Evaluation of a Psychosocial Intervention Program for Patients with Multiple Sclerosis

Mariëlle Visschedijk
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Evaluation of a psychosocial intervention program for patients with multiple sclerosis

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Mariëlle Antoinette Jozeffien Visschedijk

geboren te Almelo
promotoren: prof.dr. H.M. van der Ploeg  
prof.dr. C.H. Polman  
copromotor: dr. E.H. Collette
Voor Catelijne en Rosalin
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General introduction
1.1 Clinical aspects of multiple sclerosis

1.1.1 Pathology and epidemiology

More than 100 years have passed since Charcot, Carrell, Cruveilhier, and others described the clinical and pathological characteristics of multiple sclerosis (MS).[1.4] This enigmatic, relapsing, and often eventually progressive disorder mainly affects young adults between 20 and 45 years of age and has a worldwide predominance. However, MS is more common in Western countries with a lifetime prevalence of 1:1000.[2] In the Netherlands approximately 16,000 persons suffer from this chronic disease and every year about 270 persons are newly diagnosed. MS is considered to be an autoimmune disease and, like other autoimmune diseases, there is a predominance for women; it is approximately twice as common in women than in men.[3,4]

MS affects the central nervous system, which consists of the brain, spinal cord, and the optic nerves. Surrounding and protecting the nerve fibre of the central nervous system is a fatty tissue called myelin, which helps nerve fibres conduct electrical impulses. In MS, the body’s immune system, which normally helps to fight off infections, attacks myelin. This causes inflammation of the myelin sheath and myelin is lost in multiple areas, leaving scar tissue called sclerosis. When myelin or the nerve fibre is destroyed or damaged, the ability of the nerves to conduct electrical impulses to and from the brain is disrupted, and this produces the various neurological symptoms of MS. It is this nerve damage that causes the accumulation of disability that can occur over time.

As the central nervous system links all bodily activities, many different types of symptoms can appear in MS. The specific symptoms that appear depend upon which part of the central nervous system is affected and the function of the damaged nerve; however, there are several more common symptoms. These include motor and sensory impairments (numbness, loss of sensation), difficulty with ambulation, loss of bladder or bowel control, visual problems, sexual dysfunction, fatigue and decline in cognitive function.[5]

1.1.2 Clinical course

Symptoms of MS are unpredictable and vary from person to person and from time to time in the same person. While some symptoms will come and go over the course of the disease, others may be more lasting. In general, MS has a progressive course resulting in accumulating disability over the years. However, considerable differences in progression rate are found within the MS population.

The clinical course of MS usually can be characterized by either episodic acute periods of worsening (relapses, exacerbations or attacks) separated by periods of remissions (absence of signs or symptoms), gradual progressive deterioration of neurological functioning, or combinations of both. A relapse has been defined as lasting at least 24 hours in the context of a normal body temperature. It has been suggested that a
period of 30 days should separate the onset of two events for them to be documented as separate attacks.\textsuperscript{54} The more typical time course is for symptoms to evolve over days to 2 weeks, stabilise for 1-2 weeks, and then improve over weeks. Partial recovery with persistent residual symptoms and longer recovery periods may occur, especially with more severe relapses. Despite knowledge on several factors associated with prognosis, it remains difficult to make reliable predictions about the progression rate of the disease for individual patients. Based on epidemiological data, 50\% of patients will need help with walking within 15 years after the onset of disease.\textsuperscript{51}

Figure 1 shows the four major courses of MS. In approximately 10-15\% of the patients, the disease has a course that is progressive from onset with occasional plateaus and without evidence of relapses or remissions (primary progressive (PP) MS).\textsuperscript{7,8} In the majority of patients (80-85\%) the disease presents with a relapsing-remitting form (RR), in which the presence and absence of signs and symptoms alternate. In up to 60\% of the RR-MS patients the disease course changes into a secondary progressive (SP) form. The SP-MS course is characterized by a gradual worsening of neurological symptoms either with or without occasional relapses, minor remissions and plateaus. A small proportion of patients have progressive disease from onset with clear acute relapses, with or without full recovery and the periods between relapses are characterized by continuing progression. This type is defined as progressive-relapsing (PR) MS.\textsuperscript{8}}
Figure 1 Schematic description of the four clinical courses of multiple sclerosis: Relapsing-Remitting (RR), Primary Progressive (PP), Secondary Progressive (SP), and Progressive Relapsing (PR).

Furthermore, some patients (mostly those with a relapsing-remitting course) remain fully functional in all neurological systems 15 years after disease onset; this is referred to as ‘benign MS’. As opposed to this, occasionally patients have a rapidly progressive disease course, resulting in severe disability or death in a relatively short time after disease onset.\textsuperscript{[\textit{10}]}\n
1.1.3 Diagnosis and treatment

The diagnosis is based on established clinical and, when necessary, laboratory criteria.\textsuperscript{[\textit{10}]} Advances in cerebrospinal fluid analysis and Magnetic Resonance Imaging (MRI), in particular, can facilitate the diagnostic process.\textsuperscript{[\textit{11}]} Through the extensive use of MRI as a diagnostic tool a definite diagnosis of MS can be allowed in only a few months after the first presentation of suspected symptoms. However, before a definitive diagnosis of MS can be made, other conditions that might explain the clinical picture must be excluded.

At present, there is no therapy that can halt the accumulation of disability in MS.\textsuperscript{[\textit{5}]} Treatment focuses on 1) symptomatic therapy, like treatment for bowel and bladder
problems, spasticity and fatigue, and 2) disease-modifying therapy. Regarding symptomatic therapy, moderately effective treatments are available. Fatigue may respond to amantadine and to energy-conserving strategies. Spasticity, pain, problems with gait, decubitus ulcers, speech and swallowing disorders, and cognitive and mood disorders are best treated by a multidisciplinary approach that may involve specialists in physical medicine, rehabilitation and psychology. Regarding disease-modifying therapy, one of the main options are corticosteroids to treat clinically significant relapses in an attempt to hasten recovery and prevent permanent damage of the nerves; however, until now there is no consensus about the optimal form, dose, route (oral or injection), or duration of corticosteroid therapy. Another disease-modifying therapy is treatment with immunomodulatory drugs (such as interferon β) which are used to reduce the frequency and severity of relapses and to postpone the onset of the progressive phase of disease. The best dose and duration of interferon treatment is currently unknown, a high dose having many side effects and its beneficial effect on the progression of disability has not been confirmed beyond doubt.

1.2 Psychological aspects of multiple sclerosis

1.2.1 Emotional consequences
In addition to its physical symptoms, MS may have profound emotional consequences as well. At first, it may be difficult to adjust to the diagnosis of a disorder that is unpredictable, has a fluctuating course, and carries a risk of progressing over time to some level of physical disability. Lack of knowledge about the disease adds to the anxieties commonly experienced by people who are newly diagnosed. In addition to these emotional reactions to the disease, demyelination and damage to nerve fibres in the brain can also result in emotional changes. Several of the medications used in MS, such as steroids, can also have significant effects on the emotions. Some of the emotional changes observed in MS are: grieving for losses related to the disease, clinical depression as well as less severe depressive symptoms, and anxiety and distress.

Persons with MS often experience losses, for example, of the ability to work, to walk, or to engage in certain leisure activities. The process of mourning for these losses is considered as a 'normal' reaction to an 'abnormal' situation and it is often related to changes in self-image triggered by the disease. With time and adaptive coping strategies, grief will resolve on its own.

Depression, however, is an emotional state that is more persistent and unremitting. Moreover, a person experiencing grief may at times be able to enjoy some of life’s activities whereas a depressed person does not. Depression in its various forms is common during
CHAPTER 1

the course of multiple sclerosis; the lifetime prevalence of depression co-morbidity is 42-54%.[14-17] The precise aetiology of depression in patients with MS is unknown but may be related to the pathophysiology of MS (it is, for example, suggested that brain lesions play a causative role in the pathogenesis of depression),[16,18] to challenges of living with MS (depression can be seen as a failed coping process),[17,19-20] or to medications used to treat MS (for example, prednisone).[21,22] 

Furthermore, MS is a generally disabling, progressive, and unpredictable disease that can cause significant anxiety and distress from the moment of its first symptoms.[23-26] In contrast to depression, anxiety is thought to be of psychological origin as a result of accumulation of stressful life events. The uncertainty associated with MS is one of its most distressing aspects; people with MS never know when and if another exacerbation will occur or how severely they may be affected in the future.[27] They do not even know how they will feel from morning to afternoon or one day to the next. The loss of functions and altered life circumstances caused by the disease are also significant causes of anxiety and distress.[23-25] 

1.2.2 Health-related quality of life 

The concept of health-related quality of life (HRQoL) refers to a person or group’s perceived physical, mental and social functioning over time. HRQoL is often used to measure the effects of chronic illness in patients to better understand how an illness interferes with a person’s day-to-day life, and HRQoL has been widely examined as an outcome measure in MS. The first study of HRQoL in MS was published in 1990[28] and at least 90 studies have now measured HRQoL in patients with MS.[29,30] Many studies demonstrated that patients with MS have notable decrements in HRQoL,[29-36] mostly because the effect of disability in daily living is greater in MS (especially in its progressive form) than in other chronic diseases.[27] Compared to patients with other chronic diseases, patients with MS have the least favourable ratings of general health, vitality, physical functioning, and limitations in social roles.[37] Furthermore, at least a third of patients experience a major decline in their standard of living after the diagnosis of MS[30] and up to 70% of community-dwelling patients with MS are unemployed, half of these due to the consequences of their disease.[40] Within 10 years of onset, half of all patients with MS are unable to fulfil household and employment responsibilities; within 15 years, half are unable to walk unaided; and within 25 years, half require a wheelchair.[41] Other factors found to be determinants of poorer HRQoL in patients with MS are depression, anxiety and fatigue.[42-44] 

Assessment of HRQoL can be used as a way of checking if further treatment is required and whether interventions were as effective from the patient’s point of view as clinicians believe.[45] A further benefit of assessing HRQoL in patients with MS is that it might be an independent predictor of physical outcomes. Recently, MS-specific HRQoL instruments have been developed and proven reliable and valid.[38,44,45] Especially short
HRQoL instruments are interesting since the amount of time available in clinical trials or practice is often limited, and briefness of instruments is also important in view of respondent burden, since patients with MS can be easily fatigued.\textsuperscript{[49]}

Historically the management of MS has been predominantly about limiting disability by symptomatic management of acute relapses and attempting to influence the long-term course. Even though this type of management is important, it should be accompanied by an equal effort at improving participation, well-being, and HRQoL. HRQoL can be seen as an opportunity to assess and meet previously unmet needs, to predict previously unpredictable outcomes, and to develop broad interventions with beneficial psychological and physical effects.\textsuperscript{[50]}

1.3 Coping with multiple sclerosis

1.3.1 Self-efficacy and adjustment to MS

MS strikes relatively young adults in a life phase when many important changes take place (for example, planning to have children) and because of the diagnosis their world is turned upside down. Patients have to deal with prognostic uncertainty and it is unclear whether plans for the future can be fulfilled. Because of all this uncertainty and the progressive disabling character of the disease, coping with MS is an ongoing process. When progression goes along, but also when an important change takes place (for example, quitting work), patients are faced with a new situation. In these phases patients may seek professional help to adjust to the changed situation, because adjustment to the reality of disability allows patients to achieve personal integrity focused on skills, problem solving, and mastery over the degree of disability.\textsuperscript{[51]}

Several models of health behaviour change have been developed, in which the attitudes and beliefs people hold towards themselves, their treatment and disease are assumed to have a major impact on their coping behaviours.\textsuperscript{[52]} Self-efficacy, the individual’s confidence in being able to perform a given behaviour (for example, self-care or coping behaviour), plays an important role in adjustment to a chronic disease. As self-efficacy increases, the likelihood of an individual’s successful performance of a specific (self-care or coping) behaviour increases, as does the amount of effort and persistence in performing that behaviour in the face of obstacles.\textsuperscript{[53]} Self-efficacy may be enhanced by behavioural interventions to improve adjustment to MS.\textsuperscript{[54]}

1.3.2 Cognitive behavioural therapy

Cognitive behavioural therapy, originally developed to treat depression\textsuperscript{[55]} and anxiety\textsuperscript{[56]} has been successfully applied to a wide array of psychological problems, ranging from personality disorders to eating disorders and substance abuse.\textsuperscript{[57]}
CHAPTER 1

Cognitive behavioural therapy is described as:

“An active, directive, time-limited, structured approach (...) based on an underlying theoretical rational that an individual’s affect and behaviour are largely determined by the way in which he structures the world. His cognitions (verbal or pictorial ‘events’ in his stream of consciousness) are based on attitudes or assumptions (schemas), developed from previous experiences”.[55]

In other words, central to cognitive behavioural therapy is the assumption that behaviour and emotions are in constant interactions with cognitions. These cognitions or beliefs may be inaccurate, leading to excessive emotional reactions and a failure to cope effectively. The aim of cognitive therapy is to help patients identify their dysfunctional cognitions, test them against reality, and alter them, thereby modifying emotional disturbances and improving coping behaviour.

The assignment of meanings, explanations and expectations to internal and external events is thought to be accounted for by cognitive schemas, also called core beliefs. Core beliefs are highly individual, formed by past experiences, and are activated by particular events within or outside the person.[57] When underlying cognitive schemas are mainly negative in content, the processing of incoming information will be distorted, resulting in unpleasant, maladaptive feelings and behaviour. Depressed patients, for example, often show a characteristic cognitive pattern consisting of a negative view of themselves, the future and the world surrounding them. This can result in feelings of inadequacy, worthlessness and blame directed on oneself, hopelessness and apathy with regard to the future, and a world that is unjust and excessively demanding.

Cognitive techniques used in cognitive behavioural therapy to help patients alter these automatic thoughts involve monitoring negative, automatic thoughts and recognizing the interactions between cognition, affect and behaviour. The patient is invited to examine the evidence for his automatic thoughts and to substitute distorted cognitions with more realistic ones. In effect, patients can learn to identify and alter the underlying beliefs which lead them to think in a distorted way.[57]

A therapeutic approach that is closely related to the work of Beck and that stems from the same period is rational-emotive therapy, developed by Albert Ellis. Identical to cognitive behavioural therapy, Ellis states that thinking, feeling and acting are in constant interaction. One of the statements most central to Ellis’ work is the phrase by the ancient Greek Epictetus:[58] “People are disturbed not by things but by views they take of them”. Dysfunctional beliefs in rational-emotive therapy are termed irrational beliefs, and can, according to Ellis, be classified in three main categories: demandingness, towards the self, (“I must, under all circumstances, perform well and have the approval of others; if not, that is awful and makes me an incompetent and unworthy person!”), towards others (“You must treat me nicely, otherwise it is terrible and you are bad, unworthy people!”) and the
world (“The conditions under which I live must at all times be easy and enjoyable; if not, I can’t stand it and life isn’t worth living!”). Obviously, these beliefs can result in a variety of negative emotional states, including anxiety, self-hatred, anger, depression and dysfunctional behaviours like procrastination, withdrawal, phobias and addictions. Rational-emotive therapy has been applied to a wide variety of emotional and behavioural problems, and though there are various theoretical and philosophical differences between the two approaches, rational-emotive therapy and cognitive behavioural therapy, are not that different in clinical practice. An element important to note is the ABC model ('Activating event', 'Beliefs', and 'behavioural and emotional Consequences'), that is used in RET to identify and challenge irrational beliefs.

In line with the general model of CBT, it is assumed that previous experiences with MS colour the beliefs patients hold about the disease, the treatment and themselves. These beliefs have emotional and behavioural consequences. Examples of dysfunctional beliefs in patients with MS are: “If I can’t live my life like a healthy person, then it’s not worth living”, or, “I am a bad mother/father, because I have MS.”

Cognitive behavioural therapy has proven effective in the treatment of mood and anxiety disorders, and in the last decades its effectiveness has also been examined in programs for patients with chronic medical illnesses. These interventions focus on teaching patients that, in some diseases, although they cannot influence their illness directly, they can influence and change their attitudes and beliefs towards their illness. Thus diminishing negative emotions, and increasing feelings of control, and improving health-related behaviours.

1.4 Aim of this thesis

The overall aim of the studies in this thesis is to develop and evaluate a psychosocial intervention program for patients with MS. The intervention program is based on cognitive behavioural and rationale-emotive principles and aimed at modifying dysfunctional beliefs, thereby reducing negative emotions, improving adjustment behaviours and ultimately health-related quality of life in patients with MS.

1.5 Research objectives and outline of this thesis

One main research objective is to evaluate the impact of a psychosocial intervention program based on cognitive-behavioural and rational-emotive techniques, for patients
(recently diagnosed) with MS. Primary outcome is health-related quality of life. A second main research objective is to examine the value of health-related quality of life in predicting disability status in patients with multiple sclerosis.

In Chapter 2, a review of the literature on psychosocial group interventions for patients with multiple sclerosis is presented. Chapter 3 describes the development of a psychosocial group intervention program for patients with MS. Chapter 4 reports on the effectiveness of a psychosocial group intervention program for patients with MS, and Chapter 5 addresses the effectiveness of a psychosocial intervention program geared to the individual patient with MS. Chapter 6 describes the value of health-related quality of life in predicting disability status in patients with MS. In Chapter 7, findings described in the previous chapters are discussed, methodological considerations are addressed, and implications for clinical practice and recommendations for future research are presented.
References


The effectiveness of psychosocial interventions for patients with multiple sclerosis: a review of the literature

MAJ Visschedijk

Submitted
CHAPTER 2

Abstract

Objective – The uncontrollable and unpredictable nature of multiple sclerosis may have great psychological impact; therefore, the management of multiple sclerosis should not be restricted to medical treatment but should also include psychosocial interventions. This review describes what psychosocial interventions can offer to patients with multiple sclerosis.

Methods – A literature search on the effect of such interventions was conducted using Medline and PsychInfo, including studies published from January 1953 through November 2005. Applying strict inclusion criteria, a total of 13 studies were eventually identified and analysed.

Results – These intervention studies were grouped, described and evaluated; four interventions were primarily based on cognitive-behavioural therapy, two interventions were based on psychotherapy, two aimed at relaxation training, one aimed at teaching coping skills, one peer support program, and three interventions incorporated more than one treatment technique (e.g. multi-component program).

Conclusion – Psychosocial intervention studies for patients with MS are effective, especially with regard to improving patients’ well-being, coping behaviour, state anxiety, mood, role performance, social relations, some physical aspects, and adherence to medical treatment.
2.1 Introduction

MS has a potentially devastating impact on a person’s physical, psychological and social functioning. Foremost among the factors that make MS a difficult condition to cope with are the range and severity of the symptoms, the capricious disease process, and the psychological uncertainty that accompanies such an unpredictable illness. The disease has an enormous impact on family and social life. About 50-75% of the families studied report marital conflict, difficulty performing usual family responsibilities, and distressed parent-child relationships.\cite{1,2} Social isolation is common. One study found that 40% of people with MS spent most of their days alone,\cite{1} and another that 35% of people had contact with friends less than once a month;\cite{3} many people restrict their social activities to conserve their energy. It is therefore not surprising that emotional problems are common among people with MS.\cite{4,5} Over the past 20 years there has been growing interest in the psychological aspects of MS, resulting in an increase in the number of people with MS being referred for psychological evaluation and treatment.\cite{6}

Up to now no clear overview is available of studies on the effects of psychosocial interventions for patients with MS. A recent literature review focused on the empirical literature related to clinical health psychology in MS, and several psychological interventions were briefly described.\cite{8}

The aim of the present review is to investigate the effectiveness of psychosocial intervention studies for patients with MS. The studies are grouped according to the type of intervention used and, when possible, an extensive description of the content of the intervention is given. Additionally, comments on the studies are given and suggestions for future research on psychosocial interventions for patients with MS are presented.

2.2 Method

A literature research was performed using the computerized databases PubMed (indexed for Medline) and PsychInfo, limited to English articles published in peer-reviewed journals from January 1953 through November 2005; cross-indexing by 1) multiple sclerosis, 2) coping, 3) psychotherapy, psychotherapies, therapies, treatment(s), cognitive-behaviour therapy, CBT, counseling, intervention(s), therapy, therapies, group, cognitive therapy, program evaluation, behaviour therapy. After applying these selection criteria, the literature search yielded 255 articles. Of these, 34 were excluded because they were written in a language other than English, leaving 221 articles for further analysis. Further inclusion criteria were: I) psychosocial intervention study, II) adult patients, III) diagnosis of ‘definite’ MS, IV) non-drug, and non-medical treatment strategies, and V) at least psychological outcome measures. The one exclusion criterion was I) lack of
quantitative data. These six criteria lead to the exclusion of another 204 studies, which examined topics other than psychosocial intervention studies for patients with MS (for example, they concerned questionnaire studies, couple coping studies, neuropsychological issues, and the testing of psychological models in patients with MS). Three psychosocial intervention studies were excluded because they lacked quantitative data, two of them were conducted in 1953 and one in 1960, and one study was excluded because of methodological illegibility (for example, it was unclear how many patients were assigned to the intervention group and the control group). This resulted in the inclusion of 13 intervention studies that were further analyzed regarding the design, sample size, patient characteristics, and outcome measures (psychological parameters and eventually medical outcome measures).

2.3 Results

Table 1 presents an overview of the 13 studies on psychosocial interventions; these are described below and grouped by type of intervention.

2.3.1 Cognitive-behavioural therapy
Central to cognitive-behavioural therapy (CBT) is the assumption that behaviour and emotions are in constant interactions with cognitions. These cognitions (or beliefs) may be inaccurate, leading to excessive emotional reactions and a failure to cope effectively. The aim of cognitive therapy is to help patients identify their dysfunctional cognitions, test them against reality, and alter them, thereby modifying emotional disturbances and improving coping behaviour. CBT was originally developed to treat depression and anxiety,[9,10] and in the last decades its effectiveness has also been examined in programs for patients with chronic medical illnesses.[11-13] The application of CBT has successfully been widened to different areas of health behaviour change[14-15] and is increasingly applied within medical settings.[16] In psychosocial interventions for patients with MS it is the most frequently used method; in four studies it was the main ingredient of the intervention[17-20] and in four studies[21-23] it was part of a multi-component program. These latter studies will be described in the paragraph ‘Multi-component program’.

