Vocational rehabilitation of patients with prolonged fatigue

Joosen, M.C.W.

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Margot C.W. Joosen

Stellingen behorende bij het proefschrift:

'Vocational Rehabilitation of Patients with Prolonged Fatigue'

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1. Patiënten met vermoeidheidsklachten functioneren beter wanneer arbobegeleiding is gericht op factoren die de klacht in stand houden. *(dit proefschrift)*

2. Het combineren van interventies gericht op de patiënt én op de (werk)omgeving helpt vermoeidheidsklachten te verminderen en arbeidsparticipatie te verbeteren, ook op de langere termijn. *(dit proefschrift)*

3. Arbo-begeleidingsprogramma's zijn nog te vaak een laatste redmiddel voor patiënten in plaats van een eerste hulp strategie. *(dit proefschrift)*

4. Grensverleggend werken is onmogelijk wanneer je je eigen grenzen niet kent. Re-integratieprofessionals spelen een belangrijke rol bij het verkennen van deze grenzen. *(dit proefschrift)*

5. Kwalitatief onderzoek levert niet alleen rijke onderzoeksinformatie, maar draagt ook bij aan het beter begrijpen van de onderzoekspopulatie.

6. Het zichtbaar maken van bestaande re-integratiezorg helpt bij het beter afstemmen van zorgvraag en aanbod.

7. De onbekende pathofysiologie van vermoeidheidsklachten is geen reden om patiënten zorg te onthouden.

8. De werkgever vervult een spilfunctie binnen het re-integratieproces: hij signaleert een probleem bij een werknemer, stimuleert professionele hulp en faciliteert terugkeer naar werk.

9. De definitie van een 'sterk' onderzoeksdesign is voor de methodoloog anders dan voor de pragmaticus.

10. "Problemen zijn niet-succesvolle pogingen om moeilijkheden op te lossen." *(Selekman, 1993)*

11. Het vergt kracht om aan jezelf te durven twijfelen.

12. A bad attitude is one of the constraints in life *(naar Scott Hamilton, 1996)*

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Faculteit der Geneeskunde

Contents

Chapter 1

General Introduction

We all feel tired at times, usually after physical activity, mental exertion or when feeling ill. In most people, feelings of fatigue abate after a change in task or a period of rest.[1] However, 10-20% of the general population suffers from severe fatigue that persists and does not abate after rest.[2,3] In the Dutch working population, the prevalence of prolonged fatigue is estimated to be 22%.[4] Fatigue is a prominent symptom in chronic diseases[5] like rheumatoid arthritis[6,7], cancer[8], and depression.[9] Fatigue itself can also be a discrete disorder (i.e., chronic fatigue syndrome (CFS))[10] or can occur as a common health problem that is not related to a specific chronic disease or disorder.[11] In fact, fatigue that becomes prolonged can cause considerable suffering. Not only does prolonged fatigue affect personal well-being, but it also has negative impact on individual, social, and occupational functioning.[12,13] For example, fatigued patients might experience problems performing domestic activities, have limited social contacts, and face difficulties meeting mental, physical, and psychosocial demands at work. These functional impairments may become serious enough that workers call in sick. Therefore, apart from the physical and mental impairments it causes, fatigue can have negative consequences concerning one's ability to optimally perform at work and result in sickness absence.

Sickness absence and work disability constitute a great problem in Western society.[14-16] In the Netherlands, 30% of sick-listed workers are on sick leave due to mental health problems, which include prolonged fatigue as a major symptom.[17] Moreover, mental health complaints accounted for almost 38% of permanent work disability claims in the Netherlands in 2006.[18] More specific to the topic of this thesis, fatigue has been associated with sickness absence, ranging from more than one month[19] to permanent work disability.[20] Recently, Sabes-Figuera and colleagues[21] found that prolonged fatigue is associated with high economic costs in Great Britain (£3878 per six months). Productivity loss due to absence from work and the care from family members or friends (i.e., informal care), were the main contributors to these costs. Sick leave and work disability are not only an economic burden due to productivity loss, health care, and disability pension costs[22], but they can also negatively affect one's quality of life.[23] Therefore, options for improving work participation and preventing work disability in patients with prolonged fatigue should be further explored and evaluated.

For the purpose of this thesis, fatigue is considered as a continuum of complaints ranging from mild complaints of tiredness to severe, disabling fatigue that is neither

task-specific nor easily reversible (e.g., CFS). At any point on this continuum, fatigue can occur as a symptom of a known or unknown disease. When fatigue complaints are sustained for a long period of time and are minimally abated with rest, the condition is referred to as prolonged fatigue.[12] The study population in this thesis comprises patients with self-reported prolonged fatigue as a main or important symptom that causes functional impairments. The latter concept encompasses constraints in everyday life that cause role functioning limitations and participation restrictions.[24]

Prolonged fatigue, participation problems and perpetuating factors

The origin of fatigue complaints remains elusive, even after decades of research. In many cases of fatigue complaints, there is limited evidence for underlying disease or permanent damage, and the pathophysiology remains unclear.[25] However, it is questionable if knowledge of the exact cause of this condition (predisposing and precipitating factors) is necessary to provide effective care aiming to improve daily life functioning and participation. Health care is traditionally based on the medical model of disease: recognise patterns of symptoms, apply therapy to the underlying pathology, and expect the patient to recover.[26] This medical model was originally developed for medical conditions with a clear-cut pathology and still functions well for these conditions. The model also assumes that work disability is a consequence of disease.[26,27] However in more complex conditions, especially with long-lasting health problems, the traditional medical model is insufficient to explain underlying causes and to plan treatment that influences work participation. A biopsychosocial model is more useful than the traditional medical model in complex situations, like that of prolonged fatigue.[25,28] The biopsychosocial model states that health and sickness result from complex interactions between biological, psychological, and social factors. In prolonged fatigue, several biological, psychological, and social mechanisms are known to be associated with the development and persistence of fatigue complaints and disability. From a (neuro)biological point of view, prolonged exposure to stress and the inability to terminate stress responses, with associated fatigue, may lead to an overuse and damage of physiological stress systems.[29] Relationships between the dysregulation of stress systems (i.e., autonomic nervous system)[28,30] and the hypothalamic-pituitary-adrenal (HPA) axis hypofunction[30] in cases of prolonged fatigue complaints have been reported. In addition, cognitive and behavioural factors (e.g., causal attribution, low self-efficacy, dysfunctional beliefs about activity and

fatigue) are also believed to be involved in the persistence of fatigue complaints.[31-33] Furthermore, a lack of social support can be a perpetuating factor in fatigued patients[34], and psychosocial factors, like attitudes towards work, can play roles in function limitations and long-term sick leave.

In conclusion, although predisposing factors (e.g., family-genetic, early trauma) and precipitating factors (e.g., physical or psychological stressors) are involved in the development and triggering of fatigue, perpetuating factors may reinforce and maintain fatigue symptoms and disability (often via vicious circles), even after the original factors causing fatigue have been terminated.

Vocational rehabilitation in patients with prolonged fatigue

The previous section suggests that perpetuating factors involved in fatigue complaints and participation restrictions are important to the design and content of an appropriate intervention for these patients.[35] To stimulate effective, functional recovery in fatigued patients, treatments should consider individual, perpetuating factors.[36,37] As Waddel & Burton[38] stated, "biopsychosocial problems need biopsychosocial solutions." In medical rehabilitation, this approach is well-known and is used for both somatic and mental disorders.[39-41] However, one limitation of these rehabilitation programmes is the lack of focus on work participation. Another limitation is the lack of accessibility for impaired workers that have disorders that cannot be unambiguously diagnosed.

Vocational rehabilitation (VR) is an approach that does focus on work participation and aims to facilitate return-to-work (RTW) and work retention in addition to preventing work disability.[42,43] Due to diverse legislations, differences exist in the organisation of VR in numerous countries. In the Netherlands, employers are obliged to continue paying the salary of their sick-listed workers during the first two years of sickness absence or temporary work disability. During these two years, both the employer and worker are obliged to cooperate in the VR process of the sick-listed worker. An occupational physician (OP) is involved in this process, providing general occupational health care to workers and advice to employers. Specifically, the physician provides an assessment of ability to work, social-medical guidance, recommendations for adjusting working conditions and specialised treatment.[44] Therefore, in addition to influencing work participation, the OP has the potential to

identify a worker who is at-risk for sick leave or for developing functional impairments.[45]

Also as a part of this social system, Dutch VR treatments are offered to impaired workers and those who are on sick leave.[46] These treatments are designed by outpatient institutions and are conducted by experienced trainers and caregivers from different disciplines. VR treatments aim to improve physical, mental, and occupational functioning; they consist of several components like physical training, mental coaching, behavioural treatment, and work-directed intervention. Although these multi-component VR treatments are provided in the Netherlands, the number and specific content of these treatments are unknown. Moreover, there is a lack of evidence of the effects of these practiced treatments, especially as it relates to work participation. A better understanding of the content, underlying concepts and outcomes of VR treatment may contribute to a better understanding of the working mechanisms of the treatment and may lead to the development of more effective treatments.

Evaluating VR treatments

In Figure 1, a conceptual model describes the process and aims of multi-component VR treatment in patients with prolonged fatigue with work participation problems. This model is used in this thesis to evaluate existing VR treatments. It indicates, as mentioned above, that biological, psychological, and social factors can be involved in the perpetuating character of prolonged fatigue complaints and disability. Factors like somatic attribution, physical deconditioning, and psychosocial factors at work, can negatively affect patients' beliefs and perceptions about the condition and subsequently affect their behaviour. These mechanisms reinforce each other and the fatigue symptoms, leading to the preservation of complaints and its related disability. To improve daily life functioning and work participation, intervening on those factors that hinder recovery in an individual should be part of VR treatment. In addition, by using a combination of intervening mechanisms at different levels like influencing physiological stress systems, changing dysfunctional beliefs and improve adequate coping strategies in daily life and at work, we expect to influence those factors that obstruct recovery. This will allow patients to change their attitude and behaviour involving their daily and working life in a favourable direction. Moreover, we expect this multi-component strategy to break the vicious circle of sustained complaints and

participation restrictions (see dotted line in Figure 1), leading to improved daily life functioning, work participation and less fatigue complaints (see black arrow in Figure 1).

From the model, we hypothesise that multi-component VR treatment is an effective strategy for treating patients with prolonged fatigue complaints with participation problems. It is assumed that multi-component treatment will increase mental and physical functioning, improve work ability and work participation, and decrease fatigue complaints by intervening on individual factors that obstruct recovery using a biopsychosocial perspective. This hypothesis is tested by evaluating existing VR treatments.

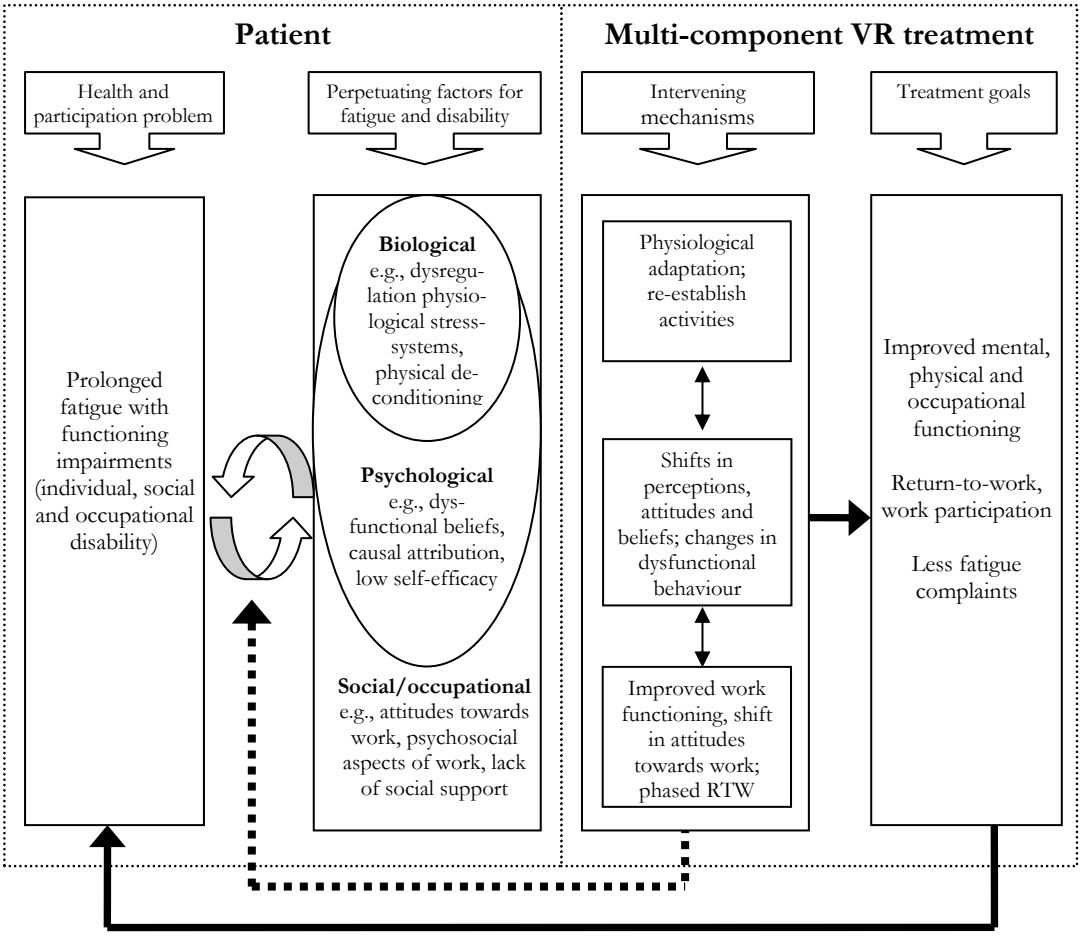

Figure 1. Model of multi-component vocational rehabilitation for prolonged fatigue

When evaluating existing treatments, special attention is needed with respect to the research design. In cases of complex health interventions with a long causal pathway from intervention to outcome, it is difficult to conduct research in tightly controlled circumstances. Thus, organizing a randomised controlled trial (RCT) may easily fail.[47,48] More suitable for evaluating multi-component treatments in real-life settings are studies with a pre/post-test design, using practice-based research.[49] This type of research includes assessments of patients treated in routine practice and addresses individual problems in a real-life setting, thus giving the research high external validity.[50-52] Staying as close a possible to the real-life situation, and monitoring the process during and after the treatment will increase internal validity as well. In this thesis, practice-based research is used to investigate the content and the short- and long-term effects of existing VR treatment in the Netherlands.

Treatments like multi-component VR treatments regard patients as active partners who are involved in treatment decision making. To be successful, these treatments require active collaboration of the patient, and the treatment prescribed must match the patients' needs.[53] In addition, patients should not be considered as an object of treatment but should instead play a key role in their treatment. In practice and clinical research, this approach is receiving growing attention. Conducting research from a patient's perspective can provide a better understanding of the problems that patients actually face, including their health-related needs and what they gain from treatments. Such knowledge has the potential to improve the quality of VR care and better meet patients' needs. Therefore, patients' perspectives are also included in this thesis.

Thesis objectives and research questions

The main objective of this thesis is to generate knowledge about the role that existing VR treatments play with respect to daily life functioning and work participation of patients with prolonged fatigue complaints. The research questions of this thesis are as follows:

1) Which VR treatments are practiced in the Netherlands, and what is their content?
2) Can VR treatments improve daily functioning and work participation of patients with prolonged fatigue on the short- and the long-term?
3) What are fatigued patients' perspectives regarding work experiences before and after receiving VR treatment?

Thesis outline

The study presented in **Chapter 2** offers an inventory of the VR treatments available in the Netherlands for workers with prolonged fatigue complaints (research question 1). The content of existing VR treatments is the focus of this chapter. The following chapters address an evaluation of existing VR treatment programmes for patients with prolonged fatigue complaints (research question 2). **Chapter 3** first explores the changes in physiological parameters and fatigue complaints after a six-week physical training programme. In **Chapter 4,** the outcomes of an outpatient, multidisciplinary treatment programme were studied using retrospective data on fatigue, daily life functioning and work participation. **Chapter 5** elaborates on Chapters 2 and 3 and presents a longitudinal study in which the process and outcomes of three existing outpatient VR treatments were evaluated. This study describes the content and process of those treatments (research question 1), including information about patient recruitment, content completeness and patient satisfaction. Furthermore, the short-term outcomes at three months after treatment are explored as they relate to fatigue complaints, work participation, work ability, daily life functioning, and heart rate variability. **Chapter 6** focuses on patients' perspectives. Using a qualitative survey, work-related limitations that workers experienced before attending VR treatment and their RTW experiences after VR treatment are explored (research question 3). In **Chapter 7,** practice-based research of long-term outcomes after VR treatment is presented. Patients from the study presented in Chapter 5 were followed for 18 months after completing VR treatment. In this study, results from the three institutions were combined and outcomes on fatigue complaints, work participation, work ability, daily life functioning, and heart rate variability are presented. Finally, in **Chapter 8**, the main research findings of this thesis are summarised and discussed, and this is followed by a discussion of recommendations for research and its practical implications.

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Chapter 2

Vocational rehabilitation treatments for fatigued workers: What is done in practice?

Margot C.W. Joosen, Monique H.W. Frings-Dresen, Judith K. Sluiter

Submitted

Abstract

Background: Patients with prolonged fatigue often experience work-related problems that contribute to higher risk of sickness absence and work disability. Vocational rehabilitation (VR) treatments aimed at improving work functioning in sick-listed workers are commonly practiced, but an overview of these treatments is lacking. An inventory of VR treatments for impaired fatigued workers was made to increase transparency related to aims and content.

Methods: We contacted 99 members of the Dutch sector organisation of VR institutions (Boaborea). The 47 VR institutions that targeted sick-listed or impaired workers with prolonged fatigue complaints were eligible for participation. A key person from the VR institution filled out an online questionnaire that investigated five domains: organisation characteristics, patient population, treatment aims, outcomes, and content.

Results: Thirteen VR treatments have been identified in ten VR institutions that fulfilled our inclusion criteria and were willing to participate. Patient populations included workers with common mental health complaints, physical complaints and chronic pain, as well as workers with prolonged fatigue complaints. All treatments aim at facilitating return to work and increased daily life functioning (11/13), improved social participation (9/13), and fewer complaints of fatigue (9/13). With regard to outcomes, treatments are mainly considered to be successful when the patient can cope with his or her own limitations and capacities (6/13), when the employer is satisfied with the outcome and cooperation with VR treatment (6/13), when patients return to their original work (5/13), and when balance is reached between daily life and work (5/13). Most VR treatments (8/13) are multi-component treatments, including physical training, psychological and/or cognitive behavioural therapy and work-directed interventions, such as graded activity, coaching, and career development. The majority of VR treatments (8/13) have a total duration between 3 and 6 months, including 8 to 40 sessions in the treatment phase, and utilise a combination of individual and group sessions.

Conclusion: The majority of specialised VR treatments offer multi-component treatments to fatigued workers to improve daily life functioning and work participation. This inventory makes the content and provision of VR health care

transparent and visible, thereby helping patients, employers and (occupational) physicians to make treatment decisions.

Background

Workers who experience long-lasting fatigue complaints that are not relieved by rest often experience substantial functional problems. Lack of energy, concentration, and physical and cognitive limitations hamper fatigued workers and prevent optimal levels of function in private life and at work.[1] Fatigued workers report having difficulty when performing work tasks, communicating with co-workers and dealing with demanding work conditions.[2] In addition, a fatigued state is a risk factor for getting injured in an occupational accident.[3] Consequently, prolonged fatigue has great impact on individual and occupational functioning and is known as a predictor of long-term sick leave[4] and future disability pension.[5] Recently, Sabes-Figuera and colleagues[6] showed that economic costs associated with chronic fatigue are very high in Great Britain (£3878 per six months). Lost productivity due to reduced work and informal care, which is care by family members or friends, were the main contributors to these costs.[6]

In the Netherlands, sick-listed workers are financially compensated for two years by their employer and stay under contract with their employer during this time. Both worker and employer are responsible for the management of sickness absence. During this process of vocational rehabilitation, an occupational physician can be consulted for occupational care and advice on starting specialised treatment.

Given the impact of fatigue complaints, there is a need for specialised treatment within the occupational health field that aims at improving work functioning, return-to-work and/or job retention for workers with limitations. These vocational rehabilitation (VR) treatments are becoming increasingly popular and are offered to impaired workers and to workers on long-term sick leave in the Netherlands.[7,8] The treatments are designed by outpatient institutions and carried out by experienced trainers and caregivers from different disciplines. However, there is no clear overview of the content of VR treatments that target impaired workers with prolonged fatigue complaints. An overview will make health care services more transparent and more visible. It can provide workers with health complaints, employers, (occupational)

physicians, and other caregivers with information that can help in making treatment decisions.

The objective of this exploratory survey is to search, list and extract data on existing VR treatments for workers with prolonged fatigue. We want to know which VR treatments are practiced in the Netherlands and what their actual content is.

Methods

Study subjects

We used an online survey to sample information on VR treatments that were used to treat impaired workers with prolonged fatigue complaints. The phrase "impaired workers" was used to denote sick-listed workers and/or workers with work participation problems. Prolonged fatigue complaints were defined as fatigue complaints as a main or important symptom in combination with functional impairments (i.e., constraints in everyday life) due to said fatigue complaints. Further criteria for inclusion were that treatments should focus on vocational rehabilitation and be available in 2010.

To find VR treatments in the Netherlands that met our inclusion criteria, we contacted members of the Dutch sector organisation of vocational rehabilitation institutions (Boaborea). Boaborea had 165 members in December 2009 who were care providers in the occupational/vocational rehabilitation field. Care providers included occupational health services, rehabilitation centres, outplacement centres, career counselling centres, vocational rehabilitation centres, and job coach organisations. From the 165 Boaborea members, 99 were selected by the member administration department of Boaborea as institutions that treated impaired workers.

Procedure and measures

The 99 VR institutions were contacted by email and telephone by MJ. When VR institutions met the inclusion criteria and were willing to participate, a key person from the institution was asked to complete an online questionnaire about the VR treatment(s) provided by the institution. The questionnaire contained five domains: organisation characteristics, patient population, treatment aims, treatment outcomes

and VR treatment content. Organisation characteristics included the number of branch locations in the Netherlands, the number of VR treatments provided by the institution, and the number of patients with prolonged fatigue treated in one year (2009). One question on the target population was included. Treatment aims were divided into overall aims and specific aims. Overall aims were pre-categorised to: less fatigue complaints, restored functioning (i.e., activate patients, improve functioning in work and private life), return-to-work (RTW), improved social participation, and miscellaneous. Specific treatment aims were answered in an open-answer format. Outcomes were included in terms of when the institution considered the VR treatment to be successful. Finally, VR treatment content was pre-categorised into: physical training, physiotherapy, graded activity, cognitive behavioural therapy, coaching, consultation with a psychologist, breathing- and relaxation exercises, work-directed sessions, career development and miscellaneous. In addition, participants could describe the content of the VR treatment freely. VR treatment content also included the methods used to communicate the treatment (individual face-to-face contact, group face-to-face contact, telephone contact), treatment duration and visit frequency. This extraction grid was constructed in accordance with a taxonomy built by Krumholz et al.[9] to help describe chronic disease management programs that covered all domains except for one: delivery personnel. We decided not to extract the professions of caregivers, but to focus on the content of the treatment provided to patients.

Results

From the 99 Boaborea members, more then half (n=52) did not meet our inclusion criteria. Of the remaining members, 28 were not reached, even after frequent attempts to contact all members. The inclusion criteria and willingness of these members to participate are therefore unknown. In total, 10 VR institutions fulfilled our criteria and were included in the study (See figure 1).

Organisation characteristics

Thirteen different VR treatments were practiced in 10 VR institutions targeting impaired workers with prolonged fatigue complaints. Eight institutions had more than one branch location, including two with nationwide coverage. The number of workers with prolonged fatigue treated by the VR institutions ranged from 3 to 335 in 2009. Four institutions saw less then 10 workers, three saw between 15 and 100 workers, and two institutions had patient populations of more than 250 fatigued workers. In one VR institution, the number of treated workers was not specified and is therefore unknown.

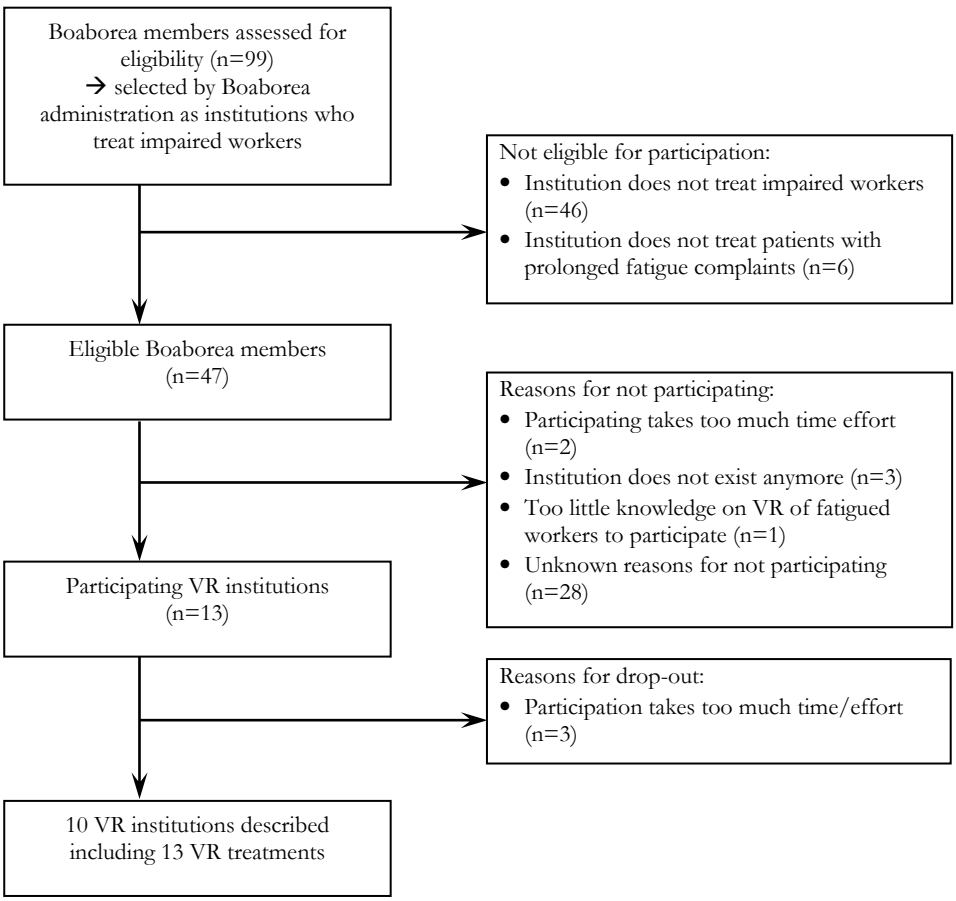

Figure 1. Flow-chart of study participants

Patient population, treatment aims and outcomes

Four VR treatments were specifically designed for workers with prolonged fatigue complaints; the nine others were not specifically designed for those with prolonged fatigue complaints, but fatigued workers were the target population. These treatments also target workers with common mental disorders, physical complaints, chronic pain and workers with complex problems (combination of physical, mental and social disabilities) (data not shown).

All 13 treatments aim to facilitate RTW and restoring daily functioning (11/13), improving social participation (9/13) and decreasing fatigue complaints (9/13) (See Table 1). Other (specific) treatment aims were: to prevent new complaints (treatment 1); to prevent sick leave, productivity loss, and stimulate personal development (treatment 2); to increase awareness of behaviour (treatment 4 and 5); to change dysfunctional behaviour (treatments 4-6); to achieve balance between activity and rest/daily life and work (treatments 4, 5, 11); to improve quality of life (treatments 4 and 5); to improve coping strategies (treatments 7 and 11); and to achieve the predetermined goals of the patient and his or her employer (treatment 9) (data not shown).

Concerning outcomes, almost half (6/13) of the VR treatments are considered successful when the worker knows his or her own capacities and limitations and can protect him/her self from exceeding these capacities. Other frequently used outcomes concerning the fatigued workers are their return to the original or adjusted job (5/13), and achieving a normal balance between activity and rest or between daily life and work (5/13). In two cases, the treatment was considered to be successful when the worker achieved personal or career development. Seven VR treatments also include outcomes concerning the employer: success is achieved when the employer is satisfied with the outcomes of the treatment and with the cooperation of the VR institution (6/13), and when the employer knows how to cope with impaired workers (1/13). In four VR treatments, success is achieved when the occupational physician is satisfied with the outcome and cooperation with the VR institution. In four cases, VR treatments include outcomes concerning the worker, the employer and the occupational physician. Three of these VR treatments utilise multi-component treatments, two of which were provided by the same VR institution. The other VR treatment involves two components, focusing on psychological and work-related sessions.

Table 1. Overall aims and outcomes of 13 VR treatments

VRt	Overall treatment aims				Treatment outcomes: Treatment is successful when…								
	De-creased fatigue com-plaints	Restored function-ing	RTW	Im-proved social partici-pation	...the patient is working in the original or adjusted job	...the patient is function-ing well at work	...the patient knows personal capacity/ limitations and can protect him/her-self from exceeding capacities	...there is a normal balance between activity and rest/work and private life	...personal and career develop-ment is achieved or is in progress	...personal goals are met (by patient, employer and/or OP)	...the employer knows how to cope with impaired workers during the VR process	...the employer is satisfied with the outcome and co-operation with VR treatment	...the occu-pational physician is satisfied with the outcome and co-operation with VR treatment
1	X	X	X		X	X							
2		X	X				X		X		X		
3	X	X	X	X	X			X					
4		X	X	X		X	X	X				X	X
5		X	X	X		X	X	X				X	X
6	X		X	X					X				
7	X		X	X	X		X					X	X
8	X	X	X	X				X		X			
9	X	X	X	X						X		X	
10		X	X				X					X	
11	X	X	X	X			X					X	X
12	X	X	X		X								
13	X	X	X	X	X			X					

VRt.: Vocational Rehabilitation treatment
RTW: return-to-work

VR treatment content

Tables 2 and 3 present the content of the VR treatments. Most VR treatments were multi-component treatments (8/13) combining physical, psychological and work-directed intervention components. Two were mono-component treatments including psychological interventions such as coaching, cognitive behavioural therapy and breathing- and relaxation exercises. In three cases, two-component treatments were provided, combining coaching or cognitive behavioural therapy with career development or work-directed sessions (2/13) or combining physical training with cognitive behavioural therapy and coaching (1/13).

Most treatments (8/13) had a total duration of three to eight months. Three treatments took between seven and 12 months, and one took less then three months. The treatment components were mainly communicated by individual face-to-face sessions but were combined with group sessions (10/13). Two VR treatments, the mono (psychological)-component treatments, used only individual sessions.

In all VR treatments, pre- and post-treatment sessions are offered. Pre-treatment sessions include an intake procedure and/or an introduction day. Post-treatment care is offered one to four times in an 11-month period. Only a few VR treatments (n=3) provided information about the content of the after-care. In these treatments, after-care consists of group sessions where work experiences are discussed and feedback is given to patients. When needed, individual sessions can be planned as well (data not shown).

Discussion

Ten VR institutions have been identified as treating impaired workers with prolonged fatigue complaints in the Netherlands. Within these institutions, 13 different VR treatments are practiced, and they focus on improving daily life functioning and work participation. Concerning outcomes, treatments are thought to be successful when the worker can cope with his or her own limitations and capacities, when the employer is satisfied with the outcome and cooperation with the VR treatment, when workers return to their original work, or when balance is reached between daily life and work. Most VR treatments are multi-component, utilizing physical training, psychological and/or cognitive behavioural therapy and work-directed intervention.

