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Prevalence, physical activity, and work in patients with spondyloarthritis

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Prevalence, physical activity, and work in patients with spondyloarthritis

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AKADEMISK AVHANDLING

Som med vederbörligt tillstånd av Medicinska fakulteten vid Lunds Universitet för avläggande av doktorsexamen i medicinsk vetenskap kommer att offentligen försvaras i Belfragesalen, BMC, Lund, fredagen den 8 november 2013, kl 9.00

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Abstract <p>Spondyloarthritis (SpA) is a group of interrelated inflammatory rheumatic diseases with the sub-diagnoses ankylosing spondylitis (AS), psoriatic arthritis (PsA), arthritis-associated inflammatory bowel disease (Aa-IBD), undifferentiated spondyloarthritis (USpA), where stiffness and pain are key symptoms. Insidious onset back pain, morning stiffness, waking up at night, and improvement from exercise are common characteristics. The disease is life-long, often with early onset, and can cause limitations in physical function, affecting the ability to work, and has a negative effect on health-related quality of life. The overall aim of the present work was to describe the prevalence of SpA and to study the consequences for the individual and society regarding physical activity and work in a population-based cohort of patients seeking health care.</p> <p>The studies are based on a cohort of patients with SpA, identified through the Skåne Health Care Register by searching for 12 ICD-10 codes for SpA that had led to a doctor's consultation 2003–2007. Two questionnaire surveys in 2009 and 2011 were sent to all the patients in the cohort ≥ 18 years and data from these formed the basis of the studies II, III, and IV.</p> <p>Study I presented an estimation of SpA prevalence based on almost 4,000 patients. It was 0.45% in adults (≥ 15 years), and equally common in women and men. The prevalence in different subgroups was 0.12% in AS, 0.25% in PsA, 0.0015% in Aa-IBD, and 0.10% in USpA with different sex distribution patterns.</p> <p>Study II dealt with the proportion of patients who met the WHO recommendations for physical activity. Seven out of ten patients with SpA met the recommendations, more often in women than in men, and with a somewhat higher proportion in the SpAScania cohort than in the general Swedish population.</p> <p>Studies III and IV examined the patterns of reduced productivity at work both cross-sectionally and longitudinally. Just under half of the patients with SpA reported reduced productivity at work, and more reduction was reported in women than in men. Reduced productivity at work was associated with, and could be predicted from several patient-reported outcome measures (PROMs) such as reduced health-related quality of life (HRQoL), higher disease activity, lower physical function, lower self-efficacy, worse mental health and low education level.</p> <p>To conclude, 45 individuals out of 10,000 have a diagnosis of SpA, and affected individuals report significant consequences of the disease. The findings presented in this thesis could help clinicians to identify patients at an early stage at risk of a worse prognosis using simple clinical questions in routine practice, and tailor the activities, treatment, and care for patients with SpA.</p>		
Key words Spondyloarthritis, ankylosing spondylitis, psoriatic arthritis, undifferentiated spondyloarthritis, prevalence, physical activity, work productivity, presenteeism, absenteeism, patient-reported outcomes		
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Prevalence, physical activity, and work in patients with spondyloarthritis

Emma Haglund



LUND
UNIVERSITY

Thesis 2013

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Every day when I can run is a good day

In loving memory of my parents Gittan and Jan

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Haglund E, Bremander AB, Petersson IF, Strömbeck B, Bergman S, Jacobsson LTH, Turkiewicz A, Geborek P, Englund M.
Prevalence of chronic spondyloarthritis and its subtypes in southern Sweden. *Ann Rheum Dis.* 2011;70(6):943-8 (Paper I)

Haglund E, Bergman S, Petersson IF, Jacobsson LTH, Strömbeck B, Bremander AB.
Differences in physical activity patterns in patients with spondyloarthritis. *Arthritis Care Res.* 2012;64(12):1886-94 (Paper II)

Haglund E, Bremander AB, Bergman S, Jacobsson LTH, Petersson IF.
Work productivity in a population-based cohort of patients with spondyloarthritis. *Rheumatology.* 2013;52(9):1708-14 (Paper III)

Haglund E, Petersson IF, Bremander AB, Bergman S.
Presenteeism in spondyloarthritis is associated with activity impairment and can be predicted by clinically used patient-reported outcome measures. Submitted (Paper IV)

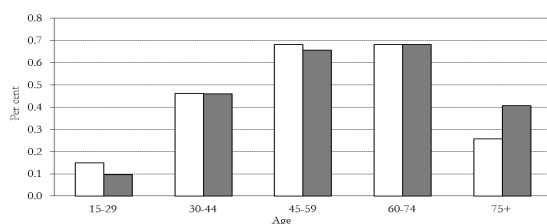
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Thesis at a glance

Study I – Prevalence of spondyloarthritis and its subgroups in Sweden

Patients and methods: 3,852 patients identified from the Skåne Health Care Register (SHCR). By searching for all health-care-seeking patients with spondyloarthritis (SpA) in the SHCR, the SpAScandia cohort was created. In this population-based study the prevalence of SpA and its subgroups in Sweden was estimated.

Conclusions: The prevalence of SpA was 0.45% in the adult population (≥ 15 years old), and was as common in women as in men. Psoriatic arthritis (PsA) and ankylosing spondylitis (AS) were the two most prevalent subgroups, followed by undifferentiated spondyloarthritis (USpA) and arthritis associated with inflammatory bowel disease (Aa-IBD) with prevalence figures of 0.25%, 0.12%, 0.10%, and 0.0015% respectively.

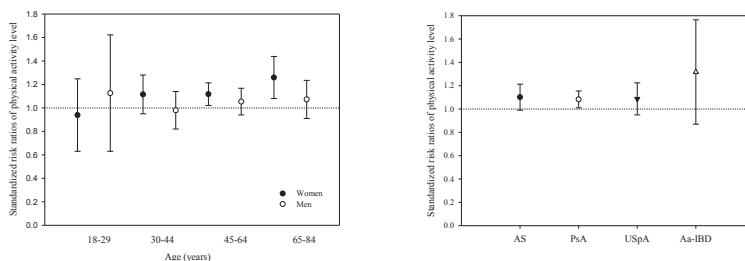


Prevalence of spondyloarthritis. White bars: women; grey bars: men.

Study II – Differences in physical activity patterns in patients with SpA

Patients and methods: A cross-sectional population-based cohort study. 2,167 patients from the SpAScandia cohort answered the SpAScandia questionnaire in 2009. The questionnaire included inquiries on patterns of physical activity. The proportion meeting the physical activity recommendation was estimated and comparisons with data from the Swedish population were made.

Conclusions: Seven out of 10 patients with SpA met the recommendations on physical activity, more frequently in women than in men and with a somewhat higher proportion in the SpAScandia cohort than in the general population. Young women with SpA tended to be less active than their counterparts in the general population.



Comparison with the general population, Meeting the physical activity recommendations in women and men with spondyloarthritis in different age groups and for meeting physical activity recommendations in different subgroups of spondyloarthritis.

Study III – Work productivity in patients with SpA

Patients and methods: A cross-sectional population-based cohort study on work productivity and associated factors. 1,773 patients in working age (18–67 years) from the SpAScania cohort answered the SpAScania questionnaire in 2009.

Conclusions: Almost half of the patients with SpA reported some reduction in work productivity and women reported a higher mean reduction than men. Reduced productivity at work was associated with higher disease activity, lower physical function, reduced quality of life, lower self-efficacy, worse mental health, and low education level in patients with SpA.

Associations between reduced productivity at work and associated factors.

Potential associations	β -est	95% CI
Disease activity (BASDAI)	7.8	(7.1;8.5)
Physical function (BASFI)	7.3	(6.8;7.9)
Quality of life (EQ-5D)	-9.6	(-10.5;-8.8)
Self-efficacy pain and symptoms (ASES)	-0.5	(-0.6;-0.4)
Anxiety (HAD)	2.3	(1.9;2.6)
Depression (HAD)	3.4	(3.0;3.8)
Education level		
≤ 12 years	3.9	(0.8;7.0)
>12 years	0	

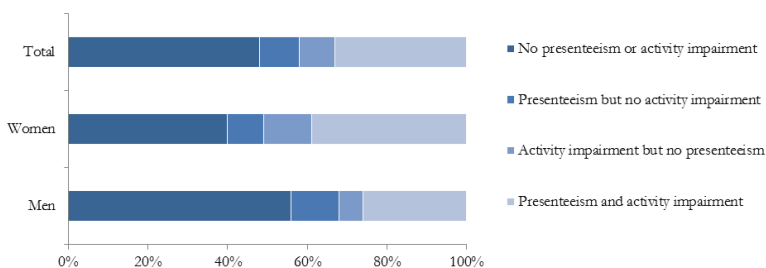
Bold text: significant level <0.05 .

Study IV – Predictors of presenteeism in patients with SpA

Patients and methods: A longitudinal study to assess predictors of presenteeism and its relationship to activity impairment outside work in patients with SpA.

1,253 patients (18–67 years) from the SpAScania cohort answered both the SpAScania questionnaire in 2009 and the follow-up questionnaire in 2011.

Conclusions: Presenteeism (reduced productivity at work) was predicted from several patient-reported outcome measures common in clinical practice: reduced quality of life, higher disease activity, lower physical function, lower self-efficacy pain, anxiety, depression, smoking, and low education level. There was a clear association between presenteeism and activity impairment outside work.



Associations in 2011 between presenteeism and activity impairment in women and men with spondyloarthritis.

Authors' contributions

Paper I

Study design: Emma Haglund, Ann Bremander, Ingemar Petersson, Britta Strömbeck, Stefan Bergman, Lennart Jacobsson, Aleksandra Turkiewicz, Pierre Geborek, Martin Englund

Data collection: Emma Haglund, Martin Englund, Britta Strömbeck, Aleksandra Turkiewicz, Pierre Geborek

Data analysis: Emma Haglund, Ann Bremander, Ingemar Petersson, Britta Strömbeck, Stefan Bergman, Lennart Jacobsson, Aleksandra Turkiewicz, Pierre Geborek, Martin Englund

Manuscript writing: Emma Haglund

Manuscript revision: Ann Bremander, Ingemar Petersson, Britta Strömbeck, Stefan Bergman, Lennart Jacobsson, Aleksandra Turkiewicz, Pierre Geborek, Martin Englund

Paper II

Study design: Emma Haglund, Stefan Bergman, Ingemar Petersson, Lennart Jacobsson, Britta Strömbeck, Ann Bremander

Data collection: Emma Haglund, Ann Bremander, Britta Strömbeck

Data analysis: Emma Haglund, Stefan Bergman, Ingemar Petersson, Lennart Jacobsson, Ann Bremander

Manuscript writing: Emma Haglund

Manuscript revision: Stefan Bergman, Ingemar Petersson, Lennart Jacobsson, Britta Strömbeck, Ann Bremander

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Study design: Emma Haglund, Ann Bremander, Stefan Bergman, Lennart Jacobsson, Ingemar Petersson

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Data collection: Emma Haglund, Ann Bremander

