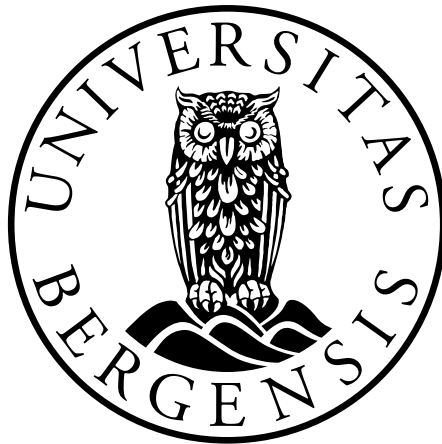


# Coping with multiple sclerosis

Kirsten Lode



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Faculty of Medicine

Institute of Clinical Medicine

University of Bergen, Norway



Stavanger University Hospital  
Stavanger Hospital Trust

Stavanger University Hospital

Stavanger, Norway



The Norwegian  
Center for Movement  
Disorders

The Norwegian Centre for Movement Disorders

Stavanger University Hospital

Stavanger, Norway

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## List of publications

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# 1. Introduction

## 1.1 MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is as an autoimmune disease that affects the central nervous system. It is progressive, has an unpredictable course and is among the most common causes of neurological disability in young and middle-aged adults. More females than males are affected by the disease and although disease modifying treatment has been available for the last twenty years, there is no curative therapy.

It was Sir Robert Carswell (1793-1857), a Scottish pathologist, and his French colleague Jean Cruveilhier (1791-1874) who independently investigated and illustrated the pathology of MS for the first time in 1837. However, it was Jean Martin Charcot (1825 - 1893), a neurologist at the Salpêtrière hospital in Paris, who described at first the clinical and pathological characteristics of MS. His one-hundred and fifty years old definition from 1868 is still used [2].

### 1.1.1 Epidemiology and etiology

The prevalence of MS varies around the world and is highest in northern Europe, middle part of North America and southern Australia [3]. In Norway the prevalence seems to be increasing and differs from 73.0 per 100.000 population in the northern part of the country to 150.8 in the west (Hordaland county, 2003) [4]. The prevalence in Hordaland county, Western Norway increased from 20 per 100.000 [5] in 1960 to 60 per 100.000 in 1983 [6] and finally 150.8 per 100.000 in 2003 [4]. The incidence is also increasing, particularly in southern Europe [3]. In Norway, the annual incidence stabilized after 1982 at about 6 per 100.000 [4] and there are about 7000 people living with MS [7]. The increasing prevalence and incidence are explained by improved diagnostic procedures and increased awareness of the disease. The cause of this



worldwide variations in prevalence and incidence is not known, but both environmental and genetic explanations have been discussed [3]. Approximately 70% of people with MS are women, and mean age at onset is between 30 and 40 years [4].

The etiology of MS is not known but both genetic and environmental factors seem to be involved. There are many genes associated with increased risk for MS, but they can not separately explain the cause of the disease [8, 9]. The Epstein-Barr virus is a risk factor that is consistently associated with MS and increases the risk with about 10 times if individuals are infected in childhood and 20 times if they as adults develop mononucleosis [10]. Other environmental factors that have been discussed are less sunlight exposure, the lack of vitamin D and cigarette smoking [11]. Stressful events have been suggested to play a role in the development of MS and may be a factor among others that influence the risk of exacerbations [12, 13].

### 1.1.2 Diagnosis

Patients describe the diagnostic phase as a period of anxious waiting filled with uncertainty [14]. In addition, the initial symptoms involve emotional distress [15]. The diagnosis is normally decided some time after the first symptoms and is based on clinical and laboratory criteria, including MRI, cerebrospinal fluid (CSF) and visual-evoked response (VER) examinations [7]. Two separate episodes with different location in the central nervous system are essential for the diagnosis. Typically, first symptoms are sensory disturbances, unilateral optic neuritis, double vision, paresthesias of trunk and limb, clumsiness, gait problems and neurogenic bladder and bowel symptoms. Many patients also describe fatigue as the first symptom of MS [3].

In the present study the criteria of Poser et al [16] were used to diagnose the patients with definite or probable MS. The Poser criteria, originally made for clinical trials, are the most commonly used diagnostic criteria in MS.

The Poser criteria define:

A) Clinically definite MS:

1. Two attacks and clinical evidence of two separate lesions.
2. Two attacks, clinical evidence of one lesion and paraclinic evidence of another, separate lesion.

B) Laboratory-supported definite MS:

1. Two attacks, either clinical or paraclinical evidence of one lesion, and cerebrospinal fluid (CSF) oligoclonal bands (OB)/Immunoglobulin G (IgG).
2. One attack, clinical evidence of two separate lesions, and CSF OB/IgG.
3. One attack, clinical evidence of one lesion and paraclinic evidence of another, separate lesion, and CSF OB/IgG.

C) Clinically probable MS:

1. Two attacks and clinical evidence of one lesion.
2. One attack and clinical evidence of two separate lesions.
3. One attack, clinical evidence of one lesion and paraclinic evidence of another separate lesion.

D) Laboratory-supported probable MS:

1. Two attacks and CSF/BO IgG.

In 2001 these criteria were replaced by the “McDonald Criteria” by the International Panel on the Diagnosis of MS and in 2005 the McDonald criteria were revised to clarify definitions, simplify and speed diagnosis [17].

### 1.1.3 Clinical picture

The clinical course of MS is heterogeneous because several parts of the CNS may be involved. In 80-85% of the patients the disease trajectory typically begins with an acute episode that evolves over several days, stabilizes and then improves spontaneously within weeks. This is the typical onset of relapsing-remitting MS (RRMS). The next episode usually occurs rather unpredictably after 1-5 years. Gradually the recovery from the relapses are incomplete and symptoms accumulate [3, 18]. A small proportion of the RRMS patients may experience a benign type of MS with an EDSS score (Kurtzke's Expanded Disability Status Scale see page 37) of  $\leq 3$  after 15 years with the disease. In more than two-thirds of the RRMS patients the disease develops into a secondary progressive phase (SPMS). In 15-20% of the patients MS is progressive from onset, primary progressive MS (PPMS). This patient group differs from the RRMS group by a greater relative frequency of males and later onset of the disease [19, 20].

Patients with MS report spasticity and weaknesses, clumsiness and slowness in the upper and lower extremities. In addition, patients may have gait and balance problems, double vision, instability, dizziness, speech problems and swallowing difficulties.

Patients may also report sensory symptoms like coldness, burning and itching.

Bowel and bladder dysfunction like constipation or diarrhoea, incontinence, urinary urgency, frequency, hesitation and retention seem to be common problems in MS. These symptoms may, together with spasticity and reduced sensitivity, also affect the patients' sexual functioning.

In addition to motor symptoms, patients with MS will often experience fatigue, cognitive impairment, neuropsychiatric symptoms, sleep disorders and pain. Fatigue is a subjective lack of physical and/or mental energy and is a common disabling symptom that frequently leads to disability [21]. As many as 10-20% individuals with MS consider fatigue as their most disabling symptom [21].

Cognitive impairment in MS is common and occurs in 45-60% of the patients [22]. Impairments in complex attention, long-term memory, executive functioning, processing speed and information processing are the most common cognitive symptoms and affects daily living by reduced ability to run household, maintain employment and participate in society [23].

Neuropsychiatric symptoms including depression, bipolar disorder, euphoria, pathological laughing and crying and psychosis are often present and reduce quality of life and may be a burden for relatives and friends [24]. Even in the early phase of the disease trajectory, these symptoms are common and associated with increased disability [25]. Treatments and preventive strategies may reduce these problems and should be taken into consideration [18, 26, 27]. These symptoms should be recognized and treated appropriately by a multidisciplinary management team [3].

Depressive symptoms are the most common neuropsychiatric symptom in MS and have a lifetime prevalence of 50% and an annual prevalence of 20%. However, methodological difficulties may have influenced these findings. The patient samples may not be representative and researchers have not agreed on a 'gold standard' for diagnosing depression in MS. In addition, the relationship between depressive symptoms and cognitive impairment is not clearly understood and the symptoms are overlapping [28]. Depression in MS differs from the classical pattern by more symptoms of irritability, discouragement and frustration than the more typical symptoms of low self-esteem and feelings of guilt [29]. As impairment increases, the risk of depressive symptoms seems to enhance to a modest degree [30] and factors like coping styles, hope and uncertainty seem to explain depressive symptoms in MS [31]. Patients' perception of the disease uncertainty and variability and the intrusiveness the disease has on daily living are factors associated with depression. In addition, changes in social role functioning that are associated with the disease and loss of social support are related to depression in MS [32]. Despite the high prevalence and the negative influence depressive symptoms have for quality of life in MS, they are often not detected or treated [33]. Physicians do not necessarily ask the

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patients for depressive symptoms and patients may be reluctant to disclose their emotional problems. A routine screening for depressive symptoms followed by an interview and appropriate treatment is important for patients with MS [34].

Psychotherapy, where active coping strategies are enhanced, and antidepressive medication are recommended as treatment for depressive symptoms [28].

#### 1.1.4 Treatment and prognosis

Patients with MS are faced with a lifelong chronic disease with a prognostic uncertainty and should be well informed about their disease from the beginning. A multidisciplinary team should be established with a neurologist, an MS-nurse as a coordinator and other health workers depending on the patient's need for help and assessment [3]. There are no curative treatments available for MS. However, to improve recovery from relapses corticosteroids are often used although there are no evidence for long-term effects of the treatment [3, 7]. To minimize disease activity and to prevent progression of disability, disease modifying treatment are introduced [7]. Since there are a lack of long-term data to prove the effect of this treatment, patients should be informed that they most likely will continue to have relapses and become increasingly disabled [3, 18]. Disease modifying treatment should be introduced early and each patient needs a careful and continuous follow-up concerning treatment response and side effects [7].

Gender, age and initial course of the disease seem to be decisive prognostic factors [19, 35]. Female gender, early onset and optic neuritis and sensory symptoms at onset have been associated with a better prognosis [36]. In addition, an interval from onset to diagnosis exceeding three years seems to be favourable [19]. Patients expect information about the prognosis at the time of diagnosis, but this is a difficult task, since the disease development is highly unpredictable especially in the early phase of the disease. However, it is important to focus on the fact that after 15 years with the

disease about 70% of the RRMS patients had no need for walking aid ( $EDSS \geq 6$ ) and nearly 85% had no need for a wheelchair ( $EDSS \geq 7$ ) [19].

#### 1.1.5 MS as chronic disease

Some people live with chronic diseases like hypertension, diabetes and MS without thinking that they are ill. Especially during times when disease symptoms are under control of medication or the disease is in a non-active phase, people consider themselves as healthy [37]. Most chronic diseases have episodes of exacerbations that lead to a shift in perspective from having wellness in the foreground and remove the focus from the diseased body to have the disease in the foreground, worrying about the strength, duration and consequences of the attack [38]. Another aspect is that patients with MS choose to conceal their disease, especially towards working colleagues, to maintain their social belonging, preserve control and avoid stigma. On the other hand, disclosure of the MS diagnosis is necessary to avoid discrimination and to get assistance from others when needed [39].

