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STUDIES OF PEOPLE LIVING WITH MULTIPLE SCLEROSIS IN STOCKHOLM COUNTY

Evaluation of methods for data collection and aspects of functioning and use of health care services

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To my family

ABSTRACT

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system with potential consequences to both the physical and psychosocial dimensions of functioning in afflicted individuals.

Aims

The aim of this thesis was to evaluate the methods of data collection by means of home visits to people with MS (PwMS) using a comprehensive protocol with structured interviews and tests on functioning, health-related quality of life (HRQoL), use of health care services and satisfaction with care, complemented by data collection through a register of use of health care services. Furthermore, the aim was to describe and analyse HRQoL and prevalence of depressive symptoms with respect to sociodemographic and disease-related factors and sense of coherence (SOC), and to describe and analyse use of health care services and satisfaction with care, in a population-based sample of PwMS in Stockholm.

Material and methods

Two separate data collections were performed via face-to face structured interviews and tests in the homes of PwMS, and via a register of health care services. The sample used for the pilot study consisted of 26 purposefully selected PwMS, with different levels of disabilities and modes of living. The sample (n=166) used in the second data collection was population-based, with PwMS identified from a stratified 15% of a pool of 2,129 individuals compiled from lists from various sources, mainly from the departments of neurology in Stockholm County, and subject to a number of inclusion criteria. The comprehensive protocol used at the home visits comprised a number of tests and questionnaires on functioning and HRQoL, including the Sickness Impact Profile (SIP), the Euroqol-5D (EQ-5D), the Beck Depression Inventory (BDI) and questionnaires on the use of services and satisfaction with care. Data on the use of health care services during a three-year period prior to each home visit to PwMS, by means of out-patient and in-patient care, was collected through a computerized register at Stockholm County Council.

Results

The pilot studies showed that the chosen methods for describing functioning, HRQoL, use of health care services and satisfaction with care were feasible for PwMS, irrespective of level of disability or mode of living. The protocol used at the home visits was well accepted by both PwMS and family caregivers, and needed only minor modifications in make them suitable for the population-based study. Further, the register of health care services was considered a reliable source of information for evaluating detailed use of services by PwMS over a three-year period.

In the population-based sample, HRQoL was negatively affected in all dimensions measured, but especially in home management, walking and recreation. HRQoL was poorer in PwMS, including those with milder disease and shorter disease duration, than in the general population. Not working, higher disease severity, and weak SOC were independently associated with major impact on HRQoL.

One fifth (19%) of the PwMS were depressed, as measured by the BDI. Depressed PwMS reported poorer HRQoL than the non-depressed in several aspects. Depressive symptoms were associated with poor memory function, but not with any of the other measures of functioning; measures on attention, walking speed, manual dexterity, ADL, or frequency of social/ lifestyle activities. Higher proportions of PwMS with depressive symptoms were found among those with weak SOC than in those with moderate to strong SOC.
During the study period of three years prior to each home visit of PwMS, high proportions of PwMS used hospital and primary care in parallel, with many departments and services involved. Primary care constituted 54% of all out-patient care and hospital neurology care constituted 20%. A mean proportion of 24% was annually admitted to in-patient hospital care. In all, 73% of the PwMS had assistive advices at home, 45% had home adaptations and 64% had permits for health-related transportation service. Some 37% used informal care from partners. PwMS were in general satisfied with care, but certain areas with which higher proportions of PwMS expressed dissatisfaction concerned accessibility of practical psychosocial advice and support and rehabilitation periods, and the participation of PwMS in planning of their care.

Conclusion
Considering the broad impact on HRQoL in most PwMS and the high prevalence of depressive symptoms, attention to health and functioning - from the perspective of PwMS - is strongly indicated in the management of MS. Further, health-care units engaged in MS management should survey the totality of services available for PwMS when planning and implementing individualized care interventions, since most PwMS will already be receiving care in more than one department or unit. The development of evidence-based, cost-effective health-care services to improve HRQoL and well-being is warranted; i.e., interventions, both somatic and psychological, that optimize health in a comprehensive perspective.

Keywords: depression, health services, multiple sclerosis, patient satisfaction, population, quality of life

SVENSK SAMMANFATTNING

Multipel skleros (MS) är en demyeliniserande sjukdom i centrala nervsystemet som kan medföra både fysisk och psykosocial påverkan på de drabbade individernas funktionsförmåga.

Syfte
Syftet med avhandlingen var att utvärdera metoder för datainsamling innebärande hembesök med tester och intervjuer om funktionsförmåga, hälsorelaterad livskvalitet, användning av hälso- och sjukvårdskontakter och tillfredställelse med vården, kompletterat med registerstudier av användning av hälso- och sjukvårdskontakter. Vidare var syftet att beskriva och analysera hälsorelaterad livskvalitet och förekomst av depressiva symptom, med hänsyn till sociodemografiska och sjukdomsrelaterade faktorer samt känsla av sammanhang, och att beskriva och analysera användning av hälso- och sjukvård och tillfredställelse med vård, hos ett svenskt befolkningsbaserat urval av personer med MS.

Material och Metoder
Två separata datainsamlingar genomfördes (en för pilotstudien och en för den befolkningsbaserade studien) med strukturerade intervjuer och tester i hemmiljö hos personer med MS, kombinerad med användning av ett datoriserat register av hälso- och sjukvård. Urvalet i pilotstudien utgjordes av 26 utvalda personer med MS med olika grad av funktionsnedsättning, kön och boendeform. Det befolkningsbaserade urvalet (n=166) av personer med MS i den andra datainsamlingen utgjordes av ett 15 % stratifierat urval från en lista med 2129 individer, vilka i huvudsak var identifierade från neurologklinikerna i Stockholms län. Vid hembesöken användes ett omfattande studieprotokoll inkluderade tester och strukturerade frågeformulär inkluderande Sickness Impact Profile (SIP), Euroqol-5D (EQ-5D), Beck Depression Inventory (BDI) och frågeformulär om användning av hälso- och sjukvård och tillfredställelse med vården. Ett datoriserat register vid Stockholms läns landsting användes för att beräkna och analysera mängden av öppenvård och slutenvård under en retrospektiv treårsperiod, räknat från varje hembesök till personerna med MS.

Resultat
Pilotstudien visade att protokollet med sammansättningen av frågeformulär och tester var väl genomförbart i hemmiljö hos personerna med MS med olika svårighetsgrad av sjukdomen, kön och boendeform. Hembesöken var uppskattade av personerna med MS och deras anhöriga, och mindre korrigeringar i protokollet var nödvändiga för att kunna användas i en större, befolkningsbaserad studie. Vidare ansågs det datoriserade registret vara en tillförlitlig källa för detaljerad utvärdering av hälso- och sjukvårdsanvändning hos ett urval av personer med MS, under en retroaktiv treårsperiod.

I den befolkningsbaserade studien framkom att den hälsorelaterade livskvaliteten var starkt negativt påverkad på alla områden, och speciellt avseende gångförmåga, skötsel av hem- och hushåll och rekreation och fritid. Den hälsorelaterade livskvaliteten, mätt med SIP och EQ-5D, var påverkad även hos personer med MS med mildare sjukdom

avseende svårighetsgrad, sjukdomsduration och förloppstyp, jämfört med normalbefolkningen. Att inte arbeta, att ha högre svårighetsgrad av sjukdomen och svag känsla av sammanhang var oberoende av varandra förenat med stor påverkan på den hälsorelaterade livskvaliteten.

En av fem (19 %) var deprimerade, mätt med BDI. De deprimerade personerna med MS rapporterade sämre hälsorelaterad livskvalitet än de icke-deprimerade avseende flera aspekter, och depression var även förenat med sämre minnesfunktion. Däremot framkom inga skillnader mellan deprimerade och icke-deprimerade i de övriga testerna/intervjuerna av funktionsförmågan; uppmärksamhet, gånghastighet, finmotorisk förmåga, ADL, eller frekvens av sociala/livstilsaktiviteter. De personerna med MS med svag känsla av sammanhang rapporterade depressiva symptom i högre grad än de med måttlig/stark känsla av sammanhang.

Under en treårsperiod räknat retroaktivt från varje hembesök, framkom att en övervägande majoritet av personerna med MS använde sjukhusbaserad specialistvård och primärvård parallellt. Primärvårdskontakter utgjorde 54% av all öppenvård och neurologisk specialistvård 20%. I medeltal var 24% av PmMS inlagda i slutenvård per år. Av alla personer med MS i studien hade 73% tekniska hjälpmedel hemma, 45% hade fått någon form av bostadsanpassning och 64% färdtjänsttillstånd. Trettiosju procent av personerna med MS använde informell vård från anhöriga. Avseende tillfredställelse med vården framkom att de flesta personerna med MS var nöjda överlag med aspekter såsom bemötande, visat engagemang och förståelse, men områden där högre andelar av gruppen var missnöjda rörde tillgång till psykosocial vård (både psykologisk t.ex. krishantering och praktisk t.ex. råd och stöd i arbetslivs- och utbildningsrelaterade frågor) och MS specifika rehabiliteringsperioder, samt delaktighet i planering av sin vård.

Slutsats
Med tanke på den negativa påverkan på den hälsorelaterade livskvaliteten inom alla undersökta delområden, och den höga förekomsten av depressiva symptom hos personer med MS, är det angeläget att uppmärksamhet riktas mot hälsa och funktionsförmåga ur deras perspektiv i MS vården. Vidare bör enheter i hälso- och sjukvården som möter personer med MS ta hänsyn till helheten av vårdkontakter i planering och genomförande av individuella vårdplaner, eftersom de flesta personer med MS redan har kontakter på mer än en klinik eller enhet. Tillgång till evidensbaserade, kostnadseffektiva vårdåtgärder för att förbättra den hälsorelaterade livskvaliteten och välbefinnandet hos personer med MS behövs, både somatiska och psykologiska sådana, vilka optimerar hälsa i vid bemärkelse.

LIST OF PUBLICATIONS

This thesis is based on the following papers, which are referred to in the following text by their roman numerals.

I. **Gottberg K**, Einarsson U, Fredrikson S, von Koch L, Holmqvist LW. Multiple sclerosis in Stockholm County. A pilot study of utilization of health-care resources, patient satisfaction with care, and impact on family caregivers. *Acta Neurologica Scandinavica* 2002; 106: 241-7

II. 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. *Clinical Rehabilitation* 2003; 17: 289-98.

III. **Gottberg K**, Einarsson U, Ytterberg C, de Pedro Cuesta J, Fredrikson S, von Koch L, Widén Holmqvist L. Health-related quality of life in a population-based sample of people with multiple sclerosis. *Multiple Sclerosis*; 2006: 12: 605-612.

IV. **Gottberg K**, Einarsson U, Fredrikson S, von Koch L, Widén Holmqvist L. A population-based study of depressive symptoms in multiple sclerosis in Stockholm County. Association with functioning and sense of coherence. *Journal of Neurology, Neurosurgery and Psychiatry*. *Published online first 17 July 2006. doi: 10.1136/jnnp.2006.090654*

V. **Gottberg K**, Einarsson U, Ytterberg C, Fredrikson S, von Koch L, Widén Holmqvist L. Use of health care services and satisfaction with care in a population based sample of people with multiple sclerosis in Stockholm County. *Submitted.*

CONTENTS

LIST OF ABBREVIATIONS

ADL	Activities of Daily Living
BDI	Beck Depression Inventory
BI	Barthel Index
CNS	Central Nervous System
CSF	Cerebrospinal Fluid
EDSS	Expanded Disability Status Scale
FAI	Frenchay Activity Index
FRR12RWT	Free Recall and Recognition of 12 Random Words Test
HRQoL	Health Related Quality of Life
KE-ADL	Katz Extended ADL Index
LMCA	Lindmark Motor Capacity Assessment
MMSE	Mini-Mental State Examination
MS	Multiple Sclerosis
9HPT	Nine-Hole Peg Test
PP	Primary progressive
PwMS	People with Multiple Sclerosis
RR	Relapsing remitting
SDMT	Symbol Digit Modalities Test
SIP	Sickness Impact Profile
SOC	Sense of Coherence
SP	Secondary progressive
SCC	Stockholm County Council
WHO	World Health Organization

1 INTRODUCTION

In my clinical work as an MS nurse, meeting people with multiple sclerosis (PwMS), I learned that individual PwMS displayed a wide range of needs; physical, social, cognitive, psychological and educational. I listened to many stories of how the PwMS perceived their symptoms, functioning, and what they thought about care for PwMS in general. Through being able to take part in the conducting of the Stockholm MS Study, I have had a chance to learn more about the impact of MS on functioning, with special regard to PwMS' own perspective and their use of health care services, as well as about methods for investigating this.

1.1 MULTIPLE SCLEROSIS

MS is a neurological, demyelinating disease[1] of the central nervous system (CNS) that is most commonly diagnosed in people who are 20-50 years of age. MS is the most common non-traumatic cause of disability in younger adults, affecting indirectly their families and the society. There is considerable variation in the consequences of MS in terms of clinical features, including course,[2] severity of disability in the long term[3] and type of symptoms.[1,4] The cause of MS is not fully understood. MS is described as a complex disease, in which several factors in the environment act together in a genetically susceptible individual to cause disease.[5]

1.1.1 Pathogenesis

The pathological process in MS is characterized by inflammation, demyelination and axonal degeneration in focal areas in the CNS – "plaques" or "lesions". In the demyelination process, the nerve axons are stripped from the myelin sheath, leading to reduced conduction velocity.[6] A broad range of neurological symptoms, depending on the localization of the plaque in CNS, may thus occur.[1] The pathological process is considered to involve T-cell mediated immunity, where these specialized types of activated white blood cell enter the blood-brain barrier into the CNS.[6] Hypotheses studied for these CNS lesions include autoimmunity[7], environmental factors[5] and primary neurodegeneration[8] which is further complicated by evidence of disease heterogeneity.[9]

1.1.2 Clinical aspects

Most PwMS experience the symptoms and consequences of MS in relapses from the disease-onset, where neurological symptoms develop over days or weeks with durations of at least 24 hours.[10] The recovery may be complete or partial, and usually takes weeks or months. This course of MS, in which relapses occur with a frequency that is unpredictable, is defined as relapsing-remitting (RR) MS.[2] Over time, after disease duration of about 10-15 years, a majority of the PwMS will have entered a progressive phase,[11] where neurological symptoms and disability worsen continuously without recovery: this is secondary progressive MS (SPMS). About 10-20% of PwMS experience the progressive course of disease directly from onset, and this is defined as primary progressive MS.[2,12]

The prognosis is difficult to make for individual PwMS. There are, however, many studies identifying factors that are favourable/unfavourable to the outcome in the long term[3,13], and recent studies suggest *inter alia* that younger age at the onset of RR disease is associated with younger age at reaching disability milestones.[13]

The broad range of symptoms includes, for example, motor disturbances (paresis/ plegia, spasticity, dysartria), sensory disturbances and pain (paraestesia; partial numbness, tingling and vibration sensations, trigeminal neuralgia), coordination and balance disturbances (intention tremor, vertigo), bowel, bladder and sexual disturbances (frequent micturation, constipation), cognitive and psychological disturbances (depression, anxiety), and fatigue.[1,10]

1.1.3 Diagnosis

Determining the diagnosis of MS is a complex procedure, involving clinical neurological examination (neurological symptoms and signs of MS disseminated in time and space, with differential diagnoses excluded), and supporting laboratory tests including lumbar punction (examining the presence of elevated IgG index and oligoclonal bands in cerebrospinal fluid, CSF) and, increasingly used, the MRI[14] (examining the presence of multifocal white matter lesions in the CNS by magnetic resonance imaging).

Due to the complexity of the diagnostic procedure, stringent diagnostic criteria have been developed over the years, of which the most commonly used are the Poser[15] and the McDonald criteria.[16-17] The Poser criteria for diagnosing clinical definite MS require at least two relapses in separate sites of the CNS and separated in time, by evidence from clinical examination and assisted by paraclinical evidence ("positive" CSF or MRI).[15] The McDonald criteria[16-17] take advantage of the developments in MRI techniques (i.e demonstration of active, Gadolinium-enhanced lesions) to show evidence of dissemination in time and space. In these newer criteria, the term "clinically definite" is no longer used.[16-17]

1.1.4 Epidemiology

MS is 2-3 times more prevalent in women than in men.[1] Throughout the world, around 2.5 million people live with MS. The geographical distribution is uneven, and low-, median- and high-risk areas may be identified.[18-19] Scandinavia is regarded as a high-risk area.[20-22] Few epidemiological studies aiming at estimating the prevalence and incidence in Swedish counties have so far been performed, but examples include studies of Värmland[23-24], Gothenburg[25] and Västerbotten[26-27] (Table 1).

Stockholm County covers 6,519 km^2 and comprises 26 municipalities.[28] Within Stockholm County, people live in the city, suburbs and the countryside, including the archipelago. In December 1997, >1,762,000 people were registered as inhabitants of Stockholm County[29] and about 2,000 PwMS were estimated to live there. However, no systematic evaluation of the prevalence of PwMS in the county was performed at the time.