Data analysis: Emma Haglund, Ingemar Petersson, Ann Bremander, Stefan Bergman

Manuscript writing: Emma Haglund

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Abbreviations

Aa-IBD	Arthritis associated with Inflammatory Bowel Disease
AS	Ankylosing Spondylitis
ASAS	Assessment of SpondyloArthritis international Society
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functional Index
EQ-5D	EuroQol-5 Dimensions
ESP	European Standard Population
ESSG	European Spondyloarthropathy Study Group
HAD	Hospital Anxiety and Depression scale
HEPA	Health-Enhancing Physical Activity
HLA-B27	Human Leukocyte Antigen B27
HRQoL	Health-Related Quality of Life
IBD	Inflammatory Bowel Disease
IBP	Inflammatory Back Pain
ICF	International Classification of Functioning, Disability and Health
ICD-10	International Classification of Diseases, Tenth Revision
JIA	Juvenile Idiopathic Arthritis
MI-PA _{rec}	Recommendations for Moderate-Intensity Physical Activity
MRI	Magnetic Resonance Imaging
NRS	Numeric Rating Scale
NSAID	Non-Steroidal Anti-Inflammatory Drugs
OMERACT	Outcome Measures in Rheumatoid Arthritis Clinical Trials
PsA	Psoriatic Arthritis
PROM	Patient-Reported Outcome Measures
PT	Physiotherapist
RA	Rheumatoid Arthritis
ReA	Reactive Arthritis
SHCR	Skåne Health Care Register
SNIPH	Swedish National Institute of Public Health
SpA	Spondyloarthritis
SPR	Swedish Population Register
SSIA	Swedish Social Insurance Agency
SSQ	SpAScania Questionnaire
TNF	Tumour Necrosis Factor
USpA	Undifferentiated Spondyloarthritis
VI-PA _{rec}	Recommendations for Vigorous-Intensity Physical Activity
WHO	World Health Organization
WHO _{rec}	World Health Organization global recommendations for physical activity for health
WPAI	Work Productivity and Activity Impairment questionnaire

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Introduction

Chronic back pain is a major health and socioeconomic problem in the western world (Bergman *et al.* 2001). Although our knowledge of the causes of back pain is growing, there is still a need to describe more distinct clinical subgroups of back pain. One subgroup is inflammatory back pain, which can be related to the group of interrelated inflammatory rheumatic diseases spondyloarthritis (SpA) (Jordan *et al.* 2013; Weisman *et al.* 2013), which is the subject of this thesis. SpA is in most cases life-long with periodic fluctuations, and has an impact on several aspects of life. The recommended treatment includes both pharmacological therapy and non-pharmacological management. In addition to an early diagnosis followed by relevant pharmacological therapy, coping with the disease is an important issue for the patient. Regular physical activity and exercise are cornerstones in the management: the skills of the physiotherapist (PT) are needed, and as a PT one often meets these individuals at an early stage in the course of the disease. The diagnosis of SpA has previously been based on observed measures, but now also includes patient-reported measures to obtain a more complete picture of the patient. Furthermore, the physiotherapy management has shifted from passive care to a more active treatment, including coaching and regime. The aim is to achieve a more independent patient who is better able to participate in and take responsibility for the care and treatment opportunities. The physiotherapy interventions for these patients have also moved to a greater extent from hospital-based in-patient care in specialist clinics to care given at out-patient hospital clinics and to long-term primary care based services, which places new demands on the care system and on health-care providers regarding greater flexibility. As a practicing PT with regular contact with this group of patients, I have seen the need for better knowledge of how to coach these patients in an evidence-based, individualized but varied way. The aim of this thesis was to improve our knowledge of the consequences of SpA, both for the individual and for society as a whole. Hopefully, this work will also be an update on the occurrence of different forms of SpA, and will help to identify relevant factors for a better or worse prognosis. This might lead to earlier diagnosis and contribute to successful and often long-term collaboration in clinical practice for this disorder.

Background

Spondyloarthritis

History

In archaeological studies, spondylitis or ankylosis of the vertebra has been found in three-thousand-year-old skeletons of Egyptian mummies, suggesting the occurrence already then of the disease now known as ankylosing spondylitis (AS) (Leden 1994; Sieper *et al.* 2002). The first literature description of the disease dates to the mid-1500s, when Colombo wrote his book “De Re Anatomica” in which he described skeletons with abnormalities typical of the disease (Sieper *et al.* 2002). Centuries later, the Irish doctor Bernard Connor described a human skeleton with marked spine curvature and also fused vertebrae and joints. He was also aware of the possible consequences of the disease on movement and respiration during the patient’s lifetime. The disease was described by several doctors in the mid-1800s, but classical descriptions were made by Wladimir von Bechterew (1893), Adolph Strümpel (1897), and Pierre Marie (1898) at the end of that century. Along with Connor, they are regarded as those who first described the disease. The Russian neurologist von Bechterew also gave rise to the term Bechterew’s disease, which was originally used in Sweden and other countries (Leden 1994; Sieper *et al.* 2002). Later on, advances in clinical sciences and medicine and the development of modern radiographic techniques helped to shape the modern concept of the disease (Sieper *et al.* 2002).

Definitions

The term spondyloarthritis (SpA) comes from the Greek terms “spondylos” (i.e. vertebra), “arthron” (i.e. joint), and “itis” (i.e. inflammation), and means arthritis of the peripheral and spinal joints (Reveille *et al.* 2005). The term SpA covers a range of diseases with clinical similarities, and in the literature various terms describing the same syndromes sometimes cause confusion. The terms SpA, spondyloarthropathy, and, occasionally without an intermediate “o”, spondylarthropathy and spondyloarthritis are used interchangeably and are also seen in plural forms with the endings -arthritides or -arthropathies (Claudepierre *et al.* 2012; Bijlsma *et al.* 2012). The related term spondylopathy refers to a disease of the vertebrae itself, and spondylitis is an inflammation of the spine without other illness, are both other diseases. In this thesis, the term spondyloarthritis with the abbreviation SpA is used.

Classification

There are no diagnostic criteria for the group of SpA diseases. To promote a common language and make research studies comparable, classification criteria have been developed instead. Such criteria may also serve as a guideline for clinicians when making a diagnosis. Classification criteria are based on frequent clinical features of the disease, with varying degrees of sensitivity and specificity. These are then combined and compared against clinical diagnoses (the gold standard) in order to define a patient group with an appropriate balance between sensitivity and specificity (Gran 1999; Rudwaleit *et al.* 2010). For a long time, the classification criteria for these patients have focused on the more severe subgroup AS, the archetype of SpA. Early classification criteria for this disease were introduced in 1961, but a better known set of criteria for AS was the New York criteria, which included definite radiographic changes (Moll *et al.* 1973a). In the early 1990s, classification criteria for SpA based on clinical information were developed by the European Spondyloarthropathy Study Group (ESSG) and Amor (Amor *et al.* 1990; Dougados *et al.* 1991; Sieper *et al.* 2009a). To improve sensitivity and specificity and to include magnetic resonance imaging (MRI) in the diagnosis setting, the international Assessment of Spondyloarthritis Society (ASAS) has worked for an international agreement on classification criteria for SpA (Rudwaleit *et al.* 2009b; Rudwaleit *et al.* 2009c; Sieper *et al.* 2009a; Rudwaleit 2010; Rudwaleit *et al.* 2011). These criteria were developed to classify individuals in clinical research in a standardized manner, not primarily to diagnose individuals in clinical practice. The ASAS's proposed criteria also include classifications for peripheral forms of SpA, where the earlier classifications were considered to be insufficient (Rudwaleit *et al.* 2011).

Subgroups of spondyloarthritis

In the group of SpA diseases, the following subgroups are included: AS, psoriatic arthritis (PsA), arthritis associated with inflammatory bowel disease (Aa-IBD), undifferentiated SpA (USpA), reactive arthritis (ReA), and juvenile idiopathic arthritis (JIA) (Dougados *et al.* 1991; Baraliakos *et al.* 2012). According to the ASAS group, the SpA is also differentiated into either axial SpA or peripheral SpA depending on the main symptoms (Figures 1, 2). The axial SpA group is also divided into AS and non-radiographic axial SpA where the term non-radiographic axial SpA is meant to cover a stage of the disease before occurrence of radiographic damage (Kiltz *et al.* 2012; Sieper *et al.* 2013). Classification criteria for the two most frequent subgroups, AS (Moll *et al.* 1973a; van der Linden *et al.* 1984) and PsA (Moll *et al.* 1973b) existed before the term SpA was introduced. The PsA classification has since been updated (Taylor *et al.* 2006). In this thesis, the term spondyloarthritis is used to refer to the subgroups AS, PsA, Aa-IBD, and USpA (Table 1, page 22). The additional subgroups belonging to the SpA group will not be discussed further. These are ReA and JIA. ReA has a more non-chronic character with peripheral arthritis occurring after a primary infection elsewhere in the body. Features of the JIA manifest initially as peripheral arthritis or enthesitis and include severe forms of iridocyclitis, sometimes with visual impairment in children before the age of 16. The disease can give both axial and/or peripheral symptoms and can also include extra-articular manifestations (Bijlsma *et al.* 2012).

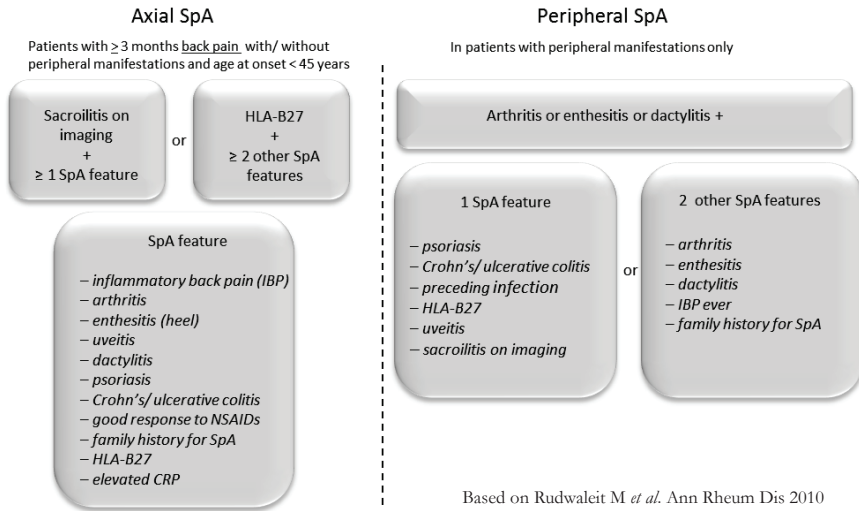


Figure 1. The ASAS classification criteria for axial and peripheral spondyloarthritis

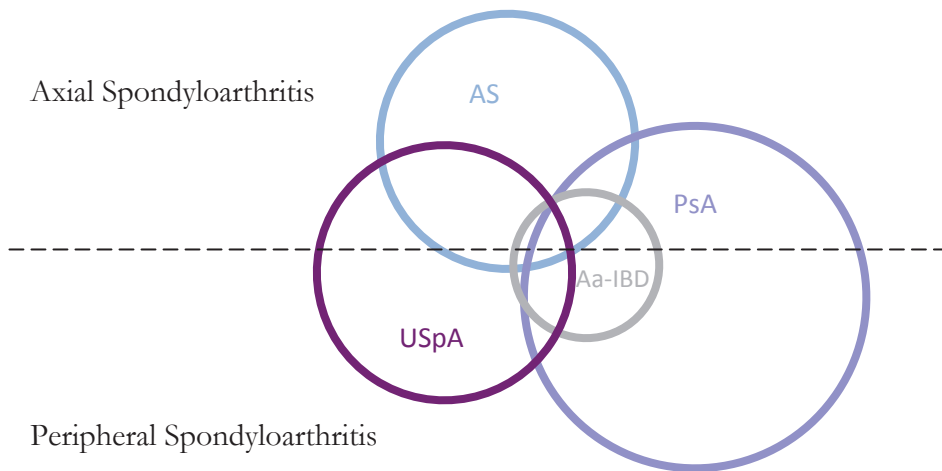


Figure 2. Axial and peripheral spondyloarthritis (SpA). This Venn diagram shows the relationship between the different diagnostic subgroups of SpA presented in the thesis. Also included are the two different clinical presentations of mainly axial or mainly peripheral SpA. During the course of disease, a particular patient can move between the different sectors/subgroups. AS: ankylosing spondylitis; PsA: psoriatic arthritis; Aa-IBD: arthritis associated inflammatory bowel disease; USpA: undifferentiated spondyloarthritis.