The first study mainly based on CBT included 19 patients who were randomly assigned to the intervention group or to the waiting-list control group[24] Nine patients underwent a six-week group CBT program and were compared with 10 (waiting-list) control patients. Subjects who were allocated to the CBT program, received weekly 1.5 hour sessions of treatment for six weeks in a group format. One therapist (a graduate student with several years of experience working with MS patients) conducted all treatment sessions. The first two sessions focused on behavioural aspects and from
sessions 3 through 6 cognitive therapy was given increasing emphasis. The aim of the behavioural element of the treatment program was to increase the frequency, quality, and range of activities and social interactions. The aim of the cognitive aspect of the treatment was to identify depressogenic and distorted cognitions and irrational beliefs, to subject these cognitions and beliefs to logical analysis and empirical testing, and to help patients think more realistically and more positively. The outcome measures: the Beck Depression Inventory (BDI), the Hamilton Rating Scale (HRS), the Mood Ratings (specifically developed for the study and designed to rate mood experienced during the day), and the Significant Other Rating Scale (also specifically developed and designed to enable a rating of overt signs of depression to be made by a significant other) were all aimed at assessing depression. The outcome measures were administered at pre- and directly post-treatment and at a one-month follow-up. Results show a significant reduction in depression for patients in the CBT group directly post-treatment, which remained stable at one-month follow-up.

The second study included 32 patients who were randomly assigned to either an 8-weekly telephone-administered CBT or to a control group receiving ‘usual care’.[8] Patients spoke with a therapist during weekly 50-minute sessions over 8 weeks, and the therapists were three advanced-level students in Psychology and one postgraduate fellow. All therapists had several years of experience working with MS patients. During the first session the principles of CBT were described and during the first two sessions the emphasis was on setting goals. In the sessions 2 through 5 the patients learned how to identify cognitive distortions and how to challenge these distortions. Additional modules were available including increasing pleasant events, and fatigue management. The Depression-Dejection scale of the Profile of Mood States (POMS) measured depressive symptomatology at pre- and directly post-treatment and adherence to medical treatment (e.g. INF-β) was measured 6 months after start of the INF-β treatment. Results indicate that patients in the intervention condition are significantly less depressed and show better adherence to INF-β treatment than patients receiving usual care.

The third study using CBT included 63 patients who were randomly assigned to three treatment conditions; 20 patients received individual CBT, 21 patients received supportive-expressive group therapy (SEG), and 22 patients received treatment with Sertraline (an antidepressant).[10] Each treatment was administered over 16 weekly sessions. A waiting period served to exclude patients whose depression spontaneously remitted, and also served as a blocking period for assigning patients to a treatment condition. In the CBT condition patients met individually for 50 minutes with a therapist once per week for 16 weeks. This treatment included both the behavioural activation and cognitive restructuring procedures common to most forms of CBT for depression. In addition, this CBT model taught specific skills for the management of MS-related symptoms and problems, including fatigue, pain and stress management, management of mild cognitive impairment, skills for intimacy, communication and sexual dysfunction,
and management of social difficulties secondary to MS impairments. Therapists did not facilitate or encourage emotional expression or arousal. Therapists were instructed to use CBT techniques to help patients manage arousal and distressing feelings. In the SEG condition, groups of 5 to 9 patients and two therapists met for 16 weekly 90-minute sessions. SEG facilitates emotional expression, particularly related to MS and the social and personal sequelae of the disease. Interpersonal group processes are fostered and used as a vehicle for change. Specific discussions on coping strategies were not initiated by the therapists but were also not actively discouraged if brought up by the patients. Treatment with Sertraline was initiated at 50 mg per day. At each visit, all side effects and level of depression were assessed by a psychologist. This assessment was performed by the psychologist rather than the neurologist to ensure adequate assessment of depression that would facilitate optimal dosing. The dosage was increased by 50 mg every 4 weeks until a maximum dosage of 200 mg was reached or until full remission was achieved as judged by the clinicians. Neurologists and psychologists discussed issues related to the medication and side effects; in all instances neurologists and psychologists maintained an empathetic stance and refrained from any other suggestions regarding general coping. Participant visits were approximately 10-15 minutes every 4 weeks. Various psychological and neuropsychological assessment measures were used as screening and outcome measure. Two psychological outcome measures were used, namely the BDI and the HRS. They assessed depression at 6 measurement points: pre-treatment followed by 3 measurements with an interval of 4 weeks during treatment, directly post-treatment, and at 6 months post-treatment. Results show that there was a significant difference on the BDI between the three treatments, with CBT and Sertraline being the most effective.

The fourth study concerns a pilot study which included 11 patients to investigate the feasibility of a CBT group program and focused mainly on the development of the CBT program. The first version of the intervention was administered over 9 group sessions of 2 hours every 2 weeks. The first 6 sessions addressed an MS specific topic, for example ‘Diagnosis MS and psychosocial problems’ or ‘MS and the future’, and sessions 7 to 9 were not allocated to any particular themes. Relaxation exercises and homework assignments were an additional part of each session. The second, and final, version of the CBT program consisted of 8 two-hour sessions each addressing a particular theme; in the first 3 sessions the rationale of CBT was explained and patients learned to work according to the CBT principles. Relaxation exercises were not included in the second version of the program. Two psychologists conducted both versions of the intervention. To assess health-related quality of life (HRQoL) two self-administered questionnaires were used: the DIP (Disability and Impact Profile) and the SF-36 (Short Form-36 Health Survey). Measurements took place pre-treatment, directly post-treatment, 6 months post-treatment, and 12 months post-treatment. Results show that the intervention program was effective and feasible; there was a statistically significant improvement in two of the HRQoL domains.
2.3.2 Psychotherapy

Although psychotherapy can be used as a generic term for psychological interventions, it is often used for ‘long-term’ intervention programs as opposed to, for example, CBT programs, which are often short-term programs. Long-term psychotherapy interventions are, for example, psychoanalysis and client-centred therapy; the basis of these interventions is previous experiences of the patients. In two intervention studies psychotherapy was used to help adjustment to MS.

In the first study, 32 inpatients at a large hospital were included and matched into triads and then randomly assigned to one of three groups: a) group psychotherapy, b) current events group, or c) non-treatment control group.[244] The emphasis in the psychotherapy group was insight-oriented, patients being actively encouraged to verbalize and confront issues of conflict. The current events group focused on discussions of newsworthy topics of a didactic or humorous type with care being taken to discourage verbalizations of an emotional or personal nature. Both the psychotherapy and the current events groups met twice weekly for 50 sessions of 1 hour each. During this period the control group received no treatment, and at the end of 50 sessions, treatment was made available for everyone participating in the study. Patients were assessed at pre-treatment and directly post-treatment. Four psychometric instruments were employed: depression was measured by the Minnesota Multiphasic Personality Inventory (MMPI), anxiety was ascertained by the Institute for Personality and Ability Testing Anxiety Scale Questionnaire (ASQ), locus of control was measured by the Adult Novicki-Strickland Internal-External Control Scale (IECS) and self-concept was determined by use of the Rosenberg Self-Esteem Scale (SES). Significant improvements were found for depression and locus of control; the psychotherapy group was less depressed than the current events group and the control group, and both the psychotherapy and current events group were more internally oriented than the control group.

In the second study, 70 patients were included; 46 chose to go to group psychotherapy and 24 received no psychological treatment.[245] The focus of the psychotherapy was client-centered with psychodrama, and patients met for 1 year on a weekly basis. As a preparation for the actual 1-year therapy, during a period of 3 months, patients received autogenic relaxation training. A group was led by one therapist, who had continuous psychoanalytic supervision. By means of in-depth interviews and a German personality test (the Giessen test), measurement of the patients’ professional and health situations and of relationships with family and friends took place at 4 time points: at the beginning of the therapy, twice during therapy, and at the end of therapy. Two years after the end of therapy, a follow-up was carried out using the Questionnaire on Assessing Changes in Experience and Behavior and a checklist of symptoms. Furthermore, the content from the written record of the taped interviews was scored and content analysis scales of verbal behaviour were assessed. Results showed significant improvements in the
therapy group compared with the control group for social relations, activities and for some physical performance capacities. The 2-year follow-up showed that the therapy group had a significantly more positive judgement of the changes that happened in the past 2 years, a tendency towards a lower general symptomatic handicap, and a significantly lower impairment in anxiety, depressed thoughts, inner tensions, feelings of freezing, headache, lack of energy and lack of appetite.

2.3.3 Relaxation
In order to manage the stress that is related to chronic illness, relaxation methods have been developed. For example, it was proposed that autogenic training (AT), were effective in counteracting many psychosocial problems associated with chronic illness.\textsuperscript{[20]} Two studies were identified focusing on relaxation techniques; in the first study 33 patients participated with 15 in the treatment group and 18 in the control group (receiving only standard medical care).\textsuperscript{[21]} Treatment consisted of 6 group sessions aimed at relaxation through biologically oriented imagery. Imagery is a psychological process that invokes and uses the senses, and which mediates the communication between perception, emotion, and bodily change. Imagery as a mind-body treatment intervention makes use of this communication process to facilitate psychophysiological or emotional changes. It is a technique that affects immune system functions and lessens stress through a decrease in sympathetic arousal.\textsuperscript{[22]} Imagery group patients participated in 6 one-hour sessions that involved the use of general, progressive relaxation training in the first session, and a biologically oriented imagery treatment process for MS in subsequent sessions. In this process the subjects focused on developing relaxation and imagining repair of damaged myelin as well as positive immune system responses. Imagery group subjects were provided with audiotapes of the relaxation and imagery protocols at the conclusion of the second group session, and were asked to practice the imagery protocol on a daily basis for the remainder of the study. Participants were assessed at pre-treatment and at post-treatment and the following measures were used: the Profile of Mood States (POMS), the State-Trait Anxiety Inventory (STAI), and the Health Attribution Test (HAT). An MS Symptom Checklist was developed and derived from the literature of the Multiple Sclerosis Foundation and imagery protocols were analyzed using a specialized analyzing system. Results showed that patients in the treatment group experienced significantly less state anxiety, experienced a more internal control of health, and experienced a positive alteration in their illness imagery.

The second study included 22 patients of which 11 were randomly assigned to 10 weeks of autogenic (relaxation) group training (AT) and 11 to a control group.\textsuperscript{[23]} In AT, an autogenic technique derived in the 1950s, the individual passively concentrates on physiologically-oriented phrases in order to bring about sensations associated with the relaxation response.\textsuperscript{[24]} The AT program consisted of one supervised training session per week for 10 weeks. The course of the AT program was incremental. In the first session, the
instructor introduced the participants to AT and the first two AT formulas (heaviness and warmth in the limbs) were introduced. Every two weeks, the other AT formulas (cardiac regulation, respiratory control and abdominal warmth and coolness of the forehead) were introduced. The participants were also asked to practice regularly (once a day) for the intervention period and record their practice and experiences in a preprinted diary. For the patients in the control group, there was no contact other than to remind them to return the questionnaires. Measurements took place at pre-intervention and at week 8 of the 10-week training program, and the following instruments were used: the Multiple Sclerosis Quality of Life Instrument (MSQOL) to assess health-related quality of life, the Profile of Mood States-Short Form (POMS-SF) to measure affective states, the Centre for Epidemiological Studies Depression Scale (CES-D) to assess depressive symptoms, and the Multidimensional Scale of Perceived Social Support (MSPSS) was used to measure social support. This latter questionnaire was only used as a statistical control for the potential positive benefits of social interaction that may be derived from participation in an intervention program in a group setting. Results, measured in effect sizes, showed some improvements of HRQoL and affect (two subscales of the POMS and CES-D), in favour of the intervention group.

2.3.4 Coping skills
Schwartz conducted a large intervention study aimed at teaching coping skills.[51] Coping skills programs are intended to help patients adapt to their altered life situation by teaching them behavioural and cognitive alternatives for certain situations in order to facilitate the use of a more effective coping style. In that randomized controlled study 132 patients participated; 64 received an 8-week coping skills group training and 68 received peer telephone support. The coping skills group was led by a health professional with a background in public health and clinical psychology, the group met for 8 weekly sessions of 2 hours each. Patients were taught various ways of dealing with some of the problems frequently faced by people with MS. Besides addressing the emotional difficulties faced by patients, the group also discussed alternative approaches to goal setting, specific strategies for dealing with cognitive deficits, and ways of improving communication with caregivers. Participants were requested to bring a support person (e.g. spouse, close friend, or relative) to the 3 sessions focused on improving communication with one’s social network, and support people were welcome to attend all sessions. At the end of the 8 weeks, group participants were matched with coping partners from the group and they were invited to telephone each other monthly for 10 months. The second intervention, peer telephone support, offered nondirective support by hired lay people with MS who were trained in active listening. The supporters called their case load (5 to 15 patients, depending on the supporters availability) monthly for one year. Phone calls should not last more than 15 minutes on average and the supporter must not give advice. The therapeutic technique is based on Rogerian client-centred psychotherapy, where the supporter reflects on what the
participant has said but does not give advice. The goal is to foster an attitudinal condition such that the individual can find the capacity and the strength to gain insight into and to cope with problems. Assessments took place 5 times during a 2-year period; pre-intervention, and at 2, 12, 18, and 24 months after the intervention. Role performance was measured by the Sickness Impact Profile (SIP) and the Multidimensional Assessment of Fatigue scale, adaptability was measured with the MS Self-Efficacy (MSSE) Function and Control subscales, the Internal subscale of the Multidimensional Health Locus of Control (MHLC) scales, and relative profile scores of the Ways of Coping Questionnaire (WCCC). Well-being was measured with the Arthritis Impact Measurement Scales (AIMS), the Quality of Life Index, and the Ryff Happiness Scale. This study suggests that the coping skills group intervention yielded significant gains over time in psychosocial role performance, coping behaviour, and numerous aspects of well-being. However, the peer telephone support intervention seemed most effective for patients with affective problems.

2.3.5 Peer support

Peer support groups differ from professional-guided psychotherapy groups in reflecting the assumption that the sharing of experiences with others in a similar situation can be of value without the presence of a health care professional. These groups are most commonly comprised of a diagnostically homogeneous group of patients without a facilitator (or the facilitator is a nonprofessional peer). The idea is that through the opportunity to share experiential knowledge, members of the group collectively seek strategies that enable them to cope more effectively with the stresses imposed by their illness and that during that process of sharing knowledge, group members themselves, in helping others, become experts.

Messner et al. conducted a peer support group intervention with 42 patients. The initial meeting was used to determine topics, followed by participants voting on a topic to discuss during the subsequent meetings. The topics most frequently chosen included family issues, employment, coping with MS, therapies and symptom management. During each subsequent group meeting, participants’ discussion focused on the pre-selected topic. Each group organizer participated in a one-day training course which addressed important issues concerning the organization of the support groups, for example information on how to get the first meeting started, basic group rules, active listening skills and suggestions for resolving problems that may arise during group meetings. Measurements of health-related quality of life (MSQOL-54), and depression (Beck Depression Inventory) took place prior to the initial meeting and at the end of the final meeting. Results showed no significant changes on the questionnaires.
2.3.6 Multi-component program
Three psychosocial interventions for patients with MS combined several treatment methods, for example stress reduction training combined with cognitive-behavioural techniques and exercises that influence body image.19-23

The first study included 54 patients of which 23 followed a group training that incorporated relaxation techniques and cognitive-behavioural strategies.20 Group sessions were scheduled once a week over 10 weeks with a follow-up of 3 sessions after a 6-week respite. The participants were provided a basic working knowledge of techniques for stress reduction and the opportunity to practice during sessions. Relaxation, cognitive and behavioural strategies were incorporated into the curriculum. The POMS was employed as the primary test set and was administered pre- and directly post-treatment. Results of the group training were compared with 21 controls who did not receive the training. Results showed a significant decrease in scores on depression and anxiety and a significant increase on vigour in favour of the intervention group.

The second study included 36 patients of which 18 were randomly assigned to an individually administered stress-inoculation training based on cognitive-behavioural principles.21 The other 18 patients served as control group and were told that the stress-inoculation training would be available in 5 weeks time. During the waiting period they received ‘treatment as usual’ which meant that all control patients received supportive psychotherapy and, in addition, 7 control patients received psychotherapeutic or medical treatments. The intervention included 6 sessions of CBT integrated with progressive deep-muscle relaxation training. Session 1 trained patients to self-monitor daily stressors and concomitant cognitive, behavioural, affective, and physiological responses. Session 2 included feedback to enhance self-monitoring and the construction of a personalized progressive deep-muscle relaxation (PDMR) tape. Session 3 evaluated cognitive self-statements in response to daily stressors. Session 4 identified stress cues to augment the in vivo use of cognitive reinterpretations, relaxation imagery, and PDMR. Sessions 5 and 6 focused on role playing how to cope with potentially distressing situations while integrating the self-monitoring, self-cueing, cognitive-behavioural, and physiological coping skills. Included measures were the BDI, the State-Trait Anxiety Inventory (STAI), the Hassles Scale (HS), the Rotter’s Internal-External Locus of Control Scale (RI-ECLS), and the Problem-focused coping subscale of the Ways of Coping Checklist (WCC). These questionnaires were administered pre-treatment, directly post-treatment and at a 6-months follow-up. Results show that patients in the intervention group had a significant reduction in depression, a significant reduction in state-anxiety, a significant reduction in daily stressors, and a significant reduction in problem-focused coping compared to patients in the control group. These results were maintained throughout the follow-up period of 6 months.

The third study, using a multi-component program included 29 patients; 14 in the intervention group and 15 controls.22 Patients were pseudo-randomized; the first 15
patients who visited the clinic were asked if they were interested to participate in psychological group therapy and the control group was formed out of the next 15 patients who visited the clinic. The intervention consisted of 7 weekly sessions and the therapies included in the treatment program were cognitive-behavioural strategies, elements of stress-coping training and specialized exercises that exert an influence on body image and body experience. Session 1 was an introductory session in which patients were informed of group rules, disease processes and treatment methods. Session 2 included a discussion on the psychophysiological consequences of the disease and the role of stress. Other activities included the conscious planning of pleasant events, and the first set of exercises for muscle relaxation is carried out and combined with imagination exercises (inner pictures of nature). Session 3 included a more in-depth discussion of the topic of stress, role playing, forms of coping, and the use of distraction strategies. Session 4 started with a discussion on the consequences of the disease, in particular, coping with illness-dependent role changes, coping with negative reactions from the environment and role playing, followed by exercises to allow the building of greater self-esteem. Session 5 repeated the discussion on coping strategies for dealing with stress and illness-dependent stress factors, followed by exercises that included body awareness and self-representation. Session 6 included exercises to improve consciousness of one’s body. Session 7 was a concluding session with oral and written evaluation of the program. The BDI, the Body image questionnaire (FKB-20), the Freiburg disease coping questionnaire (FKV-LIS SE), the STAI, and a questionnaire for therapy evaluation were assessed at pre-treatment, directly post-treatment, and at 2-months follow-up. Results show a significant reduction in BDI scores for the intervention group, and a significant time by treatment improvement in ‘depressive coping style’ and in ‘vitality and body dynamics’ in favour of patients in the intervention group.
Table 1 Overview of the psychosocial intervention studies for patients with multiple sclerosis (1953-2005) included in this review

<table>
<thead>
<tr>
<th>Ref. No.</th>
<th>Study design</th>
<th>No. of patients; sex (f/m)</th>
<th>MS type&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Years since diagnosis</th>
<th>No. of controls; sex (f/m)</th>
<th>Kind of controls</th>
<th>Intervention type(s)</th>
<th>Evaluation&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Outcome&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>Randomized-controlled</td>
<td>7/2; 7/2</td>
<td>-</td>
<td>-</td>
<td>10; 6/4</td>
<td>Waiting-list</td>
<td>Cognitive behaviour therapy</td>
<td>BDI, HRS, Mood ratings, Significant other Rating Scale</td>
<td>Significant improvement on 4 questionnaires for Time, Significant Time x Treatment interaction on 4 questionnaires</td>
</tr>
<tr>
<td>24</td>
<td>Matched-controlled</td>
<td>52 in total study; 19/13</td>
<td>-</td>
<td>-</td>
<td>Unclear Matched-control</td>
<td>Group Psychotherapy, Current Events Group, and Non-treatment controls</td>
<td>SES, ASQ, HCSC, D-30</td>
<td>Significant improvement on 2 questionnaires in favour of the psychotherapy group</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Matched-controlled</td>
<td>23; 13/10</td>
<td>-</td>
<td>-</td>
<td>21; 10/11 Matched-control</td>
<td>Relaxation group training with cognitive behavioural strategies</td>
<td>POMS</td>
<td>Significant improvement on 3 of 4 subscales</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Randomized-controlled</td>
<td>38 in total study; 31/5</td>
<td>-</td>
<td>-</td>
<td>Unclear Waiting-list</td>
<td>Individual stress inoculation training with cognitive behavioural techniques</td>
<td>BDI, STAI, WCCC, HSIS</td>
<td>Significant Time x Treatment interaction on 4 questionnaires</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>Randomized-controlled</td>
<td>15; 13/2</td>
<td>-</td>
<td>-</td>
<td>18; 12/5 Completely randomized</td>
<td>Imagery and relaxation group training</td>
<td>POMS, STAI, HAT, MS Symptom Checklist, IAT</td>
<td>Significant Time x Treatment interaction on 3 questionnaires</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>Randomized-controlled</td>
<td>64; 46/22 RR and PP 8.6 (± 6.4) 4.7 (± 1.8)</td>
<td>-</td>
<td>-</td>
<td>68; 52/12 Completely randomized</td>
<td>Coping skills group and Peer telephone support</td>
<td>Neuropsychological measures, SIP, MSSE, MHL, WCCC, AIMS, QLI, RHS</td>
<td>Four significant Time x Treatment interactions, Several significant improvements within both intervention groups</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> MS type: RR, PP

<sup>b</sup> Evaluation: BDI, HRS, Mood ratings, Other Rating Scale

<sup>c</sup> Outcome: Significant improvement on 4 questionnaires for Time, Significant Time x Treatment interaction on 4 questionnaires
<table>
<thead>
<tr>
<th>Ref. No.</th>
<th>Study design</th>
<th>No. of patients; sex (f/m)</th>
<th>MS type(^a)</th>
<th>Years since diagnosis</th>
<th>Disability status(^a)</th>
<th>No. of controls; sex (f/m)</th>
<th>Kind of controls</th>
<th>Intervention type(s)</th>
<th>Evaluation(^3)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>Randomized-controlled</td>
<td>16; 10/6 RR</td>
<td>6.1 (± 6.6)</td>
<td>16; 13/3 Completely randomized</td>
<td>Cognitive behavioural therapy by telephone</td>
<td>POMS, Cognitive functioning, Neurological functioning</td>
<td>Significant Time x Treatment on 1 questionnaire</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Randomized-controlled</td>
<td>46; 34/12 - 5.8 -</td>
<td>24; 18/6 Pseudo-randomized</td>
<td>Client-centred, Psychodrama</td>
<td>In-depth interviews</td>
<td>Significant improvement in social relations, handling of aggression and in physical performance capacities for therapy group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Randomized-controlled</td>
<td>63 in total study; 46/17 RM and SP</td>
<td>7.7 (± 3.5-31.2)</td>
<td>Three interventions with resp 20/21/22 participants per group, Pseudo randomized</td>
<td>Individual cognitive behavioural therapy, Supportive-expressive group therapy, Treatment with Sertraline</td>
<td>BDI, HRSD, SCID, LFE-H, Neuropsychological screening measures</td>
<td>Significant improvement on 1 questionnaire for all treatment groups with CBT and Sertraline being the most effective</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Randomized-controlled</td>
<td>14; 12/2 - 5.1 (± 1.3) 3.2 (± 1.3)</td>
<td>15; 13/2 Pseudo randomized</td>
<td>Behavioural, Stress-coping, Body image</td>
<td>BDI, FKB-20, FKV-LIS SE, STAI, Evaluation form</td>
<td>Significant improvement on 3 questionnaires within therapy group, Significant Time x Treatment interaction on 2 questionnaires</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>Case study</td>
<td>44; 26/18 RR</td>
<td>6.9 (± 6.14) -</td>
<td>Peer support group</td>
<td>MSQoL-54, BDI</td>
<td>No significant changes on 2 questionnaires</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Case (pilot) study</td>
<td>11; 8/3 RR</td>
<td>5.2 3.3 (2.0-4.0)</td>
<td>Cognitive behavioural</td>
<td>DIP, SF-36</td>
<td>Significant improvement on 2 questionnaires</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>Randomized-controlled</td>
<td>11; 7/4 - 9.36 (± 6.28) -</td>
<td>11; 9/2 Completely randomized</td>
<td>Relaxation intervention</td>
<td>MSQoL, POMS-SF, CES-D, MSPSS</td>
<td>Significant improvement on 2 questionnaires</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(1) MS type most frequently reported. (2) According to the Expanded Disability Status Scale. (3) Abbreviations are given in the Results section. (4) According to Guy's Neurological Disability Scale.
2.4 Discussion

The aim of this study was to group, describe and evaluate psychosocial interventions for patients with MS. Thirteen studies were established; four interventions primarily based on cognitive-behavioural therapy, two interventions based on psychotherapy, two aimed at relaxation training, one aimed at teaching coping skills, one peer support program, and three interventions that incorporated more than one treatment technique (e.g. multi-component programs). When investigating the studies that included a control group, only four studies were completely randomized.[18,27,29,31] These studies, evaluating three different intervention types, reported several significant improvements in favour of the patients in the intervention group, for example a significant improvement in psychosocial role performance, coping behaviour, state anxiety and numerous aspects of well-being, significantly less depression and a significantly better adherence to INF-β treatment. Furthermore, patients in the intervention groups experienced a more internal control of health, and experienced a positive alteration in their illness imagery HRQoL. Another seven studies included a control group; however these controls were not strictly randomized: constructions like a waiting-list control group,[27,28] a control group comprised of patients that were assigned to it following order of inclusion,[16,23] or a control group comprised of patients who chose not to join the intervention[25] were used. Results of these studies showed, for example, significant improvements in depression and mood, significant positive changes in social relations, own activities and for some physical performance capacities, as well as significant improvements in ‘vitality and body dynamics’. The remaining two studies included no control group and were so-called ‘pilot studies’; they described preliminary results in a large intervention study.[20,32] One of these studies showed a significant improvement in HRQoL.