Table 1. Prevalence and incidence of PwMS, based on Swedish studies.

Area	Incidence n/100,000/year	Prevalence n/100,000
Gothenburg[25]*	2.0	96
Västerbotten[26]	5.2	154
Värmland[24]	-	170

1.1.5 Care and rehabilitation

1.1.5.1 Medical therapy

Medical therapy available to PwMS[30-31] includes; a) symptomatic therapies e.g. for spasticity, bladder and bowel problems, neurogenic pain and depression, and b) disease-modifying therapies, all of which aim to slow down the progression of disability, mainly by reducing the number and severity of relapses. The introduction of disease-modifying therapies[32-34] (Interferon beta and glatiramer acetate) has created a need for more frequent clinical follow-up of PwMS, in the view of the need for monitoring of side-effects and overall adherence to therapies.

1.1.5.2 Multidisciplinary care and rehabilitation

Many kinds of services are involved in the care of PwMS besides physician-provided neurological care[35], for example nursing, physiotherapy, occupational therapy and psychological and counselling services. Specialist medical areas other than neurology may also be involved, for example urology and ophthalmology. In recent years, in parallel with the growing groups of PwMS who are treated with the disease-modifying agents[32-34], nurses who specialize in clinical care of MS have become common at the neurological out-patient units at the hospitals.[36-39] Rehabilitation has long formed a corner-stone in the clinical management of PwMS. There is a growing body of evidence that shows the value of rehabilitation to PwMS,[40-44] but few studies have evaluated the effects of different care models and health care services.[39, 44-45]

1.1.5.3 Organization of care for PwMS in Stockholm

In Stockholm County, the Neurology Departments at Karolinska University Hospital, at Huddinge and Solna, and at Danderyd Hospital (hospitals under the management of Stockholm County Council) bear primary responsibility for specialist MS care, but responsibilities at a more detailed level regarding care for PwMS have not formally been defined. In addition, a few private neurologists care for PwMS, but to a limited extent. Nearly all PwMS are therefore believed to have a medical record at one of the above-mentioned departments.

Primary care is also involved in the care of PwMS, mainly in the areas of rehabilitation, home care and health problems not related to MS, but to what extent is not known. Municipalities and/or companies are involved in the provision of home help service, personal assistants and safety alarm systems. Assistive devices are provided by the county council and home adaptations are provided by the municipality, after approval

of individual applications, mainly after assessment and recommendations from occupational therapists and physiotherapists.

1.2 HEALTH SERVICES RESEARCH AND HEALTH NEEDS ASSESSMENT

Health services research is concerned with the relationship between the supply, effectiveness and efficient use of health services and the health needs and demands of the population.[46] Furthermore, health services research investigates the outcome of medical and other interventions from the social, psychological and physical and economic perspectives. "Health is a state of complete physical, psychological, and social well-being, and not simply the absence of disease or infirmity" (WHO).[47] Health care needs (those that can benefit from health care[48-49]), demand for health care (what patients or the population ask for) and the supply of health care overlap, which is important to bear in mind when assessing health needs.[48] Needs for health care may differ among providers (health authorities, health care professionals) and population/patients, and may be influenced by the beliefs and knowledge of individuals, as well as by psychological, socio-economic and cultural factors.[46] Health economists argue that the capacity to benefit will always be greater than available resources, and that a financial approach (examining expenditure patterns) may assist in the procedure of evaluating changes and in priority setting.[50]

Health needs assessment is a systematic method of identifying unmet health care needs in a population and making changes to satisfy these unmet needs[48], and has come to represent the evidence-based approach to the commissioning and planning of health services. Questions to ask when making a health needs assessment include:[48-49] what is the problem and the size and the nature of the problem; what are the current services and what do the patients want?

1.3 THEORETICAL BACKGROUND TO PAPERS I AND II

In describing and measuring health and the consequences of disorders more broadly, variables such as mortality and morbidity rates are not sufficient, in view of their limited capacity to describe functioning and subjective health in individuals who live with chronic, disabling disorders such as MS.[46] In planning a procedure for a health needs assessment[48] of PwMS that aims to answer the first two questions posed in paragraph 1.2 - size and nature of the "problem" and what the current services are and what the PwMS want - there are several aspects to consider in determining what variables to measure and what methods for data collection may be used.[46]

1.3.1 A protocol for health needs assessment in PwMS

1.3.1.1 Describing functioning via a theoretical framework

The international classification of impairments, disability and handicaps[52] (ICIDH) (1980) and the subsequent international classification of functioning, disability and health[53] (ICF) (2001), may be used as a conceptual framework[54] for describing health in individuals or in groups of people (Figure 1). The point of ICF is to provide a common language for describing health and functioning worldwide and to facilitate communication of results among and within countries, and for different populations.[55]

Use of this framework may provide guidance in designing a protocol for evaluation of functioning, and therefore the overall health and disability in PwMS, which also takes into account environmental factors and personal factors.[55-56]

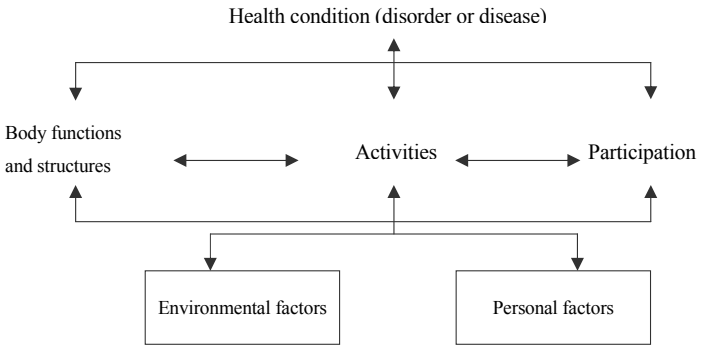

Figure 1. The theoretical model of the interactions between components of ICF[53]

Thus, use of the ICF in a procedure for health needs assessment in PwMS is not confined to the describing of symptoms and impaired body functions or structures, but also includes the overall functioning; activity (execution of tasks or actions, i.e moving, dressing); and participation (engagement in life situations, i.e. interpersonal interactions, recreation and leisure, engagement in work). There is no single questionnaire or test to assess function, activity and participation in PwMS, and a selection of variables, tests and questionnaires may thus be used in a comprehensive study protocol to cover functioning more broadly. Such a protocol may include measures of overall motor and cognitive function and depression, questionnaires on activities in daily living (ADL) and frequency of lifestyle and social activities, environmental factors (such as use of health care services, home adaptations and assistive devices) and personal factors (e.g. gender, age, coping capacity).

Regarding environmental factors, registers of routinely collected information[46] may be applied to obtain information on the use of, for example, health care services by PwMS (visits, telephone contacts, hospitalizations) over a relatively long time period, i.e. more than weeks/months. Thus, it is possible to investigate what sectors and departments are involved in the care of PwMS, and to what extent, but also to obtain greater precision in calculating total numbers of contacts made by PwMS in the health care system in Stockholm. Such a method has not previously been evaluated for PwMS.

The views of PwMS on functioning, health-related quality of life (HRQoL) and satisfaction with environmental factors are not included in the components of ICF.[57] Measures on such variables may also be added to a protocol that aims to describe needs in PwMS from different perspectives (functioning and use of health care services from the perspective of the researchers/interviewers or PwMS), especially since these perspectives may differ from each other.[58-61]

1.3.1.2 Type and setting of data collection in a health needs assessment for PwMS

The types and environments for data collection[62] of functioning, HRQoL, use of health care services and satisfaction with care in research in studies of PwMS may consist, for example, of a) mailed surveys, b) interviews and tests at a hospital clinic, c) interviews and tests in the home environment of PwMS and d) use of registers for calculating overall use of services. Both home visits and mailed surveys have been used as methods for data collection of, for instance, HRQoL in research on Swedish PwMS.[63-64]

Pilot testing of methods for data collection is preferable[65-66], in order to evaluate the possibilities for health needs assessment in PwMS in Stockholm, in a sample that is heterogeneous in terms of disease-related (disease severity) and sociodemographic factors (gender, mode of living), using home visits based on a comprehensive protocol, and the use of a computerized register.

1.4 THEORETICAL BACKGROUND TO PAPERS III, IV AND V

The exploration and analysis of HRQoL, prevalence of depressive symptoms, use of health care services and satisfaction in PwMS are important aspects of assessing overall health care needs in PwMS (as described in 1.3). Definitions of these variables are provided below, including comments on research on the matter, predominantly from population-based studies of PwMS in other countries.

1.4.1 HRQoL, including self-reported functioning (Paper III)

HRQoL[67] is a narrower concept than quality of life, being restricted to self-reported health status, general health and functional ability (Figure 2),[68] and is thus a multidimensional construct.[69] The term HRQoL is often used in clinical research on different patient groups, because the term "quality of life" is too broad in terms of defining what is asked for, as it also incorporates valued aspects of life such as income, freedom and the environment – factors that are not generally considered to fall under the heading of "health", although they may be health-related.[67] The term "self-reported functioning" is defined as a limited part of HRQoL, referring to "health status" and "functional ability" in Figure 2[68].

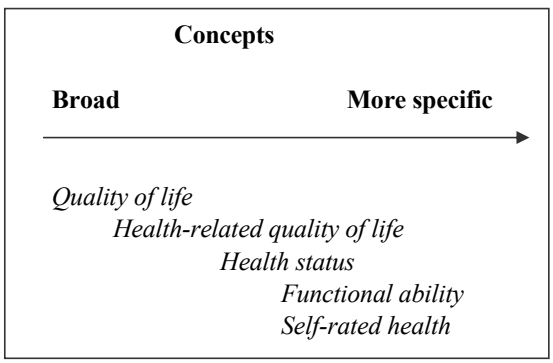

Figure 2. Concepts in quality of life research:
theoretically adopted from Björner JB et al. 1996[68]

There are several ways of evaluating HRQoL, in terms of choice of questionnaire or type of interview.[70] Questionnaires may be generic (such as the Sickness Impact Profile (SIP)[71] and the SF-36 Health Survey[72]), or disease-specific (such as the Functional Assessment of Multiple Sclerosis[73], FAMS, or the Multiple Sclerosis Quality of Life-54 Instrument[74], MSQoL-54).

HRQoL in PwMS has frequently been studied.[75-76] A growing number of studies have used a population-based approach.[77-84] Most of those studies[78-81] have been based on the SF-36 Health Survey[72], showing that HRQoL is negatively affected in PwMS compared to in the general population, and more particularly in "physical functioning" and "vitality".[78-81] Quality of life has also been studied in PwMS, using qualitative methodologies, revealing for example that being "socially active as desired" and "reasonable happy" may be central to HRQoL, irrespective of level of disability.[70] There are, to my knowledge, two published studies[63-64]on HRQoL in Swedish PwMS, although not population-based, showing that HRQoL worsens according to degree of disease severity[64] and that no significant differences exist among groups of PwMS treated or not treated with immunomodulatory therapies.[63]

1.4.2 Depression and depressive symptoms (Paper IV)

The most common symptoms in people with depression are depressed mood, anhedonia (decreased interest and joy in other people and activities), loss of appetite, changed sleep patterns, changed motor function, fatigue (physical and mental), self-accusation and feelings of guilt, difficulties in concentrating and making decisions and suicidal thoughts.[85] To acquire the medical diagnosis of major depression (according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition[86]), at least five of the above mentioned symptoms should have been present on a daily basis over the past two weeks, with the two first symptoms - depressed mood and anhedonia - always being present. Depression is common in the general population (point prevalence of 4-10%)[87], more among women than in men.[85]

Depression may be evaluated by different types of questionnaire or assessment procedure, the Beck depression inventory (BDI)[88] being one of the most commonly used.[87] Many of the symptoms described above are included in the BDI and different cut-off scores have been suggested for identifying depressed individuals. However, as it is not possible to "diagnose" or classify individuals according to DSM-IV criteria based on information solely from the BDI, the term "depressive symptoms"[89] may be used in describing what the BDI measures. Few population-based studies of depression[90-94] have been performed in MS, though reports of depression and its correlation with numerous variables in clinical samples of PwMS are frequent. The population-based studies have all reported a high prevalence of depression or depressive symptoms despite the use of different data collection methods and criteria (16-42%).[90-94] One of these population-based studies used the BDI and reported that 28% of PwMS scored ≥20, indicative of moderate to severe depression.[90]

Depressive symptoms are reportedly associated with a decrease in functioning.[95] In MS, it has been reported that depressed PwMS perform more poorly than the non-depressed in evaluations of cognitive function, for example[96], but reports conflict.[90]

Depressive symptoms in PwMS are also associated with poorer self-reported functioning and HRQoL scores[97] and depressed PwMS have been shown to be more likely to perceive their disability as being greater than their physicians' perception.[59] The prevalence of depressive symptoms has, to my knowledge, not previously been explored in Swedish PwMS from a population-based perspective, nor whether depressive symptoms are associated with functioning or HRQoL.

1.4.3 Sense of coherence (Papers III-IV)

In the salutogenic model, proposed by Antonovsky,[98-99] health is described as a continuum between ease and disease rather than as the binary opposite of disease; the model is thus appropriate for studying people afflicted with chronic disorders. Sense of coherence (SOC) refers to "general resistance resources"—capacities that facilitate coping with stressors and that thereby improve health.[98-99] The SOC describes the degree to which a person views the world as meaningful, comprehensible and manageable. This theory suggest thus that SOC could be regarded as the prerequisite of a person's adjustment to living with disease, in that the stronger the SOC, the more likely a person is to cope successfully with a stressful situation. SOC is suggested to be stable over the life courses of adult individuals in general.[98] but in some studies has been reported to change over time.[102-103] In samples of individuals from the general population and from populations with medical disorders, SOC is related to health status and HRQoL.[99-101] SOC may be viewed as a personal factor, according to the ICF[53] and may be described as "coping capacity".[104]

Though SOC has frequently been studied in Sweden in different samples of patients[105-108], only two smaller reports, not population-based studies on SOC in PwMS could be identified.[109-110] Weak SOC has been found to be associated with a higher prevalence of depression in studies of people with chronic diseases, such as rheumatoid arthritis.[111-112]

1.4.4 Use of health care services (Paper V)

Current knowledge is sparse on what services PwMS use and to what extent, from a population-based perspective, and is mainly based on clinical experience from health care professionals involved in the care of PwMS. A few population-based studies[113-116] have been performed, for example in Belgium[113] and in Minnesota (USA).[114]

In Sweden, PwMS may access health care through their national health insurance coverage (in terms of finance) and laws exist to ensure that severely disabled people are able to live at home with the help of personal assistants.[117] It is possible for a spouse or other relative to be employed, formally, as a personal assistant. Relatives of PwMS may also act as informal caregivers[116], but to what extent is not known, from a Swedish population-based perspective.

1.4.5 Satisfaction with care (Paper V)

If the care needs (physical, psychological, social) experienced from the perspective of patients do not match the care supplied, the risk is that their care will be ineffective.[118-119] This indicates that a high technical standard is not enough in modern society. When basic life and health care needs are met, the requirements increase for the care to be comprehensive.[119] This also includes psychological and social aspects of, for example, living with a chronic disease. Furthermore, patients' demands for participation and involvement in planning and decision-making increase. The participation of patients in planning and taking decisions on care is mandatory under Sweden's Health and Medical Services Act. Satisfaction with care is therefore a central multidimensional concept in determining the quality of care.[120-122] Ware suggested eight different dimensions within which satisfaction should be considered; art of care, technical quality of care, accessibility, finance, physical environment, availability, continuity, efficacy/outcome of care.[123] In research on PwMS, there are examples of studies examining satisfaction with services, but most research in this area focuses on perceived needs[124-128], met and unmet, and not on actual satisfaction with care received.

1.4.6 Health needs assessment in MS and the Stockholm MS Study

Many studies have been undertaken examining the consequences of MS on functioning. These have mainly focused on severity of disability and symptoms in PwMS. Fewer studies are, however, population-based[129-132], aiming to examine a broad range of variables within the concept of functioning [ICF] (see paragraph 1.3.1) in PwMS. Such studies include population-based studies in Ireland [131], Norway,[132] USA (Minnesota)[129] and Spain.[130] The health needs at the present time of PwMS in Stockholm or in Sweden are poorly known. One of the goals of the *Stockholm MS Study* is to provide broad knowledge on the various needs of PwMS, to enable better planning and organization of quality care for this group of people in Stockholm. The project has recently provided knowledge on functioning of PwMS, more specifically on motor and cognitive function[133] and ADL[134], taking disease severity, disease duration and courses into account, and within different sociodemographic subgroups: Examples of results from this population-based study of PwMS[133-134] are provided below:

- Motor capacity was affected in 91%
- Manual dexterity speed was below normal in 73%
- Walking speed was below normal in 92%
- Cognitive function was affected in 50%
- Personal and instrumental ADL were affected (dependency on another person in at least one activity) in 48-70%.
- Social/lifestyle activities were below normal (lower frequency) in 70%

To my knowledge, no population-based study has previously been performed regarding HRQoL, depressive symptoms, use of health care services and satisfaction with care in Sweden or in Stockholm. Knowledge on HRQoL, functioning and satisfaction of care from the perspective of PwMS and what is the current use of health care services, would complement the procedure of health needs assessment[48] in Stockholm, providing a more comprehensive picture. Results from studies in other countries cannot easily be extrapolated to Swedish conditions because of differences in the health-care and

rehabilitation systems. Furthermore, outcome or survey studies of PwMS performed at hospital clinics may include more selected groups of patients.[135] Stockholm County is a defined geographical area with different environments, suitable for the study of a population-based sample of PwMS.