The individual's perception of the disease depends on his or hers personal and social resources. Patients may find their reaction on receiving the diagnosis more disabling than the disease itself and some feel their whole existence threatened. On the other hand, patients experience the diagnosis as an explanation to their symptoms and may feel relieved [15]. The post diagnostic phase is described as facing the unknown where possible loss is an essential experience: loss of health, friends, control, function and freedom [40]. Nevertheless, empirical studies show that most patients adapt to chronic disease, despite the unstable and unpredictable disease trajectory [41]. Patients with mild or moderate MS describe their daily life with the disease as setting priorities when time and energy are limited and to change how things have been done to make it manageable [42].

### 1.1.6 Disability pension in MS

At the time of diagnosis, most patients with MS are either full-time workers or students. This changes rapidly and those who remain in full-time occupation decreases. In cross-sectional studies 50-55% of the patients are disability pensioned and with an annual increase of 10-15% [43]. Among MS patients who had recently become disability pensioned, 99% mentioned disease related factors as the main reason for not being able to continue working. In addition, increased disability correlates with decreased employment [44]. Progressive disease course, disability problems like mobility and hand function, fatigue, cognitive performance and older age are factors associated with disability pension [45]. The workplace's ability to accommodate to the individuals' need is also decisive for the possibility to continue working [46]. MS-patients at risk for disability pension are usually over the age of 39, are employed in heavy physical work and have a moderate disability [43]. To remain in work is an important value for patients, but only a few receive formal advice regarding the possibility to remain in employment. Patients need special attention from health personnel on how to cope with the impact disability has on their working capacity and employers need information about the disease and advice on how to change working environment [44].

## 1.2 COPING

### 1.2.1 Stress and coping

Life events like loosing a loved one or being diagnosed with a chronic disease or disasters like war or tsunami make us aware of how stress situations influence on our lives. Daily hassles like time pressure, disliking work and conflicts in the family are sources of stress depending on how many hassles are present at the same time and the time period they last [47]. Scientists have been concerned with the differences in how individuals cope with these situations.

In the theory, stress has been defined as either response or stimulus. Selye's response perspective focuses on the individual's reaction to stress and his or hers attempt to deal with a demanding situation. Stimuli, however, as described by Holmes and Rahe, are events in the environment such as illness or loosing a job, to which a person respond. In this stimuli perspective, the research focus is on defining the source of stress and is not concerned about the individual's different reactions to stress [48, 49]. Lazarus introduced a third model of stress; as a transaction between the person and the environment. This relationship would be the characteristics of a person in relation to the nature of the environmental event. He defined stress as a relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her well-being [49, 50]. Coping strategies are mediating factors that are important contributors to reduce stress that may lead to health problems and illness [47].

Lazarus' transactional model of stress parallels the modern view of illness, where the cause and development of a disease is not only from external organisms but also depending on the individual's ability to cope. Stress is associated with the onset of diseases as well as deterioration of symptoms. However, the psychobiological mechanisms behind these associations are not fully understood [49]. Nevertheless, research is concerned with processes that mediate the relationship between stress and



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illness. In MS the geographical differences in the incidence of the disease have challenged researchers to address factors concerning environment and climate. In addition, research in MS has shown that the individual's experience of stressful life events may cause exacerbations.

Freud's theory on defence and repression mechanisms to fend off unacceptable ideas or feelings is the precursors of the concept of coping. In the 1960s certain defense mechanisms were assessed as more adaptive and were labelled coping. Coping was conscious strategies used by the individual to react on stressful situations. The first generation of coping researchers studied almost exclusively coping reactions to life-threatening or traumatic life events. Eventually, the attention turned to study a broad range of stressful situations [51].

According to Kobasa coping theory can be based on the model that personality variables mediate stressful events [52], or as Lazarus states that coping is a process in the relationship between the person and the environment [50] or finally as Carver claims, a combination of the two [53]. Stress and coping could be seen as reciprocals to each other; when coping is effective the level of stress is expected to decline and when coping is ineffective the level of stress is likely to increase [54]. In 1984 Lazarus and Folkman published their widely accepted definition on coping describing the phenomenon as constantly changing cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person [50]. The definition is process-oriented and implies a distinction between coping and automated adaptive behavior by limiting coping to demands that are taxing or exceeding a person's resources. Lazarus and Folkman began to stress the importance of studying the situational context in which coping took place and described coping as a process [51]. Their approach has three main features. First, assessments are concerned with what a person actually thinks or does in a stressful situation. Second, what a person actually thinks or does is examined within a specific context and third, coping as a process is how thoughts and actions change during a stressful event [50]. As an example in MS a person who is informed

that he/she has MS could, on the one hand feel relieved because he/she faired a brain tumor. On the other hand he/she could feel that the diagnosis threatens important values in his/her life and become angry and refuse to talk about it. His/her reaction could be quite different if he/she was informed in a room at the hospital with several other patients present than if he/she, together with his/her next of kin, were alone with the neurologist in his office. Finally, the comprehension of being diagnosed with MS may change gradually as knowledge about the disease is achieved.

### 1.2.2 Coping functions

Coping serves primarily problem-focused and emotion-focused functions. The former is to obtain information about what to do and mobilize actions for the purpose of changing reality. The latter is to regulate emotions tied to the stress situation without changing the realities of the situation [50, 54]. Problem-focused coping involves strategies like solve, reconceptualize or minimize a stressful encounter. Emotion-focused coping includes strategies like self-occupation, fantasy, or other conscious activities that regulate emotions [51]. Emotion- and problem-focused strategies often occur concurrently when the stress situation both have emotional (what cannot be changed) and practical (what can be changed) challenges. They can also occur in sequences. For instance, after getting diagnosed with a chronic disease a period of denial or minimalization often occurs immediately. This is gradually replaced by problem-focused concerns concentrating on treatment programs and getting on with one's life [50]. Support for the existence of the two functions in coping comes from anecdotal accounts and empirical research and the two functions can both impede and facilitate each other [50].

Another basic dimension of coping is avoidance-oriented coping, such as denial and withdrawal [51]. The research on how avoidance coping influence adaption is mixed and the common apprehension is that avoidance hinders adaption. Several studies have shown that avoidance coping is associated with poorer adjustment to chronic

diseases, and with depression and distress [55]. However, to cope with a short-term stressor like myocardial infarction, avoidance coping may be effective and gives the person an opportunity to escape [56]. In the later stages of the disease it is important to move from avoidance to more problem-focused coping strategies to enhance adaptation [41]. Patients with MS tend to employ more emotion-focused and avoidance strategies when there is a likelihood of recurrence of the disease [41].

The characteristics of the stress situation will determine which coping strategies that are the most adaptive. If the stressor is appraised as changeable, problem-focused coping is preferred and will effectively reduce the stressor. Patients, when diagnosed with MS, who actively approach both emotional reactions like threat and fear and seek information and knowledge will probably experience the disease as more controllable. On the other hand, patients with MS who appraise the situation as uncontrollable where little can be done employ emotion-focused or avoidance strategies and may as a result develop helplessness and depression.

### 1.2.3 Coping as a style

Carver et al state that coping may be viewed as a style influenced by individual differences in two ways. First, the apprehension is that people have a set of coping styles that they employ in stressful situations. They do not approach each stress situation as new but rather handle the situation by using a preferred set of coping strategies that are stable across different stress situations [53]. However, according to Lazarus and Folkman assessing coping as a style impedes the possibility to study a person's freedom and flexibility to alter coping strategies in changing circumstances and locks him/her into a certain pattern of responding [50]. Second, it is reasonable to think that dimensions of the personality, like consistent patterns of thoughts, feelings and actions affect coping behavior and interact with the environment to shape the appraisal of the stress situation. Further, personality dimensions like optimism and pessimism are expected to employ respectively active coping and emotional distress

and disengagement. In addition, self-esteem seems decisive for the choice of coping strategies. People high in self-esteem choose more active coping strategies. Similarly, people who have the need to be in control of the situation, are more engaged in planning and active coping than those who believe that the consequences of one's behavior are not under one's own control [48, 53]. Finally, personality traits are linked to coping behavior e.g. the personality trait neuroticism (vulnerable to life stress) facilitates anxiety and depression, and it is reasonable to assume that this will affect coping behavior [57].

#### 1.2.4 Coping as a process

The coping process describes what a person thinks or does in a specific situation and the changes in the thoughts and actions that occur across events or as the event unfolds. There are three main features in a coping process. First, the focus is on what the person actually does and not what they usually do. Second, what they think and do is examined within a specific context. Third, the process perspective is concerned with the change in coping thoughts and acts and how the individual employ the most suitable coping strategies for the situation. The coping process is dynamic and a subject of continuous appraisals and reappraisals as the person-environment relationship is shifting. Adaption to living with a chronic disease is an example of a coping process, starting with shock and disbelief that involves denial and disengagement, then feelings of threat and loss until there finally is an acceptance for the disease as a part of one's life [50]. Exacerbations of the disease may lead to a restart of the coping process.

To measure coping as a process is to assess coping strategies that are responding to a specific stressful situation e.g. being diagnosed with MS. A way of assessing this perspective is to ask for coping strategies from a variety of situations. Respondents are then asked to think about a recent stressful event and respond to the coping items

of an instrument designed for this purpose [51]. Critics of this approach have questioned how accurate respondents recall such stress situations [57].

If health personnel did not believe in coping as a process that can change and become more appropriate, their role in guiding people to a better life with a chronic disease would be limited. At the same time it is of great importance to be able to combine the two perspectives and know something about the personality of a patient; an essential condition for building a good relationship that again will help the patient to a better life with the disease. Personality or personal dispositions will interact and shape the perceptions of a stress situation. These consistent patterns of thoughts, feelings and actions seem to occur under routine conditions. However, it has also been stated that personal dispositions are best exposed under stress [57]. In the research by Carver et al these consistent patterns and the situational coping are combined [53] and hopefully patients with MS will choose between a variety of styles to cope with their disease.

### 1.2.5 Appraisal

A central concept in Lazarus' and Folkman's coping theory is appraisal that refers to a cognitive process that evaluates what is happening and shapes the emotional and behavioral response [50]. Appraisal includes the so-called primary and secondary appraisal. Primary appraisal is the process of deciding whether what is happening is relevant to one's values, beliefs about self and the world and situational intentions and, if so, in what way. If the reverse is the case, and the result of primary appraisal is that the event is not relevant to one's well being, there is nothing further to be considered [54]. If the interpretation of the situation is positive i.e. as a challenge, positive emotions will occur. On the other hand, if the situation is appraised as negative i.e. as a threat or a loss, negative emotions like anxiety, anger or grief will occur [41]. A young mother with small children who is diagnosed with MS will

appraise the situation as a threat to most of her values and beliefs about being a young woman and a good mother.

Secondary appraisal is the process of focusing on what can be done; what coping options are available and what constraints are against acting them out. Do I need to act? What can be done? Which option is the best? [54]. The individual's appraisal decides which coping strategies that are suitable to handle the situation. For the young mother with MS, she may have to reduce or leave her job in order to have enough energy to take care of her small children. Secondary appraisal never operates independently of primary appraising.

A third step in the appraisal process is reappraisal, where an evaluation of primary and secondary appraisal on the basis of new information takes place. The individual may appraise what initially was a threat as a challenge and may reconsider the choice of coping strategy. Knowledge about the disease may stimulate patients with MS to reconsider and seek alternative actions to handle disease related problems.