Some methodological comments on these studies can be made. First, conclusions drawn without incorporating a control group should be interpreted with caution. Reported improvements are otherwise probably due to practice effects. Two studies incorporated a waiting-list control group; however, a control group that receives another intervention without overlap with the treatment, to control for the positive attention the patients received, is preferable. However, sometimes ethical or practical reasons prevented the investigators from comprising a strictly randomized control group.[20] Furthermore, it is debatable how appropriate it is to conduct randomized controlled trials (RCTs) of psychological interventions at all. This mainly has to do with the fact that in practice isolated therapies are seldom used and treatment plans are individualized to patients as complex self-management plans. Evaluation using an RCT in the clinical setting may mean that the intervention is so tightly controlled that, even if effectiveness were proven, it might be difficult to transfer the intervention into routine clinical practice.
CHAPTER 2

The second limitation involves a frequent lack of detailed information regarding sample characteristics, outcome measures, and the psychosocial intervention itself. This makes it difficult to replicate the intervention study and reproduce its findings. Third, follow-up measurements should be included to discern different patterns over time for the intervention and the control group. In addition, long-term effects of the intervention can be investigated, which is important because MS is a chronic disease.18-20,31

Fourth, the psychological outcomes examined were numerous and diverse and there seems to be no consensus as to which psychological outcomes are conceptually linked to MS or to the psychological interventions being studied. For example, although a number of studies measured depression as an outcome, the interventions used varied and the depression measurement tools also varied; this prevented any pooled result being analyzed. Careful selection of standardized instruments that resemble the intervention program should also be incorporated. At the same time, outcome measures without overlap with the intervention should be included to give insight into generalization to other functions and everyday life.

Fifth, to investigate the effect of any psychological intervention it is preferable to apply a standardized intervention, although individual differences between patients may challenge the accuracy of the therapist. Multi-component programs give rise to another question; which component or combination of components is most effective for the individual patient?

Besides the above-mentioned comments, several promising results stem from the examined intervention studies. Psychosocial intervention studies for patients with MS can be effective, for example in improving patients’ well-being, coping behaviour, state anxiety, mood, role performance, social relations, some physical aspects (e.g. vitality and body dynamics, physical capacities) and adherence to medical treatment. Furthermore, distinctive types of psychosocial treatment result in (clinically) significant outcomes. For example, cognitive-behavioural therapy, relaxation training, psychotherapy, or combinations of these treatments are proven to be effective.

These results are of clinical importance for patients with MS; they show that psychological problems that can derive from having a chronic and compelling disease like MS can be treated with success. The specialized and efficient treatment of psychological problems in patients with MS can positively affect their quality of life and the quality of life of their families.

To conclude, several effective psychosocial interventions for patients with MS have been developed. However, more research on this subject is necessary and special attention should be paid to methodological issues. For example, the examined studies had a relatively small sample size, and although we should not underestimate what we can learn from small-scale research, larger trials are needed to avoid selection bias and provide sufficient statistical power. Furthermore, psychological interventions can be effective in
many instances; however, not enough is known about selection bias, and the interactions between patient variables, treatment modalities and outcome. Research funding should target the (cost) effectiveness of psychological techniques with a sound theoretical basis applying outcome measurements that are commonly used in clinical practice and that are proven sensitive to the differing needs and rate of improvement of individual patients. By increasing our understanding of the specific effects of indications for psychosocial intervention, the care for patients with MS can be further improved.

Acknowledgements

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References


Development of a cognitive behavioural group intervention program for patients with multiple sclerosis: an exploratory study

MAJ Visschedijk, EH Collette, LEMA Pfennings, CH Polman, HM van der Ploeg

Psychological Reports 2004;95:735-746
Summary

A substantial group of patients with multiple sclerosis (MS) has difficulty coping with their disease. Cognitive behavioural group interventions may help these patients cope more effectively with MS. We developed an eight-session group intervention program for patients recently diagnosed with MS to help them cope more effectively with MS and to overcome negative thoughts and beliefs about the disease in order to improve health-related quality of life. We tested the feasibility of the group intervention program and health-related quality of life in a sample of 11 patients recently diagnosed with MS (mean age: 38 (± 7.9) years; eight women and three men). All patients were recruited through direct referral by their neurologist or by an MS nurse specialist. The program was conducted in two small groups of 7 patients each and each group was led by two psychologists. Cognitive behavioural therapy was an important ingredient in each group session as well as sharing of personal experiences and discussing homework assignments. Each session was formatted the same way but addressed a different MS-specific theme, for example ‘coping with physical impairments’ or ‘communication with medical staff’. Participants experienced a significant improvement in the health-related quality of life domains of psychological status and vitality, as measured by subscales of the Disability and Impact Profile and the Short Form-36 Health Survey. Although further studies are warranted, it appears that a short group intervention program based on cognitive behavioural techniques for patients with MS might have a positive influence on health-related quality of life.
3.1 Introduction

Multiple sclerosis (MS) is one of the most common chronic neurological diseases in the western world. It has a prevalence of about 1 per 1000 adults in the USA and Northern Europe with an age of onset between 20 and 40 years. Twice as many women are diagnosed with the disease.[1] MS is characterised by widespread inflammation and demyelination in the central nervous system. Any neurological symptom can occur, but several more common symptoms can be distinguished. These include motor and sensory impairments such as numbness and loss of sensation, difficulty with ambulation, loss of bladder and bowel control, visual problems, sexual dysfunction, fatigue and decline of cognitive function. In general, MS has a progressive course, resulting in accumulating disability over the years. However, considerable differences in progression rate are found within the MS population and despite knowledge on several factors associated with prognosis, reliable predictions on progression rate for individual patients are still difficult to make.[2]

3.1.1 Psychological consequences

The diagnosis of MS has a great impact on a person’s life and may have major psychological consequences for the patient and their family.[3] Initially, a confirmed diagnosis ends a period of uncertainty and is often accompanied by relief that there is no life-threatening illness. Later, thoughts and feelings about diminished health can become profound and many patients then experience uncertainty about the course of their MS and whether earlier personal life plans can be fulfilled. Because of the progressive nature of MS, coping with the disease is an ongoing process. Many patients with MS experience emotional problems, and mood disorders (especially depression) are frequently concomitant with other MS symptoms.[4-9] Minden and Schiffer[5] reviewed studies using reliable and valid methods of measurement of depression and reported point prevalence rates of 27-54% for patients with MS, a rate that is approximately three times that in the general population and higher than found in other medical neurological illnesses.[10]

Anxiety disorders, although less well studied, also occur regularly in the MS population,[11] and significant emotional distress occurs in up to 64% of the patients.[12] Therefore, MS patients often seek professional help to cope with the disease and its consequences.

To assist patients in learning to cope with MS, we developed a group intervention program aimed at enhancing coping skills and improving health-related quality of life (HRQoL). A group program was developed because of the known advantages of a group format (e.g. patients can share experiences and a group format is more cost-effective). Group intervention programs have been developed for numerous (chronic) medical illnesses,[13-17] and, mainly in the last decade, studies also have focused on the effects of psychosocial group interventions for patients with MS.[18-23]
3.1.2 Cognitive behavioural therapy

One of the main elements in our group program is cognitive behavioural therapy, originally developed by A.T. Beck.\textsuperscript{24} Central to cognitive behavioural therapy is the assumption that a person’s emotional problems are often founded in a system of dysfunctional or ‘distorted’ beliefs about themselves or their environment. These core beliefs generate negative automatic thoughts, that are easily triggered and often contain some sort of cognitive distortion such as “mind reading”, “magnifying”, “over-generalisation”, “personalisation”, and “all-or-nothing thinking”.\textsuperscript{25} Holding such negative beliefs causes feelings of fear, anger, and soon resulting in dysfunctional coping behaviours.\textsuperscript{26,27} Cognitive behavioural therapy aims to help patients identify and change or reframe their dysfunctional beliefs into more functional beliefs. Examples of dysfunctional beliefs in patients with MS are: “If I can’t live my life like a healthy person, then it’s not worth living”, or, “I am a bad mother/father, because I have MS.” Cognitive behavioural therapy has proven effective in the treatment of mood and anxiety disorders, and in the last decades its effectiveness has also been examined in programs for patients with chronic medical illnesses.\textsuperscript{18,28-31} These interventions focus on teaching patients that, in some diseases, although they cannot influence their illness directly, they can influence and change their attitudes and beliefs towards their illness. Thus diminishing negative emotions, and increasing feelings of control, and improving health-related behaviours. Therefore, it was hypothesized that cognitive behavioural therapy will help patients with MS to cope more effectively with the consequences of their disease.

We developed the intervention program within the scope of the MS Centre at the Vrije Universiteit University medical centre (Amsterdam) and based on our experience with psychosocial group interventions for patients with medical illnesses, such as type 1 diabetes mellitus and Parkinson’s disease, as well as our experience in counseling patients with MS. The development of the group program evolved from the need of recently diagnosed patients with MS to receive further assistance in coping with the psychological consequences of MS.

In this study, the main research question was: “What is the effect of a group intervention program based on cognitive behavioural principles, on HRQoL in patients with MS?” In addressing this question, the first step was to develop a group intervention program and investigate its feasibility and effects in a small pilot sample of patients. This article describes the first two versions of the intervention program and presents preliminary results concerning its feasibility and its effect on patients’ HRQoL.
3.2 Method

3.2.1 The intervention program
3.2.1.a First version
We designed the intervention program to be conducted in small groups (6-8 per group) of patients with recently diagnosed MS (diagnosis “definite MS” within the previous three years). The rationale to design a program for this group was based on the high level of distress and uncertainty experienced by these patients. Furthermore, many of these patients have a need for more contact with care providers and more assistance in coping with MS.

The first version of the intervention program initially consisted of six two-hour sessions of group therapy; after the fifth session, however, it was decided that three more sessions were needed. Sessions took place on a two-weekly basis and each session was based on a theme considered relevant for patients with MS. Two psychologists led each session. In the first program the session themes were: (1) Diagnosis MS and psychosocial problems, (2) Coping with fatigue and other symptoms, (3) Illness perception and illness behaviour, (4) Changing from “a healthy person” into “a person with MS”, (5) Communication with family members and medical staff, (6) MS and the future. Sessions 7 to 9 were not allocated particular themes. Relaxation exercises and homework assignments were an additional part of each session. After completion of all nine sessions, we evaluated the intervention by means of a personal interview with each participant.

3.2.1.b Second version
Based on our experiences with the first version of the program, some minor changes were made for the second version: i.e. the time schedule and some theme titles were altered. The second version consisted of eight two-hour sessions of group therapy with the following themes: (1) Diagnosis MS: How to move on?, (2) Coping with fatigue and other symptoms, (3) Assertivity, (4) Communication with family and friends, (5) Communication with medical staff, (6) Coping with psychological distress, (7) MS and the future: coping with uncertainty and fear, (8) Capita Selecta (one or more topics chosen by the participants).

3.2.2 Procedure
Two studies were performed to investigate the feasibility of the group intervention program, and a pre-post test design was applied to assess the effect of the program on HRQoL in patients recently diagnosed with MS. In both studies, four measurements of HRQoL took place: before the intervention started, immediately post-treatment, and at 6 and 12 months after completing the intervention. Feasibility was determined on the basis of attendance, trainer evaluations, and patient evaluation and satisfaction.
The intervention was delivered in two groups of recently diagnosed MS patients seen in our MS outpatient clinic between February 1999 and June 2000. Patients were recruited through direct referral by their neurologist or by an MS nurse specialist. Before the recruitment started we formulated some inclusion and exclusion criteria. The inclusion criteria were: patients who asked for assistance in dealing with MS, as well as patients who were dealing with themes that would be addressed by the intervention program. Furthermore, patients needed to be recently diagnosed. Which means that only patients who received their diagnosis within the previous three years were approached. The only exclusion criterion was: being confined to a wheelchair (although highly unlikely in patients with recently diagnosed MS). It was assumed that exposure to someone in a wheelchair would be too distressing for the other patients.

3.2.3 Participants
3.2.3.a First group
The first intervention included seven patients, six of whom completed all sessions; one patient dropped out after the fourth session due to a serious exacerbation of MS. This group consisted of four women and two men with an average age of 34 (± 7.1) years. All six patients had a relapsing-remitting form of MS and the mean disability score (measured by the Expanded Disability Status Scale, which is a rating scale ranging from 0 (no disability) to 10 (death due to MS)) was 2.8 (range: 2.0-3.5).

3.2.3.b Second group
The second intervention included seven patients of whom five completed all sessions; one patient dropped out after the second session and another dropped out after the third session, both due to emotional problems caused by intensive exposure to MS. The group consisted of four women and one man with an average age of 42 (± 6.8) years. Three patients had a relapsing-remitting form of MS, one patient had a primary progressive form, and one patient had a secondary progressive form of MS. The mean disability score in this group was 3.3 (range: 2.0–4.0).

3.2.4 Measurements
Before the group intervention started, one of the psychologists invited the patients individually for a semi-structured interview. The patients were asked about their personal history, course of MS, how they function in groups, and what motivated them to participate in the intervention program.

To assess HRQoL the following self-administered questionnaires were used:

- The Dutch version of the Disability and Impact Profile. The Disability and Impact Profile consists of 39 items and was developed as a screening instrument to assess disabilities individually weighted with respect to their relative impact as perceived by the respondent. For each item the degree of (dis)ability is rated on a 0-
10 point scale (0: maximal disability, 10: no disability), and this rating is followed by a request to rate the impact of that particular disability (weight), using the same kind of 0-10 point scale (0: not important at all, 10: most important of all). Higher scores indicate higher levels of, respectively, ability and importance. The Disability and Impact Profile contains three symptom questions, on pain, visible deformities and worry about deterioration, and 36 questions in five domains: Mobility, Self-care, Communication, Social Activities and Psychological Status. The reliability of the Disability and Impact Profile in patients with MS has proven to be acceptable, except for the internal consistency of the four symptoms items. For this study we used items referring to the subscales Mobility, Self-care, and Psychological status, because these items are part of a brief, reliable and valid HRQoL instrument constructed for use in MS patients.

- The Dutch version of the Short Form-36 Health Survey. The Short Form-36 Health Survey was developed for use with both healthy and chronically ill populations and has 36 items divided among eight scales: Physical Functioning, Role-physical Functioning, Bodily Pain, General Health Perceptions, Vitality, Social Functioning, Role-emotional Functioning and Mental Health. Extensive research has shown that it is a valid and reliable instrument. Higher scores indicate higher levels of HRQoL in the corresponding domain. For this study we used items referring to the subscales Physical Functioning, Vitality, and Mental Health, because these scales are part of a brief, reliable and valid HRQoL instrument constructed for use in MS patients.

3.2.5 Statistical analysis
The Wilcoxon Signed-Rank Test was used to compute pre-treatment and immediately post-treatment mean differences in the three subscales of the Disability and Impact Profile (Mobility, Self-care and Psychological Status) and the three subscales of the Short Form-36 Health Survey (Physical Functioning, Vitality and Mental Health). Power was also computed for each pair of variables using Cohen’s (1988) definitions of small, medium, and large effect sizes ($d = 0.20$, $d = 0.50$, $d = 0.80$, respectively).

Because of the small sample size at 6 and 12 months post-treatment ($n = 6$), we computed these results separately. For computing mean differences in this small group the Friedman’s Two-Way Nonparametric Analysis of Variance was used.

For both tests, a $p$-value of 0.05 was considered to be significant.
3.3 Results

3.3.1 Evaluation and feasibility of the program

The intervention was well appreciated by the participants, especially the sessions on assertiveness and communication training. The opportunity to share experiences with other patients was considered an important element of the program, although exposure to others with MS was occasionally burdensome for some patients. All participants in the first group indicated that six sessions were not enough to learn to apply the cognitive behavioural principles. Later, our eight-session program proved to be more satisfying in that participants could complete their homework with less help from the psychologists, and were able to apply cognitive behavioural principles beyond the group setting.

In the first group the two psychologists sometimes had difficulty adhering to the time schedule because participants had a strong need to exchange personal experiences. Therefore, in the second group somewhat more time was allocated for the exchange of experiences and interpersonal contact.

The program proved to be feasible for patients, as demonstrated by the low drop-out rate (two of 14 participants stopped due to emotional problems) and by the fact that all sessions were well-attended (two participants missed one session out of eight sessions).

3.3.2 Questionnaires

When computing the results, both intervention groups were pooled and considered as one group. We did this because both groups were comparable regarding the content of the programs: i.e. most changes in the second program concerned the time schedule whereas the important elements (e.g. cognitive behavioural therapy, homework assignments and exchanging personal experiences) remained the same. Apart from this, 14 patients in one group is not desirable: most group therapists prefer 6-8 persons in one group, otherwise there is too little time and attention for each individual member.

Table 1 gives data on pre-treatment and immediate post-treatment measurements for the 11 patients who completed the intervention. There were no significant changes in scores on the Disability and Impact Profile subscales Mobility and Self-care whereas the score on Psychological Status showed a slight but statistically significant improvement ($p = 0.013$). For the subscales of the Short Form-36 Health Survey there were no significant changes in scores on Physical Functioning and Mental Health, but there was a statistically significant improvement on the Vitality score ($p = 0.044$). Effect sizes (Cohen’s $d$) were also computed and results show small and medium effects for the test pairs.
Table 1 Nonparametric test for the comparison of means for subscales of the Disability and Impact Profile and the Short Form-36 Health Survey before and after the group intervention for patients with multiple sclerosis

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pretreatment</th>
<th>Posttreatment</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
<td>M</td>
</tr>
<tr>
<td>Mobility</td>
<td>85.2</td>
<td>11.0</td>
<td>85.4</td>
</tr>
<tr>
<td>Self-care</td>
<td>94.0</td>
<td>9.1</td>
<td>91.9</td>
</tr>
<tr>
<td>Psychological Status</td>
<td>77.0</td>
<td>11.6</td>
<td>80.7</td>
</tr>
<tr>
<td>Physical Functioning</td>
<td>64.1</td>
<td>25.3</td>
<td>68.2</td>
</tr>
<tr>
<td>Vitality</td>
<td>50.0</td>
<td>15.5</td>
<td>56.8</td>
</tr>
<tr>
<td>Mental Health</td>
<td>68.4</td>
<td>16.3</td>
<td>75.3</td>
</tr>
</tbody>
</table>

* p-values of the Wilcoxon Signed-Rank Test at 0.05 level of significance comparison between pre- and post-treatment measurements of the 11 patients who completed the intervention. d is the effect size according to Cohen (1988) with d = 0.20 small effect, d = 0.50 medium effect, and d = 0.80 large effect. Higher scores indicate higher levels of HRQoL in the corresponding domain.