Table 1. The International Classification of Diseases (ICD) 10 diagnostic codes for spondyloarthritis.

Subgroups	ICD-10 code	Diagnosis
AS	M45	Ankylosing spondylitis
PsA	L40.5	Psoriatic arthritis with joint disease
	M07.0	Distal interphalangeal psoriatic arthropathy
	M07.1	Arthritis mutilans
	M07.2	Psoriatic spondylitis
	M07.3	Other psoriatic arthropathies
Aa-IBD	M07.4	Arthropathy in Crohn's disease
	M07.5	Arthropathy in ulcerative colitis
USpA	M46.0	Spinal enthesopathy
	M46.1	Sacroilitis, not elsewhere classified
	M46.8	Other specified inflammatory spondylopathies
	M46.9	Inflammatory spondylopathy, unspecified

AS: ankylosing spondylitis; PsA: psoriatic arthritis; Aa-IBD: inflammatory arthritis associated with inflammatory bowel disease; USpA: undifferentiated spondyloarthritis.

Ankylosing spondylitis

AS is the disease archetype among the SpA subgroups. Prevalence is estimated to be in the 0.06–0.9% range in the western world (Carter *et al.* 1979; Kaipiainen-Seppänen *et al.* 1997; Braun *et al.* 1998; Andrianakos *et al.* 2003; Alamanos *et al.* 2004; Bakland *et al.* 2005; Saraux *et al.* 2005; Helmick *et al.* 2008; Geirsson *et al.* 2010) with an incidence of 6/100,000 per year (Silman 2001). The age at onset of AS is <30 years and the disease is more common in men (Carter *et al.* 1979; Khan 1995; Sieper *et al.* 2002; Feldtkeller *et al.* 2003; Alamanos *et al.* 2004; Bakland *et al.* 2005; Trontzas *et al.* 2005). Inflammatory back pain is the leading feature, but enthesopathy, peripheral arthritis, and extra-articular manifestations are also included in the pathology; the association with the human leucocyte antigen (HLA-B27) epitope is strongest in this subgroup (Baraliakos *et al.* 2009; Rudwaleit *et al.* 2009b; Rudwaleit *et al.* 2009c). The development of skeletal abnormalities such as erosions in sacro-iliac joints and syndesmophytes of the spine are more profound for patients with AS than for those with other SpAs, giving larger impairments in several dimensions of life. Pain, fatigue (Ward 1999; Zink *et al.* 2000; Hamilton-West *et al.* 2009), stiffness (Ward 1999; Hamilton-West *et al.* 2009; Halvorsen *et al.* 2012; Healey *et al.* 2013), sleeping problems (Dagfinrud *et al.* 2005a), disability and function limitations (Zink *et al.* 2000; Ward 2002; Ariza-Ariza *et al.* 2003; Dagfinrud *et al.* 2004; Dagfinrud *et al.* 2005a; Mustur *et al.* 2009; Healey *et al.* 2013; Ward *et al.* 2013), and impaired health-related quality of life (HRQoL) (Ward 1999; Ariza-Ariza *et al.* 2003; Bostan *et al.* 2003; Da Costa *et al.* 2004; Brodin *et al.* 2007; Mustur *et al.* 2009; Bodur *et al.* 2011) are common. Lower

cardiorespiratory fitness has also been reported (Hagel *et al.* 2010; Halvorsen *et al.* 2012) and patients with AS have an increased risk of extra-articular manifestations such as uveitis, bowel diseases, heart, lung, skin, bone and kidney involvement, and increased risk of cardiovascular co-morbidities (Han *et al.* 2006; Bremander *et al.* 2011; El Maghraoui 2011). Self-reported anxiety and depression have been found to be associated with higher disease activity and lower physical function (Martindale *et al.* 2006). Furthermore, AS patients have higher health-care consumption and more prescribed medications than the general population (Strombeck *et al.* 2010).

Psoriatic arthritis

PsA is the other major subgroup of SpA. For PsA, the prevalence in different studies has varied between 0.06% and 0.29% (Braun *et al.* 1998; Shbeeb *et al.* 2000; Andrianakos *et al.* 2003; Saraux *et al.* 2005; Adomaviciute *et al.* 2008; Wilson *et al.* 2009) and incidence varies from 3.4 to 8 per 100,000 per year (Gladman *et al.* 2005). The age of PsA onset is around 40 years of age and the peak incidence is at 45-54 years of age (Olivieri *et al.* 2002; Gladman *et al.* 2005). Some studies have found an equal occurrence in men and women (Alamanos *et al.* 2004; Makredes *et al.* 2009), some have found that it is more frequent in men (Kaipiainen-Seppanen *et al.* 1996; Wilson *et al.* 2009), and others have found that it occurs more frequently in women (Shbeeb *et al.* 2000). To some extent, PsA has similar clinical features to those of AS but with some differences, such as predominance of peripheral arthritis and enthesitis. The affection of the spine is also more random both in location, degree of involvement, and type of symptoms. The disease is thus characterized by peripheral arthritis, enthesitis, dactylitis, and spondylitis in addition to skin and/or nail involvement. Joint and skin disease co-exist in the vast majority of cases, although it is not mandatory (Han *et al.* 2006; Tobin *et al.* 2010; Zochling *et al.* 2010; Zhu *et al.* 2012; Mease 2013). It has been suggested that there could be gender differences, with women reporting worse HRQoL and impaired function with symmetrical polyarthritis and men having more axial involvement and radiographic joint damage (Zochling *et al.* 2010; Eder *et al.* 2013).

Arthritis associated with inflammatory bowel disease

Aa-IBD is a less common group of arthritis, where there is an association with inflammatory bowel disease (IBD). Different subtypes have been proposed, with regard to a more axial or peripheral arthritis involvement (Colombo *et al.* 2009). Previous prevalence studies have been based solely on patients with an IBD or with an AS. Approximately 5-10% of patients with AS also have IBD, but an even higher proportion has subclinical bowel inflammation. Between 4% and 10% of patients with IBD have concomitant AS. A minor proportion of patients with SpA who have subclinical bowel inflammation can also progress to development of IBD (Mielants *et al.* 2005; Rudwaleit *et al.* 2006).

Undifferentiated spondyloarthritis

USpA includes several forms of SpA, for example early AS (before definite radiographic abnormalities), but it can also be a mixture of SpA features such as inflammatory back pain (IBP), enthesopathy, uveitis, or arthritis that cannot be diagnosed as an AS, PsA, or Aa-IBD. These patients may have a milder form of disease in that they are less likely to develop syndesmophytes, although data on patient-reported outcome measures (PROMs) suggest they have at least as severe disease from a patient point of view (Kumar *et al.* 2001; Rudwaleit *et al.* 2009a; Lindström *et al.* 2013). The progression to AS strongly depends on the clinical features at baseline (Zochling *et al.* 2010), but the epidemiology of this subgroup is not well studied.

ICD-10 codes

The International Classification of Diseases, Tenth Revision (ICD-10) is a well-accepted coding system that refers to a disease, disorder, injury or trauma. It was endorsed in 1990 by the Forty-Third World Health Assembly and in Sweden it is used in the clinic for register recoding. The term SpA includes several different ICD-10 codes with limited correlation to the modern classification system for SpA presented above. For the subgroups AS, PsA, and Aa-IBD, there are broadly consistent ICD-10 codes according to the classification criteria (Table 1, page 22). Currently, however, the ICD-10 codes for the subgroup USpA do not correspond to the differentiation between mainly peripheral or axial forms of disease proposed by the ASAS criteria (Figure 1, page 21). The subgroup ReA (arthritis in lyme disease, infectious and reactive arthropathies, and other postinfectious arthropathies in diseases classified elsewhere) also has comparable ICD-10 codes, but it is not considered further in this thesis due to its more non-chronic nature.

Occurrence

SpA is among the most common of more than one hundred different rheumatic diseases, and the prevalence ranges from 0.3% to 1.9% (Braun *et al.* 1998; Saraux *et al.* 1999; Bruges-Armas *et al.* 2002; Andrianakos *et al.* 2003; Saraux *et al.* 2005; Trontzas *et al.* 2005; De Angelis *et al.* 2007; Adomaviciute *et al.* 2008; Zeng *et al.* 2008; Reveille *et al.* 2012) (Table 2). Variation in methods used and classification criteria applied have contributed to the differences in prevalence estimates. Earlier estimates were often based on the two most common subgroups: AS and PsA. SpA is correlated to the presence of HLA-B27, which varies between different countries and among ethnic groups. The prevalence of SpA is higher in populations with a higher prevalence of HLA-B27 (Boyer *et al.* 1994; Khan 1995; Alenius *et al.* 2002), which to some extent accounts for the lower prevalence of SpA in Asian populations (Hukuda *et al.* 2001). The link between SpA and HLA-B27 also differs between subgroups, and AS has the most clear association (Zochling *et al.* 2010).

Table 2. The prevalence of spondyloarthritis, reported in a selection of studies of different design and with different sets of criteria, including the study presented in Paper I.

Author	Study population (n)	Prevalens of SpA
Braun (1998)	Blood donors, Germany (348)	1.9%
Saraux (1999)	Population-based, France (3,189)	0.47%
Hukuda (2001)	Review of medical records, Japan (990)	0.0095%
Bruges-Armas (2002)	Population-based, Portugal (490)	1.6%
Andrianakos (2003)	Population-based, Greece (8,740)	0.49%
Saraux (2005)	Population-based, France (9,395)	0.30%
Trontzas (2005)	Population-based, Greece (14,233)	0.49%
De Angelis (2007)	Population-based, Italy (2,155)	1.06%
Adomaviciute (2008)	Population-based, Lithuania (4,244)	0.84%
Zeng (2008)	Review of population-based surveys in China (3,915)	0.89%
Haglund (2011)	Population-based, Sweden (849,253)	0.45%
Reveille (2012)	Population-based, USA (5,013)	0.9-1.4%

Characteristics

SpA is an autoimmune chronic disease, typically with a succession of flares and partial remissions. It contains a group of interrelated diagnoses with several common themes such as IBP, peripheral arthritis, enthesitis at the heel or other sites, dactylitis, various extra-articular manifestations (such as uveitis, skin involvement, and IBD), and association with HLA-B27 antigen (Khan *et al.* 1990; Dougados *et al.* 1991; Sieper *et al.* 2006; Baraliakos *et al.* 2011). Axial SpA onset occurs before the age of 45 years, often in adolescence or in young adults. The early onset for most patients with SpA means that it will affect them throughout their entire life. The main clinical symptoms are pain and stiffness of the axial skeleton consistent with IBP. IBP is classified as age at onset of <40 years, back pain for >3 months, insidious onset, morning stiffness, often waking up at night or in the early morning which is remedied by getting up, and improvement from exercise but not from rest (Sieper *et al.* 2009b). The disease can cause inflammation in the sacroiliac joints, vertebrae, and adjacent joints and tissues, and to varying degrees gradually leads to bone fusion in the axial skeleton (Braun *et al.* 2007).

