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**People with
Multiple Sclerosis in
Stockholm**
– aspects of motor and cognitive
function, activities of daily living
and social/lifestyle activities

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Till minne av
Anna, Ester, Einar och Hugo.
Jag är ett av alla era barnbarn som
fick möjligheter ni varken hade eller
fick, men era värderingar la grunden
till att jag fick möjligheterna många,
många år efter er. Tack!

ABSTRACT

No population-based, detailed data has been published regarding persons with multiple sclerosis (PwMS) in terms of cognitive function, manual dexterity, general motor capacity, walking capacity, activities of daily living (ADL) and social/lifestyle activities. In addition, there is a lack of knowledge about associations between cognitive function, manual dexterity, walking ability, socio-demographic factors and coping capacity; and independence in ADL and normal frequency of social/lifestyle activities in a population-based sample of PwMS.

The overall aim of the thesis – part of the Stockholm MS Study - was to describe and analyze the impact and consequences of MS on functioning in PwMS in Stockholm County, taking into account disease-related data, socio-demographic factors and coping capacity (Papers III-V). Another aim was, via a pilot study, to evaluate the feasibility of collecting data: a) using a comprehensive evaluation package administered in the home environment; and b) on health- and social-care resources, patient satisfaction and impact on family caregivers of PwMS. (Papers I, II)

Twenty-six PwMS, from the registry of the MS Center at the Department of Neurology, Karolinska University Hospital, Huddinge, were methodically selected and recruited to the pilot study. Data were collected by home visits including tests and structured interviews. A physiotherapist and a nurse conducted these home visits, (Papers I, II).

In the population-based study, data were collected during home visits to 166 randomly selected PwMS in Stockholm County. Cognitive function was assessed by the Mini-Mental State Examination (MMSE), the Free Recall and Recognition of 12 Random Words Test (FRR12RWT), and the Symbol Digit Modalities Test (SDMT). Manual dexterity was assessed by the Nine-hole Peg Test; global motor capacity by the Lindmark Motor Capacity Assessment (LMCA); and walking capacity by a timed 10-meter walk. Independence in ADL was assessed by the Barthel Index (BI), and the Katz Extended ADL Index (KE-ADL); and frequency of social/lifestyle activities by the Frenchay Activities Index. Coping capacity was assessed by the Sense of Coherence scale; and disease severity was assessed by the Expanded Disability Status Scale (EDSS), (Papers III-V).

The methods used in the pilot study for testing and interviewing the PwMS at home were found to be easy to administer and were well accepted by the PwMS, irrespective of their level of disease severity or form of living. Calculating resource utilization via use of the computerized register at Stockholm County council was found to be easy to administer. Only minor modifications were found to be necessary to adapt the methods for use in a large population-based study, (Papers I, II).

On cognitive tests, 55% (MMSE), 84% (FRR12RWT) and 45% (SDMT) of PwMS scored within the normal range; 27% of PwMS displayed normal manual dexterity, 9% had a maximum motor-capacity score (LMCA) and 8% walked at normal speed. In addition, 52% (n=85) were independent in ADL (BI), 30% (n=50) in instrumental ADL (KE-ADL) and 35% (n=57) reported normal frequency of social/lifestyle activities. Of the variables studied, disease severity of MS and current employment were found to be associated with both motor and cognitive dysfunction. Walking ability and current employment were found to be factors associated with independency in instrumental ADL and normal frequency of social/lifestyle activities. In addition, coping capacity was found to be a factor associated with normal frequency of social/ lifestyle activities, (Papers III-V).

In order to determine the impact of MS on functioning, it is appropriate to use a comprehensive evaluation package in the context of home visits. The prevalence of disability in walking ability, manual dexterity, cognitive function, in ADL, and in social/lifestyle activities is high in PwMS in Stockholm. The most important factor associated with independence in ADL and normal frequency of social/lifestyle activities was the ability to walk. Knowledge about the high prevalence in disability and the associated factors, together with evidence-based treatments, is essential in: a) setting priorities and clinical decision-making, b) planning and organizing physiotherapy and other rehabilitation resources and c) for equity in the distribution of available resources for PwMS in Stockholm

Keywords: cognition, human activities, movement, multiple sclerosis, population, prevalence, walking

LIST OF PUBLICATIONS

- I. **Einarsson U**, Gottberg K, Fredrikson S, Bergendal G, von Koch L, Holmqvist LW. Multiple sclerosis in Stockholm County. A pilot study exploring the feasibility of assessment of impairment, disability and handicap by home visits. Clin Rehabil 2003; 17: 289-298.
- II. Gottberg K, **Einarsson U**, Fredrikson S, von Koch L, Holmqvist LW. Multiple sclerosis in Stockholm County. A pilot study of utilisation of health-care resources, patient satisfaction with care, and impact on family caregivers. Acta Neurol Scand 2002; 106: 241-247.
- III. **Einarsson U**, Gottberg K, von Koch L, Fredrikson S, Ytterberg C, Jin Y-P, Andersson M, Widén Holmqvist L. Cognitive and motor function in people with multiple sclerosis in Stockholm County. Mult Scler, accepted July 2005, in press.
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LIST OF ABBREVIATIONS

ADL	Activities of daily living
CI	Confidence interval
ICF	International classification of Functioning, Disability and Health
MS	Multiple sclerosis

1 INTRODUCTION

This thesis is a part of the Stockholm MS Study, a cross-sectional, population-based, study of people with multiple sclerosis (MS) in Stockholm County. The thesis presents the results from the evaluation of the feasibility of collecting data using a comprehensive evaluation package administered in the home environment. It also presents the results from the population-based study. The results from the population-based study will mainly focus on cognitive function, global motor capacity, manual dexterity, walking ability, activities of daily living (ADL) and social/lifestyle activities.

1.1 Multiple Sclerosis

MS is a chronic neurological disease of the central nervous system, and one of the major causes of neurological disability among young and middle-aged adults. The natural history of the disease is unpredictable, varying from infrequent episodes of symptoms with complete recovery, to severe, permanent symptoms. However, the symptoms and outcome of MS vary among individuals. The most common initial disease course of MS is relapsing-remitting, and after a mean period of 15 years, approximately 50% transfer to the secondary progressive form of the disease.¹ Common symptoms are pareses, spasticity, impaired sensation, vision, bladder and bowel dysfunction, impaired balance and coordination, pain and fatigue, as well as neuropsychological dysfunction.²⁻³ MS may reduce the ability to perform ADL.⁴⁻⁷

MS is a disease with a large range of symptoms and consequences to its sufferers. To understand, describe and analyze the living situation of people with MS, the International Classification of Functioning, Disability and Health (ICF) (2001),⁸ was used as the conceptual framework in this study of people with MS in Stockholm – the Stockholm MS Study, Figure 1.

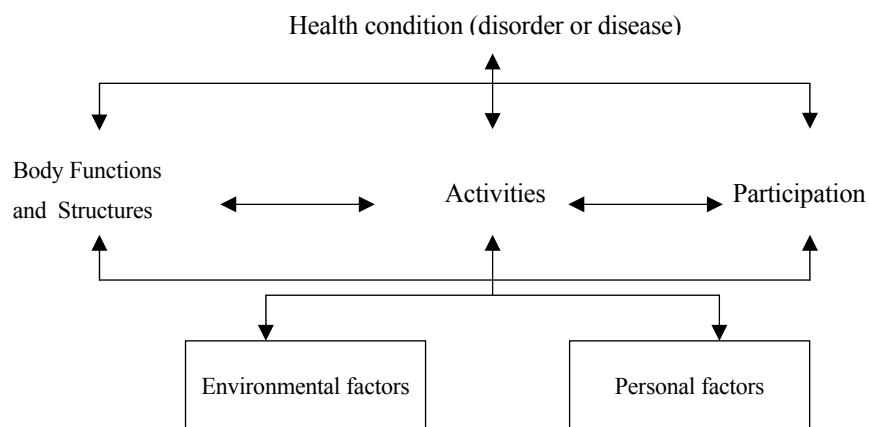


Figure 1. The theoretical model of the interactions between components of ICF.⁸

The overall aim of the ICF is to provide a framework for describing health and health-related states, by providing a scientific basis for understanding and studying health and health-related states and for improving communication between health care workers, researchers, policy-makers and the public, including people with disabilities. The ICF

has been used as a framework for studying health conditions relating to function, activity and participation, and for planning health care interventions for people with MS.^{4-5, 9-10}

The ICF is divided into two parts, each with two components:

Part 1. Functioning and Disability

Body functions and Structures

- Body functions are the physiological functions of body systems including psychological functions (e.g. Mental functions and Neuromusculoskeletal and movement-related functions)
- Body structures are anatomical parts of the body such as organs, limbs and their components (e.g. Structures of the nervous system and Structures related to movement)

Activities and Participation

- Activity is the execution of a task or action by an individual (e.g. Making decisions, Fine hand use, Walking and Dressing)
- Participation is involvement in a life situation (e.g. Interpersonal interactions and relationship and Recreation and leisure)

Part 2. Contextual Factors

Environmental Factors

- Environmental factors make up the physical, social and attitudinal environment in which people live and conduct their lives (e.g. Support and relationship, Products and technology for personal use in daily living, Health services)

Personal Factors

- Personal factors are the particular background of an individual's life and living comprise features of the individual that are not part of a health condition or health states (e.g. gender, age, coping styles, profession)

In this thesis, the ICF was not used to classify the different variables.

The diagnosis of MS is based on both clinical symptoms and laboratory investigation.¹¹⁻¹² A clinically definite MS diagnosis requires a history of at least two attacks and clinical evidence of at least two separate lesions. Laboratory-supported definite MS is diagnosed if there is a history of one attack, clinical evidence of two separate lesions and cerebrospinal fluid oligoclonal bands.¹¹ Kurtzke has defined different regions of the world by prevalence. Northern Europe, northern USA, Canada, southern Australia and New Zealand are classified as high-prevalence areas (>30/100,000).¹³ In Sweden, it is today estimated that approximately 12,000 people suffer from MS,¹⁴ but these figures are less certain. The prevalence varies in Sweden between 96/100,000 in Gothenburg,¹⁵ to 154/100,000 (CI 139 to 170) in Västerbotten.¹⁶ The incidence also varies from 2.6/100,000 (CI 2.2 to 3.0),¹⁵ to 5.2/100,000 (CI 4.4 to 6.2).¹⁶ About two thirds of people with MS are women.¹

Therapy for people with MS can be divided into two categories: disease-modifying therapy and symptomatic or supportive therapies such as physiotherapy, occupational therapy, neuropsychology and counseling, which aim to optimize functioning. In view of the progressive nature of the disease, people with MS need periodic detailed reassessment of the nature and severity of their symptoms. This applies particularly to the symptoms that impact on people with MS in their day-to-day life. A key element of symptomatic treatment is the involvement of persons with MS in managing their symptoms and that they are taught how to minimize the impact of the symptoms.¹⁷

1.2 Motor function in people with MS

As a result of demyelination, axonal damage and the formation of sclerotic plaques in the cerebral hemispheres, cerebellum, brain stem and spinal cord, movement disorders and gait disturbance are common in people with MS, but the degree of motor function may differ.¹ In people with MS, decreased upper extremity and manual dexterity are considerable, but decreased lower extremity function is more common, while weakness in upper extremity function without leg weakness is uncommon.¹ The recommendations of the American National Multiple Sclerosis Society from 1997 stated that clinical outcome measures should include components that assess function of the lower and upper extremities.¹⁸

1.2.1 Manual dexterity

Upper extremity function plays an important role in maintaining functional independency,¹⁹ but studies on manual dexterity in people with MS are rare. The two common impairments in the upper extremity, sensory loss and ataxia,¹ are difficult to measure in isolation, but can be measured with the Nine-hole Peg Test.^{18,20} The Expanded Disability Status Scale,²¹ designed to measure disease severity in people with MS, is used as the gold standard when measuring outcome in people with MS. However, in the Expanded Disability Status Scale, the degree of manual dexterity and which is the affected side is limited and ignored.²⁰ Ceiling effects were evident from the upper extremity scores in a study,²² aimed at developing a physiotherapy assessment tool to monitor motor function in people with MS. As a result, the authors recommended more sensitive tests, for example on speed of movement, to identify subtle upper extremity limitations.

1.2.2 Walking ability

Reduced walking capacity is common in people with MS, even at very early stages of MS, with no other sign of motor involvement.²³ The rating scale, the Expanded Disability Status Scale,²¹ commonly used in clinical MS trials is based largely on walking capacity, e.g. scores between 4.5-6.0 indicate the ability to walk a certain distance, while scores between 6.5-7.5 relate to the use of walking aids. The time taken to walk 8 meters and the maximum distance a person with MS can walk have been shown to deliver more precise information about walking than the Expanded Disability Status Scale and the Ambulation Index.²⁴ People with MS have a shorter stride length, slower free speed walking rates, a higher cadence, and longer double support phase than healthy people.^{23, 25-26} Moderately disabled (3.5-6.5 scores on the Expanded Disability

Status Scale) people with MS consume more energy while walking than healthy people.²⁷ Walking patterns remain consistent over the course of the day for people with MS, but self-rated fatigue levels increase from morning to afternoon.²⁸ However, in view of day-to-day variability of maximum walking distance, the mean walking speed has been recommended as a more reliable parameter.^{18,28}

1.3 Cognitive function in people with MS

The term cognition refers to all the mental functions by which information and knowledge is processed.²⁹ Cognitive functions are those that relate to the mental processes of memory, concentration, reasoning and judgement.³⁰ Cognitive dysfunctions are common in people with MS. Prevalence is estimated to vary from 43-72%.³¹⁻³³ Many MS-related cognitive dysfunctions are focal rather than global, but they vary from person to person and can be hard to detect without formal neuropsychological assessment.³³⁻³⁴ The most commonly affected cognitive domains are speed processing/working memory, learning and memory, executive functions and visual-spatial perception.^{33,35} Results from a study of gender differences in cognitive dysfunction found that males with MS were more vulnerable to cognitive dysfunction.³⁶ This was confirmed in another study, where men were over-represented in the impaired group.³¹

It was recently shown that the degree of cognitive dysfunction in people with MS was associated with longer disease duration, higher scores on the Expanded Disability Status Scale, a secondary progressive form and a lower level of education.³¹ However, another study indicates that it is unrelated to disease course or disease duration and is only weakly related to the Expanded Disability Status Scale.³³ In non-population-based studies, cognitive dysfunction is shown to have an adverse effect on employment, social activities and instrumental ADL.³⁷⁻³⁸ Cognitive dysfunction may also be a barrier to rehabilitation programs, in that people with MS may forget advice or have difficulty in acquiring new skills.³⁹

1.4 Depressed mood in people with MS

The available population-based studies on people with MS have all reported high prevalence of depressed mood or depression, compared to the general population.⁴⁰⁻⁴⁴ Depressed mood in people with MS is associated with poorer self-reported functioning and health-related quality of life ratings.⁴⁵⁻⁴⁷ In addition, depressed people with MS are also more likely to perceive their disability as being greater than the physician's perception.⁴⁸ Moderate evidence has recently been presented showing that exercise therapy can improve mood and reduce anxiety and depression in people with MS.⁴⁹⁻⁵⁰

1.5 ADL and social/lifestyle activities in people with MS

MS may reduce the ability to perform ADL,^{4-7,10} and may thus lead to dependence. ADL may be divided into personal and instrumental ADL. Personal ADL includes basic mobility and self-care activities e.g. grooming, dressing. Household activities, community activities (shopping, transportation) and social/recreational activities are classified as instrumental ADL domains.⁵¹ Population-based studies of functioning,⁸

including aspects of daily activities of people with MS in European countries,^{4,6-7,10} and in the USA,⁵ report similar percentages of people with MS who were independent in ADL such as “bathing” (68-84%), “bladder function” (72-76%), “bowel function” (83-97%), “dressing” (74-88%), “feeding” (91-95%), “grooming” (84-92%) and “transfer” (82-89%) according to the Incapacity Status Scale.⁵² So far, few studies have explored the association between motor function and ADL on the one hand and cognitive function and ADL on the other, in people with MS. However, one study showed a strong correlation between the Expanded Disability Status Scale,²¹ and ADL, and found that the mobility domain accounted for this association.⁵³ One problem in the process of developing evidence-based therapy for people with MS is the lack of population-based data. Also, differences in healthcare systems among countries render transfer and extrapolation of information on these associations difficult.

More complex activities than basic self-care such as ADL - requiring a higher level of decision-making and organization on the part of the person with MS - may be classified as social/lifestyle activities and demand a higher level of independency. When people with MS were asked whether they were as socially active as before disease onset, wider variations (27-70%),^{4-7,10} were found relative to findings for dependence in ADL when reported in percentages according to the Environmental Status Scale.⁵⁴ However, when translating and applying results from population-based studies performed in other countries with the aim of developing health-care, any differences in health-care systems must be taken into account. To my knowledge, no study has ever been performed – in Stockholm or elsewhere in Sweden of people with MS – that focuses on ADL and social/lifestyle activities from a population-based perspective.

1.6 Coping capacity

Personal factors,⁸ are contextual factors that relate to the individual, that are not part of a health condition or health state such as coping style, but that may influence functioning and disability. Aaron Antonovsky introduced the salutogenic theory “Sense of Coherence”,⁵⁵ as a global basis for viewing the world and the individual environment as comprehensible (the ability of people to understand what is happening around them), manageable (to what extent they are able to manage their situation on their own or through significant others in their social network), and meaningful (the ability to find meaning in a situation). The theory asserts that the way people view their life has a positive influence on their health. Antonovsky’s salutogenic concept “Sense of Coherence” reflects a person’s capacity to respond to stressful situations. The theory was developed from the observation that people, despite experiences in the concentration camps of the Second World War, stayed healthy. He assumed the explanation lay in the way they viewed their life and their essence of existence. The stronger the Sense of Coherence, the more likely it is that the person will be able to cope successfully with stressful situations. The fact that need, demand and supply may not always coincide has to be considered when assessing health needs.⁵⁶⁻⁵⁷ For example, the coping capacity of the people with MS may influence the demand for different types of health care, social care and information. The concept “Sense of Coherence” has to my knowledge not been used in studies including people with MS.

1.7 Family caregivers of people with MS

Although disability may develop over several decades - resulting in serious, long-lasting medical and social consequences both to people with MS and their social environment - there are few population-based studies on family caregivers and their burden.

In Sweden, it is possible to be formally employed as a personal assistant. However, we may assume that it is even more common for relatives to act as informal caregivers. A Canadian study,⁵⁸ of caregivers to people with MS indicated that their quality of life was lower than that of the general population. The caregivers studied were mostly family members. The authors also found that the quality of life of the caregivers was strongly associated with the current disease course, when other than stable, of the person with MS, as well as with greater frequency of care.⁵⁹ Relatives were found to suffer increased social strain when multiple sclerosis progressed to a moderate handicap. Thus, the quality of life for family members of people with MS may be greatly affected by the disease.⁶⁰⁻⁶² Yet, there is no knowledge of either the extent of time spent by family members of Swedish people with MS in helping their afflicted relatives with ADL, or the burden of the family caregivers.

1.8 Health-care resources for people with MS in Stockholm

Stockholm County Council's activities affect more than one fifth of Sweden's population. The geographical area covered by the council includes 26 municipalities of various sizes and types, with a total population of 1.9 million (2005). One of Stockholm County Council's mandates is to ensure that all its residents have access to health care. The resources shall be allocated with equity.⁶³

In Stockholm, specialist care of people with MS is provided mainly by the MS centers at the Departments of Neurology at Karolinska University Hospital, Huddinge; Karolinska University Hospital, Solna; and Danderyd Hospital, under the auspices of the Stockholm County Council. Primary care centers and the municipalities also contribute to the care of people with MS, as well as independent rehabilitation units and private caregivers. Health-care professionals involved in the care of people with MS include neurologists, nurses, physiotherapists, counselors, occupational therapists, neuropsychologists, psychologists and speech and language therapists.