### 1.2.6 Factors that influence coping in MS

Several factors influence appraisal and coping. Internal factors like personality and external factors like characteristics of the situation shape the individual's coping behavior. To understand coping in patients with MS it is important to address some internal and external factors that might influence their coping ability.

#### 1.2.6.1 Uncertainty

Uncertainty is known to be very stressful and coping strategies needed for an event's occurrence are different from the strategies needed for an event that is uncertain whether it will occur or not [50]. Patients with MS may experience high levels of illness uncertainty [58] that will have an influence on their coping ability. The Mishel

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Uncertainty in Illness Scale describes four key factors: ambiguity concerning the state of the illness, complexity regarding treatment and the health care system, lack of information about the diagnosis or severity of the illness, and the unpredictability of the disease course and prognosis [59]. Adaption to chronic illness depends upon the appraisal of uncertainty. If uncertainty is appraised as danger and the outcome will be harmful, coping strategies will aim at reducing uncertainty by collecting information and knowledge or by avoiding the situation. On the other hand, if the uncertainty is appraised as an opportunity with a positive outcome, i.e. not knowing when the next attack of a disease occurs gives an opportunity to think that it will not occur; coping strategies that maintain the uncertainty will be applied. In their stress and coping model, Lazarus and Folkman also describe the adaption to illness uncertainty as either appraised as a danger or as an opportunity [50]. In MS as in other chronic illnesses high levels of illness uncertainty was related to less hope, more illness intrusiveness, greater emotional distress and mood disturbances such as anxiety, tension, anger and depression. In addition, interventions to reduce illness uncertainty were associated with higher self-efficacy, less psychological distress and greater life satisfaction [59]. In our culture and in the health care system, predictability and control are major values and there are little room for chance and uncertainty. Nevertheless, people who live with a chronic disease have to accept that uncertainty is their new rhythm of life and certainty and predictability is limited. Health providers who focus on predictability and certainty will block or prolong the process of adapting to uncertainty [60].

Lack of information may enhance uncertainty. Knowledge about the actual chronic disease develops over time and those most recently diagnosed demonstrate higher levels of illness uncertainty and have a higher need for information. Information and knowledge may reduce the degree of unpredictability and strengthen coping efforts.

### 1.2.6.2 Person factors

As already mentioned person factors influence coping and Lazarus points out two person characteristics as important: commitments and beliefs. Commitments reflect what is meaningful and important to a person and determine the effort a person is willing to invest to remove what may threaten that commitment. Patients with MS may have a strong will to continue a normal life through commitments like family, friends and job. Beliefs are personally and culturally shaped and have an influence on a person's vulnerability or resistance to stress situations. Control or loss of control is basic concepts in this person characteristic. The feeling of control for patients with MS can be decisive for the degree of helplessness [48, 50].

### 1.2.6.3 Social support

Social support encompasses both personality, personal relationships and social networks and it is interesting to study how the three perspectives influence the individuals' effort to cope with life events [61]. The importance of social support in adjustment to illness is well known, but it is less known how social support actually works [50]. Social support can be conceptualized in three different ways:

- perceived social support is defined as the comprehension that others are available and willing to help when needed
- supportive relationship is social bonds that provide the individual with help in coping with a situation
- supportive network are people with personal links who provide support to the individual [50, 61].

We assume that social support helps to prevent stress and to make threatening situations less harmful. In addition, support from others can provide valuable information for coping when a difficult situation occurs [50]. MS studies have shown relationships between high perceived social support and better adjustment to the



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disease. However, supporters who are over-solicitous and critical are unhelpful in adaptation to MS [62]. We can distinguish between emotional support and informational support. Carver et al describe these coping responses as seeking social support for emotional reason or for instrumental reason. The first is to get moral support, sympathy and understanding and the latter is seeking advice, information or assistance [53].

#### 1.2.6.4 Informational social support

Many patients with MS start their information-seeking in the prediagnostic phase and continue until the diagnosis is confirmed. They seek information from health personnel, popular literature, medical text, family and friends [63]. People seek information when they become ill because the gap in their knowledge prevents them from sense-making in this new situation. Information can be used as an emotion-focused strategy to support a decision already made or as a problem-focused strategy to decide what has to be done. If a patient does not seek information about their illness, health personnel should be asking why. Some MS patients seek information to be prepared for how bad the disease can become and to stay in control over the situation, others will avoid information because they find it pushing them into a danger they cannot avoid and will wait to seek information until they know they can cope with the stress the information provoke [64].

Being diagnosed with MS has been spoken of as a phase of uncertainty, variability and unpredictability. The diagnostic phase is time consuming and a source of 'fearing the worst'[40] and after being told that they have an incurable disease, patients have been told to 'go away and live with it'[65]. Some patients experienced a sense of relief, because 'fear of the worst' could be put aside but for many patients the diagnosis was a source of severe stress and involved a range of emotional reactions. In addition, it is the patients' perception of the diagnostic phase, rather than what actually happened that influence the way they approach the future and their

relationship with the health care team [65]. The importance of patient information to gain control, reduce anxiety, create realistic expectations, promote self-care and participation and stimulate feelings of safety is considered as an important need for people who face a chronic disease. Patients with MS ask for more such supportive follow-up after the diagnosis.

### 1.2.7 Coping with chronic disease

Chronic disease is without the prospect of recovery and usually with a relatively long duration. Patients are required to live with the limitations the disease imposes on their life. There are vast differences in cause, course and final outcome both among the different diseases and within the same disease. Most of the chronic diseases have episodes of exacerbations that accumulate the disease progression.

A chronic disease confronts patients with threats and challenges like preserving a reasonable emotional balance and self-image, maintaining competence and mastery, sustaining relationships with family and friends and preparing for an uncertain future. In addition, diagnostic uncertainties, disability, dependency and life-style changes disrupt valued activities [66]. Despite severe chronic conditions, empirical studies show that most patients adapt to chronic disease [41] and the difference in health related quality of life between patients with some chronic diseases and normal controls is less pronounced than expected [67].

Avoidant, emotion-focused strategies have been related to poorer adjustment to chronic disease, whereas problem-focused strategies have been related to a more sufficient adjustment. These findings may however, be oversimplified as studies have shown that passive coping also has been positively related to adjustment in groups of chronically ill patients. In addition, characteristics of the disease and the treatment have an impact on the appraisal of the situation and together with the complexity of

the coping process and the variety of possible outcomes the association between coping and adaption may be weak [41].

Social stigma, described as the undesired differentness, has been associated with chronic diseases. A person, who fails to perform as expected, will change her definition of self and become discredited. Coping is described as a bargaining process for managing stigma and the individual try to control the body and the environment to communicate social status and identity. Further, to avoid social stigma, persons with a chronic disease may be engaged in developing a way of coping with the disease and health personnel should pay special attention to the under- or overemphasizing of the disease to obtain a balance between treating a chronically ill as normal and yet acknowledge the disease [39].

#### 1.2.8 Research on coping in patients with MS

The majority of coping research in MS is based on Lazarus and Folkman's theory and their instrument "The Ways of Coping Checklist". A tendency through these studies is that the positive relationship between problem-focused coping and adaption is less clear in MS than in chronic diseases in general. However, as in research on coping with chronic disease in general, passive, avoidant-focused strategies are related to poorer adaption [32].

A search in PubMed, Ovid Nursing and PsychInfo in July 2009 on the terms 'multiple sclerosis' and 'coping' showed a large number of papers. Thirty-seven of these assessed the relationship between coping strategies and different other variables and were considered applicable for presenting data on coping with MS. These other variables included depression, anxiety, social support and quality of life. These studies could be classified into three categories: Cross-sectional studies comparing groups and factors influencing coping, longitudinal studies comparing groups and factors influencing coping and studies on different interventions using coping as

outcome measure (Table 1). Thirteen different coping scales were applied, 12 were generic questionnaires and one was MS specific. Twenty-three studies have evaluated factors that may influence coping and 10 of these studies have compared coping among various groups, 11 studies were longitudinal with a follow-up time that varied from 3 months to 3 years, two studies measured coping as a result of an intervention and 3 studies measured coping as a part of a medical trial.

Number of participants with MS varied from 20 to 502 and 2 studies had only female participants. Seven studies compared MS-patients with normal controls and 3 studies compared them with other patient groups. Participants were recruited from one clinic or area or from the local MS Society or both and were a cross section of patients with MS in the study area. Only one study had included patients who were newly diagnosed with MS (<2years).

These studies showed a strong and consistent relationship between certain emotion-focused strategies (wishful thinking and avoidance coping) and poorer adjustment to MS. In addition, although not so strong, there is a relationship between problem-focused coping (seeking social support) and better adjustment. Patients with higher levels of psychological distress and in exacerbation employed more emotion-focused coping. Furthermore, patients were less likely to employ problem-focused coping strategies compared to normal controls. However, the assumption that coping is a predictor of adjustment is more complex; some demonstrated that coping predicts adjustment to MS and some, although fewer, did not.

Depression in patients seems to enhance emotion-focused and avoidance coping and patients who employ these strategies seem to be more depressed. However, this relationship is problematic because of the conceptual overlap. Furthermore, problem-focused or active strategies are associated with better quality of life. Teaching coping skills in group-therapy seems to improve coping ability over time.

The presented studies have some methodological limitations. These are the variety in sample sizes, coping instruments employed and variables that are controlled for. In

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addition, the differences in adjustment outcomes and in the context of the stressors participants are asked to describe. These differences may explain differences in the results [62].

Table 1. Previous studies on MS and coping.

<b>I Cross-sectional studies comparing groups and factors influencing coping.</b>				
<b>Author</b>	<b>Title</b>	<b>Sample</b>	<b>Measure</b>	<b>Key findings</b>
Warren S 1991 [68]	Emotional stress and coping in MS exacerbations.	95	WCC	Patients in exacerbation favored emotion-focused coping.
Buelow JM 1991 [69]	A correlational study of disabilities, stressors and coping methods in victims of MS.	20	Jalowiec Coping Scale	Positive correlation between future uncertainty and fatalistic coping and negative correlation between depression and optimistic coping.
O'Brien MT 1993 [70]	Multiple sclerosis: the relationship among self-esteem, social support, and coping behavior.	101	WCC	Self-esteem was positively related to problem-focused coping. No relation between social support and problem-focused coping.
Wineman NM 1994 [58]	A comparative analysis of coping behaviors in persons with MS or spinal cord injury.	433 MS 257 SCI	WCC-R	No differences between the groups. Subjects used more emotional coping at high illness uncertainty and more problem-focused coping at no uncertainty.
Mohr DC 1997 [30]	Depression, coping and level of neurological impairment in MS.	101	WCI	Patients with advanced impairment have increased risk for depression and depression and advanced impairment are associated with maladaptive coping.
Pakenham KI 1997 [71]	The role of coping in adjustment to MS-related adaptive demands.	134	WCC	Reliance on emotion-focused coping was related to poorer adjustment. In particular, avoidance was related to poorer adjustment.

**WCC** Ways of coping checklist (Folkman and Lazarus 1988), **Jalowiec Coping Scale** (Jalowiec 1989), **WCC-R** Ways of coping checklist-Revised, **WCI** Ways of coping inventory (Folkman & Lazarus 1985).