Consequences

As with other rheumatic diseases such as rheumatoid arthritis (RA), SpA also affects patients' health in a wider sense. Key symptoms are stiffness and pain, resulting in functional impairment (Heikkila *et al.* 2002) and activity limitations (Heikkila *et al.* 2002; Da Costa *et al.* 2004; Singh *et al.* 2009; Kiltz *et al.* 2012). Fatigue (Da Costa *et al.* 2004) and impaired HRQoL are other cardinal symptoms affecting the patient (Heikkila *et al.* 2002;

Da Costa *et al.* 2004; Singh *et al.* 2009; Kiltz *et al.* 2012) that may have consequences for family relationships, leisure time activities, work ability, and social interaction. Problems of self-reported anxiety and depression are reported more frequently in patients with SpA than in the general population of Sweden (Meesters *et al.* 2013). Patients with SpA and AS appear to be comparable in some clinical variables (Rudwaleit *et al.* 2009a; Kiltz *et al.* 2012) but most of the research data have been based on the AS subgroup.

Gender perspectives

In some studies, the overall occurrence of SpA has been reported to be as common in women as in men (Boyer *et al.* 1994; Saraux *et al.* 1999; Saraux *et al.* 2005; Adomaviciute *et al.* 2008; Reveille *et al.* 2012), but according to other European studies men are more frequently affected (Braun *et al.* 1998; Andrianakos *et al.* 2003). A more severe disease with structural damage and typical IBP has been reported in men with SpA, while more cervical and thoracic spine involvement, enthesopathy, and widespread pain have been described for women (Boyer *et al.* 2000; Rudwaleit *et al.* 2009a; Roussou *et al.* 2011; Slobodin *et al.* 2011). Women with SpA are often reported worse scores in PROMs on pain, fatigue, HRQoL, physical function, and mental function (Roussou *et al.* 2011; Tournadre *et al.* 2013).

Treatment

There are few treatment recommendations for SpA in the literature (Braun *et al.* 2011; Baraliakos *et al.* 2012). The most successful and recommended treatment for AS, as stated by ASAS, is a combination of pharmacological therapy and non-pharmacological treatment, a treatment that is also applicable to patients with other subgroups of SpA (Braun *et al.* 2011). The main aim is to improve HRQoL and to preserve function, activity and participation by controlling symptoms and inflammation, while preventing structural damage. Physiotherapy modalities are still an essential part of the management, almost throughout the entire progression of the disease (Sieper *et al.* 2009a; Braun *et al.* 2011). Initially, non-steroidal anti-inflammatory drugs (NSAIDs) are recommended for AS and for other SpAs that affect the axial skeleton. In cases where there is an insufficient response, treatment with anti-tumour necrosis factor (TNF) blockers has been suggested (Baraliakos *et al.* 2009; Sieper *et al.* 2009a; van der Heijde *et al.* 2011). Updated recommendations for AS have been published recently (Braun *et al.* 2011; van der Heijde *et al.* 2011; van den Berg *et al.* 2012) and there are also national guidelines in Sweden (National Board of Health and Welfare 2012). The effect of various interventions, including biologics, appears to be even greater in early disease (Sieper *et al.* 2012). For some time, a change from hospital-based in-patient and out-patient care to long-term, primary care based services for chronic conditions has become necessary to meet demands and fulfil the goals of health care (Edwards *et al.* 2008), even though the most severely ill and those on biological therapy are still referred to rheumatology units. This

gives more responsibility and assignments in primary care, but also the patient himself have to take responsibility for their health. Emphasis is put on long-term management and living a healthy life supported by the primary care services, with intermittent support from specialist care.

The International Classification of Functioning, Disability, and Health

To provide a standard framework for description of health and health-related states, the World Health Organization (WHO) presented the widely used International Classification of Functioning, Disability and Health (ICF) in 2001 (WHO 2012a). This framework is based on the bio-psychosocial model that was introduced by Engel in the 1970s (Engel 1977). The aim of introducing this framework was to provide a model for description of the disease problem, treatment, and for evaluation of the outcome, and the link between them. The framework is useful for everyone in the health-care team who is in contact with the patient. The ICF offers a universal classification system and is a useful tool when discussing and describing health and disability across different professions and in different parts of the world (Stucki 2005; WHO 2012a).

The ICF, with its emphasis on functioning and disability, is structured around the components: body functions, body structure, activities, and participation. Each component can be expressed in both positive and negative terms: functioning (body functions, body structure, activities, and participations) and disability (impairments, activity limitations, and participation restrictions). The main components also interact with contextual aspects such as environmental and personal factors.

There is no ICF core set available for the whole SpA group, but there are the ASAS ICF core set for the subgroup diagnosis AS, which were aimed at identification of the most typical and relevant consequences for functioning and health in this subgroup (Stucki *et al.* 2007; Boonen *et al.* 2010a). The ICF core set includes for example, pain, mobility, sleep functions, and exercise tolerance in the component body function. Structure of the trunk, pelvic, and lower extremities is included in the component body structure, while changing of body position, walking, working, family relationships, leisure time activities, and driving are typical of the component activities and participation. In the component environmental factors, among other things support and relationships have been mentioned as being typical of the disease (Boonen *et al.* 2010a).

Physiotherapy

Several definitions of physiotherapy have been put forward, including promotion of health and well-being and prevention of impairments, activity limitations, and participation restrictions. As a research area, it is characterized by a perception of the individual as a physical, mental, social, and existential being and PTs have a valuable role in promotion of health, care, and rehabilitation in different health-care systems around the world (Higgs *et al.* 2001; Broberg 2003; WCPT 2012). PTs need continuously updated knowledge about factors affecting health, and how these contribute to an improvement or decline in health throughout the life. Physiotherapy can be given as a single intervention or as part of a complex intervention or rehabilitation, together with other health professionals. Counselling, coaching, education, exercise, pain management, and many different types of manual treatments are widely used to maintain or improve functional limitations or disabilities from different diseases (WCPT 2012). The methods used should always be based on evidence based care and clinical experience.

Physiotherapy in spondyloarthritis

Physiotherapy has long been an important part of the treatment of patients with AS, and it is also applicable to patients with SpA (Braun *et al.* 2011), even though most research papers still refer to AS. In the past, patients with AS were quite often hospitalized in rheumatology departments for treatment (Gordon 1977). In 2005, a Cochrane review emphasized physiotherapy and group exercises to be important interventions for patients with AS, and this was also backed up in an updated review in 2008 (Dagfinrud *et al.* 2005b; Dagfinrud *et al.* 2008). The cornerstones of non-pharmacological treatment are regular exercise and patient education. The aim is to improve or maintain spinal mobility, physical fitness, and functional posture and to reduce pain (van den Berg *et al.* 2012). Home exercise is a key modality, but physiotherapy with supervised exercises, land- or water-based, individually or in a group, should be preferred, as these are more effective (Dagfinrud *et al.* 2008; Braun *et al.* 2011). Even so, home-based daily exercise programs are advocated due to their simplicity and cheapness (Aytakin *et al.* 2012). Home-based or supervised exercises have better outcomes than no intervention, and reduce the risk of disability (Dagfinrud *et al.* 2008). Furthermore, supervised group exercise also improves the well-being of the individual. Additional benefits were found with a combination of three weeks of intensive spa exercise therapy followed by weekly group physiotherapy (Dagfinrud *et al.* 2008). Different forms of rehabilitation for patients with AS have also been shown to be effective regarding physical function, mobility, pain (Fernandez-de-Las-Penas *et al.* 2006; Masiero *et al.* 2011), and aerobic capacity (Hagel *et al.* 2010). Some later studies have confirmed the effect of rehabilitation, with moderate to good effects in all ICF domains; on physical function, disease activity, HRQoL scores, and pain and mobility outcomes (Staalesen Strumse *et al.* 2011; Kjekken *et al.* 2013). Other non-pharmacological treatment modalities such as patient associations and self-help groups

are also recommended (Zochling *et al.* 2006b; Vliet Vlieland *et al.* 2009; Braun *et al.* 2011). In recent years, the awareness of the value of physical activity has been raised and interventions based on physical activity have gained considerable importance (WHO 2002; WHO; 2003; WHO 2010). Despite this knowledge, the majority of patients with AS do not exercise on a regular basis (Passalent *et al.* 2010), and for the SpA group at large it is still incompletely studied. However, interventions based on exercise, and also giving encouragement to exercise and to be physically active, are recommended for improved function in patients with AS, irrespective of whether the disease is moderate or severe (Brophy *et al.* 2013).

Physical activity

In the past decade, our awareness of physical activity in influencing human health has also been seen as a cost-effective way to promote better health. The WHO has recognized that physical inactivity is the fourth most important risk factor for mortality, and interest groups, health-care workers, and society as a whole have worked actively to disseminate information about the importance of physical activity in promoting health (WHO 2002; WHO 2010). From studies carried out worldwide, there is a large body of evidence that regular physical activity can reduce the risk of cardiovascular co-morbidities, and also a number of other co-morbidity disorders such as diabetes, obesity, hypertension, breast cancer, colon cancer, osteoporosis, and depression in a population (Warburton *et al.* 2006; Blair *et al.* 2009; Alford 2010; Lee *et al.* 2010; Sieverdes *et al.* 2010; Lee *et al.* 2012). It is also well known that patients with rheumatoid arthritis (RA) and patients with AS have an increased risk of cardiovascular co-morbidities (Han *et al.* 2006; Bremander *et al.* 2011), which makes it even more important that these patients should have a healthy lifestyle. Recommendations for physical activity in promotion of better health and prevention of disability in these specific diseases have been put forward by the WHO (WHO 2003).

Definitions of physical activity

Physical activity is a complex concept that is sometimes used interchangeably with exercise and physical fitness. The terms are inter-related but have different meanings. Physical activity is defined as “any bodily movement produced by skeletal muscles that results in energy expenditure” while exercise is a “subset of physical activity that is also planned, structured, and repetitive”, often with the objective of maintaining or improving physical fitness. In contrast, the term physical fitness is a set of attributes that relate to the ability to perform physical activity (Caspersen *et al.* 1985).

