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Perceived health status in multiple sclerosis patients

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General introduction, aims and structure of the thesis

Multiple sclerosis (MS), with its unknown etiology and still not understood occurrence, has attracted a lot of attention from researchers over the past two decades. This study tries to contribute to the understanding of perceived health status in patients with MS. This first chapter describes the disease, the aim of this study, the theoretical model used, the research questions employed and the structure of this thesis.

1.1 Multiple sclerosis

MS is considered an inflammatory neurodegenerative disease of the central nervous system, with onset usually occurring in early adult life. It is characterized by demyelination and primary or secondary axonal degeneration, with the loss of dendrites and neurons contributing to the irreversible functional impairment observed in affected individuals. It attacks more than 2 million people worldwide, the ratio of women to men affected being 2:1. Onset of the illness generally occurs between 20-50 years of age (1-3).

Although descriptions of MS symptoms date back as far as the Middle Ages, MS was first recognized as a distinct disease only in the nineteenth century. The first pathologic report was published in 1868 by J.M. Charcot, a professor of Neurology at the University of Paris. He examined the brain of a young woman and documented the characteristic scars, which he describes as “la sclérose en plaques” (1).

The prevalence of MS varies considerably around the world. It is highest in northern Europe, southern Australia and the middle part of North America. There has been a trend toward an increasing prevalence and incidence, particularly in southern Europe (3, 4, 5). Slovakia has a relatively high rate of MS prevalence, with more than 30 cases reported per 100 000 persons (6). The reasons for the variations in the prevalence and incidence of MS worldwide are not understood, as the etiology of MS is itself unknown. MS is assumed to be a multifactorial disorder, in which environmental factors are hypothesized to interact with genetically susceptible individuals. Pediatric MS and late-onset MS (i.e. clinical onset occurring later than the fifth decade) are rare (4, 7).

1.1.1 Diagnostics criteria

The most widely used criteria for the diagnosis of MS are the Poser Committee criteria and a new system of classification, the McDonald criteria. They incorporate magnetic resonance imaging (MRI) to demonstrate multiple areas of involvement and also involvement over time with the appearance of new enhancing lesions. Patients have been diagnosed as having MS or possibly having MS according to these indicators over the past two decades (8, 9). Advanced MRI and spectroscopy may allow clinicians to follow the pathological progression of the disease and to monitor the response to treatment (4).

All patients in this thesis were diagnosed in accordance with the McDonald criteria, which allows for earlier confirmation of a diagnosis of MS and an earlier decision on therapy. This diagnosis was confirmed by one neurologist (8, 9).

1.1.2 Clinical course and disability

The clinical course of MS shows heterogeneity among patients and within the same patient. Decisions on the categorization of the clinical course of MS have been made and later on reduced, thus resulting in confusing terminology:

- *relapsing-remitting MS (RR-MS)* – the disease as it occurs in the majority of MS patients (~85%) with relapses with full recovery, or with sequelae upon recovery and periods between relapses characterized by a lack of disease progression. Fifteen percent of patients with RR-MS experience a mild course with minimal disability after 15 years; this is therefore called *benign MS*.
- *progressive-relapsing MS (PR-MS)* – progressive disease from the onset on (~5%), with clear relapses, and periods between relapses showing continuing progression.
- *secondary-progressive MS (SP-MS)* – initially categorized as the RR-MS clinical course (exhibited in ~90% of the 85% RR-MS), followed by progression with or without occasional relapses, minor remissions and plateaus.
- *primary-progressive MS (PP-MS)* – the disease with progression from onset, with plateaus and temporary minor improvements (~10%) (1, 3, 4, 10).

Because of the cross-sectional design of most studies on MS, clinical course is often more simply categorized into RR-MS, SP-MS and PP-MS (7, 11). This categorization of clinical course will be used in this thesis.

The burden of disability in the cross-sectional design of MS studies is most frequently presented as the Kutzke Expanded Disability Status Score. Disability due to MS can be measured within functional neurological systems (pyramidal, cerebellar, brainstem, sensory, bowel

and bladder, visual, other) by assigning each a score. The distribution of the scores over the functional systems combined with their degree is then assigned to one of 20 categories (0, 0.5, 1, 1.5, 2,...10), which indicate the level of disability (12).

1.1.3 Treatment

Patients with MS face enormous prognostic uncertainty, and they should become well informed about their illness. Treatment focuses on acute attacks, prevention of relapses and progression, management of symptoms, and rehabilitation. In recent years advances have been made in all four areas (13). Treating physicians have to continually assess the need for psychological support for patients and their families.