<b>I Cross-sectional studies comparing groups and factors influencing coping.</b>				
<b>Author</b>	<b>Title</b>	<b>Sample</b>	<b>Measure</b>	<b>Key findings</b>
Jean VM 1997 [72]	Coping with general and disease-related stressors by patients with MS: relationship to psychological distress.	75 MS 26 HC	WCC	Patients reported higher levels of distress than controls, but similar patterns of coping.
Beatty WW 1998 [1]	Correlates of coping styles in patients with MS.	43	WCC	Patients with higher level of psychological distress are likely to use emotion-focused coping strategies.
Jean VM 1999 [73]	Psychological and neuropsychological predictors of coping by patients with MS.	56	WCC	Higher levels of distress were associated with emotion-focused coping and reduced effectiveness of the strategies employed.
Kroencke DC 1999 [74]	Stress and coping in MS: exacerbations, remission and chronic subgroups.	61	WOC	Patients in current exacerbations had more hassles and they were met by more passive avoidance or aggressive coping.
Mohr DC 1999 [75]	The psychosocial impact of MS: Exploring the patient's perspective.	94	WOCQ	Benefit-finding (deepening of relationship, enhanced appreciation of life, spiritual interest) were related to positive reappraisal and seeking social support.
deRidder D 2000 [76]	The relative benefits of being optimistic: Optimism as a coping resource in MS and Parkinson's disease (PD).	96 MS 70 PD	CISS	Optimism has a disease-specific effect on physical adjustment and the use of emotion-focused and avoidance coping strategies.

**WCC** Ways of coping checklist (Folkman and Lazarus 1988), **WOC** Ways of coping (Folkman & Lazarus 1985), **WOCQ** Ways of coping questionnaire (Scherer et al 1988), **CISS** Coping inventory for stressful situations (Endler & Parker 1994).

<b>I Cross-sectional studies comparing groups and factors influencing coping.</b>				
<b>Author</b>	<b>Title</b>	<b>Sample</b>	<b>Measure</b>	<b>Key findings</b>
Rätsep T 2000 [77]	Personality as a predictor of coping efforts in patients with MS.	49 MS 49 HC	The COPE scale	Relationship between personality traits and coping efforts in the patient group were different from control group.
Lynch SG 2001 [31]	The relationship between disability and depression in MS: the role of uncertainty, coping and hope.	188	WOC	Depression was correlated with emotion-focused and not problem-focused coping.
Pakenham KI 2001 [78]	Coping with MS: development of a measure.	414 113	CMSS WCC	Passive avoidant and emotion-focused coping are linked to poorer adjustment and problem-focused with better.
Arnett PA 2002 [79]	Relationship between coping, cognitive dysfunction and depression in MS.	55	The COPE scale	Cognitive dysfunction was associated with depression when high levels of avoidance and low levels of active coping were employed.
McCabe M 2002 [80]	Relationship functioning and sexuality among people with MS.	381 MS 291 HC	WOCQ	Coping and cognitive functioning were predictors of sexual functioning among women with MS.
McCabe M 2004 [81]	Coping and psychological adjustment among people with MS.	381 MS 291 HC	WOCQ	People with MS are less likely to adopt problem-focused coping. Coping is associated with psychological adjustment.

**The COPE scale** (Carver et al 1989), **WOC** Ways of coping (Folkman & Lazarus 1985), **CMSS** Coping with MS scale (Pakenham 2001), **WCC** Ways of coping checklist (Folkman and Lazarus 1988), **WOCQ** Ways of coping questionnaire (Scherer et al 1988).



<b>I Cross-sectional studies comparing groups and factors influencing coping.</b>				
<b>Author</b>	<b>Title</b>	<b>Sample</b>	<b>Measure</b>	<b>Key findings</b>
Chalk HM 2007 [82]	Mind over matter: Cognitive-behavioral determinants of emotional distress in MS patients.	329	CMSS	Problem-solving coping was associated with positive psychological adjustment. Disease severity was not associated with adjustment.
Montel SR 2007 [83]	Coping and quality of life in one hundred and thirty five subjects with MS.	135	WCC  CHIP	SPMS tend to use more emotional coping while PPMS use more instrumental coping.
Twork S 2007 [84]	Chronical illness and maternity: life conditions, quality of life and coping in women with MS.	482 MS mothers 607 childless	FKV-LIS	Several differences in QOL and coping between mothers and childless with MS. Mothers employed coping strategy religiosity/searching for sense in life.
Haase CG 2008 [85]	Neuropsychological deficits but not coping strategies are related to physical disability in MS.	48 MS women  38 HC women	FPI	Increased depression scores and increased cognitive deficit in advanced physically disabled patients without selection of specific coping strategies.
Kehler MD 2009 [86]	Is health anxiety a significant problem for individuals with MS?	246	WOCQ	Health and generalized anxiety were associated with emotional coping. Health anxiety was associated with problem-focused coping.
Goretti B 2009 [87]	Coping strategies, psychological variables and their relationship with quality of life in MS.	104 MS  457 HC	COPE- NVI	Patients were less likely to use problem-focused coping, avoidance were more frequent. Active coping strategies had positive influence on QoL.

**CMSS** Coping with MS scale (Pakenham 2001), **WCC** Ways of coping checklist (Folkman and Lazarus 1988), **CHIP** Coping with health, injuries and problems scale (Vitaliano et al 1985), **FKV-LIS** The Freiburg Questionnaire on Coping with Illness (Muthny 1989), **FPI** Freiburg's coping questionnaire (Muthny 1992), **WOCQ** Ways of coping questionnaire (Scherer et al 1988) **COPE-NVI** coping orientation for problem experiences-new Italian version.

<b>II Longitudinal studies comparing groups and factors influencing coping.</b>				
<b>Author</b>	<b>Title</b>	<b>Sample</b>	<b>Measure</b>	<b>Key findings</b>
Wineman NM 1996 [88]	Relationships among illness uncertainty, stress, coping, and emotional well-being at entry into a clinical drug trial.	59	Jalowiec Coping Scale	Patients entering drug trial with high levels of stress and uncertainty are likely to experience mood disturbances.
Aikens JE 1997 [89]	A replicated prospective investigation of life stress, coping, and depressive symptoms in MS.	27	WOCQ-R	MS-related depressive symptoms are a function of prior disease-related impairment, life stress and possibly escape avoidance coping.
Pakenham KI 1999 [90]	Adjustment to MS: Application of a stress and coping model	122 (96)	WCC	Better adjustment at T2 was related to less disability, greater reliance on problem-focused coping and less on emotion-focused coping.
Mohr DC 2002 [91]	Moderating effects of coping on the relationship between stress and the development of new brain lesions in MS.	36	CHIP	Some findings support that coping moderates the relationship between stress and development of new brain lesions.
Wineman NM 2003 [92]	Longitudinal analysis of illness uncertainty, coping, hopefulness, and mood during participation in a clinical drug trial.	52	Jalowiec Coping Scale	Coping effectiveness predicted hopefulness but not mood.

**Jalowiec Coping Scale** (Jalowiec 1989), **WOCQ-R** Ways of coping questionnaire-revised (Folkman and Lazarus 1985), **WCC** Ways of coping checklist (Folkman and Lazarus 1988), **CHIP** Coping with health, injuries and problems scale (Vitaliano et al 1985).

<b>II Longitudinal studies comparing groups and factors influencing coping.</b>				
<b>Author</b>	<b>Title</b>	<b>Sample</b>	<b>Measure</b>	<b>Key findings</b>
McCabe M 2005 [93]	Mood and self-esteem of persons with MS following an exacerbation.	243 MS 184 HC	WOCQ	Coping strategies did not predict mood.
McCabe M 2006 [94]	A longitudinal study of coping strategies and QOL among people with MS.	321 MS 239 HC	WOCQ	Social support, focusing on the positive and wishful thinking were predictors of QOL.
Pakenham KI 2006 [95]	Investigation of coping antecedents to positive outcomes and distress in MS.	502 (404)	CMSS	Coping predicted positive outcome at time 2 were emotional release, personal health control and physical assistance. Avoidance predicted distress. Acceptance predicted both.
Arnett PA 2006 [96]	Longitudinal course of depression symptoms in MS.	53	The COPE scale	Decreased use of active coping may increase the risk for depressed mood and increased active coping could decrease depressive symptoms.
Moreau T 2008 [97]	Coping strategy and anxiety evolution in MS patients initiating Interferon-Beta treatment.	255	CISS	In recently diagnosed RRMS patients, coping strategy as determined by CISS, impacted the level of anxiety and its evolution during the first months of IFN- $\beta$ treatment.
McCabe M 2009 [98]	Changes in quality of life and coping among people with MS over a 2 year period.	382 MS 291 HC	WOCQ	T1 patients had lower QOL and coping score than HC. After 2 years patients had increases in QOL and social/emotional support coping.

**WOCQ** Ways of coping questionnaire (Scherer et al 1988), **CMSS** Coping with MS scale (Pakenham 2001), **The COPE scale** (52) (Carver et al 1989), **CISS** Coping inventory for stressful situations (Endler & Parker 1994).

<b>III Studies on different interventions using coping as outcome measure.</b>				
<b>Author</b>	<b>Title</b>	<b>Sample</b>	<b>Measure</b>	<b>Key findings</b>
Schwartz CE 1999 [99]	Teaching coping skills enhances quality of life more than peer support: results of randomized trial with MS Patients.	64 68	WCC	Coping skills group yielded gains over time in psychosocial role performance, coping behavior and aspects of well-being. Peer support effective for those with affective problems.
Tesar N 2003 [100]	Effects of psychological group therapy in patients with MS.	29	FPI	Therapy group with cognitive and behavioral strategies showed long-term improvements in depressive stress coping style

**WCC** Ways of coping checklist (Folkman and Lazarus 1988), **FPI** Freiburg's coping questionnaire (Muthny 1992).

## 2. AIMS OF THE STUDY

The overall aim of this study was to investigate coping in patients with newly diagnosed multiple sclerosis (MS) and the longitudinal development of coping in these patients. In addition, the objective of the study was to investigate the effect of information and depression on their coping and to study how disability pensioned patients with MS cope. To obtain this information we have:

- examined coping styles in a population of recently diagnosed patients with MS and explored how the quality of the information by the time of diagnosis influence coping (Paper I)
  
- examined coping styles in patients with recently diagnosed MS as compared to normal controls and explored the relationship between depressive symptoms and coping styles in patients and controls (Paper II)
  
- examined how coping styles in patients with MS change during a 5-year period and how patients' coping styles are associated with disability pension (Paper III)

### 3. METHODS

#### 3.1 Patients at baseline and follow-up

Patients diagnosed with MS during the time period from January 1, 1998 to December 31, 2000 in Hordaland and the southern part of Rogaland in south-western Norway were invited to participate. The patient files of the Departments of Neurology at Haukeland University Hospital and Stavanger University Hospital were searched and patients included were intended to represent an unselected group of newly diagnosed patients with MS. A total of 108 patients were identified. A population of about 700 000 inhabitants lived in the study area by the time of study entry and the average annual incidence for MS was 5.06/100 000. This is comparable with the annual incidence of Hordaland County observed by Grytten et al from 1993 to 1997 [4]. By the time of study entry one patient had died and two patients had moved out of the area. Of the remaining patients, 93 agreed to participate in the study. They all met the Poser criteria of definite or probable MS.