Recommendations for physical activity

In 1995, the first more widely used public recommendations for physical activity were endorsed, promoting 30 minutes or more of moderate-intensity physical activity on most days of the week (Pate *et al.* 1995), a recommendation also adopted by the WHO (WHO/FIMS 1995). Later on, an updated version was published that recommended moderate-intensity aerobic physical activity for a minimum of 30 minutes for five days a week or vigorous aerobic activity for a minimum of 20 minutes on three days each week, or a combination of moderate-intensity and vigorous activity, for all healthy individuals aged 18–65 years. Muscle-strengthening activities should also be performed two days a week (Haskell *et al.* 2007), which has also been recommended by the WHO and adapted to individuals with inflammatory diseases. The recommendations are now expressed in total minutes per week, corresponding to 150 minutes of moderate intensity or 75 min of vigorous physical activity per week (WHO 2003; WHO 2010; Garber *et al.* 2011). For additional health benefits, adults should increase the length or the intensity of aerobic physical activity. The national board in Sweden have accepted the recommendations on physical activity to improve and maintain health i.e. health-enhancing physical activity (HEPA) as the minimum level of physical activity (Pate *et al.* 1995; National Board of Health and Welfare 2011) (Figure 3).

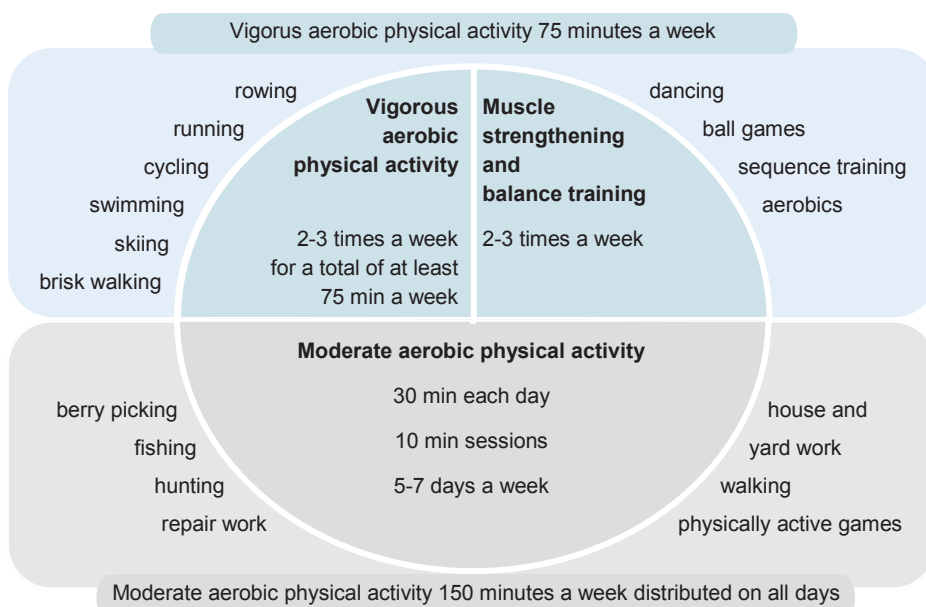


Figure 3. Pie chart of weekly physical activity. Recommendations on Health-Enhancing Physical Activity to promote health and prevent health risks associated with physical inactivity. It is preferable to take part of both halves every week, but to get at least half of the pie. Figure inspired by the UKK institute, Finland (UKK Institute 2009).

Assessment of physical activity

There are different methods to measure physical activity, which can be divided into self-reported measures or observed measures (such as when using accelerometers or pedometers). Questionnaires, and also various forms of diaries, are frequently used methods for self-reported measures and the patient's own assessment of the level of physical activity forms the basis of the outcome (Sternfeld *et al.* 2012). The questions have to provide answers to the dose of physical activity. Frequency is the number of times an activity is performed, usually expressed in sessions, episodes, or bouts per day or week. Duration is the length of the activity, often expressed in minutes, and intensity is the rate of energy expenditure required to perform the activity (U.S. Dept. of Health & Human Services 2008). With information about frequency, duration, and intensity, it can be evaluated whether the patient is meeting or not meeting the recommendations for physical activity. On the other hand, observed measures of physical activity, for example accelerometers or pedometers, assess bodily movements. It is difficult to compare self-reported measures and observed measures, and the general advice is to not mix the two methods (Prince *et al.* 2008; Slootmaker *et al.* 2009; Hagstromer *et al.* 2010). In studies comparing accelerometer data with self-reported data, both measures provided qualitatively consistent information on physical activity at the population level (Prince *et al.* 2008; Slootmaker *et al.* 2009; Hagstromer *et al.* 2010), but the absolute values differed with a modest overestimation of physical activity when using self-reported data (Hagstromer *et al.* 2010). Self-reported physical activity is, however, internationally accepted, supported by the WHO, and is often the only possible way to study this phenomenon in larger population surveys due to its ease of use and low cost, but its limitations should be considered (Sallis *et al.* 2000; WHO 2010).

Physical activity in individuals with spondyloarthritis

Physical activity patterns are seldom studied in patients with SpA. However, there have been studies of this topic in patients with AS showing that approximately two-thirds of them fulfil the recommended requirements regarding physical activity (Manning *et al.* 2012; Brophy *et al.* 2013), but in many cases at a level of intensity that is too low (Sundstrom *et al.* 2002; Passalent *et al.* 2010). Of those who met the recommendations, as many as half of them wanted further advice on physical activity (Manning *et al.* 2012). Studies in individuals with other arthritic diseases in the US and in individuals with rheumatoid arthritis in Sweden have found that a substantial proportion do not reach the recommended level of activity (Fontaine *et al.* 2004; Demmelmaier *et al.* 2013). In an older Swedish study, the majority of patients with AS had a low level of exercise, less than three times a week (76%), but the study explored exercise rather than physical activity patterns (Sundstrom *et al.* 2002). Most improvements in function were found in patients with higher levels of physical activity and in those who were more motivated. Even patients with the most severe disease activity have a lot to gain by maintaining or increasing their

level of physical activity (Brophy *et al.* 2013). Despite the positive outcomes, several patients still do not report any regular activity or exercise (Passalent *et al.* 2010). Due to the different questionnaires and methods used, the comparability between studies is low but researchers agree and advocate the use of exercise and advice on physical activity as part of the treatment in patients with AS.

Work productivity

The ability to work is a fundamental activity, and a reduced ability to work affects the well-being of both healthy individuals and people with a disease (Waddell *et al.* 2007; Arvidsson *et al.* 2011; McDonald *et al.* 2011). Work ability is important for HRQoL and has an economic impact both for the individual and for society. Research has mainly focused on the link between health risks, health conditions, and health-care costs. There have also been studies on loss of productivity, measured from the costs associated with absenteeism, the employee's time away from work, while costs for lost productivity due to different health conditions are more often ignored (Schultz *et al.* 2007). As more individuals with inflammatory diseases are treated with the new, expensive biologic drugs these days, with increasing costs to society, it is important to study the effects of the disease on productivity to obtain more information for health-economic evaluations.

Increased rates of absence from work, and short- and long-term disability in general have highlighted the importance of dealing with the relationship "work - illness" for the individual, for the health-care system, for the workplace, and for society (Drummond *et al.* 2005; Waddell *et al.* 2007). The OMERACT association (Outcome Measures in Rheumatoid Arthritis Clinical Trials) has also recommended that productivity should be used as an outcome measure in clinical trials (Beaton *et al.* 2009). Due to its early onset and chronic nature, SpA affects individuals negatively throughout their entire working life. This can cause absence from work and reduced work productivity, causing distress for the patient and economic loss for the individual, for her/his employer, and for society as a whole. Furthermore, this could mean that patients with SpA may become less employable.

Definitions of work productivity

The concept of work ability is complex, but it can be thought of as an individual's various resources in relation to the labour market's needs and requirements (Tuomi *et al.* 2001; Berglind *et al.* 2002; Tengland 2011). The reverse, work disability, can result in reduced work productivity with various consequences. In this thesis, the terms absenteeism and presenteeism are used. Absenteeism means the employee's time off work as sick-leave and/or disability pension leading to sickness benefits (Boonen *et al.* 2002). In Sweden, this

benefit is compensation for an illness that has reduced the ability to work for more than 14 days, but it is also possible to obtain it for long-term or permanent impairment (Strombeck *et al.* 2009). Presenteeism, means being present at work while sick, or the degree of reduced productivity while at work (Schultz *et al.* 2007; Beaton *et al.* 2009).

Assessment of work productivity

Different methods are used to measure work productivity. Assessment with questionnaires, observational methods, physical tests, and interviews are possible. To study absenteeism, data on sick-leave, for example, frequency of individuals on sick-leave, length of sick-leave, incidence rate, cumulative incidence, and duration of sick-leave, have been suggested (Hensing *et al.* 1998). These data can be collected through a register (sick-leave >14 days), but they may also be details provided by employers, or self-reported data. Measurement of presenteeism may involve reduced productivity due to the quantity or quality of work affected, adequate time not spent on task, or personal factors. Presenteeism is based on self-reported data (Schultz *et al.* 2007).

Absenteeism

There is a clear and well documented influence on absenteeism in individuals with musculoskeletal pain disorders (McDonald *et al.* 2011), osteoarthritis (Hubertsson *et al.* 2013), RA (Geuskens *et al.* 2008; Bansback *et al.* 2012; Kvamme *et al.* 2012), AS (Boonen *et al.* 2001; Boonen *et al.* 2002; Strombeck *et al.* 2009; Boonen *et al.* 2010b; Healey *et al.* 2011), and PsA (Kavanaugh *et al.* 2006; Armstrong *et al.* 2012; Kvamme *et al.* 2012) reported in the last decade. Large variations in prevalence among countries, may be explained by differences in social security systems, patient groups, endpoints, or recall periods (Boonen *et al.* 2002; Boonen 2006; Verstappen *et al.* 2012). For the SpA, there are fewer data on absenteeism but the results appear to be applicable even to those individuals for whom an increased risk of sick-leave and work disability has been found (Rohekar *et al.* 2010). Data on patients with AS have shown that higher disease activity (Rohekar *et al.* 2010; Healey *et al.* 2011; Armstrong *et al.* 2012), lower physical function (Ward *et al.* 2001; van der Heijde *et al.* 2006; Geuskens *et al.* 2008; Rafia *et al.* 2012), worse HRQoL (Kristensen *et al.* 2012), higher score in the depression scale (Healey *et al.* 2011), and more pain (Ward *et al.* 2001; Kristensen *et al.* 2012) have a negative influence on the ability to work. Lower education level, female gender, higher age, and other co-morbidities also have a negative effect on ability to work (Ward *et al.* 2001). Treatment with TNF blockers in individuals with AS and PsA has been shown to reduce sick-leave and work disability (Kavanaugh *et al.* 2006; van der Heijde *et al.* 2006; Keat *et al.* 2008; Kristensen *et al.* 2012). Factors associated with a high degree of absenteeism have scarcely been studied in all individuals with SpA.