In Stockholm, neurologists can refer people with MS to periods of multidisciplinary in- or out-patient rehabilitation at independent rehabilitation units in Stockholm County, units in other parts of Sweden and a unit in Tenerife, Spain. Doctors can also prescribe a period of physical or occupational therapy at specialized university-hospital based out-patient departments at primary centers or in the municipality.

The economic burden of MS care on the community is substantial.⁶⁴⁻⁶⁷ A recent study surveyed people with MS in Stockholm by mail using a self-report questionnaire on the use of health-care resources. The survey indicated the economic cost of MS in Sweden to be about SEK 4.5 billion per year.⁶⁶

1.9 Physiotherapy for people with MS

Rehabilitation is still the only way to improve function in multiple sclerosis. The recent development of disease-modifying drugs has not eliminated the need for rehabilitative strategies in the management of multiple sclerosis.⁶⁸

In-patient rehabilitation of people with progressive MS has resulted in improvements in activity and participation, well-being and health-related quality of life, as shown by studies in United Kingdom and Italy.⁶⁹⁻⁷⁰ The improvements in activity and participation were maintained for 6 months, in emotional well-being for 7 months and in health-related quality of life for 10 months.⁷¹ A study confirmed the effectiveness of a short but comprehensive (6 days a week for 6 weeks) out-patient model of rehabilitative treatment in people with MS, especially in their quality of life.⁷² The in-patient rehabilitation program in United Kingdom consisted of two 45-minute physical therapy sessions and one occupational session per day over 3 weeks.⁶⁹

One of the important health-care services for people with MS is evidence-based physiotherapy.⁵⁰ Rehabilitation including physiotherapy for people with MS is a multidisciplinary goal-oriented process. Its starting-point is when the person is diagnosed and it lasts as long as it is needed.⁷²⁻⁷³

The job of the physiotherapists is to provide the opportunity for people with MS to achieve the best level of activity relevant to his or her lifestyle at every stage of the disease.⁷⁴ People with MS have always asserted that physiotherapy plays a vital part in their ability to maintain health and independency.⁷⁵ Advice on exercise was the single most requested area in a cross-sectional survey of health-care services performed in UK.⁷⁶ Despite methodological limitations, a survey among neurologically disabled people conducted in 1997 at Huddinge Hospital, Stockholm,⁷⁷ showed similar results, in that people with MS identified the health-care system to be inadequate as regards: 1) information on different aspects of the disease and the support systems available; 2) technical aids and advice on exercise; and 3) continuation of physiotherapy and recurrent rehabilitation periods.

A recent series of randomized controlled studies,^{49, 78-79} attempting to generate high-level evidence on the effectiveness of physiotherapy showed physiotherapy and exercise to be effective. One of the studies concluded that exercise is safe for people with multiple sclerosis and should be recommended for those with mild to moderate disability.⁸⁰ A comparison of exercise therapy versus no exercise therapy for people with MS provided strong evidence indicating the benefit of exercise therapy on the outcome of muscle power functions, exercise tolerance functions and mobility-related activities.⁵⁰ Moderate evidence was found that exercise therapy improved hand and arm function, and mood.⁵⁰

1.10 Technical aids and social care

According to Swedish legislation passed in 1994 (*Lagen om ändring i lagen (1993:387) om stöd och service till vissa funktionshindrade*, SFS 1996:534), persons with severe disability have the right to live at home and to receive help from one or more personal assistants. On that basis, people with MS may in addition to receiving care from various health-care professionals, also require assistance from formal caregivers in ADL and social/lifestyle activities. In Stockholm, the County Council supplies prescribed technical aids, safety alarm systems and a health-related transport service. In addition, the municipality carries out various home and car modifications, such as the widening of doors, the removal of thresholds, and the tailoring of bathrooms and kitchens to the needs of their disabled users. This is to compensate for mobility-related dysfunction and aims at enhancing daily and social/lifestyle activities. Knowledge about the effectiveness of this service is lacking.⁸¹

1.11 Health related quality of life in people with MS

The concept of health-related quality of life is based on health dimensions, which can be determined and measured. Examples of such dimensions are physical health, physical functioning, social functioning and psychological and emotional wellbeing.⁸²

The health-related quality of life concept has frequently been used in studies evaluating the impact of MS on health status in relation to different life dimensions.⁸³⁻⁸⁴

Population-based studies assessing the health-related quality of life in people with MS show that it is negatively affected, compared to the general population in countries in Europe, USA and Canada.^{7, 58, 85-90} These results were confirmed in a recently accepted paper presenting results of the Stockholm MS Study. This paper consisted of the same study population as in this thesis, and the results showed that the health-related quality of life was widely affected, especially in home management, walking and recreation.⁹¹ Compared to the general population, the health-related quality of life was worse in people with MS in Stockholm, including those with milder disease severity and a shorter disease duration. This result was confirmed by a non-population-based study performed at Örebro University Hospital.⁹²

1.12 Patient satisfaction with care

Patient satisfaction with care has been used to measure different outcome aspects of care and cost,⁹³ and is viewed as both a determinant of the quality of care and a predictor of subsequent health-related behaviour.⁹⁴⁻⁹⁵ People, especially with chronic diseases, are not satisfied with treatment by highly skilled professionals and specialized techniques alone. They also demand that their need for psychological wellbeing should be met.⁹⁶ The need for rehabilitation services and resources is perceived differently by disabled people and professionals. It is important to determine the views of both users and provider when planning and commissioning services.⁹⁷

1.13 Self-reported falls

Fall can be defined as a subject's unintentional coming to rest on the ground or at some other lower level.⁹⁸ The risk of falling is increased in people with MS, possibly for multifactorial reasons such as poorer balance, co-ordination, strength, vision, sensation and cognitive function, as well as increased spasticity, environmental factors and use of technical aids.⁹⁹ Several studies have investigated fall-risks among the elderly,¹⁰⁰⁻¹⁰¹ but there are few studies on fall-risks for people with MS.⁹⁹

1.14 Data collection on people with MS

Referral bias is a significant problem affecting the generalizability of studies conducted in a university setting compared to population-based groups. For example, the patients are younger and have a higher mobility impairment for their age. In addition, disabled females are overrepresented, with a higher frequency of reportedly recent worsening of their condition, a higher frequency of early supported diagnosis by laboratory tests, and more frequent reliance on neurologists and therapists for routine care of their disease.¹⁰² Population-based studies to assess the degree of functioning in MS have been performed in Europe and in the USA.^{4-7, 10, 44, 103-104} Results from studies performed in one county or region are not easily extrapolated to another country or region, on account of differences in health-care systems and policies. In most of the studies referred to above (see Table 1), data were collected in out-patient clinics, rather than by interviews, and tests were conducted during home visits. The latter procedure makes validation of collected data possible.

There are three major types of data collection tools used by physiotherapists in research studies: biophysiological instruments, interviews and questionnaires. To collect data in research studies established to describe and analyze functioning, health-related quality of life, resource utilization and patient satisfaction in the care of people with MS, mailed surveys and interviews are commonly used. A comparison of the two methods indicates that interviews can achieve greater depth of response, maintain control over who actually responds and determine the opinions of those who cannot write/read. Interviews also have higher response rates. The disadvantages of interviews, compared to mailed surveys, are difficulty with coordinating researcher and subject schedules, lack of anonymity in responses and high personnel, travel and telephone costs. The advantages of mailed surveys include that they permit a larger numbers of subjects. However, low response rates are common.¹⁰⁵

Symptoms such as pareses in the upper extremities, impaired sensation in the upper and lower extremities, impaired visual function, cognitive dysfunction and fatigue are common symptoms that can influence/complicate data collection in research studies of people with MS.² Pareses and impaired sensation in the upper extremities and visual impairments are common reasons why people with MS cannot write and/or read, and proxy measures from the spouse/research assistant are necessary to avoid drop-outs. Fatigue is a common complaint reported by people with MS and this can impact on the data collection.

In addition, it may be more valuable to assess people with MS in their own home environment, rather than in the hospital environment. This is because in the home it is possible to immediately validate the information obtained there, by watching the person with MS move about and function in her/his home environment in a way that would not be possible in an interview conducted in a hospital setting, or via a postal survey.

A pilot study could evaluate the feasibility of collecting data using a comprehensive evaluation package administered in the home environment in the assessments of people with MS.

1.15 The need of a population-based study of functioning of people with MS in Stockholm

A chronic and progressive disease like MS is without doubt associated with an increased need for health services. The need for services is not homogeneous in the MS population, but is likely to vary by factors such as functioning and environmental, personal and disease-related factors. Until now, no population-based study of people with MS has been performed in Stockholm or elsewhere in Sweden, focusing on the impact and consequences of the disease on functioning. This thesis, a population-based study of people with MS, drawing on data from the Stockholm MS study is potentially of considerable value, providing, as it does, an in-depth and detailed knowledge of functioning in people with MS in Stockholm. In combination with evidence-based treatments, this knowledge is vital to an understanding of the living situation of people with MS in Stockholm. This knowledge of functioning may be of assistance in making clinical decisions; setting priorities; planning and organizing physiotherapy, other rehabilitation resources and health-care services targeted at different MS sub-groups, and in achieving equity in the distribution of resources in Stockholm County for people with MS in Stockholm.

4

Table 1. Cross-sectional population-based studies performed in Nordic and European countries and in the USA.

Variable	Västerbotten Sweden ^{16, 103-104}	Møre/Romsdal Norway ⁴	Antrim/Londonderry Northern Ireland ¹⁰	Hampshire UK ⁴⁴	Bajo Aragon Spain ⁷	Calatayud Spain ⁶	Olmstead USA ⁵
Demographic and disease related characteristics							
Patients (n)	399	124	288	305	36	34	162
Aged (y)	49	41	49	48	38	43	48
Women (%)	69	53	69	68	67	68	75
Diagnosis	Definite MS Probable MS	Definite MS Probable MS Possible MS	Definite MS Probable MS Suspected MS	Definite MS Probable MS	Definite MS Probable MS	Definite MS	Definite MS
Disease duration (y)	18 ^a 15 ^b	8 ^a	19 ^c	16 ^a	9 ^a	11 ^a	15 ^b
Age at onset (y)	30	33		33	30	33	29
Type of MS (%)							
RR/SP/PP	^c / ^c /12	^c / ^c /9	48/40/13	^c	83/14/3	41/ 53/ 6	58/28/14
Methods							
Datacollection	Medical record, follow-up interview with patient, relatives and caregivers.	Structured interview. At out-patient clinic and in a few cases at nursing homes.	Structured interview with patient, family and carers.	Interview with patient and relatives. By home-visits.	Test administered by nurse and doctor.	Patients received the scales by neurologist.	Self-reporting face to face interview. Private setting, in a few cases at nursing homes
	Neurological examination.	Neurological examination.	Neurological examination.	Neurological examination.		Neurological examination.	Neurological examination.
Measurements	EDSS ²¹	MRD ¹⁰⁶	MRD ¹⁰⁶	EDSS ²¹ HADS ¹⁰⁷ Neuropsychological tests	MRD ¹⁰⁶ FAMS ¹⁰⁸	EDSS ²¹ ESS ⁵⁴	MRD ¹⁰⁶

^amean, ^bmedian, ^cInformation not available;MRD= Minimal Record of Disability, the MRDconsists of the EDSS, the ISS, and the ESS; EDSS= Expanded Disability Status Scale; ISS= Incapacity Status Scale; ESS= Environmental Status Scale;HADS= Hospital Anxiety and Depression Scale; FAMS= Functional Assessment of Multiple Sclerosis scale; RR=Relapsing-Remitting; SP=Secondary-Progressiv; and PP=Primary-Progressive.

2 AIM

The overall aim of the thesis - part of the Stockholm MS Study - was to describe and analyse the impact and consequences of MS on functioning in people with MS in Stockholm County. Another aim was to evaluate the feasibility of collecting data using a comprehensive evaluation package administered in the home environment, and of methods of data collection of health-care and social-care resources, patient satisfaction and impact on family caregivers of people with MS.

2.1 Pilot study

2.1.1 Paper I

The aim of this study was to evaluate the feasibility of collecting data using a comprehensive evaluation package administered in the home environment in the assessments of impairment, disability and handicap aiming at exploring the consequences of multiple sclerosis.

2.1.2 Paper II

The aim of this study was to evaluate the feasibility of methods of data collection of health-care and social-care resources, patient satisfaction and impact on family caregivers of people with MS.

2.2 Population-based study

2.2.1 Paper III

The aim of this study was to describe and analyze cognitive function, manual dexterity, global motor and walking capacities in a population-based sample of people with MS from Stockholm County, while taking into account disease-related data and socio-demographic factors and coping capacity.

2.2.2 Paper IV

The aim of this study was to describe independency in personal and instrumental ADL, and frequency of social/lifestyle activities in a population-based sample of people with MS in Stockholm County.

2.2.3 Paper V

The aim of this study was to describe and analyze independency in personal and instrumental ADL, and frequency of social /lifestyle activities in a population-based sample of people with MS in Stockholm County, taking into account motor and cognitive function; socio-demographic factors; and coping capacity.

3 MATERIALS AND METHODS

3.1 Case finding and sample – Pilot study

Between January 1997 and January 1998, 26 people with MS,¹¹ were recruited to the study. The people with MS were methodically selected from the registry of the MS Center at the Department of Neurology, Karolinska University Hospital, Huddinge, on the basis of variation in gender, level of disease severity determined by the Expanded Disability Status Scale,²¹ and type of living—with a view to assembling a suitable study group.

3.2 Case finding, sample and randomization

– Population-based study

People with MS included in the population-based study were recruited from several sources, in order to attain the highest possible population-based ascertainment. In Stockholm County, most people with MS are diagnosed at the Departments of Neurology, Karolinska University Hospital, Huddinge; Karolinska University Hospital, Solna; and Danderyd Hospital. From the clinical records of these departments, 2,129 patients were identified in 1998 and registered in a temporary coordinated data pool. To determine whether any person with MS living in the area had not been registered in the temporary data pool, two other sources—the records of private neurologists and those of area nursing homes—were investigated. The names of all people with MS under the care of 10 private neurologists in Stockholm County, and of all people with MS residing in nursing homes in Huddinge Municipality in Stockholm County, were found to be present in the temporary data pool. Thus, the requirements of population-based case ascertainment were considered fulfilled.

For the purpose of recruiting approximately 10% of people with MS fulfilling the inclusion criteria, a random sample representing 15% of the total pool (n=321) was drawn from the temporary data pool (n=2,129), after stratification by hospital, gender, and age.¹⁰⁹⁻¹¹⁰ Patients not fulfilling the inclusion criteria: alive and living in, and registered as a resident of, Stockholm County; diagnosed by a neurologist with definite MS,¹¹ and informed of MS diagnosis; and lacking diagnoses indicative of severe somatic or psychiatric illness; as well as three additional people with MS included in the pilot study were excluded (Figure 2).

The remaining 196 people with MS were asked by their appointed neurologist if they were willing to receive information about the study from a physiotherapist or a nurse; 166 of these people with MS gave informed consent and agreed to participate, (Figure 2). Post-stratification distributions (with regard to hospital, gender, and age) were consistent with a priori expectations.

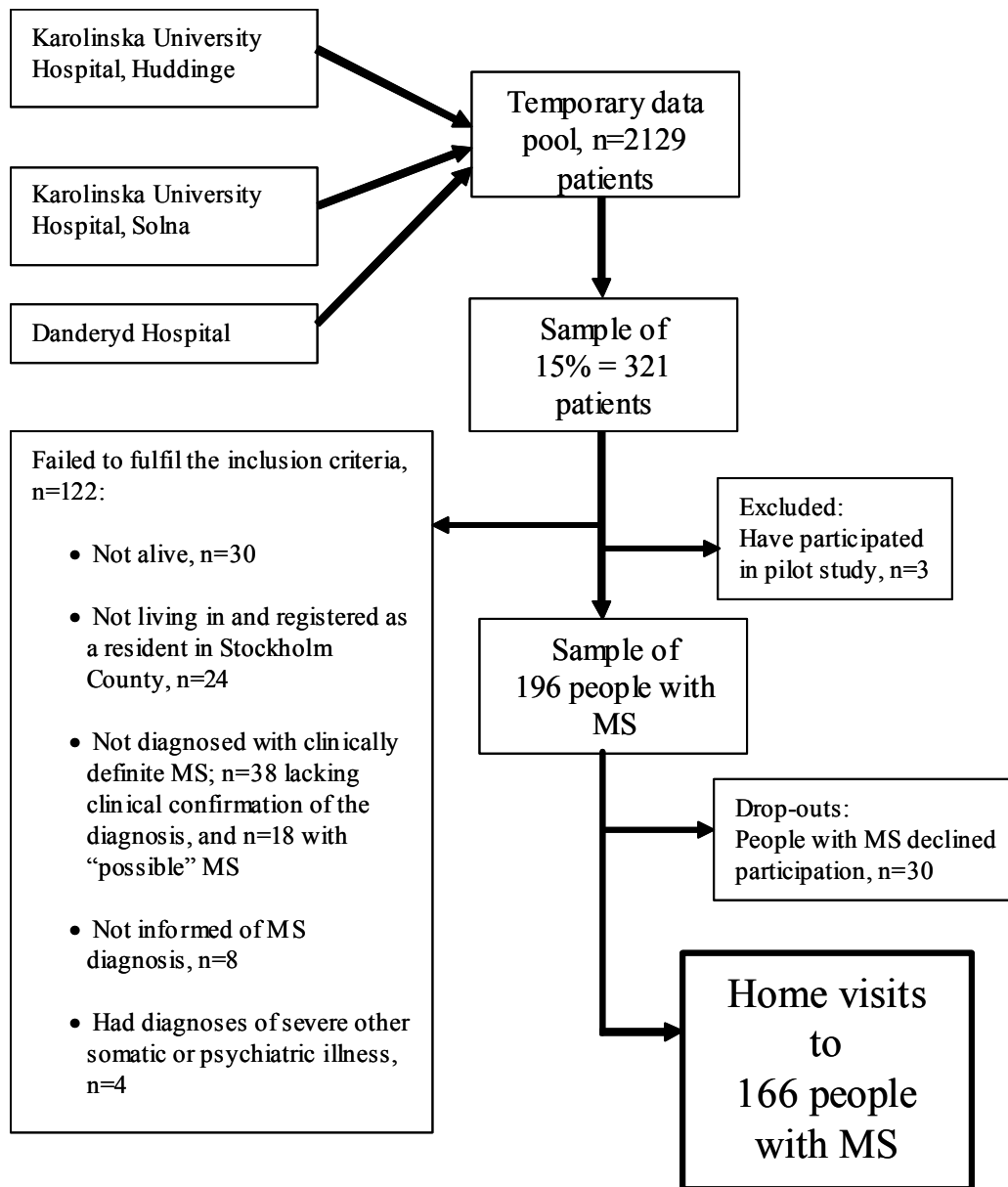


Figure 2. Flow chart of the sample, representing: 15% of the temporary data pool, with patients not fulfilling the inclusion criteria and those with MS who declined participation.

3.3 Data collection procedure

3.3.1 Pilot study

A neurologist confirmed that the patients had clinically definite MS and adjudged their disease severity to be mild, moderate or severe, according to the Expanded Disability Status Scale.²¹

The people with MS were contacted by telephone by a physiotherapist or a nurse, who informed them about the study and made an appointment with them for a weekday morning, afternoon or evening, at a time that best suited the people with MS, spouse and/or personal assistant. The people with MS also received written information about

the purpose of the study. All selected people with MS agreed to participate. Data were collected via home visits using tests and structured interviews. A physiotherapist accompanied by a nurse conducted these home visits.

3.3.2 Population-based study

In the population-based study, data were collected via home visits to 166 people with MS and were performed by a physiotherapist or a nurse, at a time that suited the people with MS, the spouse, or the personal assistant. However, whether the people with MS were experiencing a relapse at the time was not specifically taken into consideration. Data were obtained using tests and structured interviews.