At 6 and 12 months post-treatment, six patients had completed all follow-up measurements. Table 2 gives data on measurements before the intervention started (pre-treatment), immediate post-treatment and at 6 and 12 months post-treatment for those six patients only. There were no statistically significant changes in scores on the three subscales of the Disability and Impact Profile and MOS Short Form-36 Health Survey. However, the 12-month post-treatment scores remained relatively stable compared with those at immediate post-treatment; this may be of importance because it is assumed that, in general, MS patients physically deteriorate over time and that this deterioration subsequently negatively affects HRQoL. The finding that the participants did not experience such a deterioration in long-term HRQoL might by interpreted as positive.
Table 2 Nonparametric analysis of variance for comparison of means of subscales of the Disability and Impact Profile and the Short Form-36 Health Survey at pre-treatment, immediately posttreatment, and at 6 and 12 months posttreatment for patients with multiple sclerosis

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pre-treatment</th>
<th>Posttreatment</th>
<th>$d$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$M$</td>
<td>$SD$</td>
<td>Immediately</td>
</tr>
<tr>
<td>Mobility</td>
<td>82.0</td>
<td>13.2</td>
<td>81.4</td>
</tr>
<tr>
<td>Self-care</td>
<td>90.8</td>
<td>11.4</td>
<td>88.9</td>
</tr>
<tr>
<td>Psychological Status</td>
<td>75.8</td>
<td>13.3</td>
<td>78.6</td>
</tr>
<tr>
<td>Physical Functioning</td>
<td>55.8</td>
<td>29.1</td>
<td>60.8</td>
</tr>
<tr>
<td>Vitality</td>
<td>47.5</td>
<td>12.6</td>
<td>53.3</td>
</tr>
<tr>
<td>Mental Health</td>
<td>60.7</td>
<td>16.1</td>
<td>68.7</td>
</tr>
</tbody>
</table>

Data are given only for the six patients in both intervention groups who completed all measurements up to 12 months posttreatment. Higher scores indicate better HRQoL in the corresponding domain.

3.4 Discussion

The aim of this exploratory study was to develop a cognitive behavioural group intervention program for patients recently diagnosed with multiple sclerosis and to evaluate its feasibility and effectiveness with regard to HRQoL. The results indicated that this group intervention program was indeed feasible and had a promising effect on HRQoL.

Although studies on the effect of group programs for medically ill patients are increasing, few studies have investigated psychosocial group interventions for patients with MS. Therefore, the results of this study may be important not only for clinicians and their patients with MS, but also for other researchers in the field of MS.

We believe that one of the strongest elements in this study is the group format itself. We observed that bringing together patients with the same disease (at about the same stage of the disease process) enabled patients to learn a great deal from each other.

Some comments about this study should be made. Although a group format has advantages, confrontation with MS can be too distressing for some patients, as evidenced
by some hesitation to join the group. As one patient stated: “On the one hand I’m afraid to
be confronted with somebody who is more disabled than I am, on the other side I’m afraid
I’ll be the most disabled person in the group.” The two patients who stopped stated that
the confrontation with MS was too much for them. Both patients were offered individual
psychological counselling as after-care within our department.

In addition, to substantiate the results a randomised controlled design seems
warranted. We did not use such a design due to the exploratory character of the study.
Moreover, because one of the main goals of this study was to develop the intervention
program and investigate its feasibility, we did not focus only on the best possible research
design. A subsequent step could be to investigate the effect of the program using a
randomised controlled design.

The fact that we worked with a small sample size of recently diagnosed patients is
mainly due to the preliminary stage of this study. Although we did find some statistically
significant short-term effects, the sample size needs to be larger to detect more and long-
term effects of the intervention program. However, we would like to stress the difference
between the statistical significance and the clinical significance of the results. Looking at
the items that form the scales Psychological Status and Vitality, it shows that, immediately
post-treatment, the participants experienced a better HRQoL with respect to the domains
of cognitive functioning (memory and concentration), mood, existentiality (being able to
determine one’s own plan for the day and reaching one’s goal in life) and vitality (feeling
lively and energetic). From a psychological point of view, these domains are important in
that they contribute to a patient’s feeling of control and to an increased well-being. Taking
into account that MS is a progressive disease with deterioration of physical functioning, it
is promising that the psychosocial intervention improved HRQoL in these domains that
are relatively important for daily functioning, and that these clinically interesting results
persist one year after completing the intervention program.

3.5 Practical implications

The results of this study show that a psychosocial group intervention program for patients
recently diagnosed with MS is feasible and promising. Therefore it seems worthwhile to
further develop and promote multi-disciplinary projects similar to this study, and using
several questionnaires to investigate the effects of the intervention on various variables
(i.e. the effect of the intervention on coping or interpersonal relations). More specifically,
neurologists could be encouraged to support structured psychosocial intervention
programs for patients with MS and to actively refer their patients to such a program when
considered necessary. MS professionals (e.g. neurologists, psychologists, MS nurse
specialists and physiotherapists) should work together in order to continuously improve HRQoL in their patients.

Acknowledgements

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References


Evaluation of a cognitive behavioural group intervention for patients recently diagnosed with multiple sclerosis

MAJ Visschedijk, EH Collette, JWR Twisk, J Passchier, CH Polman, HM van der Ploeg

Submitted
Abstract

The diagnosis of multiple sclerosis (MS) may have major psychological consequences, such that many MS patients experience emotional problems in coping with the disease. This study evaluates the effectiveness of a new cognitive behavioural group intervention designed for patients with recently diagnosed MS, aiming to improve their health-related quality of life. Seventeen patients with MS (13 women and 4 men) participated in an eight-session group intervention program. Measurements of health-related quality of life and mood took place at pretreatment, directly posttreatment, and at 6 months and 12 months posttreatment. Results were compared with a matched control group of 17 patients with MS receiving standard medical care. For patients in the intervention group there was a gradual but nonsignificant increase in health-related quality of life in three non-physical domains (Self-care, Psychological Status, and Mental health) and a nonsignificant increase in the number of positive Social Experiences. A cognitive behavioural group intervention program for patients recently diagnosed with MS seems to be promising.
4.1 Introduction

Multiple sclerosis (MS) is a chronic neurological disease, characterized by widespread inflammation and demyelination in the central nervous system. Although a wide range of neurological symptoms may occur, the more common symptoms include motor and sensory impairments, difficulty with ambulation, loss of bladder or bowel control, visual problems, sexual dysfunction, fatigue and decline in cognitive function. MS strikes relatively young adults and has a variable and unpredictable course. Because of the progressive nature of MS, coping with the disease is an ongoing process. Many patients with MS experience emotional problems, and mood disorders (especially depression) are frequently concomitant with other MS symptoms.\textsuperscript{[1-5]} Depression, for example, may be more common in MS than in other neurological conditions\textsuperscript{[6,7]} and the lifetime risk of major depression in MS can range between 23\% - 54\%\textsuperscript{[8-11]} Anxiety disorders also occur regularly in the MS population,\textsuperscript{[12-15]} and significant emotional distress occurs in up to 64\% of the patients.\textsuperscript{[16]} Therefore, MS patients often seek professional help to cope with the both the disease and its consequences.

To assist patients in learning to cope with MS, we developed a group intervention program aimed at enhancing coping skills and improving health-related quality of life (HRQoL). Our target group was ‘the recently diagnosed patient’ (e.g. patients diagnosed with MS within the previous three years). This specific group was targeted because we wanted to anticipate coping problems, and a group program was developed because of its known advantages (e.g. sharing experiences, and time/cost effectiveness). Group intervention programs have been developed for numerous (chronic) medical illnesses,\textsuperscript{[17-21]} and (mainly in the last decade) some studies have focused on the effects of psychosocial group interventions for patients with MS\textsuperscript{[22-27]} these studies show that a group intervention program for MS patients is promising and can have a positive effect on patient’s wellbeing and HRQoL.

The primary aim of the present study was to evaluate the effectiveness of a new cognitive behavioural group intervention program on HRQoL in patients recently diagnosed with MS.

4.2 Method

4.2.1 Design and patients

For this study we initially planned a randomised controlled design with an intervention group and a waiting-list control group. However, due to recruitment difficulties (described in the intervention group section) it was not possible to compile a waiting-list control group. Therefore, in order to compare results we formed a matched control group from MS
patients receiving standard medical care who participated in an earlier study on HRQoL.\[8,29]\n
The present study included 34 patients: 17 in the intervention group and 17 in the control group. The medical ethical committee of the VU University Medical Centre approved the study protocol and all patients gave informed consent. Patients’ travel expenses were reimbursed but no fee was offered for participation. Standard medical treatment was continued as usual throughout the course of the study.

4.2.2 Intervention group
Patients for the intervention group were recruited by their neurologist based on the following inclusion criteria: 1) diagnosis of ‘definite’ MS and 2) problems in coping with MS (i.e. having difficulty in adjusting emotionally and/or practically to the disease). Initially, patients with a diagnosis ‘definite MS within the previous three years’ (which were designated as ‘recently diagnosed’) were recruited: 41 patients were eligible for the intervention. However, because 23 of these recently diagnosed patients (56%) were not willing to participate in the group program, we lengthened the period of the definite MS diagnosis to 5 years. The main reasons for nonparticipation were: lack of interest, problems getting to the hospital, lack of time, and the emotional burden of attending a group.

Finally, 18 eligible and interested patients (16 diagnosed within the previous three years and 2 diagnosed within the previous five years) were referred to the department of Medical Psychology where they were interviewed by a psychologist to assess their psychological needs. These patients were included in the intervention group unless they met the following exclusion criteria: 1) having a major psychological problem (besides problems coping with MS) which needs treatment first (e.g. serious relational problems); 2) having a serious medical condition besides MS (e.g. cancer or diabetes mellitus); 3) having severe visual impairments (e.g. unable to read the intervention material); 4) insufficient understanding of the Dutch language; 5) having a mental capacity comparable to an IQ ≤ 80; 6) having a serious alcohol or drug addiction; 7) having suicidal tendencies; 8) having psychosis or schizophrenia; 9) receiving intensive psychotherapy outside the VU University Medical Centre. One patient was excluded after the intake-interview because of major psychological problems besides problems coping with MS.

The 17 patients (13 women and 4 men) in the intervention group had a mean age of 40 (range 22-57) years and had a mean EDSS score of 3.0 (± 1.4); two of them had received their diagnosis MS more than three years previously (i.e. four and five years before inclusion). Assessments took place directly before intervention (T1), directly after intervention (T2), and 6 (T3) and 12 (T4) months post intervention.
4.2.3 Control patients
For the control group 17 patients were matched with the intervention group for gender, age and disability status. The control patients were compiled from a sample of 90 MS patients recruited by the Dutch MS Society (n = 61) and by the MS Centre of the VU University Medical Centre (n = 29) for participation in an earlier study on HRQoL in patients with MS.\cite{28,29} In that study, the MS Society (on behalf of researchers of the VU University Medical Centre) sent an invitation letter to 100 patients; these patients were selected at random from the list of patients living in and around Amsterdam. Of the 65 patients that responded, 4 were excluded because of major psychiatric disturbance or major cognitive impairment. The 29 patients recruited by the MS Centre were recruited for, and participated in, a clinical trial.

All patients in the control group had a diagnosis ‘definite MS’ and received standard medical care on an individual basis. These 17 patients (13 women and 4 men) had a mean age of 40 (range: 26-59) years and a mean EDSS score of 3.9 (± 1.4). Four assessments took place with 6 months between each assessment. Because patients in the control group had initially participated in an earlier study, the questionnaire used to assess their mood status was different from that used in the intervention group.

4.2.4 Measures
- Health-related quality of life (the primary outcome in this study) was assessed by the Amsterdam Quality of Life Questionnaire (AmsQoL).\cite{30} The AmsQoL is a Dutch quality of life questionnaire especially designed for use in patients with MS. The questionnaire is composed of several items from the Disability and Impact Profile (DIP)\cite{31,32} and the Short Form-36 Health Survey (SF-36).\cite{33} The AmsQoL consists of 40 items, divided into six subscales: Mobility, Self-care, Psychological Status (DIP), Physical functioning, Vitality, and Mental Health (SF-36). Higher scores indicate higher levels of HRQoL in the corresponding domain. The AmsQoL has good validity and internal consistency.\cite{34}
- In the intervention group, mood was assessed by the Center for Epidemiological Studies Depression scale (CES-D), a screening instrument for the presence of depressive symptoms during the past week.\cite{34,35} The scale consists of 20 items scored from 0 (less than once a day) to 3 (5 to 7 days) and contains four subscales (Somatic retarded activity, Depressed affect, Positive affect, and Interpersonal affect). The total score is formed by summing the items, with higher scores indicating the presence of more symptoms of depression. A score of ≥ 16 is considered an indication of clinical depression. The Dutch version of the CES-D has good validity and internal consistency.\cite{35}
- In the control group, mood was assessed by the Hospital Anxiety and Depression Scale (HADS).\cite{36} The HADS is used to measure depression and anxiety disorders in a non-psychiatric population. It consists of two scales, one measuring ‘anxiety’ and one
measuring ‘depression’. In the present study only the depression scale was used. This scale consists of 7 items with scores ranging from 0 to 21 and higher scores indicating more intensity. Scores > 8 indicate that patients are likely to be depressed. Reliability and validity are adequate for the Dutch population.\cite{271}

- Social experiences were assessed by the Social Experiences Checklist (SEC) an instrument developed and validated in the Netherlands\cite{28,29} The SEC measures both positively and negatively perceived social support; these two scales have 8 items each.

- Disability status was assessed by the Expanded Disability Status Scale (EDSS).\cite{140} The EDSS is rated by a neurologist and scores range from 0 (no disability) to 10 (death due to MS).

- Format and content of the intervention was evaluated by means of evaluation forms filled out after the final group meeting. Appreciation was scored on a scale from 1 (low appreciation) to 5 (high appreciation); other items, for example, pertained to strongest/weakest elements of the program, the group climate, length of the program, and the quality of the patient manual.

4.2.5 Pilot study
Two pilot studies were conducted to develop the intervention program (i.e. a patient workbook and a trainers manual) and to assess its feasibility. Results of these pilot studies are described in detail elsewhere.\cite{141}

4.2.6 Intervention program
From January 2001 to June 2002, three intervention groups with 4-8 patients per group were conducted. The program consisted of 8 two-hour sessions and was conducted by one or two psychologists (if the group consisted of 5 or more patients, two psychologists were assigned to a group). Sessions took place on a two-weekly basis and each session was based on a theme considered relevant for patients with MS. The sessions had the following themes: (1) Diagnosis MS: How to move on? (2) Coping with fatigue and other symptoms, (3) Assertiveness, (4) Communication with family and friends, (5) Communication with medical staff, (6) Coping with psychological distress, (7) MS and the future: coping with uncertainty and fear, (8) Capita Selecta (one or more topics chosen by the participants).

Each session followed a predetermined time schedule, starting with a discussion based on the central theme of that session and ending with a homework assignment for the following session. Throughout the intervention program, patients learned cognitive behavioural principles in order to change their thoughts, feelings and behaviour.

4.2.7 Loss to follow-up
Two of the 17 patients in intervention program dropped out and were lost to follow-up. One patient dropped out after the fifth group session because the confrontation with MS (and with other patients with MS) was too distressing; the other patient dropped out
before the intervention started because of being more than 15 years younger than the other participants in that group. Both patients were offered individual psychological counselling as after-care within our department but both declined this offer.

4.2.8 Statistical analysis
Baseline characteristics of the intervention group and control group were compared by means of Student’s t-tests. The difference in longitudinal development of outcome measures between the two groups was evaluated by means of MANOVA for repeated measurements (General Linear Model). To control for baseline differences between both groups, baseline scores of the outcome variables were entered as covariates in all analyses. Because no measures were available for CES-D and HADS for the control group, only the development over time in the intervention group was analysed with MANOVA for repeated measurements. All analyses were performed using SPSS for windows (release 11.0.1) and significance for all tests was set at \( p \leq 0.05 \).

4.3 Results

Table 1 shows that there were no statistically significant differences in baseline characteristics between the two groups, except for time since diagnosis. The control patients had their diagnosis ‘definite MS’ twice as long as the intervention patients. Furthermore, at baseline, 6 patients in the intervention group (35%) showed signs of clinical depression compared to 3 patients in the control group (18%).
Table 1 Baseline characteristics for patients in the intervention group and control group

<table>
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<tr>
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<th>Intervention (n = 17)</th>
<th>Control (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39.7 (11.2)</td>
<td>39.8 (11.4)</td>
</tr>
<tr>
<td>Gender female/male</td>
<td>13 / 4</td>
<td>13 / 4</td>
</tr>
<tr>
<td>Disability status</td>
<td>3.0 (1.4)</td>
<td>3.9 (1.4)</td>
</tr>
<tr>
<td>Years since diagnosis</td>
<td>2.3 (1.3)</td>
<td>4.7 (4.3) *</td>
</tr>
</tbody>
</table>

**Health-related quality of life**

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n = 17)</th>
<th>Control (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mobility</strong></td>
<td>81.3 (12.1)</td>
<td>75.4 (14.2)</td>
</tr>
<tr>
<td><strong>Self-Care</strong></td>
<td>86.9 (12.8)</td>
<td>89.7 (8.1)</td>
</tr>
<tr>
<td><strong>Psychological status</strong></td>
<td>73.2 (14.0)</td>
<td>77.7 (9.5)</td>
</tr>
<tr>
<td><strong>Physical functioning</strong></td>
<td>58.6 (30.4) *</td>
<td>48.8 (22.6)</td>
</tr>
<tr>
<td><strong>Vitality</strong></td>
<td>49.4 (20.0)</td>
<td>50.9 (18.7)</td>
</tr>
<tr>
<td><strong>Mental Health</strong></td>
<td>72.7 (18.3)</td>
<td>70.8 (16.1)</td>
</tr>
</tbody>
</table>

**Mood**

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n = 17)</th>
<th>Control (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CES-D</strong></td>
<td>12.5 (8.7)</td>
<td>-</td>
</tr>
<tr>
<td><strong>HADS depression</strong></td>
<td>-</td>
<td>4.2 (3.3)</td>
</tr>
</tbody>
</table>

**Social experiences**

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n = 17)</th>
<th>Control (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Positive</strong></td>
<td>21.6 (4.8)</td>
<td>23.8 (3.4)</td>
</tr>
<tr>
<td><strong>Negative</strong></td>
<td>11.7 (2.5)</td>
<td>12.1 (4.3)</td>
</tr>
</tbody>
</table>

Values are means (SD) or frequency of patients. Disability status was measured according to the Expanded Disability Status Scale (EDSS). * p ≤ 0.001
Table 2 gives data on the differences in longitudinal development of HRQoL (AmsQoL) and social experiences (SEC) between the two groups; no significant differences were found. Furthermore, within the intervention group, the CES-D and HADS showed no significant change over time.

**Table 2** Data on results of the questionnaires for patients in the intervention (n = 17) and control group (n = 17) at pretreatment, directly posttreatment, and at 6 and 12 months posttreatment

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Study group</th>
<th>T1 M (SD)</th>
<th>T2 M (SD)</th>
<th>T3 M (SD)</th>
<th>T4 M (SD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Health-related quality of life</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AmsQoL Mobility</td>
<td>Intervention Control</td>
<td>79.2 (13.4)</td>
<td>79.4 (13.4)</td>
<td>78.0 (13.7)</td>
<td>74.2 (17.7)</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>75.4 (14.2)</td>
<td>76.1 (12.4)</td>
<td>78.7 (11.7)</td>
<td>73.6 (13.3)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Self-care</td>
<td>Intervention Control</td>
<td>84.0 (14.1)</td>
<td>86.6 (13.6)</td>
<td>83.8 (15.8)</td>
<td>84.9 (14.9)</td>
<td>0.29</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>89.7 (8.2)</td>
<td>86.6 (10.7)</td>
<td>88.8 (6.9)</td>
<td>86.1 (10.2)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Psychological status</td>
<td>Intervention Control</td>
<td>70.7 (13.0)</td>
<td>74.3 (11.5)</td>
<td>75.5 (10.0)</td>
<td>76.4 (9.3)</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>77.7 (9.5)</td>
<td>79.1 (10.6)</td>
<td>76.6 (12.4)</td>
<td>75.5 (12.3)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Physical functioning</td>
<td>Intervention Control</td>
<td>50.8 (31.0)</td>
<td>45.6 (5.2)</td>
<td>42.5 (39.9)</td>
<td>42.9 (34.9)</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>48.8 (22.6)</td>
<td>50.8 (28.2)</td>
<td>48.2 (24.0)</td>
<td>40.0 (20.0)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Vitality</td>
<td>Intervention Control</td>
<td>48.6 (20.5)</td>
<td>45.3 (19.6)</td>
<td>37.7 (17.7)</td>
<td>32.7 (18.2)</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>50.8 (18.7)</td>
<td>43.0 (19.6)</td>
<td>50.9 (15.1)</td>
<td>45.9 (17.9)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Mental health</td>
<td>Intervention Control</td>
<td>71.6 (20.8)</td>
<td>69.3 (17.4)</td>
<td>65.5 (10.3)</td>
<td>71.3 (19.1)</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>70.8 (16.1)</td>
<td>67.3 (19.3)</td>
<td>68.7 (15.2)</td>
<td>69.0 (14.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Mood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CES-D</td>
<td>Intervention Control</td>
<td>13.2 (9.8)</td>
<td>15.1 (7.9)</td>
<td>16.6 (3.4)</td>
<td>17.3 (7.9)</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>HADS depression</td>
<td>Intervention Control</td>
<td>4.2 (3.3)</td>
<td>4.5 (2.6)</td>
<td>5.3 (3.7)</td>
<td>4.5 (2.8)</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Social experiences</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEC Positive</td>
<td>Intervention Control</td>
<td>21.3 (4.9)</td>
<td>22.3 (5.4)</td>
<td>22.6 (6.2)</td>
<td>23.6 (5.4)</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>23.8 (5.5)</td>
<td>23.1 (2.9)</td>
<td>22.8 (3.1)</td>
<td>22.5 (2.9)</td>
<td></td>
</tr>
<tr>
<td>SEC Negative</td>
<td>Intervention Control</td>
<td>11.3 (2.7)</td>
<td>11.2 (2.3)</td>
<td>11.0 (3.0)</td>
<td>11.3 (2.0)</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>12.3 (4.4)</td>
<td>13.2 (3.8)</td>
<td>13.3 (3.8)</td>
<td>12.1 (3.3)</td>
<td></td>
</tr>
</tbody>
</table>

Data are means (SD) from MANOVA Repeated Measurements design Time by Study group. p-value for the difference in development over time between the two groups (except for CES-D and HADS, where it reflects the change over time within the group). AmsQoL = Amsterdam Quality of Life questionnaire, CES-D = Centre for Epidemiological Studies Depression scale, HADS = Hospital Anxiety and Depression scale, SEC = Social Experiences Checklist, T1 = pretreatment, T2 = directly posttreatment, T3 = 6 months posttreatment, and T4 = 12 months posttreatment. Cell sample size may vary due to missing data.

The differences in development between the intervention and control group showed a trend in which the intervention group scored slightly better on the ‘non-physical’ subscales.
of the AmsQoL (i.e. Self-care, Psychological status and Mental health) and on both subscales of the SEC. For the ‘physical’ subscales of the AmsQoL (i.e. Mobility, Physical functioning and Vitality), patients in the intervention group scored slightly worse than the controls.