Table 2. Treatment content, duration of the total treatment and method of communication of 13 VR treatments

VRt.	Treatment content			Duration (total treatment)			Method of communication	
	Mono-component treatment	Two-component treatment	Multi-component treatment	< 3 months	3-6 months	7-12 months	face-to-face: group	face-to-face: individual
1			X		X		X	X
2		X (coaching + career development)				X		X (mainly)
3			X			X		X (mainly)
4			X		X		X	X
5			X			X	X	X
6			X		X		X	X
7		X (psycho + work)			X		X	
8		X (coaching + physical)			X		X	X
9			X		X			X (mainly)
10			X	X			X	X
11			X	?	?	?	X	X
12	X (psycho)				X			X
13	X (psycho)				X			X

VRt.: Vocational Rehabilitation treatment
(Mainly): only one component within the VR treatment utilising individual and group sessions

Table 3. VR treatment content (components and visit frequency/duration) specified per VR treatment

VRt.	VR treatment components				Mean visit frequency and treatment duration per phase		
	Physical	Psychological	Occupational	Others	Pre-treatment phase	Treatment phase	Post-treatment phase
1	Physical training Graded activity	Cognitive behavioural therapy Psychologist Breathing- and relaxation exercise	Work-directed sessions Career development	-	3 times for a few weeks	20 times in 3 months	1 time in 2 weeks
2	-	Coaching	Career development Coaching employers	Education	-	1x / week for 6 months	1x/ month for 6 months
3	Physical training Physiotherapy Graded activity	Cognitive behavioural therapy Coaching Psychologist Breathing- and relaxation exercise	Work-directed sessions	-	1 time in 2 weeks	2 x/ week for 10-20 weeks	2 times in 9 months
4	Graded activity Unrestricted moving	Cognitive behavioural therapy Coaching Psychologist Cognitive therapy	Work-directed sessions	Energy engineering	1 day	Max. 18 sessions in 2 weeks	4 times in 3,5 months
5	Graded activity Unrestricted moving	Cognitive behavioural therapy Coaching Psychologist Cognitive therapy	Work-directed sessions	Energy engineering	1 day	from 5x/ week to 1x/ week in 4-6 weeks	4 times in 11 months
6	Physical training Graded activity	Cognitive behavioural therapy Coaching Psychologist Breathing- and relaxation exercise	Work-directed sessions Career development	Dietary	3x/ week for 2 weeks	2x/ week for 15 weeks	1x/ week for 5 weeks
7	-	Cognitive behavioural therapy Coaching Psychologist Breathing- and relaxation exercise	Work-directed sessions	-	1 day	12 sessions in 3 months	1 day
8	Physical training	Coaching Breathing- and relaxation exercise	-	-	1 day	3x/ week (group) and 1x/ 3 week (individual) in 100 days	2 times by telephone

VRt.	VR treatment components				Mean visit frequency and treatment duration per phase		
	Physical	Psychological	Occupational	Others	Pre-treatment phase	Treatment phase	Post-treatment phase
9	Physical training Physiotherapy Graded activity	Cognitive behavioural therapy Coaching Psychologist Breathing- and relaxation exercise	Work-directed sessions Career development	-	3x/ week for 2-6 weeks	from 2x/ week to 1x/ week in 6-12 weeks	2 times
10	Physical training	Coaching Psychologist	Work-directed sessions Career development	-	1 day	6 weeks	1 day
11	Physical training	Coaching Psychologist	Work-directed sessions	Neuro-feedback	1-2x/ 2 weeks duration: tailored to needs	1x/ 2 weeks duration: tailored to needs	1x/ 2-4 weeks duration: tailored to needs
12	-	Cognitive behavioural therapy Coaching Breathing- and relaxation exercise	-	-	3 weeks	from 1-2x/ month to 1x/ 2 month in 2-4 months	from 1x/ 2months to 1x/ 3months in 1-3 months
13	-	Cognitive behavioural therapy Psychologist	-	-	1-4x/ month for 2 months	1-2x/ month for 4-6 months	1x/2-3 month for 1-3 months

Most VR treatments (10/13) combine worker-directed and work-directed interventions. Although we do not know the exact content of these interventions, especially the work-directed sessions, this seems promising. In addition, given the results on outcomes, five VR treatments did *not* address the employer or occupational physician. Two of these treatments were mono-component interventions. Therefore, most of the multi-component treatments did involve the workplace, employer, and/or occupational physician within the treatment. Although we cannot judge the quality of care provided by the VR treatments included in this study, previous research indicates that combined or multi-component treatments (worker-directed and work-directed) are preferred in complex conditions, such as prolonged fatigue.[10,11]

A strength of this study is that it demonstrates what is done in practice regarding VR in fatigued workers. Much research is focussed on investigating newly developed interventions, which are designed according to the latest insights or research paradigms.[12,13] In this study, we show that a lot is being done in practice to treat impaired, fatigued workers. It therefore seems advisable for future studies to combine research and practice. The benefits of this kind of practice-based research are two-fold. Professionals are experienced in treating patients in a specific context. Therefore, conducting research in a real-life setting provides knowledge that is often directly applicable to daily practice. Consequently, no difficulties concerning implementation of experimental interventions are to be expected. Second, practice-based research allows health-care providers to improve their practices. For health-care providers, it can be difficult to keep up-to-date with the best available evidence and differentiate between evidence that is and is not applicable to a particular situations.[14] Similarly, it can be difficult for care providers to conduct research themselves and/or publish in scientific journals.

As mentioned before, no conclusions can be drawn concerning the effect or quality of the included VR treatments. However, this inventory makes VR health care content and provision transparent and more visible. The inventory may be useful in several ways: 1) impaired workers can find help and encouragement in making treatment decisions that match their preferences; 2) employers, who are often financing VR treatments, are provided with insight into specific VR strategies; 3) occupational physicians can use the information when referring to specialised care; and 4) researchers and care providers worldwide can learn from the situation in the Netherlands, with regard to the organisation and provision of VR care.

Limitations

Our results need to be interpreted in light of certain limitations. First, because this study was exploratory, the listing and description of the VR treatments included cannot be considered exhaustive. The Dutch organisation of vocational rehabilitation institutions (Boaborea) provides nationwide coverage of VR institutions, and its members are responsible for 75% of the total VR care costs in the Netherlands. So we believe this was a representative sample of the VR institutions in the Netherlands. However, it is possible that VR institutions for fatigued workers practice without having a Boaborea membership. A second concern may related to the pre-selection of VR institutions by Boaborea administration. This was done in consultation with Boaborea to protect their 'not eligible' members from being bothered unnecessarily. However, by doing so, eligible VR treatments may have been missed. Furthermore, despite multiple attempts to contact a key person within all VR institutions, we have no records for 28 VR institutions. These institutions might have considered themselves as not-eligible for participation or thought it was too much trouble to participate in research, as was the case for five others who did respond. Another explanation for the non-response might be that the VR institutions want to 'protect' their product, considering the commercial setting in the Netherlands.

Second, we used online questionnaires to extract data related to the aims and content of the VR treatments. This questionnaire was tailored to increase usability and was tested in a VR care setting. Although the questionnaire was user friendly and contained enough space to elaborate on the content, aims, and duration of treatments, detailed information was sometimes missed. Some participants remarked that they found it difficult to answer questions, especially about visit frequency and duration, because their treatments were not clear-cut; rather, care was often patient-centred and/or tailored to workers' needs.

Conclusions

VR treatments that target impaired fatigued workers mainly focus on improving daily life functioning and work participation. Content in the majority of VR treatments is multi-component, combining physical, psychological and work-directed interventions. Most VR treatments have a total duration between 3 and 6 months and utilise a combination of individual and group sessions to communicate the treatment components. VR health care content and provision are more transparent and visible.

This can help impaired workers, employers, and (occupational) physicians to make treatment decisions.

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Chapter 3

Evaluation of the effects of a training programme for patients with prolonged fatigue on physiological parameters and fatigue complaints

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Abstract

Objectives: Complaints of prolonged fatigue are considered as a major health problem, as it can effect daily functioning and may lead to work disability. To increase knowledge about the effectiveness of interventions focussing on fatigued patients, a pre-post study was designed to evaluate an established training programme for patients with prolonged fatigue.

Materials and Methods: Eighteen patients who reported fatigue to be one of their major health complaints and who were suffering from functional impairments attended a training programme of six weeks, three times a week. The training consisted mainly of physical endurance training, relaxation therapy and breathing exercises in rest. At baseline, time- and frequency domain measures of heart rate variability (HRV) and respiration rate measurements were recorded during rest and during recovery after bicycle exercise. Furthermore, fatigue complaints were assessed with the Checklist Individual Strength (CIS). These measurements were repeated at three weeks and six weeks from baseline.

Results: After three and six weeks, HRV increased significantly in rest (SDNN (i.e. standard deviation of normal beat-to-beat intervals) ($p=0.02$), very low frequency ($p=0.04$) and low frequency ($p=0.04$)), and showed a positive trend in the remaining HRV components. No significant HRV changes during recovery were found. Respiration rate decreased significantly after six weeks during rest (from 11.8(SD =4.65) to 8.1(SD =2.57) b·min^{-1}) and during recovery (from 15.1(SD=4.90) to 10.4(SD=2.97) b·min^{-1}). In all patients, CIS scores diminished after six weeks training (from 106(SD =13.3) to 78 (SD =21.8),$p= .001$).

Conclusions: The results suggest that a six-week training programme has a positive effect on physiological and subjective parameters in patients with severe complaints of fatigue.

Introduction

Feelings of fatigue are common complaints among both the general and working population.[1-3] It's a normal phenomenon after physical or mental exertion, that usually abates after a period of rest, when tasks are changed or when coping strategies are used.[4,5] Sometimes, however feelings of fatigue persist. Unlike acute fatigue, prolonged fatigue is not task-specific, does not recover in short term and effects an individual's work performance and activities of daily living. This may result in sick leave and/or work disability.[6,7] Compensation mechanisms (e.g. reducing activity) are not successful in this context, and they do not decrease fatigue feelings.[5]

To date, researchers have not reached consensus about the aetiology of prolonged fatigue. One hypothesis is that fatigue develops from chronic stress reactions. A 'stress alarm' occurs when an individual experiences stress, for example when job demands are high and coping (i.e. the expectancy of being able to cope and handle the situation with a positive result) is low.[8] This alarm increases wakefulness and alertness (i.e. arousal) and can eventually lead to a dysfunction of the autonomic nervous system, particularly with regard to the sympathetic nerves. Increased sympathetic activity can be identified by increased heartbeats (i.e. decreased heart rate variability (HRV))[9] and an increased respiration rate.[10] These reactions can be seen as anticipation for action, and cause the body to consume more energy. The amount of glucose, which is used as fuel, increases with activity (e.g.[11]). When the body is in a state of sustained arousal (i.e. extra alert and active for a longer period of time), the energy supply is thus likely to be depleted, possibly leading to fatigue, exhaustion and similar complaints. If they persist, such complaints can provoke problems at work and in the daily routine. Thus, chronic stress, resulting in overactive stress systems (e.g. autonomic nervous system), can lead to long-term negative physiological effects and resulting in prolonged fatigue complaints.[12] The relationship between dysregulation of the autonomic nervous system and chronic fatigue complaints has been reported in several studies.[13-15] Interventions regarding prolonged fatigue have focussed primarily on the cognitive components of stress-related complaints and fatigue.[16,17] In view of the above mentioned theoretical ideas, it seems that breaking through the vicious circle by means of an intervention aimed at physiological and physical components may provide a number of interesting results. It appears that physiological parameters can be influenced by physical training in normal individuals. In addition, it is clear that

physical training has positive effects in terms of increased HRV in healthy individuals[18-20] and in chronic heart failure patients.[21-23] However, the effects of physical training on physiological parameters in patients with complaints of fatigue have not yet been studied.

In this present study an established six-week intervention, consisting of endurance training, relaxation therapy and breathing exercises is evaluated to answer the following research question: What are the changes in physiological parameters and fatigue feelings in patients with prolonged fatigue after a six week training programme? Fatigue-related complaints were expected to reduce after the intervention. Furthermore, the training was expected to have positive effects on physiological parameters (i.e. it raises HRV, while lowering respiration rate) at rest and during recovery after exercise. Both parameters were measured to study if physiological responses occur when they are not needed (i.e. in rest) and to study if patients recuperate after physical activity (i.e. during recovery).

Materials and Methods

Patients

The patients were recruited from among new clients of an outpatient clinic for rehabilitation and medical fitness (Energy Control, Weesp, the Netherlands). Clients (self-referred) who wanted to attend a training at the outpatient clinic, were asked to participate in the current study when they met the following inclusion criteria: 18 to 65 years of age, prolonged complaints of fatigue as a main or important problem and suffering from functional impairments (e.g. constraints in everyday life). Patients who reported a somatic condition (e.g. cancer, HIV, multiple sclerosis or chronic obstructive pulmonary disease) which could explain fatigue complaints were excluded from participating in the study. All patients were enrolled within a period of five months.

Information about personal characteristics was collected, including the duration and subjective reasons for the complaints of fatigue. At the same time, patients were asked about their activities in both work and home setting. A written informed consent was obtained from each participant in this study.

Previously collected pre-post HRV data from the outpatient clinic were used to estimate the effect-sizes and determine the sample-size of this study by a power analysis programme (G*POWER).[24] Fifteen patients were necessary to obtain a power value of 0.82 and an alpha of 0.05. A decision was made to include a total number of 16 patients.

Protocol

A pre-post design with repeated measurements, at baseline and at three and six weeks after baseline, was used. At the assessment days, patients completed a questionnaire concerning their fatigue complaints. Secondly, patients remained in a sitting rest position, while heart rate and respiration signals were recorded for ten minutes, using the Co2ntrol recording device (Decon Medical Systems, Weesp, the Netherlands). Adhering the test procedure of the clinic, patients performed a peak exercise test (see further below). The procedure ended with a recovery phase of ten minutes in sedentary position on the bicycle, while heart rate and respiration signals were recorded.

Intervention

Prior to the above mentioned recovery phase, patients performed a peak exercise test on a bicycle-ergometer (EC-Bike 1000WS) to determine their physical status. This test, carried out by an exercise instructor, is part of a physical examination which the outpatient clinic uses to write a personal training programme. All patients, who participated in the pilot study performed the exercise test.

Before the bicycle exercise test, patients were not allowed to eat or drink coffee for two hours. All tests were performed using a standardized exercise test at the same time of day before and after the training period of three and six weeks. The work rate was increased by 10 W·min^{-1} for women and 20 W·min^{-1} for men, both starting with unloaded pedalling. The patients were instructed to continue pedalling at a rate of 70 – 75 rpm until volitional exhaustion. After the subjective maximum was reached, patients remained cycling for five minutes at a resistance of 40% of their maximum performed load, in order to cool down. During the test, heart rate and respiration signals were recorded by the Co2ntrol recording device (Decon Medical Systems, Weesp, the Netherlands). The aerobic threshold (i.e. respiration rate of 30 times·min^{-1} and estimated Respiratory Quotient (RQ) ($\dot{V}CO_2/\dot{V}O_2$) of approximately 1.00) was

determined individually during the exercise test, using data from the Co2ntrol recordings (i.e. respiration rate, inhalation and exhalation time and chest extension).

A personal workout schedule was made based on the results of the peak exercise test. Heart rate limits thought to be corresponding to RQ-measures were used as references, and patients were provided with heart-rate monitors (Polar Electro) to monitor these limits during physical exercises. This personalized workout scheme was meant to ensure optimal training and prevent overload and increasing complaints of fatigue.

The training programme comprised three two-hour sessions per week for a period of six weeks, and consisted each session of:

- 'Passive' warming up for 15 minutes: Patients receive a massage (through a massage mattress), magnetic-field therapy and infrared therapy in supine position, to increase body temperature.
- 'Active' warming up for six minutes: Patients ride a bicycle at an intensity corresponding to an RQ of 0.70 and respiration rate up to 22 times $\cdot min^{-1}$, in order to increase muscle temperature. During this exercise, extra oxygen (up to 35%) is applied through a nasal tube.
- Exercises on the bicycle for 20 minutes, to increase aerobic fitness: The intensity corresponds to an RQ of 0.85 and respiration rate between 22 and 26 times $\cdot min^{-1}$. During this exercise, extra oxygen (up to 35%) is applied through a nasal tube.
- Exercises (walking or rowing) for six minutes, to increase aerobic fitness: This exercise is performed at an intensity corresponding to an RQ of 0.93 and respiration rate between 26 and 30 $\cdot min^{-1}$.
- Strength exercises on a vibration platform (Power Plate® International, Badhoevedorp, the Netherlands) for a maximum of 20 minutes: seven exercises to strengthen the lower extremity (e.g. the buttocks, hamstrings, quadriceps and calves muscles). During each 30-second exercise, the vibrations are set to a speed of 30 to 40 times per second. The frequency of the vibration platform during the exercises is 35Hz, with amplitude between 2mm (20% of the exercises) and 4mm (80% of the exercises), in a vertical direction.
- 'Active' cooling down for six minutes: Patients ride the bicycle at an intensity corresponding to an RQ of 0.70 and respiration rate up to 22 times $\cdot min^{-1}$, to decrease muscle temperature and remove residual products from the muscles.

- Breathing exercises for 15 minutes, monitored by Co2ntrol output, in order to provide visual feedback. Breathing exercises consists of practising a relaxing respiratory pattern: two seconds of inhalation, four seconds of exhalation and two seconds waiting before the next inhalation. This is thought to bring about an even breathing pattern and relaxation. Practicing this respiration pattern was given as homework.
- 'Passive' cooling down for 15 minutes: Patients receive a massage (through a massage mattress), magnetic-field therapy and infrared therapy in supine position for faster and better total recovery.

The workload of this programme increased each week: the 20-minute exercises increased by four minutes each week, while the exercise intensity remained at an RQ of 0.85. After three weeks, the training programme was evaluated (using the exercise test) and adjusted when necessary.

Data collection

Fatigue

The Checklist Individual Strength (CIS)[25], was used to measure fatigue. The CIS consists of 20 statements that cover several aspects of fatigue. Each item is scored on a 7-point Likert scale (1 = Yes, that is true; to 7 = No, that is not true). The scores range from 20 to 140 and a total score can be calculated by adding all item scores. Higher score indicate a higher severity of fatigue complaints.[25] The CIS was found reliable (α = 0.90)7[25] and the scale has been validated in the Dutch working population.[26]

Physiological measures

Heart rate variability and respiration rate measurements were determined from the data collected following the protocol described above. These physiological measurements were recorded using the Co2ntrol (Decon Medical Systems, Weesp, the Netherlands), a small and light device which is attached to a chest strap. The Co2ntrol detects R-tops of the QRS complexes in the beat-to-beat heart rate signal. The normal-to-normal (NN) intervals (i.e. the normal RR intervals between adjacent QRS complexes) are determined from these R-tops with an accuracy of 1 ms. Time-domain and frequency-domain (HRV) measurements were calculated from these NN intervals. The elastic chest strap, which the Co2ntrol is attached to, records chest expansion. To

measure respiration rate, inhalation and exhalation times, chest extension and breathing signals are logged every 1ms from these records.

The Co2ntrol was developed according to the guidelines of the European and North American Task Force.[27] It was found to provide reproducible HRV and respiration rate measurements in both healthy individuals[28] as in patients with prolonged fatigue.[29]

Data analysis

Data reduction

Heart rate variability was assessed by means of i) time-domain characteristics; the standard deviation of NN intervals (SDNN) and the square root of the mean of the sum of squares of differences between adjacent NN intervals (RMSSD) and ii) frequency-domain characteristics; very low frequency (VLF) (0.003-0.05 Hz), low frequency (LF) (0.05-0.15 Hz), high frequency (HF) (0.15-0.4 Hz) and the ratio between low frequency and high frequency (LF:HF ratio), according to the guidelines of the European and North American Task Force.[27] To define these measurements, data were transferred to HRV Analysis Software (http://venda.uku.fi/research/biosignal).[30] The Fast Fourier transform (FFT) option was used to determine the spectrum of HRV and RR series were re-sampled at a rate of 4 Hz using cubic interpolation. To define rest values, the final seven minutes of the ten minute recording period in sedentary resting position were selected. To define recovery values, the final five minutes of the ten minute recording period during the recovery phase were selected. The same data selection was used to define the respiration rate.

Statistical analysis

To assess the changes in physiological parameters and fatigue feelings after a six week physical training, (within-subject) analysis of variance between the measurements at baseline (t0), at three weeks (t1) and six weeks (t2) from baseline were conducted. Differences in the variables (i.e. rest and recovery values of HRV and respiration rate and the fatigue score) were compared using the General Linear Models procedure for repeated measurements. A post-hoc multiple-comparisons procedure was followed to test significant differences between test moments. Values of $p<.05$ were considered statistically significant. The statistical analyses were performed using SPSS version

12.0.1 for Windows (SPSS inc., Chicago, IL, USA). In addition, the results of the physiological characteristics were described separately for men and women.

Results

Personal characteristics

Eighteen clients (7 men and 11 women) were included in the sample. Ages varied between 20 and 63 years (mean = 48 years, SD = 11.8). At baseline, two patients were working full-time, three worked part-time and 13 were unemployed. Sixteen out of 18 patients completed the entire six-week training programme. Two patients dropped out, one because of back problems and one because of lack of motivation. The mean number of training sessions was 17 (SD = 1.0) in the six-week period, with a frequency of approximately three sessions a week.

Heart Rate Variability

As shown in Table 1, the mean resting SDNN values increased significantly (P= 0.02) from 29ms (SD= 12.0) at baseline to 39ms (SD= 23.4) after three weeks, and to 40ms (SD=23.6) after six weeks. Post-hoc analysis showed that changes between baseline and three weeks and between baseline and six weeks were significant (not shown in Table 1: both P= 0.03). There was no significant difference between baseline and follow-up tests on RMSSD rest values (P= 0.07).

Two out of three frequency-domain characteristic showed significant results: VLF power in rest increased from 56ms^2 (SD= 34.3) at baseline to 88ms^2 (SD= 77.5) after six weeks. Post-hoc analysis showed a significant change between baseline and six weeks (P= 0.05). LF power in rest increased from 318ms^2 (SD= 280.9) to 809ms^2 (SD= 989.4) after six weeks with post-hoc tested significant changes between baseline and three weeks and six weeks (P= 0.03 and P =0.05 respectively). Furthermore, in rest HF power increased non-significantly from 104ms^2 (SD= 99.9) to 138ms^2 (SD= 117.2) after six weeks. The LF:HF ratio increased but these changes were not significant.

As for the recovery measurements, neither frequency-domain parameters nor time-domain parameters did show significant changes between baseline and follow-up tests (Table 1).

Table 1. Number of patients (men and women), means, standard deviations (SD) and p-values before baseline) and after treatment (three and six weeks) on heart rate variability (SDNN, RMSSD, VLF, LF, HF and LF:HF ratio), respiration rate and fatigue, based on General Linear Model (GLM) analysis.

		Baseline (t0)		Three weeks from baseline (t1)		Six weeks from baseline (t2)		GLM
Variable	N	Mean	(SD)	Mean	(SD)	Mean	(SD)	overall *P*-values
HRV rest								
SDNN (ms)	16	29	(12.0)	39	(23.4)*	40	(23.6)*	.02
RMSSD (ms)	16	21	(12.2)	26	(15.4)	30	(19.1)	.07
VLF (ms^2)	16	56	(34.3)	53	(36.6)	88	(77.5)*	.04
LF (ms^2)	16	318	(280.9)	761	(895.0)*	809	(989.4)*	.04
HF (ms^2)	16	104	(99.9)	144	(181.5)	138	(117.2)	.55
LF:HF (%)	16	4.8	(3.86)	6.6	(5.84)	5.6	(3.86)	.12
HRV recovery								
SDNN (ms)	16	12	(5.1)	13	(8.3)	13	(8.4)	.69
RMSSD (ms)	16	6	(2.9)	7	(4.9)	6	(4.8)	.28
VLF (ms^2)	16	20	(22.8)	18	(27.4)	12	(8.8)	.46
LF (ms^2)	16	54	(40.2)	97	(129.7)	95	(126.8)	.18
HF (ms^2)	16	9	(12.6)	24	(54.0)	19	(43.4)	.30
LF:HF (%)	16	9.9	(7.08)	12.3	(12.35)	9.2	(8.16)	.60
Respiration Rate rest (breaths min^{-1})	14	11.8	(4.65)	8.8	(3.89)*	8.1	(2.57)**	.001
Respiration Rate recovery (breaths min^{-1})	14	15.1	(4.90)	10.4	(3.38)*	10.4	(2.97)*	.001
Fatigue (total CIS score, range 20-140)	16	106	(13.3)	87	(22.5)***	78	(21.8)***	.001

HRV rest = heart rate variability during rest; HRV recovery = heart rate variability during recovery
SDNN = standard deviation of NN intervals; RMSSD = square root of the mean of the sum of squares of differences between adjacent NN intervals; VLF = very low frequency (0.003-0.05 Hz); LF = low frequency (0.05-0.15 Hz; HF = high frequency (0.15-0.4 Hz)
Post-hoc analyses within subjects (compared to t0): *P <0.05; **P <0.01; ***P <0.001

Respiration Rate

The mean rest respiration rate values decreased significantly (*P*= 0.001) from 11.8 breaths·min^{-1} (SD= 4.65) to 8.8 b·min^{-1} (SD= 3.89) after three weeks, and to 8.1 b·min^{-1} (SD= 2.57) after six weeks from baseline. Post-hoc analysis showed that the difference between baseline and three weeks was significant (*P*= 0.014), as was the difference between baseline and six weeks (*P*= 0.003) (Table 1).

The mean recovery respiration rate values also changed significantly (*P*= 0.001) between the three measurement points, with mean values from 15.1 b·min^{-1} (SD= 4.90) to 10.4 b·min^{-1} (SD= 3.38) after three weeks, to 10.4 b·min^{-1} (SD= 2.97) after six weeks. The *P*-values between baseline and three weeks and between baseline and six weeks were both .001 (Table 1).

Fatigue

Duration of fatigue complaints ranged from six months to 22 years at the start of the training. Twenty-two percent of all patients attributed their complaints to work characteristics; 11% reported that the complaints had been caused by private psychosocial factors, 50% reported that a combination of these two factors caused their symptoms and 6% attributed their symptoms to something else.

Significant differences in mean CIS scores, which represent fatigue complaints, were found between the three measurements in time. A significant decrease (*P*= 0.001) of the mean fatigue values was determined from 106 (SD= 13.3) at baseline, to 87 (SD= 22.5) after three weeks, and to 78 (SD= 21.8) after six weeks. Post-hoc analysis showed that the differences were significant across all three groups. The *P*-value between baseline and three weeks was 0.001, and between baseline and six weeks, the value was *P*= 0.001 as well (Table 1).

To give an impression on how gender may have influenced the results, the results of HRV and respiration rate analysis are described for women and men in Table 2 and 3, respectively.

Table 2. Number of patients (women), means and standard deviations (SD) before (baseline) and after treatment (three and six weeks) on heart rate variability (SDNN, RMSSD, VLF, LF, HF and LF:HF ratio) and respiration rate.

		Baseline (t0)	Three weeks from baseline (t1)	Six weeks from baseline (t2)
Variable	N	Mean (SD)	Mean (SD)	Mean (SD)
HRV rest				
SDNN (ms)	11	32 (11.5)	46 (24.0)	46 (24.5)
RMSSD (ms)	11	24 (12.7)	31 (15.6)	35 (20.1)
VLF (ms^2)	11	60 (34.3)	58 (38,7)	84 (72.3)
LF (ms^2)	11	382 (302.9)	1038 (961.8)	1046 (1104.2)
HF (ms^2)	11	127 (107.0)	183 (206.7)	166 (122.1)
LF:HF (%)	11	4.6 (3.69)	7.4 (6.18)	6.2 (4.34)
HRV recovery				
SDNN (ms)	11	13 (5.5)	13 (7.5)	13 (8.0)
RMSSD (ms)	11	6 (3.1)	6 (4.0)	6 (4.5)
VLF (ms^2)	11	23 (26.1)	15 (26.0)	13 (9.3)
LF (ms^2)	11	55 (41.0)	92 (97.7)	95 (114.2)
HF (ms^2)	11	10 (13.8)	13 (20.2)	10 (11.0)
LF:HF (%)	11	9.2 (7.03)	12.9 (11.96)	8.6 (8.57)
Respiration Rate rest (breaths $\cdot min^{-1}$)	10	10.3 (4.21)	6.7 (1.56)	6.9 (1.37)
Respiration Rate recovery (breaths $\cdot min^{-1}$)	10	13.5 (4.32)	9.0 (2.43)	9.5 (2.16)

HRV rest = heart rate variability during rest; HRV recovery = heart rate variability during recovery
SDNN = standard deviation of NN intervals; RMSSD = square root of the mean of the sum of squares of differences between adjacent NN intervals; VLF = very low frequency (0.003-0.05 Hz); LF = low frequency (0.05-0.15 Hz; HF = high frequency (0.15-0.4 Hz)

Table 3. Number of patients (men), means and standard deviations (SD) before (baseline) and after treatment (three and six weeks) on heart rate variability (SDNN, RMSSD, VLF, LF, HF and LF:HF ratio) and respiration rate.

		Baseline (t0)	Three weeks from baseline (t1)	Six weeks from baseline (t2)
Variable	N	Mean (SD)	Mean (SD)	Mean (SD)
HRV rest				
SDNN (ms)	5	22 (10.9)	22 (10.3)	27 (17.1)
RMSSD (ms)	5	14 (7.8)	15 (9.1)	18 (11.6)
VLF (ms^2)	5	47 (36.8)	41 (32.1)	99 (96.1)
LF (ms^2)	5	177 (174.8)	151 (117.6)	287 (356.8)
HF (ms^2)	5	54 (65.3)	57 (54.9)	76 (85.9)
LF:HF (%)	5	5.2 (4.63)	5.0 (5.24)	4.2 (2.31)
HRV recovery				
SDNN (ms)	5	10 (4.4)	13 (10.8)	12 (10.2)
RMSSD (ms)	5	4 (2.1)	9 (6.7)	6 (6.2)
VLF (ms^2)	5	14 (13.4)	23 (32.9)	9 (7.8)
LF (ms^2)	5	54 (42.9)	110 (197.3)	93 (166.3)
HF (ms^2)	5	7 (10.7)	47 (94.8)	37 (78.3)
LF:HF (%)	5	11.6 (7.69)	10.9 (14.52)	10.4 (7.95)
Respiration Rate rest (breaths $\cdot min^{-1}$)	4	15.6 (3.81)	14.0 (2.68)	11.2 (2.26)
Respiration Rate recovery (breaths $\cdot min^{-1}$)	4	19.1 (4.25)	13.7 (3.27)	12.6 (3.88)

HRV rest = heart rate variability during rest; HRV recovery = heart rate variability during recovery
SDNN = standard deviation of NN intervals; RMSSD = square root of the mean of the sum of squares of differences between adjacent NN intervals; VLF = very low frequency (0.003-0.05 Hz); LF = low frequency (0.05-0.15 Hz; HF = high frequency (0.15-0.4 Hz)

Discussion

The main results of this study suggest that after physical training, patients with fatigue complaints experience positive changes in HRV, respiration rate and fatigue. A significant increase in HRV (determined by rest SDNN, VLF and LF components) was observed after the training. A trend towards increased HRV was found in the remaining HRV rest values. Non-significant changes in HRV recovery values were observed after the training. Thus, positive HRV changes can be observed in rest, but patients did not recover faster from physical exertion after six weeks training. To our knowledge, few if any studies have investigated the effects of physical training in patients with complaints of fatigue. Nonetheless, the results of several previous studies that used different populations are consistent with the current results.[18-23] These studies showed increased HRV (SDNN, HF, LF, and/or LF:HF ratio components) after physical training in healthy individuals and in chronic heart failure patients.

HRV components SDNN, RMSSD and HF power are known to be mediated by vagal activity and an increase of these components therefore indicates an increase of parasympathetic activity.[22,31] The interpretations of LF power and LF:HF ratio are somewhat controversial. The ratio between LF and HF power is the sympathovagal balance, but lacks physiological base.[20] LF power is by some considered as a mediator of both the parasympathetic and sympathetic nervous system.[27] The increased LF power found in this study may seem in contrast with this explanation, but has been found before by Sandercock et al. (2007)[22] after eights weeks of cardiac rehabilitation. As for the VLF component, a significant change was observed after the six weeks training period. However, physiological interpretation can not be made, since VLF power is a dubious measure.[27]

Large variations in individual effects were found within and between sexes (Table 2 and 3), especially in the LF and HF power components. Post-hoc analyses showed that the individual LF power differences in women between baseline and six weeks training ranged from -180ms^2 to 3439ms^2. In men, individual changes between baseline and six weeks training ranged from -32ms^2 to 425ms^2. Additional analysis of the HF power component showed relatively even larger individual differences within men and women. These differences were partly due to some extreme values but may have influenced the results since previous studies found that aging is associated with a

reduction in parasympathetic control and that autonomic differences are gender-specific.[20] However in this study, no indications of even intermediate correlations between age and gender and any HRV component and respiration measurement were found after post-hoc analysis. Because of the small number of subgroups of patients included in this study, we did not test these indications statistically.

As hypothesized, the second physiological parameter, respiration rate, decreased significantly. The results show that, with the exception of two individuals, the respiration rate of all patients decreased both during rest and during recovery after physical exertion. A possible explanation is consistent with the authors' hypothesis: chronic stress reactions, which were assumed to occur in this population, might have been reduced due to relaxation, exercise or a combination of the two. The reduction of chronic stress reactions may decrease the stress alarm and thereby the sympathetic activity. In combination with the relaxing breathing impulses that are given during the breathing exercises, patients might have been able to decrease their respiration rate. An alternative explanation for the findings is that the decreases in respiration rate were due to the combination of breathing exercises with physical training, which was an important component of the programme.

A significant decrease in fatigue symptoms was found. All patients experienced fewer complaints at the end of the intervention period, compared to baseline. At baseline, a mean CIS score over 100 was found. This score was only slightly lower than the total CIS score of patients with chronic fatigue syndrome (mean = 113)[25], but higher than the total score for patients reporting mental reasons for fatigue (mean = 90).[26] Furthermore, the personal CIS scores are also worth mentioning. At baseline, all patients had CIS scores above 76 (range from 86 to 129), which was determined as the cut-off point for chronic fatigue.[32] This cut-off point can be associated with increasing risk level for sick leave or work disability. After three weeks, the scores of four out of 16 patients were below the cut-off point; after six weeks, six patients had scores of 74 or lower. In other words, all patients reported less fatigue symptoms after the six-week training period, and the complaints decreased in one quarter of the cases from severe to moderate.

The existing training programme that was evaluated in this study consists primarily of endurance training and breathing exercises. Several other components were part of the programme as well, including magnetic-field therapy, infrared therapy, power-plate exercises and application of extra oxygen. The effectiveness of

these solo components is unclear. However, they are part of the original training programme of the outpatient clinic and were, therefore, not excluded.

The following limitations should be taken into account. First, no control group was included in this evaluation study. Therefore it is not possible to ascribe all of the observed results to the intervention. However, the patients reported to have their complaints for long periods of time and no other interventions took place during the study period. A second limitation may be found in the short duration of the intervention. A longer training period may produce increased physiological changes and additional follow-up measures can provide more information about the long-term effects. Therefore, it is suggested to extend the training programme duration to follow-up physiological effects after a longer intervention period. Furthermore, due to the small number of subgroups of patients included in this study, we were not able to perform separate analysis for men and women. In future studies, when more patients can be included, it is suggested to present the data according to gender and take age into account. In the end, it might be interesting to study the effects of a physical training programme on return-to-work in future research, since a majority of the patients participating in this study were unemployed.

Conclusion

In summary, the results of the current study suggest that a six week physical training changes heart rate variability and respiration rate in patients with complaints of prolonged fatigue. Furthermore, patients reported a significant and clinically relevant decrease in fatigue complaints after the training programme. These results look promising for treatment of patients with prolonged and severe fatigue complaints.

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Chapter 4

Evaluating a multidisciplinary treatment programme in patients with prolonged fatigue complaints

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Abstract

Complaints of prolonged fatigue are common in the working population and may lead to functional impairments and work disability. A multidisciplinary treatment programme, consisting of physical training and psychological sessions, was evaluated. Thirty-two new patients of an outpatient institution with prolonged fatigue were included during the period 2002-2006. Fatigue complaints, quality of life and work participation were measured pre- and post treatment and at three months follow-up. Furthermore, patient and employer satisfaction was measured. Fatigue complaints decreased significantly and quality of life and work participation increased significantly after the training period. Furthermore, 90% of the patients reported that their complaints were diminished after the training and 82% of the employers were satisfied with the results achieved. The results suggest that a multidisciplinary treatment programme has significant and clinically relevant influence on decrease of fatigue complaints and improvement of quality of life and work participation in patients with prolonged fatigue complaints.