Home visits were performed during two different periods: from September 1999 to August 2000 (n=102); and from November 2001 to July 2002 (n=64). People with MS were visited during the second period for primarily two reasons: 1) difficulties with getting in contact with them; or 2) difficulties with arranging a home visit. In the former case, problems most often stemmed from the fact that the people with MS were no longer in regular contact with the Neurological Departments; in the latter case, the difficulties usually related to the employment status or family situation of people with MS, or to the coordination of visits with the schedules of spouses and professional personal assistants.

3.4 Tests and structured interviews

In the pilot study, the time needed to perform the different tests and structured interviews was noted in a time schedule. Comments from the people with MS and from the physiotherapist and nurse performing the data collection regarding necessary modifications of the included tests and structured interviews were noted in a diary. In addition, the temperature was noted, since temperature can influence the ability of the people with MS to function. An overview of the different tests and structured interviews used in the pilot and population-based studies is presented in Table 2.

3.4.1 Motor function

3.4.1.1 Global motor capacity

A shortened version of the Lindmark Motor Capacity Assessment,¹¹¹ comprising the sub-scales for active movements (31 items) and co-ordination (rapid movement changes) (four items) in the upper and lower extremities and for balance (seven items) and mobility (eight items) was used to assess global motor capacity. In the Lindmark Motor Capacity Assessment, the items are mostly scored on a four-point scale from no function/cannot perform the activity (0) to normal function/can perform the activity without help (3). The total score is a summation of the sub-scales, with a total range of 0 to 258 and the higher the score, the better the motor capacity. The Lindmark Motor Capacity Assessment is considered reliable and valid.¹¹²⁻¹¹³ In the population-based study, the Cronbach's Alpha coefficient for the total score was 0.94. Originally the Lindmark Motor Capacity Assessment was developed to evaluate functional capacity after stroke,¹¹¹ but it has been used in the assessment of individuals with other neurological disorders, i.e. Guillian-Barré syndrome.¹¹⁴

Table 2. Overview of tests and structured interviews used for the people with MS in the different studies.

Variables	Pilot study		Population based study		
	Paper I	Paper II	Paper III	Paper IV	Paper V
Motor function					
Global motor capacity					
Lindmark Motor Capacity Assessment	x		x		
Manual dexterity					
Nine-hole Peg Test	x		x		x
Walking					
10-meter walk	x		x		x
Cognitive function					
Mini-mental State Examination	x		x		
Free Recall and Recognition of 12 Random Words Test	x		x		
Symbol Digit Modalities Test	x		x		x
Depressed mood					
Beck Depression Index	x				
Activities of daily living (ADL)					
Barthel Index	x			x	x
Katz Extended ADL Index	x			x	x
Social/lifestyle activities					
Frenchay Activity Index	x			x	x
Demographic characteristics	x	x	x	x	x
Coping capacity					
Sense of Coherence Scale		x	x		x
Resource utilization		x			
Technical aids and social care		x			
Disease-related factors					
Disease-related characteristics	x	x	x	x	x
Expanded Disability Status Scale	x	x	x	x	x
Health-related quality of life					
Sickness Impact Profile	x	x			
Patient satisfaction with care questionnaire	x				
Self-reported falls	x				

3.4.1.2 Manual dexterity

Manual dexterity was tested using the Nine-hole Peg Test,¹¹⁵ which is widely used and has been recommended for the assessment of people with MS.¹⁸ Seated at a table, the person with MS is timed with a stopwatch, while, with one hand, picking up nine pegs from a box and placing them in a board with nine holes. The person with MS is considered capable of performing the test if all nine pegs can be picked up and placed in the board within 60 seconds. The Nine-hole Peg Test is considered reliable and valid.¹¹⁶ Inability to perform the Nine-hole Peg Test was in the population-based study categorized as zero pegs per second. A result of 0.5 pegs per second or better by people with MS in the population-based study was categorized as within the normal range.¹¹⁶

3.4.1.3 Walking

Timing of a rapid walk over a distance of 10 meters, recommended in the assessment of people with MS,¹⁸ and considered a reliable and valid test, was used to evaluate walking ability and capacity.¹¹⁷⁻¹¹⁸ Persons with MS were asked to walk 10 meters as rapidly as possible without compromising safety, and the time taken was recorded with a stopwatch. Walking aids were allowed, but not assistance. The use of walking aids was noted. In addition, the number of steps used was counted, since this may indicate that the quality of walking was not normal, even if the 10 meters may have been walked at normal speed. In the pilot study, the 10 meter walk proved possible at all home visits. However, it may be that an unimpeded distance of 10 meters is not available in all forms of living, and in the population-based study the 10-meter walk was therefore performed with a turn on a 5-meter course.¹¹⁹

In the population-based study, an inability to walk 10 meters was categorized as zero meters per second. For people with MS, times exceeding reference times based on mean fast gait speed and mean step length of age- and gender-matched healthy controls,¹²⁰ less one standard deviation, were categorized as within the normal range.

3.4.2 Cognitive function

Cognitive function, general cognitive performance, verbal memory, and speed processing/working memory further mentioned as attention, was assessed using the Mini-Mental State Examination,¹²¹ the Free Recall and Recognition of 12 Random Words Test,¹²² and the Symbol Digit Modalities Test.¹²³

The Mini-Mental State Examination is a widely used test for screening of general cognitive performance. The Mini-Mental State Examination includes 11 items, divided into two sections; the first section requires verbal responses to orientation, memory and attention questions. The second part requires reading and writing and includes the ability to name, follow verbal and written commands, write a sentence and copy a polygon.¹²¹ Thirty is the maximum score and the most commonly used cut-off point to indicate cognitive dysfunction meriting further investigation is 23/24.¹²⁴ In the population-based study, scores of 28 or higher were categorized as within the normal range.¹²⁵ People with MS unable to perform the Mini-Mental State Examination, mainly because of severe cognitive dysfunction, were not included in the analysis in the population-based study. Reliability and validity are considered good.¹²⁴

The Free Recall and Recognition of 12 Random Words Test is designed to test verbal memory in elderly Swedish subjects. A similar test has been used previously on people with MS.¹²⁵ In the test, the person with MS is continuously presented with words at a rate of one word every 5 seconds from two word lists—a free recall list and a word recognition list, containing 12 and 24 words, respectively. The words from the free recall list are read out loud and displayed simultaneously on printed cards. People with MS were instructed to try to remember the words for later recall. After the words have been presented, the people with MS were asked to recall as many words as possible. In the recognition word list, 12 target words from the free recall list are presented

intermixed with an equal number of distracters. People with MS were asked to respond by yes-no recognition. The score is based on the number of right and wrong answers. In the population-based study of people with MS, scores on the Free Recall and Recognition of 12 Random Words Test higher than the mean score of a reference group less one standard deviation,¹²⁶ were categorized as within the normal range. People with MS unable to perform the Free Recall and Recognition of 12 Random Words Test, mainly because of severe cognitive dysfunction, were not included in the analyses. In the population-based study, only the results of the free recall part were analyzed.

The Symbol Digit Modalities Test requires the person with MS to use his or her capacity to direct attention in a quick and accurate manner. The Symbol Digit Modalities Test has frequently been used and recommended in MS as an instrument that is sensitive to cognitive dysfunction.¹²³ A key featuring arbitrary pairings of numerical digits and geometric symbols is presented to the person with MS. That person is then asked to verbally substitute numbers for the various geometric symbols according to the key. The score is based on the number of correct responses within a 90 second period.¹²³ In the pilot study, the people with MS were asked to respond orally. However, in the population-based study, the people with MS were asked to respond in writing except for those people with MS with motor dysfunction in the upper extremities who were allowed to reply orally.¹²⁵ In the people with MS, scores in the Symbol Digit Modalities Test (completed by oral or written reply) higher than the mean score for a group of age-matched healthy controls, less one and a half standard deviations,¹²⁵ were categorized as within the normal range. People with MS unable to perform the Symbol Digit Modalities Test, mainly because of severe cognitive dysfunction, were not included in the analyses. Reliability and validity are considered good.¹²⁷

3.4.3 Depressed mood

Depression was assessed via the Beck Depression Index, a widely used self-reporting questionnaire assessing mood.¹²⁸ The Beck Depression Index has previously been used on people with MS in the home environment.¹²⁹ The Beck Depression Index evaluates 21 symptoms of depression and so the index comprises 21 categories from which the total score is derived. Each category contains four statements corresponding to the absence of depression, mild depression, moderate depression and severe depression. The cut-off score for the presence of depression is >9 points, on a scale ranging from 0 to 63.^{128, 130} Reliability and validity are considered good.¹²⁴

3.4.4 ADL

Information about dependence on another person in the performance of personal and instrumental ADL was collected by interviews with the people with MS and/or caregiver and/or personal assistant. Independency in ADL was measured using the Barthel Index,¹³¹ while independency in personal and instrumental ADL was measured using the Katz Extended ADL Index.¹³²

The Barthel Index, a widely used measure, comprises 10 items. The total score range is 0-100. Scores for each item are weighted, contributing 5, 10 or 15 points to the total score. The maximum total scores in the Barthel Index were categorized as independent in ADL, implying that the person with MS did not require any assistance or supervision by another person when performing the activities, but assistive devices were allowed. The Barthel Index includes ten items: “feeding”, “bathing”, “grooming”, “dressing”, “bowels”, “bladder”, “toilet use”, “transfers”, “mobility”, and “stairs”. The Barthel Index is considered reliable and valid.¹³³⁻¹³⁴ In the population-based study, the Cronbach’s Alpha coefficient for the total score was 0.95.

Independency in personal and instrumental ADL was measured using the Katz Extended ADL Index, also a widely used instrument. In the Katz Extended ADL Index, the total range of scores is 0 -10. The maximum score of individuals using the Katz Extended ADL Index items varies from 0 (dependent) to 1 (independent). The Katz Extended ADL Index includes six personal ADL items: “feeding”; “bathing”; “dressing”; “continence”; “toileting”, and “transfer” and four instrumental ADL items: “shopping”; “cooking”; “cleaning indoors”, and “outdoors transportation” Little evidence has been published on its reliability and validity.¹²⁴ In the population-based study, the Cronbach’s Alpha coefficient for the score in personal ADL, instrumental ADL and total score was 0.94, 0.87 and 0.92, respectively.

The maximum total scores in the Barthel Index and the Katz Extended ADL Index were categorized as independent in ADL, implying that the people with MS did not require any assistance or supervision by another person when performing the activities, but assistive devices were allowed.

3.4.5 Social/lifestyle activities

The frequency of social/lifestyle activities during the past 3-6 months was measured using the Frenchay Activities Index.¹³⁵ The index consists of 15 items pertaining to general activities that require some initiative on the part of the person being assessed, including domestic tasks, leisure and work-related activities, and other outdoor activities. For most items, scoring is based upon the frequency with which a particular activity has been performed. For two items (“gardening”, “household maintenance”), however, the score is based on tasks subsumed within the activity performed by the person with MS. The total score ranges from 0 to 45, with a high score indicating a high frequency of social/lifestyle activities. The maximum scores of the individual 15 items vary from 0-3.

The Frenchay Activities Index was originally developed and validated for stroke patients, but it has also been used in studies of people with MS.¹³⁶ In people with MS, scores on the Frenchay Activities Index higher than the 25th percentile score for a group of age-matched and gender-matched reference population were categorized as within the normal range.¹³⁷ In the population-based study, the Cronbach’s Alpha coefficient for the total score was 0.89. Reliability and validity are considered good.¹³⁷

3.4.6 Demographic characteristics

Demographic characteristics; age, gender, nationality, family situation, type of housing, education and employment status were collected at the home visit.

In the analysis in the population-based study, residence in care homes and apartments adapted for the disabled, as well as forms of care whereby people with MS spent alternate weeks at a nursing home and their private residence (cohabiting with a partner), were all classed as sheltered living. People with MS who were fully engaged in the home with family responsibilities, but were not otherwise employed, were included in the sub-group “not working”, while people with MS who had retired because of age were excluded from analyses of the sub-groups “working” and “not working”.

3.4.7 Coping capacity

Coping capacity was measured via the short version of the Sense of Coherence Scale,^{55, 138} which has been used in the assessment of individuals with a variety of diseases.^{55, 139-140} The 13 items making up the Sense of Coherence Scale are constructed as statements, which are rated by the person with MS on a Likert-type scale from 1 to 7. In the population-based study, a moderate/strong Sense of Coherence will be referred to as normal coping capacity and weak Sense of Coherence as below normal coping capacity. For the purpose of sub-group analysis, people with MS were categorized - on the basis of their Sense of Coherence Scale scores and relative to a reference group of subjects living in Stockholm,¹⁴¹ - into one of the two sub-groups “below normal”, or “normal or above normal”. In the population-based study, the Cronbach’s Alpha coefficient for the total score was 0.83. Reliability and validity are considered good.⁵⁵

3.4.8 Family caregivers

The spouse or the partner of the people with MS and two adult daughters (>18 years), were interviewed as family caregivers. Data were compiled on utilization, over the past 6 months, of informal assistance from family caregivers. Help from family caregivers was defined as assistance with ADL (Katz Extended ADL Index).

3.4.9 Resource utilization

To calculate use of health-care resources by people with MS within the Stockholm County in the pilot study and to detect changes in resource use over time, summaries were made of the results with regard to the feasibility of: 1) using the computerized register at the Stockholm County Council, and 2) interviewing people with MS about data not available through the computerized register at the Stockholm County Council, over the past 6 months. A questionnaire on utilization over the past 6 months of day care, independent rehabilitation units, private caregivers, home-help service, salaried personal assistants and informal assistance from family caregivers was used.

The nurse or the physiotherapist asked all the people with MS, or their proxy-caregiver, for permission to calculate utilization of health-care resources before using the computerized register at the Stockholm County Council.

3.4.10 Technical aids and social care

Information on the use of different kinds of technical aids, in personal care, mobility and household management, was collected via a separate questionnaire¹⁴⁰, which was completed during the home visit, on the basis of the information provided by the people with MS and observations by the nurse and physiotherapist. The questionnaire also included information on home modifications, safety alarm systems, health-related transportation service, handicap modification of car and contact with patient organizations.

3.4.11 Disease-related variables

Information on disease duration; disease course; ongoing treatment of immunomodulating drugs and symptomatic drugs were collected from the medical records and verified at the home visit.

The Expanded Disability Status Scale,²¹ is designed to measure disability in people with MS, in this thesis defined as disease severity. The scale includes measurements of MS-related impairment of pyramidal, cerebellar, brain stem, sensory, bowel and bladder, visual and mental functions. Scores for the various functional systems and other measures of function such as walking distance, need of aid when ambulating and ultimate dependence on carers are then used to determine an overall score for disease severity which is measured in half point increments from 0-10. Problems with reliability and rater-to-rater variability is documented.¹⁴²

The people with MS were methodically selected in the pilot study from three neurologist-classified sub-groups; mildly disabled (0 to 3.0), moderately disabled (3.5 to 6.0) and severely disabled (≥ 6.5).

In the population-based study, the scores from Expanded Disability Status Scale - performed at a similar time as the home visit and verified by a senior neurologist (SF) - were used to classify people with MS into the following four disease-severity sub-groups: mildly disabled (0 to 3.0), moderately disabled (3.5 to 5.5), severely disabled (6.0 to 6.5), and very severely disabled (≥ 7.0).⁶⁶

3.4.12 Health-related quality of life

In order to evaluate the subjective health-related quality of life of people with MS and their caregiver, a Swedish version of the Sickness Impact Profile was administered by interview.¹⁴³⁻¹⁴⁴ The Sickness Impact Profile is a generic self-report questionnaire on health-related quality of life, which examines the individual's perception of the impact of the disease process on behavior in everyday life.¹⁴³ The Sickness Impact Profile has been used previously to assess quality of life in a variety of chronic diseases, including

MS.¹⁴⁵ It was designed to be broadly applicable across types and severities of illness and across demographic and cultural sub-groups. The measure comprises 136 items grouped into 12 sub-scales; “sleep and rest”, “emotional behavior”, “body care and movement”, “home management”, “mobility”, “social interaction”, “ambulation”, “alertness behavior”, “communication”, “work”, “recreation and pastimes”, and “eating”. The respondents have to mark those statements in all the 136 items that describe them on a given day and are related to their health. Scores were calculated using item weighting to indicate the relative severity of limitation implied by each statement. From the sub-scales, it is possible to calculate two-dimensional scores (physical and psychosocial). Likewise, a total score over the entire profile, and for each category, may be calculated. The score range is 0 to 100, where 0 indicates the best possible health-related quality of life and 100 a low health-related quality of life.^{82, 124, 146} Reliability and validity are considered good.^{124, 143}

3.4.13 Patient satisfaction with care

A patient-satisfaction questionnaire used in earlier studies of individuals with rheumatoid arthritis and stroke,^{96, 140} was used in a modified and shortened version comprising 18 items. These were constructed as statements, which the respondents were asked to agree or disagree with on a 5-grade Likert scale. The questionnaire was based on Ware's taxonomy for patient satisfaction,⁹⁵ except for items relating to the physical environment. These were not included, in that the interview covered many different physical environments. According to Sweden's health-care laws, the patient's participation in planning of his/her care is obligatory. Against that background, items relating to that subject were included in the questionnaire.

3.4.14 Self-reported falls

The frequency of falls and injurious falls over the past three months was retrospectively recorded. A fall was defined as a subject's unintentional coming to rest on the ground, or at some other lower level.⁹⁸ If the person with MS replied affirmatively, that falls had in fact occurred, then the number of falls and the consequences of each fall were recorded.

3.4.15 Standardized order and enlarged font size of tests and structured interviews

During the first five home visits in the pilot study, the order of performance for the various parts of the comprehensive evaluation was investigated. During home visits 6 to 26, and during all home visits in the population-based study the elements of the comprehensive evaluation were administered in the following standardized order: 1) collection of biographical data; 2) Mini-Mental State Examination; 3) Free Recall and Recognition of 12 Random Words Test; 4) Symbol Digit Modalities Test; 5) Sickness Impact Profile; 6) Nine-hole Peg Test; 7) Beck Depression Index; 8) Frenchay Activities Index; 9) Barthel Index; 10) Katz Extended ADL Index; 11) Lindmark Motor Capacity Assessment; 12) Sense of Coherence Scale; 13) collection of information on the use of health care and patient satisfaction; 14) measurement of time taken to walk

10 meters; and 15) questions concerning frequency of falls and injurious falls. During the home visit in the pilot study, the physiotherapist performed the Mini-Mental State Examination; the Symbol Digit Modalities Test; the Nine-hole Peg Test; the Frenchay Activities Index; the Lindmark Motor Capacity Assessment; the timed 10-meters walk test; and asked the questions concerning falls and injurious falls. Collection of biographical data; the Free Recall and Recognition of 12 Random Words Test; the Sickness Impact Profile; the Beck Depression Index; the Barthel Index; the Katz Extended ADL Index; the Sense of Coherence Scale was performed by the nurse, who also collected information on the use of health care and conducted the patient satisfaction questionnaire.

The text of the forms used for the Free Recall and Recognition of 12 Random Words Test, the Symbol Digit Modalities Test; the Sickness Impact Profile; the Beck Depression Index; and the Frenchay Activities Index, was enlarged to font size 20 to assist people with MS with visual problems. However, if people with MS were unable to read or mark their forms because of severe visual dysfunction and/or severe ataxia, despite this enlarged font size, they were given the questions orally, and asked to reply orally. Their replies were then marked by the examiner. All questions included in the instruments were read aloud in the presence of the person with MS, to minimize the risk of misunderstanding.

3.5 STATISTICAL ANALYSIS

3.5.1 Pilot study (Papers I-II)

Descriptive statistics were used. Mean and median scores, ranges, and the percentage of people with MS scoring the minimum (floor) and maximum (ceiling) possible scores were examined to assess variation and floor and ceiling effects.