Patients included had been followed regularly at the hospitals and were invited by letter to a 5-year follow-up. A total of 83 patients attended the follow-up visit. Reasons for not participating in the study were moved out of the study area (n=5), withdrawal of consent (n=4) and death (n=1). Of these remaining patients 76 completed the COPE scale both at baseline and at the 5-year follow-up.

#### 3.2 Normal controls

Two-hundred and twenty age, gender, geography matched and randomly chosen controls were selected by the National Population Registry. Ninety-six gave their informed consent to participate.

### 3.3 Assessment of disability

Disability was assessed by Kurtzke's Expanded Disability Status Scale (EDSS). EDSS is the most commonly used scale in MS research, is neurologist-rated and rates disability caused by MS on a continuum of 0 (no impairment) to 10 (death due to MS). The scale includes pyramidal function, cerebellar function, brainstem function, sensory function, bladder/bowel function, visual function and mental function [101].

### 3.4 Assessment of coping

The COPE scale was developed by Carver, Scheier and Weintraub in 1989 as a result of a critical survey of the existing coping measures among those the most widely used scale, Lazarus and Folkmans 'The ways of coping checklist'. Carver et al discovered a lack of focus and an ambiguity in some of the coping items and that the scales were empirically and not theoretically based [53]. After several revisions in its development, the scale was tested in a sample of 978 students. The final version contained 13 scales with 4 items each [102]. Later the authors have added two additional scales and in this study we have used the version with 15 scales and 60 items.

The first five scales are subdimensions of problem-focused coping:

- Active coping: taking active steps to try to remove stressor. Example of item: 'I do what has to be done, one step at the time'.
- Planning: thinking about how to cope with the stressor. Example of item: 'I make a plan of action'.
- Suppression of competing actions: putting other projects aside in order to deal with the stressor. Example of item: 'I keep myself from getting distracted by other thoughts or activities'.

- Restraint coping: waiting until an opportunity to act presents itself. Example of item: 'I force myself to wait for the right time to do something.'
- Seeking social support for instrumental reasons: seek advice, information and assistance. Example of item: 'I ask people who have the same experience what they did'.

The next five scales are subdimensions of emotion-focused coping:

- Seeking social support for emotional reasons: get moral support, understanding and sympathy. Example of item: 'I talk to someone about how I feel'.
- Positive reinterpretation and growth: positive reappraisal that one may learn from. Example of item: 'I look for something good in what is happening'.
- Acceptance: Example of item: 'I learn to live with it'.
- Turning to religion: Example of item: 'I put my trust in God'.
- Focus on and venting of emotions: to focus on distress and ventilate feelings. Example of item: 'I get upset and let my emotions out'.

The next three scales are subdemensions of avoidance coping:

- Denial: Example of item: 'I refuse to believe that it happened'.
- Behavioral disengagement: Reduce and even give up the effort to deal with the stressor. Example of item: 'I just give up trying to reach my goal'.
- Mental disengagement: Distraction from thinking about the goal the stressor interferes with. Example of item: 'I daydream about things other than this'.

The last two scales are concerned with alcohol and humour:

- Alcohol-drug disengagement: Example of item: 'You drink alcohol or take drugs in order to think less about it'.



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- Humour: Example of item: 'You make jokes about it'.

The scales are theoretically based except for 'positive reinterpretation and growth', 'denial', 'acceptance', 'turning to religion', 'alcohol-disengagement' and 'humour' that are empirically based. The questionnaire has a six-point Likert scale from 0=not at all to 5=a lot. For each subscale, a sum score is calculated and high sum scores indicate more use of that particular coping style [53].

We selected the 9 scales believed to be the most relevant for patients with MS (3 problem-focused, 3 emotion-focused and 3 avoidance strategies) partly to avoid multicollinearity because of the rather low number of participants and the high number of variables in the COPE scale. We removed the strategies active coping, suppression of competing activities and acceptance. They were corresponding to planning, restraint coping and positive reinterpretation and growth [53]. In addition, active coping and planning showed a strong association statistically. Statistical analysis exposed less diversity in the scores for restraint coping than for suppression of competing activities. The strategies turn to religion, alcohol-drug disengagement and humour were removed because of their skewed distribution.

The COPE scale can be used in different formats. In the dispositional or trait-like version the respondents report the extent to which they usually do or feel when they are stressed. In the situational version respondents are asked to think about their most stressful situation in the last two months and then complete the ratings [53]. In our study we have used the dispositional version. First we asked the patients and the controls what they usually do or feel in general when they experienced stressful situations. Furthermore, we asked the patients what they usually do when experiencing stressful situations in connection with their disease. Finally, this last version was repeated at the 5-year follow-up.

### 3.5 Assessment of the quality of patient information

For this study we developed an instrument to examine the quality of perceived information by the patients. The instrument is based on discussions with neurologists and patients about the content of the information by the time of diagnosis and relevant literature [15, 63, 103, 104]. The patients were asked to think about the situation when they were told they had MS and indicate how they experienced the information they were given at that time. The questionnaire contains four questions on the content of the information:

'Was the information about the disease MS satisfactory?

'Did they inform you about the treatment for the disease?'

'Did you get information about how to handle your job, family and friends?'

'Did you get information about what it implies to live with MS?'

The response alternatives were 'yes', 'some', 'too little' and 'no'.

In addition, the instrument consists of five statements about the experience of the information:

'They gave me adequate information about MS',

'I had time enough to think through what they told me and to ask questions',

'They told me the consequences MS could have for my daily life',

'They encouraged me to ask questions'

'I felt cared for'.

On these five statements the participants could indicate their degree of agreement/disagreement on a five point Likert scale; one indicating 'fully agree' and five 'don't agree'. Based on the results from the 9 items on the questionnaire the patients' degree of satisfaction with the information was categorized into a scale from 0 – 4. Individuals with scores 0 through 1 were categorized as 'very dissatisfied', more than 1 through 2 as 'dissatisfied', more than 2 through 3 as 'satisfied', and finally, more than 3 through 4 as 'very satisfied'.

Two patients with MS tested the questionnaire before study start. To test the dimensionality of the items from the quality of the information questionnaire factor, we conducted analysis implementing principal axis factoring and a minimum eigenvalue of 1. This analysis showed a one-factor solution, whereas a reliability analysis yielded a Cronbach's alpha of 0.93. These results indicate that the scale on information quality is internally consistent and assesses a uniform concept.

### 3.6 Assessment of depression

The Beck Depression Inventory (BDI) is a self-rating scale for depression. Furthermore, it represents the gold standard for self-rating of depression [105] and is widely used in studies of patients with MS [106, 107]. It is a 21-item scale with a series of statements rated from 0 to 3, denoting increasing severity of symptoms. Patients were asked to select the one item that best describes the way they feel at the moment. Examples of items include feeling of sadness, concerns about the future, suicidal ideation, tearfulness, sleep, fatigue, interests, worries about health, sexual interest, appetite and general enjoyment. The scale has been validated and has shown excellent consistency [106]. We assessed patients and controls with the BDI both at baseline and at the 5-year follow-up.

### 3.7 Assessment of cognition

Cognition was measured by four instruments:

- Paced Auditory Serial Addition Test (PASAT) is an operationalization of working memory where the score represents the number of correct answers [108].

- Symbol Digit Modality Test (SDMT) is to assess visual scanning and tracking aspects of attention and the amount of correct answers in 90 seconds make up the score [109].
- Buschke Selective Reminding Test (SRT) is to measure verbal learning and memory that includes measures for Long Time Storage (SRT-LTS), Consistent Long Term Retrieval (SRT-CLTR) and Delayed Recall (SRT-DR) [110].
- Kurtzke's Functional Score (KFS) is the score for cerebral or mental function in EDSS and ranges from 0 (normal) to 5 (dementia or chronic brain syndrome – severe or incompetent) [101].

### 3.8 Statistical analysis

In study 1 the prevalence of general and MS-related coping styles were demonstrated with mean scores and standard deviations. In addition, we produced differential scores by subtracting the score for general coping from the score for MS-related coping, and by that we demonstrated to which degree the patients used the same coping styles for MS-related as for general stress situations. The dimensionality of the items from the quality of the information questionnaire factor was tested by principal factor analysis. Furthermore, we conducted reliability analysis to test the internal consistencies of the different scales used. A multivariate procedure, general linear modelling (GLM) was used to demonstrate the associations between quality of perceived information and MS-specific coping styles.

In study 2 we analyzed differences in scores for depressive symptoms between the two sub-samples, patients and controls, by both an independent t-test and a Mann-Whitney U test for non-normal distribution. Furthermore, we conducted analysis of correlations and partial correlations of scores for MS-specific coping styles with scores for depressive symptoms among the MS-sample and for general coping styles and depressive symptoms among the control sample. GLM was used to test

differences in mean scores between sub-samples in scores for general MS-coping in patients and general coping styles in controls.

In study 3 we applied a Chi-squared test for testing differences in portions for categorical variables, Student's t-test to compare means for continuous variables in two groups, and paired Student's t-test to compare means for continuous variables at baseline and at five years. GLM was applied to compare means for continuous independent variables when comparing coping in two groups where the repeated measurements was accounted for. In addition, the GLM was applied when comparing coping strategies in the two groups of patients at baseline and patients at five years.

## 4. RESULTS

### Paper I

We found that 43.2% of the patients were dissatisfied or very dissatisfied with the information by the time of diagnosis. Furthermore, we found that MS-related coping styles were influenced by the individual's general coping styles. In our patient sample the most frequently employed MS-related strategies were positive reinterpretation and growth, planning and restraint coping while denial was the most infrequently employed strategy. In addition, we showed that patients who were satisfied with the information about the diagnosis employed to a lesser extent avoidance coping and more actively both planned and sought information about the situation.

### Paper II

In this study we found that patients with MS employed significantly less the problem-focused strategies planning, restraint coping and seeking social support for instrumental reasons compared to normal controls. Furthermore, compared to normal controls patients used less the emotion-focused strategies positive reinterpretation and growth and seeking social support for emotional reasons. The mean BDI scores for depressive symptoms were 10.9 in patients with MS and 4.7 in normal controls. In stress situations connected to MS, depressive symptoms was in these patients related to the problem-focused strategies of restraint coping and planning, the emotion-focused strategy of focusing on and venting of emotions, and the avoidance strategies of behavioural- and mental disengagement and denial. The associations to depressive symptoms were similar for coping with stress situations in general, except for the coping strategy of planning that showed no relation to depressive symptoms.

### Paper III

In MS patients who were followed throughout a 5-year study period, patients' scores on problem- and emotion-focused strategies showed no significant change but a trend (statistically non-significant) towards lower scores than at baseline and significantly lower as compared to general coping in normal controls. The results from baseline on avoidance coping did not change at the 5-year follow-up, and were similar as compared to normal controls at baseline. The portion of patients with disability pensioned increased from 51% at baseline to 73% at the 5-year follow-up and patients with disability pension had significantly higher age, more disability and depression and lower scores on three of six cognitive tests than those without. Patients who were disability pensioned also had significantly higher scores on the problem-focused strategy seeking instrumental social support, emotion-focused strategy focus on and venting of emotion, and the avoidance strategy behavioural disengagement.