Corticosteroid therapy is often used to treat clinically significant relapses in an attempt to stop the relapse and consequently to hasten recovery. Current therapeutic agents for MS patients are anti-inflammatory or immunomodulatory in nature (1, 4). Treatment with interferon-beta and glatiramer acetate may delay the development of a second, diagnosis-defining bout. Interferon-beta may delay the progression of disability in patients with minor disability who have a relapsing form of MS (3, 4, 14). The advent of natalizumab for the treatment of multiple sclerosis opens up a new era of immune-specific therapy. At present, the available therapeutic repertoire to fight against multiple sclerosis remains limited and is primarily aimed at targeting the activity of the immunocompetent cells (4, 15, 16).

Unfortunately, no proven therapies for PP-MS exist which would be able to reverse the neurological disabilities in MS patients (4). There are, however, moderately effective treatments for several of the complications of MS, like fatigue, pain, gait problems, spasticity, speech and swallowing disorders, weakness of legs, bladder and bowel disturbances, sexual dysfunction, cerebellar tremor, sleep disorders, cognitive and mood disorders, etc. (3, 4).

1.1.4 Prognosis

One limiting factor in determining the potential improvement in outcome with new therapies is the lack of a direct biomarker for disease outcome. Over 120 randomized clinical trials are currently underway in MS involving 30 agents or combinations of agents, so the outlook for better therapies in the future is hopeful. Advances in the understanding of the underlying mechanisms of MS are allowing a more focused approach to the development of the new therapies for MS patients (13). Research and clinical developments in the field of multiple sclerosis appear to be very active and dynamic at present; it is therefore hoped that some of the promising compounds may broaden the still limited therapeutic arsenal for this disabling disease (16).

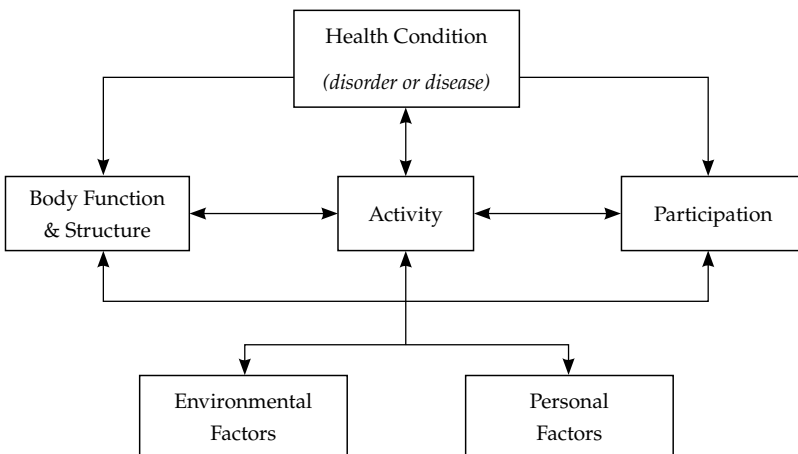
1.2 Structure of health status

When trying to explain the structure of health status, some questions on health can be raised: Is health the absence of disease symptoms? Is health the ability to work and carry out one's role? Does health include emotional and spiritual components? What is optimal health? The answers to these questions might only approach an explanation of health, however, because there is not really consensus on the definition of health the content of which has changed over time (17, 18).

The concept of health as well-being was introduced in the World Health Organization (WHO) as a definition of health as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (19). Other authors have characterized well-being as being able to feel well during a life of mobility, enjoyment and social relationships (20), and as an optimal individual fitness, so that one lives a full, creative life (21). The WHO definition also provides a popular consideration of several different dimensions of health, such as physical (structure and function), social, role, mental (emotional and intellectual) and general perceptions of health status (17, 19). An important feature of health is its dimensionality. Health has distinct components, as can be derived from the definition of health offered by the WHO (19, 22).

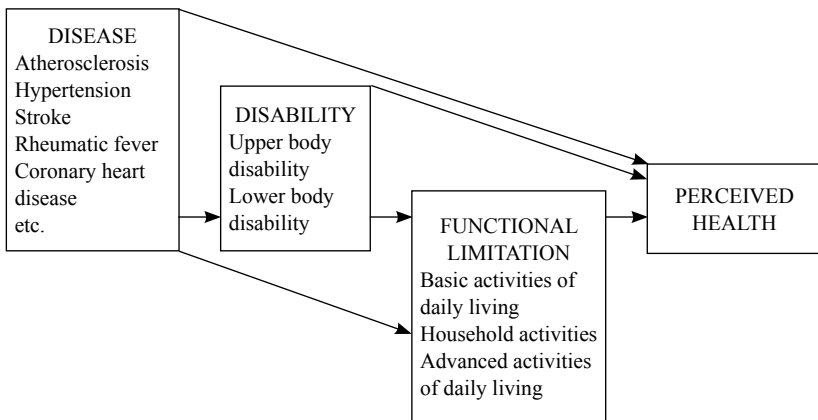
Figure 1 presents a graphic representation of the International Classification of Functioning, Disability and Health (ICF) model formally endorsed as the "International classification of impairment, disability and health" by WHO, in which health conditions interact with environmental and personal factors, and result in functioning or disability in one or more components or levels (23, 24).