4.3.1 Evaluation of the intervention
All patients in the intervention group filled in an evaluation form which contained both structured and open-ended questions. On a scale from 1 (low) to 5 (high), the mean appreciation-score was 3.8 (± 0.8). On the question as to whether patients had learned from the intervention, the mean learning score was 3.6 (± 1.1) on a scale from 1 (low) to 5 (high). On the open-ended question addressing which part of the intervention was considered the strongest element: 9 patients (53%) answered ‘the cognitive behavioural techniques’, 6 (35%) answered the ‘interpersonal contact’, and 2 (12%) experienced the theory and the role playing, respectively, as the strongest elements. On the open- ended question about which part of the intervention was considered the weakest element: 4 (24%) answered ‘no weak parts’, 4 (24%) experienced ‘the time schedule’ (more time per session was desirable) as the weakest part, and 2 (12%) experienced the sessions as ‘sometimes too emotionally distressing’. Other weak parts mentioned by the patients in the intervention group were: ‘working in subgroups’, ‘goal setting’, and ‘too much theory’.

4.4 Discussion
Some limitations about this study should be addressed. First, the patient improvements emerging from our study were not statistically significant; to detect statistically significant effects, sample sizes need to be larger. A power analysis for two samples with unequal variances (with significance set at 0.05 (one-sided) and power set at 0.80) shows that in the present study the sample size would have to range from 52 (subscale SEC positive) to 2,127 (subscale Vitality) for patients in the intervention group, and from 37 (subscale SEC positive) to 1,989 (subscale Vitality) for patients in the control group. This is hardly feasible in a psychosocial intervention study; moreover, the clinical relevance of a treatment effect that needs such large numbers to be statistically significant, is debatable.

Second, taking into account our recruitment difficulties we are of the opinion that a group program with a psychosocial character is probably not particularly attractive for patients recently diagnosed with MS. Although a group format has known advantages, confrontation with MS can be too distressing for some patients, as evidenced by hesitation to join the group. As one patient stated: “On the one hand I’m afraid to be confronted with somebody who is more disabled than I am, on the other hand I’m afraid I’ll be the most disabled person in the group.” We assume that these recruitment difficulties could be a
result of some particular ‘patient characteristics’. For example, one study revealed a key role for neuroticism in the development of anxiety and depression in physically ill patients.\textsuperscript{[45]} Neurotic patients tend to experience negative emotions, will therefore suffer more quickly from depressive symptoms and may seek psychological help more often than patients who are less neurotic. Denial may also play a role in the recruitment difficulties; denial is common and its impact may vary over time.\textsuperscript{[45,46]} Moreover, it can often occur among recently diagnosed patients. Pre-intervention denial of negative emotions about MS may help to reduce pre-intervention feelings of anxiety and depression, but attending a psychosocial intervention program denial is no longer an option. Patients in denial may be less inclined to attend a specialized group program that focuses on their disease.

Third, due to the recruitment difficulties our results may have been affected by selection bias and, for medical-ethical reasons, it was not possible to examine the characteristics of patients who declined participation. Also because it was impossible to compile a waiting-list control group, we comprised a matched control group from MS patients who participated in an earlier study.\textsuperscript{[38,40]} We decided to include a control group (rather than having no controls at all) in order to be able to compare results of ‘treated’ versus ‘untreated’ patients.

Finally, our recruitment difficulties are similar to those of an earlier study on the effects of a psychosocial group intervention for patients with MS\textsuperscript{[46]} in that study, 325 MS patients were invited to participate, 29% showed interest and after the intake interview only 13% actually participated. In the future, researchers and psychologists should consider this and perhaps give patients the opportunity to follow a specialized psychosocial program on an individual basis.

\subsection{4.4.1 Conclusion}

This study evaluated the effectiveness of a cognitive behavioural group intervention program for patients recently diagnosed with MS. An eight-session cognitive behavioural group program showed a positive trend for HRQoL in the domains of self-care, psychological status, and mental health, whereas for the domains of mobility, vitality and physical functioning a negative trend for HRQoL was observed. Patients in the intervention group also showed a positive trend for the number of positive social experiences.

Considering the recruitment difficulties in the present study, a group intervention program apparently is not the best option for patients recently diagnosed with MS. For these patients it may be more appropriate to offer an educational program that focuses on the emotional aspects of having a chronic disease. Further studies are needed to assess the needs in psychosocial care for patients with recently diagnosed MS, and to examine whether an intervention program based on individual counselling is a better option for this group.
CHAPTER 4

We believe that MS professionals (e.g. neurologists, psychologists, MS nurse specialists and physiotherapists) should work together to continuously improve the care of their patients in order to improve HRQoL.

Acknowledgements

We gratefully acknowledge the financial support of the Dutch foundation *Stichting MS Research* (Project No. 98-344 MS) and the expert assistance of the psychologists of the VU University Medical Centre D. Sellenraad, S.J.E Tibbe and A.M.E. Tromp-Weyer.
References


5 Evaluation of a cognitive behavioural intervention on an individual basis for patients with multiple sclerosis

MAJ Visschedijk, EH Collette, JWR Twisk, J Passchier, CH Polman, HM Van der Ploeg

Submitted
CHAPTER 5

Abstract

Background – Multiple sclerosis (MS) is a chronic neurological disease mainly affecting relatively young people and due to its characteristics, MS has a major impact on the lives of patients and their families.

Purpose – To examine the effectiveness of a cognitive behavioural intervention program for patients with MS aimed at enhancing coping skills and health-related quality of life (HRQoL). The effectiveness of the intervention program used in group counselling was compared with its use in individual counselling.

Method – Thirty-six patients (25 women, 11 men) participated in this study: 19 patients participated in individual counselling and 17 in group counselling. Measurements of HRQoL (AmsQoL), mood (CESD), and number of social experiences (SEC) were made pretreatment, directly posttreatment, and at 6 and 12 months posttreatment. Results of both groups were compared.

Results – Patients in individual counselling had a statistically significant longitudinal improvement in health-related quality of life in the domain of Vitality (p = 0.02) and an almost statistically significant long-term increase in depressive symptoms (p = 0.06). No other statistical significant differences were found between the two groups.

Conclusion – A psychosocial intervention program on an individual basis seems promising in the aim to enhance health-related quality of life and mood in patients with MS.
5.1 Introduction

Multiple sclerosis (MS) is a chronic neurological disease mainly affecting relatively young people aged 20 to 40 years. Any neurological symptom may occur, but the more common symptoms include motor and sensory impairments (e.g. numbness, loss of sensation), difficulty with ambulation, loss of bladder or bowel control, visual problems, sexual dysfunction, fatigue and decline in cognitive function. Due to its characteristics, MS has a major impact on the lives of patients and their families; it substantially interferes with daily activities and family, social and working life, disturbs emotional wellbeing, and reduces quality of life.\textsuperscript{1-7}

To assist patients in learning to cope with the disease and its consequences, we developed a psychosocial intervention program aimed at enhancing coping skills and improving health-related quality of life (HRQoL). Initially we developed a group program based on cognitive behavioural techniques for patients (recently diagnosed) with MS.\textsuperscript{8} Group intervention programs have been developed for numerous (chronic) medical illnesses\textsuperscript{9-13} and (mainly in the last decade) some studies have focused on the effects of psychosocial (group) interventions for patients with MS\textsuperscript{14-16} these studies show that an intervention program for MS patients is promising and can have a positive effect on patient’s wellbeing and HRQoL.

Due to recruitment difficulties (56% of the eligible patients declined participation), we concluded that a group counselling program might not be sufficiently attractive for (recently diagnosed) patients with MS. Therefore we decided to rewrite the intervention program for use in individual counselling. The primary aim of the present study is to evaluate this cognitive behavioural intervention on an individual basis for patients with MS. We hypothesize that such an intervention program will be more attractive for patients with MS than a group intervention program. Therefore, we compare results on HRQoL, depression and number of social experiences of patients in individual counselling with results of patients in group counselling.

5.2 Method

5.2.1 Design and patients
Initially we developed a cognitive behavioural group program; however, as a result of recruitment difficulties which are described in detail elsewhere,\textsuperscript{18} we decided to rewrite the program for use in individual counselling. To be able to compare and frame results, patients who participated in the group intervention program formed the control group in the present study.
The present study included 36 patients: 19 in individual counselling and 17 in group counselling. The medical ethical committee of the VU University Medical Centre approved the study protocol and all patients gave signed informed consent. Patients’ travel expenses were reimbursed but no fee was offered for participation. Standard medical treatment was continued as usual throughout the course of the study.

5.2.1.a Patients in individual counselling
Patients for individual counselling were referred to the Department of Medical Psychology by their neurologist on the following inclusion criteria: 1) diagnosis of ‘definite’ MS, and 2) problems in coping with MS (i.e. having difficulty in adjusting emotionally and/or practically to the disease). No limit was set on the years passed since patients received their diagnosis. At the Department of Medical Psychology, 26 patients received an intake interview during which they were screened on the following exclusion criteria: 1) having a major psychological problem (besides problems coping with MS) which needs treatment first (e.g. serious relational problems); 2) having a serious medical condition besides MS (e.g. cancer or diabetes mellitus); 3) having severe visual impairments (e.g. unable to read the intervention material); 4) insufficient understanding of the Dutch language; 5) having a mental capacity comparable to an IQ < than 80; 6) having a serious alcohol or drug addiction; 7) having suicidal tendencies; 8) having psychosis or schizophrenia; and 9) receiving intensive psychotherapy outside the VU University Medical Centre. Twenty-four patients were eligible for participation. Two patients were excluded after the intake interview because of major psychological problems besides problems coping with MS and received individual counselling outside our study protocol. Five patients (19%) declined participation; these patients did not want to participate in a protocolized program and received individual counselling outside our MS protocol.

The 19 patients (12 women and 7 men) in the individual counselling program had a mean age of 36 (range 19-58) years and a mean disability status (EDSS score) of 2.7 (± 0.9). The mean time passed since their diagnosis ’definite MS’ was 3.4 (± 4.6) years. Assessments took place directly before intervention (T1), directly after intervention (T2), and at 6 (T3) and 12 (T4) months after intervention.

5.2.1.b Patients in group counselling
Patients for group counselling were recruited by their neurologist according to the same inclusion criteria as the patients in individual counselling. Initially, patients with a diagnosis ‘definite MS within the previous three years’ (which were designated as ‘recently diagnosed’) were recruited: 41 patients were eligible for participation. However, because 23 of these recently diagnosed patients (56%) were not willing to participate in the group program, we dropped this inclusion criterion and included two interested patients with a diagnosis MS of more than three years. The main reasons for nonparticipation were: lack
of interest, problems getting to the hospital, lack of time, and the emotional burden of being involved in a group.

Finally, 18 eligible and interested patients (16 patients diagnosed within the previous three years and 2 diagnosed within the previous five years) were referred to the Department of Medical Psychology where they were interviewed by a psychologist to assess their psychological needs. These patients were included unless they met the same exclusion criteria as patients in individual counselling. One patient was excluded after the intake interview because of major psychological problems (besides coping problems with MS) and received individual counselling outside our (group) protocol.

The 17 patients (13 women and 4 men) in the group intervention had a mean age of 40 (range: 22-57) years and a mean disability status (EDSS score) of 3.0 (± 1.4). The mean time passed since they received their diagnosis ‘definite MS’ was 2.3 (± 1.3) years.

Assessments took place directly before intervention (T1), directly after intervention (T2), and at 6 (T3) and 12 (T4) months after intervention.

5.2.2 Measures
- Health-related quality of life (the primary outcome in this study) was assessed by the *Amsterdam Quality of Life Questionnaire* (AmsQoL).[26] The AmsQoL is a Dutch quality of life questionnaire especially designed for use in patients with MS. The questionnaire is composed of several items from the Disability and Impact Profile (DIP)[21,22] and the Short Form-36 Health Survey (SF-36).[23] The AmsQoL consists of 40 items, which can be divided in six subscales: Mobility, Self-Care, Psychological Status (DIP), Physical functioning, Vitality, and Mental Health (SF-36). Higher scores indicate higher levels of HRQoL in the corresponding domain. The AmsQoL has good validity and internal consistency.[26]
- Mood was assessed by the *Center for Epidemiological Studies Depression* scale (CES-D), a screening instrument for depressive symptoms during the past week.[24,25] The scale consists of 20 items, which can be scored from 0 (less than once a day) to 3 (5 to 7 days). The scale contains four subscales: Somatic retarded activity, Depressed affect, Positive affect, and Interpersonal affect. The total score can be formed by summing the items, with higher scores indicating more symptoms of depression being present. A score of ≥ 16 is considered an indication of clinical depression. The Dutch version of the CES-D has good validity and internal consistency.[26]
- Social experiences were assessed by the *Social Experiences Checklist* (SEC).[26,27] The SEC measures both positively and negatively perceived social support. The instrument was developed and validated in the Netherlands. The two scales consist of 8 items each.
- Disability status was assessed by the *Expanded Disability Status Scale* (EDSS).[26] The EDSS is rated by a neurologist and scores range from 0 (no disability) to 10 (death due to MS).
5.2.3 The intervention programs
From January 2001 to June 2002, three counselling groups with four to eight patients per group were conducted, and from October 2002 to June 2003 the patients in individual counselling were seen. Both, the group counselling sessions and the individual counselling sessions took place at the Vrije Universiteit University Medical Centre. The intervention program consisted of eight sessions and each session was based on a theme considered relevant for patients with MS. The sessions had the following themes: (1) Diagnosis MS: How to move on? (2) Coping with fatigue and other symptoms, (3) Assertiveness, (4) Communication with family and friends, (5) Communication with medical staff, (6) Coping with psychological distress, (7) MS and the future: coping with uncertainty and fear, (8) Capita Selecta (one or more topics chosen by the participants). Each session followed a prefixed time schedule: in the group intervention it started with a discussion based on the central theme of that session and ended with a homework assignment for the next session. Throughout the intervention program, patients learned cognitive behavioural principles aimed to change their thoughts, feelings and behaviour.

Some practical differences existed between the individual and group counselling programs. The individual counselling took place on a weekly basis with eight one-hour sessions conducted by one psychologist, while the group counselling took place once in two weeks with eight two-hour sessions conducted by one or two psychologists (depending on the number of participants; if the group consisted of five or more patients, two psychologists were assigned to a group).

5.2.4 Loss to follow-up.
In individual counselling, five patients (19%) dropped out of the program and were lost to follow-up. These patients dropped out after they had finished all eight sessions of the intervention; four patients dropped out at the third measurement (6 months post-intervention) and the fifth patient dropped out at the fourth measurement (12 months post-intervention).

In group counselling, two patients (12%) dropped out of the program and were lost to follow-up. One patient dropped out after the fifth group session because the confrontation with MS (and other patients with MS) was too distressing. The other patient dropped out before the intervention started because of an extensive age difference (more than 15 years younger) with the other participants in that group. Both patients were offered individual psychological counselling as after-care within our department; this was declined by both of them.

5.2.5 Statistical analysis
Baseline characteristics of patients in individual counselling and group counselling were compared by means of Student’s t-tests for continuous variables and with chi-square tests.
for dichotomous variables. Differences in longitudinal development of each outcome measure between the two study groups were evaluated by means of a general linear model for repeated measurements (i.e. MANOVA for repeated measurements). To control for baseline differences for both study groups, baseline scores of each outcome variable were entered as covariates in all analyses. All analyses were performed using SPSS for Windows (release 11.0.1) and significance for all tests was set at \( p \leq 0.05 \).

### 5.3 Results

Table 1 presents baseline characteristics for patients in individual counselling and group counselling. There was a significant baseline difference between patients in individual counselling and group counselling on two of the six domains of HRQoL (AmsQoL): Self-Care \( (p = 0.05) \) and Mental Health \( (p = 0.02) \). Patients in individual counselling have a significantly higher score on the subscale Self-Care and a significantly lower score on the subscale Mental Health, indicating a higher respectively lower HRQoL in the corresponding domains. Furthermore, there is a significant baseline difference between the two study groups for depression (CES-D) \( (p = 0.02) \). At baseline, patients in individual counselling show significantly more signs of clinical depression compared to patients in group counselling. There are no statistically significant differences at baseline between both study groups on age, gender, disability status, years passed since diagnosis, and number of social experiences (SEC).
Table 1 Characteristics of multiple sclerosis patients in individual counselling and group counselling

<table>
<thead>
<tr>
<th></th>
<th>Individual counselling (n = 19)</th>
<th>Group counselling (n = 17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36 (10.2)</td>
<td>40 (11.2)</td>
<td>0.29</td>
</tr>
<tr>
<td>Gender female/male</td>
<td>12/7</td>
<td>13/4</td>
<td>0.40</td>
</tr>
<tr>
<td>Disability status</td>
<td>2.7 (0.9)</td>
<td>3.0 (1.4)</td>
<td>0.47</td>
</tr>
<tr>
<td>Years since diagnosis</td>
<td>3.4 (4.6)</td>
<td>2.3 (1.3)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Health-related quality of life

- **Mobility**: 87.3 (8.4) vs. 81.3 (12.1), p = 0.09
- **Self-Care**: 94.0 (7.3) vs. 86.9 (12.8), p = 0.05
- **Psychological status**: 72.1 (13.9) vs. 73.2 (13.9), p = 0.80
- **Physical functioning**: 70.8 (27.4) vs. 58.5 (30.4), p = 0.21
- **Vitality**: 42.9 (17.4) vs. 49.4 (20.0), p = 0.30
- **Mental Health**: 57.7 (19.0) vs. 72.7 (18.3), p = 0.02

Mood

- **CES-D**: 20.2 (10.2) vs. 12.5 (8.7), p = 0.02

Social experiences

- **Positive**: 20.7 (4.1) vs. 21.6 (4.5), p = 0.50
- **Negative**: 12.2 (4.0) vs. 11.7 (2.8), p = 0.60

Values are means (SD) or frequency of patients. Disability status was measured according to the Expanded Disability Status Scale (EDSS). p-value according to Student’s t-tests except for Gender (chi-square test).

Table 2 shows results of the repeated measurement analyses to evaluate the differences in longitudinal development (T1, T2, T3, T4) of HRQoL (AmsQoL), depression (CES-D), and social experiences (SEC) between patients in individual and group counselling. There is a significant difference in longitudinal development for the subscale Vitality (AmsQoL) in favour of the patients in individual counselling ($p = 0.02$). For Vitality there was an increase in HRQoL for patients in individual counselling from 45.7 at T1 to 54.3 at T4, while for patients in group counselling there was a decrease from 48.8 at T1 to 32.7 at T4. Another statistically interesting difference between the two study groups can be observed for scores on the CES-D ($p = 0.06$); patients in individual counselling experienced a decrease in depressive symptoms from 18.6 at T1 to 11.3 at T4, whereas patients in group counselling experienced an increase in depressive symptoms from 13.2 at T1 to 17.3 at T4. No other significant differences between the two study groups were found.
Table 2 Data on multiple sclerosis patients in individual counselling (n = 19) and group counselling (n = 17) at pre-treatment, directly post-treatment, and at 6 months and 12 months post-treatment.

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Intervention</th>
<th>T1 (M, SD)</th>
<th>T2 (M, SD)</th>
<th>T3 (M, SD)</th>
<th>T4 (M, SD)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Health-related quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AmsQoL Mobility</td>
<td>Individual</td>
<td>88.4 (8.3)</td>
<td>88.4 (9.2)</td>
<td>87.2 (8.9)</td>
<td>88.9 (10.7)</td>
<td>0.31</td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>79.2 (13.4)</td>
<td>79.4 (13.4)</td>
<td>78.0 (13.7)</td>
<td>74.2 (17.7)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Self-care</td>
<td>Individual</td>
<td>94.4 (7.6)</td>
<td>94.1 (7.2)</td>
<td>92.5 (7.9)</td>
<td>93.9 (9.9)</td>
<td>0.95</td>
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<tr>
<td></td>
<td>Group</td>
<td>84.0 (14.1)</td>
<td>86.6 (13.6)</td>
<td>83.8 (15.7)</td>
<td>84.9 (14.9)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Psychological status</td>
<td>Individual</td>
<td>74.8 (12.5)</td>
<td>75.7 (11.0)</td>
<td>77.7 (12.4)</td>
<td>79.8 (12.5)</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>70.7 (15.0)</td>
<td>74.5 (11.5)</td>
<td>75.5 (10.0)</td>
<td>75.5 (12.3)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Physical functioning</td>
<td>Individual</td>
<td>72.1 (27.9)</td>
<td>66.8 (29.2)</td>
<td>66.1 (28.8)</td>
<td>66.8 (22.6)</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>50.8 (31.0)</td>
<td>46.7 (31.4)</td>
<td>42.5 (31.0)</td>
<td>42.1 (34.0)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Vitality</td>
<td>Individual</td>
<td>45.7 (18.3)</td>
<td>48.2 (21.1)</td>
<td>51.8 (23.3)</td>
<td>54.3 (10.5)</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>48.6 (20.3)</td>
<td>43.6 (19.6)</td>
<td>37.7 (17.7)</td>
<td>32.7 (18.2)</td>
<td></td>
</tr>
<tr>
<td>AmsQoL Mental health</td>
<td>Individual</td>
<td>59.4 (17.9)</td>
<td>64.3 (18.5)</td>
<td>72.9 (18.0)</td>
<td>72.6 (13.7)</td>
<td>0.40</td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>71.6 (20.8)</td>
<td>63.3 (17.4)</td>
<td>65.5 (10.3)</td>
<td>71.3 (19.1)</td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CES-D</td>
<td>Individual</td>
<td>18.6 (7.9)</td>
<td>17.1 (9.5)</td>
<td>13.9 (9.9)</td>
<td>11.3 (9.5)</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>13.2 (9.8)</td>
<td>15.1 (7.9)</td>
<td>16.6 (3.1)</td>
<td>17.3 (7.9)</td>
<td></td>
</tr>
<tr>
<td>Social experiences</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEC Positive</td>
<td>Individual</td>
<td>21.4 (4.1)</td>
<td>22.0 (3.6)</td>
<td>21.5 (3.0)</td>
<td>22.8 (4.2)</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>21.3 (4.9)</td>
<td>22.3 (5.4)</td>
<td>22.6 (6.2)</td>
<td>23.0 (5.4)</td>
<td></td>
</tr>
<tr>
<td>SEC Negative</td>
<td>Individual</td>
<td>11.8 (3.8)</td>
<td>10.8 (2.1)</td>
<td>11.1 (2.7)</td>
<td>11.6 (2.7)</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>Group</td>
<td>11.3 (2.7)</td>
<td>11.2 (2.3)</td>
<td>11.0 (3.0)</td>
<td>11.3 (2.0)</td>
<td></td>
</tr>
</tbody>
</table>

Data are means (SD) from patients who attended all four measurements and therefore were included in the MANOVA Repeated Measurements design Time by Study group. Baseline values differ from those in Table 1 due to patients who dropped out. p-value for the difference in development over time between the two groups with baseline scores as covariates. AmsQoL = Amsterdam quality of Life Questionnaire, CES-D = Center for Epidemiological Studies Depression scale, SEC = Social Experiences Checklist. T1 = pre-treatment, T2 = directly post-treatment, T3 = 6 months post-treatment, and T4 = 12 months post-treatment.