Introduction

Fatigue is a common complaint in the general population and the working population.[1-3] Acute fatigue can occur following a period of mental or physical exertion and be of temporary duration. In some cases, however, fatigue is prolonged, with serious effects on personal, social and occupational functioning, which can result in sickness absence and/or work disability.[4,5] The prevalence of prolonged fatigue is between 10% and 20% in the general population[2,3,6] and 22% in the Dutch working population.[1] There is no clear aetiology of fatigue, but it would appear to be multifactorial.[5] Risk factors for the development of prolonged fatigue are psychosocial factors[3] and work characteristics.[7,8] There are also indications that chronic stress and physiological reactions to stress are a factor in the development and persistence of prolonged fatigue.[9]

In view of the foregoing, treatments for patients with fatigue problems need to target both physiological and psychological aspects of individual and social/occupational functioning. In the Netherlands, patients with prolonged fatigue are offered various treatment cycles based on a multifactorial approach. These differ in the emphasis placed on physical training, cognitive restructuring, relaxation exercises and/or involving the employer/workplace situation in the process. Although a lot is being done in practice to treat patients with fatigue, there has been no research yet into the effectiveness of treatment cycles.

This study evaluates an existing multidisciplinary treatment programme for patients with prolonged fatigue. The aim is to assess the outcomes of the treatment programme on patients with prolonged fatigue by answering the following questions: (1) What effect does a treatment programme have on the degree of fatigue, quality of life and work participation in patients with prolonged fatigue? (2) What are the perceived results of a treatment programme from the point of view of patients and employers?

Method

Population

The research data relates to patients enrolled at a vocational rehabilitation institution (Reaplus BV, Dordrecht) during the 2002-2006 period. They were referred to the institution by an occupational physician, employer or benefits agency. From the total population, the institution selected those patients who had prolonged fatigue upon intake, had a good command of spoken and written Dutch and were motivated to take part in the programme. Patients were excluded if they had a somatic disorder or if the employer or the patient set unrealistic targets regarding return to work.

Design

The study was based on retrospective data. In order to evaluate the effect of the treatment programme, repeated measurements within subjects were carried out. These took place upon intake (t0), six weeks (t1) and 12 weeks (t2) after the start of the programme, upon completion of the programme after a minimum of 18 weeks (t3) and three months after completion (t4).

The following variables were operationalised to answer Question 1 (see Table 1):

Fatigue

In order to ascertain the degree of fatigue, patients completed the Checklist Individual Strength (CIS) at t0, t1, t2 and t3.[10] The total score ranges from 20 to 140, with higher scores reflecting higher degrees of fatigue. The CIS is a reliable tool (α=0.90)[10], which has been validated in a Dutch working population.[11]

Quality of life

Quality of life was measured at t0 and t3 using the validated RAND-36.[12] The researchers used five scales in the study: physical functioning, physical role limitation, emotional role limitation, mental health and vitality. The score on each scale ranges from 0 to 100, higher scores being better.

Work participation

Data on work participation comprised the number of contractual hours at t0 and the number of hours the patient was working at t0, t3 and t4. The data were collected in interviews at t0 and t3 and using a questionnaire at t4.

The following variables were used to answer Question 2 (see Table 1):

Perceived outcome from the patient's perspective

At t4, patients stated how much their symptoms had changed during the programme and in the three months afterwards. Scoring was on a five-point scale, ranging from 1 = 'seriously deteriorated' to 5 = 'highly diminished'. Upon completion of the programme (t3), there was a written evaluation of the personal targets set at t0. Patients scored each target separately on a five-point scale, ranging from 1 = 'fully met' to 5 = 'not met'.

Perceived outcome from the employer's perspective

The employer indicated how satisfied he was with the outcome in a questionnaire (at t4). Scoring was on a five-point scale, ranging from 1 = 'very dissatisfied' to 5 = 'very satisfied'. If the employer did not return the questionnaire the researchers contacted him by telephone.

Table 1. Overview of measuring points and variables measured

	T0	T1	T2	T3	T4
	Intake	6 weeks after start	12 weeks after start	Completion (> 18 weeks)	3 months after completion
Fatigue (CIS)	X	X	X	X	
Quality of life (RAND-36)	X			X	
Work participation	X			X	X
Changes in symptoms: patient's perspective					X
Targets met: patient's perspective	X			X	
Satisfaction: employer's perspective					X

Analysis

Fatigue

The CIS total scores were subjected to a General Linear Model analysis for repeated measurements. The scores at t1, t2 and t3 were compared with the score at t0. If there were values for t0 and t3 and no more than one missing value for either t1 or t2, the data were included in the analysis. For any missing values the researchers inserted the average of the surrounding CIS scores.

Quality of life

The RAND-36 scores for each sub-scale were checked using the Shapiro-Wilk test[13] for the normal distribution of the scores that differed between t3 and t0. A paired t-test was carried out where the distribution was normal, and a Wilcoxon signed-rank test where it was not.

Work participation

The number of hours worked at t0, t3 and t4 was compared with the number of hours in the employment contract at t0. As the data were not distributed normally they were tested using a non-parametric Friedman test.

Perceived outcome

The scores for the target were transformed into dichotomous data. Original scores of 1 (= 'fully met') and 2 (= 'largely met) were interpreted as 'target met'. The analyses of both the outcomes of the targets and patient and employer satisfaction were descriptive. All the statistical analyses were performed in SPSS 12.0.1 (SPSS Inc., Chicago, IL, USA). A significance level of α=.05 was maintained.

Treatment

The aim of the treatment was to vitalise patients and enable them to participate optimally at work.

Intake

Each patient was seen by a multidisciplinary team at an intake procedure that took four hours. The psychologist carried out a psychological examination, ascertaining

during the interview whether the patient had any mental needs and whether there were any mental aspects that had a negative influence on the present situation and potential recovery. The patient also talked to the occupational and organisational expert about work-related matters. The (occupational) physiotherapist carried out a mobility test and assessed activity pattern in terms of exertion and relaxation. There was also a physiological examination: a human movement scientist or physiotherapist checked lung function and the breathing pattern at rest (Ergostar, Energy Control, Weesp). The patient also took a submaximal exertion test on the bicycle ergometer to ascertain his or her physical condition in terms of peak oxygen uptake ($VO2_{peak}$) and peak resistance (P_{peak}). The aerobic threshold was determined on the basis of breathing pattern (an exponential increase in respiratory rate).

The aim of the intake procedure was to gain an understanding of the patient's current situation and how it developed. This information was incorporated in the 'treatment plan'. The participants also set targets relating to physical condition, mental condition and the work situation. The employer's target was then set at an interview with him. The treatment duration and programme were drawn up based on the complexity and diversity of the problems as estimated by the team. A treatment cycle could take 18 to 24 weeks. Once the treatment plan had been approved by the patient and the employer, treatment commenced. The time between intake and start (averaging 32 days) depended mainly on the speed with which the employer acted.

Programme

Depending on the physical, mental and/or work-related problems and issues, treatment could consist of a combination of various group modules (with a maximum of six patients) and individual sessions (see Table 2). The group sessions and disciplines involved were as follows:

(1) Two (occupational) physiotherapists ran the 'physical training' group module. Based on the results of the exertion test during the intake procedure (heart rate corresponding with aerobic threshold), a progressive personal workout scheme was drawn up to improve physical condition. Heart rate limits were used as a reference, and patients were given a heart rate monitor (Polar Electro) to monitor their limits. The two-hour condition training session was increased by two minutes a week from 20 minutes to a maximum of 40 per session. Exercises designed to improve strength, coordination, stability and

mobility of muscle and joint and exercises to improve perception of exertion and relaxation were done on a power station (Bowflex®, USA). Training sessions took place three times a week in the first six weeks of the programme, twice a week in the second six weeks and once a week in the third (and where appropriate fourth) six-week period. Once the patient had completed the second period he or she was expected to make up the number of sessions to twice a week.

(2) Five sessions included one-hour education on sickness behaviour and training theory.

(3) Another five hours were spent on the Breathing, Awareness and Relaxation module (where this was indicated), the aim of which was to increase body awareness and reduce any tensions.

(4) The Group Coaching module, based on the principle of Neuro-Linguistic Programming (NLP), was run by two NLP coaches. The purpose of these sessions was to gain fresh insights into problems and how to function with them.

In addition to these group modules, the programme included the following individual sessions:

(1) Work and organisation: the occupational and organisational expert discussed work-related matters, such as returning to work, communication, work ethos and character traits that can be an impediment (e.g. extreme perfectionism).

(2) The psychologist worked on aspects that could be improved to enable patients to function the way they would like in their working and private lives, such as setting boundaries, self-respect and overcoming negative patterns that have crept in.

(3) If the patient was no longer able to properly interpret mental or physical signals of overload, the coach provided assistance with body awareness.

(4) Patients who had physical problems, or who needed to change their attitude or behaviour in order to reduce the problems being experienced, received treatment or coaching from the physiotherapist.

The number of sessions required for the various individual modules was estimated during the intake procedure. If it emerged during treatment that additional sessions were needed in order to achieve the target or maintain the outcome, these were scheduled at no additional cost to the employer. At six-week intervals in the

programme, respiratory variables were measured and the submaximal exertion test was repeated in order to detect changes in physical condition so that the personal workout scheme could be adjusted if necessary. If P_{peak} had remained the same or gone down (whereas the session length had increased) there was a risk of over-training.[14] In this case, the session length was reduced by eight minutes so that it could subsequently be increased by two minutes a week. If P_{peak} had gone up the session was increased by two minutes a week up to a maximum of 40 minutes.

Table 2. Modules used to treat employees with prolonged fatigue

Module	Provided by	Time per session	Number of sessions
Group sessions			
Physical training	2 physiotherapists	2 hours	30–36
Theory lessons	Physiotherapist	1 hour	5
Breathing, Awareness and Relaxation	Physiotherapist	1 hour	5
Group coaching	2 NLP coaches[1]	2 hours	5
Individual sessions			
Work & Organisational	Occupational and organisational expert	1 hour	Determined individually
Psychologist	Psychologist	1 hour	Determined individually
Body awareness	Coach	1 hour	Determined individually
Physiotherapy	Physiotherapist	20–30 minutes	Determined individually
Physical coaching	Physiotherapist	30–60 minutes	Determined individually
Exertion test	Human movement scientist Physiotherapist	1 hour	At 6-week intervals

[1] Neuro-Linguistic Programming

Results

Population

Data was collected on 32 patients with prolonged fatigue, 23 female and 9 male. The average age was 37 years (SD = 11.3), ranging from 21 to 58 years. Average sick leave up to t0 was 27 weeks (SD = 18.5), with three patients not on sick leave and 21 on full sick leave. The diagnoses with which they were enrolled were burn-out, frequent absences from work, mental problems, stress or tension problems, Chronic fatigue syndrome (CFS) and fibromyalgia.

Fatigue

Data were available for analysis on 21 patients. Eleven patients did not complete (or fully complete) the questionnaire at both t1 and t2. The average CIS score reduced significantly during treatment (see Table 3).

Quality of life

Twenty-three patients fully completed the RAND-36 at t0 and t3. During the period from intake to completion of the treatment, the average score rose significantly ($p<0.01$) on the five sub-scales: physical functioning, vitality, mental health, physical role limitation and emotional role limitation (see Table 4).

Work participation

This analysis contained complete data on 31 patients. One patient did not have a permanent employment contract at t0 but had previously been working freelance. At t0 the patients were working 21.9% (SD = 34.03) of their contractual hours, on average; this percentage had increased significantly by t3 and t4 (see Table 5). In the case of three of the 31 patients the number of contractual hours was reduced at their request between t0 and t4. Another three patients had their employment contracts terminated: one was dismissed and two resigned. The work participation percentage at t4 compared with the number of contractual hours at t4, i.e. adjusted for the changed contracts (n = 28), shows that the patients were working 96.0% (SD = 11.86) of their contractual hours.

Table 3. Degree of fatigue as measured using the Checklist Individual Strength (CIS) during a treatment programme

Measuring points		**Fatigue**	
	n	M	SD
Intake (t0)	21	102	(19.0)
6 weeks after start (t1)	21	87	(33.8)[1]*
12 weeks after start (t2)	21	76	(36.0)[1]*
Upon completion (t3)	21	64	(35.0)[1]*

The table shows numbers (n), average total scores (M) and standard deviations (SD). The higher the value, the more fatigue problems.
[1] General Linear Model for repeated measurements (compared with t0); * p<.01

Table 4. Quality of life as measured using RAND-36 prior to and after completion of a treatment programme

Quality of Life		**Intake (t0)**		**Upon completion (t3)**	
	n	M	SD	M	SD
Physical functioning	23	58.3	(20.03)	84.1	(19.52)[2]**
Vitality	23	33.3	(19.92)	60.2	(20.36)[2]**
Mental health	23	57.2	(17.78)	72.9	(19.85)[2]*
Physical role limitation	23	9.8	(23.25)	63.0	(39.79)[1]**
Emotional role limitation	23	44.9	(34.25)	71.0	(30.66)[1]*

The table shows numbers (n), average scores (M) and standard deviations (SD). The higher the score, the higher quality of life.
[1] Wilcoxon signed-rank test, two-sided or [2] paired t-test, two-sided; *p<.05 and **p<.01

Table 5. Work participation percentage during the treatment programme

Measuring points		**Work participation**	
	n	M	SD
Percentage of hours worked at t0	31	21.9	(34.03)
Percentage of hours worked at t3	31	65.7	(29.30)[1]*
Percentage of hours worked at t4	31	84.1	(30.61)[1]*

The table shows numbers (n), averages (M) and standard deviations (SD).
[1] Friedman test (compared with t0); *p<.001

Perceived outcome from the patient's perspective

Twenty patients returned the questionnaire. Two said their symptoms were 'unchanged' during the programme, five 'somewhat diminished' and 13 'greatly diminished'. After completion of the programme, three subjects' symptoms were 'somewhat worse', two 'unchanged', eight 'somewhat diminished' and seven 'greatly diminished' compared with the end of the programme.

Twenty-eight patients set physical targets, e.g. improving their physical condition or reducing pain or physical symptoms, and evaluated them at t3: twenty-one said they had met their physical targets. Twenty-six patients set mental targets, e.g. being able to relax more or becoming more self-confident: at t3 twenty-three said they had met their targets. Twenty-seven patients set work-related targets, e.g. full return to their previous work or exploring the job opportunities: at t3 eighteen said they had met their targets.

Perceived outcome from the employer's perspective

Twenty-two employers returned the questionnaire or answered it by telephone. In the case of eight patients, the original contact person was no longer working for the company, and two employers could not be contacted even after repeated calls. One employer was dissatisfied with the outcome, three were neutral, nine satisfied and nine very satisfied.

Discussion

This study evaluated the outcomes of an existing treatment programme for patients with prolonged fatigue. The multidisciplinary programme included both physical and cognitive behavioural aspects, with both individual and group sessions taking place. The treatment was expected to influence certain outcome measures, e.g. diminished fatigue problems, better functioning in day-to-day life and return to work. The current research design was selected and the outcome measures were operationalised on the basis of this expectation.

At the start of the treatment programme, the patients were seriously fatigued, with an average CIS score of 102. This is slightly lower than the average CIS score for

CFS patients (average = 113)[15], but higher than that for fatigued workers (on sick leave) (average = 90).[15] Looking at the initial individual scores, we note that all the patients except one (CIS = 69) had a CIS score of over 76. This was set as the cut-off point for increased risk of sickness absence due to fatigue.[15] After completion of the programme, not only had the average CIS score diminished significantly, 14 of the 21 patients also had a CIS score of less than 76.

After completion of the programme, the average score on the RAND-36 physical functioning sub-scale (84.1) was slightly better than for the Dutch population as a whole (83.0).[16] The scores after completion of the programme on the vitality (60.2) and mental health (72.9) scales are close to the Dutch norm (68.6 and 75.9 respectively).[16] The results show that three months after completion of the programme (t4) work participation rose to 84%. Five patients had their contracts changed during the study period, with the result that at t4 96% of the current contractual hours were being worked at t4. One of the aims of the programme was for patients to gain a better feeling for where their boundaries lay. It may be as a result of gaining this insight that five patients changed their employment contracts.

The following points should be taken into account when interpret the results. First, this was an evaluation study without a control group, so all the results observed cannot necessarily be attributed to the treatment programme. Given the longstanding nature of the problems and the sickness absence at the start of the programme, however, spontaneous recovery from fatigue was unlikely. Second, when collecting data on the outcome measures fatigue and quality of life there were found to be 'missing values'. The vocational rehabilitation institution added new questionnaires during the 2002-2006 period, with the result that not all 32 patients completed all the questionnaires, leading to a limited sample size. Having analysed the outcome measures, however, we observed a large effect on both fatigue (effect size = 1.41) and quality of life (effect size = 0.68).

Ten patients did not participate in the programme following the intake procedure: two decided not to because they were not confident of achieving a good outcome, and in the case of the other eight, the employer considered that the investment in terms of time or money outweighed the possible benefits. Given this last finding, it would be interesting for future research to examine the cost-effectiveness of the treatment programme. Also, in view of the improvements observed, it would be worthwhile to continue research into treatment programmes for patients with fatigue both in a

controlled setting and in the longer term. This recommendation is being implemented in a follow-up study.

Conclusion

The results of this evaluation study suggest that a multidisciplinary treatment programme significantly reduces fatigue problems and improves quality of life and work participation. These outcomes are of clinical relevance. It also emerged that both patients and employers perceived the programme as having had a positive outcome.

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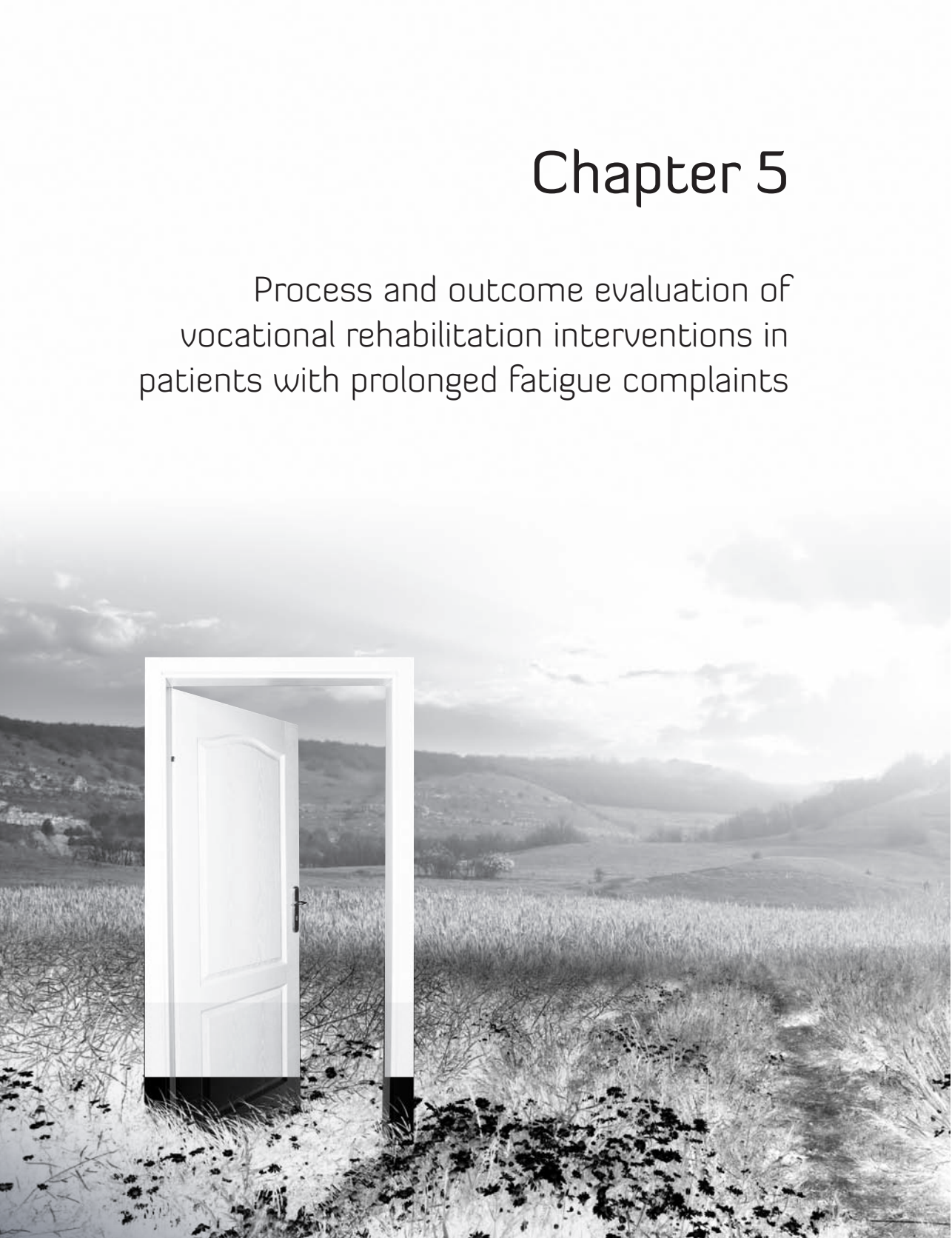
Chapter 5

Process and outcome evaluation of vocational rehabilitation interventions in patients with prolonged fatigue complaints



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Abstract

Background: Prolonged fatigue can cause physical, mental and occupational disability. Fatigue often persists because of a combination of biopsychosocial factors.

Purpose: To evaluate the process and outcomes of three existing outpatient vocational rehabilitation interventions (VRI) in patients with prolonged fatigue complaints. The VRIs differ with regard to the content and treatment duration, enrolment procedure and financing.

Method: A pre-post design was used with repeated measurements before treatment, after treatment and three months after treatment. Primary outcomes (fatigue and work participation) and secondary outcomes (physical and social functioning, mental health and physiological indicators (heart rate variability)) were assessed over time using linear mixed models analysis. A process evaluation (i.e., patient reach, content completeness and patient satisfaction) was conducted as well.

Results: One hundred patients participated. Post treatment, fatigue decreased ($p<.001$) and work participation ($p<.010$), physical functioning ($p<.001$), mental health ($p<.001$) and social functioning ($p<.001$) improved considerably in all three VRIs. Physiologically, heart rate variability improved in two VRIs ($p=.044$, $p=.038$, respectively). VRIs were administered according to the programme protocol. Almost all patients met their personal goals and the majority was satisfied with the outcomes of diminished constraints at work.

Conclusion: Three VRIs showed significant and clinically relevant outcomes over time regarding decreased fatigue and improved functioning and work participation in fatigued patients. The VRIs administered patient-tailored biopsychosocial interventions as planned and patients were satisfied with the interventions.

Introduction

It is known that fatigue is a common complaint in the general and working population, both in healthy people and those in ill health.[1] In the general population, the prevalence of severe fatigue complaints is 10 to 20%, while in the Dutch working population it is up to 22%.[2,3] However, the definition and origin of fatigue are elusive, even after years of research.[4] Fatigue can be seen as a discrete disorder (e.g., chronic fatigue syndrome (CFS))[5], a symptom of chronic diseases[1], or as an uni-dimensional continuum of complaints.[4] In this latter view, fatigue can develop from common mild complaints of tiredness to severe disabling fatigue that is not task-specific or easily reversible.[4,5] Prolonged severe fatigue complaints often affect individual, social and occupational functioning and would appear to be of multi-factorial origin.[1,5] Hence, using a traditional medical model of disease to explain prolonged fatigue would be insufficient.[6] The biopsychosocial model[7], which states that sickness and health results from a complex interaction between biological, psychological and social factors, seems to be more appropriate to explain prolonged fatigue and is used by several fatigue researchers.[8,9]

In line with the biopsychosocial model, mechanisms responsible for the perpetuating character of prolonged fatigue have been investigated. From a (neuro)biological point of view, prolonged exposure to stress, accompanied by the inability to terminate stress responses, may lead to overuse and damage of physiological stress systems.[10] Relationships between dysregulation of stress systems (i.e., autonomic nervous system)[11,12], HPA axis hypofunction[13] and prolonged fatigue complaints have been reported. Second, cognitive and behavioural factors are found to be involved in the perpetuation of fatigue complaints.[14,15] These perpetuating factors are important for designing an appropriate intervention.[16] Treatment should therefore include physical, psychological or cognitive-behavioural and (psycho)social interventions. To be more specific, intervening on those factors that perpetuate symptoms of the individual patient should be the target of interventions.[17] This approach has already shown positive effects in RCT research in CFS[9] and cancer-related fatigue[18] and in treating CFS patients in clinical practice.[19] Furthermore, intervention research in fatigued patients directed towards symptoms and complaints has been done.[20,21] However, research focussing on participation, especially work participation, is scarce.

In the Netherlands, multicomponent interventions are being offered to workers with participation problems.[20,22] Although these vocational rehabilitation interventions (VRIs) are practiced, there is a lack of evidence for the effects and content of these treatments. In this study, three different existing VRIs for fatigue patients are evaluated. When studying interventions in their usual settings, researchers are not able to manipulate content and organisation.[23] A process evaluation provides understanding of how an intervention was conducted and received.[24]

The aim of this study, therefore, is to assess the outcomes of three VRIs up to three months after completion in patients with prolonged fatigue. A second aim is to evaluate the process of the interventions, to gain insight into the outcomes and the content of the interventions. Research questions are as follows:

1. How were the VRIs conducted, in terms of reach of the target population, completeness of the administered intervention and patient's satisfaction?
2. Will fatigue complaints decrease and work participation increase after completion of the VRIs?
3. Will physical and social functioning, mental health and physiological indicators show positive changes after completion of the VRIs?

Method

Participants

The research population included patients enrolled in one of the three selected VRIs during the period 2006 – 2008. The VRIs used inclusion criteria to select their clients before treatment, including: good command of spoken and written Dutch, being motivated to take part in the intervention and not suffering from a psychiatric disorder. From this population, patients between the age of 18 and 60 years who reported to have fatigue complaints (for a longer period of time) as a main or important symptom and suffering from functional impairments (i.e., constraints in everyday life) due to fatigue complaints were eligible for participating in the study. These inclusion criteria were checked by a supervisor of the VRI during an intake procedure. Eligible patients were approached and informed about the study before

they provided written consent. This study was approved by the Medical Ethical Committee of the Academic Medical Center.

Design

Three institutions providing outpatient VRIs participated in this study. All three saw patients with prolonged fatigue complaints and problems with (work)participation. Differences between the institutions included content and duration of the treatment programmes, enrollment procedures and financing of treatment (Table 1).

A pre-post design with repeated measurements was carried out at each of the sites. Measurements took place at baseline (t0), upon completion of the intervention (t1) and three months after completing the intervention (t2). The results observed during t1 and t2 were compared with respect to baseline results. Because it is likely that the three VRIs had different target populations (including factors such as motivation, sick leave duration and disability level), it was not possible to compare the intervention outcomes of the three VRIs. In addition to evaluating outcomes of the VRIs, a process evaluation was conducted to assess the process and content of each intervention.

Table 1. Characteristics of the three Vocational Rehabilitation Interventions (VRIs)

	VRI 1	**VRI 2**	**VRI 3**
Target group	Patients with fatigue complaints and functional impairments	Workers with fatigue complaints and functional (work) impairments	Workers with fatigue complaints and functional (work) impairments
Recruitment strategies	Self referred	Referred by an occupational physician or benefits agency	Referred by an occupational physician or benefits agency
Financing of the intervention	By patients themselves	By the employer of the patient	By the employer of the patient
Overall goal	Reduce fatigue complaints and regain balance between activity and rest	Achieving a normal balance between daily life and work	Achieving a normal pattern of functioning including return to work
Duration	18 weeks	18 weeks (3 x 6 weeks)	4, 5 or 6 weeks
Days	3 times a week	3, 2, 1 times a week	From 5 to 2 times a week
Level	Individual	Individual and group level	Group and individual level

Vocational Rehabilitation Interventions (VRI)

VRI 1

The first VRI was carried out in a regional outpatient clinic (Energy Control), mainly consisting of physical training, relaxation and breathing exercises. Based on an exercise test, in which individual heart rate levels were registered, a progressive personal workout scheme was developed to improve physical/aerobic fitness. For a detailed description of the intake procedure, see Joosen et al.[20] During the training, heart rate values were monitored and used as references to determine the load of the training. VRI1 took 18 weeks, with a clinic visit frequency of three times a week (Table 1).

VRI 2

A regional vocational outpatient clinic (Reaplus) carried out a multicomponent treatment programme. The programme consisted of physical training (i.e., progressive personal workout scheme was used based on an exercise test in which heart rate levels were registered), psychological and cognitive behavioural sessions and return-to-work sessions.[22] VRI2 took 18 weeks, with a frequency of three times a week during the first six weeks, decreasing from two to one time per week for the following six weeks. During the third period, patients were expected to engage in physical training two times per week (Table 1).

VRI 3

The third VRI, a multicomponent treatment programme, was carried out by a national vocational outpatient clinic (Winnock). Four of its ten locations were included for this study and followed the same protocol. The duration of the programme depended on the duration of sick leave; the intervention was set at four weeks when the patient was absent from work less than 18 consecutive weeks, five weeks at 18-26 weeks sickness absence and six weeks when absence duration was longer than 26 weeks. The first one, two or three weeks of intervention consisted of a five days-a-week programme of cognitive behaviour therapy principles, physical training (i.e., graded activity using time-contingent training) and return-to-work sessions. Frequency diminished to one or two times a week in the weeks following (Table 1).

Process evaluation

Based on key elements in process evaluation research, i.e., reach, dose delivered and dose received, an evaluation was conducted on each programme intervention.[24] Reach addressed 1) patient characteristics (i.e., demographics, degree of fatigue, duration of fatigue and disability), collected at baseline by means of a self-administered questionnaire; and 2) data about frequency of and reasons for intervention dropouts were collected by the researcher during the intervention period.

Dose delivered analysis reviewed whether the interventions were administered as planned. Following each session or training day, supervisors or trainers completed a structured process evaluation form. Presence of patients and reasons for not attending meetings and intervention components delivered of the specific session were registered for each participant. Frequency of components delivered was compared with the programme protocol to check the completeness of the interventions. Completeness was determined to be 'full' when more than 74% of the prescribed amount of components took place, 'fair' between 50-74% and 'incomplete' when less than 50% of the programme protocol was delivered.

Dose received, as measured by patient satisfaction, was recorded at t1. Personal goals were evaluated through open-ended questions and the perceived effectiveness of the intervention on experienced constraints at work was also assessed by questionnaire.

Outcome evaluation

Data to assess the outcomes of the VRIs were collected at t0, t1 and t2. Outcome variables were divided into primary outcomes and secondary outcomes.

Primary outcomes

To investigate fatigue complaints, three questionnaires were used. First, severity of fatigue complaints was measured with the Checklist Individual Strength (CIS)[25], which consists of 20 statements that cover several aspects of fatigue. The total score was calculated by adding all item scores and ranged from 20 to 140. Higher scores indicated a higher severity of fatigue. The CIS has been validated in the Dutch working population.[26] The Vitality subscale, one subscale of the Dutch version of the RAND-36 Health survey[27], which is almost identical to the MOS SF-36[28], was used to measure fatigue as well. The score ranged from 0 to 100, higher scores being better.

The RAND-36 is a reliable and validated generic instrument.[27] Third, work-related fatigue was measured with the Need for Recovery After Work scale.[29] This scale comprises 11 dichotomous items. The total score was calculated by adding the item scores and transformed into a scale ranging from 0 to 100. Higher scores indicated a higher degree of need for recovery after work. The Need for Recovery scale was found reliable in a working population.[30]

Data on work participation were collected at t0, t1 and t2 by researcher-formulated questionnaire. Data consisted of 1) current work status, in terms of employed or unemployed; 2) number of contractual hours; and 3) absolute number of hours the patient was working. These data were used to determine the percentage of return-to-work, defined as the mean percentage of return to original working hours at t0. Self-reported work ability was assessed using two items from the Work Ability Index (WAI)[31] 1) current work ability compared with lifetime best, scoring between 0 ('not being able to work') and 10 ('lifetime best work ability'); and 2) personal prognosis of work ability in the next two years, scored on a three-point scale ('hardly able to work', 'not sure', 'fairly sure to be able to work').

Secondary outcomes

Subscales of the RAND-36 Health survey[27] were used to measure physical functioning and physical role limitation, mental health and emotional role limitation, and social functioning. The scores on each scale range from 0 to 100, higher scores being better.

Heart rate variability (HRV) was used as a physiological indicator and is a marker that reflects sympathetic and parasympathetic activity of the autonomic nervous system. Prolonged exposure to stress, can lead to dysregulation of this system (i.e., lower parasympathetic activity)[10,32] and can be identified by decreased HRV.[33] HRV was recorded using the Co2ntrol (Decon Medical Systems, Weesp, the Netherlands), a small device attached to a chest strap that detects beat-to-beat intervals of the heart rate signal.[20] HRV was measured at t0 and t1 (only in patients of VRI1 and VRI2) during a standardised test protocol: five minutes seated in a resting position for adaptation, followed by 12 minutes light exercise on a bicycle ergometer using a single load of 50W with a pedal frequency between 60 and 65 min^{-1}. The Co2ntrol was developed according to the guidelines of the European and North American Task Force (1996).[34] It was found to provide reproducible HRV measurements in healthy individuals and in patients with prolonged fatigue.[35]

HRV data reduction

To define HRV, raw data were transferred to HRV Analysis Software version 2.0 (http://venda.uku.fi/research/biosignal), data artefacts were detected and processed by the software. The data were de-trended using the smoothn prior option. To determine the spectrum of HRV, the Fast Fourier Transform (FFT) option was used and data were re-sampled at a rate of 4 Hz using cubic interpolation. The final nine minutes of the 12 minute recording period during light exercise were selected. HRV was measured by means of heart period High Frequency (HF) power. HF power values were used to estimate Respiratory Sinus Arrhythmia (RSA), the variability of heart period in the respiratory frequency band. RSA is considered a valid index of changes in cardiac vagal tone, which interacts with parasympathetic activity.[32,33] In this study HF power was computed in the 0.15-0.5 Hz respiration window. The VRIs were expected to have beneficial effects on physiological status (i.e., raise HF power after completion of the interventions).