3.5.2 Population-based study (Papers III-V)

All statistical analyses were performed using SPSS version 11.5 (Papers III, V) and version 13.0 (Papers IV-V) (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics were used. In univariate analyses, differences in proportions were examined by a chi-squared test, and the significance of differences between sub-groups assessed by the Wilcoxon-Mann-Whitney test or the Kruskal-Wallis test. In box plots of scores, the boundaries of the boxes represent interquartile ranges, while transverse lines represent medians and whiskers the non-outlier range. Outliers are cases between 1.5 and 3 box lengths from the upper or lower edge of the box; extremes are cases with values more than 3 box lengths from the upper or lower edge of the box. Probability values of less than 0.05 were considered statistically significant. To adjust for multiple comparisons, probability values of < 0.001 were considered statistically significant in Paper V.

Initially, in the first multivariate analysis (Paper III), associations between potential predictors of disease-related characteristics (Expanded Disability Status Scale, disease course, and duration of disease); socio-demographic factors (gender, living conditions, education, employment status); and outcome variables attention (Symbol Digit

Modalities Test); manual dexterity (Nine-hole Peg Test); and walking ability (ability to walk 10 meters) were assessed using a chi-squared test or Fisher's exact test. In the second multivariate analysis (Paper V), associations between potential predictors, attention (Symbol Digit Modalities Test); manual dexterity (Nine-hole Peg Test); ability to walk with/without walking aid or support from another person; socio-demographic factors (gender, living conditions, education, employment status); and coping capacity and outcome variables, ADL and social/lifestyle activities (Barthel Index, Katz Extended ADL Index and Frenchay Activities Index) were assessed using a chi-square test. On account of the multivariate structure of the data, a forward, stepwise logistic-regression analysis was needed to allow the identification of the most important predictive factors. Any variable with a probability value of less than 0.25 in the univariate test was considered to be a candidate for the multiple-regression models. For the stepwise selection, the criteria used were, for entry, a probability value of less than 0.10, and, for removal, a probability value of greater than 0.15.¹⁴⁷

Via the method of structured interview and tests in the home environment, a clinical validation of many of the variables was possible. To establish the internal consistency in the instruments and sub-scales, Cronbach's Alpha coefficient was calculated for the total score and the sub-scales. Cronbach's Alpha is essentially a form of correlation coefficient, and a value of 0 would indicate that there was no correlation between the items that make up the scale. A value of 1 would indicate complete correlation.¹⁴⁸

3.6 ETHICAL CONSIDERATIONS

Ethical approval for the studies was obtained from the Ethics Committee of Huddinge University Hospital, (Dnr: 164/97). In addition, permission was obtained from the Data Inspectorate for establishing a database.

4 RESULTS

4.1 Pilot study (Papers I-II)

Demographic, disease-related data and information concerning coping capacity of the 26 people with MS included in the study are summarized in Table 3.

Table 3. Demographic and disease-related characteristics of 26 people with multiple sclerosis in the pilot study and of 166 people with multiple sclerosis in the population-based study

Variable	Pilot study n (%)	Poulation-based study n (%)
Age at recruitment (years)	47(12) ^a	51 (12) ^a ; 50.5 (43-60) ^b
Women/men	18/8 (69/31)	118/48 (71/29)
Coping capacity (SOC ^c)	72 (11) ^a ; 73 (65.5-83.5) ^{bd}	71 (12) ^a ; 73 (62-80) ^{be}
Below normal/normal/above normal	1/7/12 (5/35/60)	15/39/91 (10/27/63)
Living conditions		
Living with a partner	7 (27)	65 (39)
Living with partner and children	7 (27)	37 (22)
Living with children	2 (8)	14 (8)
Living without partner or children	10 (38)	50 (30)
Apartment/detached house/sheltered living	14/7/5 (54/27/19)	88/67/11 (53/40/7)
Basic/university-level education	20/6 (77/23)	100/66 (60/40)
Employment status		
Working full-time	2 (8)	28 (17)
Working part-time	10 (38)	40 (24)
Not working	14 (54)	97 (58)
Retired, medical reasons	7 (27)	51 (31)
Retired, age	2 (8)	22 (13)
On full-time sick leave	2 (8)	24 (15)
Studying	3 (12)	
Unemployed (eligible for work)		1
Swedish/other origin	23/3 (88.5/11.5)	151/15 (91/9)
Age at disease onset (years)	^f	31 (10) ^a ; 31.5 (24-39) ^b
Disease duration (years)	^f	19 (11) ^a ; 17.5 (11-26) ^b
Disease severity (Expanded Disability Status Scale)		
Mild disabled (0-3.0)	6 (23)	42 (25)
Moderately disabled (3.5-5.5)		35 (21)
Severely disabled (6.0-6.5)		47 (28)
Very severely disabled (≥7.0)		42 (25)
Moderately disabled (3.5-6.0)	8 (31)	
Severely disabled (≥6.5)	12 (46)	
Disease course		
Relapsing-remitting	^f	70 (42)
Secondary progressive	^f	80 (48)
Primary progressive	^f	16 (10)
Ongoing treatment at recruitment		
With immunomodulatory drug	^f	68 (41)
Symptomatic treatment	^f	129 (78)

^a mean (standard deviation); ^b median (interquartile range); ^c SOC=Sense of Coherence Scale; ^d n=20; ^e n=145; ^f Information not available

The mean time needed to perform the home visit was 1 h 57 min (SD \pm 19 min). This did not include time required for traveling and administration. In 16 out of the 26 cases of people with MS (62%), the home visits were completed within the allocated 2 hours, and all home visits were performed within 2½ hours.

With the assistance of the spouses of three severely disabled people with MS and the personal assistant of one severely disabled person with MS, it was possible for a comprehensive evaluation to be performed for the majority of the participants with MS, including all planned tests and structured interviews during home visits. The percentages of people with MS participating in the various tests and structured interviews were as follows: Lindmark Motor Capacity Assessment, 85%; 10-meter walk, 58%; Nine-hole Peg Test, 74%; Mini-Mental State Examination, 100%; Free Recall and Recognition of 12 Random Words Test, 96%; Symbol Digit Modalities Test, 88%; Sense of Coherence, 77%; Beck Depression Index, 91%; Barthel Index, 96%; Katz Extended ADL Index, 96%; Frenchay Activities Index, 96%, Sickness Impact Profile, 100%; and questions concerning self-reported falls during the past three months, 92%.

4.1.1 Motor function (Paper I)

One person with MS in the study scored a maximum score in the Lindmark Motor Capacity Assessment. No apparent floor effects were observed for the Lindmark Motor Capacity Assessment. The variation in the time taken to walk 10 meters and to perform the Nine-hole Peg Test was acceptable.

4.1.2 Cognitive function and depressed mood (Paper I)

The first four people with MS were only tested via the Mini-Mental State Examination. Thereafter, the evaluation was expanded to also include the Free Recall and Recognition of 12 Random Words Test, the Symbol Digit Modalities Test and the Beck Depression Index. Six (33%) of the tested people with MS had depressed mood according to the Beck Depression Index. The variation in the Mini-Mental State Examination; the Free Recall and Recognition of 12 Random Words Test; the Symbol Digit Modalities Test was acceptable; the tests displayed no apparent floor effects and no marked ceiling effects. Compared to the Mini-Mental State Examination Test, and the Free Recall and Recognition of 12 Random Words Test, most people with MS (58%) performed below normal in the Symbol Digit Modalities Test.

4.1.3 ADL and social/lifestyle activities (Paper I)

An acceptable variation in scores was observed for Barthel Index, Katz Extended ADL Index and Frenchay Activities Index. Neither Barthel Index nor Katz Extended ADL Index displayed any marked floor effects; however, ceiling effects were observed for both instruments. No floor or ceiling effects were observed in the Frenchay Activities Index.

4.1.4 Coping capacity (Paper II)

The coping capacity of the people with MS as measured by the Sense of Coherence scale depicted a wide variation in scores. No floor or ceiling effects were apparent. Six people with MS were not interviewed because of emotional instability (n=2), lack of time (n=2), cognitive dysfunction (n=1), or fatigue (n=1). It seems that the questions for Sense of Coherence scale used in this study may be too difficult for people with MS with severe cognitive dysfunction and/or depressed mood to understand and answer.

4.1.5 Family caregivers (Paper II)

Sixteen (62%) people with MS lived with a spouse or partner. Twelve (75%) of them agreed to be interviewed about demographic characteristics. The daughter of one of the persons with MS also consented to being interviewed, making a total of 13 persons.

Nine agreed to answer the health-related quality of life questionnaire called the Sickness Impact Profile. This questionnaire was found to be useful in obtaining information on the health-related quality of life of family caregivers of the people with MS.

As regards interviews of family caregivers on health-related quality of life and the time spent on helping the people with MS, only spouses and partners - or significant others such as adult children or personal assistants - should be included in a population-based study, so that a homogeneous group of caregivers is evaluated.

4.1.6 Resource utilization, technical aids and social care (Paper II)

The number of visits to the Emergency Department, lengths of hospital stays in days, and frequency of contacts with physicians, nurses, physiotherapists, occupational therapists and other health-related professionals, both in hospital out-patient clinics and in primary care, over the past 3-year period were calculated for all the people with MS. The method of calculating resource utilization within Stockholm County Council and of detecting changes over time using the computerized register was thus found to be feasible and sufficiently detailed for such a study.

Details on use of health-related services by the people with MS during the 6 months prior to the home visit were available from all people with MS, whatever their level of disability, cognitive function or fatigue-related problems. Although, this implied that family caregivers and personal assistants were able to take part in the interview for some of the people with MS. In the interview, people with MS reported 93% of those contacts, with health-care professionals over the past half-year that were entered in the computerized register. The conclusion was that the people with MS had a clear memory of which health-care professionals they had had contact with over the past 6 months, but not the frequency of those contacts. This suggests that the use of some health-related services not recorded in the database, such as home-help services, may very well be underestimated by people with MS during an interview.

The comprehensive questionnaires used for collecting information on health-related services, technical aids, home modifications and transportation service were found, as they were conducted, to be suited for use during home visits and sufficiently detailed. Above all, home adaptations and technical aids were clearly visible to the investigators, and the people with MS could easily discuss and point to aspects of their current home environment.

4.1.7 Health-related quality of life (Paper I)

The variation in scores of the Sickness Impact Profile was acceptable, and no marked floor or ceiling effects were apparent. Ceiling effects were found in 5 - “emotional behavior”, “mobility”, “alertness behavior”, “communication” and “eating” of the 12 sub-scales of the Sickness Impact Profile .

4.1.8 Patient satisfaction with care (Paper II)

The feasibility of the patient satisfaction questionnaire was found to be satisfactory, with people with MS showing a high level of interest in sharing their experiences of MS care. However, in view of the observations the people with MS on items lacking, it was concluded the patient satisfaction questionnaire needs modification. The questionnaire also needs to include items relating to: information and advice on social security matters and psychosocial issues; information delivered during early stages of the disease; and the perception of the situation when the diagnosis of MS was first given.

4.1.9 Self-reported falls (Paper I)

Thirteen of 23 people with MS tested reported a fall during the past three months. One person suffered a fracture as the result of a fall.

4.2 Population-based study (Papers III-IV)

4.2.1 Demographic, disease-related data and coping capacity (Papers III-V)

Home visits were made to 166 people with MS. Among them, 16 (10%) needed two visits to complete the comprehensive evaluation. Demographic and disease-related characteristics, with information on coping capacity for the total sample of people with MS in Stockholm County are summarized in Table 3. Relative to an age-matched sample of healthy subjects from Stockholm County, fewer people with MS lived alone and worked full- or part-time, but a higher proportion had a university level education.¹⁴⁹ A total of 11 people with MS made use of sheltered living— 4 in care homes, 6 in apartments for the disabled, and 1 in a nursing home. One person with MS in the sample declined to perform the tests included in this study.

4.2.2 Cognitive function, motor function, ADL and social/lifestyle activities (Papers III-IV)

Results from tests measuring global motor capacity, manual dexterity, walking capacity, cognitive function, ADL and social/lifestyle activities for the total sample of people with MS from Stockholm County are summarized in Table 4.

Table 4. Global motor capacity, manual dexterity, walking ability, cognitive function, activities of daily living (ADL), social/lifestyle activities in 166 people with multiple sclerosis in the population based study

Variable (range of scores)	n (%)
Global motor capacity (n=164)	
Total score Lindmark Motor Capacity Assessment (0-258)	232 (164-253) ^b
Maximum score Lindmark Motor Capacity Assessment	14 (9)
Manual dexterity (n=165)	
Able to perform Nine-hole Peg Test with both hands	139 (84)
Time to perform Nine-hole Peg Test per hand (seconds; n=139)	27 (23) ^a ; 21 (16-29) ^b
Within normal range (0.5 pegs/seconds)	45 (27.1)
10-meters walk (n=166)	
Able to walk without/with aid	87/36 (52/22)
Walking time (seconds; n=123)	20 (30) ^a ; 11 (8-22) ^b
Walking speed (meter/seconds; n=123)	0.9 (0.5) ^a ; 0.9 (0.5-1.3) ^b
Within normal range (n=123)	14 (11)
Walking speed (meter/seconds)	0.7 (0.6) ^a ; 0.6 (0.0-1.1) ^b
Within normal range	14 (8)
Step length (meter; n=119)	0.5 (0.2) ^a ; 0.5 (0.4-0.6) ^b
Within normal range	40 (34)
Step length (meter)	0.4 (0.3) ^a ; 0.4 (0.0-0.6) ^b
Within normal range	40 (24)
Cognitive function	
Mini-Mental State Examination (n=163)	
Total score (0-30)	27 (4) ^a ; 28 (26-29) ^b
Within normal range	89 (55)
Free Recall and Recognition of 12 Random Words Test (n=160)	
Free recall within normal range	135 (84)
Symbol Digit Modalities Test (n=155)	
Within normal range	69 (44.5)
ADL, (n=165)	
Barthel Index	
Independent in all the Barthel Index items	81 (30) ^a ; 100 (75-100) ^b
Independent in all the Katz personal ADL items	85 (52)
Independent in all the Katz personal ADL items	118 (72)
Independent in all the Extended Katz ADL index items	50 (30)
Social/lifestyle activities, (n=164)	
Frequency within normal range in Frenchay Activities Index	21 (12) ^a ; 22 (9-31) ^b
Frequency within normal range in Frenchay Activities Index	58 (35)

^a mean (standard deviation); ^b median (interquartile range)

21 persons with MS with motor dysfunction in the upper extremities replied orally in the Symbol Digit Modalities Test. Balance and coordination were the most affected aspects of global motor capacity according to the Lindmark Motor Capacity Assessment. Four of the 14 people with MS who walked at normal speed had reduced step length. (Paper III)

In the various items in the Barthel Index, the percentages of people with MS who were independent varied from 61-91% (n=100-150). Items where most - 80-91% (n=133-150) - people with MS were independent were “grooming”, “bowels”, “toilet use”, and “transfers”. Most frequently affected items - 27-39% (n=45-66) - were “mobility”, “stairs”, and “dressing”. In the different Katz ADL Index items, the percentages of people with MS who were independent varied from 38-92% (n=62-152). Items where most - 80-91% (n=133-150) - people with MS were independent were “feeding”, “transfer”, and “toileting”. Most frequently affected items - 38% (n=62-63) - were “cleaning indoors” and “outdoor transportation”. (Paper IV)

In the different items in the Frenchay Activities Index, the percentages of people with MS who reported full activity varied from 8-54% (n=13-88). Items where most - 53-54% (n=87-88) - people with MS reported full activity were “local shopping”, and “light housework”. Items where most - 59-68% (n=97-112) - people with MS reported no activity were “gardening”, “heavy housework”, “household maintenance” and “walking outside for more than 15 min”. Compared to an age- and gender-matched population, 35% (n=57) performed within the normal range in social/lifestyle activities, according to the Frenchay Activities Index. (Paper IV)

4.2.3 Subgroup analyses (Papers III, V)

Significantly higher percentages of people with MS able to perform the Nine-hole Peg Test with both hands and able to walk 10 meters were found in the following sub-groups: people with MS with a lower level of disease severity, people with MS with a relapsing-remitting disease course, people with MS living in a private household and people with MS working full- or part-time. In addition, significantly higher percentages of people with MS able to walk 10 meters were found in the following sub-groups: people with MS with disease duration of 10 years or less and people with MS living with a partner. (Figure 3) (Paper III)

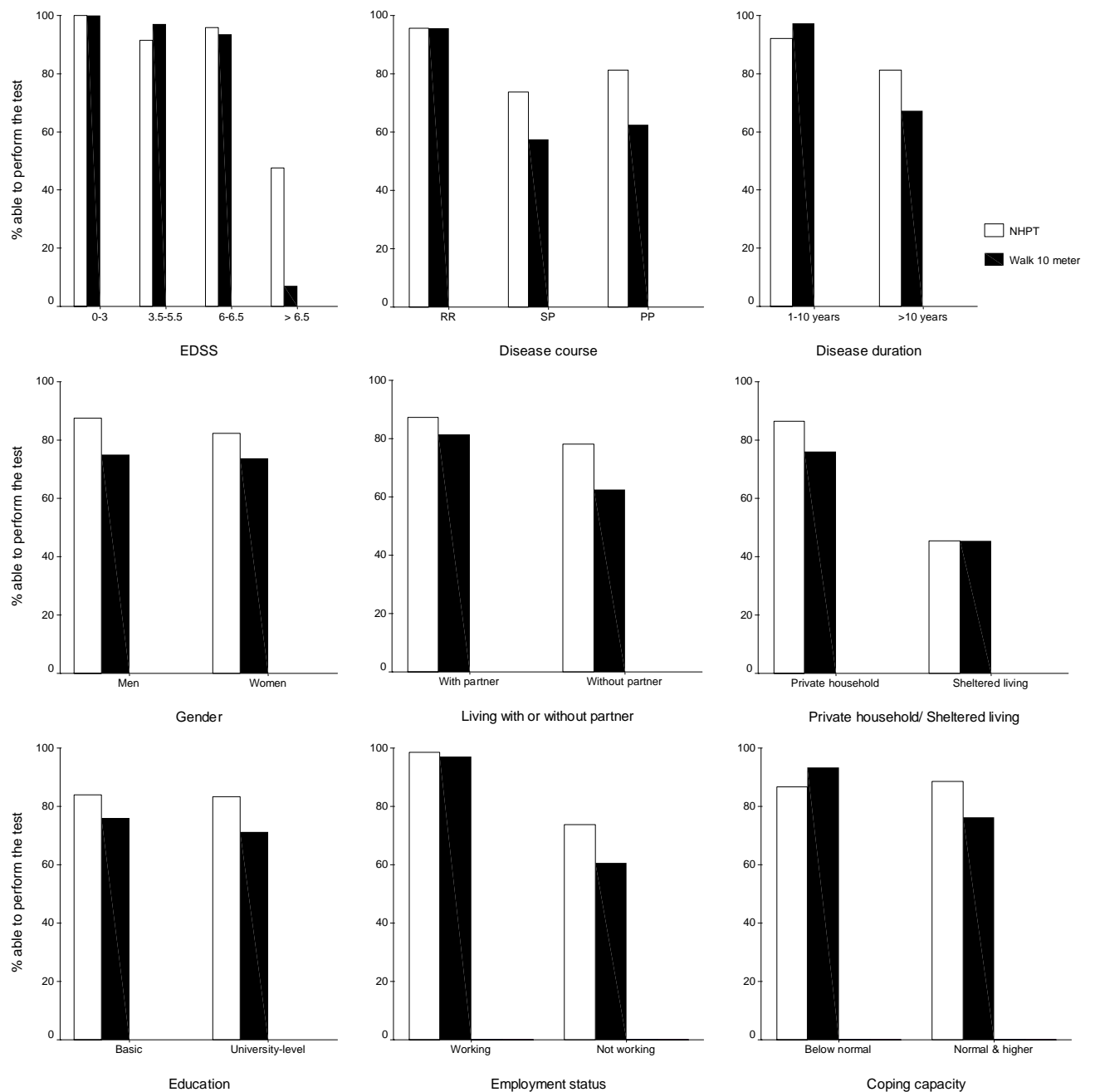


Figure 3. Percentages of persons with MS able to perform Nine-hole Peg Test with both hands and able to walk 10 meters with or without walking aids, taking into account disease-specific information, demographic characteristics and coping capacity. EDSS=Expanded Disability Status Scale; RR=relapsing-remitting; SP=secondary progressive; PP=primary progressive.