Presenteeism

In order to have a broader view of work productivity, it is important to study more subtle measures such as presenteeism, i.e. the degree of reduced work productivity due to the disease in those still working (Beaton *et al.* 2009; McDonald *et al.* 2011). Some authors have claimed that presenteeism is the main source of loss of work productivity; the negative economic effects are several times greater than health-care costs and larger than the costs of absenteeism (Mattke *et al.* 2007; Schultz *et al.* 2007). Presenteeism has been shown to be common in musculoskeletal pain disorders (McDonald *et al.* 2011), in chronic arthritis (Burton *et al.* 2006; Schultz *et al.* 2007), and in AS (Boonen *et al.* 2010b; Maksymowych *et al.* 2010; Healey *et al.* 2011), while this variable has scarcely been studied in all individuals with SpA. Associations between presenteeism and higher disease activity (van der Heijde *et al.* 2006; Boonen *et al.* 2010b; Maksymowych *et al.* 2010; Rohekar *et al.* 2010; Rafia *et al.* 2012), lower physical function (van der Heijde *et al.* 2006; Geuskens *et al.* 2008; Boonen *et al.* 2010b; Maksymowych *et al.* 2010; Rohekar *et al.* 2010; Rafia *et al.* 2012), reduced HRQoL (Maksymowych *et al.* 2010; Rohekar *et al.* 2010), higher scores in depression and anxiety (Healey *et al.* 2011), more pain (Geuskens *et al.* 2008; Maksymowych *et al.* 2010), lower self-efficacy (Healey *et al.* 2011), and increased age (Healey *et al.* 2011) have been reported in patients with AS, while very little information is available for other individuals with SpA. Whereas presenteeism measures reduced productivity at work, activity limitations measure reduced productivity outside work. Activity limitations have been found to be present in one out of four patients with AS (Maksymowych *et al.* 2010) and to be associated with HRQoL, physical function, disease activity, and pain (Maksymowych *et al.* 2010). Associations between activity limitations and presenteeism are not yet studied.

Rationale for this thesis

Better knowledge of the epidemiology of different rheumatic diseases and their burden to society is needed to increase the likelihood of better health-care planning and use of resources. Until now, the occurrence calculations are often based only on studies of patients in the different subgroups, while patients affected by the whole group of SpA diseases, have scarcely been studied.

As patients with SpA often have early onset and life-long disease causing limitations affecting several aspects of life, an awareness of the consequences can help the patients to cope with the disease, and can help health-care providers to support the patient in the best possible way. Previous research in SpA has mainly focused on the ICF components, body function, body structure, and activities whereas this thesis adds outcomes related to participation. Stiffness, pain, impaired physical and mental function, and reduced HRQoL are common and well-known consequences, which the patients are also aware of and may get help with from the health-care providers. However, in recent years promotion and maintenance of physical activity for health has been recognized as an important outcome, also showing effects on several dimensions of health in patients with arthritis. Helping patients to follow these recommendations on physical activity has become an important part of the regime, and better knowledge of the pattern of physical activity can help tailor activities and facilitate coaching strategies in clinical routine.

Yet another consequence that affects the patient with a life-long disease is the ability to work. Studies focusing on how to identify the patients who are at risk of a worse prognosis in working life would be useful for patients, for health professionals, and for society as a whole. In the clinical situation, knowing what to measure, what to be aware of, and how to predict reduced productivity both at work, and outside work is valuable and promotes management that is tailored to the patient. There is therefore a need for better knowledge concerning the occurrence and the consequences of SpA.

Aims

The overall aim was to study the prevalence of SpA and the consequences of the disease for the individual and for society regarding physical activity and work, in a well-defined population-based cohort of patients.

The specific aims were:

- I. To estimate the prevalence of SpA in subjects seeking health care in the Skåne region, and to define the age and gender characteristics for the whole SpA group and for the different subgroups (Paper I).
- II. To study self-reported physical activity in patients with SpA, and possible differences associated with gender and the SpA subgroups. A second aim was to study factors associated with the different physical activity patterns (Paper II).
- III. To evaluate work productivity and compare differences between women and men and for subgroups of SpA. A second aim was to study factors associated with reduced productivity at work in patients with SpA (Paper III).
- IV. To study predictors of presenteeism and possible differences with regard to gender and the SpA subgroups. A secondary aim was to study associations between presenteeism and activity impairment outside work (Paper IV).

Methods

Study design

This thesis is based on four epidemiological studies using different information from population-based cohorts of patients with SpA. Paper I is a population-based prevalence study based on the Skåne Health Care Register (SHCR). Papers II and III are cross-sectional population-based cohort studies, and Paper IV is a longitudinal population-based cohort study (Table 3), all three of them being based on data mainly derived from the SpAScania Questionnaires (SSQ).

Table 3. Characteristics of studies I—IV.

Paper	Study collection year	Subject of study	Study design	Data sources	No. of participants (% men)	Age year, mean (SD)	Disease duration years, mean (SD)
I	2007	Prevalence	Population-based (*health-care seeking)	SHCR ¹ SPR ² ESP ³	3,852 (49%)	53 (15)	-
II	2009	Physical activity	Population-based cohort* Cross-sectional	SHCR ¹ SPR ² SSQ ⁴ 2009 SNIPH ⁵	2,167 (48%)	55 (14)	14 (12)
III	2009	Work productivity	Population-based cohort* Cross-sectional	SHCR ¹ SPR ² SSQ ⁴ 2009 SSIA ⁶	1,773 (48%)	51 (11)	13 (10)
IV	2009, 2011	Presenteeism	Population-based longitudinal cohort*	SHCR ¹ SPR ² SSQ ⁴ 2009 SSQ ⁴ 2011	1,253 (47%)	51 (11)	13 (10)

¹SHCR: Skåne Health Care Register, ²SPR: Swedish Population Register, ³ESP: The European Standard Population, ⁴SSQ: SpAScania Questionnaire, ⁵SNIPH: Swedish National Institute of Public Health, ⁶SSIA: Swedish Social Insurance Agency

The Skåne Health Care Register

In Sweden, free health care is provided by both public and private health-care providers, all through the same tax-based financing system. All providers are required to provide information for reimbursement purposes, which ensures a high quality of reporting. In

the Skåne region, all health-care visits, public and private, in-patient and out-patient, are registered in the Skåne Health Care Register (SHCR). The register includes information on the health-care provider and the date of the health-care visit, and it is linked to the Swedish Population Register (SPR) with a 10-digit personal identification number providing information on date of birth. Since 1997, codes on the International Classification of Diseases, Tenth Revision (ICD-10) as given by any physician have been registered in the SHCR for public care. The population of Skåne was 1,263,088 by the end of December 2012, which means that the SHCR covers one-eighth of the Swedish population (Statistics Sweden 2012). Data from the SHCR were used in studies I–IV for identification of the patients in the SpAScania cohort, the cohort which this thesis is based on. Data from the SPR were used in studies I–IV for information on sex, residential address, and date of death to ensure exclusion of patients who had died or moved out of the region.

Study population

The SpAScania cohort

The individuals on whom this thesis is based were identified by searching for all health-care seeking patients aged ≥ 15 years with SpA in Skåne (on 31 December 2007), according to chosen ICD-10 codes in the SHCR. At that time, the county of Skåne had 999,121 inhabitants ≥ 15 years. The ICD-10 codes that could be linked to SpA were based on the literature and on clinical consensus, resulting in 6,799 valid cases and this group of patients was named the SpAScania cohort (Figure 4). The cohort included all cases who at any time over five calendar years (2003–2007) had received a diagnosis of SpA. This was achieved by searching for 12 separate ICD-10 codes for AS, PsA, Aa-IBD, and USpA (Table 1, page 22) and 8 ICD-10 codes for possible SpA (M08.1, M01.2, M02.0, M02.1, M02.2, M02.8, M02.9, M03.2; juvenile ankylosing spondylitis, arthritis in Lyme disease, infectious and reactive arthropathies, and other postinfectious arthropathies in diseases classified elsewhere) (Figure 4, Table 1 page 22).

Data sources

SpAScania Questionnaires

The collection of data from the patients in the SpAScania cohort involved two questionnaire-based postal surveys. The baseline SpAScania questionnaire (2009 SSQ) was sent out between May and August 2009 to all patients in the SpAScania cohort who were ≥ 18 years of age, still alive, and resident in the county in 2009 ($n=5,771$). Data from the 2009 SSQ were used in studies II, III, and IV. The follow-up SSQ (2011 SSQ) was

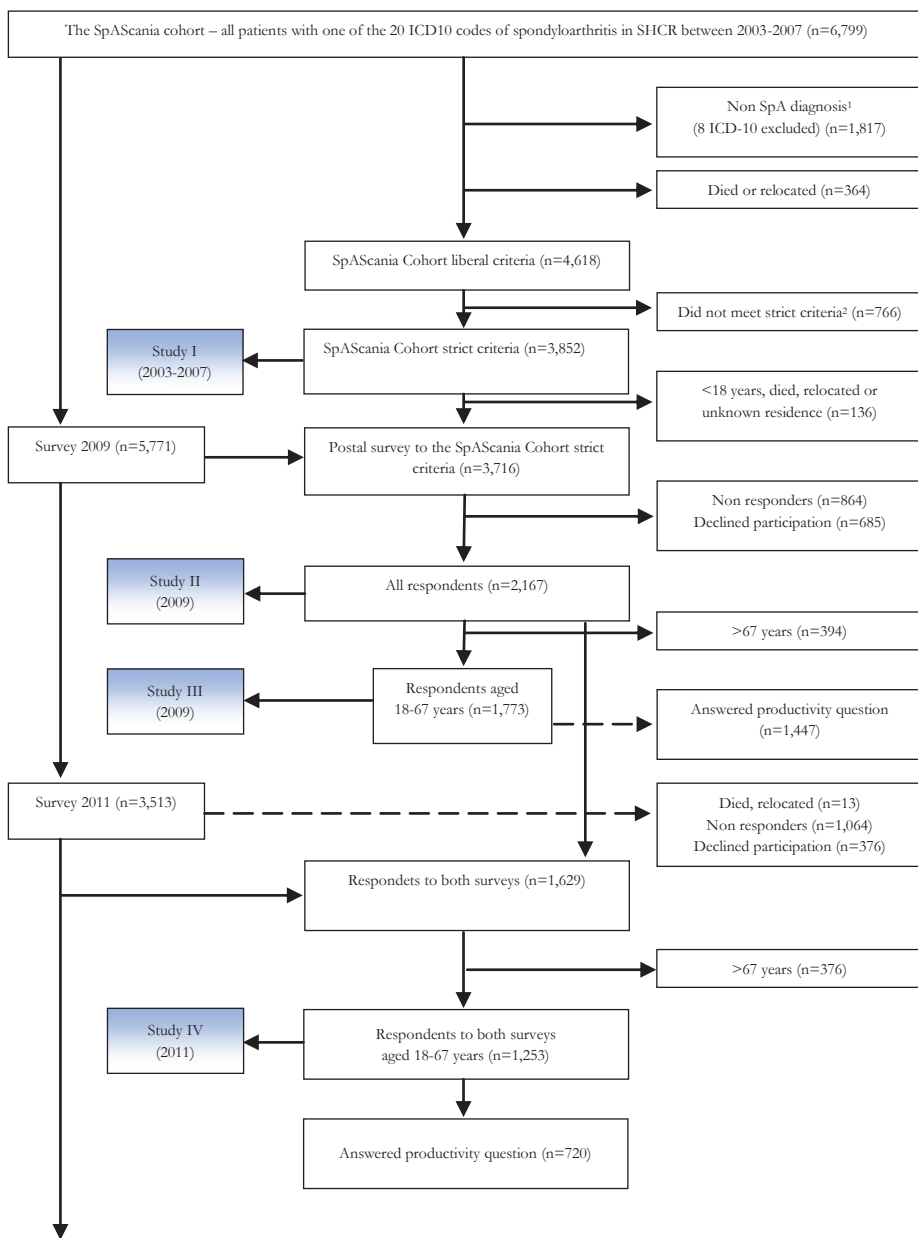


Figure 4. Flow chart of the patients at each stage of study I-IV. ¹M08.1, M01.2, M02.0, M02.1, M02.2, M02.8, M02.9, M03.2. ²The spondyloarthritis (SpA) diagnosis were required at least once by a rheumatologist or internist, or at least on two separate occasions by any other physician.

sent out between November 2011 and January 2012, 2.5 years after the 2009 SSQ. It included patients in the SpAScania cohort who were still alive and resident in the county in November 2011 (n=3,513), and who had not declined further participation. Data from the 2011 SSQ were used in study IV.