Statistical analysis

Statistical analyses were performed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Values of $p<.05$ were considered statistically significant. To analyse the changes of the three VRIs on the outcome variables over time, linear mixed-model analyses were performed based on repeated measures. The best fitting covariance–variance model was tested before the analysis was applied. A post-hoc procedure (Bonferroni correction: unadjusted p value times 2) was followed to test significant differences between test moments (t1 and t2 compared with t0). Analyses were conducted for each VRI separately. To assess the changes in HRV over time, a paired t-test was carried out.

Results

Process evaluation

Reach

In total, 35 patients enrolled in VRI1, 30 patients in VRI2 and 45 patients enrolled in VRI3. Due to dropouts, analyses were performed for 30, 29 and 41 patients respectively. See Figure 1 for a flowchart and reasons for dropout.

Patient's characteristics by VRI group are shown in Table 2. In all three interventions patients had, on average, severe disabling fatigue complaints for many years (mean over 2.5 years). In the VRI1 and VRI2 groups, most patients (58% in each group) were on sick leave at baseline. In the VRI3 group, most patients (53%) were fully at work at baseline.

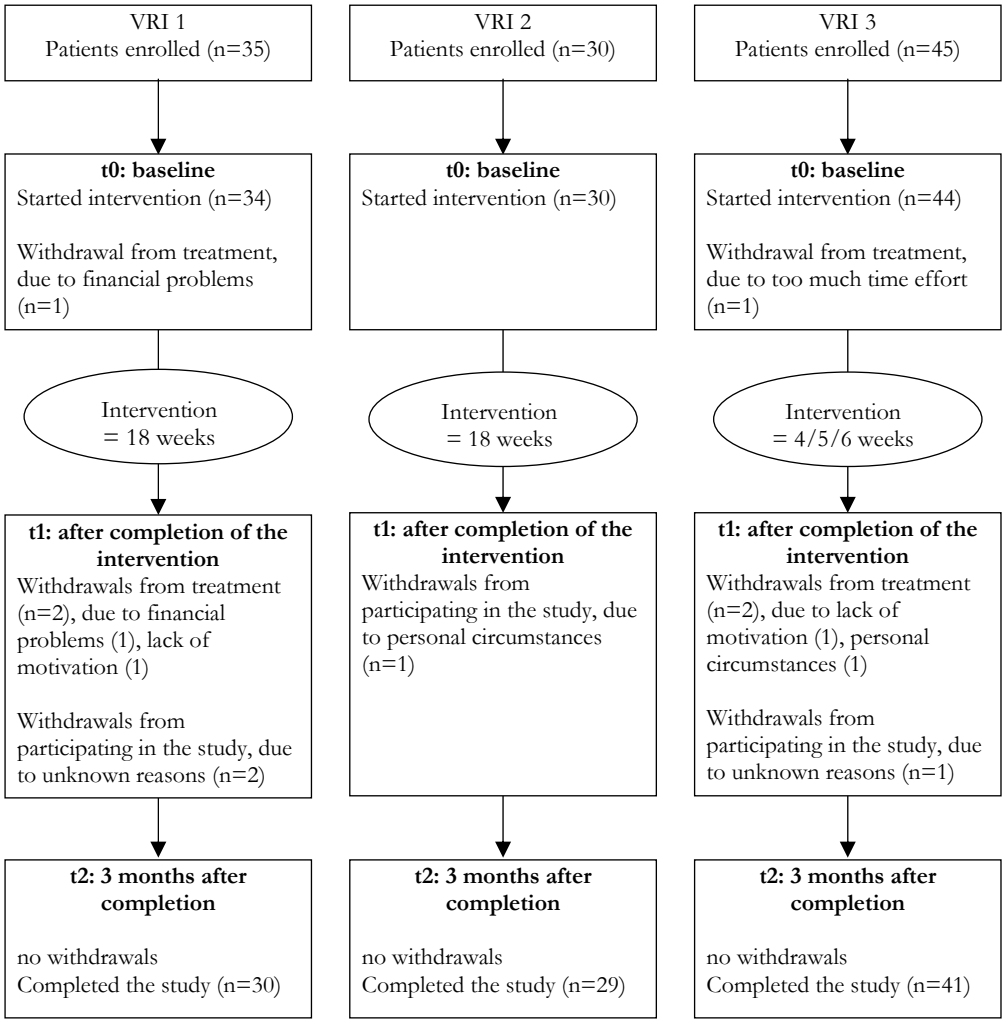

Figure 1. Flow-chart of patients through the study

Table 2. Characteristics of the patients of VRI1, VRI2 and VRI3

	VRI 1	**VRI 2**	**VRI 3**
	Mean (SD) or Freq. (%)	Mean (SD) or Freq. (%)	Mean (SD) or Freq. (%)
Intervention completed (n)	30	29	41
Age	47 (8.1)	45 (12.1)	45 (10.4)
Male	5 (17%)	16 (55%)	24 (59%)
Female	25 (83%)	13 (45%)	17 (41%)
Severe fatigue (CIS score >76)[1]	83%	90%	95%
Duration of fatigue complaints in years	5.8 (5.6)	3.0 (3.6)	3.7 (4.7)
Duration functional impairments in years	4.0 (4.7)	2.5 (3.2)	3.4 (5.4)
Employment status			
Paid job, fully at work	10 (33%)	11 (38%)	20 (49%)
Paid job, partly on sick leave	8 (27%)	13 (45%)	15 (37%)
Paid job, fully on sick leave	6 (20%)	2 (7%)	3 (7%)
No paid job	6 (20%)	3 (10%)	3 (7%)

[1]CIS score above 76 was set as the cut-off point for chronic fatigue and increased risk of sickness absence due to fatigue[36]

Dose delivered

On average, the VRI1 participants missed three training days because of illness, vacations or bad weather/traffic. In five patients, the programme protocol was adjusted from three times a week to two times a week due to time constraints. In the VRI2 group, patients missed on average four sessions. Reasons for not attending a session were primarily illness and vacation. During the intake procedure, individual goals were set and the programme protocol was tailored to participant needs. The duration of the VRI3 programme depended on the participant's sick leave duration; 21 patients attended the programme for four weeks, ten for five weeks and 14 patients attended for six weeks.

The components of the VRIs, intended frequency per patient, frequency actually delivered and completeness are shown in Table 3. Varieties in the programme protocol (duration and/or components) per patient are taken into account. On average, the completeness of three out of five components of VRI1 was 'fair'. In VRI2 and VRI3, all but one session were carried out as planned ('fair' to 'full' completeness).

Table 3. Process evaluation: Content, aims of components, frequency of dose in protocol (average number of sessions per patient), dose delivered (incl. range) and completeness (%) of the VRIs.

	Session type	Components / sessions	Aim	Freq. dose protocol (range)[1]	Freq. dose delivered (range)	Completeness % (range)
VRI 1 18 weeks: 3 times a week	Exercise test	Exercise test	Examine physical condition (basis for workout scheme)	3 (3)	2 (1-6)	59 (33-100)
	Physical training	Progressive workout scheme (incl. warm-up, aerobic training, muscle strength training, cool-down)	Reconditioning, improve aerobic fitness	51 (36-54)	29 (13-48)	57 (28–94)
	Relaxation	Relaxation techniques (prior and after each physical training)	Relaxation / stress reduction	51 (36-54)	26 (10-47)	51 (27–94)
		Breathing exercises (visual feedback)	Relaxation	51 (36-54)	25 (9-45)	49 (25–92)
	Psychological	Informal conversations about cognition of illness and training.	Improve coping with the illness / increase knowledge sickness behaviour and training theory	Not in protocol	12 (3-36)	100% of the patients

	Session type	Components / sessions	Aim	Freq. dose protocol (range)	Freq. dose delivered (range)	Completeness % (range)
VRI 2 18 weeks (3 times 6): 3, 2, 1 times a weeks	Assessment	Intake procedure (exercise test, psychological examination, goal setting)	Examine physical and mental condition (basis for workout scheme and session delivered)	3 (0)	3 (2-4)	92 (67-100)
	Physical training	Progressive workout scheme (warm-up, aerobic training, muscle strength training, cool-down)	Reconditioning, improve aerobic fitness	36 (0)	30 (9-37)	83 (25-100)
	Psychological / Cognitive behavioural	Breathing, awareness and relaxation	Body awareness / stress reduction	5 (0)	3 (0-5)	59 (0-100)
		Group coaching module	Improve coping strategies	4 (0)	2 (0-7)	88 (0-100)
		Psychologist (individual counselling, cognitive therapy (RET)	Stress reduction, improve coping strategies	Max 10[2]	3 (0-11)	73 (0-100)
		Energy engineering (individual)	Physical coaching, body awareness, relaxation	Max 10[2]	4 (0-10)	100 (0)
		Education	Increase knowledge about illness, sickness behaviour and training theory	8 (0)	4 (2-8)	47 (25-100)

	Return-to-work	Work & Organisation (discussing strengths/weaknesses, preparing for return to work, work experiences)	Return to work	Max 10[2]	5 (0-11)	100 (0)

	Session type	Components / sessions	Aim	Freq. dose protocol (range)[1]	Freq. dose delivered (range)	Complete-ness % (range)
VRI 3 4, 5, 6, weeks	Physical (training)	Graded activity training	Reconditioning, body knowledge	12 (5-25)	12 (1-28)	85 (20-100)
		Unrestricted moving	Body knowledge	3 (1-4)	2 (1-4)	89 (33-100)
	Cognitive behavioural	Cognitive therapy (e.g., RET)	Stress reduction, improve coping strategies	7 (4-11)	7 (2-13)	88 (29-100)
		Education	Increase knowledge about illness and sickness behaviour	2 (1-3)	2 (0-6)	90 (0-100)
		Partner session	Increase knowledge about illness and sickness behaviour	1 (0-1)	0.2 (0-1)	28 (0-100) [3]
		Energy engineering	Body awareness, relaxation	1 (1-3)	2 (1-3)	96 (50-100)
		Evaluation	Goal setting (personal goals), evaluating progress	2 (2-3)	2 (0-5)	87 (0-100)
	Return-to-work	Work (preparing for return to work, workplace visit)	Return to work	5 (2-7)	4 (0-10)	74 (0-100)
		Follow-up (work experiences)	Return to work, improve coping strategies	3 (2-4)	3 (0-7)	76 (0-100)

Completeness: average of dose delivered in percentage compared to dose in protocol per individual

[1] Frequency ranges because of differences in modules or duration of the intervention, determined individually post intake.

[2] Number of sessions was individually determined during the intervention, but with a maximum of 10 sessions.

[3] Not an accurate figure because of lack of information about number of sessions in the protocol, individually determined.

Table 4. Mean scores (95% Confidence Intervals) on degree of fatigue parameters and work participation at t0 (baseline), t1 (at completion of the intervention) and t2 (three months after completion) in three VRIs and p-values for the differences over the three measurements.

			Degree of fatigue			**Work participation**	
			Fatigue (CIS) 20-140 (scale)	*Work related fatigue (VBBA)* 0-100 (scale)	*Vitality (SF-36)* 0-100 (scale)	*Return-to–work %* 0-100	*Work ability (WAI)* 0-10 (scale)
VRI 1		*N*	30	24	30	24	30
	t0	M (95% CI)	98 (88.9-106.6)	68 (54.8-81.7)	32 (27.5-36.2)	63 (45.5-81.0)	4 (2.8-4.7)
	t1	M (95% CI)	67 (58.3-76.1)***	47 (34.4-60.5)**	55 (49.2-61.4)***	76 (61.2-91.6)*	6 (5.0-6.9)***
	t2	M (95% CI)	62 (52.6-71.0)***	46 (33.0-58.8)**	59 (52.3-66.3)***	81 (68.7-94.0)**	6 (5.5-7.4)***
		Overall p-value	<.001	.001	<.001	.008	<.001
VRI 2		*N*	29	25	29	26	29
	t0	M (95% CI)	107 (99.2-115.3)	78 (64.8-91.5)	34 (27.1-39.9)	31 (16.6-45.9)	3 (2.2-3.8)
	t1	M (95% CI)	64 (50.7-76.6)***	33 (19.1-46.2)***	62 (53.7-70.6)***	67 (51.5-83.3)***	7 (5.8-7.3)***
	t2	M (95% CI)	66 (52.8-79.6)***	40 (24.2-55.5)**	59 (50.2-68.1)***	80 (65.6-95.0)***	7 (5.7-7.6)***
		Overall p-value	<.001	<.001	<.001	<.001	<.001
VRI 3		*n*	41	40	41	38	41
	t0	M (95% CI)	107 (101.6-111.6)	81 (73.8-87.4)	30 (26.4–34.6)	31 (21.0-41.0)	3 (2.9-4.0)
	t1	M (95% CI)	78 (71.3-85.0)***	55 (45.3-64.4)***	51 (45.7-55.6)***	57 (46.7-66.9)***	6 (5.0-6.1)***
	t2	M (95% CI)	75 (65.6-84.2)***	52 (39.8-63.2)***	52 (45.3-59.1)***	84 (73.5-94.5)***	6 (5.6-7.0)***
		Overall p-value	<.001	<.001	<.001	<.001	<.001

post-hoc analysis (Bonferroni adjustments) within subjects (compared to t0): *p<.02; **p<.01; ***p<.001

Table 5. Mean scores (95% Confidence Intervals) on physical functioning, mental health, social functioning and mean scores (standard deviations) on heart rate variability at t0 (baseline), t1 (at completion of the intervention) and t2 (three months after completion) in three VRIs and p-values for the differences over the three measurements.

			Physical functioning		**Mental Health**		**Social functioning**	**Heart rate variability**
			Physical functioning (SF-36) 0-100	*Physical role limitation (SF-36)* 0-100	*Mental health (SF-36)* 0-100	*Emotional role limitation (SF-36)* 0-100	*Social functioning (SF-36)* 0-100	*HF power (ms)*
VRI 1		*n*	30	30	30	30	30	29
	t0	M (95% CI)	74 (68.0-81.0)	14 (4.2-24.2)	57 (50.7-63.4)	47 (29.5-63.8)	45 (36.0-54.8)	64 (SD=79.5)
	t1	M (95% CI)	86 (79.5-92.6)***	61 (44.0-78.4)***	71 (65.1-76.4)***	87 (77.0-97.8)***	67 (58.0-76.5)**	164 (SD=295.4)
	t2	M (95% CI)	86 (79.6-92.8)***	64 (46.3-80.9)***	73 (67.5-77.6)***	75 (60.7-89.1)**	71 (61.8-80.5)***	not measured
		Overall p-value	<.001	<.001	<.001	.001	<.001	.044
VRI 2		*n*	29	29	29	29	29	26
	t0	M (95% CI)	62 (54.3-70.4)	9 (.2-18.2)	56 (48.7-63.0)	45 (28.1-61.5)	50 (39.9-59.2)	27 (SD=31.2)
	t1	M (95% CI)	83 (75.8-90.4)***	52 (36.3-68.4)***	75 (69.1-81.2)***	67 (50.5-84.1)	77 (67.0-86.6)***	71 (SD=122.9)
	t2	M (95% CI)	82 (73.5-90.6)***	61 (45.0-77.6)***	72 (63.9-80.2)***	62 (45.0-79.5)	75 (65.2-84.8)**	not measured
		Overall p-value	<.001	<.001	<.001	.098	<.001	.038
VRI 3		*n*	41	41	41	41	41	
	t0	M (95% CI)	66 (59.2-73.0)	13 (3.1-22.6)	50 (44.5-55.6)	28 (15.9-41.1)	43 (36.3-50.3)	not measured
	t1	M (95% CI)	81 (74.4-88.3)***	41 (27.8-54.1)***	64 (58.4-69.6)***	53 (40.6-66.1)**	67 (59.7-73.3)***	not measured
	t2	M (95% CI)	82 (75.2-89.1)***	53 (39.4-67.0)***	68 (62.7-73.8)***	71 (58.5-84.0)***	73 (66.0-80.8)***	not measured
		Overall p-value	<.001	<.001	<.001	<.001	<.001	

post-hoc analysis (Bonferroni adjustments) within subjects (compared to t0): *p<.02; **p<.01; ***p<.001

Dose received (data not shown)

In total, 29 patients in the VRI1 group set personal goals, such as improving energy level or physical condition or being able to relax more. At t1, 24 patients (83%) stated their targets were partly to fully met. Out of 28 patients in the VRI2 group, 24 (86%) had partly or fully met their goals at t1; stated goals included improving energy level or physical condition, being able to relax more, improving physical and mental functioning and/or improving work participation. In the VRI3 group, 36 patients set personal targets, including improving energy level, concentration, cognitive functioning, general health and/or work participation. At t1, 34 (94%) had partly or fully met their goals.

Furthermore, 16 (55%) out of 29 patients in the VRI1 group stated that the intervention was effective in diminishing perceived constraints at work. In the VRI2 sample, this figure was 20 (74%) out of 27; and in VRI3 participants, 26 (68%) out of 38 patients stated the intervention was effective on constraints at work.

Outcome evaluation

Primary outcomes

In Table 4, mean scores with confidence intervals and overall p-values for primary outcomes are reported per VRI per measurement.

In all VRIs, fatigue (i.e., fatigue severity, vitality, work related fatigue) significantly decreased over time (between $p<.001$ and $p=.001$). In the VRI1, VRI2 and VRI3 groups, 83%, 90% and 95%, respectively, of patients had CIS scores above the cut-off scores (indicating chronic fatigue)[36] at baseline. At t2, these percentages diminished to 19%, 46% and 50%, respectively.

Significant increases were found in percentage of return-to-work (between $p<.001$ and $p=.01$) and in perceived workability ($p<.001$) for all VRIs over time. As for the personal prognosis of work ability, in the VRI1 group, 13 (39%) out of 33 patients stated at baseline that they were "fairly sure" they would be able to work in two years. At t1, this figures was 21 (72%) out of 29 patients. Out of 30 patients in the VRI2 group, 15 (50%) were "fairly sure" to be able to work in two years at baseline, and at t1, this figure was 21 (78%) out of 27. While in the VRI3 group, 24 (55%) out of 44 patients at baseline and 26 (65%) out of 40 at t1 felt this way (data not shown).

Secondary outcomes

Table 5 shows mean scores and confidence intervals for secondary outcomes (standard deviations for heart rate variability) and overall p-values per measurement for each VRI.

Physical functioning, physical role limitation, mental health and social functioning improved significantly ($p<.001$) over time in all three VRI groups. Emotional role limitation improved significantly over time in the VRI1 and VRI3 groups ($p=.001$ and $p<.001$, respectively). Non-significant changes in emotional role limitations were found in VRI2 group participants ($p=.098$).

Heart rate variability, i.e., HF power values, increased significantly in the VRI1 and VRI2 groups ($p=.044$ and $p=.038$, respectively) after completion of the interventions.

Discussion

The process and outcomes of three existing vocational rehabilitation interventions aimed at improving individual and occupational functioning in fatigued patients using a biopsychosocial approach were studied. All interventions were conducted in a sample of patients with prolonged disabling fatigue. The most important components of each intervention were administered as planned, and few dropouts were reported. Furthermore, the majority of the population met their personal goals and stated that the attended intervention was effective in diminishing constraints at work. After treatment and three months later, patients had on average significantly fewer fatigue complaints and had improved their individual and occupational functioning. One secondary outcome showed no significant effect in one VRIs.

Specific content of the interventions was determined and all VRIs used a biopsychosocial approach in their intervention, but differed in the components primarily focused upon. VRI1 focused primarily on physiological improvement by means of an extensive workout scheme. Patients in the VRI1 group completed, on average, 57% of the planned physical training sessions. Even though this was stated as 'fairly' complete, only four patients completed over 75% of the training sessions planned. It appears that keeping up with a training frequency of three times a week

(each 2.5 hours) for 18 weeks is a difficult task in this population. Furthermore, informal conversations about patient's feelings, thoughts and concerns about their illness and the training were not detailed in the VRI1 protocol, but were conducted in all patients. The content of VRI2 was individually tailored to patients' needs. The intervention focused on physiological adaptation (by physical training) and on psychosocial functioning (by cognitive behavioural sessions in groups and in individuals), and were 'fairly' or 'fully' completed. VRI3 focused on cognitive behavioral therapy on physical, personal and social/work level, provided mostly in group sessions. These components were delivered as planned. However, completeness of partner sessions was below 50%. This figure may be misleading because the sessions were non-compulsory, and it is unknown whether the partner sessions were planned for each patient.

In this study, patients enrolled in one of the VRIs by 'normal' enrolment procedures. The VRIs have different ways of recruiting their clients; in VRI2 and VRI3, occupational physicians often refer sick-listed workers to the clinics. The clients of VRI1 are often advised to visit the clinic by people in their social environment and/or caregivers, but are self referred. Consequently, clients in VRI1 have to finance the treatment themselves, whereas in VRI2 and VRI3 the employer of the clients pays for the treatment. Therefore, the VRIs could have slightly different target populations, with regard to motivation and employment status. Nevertheless, the current results on patient's personal goals show that the content of the interventions individually match these individual goals.

Despite the differences in content, fatigue complaints decreased significantly at completion and at three months follow-up in all interventions. At baseline, mean CIS scores were around 100, only slightly lower than CIS scores in CFS patients (mean=113).[36] After treatment and three months later, CIS scores diminished to below the cut-off point indicating chronic fatigue[36] (CIS=76), but were still higher compared to the Dutch working population (mean=47).[36] As for work participation, mean percentage return-to-work rose to over 80% at t2 in all VRIs. Remarkably, this is even the case in the VRI1 group, in which return-to-work was not a specific component of the intervention. However, work participation in the VRI1 sample was higher at baseline compared to VRI2 and VRI3 groups. After completion of the VRIs, physical functioning and mental health moved towards the scores of the Dutch population (resp. mean=83 and mean=77).[37] Social functioning improved significantly

in all VRIs, but stayed below the scores found in the Dutch population (mean=84).[37] It may be hypothesised that improvement comparable with the social functioning level of the Dutch population requires more time, especially in patients with longstanding disabling fatigue.

As for heart rate variability, both patients in VRI1 and VRI2 showed significant improvements in HF power after treatment. This reflects an increase of parasympathetic activity of the autonomic nervous system. Few if any studies have investigated the effects of vocational interventions on HRV in fatigued patients. In healthy individuals and coronary patients, aerobic exercise, comparable to physical exercise in VRI1 and VRI2, significantly increases HF power.

The results of the current study are in line with previous research. In CFS patients, biopsychosocial interventions showed positive effects on physical, psychological and quality of life outcomes.[9] In different populations, that is, in patients with upper extremity musculoskeletal disorders[38], low back pain[39] and patients on long-term sick leave[40], multidisciplinary biopsychosocial rehabilitation showed positive effects on work participation, as well. However, few if any studies have evaluated biopsychosocial interventions in practice on work participation in fatigued patients. The VRIs in this study were not specifically designed for fatigue patients. Patients with different diseases and disabilities were treated as well.

In this study, interventions were evaluated in a real life setting. Outpatient clinics in the Netherlands have to deal with issues such as creating contracts with clients and employers, competition with other clinics and protection of their product. Therefore, as in all business enterprises, they have financial motives in addition to providing the best care to the patient. Consequently, conducting a randomised controlled study was not feasible. However, these outpatient interventions were already practised in real-life situations, with their own patient population and carried out by experienced trainers and supervisors. It is therefore of great importance to evaluate the outcomes of these everyday practices with many fatigued patients seeking help. Because of its uncontrolled design, the results of this study cannot directly be attributed to the interventions. However, a number of measures were taken to strengthen the design. First, the VRIs content and theory was specified and outcomes were selected close to the interventions and were measured using reliable and validated outcomes variables. The results pointed in the same direction. This was shown, by longitudinal data, as well as in the process evaluation which confirmed that the VRIs were also conducted

as planned. Second, the outcomes variables which were thought to be affected by the VRIs showed positive results. The outcomes variables which were thought to be not or less affected by the VRIs (e.g. social functioning in VRI1 and VRI2) did *not* show positive results. Third, by using triangulation of methods, different perspectives were taken into account and we found that patient's interpretation of the outcomes did not differ from the researcher's perspective. Finally, the patients within this study were suffered from disabling fatigue for many years on average. Given the longstanding nature of fatigue complaints and perceived disabilities, spontaneous recovery of these problems was unlikely. Considering the above mentioned points, we believe that the outcomes of this study may be attributed to the interventions as provided by the outpatient clinics in a population of prolonged fatigue patients with participation problems.

The results of this study therefore suggest that these three VRIs, guided by principles of the biopsychosocial model, provide significant and clinically relevant outcomes regarding decreased fatigue symptoms and improved functioning and participation in patients with prolonged fatigue up to three months after intervention. It is therefore recommended that biopsychosocial interventions (patient-tailored) be used for patients with disabling prolonged fatigue complaints. The results are of importance for occupational physicians, among others. Occupational physicians play an important role in preventing and managing sickness through referral to VRIs. It is, however, unclear whether the positive short-term outcomes obtained in this study will be sustained. Research into durability of these outcomes will be of importance for those involved in treating this population and is therefore recommended.

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Chapter 6

Work-related limitations and return-to-work experiences in prolonged fatigue: workers' perspectives before and after vocational treatment

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Submitted

Abstract

Purpose: To gain insight into fatigued workers' perspectives regarding work experience before and after receiving vocational rehabilitation (VR) treatments.

Method: A qualitative survey was conducted using semi-structured interviews with 21 fatigued workers who attended an outpatient multi-component VR treatment. Six months after treatment, work-related limitations and employed VR strategies at work before treatment were explored. Next, VR treatment experiences regarding return-to-work (RTW) were explored. Two researchers performed partially independent, qualitative analyses that revealed topics, discussed by the project team, and organised into domains, categories, and sub-categories.

Results: Work-related limitations were: symptoms of prolonged fatigue, personal limitations (e.g. lack of self-reflection on individual capacity and limitations), interpersonal factors, activities and conditions at work, and life/work imbalance. Before the treatment, VR strategies such as work adaptations, well-intentioned advice and support, and/or referral to psychological or physical care were employed. VR treatment experiences on RTW were: personal challenges (e.g. gained awareness and coping skills), improved activities during work, work adaptations, and unresolved problems (e.g. remaining fatigue symptoms and sickness absence).

Conclusions: New information about work experiences before and after multi-component VR treatments in workers with prolonged fatigue may help employers, occupational physicians and other caregivers to develop VR strategies that better meet individuals' needs.

Introduction

The ability of a worker to perform optimally at work can be affected by having health problems, functional impairments, activity limitations and a range of factors in the individual and environmental context.[1] Prolonged fatigue is a health problem that is associated with impaired functioning.[2,3] Fatigue complaints can be seen as a continuum, ranging from mild complaints of tiredness to severe disabling fatigue that is not task-specific nor easily reversible.[4] When fatigue is severe and prolonged, individual and social functioning are affected and as a consequence, so is the ability to participate at work. From previous research, we know that various factors are associated with the employment situation of workers with general health complaints and with fatigue-related conditions. Symptom severity[5,6], cognitive difficulties, behavioural factors[7], and work organisational factors[8] are reported as being associated with sick leave and/or work disability. In addition, perceived health complaints, limitations in daily physical activities, heavy manual work, and female gender were found to be prognostic factors for work disability in various chronic (somatic) diseases.[9]

Knowing that personal and environmental factors may obstruct work participation in individuals, treatments that focus on diminishing limitations and restrictions affecting work participation should be encouraged. Vocational rehabilitation (VR) treatments are used to facilitate return-to-work (RTW) and work retention, as well as to prevent future loss of work.[10,11] In addition, these strategies may be of importance because impaired work ability has a negative impact on people's quality of life[12] and has grave economic consequences.[13,14]

Due to diverse legislations, differences may occur in the organisation of VR between countries. In the Netherlands, employers have to continue paying the salary of their sick-listed employees during the first two years of sickness absence or (temporary) work disability. During these two years, both employer and worker must cooperate in the VR process of the sick-listed worker. As a consequence, Dutch outpatient VR treatments that focus on job retention are offered to impaired workers and to workers on sick leave.[15,16] Some of the VR treatments that use multi-component treatment for fatigued workers were evaluated and found to be effective in reducing fatigue symptoms, and improving activities, and work participation over time.[17]

As described above, risk factors for being off work have been studied, and treatments that focus on improving work participation of fatigued patients have been previously evaluated. However, perspectives of patients on work-related problems and RTW experiences have rarely been explored. Conducting research from the patient's point of view can provide a better understanding of the problems that patients actually face, how they perceive these problems and how the treatment that is offered is experienced.[18-20] Moreover, this knowledge has the potential to guide the development of VR that better meets patients' needs.

Therefore, we conducted a study in patients with prolonged fatigue complaints who were limited in their ability to perform their job (defined as fatigued workers) and who went on to attend an outpatient multi-component VR treatment. The aim of this study was to gain insight into the perspective of fatigued workers regarding work experiences before and after receiving VR treatment. This paper reports on 1) work-related limitations that fatigued workers experienced before receiving VR treatment, 2) VR strategies employed at work before receiving VR treatment, and 3) workers' VR treatment experiences of work participation.

Method

Participants

This qualitative study was nested within a longitudinal intervention study investigating the outcomes of VR treatments in fatigued workers, provided by three established outpatient institutions. Our target population consisted of fatigued workers who enrolled (by referral by occupational physicians or self-referred) in one of the outpatient institutions during the period 2006 – 2008. The outpatient institutions had specific inclusion criteria to select their clients before treatment, including: having complaints for more than three months, good command of spoken and written Dutch, being motivated to take part in the treatment and not suffering from a psychiatric disorder. The inclusion criteria to participate in the evaluation study were: aged between 18 to 60 years, fatigue complaints as a main or important symptom, and suffering from functional impairments (i.e. constraints in everyday life) due to fatigue complaints (self-reported). Patients were included in the study after an informed

consent procedure. This study was approved by the Medical Ethical Committee of the Academic Medical Center.

In total 110 patients enrolled in the intervention study. Ten dropped out because of financial problems (n=2), lack of time (n=1) or motivation (n=2), personal circumstances (n=2) or because of unknown reasons (n=3). The remaining 100 participants agreed to take part in an interview after receiving VR treatment, as part of the intervention study. For the purpose of this qualitative survey we used a sample of these interviews. A subsample was taken to achieve a sample of fatigued workers with a variety in five factors, reflecting fatigued workers participating in a VR treatment: gender, symptom severity, symptom duration, sickness leave (fully, partly, no sick leave) and outpatient institution where VR treatment was attended. A random sampling strategy was first used to select 30 out of 100 workers stratified per outpatient institution. If this strategy was not successful in obtaining diversity in the sample based on above described five factors, an extra purposive sample was conducted.

Vocational Rehabilitation (VR) treatments

All workers attended VR treatments, provided by three existing outpatient institutions in the Netherlands. From previous research we know that these three institutions are all using a biopsychosocial-based multi-component treatment.[17] The main aim of the VR treatments was to improve individual and occupational functioning in workers with prolonged fatigue complaints by achieving a normal balance between activity and rest, and subsequently between daily life and work. The VR treatments consisted of a combination of biological/physical components, psychological/cognitive behavioural components and social/work-directed components.

Biological/Physical component. Physical training included an individualized progressive personal workout scheme based on daily heart rate levels or graded exercise programme using time-contingent training. Physical training was guided by a movement specialist and/or physiotherapist and exercises were done on bicycle, treadmill, cross trainer and/or a power station. Physical training was aimed at improving physical fitness, and increasing activity levels and body awareness. Relaxation and breathing exercises were given, aimed to reduce stress and increase body awareness.

Psychological component. Group and individual sessions with a psychologist or personal/mental coach used cognitive-behavioural principles aimed at relieving distress and increasing illness knowledge, awareness of perceptions, attitudes, and beliefs. Moreover, improving coping strategies and changing dysfunctional behaviour were also goals.

Social/work-directed component. RTW sessions (individual or group sessions) with a psychologist or occupational expert addressed patient's attitude towards work, job conditions and work adaptations, and involvement of the social environment (partner). In addition, a patient-tailored phased-RTW plan was made, in which RTW was gradually increased (e.g. gradual increase in number of working hours, work task and work demands). These sessions were aimed to increasing awareness of behavioural patterns at work and in private lives, improving coping skills and facilitating work participation. The VR treatments took in total 4 to 18 weeks with a clinic visit frequency of 3 to 5 times a week in the first part of the treatment period (1/3), decreasing from 2 times in the second part to 1 time a week in the third part of the treatment period. For detailed information about the content of the VR treatments see Joosen et al.[17]

Study design and procedure

This qualitative survey was conducted six months after fatigued workers completed the VR treatment and included questions about the situation of the patient before the VR treatment and after the VR treatment. We used a semi-structured interview based on a topic list. The interview questions were based on earlier research on barriers for work participation in chronic diseases patients[21], pilot interviews, and the expertise of the research team. To enable readers to evaluate the possible effects that the researchers' backgrounds might have on their interpretation of the results, the following information is included. The research team had expertise in occupational medicine, psychology and physiotherapy in general, and in conducting qualitative research in work experiences within several chronic diseases (e.g. rheumatoid arthritis, repetitive strain injury, acute coronary syndrome). All of the researchers helped develop the schedule of questions used in the interviews. None of the researchers knew any of the participants before the start of the VR treatment.

The face-to-face interviews were conducted in a private room in the institution where workers attended the treatment and had an average of 23 minutes in duration.

All interviews were held by MJ (Woman, 27 years, physiotherapist and health scientist, and practiced in patient communication and qualitative research) between May 2007 and August 2008. The interviewer explained the purpose of the interview, that the interview was confidential and asked for permission to audiotape the interview. Personal demographics, symptom severity and duration, and the employment situation of the workers were obtained by questionnaires given before the start of the treatment and six months after its completion.