## 5. DISCUSSION

To be diagnosed with a chronic, progressive disease without cure as a young or middle aged adult is to cope with high levels of stress. In the early stage with a disease, stress may be related to the uncertainty of the first symptoms and the recognition of having a serious disease that will affect the rest of your life. Later it becomes important to gain control over the influence that the disease have on one's life and to cope with a set of ever-changing stressors. This process depend heavily on the individuals appraisal of the stress situation, their coping ability and their social network [41].

### 5.1 General aspects of methodology

When studying epidemiological features of a disease it is important that it is an unselected sample, correct diagnosis and that the instruments are well-tested and valid.

The study population from southern Rogaland and Hordaland consisted of all patients who were diagnosed with MS in 1998, 1999 and 2000. The diagnosis of MS was established according to the Poser criteria and by experienced neurologists. Several prevalence and incidence studies have been performed in the Hordaland area [4, 6, 111] and the annual incidence has been about 6.0 new patients pr 100.000 population during the last twenty years. In our study a total of 108 patients with MS were identified and approximately 700.000 inhabitants were living in the study area. This gives an average annual incidence of 5.1/100.000 and is comparable to previous findings. Study recourses did not allow the ideal door-to-door survey. However, MS patients in the two areas are referred to either Stavanger University Hospital or Haukeland University Hospital and to obtain an unselected group of patients, the files at the departments of Neurology were searched for MS-patients diagnosed from 1998 to 2000. At baseline 93 of the 108 detected patients gave their consent to participate



in the study and 86 of these completed the COPE scale. The non-completers were not different from the participating patients in terms of demographic and clinical variables. We therefore believe that the majority of the patients in the study area were detected and that the cohort is representative for early MS populations in Western Norway.

At the 5-year follow-up 83 patients with MS were included and 76 completed the COPE scale. Among the seven patients who failed to complete the COPE scale there were three patients who refused to participate and in four patients the consequences of the disease made it impossible for them to do so.

After one reminder 96 (44%) of the 220 normal controls gave their consent to participate in the study. The rather low response rate affected only to a minor degree the gender and age distribution of the participating control group. Attrition is seldom totally random and the higher rate of attrition the greater likelihood of bias [112]. 44% response rate is low and since we do not know much about the non-responders a possible bias should be of concern.

Another important issue in studies like ours is to use appropriate measurement instruments. The COPE scale is a validated instrument that has been used to study coping with different health problems including MS [79, 96, 113]. The COPE scale reflects a balanced view of dispositional versus situational or time-limited coping and has been tested for both versions. In our first study, we compared the patients' coping ability towards general stress situations and disease related stressors and found a strong correlation between the two. The same pattern of coping strategies as in our first study still existed after five years with the disease.

The full COPE scale has 60 items and patients may become tired in completing the instrument because of its length [114]. The application of such a demanding instrument on a population who suffers from a relatively severe disease may be difficult. In addition, the COPE scale was one of many instruments that were applied. For further studies it would be wise to consider The Brief COPE with 28 items.

As there were no validated instruments to assess the quality of the information given to patients with MS, it was necessary to develop our own instrument. The instrument was based on interviews with MS-patients and clinicians and furthermore it was tested on a group of patients. Creating a new instrument is demanding because it is difficult to develop an accurate and valid scale, but we attempted to solve this by testing the instrument statistically. The results of the factor analysis indicate that the scale on information quality is internally consistent and assesses a uniform concept.

BDI is the most commonly used depression scale and is considered as the best approach for screening depression in MS [115]. A cut-off score of 13 is recommended as optimal for screening depression and seems to screen for about 70% of MS patients [115, 116]. A problem with assessing depression in MS is the overlap between depression and MS-related symptoms like fatigue, work problems and concerns about health [106]. This may result in an overestimation of depression. [117].

In study I and II we have used a cross-sectional design and studied different characteristics of the patient population at one time point. The purpose was to determine associations between variables like the quality of the information and coping ability. The advantages of this design are that it is relatively economical and easy to perform. In study III we have applied a longitudinal design where new data were collected from the same population after five years. This design allows the researcher to identify change over time like coping styles after five years with MS. The challenge in this design is attrition over time. In our study the number of participants decreased from 86 to 76 after five years. Some of the drop-outs were too disabled to participate and this may bias the study population and decrease the generalizability of the findings [112].

## 5.2 Is it possible to measure coping and does it make sense?

Most of the research in MS has focused on the biology to understand the disease process with the purpose to find a treatment. In addition, the focus has been on treating symptoms or complications of the disease. However, the patients' experience with MS will reflect both its biology and the psychological and social aspects of living with the disease. As there is no cure for MS, both patients and health personnel should focus on adaption to the disease and coping as an important mediator in that process.

Gradually coping has been viewed as a normal, healthy and conscious process that enables people to deal with problems in their lives [50]. This was followed by the development of measurement instruments that should reflect the individuals' effort to cope with stressful life events; an effort that were described as strategies and enabled researchers to conceptualize coping responses [51]. Research on coping were greatly stimulated by the development of The Ways of Coping Checklist in the 1970s and opened for studies on large groups of individuals. Furthermore, it became possible to quantify the coping process and this may be useful and important in understanding persons' reactions towards stress situations in having a chronic disease and to develop strategies to help persons to a better living with the disease [54].

There are, however, critiques of the research on stress and coping. The gap between the process and individualized theory of stress and coping and the methodology of coping research calls for a longitudinal, process-oriented research design. However, most studies are cross-sectional designs that may not capture this dynamic process [118, 119].

Another criticism of coping research is confounding, that is the risk that measures of coping may contain other variables than intended. An example from our study is that we have discussed the risk for overlap between avoidance coping and depressive symptoms. However, confounding has always been a challenge for the measurement of psychological processes [54]. In the study of coping and depression in MS we have

used normal controls, comparable for age and sex, to compensate for this problem with confounding.

Coping is a wide concept with different definitions and several conceptual problems and although analysis of coping has not yet developed a concept with clear answers, some of these issues are being clarified by further exploration of the concept.

Despite the critics, we would claim that it is possible to measure coping, but to do so researchers have to be aware of the limitations. Measuring coping by self-reports and coping instruments is one way to learn more about the concept. Other research methods could bring an expanded understanding of the concept.

Research on coping makes sense if it brings new or confirm existing knowledge that give patients a better life with MS. The experiences of two young women being diagnosed with MS and their stories on how they were left alone to sort out their lives after being informed about the disease were my inspiration for doing this study. What does a person think and do and what factors may influence in a situation like this? The results from this study indicate that coping theory and the COPE scale describe important issues regarding this stressful event.

We first examined patients' perceived quality of the information given at the time of diagnosis and the influence of this experience eventually had on patients' coping styles. It has been shown that even several years after patients had their diagnostic consultation with a neurologist they remembered in detail what was said and their emotional reactions both during the consultation and afterwards. Patients describe that they are told "to go home and live with it". This feeling of being abandoned and isolated may make it difficult to cope with the stress associated with the disease symptoms and everyday problems. Our study shows that with the traditional doctor/nurse approach to provide information about the diagnosis, the findings indicate that better perceived quality of the information may reduce inappropriate coping strategies like denial and enhance adaptional strategies like seeking social support. Denial is considered ineffective in the sense that it makes a person more

vulnerable, closes the mind to what could be threatening and may lead to loss of energy and even depression [50]. Searching for support, information and advice seem to be important in coming in terms with uncertainty caused either by the nature of the disease or by the health care system in its communication with patients.

In the second study we explored coping in patients with MS compared to that of normal controls. As expected we found that patients employed less problem-focused strategies than controls. More surprisingly was the discovery that they also employ less emotion-focused strategies. Together with the low scores on avoidance, as compared to the scores for normal controls, this shows that MS patients as a group behave passive to disease related stress situations. Patients also had more depressive symptoms than controls, but these symptoms did not explain the differences in coping between patients and normal controls. These findings are partly in line with other studies and confirm that patients with MS have problems with coping in an early phase of the disease. We also know from other studies that this early phase is important for the patients and they experience both anxiety and helplessness and may be in need for assistance to handle both problems with the disease and other areas of life affected by the disease. These findings have a direct relevance for the management of patients with MS and should encourage health personnel to establish multidisciplinary teams that can help patients with the consequences MS may have for family, social life and work.

In a recent published study McCabe et al [98] has examined coping and quality of life in 382 people with MS and 291 normal controls. As in other studies their findings suggested that people with MS adapt to the disease over time by the fact that they have lower scores on problem-focused coping strategies and lower quality of life at baseline as compared to two years later. In our study we did not find this tendency for MS patients to adapt to the disease. Our findings showed a remarkable stability of applied coping with strategies that are considered as maladaptive. The patients continued their pattern of passive coping. The explanation for this is unclear. Perhaps the health care system in Norway does not stimulate patients to cope with MS. As this

group is in the early phase of the disease, the assumption could be that they choose to live as normal as possible and avoid to proceed with the adaptation of the disease. Another explanation could be fear for what the future will bring. Further, it seems important to avoid the stigma of having this disease.

We also found that patients were depressed and we know that depression is not well treated in MS. Depression may influence coping and should therefore be detected and treated but depression could not, as mentioned above, explain the majority of inappropriate coping.

In paper 3 we also studied characteristics of MS patients who had been disability pensioned. As in other studies the group of patients who were disability pensioned was older and had more functional and cognitive problems. Furthermore, the findings on coping were diverging and did not form a typical coping pattern for these patients and it is difficult to draw any conclusions about the association between disability pension and coping style in this study. However, an important finding was that compared to those who were still working, disability pensioned patients sought more social support, were more behavioural disengaged and had more focus on and venting of emotions. This may indicate that these patients had less drive and felt more dependent on others.

In summary, we have found that these patients with MS do not employ what is assessed as adaptive coping strategies either at baseline or at the 5-year follow-up. Good and adequate information by the time of diagnosis seem to reduce ineffective coping and enhance adaptive coping. Patients with MS experience depressive symptoms, but depression does not explain their different coping pattern compared to normal controls.

Based on our examinations we have been able to bring new and important information on coping in early MS. We have shown that available rating scales provide meaningful and valuable information on coping with MS in both cross-sectional and longitudinal studies.

## 6. CONCLUSIONS

The aims of this thesis were to examine coping styles in patients with MS and the longitudinal development of coping in these patients. The instruments applied are self-reports and represent the subjective experience of the patients themselves. Our studies bring meaningful and important information on coping in patients with MS.

In this thesis we have studied how patients with MS cope in the early phase of the disease and how the perceived quality of the information by the time of diagnosis may influence their further ability to cope with the disease. We have showed that MS-patients cope differently from normal controls. In addition, patients have more depressive symptoms, but these symptoms do not explain the differences in coping between patients and controls. Furthermore, our study shows how this group of patients copes during a 5-year follow-up. Finally, we have examined characteristics of those patients who perceived disability pension and studied their ability to cope.

How patients with MS cope has been studied previously. We do, however, extend this knowledge by providing information on patients' coping style in the early phase of the disease and during a 5-year follow-up period. In addition, we have studied factors that may influence coping ability in patients with MS.

### 6.1 Implications for practice

Our study shows that patients with MS seem to employ coping strategies that are not optimal for the adaption to their disease. The explanations for this are probably multifactorial but our findings should stimulate health personnel to provide a better care for these patients. Our research strengthens the apprehension that patients with MS need more help to cope with difficult situations regarding their disease. A closer

follow-up by the neurologist and MS-nurse, involvement of a multidisciplinary team and teaching courses should be available for these patients.