The SSQs consisted of eight (2009 SSQ) and twelve (2011 SSQ) commonly used and well-validated self-reported outcome instruments, in addition to questions on patient characteristics, demographics, and lifestyle issues, which are described in detail below. Both SSQs developed for the survey had the same content, except for a few questions that were different in the follow-up. Issues concerning health economics were also included in the SSQs, which were not studied further and are not described in this thesis. The SSQs were drawn up by a panel of three physicians (two specialists in rheumatic diseases and one general practitioner), three PTs (specialists in rheumatic diseases), and one health economist. Before the first survey, the composite SSQ was tested in three focus groups consisting of 20 patients in total with different SpA diagnoses, and one patient research partner from the Swedish Rheumatism association in order to improve face and content validity. This resulted in minor corrections to improve patients' understanding. Reminders were sent on two separate occasions within ten weeks of the first mailing.

The Swedish National Institute of Public Health

The main task of the Swedish National Institute of Public Health (SNIPH) is to provide data and support to the government, state agencies, and other organizations in the field of health promotion and disease prevention. A national public health survey involving ~20,000 individuals 16-84 years of age is conducted each year. Data on physical activity patterns from the survey in 2010 were included for comparison in study II. The reference data were based on responses from 9,972 individuals (Swedish State Institute of Public Health 2010); these data are currently available online (<http://www.fhi.se/Statistik-uppfoljning/Nationella-folkhalsoenkaten/Levnadsvanor/Fysisk-aktivitet/>).

The Swedish Social Insurance Agency

The Swedish Social Insurance Agency (SSIA) provides financial protection for everyone in the event of work incapacity owing to sickness, disability, or injury and covers all inhabitants living in Sweden. By law, all Swedish residents aged 16-64 years are granted economic compensation (i.e. sickness benefit) from SSIA in case of work incapacity longer than 14 days. The first period (≤ 14 days) is paid directly by the employer, and these benefits are not registered by the SSIA. The sickness benefit from SSIA is payable as full, three-quarter, half, or one-quarter day compensations due to sickness, disability, or injury and is limited to one year. For patients with more permanent work incapacity due to a disease, disability pension is granted (Strombeck *et al.* 2009). Data from the SSIA

concerning sick-leave (absenteeism) were used in studies III and IV. The data included the number of days of sickness benefit (longer than 14 days) and disability pension related to SpA and to other diagnoses. The number of gross days with any degree of sick-leave (25%, 50%, 75%, and 100%) was converted to net days, including the 2009 survey response date. This is expressed as the number of net days with full sick-leave in a 3-month period (0–91 days).

Procedures

Data describing the flow chart are presented in Figure 4 (page 39) and the patients included in the four different studies are described in Figure 5.

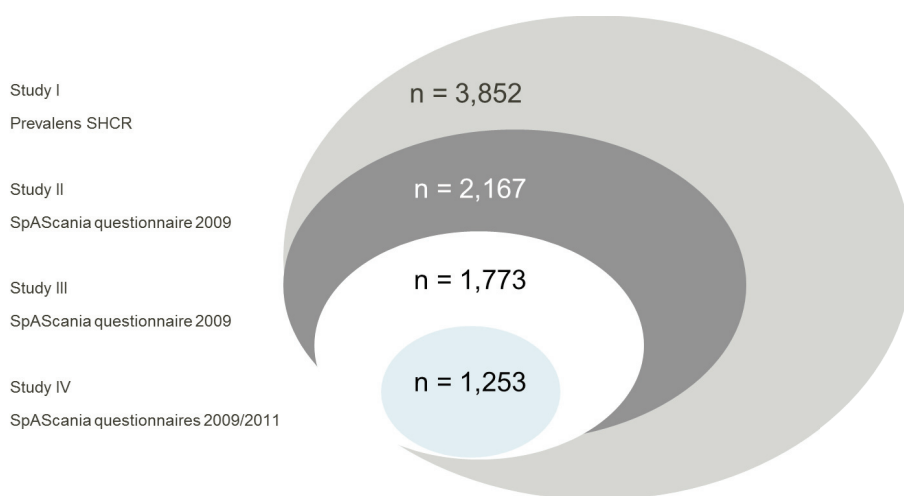


Figure 5. Numbers of patients with spondyloarthritis who were included in studies I–IV.

Study I

All potential cases (n=6,799) identified in the SHCR were cross-referenced with information in the population register at 31 December 2007, the end of the study period, to exclude patients who had died or moved out of the county (n=364). Eight ICD-10 codes for “possible” SpA were excluded (n=1,817) leaving twelve included ICD-10 codes (Table 1, page 22). A total of 4,618 patients from the SpAScania cohort remained, and were included in study I. To ensure higher specificity of the SpA diagnoses when estimating the prevalence, a stricter inclusion criteria were used and the diagnoses were required to be registered at least once by a rheumatologist or internist, or at least on two

separate occasions by any other physician in primary or secondary care. This step eliminated 766 cases and a total of 3,852 patients remained for estimation of the prevalence (Figure 4, page 39). In epidemiological studies, when comparing the occurrence of a disease between different populations the direct method of standardization is commonly used. The data set estimates the numbers of expected prevalent cases relative to the number of observed cases. Data from the European Standard Population (ESP) were used for comparisons in study I (Waterhouse *et al.* 1976).

Study II

Study II had a cross-sectional design. All patients with SpA (12 ICD-10 codes) in the stricter inclusion with diagnosis registered once by a rheumatologist or internist, or on two occasions by any other physician, and who had responded to the 2009 SSQ were included in the analysis. Out of 3,716 patients with SpA in the stricter SpAScania cohort who received the 2009 SSQ, 2,852 (77%) responded to the survey; of these, 685 declined participation and 2,167 (58%) returned the 2009 SSQ (Figure 4, page 39 and Figure 5, page 41).

Study III

Study III also had a cross-sectional design and included all patients of working age (range 18-67 years) in the stricter inclusion who had responded to the 2009 SSQ (n=1,773) (Figure 4, page 39 and Figure 5, page 41).

Study IV

Study IV had a longitudinal design and was based on data from all patients of working age (range 18-67 years at the end of the study period 2011) in the stricter inclusion who had answered both the 2009 SSQ and the 2011 SSQ (n=1,253). Of these patients, 757 reported being in work and 720 responded to the question on presenteeism (Figure 4, page 39 and Figure 5, page 41).

Variables studied

Several outcome variables were considered in this thesis. An overview of the PROMs included in studies II-IV is given in Table 4, and the outcome variables are listed according to the ICF.

Descriptive data

Descriptive data about education level, work status, smoking habits, disease duration, and duration of symptoms, and also questions assessing co-morbidity were self-reported through the SSQ. In addition, information on patient characteristics such as age, gender, and ICD-10 diagnosis were collected from the SHCR.

Table 4. Outcome variables used in studies II-IV, classified according to the ICF

Outcome variable	ICF-component	References	Study II	Study III	Study IV
Physical activity	Activities and participation	Fekete 2012	x	x	x
Fatigue (VAS)	Body function	Stamm 2013	x		
Pain (VAS)	Body function	Hagel 2011	x		
EQ-5D	Body function, Activities and participation, Environmental factors	Boonen 2009 Hagel 2011	x	x	x
BASDAI	Body function	Boonen 2009 Hagel 2011	x	x	x
BASFI	Body function, Activities and participation, Environmental factors	Boonen 2009 Hagel 2011	x	x	x
HAD	Body function, Activities and participation	Prodinger 2008	x	x	x
Presenteeism	Activities and participation	Escorpizo 2009		x	x
WPAI-SpA	Activities and participation	Escorpizo 2009			x
ASES pain	Body function, Activities and participation	Haglund 2013 ¹		x	x
ASES symptom	Body function, Activities and participation	Haglund 2013 ¹		x	x
Sick-leave	Activities and participation	Escorpizo 2009		x	x

¹In manuscript, Haglund *et al.*

Physical activity

From the SSQ in 2009, information on physical activity was collected from three questions taken from recommendations on how to measure self-reported physical activity (Haskell *et al.* 2007). This included information on intensity (moderate/intense physical activity), duration (30 minutes or more), and number of days per week (0–7). Patients who reported activities 5–7 days per week of moderate intensity (defined as aerobic exercise that causes mild breathlessness, e.g. walking or gardening etc.) for at least 30 minutes a day were considered to meet the moderate-intensity physical activity recommendations (MI-PA_{rec}). Those who exercised on a vigorous level for at least 30 minutes 2-3 times a week or more were considered to meet the vigorous physical activity

recommendations (VI-PA_{rec}). These two recommendations (MI-PA_{rec}, VI-PA_{rec}) were then merged and categorized into either meeting or not meeting the WHO recommendations (WHO_{rec}) (Haskell *et al.* 2007; WHO 2010). Categorization of data in this way has already been done in large studies in Sweden, both on arthritis and in the general population (Eurenius *et al.* 2005; Swedish State Institute of Public Health 2010). Physical activity was the outcome variable in study II and an independent variable in studies III and IV.

Fatigue and pain

Fatigue and pain during the previous week were recorded using numeric rating scales (NRS), 0-10 (best to worst). NRS pain has been shown to be reliable and valid (Englbrecht *et al.* 2012). NRS fatigue has been used for evaluation of fatigue in other rheumatic diseases (Gossec *et al.* 2011).

Health-related quality of life

EuroQol-5 domain (EQ-5D) was used to measure HRQoL. EQ-5D is a widely used generic questionnaire consisting of five questions covering mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The EQ-5D has a summary score ranging from 0 to 1 (no health to full health) (TheEuroQolGroup 1990).

Disease activity and physical function

The Bath Ankylosing Spondylitis Indices were used as self-reported disease-specific measures to assess disease activity (BASDAI) and function (BASFI). The indices are primarily validated for patients with AS (Calin *et al.* 1994; Garrett *et al.* 1994; Cronstedt *et al.* 1999; Waldner *et al.* 1999; Van Tubergen *et al.* 2002) but they have been found to be valid in patients with early non-radiographic axial SpA (Rudwaleit *et al.* 2009a). Recently, the BASDAI was also validated for patients with PsA with good-to-moderate validity (Eder *et al.* 2010). In the indices, the total score range between 0 to 10 (best to worst). The BASDAI consists of six questions on fatigue, pain, tenderness, and morning stiffness. The BASFI consists of ten questions; eight are concerned with body function, two concerned with activity and participation and environmental factors (Boonen *et al.* 2009). The final scores in each index are estimated by calculating the means (Calin *et al.* 1994; Garrett *et al.* 1994).