Interview

The topic list we used in the interviews started with an introduction phase. The interviewer and the worker reviewed the worker's situation regarding employment status from before the start of the treatment to date. Next, the interview contained questions about the worker's situation before receiving the VR treatment: (i) problems experienced with functioning at work and (ii) arrangements/strategies taken at the work site to improve work participation. Questions about the situation after VR treatment included (iii) the extent to which the treatment affected functioning in daily life and (iv) in current functioning at work. When collecting the qualitative data, the interviewer would ask the opening questions, listen to the response, and encourage the participants to elaborate their story through questions that emerged from this conversation. Typical questions were: 'How did this affect you?' or 'Would you tell me more about this experience?'. Then the interviewer attempt to summarize and check back with the worker to determine if their summary was correct. This way, the key information captured was checked and it gave workers time to reflect on their answers and correct themselves if they thought that something else had been important. This procedure supports validation of the data. The topics and questions are presented in Appendix I.

Analysis

All interviews were audio taped and were fully transcribed verbatim. We used MAXqda software 2007 (Udo Kuckartz, Berlin, Germany) for coding the transcripts. First, we developed a code structure based on the topic list as well as the research questions and used this as a framework. The topics within this framework were: 'work-related limitations', 'VR strategies employed at work', and 'VR treatment experiences on RTW'. One researcher (MJ) read and open-coded all transcripts; text

fragments were given a code representing this fragment and were assigned to one of the framework-topics. To improve the reliability of the analysis process, a second researcher (JS) read and open-coded three transcripts independently of the first researcher. One interview per institution was selected. The two researchers then compared their codes. At this meeting, different codes were discussed and refined until consensus was reached. Then similar codes were grouped together into an open-coding system. Next, MJ open-coded the remaining transcripts. Within the framework-topics codes were organised in broad domains. Within each domain, we looked for categories and sub-categories that were representative of that domain. This process was discussed in the research team and progressed until main domains and categories emerged. Coding the transcripts took place until saturation of the data was reached to answer the research questions.[22,23] Using this strategy, 21 interviews were analysed. Within this sample, diversity was reached in gender, symptom severity, symptom duration, sick leave, and outpatient institutions (see workers' characteristics below and in table 1).

Results

Workers' characteristics

A total of 21 interviews with fatigued workers, 11 women and 10 men, were analysed. Ages ranged from 34 to 57 years, with a mean age of 47 years. The three VR treatments were equally represented. Before the start of the treatments, the mean duration of fatigue complaints was 3.3 years (ranging from 2 months to 15 years), and 19 workers (90%) had severe fatigue complaints (indicated by a score >76 at the Checklist Individual Strength).[24] At the time of the interview, six months after completing the treatment, six workers (29%) still had severe fatigue complaints. Characteristics are further described in table 1.

Work-related limitations before VR treatment

In retrospect, fatigued workers experienced a large number of limitations for participating in their work situation before the start of the treatment. We organised these problems into six domains: 1) symptoms of prolonged fatigue, 2) personal

limitations, 3) interpersonal factors at work, 4) activities during work, 5) work conditions, and 6) life/work imbalance. These domains are further discussed below. Table 2 summarises the findings and provides illustrative quotes to support the domains on work-related limitations before VR treatment.

Table 1. Characteristics of the workers (n = 21)

Variable	**Value**
Male	11 (52%)
Female	10 (48%)
Age, years	
34-39	3 (14%)
40-49	9 (43%)
50-57	9 (43%)
Duration of fatigue complaints in years, mean ± SD	3.3 ± 4.6
Duration functional impairments in years, mean ± SD	2.5 ± 3.8
Type of work:	
Management	6 (29%)
Consulting	3 (14%)
Office and administrative	2 (10%)
Education	2 (10%)
Financial	2 (10%)
Health care	2 (10%)
Technical	2 (10%)
Aviation	1 (5%)
Other	1 (5%)

	Values before the start of the VR treatment	**Values six months after completion**
Severe fatigue (CIS score >76)[1]	19 (90%)	6 (29%)
Employment situation		
Paid job, fully at work[2]	2 (10%)	9 (43%)
Paid job, partly on sick leave[3]	8 (38%)	7 (33%)
Paid job, fully on sick leave[4]	11 (52%)	2 (10%)
No paid job[5]	0	3 (14%)

[1]CIS (Checklist Individual Strength) score above 76 was set as cut-off point for chronic fatigue and increased risk of sickness leave due to fatigue[24]; [2]workers with an employment contract and working 100% of the contracted working hours; [3]workers with an employment contract and working less than 100% of the contracted working hours; [4]workers with an employment contract and being absent from work for 100% of the contracted working hours; [5] people with no (longer an) employment contract

Table 2. Work-related limitations before VR treatment, presented in domains, categories and subcategories including representative quotes of individual workers per domain.

Domains	Categories (subcategories)	Illustrative quotes
Symptoms of prolonged fatigue	- Reduced concentration - Physical limitations - Lack of energy / being exhausted - Cognitive limitations (Incapacity to assess situations; Difficulties with processing information; Memory loss)	P02.02: As soon as I got tired, which happened quite soon during the day, I had difficulty concentrating and remembering things. In the worst case, I had problems with typewriting, like mistyping numbers. I couldn't think straight and was very slow in processing information. (female 34 yrs; VRI1) P02.09: During long flights, I got migraine headaches and felt nauseous. They came out of nowhere, getting worse slowly. Then it just takes a lot of energy to keep the rudder straight. (male 54 yrs; VRI1) P02.09:…and because of this [Fatigue] you can't set priorities properly. You can't respond adequately and fast enough to what is needed and that is very annoying. (male 54 yrs; VRI1)
Personal limitations	- Self-reflection (Difficulty defining own limits; Difficulty to set limits to current capacity; Not receptive for feedback) - Emotional problems (Fear of sickness absence; Not accepting having prolonged fatigue complaints and limitations; Lack of self-confidence/doubting own abilities; Lack of persuasiveness) - Attitude towards work organisation	P03.13:…good advice was given, but I was quite stubborn and I didn't want to see it [that I was doing badly]. Because you're afraid that if you give up, you failed. Or at least, that others might think so. (...) I just wanted too much, and I wasn't clear in indicating when I had no time and when I didn't feel like it. (...) I was working long days, and at some point you're in this situation that you completely forget yourself. (male 52 yrs; VRI2) P02.08: ...you need to adjust your life to your new situation and discuss this [process] each week or each month. But I just wanted to do something from which I hoped to get better and regain my health... (female 41 yrs; VRI1) P03.03: What was part of the problem as well, (...) was the way the job was changing. The reason why I once choose to do this work, the current policies and various measures from the government [changed]. My vision [on the job] was different than the organisation's vision. For years this has been the same, but it got more and more divergent. (female 41 yrs; VRI2)
Interpersonal factors at work	- Interpersonal relationships with co-workers (Not being able to function socially; React negatively on social environment / feeling irritated; Dealing with contradictive ideas about work ethic)	P03.06: Non-verbally, I expressed myself as: "stay out of this" (...). I've been keeping everyone and everything out; I stubbornly continued to do my work and, therefore achieved a negative effect. (...) [Coping with colleagues and supervisor] went bad. I wasn't open to reason. I constantly tried to defend myself because I was trying so hard. But that wasn't the problem; I just couldn't take it anymore. (female 42 yrs; VRI2)

Domains	Categories (subcategories)	Illustrative quotes
	- Interpersonal relationships with supervisor and occupational physician (Negative attitude of employer towards limitations of the worker; Employer perceives limitations but worker not)	P03.03: I mentioned [to my supervisor] that I didn't want to work there anymore. Because the vision they have and the way they want to organise it [the work] (…) I don't think that it will work with the colleagues in that team. (female 41 yrs; VRI2) P03.08: They [supervisors] were afraid I would collapse at some point. I had many headaches and physical complaints such as colds that stayed on. Normally you would recover within a few days, but they [the complaints] stayed on and they turned into chronic complaints. I wasn't on sick-leave, but they [supervisors] noticed my complaints at work. (...) At some point, they sent me home. In the first week nothing happened, I was just angry that I was sent home. Then, the second week, I collapsed completely, I couldn't even get off the couch. (female 43 yrs; VRI2)
Activities during work	- Limited work capacity - Diminishing output - Limitations in the process of work (Difficulty performing and structuring work tasks; Making mistakes at work; Inability to handle demanding situations appropriately)	P03.13: He [the supervisor] noted that the quality of my work declined because of the amount of work I wanted to do. I could no longer fulfil all these things. (...) I had unfinished work everywhere, but nothing was completed. I had answered all the questions, but not in the way I wanted to answer them. One moment, I had piles of work, and then, increasingly, the pressure rises. (female 41 yrs; VRI2) P04.18: I couldn't handle the class, that was the problem. I could not discuss this with my supervisors, nor with colleagues, and I was up to my ears in work. I mean, during the weekend I worked 12 hours on Saturday, 12 hours on Sunday and I couldn't manage it. So I needed help, my husband helped me; he took over parts of my work. Especially checking homework, filling in grade lists, because I made many mistakes doing that. [I spent] hours filling in grades and when I arrived at school on Monday, I discovered I forgot to click on save, and everyone said: "Well, you did not hand in the grades!". Then I thought, shit, I worked 12 hours yesterday. (female 52 yrs; VRI3) P02.09: I couldn't function properly in the cockpit, I felt like I experienced the outside world around me as through a haze. Often I couldn't respond adequately to things that were necessary or responded too slow. I knew this, I felt it, but I couldn't change it and that was very frustrating. (male 54 yrs; VRI1)
Work conditions	- Experiencing to much work stress/pressure - Problems with noise in work environment	P03.07: I was working on routine, but the organisational structure and work procedures changed and that was very difficult for me. As long as it remained the same, I would have been able to manage the work, but because of all the changes and stuff [I couldn't]...(male 56 yrs; VRI2)

Domains	Categories (subcategories)	Illustrative quotes
	- Problems with irregular working hours - Difficulty with commuting - Negative atmosphere at work	P02.06: everything just goes slower and you try to keep up. But you just feel like you are failing, it is like you're on a soapy slope trying to climb up. But you still try to do things; you try to do what you want to do because you are hired for that job after all. (female 54 yrs; VRI1) P03.11: My concentration is bad. My room is very busy, people talk a lot and the phone is ringing a lot. So it takes a lot of energy to ignore it and to focus on my own work. (female 38 yrs; VRI2) P03.03: For about 8 years I have done 24 hour shifts. That is, early or late shifts, sleeping or weekend shifts and during holidays. I had thought before "I don't want to do that anymore, I want [to work] from Monday to Friday". But in this work [it is not possible], and you still enjoy it… But I was struggling with this more and more. (female 41 yrs; VRI2) P04.15: ...people [at work] were complaining and were unsatisfied [with the situation at work]. This led to bad collegiality and created friction. (...) It [the team] was no longer a "well-oiled machine. (male 56 yrs; VRI3)
Life/work imbalance	- Problems with finding the balance between demands in work and private life	P03.13:...my children already moved out, but I couldn't give attention to... Some attention for this, and some for that. (...) but I couldn't give enough attention to work and not enough to my private life. I was trying to find the balance. (female 41 yrs; VRI2) P03.05: If everything is in balance: work, home and of course just taking care of yourself, keeping in shape and not neglecting your personal health, you are able to handle a lot at work. And you know it is not a problem. But the other two [factors: home and personal health] should stay in balance. There it went wrong and it made that I could no longer function at that high level. (male 43 yrs; VRI2) P03.03: I realised,… that it was a combination of private life, work, irregular working hours and the problems at home that I had to deal with at work, that was the problem. (...) This was the reason for me to call in sick…that a situation at work referred to my problems at home in a way that it made me unable to work anymore and unable to return. (female 41 yrs; VRI2)

Symptoms of prolonged fatigue

Almost all workers mentioned that mental and physical symptoms associated with the prolonged fatigue condition influenced their ability to work: being too tired to function at work and in private life, tasks took too much energy and/or more than normal, experiencing a lack of concentration, and having physical complaints, such as muscle and headaches. Cognitive difficulties, such as lacking the ability to assess situations properly and set priorities, and difficulties with processing information and with memory loss were also mentioned as limiting work ability.

Personal limitations

Three categories were found concerning personal problems: lack of self-reflection, emotional difficulties, and attitude towards work. With respect to self-reflection, workers mentioned having difficulties defining their own limits and setting limits to their current capacity. Because of their fatigue complaints, energy supplies had dropped and so did their general work capacity. It was hard for workers to adjust and take 'a step back'. Another barrier related to self-reflection was that workers noted that in retrospect, they were stubborn, did not want to show that they were not doing fine and were afraid to fall short. This attitude led to not being receptive to feedback from co-workers and/or supervisors.

Being afraid of having a relapse and doubting oneself and their one's own abilities were emotions which were mentioned as affecting work ability. Moreover, the feeling of being unable to persuade others and or to persuade oneself was mentioned. Furthermore, not accepting their condition, their limitations and the fact that they had to adjust their life to their disability were noted as barriers to functioning at work.

Additionally, workers stated that a negative attitude towards work was limiting their ability to participate. This attitude became negative with reorganisations in progress which workers found frustrating (to not have control), which they could not unite with or which gave them a feeling of distrust concerning their position in the organisation.

Interpersonal factors at work

Interpersonal barriers at work were mentioned, especially in relationships with co-workers. Workers had difficulties in performing social activities (e.g. socialise with co-workers), react negatively on their social environment and also feel irritated. In

addition, a few workers mentioned to have different ideas about work ethic and changes made in the organisation structure, this led to misunderstandings with co-workers.

Barriers to participation were also mentioned in the relationship with supervisors and occupational physicians. Some workers felt that their employer did not really listen to their complaints and their perceived limitations and they felt misunderstood. However, one worker noted that her supervisor was concerned about her health condition but she herself was not.

Activities during work

We organised problems concerning activities during work into limited work capacity, diminished output of work, and difficulties in processing work. In general, limited individual work capacity and not being able to handle the responsibility of the job were mentioned. Workers also noticed their work output or quality of work was reduced. With regard to processing work, workers had difficulties performing work tasks, their work pace slowed down, they lost control of work, and they had difficulties structuring work tasks. Workers made mistakes, were not responsive during work and could not appropriately handle critical situations. These limited and/or reduced activities at work were affecting participation and well-being at work. Often, workers mentioned they had multiple problems with performing activities.

Work conditions

Experiencing too much pressure at work (overload), a noisy work environment, irregular working hours, and commuting to and from work was mentioned a lot as demanding work conditions. Workers mentioned that in some cases they experienced pressure at work because of changes in organisation structure or work procedures, which they couldn't keep up with. As long as nothing changed, they would have been able to manage because of their experiences. Next, a negative atmosphere at work was also mentioned as being a problem for participation. This type of atmosphere led to poor work relationships, and workers felt inhibited to talk about their problems in these conditions.

Life/work imbalance

With respect to life and work, workers struggled to find a balance between demands at work and in their private life. When private life claimed attention from the worker, workers mentioned that it was difficult to concentrate and to keep functioning at the same level at work. Moreover, demands at work that referred directly to unresolved personal problems or problems at home made it difficult to participate at work and in one case was the direct reason to call in sick.

VR strategies employed at work before VR treatment

Various VR strategies were conducted at the work site before the workers started the outpatient vocational treatments. These strategies were employed by the worker's employer to prevent and/or reduce sickness absence and improve work participation. Domains concerning employed strategies were as follows: 1) work adaptations, 2) advice/communication, and 3) referral strategies. In addition, failed strategies were also mentioned. The strategies are discussed below and summarised in table 3, including illustrative quotes..

Work adaptations

Employers used various strategies to facilitate work participation by modifying job conditions; work tasks and work demands were reduced, work content was adjusted by switching jobs within the organisation and working hours were scheduled more flexibly according to current work capacity. Often these adaptations were made in accordance with the worker, however sometimes workers were complaining that individual preferences were not taken into account. Before the start of VR treatment some workers were fully or partly on sick leave. Employers tried to facilitate the RTW process by tailoring the number of work tasks and working hours a week.

Advice / communication

Workers received support from their co-workers by showing understanding for their situation and giving feedback about their work capacity and functioning. For some workers, the occupational physician and/or the supervisor gave supportive communication and advice (e.g. "when you feel very fatigued, first take rest and take

Table 3. Strategies employed at work before VR treatment, presented in domains, categories and subcategories including representative quotes of individual workers per domain.

Domains	Categories (subcategories)	Illustrative quotes
Work adaptations	- Adjust work tasks - Switch to another job within the organisation - Diminish pressure at work - More flexible working hours - Adjust number of working hours	P03.03:..then they offered me a different place to work, but that didn't fit my preferences. It was more like, this way you stay within the organisation and you keep working the same hours. But they didn't take into account what you had done previously, what you had achieved, what your preferences were and what matched to what was happening to me personally. They didn't take that into account. (female 41 yrs; VRI2) P02.02: For instance, changing the time I started the workday. There was a time, that I worked just as long as I could, as often as I could and was partially on sick leave. (female 34 yrs; VRI1) P03.11: I have worked less hours for a while. And sometimes I started an hour later, so that I had time to rest before I went to work in the morning. (female 38 yrs; VRI2) P04.33: ... When I was on sick leave full-time they said I should at least come over for coffee, just to be present [at the work site]. Later, I started to read my email and similar tasks, and, at some point, I worked 2 times 2 hours. (male 38 yrs; VRI3)
Advice / communication	- Support from co-workers and supervisor - Advice from supervisor and occupational physician (Advice to keep physically active; Advice to take rest; Supportive communication)	P04.39: Everyone was surprised that it [sick leave due to prolonged fatigue complaints] happened to me, it happens to the best, apparently. One colleague supported me a lot and often pointed out to me that I was overdoing it, exceeding my limits… (male 49 yrs; VRI3) P03.08: The occupational physician knew [about the fatigue complaints] and said: stay at home, stay at home, stay at home. But, I didn't want to. So I made a lot of effort… phoning people, putting things into action; to make sure that in some way or another I could return to work quickly (female 43 yrs; VRI2) P03.07: During the conversations I had with my supervisor every 14 days, it [fatigue complaints] was a topic of conversation [...] He gave advice too, but I think I was a bit stubborn, in a way that I simply didn't see the point in the suggestions he made. (...) At that time he did try to stimulate me, he was good at that. Until I jut couldn't manage anymore. (male 56 yrs; VRI2)
Referral…	- to (company) physiotherapy - to a social worker - to a career counselling	P04.33: The occupational physician referred me to social work. (...) I went there once, but I didn't think it suited me. The advice he gave me… I already did those things; it [guidance] didn't work out. Then, I was sent to a company physiotherapist for relaxation exercises mainly because I was tight with tension.

Domains	Categories (subcategories)	Illustrative quotes
	- to a mental coach	At that time I didn't really work. (male 38 yrs; VRI3) P03.03: [The occupational physician] told me to go to the LAK, that's the career advice centre within our organisation, to see if you can work somewhere else. That is how I ended up at that last working place, but it was counterproductive. (female 41 yrs; VRI2)
Failed strategies	- Measures tried to take, but did not manage to - Inadequate / insufficient action	P04.32: I tried to give the workmen [other co-workers] more responsibilities, but that was very difficult because one didn't want to and the other couldn't. (male 49 yrs; VRI3) P03.06: I almost went on sick leave before and had previously said, 'this is not working anymore', that I didn't like it anymore and I couldn't handle it. (…) Then they [supervisors] said they were going to take some work off me and they did. But at the same time, 4 or 5 [projects] came in. They hadn't noticed how deep I was in. (female 42 yrs; VRI2) P04.15: [Work adjustments] couldn't be achieved. If they [supervisors] had just listened to me, when for example I said I don't agree with this and they had given in... But, you simply weren't heard, yes, they were listening superficially but they didn't do anything. (male 56 yrs; VRI3)

off from work to recuperate"). Although, this were not always leading to positive results, as some workers mentioned to be stubborn in taken advice.

Several workers mentioned that they communicated with their supervisor about their impairments and limitations and/or had monthly evaluations regarding the RTW process. In addition, in some cases strategies for coping with specific problems faced at work were discussed with the supervisor.

Referral

Next to conducting VR strategies at the work place, employers also used external services to facilitate work participation. A few workers were referred to individual (company) physiotherapy care, social work, mental coaching and/or career counselling. Although these services were sometimes perceived as helpful, none was effective to improve work ability sufficiently.

Failed strategies

A few workers noted that either they or their employer tried to make VR arrangements but failed because it was not possible to find a suitable replacement to take over tasks, it was impractical to reduce responsibilities or it did not manage to delegate tasks. Also, workers mentioned that supervisors weren't really listening to their complaints and limitations or that they were listening but did not take action. Some workers mentioned that no other strategies but the VR treatments were employed.

VR treatment experiences on RTW

Workers' VR treatment experiences regarding RTW and work participation concerned three domains: personal challenges (i.e. improved awareness, coping skills and confidence), improved activities during work and work adaptations. The domains are discussed below and summarised in table 4, including illustrative quotes.

Personal challenges

Improved personal factors, especially awareness, were mentioned by almost all workers. During the treatment, workers learned meta-cognitive skills about their functioning in private and working life. Workers mentioned being more aware of

themselves and their wishes, thoughts and attitudes towards work. This awareness helped them gain insight into their own capacity and pitfalls.

Being aware of their personal identity and knowing their abilities and limitations was important before learning how to deal with these personal characteristics. Workers mentioned that learning coping skills helped them to participate at work. In general, workers mentioned learning how to deal with their limitations and how to protect themselves from exceeding their capacity (i.e. learning to set boundaries and how to "say no"). Workers also learned tools to cope with their condition at work (e.g. using relaxation techniques or taking breaks) and/or with specific limitations at work (e.g. learned to use a more efficient work strategy). In addition, workers mentioned that their self-confidence increased and/or that the treatment helped to reduce concerns about their physical complaints.

Improved activities during work

Workers mentioned that by attending VR treatment their mental and physical functioning improved. They were feeling stronger physically (e.g. using the stairs more easily) and mentally (e.g. emotionally more capable to work). Workers also mentioned that physical activity during the treatment regained their energy level and improved their ability to concentrate as well as think clearly.

With regard to RTW strategies, some workers who were on sick leave used a plan to gradually RTW. These plans were patient-tailored and discussed together with the worker, their supervisor and a treatment caregiver. Work tasks, work demands, and working hours were customised and were intended to gradually increase during the RTW phase.

Some workers were able to work at their former capacity and/or perform even better due to the coping strategies learned (e.g. 'I work better because I take more time and space for doing my job properly').

Work adaptations

Workers mentioned that they were able to participate better at work because of changes made in the work setting. These modifications were influenced, directly or indirectly, by the treatment and included arranging to work fewer contractual hours, reducing workload due to extra manpower or deciding to quit the current job to make a career turn .

Table 4. Workers' RTW experiences regarding the attended VR treatment in relation to work participation, presented in domains, categories and subcategories including representative quotes of individual workers per domain.

Domains	Categories (subcategories)	Illustrative quotes
Personal challenges	- Awareness (Being more aware of oneself; Exploring wishes and thoughts/cognitions towards work; Knowing their own capacities and limitations) - Coping (Coping with limitations; Learning to protect oneself; Learning tools to cope with (fatigue) symptoms/ disease; Learning a different work strategy) - Confidence (Gaining self-confidence)	P04.39: …not by the theory that was educated, but particularly by the group discussions, I realised that I it was foolish the way I was working. It just was mad what I did, and unnecessary as well. During my [VR treatment] I started to work again and I tried to apply what I had learned. (male 49 yrs; VRI3) P03.13: …pitfalls will always remain. I did learn that, when I really don't want to do something, I don't. And when I think: 'this becomes too much', I take an afternoon off. I just go away. And that's not running away [from the problem]. It's reading a nice book at home, 'building up reserves', dealing with it my way ... (female 41 yrs; VRI2) P04.14: Body and mind both didn't work properly. Then you start to doubt yourself a lot and this program has really helped, in that you can do things without getting tired. And that gave me back a little confidence, like "I can still do more than I expected". When I left [VR treatment] after three weeks, I continued going to the gym, to work on my physical fitness and being active. Before I would have never started that. (male 46 yrs; VRI3)
Improved activities during work	- Mental functioning (Mentally stronger) - Physical functioning (Physically stronger; More energy) - Work functioning (RTW strategies; Working at former capacity)	P03.06: Here [VR treatment] they first made sure that you improved physically, so you felt fitter, so you can think more clearly. Secondly, by the total programme, they made you aware of the problems you are facing, what your weaknesses are and how to tackle them differently? And that really made me think. The fact that the physical training is there, ensures that you get stronger and become more able to think. (female 42 yrs; VRI2) P04.39: I found it very disappointing that I was not allowed to return to 40 hours immediately, because I felt quite capable to work 40 hours. But at the same time that was my pitfall. (…) I went back to my normal work again, and I felt capable of doing it, I dared to take responsibility, felt energetic and was able to work throughout the day. (male 49 yrs; VRI3) P04.39: I think I am on my original level, with everything I have learned, at least in terms of work I am back at the level before my depression two years ago. Including things just going well automatically. (male 49 yrs; VRI3)

Domains	Categories (subcategories)	Illustrative quotes
Work adaptations	- VR strategies at work employed	P04.32: First, tasks were reduced to make it easier to come back. Then a new colleague started, so parts of the tasks were divided. Hereby, the workload was clearly less. (male 49 yrs; VRI3) P04.33: I am just doing the same work, only less hours. (...) I have applied for a WIA [disability pension], because I worked 28 hours before and we decided that the goal was to go back to 20 hours. But, I had the feeling that between 16 and 20 hours would be reasonable and we have now reached 16 hours. (male 38 yrs; VRI3)
Unresolved problems	- No full-time return to work achieved - Fatigue symptoms remain - Not accepting limitations - Difficulty to coping with limitations	P04.32: ...this [VR treatment] opens your eyes to who you really are. You will recognize your pitfalls and know how to handle them. (...) But it doesn't always work out [to cope with pitfalls]. I sometimes get kicked back. (male 49 yrs; VRI3) P02.08: [The program hasn't helped] in that I have returned to work, because I didn't improve that must yet. I had really hoped I would have, and I had expected it. You think you will start and after 18 weeks I'll be up and running again and be able to do anything. Well, that was disappointing. (female 41 yrs; VRI1) P02.02: My body is stronger, so that's handy when you have to walk the stairs. But in terms of concentration and getting tired of conversations or just noise around me or whatever, no that hasn't improved. (female 34 yrs; VRI1)

Unresolved problems

Some workers mentioned that they had not yet achieved full-time RTW and/or were still suffering from fatigue complaints and limitations in daily life and work. Furthermore, workers stated that it was sometimes hard to cope with their limitations despite learned coping skills. One worker said she had not accepted her condition and remained suffering from limitations.

Discussion

First, this study highlights perceived limitations to participate at work in fatigued workers. In general, fatigue symptoms and personal limitations, such as lack of self-reflection on individual capacity, were perceived as limiting work ability. Work issues concerning difficulties with interpersonal relations, performing activities during work, demanding work conditions and work/life imbalance were problems that affected participation. Second, by conducting this study, insight into the VR strategies that were conducted at the work site by the employer to prevent further sick leave and/or facilitate RTW was gained. Overall, several work adaptations were made. On personal level, co-workers and supervisors showed support, and psychological or physical care was given. Lastly, this study reports on workers' experiences of attending an outpatient multi-component VR treatment on work participation. Afterwards, fatigued workers had positive experiences towards work including personal challenges (i.e. increased awareness, coping skills and confidence), improved activities during work and several work adaptations. However, in some workers, satisfactorily recovery was not achieved.

Our results are partly in line with previous research concerning risk factors for work loss or work disability. These studies confirm that lack of support from co-workers or supervisors[21], demanding working conditions, problems with social relations[25], and work-family conflicts[26,27] limits workability in fatigue-related conditions. Interestingly, our findings emphasise personal factors that also limit workability. Although personal characteristics such as lack of self-acceptance, self-efficacy[21], cognitions and behavioural factors are known to be related to fatigue complaints[7], according to our results, lack of self-reflection and lack of awareness of

reduced capacity were mentioned to limit workability. Workers mentioned that in the period before receiving VR treatment, they were not aware of their own capacity and limitations. Moreover, they were stubborn and not receptive to any advice or feedback on their ability to function. In other words, workers were not aware of their behaviour and their abilities and could not correctly interpret advice that was given.

In this view, it is not surprising that the numerous VR strategies employed in the work situation before receiving the VR treatment were not as effective at achieving satisfactory recovery and work participation. This was especially true because these strategies mainly consisted of work adaptations and support and advice from co-workers and supervisors, to which workers were not open at that time. Finally, in all workers, the decision was made to start an external multi-component VR treatment. These treatments all included physical, psychological (e.g. cognitive behavioural therapy) and work-directed components using a biopsychosocial approach in guiding their patients[17] We found that workers gained awareness of their personal identities, capacities and limitations during the treatment. Additionally, workers learned to reflect on their cognitions, emotions (illness perceptions) and their behaviour, and learned to cope with their limitations and to protect themselves from exceeding their personal capacities. Workers expressed that learning about these perceptions and behaviours affected their work participation positively. Next, we found that functioning at work was improved by means of formulating a phased-RTW plan. This plan, initiated by the VR treatment, was made in accordance with the worker, employer and care givers of the treatment and was tailored to the worker's work capacity.

We found that the vocational strategies made at the work site before the treatments were almost identical to the aspects addressed in the VR treatments; both addressed work adaptations and advising workers about dealing with functional problems. However, during the VR treatments, prominent attention was given to personal factors that hindered the ability to change workers' behaviours. In addition, these perpetuating personal factors were treated, leading to recovery. Workers see additional value for the process of their recovery and RTW in learning to recognise their own behaviour patterns at work and in their private lives, and, subsequently, in training to cope with their limitations and capacities. We think that the outpatient setting of the VR institutions is of importance for this process. By taking the worker out of the work site, perpetuating personal factors can be examined and interfered with thoroughly, without being distorted by relations at work. However, it is of

importance to also involve the workplace and provide an active role for the employer in the rehabilitation process because we know that this can facilitate RTW.[10,28,29]

Not all workers had positive experiences, and unsolved limitations were also mentioned. These remaining problems concerned fatigue symptoms, difficulties coping with limitations and not yet being able to work full-time. Huibers and colleagues[7] found that recovery from prolonged fatigue and resuming work entangles different underlying processes and that improved health perception and RTW do not necessarily coincide. This observation is in line with our findings because workers with a wide variety of fatigue severities, duration of fatigue complaints, functional impairments and employment status were included. Consequently, individual differences in duration of the recovery process are to be expected.

The work-related problems experienced by fatigued workers and their experiences after receiving VR treatments, revealed by this current study, have important implications for professionals for the design of treatments for fatigued workers. Professionals need to consider perpetuating personal limitations which could hinder recovery. Strategies to deal with these problems seem important for treatment, in combination with conducting VR strategies at the work site (e.g. using gradual RTW plans and involving the employer in the RTW process). For employers it might be difficult to recognise and cope with the complexity of fatigue conditions and impaired personal factors of their employees. Cooperation with health care providers and combining forces to employ patient-tailored VR strategies at the work site are recommended.

The first two questions of the current study regarding experiences before receiving VR treatment were explored retrospectively. The interviews took place six months after the treatment was followed. Therefore, recall loss has the potential to be an issue. However, workers had experienced fatigue complaints and functional impairments for many years; thus, their condition was not a fleeting phenomenon. In addition, research has demonstrated that people are able to remember with good accuracy events related to their ability to perform tasks and actions for as long as ten years following complaints.[30] For some workers, details were sometimes difficult to recall (e.g. exact dates). However, the majority of the workers could, during the interview, recall detailed memories of the events and feelings before the treatment. Therefore, it would appear that loss of recall was not highly prevalent. Nonetheless, recall bias may remain a threat since participants' memories may change or distort

over time. On the contrary, by using this method, we were able to highlight 'new' insight into problems faced by fatigued workers. It takes reflectivity to recognise your own problems and interpret what exactly it was/is that limits you. By the richness of the results of this study, we know that workers had this reflectivity at the time of the interview, but might not have had in the period before the treatment when suffering from prolonged fatigue complaints. So, the workers in this study all participated in a VR treatment and were motivated to change their health and work situation, as being motivated was an inclusion criteria set by the individual VR treatments. This issue should be taken into account when interpreting and trying to generalize the findings. This is one qualitative study in an area that is currently not well-investigated. Findings only reflect what is considered important by this specific group of participants. That is, workers with prolonged fatigue complaints with functional impairments, who participated in a VR treatment. Besides, motivation may have influenced the findings in this study since it is plausible that motivated workers have different views on return to work than non-motivated workers. However, as we included only workers who were 'normally' enrolled in the VR treatment, our sample seems to reflect a considerable patient group in real life practice.

In conclusion, whilst aggravating working conditions, difficulties with activities during work, and interpersonal relations, all have roles in limiting work ability; the current findings suggest that lack of self-reflection on individual capacities and limitations also greatly affects work ability in fatigued workers. Vocational treatments that encouraged participant reflection on personal characteristics and life- and work style, learning coping strategies, and phased RTW positively affected work participation. These findings stress the importance of involving personal factors in the process of recovery and RTW beyond modifying the worksite. These results are useful for employers and professionals working in the occupational health field in the development of VR strategies that better meet patients' needs. To apply these results in other populations, researchers should reproduce this study in different settings, for example in other countries with different social systems.

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Appendix I

Topics and interview questions in a semi-structured interview

Employment situation and timetable from start of VR treatment to date

1. starting date of the VR treatment
2. employment situation before the start of VR treatment
3. occupation before the VR treatment
4. time schedule from the start of VR treatment to date

Work-related problems faced before VR treatment

Which problems did you experience that prevented you from participating in your work environment?

- What was it about this barrier that was a problem at work?
- How did it affect your work?

Strategies employed to improve work participation (before VR treatment)

Were there any strategies taken to improve functioning at work?

- What were these strategies?
- How did you experience these strategies?