To achieve that the quality of the perceived information of patients with MS is improved, it is important that health personnel offer time, privacy and dialog. In addition, patients should be offered the possibility to bring a next of kin and oral information should be supplemented by written information designed for newly diagnosed patients.

Depression should be detected and treated in patients with MS, since depressive symptoms seem to enhance non-adaptive coping strategies.

Both health personnel and employers should have special focus on the possibilities for patients to keep on working even though they may need special equipment or assessment.

## 6.2 Implications for further research

Further studies should explore possible intervention to improve coping and the management of patients with MS.

Future studies are needed to replicate and supplement our findings. Follow-up studies over a longer period of time and with more participants would to a greater extent determine the impact of coping as the disease progresses.



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## Source of data

1. Beatty, W.W., et al., *Correlates of coping style in patients with multiple sclerosis*. *Mult Scler*, 1998. **4**(5): p. 440-3.
2. Pearce, J.M.S., *Historical Descriptions of Multiple Sclerosis*. *Eur Neurol*, 2005. **54**: p. 49-53.
3. Noseworthy, J.H., et al., *Multiple sclerosis*. *N Eng J Med.*, 2000. **343**(13): p. 938-52.
4. Grytten, N., et al., *A 50-year follow-up of the incidence of multiple sclerosis in Hordaland County, Norway*. *Neurology*, 2006. **66**(2): p. 182-6.
5. Presthus, J., *Report on the multiple sclerosis investigations in West-Norway*. *Acta Psychiatr Scand Suppl*, 1960. **35**(147): p. 88-92.
6. Larsen, J.P., et al., *Western Norway, a high-risk area for multiple sclerosis: a prevalence/incidence study in the county of Hordaland*. *Neurology*, 1984. **34**(9): p. 1202-7.
7. Myhr, K.M., *Diagnosis and treatment of multiple sclerosis*. *Acta Neurol Scand*, 2008. **117**: p. 12-21.
8. Sadovnick, A.D., D. Dymont, and G.C. Ebers, *Genetic epidemiology of multiple sclerosis*. *Epidemiol Rev*, 1997. **19**(1): p. 99-106.
9. Dymont, D.A., G.C. Ebers, and A.D. Sadovnick, *Genetics of multiple sclerosis*. *Lancet Neurol*, 2004. **3**(2): p. 104-10.
10. Ascherio, A. and K.L. Munger, *Environmental risk factors for multiple sclerosis. Part I: the role of infection*. *Ann Neurol*, 2007. **61**(4): p. 288-99.
11. Ascherio, A. and K.L. Munger, *Environmental risk factors for multiple sclerosis. Part II: Noninfectious factors*. *Ann Neurol*, 2007. **61**(6): p. 504-13.
12. Mohr, D.C., *Stress and multiple sclerosis*. *J Neurol*, 2007. **254** **Suppl 2**: p. II65-8.
13. Li, J., et al., *The risk of multiple sclerosis in bereaved parents: A nationwide cohort study in Denmark*. *Neurology*, 2004. **62**(5): p. 726-9.
14. Koopman, W. and A. Schweitzer, *The journey to multiple sclerosis: a qualitative study*. *J Neurosci Nurs*, 1999. **31**(1): p. 17-26.
15. Isaksson, A.K. and G. Ahlstrom, *From symptom to diagnosis: illness experiences of multiple sclerosis patients*. *J Neurosci Nurs*, 2006. **38**(4): p. 229-37.
16. Poser, C.M., et al., *New diagnostic criteria for multiple sclerosis: guidelines for research protocols*. *Ann Neurol*, 1983. **13**: p. 227-231.
17. Polman, C.H., et al., *Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria"*. *Ann Neurol*, 2005. **58**(6): p. 840-6.
18. Compston, A. and A. Coles, *Multiple sclerosis*. *Lancet*, 2008. **372**(9648): p. 1502-17.
19. Myhr, K.M., et al., *Disability and prognosis in multiple sclerosis: demographic and clinical variables important for the ability to walk and awarding of disability pension*. *Mult Scler*, 2001. **7**(1): p. 59-65.

20. Confavreux, C. and S. Vukusic, *Natural history of multiple sclerosis*. Brain, 2006. **129**: p. 606-616.
21. Krupp, L.B., *Fatigue in multiple sclerosis: definition, pathophysiology and treatment*. CNS Drugs, 2003. **17**(4): p. 225-34.
22. Rao, S.M., *Neuropsychology of multiple sclerosis*. Curr Opin Neurol, 1995. **8**(3): p. 216-20.
23. Chiaravalloti, N.D. and J. DeLuca, *Cognitive impairment in multiple sclerosis*. Lancet Neurol, 2008. **7**(12): p. 1139-51.
24. Feinstein, A., *The neuropsychiatry of multiple sclerosis*. Can J Psychiatry, 2004. **49**(3): p. 157-63.
25. Figved, N., et al., *Neuropsychiatric symptoms in patients with multiple sclerosis*. Acta Psychiatr Scand, 2005. **112**(6): p. 463-8.
26. Nortvedt, M.W., et al., *Prevalence of bladder, bowel and sexual problems among multiple sclerosis patients two to five years after diagnosis*. Mult Scler, 2007. **13**(1): p. 106-12.
27. Beiske, A.G., et al., *Pain and sensory complaints in multiple sclerosis*. Eur J Neurol, 2004. **11**(7): p. 479-82.
28. Siegert, R.J. and D.A. Abernethy, *Depression in multiple sclerosis: a review*. J Neurol Neurosurg Psychiatry, 2005. **76**(4): p. 469-75.
29. Minden, S.L. and R.B. Schiffer, *Affective disorders in multiple sclerosis. Review and recommendations for clinical research*. Arch Neurol, 1990. **47**(1): p. 98-104.
30. Mohr, D.C., et al., *Depression, coping and level of neurological impairment in multiple sclerosis*. Multiple Sclerosis, 1997. **3**: p. 254-8.
31. Lynch, S.G., D.C. Kroencke, and D.R. Denney, *The relationship between disability and depression in multiple sclerosis: the role of uncertainty, coping and hope*. Multiple Sclerosis, 2001. **7**: p. 411-416.
32. Mohr, D.C. and D. Cox, *Multiple sclerosis: empirical literature for the clinical health psychologist*. J Clin Psychol, 2001. **57**(4): p. 479-99.
33. Lobentanz, I.S., et al., *Factors influencing quality of life in multiple sclerosis patients: disability, depressive mood, fatigue and sleep quality*. Acta Neurol Scand, 2004. **110**: p. 6-13.
34. Mohr, D.C. and D.E. Goodkin, *Treatment of Depression in Multiple Sclerosis: Review and Meta-analysis*. Clinical Psychology: Science and Practice, 1999. **6**: p. 1-9.
35. Confavreux, C. and S. Vukusic, *Age and disability milestones in multiple sclerosis*. Brain, 2006. **129**: p. 595-605.
36. Kantarci, O., et al., *Survival and predictors of disability in Turkish MS patients. Turkish Multiple Sclerosis Study Group (TUMSSG)*. Neurology, 1998. **51**(3): p. 765-72.
37. Corbin, J.M., *The body in health and illness*. Qual Health Res, 2003. **13**(2): p. 256-67.
38. Paterson, B.L., *The shifting perspectives model of chronic illness*. J Nurs Scholarsh, 2001. **33**(1): p. 21-6.

39. Grytten, N. and P. Maseide, '*What is expressed is not always what is felt*': coping with stigma and the embodiment of perceived illegitimacy of multiple sclerosis. *Chronic Illn*, 2005. **1**(3): p. 231-43.
40. Barker-Collo, S., C. Cartwright, and J. Read, *Into the unknown: the experiences of individuals living with multiple sclerosis*. *J Neurosci Nurs*, 2006. **38**(6): p. 435-41, 446.
41. Maes, S., H. Leventhal, and D.T.D. de Ridder, *Coping with Chronic Diseases.*, in *Handbook of Coping.*, E.N. Zeidner M, Editor. 1999, John Wiley & Sons Inc.: New York. p. 221-251.
42. Yorkston, K.M., et al., *Getting the work done: a qualitative study of individuals with multiple sclerosis*. *Disabil Rehabil*, 2003. **25**(8): p. 369-79.
43. Busche, K.D., et al., *Short term predictors of unemployment in multiple sclerosis patients*. *Can J Neurol Sci*, 2003. **30**(2): p. 137-42.
44. O'Connor, R.J., et al., *Factors influencing work retention for people with multiple sclerosis: cross-sectional studies using qualitative and quantitative methods*. *J Neurol*, 2005. **252**(8): p. 892-6.
45. Julian, L.J., et al., *Employment in multiple sclerosis. Exiting and re-entering the work force*. *J Neurol*, 2008. **255**(9): p. 1354-60.
46. Johnson, K.L., et al., *The cost and benefits of employment: a qualitative study of experiences of persons with multiple sclerosis*. *Arch Phys Med Rehabil*, 2004. **85**(2): p. 201-9.
47. Kohn, P., *On Coping Adaptively with Daily Hassles in Handbook of Coping*, M. Zeidner and N.S. Endler, Editors. 1996, John Wiley & Sons Inc: New York.
48. Cassidy, T., *Stress, cognition and health*. 1999, London: Routledge.
49. Rice, V.H., *Handbook of Stress, Coping and Health. Implications for Nursing Research, Theory and Practice*. Major Life Stressors and Health Outcomes, ed. F.M. Werner JS. 2000, Thousand Oaks: Sage Publications.
50. Lazarus, R.S. and S. Folkman, *Stress, appraisal and coping*. 1984, New York: Springer Publishing Company.
51. Parker, J.D.A. and N.S. Endler, *Coping and Defense: A Historical Overview.* , in *Handbook of Coping*, J.D.A. Parker and N.S. Endler, Editors. 1996, John Wiley & Sons Inc: New York.
52. Kobasa, S.C. and M.C. Puccetti, *Personality and social resources in stress resistance*. *J Pers Soc Psychol*, 1983. **45**(4): p. 839-50.
53. Carver, C.S., M.F. Scheier, and J.K. Weintraub, *Assessing Coping Strategies: A Theoretically Based Approach*. *Journal of Personality and Social Psychology.*, 1989. **56**(No 2): p. 267-283.
54. Lazarus, R.S., *Toward better research on stress and coping*. *Am Psychol*, 2000. **55**(6): p. 665-73.
55. Mikulincer, M. and V. Florian, *Coping and Adaption to Trauma and Loss*, in *Handbook of Coping*, E.N. Zeidner M, Editor. 1996, John Wiley & Sons, Inc: New York.