2 AIMS

The overall aim of this thesis was to evaluate the methods of data collection by means of home visits to PwMS using a comprehensive protocol with structured interviews and tests, complemented by data collection through a register of use of health care services. Furthermore, the aim was to describe and analyse HRQoL, prevalence of depressive symptoms, use of health care services and satisfaction with care, in a population-based sample of PwMS in Stockholm.

The specific aims of the pilot studies presented in this thesis, were

- to evaluate the methods for collection of data on health care services, satisfaction with care and impact on family caregivers (Paper I)

- to evaluate the methods for collecting data using a comprehensive protocol administered in the home environment to assess impairment, disability and handicap, in order to explore the consequences of multiple sclerosis (Paper II)

The specific aims in the population-based study of PwMS in Stockholm County, presented in this thesis were:

- to analyze HRQoL with respect to disease-related and sociodemographic factors and to sense of coherence (Paper III)

- to explore the prevalence of depressive symptoms, taking into account disease-related and sociodemographic factors (Paper IV)

- to analyze the association between depressive symptoms and functioning (tested and self-reported) and sense of coherence, respectively (Paper IV)

- to explore and describe the use of health care services and satisfaction with care (Paper V).

3 MATERIAL AND METHODS

3.1 CASE FINDINGS AND SAMPLE OF PwMS − PILOT STUDY

Twenty-six persons with clinically definite MS, from the MS Centre at the Departments of Neurology and Physiotherapy of the former Huddinge University Hospital, were purposefully selected on the basis of variation of gender, level of disability and mode of living, with a view to assembling a suitable pilot study group. Six PwMS were classified by a neurologist, using the Expanded Disability Status Scale (EDSS),[136] (see section 3.3.1.1) as having mild disability (score 0−3.0), while 8 PwMS had moderate disability (EDSS 3.5−6.0) and 12 PwMS severe disability (EDSS ≥ 6.5). Eighteen PwMS were women (69%). Fourteen PwMS were living in flats, 7 in private houses and 5 were in sheltered accommodation.

3.2 DATA COLLECTION IN PILOT STUDY

3.2.1 Home visits to PwMS

Two health care professionals, experienced in the care of PwMS (myself – a nurse – and a physiotherapist), together performed home visits to the 26 PwMS. During the home visits, data were obtained through the use of structured, face-to-face interviews and tests, which were based on a number of selected questionnaires, formerly used in a randomized study of home rehabilitation for patients with stroke.[137]
Specific consideration was taken to the following questions; a) is it possible for PwMS with various levels of disability, including presence of fatigue and neuropsychological impairment, to participate in a comprehensive evaluation at home within the planned limit of 2 hours? b) are the chosen methods of testing and conducting interviews in the home environment or in sheltered accommodation acceptable and sensitive for PwMS in different stages of disease progression?

3.2.2 Computerized register of health care contacts

Information on the use of health care services, both in the context of hospital-based in-patient and out-patient care and in the context of primary care, were collected through the computerized register at Stockholm County Council (SCC). Information on each individual's use of health care was searched for in the three-year period prior to the date of the home-visit. Information was obtained and analyzed regarding total number of contacts at different departments and units within hospital specialist care and primary care, as well as in-patient periods (including length of stay in days) at different hospital departments.

3.3 PROTOCOL OF TESTS AND QUESTIONNAIRES IN THE PILOT STUDY

During the first five home visits in the pilot study, the order of performance of the various parts of the protocol was investigated, based on the interviewers' perception of what was most convenient for PwMS, taking into account possibility for mixing testing and interviewing. During home visits 6 to 26, the tests and questionnaires were

administered in a standardized order by a nurse (RN) or a physiotherapist (RPT), as shown in Table 2.

Table 2. Protocol of tests and questionnaires in the pilot study in order of performance.

Test or questionnaire (performed by RN or RPT)
1) Collection of sociodemographic data (RN)
2) Mini-Mental State Examination (RPT)
3) Free Recall and Recognition of 12 Random Words Test (RN)
4) Symbol Digit Modalities Test (RPT)
5) Sickness Impact Profile (RN)
6) Nine-Hole Peg Test; (RPT)
7) Beck Depression Index (RN)
8) Frenchay Activities Index (RPT)
9) Barthel Index (RN)
10) Katz Extended ADL Index (RN)
11) Lindmark Motor Capacity Assessment; (RPT)
12) Sense of Coherence Scale (RN)
13) Collection of information on the use of health care services and satisfaction with care (RN)
14) Measurement of time taken to walk 10 metres (RPT)
15) Questions concerning frequency of falls and injurious falls (RPT)

3.3.1 Sociodemographic and disease-related information

Information on age, gender, number of children, number of persons living in the same residence, closest relative, nationality, mode of living, level of education, and work status including information on reasons for not working were collected at the home visits from PwMS. Information age, gender, country of origin, level of education and work status was also collected from family caregivers.

Information on disease duration; disease course; ongoing treatment via disease-modifying and symptomatic therapies were collected from the medical records and verified at the home visit.

3.3.1.1 The EDSS

In this thesis, the EDSS[136] was used to assess disease severity. The scale was originally designed to measure disability in people with MS, including evaluations of pyramidal, cerebellar, brain steam, sensory, bowel and bladder, visual and mental functions. Scores for the various functional systems and other measures of function such as walking distance and need for aid when ambulating are then used to determine an overall score for disease severity which ranges from 0 to 9.5 and to 10 which equals dead.

3.3.2 SOC

SOC was evaluated using the short, Swedish version[104] of the SOC scale[138] which has been used in the assessment of individuals with a variety of diseases. The 13 items making up this version of the SOC scale are constructed as statements, which are rated by the respondents on a Likert-type scale from 1 to 7. Both the longer 29-item and the

13-item versions have been used in >16 countries in studies of various samples of people, including samples of people with chronic disorders and cancer.[100-101,139] An example of an item is shown below:

Doing the things you do every day is:

1	2	3	4	5	6	7
A source of deep pleasure and satisfaction					A deep source of pain and boredom	

3.3.3 Cognitive function

Cognitive function - general cognitive performance, verbal memory, and speed of processing/working memory - also mentioned as attention, was assessed using the tests described below. A neurophysiologist assisted in analyzing and classifying the scores.

3.3.3.1 The Mini-Mental State Examination

The Mini-Mental State Examination (MMSE)[140] is a widely used test for screening of general cognitive performance. The MMSE includes 11 items measuring orientation, memory, attention, reading, writing, drawing and the ability to follow verbal and written commands.[ref] A total sum score is calculated ranging from 0 to 30. Reliability and validity are considered good.[141] The test has been frequently used in studies of people with neurological disorders[108, 137]

3.3.3.2 The Free Recall and Recognition of 12 Random Words Test

The Free Recall and Recognition of 12 Random Words Test (FRR12RWT)[142] comprises two parts, i.e. two word lists - a free recall list and a word recognition list, of 12 and 24 words, respectively. Firstly, the person with MS is continuously presented with the 12-word list, one word every 5 seconds read out loud. Respondents are instructed to try to remember the words and then asked to recall as many words as possible immediately after the presentation. Secondly, respondents are asked to answer by yes-no recognition whether the 12 words from the first list were present or not in the second 24-word list. The scores on the two parts are based on the number of right and wrong answers. The test has recently been validated for use in PwMS.[143]

3.3.3.3 Symbol Digit Modalities Test

The Symbol Digit Modalities Test (SDMT)[144] requires the person with MS to use his or her capacity to focus attention quickly and accurately. A key made up of pairings of numerical digits and geometric symbols is presented to respondents. The respondent is asked to verbally substitute numbers for the various geometric symbols according to the key, as many as they can manage from a list within 90 seconds. The score is based on the number of correct responses within the time period.[ref] The SDMT has frequently been used and recommended in MS as an instrument that is sensitive to cognitive dysfunction.[145]

3.3.4 Depressive symptoms

Depressive symptoms were assessed by the BDI.[88] The BDI evaluates 21 symptoms of depression, 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 minimal depression is ≥10 points, on a scale ranging from 0 to 63.[88] The ranges in scores for minimal and moderate to severe depression according to BDI is; minimal depression 10-15, mild-moderate depression 16-19, moderate-severe depression 20-29, severe depression 30-63.[51]An example of an item from the BDI is described below, where the respondent is requested to choose one alternative from the following four statements:

0. I have not lost interest in other people
1. I am less interested in other people now than I used to be
2. I have lost most of my interest in other people and have little feeling for them
3. I have lost all my interest in other people and don't care about them at all.

Reliability and validity are considered good.[141] The BDI has frequently been used in studies of PwMS, including by data collection in the home environment.[146]

3.3.5 Motor function

3.3.5.1 Global motor capacity

A shortened version of the Lindmark Motor Capacity Assessment (LMCA),[147] 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 LMCA, 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. The higher the score, the better the motor capacity. The LMCA is considered reliable and valid.[148]

3.3.5.2 Manual dexterity

Manual dexterity was tested using the Nine-Hole Peg Test (9HPT),[149] which is widely used and has been recommended for the assessment of PwMS.[150] 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 PwMS is considered capable of performing the test if all nine pegs can be picked up and placed in the board within 60 seconds. The NHPT is considered reliable and valid.[151]

3.3.5.3 Walking

Timing of a rapid walk over a distance of 10 metres, recommended in the assessment of PwMS,[150] and considered a reliable and valid test, was used to evaluate walking ability. PwMS were asked to walk 10 metres as rapidly as possible without compromising safety, and the time taken was recorded with a stopwatch. Assistive devices such as a cane or a crutch were allowed, and their use was noted.

3.3.6 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 partner and/or personal assistant.

3.3.6.1 The Barthel Index

The widely-used Barthel Index (BI)[152] measure assesses ADL. The total score range is 0-100, summed up by scores on 10 items; Feeding, Bathing, Grooming, Dressing, Bowels, Bladder, Toilet use, Transfers, Mobility and Stairs. The maximum total scores in the BI 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.

3.3.6.2 Katz Extended ADL Index

Independency in personal and instrumental ADL was measured using the Katz Extended ADL Index (KE-ADL).[153] In the Katz Extended ADL Index, the total range of scores is 0 -10. The maximum score of individuals using the KE-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, Outdoor transportation.

3.3.7 Social and lifestyle activities

The frequency of social/lifestyle activities during the past 3-6 months was measured using the Frenchay Activities Index (FAI).[154] The questionnaire 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. The scoring is mainly based upon the frequency at which a particular activity has been performed. The scores of the individual 15 items vary from 0-3, and the total score ranges from 0 to 45, where 45 indicates a high frequency of social/lifestyle activities. Reliability and validity are considered good.[154] The FAI was originally developed and validated for stroke patients, but it has also been used in studies of people with neurological disorders including MS.[155]

3.3.8 HRQoL

3.3.8.1 The SIP

The Swedish version [156] of the generic, HRQoL questionnaire SIP,[71] which more specifically measures self-reported functioning, was used in structured interviews. The SIP examines the individual's perception of the impact of the disease process on behaviour in everyday life.[51] The questionnaire comprises 136 statements grouped into 12 categories, belonging to two different dimensions or termed "independent";

- Physical dimension categories: Body care and movement, Mobility, Ambulation

- Psychosocial dimension: Emotional behaviour, Social interaction, Alertness behaviour, Communication
- Independent categories: Sleep and rest, Home management, Work, Recreation and pastimes, Eating

The respondents answer "yes" or "no" to each statement, depending on whether the statements are true to them, in relation to their health. Scores are calculated using item weighting to indicate the relative severity of limitation implied by each statement. A total score and two-dimensional scores (physical and psychosocial) are calculated, along with each category score. The scores range from 0 to 100, where 0 indicates the best possible health-related quality of life - or no impact at all on the respondent's self-reported functioning - and 100, a low health-related quality of life or maximum impact on the self-reported functioning. In the studies comprised by this thesis, all statements in the SIP were read out loud to the PwMS and they read the statements themselves simultaneously. Reliability and validity are considered good.[51] The SIP has been used previously to assess HRQoL in a variety of chronic diseases,[157-158] including MS.[159]

3.3.9 Satisfaction with care

A questionnaire on satisfaction with care used in earlier studies of persons with rheumatoid arthritis[118-119] and neurological disorders[160-161] was used in a modified and shortened version consisting of 18 items. The items were constructed as statements, which the PwMS had to agree or disagree with on a 5-graded Likert scale. The questionnaire was based on Ware's taxonomy for patient satisfaction,[123] with the exception of items relating to the physical environment. According to Swedish health-care legislation, the patient's participation in the planning of his/her care is mandatory; against that background, items relating to this issue were included in the questionnaire. PwMS who answered "agree" and "disagree" were classified as "satisfied" and "dissatisfied", respectively, and those who chose in between these alternatives were classified as "uncertain". An example of a statement translated into English is shown below:

It has been very easy to come into contact with health care professionals when it has been required

3.3.10 Use of health care services

Data on resource use, in the context of municipal health care and municipal social care, and on contributions by family caregivers were not available through the computerized register at the SCC. As a result, a protocol based on information gathered during interviews with the PwMS and, where appropriate, a family caregiver and/or personal assistant, was used. This enabled data to be compiled on utilization over the past 6 months of day care, rehabilitation, home-help service, salaried personal assistants and informal assistance from family caregivers. The following variables were also included in the protocol: Information on the use of different kinds of assistive devices in the

areas of personal care, mobility and household management, home adaptations, safety alarm systems, health-related transportation service, driving licenses, disability adaptation of car, and contact with patient organizations. A similar protocol has been used in the past for data collection in the home environment in a study of persons with neurological disorders.[160-161]

Information on contacts with different health-care professionals or services during the past 6 months was also included for the purpose of comparison with the information available through the computerized register at the SCC; total number of health care contacts reported by PwMS was compared to contacts found in the register during the period.

3.3.11 Help from family caregivers and their HRQoL

Data were compiled on use of informal assistance from family caregivers over the past 6 months, defined as assistance with KE-ADL[153], in hours per week. The SIP[156] was used for assessing family caregivers HRQoL (described above in paragraph 4.3.3). If the family caregiver was not able to be present at the time of the patient interview, the questionnaire was left to be filled in later and mailed to the authors.

3.3.12 Falls and injuries

Self-reported frequency of falls and injurious falls over the past three months was recorded (number of falls and consequences). A fall was defined as a subject's unintentional coming to rest on the ground, or at some other lower level.[162]

3.4 CASE FINDINGS IN THE POPULATION-BASED STUDY

The PwMS included in this study were recruited from several sources to attain the highest possible population-based ascertainment. The main sources were the lists of MS patients from the three departments of neurology at the hospitals in Stockholm at the time of the case finding procedure. These were: the former Huddinge Hospital, the former Karolinska Hospital and Danderyd Hospital. The list from Huddinge hospital consisted of:

a) the clinical list of MS patients (n=1,141)
b) the lists of patients from neurologists who met patients with MS but were not participating in the specific activities of the MS centre (n=594)
c) lists from researchers who have included patients with MS or possible MS in their research (n=949)
d) a list from a neurologist with recently diagnosed patients who were not yet registered in the clinical list (n=13)
e) the list of patients with MS from former departments of neurology at Södersjukhuset (which was transferred to Huddinge Hospital in 1997, all medical records were moved) (n=82)

All duplicates were eliminated in the lists. The pooling results of the lists from the three hospitals are shown in Table 3.

Table 3. Patients in the pooled database by gender and hospital, from the three Stockholm hospitals (n=2,129).

Source	Female	Male	All	F/M ratio	Age (SD)	Age range
Danderyd	192	71	263	2.70/1	52 (12)	22-87
Karolinska	326	141	649	2.31/1	48 (14)	17-84
Huddinge	962	437	1399	2.20/1	50 (13.5)	15-92
Total	1480	649	2129	2.28/1	50 (13.5)	15-92

In order to obtain a sample consisting of approximately 200 PwMS and estimating that all individuals would not fulfil the criteria of clinical definite MS - a 15% sample was drawn from the temporary data pool (n=2,129), stratified by hospital, sex and age[163-164] resulting in 321 cases (Table 4).

Table 4. Age and gender distribution in the 15% sample at January 1st 1999 (prevalence date) (n=321).