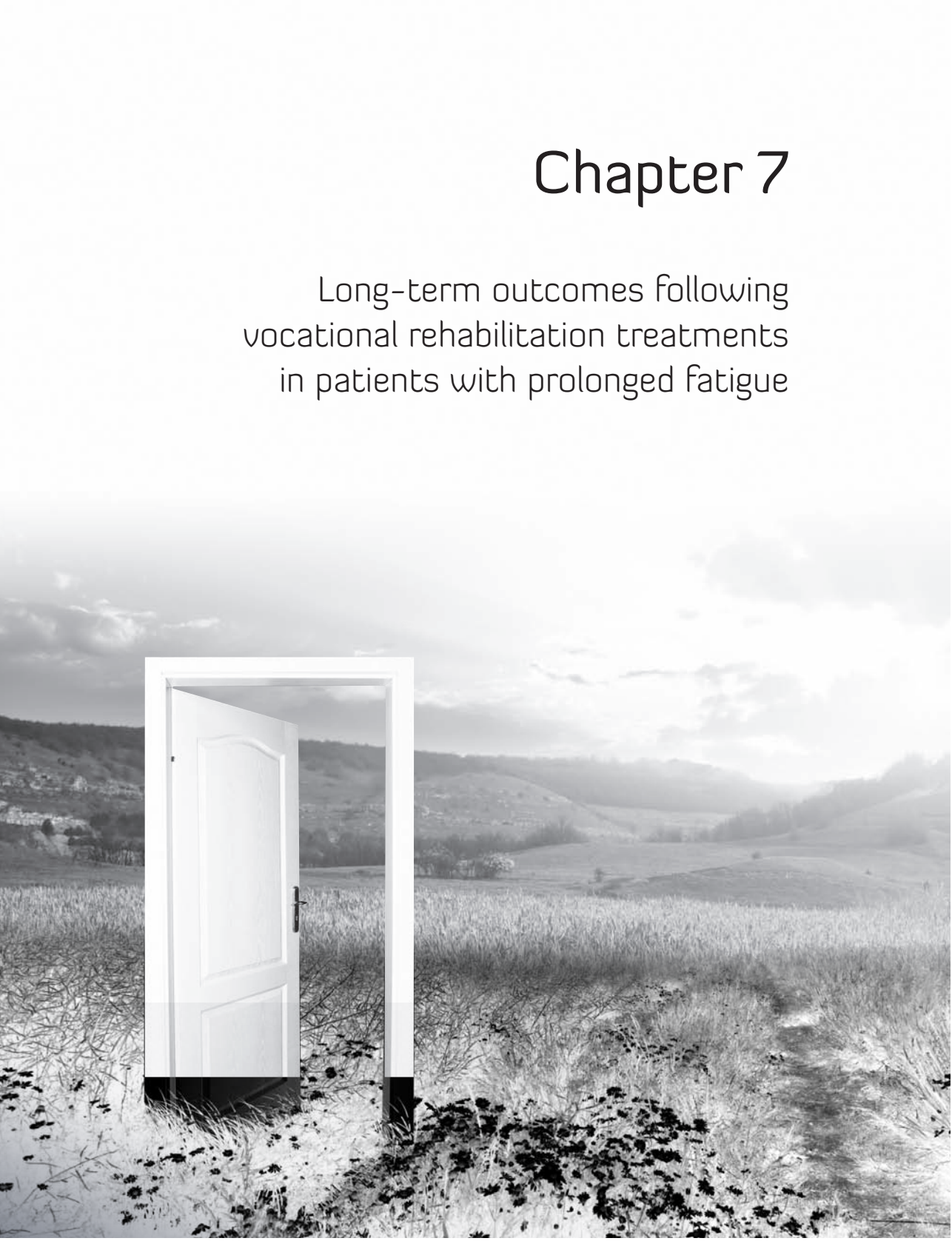
VR treatment experiences

Did attending the VR treatment affect your ability to function?

- How did attending the VR treatment affect your ability to function at work?

Chapter 7

Long-term outcomes following vocational rehabilitation treatments in patients with prolonged fatigue



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Submitted

Abstract

Purpose: Prolonged fatigue is a complex condition that can cause individual and occupational disabilities. Multi-component vocational rehabilitation (VR) treatments in patients with prolonged fatigue complaints were evaluated for up to 18 months.

Methods*:* Measurements were taken before treatment (t0), after treatment (t1) and in long-term follow-ups at six (t2), twelve (t3) and eighteen months (t4) after treatment. Primary outcomes (fatigue, work participation and work ability) and secondary outcomes (physical and social functioning, mental health and heart rate variability (HRV)) were assessed over time using linear mixed models analyses. Post-hoc, long-term outcomes were compared with t0 and t1.

Results: Sixty patients with severe fatigue complaints participated. The primary outcomes significantly ($p<.001$) improved at follow-ups compared with t0 and showed no relapse compared with t1. Moreover, fatigue decreased ($p<.002$) whereas work ability ($p<.001$) and work participation ($p<.001$) increased further after treatment (t1). The secondary outcomes, physical functioning, mental health, social functioning, and HRV, improved significantly ($p<.001$, $p<.001$, $p<.001$ and $p=.049$ respectively) over the long-term compared with t0. At six-month follow-up (t2), mental health ($p<.003$) and social functioning ($p=.003$) further increased after the treatment was stopped.

Conclusions: Multi-component VR treatments seem to significantly and in a clinically way decrease fatigue symptoms and improve individual functioning and work participation in patients with severe prolonged fatigue over the long-term and without showing relapse.

Introduction

Prolonged fatigue is highly prevalent in the general population[1,2] and is also a prominent symptom in chronic diseases such as rheumatoid arthritis[3], cancer[4] and depressive disorders.[5] In addition, fatigue can be a discrete disorder (i.e., chronic fatigue syndrome (CFS))[6] or occur independent of a specific chronic disease or disorder (i.e., common health problem).[7] In all cases, in addition to individual suffering, prolonged fatigue can affect social and occupational functioning that may result in negative consequences concerning work capacity. Sickness absence due to prolonged fatigue may result in poor quality of life[8] and serious economic consequences.[9] If effective treatments in disabled workers with prolonged fatigue were available, work participation and health could be improved.

Because of its multi-factorial origin, the biopsychosocial model[10], which states that sickness and health result from a complex interaction between biological, psychological and social factors, seems appropriate to explain prolonged fatigue.[11,12] In line with this model, mechanisms responsible for the perpetual nature of prolonged fatigue have been investigated. From a biological perspective, prolonged fatigue is related to dysregulation of physiological stress systems due to overuse of these systems.[11,13,14] In addition, cognitive and behavioural factors (e.g., causal attribution, low self-efficacy, dysfunctional beliefs about activity and fatigue) are also involved in the perpetuation of fatigue complaints.[15-17] Furthermore, lack of social support can be a perpetuating factor in fatigued patients.[18] To stimulate effective recovery in fatigued patients, treatments should take individual perpetuating factors into account.[19,20] In the Netherlands, outpatient Vocational Rehabilitation (VR) institutions guide workers with prolonged fatigue and functional limitations. These institutions use multi-component treatments to increase physical and mental functioning and facilitate work participation. These real-life practices were evaluated before, using process and outcome measures in a population of disabled fatigued patients recruited from the practice setting.[21] This kind of research can be identified as practice-based research, and is suitable for evaluating multi-component treatments in real-life settings in an everyday patient population.[22,23] In addition, these multi-component treatments showed significant and clinically relevant outcomes in symptomatic and functional improvements and work participation up to three months after treatment.[21] However, it is unclear whether these positive short-term outcomes will be sustained over time.

Long-term outcomes of treatments are of special interest because of the long-lasting character of fatigue complaints; the perpetuating factors often lead to long-lasting and deeply ingrained patterns.[12] Moreover, multi-component interventions that target behavioural change (e.g., by intervening with perpetuating factors such as dysfunctional beliefs and coping strategies in work and private life) may have the potential to be effective in the long-term (one year after discharge of treatment).[24] Therefore, we evaluated the long-term outcomes of VR treatments in the Netherlands in patients with prolonged fatigue complaints and participation problems. The purpose of this study is to answer the following question: In patients with prolonged fatigue, what are the outcomes up to 18 months after VR treatment on fatigue symptoms, work participation, work ability, daily functioning and a physiological parameter (heart rate variability)?

Method

Patients

Our target population consisted of patients who enrolled in one of the participating outpatient institutions for VR treatments from 2006 – 2008. The outpatient institutions used specific inclusion criteria to select clients before treatment, including the following: good command of spoken and written Dutch, motivation to take part in the treatment, complaints for (in general) more than three months and no diagnosis of a psychiatric disorder. The inclusion criteria to participate in this study were as follows: aged between 18 to 60 years, fatigue complaints as a main or important symptom and suffering from functional impairments (i.e., constraints in everyday life) due to fatigue complaints. Eligible patients were approached and informed about the study before they provided written consent. This study was approved by the Medical Ethical Committee of the Academic Medical Center.

Design

In this practice-based research, we evaluated VR treatments in their natural setting[22,23] and used the TREND (Transparent Reporting of Evaluations with Non-randomised Designs) statement[25] in designing and reporting this study. We used a pre-post design

with repeated measurements at baseline (t0), upon completion of the treatment (t1) and three months (t'), six months (t2), twelve months (t3) and eighteen (t4) months follow-up (Figure 1). The study participants were recruited in two phases. First, patients were asked to participate in the study until six months after treatment. After six months, we asked if patients would participate in the second phase of the study until eighteen months after treatment. In the current study, we focused on the long-term outcomes (6, 12 and 18 months after treatment) and report outcomes at these follow-up measurement compared to t0 and t1. The short-term outcomes of the VR treatments (t1 and t' versus t0) are described in a previous publication.[21]

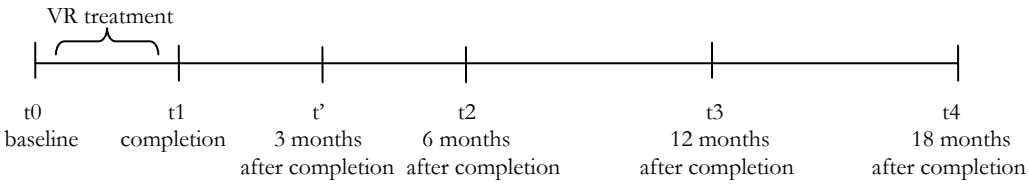


Figure 1.

Vocational Rehabilitation (VR) treatments

The VR treatments were provided by three practiced outpatient institutions in the Netherlands. These institutions are focused on patients with fatigue complaints who were on sick leave and/or had limitations in work function. Usually patients were referred by occupational physicians or self-referred (e.g., advised to visit the institution by people in their social environment and/or other caregivers). The main aim of the VR treatments was to improve individual and occupational functioning in patients with prolonged fatigue complaints by achieving a normal balance between activity and rest, and subsequently between daily life and work. From previous research, we know that these three institutions use a biopsychosocial-based multi-component treatment.[21] That is, these treatments consisted of biological/physical components, psychological/cognitive behavioural components and social/work-directed components.

Biological/Physical component. Physical training included an individualised progressive personal workout scheme based on daily heart rate levels or a graded exercise programme using time-contingent training. Physical training was guided by a movement specialist and/or physiotherapist and exercises were done on a bicycle, treadmill, cross trainer and/or power station. Physical training was aimed at improving physical fitness, increasing activity levels and body awareness. Relaxation and breathing exercises were provided in an attempt to reduce stress and increase body awareness.

Psychological component. Group and individual sessions with a psychologist or personal/mental coach used cognitive-behavioural principles aimed at relieving distress, increasing illness knowledge, and raising awareness of perceptions, attitudes, and beliefs. Improving coping strategies and changing dysfunctional behaviour were goals as well.

Social/Work-Directed component. Return-to-work (RTW) sessions (individual or group sessions) with a psychologist or occupational expert addressed patients' attitudes towards work, job conditions and work adaptations, and social environment (partner). In addition, a patient-tailored phased RTW plan was made, in which RTW (e.g., number of working hours, work task and work demands) was gradually increased. These sessions were intended to increase awareness of behavioural patterns at work and in private life, improve coping skills and facilitate work participation. The VR treatments took in total 4 to 18 weeks with a visit frequency of 3 to 5 times per week in the first part of the treatment period (1/3) and decreased from 2 times in the second part to 1 time per week in the third part of the treatment period. For detailed information about the content of the VR treatments, see Joosen et al. 2010.[21]

The specific content of the VR treatment (e.g., number of sessions, topics focussed upon, duration of the treatment) can differ somewhat between patients in this study because the treatment is provided by three different institutions. Indeed, the three institutions pursue the same goal in a population of disabled fatigued patients using the same approach but with a focus on the content that is tailored to meet individual needs.[21] According to practice-based research methodology[22,23,26], we aimed at evaluating real-world practice. Therefore we decided to combine the three treatments and report on the long-term outcomes of the total group of patients.

Primary outcome measures

Primary outcome measures were degree of fatigue, work participation, and work ability. To assess fatigue, three questionnaires were used. First, fatigue complaints were measured using the Checklist Individual Strength (CIS)[27], which consists of 20 statements. The CIS has been validated in the Dutch working population.[28] Second, we used the Vitality subscale of the Dutch version of the RAND-36 Health survey[29], which is almost identical to the MOS SF-36[30] and is a reliable and validated generic instrument.[29] Third, work-related fatigue was measured with the Need for Recovery After Work scale[31], with 11 yes/no items. The Need for Recovery scale was found reliable and valid in a working population.[32,33]

Data on work participation were collected by researcher-formulated questions at different measurement times. Data consisted of the following: 1) current work status, in terms of employed or unemployed; 2) number of contractual working hours; and 3) absolute number of hours the patient was working at that moment. With these data we determined the following: 1) percentage of return-to-original-work, defined as the mean percentage of return working to the original contracted working hours at t0, and 2) percentage of return-to-work, defined as the mean percentage of return working to the contracted working hours at the measurement time.[34] In this latter variable, changes in contracted working hours during the study period were taken in account.

Self-reported work ability was assessed using two items from the Work Ability Index (WAI)[35]: 1) currently perceived work ability compared with lifetime best, scoring between 0 ('not being able to work') and 10 ('lifetime best work ability'); and 2) personal prognosis of work ability in the next two years, scored on a three-point scale ('hardly able to work', 'not sure', and 'fairly sure to be able to work').

Secondary outcome measures

The secondary outcome measures included physical functioning, mental health, social functioning and heart rate variability (HRV). Subscales of the RAND-36 Health survey[29] were used to measure physical functioning and physical role limitation, mental health and emotional role limitation, and social functioning.

HRV was used as a physiological indicator that reflects sympathetic and parasympathetic activity of the autonomic nervous system. Prolonged exposure to stress can lead to dysregulation of this system (i.e., lower parasympathetic activity)[14,36] and can be identified by decreased HRV.[37,38] HRV was recorded using the Co2ntrol

(Decon Medical Systems, Weesp, the Netherlands), a small device attached to a chest strap that detects beat-to-beat intervals.[39] Due to practical constraints, HRV was only measured at t0, t1 and t2 during a standardised test protocol: five minutes seated in a resting position for adaptation, followed by 12 minutes light exercise on a bicycle ergometer using a single load of 50 W with a pedal frequency between 60 and 65 min^{-1}. The Co2ntrol was developed according to the guidelines of the European and North American Task Force (1996).[40] It was found to provide reproducible HRV measurements in healthy individuals[41] and in patients with prolonged fatigue.[42]

In addition, personal demographics, duration of fatigue symptoms and duration of functional impairments were obtained by questionnaires before treatment (patient characteristics at baseline). Furthermore, additional treatments and sick leave duration were recorded at two points in time (t3 and t4). At follow-up, patients were asked to report which health care providers they had visited concerning fatigue complaints during the last six months to monitor additional treatments. Next, sick leave duration during the last six months was recorded.

Data reduction

Data from the questionnaires were reduced and/or transformed into total scores. In CIS data, we added the item scores to a total score ranging from 20 to 140. Higher scores indicated a higher severity of fatigue. Item scores from the Need for Recovery scale were added and transformed[29] into a scale ranging from 0 to 100. Higher scores indicated a higher degree of need for recovery after work. SF-36 scores were added separate per scale and transformed[29] into a score ranging from 0 to 100; higher scores represent better outcomes.

To define HRV, raw data were transferred to HRV Analysis Software version 2.0 (http://venda.uku.fi/research/biosignal) and data artefacts were detected and processed by the software. The data were de-trended using the smoothn prior option. To determine the spectrum of HRV, the Fast Fourier Transform (FFT) option was used and data were re-sampled at a rate of 4 Hz using cubic interpolation. The final nine minutes of the twelve minute recording period during light exercise were selected. HRV was measured by means of heart period High Frequency (HF) power. HF power values were used to estimate Respiratory Sinus Arrhythmia (RSA), the variability of heart period in the respiratory frequency band. RSA is considered a valid index of changes in cardiac vagal tone, which interacts with parasympathetic

activity.[38,43] In this study, HF power was computed in the 0.15-0.5 Hz respiration window. The VR treatments were expected to have beneficial effects on physiological status (i.e., raise HF power after completion of the interventions).

Statistical analysis

Our target sample size was 110 patients from the first phase of the evaluation study.[21] Because we knew that part of this sample dropped out of the study after the first phase, we performed a non-response analysis to check for possible bias. Differences in baseline characteristics and primary short-term outcomes (i.e., degree of fatigue and return-to-work) were tested with t-tests for continuous variables and chi-tests for categorical variables.

To analyse the long-term outcomes of the variables over time up to 18 months, we performed linear mixed-model analyses based on repeated measures. The best fitting covariance–variance model was tested before the analysis was applied. If a statistically significant overall effect was found, post-hoc tests using Bonferroni correction (taking into account the multiple comparisons) were performed to compare outcomes between follow-up measurements and t0 and t1. To assess the changes in HRV between t0 and t1 and between t0 and t2, non-parametric Wilcoxon signed-rank tests were carried out. Statistical analyses were performed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Values of $p<.05$ were considered statistically significant. Post-hoc values in primary and secondary outcome measures were considered significant at $p<.0083$ due to Bonferroni corrections (p-value divided by the number of comparisons, i.e., six).

Results

Patient characteristics

A total of 110 patients, 50 men and 60 women, enrolled in this study and 60 patients completed the 18-month follow-up measurement (Fig. 2). Reasons for failure to follow up are presented in Figure 2. Only "completers", 60 patients (28 men and 32 women) who completed the 18-month follow-up measurement, were included in the analysis. Patients had, on average, severe disabling fatigue complaints for many years

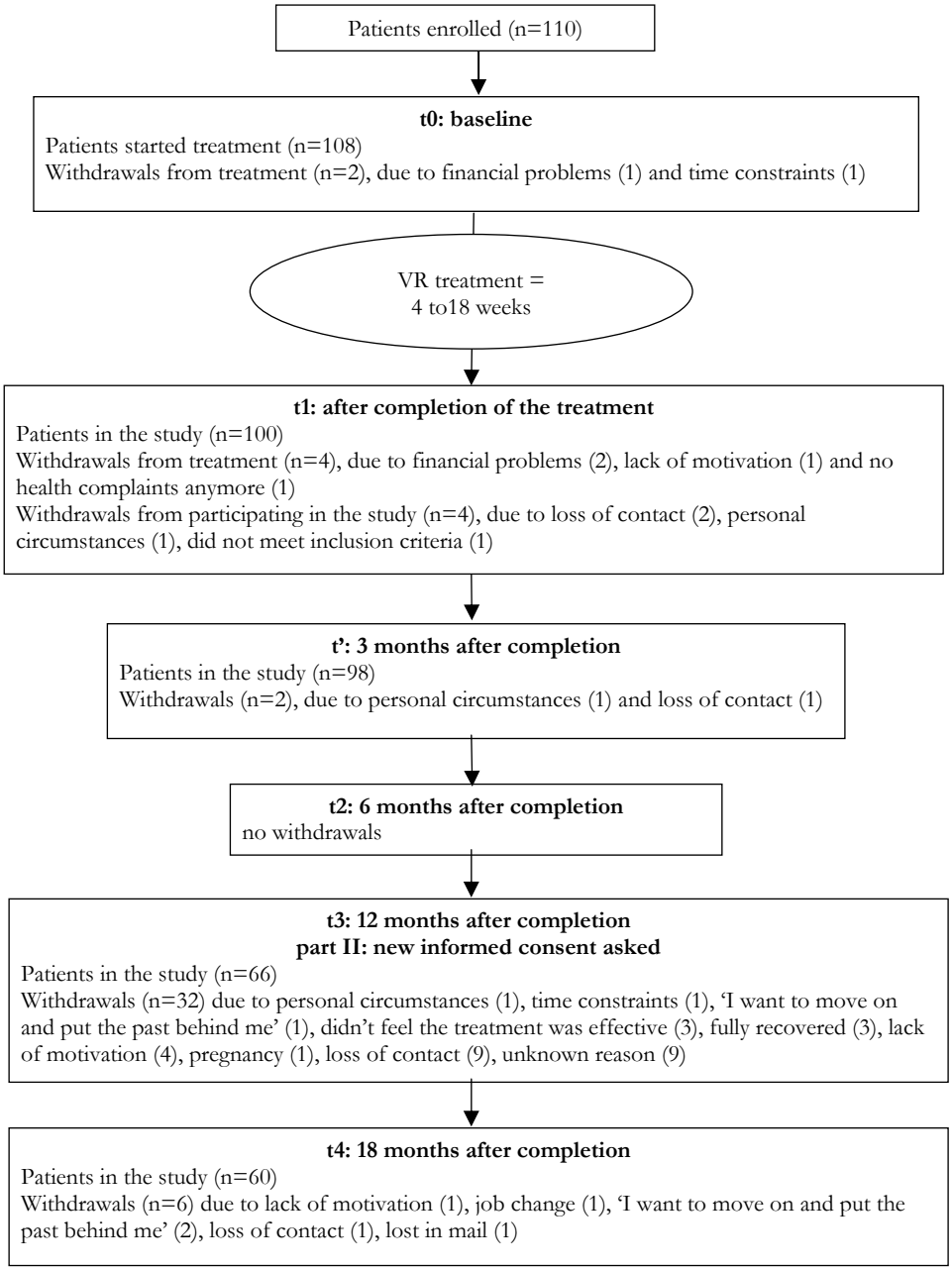


Figure 2. flow-chart of patients through the study

(mean 3.4 years). Most patients (73%) were partly or fully on sick leave, 17% were working full time and 10% had no paid job (Table 1).

We performed a non-response analysis and compared "completers" with "non-completers". No significant between-group difference was found on gender, age, duration of fatigue complaints, duration of functional impairments and fatigue severity at baseline. "Completers" and "non-completers" did not differ in fatigue severity levels (i.e., mean CIS scores) between t1-t0, nor did the groups differ in return-to-original-work percentage between t1 and t0.

Half of the 60 patients (52%) volunteered to participate in various additional treatments between 6 and 18 months after completing the VR treatments. Many of these patients (21-23%) were treated by general practitioners and medical specialists or took extra sessions in the VR institution. However, most patients (61%) sought care in the complementary and alternative medicine field (including acupuncture, homeopathy and orthomolecular medicine). Type and number of additional treatments are reported in Table 2.

In the period between six and eighteen months after treatment, 17 patients (28%) had not been on sick leave for one year. In this period, 14 patients (24%) had been on sick leave due to fatigue complaints. The mean duration of sick leave was nine weeks, ranging from two days to one year. Two patients were on sick leave for the full one-year period (data not shown).

Table 1. patients' characteristics

	Mean (SD) or Freq. (%)
Completers (n patients in the study at t4)	60
Age	47 (8.7)
Male	28 (47%)
Female	32 (53%)
Severe fatigue (CIS score >76)[1] (percentage)	87%
Duration of fatigue complaints in years	4.6 (5.1)
Duration functional impairments in years	3.4 (4.4)
Employment status	
Paid job, fully at work	10 (17%)
Paid job, partly on sick leave	24 (40%)
Paid job, fully on sick leave	20 (33%)
No paid job	6 (10%)

[1] Bültmann et al.[44]

Table 2. Additional treatments. Type and number (percentage) of additional treatments between six and 18 months follow-up

Additional treatment at follow-up (6-18 months)	Type of treatment	n (%)*
VR treatment	Extra sessions e.g.,: physical training, physical therapy, mental coach, psychologist, advice	13 (42%)
General practitioner		13 (42%)
Occupational physician		7 (21%)
Medical Specialist	Internist (2), neurosurgeon (3), rheumatologist (2), lung specialist (1), ear, nose and throat specialist (1), specialist in Metabolic Diseases (1), psychiatrist (1), cardiologist (1), neurologist (1), insurance physician (1).	14 (45%)
Psychologist		9 (29%)
Physiotherapist		7 (21%)
Vocational rehabilitation counsellor		1 (3%)
Career counselor		2 (6%)
Complementary and Alternative Medicine	Whole medical systems: homeopathy (2), naturopathic medicine (2)	4 (13%)
	Biological based practices: Orthomolecular medicine (1)	1 (3%)
	Mind-body Medicine: healing (1), paranormal medicine (1)	2 (6%)
	Manipulative and body-based practices: haptonomy (1), osteopathic (1), Bowen therapy (2), acupuncture (4), bio-energetic therapy (1)	9 (29%)
	Energy Therapies: Kinesiology (2), prognos therapy (1), Bio-resonance therapy	3 (10%)
Others	Nutrition: B12 insufficiency therapy (1)	1 (3%)
	Sleeping clinic (1), Coach (1), Mensendieck therapy (1), Course: personal development (1)	4 (13%)

* Number of patients (%) receiving additional treatment 6-18 months. More than one type of treatment per patient could be included.

Primary outcome measures

Figure 3 shows the results (mean scores, confidence intervals and p-values) of primary outcomes. Fatigue severity, work-related fatigue, vitality, percentage return-to-original-work, percentage return-to-work and perceived work ability all improved significantly ($p<.001$) over time. In post-hoc analyses, all outcomes improved significantly

(p<.001) in follow-up measures compared to baseline. In addition, the percentage of cases with chronic fatigue (CIS score above 76)[44] decreased from 87% at baseline to 46% after treatment and to 37% at 18 months follow-up.

Compared to t1, long-term improvements were less clear. No relapse in the assessed outcomes was found at 6, 12 and 18 months after treatment compared to t1. Moreover, two out of three fatigue outcomes significantly improved at six months after treatment (t2) compared to t1 (work-related fatigue (p=.002) and vitality (p=.004), as did work ability (p<.001). In addition, both work participation long-term improvements (t2, t3 and t4) were significant (p<001) compared to t1.

Out of 60 patients, 28 (47%) stated at baseline that they were "fairly sure" they would be able to work in two years. At t1, this number rose to 44 patients (73%). At 12 months and 18 months follow-up, 39 out of 53 patients (74%) and 44 out of 58 patients (76%), respectively, were "fairly sure" they would be able to work in two years (data not shown).

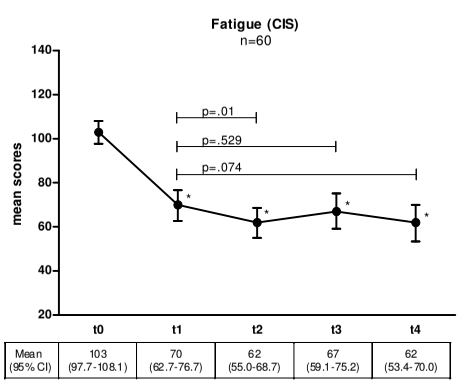
Secondary outcome measures

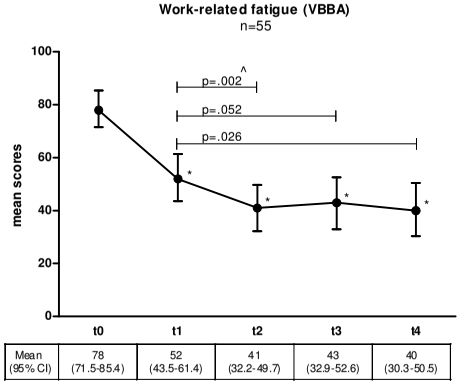
Table 3 reports mean scores, confidence intervals and overall p-values in the secondary outcomes per measurement. Five secondary outcomes (physical functioning, physical role limitation, mental health, emotional role limitation, and social functioning) improved significantly (p<.001) over time. These outcomes improved significantly (p<.001) at all follow-up measures compared to baseline.

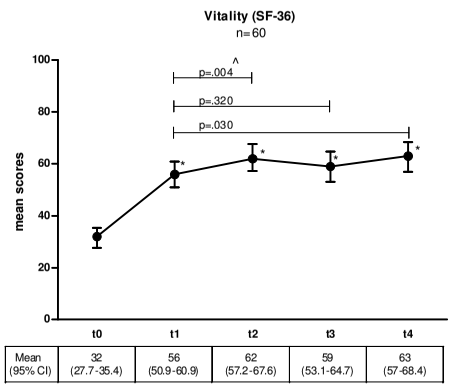
In post-hoc analyses compared to t1, non-significant long-term improvements at t2, t3 and t4 were found in physical functioning (p=.470, p=.239, and p=.396, respectively) and physical role functioning (p=.012, p=.035, and p=.041, respectively). In mental health, mean scores at six months after treatment improved significantly (p<.001) and emotional role limitation improved significantly six months (p=.003) and twelve months (p=.004) after treatment compared to t1. Social functioning increased significantly as well after the treatment was stopped (p=.003 at six months follow-up compared to t1).

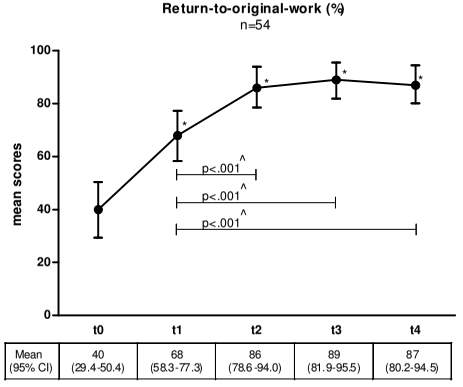
For heart rate variability, compared with baseline, HF power values improved significantly (p<.001) after treatment and at six months follow-up (p=.049). However, HF power did not improve significantly at six-month follow-up compared with t1 (p=.119).

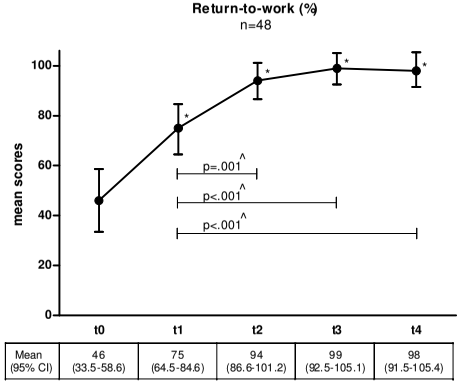
Figure 3. Primary outcomes: fatigue severity, work-related fatigue, vitality return-to-original-work, return-to-work and work ability.
Mean scores (95% Confidence intervals) on primary outcomes at t0 (baseline), t1 (at completion of the treatment), t2 (six months follow-up), t3 (12 months follow-up) and t4 (18 months follow-up) and p-values for the differences between follow-up measures and t1.

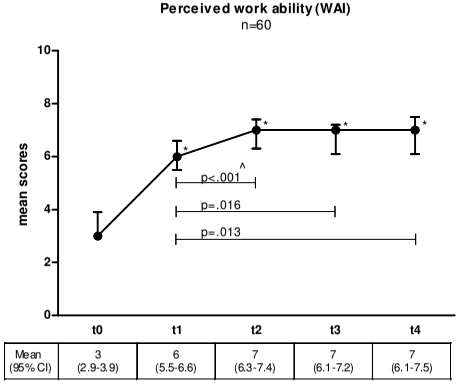












*p<.001: Significant post-hoc outcome w ithin subjects compared w ith t0. Significant w hen p<.0083 (Bonferroni corrected)
^p<.0083: Significant post-hoc outcome w ithin subjects compared w ith t1 (p<.0083 Bonferroni corrected)

Table 3. Secondary outcomes: physical functioning, mental health and social functioning
Mean scores (95% Confidence Intervals) on physical functioning, mental health, social functioning at t0 (baseline), t1 (at completion of the treatment), t2 (six months follow-up), t3 (12 months follow-up) and t4 (18 months follow-up) and p-values for the differences over the five measurements.

		Physical functioning		**Mental Health**		**Social functioning**
		Physical functioning (SF-36) 0-100	*Physical role limitation (SF-36)* 0-100	*Mental health (SF-36)* 0-100	*Emotional role limitation (SF-36)* 0-100	*Social functioning (SF-36)* 0-100
	n	60	60	60	60	60
t0	M (95% CI)	69 (62.9-74.1)	13 (5.9-20.8)	53 (48.5-58.2)	41 (30.0-52.3)	49 (41.9-55.6)
t1	M (95% CI)	85 (80.4-90.2)*	54 (43.1-65.3)*	69 (64.2-73.0)*	67 (56.2-77.2)*	68 (62.0-74.3)*
t2	M (95% CI)	86 (81.4-91.3)*	68 (58.1-78.6)* ^^	76 (72.1-79.4)* ^^	83 (74.2-91.4)* ^^	76 (69.2-82.0)* ^^
t3	M (95% CI)	88 (82.7-92.7)*	67 (57.0-78.0)* ^	73 (68.3-77.1)*	85 (76.8-93.1)* ^^	74 (67.3-81.4)*
t4	M (95% CI)	87 (82.4-92.0)*	68 (57.1-78.8)* ^	75 (70.2-79.3)* ^	82 (71.9-91.3)* ^	77 (70.0-83.3)* ^
	Overall p-value	<.001	<.001	<.001	<.001	<.001

*p<.001: post-hoc outcome within subjects compared with t0. Significant when p<.0083 (Bonferroni corrected)
^p<.05: post-hoc outcome within subjects compared with t1. Significant when p<.0083 (Bonferroni corrected)
^^p<.0083: post-hoc outcome within subjects compared with t1. Significant when p<.0083 (Bonferroni corrected)

Table 4. Heart rate variability
Mean scores (standard deviations) on HF power. Comparisons were made between t1-t0, t2-t0 and t2-t1.

	t0	t1	t2
n	58	37	55
HF power in ms^2 (SD)	50 (64.4)	126 (246.7)*	75 (126.0)**

*p=.001 Wilcoxon signed rank test (t1 compared with t0)
**p=.049 Wilcoxon signed rank test (t2 compared with t0)

Discussion

The results of our study suggest that in patients with prolonged fatigue, multi-component VR treatments significantly decrease fatigue symptoms and improve work participation, work ability, and physical-, mental-, and social functioning over the long-term. In addition, HRV as a physiological parameter did improve six months after the VR treatments. The results show that the positive changes in patients measured immediately after completing the treatment were maintained over the long term. Moreover, positive changes for fatigue complaints, work participation, work ability, mental health, and social functioning improved further up to 18 months after treatment.