With regard to general cognitive performance (as assessed by the Mini-Mental State Examination), significantly higher proportions of people with MS showing general cognitive performance within normal limits were found in the following sub-groups: people with MS with a lower level of disease severity, people with MS with a disease duration of 10 years or less and people with MS working full- or part-time. In addition, with regard to verbal memory (as assessed by the Free Recall and Recognition of 12 Random Words Test), significantly higher percentages of people with MS with verbal

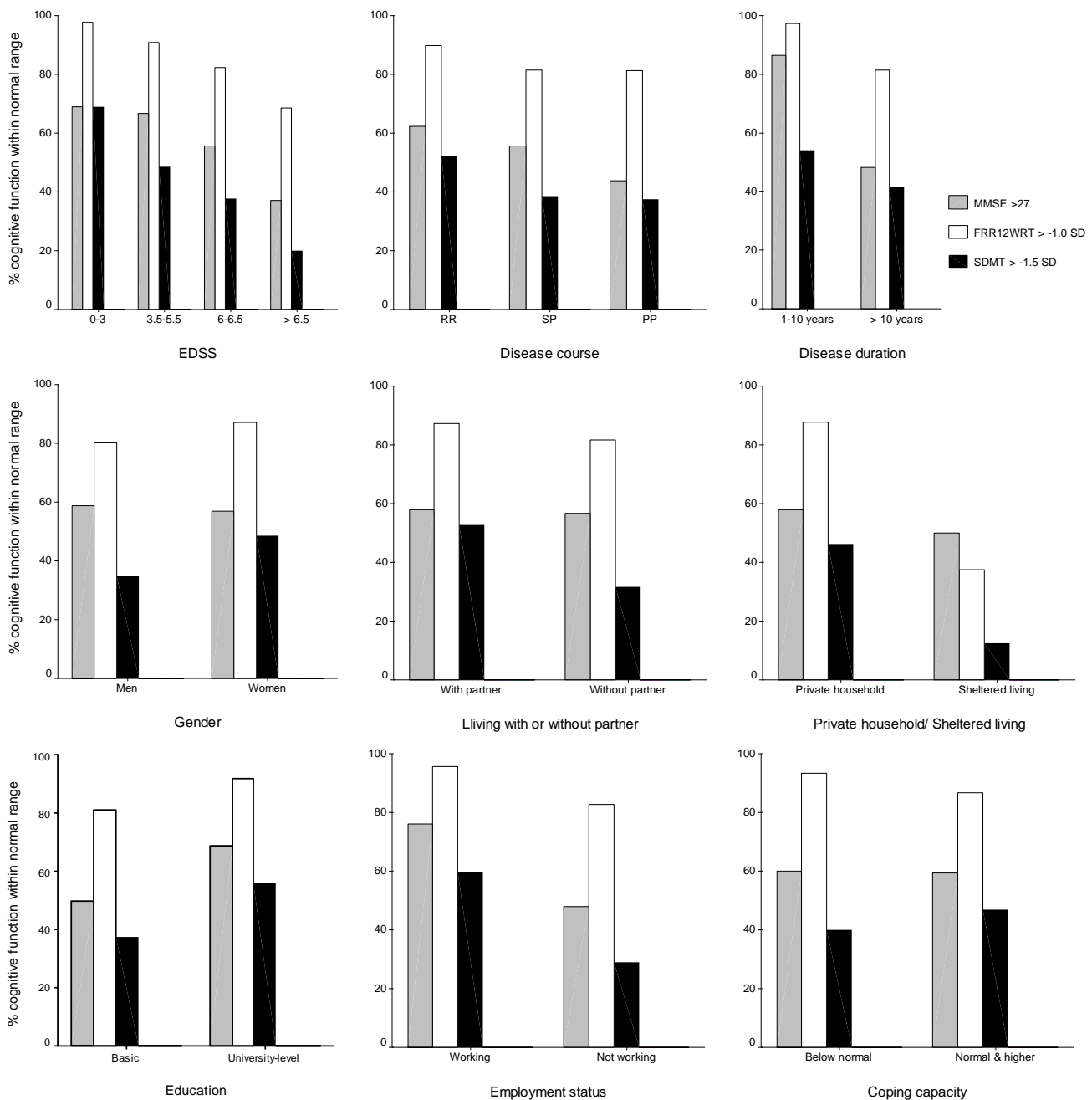


Figure 4. Percentages of persons with MS performing within normal range in general cognitive performance, verbal memory and attention taking into account disease-specific information, demographic characteristics and coping capacity. EDSS=Expanded Disability Status Scale; RR=relapsing-remitting; SP=secondary progressive; PP=primary progressive.

memory within normal limits were found in the following sub-groups: people with a lower level of disease severity, people with a disease duration of 10 years or less, people living in a private household and people working full- or part-time. Lastly, with regard to attention (as assessed by the Symbol Digit Modalities Test), significantly higher proportions of people with MS showing attention within normal limits were found in the following sub-groups: people with a lower level of disease severity, people living with a partner, people with a university-level education and people working full- or part-time. (Figure 4) (Paper III)

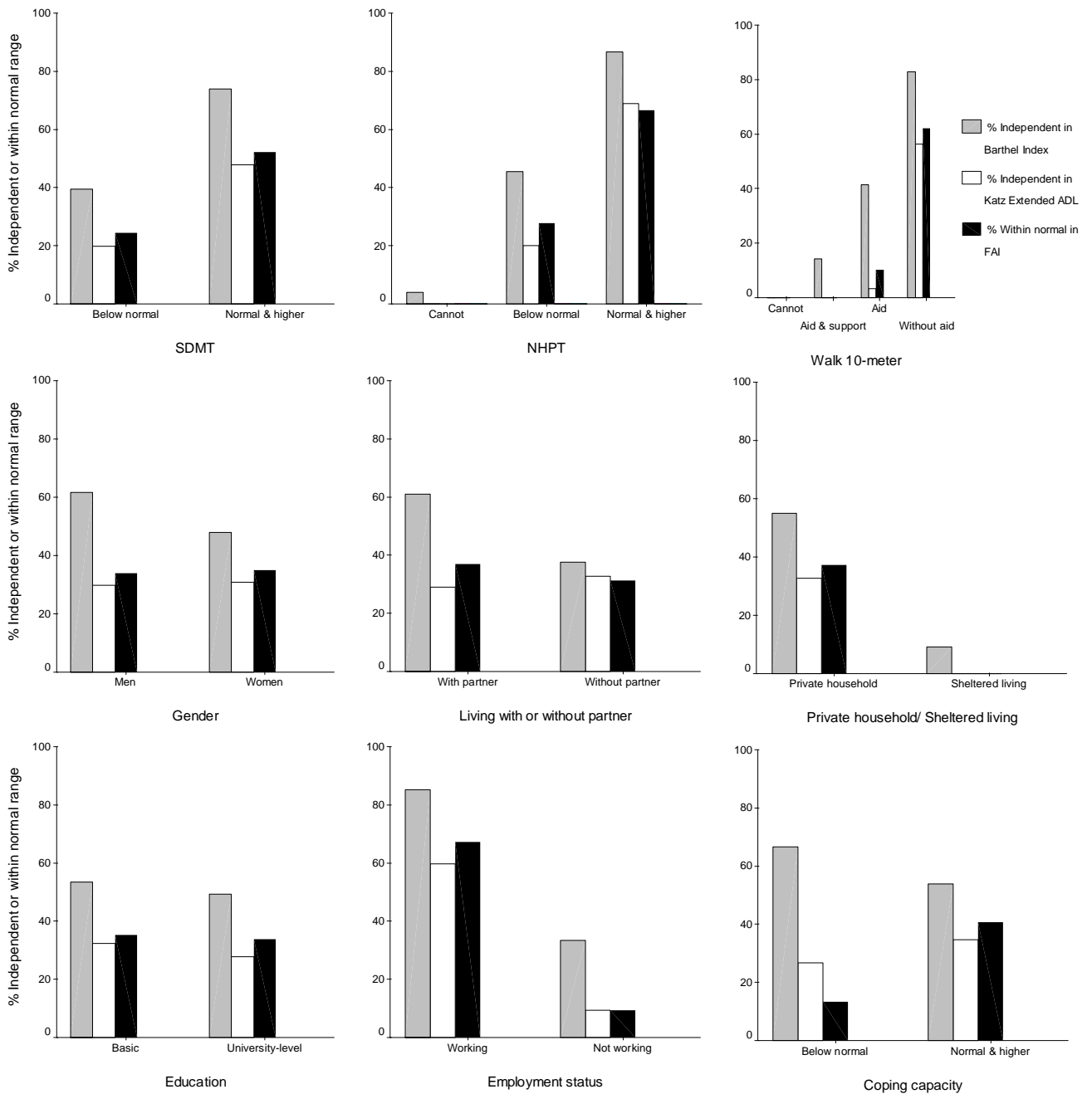


Figure 5. Percentages of people with MS independent in personal and instrumental ADL measured by the Barthel Index and the Katz Extended ADL, with normal frequency of social/lifestyle activities measured by the Frenchay Activities Index (FAI) taking into account cognitive function as regards attention, manual dexterity speed, walking ability, socio-demographic factors and coping capacity. EDSS=Expanded Disability Status Scale; RR=relapsing-remitting; SP=secondary progressive; PP=primary progressive.

Significantly higher percentages of people with MS who are independent in ADL as regards the Barthel Index and the Katx Extended ADL Index, with frequency of activities within normal limits, were found in the following sub-groups: people with a normal attention (Symbol Digit Modalities test), people with higher level of manual

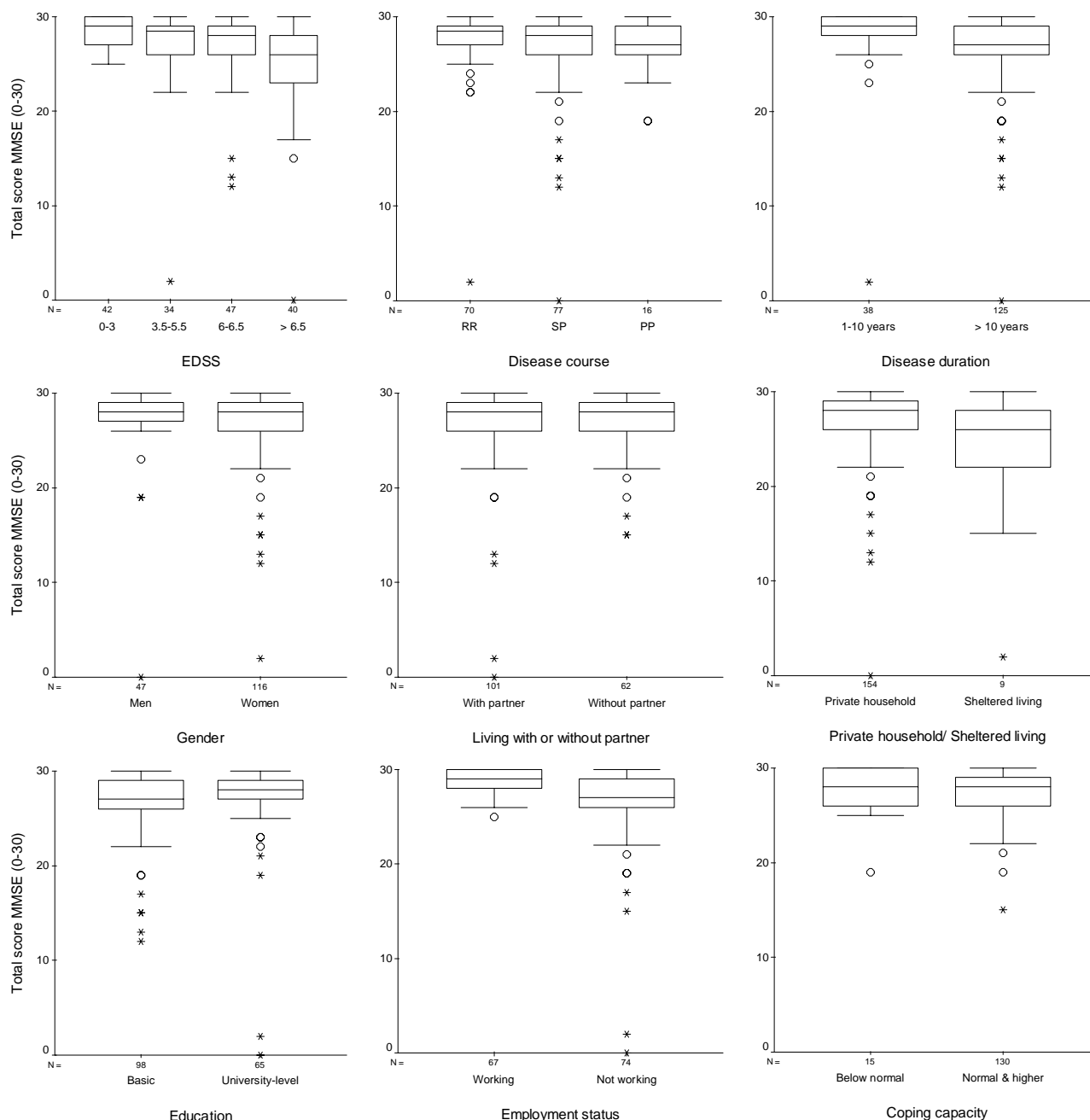


Figure 6. Mini-Mental State Examination (MMSE); score in people with multiple sclerosis, relative to disease-related factors, demographic characteristics and coping capacity. EDSS=Expanded Disability Status Scale; RR=relapsing-remitting; SP=secondary progressive; PP=primary progressive.

dexterity function, people with higher level of walking ability, people living in a private household and people working full- or part-time. In addition, with regard to independency in ADL (the Barthel Index), people living with a partner; and with regard to frequency of activities within normal limits people with normal or higher coping capacity. (Figure 5) Box plots of scores on the Mini-Mental State Examination and the Lindmark Motor Capacity Assessment and of results of the Nine-hole Peg Test (in

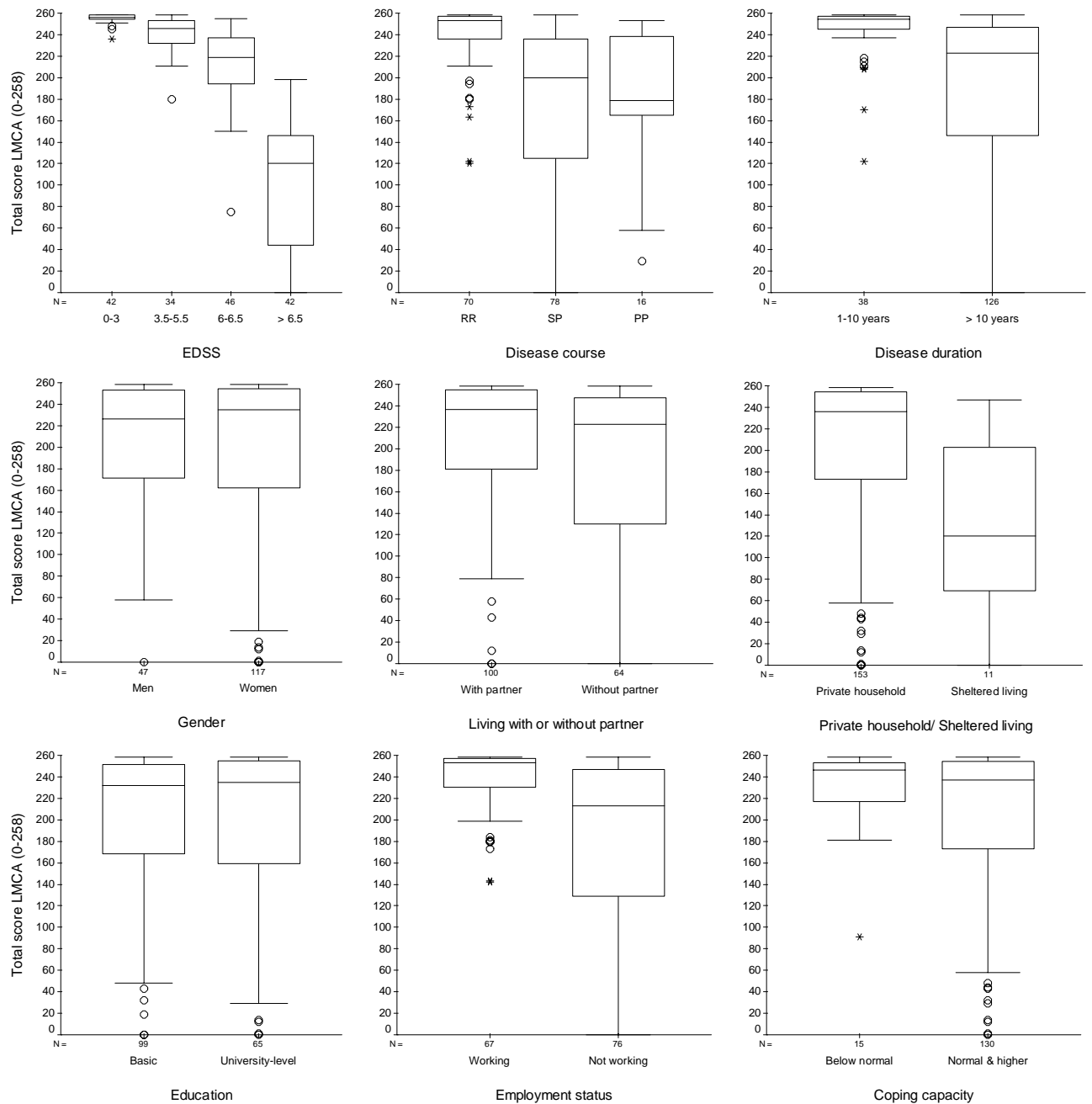


Figure 7. Lindmark Motor Capacity Assessment (LMCA) score for people with multiple sclerosis, relative to disease-related factors, demographic characteristics and coping capacity. EDSS=Expanded Disability Status Scale; RR=relapsing-remitting; SP=secondary progressive; PP=primary progressive.

pegs/seconds) and the 10-meter walk (in meter/seconds), relative to disease-related factors, demographic characteristics and coping capacity, are presented in Figures 6-9.