Source	N	Mean (SD) age	F/M ratio
Danderyd	40	53 (10)	2.64/1
Karolinska	70	48 (13)	2.33/1
Huddinge	211	49 (14)	2.20/1
Total	321	49.5 (13)	2.28/1

After perusal of the medical records and of the records of the Swedish National Population Registry,[165] it was determined that 125 patients failed to fulfil the inclusion criteria (Table 5). One hundred and ninety six PwMS thus fulfilled the inclusion criteria and 166 (85 %) PwMS gave informed consent and agreed to participate.

Table 5. Inclusion criteria in the population-based study of PwMS in Stockholm.

15 % sample from temporary data pool, n=321	Included PwMS, n=196, n (%)	Patients not fulfilling inclusion criteria, n=125, n (%)
Dead	-	30 (24)
Not living and registered as a resident in SC	-	24 (19)
Lacking clinical confirmation of MS diagnosis	-	38 (30.5)
Not informed of MS diagnosis	-	8 (6.5)
Possible MS	-	18 (14.5)
Diagnosis of severe other neurological or psychiatric illness	-	4 (3)
Participated in pilot study	-	3 (2.5)
Declined participation	30 (15)	-
Agreed to participate with home visit	166 (85)	-

3.5 DATA COLLECTION IN THE POPULATION-BASED STUDY

All identified 196 PwMS fulfilling the inclusion criteria of the study received a letter from their treating neurologist with information about the study, giving the PwMS the option of declining contact with clinically experienced health care professionals in asking for participation in the study. The PwMS were then contacted by telephone in order to offer more information and to book a suitable time for a home visit, at a time that best suited the PwMS.

Data were then obtained by these home visits to the PwMS, using structured face-to-face interviews and tests. The interviews were performed by either the nurse (KG) or one of the physiotherapists. The interviews lasted up to two-and-a-half hours and were conducted using a comprehensive protocol in a standardized order, according to the method previously presented in 3.2 and 3.3. The periods in which the home visits took place were September 1999 to August 2000 (102 visits) and November 2001 to July 2002 (64 visits).

3.6 MODIFICATIONS OF THE PROTOCOL IN THE POPULATION-BASED STUDY

The method of using the computerized register at SCC for calculating the use of health care in PwMS was applied with no modifications or additions as compared to the pilot study. The protocol of tests and questionnaires shown in Table 4 and described in paragraph 4.3 was used in the population-based study with the following modifications and additions:

3.6.1 Disease-related information

Evaluation of disease-severity was collected from the medical records, evaluated at the home visit and then verified by a senior neurologist; results from tests (i.e. walking ability and need for walking aid, global motor function, self-reported symptoms) and overall clinical view from the perspective of the interviewers assisted in this evaluation. Data on type of therapy (disease-modifying and symptomatic therapy) including psychotropic medication was collected through the interview with the PwMS, and data was also obtained on the presence of any (self-reported) concurrent diseases.

3.6.2 Cognitive function

Regarding performance of the SDMT, PwMS were asked to respond in writing except for those with MS with motor dysfunction in the upper extremities, who were allowed to reply orally.

3.6.3 Motor function

The 10-metre walk was performed with a turn on a 5-meter course,[165] in view of the fact that a 10-metre distance may not be available in all modes of living.

3.6.4 HRQoL

The median SIP scores (total, physical and psychosocial dimension and 12 category scores) of the PwMS were compared with age-group matched scores from the general population living in Stockholm.[104]

To complement the interview on HRQoL, an additional questionnaire was included in the protocol. The Swedish version of the preference-based measure EuroQol-5D (EQ-5D)[167-168] contains five items (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and the scores are converted to an index value ranging from 0 (death) to 1 (full health).[167] The mean EQ-5D scores of the PwMS were compared with an age-group matched general population in Stockholm[169]

3.6.5 Interview on use of health care services and satisfaction with care

Variables on the use of health care contacts and hospitalizations in the past six months were not included, since this information could be found more accurately in the computerized register at SCC, according to the results of the pilot study. Questions on use of services that is not available through the SCC register (such as home help service) remained in the protocol.

The satisfaction with care questionnaire was subject to modification after the pilot study. Firstly, four items were added regarding information delivered during the early stages of the disease (one item), the perception of the situation when the diagnosis was first given (one item), and the accessibility of psychosocial care (two items). Secondly, the format used for answering items related to the dimension “art of care” and “information on the disease” was changed to the following: the item was divided into several sub-items to create the opportunity to rate “satisfied” or “dissatisfied” concerning several types of health care professionals. After modification, the questionnaire consisted of 22 items, and the PwMS had the option of adding a verbal comment on the care of PwMS in Stockholm.

3.7 CATEGORIZATIONS OF DISEASE-RELATED AND SOCIODEMOGRAPHIC INFORMATION IN THE POPULATION-BASED STUDY

PwMS were classified into the following four disease-severity subgroups, according to the EDSS:[136]

- mildly disabled (0 to 3.0)
- moderately disabled (3.5 to 5.5)
- severely disabled (6.0 to 6.5)
- very severely disabled (≥7.0).

PwMS were further classified into

- disease duration: shorter or longer than 10 years
- disease courses: relapsing remitting (RR), secondary progressive (SP) or primary progressive (PP) MS.

PwMS were also classified into sociodemographic subgroups according to

- gender
- living with partner/alone,
- type of housing (private/sheltered accommodation)
- level of education (basic/university level education)
- work status (working/not working).

In subgroup analysis of work status, PwMS who had retired because of their age were excluded. Living in an apartment for disabled persons supplied by the municipality, in a nursing home or spending alternate weeks at a nursing home and their private residence were classified as sheltered living.

3.8 CATEGORIZATIONS OF FUNCTIONING VARIABLES AND HRQOL IN THE POPULATION-BASED STUDY

3.8.1.1 SIP and BDI categorizations

A total SIP score above or equal to the median SIP scores of the PwMS was classed as major impact on HRQoL.

PwMS in the sample with BDI scores of 13 or higher[170-171] were classed as depressed. In subgroup analyses, BDI cut-off scores of both 13 and 10[51,88] were used.

3.8.1.2 Functioning and SOC categorizations

The cut-off levels used for categorization of below-normal performance in cognitive function,[144,172] walking capacity,[173] manual dexterity[151], independency in ADL,[134] below-normal frequency of social/ lifestyle activities,[174] and weak SOC[104] are described in Table 6. Regarding SOC scores, the PwMS were compared to a Swedish reference population;[104] scores within the lowest reference quartile were classed as weak SOC, and scores above the lowest reference quartile were classed as moderate to strong SOC. PwMS unable to perform the cognitive tests mainly because of severe cognitive dysfunction were not included in the analysis. Inability to walk 10 metres was set at zero metres per second and inability to perform the NHPT was set at zero pegs per second.

Table 6. Cut-off levels used for categorization of below-normal performance of cognitive function, walking capacity, manual dexterity, dependency in activities of daily living, below-normal frequency of social/lifestyle activities and sense of coherence.

Variable	Questionnaire/Instrument	Criteria
Cognitive function	The Symbol Digit Modalities Test	Age-related norms, written or oral reply – 1.5 SD[144]
	The free recall portion of the Free Recall and Recognition of 12 Random Words Test	Age-/gender-related norms, -1 SD[172]
Walking capacity	Walking speed 10 metres (5 × 2)	Age-/gender-related norms, -1 SD[173]
Manual dexterity	The Nine-Hole Peg Test	< 0.5 pegs/second[151]
Activities of daily living	Barthel Index	<100[134]
	Katz Extended ADL Index	Dependent in one or more items[134]
Frequency of social/lifestyle activities	Frenchay Activities Index	Age-/sex-related norms < lower quartile[174]
Sense of coherence	Sense of coherence scale (SOC)	Weak SOC: 13-54 points; moderate-strong SOC: 55-91 points[104]

3.9 STATISTICAL METHODS

3.9.1 Pilot study

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

3.9.2 Population-based study

All statistical analyses were performed using SPSS version 11.5 (Papers III), version 13.0 (Papers IV) and version 14.0 (Paper V) (SPSS Inc., Chicago, Illinois, USA).

Descriptive statistics were used. For comparisons of groups, Student's *t* Test was used for continuous data (walking speed, pegs per second in the NHPT) and the Mann-Whitney test or the Kruskal-Wallis test for ordinal data (for example, ADL and the SIP). For analyses of categorical data (for example, dependent or independent in ADL, depressed or non-depressed), a chi-squared test or Fisher's exact test was used.

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.

The method of structured interview and tests in the home environment provided an opportunity for a clinical validation of many of the variables.

3.9.2.1 Multivariate analyses and consideration of multiple comparisons

In Paper III, probability values of less than 0.05 were considered statistically significant. To account for multiple comparisons of the outcome (SIP - in relation to the independent categories (disease-related and sociodemographic factors and SOC)), a multivariate analysis was performed (Paper III). Initially, associations between potential predictors of the independent variables and the outcome variable SIP (≥ the median total SIP score of the sample of PwMS) was assessed using a chi-squared test or Fisher's exact test. Next, a forward, stepwise logistic-regression analysis was needed to allow the most important predictive factors to be identified. 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.[175]

In Paper IV, probability values of less than or equal to 0.01 were considered statistically significant, to account for multiple comparisons.

3.9.2.2 Comparison with the results of the general population

The Sign Test was applied for the purpose of comparing results from PwMS with the general population. Probability values of less than 0.05 were considered statistically significant.

3.10 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 a database to be established.

In the planning of the studies within this thesis, several ethical considerations were made, for instance;

- Is it ethically defensible to make a home visit lasting approximately 2 hours to PwMS and their partners?
- Is it ethically defensible to conduct tests and interviews including questions on functioning, HRQoL, use of health care services and satisfaction with care?

The clinical experience of the MS Center, Karolinska University Hospital, Huddinge, is that PwMS demand more time and efforts of health care professionals to discuss their care and disease. The home visits within the Stockholm MS study were not considered to harm or expose PwMS to unnecessary risk. Furthermore, the results of the papers included in this thesis will contribute to the base needed for planning and organizing health care services in Stockholm, which may be beneficial for PwMS.

4 RESULTS

4.1 PILOT STUDY (PAPER I AND II)

The mean time needed to perform the home visit was 1 h 57 min (SD ± 19 min) and all home visits were performed within 2½ hours. This did not include the time required for travelling and administration. With the assistance of the family caregivers and/or personal assistants, it was possible to perform the home visit with the comprehensive evaluation protocol for the majority of the participants with MS. The mean (SD) age of the PwMS was 47 years (12), ranging from 28 to 69 years. Half of the PwMS (13/26) were living with a partner. More than half of the PwMS (14/26) were not working (retired or other).

4.1.1 SOC, functioning and HRQoL

High percentages of people with MS participated in the various tests and structured interviews (69% - 100%), with the exception of walking 10 metres where 50% did not perform the test, mainly due to severe motor-capacity problems (Table 7). Reasons for not performing the tests or answering questionnaires included severe visual problems, severe ataxia, severe motor-capacity problems, severe neuropsychological impairments, fatigue, emotional instability, instrument absent from test battery, and/or lack of time during the visit.

Table 7. Participation and performance of tests and questionnaires regarding sense of coherence, functioning and HRQoL in PwMS in the pilot study (n=26).

Test or questionnaire	Participated n (%)	Median (IQR)
Sense of Coherence	20 (77)	73 (66-84)
Mini-Mental State Examination	26 (100)	28 (25-29)
Free Recall and Recognition of 12 Random Words Test, n=22		
Free recall list, below/average/above	21 (95)	8/10/3 [a]
Recognition list, below/average/above	21 (95)	5/11/5 [a]
Symbol Digit Modalities Test, below average/normal, n=22	19 (86)	11/8[a]
Beck Depression Inventory, n=22	18 (82)	6/12[a]
Lindmark Motor Capacity Assessment	21 (81)	189 (108-242)
Walking time, seconds	13 (50)	13 (10-18)
Performance of Nine-Hole Peg Test	19 (73)	9[b]
Barthel Index	25 (96)	85 (65-100)
Katz Extended ADL Index, independency in personal/instrumental ADL	23 (88)	14/7[a]
Frenchay Activities Index	24 (92)	25 (8-33)
Reported falls	23 (88)	13 (57%)[a]
Sickness Impact Profile, total score	26 (100)	24 (15-37)

[a]number of PwMS (%), [b]numbers of PwMS who performed ≤18sec

The results of the tests and questionnaires on SOC, functioning and HRQoL are presented in Table 7. Acceptable variations in scores were observed. Ceiling effects were found for BI and KE-ADL. In this selected hospital-based sample of PwMS, 58% and 38% performed below normal in the SDMT and the free recall part of the RR12RWT, respectively, and 33% were depressed according to the BDI. Furthermore, 47% were able to perform the NHPT ≤ 18 seconds and 70% were dependent in ADL according to the KE-ADL. The most affected categories of the SIP were, in this sample of PwMS, home management (median 54), work (median 62), recreation and pastime (median 43) and ambulation (median 40).

4.1.2 Satisfaction with care

The feasibility of the satisfaction with care questionnaire was found to be good, with PwMS showing a high level of interest in sharing their experiences of MS care. Importantly, PwMS brought up additional issues that had not been covered in the questionnaire, e.g., information and advice in social security matters, psychosocial issues, the importance of receiving information about MS at an early stage of the disease, and issues concerning the handling of the situation when the diagnosis of MS was first given. The questionnaire thus needed certain modifications to suit the purposes of a larger population-based study. One PwMS could not answer the questionnaire because of emotional instability. The mean rate of satisfaction with the various dimensions of care, as measured by the questionnaire was, 70% (range 32%-100%). The dimensions where PwMS were most satisfied were; continuity, art of care and accessibility of health-related transportation services. The dimensions where PwMS were least satisfied were accessibility of physiotherapy, participating in the planning process of their care and information about their disease.

4.1.3 Use of health care services

The method of calculating use of health-care by the 26 PwMS during the 3-year period prior to the home visit (1995-1998), as reflected by entries in the computerized register at the SCC, was feasible in terms of identifying sectors (hospital and primary care), departments (neurology and other) and units/services where PwMS had been in contact formally. All planned variables of use of health care contacts and hospitalizations (i.e length of stay in wards at different departments) could thus be calculated for each PwMS. The proportion of PwMS visiting the emergency department at the hospital was 42% and the proportion of PwMS who had been in contact with different services/health care professionals varied over the years studied; neurologists 65%-96%; nurses working at departments of neurology: 4%-73%; physiotherapists: 27%-54%; primary care physicians: 46%-96%. The method of using the computerized register at SCC was found to be feasible and sufficiently detailed for a population-based study.

The comprehensive protocols used for collecting information on health-related services, assistive devices, home adaptations and transportation service were found to be feasible for use during home visits and sufficiently detailed as they were carried out—in particular because home adaptations and assistive devices were clearly visible to the investigators, and because PwMS could easily discuss and exhibit their current home environment.

One PwMS used day care, 6 PwMS (23%) had undergone rehabilitation outside their homes, 3 PwMS (12%) used a home-help service and 6 PwMS (23%) used personal assistants. Twenty of the 23 PwMS interviewed (91%) used 9 different assistive devices, 16 PwMS (67%) had received home adaptations and 19 PwMS (76%) had permits for a health-related transportation service.

4.1.3.1 Comparison of methods for evaluating use of health care services

During the interview, PwMS were able to report 93% of the total contacts from the past half-year entered in the computerized register. Twenty-one PwMS (81%) reported a total number of contacts during the past 6 months that differed from the number recorded in the register. PwMS remembered well what health care contacts they had, but to a lesser extent the exact numbers of contacts the past 6 months.

4.1.4 Family caregivers

Sixteen PwMS (62%) lived together with a spouse or partner. Twelve of them (75%) accepted being interviewed about demographic characteristics. One adult daughter of a female PwMS, who did not live with her mother, was also interviewed. A mean of 19 hours per week (range, 2−45) was spent by informal family caregivers (n=11) in helping the PwMS with personal or instrumental ADL, highlighting the importance of including evaluation of the input of the family caregivers.

4.1.4.1 HRQoL of family caregivers

Nine of 13 family caregivers (69%) accepted having their subjective dysfunction evaluated by the SIP. The SIP was found to be useful in determining the HRQoL of family caregivers of the PwMS. However, it may be necessary to include additional items in a separate questionnaire, in order to assess the impact on daily life of caring for and living with a PwMS. One third of the family caregivers participated in the study by returning the SIP by post. The overall mean SIP score for family caregivers was 2.6 %, indicating modest subjective dysfunction.

4.2 POPULATION-BASED STUDY (PAPER III, IV AND V)

Visits were performed in the homes of PwMS situated in the various environments of Stockholm County; in the city, in the suburbs, in the countryside or on islands of the archipelago; in apartments, private houses, on farms or in forms of sheltered living. 16/166 (10%) required two visits in order to complete all tests and structured interviews.

4.2.1 Sample characteristics

The sociodemographic and disease-related information is specified in Table 8.