Not surprisingly, the largest improvements compared to baseline were found immediately after completing the VR treatment. More surprisingly, the results show that short-term improvements are maintained over the long term, after treatment was stopped. These long-term improvements can be interpreted as clinically relevant outcomes, that is Cohen's effect size statistic $d > .50$[45], due to large effect sizes ($d > 1.2$) in all outcome measurements. First, the three fatigue measures show the same pattern of recovery. Moreover, mean fatigue severity scores (CIS) and mean scores in work-related fatigue decreased below the cut-off points of these scales, indicating chronic fatigue (mean=76)[44] and high risk of receiving treatment (mean=55), respectively.[46,47] Despite these significant and clinically relevant results, after 18 months patients in this study reported still more fatigue complaints than the Dutch (working) population (mean CIS score=47 and Vitality score=69).[44,48] Second, both work participation

measures improved further after treatment. Eighteen months after completing the treatment, return-to-original-work rose to 87%. That means that on average, patients worked for 87% of their contract hours at baseline. This result is similar to studies reporting RTW after multi-component treatment in upper extremity complaints[34] and in previous retrospective data.[49] Taking into account that some patients (n=15) modified their employment contract (i.e., less contracted hours) during the study period, return-to-work rose to 98% at 18 months follow-up. The VR treatment was aimed at facilitating full RTW by using work-directed components. However, another important aim of the treatment was to increase awareness of attitudes towards work and improve coping strategies and behaviour. In addition, patients have indicated that their work participation increases by learning to recognise their behavioural patterns at work and in private lives, and training to cope with their limitations and capacities (e.g., setting boundaries).[50] As a result of gaining this insight, patients may have changed their employment contract to avoid exceeding their capacities, thus resulting in a higher return-to-work percentage. It should be noted that eight patients were not included in the return-to-work analysis because they had no paid job anymore at 18 months follow-up. Because we do not know why these patients lost their employment contract (e.g., retirement, going back to college, permanent work disability) and if this job loss was the result of attending the VR treatment, we can not draw conclusions from this.

The secondary outcomes, physical functioning, mental health, and social functioning showed long-term improvements. Physical functioning mean scores at 18 months follow-up were higher than scores in the Dutch population (mean=83).[48] Mental health and social functioning improved significantly after the treatment was stopped. Eighteen months after treatment, mental health scores moved towards the scores found in the Dutch population (mean=77)[48], but social functioning scores stayed below the scores of the Dutch population (mean=84). As for HRV, we found six-month follow-up (t2) improvements compared with baseline. Mean HF power worsened compared with t1, however not significantly. Few, if any, studies have investigated the effects of vocational interventions on HRV in fatigued patients. Though, we do know that physical exercise that is focussed on physiological adaptation improves HF power in other populations (e.g., healthy and coronary patients) over the short term.[51,52] However, these effects may be maintained only if the

exercise is continued. We do not know if the patients in our study continued physical training in their private time.

The main aim of the VR treatments was to improve individual and occupational functioning by achieving a normal balance between activity and rest, and subsequently between daily life and work. To achieve this normal balance, perpetuating factors that hindered recovery were addressed from a biopsychosocial perspective. The complexity of the treatment and outcomes, that is a combination of body awareness, increased physical fitness, awareness of attitudes and beliefs towards work and in private life, improving coping strategies and making a gradual RTW plan, are thought to increase daily functioning and, moreover, change patients' behaviour (e.g., adopt a new lifestyle). Consequently, this would improve participation over the long-term. The current results show that although fatigue symptoms remain prevalent, outcomes on functioning in daily life and work participation improve over the long-term and improve further after treatment is stopped. This suggests that patients are better capable of coping with perceived complaints in their private and working lives. These findings are supported by the findings of patients' RTW experiences after treatment in this same population.[50] In addition, in upper extremity musculoskeletal disorders[34] and in low back pain[53], biopsychosocial rehabilitation showed positive effects on work participation over the long-term (one year follow-up).

This study was designed as a practice-based research attempting to answer a question that originates from everyday practice. In the Netherlands, outpatient VR care is decontrolled. Thus, various treatments are designed by outpatient institutions and carried out by experienced trainers, caregivers and supervisors. It is of great importance to evaluate the outcomes of these everyday practices, as many fatigued patients who seek help attend these treatments. However, conducting a randomised controlled study in this setting was not feasible; among other reasons, institutions were bound by contracts with employers. In practice-based research, the content of the intervention and patients participating in the study should be the same as in "clinical" practice. Next, a broad range of real-life outcomes should be collected. These factors were taken into account, which gives this study high external validity.[22,26,54] Due to the absence of a control group, which is not unusual in practice-based research, a number of measures were taken to strengthen the design (and thereby internal validity) according to the TREND statement.[25] The content of VR treatment was theoretically specified, and outcomes were selected based on the

interventions and measured using reliable and validated outcome variables. The results of this study are in line with and confirmed by different perspectives by longitudinal data (current study), process evaluation (described in[21]) and patients' perspectives.[50] In addition, considering the long-standing nature of fatigue complaints and perceived disabilities, spontaneous recovery of these problems was unlikely. Considering these points, we believe that the outcomes of this study may be attributed to the VR treatment provided by the outpatient institutions in a population of prolonged fatigue patients with participation problems.

We conclude that multi-component VR treatments have the potential to reduce fatigue symptoms and improve individual functioning and work participation in patients with severe prolonged fatigue complaints over the long-term without relapses. It is therefore recommended to use multi-component VR treatments with a biopsychosocial approach for patients with disabling prolonged fatigue complaints. These results are of importance to the occupational health field in preventing and managing sickness absence in fatigued workers through referral to VR treatments.

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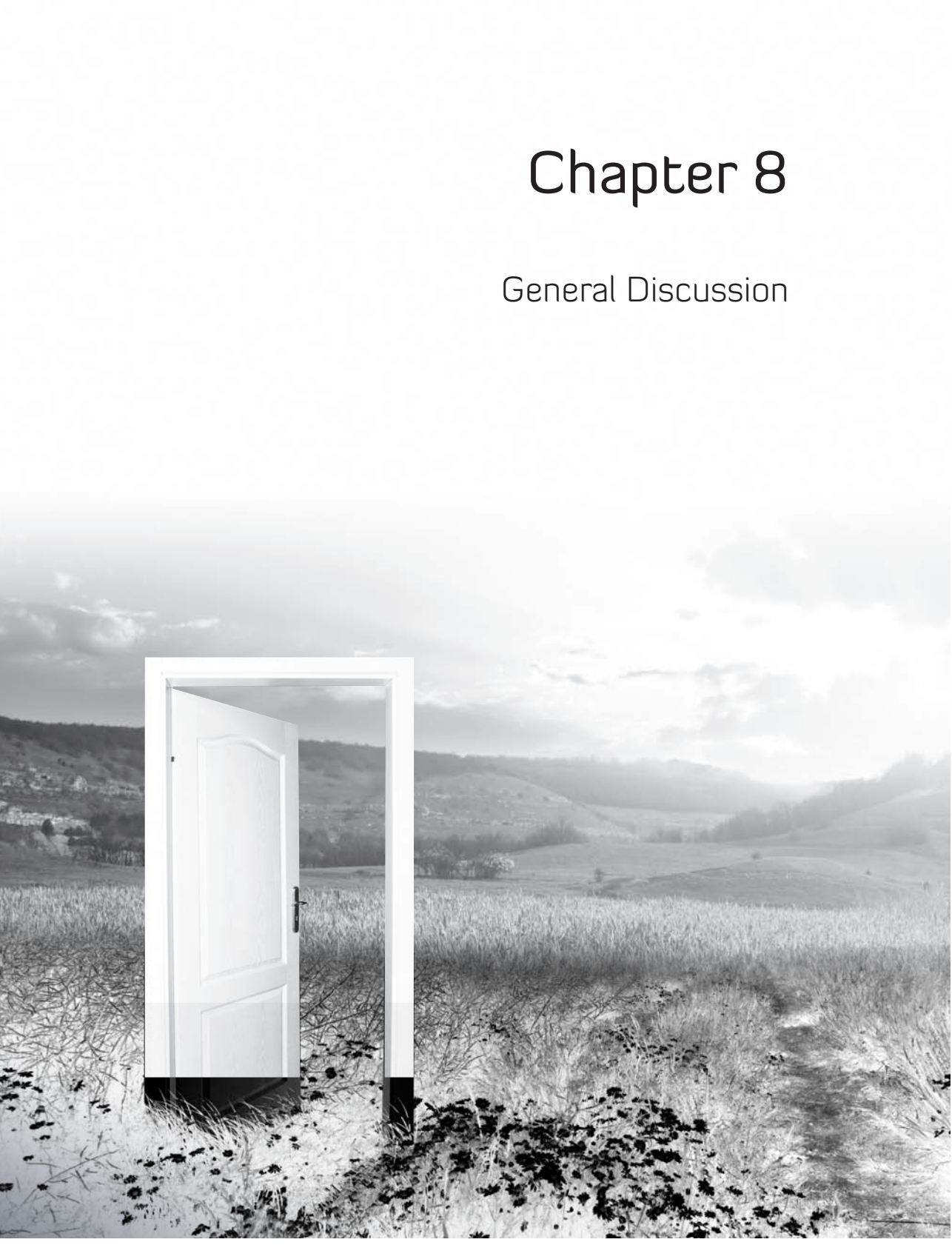
Chapter 8

General Discussion



The main objective of this thesis was to generate knowledge about the role of different existing vocational rehabilitation (VR) treatments with respect to daily life functioning and work participation of patients with prolonged fatigue complaints. In this chapter, the main research findings of this thesis are presented, and strengths and weaknesses of the research are discussed. Furthermore, recommendations for future research and practice are presented.

Main findings

1) Which VR treatments are practiced in the Netherlands and what is their content?

Among the 10 VR institutions that were identifiable as treating impaired workers with prolonged fatigue in the Netherlands, 13 different types of VR treatments were used in 2010. The main purpose of VR treatments was to facilitate return-to-work (RTW) and improve daily life functioning. In the case of most treatments, the content was multi-component focussed (n=8), combining physical, psychological, and work-directed interventions. In the case of three treatments, content was focussed on only two components; in the case of two treatments only psychological intervention was provided. Eight treatments took between 3 and 6 months in total and combined individual with group sessions. Treatments were mainly considered to be successful when the patient could cope with his or her own limitations and capacities, when the employer was satisfied with the outcome and cooperation with VR treatment, when patients returned to their original work, and when balance was reached between daily life and work. Thus, the majority of the specialised VR treatments in the Netherlands offer multi-component interventions to fatigued workers with the aim of improving both daily life functioning and work participation.

That multi-component treatments are actually carried out is confirmed by the outcomes of a process evaluation of three existing VR treatments (Chapter 5). This process evaluation demonstrates that the three VR treatments were administered according to their pre-defined treatment protocol, which consisted of multi-component treatments using a biopsychosocial approach in each case.

2) Can VR treatments improve daily functioning and work participation of patients with prolonged fatigue on the short- and the long-term?

Three multi-component VR treatments were evaluated based on their outcomes on patients with prolonged fatigue and work participation problems. These VR treatments were designed and carried out by outpatient institutions in the Netherlands. Using a practice-based research design (Chapters 5 and 7), short and long-term outcomes were studied. The three existing, multi-component VR treatments were successful with improving individual and social functioning, work ability, and work participation. These outcomes were significantly improved directly after treatment compared to measurements before treatment, and improvement was maintained after a long-term measurement, which was taken at 18 months after completing treatment. Moreover, mental health, social functioning, work ability, and work participation continued to improve significantly after treatment was stopped. Lastly, VR treatments also affected fatigue complaints. After 18 months, 37% of patients were no longer cases suffering from severe fatigue compared with 87% at baseline; however, on average the degree of fatigue complaints was still higher among participants compared to the general Dutch working population.

In conclusion, multi-component treatments using a biopsychosocial approach appear to improve the daily life functioning and work participation in patients with prolonged fatigue for as many as 18 months after treatment was completed.

3) What are fatigued patients' perspectives regarding work experiences before and after receiving VR treatment?

From the qualitative survey in Chapter 6, we learn that workers with prolonged fatigue complaints report work-related problems in several domains. According to workers, aggravating working conditions, difficulties with activities during work, and interpersonal relations all have roles in limiting work abilities. Additionally, fatigued workers described that a lack of self-reflection on individual capabilities and limitations affect their work ability. Due to these latter problems, workers explained that they were not receptive to advice from supervisors or co-workers, thus further hindering the RTW process.

Fatigued workers explained that work participation improved after VR treatment once they learned coping strategies and reflected on personal characteristics, lifestyle and work style. Also, according to workers, a phased-RTW strategy and work

adaptations (like working fewer hours) had a positive effect on their work ability. Findings from the qualitative survey in Chapter 6 were supported by evaluations in Chapters 4 and 5. In those evaluations, more than half of fatigued workers stated that the treatment was effective in reducing work functioning limitations and that their personal aims (including work-related goals) were met. These findings emphasise the importance of addressing personal characteristics in treatments and in the RTW process in addition to modifying the worksite.

Interpretations of findings

Content, aims and outcomes of multi-component VR treatment

In Chapter 1, a conceptual model describes the process and aims of VR in patients with prolonged fatigue (Figure 1). This model presents biological, psychological, and social/occupational factors as factors that can be involved in the perpetuation of fatigue complaints and related disability. We hypothesised that work participation could be improved if VR treatments focus on those factors that obstruct recovery, using a combination of biological, psychological, and social-occupational components. First, Chapter 2 shows that the majority of specialised VR treatments in the Netherlands do indeed use multi-component treatments. In addition, Chapter 5 provides new information about the treatment process and the specific content of existing VR treatments. By evaluating three existing, multi-component VR treatments closely, we found that these approaches do indeed address factors that obstruct patient recovery from fatigue symptoms and the restoration of daily life functioning and work participation. The VR treatments integrated therapeutic approaches with a combination of biological/physical, psychological/cognitive behavioural, and social/work-directed components. Perpetuating factors like the dysregulation of physiological stress systems and physical deconditioning were influenced by physiological adaptation in physical training sessions, body awareness in graded exercise training, and in relaxation and breathing exercises. Next, cognitive behavioural sessions and psychological therapy sessions were employed to influence dysfunctional beliefs and behaviour, and causal attribution. These sessions offered patients insight into their attitudes and beliefs involving work and private life; they

also improved patient knowledge and coping skills. During RTW sessions, psychosocial factors were addressed by teaching workers mechanisms to change attitudes towards work, increase awareness of behavioural patterns at work and in private life, improve job conditions, and involve the employer with making a phased-RTW plan. Upon evaluating these three treatments, differences were identified with regards to 1) the method used to communicate with the patient (group or individual sessions) and 2) the specific intervention techniques used (physical training vs. graded activity, coaching vs. cognitive therapy, addressing work-related problems vs. involving the employer). Deciding how to communicate and which specific intervention technique to use was based on VR institution's preference or was tailored to patient's needs.

The conceptual model in Chapter 1 (Figure 1) also suggests that multi-component VR treatment, using a biopsychosocial approach, would be an effective strategy to increase daily functioning and work participation and decrease fatigue complaints. This approach is unique in the field of fatigue research, as it concerns evaluating treatments in the RTW context. In addition, the treatments focus on functional recovery rather than symptomatic recovery. Though reduction in fatigue symptoms can be seen as an additionally outcome. The results presented in Chapters 5 and 7 indicate that using a combination of therapeutic approaches and addressing biological, psychological, and social factors can together increase daily functioning and work participation, lead to more effective behaviour (e.g., adopt a new life/work style) and reduces fatigue complaints. Consequently, these outcomes are likely to maintain or improve further over the long-term.

Few, if any, studies have evaluated the long-term effects of biopsychosocial multi-component treatment on work participation in fatigued patients. One evaluation of a comparable, multi-component treatment approach in patients with non-specific upper extremity complaints showed improvements in daily functioning and work participation after one year as well.[1] A study of a body awareness programme in patients with chronic, non-specific psychosomatic symptoms showed positive, long-term one year results on body awareness, self-efficacy and quality of life one year after the intervention.[2] Although it was uni-modal, this programme was comparable to some of the psychological components of VR treatment in our research. These results support our findings regarding behaviour change through body awareness, thus suggesting a comparable process of behaviour change.

In conclusion, the study results confirm our hypothesis that a combination of therapeutic approaches, integrated through different treatment components (aimed at both the individual and his (work)environment), have a positive effect on daily functioning and work participation. These findings contribute to our growing understanding of the working mechanisms and outcomes of VR treatment in impaired workers with prolonged fatigue.

Clinically relevant long-term outcomes

When interpreting results from an evaluation study, knowledge of statistical significance is useful in some respects but does not provide information about the clinical relevance of the outcomes, particularly with regard to fatigue and daily functioning outcomes. Two studies in this thesis (Chapters 4 and 7) present effect sizes to assess the clinical relevance by using Cohen's effect size *d* for repeated measurements.[3] In all statistically significant results from the long-term evaluation (Chapter 7), we found effect sizes of $d>1.2$, indicating large, clinically relevant effects. Furthermore, results from the evaluation studies conducted for this thesis were compared with norm figures from large samples of the Dutch (working) population. In doing this comparison, we found that our population had on average a high rate of severe fatigue complaints at baseline. A total of 87% of patients were suffering from chronic severe fatigue, indicated by the Checklist Individual Strength (CIS) cut-off point above 76.[4] This percentage decreased to 45% at the completion of treatment and to 37% at 18 months after treatment. Despite these clinically relevant results, on average patients still reported more fatigue complaints after 18 months compared with the Dutch working population.[4] These results were confirmed with both the CIS scores and the vitality scores (SF-36). Secondary outcomes (physical functioning, mental health, social functioning) showed long-term improvement. Moreover, physical functioning scores at 18 months follow-up had increased and were better than scores measured in the general Dutch population.[5] Mental health and social functioning increased as well and continued improving after treatment, although they remained lower than the Dutch norm 18 months after treatment. With regards to work participation, return-to-original-work significantly increased from 22% before treatment to 84% at 18 months follow-up. In addition, patients found themselves better able to work immediately after treatment and also 18 months after treatment. Considering that some patients (15/60) modified their employment contract (i.e.,

fewer contracted hours) during the study period, RTW increased to 98% at 18 months follow-up. An important aim and therapeutic approach of VR treatment was to increase awareness of cognitions with respect to work and change dysfunctional beliefs and behaviour. Patients explained that their ability to work increased after both learning to recognise their behavioural patterns at work and in their private lives and after training to cope with their limitations and capacities (e.g., setting boundaries). As a result of gaining this insight, patients may have changed their employment contract to avoid exceeding their capacities, thus resulting in a higher RTW percentage. However, it should be noted that 8 (out of 60) patients no longer had a paying job at the 18-month follow-up and therefore were not included in the RTW analyses. It is unclear whether these patients lost their employment contract by choice (e.g., returned to school, sabbatical, retirement) or because of permanent work disability. Therefore, we cannot draw a concrete conclusion from this finding.

Interestingly, the fact that half of the patients participated in additional treatment during the last year of our study (Chapter 7) indicates that patients were not free of complaints. Perhaps patients were searching for care that would address their remaining symptoms. This theory is supported by the fact that the majority of these patients sought help in complementary and alternative therapies, which often focus on symptomatic relief.[6] However, it remains unclear to what extent these additional treatments either negatively or positively contributed to the outcomes observed in our study (Chapters 5 and 7).

Thus, although fatigue complaints remained prevalent, patients reported being more able to work and outcomes on individual and social functioning, and work participation improved overall in a clinically relevant way, both immediately after VR treatment and on a long-term basis. In fact, outcomes continued to improve long after VR treatment stopped. This finding suggests that patients were more capable of coping repeatedly, day-to-day and week-by-week, with their perceived complaints in both their private and working lives.

Changes in physiological stress-systems

One factor possibly associated with the persistence of fatigue complaints and related disability is the dysregulation of physiological stress-systems, particularly cardiac autonomic imbalance.[7] Before using physiological parameters as outcome measures in our long-term evaluation study, we wanted to investigate whether or not cardiac

autonomic balance would change after physical training in patients with prolonged fatigue complaints. Heart rate variability (HRV) was used as a marker to reflect cardiac autonomic activity. In the first study (chapter 3), we used both time-domain and frequency-domain characters to measure HRV. In later studies we focused on high frequency (HF) power values, as it estimates changes in cardiac vagal tone. Higher vagal control is related to reduced heart rate and is involved in the process of recovery and restoration.[8] In the pilot study described in Chapter 3, a six-week training programme was evaluated to explore if HRV would increase after VR treatment. After patients (n=18) with severe fatigue complaints completed the training programme, HRV significantly increased and fatigue complaints significantly decreased. In further short- and long-term evaluation studies (Chapters 5 and 7), we found that HRV positively changed compared to baseline measures after VR treatment that aimed at physiological adaptation by physical training. However, interpreting HRV (and other physiological parameters) remains problematic because of a lack of reliable norm figures.[9] In addition, studies on the differences in physiological mechanisms in specific patient groups show conflicting results.[10-12] Moreover, previous research showed no differences in peripheral physiological measurements between extremely different groups (burnout patients and engaged workers).[13] Therefore, physiological measurements like HRV may currently not be very useful in the detection of physiological deviations at a group level or to predict future health status.[13] However, HRV is a suitable tool for tracking modifications in clinical state at an individual level.[14] In addition, there are indications that there are gender differences in autonomic cardiovascular regulation after training.[15] Within this context, we can calculated effect sizes to comment on the relevance of the modifications. We did so post-hoc and found "medium" effects (Cohen's *d* just below .50) in short and long-term outcomes in the total group. When calculating effect sizes separate for men and women, we found that women had the largest, clinical relevant, change in HRV direct after training (Cohen's *d* .51). Hereby, HRV offers insight into the mechanisms of physical training by confirming a positive physiological adaptation after physical training in patients with severe fatigue complaint. In general, these findings correlate with those of previous studies on other populations, like coronary and cancer patients.[16-18] Additionally, HRV may also be a useful tool for monitoring training responses and subsequently to ensure optimal training (e.g., preventing unfavourable training responses due to over- or under-load) at the individual level[19], as exemplified

by two VR treatments discussed in this thesis. Thus, HRV or other parameters measuring cardiac autonomic activity may be less suitable for diagnosing purposes or judging patient participation or functioning levels in clinical practice, but they can be useful for evaluation purposes.

RTW experiences

Findings of the qualitative survey presented in Chapter 6 emphasise the importance of viewing recovery and the RTW process from a biopsychosocial perspective. Our analysis of work-related problems experienced by patients with extreme fatigue complaints and of the VR treatment strategies the patients believed worked well draws attention to the importance of considering each impaired worker in his or her specific situation, including personal (cognitive) characteristics, when applying VR strategies.

Special attention should be given to the (meta)cognitive abilities of impaired workers with severe fatigue complaints. In our study, workers mentioned that before the VR treatment, they felt stubborn and unreceptive to advice or feedback from co-workers, employers or family members. They were not aware of their behaviour and could not interpret or handle advice from others. This problem calls for certain actions to facilitate the recovery process. Workers placed additional value on receiving intensive, multi-component VR treatment that included work-directed interventions and worker-directed interventions. Specifically, learning to recognise their own behavioural patterns in daily life and at work, and learning strategies to deal with their limitations and capacities were mentioned by workers as important components of their therapy that positively affected work participation. Apparently the outpatient setting in which the VR treatments were conducted was important as well. Workers reported that they had suffered from fatigue for many years, relying on willpower and a daily routine before they finally "collapsed" and called in sick to work. In these cases, by removing the worker from the work site, perpetuating personal factors can be examined and addressed thoroughly without distractions from the work environment. However, aside from focussing on the worker and taking individual processing and recovery time into account[20,21], involving the workplace and provide an active role for the employer during an early stage of the rehabilitation process is of great importance, because we know this approach can facilitate the RTW process.[22,23]

Methodological considerations

In this section, the methodological issues of this thesis are discussed, as well as the strengths and weaknesses of the study design, study population selection and the outcome measurements used.

Study design

The outcomes of VR treatment were investigated using a pre-/post-test design with repeated measurements as far as 1.5 years after completion of treatment. Although a randomised controlled trial (RCT) design is considered to be the best method to evaluate an intervention, it is not always feasible to perform such a trial. In this case, we were unable to create a controlled design because of the outpatient setting in which the study was performed, as well as financial and ethical constraints. To withdraw care from patients on sick leave, thereby costing society and the employer an enormous amount of money, was not considered to be moral. Besides, the supposed superiority of an RCT in public health research has been discussed by several others.[24-26] Often, RCTs lack external validity because they do not produce findings applicable to a real-life context and to the population currently being seen in daily practices (often atypical patients).[27] Furthermore, crossover effects between experimental and control groups occur when blinding is not possible, which is particularly likely with public health interventions where long causal pathways are common.[28,29] Moreover, when people are monitored, they will react accordingly.[30] Thus, even participants in a control group or on a waiting list may alter their behaviours and influence the results. Initially, a study design using two comparison groups within each VR institution was considered. However, the treatments were patient-centred, and care providers found it complicated to allocate patients randomly to structured, standardised treatments. Additionally, it became not possible to create two interventions that were different enough to be real comparisons. The evaluations conducted for this thesis focused therefore only on intervention groups and did so with the best possible study design. This design was strengthened by certain aspects of the process evaluation we performed. From this evaluation, we know that VR treatments were conducted as described in the pre-defined protocol and that they entailed a multi-component, biopsychosocial approach. We also conducted a qualitative survey to strengthen the study design. By doing so, a more in-depth, comprehensive understanding of the

effects of VR treatment was provided.[31] This method also validated the importance of listening to patients as they play a central and active role in the VR process.[32] Findings from the qualitative survey confirmed data from our quantitative studies.

As is often the case with intervention studies using a longitudinal design, we faced the problem of missing data. Missing data occurs when one or more measurement sequences for participants are incomplete, which therefore complicates statistical inference.[33] Removing all cases of missing data would have negatively affected the power of our study. Therefore, we used linear mixed-model analyses to best fit the longitudinal data in the presence of missing data (4.4% of the total data was missing). With this model, we could also select the best fitting variance-covariance model for the present data and investigate trends over time. When overall effects were significant, we performed post-hoc analyses to detect differences between measurements. However, post-hoc analyses should be interpreted with care because multiple testing can lead to high false positive rates[34] and multiple comparisons procedures are recommended.[35] Therefore, we performed bonferroni adjustments and presented the actual p-values with our results for transparency purposes (Chapter 7).

Overall, in evaluating existing VR treatments we used a sound design that was also applicable in practice, conforming to the principles of practice-based research[36] and the TREND statement.[37] This is seen as a strength of this thesis.

Selection of the study population

We used limited selection criteria to include a sample that represent patients in outpatient VR institutions in practice. The VR institutions had their own inclusion criteria, like being motivated to take part in treatment, good command of the spoken and written Dutch language and no diagnosis of a psychiatric disorder. Such a patient group might represent a heterogeneous group that, in the case of an RCT, may threaten validity. However, from the perspective of a practice-based research, selection of participants for this study resembles daily practice and therefore ensures ecological validity.[24]

One of the few inclusion criteria included in this study was that patients suffer from self-reported fatigue complaints. In the pilotstudy presented in Chapter 3 we used exclusion criteria regarding somatic diseases. However, given the impact fatigue complaints (regardless the diagnosis, e.g., burnout, CFS, fibromyalgia, cancer) have on individual, social, and occupational functioning we chose not restrict inclusion to

diagnostic criteria in the other studies. This choice however, may have caused some resistance in accepting our results in the clinical scientific field of mental health and fatigue care. A point of consideration is whether or not we missed eligible patients due to an unclear definition of prolonged fatigue. Practitioners of the VR institutions screened every new client for inclusion in the study. During the inclusion phase, the researchers noticed that some practitioners had doubts about specific cases that they had already excluded from the study. Given the number of practitioners involved in the inclusion process (approximately 30 practitioners from a total of 6 centres), under-representation of the target population might have resulted. However, selection bias is not likely a problem because this doubt was detected at an early stage of the inclusion period, and the definition of prolonged fatigue was then established more clearly and explained to the participating practitioners in all centres.

One problem in the long-term study (Chapter 7) was the high proportion of drop-outs compared to the short-term study (Chapter 5); this problem may have resulted in attrition bias. Patients who benefited from treatment on a short-term basis (first phase of the study) may have been more likely positively respond to the second (long-term) phase of the study. However, a non-response analysis showed no statistical differences between the baseline characteristics and short-term effects of both groups. Moreover, the reasons for dropping out were diverse and included patients with both positive and negative treatment experiences. So, we believe that the 'long-term' group was not a select patient group and resembles the original sample in the study. Additionally, this patient group still represents patients with long-lasting fatigue in VR treatments.

Outcomes

The outcomes parameters that were used to evaluate existing VR treatments were chosen in accordance with the goals of VR treatments. Work participation or RTW is the main aim of VR treatments and was defined as the percentage return-to-original-work (mean percentage of the absolute number of working hours, compared to contractual working hours before treatment) and return-to-work (mean percentage of the absolute number of working hours compared to current contractual working hours) (Chapter 4, 5 and 7). At different time points, patients were asked about their current contractual working hours and absolute number of working hours. Because we did not have access to sick leave registration systems, this method was deemed to be the most reliable.[38] Self-reported sick leave data are sometimes questioned with

respect to reliability because people may find it difficult to remember frequency and duration of sick leave, especially when it relates to a long period of time.[39] Because patients in our study were only reporting the current situation, reliability was ensured. A second advantage of this method is measuring "return-to-work" allowed for the identification of modifications in employment contract. In Chapter 7, we report that in 15 patients, contract hours were changed. By using this measure, we collected the most accurate data possible. Next to measuring RTW objectively, we studied perceived work ability using one item of the Work ability Index (WAI).[40] A second item from the WAI was used to study personal prognosis of work ability in the next two years. This provided us insight into the patient's ability to work and if they felt their work ability would improve over the years.

Decreasing fatigue symptoms was not a direct aim of VR treatment but was a condition central to this thesis. Fatigue is also a known predictor for sick leave and disability.[41,42] For these reasons, we chose degree-of-fatigue as a primary outcome along with work participation. Along with these primary outcomes, we included the following secondary outcomes to gain knowledge about the therapeutic process: physical functioning (including physical role limitations), mental health (including emotional role limitations), social functioning and HRV.

Although VR treatments also use therapeutic approaches that address insight into attitudes and beliefs, improve coping strategies, and change dysfunctional behaviour, we did not measure these process outcomes in the evaluation studies. Besides, variables such as attitudes, coping strategies and perceptions are not easily measured and lack standardised questionnaires related to RTW and applicable for patient with prolonged fatigue. Yet, in the qualitative interviews, patients reported that gaining awareness of their own behaviour and learning to cope with their limitations and capacities positively influenced work participation (Chapter 6).

Thus, along with standardised and validated questionnaires, we used self-formulated questions, process evaluation and qualitative interviews to collect data. The results of this research project are confirmed by these different perspectives and methods. The strategy using mixed-methods is considered to be a strength of this project.

Recommendations for research

In the Netherlands, employers are co-responsible for VR of disabled workers and become important partners in the RTW process. It is therefore important to explore employers' perspectives along with the experiences of patients. This research should combine expectations of employers regarding VR treatment for disabled workers, with matched employers' experiences with these treatments. Also, such research may focus on workplace disability management to investigate what employers themselves do to prevent work disability and facilitate RTW in disabled workers. We actually performed a small study concerning the VR efforts made by employers in fatigued workers with functional impairments (not published). The importance of good collaboration between employer, worker and health care professionals, such as occupational physicians and VR care providers, in the RTW process was stressed. Thus, research from an employer's perspective may provide knowledge that can be used to stimulate and facilitate cooperative VR strategies.

Multi-component VR treatment seems to positively affect daily life functioning and work participation in patients with prolonged fatigue complaints as their main symptom affecting work ability. This biopsychosocial treatment approach, tailored to patients' needs, may also be successful in populations with other complex conditions, such as patients with other common mental health disorders, chronic medical conditions or chronic pain patients. Considering that these types of patients, like fatigue patients, are already seen by outpatient VR institutions, such research is warranted.

A final recommendation for future research is to investigate the costs and benefits of existing VR treatments. Especially in the Netherlands, where employers make financial investments to provide workers with VR care at outpatient clinics, such research would be important for the sake of exploring the costs of medical health care and VR care and costs incurred with sickness absence.

Recommendations for practice

Workers and employers

When a worker experiences work participation problems, Dutch legislation requires that both worker and employers are responsible for the RTW process. Because of the complexity of prolonged fatigue complaints, specialised care is often needed. It is therefore recommended that employers find professional help from an occupational physician or outpatient VR service at an early stage to prevent long-term work disability. Along with specific treatment strategies, good cooperation and communication are essential to the RTW process. Patients should try to specify constraints they face in daily life and work, including the consequences of work participation. Conversely, employers should be aware of the implications that fatigue complaints can have for workers as they pertain to emotional and cognitive problems, daily functioning, and work ability and should feel partially responsible for the recovery process of the worker.

The occupational health setting

In our study, patients were suffering from fatigue complaints and functional impairments for over 2.5 years on average before they participated in VR treatment. This is an undesirable situation because of ethical issues (loss of health care) and possible financial consequences due to productivity loss and sick leave costs. Among these patients, long-term positive effects were reported on daily functioning and work participation after multi-component VR treatment. Before treatment, impaired workers felt emotionally distressed and not receptive to advice. Therefore, multi-component VR treatments should be used for disabled patients with prolonged fatigue complaints; preferably early in the course of the condition to prevent long-term sick leave. The occupational physician plays an important role in preventing and managing sickness (absence). Therefore, occupational physicians should consider referral to multi-component VR treatment in impaired workers with prolonged fatigue complaints as a first aid strategy rather than a patient's last option.