Despite large overlaps in performance between sub-groups, significantly more favorable results with regard to general cognitive performance, global motor capacity, manual dexterity and walking speed were found in the following sub-groups: people with a lower level of disease severity, people with a disease duration of 10 years or less,

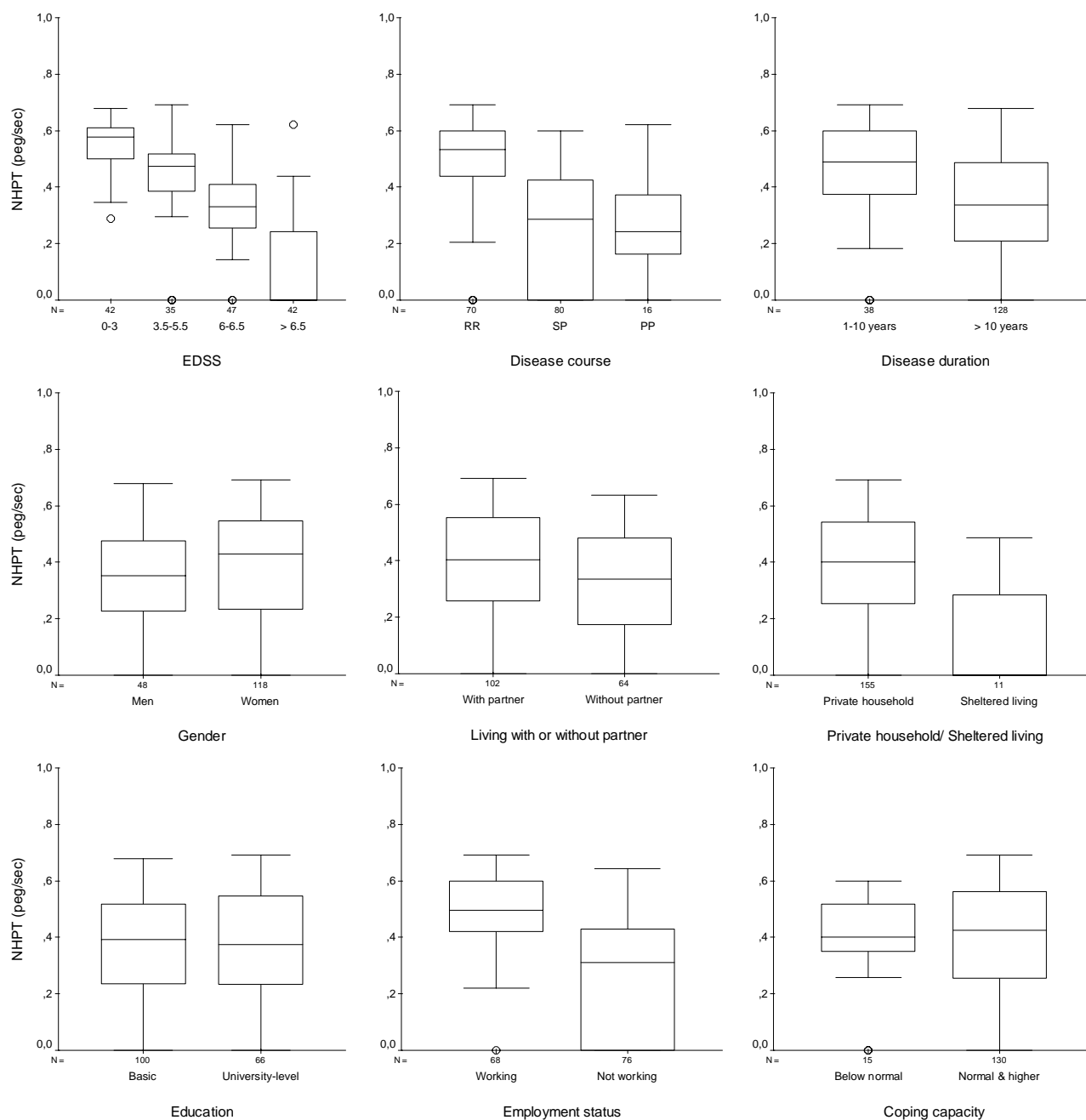


Figure 8. Results of Nine-hole Peg Test (NHPT; in pegs/seconds) in people with multiple sclerosis, relative to disease-related factors, demographic characteristics and coping capacity. EDSS=Expanded Disability Status Scale; RR=relapsing-remitting; SP=secondary progressive; PP=primary progressive.

and people working full- or part-time. In addition, significantly better global motor capacity, manual dexterity and walking speed were found in sub-groups of people with a relapsing-remitting disease course; people living with a partner; and people living in a private household. No significant differences were found with regard to gender, level of education or coping capacity. (Paper III)

Box plots of scores on the Barthel Index, the Katz Extended ADL Index and the Frenchay Activities Index, relative to attention (Symbol Digit Modalities Test); manual

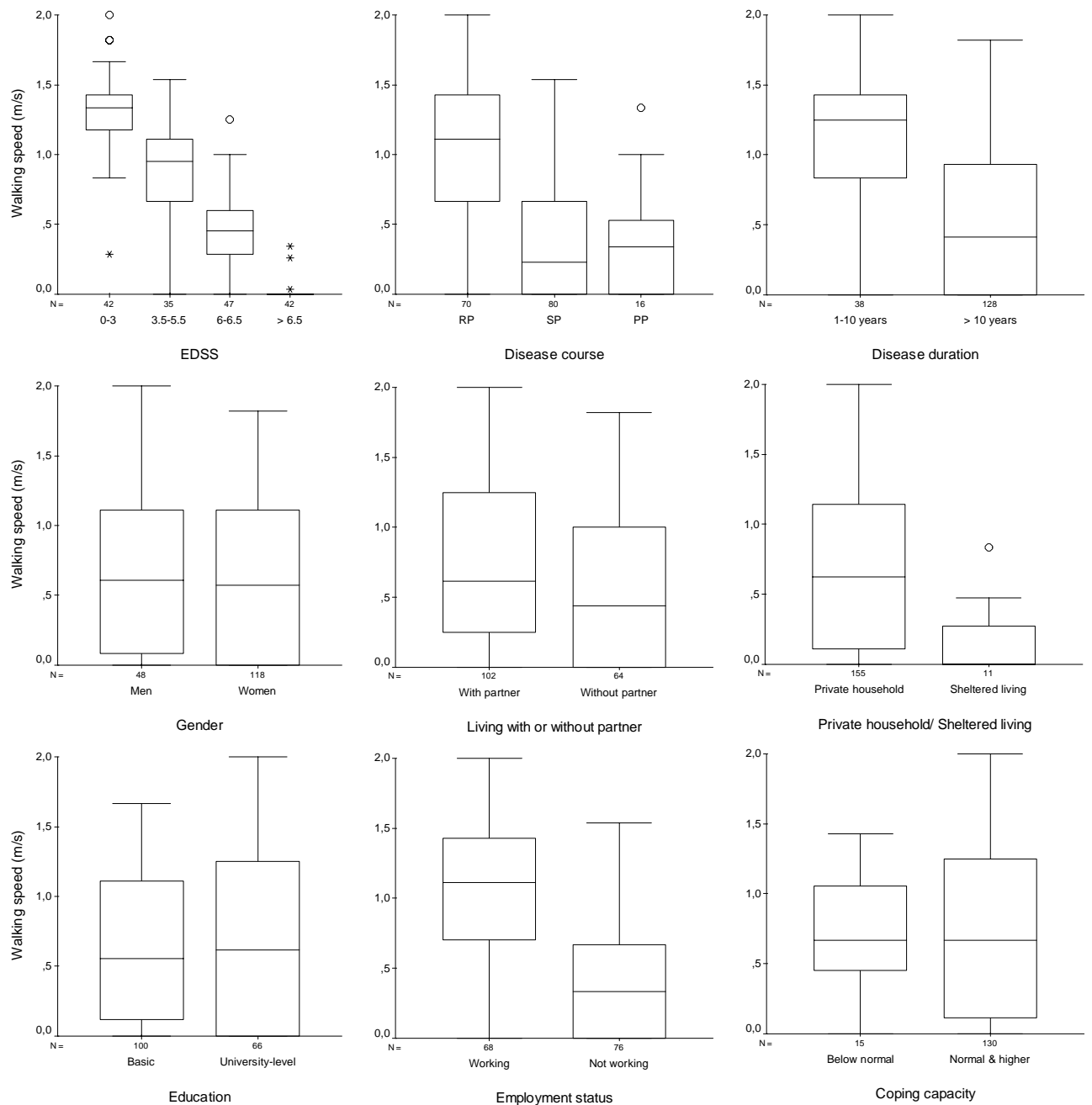


Figure 9. Walking speed (in meter/seconds) in people with multiple sclerosis, relative to disease-related factors, demographic characteristics and coping capacity. EDSS=Expanded Disability Status Scale; RR=relapsing-remitting; SP=secondary progressive; PP=primary progressive.

dexterity; walking ability; socio-demographic factors; and coping capacity are presented in Figures 10-12.

Significantly higher scores with regard to personal and instrumental ADL (as assessed by the Barthel Index and the Katz Extended ADL Index) and frequency of social/lifestyle activities were found in the sub-groups of people with MS with normal attention; normal manual dexterity; ability to walk without walking aid and support from another person; living in a private household and working part-/full-time. In addition, with regard to the Barthel Index significantly higher scores were recorded

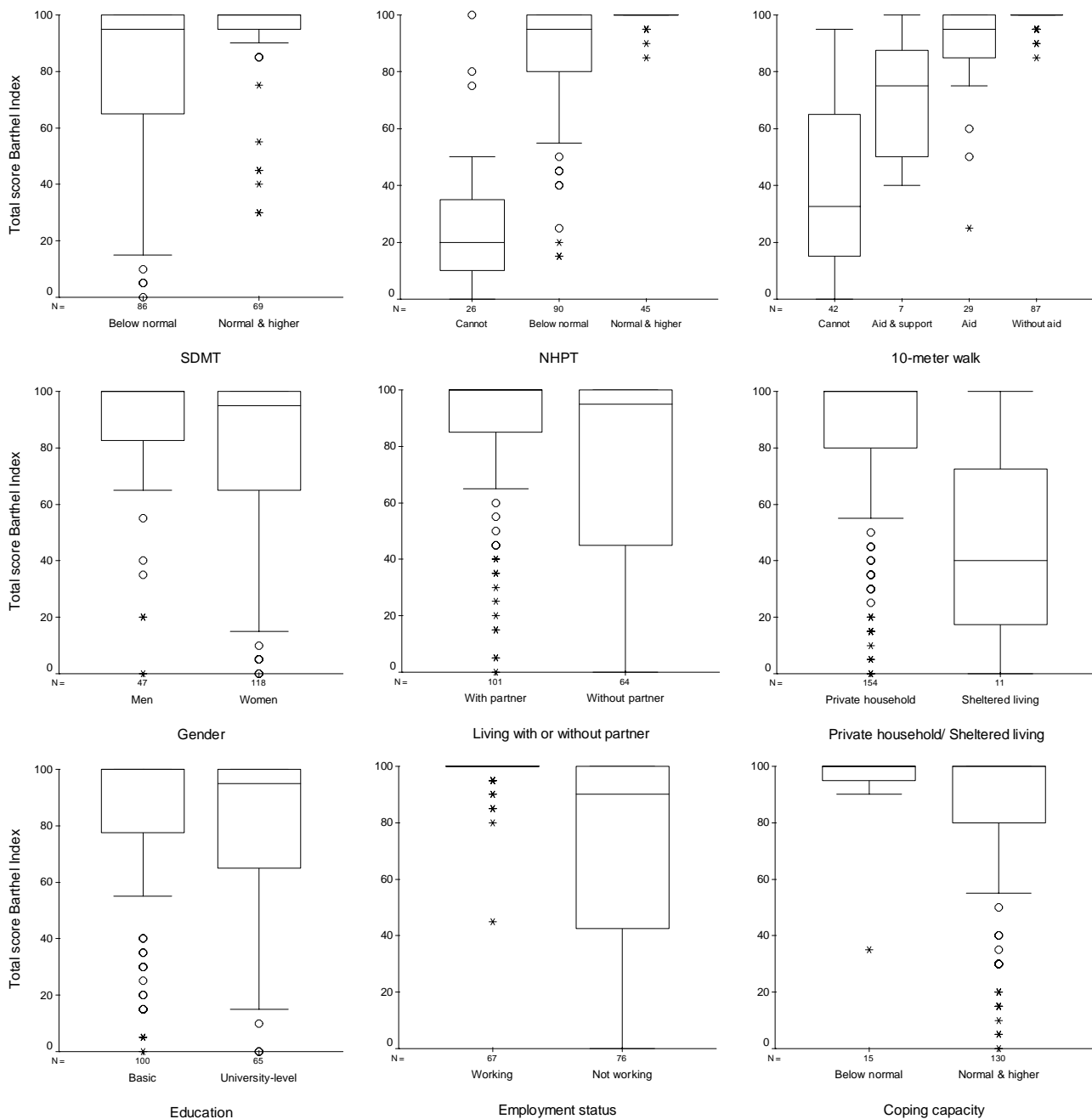


Figure 10. Barthel Index score in people with MS, in relation to cognitive function as regards attention, manual dexterity speed, walking ability, socio-demographic factors and coping capacity. SDMT=Symbol Digit Modalities Scale; NHPT=Nine-hole Peg Test.

among those living with a partner. No significant differences were found with regard to gender, level of education and coping capacity.

The significantly greatest gain was seen: a) in the Barthel Index and the Katz Extended ADL Index between those with slow manual dexterity (<0.5 pegs/second) and those with no manual dexterity, followed by those who needed no walking aid, relative to those who needed aid with walking; and b) in the Frenchay Activities Index between

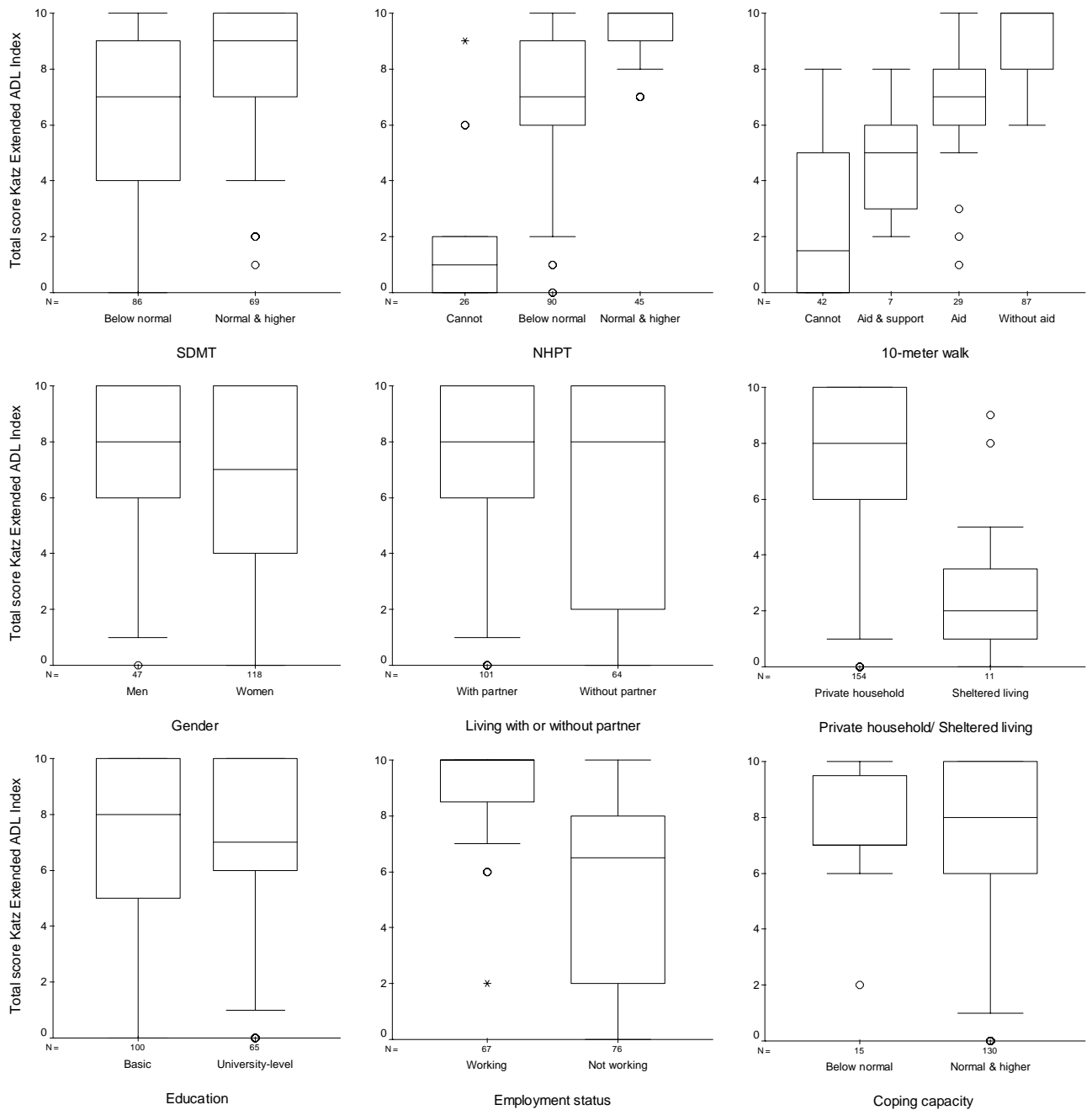


Figure 11. Katz Extended ADL Index score in people with MS, relative to cognitive function as regards attention, manual dexterity speed, walking ability, socio-demographic factors and coping capacity. SDMT=Symbol Digit Modalities Scale; NHPT=Nine-hole Peg Test.

those with slow manual dexterity and those with no manual dexterity; followed by those with normal manual dexterity speed relative to those with slow manual dexterity; and followed next by those who needed no walking aid relative to those who needed walking aid.

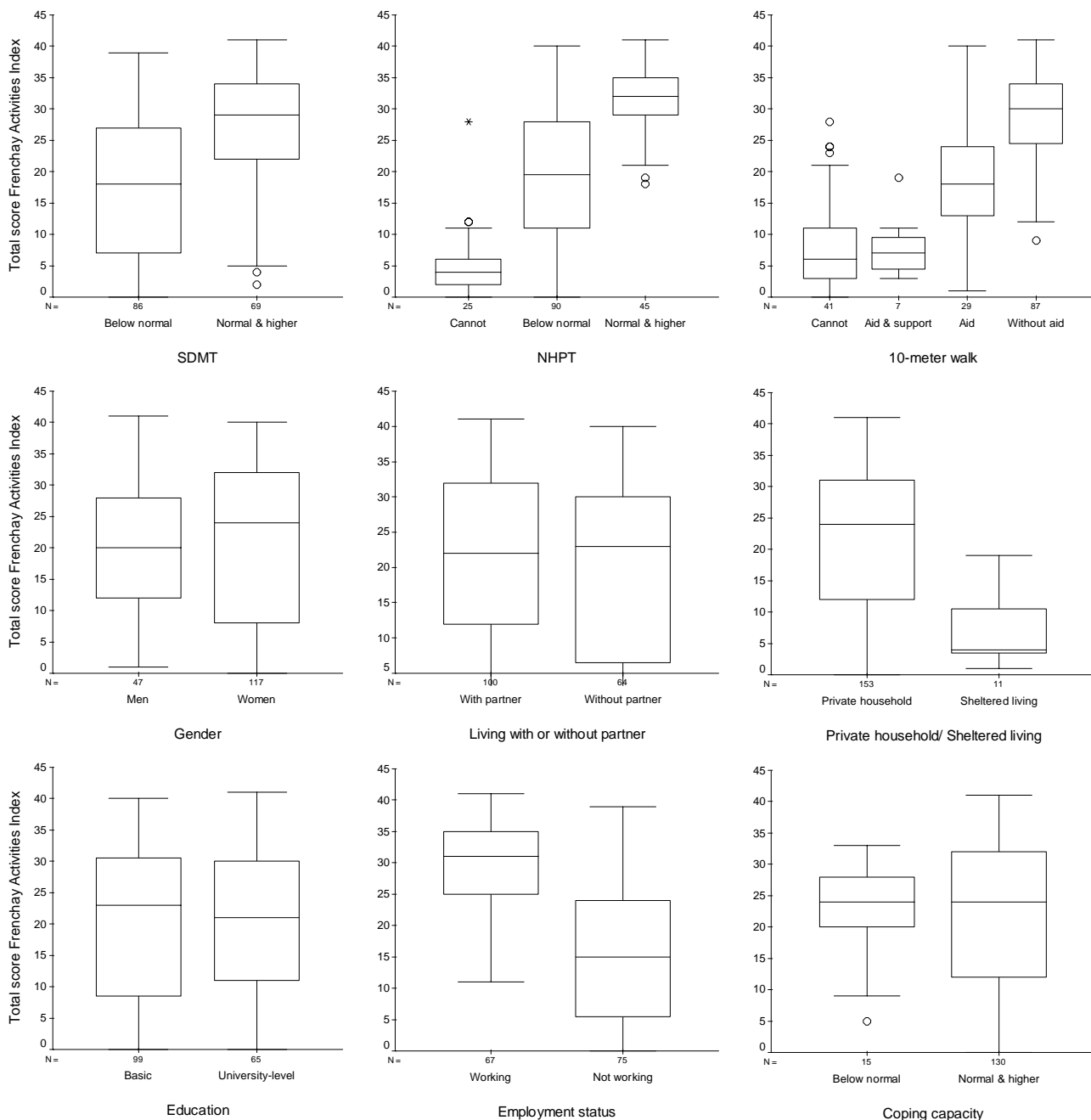


Figure 12. Frenchay Activities Index score in people with MS, relative to cognitive function as regards attention, manual dexterity speed, walking ability, socio-demographic factors and coping capacity. SDMT=Symbol Digit Modalities Scale; NHPT=Nine-hole Peg Test.