Table 8. Sociodemographic and disease-specific information on the sample of people with multiple sclerosis (PwMS) in Stockholm (n=166)

Variable	PwMS n (%)
Age when surveyed (years)	51 ± 12[a] (19–79)[b]
Women/Men	118 / 48 (71/29)
Living with a partner	102 (61)
Type of housing/sheltered accommodation	11 (7)
University level education	66 (40)
Working	68 (41)
Swedish origin	151 (91)
Age at disease onset (years)	31 ± 10[a] (11–58)[b]
Disease duration (years)	19 ± 11[a] (1–55)[b]
Disease severity (EDSS)	
Mild (0–3)	42 (25)
Moderate (3.5–5.5)	35 (21)
Severe (6–6.5)	47 (28)
Very severe (>7)	42 (25)
Disease course:	
Relapsing/remitting	70 (42)
Secondary progressive	80 (48)
Primary progressive	16 (10)
Ongoing pharmacological treatment when surveyed:	
Disease modifying	68 (41)
Symptomatic treatment	129 (78)
Antidepressants	18 (11)
Weak sense of coherence[c]	15 (10)

[a]mean /SD), [b]range, [c]based on 145 people with MS

4.2.2 Paper III - HRQoL

One hundred and fifty two PwMS completed the EQ-5D, giving a median (IQR) of 0.66 (0.15-0.74). One hundred sixty-five PwMS completed the SIP (one PwMS declined participation). Seven PwMS (4%) scored zero on the SIP (meaning no reported impact from MS in the various categories). The median (IQR) SIP score was 24 (11-33) and scores ranged from 0 to 57. The most affected SIP categories were home management, ambulation and recreation and pastime (Fig. 3).

4.2.2.1 HRQoL in PwMS versus general population

In comparison with the age-matched Swedish population, the PwMS reported significantly poorer HRQoL ($p < 0.05$) according to both the EQ-5D index value (Figure 6) and all SIP scores including SIP categories and EQ-5D dimensions. Using the SIP scores in all categories, PwMS of mild severity according EDSS 0–3; RR course of MS; and disease duration of less than 10 years also reported significantly poorer SIP scores ($p < 0.001$) than the Swedish population group, except for in the SIP category “eating”.

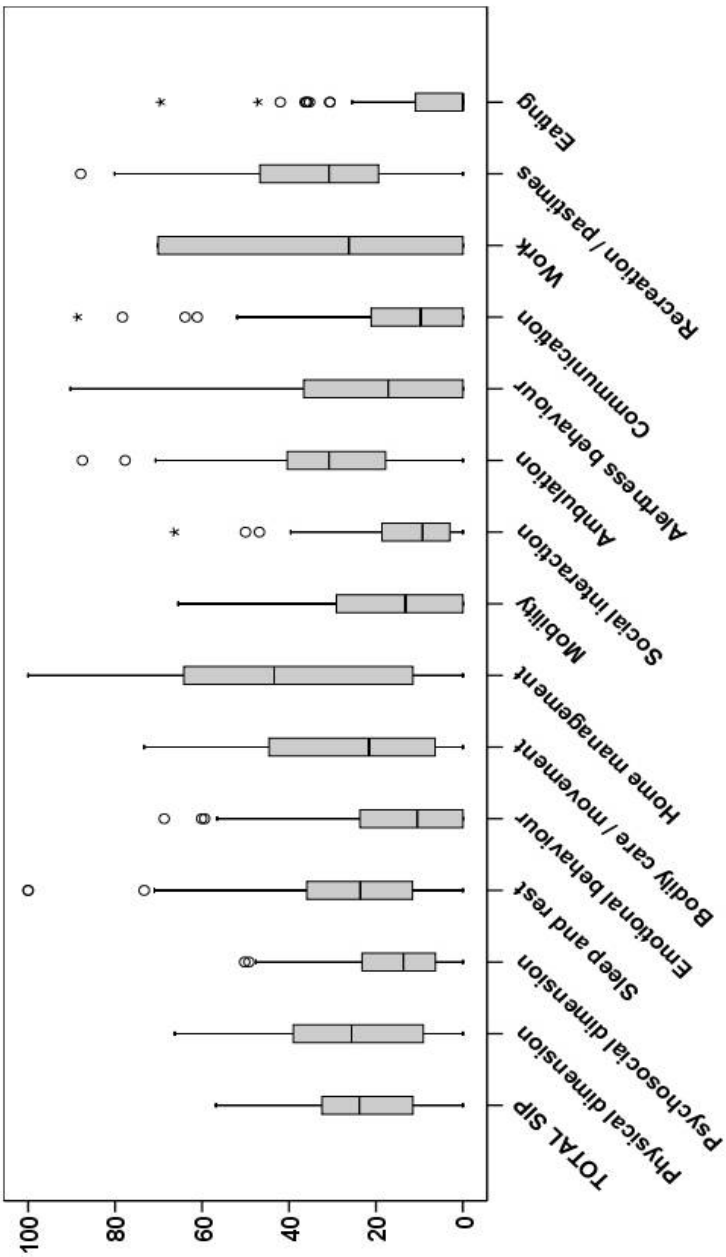

Figure 3. Boxplots of Sickness Impact Profile scores of people with multiple sclerosis in Stockholm (n=165).

4.2.2.2 Association with sociodemographic and disease-related factors

There were no significant associations between EQ-5D or SIP scores and gender, level of education or living with/without a partner (other than in one SIP category, communication, where men scored lower than women). Significantly poorer SIP and EQ-5D scores were reported by PwMS who were not working (PwMS aged 65 or above were excluded from these analyses) or who were living in sheltered accommodation, compared to those working or in private accommodation (Table 9).

Table 9. Difference in EQ-5D index scores and SIP scores (expressed as p-values) among the subgroups of sociodemographic factors.

SIP and EQ-5D scores	Private/ sheltered accom-modation	Working / not working
EQ-5D index score	0.003	<0.001
Total SIP	0.025	<0.001
Physical dimension	0.047	<0.001
Psychosocial dimension	0.096	<0.001
Ambulation	0.573	<0.001
Mobility	0.102	<0.001
Body Care /Movement	0.013	<0.001
Social interaction	0.184	<0.001
Alertness behaviour	0.053	0.024
Emotional behaviour	0.146	0.392
Communication	0.001	<0.001
Sleep and rest	0.364	<0.001
Eating	0.008	<0.001
Work	0.140	<0.001
Home management	0.008	<0.001
Recreation and pastime	0.263	<0.001

PwMS with severe MS, a progressive course of MS and a disease duration of more than 10 years reported poorer EQ-5D and SIP scores than PwMS with less severe MS, a RR course of MS and disease duration of less than 10 years, with the exception for certain SIP categories of a psychosocial nature (Table 10). Boxplots of total SIP scores and physical and psychosocial dimension scores among disease-severity subgroups, by EDSS groups from mild to very severe are shown in Figure 4.

4.2.2.3 HRQoL – association with SOC

PwMS with weak SOC (13-54 points on SOC scale) reported significantly worse SIP scores in the psychosocial dimension score ($p = 0.005$) and in the categories emotional behaviour ($p < 0.001$) and alertness behaviour ($p=0.042$) than those with moderate to strong SOC.

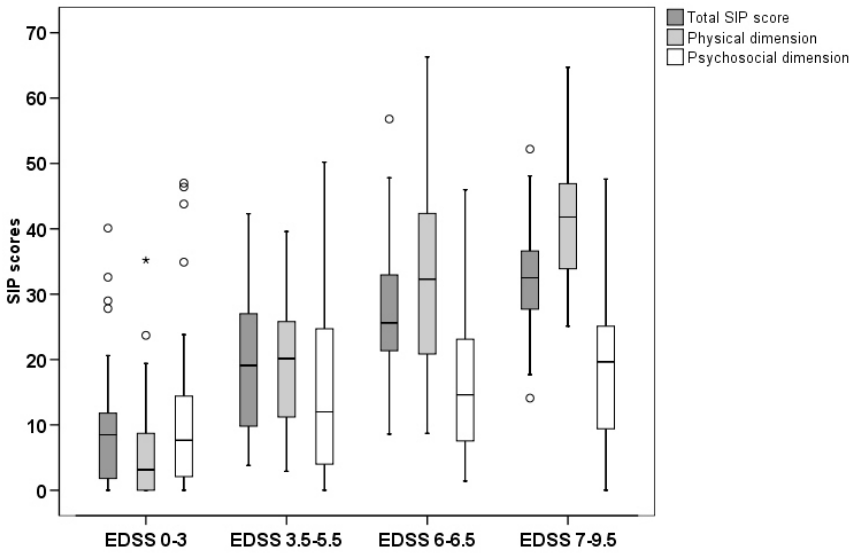

Figure 4. Boxplots of total SIP scores and physical and psychosocial dimension scores among disease-severity subgroups, by EDSS groups from mild to very severe.

Table 10. Difference in SIP and EQ-5D scores (expressed as p-values) between the subgroups of disease-related factors.

Variable (SIP score)	Disease severity (EDSS)	Disease course (RR, SP, PP)	Duration (≤10 years / > 10 years)
EQ-5D index score	<0.001	<0.001	0.011
Total SIP	<0.001	<0.001	<0.001
Physical dimension	<0.001	<0.001	<0.001
Psychosocial dimension	<0.001	0.086	0.203
Ambulation	<0.001	<0.001	0.001
Mobility	<0.001	<0.001	<0.001
Body Care / Movement	<0.001	<0.001	<0.001
Social interaction	<0.001	0.316	0.118
Alertness behaviour	0.320	0.762	0.978
Emotional behaviour	0.435	0.760	0.511
Communication	<0.001	<0.001	0.005
Sleep and rest	0.010	0.124	0.399
Eating	<0.001	<0.001	<0.001
Work	0.003	0.067	0.201
Home management	<0.001	<0.001	<0.001
Recreation and pastime	<0.001	0.009	0.015

4.2.2.4 Multivariate analyses of HRQoL

The multivariate analysis showed that not working versus working; severe to very severe disease versus mild disease; and weak SOC versus moderate to strong SOC were independent predictors of major impact on HRQoL (Table 11).

Table 11. Multivariate analysis[a] of predictors for major impact on HRQoL according to Sickness Impact Profile score ≥ 24 in People with Multiple Sclerosis in Stockholm

Variable	OR (95 % CI.)	p-value
Weak versus moderate to strong SOC	5.27 (1.22–22.77)	0.026
Not working versus working	12.70 (4.17–38.69)	<0.001
EDSS		0.004
Moderate versus mild	2.63 (0.59–11.80)	0.206
Severe versus mild	6.00 (1.54–23.33)	0.010
Very severe versus mild	15.41 (3.24–73.24)	0.001

Prediction Model Characteristics: $R^2 = 0.57$, Hosmer and Lemeshow Test p-value = 0.926 and overall correct classification = 89.2 %. [a]Model based on 145 PwMS as Sense of Coherence score is missing for 21 PwMS

4.2.3 Paper IV − Depressive symptoms

One-hundred and forty-nine PwMS answered the BDI questionnaire. The median (IQR) score was 7 (3-12). Nine PwMS (6%) scored zero points. Twenty-eight (19%) were depressed (BDI ≥ 13) and 59/149 (40%) scored ≥ 10 points. The five most commonly reported items were Fatigability (82%), Loss of libido (54 %), Sleep disturbance (51%), Work inhibition (46%) and Irritability (46%) (Figure 5).

4.2.3.1 Association with functioning

Regardless of whether a BDI cut-off score of 10 or 13 was used, there were no significant differences between depressed and non-depressed PwMS in terms of percentage with cognitive dysfunction (SDMT), below-normal walking capacity or manual dexterity; percentage dependent in ADL; or percentage with a below-normal frequency of social/lifestyle activities . With a BDI cut-off score of 13, a higher proportion of PwMS with below-normal memory function according to FRR12RWT were found among the depressed (29%) than among the non-depressed (9%) (p =0.005).

Depressed PwMS (BDI ≥ 13) had poorer SIP scores mostly in the categories of a psychosocial nature (sleep and rest, emotional behaviour, social interactions, alertness behaviour, and work), and in addition, depressed PwMS (according to BDI ≥ 10) had significantly poorer HRQoL in the categories Mobility and Ambulation (Table 12).

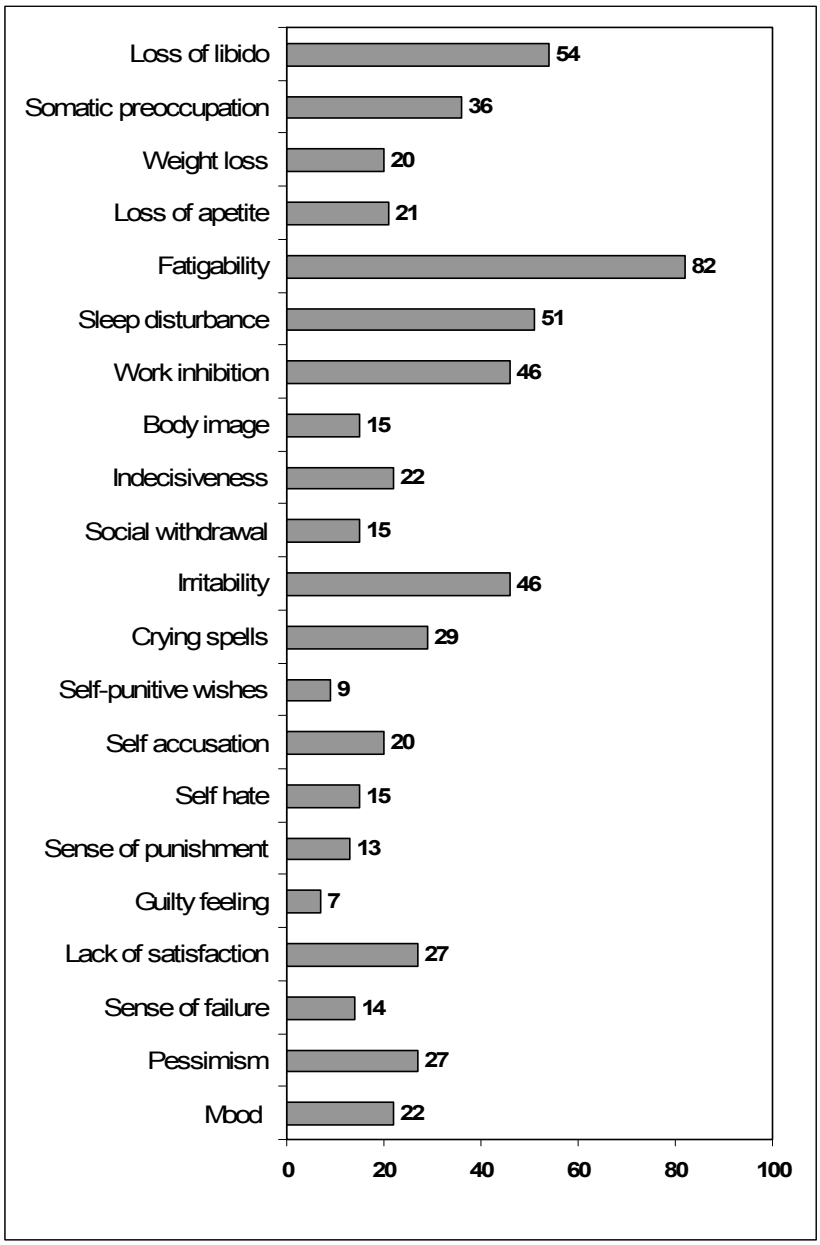

Figure 5. Percentages of People with Multiple Sclerosis who scored 1-3 on the Beck Depression Inventory items, indicating presence of depressive symptoms (n=149).

Table 12. Median (interquartile range) Sickness Impact Profile (SIP) scores in depressed and non-depressed People with Multiple Sclerosis (n=149) in Stockholm.

Variable	Depressed BDI ≥ 10	Non-depressed BDI <10	P
SIP total score	28 (18-34)	17 (7-28)	0.001
Physical dimension	28 (13-43)	20 (4-34)	0.018
Psychosocial dimension	21 (14-29)	8 (3-14)	<0.001
Sleep and rest	34 (21-46)	19 (10-34)	<0.001
Emotional behaviour	25 (11-43)	0 (0-11)	<0.001
Body care and function	22 (11-41)	15 (2-37)	0.045
Home management	43 (21-67)	34 (0-58)	0.044
Mobility	17 (9-27)	6 (0-25)	0.004
Social interaction	17 (7-25)	5 (0-12)	<0.001
Ambulation	31 (24-49)	24 (10-40)	0.004
Alertness behaviour	29 (10-53)	10 (0-21)	<0.001
Communication	10 (0-21)	9 (0-19)	0.087
Work	45 (8-70)	27 (8-70)	0.610
Recreation and pastimes	32 (22-49)	29 (9-41)	0.016
Eating	5 (0-11)	0 (0-6)	0.147

4.2.3.2 Association with sociodemographic and disease-related factors

Depressive symptoms were equally common (proportions of PwMS scoring > 9 or ≥13) among PwMS in the disease-related subgroups. Boxplots of BDI scores in disease-severity subgroups are shown in Figure 6. Depressive symptoms were also equally common among those with shorter and longer disease duration and among those with a RR, SP or PP disease course. No association was found either between the prevalence of depressive symptoms or any of the sociodemographic factors.