The (non-significant) trend in the longitudinal development of scores between individual and group counselling is in favour of the patients in individual counselling, except for the development of scores on the subscales Self-Care (AmsQoL) and on both subscales of the SEC.
5.4 Discussion

5.4.1 Practice implications

This study aimed to evaluate the effectiveness of a psychosocial intervention program on an individual basis for patients with MS. Although a group format has advantages, for example its cost-effectiveness, we hypothesized that an intervention on an individual basis would be more attractive for patients with MS than a group intervention.

Results showed a significant improvement in HRQoL in the domain of Vitality for patients in individual counselling compared to patients in group counselling. The Vitality domain contains questions such as ‘How much of the time during the past four weeks... did you have a lot of energy?’ Thus, patients in individual counselling appear to have better perceived energy levels one year after individual counselling compared to patients in group counselling. This finding is of particular importance because especially fatigue (a symptom experienced by approximately 80% of MS patients) can have a profound effect on social and psychological functioning. It can, for example, restrain patients from visiting friends and family, making patients dependent on others to visit them and may also influence mood. Furthermore, several studies have demonstrated significant associations of fatigue with disability status, depression and quality of life in MS. Examination of the scores on the CES-D of the two groups reveals an almost statistically significant decrease in depressive symptoms for patients in individual counselling; patients in individual counselling show a 39% decrease in depressive symptoms one year after the intervention. This finding is of clinical relevance because depression is frequently concomitant with other MS symptoms. Depression, for example, may be more common in MS than in other neurological conditions and some studies have indicated that the lifetime risk of major depression in MS is between 23% and 54%. Furthermore, depression is associated with higher levels of disability and poorer HRQoL in patients with MS. This means that an improvement in depressive feelings can affect the patient’s quality of life and disability status. The increase in depressive symptoms for patients in group counselling could be a result of the confrontation with other patients with MS. Confrontation with patients who are more disabled may cause feelings of distress, such as anxiety and depression. Another possibility could be the role of denial; denial is common and its impact may vary over time. Patients in group counselling were recruited more pro-actively than patients recruited for individual counseling (i.e. these latter patients were referred to the Department of Medical Psychology to receive psychological counseling, either inside or outside the intervention protocol). Pre-intervention denial of negative emotions about MS may help to reduce pre-intervention feelings of anxiety and depression, but when attending a psychosocial group intervention program denial is no longer an option.
5.4.2 Limitations
Some limitations of this study should be addressed. First, sample sizes need to be larger to improve the power of this study. A power analysis for two samples with unequal variances (with significance set at 0.05 (one-sided) and power set at 0.80) shows that in the present study the sample size would have to range from 18 (subscale Self-Care) to 6,654 (subscale Mobility) for patients in individual counselling, and from 17 (CES-D) to 9,586 (subscale Mobility) for patients in the control group. This is not feasible in a psychosocial intervention study with patients with MS; moreover, the clinical relevance of a treatment effect that needs such large numbers to be statistically significant, is debatable.

Second, we performed several tests to compare measurements of both study groups. Due to this multiple testing, the statistically significant results should be interpreted carefully.

Third, patients in individual counselling were recruited after their neurologist referred them to the Department of Medical Psychology, whereas patients in group counselling were recruited at the Department of Neurology. This could imply that the patients in individual counselling were in greater psychological distress than the patients in group counselling, which is evidenced by the baseline difference in depressive symptoms between the two study groups. However, we decided to recruit patients with greater psychological distress to prevent the recruitment difficulties we experienced in the group intervention. We concluded that a group intervention is less attractive for most patients with MS and that a psychosocial intervention program in general is more feasible for patients already referred for psychological assistance. We think that the content of the program better fits the needs of patients who are referred for a psychological consult, than it fits the needs of ‘the average’ patient with MS. For this latter group, it may be more appropriate to offer an educational (and not primarily psychosocial) program which focuses on the emotional aspects of having a chronic disease.

Finally, we measured symptoms of depression by use of a self-report questionnaire. A problem with self-report questionnaires is that they may be susceptible to social desirability factors and therefore cannot distinguish between ‘true’ and ‘masked’ levels of depression. To adjust for the level of masking, clinical ratings could be included. Another possible solution for this problem is to include proxy ratings on depression.

5.4.3 Conclusions
Although more studies are needed to further evaluate the intervention program and to continuously improve it we believe that our results show that a protocolized psychosocial intervention program on an individual basis is promising and of significance in enhancing HRQoL and mood in patients with MS.
CHAPTER 5

Acknowledgements

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References


6

Value of health-related quality of life to predict disability course in multiple sclerosis

MAJ Visschedijk, BMJ Uitdehaag, M Klein, E van der Ploeg, EH Collette, L Vleugels, LEMA Pfennings, ELJ Hoogervorst, HM van der Ploeg, CH Polman

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CHAPTER 6

Abstract

Objective – To determine the value of health-related quality of life to predict change in disability status in patients with multiple sclerosis (MS).

Methods – Over a five-year period we collected data on health-related quality of life (MOS SF-36 Health Survey) and disability status (Expanded Disability Status Scale) from a heterogeneous group of 81 Dutch-speaking MS patients.

Results – Multivariate logistic regression analysis showed that HRQoL in the domains of Physical functioning and Role-physical functioning is a significant predictor of change in disability status.

Conclusions – The results indicate that a patient’s subjectively perceived health-related quality of life may not only be a clinically and psychosocially meaningful outcome per se, but may also be a predictor of objective outcomes such as change in disability status over a substantial period of time.
6.1 Introduction

Considerable differences in progression rate are found in patients with MS. Despite knowledge of several factors associated with prognosis, reliable predictions concerning the prognosis for individual patients are still difficult to make.\textsuperscript{[5]} Health-related quality of life (HRQoL) is now recognized as an essential measure to determine the impact of a disease as well as the potential effects of treatment interventions. HRQoL essentially reflects an evaluation of health and wellbeing from the patient’s perspective. Although several studies examined the potential prognostic value of HRQoL on medical outcome,\textsuperscript{[2-8]} only a single study examined its value in an MS population.\textsuperscript{[50]} This latter study investigated the predictive value of HRQoL (measured by the MOS SF-36 Health Survey (SF-36)) on subsequent changes in disability status (measured by the Expanded Disability Status Scale (EDSS)) in patients with MS. It showed that low scores on the SF-36 subscale Mental Health and low scores on Self-rated health (measured by the first question of the SF-36) were correlated with increased disability.

The present study also aimed to determining the value of HRQoL to predict change in disability status but, whereas the follow-up of the above-mentioned study was restricted to one year,\textsuperscript{[51]} our study has a five-year follow-up.

6.2 Method

6.2.1 Design and patients

A heterogeneous group of 144 Dutch and Belgian patients with MS participated in this study. All patients participated in an earlier longitudinal study\textsuperscript{[60]} on the construction of an MS-specific HRQoL instrument. In the present study, follow-up measurements took place over 60 months (i.e. five years) after baseline measurements. At five-years follow-up, 31 patients (20%) had dropped out of the study. Of these patients, 11 could not be reached, nine were not willing to participate again, six patients died, and five patients dropped out due to various reasons (e.g. serious illnesses). Baseline data of 32 Belgian patients (22%) turned out to be insufficiently complete to be used for this study. Data collected from 81 patients (61 Dutch patients and 20 Belgian patients) were used to examine the predictive value of HRQoL on change in disability status.
6.3 Measurements

We measured HRQoL at baseline, and at 6, 12, 18, 24 and 60 months follow-up (i.e. five years). Disability status was measured at baseline and at five-years follow-up.

In the Dutch sample, the questionnaire was completed at home by the patient themselves. In the Belgian sample, the questionnaire was completed in the presence of a specialized person who could provide assistance when necessary. Within two weeks of having completed the HRQoL questionnaire, a neurologist experienced in MS assessed the disability status of all patients by telephone using a standardized scale.\(^{[12]}\)

- To assess HRQoL, the Dutch version of the MOS Short Form-36 Health Survey (SF-36)\(^{[11,13]}\) was used. The SF-36 is developed for use in both healthy and chronically ill populations and has 36 items divided among eight subscales: Physical functioning, Role-physical functioning, Bodily pain, General health perceptions, Vitality, Social functioning, Role-emotional functioning and Mental health. The scores range from 0 to 100, with higher scores indicating higher levels of HRQoL in the corresponding domain. The SF-36 has been shown to be a valid and reliable instrument.

- In line with an earlier study on the predictive value of HRQoL on change in disability in patients with MS,\(^{[10]}\) we used the first question of the SF-36 to assess Self-rated health. This question is formulated as: “In general would you say your health is...” and can be scored on a five-point scale ranging from 5 (excellent) to 1 (poor).

- To assess disability status, the Expanded Disability Status Scale (EDSS) was used.\(^{[14]}\)

  The EDSS is rated by a neurologist and scores range from 0 (no disability) to 10 (death due to MS). According to neurological standards, a clinically meaningful change in EDSS score is specified as a change of 1 point in baseline EDSS scores ≤ 5.5, and as a change of 0.5 point in baseline EDSS scores ≥ 6.0 (15).

6.3.1 Statistical analysis

The association between HRQoL and change in disability status was assessed in three steps. First, a logistic regression analysis was performed to investigate the relationship between baseline Self-rated health (measured by the first question of the SF-36) and the presence or absence of a clinically meaningful deterioration in disability status five years later. To control for age, gender, and baseline disability status these variables were entered into the equation. Results are presented as regression coefficients (B) with 95% confidence intervals (CI). To analyse the significance of the relationship a Pearson chi-square test was performed. Second, the relationship between baseline HRQoL (measured by the eight subscales of the SF-36) and change in disability status five years later was further investigated by comparing patients who did or did not experience a clinically meaningful deterioration in disability status; this relationship was analysed with a Student’s t-test for independent samples. To control for multiple testing, the level of significance of the t-tests
was set at $p < 0.00625$ (according to Bonferroni’s method). Third, a multivariate logistic regression analysis was performed to determine the predictive value of HRQoL on change in disability status with change in disability status (i.e. presence or absence of a clinically meaningful deterioration in disability status) as the dependent variable. To control for gender, age and baseline disability status these variables were entered into the equation. The variables measuring HRQoL were entered into the model by a forward stepwise selection procedure using a likelihood ratio (LR) chi-square statistic. The level of significance of all tests (except for Student’s t-tests) was set at $p < 0.05$. Statistical analyses were performed using SPSS for Windows, version 11.0 (SPSS, Inc., Chicago, IL).

### 6.4 Results

The patient characteristics are presented in Table 1. At baseline, the 81 patients had a mean age of 44 (range 26 to 75) years and 55 (68%) of them were women. The mean duration of MS was 9 (± 8) years and the mean EDSS score was 5.1 (range 2.0 to 8.5). The Belgian sample showed a higher EDSS score at baseline ($\mu = 5.6 \pm 1.3$) than the Dutch sample ($\mu = 4.9 \pm 1.6$).

#### Table 1 Patient characteristics (n = 81)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Five-year follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>44 (11)</td>
<td>-</td>
</tr>
<tr>
<td>Gender (female/male)</td>
<td>55/26</td>
<td>-</td>
</tr>
<tr>
<td>Time since diagnosis (years)</td>
<td>9 (8)</td>
<td>-</td>
</tr>
<tr>
<td>EDSS score</td>
<td>5.1 (1.5)</td>
<td>5.7 (1.9)</td>
</tr>
<tr>
<td>Self-rated health (n = 80)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>poor</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>fair</td>
<td>42</td>
<td>-</td>
</tr>
<tr>
<td>good</td>
<td>26</td>
<td>-</td>
</tr>
<tr>
<td>very good</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>excellent</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Change in EDSS (n = 79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>unchanged</td>
<td>-</td>
<td>26</td>
</tr>
<tr>
<td>deteriorated</td>
<td>-</td>
<td>41</td>
</tr>
<tr>
<td>improved</td>
<td>-</td>
<td>12</td>
</tr>
</tbody>
</table>

Values are means (SD) or frequencies. EDSS = Expanded Disability Status Scale, Self-rated health = first question of the SF-36.

At baseline, one patient provided no data on the first question of the SF-36 (i.e. Self-rated health). Of the remaining 80 patients, five (6%) evaluated their health as poor, 42 (53%) as fair, 26 (33%) as good, six (8%) as very good, and one as excellent. At five-years follow-up,
CHAPTER 6

EDSS data of two patients were missing. Of the remaining 79 patients, 26 (33%) had an unchanged EDSS score, 41 (52%) experienced a clinically meaningful increase in EDSS score (i.e. deterioration), and 12 (15%) experienced a clinically meaningful decrease in EDSS score (i.e. improvement). Change in disability status from baseline to five-years follow-up ranged from an increase in EDSS score (i.e. deterioration) of 3.5 to a decrease in EDSS score (i.e. improvement) of 3.0. Change in disability status was categorized into two ordinal groups according to neurological standards: ‘clinically meaningful deterioration in disability status’ (n = 41), and ‘no clinically meaningful deterioration in disability status’ (n = 38); the latter group comprised patients with an improved or an unchanged EDSS score.

Table 2 shows the results of a logistic regression analysis performed to determine the relationship between Self-rated health at baseline and change in disability status at five-years follow-up. After controlling for gender, age, and disability status at baseline, there is no association between Self-rated health at baseline and change in disability status (B = 1.59, p = 0.34).

<table>
<thead>
<tr>
<th></th>
<th>B [95% CI]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0.38 [0.14-1.04]</td>
<td>0.06</td>
</tr>
<tr>
<td>Age</td>
<td>1.01 [0.97-1.06]</td>
<td>0.61</td>
</tr>
<tr>
<td>Disability status at baseline</td>
<td>0.95 [0.69-1.31]</td>
<td>0.74</td>
</tr>
<tr>
<td>Self-rated health at baseline</td>
<td>1.59 [0.62-4.10]</td>
<td>0.34</td>
</tr>
</tbody>
</table>

*Logistic regression analysis (SPSS). B = regression coefficient, CI = confidence interval. Dependent variable: change in disability status (no clinically meaningful deterioration in disability status = 0, clinically meaningful deterioration in disability status = 1). Self-rated health = first question of the SF-36.*

Table 3 presents the frequency of patients with a change in disability status according to Self-rated health at baseline. Of the 46 patients who evaluated their health at baseline as poor or fair, 22 (48%) experienced deterioration in disability status five years later; of the 33 patients who evaluated their health at baseline as good, very good or excellent, 19 (58%) experienced deterioration in disability status at five-years follow-up. For patients who rated their health at baseline as poor or fair, this gives a relative risk of having a deteriorated disability status five years later of 0.83 (X² = 0.73, p = 0.39).
Table 3 Change in disability status according to Self-rated health at baseline

<table>
<thead>
<tr>
<th>Change in disability status</th>
<th>Deterioration</th>
<th>No deterioration</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-rated health poor/fair</td>
<td>22</td>
<td>24</td>
<td>46</td>
</tr>
<tr>
<td>Self-rated health good/very good/excellent</td>
<td>19</td>
<td>14</td>
<td>33</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>38</td>
<td>79</td>
</tr>
</tbody>
</table>

Values are frequency of patients. Change in disability status = presence or absence of a clinically meaningful deterioration in disability status, Self-rated health = first question of the SF-36.

The relationship between baseline HRQoL and change in disability status five years later was further investigated by comparing mean scores on the subscales of the SF-36 of patients with or without deterioration in disability status; this was analysed with the independent samples t-test. The results presented in Table 4 show that there were no significant differences in SF-36 scores between the two groups.

Table 4 Comparison of baseline HRQoL between patients with and without a clinically meaningful deterioration in disability status

<table>
<thead>
<tr>
<th>Disability status (EDSS)</th>
<th>Deterioration (n = 41)</th>
<th>No deterioration (n = 38)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health-related quality of life (SF-36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical functioning</td>
<td>31.7 (19.9)</td>
<td>43.6 (26.8)</td>
<td>0.03</td>
</tr>
<tr>
<td>Role-physical functioning</td>
<td>40.2 (37.5)</td>
<td>34.5 (39.7)</td>
<td>0.51</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>76.3 (26.0)</td>
<td>74.6 (20.7)</td>
<td>0.74</td>
</tr>
<tr>
<td>General health</td>
<td>46.0 (21.5)</td>
<td>45.7 (20.6)</td>
<td>0.95</td>
</tr>
<tr>
<td>Vitality</td>
<td>54.3 (19.6)</td>
<td>53.8 (21.6)</td>
<td>0.75</td>
</tr>
<tr>
<td>Social functioning</td>
<td>69.8 (23.0)</td>
<td>73.4 (19.7)</td>
<td>0.47</td>
</tr>
<tr>
<td>Role-emotional functioning</td>
<td>79.7 (35.7)</td>
<td>67.6 (38.1)</td>
<td>0.15</td>
</tr>
<tr>
<td>Mental health</td>
<td>73.2 (18.7)</td>
<td>70.3 (21.9)</td>
<td>0.53</td>
</tr>
</tbody>
</table>

Values are means (SD). P-values are based on independent samples t-tests (SPSS). Significance was set at p < 0.00625 (according to Bonferroni’s method). * p-values all nonsignificant.
Table 5 presents results of a multivariate logistic regression analysis to determine the predictive value of HRQoL on change in disability status. After controlling for gender, age and disability status at baseline, subscales Physical functioning and Role-physical functioning appeared to be significant predictors of change in disability status five years later; i.e. a decrease of HRQoL in the domain of Physical functioning is associated with deterioration in disability status and, an increase of HRQoL in the domain of Role-physical functioning is associated with deterioration in disability status. The regression model shows good fit according to the Hosmer-Lemeshow goodness-of-fit statistic ($X^2 = 3.78, df = 8, p = 0.88$), and the total amount of variance explained by the model is 28% ($R^2 = 0.28$). Subsequently, odds ratios (OR) were calculated for the smallest unit change in both HRQoL subscales. A 5 point decrease in HRQoL on the subscale Physical functioning gives an OR of 1.67 (95% CI, 1.30-2.16) of having a deteriorated disability status five years later, and a 25 point increase in HRQoL on subscale Role-physical functioning gives an OR of 1.61 (95% CI, 1.03-2.50) of having a deteriorated disability status five years later.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Predictor</th>
<th>B</th>
<th>SE</th>
<th>OR  [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in disability status</td>
<td>Gender</td>
<td>-1.143</td>
<td>0.624</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>-0.009</td>
<td>0.027</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>Disability status at baseline</td>
<td>-1.069</td>
<td>0.334</td>
<td>0.343 [0.178-0.661]**</td>
</tr>
<tr>
<td></td>
<td>Physical functioning</td>
<td>-0.103</td>
<td>0.026</td>
<td>0.902 [0.857-0.950]**</td>
</tr>
<tr>
<td></td>
<td>Role-physical functioning</td>
<td>0.019</td>
<td>0.009</td>
<td>1.020 [1.001-1.038]*</td>
</tr>
</tbody>
</table>

Multivariate logistic regression analysis (SPSS) adjusted for gender, age and disability status at baseline. Dependent variable: change in disability status (no clinically meaningful deterioration in disability status = 0, clinically meaningful deterioration in disability status = 1). B = regression coefficient, SE = standard error, OR = odds ratio, CI = confidence interval. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

6.5 Discussion

We have replicated and expanded findings from a previous study (in an MS population in Norway) which reported a significant relationship between Self-rated health (i.e. the first question of the SF-36) and Mental health scores at baseline and change in disability status.
one year later, suggesting that HRQoL has a predictive value for subsequent disability development in MS. Our study enlarges on this latter study by extending the follow-up period, which we think is important in a chronic disease such as MS. In addition, changes in EDSS scores measured during one year only are less robust and may include more ‘errors of measurement’. Therefore, we examined the predictive value of HRQoL on changes in disability status over a period of five years.

Although our study confirms the predictive value of HRQoL on change in disability status in patients with MS, our findings differ from the above mentioned, in that we found no significant relationship between baseline Self-rated health and change in disability over time. Comparison of mean scores on the baseline SF-36 subscales for patients with and without deteriorated disability status revealed no significant differences in SF-36 scores between the two groups. However, multivariate logistic regression analysis revealed that the two HRQoL domains Physical functioning and Role-physical functioning are significant predictors of change in disability status in patients with MS over a period of five years.

Our results are consistent with earlier reports of a significant relationship between HRQoL in the domain of physical functioning and medical outcome in various diseases. For example, one study identified physical functioning and role functioning as significant and independent prognostic factors for overall survival in patients with bladder cancer, and another study found a significant relationship between low HRQoL in the domain of physical functioning and increased risk of death and hospitalization for patients with obstructive lung diseases.

One possible explanation for the relationship between HRQoL in the domain of physical functioning and change in disability status is that assessment of HRQoL in physical functioning reveals more practical and more diverse information about a patient’s limitations in daily functioning compared to scales that measure ‘pure’ functional status; for example, the EDSS is mainly based on measurement of ambulation. In general, self-rating of HRQoL integrates not only the objective functional or physical aspects of the disease, but also the patient’s perspective on their health and wellbeing. For example, the SF-36 Physical functioning scale (10 items) assesses limitations in activities ranging from self-care (e.g. washing or dressing oneself) to vigorous activities (e.g. lifting or carrying groceries) whereas the Role-physical functioning scale (4 items) measures the extent to which physical problems interfere with regular daily activities (e.g. shortening the amount of time spent on work or other activities as a result of one’s physical health). Because MS patients can experience a large variety of symptoms (e.g. motor impairments, numbness, loss of sensation, loss of bladder or bowel control, visual problems, sexual dysfunction, fatigue, etc.), and the EDSS disregards many of these, HRQoL probably captures more of these symptoms.

Another possible explanation for the relationship between HRQoL in the domain of physical functioning and change in disability status is that patients who experience a high
HRQoL on the physical dimension are in fact healthier (i.e. have a healthier lifestyle) compared to patients reporting a low HRQoL in physical functioning. Also, patients who consider themselves physically more efficient (i.e. have better perceived physical abilities) are less vulnerable regarding deterioration of physical functioning over time.