Figure 1 WHO model of the International Classification of Functioning, Disability and Health (24)



As a conceptual framework for disability studies, Nagi's model from 1965 is well-known. When conceptualizing disability, he thought in terms of a four-stage sequential process: *disease – physiological impairment – limitations in the physical and emotional dimensions – disability*. Nagi's model was modified by Johnson and Wolinsky (1993), who used slightly different terminology in some instances. The four terms in their model were substituted: *disease – disability – functional limitation – perceived health* (25) (Figure 2).

Figure 2 Conceptual model of disability by Johnson and Wolinsky (1993)



Johnson and Wolinsky (1993) expected that all of the dimensions of health status affected an individual's global perception of his or her health status. The concept of perceived health status may reflect the transitional status of acute symptoms unrelated to the more stable influences of chronic disease, disability and functional limitations. That is, perceived health can also be linked to a wider range of health status measures, and therefore is frequently used as a proxy for other physical and mental health status measures (22, 25). Knowledge of the underlying disease, recognition of physical disabilities and awareness of functional limitation affect perceived health status negatively (25).

It is still under debate whether health, defined comprehensively, can be equated with quality of life, which is defined as a much broader concept than health. Quality of life and well-being represent subjective perceptions and expectations of individuals about their health. Perceived health status reflects a complex of internalized calculations based on life experience and knowledge of disease causes and consequences, or the influences of chronic disease, disability and functional limitations (22, 23, 25-32).

Considering the outcome of MS, it is possible to conceptualize the consequences as lying on a continuum of outcome (Figure 3) running

from disease through impairment, disability (activities) and handicap (participation) – formalized in the International Classification of Impairments, Disabilities and Handicaps (ICIDH) (33, 34).

Figure 3 Outcome continuum in MS of the ICIDH (33, 34)

Disease	Impairment	Disability	Handicap	Quality of life
Relapse rate	Weakness	Locomotor	Physical-independence	Well-being
MRI	Sensory dysfunction	Dexterity	Mobility	
	Fatigue	Personal care	Occupation	
	Bladder/bowel dysfunction	Reading	Social integration	
	Imbalance	Sexual function	Economic	
	Visual loss			
	Cognitive decline			

Physical illness, particularly in chronic disorders, can be considered as one of the main causes of a loss of access to valued resources and, consequently, of valued goals. Loss for the individual involves, for example, a loss of independence, a reduced social mobility, reduced capacity to work, exposure to pain, fatigue and threat of disfigurement (and eventually death) (35, 36). The impact of some specific MS disabilities on perceived health status has been studied. Therefore, we now have evidence confirming that cognitive and emotional functions and chronic pain correlate particularly with the physical and mental domains of perceived health status, that depression and anxiety significantly influence the mental domains of perceived health status especially, that bladder, bowel and sexual functioning are related to reduced quality of social functioning, and that fatigue has an important impact on perceived health status in MS patients (26, 30, 37-41).

MS influences a wide range of social and personal dimensions in life. When a person has MS the whole family “is affected” as well. The family of MS patients are often the most immediate and obvious source of social support, and the development of MS has a significant effect on family dynamics as a whole. Patients without family, living alone because they are single, separated, divorced or widowed, may have a sense of isolation and uncertainty about the formation of new relationships. They very often need high levels of physical assistance and emotional support. Moreover, the somatic symptoms involved in MS can cause the loss of current employment and reduce economic status (42-45).