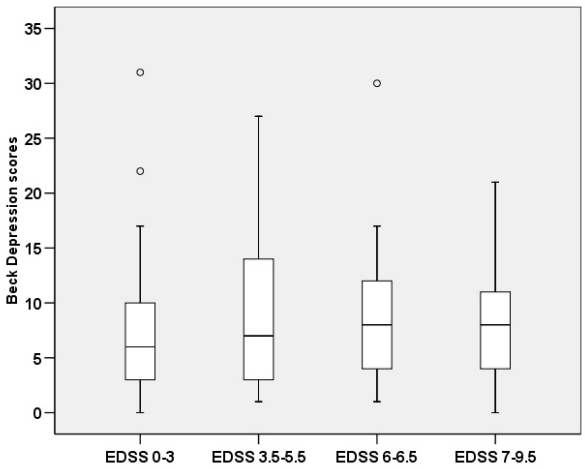

Figure 6. BDI scores of PwMS among disease severity subgroups, by EDSS group mild to very severe (n=149).

4.2.3.3 Association with SOC

Higher percentages of depressed PwMS were found among those with weak SOC than among those with moderate to strong SOC (using BDI ≥ 13; 53% vs. 15%, $p < 0.001$).

4.2.4 Paper V - use of health care services and satisfaction with care

All PwMS except one accepted having their health care contacts collected from the computerized register and analyzed according the method planned.

4.2.4.1 Use of out-patient care

Analyzing what proportion had any contact with a certain care sector or department revealed that the great majority (92%) had been in contact with out-patient departments of neurology (Table 13 and 14) and over two thirds had been in contact with other hospital out-patient departments (76%).

Table 13. Number (%) of People with Multiple Sclerosis (n=165) who had any type of out-patient contact* during the study period, in ranking order within hospital out-patient care.**

Department	Mean n/year	Total, three years n (%)
Hospital		
Neurology	131 (79)	152 (92)
Emergency room	52 (32)	102 (62)
Urology	28 (17)	46 (28)
Surgery	20 (12)	41 (25)
Ophthalmology	19 (12)	39 (24)
Physiotherapy	21 (13)	38 (23)
Medical social workers' counselling	17 (10)	32 (19)
Women's	10 (6)	23 (14)
Occupational therapy	10 (6)	21 (13)
Oncology	10 (6)	17 (10)
Psychiatry	6 (4)	14 (9)
Medicine	6 (4)	14 (8.5)
Orthopaedics	17 (10)	13 (8)
Endocrinology	7 (4)	9 (5.5)
Rehabilitation	3 (2)	8 (5)
Dermatology	2 (1)	7 (4)
Haematology	3 (2)	6 (4)
Infection	1 (1)	3 (2)
Psychology	1 (1)	4 (2)

*Contacts i.e. appointments, home-visits, telephone consultations or other that render individual documentation in the records of PwMS. **Departments with less than 1 percent of PwMS during study period not listed.

Table 14. Number (%) of People with Multiple Sclerosis (n=165) who had any type of out-patient contact* during the study period, in ranking order within primary care.**

Department	Mean n/year	Total, three years n (%)
Primary care, total	117 (71)	137 (83)
Physicians	82 (50)	113 (68)
Nurses	38 (23)	61 (37)
Physiotherapy	33 (20)	56 (34)
Occupational therapy	28 (17	47 (28.5)
Home-care	11 (7)	22 (13)
Gynaecology/midwifery	9 (5)	17 (10)

*Contacts i.e. appointments, home-visits, telephone consultations or other that render individual documentation in the records of PwMS.** Departments with less than 1 percent of PwMS during study period not listed.

During the study period, one PwMS had no health care contacts at all and 33 (20%) PwMS had more than 100 contacts (101 – 525). In total, the 164/165 PwMS had altogether 10,275 health care contacts in primary and hospital out-patient care. The mean annual number of out-patient contacts per PwMS was similar during the three years (18-22). Over half (54%) of the out-patient contacts were within the primary care sector and one fifth (20%) of the contacts were at departments of neurology in hospitals (Figure 7). The large proportion of primary care contacts consumed by PwMS was mainly home care (25%) and appointments or telephone consultations with physiotherapists (25%) or with physicians (20%). PwMS who were aged ≥ 65 years (13%) and those who reported concurrent health problems had used more primary care than those without concurrent health problems and of lesser age.

Over half of the contacts within departments of neurology (59%) comprised telephone contacts, administration of referrals and drug prescriptions administered by physicians (41%) and contacts with nurses (18%) (Figure 8). The remaining 41% of contacts were appointments with physicians. The mean (SD) annual number of appointments with physicians per PwMS within departments of neurology was 1.7 (range 0-11). The highest numbers of out-patient contacts at other hospital departments were for physiotherapy (23%), urology (11%) and counselling service by medical social workers (10%).

4.2.4.2 In-patient care

Seventy-seven PwMS (47%) had been admitted to hospital in-patient care (mean proportion per year 24%). The annual and total mean number of in-patient care days was 2.8 and 8.3, respectively. The highest proportion of in-patient care days was spent in wards of departments of neurology (30%), followed by department of geriatrics (17%) and departments of medicine (11%).

4.2.4.3 Use of self-reported health care services

About one third (32%) used home help service or personal assistants. In all, 61 PwMS (37%) used informal care from partners. The mean (SD, range) number of hours spent by partners or spouses per week was 20 (24, 1-116). High proportions of PwMS made use of different services, for instance permits for health-related transportation service, assistive devices and adaptations made at home by help from the municipality (Table 15). In the last year prior to the home-visit, thirty-six PwMS (22%) reported that they had been admitted to a specific rehabilitation unit organized externally from SCC.

Table 15. Use of health care services; home help service, personal assistants, transportation and other resources in people with multiple sclerosis in Stockholm (n=166).

Type of service	n (%)
Home help service or personal assistants	53 (32)
Home help service	28 (17)
Personal assistants	32 (19)
Help from spouses or partners	
Personal ADL	19 (11)
Instrumental ADL	51 (31)
Other	47 (28)
Total	61 (37)
Help from other persons, unspecified/unsalaried	21 (13)
Health-related transportation service	107 (64)
Home adaptation	75 (45)
Safety alarm system	46 (28)
Assistive devices	122 (73)
Economic help to purchase or adapt car, n=164	33 (20)

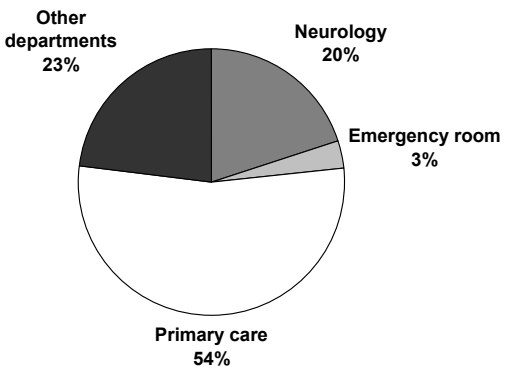

Figure 7. Distribution of all care contacts (n=10,275) among different care sectors in People with Multiple Sclerosis in Stockholm (n=165) during the study period.

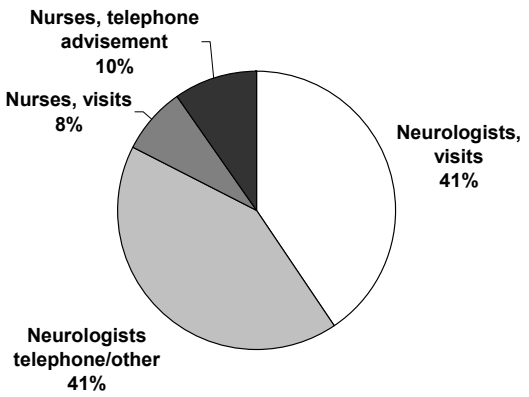

Figure 8. Distribution of specialist neurology care contacts (n=2050) in people with multiple sclerosis in Stockholm (n=165) during the study period

4.2.4.4 Satisfaction with care

One-hundred and sixty-one PwMS (97%) participated in the structured interview regarding satisfaction with care, and one of them reported "manifested need" only regarding "information about the disease from physicians".

The great majority of PwMS were of the opinion that it is very important to receive early knowledge of the diagnosis, but over half of them (55%) expressed dissatisfaction with the situation in which they first received the MS diagnosis. The majority were satisfied with general information on MS (57-90%) and with the art of care (sympathy from or engagement of staff and kind treatment) (63-99%) from various health care professionals.

Of those who expressed a need for accessibility of different services (42-84%), more than half of the PwMS were satisfied (64-90%) other than in the cases of: accessibility of rehabilitation (42 %), psychosocial counselling (48%) and information and advice on social insurance matters, work and education-related rehabilitation (27%) (Table 16).

Regarding the efficacy or outcome of care, high proportions of PwMS (77-85%) were satisfied, but only about half of those who wanted to participate in the planning of their care (52%) perceived that they actually had participated (Table 16).

Table 16. Satisfaction with care regarding accessibility, continuity, finances, efficacy and participation in planning, by People with Multiple Sclerosis in Stockholm (n=161).

Dimensions and related matters	Manifested need*	Satisfied/Uncertain/ Dissatisfied	
	n (%)	n	%
Accessibility			
Physiotherapy	136 (84)	93 / 9 / 34	68 / 7 / 25
Occupational therapy	98 (61)	63 / 12 / 23	64 / 12 / 24
Rehabilitation periods	113 (70)	47 / 8 / 58	42 / 7 / 51
Assistive devices	113 (70)	103/5/5	91 / 4.5 / 4.5
Workplace adaptation	67 (42)	44 / 6 / 17	66 / 9 / 25
Health-related transportation service	108 (67)	97 / 2 / 9	90 / 2 / 8
Home adaptations	89 (55)	71 / 9 / 9	80 / 10 / 10
Home help service or personal assistants	68 (42)	48 / 4 / 16	71 / 6 / 23
Psychosocial support/ counselling	85 (53)	41 / 4 / 40	48 / 5 / 47
Advice/support in social insurance/work rehabilitation	109 (68)	29 / 17 / 63	27 / 16 / 58
Availability			
Physicians	153 (95)	71 / 26 / 56	46 / 17 / 37
Nurses	123 (76)	87 / 15 / 21	71 / 12 / 17
Physiotherapists	91 (56)	72 / 7 / 12	79 / 8 / 13
Occupational therapists	63 (39)	43 / 11 / 9	68 / 18 / 14
Medical social workers	49 (30)	37 / 4 / 8	76 / 8 / 16
Psychologist	17 (11)	10 / 2 / 5	59 / 12 / 29
Others	22 (14)	14 / 2 / 6	64 / 9 / 27
Contact with all expertise needed	159 (99)	116 / 16 / 27	73 / 10 / 17
Continuity			
Meeting the same staff	156 (97)	116 / 10 / 30	74 / 6 / 19
Finances	159 (99)	99 / 16 / 44	62 / 10 / 28
Efficacy/outcome of care			
Hospital in-patient care	100 (62)	78 / 6 / 16	78 / 6 / 16
Hospital out-patient care	159 (99)	123 / 14 / 22	77 / 9 / 14
Primary care	116 (72)	90 / 6 / 20	78 / 5 / 17
Rehabilitation	87 (54)	74 / 4 / 9	85 / 5 / 10
Participation in planning care			
Want to participate in planning care	154 (96)	139 / 8 / 7	90 / 5 / 5
Have participated in planning care	144 (89)	75 / 15 / 54	52 / 10 / 38

*Manifested need, or applicable from the perspective of PwMS

5 DISCUSSION

5.1 THE PILOT STUDY

The pilot study, which assessed the methods for data collection with Swedish PwMS with varying levels of disability and modes of living, was the first step in the Stockholm MS Study. The WHO's theoretical model (the former ICIDH[52]) was found useful in describing the health and functioning of PwMS from a broader perspective, combined with measures focusing on HRQoL, and PwMS' use of health care services and their satisfaction with care. When the pilot study was being planned and performed, the current ICF[53] (2001) was not yet available and the ICIDH[52] served as a theoretical model for this research. In the pilot study, environmental factors were addressed (by assessing the use of health care services) and personal factors (by assessing SOC). The tests and questionnaires suggested in the planning of the pilot study were mostly common methods for evaluating health[51] and had previously been used in neurological groups of patients.[137]

The pilot study of 26 PwMS aimed to evaluate the methods of performing home visits, including tests and structured interviews, to PwMS with various levels of disability and modes of living (private/sheltered). In more than half of cases, the time needed to perform the home visits was less than 2 hours, and all visits were completed within 2.5 hours. Through the pilot study, the health care professionals who performed the home visits were able to standardize their performance in giving information and instructions and asking questions in a fixed order. As a result, a decision was taken to have the home visits conducted by one interviewer in any future larger study, in order to save time for data collection.

The main findings of the pilot study that showed up needs for modifications of the protocol were as follows:

a) Use of health care services: PwMS remembered clearly which health-care professionals they had had contact with over the past 6 months, but not the frequency of those contacts. Therefore, the computerized register of health care contacts was considered the most reliable source of information for evaluating detailed use of services by PwMS over a three-year period, and interviewing for these data is not considered necessary
b) Satisfaction with care: PwMS showed a high level of interest in sharing their experiences of MS care and, importantly, raised additional issues that had not been covered in the questionnaire. These included items relating to information and advice on social security matters and psychosocial issues, items relating to information delivered during early stages of the disease, and items relating to the perception of the situation when the diagnosis of MS was first given
c) Cognitive function and depressive symptoms: The MMSE was not, on its own, sufficient to detect cognitive dysfunction and was complemented during the pilot study by the use of SDMT and FRR12RWT, as suggested by a neuropsychologist. The BDI was also added to detect depressive symptoms

d) Motor function: The evaluation of a timed 10-metre walk was difficult to perform in all homes, and thus required modification to a 5x2 metre walk for use in various homes of PwMS.

Both PwMS and family caregivers were eager to provide the requested information and to share their experiences of MS care and their situation, irrespective of the severity of the disability, of gender or of mode of living. No PwMS refused to participate in the study when asked. The investigators met with each PwMS in his/her current living situation, with technical aids and home adaptations being readily observable. Examples of reasons for PwMS not performing the tests or answering questionnaires included severe visual problems, severe ataxia, severe motor-capacity problems, or severe neuropsychological impairment, which shows the difficulty of evaluating severely disabled PwMS in detail as regards functioning.[69] However, all PwMS participated in the SIP interview despite its length of 136 statements, highlighting the advantage of simple answering formats (e.g. yes/no format) for gaining knowledge on HRQoL.

5.2 THE POPULATION-BASED STUDY

5.2.1 Major findings

HRQoL was severely affected in this population-based sample of PwMS in Stockholm, in all dimensions measured, but especially in home management, walking and recreation. HRQoL was poorer in PwMS, including those with milder disease and shorter disease duration, than in the general population. One fifth of the PwMS were depressed and 4 of 10 reported depressive symptoms corresponding to a BDI score above or equal to 10. Differences were recorded among the disease-related and sociodemographic subgroups studied regarding HRQoL but not regarding prevalence of depressive symptoms. Higher disease severity, not working and weak SOC were independently associated with major impact on HRQoL. Depressed PwMS reported poorer HRQoL than non-depressed PwMS in several aspects, and weak SOC was associated with both poorer HRQoL and the prevalence of depressive symptoms. Depressive symptoms were associated with poor memory function, but not with any of the other measures of functioning, such as of measures of walking, manual dexterity or ADL. High proportions of PwMS used hospital and primary care in parallel, with many departments and services being involved. Primary care constituted 54% of all out-patient care, and hospital neurology care 20%. PwMS were in general satisfied with care, but certain areas of which larger proportions of them were dissatisfied were accessibility of practical psychosocial advice and support and rehabilitation periods, the participation of PwMS in the planning of their care, and the situation in which diagnosis was given.

5.2.1.1 HRQoL in PwMS (Paper III)

The most affected categories of HRQoL, as measured by SIP, were walking, home management and recreation and pastimes, but all categories or dimensions of SIP and EQ-5D were affected. According to these results, MS affects not only physical aspects (walking, mobility, self-care) but also social aspects (family life, recreation, work life) and psychological/mental aspects (emotional functioning, alertness and communication) from the perspective of PwMS. Notably, HRQoL by SIP scores in all categories was significantly worse than in the general population[104] even in PwMS with

mild disease severity (EDSS score 0 – 3), except for in the category "eating", and this may call into question the wording "mild". It has been suggested that a score of 10 or higher indicates "clinical relevance" of dysfunction, as measured by SIP.[176] According to the median SIP scores of PwMS in Stockholm; high proportions of PwMS reported clinically relevant dysfunction in HRQoL in most categories. The pattern of HRQoL in Swedish PwMS, with all subcategories affected according to the questionnaires used, does not differ substantially from the results of population-based studies on HRQoL[76-84] in other countries. This implies that there is an overall impact on HRQoL dimensions in PwMS, irrespective of which country they live in.