Furthermore, the present study showed a significant positive relationship between Role-physical functioning and change in disability status, indicating that patients reporting a high baseline HRQoL in Role-physical functioning, have a greater chance of experiencing deterioration in disability status five years later; however, this relationship is weak and seems counterintuitive. A possible explanation for this finding is a change in expectations and behaviour in patients who have a low level of physical functioning; by adjusting their ambitions and targets, their role-physical functioning may increase. This could explain the opposite relationship between Physical functioning and EDSS progression on the one hand, and Role-physical functioning and EDSS progression on the other. This explanation is supported by the observation that those patients who experienced deterioration in disability status, HRQoL in the domain of Role-emotional functioning is also somewhat higher.

Some limitations to our study need discussing. One concerns the longitudinal observational design whereby changes in the patients’ lives over time may influence their HRQoL and consequently their scores on HRQoL instruments. Such changes (varying e.g. from a severe relapse, the occurrence or disappearance of symptoms, use of a wheelchair, the death of a parent or partner, getting married, moving house, to the birth of a child, etc.) may be directly related to HRQoL, but can nevertheless impact on it. Most of these changes can occur without the knowledge of the investigator. Moreover, because most patients receive treatments during the follow-up period this may also influence the HRQoL scores.

Another limitation of our study is that we did not consider the role of (psychological) confounding factors, such as depression, anxiety, and fatigue. Several studies on MS patients have reported a significant relationship between depression and HRQoL, and between fatigue with EDSS. Other studies have shown that depression is an important predictor of both the physical and mental health scores of HRQoL, independent of clinically-assessed disability status. One study suggested that in patients with more symptoms of anxiety and depression, physical limitations may have a greater impact on the quality of physical health as assessed by the SF-36. Fatigue could represent another intermediate factor in the relationship between disability status and HRQoL. However, one study showed that fatigue contributed significantly only to the prediction of Role-physical functioning and General health scores, but not to other SF-36 scales.

More research is needed to validate our model of the long-term predictive value of HRQoL on change in disability status in different populations of patients with MS, and to investigate whether interventions directed at improving HRQoL have a favourable impact on the subsequent course of disability.
Acknowledgements

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References


General discussion
CHAPTER 7

This chapter presents the main results of the work in this thesis and discusses the methodological considerations, meaning and significance of the findings. In addition, some general conclusions are drawn.

Section 7.1 presents the results of the two main research questions and the four sub-questions that were investigated. In section 7.2 the methodological considerations are described in order to address the legitimacy of the results of the studies. Section 7.3 addresses the meaning and significance of the findings of this thesis and discusses them in relation to the international literature. Section 7.4 further discusses the implications of our work for clinical practice and makes some recommendations for future research. Finally, section 7.5 presents some concluding remarks about the studies in this thesis.

7.1 Research questions and findings

This section addresses the research questions posed in the General Introduction (Chapter 1). The first main research question of this thesis was:

1) What is the impact of a psychosocial intervention program, based on cognitive-behavioural and rational-emotive techniques, on health-related quality of life (HRQoL) in patients with multiple sclerosis (MS)?

Before this main research question is addressed, four sub-questions can be distinguished:

a) What is the effectiveness of psychosocial interventions for patients with MS in general?

A search of the literature research shows that several effective psychosocial interventions for patients with MS have been developed (see Chapter 2). A total of 13 studies in total were identified; four interventions were primarily based on cognitive-behavioural therapy, two interventions were based on psychotherapy, two aimed at relaxation training, one aimed at teaching coping skills, one was a peer support program, and three interventions incorporated more than one treatment technique (e.g. multi-component program). The results of these studies show that psychosocial interventions for patients with MS can be effective, especially in improving patients’ well-being, coping behaviour, state anxiety, mood, role performance, social relations, some physical aspects, and adherence to medical treatment.

b) What is the content and feasibility of a psychosocial group intervention, based on cognitive-behavioural and rational-emotive principles, for patients recently diagnosed with MS?

The results regarding this sub-question showed that a ‘per protocol’ psychosocial group intervention program for patients recently diagnosed with MS is feasible and promising
(see **Chapter 3**). Participants experienced a significant improvement in the HRQoL domains of Psychological status and Vitality.

c) **What is the impact of a psychosocial group intervention, based on cognitive behavioural and rational-emotive principles, for patients with MS?**

Findings related to this sub-question show a gradual though nonsignificant increase in HRQoL in three domains (Self-care, Psychological Status, and Mental health), and a nonsignificant increase in the number of positive Social Experiences for patients in the intervention group compared to patients who did not undergo a psychosocial intervention (see **Chapter 4**). The findings also revealed a negative trend for HRQoL in the domains of Mobility, Vitality, and Physical functioning. Taking into consideration the difficulty associated with patient recruitment and the results of this study, the conclusion is that a group intervention program is not the best option for most patients recently diagnosed with MS.

d) **What is the impact of a psychosocial intervention, based on cognitive–behavioural and rational-emotive principles, on an individual basis for patients with MS compared to the effectiveness of the intervention applied in groups of patients with MS?**

The results regarding this sub-question show that patients undergoing individual counselling had a statistically significant longitudinal improvement in HRQoL in the domain of Vitality and that patients tend to report a decrease (although nonsignificant) in depressive symptoms compared to patients in group counselling (see **Chapter 5**).

The second main research question of this thesis was:

2) **What is the value of health-related quality of life in predicting disability status in patients with MS?**

Findings regarding this main research question reveal that the two HRQoL domains Physical functioning and Role-physical functioning are significant predictors of change in disability status in patients with MS measured over a period of five years (see **Chapter 6**). This means that a decrease of HRQoL in the domain of Physical functioning is associated with deterioration in disability status, and an increase of HRQoL in the domain of Role-physical functioning is also associated with deterioration in disability status. The results also show the absence of an association between self-rated health and change in disability status.

In conclusion, the main results are that a short and ‘per protocol’ psychosocial intervention program based on cognitive-behavioural and rational-emotive techniques can have a positive effect on some, but not all, domains of HRQoL. More specifically, the effects on HRQoL are somewhat better when patients follow the program during individual counselling compared to patients who join the program in a group.
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Furthermore, the results indicate that a patient’s subjectively perceived HRQoL may also be a predictor of objective outcomes, such as change in disability status over a period of five years.

7.2 Methodological considerations

In order to conclude whether the findings of this thesis, as summarized above, are valid and generalizable, several methodological factors that might have influenced the results need to be discussed.

7.2.1 Participants
Selection of patients is an important step in research since, ideally, the population tested should be representative for the larger population to which one aims to generalize the results. Selection bias may limit the external validity of the research findings. Ideally a random sample is selected, but for practical reasons random selection is rare. For the intervention studies described in Chapters 3, 4, and 5 patients were recruited from two outpatient clinics of the VU University medical centre; i.e. the Department of Neurology and the Department of Medical Psychology. Since patients were recruited from a university hospital, some of them may have visited the hospital for a second opinion and/or for problems of more than average complexity. This could have influenced several of the findings. However, according to the baseline characteristics (Chapter 4; Table 1) no differences in psychological outcome measures were found between patients participating in the group intervention (recruited at the Department of Neurology) and patients in the control group (recruited from two sources; the Dutch MS Society and the university hospital). It is, therefore, not likely that MS patients recruited at a university hospital (i.e. patients with a second opinion and/or with problems of more than average complexity) are dissimilar regarding psychological characteristics to patients recruited from other sources.

For the individual counselling program described in Chapter 5, we recruited patients at the Department of Medical Psychology. According to the baseline characteristics, patients recruited at that department show significantly more signs of depression (Chapter 5; Table 1) compared to patients recruited at the Department of Neurology of the same university hospital. This implies, and confirms, that patients who are referred to a medical psychologist are in greater psychological distress than patients who are not. However, we decided to recruit patients with greater psychological distress in order to avoid the recruitment difficulties we experienced in the group intervention.

Another possible source of selection bias is the motivation of the participating patients. For the group intervention study described in Chapter 4 we had difficulty in
recruiting patients; of all eligible patients, 59% declined to join the group program for various reasons (i.e. lack of interest, problems getting to the hospital, lack of time, and the emotional burden of participating in a group). This may have resulted in a selected sample of highly motivated patients. For medical-ethical reasons it was not possible to examine the characteristics of patients who declined participation. Based on these recruitment problems we concluded that a group intervention is less attractive for most patients with MS and that the content of the program better fits the needs of patients who are referred for a psychological consultation (Chapter 5).

In conclusion, our findings are particularly representative for patients with MS treated by a neurologist in a university hospital and who are both highly motivated and not afraid of group processes or who are referred to a medical psychologist.

7.2.2 Design
The impact of the study design on the results also needs to be addressed. In the studies described in this thesis we used a longitudinal design, whereby the patients in the intervention studies were followed for more than one year and assessed at four time points; directly before intervention, directly after intervention, and at 6 and 12 months after intervention. Longitudinal research is time consuming and thereby costly, but in order to explore, for example, topics such as long-term effects and developmental processes such a study design is essential.14-2 A disadvantage of a longitudinal observational study is that changes in the lives of the participants and changes in the health status of participants may occur in the period between measurements, which may influence the HRQoL of these participants and consequently their scores on HRQoL questionnaires. These changes may have an impact on many aspects of HRQoL; for example, important changes can include severe exacerbations of MS, the occurrence or disappearance of symptoms, the use of walking aids (i.e. a wheelchair), the death of a parent or partner, getting married, losing one’s job, moving house, and the birth of a child. Although some of these changes may not be directly related to HRQoL they can definitely have an impact on it. However, nearly all of the above factors are beyond the control of and/or the knowledge of the investigator. Furthermore, most participants are under medical supervision and may receive various treatments from their physician in the period between two measurements. Changes in the lives of patients are natural and, depending on the duration of the impact (short-term versus long-term) and on the perceived control by the participant, may have an influence on HRQoL scores.

In a longitudinal study, a randomized controlled design is the best option to minimize threats to validity; initially we intended to use such a design by including a waiting-list control group and to randomly assign patients to either the intervention group or the waiting-list control group. However, due to the recruitment difficulties described in Chapters 4 and 5 it was not possible to compile a waiting-list control group. For the group
intervention study (described in Chapter 4) we decided to include a matched control group compiled from MS patients who participated in an earlier study on HRQoL, in order to be able to compare results of ‘treated’ versus ‘untreated’ patients. These matched control patients received ‘standard medical care’, and therefore their results on the questionnaires reflect the ‘normal’ longitudinal development of HRQoL in patients with MS, including any effects of life events and changes in health conditions.

Furthermore, it is debatable how appropriate it is to conduct randomized controlled trials (RCTs) of psychological interventions at all. This is mainly due to the fact that, in practice, isolated therapies are seldom used and treatment plans are individualized to patients as complex self-management plans. Evaluation using an RCT in the clinical setting may mean that the intervention is so tightly controlled that even if effectiveness were proven, it might be difficult to transfer the intervention into routine clinical practice.

In longitudinal research there is always a risk of losing participants during the study, which may result in a biased sample. In the group intervention study, two patients (12%) dropped out and were lost to follow-up; one of them dropped out after the fifth group session because the confrontation with MS (and other patients with MS) was too distressing, and the other patient dropped out before the intervention started because of the more than 15-year age difference between her and the other participants in that group. In the individual intervention study, five patients (19%) dropped out and were lost to follow-up. These patients dropped out after they had finished all eight sessions of the intervention; four patients dropped out at the third measurement (6 months post-intervention) and the fifth patient dropped out at the fourth measurement (12 months post-intervention). Their reason for drop-out was loss of interest in the study.

Another threat to validity could be the sample size. In this study we used relatively small sample sizes (i.e. n=17 for the group intervention study and n=19 for the individual counselling study). A power analysis for two samples with unequal variances, with significance set at 0.05 (one-sided) and power set at 0.80, shows that, for example, in the individual counselling study the sample size would have to range from 18 (subscale Self-Care) to 6,654 (subscale Mobility) for patients in individual counselling, and from 17 (CES-D) to 9,586 (subscale Mobility) for patients in the control group (i.e. group intervention). This is not realistic for a psychosocial intervention study; moreover, the clinical relevance of a treatment effect that needs such large numbers to be statistically significant, is debatable. Therefore we believe that, although large numbers of participants are desirable, it is not always realistic to aim for large groups. Furthermore, most of the psychosocial intervention studies for patients with MS (Chapter 2) are based on relatively small sample sizes. The average sample size of these studies is 27 patients in total and none of the studies included more than 70 patients (Chapter 2; Table 1). This is in line with the sample sizes in our studies (Chapter 4 and Chapter 5), and shows that in psychosocial intervention studies for patients with MS, it is not to be expected to include large numbers of patients should not be expected.
In conclusion, notwithstanding the above mentioned potential biases regarding study design, it appears that the type of design did not influence the effectiveness of our psychosocial intervention and, therefore, it is justified to consider our findings as being relatively valid.

7.2.3 Assessment instruments
A broad range of patient characteristics was assessed in this study (including generic as well as MS-specific measures) and the majority of instruments used were validated, reliable measures. The validity of two (kinds of) instruments is discussed in more detail: the use of self-report questionnaires in general and, more specifically, the assessment of clinical disability by means of the Expanded Disability Status Scale (EDSS).

Most instruments used for the studies in this thesis were self-report questionnaires, which have been proven valid in clinical practice and scientific research. Self-report instruments are very suitable for the measurement of HRQoL, since HRQoL is generally considered a subjective perception. However, in any research measuring aspects of reality, bias can occur. Bias is identified as an inaccurate reflection of reality due to systematic measurement error. By using instruments that are validated and known to be reliable, bias can be diminished. The AmsQol is a newly developed MS-specific HRQoL questionnaire, and is composed of several items from two existing and well-constructed HRQoL questionnaires; the Short Form-36 Health Survey (SF-36) and the Disability and Impact Profile (DIP).[5]

A problem with self-report questionnaires is that they may be susceptible to social desirability factors and therefore cannot distinguish between ‘true’ and ‘masked’ levels of a certain characteristic, for example, depression. To adjust for the level of masking, clinical ratings could be included.[4] Furthermore, self-report questionnaires may be less suitable for patients experiencing cognitive or emotional problems because they will interfere with self-assessment of health status, which may affect reliability. Applying self-report measurements in these patients could lead to biased or unreliable information or loss of information.[5,6] A solution for this problem would be to include proxy ratings; in particular, partners as proxies are known to be useful sources when assessing the impact of MS.[7]

For assessment of disability status, we used the Expanded Disability Status Scale (EDSS), which is widely used by physicians (i.e. neurologists). The EDSS has some imperfections; the instrument has poor responsiveness, large inter-rater variability and primarily focuses on mobility and ambulation.[8,9] It can be argued that in a relatively homogenous population the EDSS is inadequate for the measurement of small differences in disability status. However, in the intervention studies (Chapter 4 and Chapter 5) we used the EDSS to assess pre-study disability status and did not examine possible change between pre- and post-intervention disability status. For the study described in Chapter 6,
the EDSS was used to predict change in disability status over a period of five years. It is reasonable to assume that over five years clinically significant changes in disability will take place in patients with MS.

In conclusion, by using well-constructed and validated patient-assessed and physician-assessed instruments, the whole spectrum of physical and psychological aspects of patients’ functioning was examined. Therefore, it is justified to consider the results of our study as valid and reliable.

7.2.4 Conclusions regarding methodology
After taking into account the several methodological considerations it might be concluded that, as a result of the selection of the participants, the type of design and the choice of instruments, our findings can be attributed to the interventions and, in general, that our findings are relevant for MS patients treated in (university) hospitals.

7.3 Relevance of findings

Several similarities exist between the findings of the current thesis and those of previous studies on psychosocial interventions for patients with MS.

First, our finding that an individual counselling program for patients with MS can improve HRQoL in the domain of Vitality is particularly relevant. The Vitality domain of the Amsterdam Quality of life Questionnaire (AmsQoL) contains questions such as ‘How much of the time during the past four weeks... did you have a lot of energy?’. This means that patients, one-year after completing the individual counselling program, report to have an improved energy level compared to their pre-interventional energy level. This finding is of importance because especially fatigue (a symptom experienced by approximately 80% of MS patients) can have a profound effect on social and psychological functioning.\cite{10} It can, for example, deter patients from visiting friends and family (making patients dependent on others to visit them) and may also influence mood. Furthermore, several studies have demonstrated significant associations between fatigue and disability status, depression and quality of life in MS.\cite{11-14}

Second, examination of the scores on the CES-D reveals an almost statistically significant improvement in depressive symptoms for patients in individual counselling; patients in individual counselling show a 30% decrease in depressive symptoms one year after the intervention. This finding is of clinical relevance because depression frequently co-occurs with other MS symptoms (102-106). Depression, for example, may be more common in MS than in other neurological conditions\cite{20,21} and some studies have indicated that the lifetime risk of major depression in MS is between 23% and 54%.\cite{22-25}
Furthermore, depression is associated with higher levels of disability and poorer HRQoL in patients with MS.\textsuperscript{[26]} This means that an improvement in depressive feelings can affect the patient’s quality of life and disability status.

Third, our recruitment difficulties in the group intervention study (56% of the eligible patients was not willing to participate in the group program) are similar to those of an earlier study on the effects of a psychosocial group intervention for patients with MS.\textsuperscript{[27]} In that study, 325 MS patients were invited to participate, 29% showed interest and after the intake interview only 13% actually participated. Our study demonstrates that a group program with a psychosocial character is probably not particularly attractive for patients recently diagnosed with MS. Although a group format has known advantages, confrontation with MS can be too distressing for some patients, as evidenced by hesitation to join the group. As one patient stated: “On the one hand I’m afraid to be confronted with somebody who is more disabled than I am, on the other hand I’m afraid I’ll be the most disabled person in the group.” We assume that these recruitment difficulties could be a result of some particular ‘patient characteristics’. For example, one study revealed a key role for neuroticism in the development of anxiety and depression in physically ill patients.\textsuperscript{[28]} Neurotic patients tend to experience negative emotions, will therefore suffer more quickly from depressive symptoms and may seek psychological help more often than patients who are less neurotic. Denial may also play a role in the recruitment difficulties. Denial is common and its impact may vary over time;\textsuperscript{[29,30]} moreover, it can often occur among recently diagnosed patients. Pre-intervention denial of negative emotions about MS may help to reduce pre-intervention feelings of anxiety and depression, but attending a psychosocial intervention program denial is no longer an option. Patients in denial may be less inclined to attend a specialized group program that focuses on their disease.

In conclusion, our finding that a psychosocial group intervention program is less attractive for most of the recently diagnosed patients with MS as well as our finding that a psychosocial intervention program on an individual basis has a greater effect on HRQoL than does a group intervention, contributes to the current literature on psychosocial intervention studies for patients with MS.

7.4 Implications for clinical practice and suggestions for future research

7.4.1 Implications for clinical practice
Having discussed the methodological strengths and weaknesses of the studies in this thesis and having addressed the value of the findings, several implications for clinical practice
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should be mentioned. A distinction will be made between clinical implications for a) patients with MS, b) partners of patients with MS, and c) professionals.

7.4.1.a Patients

A psychosocial intervention program is particularly suitable for MS patients with serious psychosocial problems as a result of their disease. It is advised to approach those patients who, for example, show signs of clinical depression or who report to suffer from the burden of having an unpredictable, progressive and disabling disease. For recently diagnosed patients who are not in great psychological distress, it may be more appropriate to offer an educational program. An educational program, for example, focuses less on psychosocial and psycho-behavioural issues compared to a psychological-based intervention. Instead of solving emotional difficulties in adjusting to MS, an educational program mainly provides patients with practical information concerning MS (i.e. information about symptom and disease management, treatment and medication, or about physical and emotional aspects of MS in general).

7.4.1.b Partners

Since MS causes many changes in the lives of patients the same applies to their partners, who also have to cope with many changes. A few studies have explored the impact on HRQoL and emotional well-being of the partners of patients with MS. Not surprisingly, these studies found that HRQoL of partners was poorer compared to that of the general population. Therefore, partners of patients with MS should also be encouraged to express their needs for psychosocial care, and hospitals should facilitate access to specialized intervention programs (for example, a (psycho-) educational program) for partners of patients with MS or specialized partner sessions could be incorporated in an intervention program for patients with MS.

7.4.1.c Professionals

MS professionals (e.g. neurologists, MS nurse specialists or physiotherapists) should be aware of psychosocial problems in patients with MS and should recognize that some patients are, psychologically, more vulnerable than others (e.g. patients who show signs of clinical depression), which implies that these patients need a different kind of psychological counselling than patients who are less vulnerable. It is important for health professionals to refer patients to a medical psychologist when they report having psychological distress concerning MS in order to properly assess their psychological situation. In addition, assessment of HRQoL should be a part of the assessment program for patients with MS because HRQoL is related to disability status in the long term.

Furthermore, health professionals should recognize that there are several distinct courses of MS and each course may confront patients with somewhat different psychological challenges. Even for individual patients with the same course, the prognosis
is diverse and uncertain. It is, therefore, important to develop disease-specific psychosocial intervention programs (such as the program examined in this thesis) because these programs best fit the psychosocial needs of patients with MS (and their partners).

7.4.2 Suggestions for future research

Based on the findings of the studies presented in this thesis, several recommendations for future studies on the effects of psychosocial interventions for patients with MS can be made.

First, more studies are needed to assess the needs in psychosocial care for patients with (recently diagnosed) MS. It needs to be established which type of care best suits the diverse phases of MS and the intensity of the reported psychological distress in patients with MS. For example, it should be explored what the effect is of a (psycho-) educational program versus the effect of a psychosocial intervention program on HRQoL in patients with MS. Furthermore, it needs to be established which type of MS patient (defined by, for example, disease characteristics, or particular patient characteristics or type and/or impact of psychosocial problems) benefits most from a group intervention program and which type of MS patient benefits most from an individual counselling program.

Second, it needs to be examined whether a specialized educational or psychosocial partner program will be feasible and effective in improving HRQoL of partners of patients with MS. By adequately supporting the close relatives of MS patients, the psychological well-being of a patient’s social care system might be maintained or improved.

Third, future research should investigate the effectiveness of follow-up sessions for patients who participated in the intervention program. Follow-up sessions might contribute to a long-lasting change in cognitions, feelings and behaviour of participants. This can be particularly relevant since MS is a chronic and progressive disease.

Fourth, important in future research could be the study of the impact of new types of counselling, for example, internet therapy or self-help programs (i.e. books) for patients with MS (and their partners). These novel types of counselling can be of special interest for the MS population because they will facilitate access to therapy programs. Internet counselling and self-help programs could be a useful solution or option for some patients, such as for patients who are dependent on others for driving them to a therapy location or for patients who suffer severely from fatigue.