4.2.4 Multivariate analyses (Papers III, V)

In the logistic-regression model (Table 5), a lower level of disease severity and current employment were found to be significantly and independently associated with the ability to perform the Nine-hole Peg Test with both hands and to walk 10 meters. In addition, living in a private household was a significant factor associated with the ability to perform the Nine-hole Peg Test and living with a partner was a significant, independent factor associated with the ability to walk 10 meters. A lower level of disease severity and a higher level of education were found to be significantly and

Table 5. Factors independently predictive of normal cognitive function (attention, as assessed by the Symbol Digit Modalities Test [SDMT]), of the ability to perform the Nine-hole Peg Test (NHPT), and of the ability to walk 10 meters in 166 people with MS.

Variables	SDMT	NHPT	10-meter walk
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Disability (EDSS)			
Mild vs. very severe	8.52 (2.80-25.89)		
Moderate vs. very severe	3.75 (1.23-11.43)		
Severe vs. very severe	2.23 (0.77-6.49)		
Mild/moderate vs. severe/very severe		4.10 (1.09-15.44)	1.48 (2.04-150.10)
Disease course			
RR vs. PP	x	x	5.13 (0.76-34.87)
SP vs. PP	x	x	0.81 (0.22-3.02)
Disease duration			
10 years vs. >10years	x	x	x
Female vs. male	2.00 (0.90-4.35)	b	b
Age	x	x	x
Living with partner vs. living without partner	2.00 (0.94-4.23)	x	3.78 (1.40-10.19)
Private household vs. sheltered living	x	3.93 (1.04-14.88)	x
Higher education vs. basic education	2.38 (1.15-1.49)	b	b
Working vs. not working	x	10.97 (1.35-88.98)	9.80 (1.96-48.85)
Coping capacity (SOC)			
Normal/above normal vs. below normal	b	b	x
Prediction model, characteristics:			
R ²	0.25	0.31	0.56
Overall proportion correct	62%	68%	79%
Hosmer GOF (r value)	0.71	0.67	0.28

OR=odds ratio; CI=confidence interval; EDSS=Expanded Disability Status Scale; RR=relapsing-remitting; PP=primary progressive; SP=secondary progressive; SOC= Sense of Coherence Scale; GOF=goodness of fit; ^an=155; ^bdid not fulfill entry criteria

independently associated with attention within normal limits (as assessed by the Symbol Digit Modalities Test). The explanatory value of the variables included in the analyses of the study ranged from 25% to 56%. (Paper III)

In the logistic-regression model (Table 6), the ability to walk 10 meters without aid and/or support; and current employment were found to be significantly and independently associated with being independent in personal and instrumental ADL and for normal frequency of social/lifestyle activities. In addition, living with a partner was a significant, independent factor associated with independency in the Barthel Index; normal manual dexterity speed with independency in the Katz Extended ADL Index; and normal coping capacity with normal frequency of social/lifestyle activities. The explanatory value of the variables included in the analyses of the study ranged from 61% to 64%. (Paper V)

Table 6 Factors independently predictive of independency in activities of daily living, as assessed by the Barthel Index (BI) and the Katz Extended ADL Index (KE-ADL) and frequency of social/lifestyle activities within normal, as assessed by the Frenchay Activities Index.

Variables	BI ^a OR (95% CI)	KE-ADL ^a OR (95% CI)	FAI ^b OR (95% CI)
Manual dexterity (Nine-hole Peg Test) Normal/above normal speed versus cannot perform test/below normal speed	x	2.89 (1.09-7.63)	x
Walking (10 meters) Walk without aid/support versus cannot walk/walk with aid/support	20.10 (6.94-58.20)	41.08 (5.17-326.12)	19.25 (5.08-72.91)
Cognitive function (SDMT) Normal/above normal versus below normal	2.32 (0.88-6.14)	x	x
Gender Female versus male	x	c	c
Living conditions Living with partner versus living without partner	4.02 (1.38-11.76)	c	c
Private household versus sheltered living	x	x	x
Employment status Working versus not working	6.91 (2.54-18.80)	5.31 (1.99-14.18)	10.19 (3.78-27.46)
Coping capacity (SOC) Normal/above normal versus below normal	c	c	6.49 (1.08-39.13)
Prediction model, characteristics:			
R ²	0.64	0.61	0.62
Overall proportion correct (%)	82.12	83.44	85.00
Hosmer GOF (r value)	0.12	0.83	0.96

^an=151; ^bn=140; ^cdid not fulfill entry criteria; OR, odds ratio; CI, confidence interval; SDMT, Symbol Digit Modalities Test; SOC, Sense of Coherence Scale; GOF, goodness of fit.

5 DISCUSSION

5.1 Main findings

5.1.1 Pilot study (Papers I-II)

The pilot study evaluated the feasibility of a comprehensive evaluation package, administered in the home environment, measuring functioning, patient satisfaction, resource utilization, and health-related quality of life of people with MS and their family caregivers. The methods used in this study for testing and interviewing the persons with MS at home were found to be easy to administer and were well accepted by the persons with MS, irrespective of their level of disease severity or form of living. Calculating resource utilization via the computerized register at Stockholm County Council was found to be easy to administer. Only minor modifications proved to be necessary to make the methods suitable for application in a large population-based study. For 38% of the persons with MS, the time needed to complete the evaluation exceeded 2 hours, although in no case did it exceed 2½ hours. The possibility of collecting data over two separate home visits, in order to prevent fatigue and loss of attention on the part of the people with MS, was to be considered in the population-based study.

5.1.2 Population-based study (Papers III-V)

This population-based study is the first to present detailed data on cognitive function, manual dexterity, general motor capacity, walking capacity, ADL and social/lifestyle activities. It is also the first to present data on the associations between cognitive function as regards attention, manual dexterity, walking ability, socio-demographic factors and coping capacity, as well as on independency in ADL and normal frequency of social/lifestyle activities, in a population-based sample of people with MS.

The results showed that motor functions, such as walking and manual dexterity, and cognitive function, are reduced in the vast majority of people with MS. Other findings were that 50% are independent in personal ADL, but only 30-35% are independent in instrumental ADL and show a normal frequency of social/lifestyle activities.

Disease severity of MS as indicated by the Expanded Disability Status Scale,²¹ was, in the multivariate analyses, found to be the most important factor associated with both motor and cognitive dysfunction. Socio-demographic factors were also found to be important, especially current employment.

Major differences were found by the measures of ADL and social/lifestyle activities in favor of both those with ability in manual dexterity and those with ability to walk without aid in the home environment. The multivariate analyses showed walking ability to be the most important factor to independency in instrumental ADL and normal frequency of social/lifestyle activities. In addition, socio-demographic factors and coping capacity were found to be factors of importance to normal frequency of social/lifestyle activities.

The findings that a majority of people with MS in Stockholm were ambulatory are in line with the results of population-based studies performed in Norway, England and Spain.^{4,7,44} However, when the data was analyzed in greater detail and compared with data from the general Swedish population, the results were discouraging: only 8% showed a normal walking speed. 23 percent of people with MS had a walking speed higher than 1.3 m/s, the pace needed to traverse a crosswalk before the traffic light had changed,¹⁵⁰ a feat of major importance in the urban environment of Stockholm. Moreover, in the context of European standards,¹⁵⁰ which are based on walking speeds greater than 1.5 m/s, only 13% of people with MS in the present study would be able to traverse a crosswalk before the traffic light had changed. On the Lindmark Motor Capacity Assessment,¹¹⁰ 16% had maximum scores on the co-ordination sub-scale, 20% on the balance sub-scale, and 23% on the mobility sub-scale. Ambulation and different forms of public transportation are adversely affected by difficulties with these aspects of motor activity. In addition, when the data on manual dexterity was analyzed in greater detail and compared with data from the general population, the results were also discouraging: only 27% had normal manual dexterity.

A majority of people with MS in Stockholm displayed cognitive function (i.e. verbal memory, as assessed by the Free Recall and Recognition of 12 Random Words Test,¹²²) within normal limits, coinciding with the results of population-based studies performed in Norway, England, and Spain.^{4,7,44} However, when the data were analyzed in greater detail, 55% of people with MS showed normal general cognitive performance (as assessed by the Mini-Mental State Examination Test,¹²¹) and 45% normal attention (as assessed by the Symbol Digit Modalities Test,¹²³), as compared with data from the general population. The impact of reduced attention and manual dexterity on, for example, the use of computers, cell phones and automatic cash-dispensing machines is not known. Furthermore, research is needed into how people with MS might benefit from the use of technical devices designed to compensate for such disabilities.

The percentages of people with MS in Stockholm who were independent in personal ADL were similar to those indicated in other population-based studies,^{4,7,10} although information on independency in instrumental ADL is not available from those studies. The importance of identifying limitations in instrumental ADL in rehabilitation has been highlighted in studies showing that people with MS can be independent in personal ADL but still limited in instrumental ADL.¹⁵¹⁻¹⁵² The most frequently affected ADL and social/lifestyle activity items were “cleaning indoors”, “outdoor transportation”, “household maintenance”, “walking outside”, “heavy housework”, and “gardening”. All these activities may be considered mobility-related and physically demanding.¹⁵³ Exercise therapy has been shown to benefit mobility-related activities and is considered an important part of symptomatic and supportive treatment.⁵⁰ However, the extent to which it is provided to people with MS in Stockholm is not known. Knowledge is also needed on whether improved cardiovascular fitness might affect independency in ADL and the frequency of social/lifestyle activities in which the person participates.⁷⁹ As neither the application of assistive technologies for people with MS nor current recommendations are based on quantitative research,⁸¹ evidence is needed on effective assistive technical devices for people with MS, capable of

improving their independency in ADL and them to participate in self-care, work and social activities.^{50, 154}

Possible explanations for the major variations in the reported percentages of people with MS with reduced social activity, shown in population-based studies based on the Environmental Status Scale,⁴⁻⁷ include differences in some demographic or disease-related characteristics and/or the patients' socio-economic situation. Relative to these studies, higher percentages of people with MS in Stockholm generally showed a lower frequency of social/lifestyle activities. However, it may not be relevant to compare these results with those of other studies, in view of the different methods used, see Table 1. In the other studies, the question asked was whether the person was as socially active as before the onset of MS. This question may be difficult to answer, because of long disease duration and possible changes in interest in social/lifestyle activities as a result of age and level of functioning. A Danish study, with similar demographic and disease-related characteristics as in the population-based study (also including only people with definite MS and 95% living in private households) also reported less impact on social activity, with 45% reporting a lower level of outgoing contacts.¹⁵⁵

In rehabilitation, the patient's perspective plays a very important role.¹⁵⁶ In a recently accepted paper on another part of the Stockholm MS Study, not included in this thesis,⁹¹ the health-related quality of life was found to be widely affected. In particular, the domains "home management", "walking" and "recreation" were affected, which subjectively confirmed the objective results concerning walking, ADL and social/lifestyle activities found in this study. This combination of objective and subjective knowledge may be of great value in planning and organizing physiotherapy and other rehabilitation resources.

5.1.2.1 Subgroup analyses

In previous, non-population-based studies,³⁶ females with MS have performed better than males with MS in cognitive tests. In the population-based study, however, statistically significant differences in cognitive performance between the genders were not detected. Moreover, while females with MS performed the manual dexterity test slightly faster than males with MS, and males with MS walked slightly faster than females with MS, these differences were not statistically significant either. The lack of statistical significance in the study in detecting any differences in cognitive or motor function, independency in ADL and frequency of social/lifestyle activities between the genders may be attributable to the nature of the tests used or to the limited size of the sample.^{118, 157}

The coping capacity score was higher for people with MS than for the general population. Similar results have been found in long-term cancer survivors.¹⁵⁸ It is not fully known to what degree antidepressants and anxiolytics, or attending sessions with counselors and/or psychiatrists, may influence the coping capacity, or to what degree a diagnosis associated with the likelihood of major disability and the struggle to avoid this fate might lend greater meaning to a person's life.¹⁵⁸

People with MS had a higher educational level than the non-MS population in Stockholm. In the literature, results of studies exploring the relationship of level of education to the risk of MS have been inconsistent,¹⁵⁹⁻¹⁶⁰ and the issue remains unresolved.

In Stockholm, many people with MS lived in a private household or alone, despite very severe disability. This was presumably because of the Swedish practice of not requiring a change of residence for the provision of professional personal assistance and home-help service,¹⁰⁴ which may explain why only 5% of people with MS made use of sheltered living. The relationship between the need for and the provision of health services, such as professional assistants and sheltered living, to people with MS and varying levels of disability, has never been investigated in a population-based study.

Limitations in motor capacity, manual dexterity, and walking capacity were as extensive in people with MS who worked full- or part-time, as in people with MS who were unable to work. At the same time, a majority of people with MS with cognitive dysfunction were unable to work. This finding accords with the results of the population-based study performed in England.⁴⁴ We may assume that this reflects not only limitations in intellectual capacity but also the failure of compensatory strategies in cognitively impaired people with MS.^{44, 104} In addition, the percentage of people with MS who were eligible for work and were in fact employed was higher in the study than in other population-based studies performed in Europe,^{4, 6-7, 10, 44} and the United States.⁵ However, a lower percentage of these people with MS were employed full-time. This discrepancy is assumed to reflect the availability in Sweden of subsidized full- and part-time sick leave; indeed, similar percentages of people with MS in Stockholm and northern Sweden were on full-time sick leave.¹⁰⁴

5.1.2.2 *Multivariate analyses*

In the logistic-regression model, disease severity (as assessed by the Expanded Disability Status Scale) was the most important factor associated with normal attention in terms of the Symbol Digit Modalities Test, the ability to perform the Nine-hole Peg Test,¹¹⁵ and the ability to walk 10 meters. The importance of disease-related factors as independent predictors of function has been demonstrated previously.¹⁶¹

Expanded Disability Status Scale has been criticized for problems with sensitivity, reliability, rater-to-rater variability,¹⁴² for inadequately evaluating the upper extremity and cognitive function, and for a mix of impairment and disability measurements.¹ Outcome measures including measures of manual dexterity and ambulation has been recommended, in clinical trials,^{162, 18} Although, the Expanded Disability Status Scale has remained a useful tool for classifying people with MS by disease severity and has been used to assess disability.¹ In this population-based study the Expanded Disability Status Scale was the most important factor associated with attention, manual dexterity and walking. Despite, the drawbacks of the Expanded Disability Status Scale, and development of new measurements e.g. the MS Functional Composite,¹⁴² the

Expanded Disability Status Scale has not been replaced yet and still it is used as the gold standard.

According to the ICF,⁸ environmental and personal factors may impact greatly on an individual's health. The effect of socio-demographic factors and coping capacity on functioning has, to my knowledge, never before been presented in a population-based study of people with MS. A higher level of education was found to be an independent factor associated with normal attention (according to the Symbol Digit Modalities Test). In addition, working full- or part-time and living in a private household were associated with the ability to perform the Nine-hole Peg Test. Working full- or part-time and living with a partner was associated with the ability to walk 10 meters. In addition, associations were found with working full- or part-time and living with a partner and independency in ADL and normal frequency of social/lifestyle activities.

The specific areas of MS that impact on work retention are incompletely understood.¹⁶³ The causal relationship between the associations of working and independency in ADL and normal frequency of social/lifestyle activities, are not known and the explanation for the result may lie in confounding factors. A cross-sectional study,¹⁶³ found that an unemployed group of people with MS had significantly more disability than an employed group as measured by Barthel Index and Expanded Disability Status Scale scores. This result was confirmed in a population-based study from northern Sweden where disease severity (assessed by the Expanded Disability Status Scale) was the most important factor associated with full sick leave.¹⁰⁴ Interviews with the persons with MS also identified areas such as handwriting, hand-to-eye co-ordination, fatigue, balance and walking difficulties as having a major impact on their ability to work and remain in work. In addition, people with MS also described symptoms of MS that impacted on all activities, both in work and at home, e.g. fatigue.¹⁶³ More knowledge is needed to help people with MS return to work or retain employment. Rehabilitation professionals must understand the barriers that result in unemployment and implement interventions to reduce or remove those factors.¹⁶⁴

More detailed knowledge is also needed on the family situation, such as whether living with or without a partner and caring for children etc. and the possible associations of these factors with ADL and frequency of social/lifestyle activities.

Coping capacity has not, to my knowledge, been analyzed in studies on people with MS. In the population-based study, coping capacity was found to be a factor of importance to normal frequency of social/lifestyle activities. A study of people with rheumatoid arthritis suggested that a Sense of Coherence might be understood as a mediator between activity and participation,¹⁶⁵ and so further studies are needed on possible associations with these factors in people with MS.

Walking ability has previously been shown in a survey of stroke patients to be the most important factor to independency in ADL.¹⁶⁶ The strong impact of independency on walking ability in the home environment is an important factor for physiotherapists to consider when prioritizing among treatment options. This is because compelling

evidence has recently been presented indicating that exercise therapy can increase mobility-related functions in people with MS.⁵⁰ Indeed, many of the items included in the Barthel Index and the Katz Extended ADL Index are mobility-related, namely “transfers”; “mobility”; “stairs”; “shopping”; and “outdoor transportation”. Thus, improving mobility-related functions is highly relevant to physiotherapy treatment aiming to make people with MS independent in ADL. Future studies are needed to evaluate different type of interventions designed to improve walking ability, preferably using independency and frequency in ADL and social/lifestyle activities as outcome measures.

Manual dexterity has also been found to be a factor of importance to independency in instrumental ADL in the multivariate analyses. In addition, significantly higher scores in the Barthel Index, the Katz Extended ADL Index and the Frenchay Activities Index were found among those with some manual dexterity, compared to those with no manual dexterity. Instances of effective interventions with effective manual dexterity programs are rare.⁸⁰ A recent study found that exercise increased upper extremity endurance. People with impaired manual dexterity in Stockholm are mostly referred to occupational therapy programs. The aim of occupational therapy is to enable individuals to participate in self-care, work and social activities in their everyday life,¹⁶⁷ but since no evidence exists showing improvements in people with MS, as a result of treatment of manual dexterity, future intervention studies are needed to evaluate effectiveness.¹⁵⁴

Normal attention, (as assessed by the Symbol Digit Modalities Test), was not a significant factor to independency in ADL and to normal frequency of social/lifestyle activities identified in the multivariate analyses. But the univariate analysis showed significantly higher scores in the Barthel Index,¹³¹ the Katz Extended ADL Index,¹³² and the Frenchay Activities Index,¹³⁵ among those with normal attention. Cognitive dysfunction has been shown to be a strong predictor for independency in ADL in the elderly,¹⁶⁸ although there is still a lack of evidence on the effect of cognitive interventions for people with MS.³⁹

As regards people with MS in whom the disease is mildly or moderately severe, it has recently been shown that a six-month exercise program can produce clinically meaningful improvements in walking speed and upper-extremity endurance.⁸⁰ Also, as has been shown in heterogeneous groups of people with MS,⁵⁰ exercise therapy can benefit isometric strength, physical fitness, time needed for transfer, walking cadence and balance time. By contrast, a study of a heterogeneous group of people with MS living independently at home failed to indicate any benefit to cognitive interventions.³⁹ Nevertheless, it has been suggested that rehabilitation programs for people with MS should take into account any cognitive dysfunction that may be present. The availability in Stockholm of rehabilitation services aimed at improving the cognitive function and motor capacities of people with MS will need to be explored in future studies.