5.2.1.2 HRQoL in subgroups of PwMS (Paper III)

In general, poorer HRQoL was seen with increasing disease severity, a progressive course of MS and a disease duration of longer than 10 years. In categories of HRQoL of a more psychosocial nature and sleep and rest, these differences were not as marked. The results here indicate that the overall psychosocial impact from MS is quite similar, irrespective of specific disease-related or sociodemographic subgroup, and may also reflect adaptation to living with MS.[177] Other population-based studies of HRQoL in PwMS[78-80] have reported similar findings. It has been suggested that a response shift[177] may occur in PwMS, meaning changes in the meaning of self-evaluations of HRQoL, which in turn result from changes in internal standards, values or conceptualization. As a result, HRQoL may remain at a certain level or improve in PwMS, despite evidence of deterioration from the perspective of health care professionals or others. Since the study on HRQoL in this thesis is cross-sectional, no such hypothesis could be evaluated.

There were few differences in HRQoL among the sociodemographic subgroups studied, other than in work status and type of accommodation. PwMS in sheltered accommodation reported poorer HRQoL than those living at home, by the measures of communication, eating, home management and body care and function, reflecting their greater need for nursing care including assistance with ADL.[178] PwMS who were not working reported markedly poorer HRQoL scores in most aspects than those who were working . This relationship has been reported in other population-based studies of HRQoL in PwMS,[81] but also in the general population in Sweden.[179] HRQoL and sociodemographic factors, other than employment or work status,[81,180] are not frequently studied in PwMS. In the sample of PwMS in Stockholm, 59% of employed PwMS were working part-time combined with financially-supported periods of sick-leave. Remaining in gainful employment, therefore, seems important to HRQoL in MS, with a preference for reducing work-hours per week rather than leaving work completely.

The majority of the PwMS in the study (90%) were categorized as having moderate-to-strong SOC, indicating that many of them view life as meaningful, comprehensible and manageable,[98] despite living with MS. Similar results have been found in long-term cancer survivors.[139] The association between weak SOC and poorer psychosocial HRQoL scores is consistent with findings for the general population in Sweden.[104] In MS management, increased focus on the resources of individual PwMS and not solely on their obstacles in life in relation to health might be of relevance.[101] Interventions

such as the teaching of coping skills have been identified as improving quality of lifes.[181]

Exploring what sociodemographic or disease-related factors, or if SOC, were independently associated with major impact on HRQoL (≥median SIP score of all PwMS), multivariate analyses were performed; a stepwise, forward logistic regression analysis.[163] In this statistical procedure, work status was chosen as the first variable to enter, as the most important "predictor", then EDSS group and lastly SOC. Together these accounted for 57% of the variance in predicting major impact on HRQoL. These three factors are therefore relevant to clinical care, in identifying PwMS at particular risk of severely affected HRQoL, bearing in mind that no evidence of causal relationship is provided. The negative aspects of HRQoL were evaluated, such as perceived dysfunction and negative behaviour, but not a single overall score or statement of health status or overall HRQoL of PwMS. Influences from overall HRQoL and quality of life of PwMS, for example influence from individual MS symptoms,[181-182] may thus contribute to the variance in the analysis described above.

5.2.1.3 Depressive symptoms in PwMS (Paper IV)

One out of 5 PwMS was depressed and 4 out of 10 reported depressive symptoms that generated a score of 10 or higher on the BDI, results that confirm the international picture of depression being common in PwMS.[90-94] As regards the most serious item of the BDI - suicidal ideation - 9% of PwMS confirmed that they had such thoughts to a certain extent. In the single question included in the EQ-5D on anxiety and depression, 46% of the PwMS stated that they perceived moderate or severe feelings of depression or anxiety, further highlighting the need to consider mental health issues in the care of PwMS. The most frequently observed BDI symptom was "fatigability" - reported by 82%. Fatigue is a common symptom of MS, and its association with depression in PwMS is not fully understood.[184] For clinical purposes, questionnaires may assist in elucidating what symptoms are present and their severity. There is no clear clinical limit or "cut-off" to distinguish among PwMS who would be diagnosed with an affective disorder[86] and those who are in a grey zone, manifesting depressive symptoms. A comparison with another population-based study in Ireland,[90] which also applied BDI through interviews with PwMS, reveals that fewer PwMS in Stockholm report moderate to severe depressive symptoms, which may be attributed to differences in prevalence of these symptoms and their severity among our countries.

5.2.1.4 Depressive symptoms in sociodemographic or disease-related subgroups of PwMS and SOC (Paper IV)

Evidence from the literature on depression among subgroups of PwMS is inconsistent.[90-94] One example of an issue where results differ among population-based studies is gender, with depression reported as being higher in women than in men[91-92], higher in men than in women[94] and showing a similar prevalence among men and women[93] (as in the present thesis). Another example of inconsistency is the issue of disease severity, where some studies report an association between EDSS and depressive symptoms among PwMS[93-94]while others report no association between these variables.[90] In an American, mail-surveyed, population-based sample of PwMS,[93] disease-severity, shorter disease duration, less education, and lower age were

independently predictive of clinically significant depressive symptoms, where these variables were self-assessed by PwMS. It is concluded that there may be real differences among countries regarding prevalence of depressive symptoms in different subgroups of PwMS, but there are also methodological aspects to this issue, such as the response rate of the sample and the method of data collection (interview versus mail survey).

Higher percentages of depressed PwMS were found among those with weak SOC than among those with moderate to strong SOC, supporting the notion that strong SOC may act as a protective factor against depressive symptoms.[111] SOC has been reported to be associated with different aspects of mental health, including depression,[100] and the associations found in PwMS are thus in line with previous research.

5.2.1.5 Depressive symptoms - association with functioning and HRQoL (Paper IV)

Depressed PwMS did not perform more poorly than the non-depressed in tests of cognitive function (attention), walking speed, manual dexterity speed, nor did they report poorer ADL or frequency of social or lifestyle activities, though they performed more poorly in tests of memory function. However, according to the associations found between depressive symptoms and SIP scores, depressed PwMS may underestimate their ability in reporting their functioning compared to the non-depressed, which is important to remember in clinical assessment and follow-up. Similar results have been reported in an Irish population-based study[90] using the BDI and the MSIS-29.[185] In a population-based study of depressive disorders in Stockholm,[186] depressed individuals showed impairments in tasks requiring episodic memory, but the pattern of impairments varied according to the type of depression (major and minor depression, dysthymia, etc.). In PwMS in Stockholm, depressive symptoms were associated with below-normal performance in tests of memory function (free recall of words). Other studies have also found this relationship, and it has been suggested that depression adversely affects working memory.[96,187]

5.2.1.6 Use of health care services (Paper V)

During the study period of three years, the great majority of PwMS (76-92%) had been in contact with both the specialist care and the primary care sectors, and primary care constituted over half of all out-patient care. Neurology care contacts constituted only 20% of all out-patient care. Above 60% of the PwMS had visited hospital emergency rooms and 47% had been admitted to in-patient hospital care during the three years. In all, 32% of the PwMS used home help service or personal assistants but higher proportions used informal, unpaid help from partners (37%). Some 45% had home adaptations carried out, and 73% had assistive devices.

Relatively low out-of pocket expenses in Sweden, as well as routines for referrals, could in part explain the relatively high use of care contacts and other services in PwMS in Stockholm. The mean number of about 20 out-patient contacts per year per PwMS could, on the other, hand be regarded as sparse, considering the complexity of the MS disease. During 2002, use of primary care represented the largest part of out-patient care for the residents of Stockholm County and the mean number of visits to primary care physicians was per capita 1.3.[188.] PwMS had a mean number of 2.2

contacts per year with primary care physicians, thus using more primary care than the general population. A relatively large proportion of the PwMS reported health problems other than MS and this subgroup used more primary care than the other. However, excluding those who reported medical problems other than MS in the analysis, the PwMS still displayed higher mean numbers of contacts (1.7/year).

Less than one third of PwMS were annually in contact with nurses at departments of neurology, but looking at the full three-year period, half of the PwMS had been in contact with neurology nurses based in out-patient care. This type of pattern was seen for other services/departments as well, with a difference between the mean rate of PwMS per year and the total rate of PwMS in the three-year period using a specific service. This may indicate that different PwMS come into contact with a certain service at different points in time and that it is not entirely the same PwMS who use a service repeatedly. This then raises the question of what characterizes those PwMS who have come into contact with different departments/services in terms of disease-related or sociodemographic features, but the issue is not addressed within this thesis.

A few population-based studies[113-116] of resource use and/or perceived needs of PwMS have been performed, based on different methodologies, challenging the possibilities of comparing results. Different time frames are used in these studies and most of them use self-report questionnaires for evaluating use of health care. A recent European study on costs and quality of life in MS[189] examined aspects of use of health care services by 13,186 PwMS in nine countries, including Sweden, mainly via mailed questionnaires. It was concluded that resources such as medical consultations and hospitalizations varied considerably from one country to another, while use of other services such as assistive devices, and home care was comparable. Compared to the samples of Swedish PwMS in these cost studies[64,189] the results of this thesis revealed lower annual mean numbers of visits to neurologists[64] and in-patient care days per PwMS.[64,189]

5.2.1.7 Satisfaction with care (Paper V)

Regarding satisfaction with information on MS in general in the study of PwMS in Stockholm, 10-33% were dissatisfied and as many as 55% were dissatisfied with the situation in which diagnosis was given to them. The reason for the latter is unclear, and should not be seen as an evaluation of how the MS diagnosis is given today in general, since many of the PwMS was diagnosed a considerably number of years before this study. A German study[191] on the way the MS diagnosis was delivered revealed that PwMS perceived that the time taken for explaining MS was too short and too cautious. The need for information in PwMS is multifaceted and not always met,[127,192] ranging, for example, from basic understanding of what MS is and why symptoms occur and understanding of therapies and side-effects, to available health care resources and the resources of society and rights of disabled people. Studies have shown that PwMS want information tailored to their individual requirements and delivered in different formats and within a suitable time frame.[190] The above mentioned aspects were not elucidated in the satisfaction with care interview with PwMS in Stockholm, but may be addressed in future studies in exploring detailed information needs. In recent years, a trend has emerged towards more written information available for PwMS, i.e via the Internet,

books, and information courses for the newly diagnosed,[193-194] but it is not known whether the content of these sources of information accords with the wishes of PwMS.

The majority of PwMS were satisfied with "art of care", meaning that in general they perceived engagement and kind treatment from health care professionals, results that are similar to those of other studies of people with neurological disorders.[160-161] Looking at the general population, high proportions are satisfied with the art of care (around 80%) but fewer people are satisfied with accessibility (around 70%) and readily accessible information (around 50%).[188] Most dissatisfaction among the PwMS concerned accessibility of services of a psychosocial nature and of MS-specific rehabilitation and their participation in planning of their care. Disabled people and professionals may differ in their perceptions of rehabilitation needs.[58,60] In an Australian survey of disability and quality of life,[195] 39% reported difficulty in accessing rehabilitation services because of either lack of service provision or inadequate information on how to access the services.
The majority (85%) of PwMS who had experience of MS-specific rehabilitation were satisfied with the outcome. The overall use of out-patient care in PwMS was spread evenly across specialist hospital care and primary care, and the dissatisfaction of PwMS with their ability to participate in the planning of their care may partly be because of the lack of coordination or communication between different care sectors and/or services. Almost one third (28%) stated that the costs of their MS-related care was burdensome, which might be because of the financial situation of living with MS and the costs of sick-leave periods, or other unknown causes. Similar results have been reported in other studies of people with neurological disorders in Sweden.[160-161] A high proportion of PwMS were dissatisfied with accessibility of advice and support in work and education-related rehabilitation and social insurance,[61] which might reflect low provision of such services in Stockholm, or lack of information on the availability of such advice or support.

5.2.2 Methodological considerations

The papers presented in this thesis are parts of the project "the Stockholm MS Study", which aims to explore overall health needs, in order to improve health care services for PwMS in Stockholm. Evaluation of the methods used for this health needs assessment procedure, the drafting of the final protocol and the identification of the sample of PwMS preceded the larger data collection in the form of home visits in the population-based study. Each home visit performed was a unique situation: entering into a private home as a guest and asking individuals to share their experiences and their perceptions of certain aspects of living with MS. In the population-based study, we (myself and the physiotherapists) had not met most of the PwMS before in clinical work. This was a change compared to the pilot study, in which almost all of the PwMS were well-known patients and visitors to the Department of Neurology at the former Huddinge University Hospital. As a result, less bias[46] regarding the possible impact on PwMS from us interviewers was probably introduced in the population-based study as compared to that in the pilot study.

5.2.2.1 Case finding, estimated prevalence and sample of PwMS

The large number of patients in the temporary data pool who failed to meet the Poser criteria[15] for definite MS can be explained by the fact that the Swedish MS Registry[196] had not yet been established at the time of the study. An estimated calculation of the prevalence of MS in Stockholm County was undertaken on the following basis: the population of SC numbered 1,762 million inhabitants in December 1997, and after exclusion of those who were not diagnosed with MS - although registered - and exclusion of those who were not alive or were not living in and registered as a resident of Stockholm County, the MS cases identified in this study (n=211 including PwMS who were not informed, but excluding patients with possible MS) would correspond to a prevalence of 80/100,000 inhabitants (95% CI 69-92/100,000).

This estimated prevalence could be regarded as low, considering previous Swedish reports.[24-27] Firstly, it is possible that there were losses of MS patients in the temporary data pool with a clinical onset prior to 1999, who may have fulfilled the MS criteria later or today.[11,12] Secondly, only one municipality was evaluated in terms of cases of PwMS living in nursing homes or sheltered accommodation, and it is unknown whether more cases would be "found" by searching in the nursing homes of all municipalities in Stockholm County. Primary care centres are another source of case findings for PwMS. However, there are numerous primary centres in Stockholm County, and most PwMS are believed to have a medical record at one of the hospitals, at departments of neurology, and such a procedure was not considered feasible in identifying a heterogeneous sample of PwMS for the aim of health needs assessment. In summary, all other possible sources for assembling a pool with a high level of sensitivity to PwMS were applied, and collaboration was excellent. Furthermore, 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.

The sample is believed to be representative of PwMS in Stockholm, though the effect of the 15% PwMS who declined participation on study validity is not known. However, the sample characteristics of PwMS who participated in the study are similar to those presented in other population-based studies.[129-132] The population of Stockholm County amounts to about one fifth of the population of Sweden, and so the results of this thesis are believed to be representative of PwMS in Sweden in general. Exceptions identified are local circumstances that may influence data, e.g. access to specialist neurology care and immunomodulating drugs at the time of the study,[197] and, possibly, differences in attitudes in health care services as compared to other parts of the country.

5.2.2.2 Home visits with face-to face structured interviews and tests

The method of home visits to PwMS including tests and structured, face-to face interviews has several advantages; control is maintained over who actually responds, and symptoms of MS such as fatigue and motor/cognitive dysfunction are taken into account when designing the protocol for optimizing response rate. Furthermore, it enables both interviews and tests to be conducted on the same occasion, and in an environment that is not artificial but realistic to PwMS. During home visits, validation of the information obtained is possible by observing functioning and use of assistive

devices in the home environment of PwMS. The disadvantages of interviews,[62] compared to other types of data collection, are difficulty in coordinating schedules of researcher and PwMS, lack of anonymity in responses and possibility of interviewer bias, high costs of data collection and limitation in number of PwMS who may be included in a study. In all, 166 home visits, plus an additional 16 for those who required two visits in order to complete the protocol, were performed.

5.2.2.3 Use of tests, structured interviews and computerized register

Participation in the structured interviews including the various instruments was high (92-100%), considering the high - 25% - proportion of PwMS with severe disability (EDSS ≥7).

Use of the SIP[71] offered several advantages. SIP is characterized by the simplicity of its response format: yes or no to statements read out loud, the use of the current time frame - not forcing participants to remember how they functioned several weeks before - and the ability of PwMS to choose among many answer options.[69] This was particularly useful in interviews of PwMS with marked cognitive dysfunction or speech difficulties.

We did not have access to validated MS-specific HRQoL measures[74, 185] (e.g. MSQoL-54[74]) when the present study was planned, but such measures should be useful in clinical care, in identifying detailed problem areas from the perspective of PwMS. Despite the SIP being a generic questionnaire, it enables MS-specific issues to be highlighted, in analyses of the most frequently marked items within each category. Issues added to the SF-36 in the MSQoL-54[74] questionnaire are indeed to be found in SIP as well, for example, urinary and bowel incontinence and constipation, sexual dysfunction and fatigue. SIP was found to cover most aspects relevant to HRQoL in PwMS as reviewed by Grunewald et al.[69] We used the combination of two different HRQoL measures, the SIP and the EQ-5D,[167] to be able to compare our results with results from the general populations.[104, 169] The EQ-5D is suggested as a standard indicator for HRQoL in the population within Stockholm County, and is commonly used in public health surveys.[169] In this thesis, no overall HRQoL score evaluation of the PwMS was presented, such as the first health rating question of the SF-36,[72] which might be a disadvantage. The MSIS-29[185] has increasingly been used in Swedish clinical follow-up and research of PwMS, but this questionnaire does not, either, provide an overall estimation of HRQoL from PwMS in a single question. In deciding what future HRQoL measures are useful to research in PwMS, several instruments might therefore be considered, both generic and disease-specific.