In the Netherlands, outpatient VR care is not centrally controlled, resulting in a wide range of available treatments that are not always clearly visible. The results of Chapter 2 contribute to better visibility and transparency of VR treatment providers

specialised in serving fatigued workers in the Netherlands. Occupational physicians are recommended to use this inventory to gather information about the aims and content of treatments, which can help them make better treatment decisions (referral advice) that best match the preferences of patient and employer.

VR institutions

As abovementioned, making the available care transparent in terms of treatment aims and content is important for treatment decision making but also for the development of knowledge in the vocational rehabilitation field. Although competitive motives may obstruct giving complete insight, VR institutions should try to make their treatments (theory and content) more transparent. In this way, professionals can learn from each other which can improve quality of care and professionalization of the vocational rehabilitation field.

We found that various factors hampered patients' participation at work, including cognitive abilities and social factors. Exploring these factors when patients present with prolonged fatigue complaints would give more insight into the factors that hinder recovery and give direction for individually tailored treatment. Moreover, to be effective at the work participation level, these treatments should combine worker-directed interventions with work-directed interventions. Patient's personal challenges should be addressed within their social and occupational context, and the employer and the work place should be involved. In addition, work disability demonstrates the existing gap between personal capacity and employers' and societal demands. Thus, commitment and cooperation among the worker, employer, treatment providers and occupational physicians will result in a more successful approach to prevent long-term work disability. We therefore recommend that all parties invest in a fruitful cooperation and combine forces to address this problem.

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Summary

Fatigue is a common complaint in both the general and working populations. In most cases, fatigue is a temporary state that abates after rest. However, sometimes fatigue persists and develops into a long-lasting condition with little chance of recovery without therapy. These complaints of prolonged fatigue are accompanied by individual, social, and occupational problems and may lead to sickness absences and/or work disability. Therefore, prolonged fatigue is a serious health problem, affecting not only the patient but also posing grave economic consequences. Consequently, caregivers, occupational physicians, employers and the patients itself are involved in the (occupational) recovery process.

In most cases, fatigue cannot be explained by a single factor. Moreover, the precise aetiology of prolonged fatigue is still unknown. However, factors involved in the persistence of fatigue complaints and related disability have been identified and appear to be of biopsychosocial origin. These perpetuating factors are of great importance in the treatment of prolonged fatigue. In the Netherlands, outpatient vocational rehabilitation (VR) institutions offer services for workers with prolonged fatigue. These institutions use multi-component treatments to increase physical and mental functioning and facilitate work participation. However, knowledge of the precise content and effects of these treatments in practice is lacking. We hypothesise that (multi-component) VR treatment will positively affect daily life functioning and work participation in patients with prolonged fatigue complaints.

The main objective of this thesis is to generate knowledge about the role that different existing VR treatments play with respect to daily life functioning and work participation of patients with prolonged fatigue complaints. In this thesis, the following research questions are answered:

1) Which VR treatments are practiced in the Netherlands and what is their content?

2) Can VR treatments improve daily functioning and work participation in patients with prolonged fatigue on the short- and the long-term?

3) What are fatigued patients' perspectives regarding work experiences before and after receiving VR treatment?

Chapter 2 addresses the first research question and provides an inventory of VR treatments in use in the Netherlands. The purpose of this inventory was to increase visibility and transparency of current care for fatigued workers. We contacted 99 members of the Dutch sector organisation of vocational rehabilitation institutions

(Boaborea) to search, list and extract data on existing VR treatments used for sick-listed or impaired workers with prolonged fatigue complaints. VR institutions were contacted by email and telephone, and a key person involved with VR treatment was asked to complete an online questionnaire containing five domains: organisation characteristics, patient population, treatment aims, outcomes, and VR treatment content.

Thirteen VR treatments were identified from the ten VR institutions that were willing to participate and met our inclusion criteria. The treatments are used not only for patients with prolonged fatigue complaints, but also for patients with chronic pain, common mental health and physical complaints. The 13 treatments aimed to facilitate one's return-to-work (RTW), increase functioning in daily life activities (n=11), improve social participation (n=9) and decrease fatigue complaints (n=9). Regarding the outcomes, treatments were mainly considered to be successful when the patient could cope with his or her limitations and capacities (n=6), when the employer was satisfied with the outcome and collaboration with VR treatment (n=6), when patients returned to their original jobs (n=5) and when balance was reached between daily life and work (n=5). Most VR treatments (n=8) used multi-component treatments, that included physical training, psychological or cognitive behavioural therapy, and work-directed interventions. Furthermore, most VR treatments had a total duration of 3 to 6 months, with 8 to 40 sessions during the treatment phase and they employed a combination of individual and group sessions to deliver treatment components. In conclusion, the majority of specialised VR institutions offer multi-component treatments with fatigued workers to improve functioning in daily life and participation at work. This inventory allows for the content and aims of treatments offered at VR institutions to be transparent and visible, thereby helping patients, employers, and (occupational) physicians to make treatment decisions.

The pilot study presented in **Chapter 3** served as the first step in answering the second research question by exploring patient changes in physiological parameters and fatigue complaints after a six-week physical training programme. Dysregulation of physiological stress-systems may be associated with fatigue complaints, particularly in the persistence of prolonged fatigue. Therefore, we investigated whether or not physiological parameters and fatigue complaints would change after participation in a physical training programme. The training consisted mainly of physical endurance

training using an individualised, progressive workout plan based on daily heart rate levels, next to relaxation therapy, and breathing exercises. Eighteen fatigued patients participated and visited the training three times a week in 2005. Before the training programme began, fatigue complaints were assessed with the Checklist Individual Strength (CIS). Physiological parameters (heart rate variability (HRV) and respiratory rate) were recorded at rest and during recovery after a bicycle exercise test. After the programme began, these measurements were repeated at three weeks and six weeks. After six weeks, fatigue scores decreased in all patients, with the mean fatigue scores decreasing significantly compared to baseline values ($p=.001$). HRV improved (increased) significantly (related to recovery and restoration) as we expected at rest ($p<.04$) but not during recovery. Respiratory rates both at rest and during recovery improved (decreased) significantly, as expected after six weeks ($p=.001$ for both). These results suggest that a six-week training programme in patients with severe complaints of fatigue has the potential to improve physiological parameters and fatigue symptoms.

Chapter 4 also addresses the second research question and describes a retrospective study encompassing the evaluation of a multi-component treatment programme, practiced by an outpatient institution. The treatment lasted 18 weeks and consisted of physical training, psychological sessions and RTW sessions. The treatment was aimed to decrease fatigue complaints, improve daily life functioning and facilitate RTW. Thirty-two patients with prolonged fatigue and functional impairments were included, from 2002 to 2006. Fatigue complaints, mental health, physical functioning, and work participation (i.e., mean percentage of the working hours, compared to contractual working hours before treatment and after treatment) were measured pre-treatment, post-treatment and at three months follow-up. Finally, patient and employer satisfaction were measured.

Results showed that after the training period, fatigue complaints decreased significantly ($p<.001$) and work participation increased significantly ($p<.001$) from 22% to 84% return to the original hours worked. Additionally, physical functioning and mental health improved significantly ($p<.05$). Furthermore, 90% of patients reported that their complaints were diminished after completing the programme, and 82% of the employers were satisfied with the results achieved. Given these results, it

seems that multi-component treatments improves fatigue complaints, daily functioning, and work participation in fatigued patients with functional limitations.
The research presented in **Chapter 5** continues on the previous two studies to answer the second research question and describes an evaluation of the process and outcomes of three existing VR treatments in patients with prolonged fatigue. The VR treatments were designed and practiced by outpatient institutions. Using a prospective pre-/post-test design with repeated measurements (before treatment, immediately after treatment, and three months after treatment), we evaluated the process and short-term outcomes of each VR treatment (between 2006 and 2008). Primary outcomes (fatigue, work participation) and secondary outcomes (physical and social functioning, mental health, HRV) were assessed over time using linear mixed model analyses. To conduct the process evaluation, information about patient recruitment, content completeness, and patient satisfaction were examined. .

One hundred patients (30 patients in VR treatment 1, 29 in VR treatment 2 and 41 in VR treatment 3) who had reported severe, disabling fatigue for many years (mean=2.5 years) participated. The three VR treatments were administered according to the pre-defined programme protocols; all used multi-component treatments with a biopsychosocial approach. All three VR treatments targeted biological/physical, psychological, social/occupational factors that were thought to hamper patient ability to recover and participate in daily life and at work. However, differences in content of the VR treatments mainly involved the specific intervention technique used and the manner in which treatment was communicated. Almost all patients met their personal goals, and the majority of patients stated that the intervention effectively diminished factors constraining them at work. The aims of the VR treatments were achieved after three months: work participation ($p<.010$), physical functioning ($p<.001$), mental health ($p<.001$), and social functioning ($p<.001$) improved considerably in all three VRIs. Furthermore, fatigue decreased ($p<.001$) in patients in all three VR treatments, with mean scores below scores, that indicate severe chronic fatigue (mean CIS score=76) and a high risk of receiving treatment (mean VBBA need for recovery score=55). Physiologically, HRV improved in two VR treatments ($p=.04$); HRV was not measured in the remaining VR treatment due to logistic constraints. In conclusion, our results suggest that the three, biopsychosocial, patient-tailored VR treatments provided clinically relevant and statistically significant short-term outcomes regarding symptoms, daily functioning, and participation at work for fatigued patients.

Chapter 6 addresses the third research question and presents results from a qualitative survey. The purpose of this study was to gain insight into fatigued workers' perspectives regarding work experiences before and after receiving VR treatments. Six months after treatment, patients were interviewed about work-related problems, arrangements made before the VR treatment and how the VR experience affected work participation. We used a sub-sample of participants from the evaluation study presented in chapter 5. A random sampling strategy was used to select 30 of the 100 workers, stratified by treatment; 21 interviews were analysed before saturation of data was reached. Two researchers performed partially independent qualitative analyses. The results revealed themes that were discussed by the project team and were organised into domains, categories and sub-categories.

Participants believed that the following problems limited their ability to work: symptoms of prolonged fatigue and personal limitations like a lack of self-reflection on individual capacity and limitations. Additional difficulties with interpersonal relations, performing activities at work, demanding work conditions, and work-life imbalance contributed to problems with work participation. Prior to the VR treatment, VR strategies like work adaptations, social support, and advices or referrals by occupational physician to psychological or physical care were employed. After attending a VR treatment, fatigued workers reported positive experiences with work and personal challenges (i.e., increased awareness, coping skills and confidence), improved activities at work, and effective work adaptations. However, some workers reported unsatisfactory recovery and stated that fatigue symptoms and absence from work persisted. Thus, while aggravating working conditions, difficulty with work activities, and interpersonal relations can limit one's functioning at work, our findings suggest that a lack of self-reflection on individual capacities and limitations can also greatly affect work ability in fatigued workers. VR treatments that encourage workers to reflect on personal characteristics (behavioural patterns in daily life and work), learn coping strategies, and stimulate a phased-RTW strategy, serve to positively affect work participation. These findings stress the importance of involving such personal factors in the recovery process and RTW beyond singly adapting the worksite.

Chapter 7 presents the long-term outcomes of existing multi-component VR treatments offered in outpatient institutions. This study addresses the second research question of this thesis. For this study, participants from the evaluation study described

in chapter 5 were followed for 18 months after completing VR treatment. To evaluate real-world VR care, we studied participants who received any of the three treatments and reported the long-term outcomes of the entire group of patients. The main goal of the VR treatments was to improve individual and occupational functioning in patients with prolonged fatigue complaints by achieving a normal balance between activity and rest, and subsequently between daily life and work. We measured outcomes before treatment (t0), after treatment (t1) and at long-term follow-ups: six (t2), 12 (t3) and 18 months (t4) after treatment. Primary outcomes (fatigue, work participation, work ability) and secondary outcomes (physical functioning, mental health, social functioning, HRV) were assessed using linear mixed model analyses. Post-hoc, long-term outcomes were compared with t0 and t1.

Of the 100 patients who started treatment, 60 remained and could be assessed after 18-months. These 60 patients did not differ from the drop-outs with regard to personal characteristics, fatigue duration, fatigue severity and RTW percentage upon evaluation of short-term outcomes. The primary outcome parameters significantly improved ($p<.001$) upon the follow-up measurements compared with t0 and showed no relapse when compared with t1. Moreover, the percentage of cases with severe fatigue (CIS score>76) decreased from 87% at baseline to 46% after treatment and to 37% after 18 months. Additionally, work ability and work participation increased ($p<.001$) after treatment stopped. The secondary outcomes (physical functioning, mental health, social functioning, HRV) improved significantly ($p<.001$, $p<.001$, $p<.001$ and $p=.049$, respectively) over the long-term compared with t0. After six-months (t2), mental health and social functioning further increased compared with the end of treatment (t1) ($p<.003$, $p=.003$, respectively). These long-term improvements can be interpreted as clinically relevant due to the large effect sizes ($d>1.2$ for all significant outcomes). In conclusion, multi-component VR treatments can decrease fatigue symptoms and improve individual and social functioning and work participation in patients with severe prolonged fatigue over a long-term period without a relapse of symptoms and activities. These results are important in the field of occupational health for the prevention and management of sickness absences in patients with prolonged fatigue complaints.

In **Chapter 8,** the main research findings and recommendations for further research and practice are discussed. The three research questions of this thesis can be answered as follows:

1. In the Netherlands, the majority of specialised VR treatments use multi-component treatments to treat impaired workers with prolonged fatigue. These VR treatments include physical, psychological, and work-directed interventions and are aimed to improve daily functioning and facilitate work participation.
2. Short-term and long-term outcome evaluation of multi-component VR treatment shows that these strategies significantly improve individual functioning and work participation and decrease fatigue symptoms without relapse. In addition, VR treatments result in clinically relevant improvements in fatigue complaints, daily functioning, physiological parameters, and occupational participation level in patients with severe prolonged fatigue.
3. According to the patients themselves, VR treatments that encourage patients to reflect on personal characteristics, lifestyle and work habits; learning coping strategies and use a phased-RTW strategy may yield positive results with respect to work participation.

These findings stress the importance of the multi-component VR treatments practiced in the Netherlands for impaired workers with prolonged fatigue. Therefore, we recommended the use of such biopsychosocial-based treatments in patients with disabling, prolonged fatigue. Additionally, addressing personal factors during the recovery process and RTW process beyond modifying the worksite can be of additional value. These results are of importance in the field of occupational health for the prevention and management of sickness absence, like referral to VR treatment. However, as employers play an important role in the RTW process of impaired workers and often finance the actual outpatient VR treatments, future research should investigate the employers' perspectives of this process. Moreover, a study of the costs incurred for VR treatments and sickness absence is also warranted.

Samenvatting

Iedereen is wel eens vermoeid; bijvoorbeeld na een periode van fysieke en/of mentale inspanning. Meestal verdwijnt deze vermoeidheid door het nemen van rust. In sommige gevallen houden vermoeidheidsklachten echter langer aan en kunnen chronisch van aard worden. Deze zogenoemde aanhoudende vermoeidheidsklachten kunnen problemen geven bij het functioneren in het dagelijks leven. Patiënten met aanhoudende vermoeidheid ervaren vaak zowel fysieke als mentale problemen die hen beperken in het uitvoeren van activiteiten, zowel thuis als op het werk. Uiteindelijk kunnen aanhoudende vermoeidheidsklachten leiden tot participatieproblemen, zoals ziekteverzuim en/of arbeidsongeschiktheid. Hierdoor is aanhoudende vermoeidheid niet alleen een groot probleem voor het individu, maar heeft het ook maatschappelijke en economische consequenties.

De oorzaak van vermoeidheidsklachten is vaak onbekend, maar het aanhoudende karakter van vermoeidheid lijkt door meerdere factoren beïnvloed te worden. Zo kunnen factoren van biologische/fysiologische aard, psychologische/cognitieve aard en sociale/werkgerelateerde aard een rol spelen bij het in stand houden van klachten. Om aanhoudende vermoeidheidsklachten te verminderen en het functioneren en de arbeidsparticipatie van patiënten te verbeteren is het belangrijk in te spelen op deze instandhoudende factoren. In Nederland worden arbo-begeleidingsprogramma's aangeboden door re-integratiecentra die zich richten op werknemers die beperkingen ervaren bij het functioneren in werk. Ook patiënten met aanhoudende vermoeidheidsklachten worden begeleid in deze programma's. Het doel van dit proefschrift is om wetenschappelijke kennis te verkrijgen over de rol die arbo-begeleidingsprogramma's spelen bij het verbeteren van het dagelijks functioneren en de arbeidsparticipatie bij patiënten met aanhoudende vermoeidheidsklachten. De volgende onderzoeksvragen zijn onderzocht:

1. Welke arbo-begeleidingsprogramma's voor werknemers met aanhoudende vermoeidheidsklachten worden in Nederland toegepast en waar bestaan deze programma's inhoudelijk uit?
2. Kan door middel van arbo-begeleidingsprogramma's het dagelijks functioneren en arbeidsparticipatie van patiënten met aanhoudende vermoeidheidsklachten worden verbeterd op de korte en op de lange termijn?
3. Wat zijn de ervaringen van langdurig vermoeide werknemers, met betrekking tot hun werkervaringen vóór en na het volgen van arbo-begeleidingsprogramma?

Arbo-begeleidingsprogramma's voor werknemers met aanhoudende vermoeidheidsklachten in Nederland

Voor het beantwoorden van de eerste onderzoeksvraag wordt in **Hoofdstuk 2** een onderzoek gepresenteerd waarin een overzicht wordt gegeven van bestaande begeleidingsprogramma's in Nederland voor langdurig vermoeide werknemers. Dit onderzoek is uitgevoerd om de transparantie en zichtbaarheid van aanwezige arbobegeleiding voor werknemers met aanhoudende vermoeidheidsklachten te vergroten. Onder de leden van de brancheorganisatie voor arbodiensten en re-integratiebedrijven (Boaborea) waren 10 re-integratiecentra, die vermoeide werknemers begeleiden, bereid om een online vragenlijst in te vullen over de inhoud van hun programma(s). Binnen deze centra werden 13 verschillende begeleidingprogramma's geïdentificeerd die zich naast vermoeidheidspatiënten richtten op patiënten met psychische-, fysieke- en pijnklachten. Alle 13 begeleidingsprogramma's hadden als doel om terugkeer naar werk te bevorderen. Andere doelen waren het verbeteren van functioneren in het dagelijks leven, verbeteren van deelname aan het maatschappelijk leven en verminderen van vermoeidheidsklachten. Het merendeel van de programma's (8 van de 13) bestond uit multi-modale begeleiding, waarbij zowel fysieke training, psychologische- en/of cognitief gedragsmatige sessies en werkgerichte interventies werden aangeboden. De duur van de meeste programma's lag tussen de drie en de zes maanden in totaal, waarbij individuele en groepssessies werden gecombineerd. De programma's werden als succesvol beoordeeld als de patiënt heeft leren omgaan met de eigen beperkingen en mogelijkheden, als de werkgever tevreden is over de re-integratie en met de samenwerking met de behandelaars van het begeleidingsprogramma, als de patiënt terug is gekeerd naar zijn/haar originele werk en/of als er een verbeterde balans is tussen werk en privé.

Het verkregen overzicht van de inhoud van bestaande arbo-begeleidingsprogramma's in Nederland kan bruikbaar zijn voor verschillende actorgroepen: 1) het kan vermoeide werknemers helpen bij het maken van behandelkeuzes die passen bij hun behoeften, 2) werkgevers krijgen meer inzicht in specifieke terugkeer naar werk strategieën, 3) bedrijfsartsen kunnen de informatie gebruiken bij het verwijzen naar specialistische re-integratie zorg, en 4) onderzoekers en zorgverleners kunnen leren van de situatie in Nederland met betrekking tot de organisatie en uitvoering van arbozorg.

In **Hoofdstuk 5** werden drie bestaande arbo-begeleidingsprogramma's nader onderzocht. In een procesevaluatie van uitvoering van de programma's kwam naar voren dat de drie arbo-begeleidingsprogramma's werden uitgevoerd zoals ook vooraf beschreven stond in het protocol. Bij alle drie de programma's werd een multi-modale behandeling gegeven vanuit een biopsychosociale benadering. Dit betekent dat er werd geïntervenieerd op biologische/fysieke, psychische en sociale/werkgerelateerde factoren die de persoon hinderen bij het herstel en re-integratie proces. Desondanks verschilden de programma's van elkaar door de nadruk die werd gelegd op de verschillende componenten en de uitvoering ervan.

Korte en lange termijn effecten van arbo-begeleidingsprogramma's op het functioneren en arbeidsparticipatie van patiënten met aanhoudende vermoeidheidsklachten.

Voordat de korte en lange termijn effecten van drie arbo-begeleidingsprogramma's werden onderzocht bij 100 werknemers (Hoofdstuk 5 en 7) is eerst een pilotstudie (Hoofdstuk 3) en een retrospectieve studie (Hoofdstuk 4) uitgevoerd.

De pilotstudie (**Hoofdstuk 3)** werd uitgevoerd om te onderzoeken of fysiologische parameters en vermoeidheidsklachten te beïnvloeden zijn door fysieke training bij 18 patiënten met aanhoudende vermoeidheidsklachten. Eén van de factoren die een rol lijkt te spelen bij het in stand houden van vermoeidheidsklachten is disregulatie van fysiologische stress systemen, waaronder het cardiovasculaire systeem. Hartslag variabiliteit (HRV) en ademhalingsfrequentie werden in dit onderzoek meegenomen om een indruk te krijgen van de toestand van het cardiovasculaire systeem, in het bijzonder de balans tussen sympathische en parasympathische activiteit. De verwachting was dat na fysieke training, parasympathische activiteit zou toenemen (dat wil zeggen, HRV verhoogt en ademhalingsfrequentie daalt) bij patiënten met aanhoudende vermoeidheidsklachten. Het trainingsprogramma van zes weken bestond voornamelijk uit fysieke training gericht op uithoudingsvermogen, waarbij gebruik werd gemaakt van een persoonlijk trainingsschema gebaseerd op hartslag niveaus. Verder werden ontspannings- en ademhalingsoefeningen gegeven. Het programma werd drie keer per week gegeven en was ontwikkeld voor patiënten met aanhoudende vermoeidheidsklachten. Van de 18 patiënten die deelnamen aan de

studie werd voorafgaand en na afloop van het programma vermoeidheidsklachten gemeten met een vragenlijst en werden fysiologische parameters, hartslag variabiliteit (HRV) en ademhalingsfrequentie, onderzocht vóór en na een fietstest.

Na afloop van de trainingsperiode waren de patiënten gemiddeld minder vermoeid dan voorafgaand aan de trainingsperiode. Zowel HRV als ademhalingsfrequentie verbeterde (HRV verhoogt en ademfrequentie daalt) na afloop. Deze resultaten laten zien dat een 6-weken durend trainingsprogramma de (fysiologische) balans van het cardiovasculaire systeem en vermoeidheidsklachten meetbaar positief kan beïnvloeden.

Vervolgens werd een retrospectieve studie (**Hoofdstuk 4)** uitgevoerd om te onderzoeken of het mogelijk is om het functioneren in het dagelijks leven en arbeidsparticipatie te verbeteren door een multidisciplinair begeleidingsprogramma. Dit 18 weken durende programma bestond uit fysieke training (persoonlijk trainingsschema gebaseerd op harstslag niveaus), psychologische sessies en terugkeer naar werk sessies. Het programma was gericht op het verminderen van vermoeidheidsklachten en het verbeteren van het dagelijks functioneren en specifiek het functioneren in het werk. Van 23 patiënten met aanhoudende vermoeidheidsklachten en beperkingen in het dagelijks leven werd retrospectieve data over de mate van vermoeidheid, het dagelijks functioneren (fysiek functioneren en mentale gezondheid) en arbeidsparticipatie (percentage van werkzame uren vergeleken met uren in het arbeidscontract) geanalyseerd. Deze data werd voor en na het programma en drie maanden na afloop van programma verzameld. Daarnaast werden de ervaringen van patiënten en van hun werkgever met betrekking tot het behaalde resultaat geanalyseerd.

Na afloop van het programma hadden patiënten gemiddeld significant minder vermoeidheidsklachten en verbeterde het dagelijks functioneren significant (verschillen zijn niet op toeval gebaseerd). Ook arbeidsparticipatie verbeterde significant; patiënten werkten na de begeleiding gemiddeld 84% van hun contracturen ten opzichte van 22% voorafgaand aan de begeleiding. Tevens was 82% van de werkgevers tevreden met de behaalde resultaten. De conclusie is dat toepassing van een multidisciplinair arbo-begeleidingsprogramma effect lijkt te hebben met betrekking tot het verminderen van vermoeidheidsklachten en het verbeteren van het

dagelijks functioneren en arbeidsparticipatie bij mensen met aanhoudende vermoeidheidsklachten en participatieproblemen.

Omdat zowel de pilotstudie (hoofdstuk 3) als de retrospectieve studie (hoofdstuk 4) positieve resultaten lieten zien, werd er een longitudinale evaluatiestudie opgezet om het proces en de uitkomsten van drie bestaande arbo-begeleidingsprogramma's te onderzoeken. Deze studie staat beschreven in **Hoofdstuk 5**. De drie arbo-begeleidingsprogramma's werden ontwikkeld en uitgevoerd door drie re-integratiecentra. Deelnemers aan het onderzoek waren langdurig vermoeide patiënten met beperkingen in het dagelijks functioneren die nieuw instroomde bij één van de drie programma's en tot drie maanden na afloop van de programma's werden gevolgd. Van de 110 patiënten die deelnamen, hebben uiteindelijk 100 patiënten alle metingen afgerond en werden meegenomen in de analyse. Deze deelnemers hadden voorafgaand aan de behandeling ernstige vermoeidheidsklachten die gemiddeld al meer dan 2,5 jaar aanwezig waren.

Alle drie de programma's lieten positieve effecten zien na afloop. Drie maanden na afloop van de arbo-begeleidingsprogramma's hadden patiënten significant en klinisch relevant minder vermoeidheidsklachten en verbeterde arbeidsparticipatie (patiënten gingen gemiddeld weer meer uren aan het werk). Ook het fysiek functioneren, de mentale gezondheid, sociaal functioneren en HRV verbeterd significant en op relevante wijze na het volgen van het programma. De conclusie is dat de drie multi-modale arbo-begeleidingsprogramma's positieve effecten hebben met betrekking tot het verminderen van vermoeidheidsklachten en verbeteren van zowel arbeidsparticipatie en fysieke, sociaal en mentaal functioneren.

Het onderzoek beschreven in **Hoofdstuk 7** onderzoekt het laatste deel van de tweede onderzoeksvraag van dit proefschrift, namelijk de evaluatie van de lange termijn uitkomsten van bestaande arbo-begeleidingsprogramma's. De deelnemers van de studie uit hoofdstuk 5 werden tot 1,5 jaar na afloop van de begeleiding gevolgd. In totaal hebben 60 patiënten alle metingen doorlopen en werden als één groep geanalyseerd.

De resultaten laten zien dat arbo-begeleidingsprogramma's op lange termijn positieve en klinisch relevante effecten hebben. Anderhalf jaar na afloop van de begeleiding zijn de vermoeidheidsklachten significant verminderd en de

arbeidsparticipatie (terugkeer naar eigen werk percentage) significant ten opzichte van voor de begeleiding. Ook het fysiek functioneren, mentale gezondheid, sociaal functioneren en hartslagvariabiliteit verbeterde significant. Nadat de begeleiding werd gestopt verminderden de vermoeidheidsklachten verder en verbeterden arbeidsparticipatie, mentale gezondheid en sociaal functioneren ook significant verder. De resultaten laten ook zien dat, na 1,5 jaar, de gemiddelde vermoeidheidsscores van de patiënten zover zijn gedaald dat er minder risico is op toekomstig ziekteverzuim of een behandeltraject. Daarnaast waren de scores op fysiek functioneren en mentale gezondheid vergelijkbaar met scores van de algemene Nederlandse bevolking. Tot slot blijkt dat 15 patiënten in de loop van het onderzoek hun arbeidscontract hebben aangepast. Hierdoor is het gemiddelde percentage terugkeer naar werk gestegen tot 98% na 1,5 jaar. Concluderend, werden in deze studie na multi-modale begeleiding van patiënten met aanhoudende vermoeidheidsklachten op de lange termijn, positieve en klinisch relevante uitkomsten gevonden op vermoeidheidsklachten, arbeidsparticipatie en op het persoonlijk en sociaal functioneren.

Ervaringen van vermoeide werknemers, met betrekking tot hun werk-ervaringen vóór en na het volgen van arbo-begeleidings-programma's.

Hoofdstuk 6 presenteert de resultaten van een kwalitatieve studie naar de werkervaringen van werknemers met aanhoudende vermoeidheidsklachten. Bij de deelnemers uit de studie beschreven in hoofdstuk 5 werden, zes maanden na afloop van de behandeling, semigestructureerde interviews afgenomen. In deze interviews werd gevraagd naar de problemen die vermoeide werknemers in het werk ervaarden vóór de arbo-begeleiding en welke maatregelen waren ondernomen om deze problemen op te lossen. Vervolgens werd gevraagd wat de terugkeer naar werk ervaringen waren ná de arbo-begeleiding en hoe de begeleiding het functioneren in het werk had beïnvloed. De interviews van 21 patiënten, die werk hadden aan het begin van de begeleiding, werden geanalyseerd.

Vermoeide werknemers gaven aan dat zowel de vermoeidheid zelf als ook persoonlijke factoren belemmerend waren om te functioneren in het werk. Persoonlijke factoren zoals gebrek aan zelfreflectie en verminderd inzicht in eigen mogelijkheden en beperkingen werden genoemd. Verder gaven werknemers aan dat werkgerelateerde factoren, zoals de relatie en communicatie met collega's en

leidinggevenden, het uitvoeren van werktaken, zware werkcondities en een disbalans tussen werk en privé activiteiten van invloed waren op het goed functioneren in het werk. Voorafgaand aan het arbo-begeleidingsprogramma werden er op de werkvloer maatregelen getroffen zoals werkaanpassingen, advies en steun van leidinggevende en/of doorverwijzing naar psychologische zorg of fysiotherapeut. Deze maatregelen waren echter niet effectief genoeg om weer goed te functioneren. Na afloop van het arbo-begeleidingsprogramma waren vermoeide werknemers positief over het effect van de gevolgde begeleiding. Persoonlijke ontwikkeling, zoals bewustwording van eigen mogelijkheden en beperkingen, verbeteren van coping strategieën en verbeterd zelfvertrouwen hielpen om beter te functioneren in het werk. Daarnaast gaven werknemers aan dat verbeterde werkactiviteiten en ondernomen werkaanpassingen, door tussenkomst van het arbo-begeleidingsprogramma, het functioneren in het werk had verbeterd. Sommige patiënten hadden echter nog steeds aanzienlijke vermoeidheidsklachten of bleef ziekteverzuim bestaan. Uit deze studie komt naar voren dat, volgens de patiënten zelf, persoonlijke beperkingen naast belastende werkcondities en symptomen van vermoeidheid, een rol speelden bij het verminderde werkvermogen. Ook gaven ze aan dat het beïnvloeden van juist deze persoonlijke factoren een positieve invloed had op het functioneren in het werk en in het dagelijks leven.

Deze positieve ervaringen met arbo-begeleidingsprogramma's die vanuit de kwalitatieve studie werden gevonden, kwamen overeen met bevindingen uit de evaluaties beschreven in hoofdstuk 4 en 5. Bijna alle patiënten (90%) gaven aan dat hun klachten waren verminderd na de begeleiding (**Hoofdstuk 4**). Verder gaven vrijwel alle patiënten (88%) aan hun persoonlijke doelen, tijdens of na de begeleiding, te hebben behaald. Ook vond de meerderheid (66%) van de patiënten dat de begeleiding effectief was in het verminderen van de beperkingen in het werk (**Hoofdstuk 5**).

Conclusies en aanbevelingen

De belangrijkste resultaten van dit proefschrift en aanbevelingen voor verder onderzoek en de praktijk werden in **Hoofdstuk 8** besproken. De drie onderzoeksvragen van dit proefschrift kunnen als volgt worden beantwoord:

1. De meeste gespecialiseerde arbo-begeleidingsprogramma's voor vermoeide werknemers in Nederland zijn gericht op het verbeteren van functioneren in het dagelijks leven en arbeidsparticipatie en bieden multi-modale begeleiding: een combinatie van fysieke, psychologische en werkgerichte interventies.
2. Zowel op de korte als op de lange termijn tot 18 maanden na begeleiding hebben drie bestaande multi-modale arbo-begeleidingsprogramma's positieve effecten met betrekking tot het verminderen van vermoeidheidsklachten en het verbeteren van functioneren in het dagelijks leven en arbeidsparticipatie.
3. Omdat patiënten zelf aangeven dat bewustwording van cognities en (werk)patronen en het leren omgaan met beperkingen een positieve invloed heeft op arbeidsparticipatie, lijkt het belangrijk om naast aanpassingen in het werk, aandacht te geven aan persoonlijke factoren in het herstel- en re-integratieproces van langdurig vermoeide werknemers.

Naar aanleiding van deze bevindingen wordt aanbevolen om multi-modale arbo-begeleidingsprogramma's in te blijven zetten en te stimuleren bij werknemers met aanhoudende vermoeidheidsklachten en participatieproblemen. Deze aanbeveling richt zich voornamelijk op bedrijfsartsen, maar heeft ook betrekking op werkgevers, die mede verantwoordelijke zijn voor het re-integratieproces van de werknemer. Aangezien de begeleiding nu pas gemiddeld na 2,5 jaar wordt gestart is het aan te bevelen om arbo-begeleidingsprogramma's vroeger in te gaan zetten, zodat ziekteverzuim en bijkomende kosten voorafgaand aan de begeleiding beperkt blijven. Het onderzoeken van het effect van het vroeg inzetten van begeleiding was echter niet de focus van dit proefschrift en zal in de praktijk verder onderzocht moeten worden, evenals de kosten t.o.v. de opbrengsten van de arbo-begeleidingsprogramma's bij deze groep werknemers. Gezien het feit dat werkgevers een steeds actievere rol spelen bij het re-integratieproces van werknemers die zijn uitgevallen of dreigen uit te vallen, lijkt het op zijn plaats ook het perspectief van werkgevers op re-integratie van werknemers met beperkingen mee te nemen in verder onderzoek.

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