56. Zeidner, M. and D. Saklofske, *Adaptive and Maladaptive Coping.*, in *Handbook of Coping*, E.N. Zeidner M, Editor. 1996, John Wiley & Sons: New York. p. 505-531.
57. Costa, P.T., M.R. Somerfield, and R.R. McCrae, *Personality and Coping: A Reconceptualization*, in *Handbook of Coping*, E.N. Zeidner M, Editor. 1996, John Wiley & Sons Inc: New York. p. 44-61.
58. Wineman, N.M., E.J. Durand, and R.P. Steiner, *A comparative analysis of coping behaviors in persons with multiple sclerosis or a spinal cord injury*. *Res Nurs Health*, 1994. **17**(3): p. 185-94.
59. Wright, L.J., A. Niloofar, and A. Zautra, *The Illness Uncertainty Concept: A Review*. *Current Pain and Headache Reports*, 2009. **13**: p. 133-138.
60. Mishel, M.H., *Uncertainty in chronic illness*. *Annu Rev Nurs Res*, 1999. **17**: p. 269-94.
61. Pierce, G.R., I.G. Sarason, and B.R. Sarason, *Coping and Social Support*, in *Handbook of Coping*, E.N. Zeidner M, Editor. 1996, John Wiley & Sons: New York.
62. Dennison, L., R. Moss-Morris, and T. Chalder, *A review of psychological correlates of adjustment in patients with multiple sclerosis*. *Clin Psychol Rev*, 2009. **29**(2): p. 141-53.
63. Baker, L.M., *Sense making in multiple sclerosis: the information needs of people during an acute exacerbation*. *Qual Health Res*, 1998. **8**(1): p. 106-20.
64. Baker, L.M., *A new method for studying patient information needs and information-seeking patterns*. *Top Health Inf Manage*, 1995. **16**(2): p. 19-28.
65. Johnson, J., *On receiving the diagnosis of multiple sclerosis: managing the transition*. *Mult Scler*, 2003. **9**(1): p. 82-8.
66. de Ridder, D. and K. Schreurs, *Developing interventions for chronically ill patients: is coping a helpful concept?* *Clin Psychol Rev*, 2001. **21**(2): p. 205-40.
67. de Ridder, D., et al., *Psychological adjustment to chronic disease*. *Lancet*, 2008. **372**(9634): p. 246-55.
68. Warren, S., K.G. Warren, and R. Cockerill, *Emotional stress and coping in multiple sclerosis (MS) exacerbations*. *J Psychosom Res*, 1991. **35**(1): p. 37-47.
69. Buelow, J.M., *A correlational study of disabilities, stressors and coping methods in victims of multiple sclerosis*. *J Neurosci Nurs*, 1991. **23**(4): p. 247-52.
70. O'Brien, M.T., *Multiple sclerosis: the relationship among self-esteem, social support, and coping behavior*. *Appl Nurs Res*, 1993. **6**(2): p. 54-63.
71. Pakenham, K.I., C.A. Stewart, and A. Rogers, *The role of coping in adjustment to multiple sclerosis-related adaptive demands*. *Psychology, Health and Medicine*, 1997. **2**(3): p. 197-211.
72. Jean, V.M., et al., *Coping with general and disease-related stressors by patients with multiple sclerosis: relationship to psychological distress*. *Multiple Sclerosis*, 1997. **3**: p. 191-6.

- 
73. Jean, V.M., R.H. Paul, and W.W. Beatty, *Psychological and neuropsychological predictors of coping patterns by patients with multiple sclerosis*. J Clin Psychol, 1999. **55**(1): p. 21-6.
  74. Kroencke, D.C. and D.R. Denney, *Stress and coping in multiple sclerosis: exacerbation, remission and chronic subgroups*. Mult Scler, 1999. **5**(2): p. 89-93.
  75. Mohr, D.C., et al., *The psychosocial impact of multiple sclerosis: exploring the patient's perspective*. Health Psychol, 1999. **18**(4): p. 376-82.
  76. De Ridder, D., K. Schreurs, and J. Bensing, *The relative benefits of being optimistic: Optimism as a coping resource in MS and Parkinson's disease*. British Journal of Health and Psychology, 2000. **5**: p. 141-155.
  77. Rätsep, T., et al., *Personality as a predictor of coping efforts in patients with MS*. Multiple Sclerosis, 2000. **6**: p. 397-402.
  78. Pakenham, K.I., *Coping with Multiple Sclerosis: development of a measure*. Psychology, Health and Medicine, 2001. **6**(4): p. 411-428.
  79. Arnett, P.A., et al., *Relationship Between Coping, Cognitive Dysfunction and Depression in Multiple Sclerosis*. The Clinical Neuropsychologist, 2002. **16**(3): p. 341-355.
  80. McCabe, M.P., *Relationship Functioning and Sexuality Among People With Multiple Sclerosis*. The Journal of Sex Research, 2002. **39**: p. 302-309.
  81. McCabe, M.P., S. McKern, and E. McDonald, *Coping and psychological adjustment among people with multiple sclerosis*. J Psychosom Res., 2004. **56**(355-61).
  82. Chalk, H.M., *Mind over matter: cognitive - behavioral determinants of emotional distress in multiple sclerosis patients*. Psychol Health Med, 2007. **12**(5): p. 556-66.
  83. Montel, S.R. and C. Bungener, *Coping and quality of life in one hundred and thirty five subjects with multiple sclerosis*. Multiple Sclerosis, 2007. **13**: p. 393-401.
  84. Twork, S., et al., *Chronical illness and maternity: life conditions, quality of life and coping in women with multiple sclerosis*. Qual Life Res, 2007. **16**(10): p. 1587-94.
  85. Haase, C.G., M. Lienemann, and P.M. Faustmann, *Neuropsychological deficits but not coping strategies are related to physical disability in multiple sclerosis*. Eur Arch Psychiatry Clin Neurosci, 2008. **258**(1): p. 35-9.
  86. Kehler, M.D. and H.D. Hadjistavropoulos, *Is health anxiety a significant problem for individuals with multiple sclerosis?* J Behav Med, 2009. **32**(2): p. 150-61.
  87. Goretti, B., et al., *Coping strategies, psychological variables and their relationship with quality of life in multiple sclerosis*. Neurol Sci, 2009. **30**(1): p. 15-20.
  88. Wineman, N.M., et al., *Relationships among illness uncertainty, stress, coping, and emotional well-being at entry into a clinical drug trial*. Appl Nurs Res, 1996. **9**(2): p. 53-60.

- 
89. Aikens, J.E., et al., *A Replicated Prospective Investigation of Life Stress, Coping, and Depressive Symptoms in Multiple Sclerosis*. Journal of Behavioural Medicine., 1997. **20**(5): p. 433-445.
  90. Pakenham, K.I., *Adjustment to multiple sclerosis: application of a stress and coping model*. Health Psychology, 1999. **18**: p. 383-92.
  91. Mohr, D.C., et al., *Moderating effects of coping on the relationship between stress and the development of new brain lesions in multiple sclerosis*. Psychosom Med, 2002. **64**(5): p. 803-9.
  92. Wineman, N.M., et al., *Longitudinal analysis of illness uncertainty, coping, hopefulness, and mood during participation in a clinical drug trial*. J Neurosci Nurs, 2003. **35**(2): p. 100-6.
  93. McCabe, M.P., *Mood and self-esteem of persons with multiple sclerosis following an exacerbation*. J Psychosom Res, 2005. **59**(3): p. 161-6.
  94. McCabe, M.P., *A Longitudinal Study of Coping Strategies and Quality of Life Among People with Multiple Sclerosis*. J Clin Psychol Med Setting, 2006. **13**: p. 369-379.
  95. Pakenham, K.I., *Investigation of coping antecedents to positive outcomes and distress in multiple sclerosis (MS)*. Psychology and Health., 2006. **21**(5): p. 633-649.
  96. Arnett, P.A. and J.J. Randolph, *Longitudinal course of depression symptoms in multiple sclerosis*. J Neurol Neurosurg Psychiatry, 2006. **77**: p. 606-610.
  97. Moreau, T., et al., *Coping strategy and anxiety evolution in multiple sclerosis patients initiating interferon-beta treatment*. Eur Neurol, 2009. **62**(2): p. 79-85.
  98. McCabe, M.P., M. Stokes, and E. McDonald, *Changes in quality of life and coping among people with multiple sclerosis over a 2 year period*. Psychol Health Med, 2009. **14**(1): p. 86-96.
  99. Schwartz, C.E., *Teaching Coping Skills Enhances Quality of Life More Than Peer Support: Results of a Randomized Trial With Multiple Sclerosis Patients*. Health Psychology, 1999. **18**: p. 211-220.
  100. Tesar, N., et al., *Effects of psychological group therapy in patients with multiple sclerosis*. Acta Neurol Scand, 2003. **107**(6): p. 394-9.
  101. Kurtzke, J.F., *Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS)*. Neurology, 1983. **33**: p. 1444-1452.
  102. Schwartz, R. and C. Schwartz, *A Critical Survey of Coping Instruments*, in *Handbook of Coping*, M. Zeidner and N.S. Endler, Editors. 1996, John Wiley & Sons Inc: New York.
  103. Box V, H.M., Harrison J, *Identifying information need of people with multiple sclerosis*. Nurs Times, 2003. **99**(49): p. 32-6,.
  104. Johnson, J., *On receiving the diagnosis of multiple sclerosis: managing the transition*. Multiple Sclerosis, 2003. **9**: p. 82-88.
  105. Burns, A., B. Lawler, and S. Craigh, *Assessment Scales in Old Age Psychiatry*. 1999, London: Martin Dunitz Ltd.
  106. Mohr, D.C., et al., *Identification of Beck Depression Inventory items related to multiple sclerosis*. J Behav Med, 1997. **20**(4): p. 407-14.

- 
107. Beck, A.T., et al., *An inventory for measuring depression*. Arch Gen Psychiatry, 1961. **4**: p. 561-71.
  108. Gronwall, D.M., *Paced auditory serial-addition task: a measure of recovery from concussion*. Percept Mot Skills, 1977. **44**(2): p. 367-73.
  109. Smith, A., *Symbol Digit Modality Test: Manual*. . 1982, Los Angeles: Western Psychological Services.
  110. Buschke, H. and P.A. Fuld, *Evaluating storage, retention, and retrieval in disordered memory and learning*. Neurology, 1974. **24**(11): p. 1019-25.
  111. Gronning, M., et al., *Incidence of multiple sclerosis in Hordaland, western Norway: a fluctuating pattern*. Neuroepidemiology, 1991. **10**(2): p. 53-61.
  112. Polit, D.F. and C.T. Beck, *Nursing research: Principles and Methods*. 7th ed. 2004, Philadelphia: Lippincott, Williams & Wilkins.
  113. Ratsep, T., et al., *Personality as a predictor of coping efforts in patients with multiple sclerosis*. Multiple Sclerosis, 2000. **6**(397-402).
  114. Carver, C.S., *You want to measure coping but your protocol's too long: consider the brief COPE*. Int J Behav Med, 1997. **4**(1): p. 92-100.
  115. *The Goldman Consensus statement on depression in multiple sclerosis*. Mult Scler, 2005. **11**(3): p. 328-37.
  116. Sullivan, M.J., et al., *Screening for major depression in the early stages of multiple sclerosis*. Can J Neurol Sci, 1995. **22**: p. 228-31.
  117. Moran, P.J. and D.C. Mohr, *The validity of Beck Depression Inventory and Hamilton Rating Scale for Depression items in the assessment of depression among patients with multiple sclerosis*. J Behav Med, 2005. **28**(1): p. 35-41.
  118. Somerfield, M.R. and R.R. McCrae, *Stress and coping research. Methodological challenges, theoretical advances, and clinical applications*. Am Psychol, 2000. **55**(6): p. 620-5.
  119. Coyne, J.C. and M.W. Racioppo, *Never the Twain shall meet? Closing the gap between coping research and clinical intervention research*. Am Psychol, 2000. **55**(6): p. 655-64.