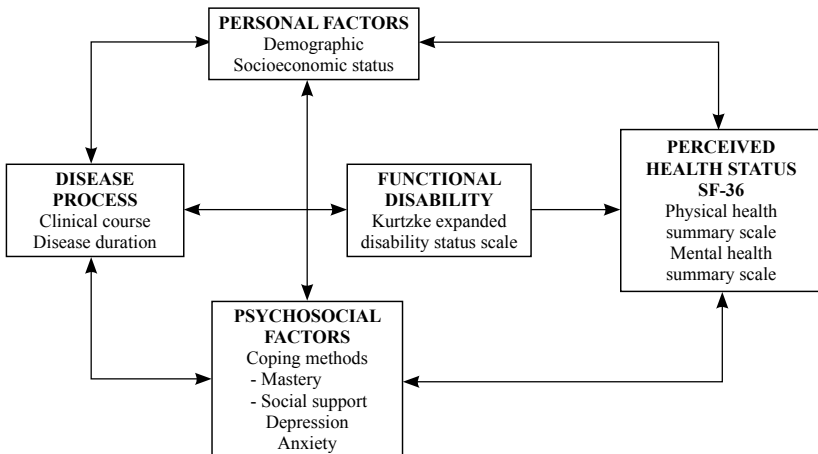
Measures that address impairment and disability have traditionally been referred to as measures of health status (34, 46). It has become common to describe the same dimensions of health status (i.e. impairment,

disability and handicap) as health-related quality of life measures. In this study the construct 'perceived health status' is preferred over the use of 'quality of life', which was more or less 'fashionable' during the last decade. The full SF-36 was originally designed as a generic indicator of health status in the chronically ill (47). *Chapter 2* provides a description of other useful health status measures apart from the SF-36. For example, the Multiple Sclerosis Quality of Life 54 Questionnaire (MSQoL-54) was expanded from the original the SF-36 Health Survey by adding an additional 18 items that were thought by experts to be relevant for patients with MS (34, 48). Items from the SF-36 are also a part of the European Quality of Life Scale (EuroQoL-5D) (49-51). Therefore the SF-36 Health Survey represents the heart of this study with regard to the evaluating the health status of MS patients.

1.3 Aims of the study and research questions

The influence of MS on health status has been studied on an individual level. MS, along with its disease symptoms, influences the activity, participation and well-being of patients. The association between MS and social and personal participation in daily activities or with decreased work ability and economic status of whole families is strong. Interaction directions as evaluated in this thesis and arising from the theoretical background of health status, are depicted in Figure 4.

Figure 4 Design of this thesis



The main objectives of the thesis therefore include:

- 1) To explore the relationships between psychosocial factors and perceived health status in MS patients,
- 2) To study the outcomes in perceived physical and mental health summary scales as measured by the SF-36 in MS patients.

The objectives led to the following general research questions (RQ):

- 1) To review the literature focusing on the associations between disease duration, disability and perceived health status as measured by the SF-36, as well as the psychological well-being related to perceived health status in MS patients (*Chapter 2*).
- 2) To explore the association between self-rated health and employment status in MS patients when controlling for age, gender, functional disability, disease duration and psychological well-being (*Chapter 3*).
- 3) To investigate whether different levels of perceived social support are associated with different levels of perceived health status in MS patients (*Chapter 4*).
- 4) To clarify whether mastery is associated with functional disability and perceived health status in MS patients, and how such an association might function (*Chapter 5*).
- 5) To investigate the discrepancies in the association of depression and anxiety with perceived physical and mental health status, and whether these associations differ in younger (<45 years) and older (≥45 years) MS patients (*Chapter 6*).

1.4 Structure of this thesis

The outline of this thesis provides a first insight into the studies addressing the disease of multiple sclerosis, health status with its structure and the specific components of perceived health status in MS patients.

In *Chapter 2* of this study an overview is given of perceived health status as measured using the SF-36 Health Survey in recent studies.

Chapter 3 will describe the association between self-rated health and employment status in MS patients. The ability to maintain one's job often depends on the progression of disease, and therefore this study sees the subjective assessment of health as a very helpful indicator of the current health status for further work of MS patients. Good self-rated health in association with the ability to work will be studied, and this which association will be controlled for age, gender, functional disability, disease duration, depression and anxiety.

Subsequently, *Chapter 4* will report on social support as a predictor of perceived health status in MS patients. The health status of MS patients may be improved when patients receive social support from their environment. To study this point of view, we will investigate whether

social support from family, friends or significant others associates with different levels of perceived physical and mental health status in MS patients independently from basic demographic variables and functional disability.

Chapter 5 explores the contribution of mastery and functional disability to perceived health status in MS patients. Next, we are interested in knowing whether younger MS patients (<45 years of age) differ in the evaluation of mastery and in their health status when compared to older MS patients (≥45 years of age).

In *Chapter 6* the study takes into account the relationship between depression and anxiety and perceived health status in the total sample, and possible discrepancies in the levels of depression and anxiety in younger (<45 years) and older (≥45 years) MS patients as well.

Finally, in *Chapter 7* the main results of this study are summarized and discussed, and general conclusions, clinical implications and recommendations for future research are made.

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