5.2 Methodological considerations

5.2.1 Case ascertainment

The accuracy of estimated prevalence from the sample is high, for several reasons: 1) the sensitivity of the MS register to MS is high, since case findings were based on all possible sources of MS diagnosis in Stockholm and collaboration was excellent; and 2) case or diagnostic ascertainment was performed by qualified specialists using clinical information generated by neurologists and diagnostic criteria appropriated in 1998, to ensure that the positive predictive value of registered MS cases would be high. However, it is possible there were losses of MS patients with clinical onset prior to 1999, who may have fulfilled MS criteria,^{11, 12} at later points in time. Another limitation of the sample could be its limited size. Although 211 people with MS provide an appropriate background for differentiating the most important functional MS sub-groups, sample size may not be sufficient to enable a detailed description of primary progressive and/or mild MS, and/or younger people with MS. The population of Stockholm County numbered 1.762 million inhabitants in December 1997; thus, after exclusion of people who were not non-MS registered, not alive, not living in and registered as a resident of Stockholm County, the MS cases identified in this study would correspond to a prevalence of 80/100,000 inhabitants (95% CI 69-92/100,000).¹⁶⁹

The prevalence varies in Sweden from 96 to 154/ 100,000 in Västerbotten,^{103, 104} and the current Swedish MS register,¹⁴⁹ estimates prevalence at 120/100,000. A possible explanation for the low prevalence in this study is that, unlike in the other studies, probable MS wasn't included in the figures, resulting in the figure of 80/100,000.

5.2.2 Sample

The large number of patients in the temporary data pool who failed to meet the criteria for definite MS can be explained by the fact that the Swedish MS Registry,¹⁴⁹ was not yet accessible at the time of the study. Some previous population-based studies made use of the registries of MS patient associations to identify cases.^{6, 44} The Swedish Association of Persons with Neurological Disabilities is an organization for patients with a variety of disorders, and not strictly people with MS. As a result, its registry could not be used in the study to identify cases of definite MS. However, on the basis that the population of Stockholm County amounts to about one fifth of the population of Sweden, and in view of similarities in female-to-male ratio, percentage of people with MS with a primary progressive disease course, mean age at disease onset and mean disease duration between the sample and a prevalence cohort from northern Sweden,^{16, 103-104} the results of the study may be taken as being representative of Sweden in general. Nevertheless, the percentage of people with MS treated with immunomodulatory drugs in the sample (41%) - which was much higher than the percentage in Sweden as a whole (15%),¹⁷⁰ - might limit the feasibility of extrapolating the results.¹⁷¹

Similarities in demographic and disease-related characteristics between this population-based study and others,^{4-7, 10} see Table 1 - including female-to-male ratio,⁵⁻⁷ mean age

at disease onset,⁴⁻⁷ proportion of people with MS with a primary progressive disease course,^{4-5, 10} and mean age at recruitment,^{5, 10} - suggest that the results may also be comparable with and/or applicable to other MS populations in other countries.

5.2.3 Data collection procedure

Performing a pilot study to evaluate the feasibility of a comprehensive evaluation package administered in the home environment was a strength. No pilot study had previously been published regarding evaluation of functioning and disability in a population-based sample of people with MS.

The necessary modifications detected in the pilot study might have limited drop-outs in the tests and interviews included, for example because of depression or the inability to walk 10 meters in a home environment. In addition, if the Mini-Mental State Examination alone had been used, the cognitive results would not have been as detailed as in the population-based study. It was important to standardize the order in which tests and structured interviews were performed, to prevent problems with cognitive dysfunction and fatigue, to make the evaluation as effective as possible and to minimize the time taken. Another potential gain is the possibility of developing concordance between the nurse and the physiotherapist. The most important reason for performing a pilot study before performing a comprehensive evaluation of 10% of people with MS in Stockholm in their home environment lies in the ethical domain.

The main strengths of the population-based study were the use of interviews during home visits and a response rate of 85% among eligible people with MS who were targeted for recruitment in the study. The goal of obtaining valid, detailed information on the functioning of people with MS is best achieved by assessing people with MS in their own home environment, rather than in the hospital environment. This is because of the frequent occurrence in MS of cognitive dysfunction, visual problems and fatigue. In addition, information obtained during home visits can be validated immediately, for example, by watching the person with MS move and act in her/his home and in her/his home environment, in a way that would not be possible during an interview conducted in an out-patient clinic at a hospital, or via a postal survey.

The interviewers were clinically experienced, a nurse and two physiotherapists associated with the MS center under one of the participating neurological departments. However, this could be viewed as both an advantage and a drawback. It may have been considered an advantage that the interviewer was able to understand the symptoms that the persons with MS referred to. But on the other hand this preunderstanding may have worked as a bias, inasmuch as the people with MS would express and describe things differently to the perceptions of the professionals.⁹⁷ Depending on which professional performed the home visit, the people with MS might also have asked, and expressed themselves in more detail, about the subjects they thought would please the professional. However, the data collection method chosen, with well-established, standardized, structured interviews, limited these biases.

5.2.4 Tests and structured interviews

A further strength of this study was the use of non-time-consuming methods that may be administered one by one, simply in a clinical setting by physiotherapist and other rehabilitation professionals.

Despite being an important instrument for demonstrating decline in general cognitive performance, the Mini-Mental State Examination Test,¹²¹ is not sensitive enough to precisely identify cognitive dysfunction in people with MS, compared to other screening instruments.¹²⁵ After the fourth home visit in the pilot study, the comprehensive evaluation was supplemented by the Free Recall and Recognition of 12 Random Words Test,¹²² and the Symbol Digit Modalities Test,¹²³ in order to include higher-sensitivity instruments for cognitive dysfunction. Most people with MS (94-99%) were able to perform all the cognitive tests, and no obvious floor or marked ceiling effects were found, compared to the recommended Paced Auditory Serial Attention Test that has been criticized for floor effects and being stressful to people with MS.^{20, 172} The main reason why people with MS could not perform the Mini-Mental State Examination Test, the Free Recall and Recognition of 12 Random Words Test and the Symbol Digit Modalities Test in the population-based study was severe cognitive dysfunction. The percentages stated above for people with MS who displayed cognitive function within the normal range decline slightly when people with MS unable to perform cognitive tests are included in the denominator: 54% in the Mini-Mental State Examination Test, 83% in the Free Recall and Recognition of 12 Random Words Test and 42% in the Symbol Digit Modalities Test. The results observed in the population-based study of 55% of people with MS below normal in Symbol Digit Modalities Test (attention), indicate that the neuro-psychological impairments in this group are rather specific neuropsychological impairments related to MS.³³⁻³⁵ In the population-based study, people with MS with impaired manual dexterity were asked to respond orally, rather than in writing, in the Symbol Digit Modalities Test, so that people with MS with impaired manual dexterity could be included.

Assessment scales evaluating motor function are rare. The Motor Club Assessment Scale, originally developed for stroke patients, has been modified for people with MS, in the form of the Amended Motor Club Assessment.¹⁷³ In this population-based study, it was considered less suited for use in the home environment, in that the instrument includes a 50 meter walk. It was replaced by the Lindmark Motor Capacity Assessment¹¹⁰, which was also originally developed for use with stroke patients. Only one of the persons with MS in the pilot study scored a maximum in the Lindmark Motor Capacity Assessment. In the population-based study, it was important to the assessment of people with MS with less severe motor dysfunction that the Lindmark Motor Capacity Assessment was supplemented by both Nine-hole Peg Test and time to walk 10 meters. High percentages of people with MS were able to perform the Lindmark Motor Capacity Assessment (99.5%) and the Nine-hole Peg Test (90%), and were able of walk 10 meters (75%) in the study. In the pilot study, 10-meter walks were performed in all home visits. However, we thought an unimpeded distance of 10 meters

may not be available in all forms of living, and so in the population-based study the people with MS were asked to walk 2 × 5-meter distances.¹¹⁹

ADL was measured by the widely used Barthel Index and Katz Extended ADL Index. The Barthel Index was chosen because it is quick and simple and can be administered by self-report. A more elaborate instrument, the Functional Independence Measure, reportedly provides no advantages over the Barthel Index in the assessment of people with MS.¹⁷⁴ The Katz Extended ADL Index was found to be a useful complement to Barthel Index by virtue of the detailed information it provided about people with MS dependence in instrumental ADL: cleaning, shopping, transportation and cooking. The Frenchay Activities Index is not a commonly used instrument in MS studies, but its use appears feasible.¹³⁶ The latter index also includes domestic chores, but in the past has been criticized for excluding such activities as sports and exercise, holidays and caring for children, grandchildren and pets.¹³⁷ In addition, the experience from home visits to people with MS highlighted that it might be important to include, as social/lifestyle activities in people with MS, Internet activity, social activity performed by e-mail contacts and cell phones, shopping for pleasure and going for a walk using an electric scooter for the disabled or an electric wheelchair. The items included in the Barthel Index and the Katz Extended ADL Index, still seem to be representative for evaluation of independency in ADL, but the Frenchay Activities Index needs continuous modification to reflect changes in how social/lifestyle activities are performed in society. Despite the criticism, the combination of measures such as the Barthel Index, the Katz Extended ADL Index and the Frenchay Activities Index provided detailed information not only on whether the people with MS were independent in daily activities, but also on how frequently the various activities were performed. It also eliminated the possible limitations of the apparent marked ceiling effects in the Barthel Index and the Katz Extended ADL index.

There is no gold standard for measuring walking ability in individuals with central neurological pathology. Walking speed is recommended to be the best single measure of walking impairment in people with MS.^{18, 28} No recommendations were available regarding normal ranges in people with MS for the timed 10-meter walk, or step length. Since clinicians generally underestimate the speed and distance needed to function independently within a community environment,¹⁷⁵ the people with MS were compared with a Swedish reference material.¹²⁰ In order not to underestimate disability in the context of the planning and organization of health-care services for people with MS, a lower threshold was chosen, mean minus one standard deviation.

Upper extremity function is the basis for the fine motor skills important to personal ADL activities such as feeding, dressing, and grooming. Only 27 % of people with MS showed manual dexterity within the normal range, although the relevance of these results is limited by the fact that the only general reference population available used had a mean age of 73 years.¹¹⁶ This indicates that 27% may be a high proportion of people with MS with normal manual dexterity, as the mean age, 51 years, in this population-based group is much lower.

When the commonly recommended cut-off score of 24 and below is applied, the Mini-Mental State Examination Test, has been criticized for lack of sensitivity in detecting cognitive dysfunction in people with MS.¹²⁵ In the population-based study, a cut-off score of 27 points and above - as recommended for people with MS in order not to underdiagnose subcortical white matter dementia,¹⁷⁶ - was used. Recommendations for cut-off levels for the Free Recall of 12 Random Words Test and the Symbol Digit Modalities Test for people with MS are not available. The cut-off levels were chosen in order to avoid underestimating the cognitive dysfunction in people with MS.

In view of the young, mid-life population included in the study, the chosen limit for independency in the Barthel Index and the Katz Extended ADL Index was demanding – a maximum score. This decision is open to discussion, since a study suggests that a score of 60 in the Barthel Index represents a dividing line between dependence and independence.¹⁷⁷

Antonovsky recommended the Sense of Coherence,⁵⁵ concept to be examined without dividing the sum of the item values into a low or high Sense of Coherence. Consequently, he never expressed what would be a normal level for a Sense of Coherence. However, numbers of studies report divisions into a low, moderate or high Sense of Coherence.¹⁷⁸ In the population-based study, the cut-off scores used for classifying the subjects into the sub-groups “below normal” and “normal and higher” Sense of Coherence were taken from a study with a sample from Stockholm County.¹⁴¹ 13 % of people with MS could not perform the Sense of Coherence Scale mainly because of cognitive dysfunction. As a result, conclusions about coping capacity are limited to the 85% of the population of people with MS.

5.2.5 Statistical analyses

The explanatory values of the variables included in the multi-analyses of the study ranged from 25% to 56% (Paper III), and 61-64%, (Paper V), indicating the existence of other factors of relevance to the functioning of people with MS. In addition, the cross-sectional design precludes any conclusions regarding possible causal relationships between the variables studied. On that basis, the results should be interpreted taking these limitations into account.

5.3 Ethical considerations

The ethical considerations center on whether it is ethically defensible to make a home visit lasting 2 hours to people with MS and their family caregivers, visits that include tests and structured interviews on functioning, health-related quality of life, resource utilization in health care and patient satisfaction. The clinical experience of the MS Center, Karolinska University Hospital, Huddinge, is that the people with MS demand home visits to discuss their disease. This experience accords with the principle of nonmaleficence, the principle of beneficence, the principle of utility prior.¹⁰⁵ The pilot study showed that all the people with MS were very willing to share with the investigators, their experience of having the disease. This hitherto unavailable knowledge, reported in this thesis, is not expected to harm or expose the people with

MS to unnecessary risk. Indeed, it may benefit people with MS and their family caregivers by the development of more efficient and effective evidence-based forms of physiotherapy treatment, rehabilitation and health care.

In line with the principle of autonomy,¹⁰⁵ all data was handled anonymously and all people with MS were verbally informed by telephone when the time for their home visit had been decided. Next, written confirmation was sent to the person with MS and her/his family caregiver. Each home visit was preceded by verbal and written information to the people with MS and their family caregivers. Then, before informed consent was requested again, the nurse or physiotherapist reassured the person that his/her care would not suffer if he/she chose not to participate. Proxy consent was added when it was established that the person with MS was suffering cognitive dysfunction. In addition, permission from the Data Inspectorate was obtained for the establishment of a database.

Physical risk,¹⁰⁵ in this study was estimated to be low, but it was recognized that the research questions raised may have affected the people with MS and their family caregivers, and made them reflect and wonder about domains they had not been thinking about earlier. To minimize the negative aspect of these psychological risks,¹⁰⁵ a clinical judgement was made at every home visit regarding the need for professional support connected with the home visit of all people with MS and their family caregivers. All the people with MS participating were offered the possibility of telephone contact with the interviewer the day after the home visit, as well as contact with a doctor, a counselor or other professional from the various MS-centers in Stockholm. In view of confidentiality requirements, and to minimize social risks,¹⁰⁵ all the people with MS participating in the study, and all those who declined participation, were asked by mail by the neurologist responsible whether they wanted a nurse or a physiotherapist to inform them about a study they may be participating in. In addition, all the people with MS, or their proxy-caregivers, were asked for permission to calculate the extent of their utilization of health-care resources before the computerized register at the Stockholm County Council was used. To minimize the economic risk,¹⁰⁵ such as additional cost through lost work hours, baby-sitting fees and transportation costs, the people with MS were offered home visits at a time that best suited them e.g. evenings or weekends.

The goal for people with MS is to increase or remain functioning. The goal of the researcher to develop knowledge.¹⁰⁵ It is to be hoped that both these goals are fulfilled in this thesis. The benefit to the people with MS who participated in the studies covered by this thesis is more effective health-related services for people with MS in Stockholm in the near future.

6 CONCLUSIONS

6.1 Pilot study (Papers I-II)

The evaluation package and computerized calculation of health-care resources used in this study is suitable in population based studies as it should provide comprehensive information on impact and consequences of the disease on people with MS, and should contribute to identification of areas in which the provision of rehabilitation and health-care services needs to be improved. In order to capture the impact of MS on functioning, it is appropriate to use a comprehensive evaluation package, in the context of home visits. The majority of the people with MS in this study were able to participate in all parts of the comprehensive evaluation, except for Nine-hole Peg Test and the 10-meter walk. With the help of a spouse or salaried personal assistant, it should be possible to collect for all MS people with MS biographical data and information concerning, ADL, social/lifestyle activities and health-related quality of life. The data collection method, based on home visits, was well accepted by people with MS, irrespective of level of disease severity or form of living, by their spouses and by the salaried personal assistants. A population-based survey using the methods of this pilot study, with minor modifications complimented with utilization of health-care resources, and patient satisfaction—as well as the impact of the disease on family caregivers should provide in-depth information concerning people with MS, and should allow identification of areas in which the provision of physiotherapy and other rehabilitation resources and health-care services needs to be improved.

6.2 Population-based study (Papers III-V)

In this first population-based study, conducted in Stockholm County using data collected during home visits, a majority of people with MS displayed normal verbal memory and were able to perform the Nine-hole Peg test and walk 10 meters. By contrast, only about half of the people with MS in the sample displayed normal cognitive function, and normal manual dexterity and normal walking speed were present in a minority. ADL and social/lifestyle activities were affected in two thirds of people with MS in Stockholm. The most affected items were items that could be classified as mobility-related and physically demanding, underlining the importance of developing and using evidence-based forms of exercise treatment and rehabilitation to increase independency in people with MS in Stockholm.

Disease severity and current employment, was the most important factors significantly and independently associated with both motor and cognitive function. The most important factor significantly and independently associated with independency in ADL and normal frequency of social/lifestyle activities was the ability to walk. In addition, coping capacity was found to be significantly and independently associated with normal frequency of social/ lifestyle activities.

The prevalence of disability in walking ability, manual dexterity, cognitive function and in ADL and social/lifestyle activities is high in PwMS in Stockholm. The most important factor associated with independence in ADL and normal frequency of

social/lifestyle activities was the ability to walk. Knowledge about the high prevalence in disability and the factors associated with disability, together with evidence-based treatments, is essential in: a) setting priorities and in clinical decision-making, b) planning and organizing physiotherapy and other rehabilitation resources, and c) for equity in the distribution of available resources for people with MS in Stockholm.

7 CLINICAL IMPLICATIONS

There is a great need for effective rehabilitation interventions focusing on cognitive function, manual dexterity, walking ability, ADL and social/lifestyle activities for people with MS in Stockholm, as only:

- Cognitive function was normal in 50%.
- Manual dexterity speed was normal in 27%.
- Walking speed was normal in 8%.
- 50 % were independent in personal ADL.
- 30% were independent in instrumental ADL.
- Social/lifestyle activities were normal in 30%.

In addition:

- Disease severity was the most important factor associated with both motor and cognitive dysfunction.
- Ability to walk was the most important factor associated with independency in ADL and normal social/lifestyle activities.
- Normal coping capacity was a factor associated with normal frequency of social/lifestyle activities.

8 FURTHER STUDIES

Family life

More detailed knowledge is needed on associations between independency in ADL and frequency of social/lifestyle and the family situation, e.g. caring for children or adolescents, with or without help from a partner. Many of the domestic activities associated with the care of children is not reflected in standardized measurement of ADL, e.g. changing and bathing the baby/children, collecting children from school, playing with children etc. Independency in instrumental ADL, including preparing food, shopping, cleaning indoors, and washing clothes, may also be determined by the number of family members and/or by housing facilities, e.g. access to sheltered living, professional personal assistance and any home-help service.

Falls

In spite of the frequent use of technical aids and home adaptations, people with MS report falls. It is important to identify any increased risk of falls in a population-based study of people with MS in Stockholm, as this may have medical, social and health-economic implications. To prevent falls in people with MS in Stockholm, detailed knowledge is needed as regards functioning, and the environmental and personal factors of the sub-groups of people with MS known as “fallers” and “non-fallers”.

Rehabilitation

There is a need to identify the most promising evidence-based intervention strategies for the purpose of improving independence and participation in ADL and social/lifestyle activities for different sub-groups of people with MS and to ensure equity in access to such services.

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