Finally, it is important to keep improving psychosocial intervention programs for patients with MS and adjusting them not only to relevant findings in medical psychology but also to relevant findings in MS research in general.
7.5 Final remarks

First, the current thesis demonstrates that a short-term psychosocial (group) intervention program for patients with MS can have a positive effect on some, but not all, domains of HRQoL. More specifically, patients in individual counselling had a statistically significant longitudinal improvement in HRQoL in the domain of Vitality and an almost statistically significant long-term decrease in depressive symptoms compared to patients in group counselling. The results of this thesis also show a gradual increase of HRQoL in three domains (Self-care, Psychological Status, and Mental health) and a gradual increase in the number of positive Social Experiences for patients in the intervention group compared to patients who received ‘standard medical care’.

Second, the current thesis also shows that HRQoL is a significant predictor of long-term change in disability status in patients with MS.

To conclude, this thesis demonstrates that a psychosocial group intervention program is not particularly attractive for most patients recently diagnosed with MS, and that patients who seriously suffer from the burden of having MS are likely to benefit the most from psychosocial intervention programs, such as the intervention examined in this thesis. Furthermore, the results of this thesis indicate that a patient’s subjectively perceived HRQoL may not only be a clinically and psychosocially meaningful outcome per se, but may also be a predictor of objective outcomes such as change in disability status over a substantial period of time.
References


Summary
Multiple sclerosis (MS) affects the central nervous system, which consists of the brain, spinal cord, and the optic nerves. Surrounding and protecting the nerve fibres of the central nervous system is a fatty tissue called myelin, which helps nerve fibres conduct electrical impulses. In MS, the body’s immune system, which normally helps to fight off infections, attacks myelin. This causes inflammation of the myelin sheath and myelin is lost in multiple areas, leaving scar tissue called sclerosis. When myelin or the nerve fibre is destroyed or damaged, the ability of the nerves to conduct electrical impulses to and from the brain is disrupted, and this produces the various neurological symptoms of MS. It is this nerve damage that causes the accumulation of disability that can occur over time. As the central nervous system links all bodily activities, many different types of symptoms can appear in MS. The specific symptoms that appear depend upon which part of the central nervous system is affected and the function of the damaged nerve; however, several symptoms are more common. These include motor and sensory impairments (numbness, loss of sensation), difficulty with ambulation, loss of bladder or bowel control, visual problems, sexual dysfunction, fatigue, and decline in cognitive function. In addition to its physical symptoms, MS may have profound emotional consequences as well; MS strikes relatively young adults in a life phase when many important changes take place (for example, planning to have children) and because of the diagnosis their world is turned upside down. Patients have to deal with prognostic uncertainty and it is unclear whether plans for the future can be fulfilled. Because of all this uncertainty and the progressive disabling character of the disease, coping with MS is an ongoing process. Historically the management of MS has been predominantly about limiting disability by symptomatic management of acute relapses and attempting to influence the long-term course. Even though this type of management is important, it should be accompanied by an equal effort at improving participation, well-being, and health-related quality of life (HRQoL). HRQoL can be seen as an opportunity to assess and meet previously unmet needs, to predict previously unpredictable outcomes, and to develop broad interventions with beneficial psychological and physical effects.

One main research objective of this thesis is to develop and evaluate a psychosocial intervention program for patients (recently diagnosed) with MS. The intervention program is based on cognitive behavioural and rational-emotive principles and aimed at modifying dysfunctional beliefs, thereby reducing negative emotions, improving adjustment behaviours and ultimately HRQoL. in patients with MS. A second main research objective of this thesis is to examine the value of HRQoL in predicting disability status in patients with MS. To investigate these two main research objectives several studies were conducted.

Chapter 2 provides information on the effectiveness of psychosocial interventions for patients with MS in general. Literature research shows that several effective psychosocial interventions for patients with MS have been developed. A total of 13 studies were identified; four interventions were primarily based on cognitive-behavioural therapy,
two interventions were based on psychotherapy, two aimed at relaxation training, one aimed at teaching coping skills, one was a peer support program, and three interventions incorporated more than one treatment technique (e.g. multi-component programs). The results of these studies show that psychosocial intervention studies for patients with MS can be effective, particularly in improving patients’ well-being, coping behaviour, state anxiety, mood, role performance, social relations, some physical aspects, and adherence to medical treatment.

**Chapter 3** describes the results of a study on the development and feasibility of a psychosocial group intervention, based on cognitive-behavioural and rational-emotive principles, for patients recently diagnosed with MS. The results show that a ‘per protocol’ psychosocial group intervention program for patients recently diagnosed with MS is feasible and promising. Participants experienced a significant improvement in the HRQoL domains of Psychological status and Vitality.

**Chapter 4** presents the results of a study on the impact of a psychosocial group intervention, based on cognitive behavioural and rational-emotive principles, for patients with MS. Findings show a gradual though nonsignificant increase in HRQoL in three domains (Self-care, Psychological Status, and Mental health) and a nonsignificant increase in the number of positive Social Experiences for patients in the intervention group compared to patients who did not undergo a psychosocial intervention. The findings also reveal a negative trend for HRQoL in the domains of Mobility, Vitality, and Physical functioning. Taking into consideration the recruitment difficulties and the results of this study, the conclusion is that a group intervention program is not the best option for most patients recently diagnosed with MS.

The study in **Chapter 5** investigates the impact of a psychosocial intervention, based on cognitive-behavioural and rational-emotive principles, on an individual basis for patients with MS. The psychosocial intervention on an individual basis was compared with the intervention used in groups of patients with MS. The results of this study show that patients in individual counselling had a statistically significant longitudinal improvement in HRQoL in the domain of Vitality and, although nonsignificant, patients tend to report a decrease in depressive symptoms compared to patients in group counselling.

**Chapter 6** presents the results of a study on the value of HRQoL in predicting disability course in patients with MS. Findings in this study show that the two HRQoL domains Physical functioning and Role-physical functioning are significant predictors of change in disability status in patients with MS measured over a period of five years. This means that a decrease of HRQoL in the domain of Physical functioning is associated with deterioration in disability status, and an increase of HRQoL in the domain of Role-physical functioning is also associated with deterioration in disability status. The findings also show the absence of an association between self-rated health and change in disability status.
SUMMARY

Chapter 7 discusses the main findings of the studies in this thesis from a methodological viewpoint to establish whether methodological choices made concerning the inclusion of participants, the study design, and the measurement instruments might have influenced the validity of the findings. Chapter 7 also describes the relevance of the findings of the current thesis and relates them to the literature on psychosocial interventions for patients with MS. Furthermore, some implications for clinical practice and suggestions for future research are addressed.

In conclusion, this thesis shows that a psychosocial group intervention program is not particularly attractive for most patients recently diagnosed with MS, and that patients who seriously suffer from the burden of having MS, are likely to benefit the most from psychosocial intervention programs, such as the intervention examined in this thesis. Furthermore, the results in this thesis indicate that a patient’s subjectively perceived HRQoL may not only be a clinically and psychosocially meaningful outcome *per se*, but may also be a predictor of objective outcomes such as change in disability status over a substantial period of time.
Samenvatting
SAMENVATTING

Multiple Sclerose (MS) is een ziekte van het centrale zenuwstelsel, dat bestaat uit de hersenen, het ruggebeen en de oogzenuwen. De zenuwbanen van het centrale zenuwstelsel worden beschermd door een vetttige laag (myeline) die ervoor zorgt dat de zenuwbaan een electrische impuls kan voortbrengen. Bij MS valt het immuunsysteem, dat normaaliter infecties bestrijdt, de myeline aan. Hierdoor ontstaan er op meerdere plaatsen ontstekingen in de myelinelaag waardoor de myeline verloren gaat en er littekenweefsel (sclerose) achterblijft. Wanneer de myelinelaag of een gehele zenuwbaan is vernietigd of beschadigd, kan de zenuwbaan geen of slechts gedeeltelijk electrische impulsen vanuit de hersenen voortbrengen en hierdoor ontstaan de verscheidene neurologische symptomen van MS. De voortschrijdende beschadiging van zenuwbanen veroorzaakt in de loop van tijd een verslechtering van het lichamelijk functioneren. Omdat het centrale zenuwstelsel betrokken is bij alle lichamelijke activiteiten, kunnen bij MS allerlei verschillende symptomen optreden. Welk symptoom optreedt is afhankelijk van het deel van het centrale zenuwstelsel dat is aangetast en van de functie van de beschadigde zenuwbaan, maar sommige symptomen komen vaker voor dan andere. Problemen met de sensoriek en motoriek, het lopen, de blaas, de darmen, de ogen, het seksueel en cognitief functioneren komen veel voor. Verder zijn veel mensen met MS vaak moe. Naast lichamelijke symptomen kan MS ook emotionele consequenties hebben; MS treft vaak relatief jonge mensen die in een levensfase zijn waarin belangrijke veranderingen plaatsvinden (bijvoorbeeld gezinsuitbreiding) en de diagnose kan alles in een ander licht zetten. Mensen met MS moeten omgaan met onzekerheid over hun prognose en het is onduidelijk of toekomstplannen kunnen worden uitgevoerd. Door de onzekerheid en het progressieve karakter van MS, is het omgaan met deze ziekte een continu proces. De behandeling van MS concentreert zich vaak, ook vanuit historisch perspectief, op het beperken van lichamelijke symptomen bij een acute terugval en het beïnvloeden van het verloop op lange termijn. Hoewel dit type interventie belangrijk is, zou het moeten samengaan met interventies gericht op het verbeteren van gezondheidsgerelateerde kwaliteit van leven (KvL) en algemeen welbevinden. KvL heeft een multi-dimensioneel karakter waarbij drie domeinen worden onderscheiden: fysiek, psychologisch en sociaal functioneren. Vanuit deze definitie kan KvL een uitdaging bieden voor het ontwikkelen van ‘brede’ interventies gericht op het verbeteren van lichamelijke en psychosociale problemen.

Een hoofddoel van de onderzoeken in dit proefschrift is het ontwikkelen en evalueren van een psychosociaal interventieprogramma voor mensen (recent gediagnosticeerd) met MS. Het interventieprogramma is gebaseerd op cognitief gedragstherapeutische en rationeel-emotieve principes en heeft tot doel om, naast het modificeren van disfunctionele overtuigingen en het verbeteren van negatieve emoties, mensen met MS (beter) te leren omgaan met hun ziekte om uiteindelijk hun KvL te verbeteren. Een tweede hoofddoel van de onderzoeken in dit proefschrift is om na te gaan in hoeverre KvL het lichamelijk functioneren van mensen met MS kan voorspellen. Om
deze twee hoofddoelen te bereiken, zijn meerdere deelonderzoeken uitgevoerd en beschreven in dit proefschrift.

In Hoofdstuk 2 worden de resultaten beschreven van een literatuuronderzoek naar de effectiviteit van psychosociale interventies voor mensen met MS. Uit dit literatuuronderzoek blijkt dat er verscheidene effectieve psychosociale interventies voor mensen met MS zijn ontwikkeld. In totaal werden 13 interventiestudies geïdentificeerd; vier interventiestudies waren gebaseerd op cognitieve gedragstherapie, twee interventiestudies waren gebaseerd op psychotherapie, twee studies baseerden zich op ontspanningstechnieken, één richtte zich op het beter leren omgaan met MS (een ‘copingvaardigheidstraining’), één studie betrof een begeleidingsprogramma door medepatiënten, en drie interventiestudies waren gebaseerd op meerdere behandelingsmiddelen (zogenaamde multi-component programma’s). De resultaten van deze interventiestudies laten zien dat psychosociale interventieprogramma’s voor mensen met MS effectief kunnen zijn, met name op het gebied van het verbeteren van welbevinden, ‘coping-gedrag’, angst, stemming, rol-functioneren, sociale relaties, een aantal lichamelijke aspecten en therapietrouw.

In Hoofdstuk 3 wordt de ontwikkeling en haalbaarheid beschreven van een eerste versie van het psychosociale groepsinterventieprogramma gebaseerd op cognitief-gedragstherapeutische en rationeel-emotieve principes, voor mensen die recent de diagnose MS hebben gekregen. De resultaten van dit deelonderzoek laten zien dat een geprotocolleerde psychosociale groepsinterventie voor mensen met MS haalbaar is en potentie heeft. De deelnemers aan het groepsinterventie lieten een statistisch significante verbetering van KvL zien in de domeinen Psychologische status en Vitaliteit.

In Hoofdstuk 4 wordt de effectiviteit beschreven van de definitieve versie van het psychosociale groepsinterventieprogramma voor mensen met MS, gebaseerd op cognitief-gedragstherapeutische en rationeel-emotieve principes. Hiertoe werden de resultaten van de deelnemers aan de psychosociale groepsinterventiestudie vergeleken met MS patiënten die ‘standaard medische zorg’ ontvingen. De resultaten van dit deelonderzoek laten een gelijdelijke, maar niet statistisch significante, toename van KvL op drie gebieden zien voor de deelnemers aan de interventiestudie (Zelf-verzorging, Psychologische status en Geestelijke gezondheid) en daarnaast een niet-statistisch significante toename van het aantal Sociale contacten voor de deelnemers aan de interventiestudie. Ook laten de resultaten een negatieve trend zien voor de KvL-domeinen Mobilitéit, Vitaliteit en Fysiek functioneren. In aanmerking genomen de wervingsmoeilijkheden en de resultaten van deze deelstudie is de algemene conclusie dat een groepsinterventie niet de beste optie is om KvL te verbeteren bij recent gediagnosticeerde mensen met MS.

In Hoofdstuk 5 wordt de effectiviteit beschreven van een psychosociaal interventieprogramma voor mensen met MS op individuele basis en gebaseerd op cognitief-gedragstherapeutische en rationeel-emotieve principes. De resultaten van het interventieprogramma voor gebruik in individueel patiëntenco contact werden vergeleken
SAMENVATTING

met de resultaten van het interventieprogramma voor gebruik in een groep patiënten. Uit
de resultaten van dit deelonderzoek kwam naar voren dat de deelnemers aan het
individuele interventieprogramma een statistisch significante longitudinale verbetering in
het KvL-domein Vitaliteit rapporteerden vergeleken met de deelnemers aan het
groepsprogramma. Daarnaast bleek dat de deelnemers aan het individuele
interventieprogramma een (niet-significante) afname van depressieve klachten
rapporteerden.

In Hoofdstuk 6 worden de resultaten beschreven van een studie naar de waarde
van KvL bij het voorspellen van mate van invaliditeit van mensen met MS. De resultaten
van dit onderzoek laten zien dat de twee KvL-domeinen Fysiek functioneren en Rol-fysiek
functioneren statistisch significante voorspellers zijn van verandering in mate van
invaliditeit op langere termijn (vijf jaar). Meer specifiek, deze studie toont aan dat bij
mensen met MS een afname van KvL in het domein Fysiek functioneren is geassocieerd
met een toename van de mate van invaliditeit vijf jaar later en ook dat een toename van
KvL in het domein Fysieke rolbeperking is geassocieerd met een toename van de mate van
invaliditeit vijf jaar later. Daarnaast toont deze studie aan dat er geen verband bestaat
binnen ‘self-ervaren algemene gezondheid’ (self-rated health) en verandering in mate van
invaliditeit van mensen met MS.

In Hoofdstuk 7 worden de belangrijkste bevindingen van de onderzoeken
beschreven in dit proefschrift samengevat en besproken, gevolgd door methodologische
overwegingen wat betreft de inclusie van deelnemers, het onderzoek design en de
meetinstrumenten. Daarnaast beschrijft Hoofdstuk 7 de relevante van de resultaten
gerelateerd aan wat in algemene zin bekend is over psychosociale interventies voor
mensen met MS. Vervolgens worden aanbevelingen gedaan voor de klinische praktijk en
verder onderzoek.

Concluderend blijkt uit dit proefschrift dat een psychosociaal
groepsinterventieprogramma niet bijzonder attractief is voor de meeste MS patiënten die
recent gediagnosticeerd zijn en dat MS patiënten die een zekere mate van lichamelijke
ervaren door hun ziekte, de grootste kans maken te profiteren van psychosociale
interventieprogramma’s zoals beschreven in dit proefschrift. Bovendien blijkt uit dit
proefschrift dat het subjectieve concept Kwaliteit van Leven niet alleen in klinisch en
psychosociaal opzicht een betekenisvolle uitkomstmaat is, maar dat het ook over langere
termijn een voorspeller kan zijn van een objectieve uitkomstmaat zoals verandering in
mate van invaliditeit.
Appendix
APPENDIX

Inhoud en werkwijze van ‘Leren omgaan met MS’: een cursus voor mensen met multiple sclerose

Het psychosociale interventieprogramma ‘Leren omgaan met MS’ bestaat uit acht bijeenkomsten die eens in de twee weken plaatsvinden. Er zijn twee versies van het zorgprogramma ontwikkeld: één versie voor gebruik in kleine groepen (6-8 deelnemers) en één versie voor gebruik in individueel patiëntencentrum. Beide programma’s zijn inhoudelijk gelijk, maar verschillen met name in de duur van de bijeenkomsten (elke groepsbijeenkomst duurt 2 uur, inclusief een pauze van ongeveer 15 minuten, en elke individuele bijeenkomst duurt 45 minuten). Het intensieve programma vraagt actieve participatie van deelnemers in de vorm van huiswerkopdrachten en oefeningen. Deelnemers ontvangen aan het eind van elke bijeenkomst een nieuw hoofdstuk uit het werkboek, met daarin informatie en huiswerkopdrachten. De informatie en de huiswerkopdrachten zijn gekoppeld aan de thema’s die in de bijeenkomsten centraal staan. De rode draad door de bijeenkomsten wordt gevormd door de Doelenschema’s en de Gedachtenschema’s. De laatste bijeenkomst heeft geen vooraf vastgelegd thema, het thema voor deze bijeenkomst wordt door de deelnemer(s) zelf bepaald. Voor de begeleiding van deelnemers aan het groepsprogramma wordt geadviseerd om met twee (BIG-geregistreerde) psychologen te werken, voor de begeleiding van deelnemers aan het individuele programma wordt geadviseerd om met één (BIG-geregistreerde) psycholoog te werken.

Bijeenkomst 1: Diagnose MS en wat nu?
De eerste bijeenkomst staat in het teken van kennismaking, uitleg van het doel en de opzet van de cursus en een inleiding in de achtergrond van en het werken met de RET-methode. De relatie tussen denken, voelen en doen wordt uitgelegd aan de hand van een oefening en de deelnemers gaan aan de slag met een inzichtgevende persoonlijke opdracht.

Bijeenkomst 2: Wat vind ik belangrijk?
In het eerste deel van deze bijeenkomst staat het bespreken van de huiswerkopdrachten centraal. Door elke bijeenkomst veel aandacht aan het huiswerk te besteden, wordt het belang van het maken van het huiswerk benadrukt. Tevens komen in de huiswerkopdrachten persoonlijke situaties aan bod, waardoor ervaringen kunnen worden uitgewisseld. ‘Steunen’ is belangrijk in dit eerste gedeelte van de bijeenkomst. Belangrijk is dat de deelnemers gemotiveerd zijn en blijven om het huiswerk te maken. In het tweede deel van deze bijeenkomst ligt de nadruk op het belang van het stellen van doelen voor het sturen van gedrag. De deelnemers gaan aan de slag met het stellen van realistische en

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haalbare lange- en korte termijn doelen en maken een stappenplan om de doelen te bereiken.

Bijeenkomst 3: Opkomen voor jezelf
In deze bijeenkomst staat assertiviteit centraal. In het eerste deel wordt stil gestaan bij de huiswerkopdrachten rondom assertief gedrag. De deelnemers formuleren een gedragsbeperking die zij hebben als gevolg van een MS-gerelateerde (lichamelijke) klacht en ze hebben brengen onder woorden wat het voor hen betekent om deze beperking te hebben. Vervolgens formuleren zij tenminste één gedachte die zij in die situatie hebben. Verder gaan de deelnemers aan de slag met het herkennen en begrijpen van niet-helpende gedachten. In het tweede deel van de bijeenkomst wordt uitgelegd wat assertief gedrag is en wat het belang van assertief gedrag is.

Bijeenkomst 4: Communicatie met je brede omgeving

Bijeenkomst 5: Communicatie met je directe omgeving
Deze bijeenkomst is qua inhoud en opzet hetzelfde als de vierde bijeenkomst. De deelnemers hebben een Gedachtenschema ingevuld rondom het thema communicatie met naasten (familie, vrienden, buren, etc). Ook in deze bijeenkomst wordt in een rollenspel geofend met een persoonlijke casus waarin de deelnemers communicatieproblemen ondervonden.

Bijeenkomst 6: Omgaan met psychisch onwelbevinden
In deze bijeenkomst staan gevoelens centraal die horen bij een aanpassingsproces. Deze onbehaaglijke gevoelens kunnen divers zijn, per persoon verschillen en leiden tot ‘psychisch onwelbevinden’. De boodschap van deze bijeenkomst is dat deze gevoelens ‘normaal’ zijn en ergens toe dienen (aanpassing). Door de aanleiding van het onbehaaglijke gevoel (stress, spanning, verdriet, somberheid) en de bijbehorende gedachten en gevoelens onder de loep te nemen, kunnen er indien nodig en gewenst, nuances in het onbehaaglijke gevoel worden aangebracht. In het eerste deel van deze bijeenkomst wordt ruim aandacht besteed aan de voor het huiswerk ingevulde Gedachtenschema’s. In het tweede deel wordt ingegaan op hoe de deelnemers zich per dag voelen en waar dat mee te maken kan hebben.
APPENDIX

Bijeenkomst 7: MS en de toekomst
In deze bijeenkomst staan gevoelens van onzekerheid en angst voor de toekomst centraal. Naast een Gedachtenschema hebben de deelnemers ook een Angstschema ingevuld. Hierin hebben zij hun grootste angst met betrekking tot MS ingevuld en een actieplan gemaakt voor het geval deze angst waarheid wordt. Vervolgens wordt dieper ingegaan op deze angsten en de gedachten, gevoelens en het gedrag die ermee gemoeid zijn. Als laatste onderdeel van deze bijeenkomst wordt het definitieve thema voor de laatste bijeenkomst bepaald.

Bijeenkomst 8: Inval-bijeenkomst
In deze bijeenkomst staan één of meer thema’s centraal die vooraf door de deelnemers zijn bepaald. In het eerste deel wordt aandacht besteed aan de gekozen thema’s en in het tweede deel van de bijeenkomst wordt de cursus schriftelijk en mondeling geëvalueerd en wordt afscheid genomen.

Het complete interventieprogramma kan worden aangevraagd via het MS Centrum Amsterdam:
MS Centrum Amsterdam
VU medisch centrum, kamer 4X180
Postbus 7057
1007 MB Amsterdam
020-4449088
www.mscentrumansterdam.nl
bureauMSCentrum@vume.nl
Dankwoord

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Curriculum Vitae