The BDI is one of the most frequently used questionnaires for assessing depression[87] and was recently recommended for use in MS populations in a clinical context to identify those PwMS who may merit special attention and follow-up.[170] Use of the BDI was feasible with the PwMS at home visits and in structured interviews, despite the severe and sad nature of the questions. As in many other studies of depressive symptoms in PwMS, it is recognized that physical items are frequently marked, and that they are difficult to differentiate from symptoms related to MS. Use of the full 21-item BDI has been recommended, since all BDI items decreased significantly in a treatment study of psychological and pharmacological interventions for depression.[198]

A shorter questionnaire, named the BDI-Fast Screen,[199] has been developed to assess depression in populations with medical disorders, but to my knowledge is not available in Swedish. In the course of future research to assess depressive symptoms in PwMS, instruments other than the original BDI may be considered, which also take into account the possibility of and need for comparing results among studies.

The interview on satisfaction with care, comprising 22 structured questions, provided a detailed view of the experiences of PwMS in different dimensions of care. This could be supplemented by, for example, a study based on qualitative methodology such as semi-structured interviews on the quality and experience of care in different areas, including experiences of and preferences for information or support given in care. A future questionnaire may be developed for use with people with neurological disorders, comprising questions covering, but differentiating among, all sectors and divisions of care (e.g. primary care, hospital specialist care, questions on overall co-ordination and information of different kinds), and the results of a measure of this kind may be used as a qualitative indicator of outcome of total use of care in a patient group. Other questionnaires on patient satisfaction[122] are intended for use at particular departments, units or wards for clinical or research purposes. The Swedish "Vårdbarometern"[200] has for recent years surveyed satisfaction with care in general, in Swedish counties including Stockholm, and such information may be used for comparison.

The use of a computerized register, where most health care contacts of the PwMS were identified, valuably supplemented the data collection protocol. According to the results of the pilot study on this method, PwMS had certain difficulties in remembering the exact numbers of health care contacts taken over a longer period of time. As the exact identification and count of different types of contacts were not dependent on the memory of the PwMS in the population-based study, a period of three years could be chosen to account for variability of care need over time. In the case of variables such as amount of home help service or assistive devices, no central register existed for data collection, but face-to-face structured interviews in the homes of PwMS complemented the picture of the total use of services. Regarding the total resource use by PwMS, the number of health care contacts might be underestimated, since contacts within company (occupational) health services and within alternative or complementary medicine have not been registered or presented here.

5.2.2.4 Statistical considerations

The sample size of 166 PwMS who agreed to participate in the study may not be sufficient to enable a detailed analysis of differences in all sociodemographic and disease-related subgroups, and lack of significant differences among subgroups may be because of small numbers in certain groups of PwMS. For example, the proportion of depressed PwMS among those who were not working was higher than in those working - the p-value was 0.017 - and the level of significance was set at 0.01 in view of the high number of analyses in this particular study not overestimating differences in scores or proportions. Such analyses may be repeated in larger sample of PwMS to confirm the results presented in this thesis. Correcting for multiple comparisons may require, for example, a Bonferroni correction to lower the limit for probability values to be

significant or multivariate analyses.[163] The two latter alternatives were applied in this thesis.

5.2.3 Reflections on health needs assessment, the Stockholm MS Study and future research

The knowledge provided through the results of this thesis, and other publications within the Stockholm MS Study, will add to the base needed for planning care for PwMS in Stockholm and provide guidance for further research and development in certain areas, as discussed below.

5.2.3.1 Studying HRQoL and SOC in PwMS

Management of MS should focus on enhancing the health of PwMS by slowing disease progression and by improving functioning[53] and HRQoL through evidence-based interventions. Considering the high impact on HRQoL, and that the perspective of PwMS may differ from that of health care professionals,[201] HRQoL is a relevant issue in the care of and research into PwMS. HRQoL in PwMS is now described in numerous publications since it started to attract interest in MS research, but HRQoL has to a lesser extent been used as an outcome measure in clinical trials. Examples of randomized controlled trials in recent years using HRQoL as an outcome measure and based on highly selected samples of PwMS,[181,202-204] indicate that HRQoL of PwMS may be improved by different interventions; exercise therapy,[202] home-based management,[203] psychological interventions,[181] and drugs.[204] HRQoL also needs to be included as an outcome variable in future clinical studies of PwMS as part of the process to gain further knowledge of what type of interventions are effective in maintaining or improving health and functioning from the perspective of PwMS, despite the threat of deterioration of MS.

The impact on HRQoL in PwMS in Stockholm has been described in detail in this thesis, but the association between HRQoL and the use of services and satisfaction with care has not yet been explored, nor the association between HRQoL and functioning variables such as ADL and motor and cognitive function. Such exploration may elucidate what implications there are to studying HRQoL as a determinate for use of health-care, or the importance of environmental factors (e.g. use of health care) and functioning to the HRQoL. SOC was associated with HRQoL in PwMS in Stockholm, and was studied as an independent factor and dichotomized into weak or moderate/strong SOC.[104] However, SOC may be studied per se, as a dependent variable and in relation to sociodemographic and disease-related subgroups of PwMS.

5.2.3.2 Studying depressive symptoms in PwMS

The prevalence of depressive symptoms was also assessed in detail within this thesis. Though depression and its association with HRQoL is frequently studied in MS, few randomized clinical trials have been performed studying outcomes of different psychological interventions or antidepressant therapies for depression. No definite conclusions have been drawn from a Cochrane report on the matter,[205] other than that there is reasonable evidence to argue that cognitive behavioural therapy (CBT) approaches are beneficial in the treatment of depression.[206] The delivery of CBT to PwMS in Stockholm has not been investigated in detail, and other strategies offered to

meet needs of a psychological nature should be explored and evaluated, including the prescription of antidepressants[87] and the role of nursing care in the context of neurological hospital care.[38] Besides psychopharmacological or psychological interventions, the effects of individualized MS management, rehabilitation and physical activity on depression deserve further study, to provide future guidelines on recommendations regarding the supply of care to PwMS. It has not yet been explored whether depressed and non-depressed PwMS were satisfied with care in general or with specific dimensions such as accessibility of psychosocial services, or whether these subgroups differ in their total use of health care services.[207-208]

In the cross-sectional studies of depressive symptoms and their associations with functioning in PwMS in Stockholm, an assumption was made that prevalence of depressive symptoms could affect performance in functioning tests in PwMS. It is possible though to hypothesize that depressive symptoms are prevalent in PwMS as a result - a reactive condition - to performance in functioning, such as PwMS reacting to, for example, indications of diminution in their ability to walk or to maintain normal manual dexterity or cognitive function. For example, Voss et al[209] found that fatigue and physical disability were indirectly and directly predictive of depression in PwMS through their effects on recreational functioning, and hypothesized that a disease will lead to a depressive effect only if it disrupts physical or psychosocial functioning.

5.2.3.3 Use of health care services, satisfaction with care and sociodemographic and disease-related factors

The use of health care services and satisfaction with care of PwMS in Stockholm has been explored in this thesis, but not yet in terms of disease-related or sociodemographic factors. Use of health care services has partly been explored in subgroups of PwMS aged <65 and in those with self-reported, concurrent disorders, but other sociodemographic factors also need to be explored. In health economics research and in population-based studies of PwMS,[113] total use of services and/or costs are found to rise with increasing disability[64,] and correlations of this kind need to be confirmed in the sample of PwMS used in this thesis, where register data were applied for data collection. The relation between sociodemographic factors and use of services or satisfaction with care has been less studied in PwMS and more knowledge on this is thus warranted in order to assure equity in distributing available resources. Regarding sociodemographic factors, analyses of the relationship between potential predictors and work performance would be valuable,[180] since sick leave periods and disability pensions are among the largest drivers of cost for MS in the society.

In relation to the health needs assessment and relevant questions to ask, no direct questions were put to PwMS on their perceived needs or priorities of health care.[192] Rather, their satisfaction or dissatisfaction with the overall care experienced was explored, with the restriction to the dimensions taken into account in the structured questionnaire. Nevertheless, the results of the satisfaction with care interview with PwMS in Stockholm may be regarded as guidance for "what the patients want", and as subjective evaluations of environmental factors set out in the ICF model. Another issue that may be elucidated in future studies may be the exploration of the relationship between use of health care services and satisfaction with care;[118] i.e. are those who are

major consumers of a certain service the most or least satisfied with the service? Since a high proportion (58%) of the partners to PwMS were involved in informal care, according to the results of this thesis, their situation including HRQoL should be further investigated,[210] for also including them in health needs assessment of PwMS in Stockholm.

As financial resources are limited, questions of resource allocation - in terms of what groups of PwMS have capacity to benefit[48] - rises. As a result, there is a considerable need for more scientific evidence on methods and their cost-effectiveness in meeting health care needs in PwMS. In clinical MS research, the focus lies on evaluation of methods for slowing down progression and the relapse rate - drug interventions - but there is also a need to focus on what methods to use to help PwMS with everyday solutions to cope with and manage MS.

5.2.3.4 Reflections on results in terms of care for PwMS in Stockholm

The Department of Neurology at Karolinska University Hospital bears primary responsibility for neurological care and treatment in Stockholm County. However, allocation of responsibilities regarding different treatments, rehabilitation and counselling are not clearly stated in the hospital and primary sector for PwMS in Stockholm (to my knowledge), other than for that which MS therapies are prescribed and monitored at departments of neurology. Thus, what is considered as specialist MS care is more clearly defined regarding medical care treatments, but less so regarding the social and psychological needs of PwMS, where services such as nursing care[37] and rehabilitation[40] play a role in meeting these needs.

According to the results of this thesis, it is confirmed that all sectors are involved in the care of large proportions of PwMS in Stockholm - hospitals and primary care departments, including service units for assistive devices and health-related transportation (units of Stockholm County Council), the municipalities and rehabilitation units organized outside the Council. According to the high numbers of PwMS who were not working, contacts with the social insurance offices should also be taken into account, as well as contacts with company (occupational) health services. It has not been explored to what degree all these units and departments are integrated - or whether and how the individual PwMS perceive that an integrated care plan exists, relative to their present needs. The continuum of integration of health care units may range from linkage (adequate referral to the right unit at the right time with good communication among units) to full integration, including for example pooled budgets and one record for documentation.[211] A position in-between these states in that continuum - co-operation - where key professionals are appointed to improve the contacts among organizational units[211], seems appealing in terms of the organization of MS care, in my opinion. Research has shown that barriers to effective co-ordination of care, as perceived by people with physical disabilities including PwMS, are lack of disease- and disability-specific knowledge, time and effort to invest in care co-ordination and insufficient communication among providers.[212-213] "Providing seamless services" was one of six key priorities to implementation, within the MS Guidelines of the National Institute of Clinical Excellence in Great Britain (NICE).[214]

Co-ordination is one of the central, nursing interventions[215]in which nurses are to support and plan co-ordination for PwMS.[37,39,216] This co-ordination of care may take place among different caregivers at special unit, but also among different units within a defined geographical area. Certain evidence suggests that providing MS specialist nursing may shorten the time for accessibility of treatments,[216] improve the availability of a named contact person,[39] and that knowledge of MS, coping, mood, confidence and family relationships might be improved in PwMS.[37] To my knowledge, no Swedish research exists on the evaluation of MS nursing services. Further development of such services may take advantage of the possibility of nurses to act as key professionals.

Certain quality indicators for MS care in Sweden have been proposed.[217] Local guidelines on allocation of responsibilities of clinical care in different areas, such as relapse management, urinary dysfunction, depression or inability to manage ADL independently, may have effect on the total use of health care services. The results in the present thesis and in other publications from the Stockholm MS Study[133-134] may contribute to discussions and efforts for specifying detailed, clinical care programs for PwMS and guidelines, such as the efforts made by the NICE in Great Britain.[214] The implementation of care programmes or changes in the way MS care is provided in society should be the subject of health economic evaluation, as well as evaluation of functioning and HRQoL, use of services and satisfaction with care of PwMS.

6 SUMMARY AND CONCLUSION

The studies presented within this thesis are the first to provide detailed knowledge on HRQoL, depressive symptoms, use of health care services and satisfaction with care in a Swedish, population-based sample of PwMS. Together with detailed knowledge of functioning of PwMS, the results presented within this thesis complement the procedure of health needs assessment of PwMS in Stockholm. The major strengths of the studies were the population-based approach with home visits and structured interviews and tests which facilitated the use of a comprehensive protocol, and that this was evaluated in advance in pilot studies. The results of the pilot studies showed that the proposed protocol was viable with most PwMS with various disease severity, gender and form of accommodation (private/sheltered) and was possible to perform within a reasonable time frame.

In the population-based sample of PwMS, the HRQoL with emphasis on self-reported functioning was severely affected as compared to the general population, including those with milder disease according to severity, duration and course of MS. HRQoL differed among sociodemographic and disease-related subgroups of PwMS, and work status (not working vs. working), disease severity (severe vs. mild EDSS), and SOC (weak vs. moderate/strong) were independently associated with major impact on HRQoL. In all, 19 % were depressed, and there were no significant differences in prevalence of depressive symptoms among sociodemographic or disease-related subgroups of PwMS. Depressive symptoms were associated with HRQoL, such as that depressed PwMS reported worse functioning in several aspects than the non-depressed. The depressed PwMS did not perform worse than non-depressed in tests of cognitive function (attention), walking speed, manual dexterity speed or reported worse ADL or frequency of social or lifestyle activities, though they performed worse in tests of memory function. The great majority of PwMS used hospital specialist care and primary care in parallel. Primary care constituted 54% of all out-patient care and hospital neurology care constituted 20%. A mean of 24% of PwMS was annually admitted to in-patient care. Large proportions of PwMS had assistive devices, home adaptations made and permits for health-related transportation service, implying the involvement of municipalities and other organisational units in the care of PwMS. Some 37% of PwMS used informal care and help from partners. PwMS were in general satisfied with care, but certain areas where larger proportions were dissatisfied concerned accessibility to psychosocial practical advice and support, and rehabilitation periods, and their participation in planning of their care.

Considering the broad impact on HRQoL in most PwMS and the high prevalence of depressive symptoms, attention to health and functioning - from the perspective of PwMS - is strongly indicated in the management of MS. Further, health-care units engaged in MS management should survey the totality of services available for PwMS when planning and implementing individualized care interventions, since most PwMS will already be receiving care in more than one department or unit. The development of evidence-based, cost-effective health-care services to improve HRQoL and well-being is warranted; i.e., interventions, both somatic and psychological, that optimize health in a comprehensive perspective.

7 CLINICAL IMPLICATIONS

Health-care professionals involved in clinical care of PwMS that aims to maintain or improve HRQoL and well-being may find useful the following implications of the results of this thesis:

►HRQoL, including self-reported functioning, is affected in all health areas covered by typical questionnaires; hence, it is relevant to in detail evaluate all of these areas—physical, psychological, cognitive, and social functioning; and, in particular, ambulation, home management, and recreation and pastimes—in order to characterize functioning from the perspective of PwMS. This implication is also valid for PwMS with milder disease (in terms of severity, duration or course).

►The knowledge that HRQoL differs among subgroups of PwMS—for example, that it is poorer in those not working, with severe disability, and in those with weak SOC—may be used to identify PwMS at high-risk for major negative impact on HRQoL

►Given the fact that depression may be present in 1 of 5 PwMS, and that the prevalence of depressive symptoms differs little across sociodemographic and disease-related subgroups, awareness of, and attention to, the mental health of *all* PwMS is advocated.

► Depressed PwMS may report poorer HRQoL than the non-depressed, including in aspects of walking and mobility. Depressive symptoms may be associated with poor memory function, while at the same time displaying no association to other measures of functioning, such as measures of attention, walking speed, manual dexterity, ADL, or frequency of social/ lifestyle activities. The above differences in the way functioning appears to be affected by depressive symptoms are important to consider in clinical evaluations of the functioning of PwMS.

►The total use of health-care services by individual PwMS should be considered when planning or implementing an individual care plan, since the use of health-care services is seldom restricted to one sector, department, or type of service for most PwMS. Given the fact that MS is a chronic disease, entailing continuous health needs and engaging multiple caregivers, the question of how providers of services and caregivers communicate, and to what extent their efforts are integrated, may be of vital importance.

►Satisfaction with care on the part of PwMS can be regarded as a quality indicator for patient-focused health-care services; it should be considered when making clinical decisions, especially decisions regarding the need for psychosocial care and rehabilitation, and PwMS should be actively encouraged to participate in the planning of their care.

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