Anxiety and Depression

The Hospital Anxiety and Depression (HAD) scale has been constructed to assess psychological status for scoring of anxiety (HAD anxiety) and depression (HAD depression). The two subscales each consist of seven questions ranging between 0 and 3 on a four-point Likert scale. The subscales have a summary score ranging from 0 to 21 (no distress to maximum distress). A score of less than 8 indicates absence of psychiatric morbidity, a score of 8-10 indicates possible anxiety or depression, and a score of more than 10 points indicates probable anxiety or depression (Zigmond *et al.* 1983).

Self-efficacy

The Arthritis Self-Efficacy Scale (ASES) is concerned with coping with the consequences of the disease, with subscales for pain, function, and symptoms. This was used to assess self-reported self-efficacy in pain and symptoms. The subscales for pain have five items and those for other symptoms have six items. Each item is scored on a scale between 10 to 100 (low self-efficacy to greater self-efficacy) (Lorig *et al.* 1989). The ASES has acceptable validity and responsiveness, supporting its use on patients with AS (Sandhu *et al.* 2011).

Presenteeism

In the 2009 survey, one screening question assessed work impairment in the previous seven days (yes or no). If the answer was yes, patients were also asked to report their reduced productivity at work (presenteeism) by answering the question “During the past seven days, how much did SpA affect your productivity while you were working?”. This question was taken from the valid, reliable, and disease generic instrument Work Productivity and Activity Impairment Questionnaire, which is also used for patients with AS (WPAI-SpA). The question measures the degree of impairment, and patients rate the percentage of reduced productivity at work on a numeric rating scale (0–100%) where a higher percentage indicates a greater reduction in productivity at work (Reilly *et al.* 1993; Prasad *et al.* 2004; Reilly *et al.* 2010). Patients who answered “no” to the initial question were not asked to rate the degree of reduction but were included in the analysis with 0% reduction in productivity. Presenteeism was an outcome variable in studies III and IV.

Work productivity and activity impairment questionnaire (WPAI)

In the 2011 SSQ, the full WPAI-SpA was used. The WPAI-SpA consists of six questions assessing the impact of the disease on work and other daily activities during the previous seven days. This instrument determines employment status, number of hours missed from work due to the disease, hours missed from work for other reasons, hours worked,

degree to which the disease reduces productivity at work, and degree to which the disease reduces productivity in other activities outside work (exemplified as housework, shopping, babysitting, exercising and studying). The results are presented in four different components (absenteeism, presenteeism, impaired activities outside work, and overall work impairment). Each component is expressed as percentage of impairment due to the disease (0–100%) where a higher percentage indicates a greater reduction (Reilly *et al.* 2010). The question concerning presenteeism was the same in the two surveys, but without the initial screening question in the follow-up. The component impaired activities outside work was a secondary outcome variable in study IV.

Data on demographics and characteristics of the patients included in studies I–IV are given in Table 5 and for the patients responded to the 2009 SpAScania questionnaire in Table 6, by gender and by spondyloarthritis subgroups.

Table 5. Demographics and characteristics for the study population in studies I-IV

	Study I	Study II	Study III	Study IV	Study IV ¹ (Presenteeism)
	n=3,852	n=2,167	n=1,773	n=1,253	n=720
Gender, % men	49%	48%	48%	47%	49%
Age, years	53 (15)	55 (14)	51 (11)	51 (11)	48 (10)
Disease duration, years	-	14 (12)	13 (10)	13 (10)	12 (9)
Symp-diagnosis, years ²	-	6 (7)	5 (7)	6 (7)	5 (6)
BASDAI, 0-10	-	4.4 (2.2)	4.4 (2.2)	4.3 (2.2)	3.8 (2.0)
BASFI, 0-10	-	3.2 (2.5)	3.0 (2.4)	3.0 (2.4)	2.3 (2.0)
ASES pain, 10-100	-	50 (22)	51 (22)	52 (21)	55 (21)
ASES symp 10-100	-	57 (21)	59 (21)	59 (21)	62 (20)
EQ-5D, 0-1	-	0.75 (0.17)	0.75 (0.16)	0.75 (0.16)	0.78 (0.13)
HAD anxiety, 0-21	-	5.9 (4.3)	5.9 (4.3)	5.8 (4.2)	5.6 (4.0)
HAD depression, 0-21	-	4.4 (3.6)	4.3 (3.7)	4.2 (3.5)	3.9 (3.3)
Physical activity ³	-	68%	68%	69%	68%
Education level ⁴	-	35%	37%	38%	45%
Non-smokers	-	44%	45%	46%	51%
Absenteeism ⁵			28%	29%	30%
Presenteeism				20 (29)	25 (23)
Activity impairment outside work ⁶			-	84%	80%

Unless otherwise stated, values are mean (SD). ¹720 patients responded to the presenteeism question in both 2009 and 2011 SpAScania questionnaires. ²Years between first symptoms and diagnosis. ³Percentage meeting the WHO recommendations for physical activity. ⁴Percentage with a level of education >12 years.

⁵Absenteeism: percentage with any sick-leave >14 days. ⁶Activity impairment outside work: percentage with any reduction of activity impairment outside work at follow-up

Table 6. Demographics and characteristics for the patients responded to the 2009 SpAScania questionnaire (n=2,167), by gender and by spondyloarthritis subgroups

	Women	Men	AS	PsA	USpA	Aa-IBD
	n=1,121	n=1,046	n=571	n=1,185	n=370	n=41
Gender, % men	-	-	66%	43%	42%	32%
Age, years	55 (14)	56 (13)	55 (14)	58 (13)	49 (14)	57(12)
Disease duration, years	13 (11)	16 (13)	20 (14)	13 (11)	10 (10)	11 (9)
Symp-diagnosis, years ¹	6 (8)	5 (7)	7 (7)	5 (7)	6 (8)	6 (7)
BASDAI, 0-10	4.2 (2.3)	4.0 (2.2)	3.9 (2.2)	4.8 (2.1)	4.2 (2.2)	5.1 (1.9)
BASFI, 0-10	3.5 (2.5)	2.8 (2.4)	3.3 (2.6)	3.2 (2.6)	2.9 (2.4)	3.3 (2.7)
ASES pain, 10-100	49 (21)	51 (22)	51 (22)	49 (21)	52 (21)	54 (23)
ASES symp 10-100	55 (21)	59 (22)	58 (21)	56 (22)	59 (21)	63 (22)
EQ-5D, 0-1	0.74 (0.16)	0.76 (0.17)	0.75 (0.17)	0.74 (0.17)	0.76 (0.17)	0.74 (0.15)
HAD anxiety, 0-21	6.3 (4.4)	5.4 (4.2)	6.0 (4.2)	5.9 (4.4)	5.8 (4.1)	5.8 (4.4)
HAD depression, 0-21	4.5 (3.7)	4.2 (3.6)	4.3 (3.6)	4.4 (3.6)	4.2 (3.6)	3.7 (3.6)
Physical activity ²	70%	66%	69%	67%	69%	81%
Education level ³	38%	31%	41%	28%	45%	39%
Non-smokers	43%	45%	46%	38%	61%	29%

Unless otherwise stated, values are mean (SD). ¹Years between first symptoms and diagnosis. ²Percentage meeting the WHO recommendations for physical activity. ³Percentage with a level of education >12 years.

Analysis of non responders in the 2009 SSQ (n=1,549/3,716) mean age 52 years, showed that patients with AS were more likely to respond to the questionnaire and that patients with Aa-IBD were the least likely to respond. Higher age also significantly predicted a higher response rate in men. Women tended to respond more with higher age except in the subgroup AS.

Statistical methods

In study I, both crude and age-standardized estimates of the prevalence were calculated with 95% confidence interval (CI) using Stata/IC 10.0. ESP was used to enable comparisons with other countries (Waterhouse *et al.* 1976). The total population of Skåne at 31 December 2007 was used as the denominator, compensated for by a 15% reduction to simulate loss of patients seen by private practitioners, whose diagnoses were not forwarded to the register. Validation of the diagnostic coding was done by reviewing medical records of patients visiting a rheumatology clinic within the county. Sensitivity analyses were done in three ways. Firstly, we modified the case criteria from strict (whereby the diagnosis was given at least once by a rheumatologist or internist, or after at least two visits with diagnosis by any other physician) to more liberal (with the diagnosis made at least once by any physician). Secondly, we varied the adjustment to the denominator of the total population by -5% to -25% to simulate the range of uncertainty in the proportion of cases only diagnosed by private health-care providers. Thirdly, we evaluated the prevalence in a district with no private rheumatologist and few private general practices, without any reduction in the denominator.

All analyses in studies II–IV were performed using SPSS software for Windows versions 16–19. Patient characteristics were described with means, standard deviations (SDs), and 95% CI. Mann-Whitney U test, Chi-square test, t-test, and analyses of variance (ANOVAs) were used to analyse differences between groups. A significance level of <0.05 was used. For EQ-5D, the US tariff was used to transforming results to a summary index.

In study II, standardized risk ratios (RRs) and 95% CI for meeting the WHO_{rec} were calculated. The ratios observed in the SpA cohort were divided by their expected ratios for meeting the WHO_{rec} in the population, adjusted for age and gender (Swedish State Institute of Public Health 2010). Multivariate logistic regression analysis with odds ratios (ORs) and 95% CI were used to study associations with MI-PA_{rec} and VI-PA_{rec} as dependent variables and gender, SpA subgroups, age, smoking habits, education level, anxiety, depression, physical function, disease activity, and HRQoL as independent variables. Due to high correlation between BASDAI, BASFI, EQ-5D, HAD anxiety and depression with Spearman's correlations (r_s) >0.3 , each of these variables was included separately in the regression together with other independent variables.

In study III, the analysis of covariance (ANCOVA) with beta-estimate (β -est) was used to study factors associated with reduced productivity. A β -est of x means that the productivity is reduced by x % (or steps) when the score of the factor under study has increased by one step. Due to the high correlation between productivity at work and other variables (Pearson correlation analysis), an acceptable correlation was considered to be >0.5 . The β -est described the true coefficient in the population, based on a sample from the population. The analyses are presented for all patients, and for twelve different strata, by gender, age, and SpA subgroup (AS, PsA, and USpA).

In study IV, multivariate logistic regression analyses with OR and 95% CI were used to study predictors of presenteeism. Presenteeism at follow-up as the dependent variable was dichotomized based on the mean value (24.9%). Values of $\geq 24.9\%$ were regarded as presenteeism (reduced productivity). A base model included gender, age, SpA subgroups, and presenteeism at baseline in 2009 as independent variables. HRQoL, disease activity, physical function, anxiety, depression, self-efficacy pain and symptoms, smoking habits, disease duration, education level, reaching recommended level of physical activity, and sick-leave were other possible predictors that were added separately to the base model due to high correlation (>0.5 , Pearson correlation analysis). The models were controlled for interactions between gender, different SpA subgroups, and short and long disease duration (split by median duration of 0-8 years vs. ≥ 9 years). Chi-square test was used to analyse the association between presenteeism and activity impairment outside work (dichotomized based on the mean value of 32.7%).

Ethics

The Regional Ethical Review Board of Lund University, Sweden approved the studies (301/2007, 406/2008). Informed consent was obtained from all patients, in compliance with the Helsinki Declaration.

Results

Prevalence of spondyloarthritis (Paper I)

The overall crude prevalence of SpA was 0.45% (95% CI 0.44–0.47). The mean age (SD) of SpA patients was 53 (15) years. The peak prevalence was found in the 45-59 year and the 60-74 year stratas (Figure 6, Table 7).

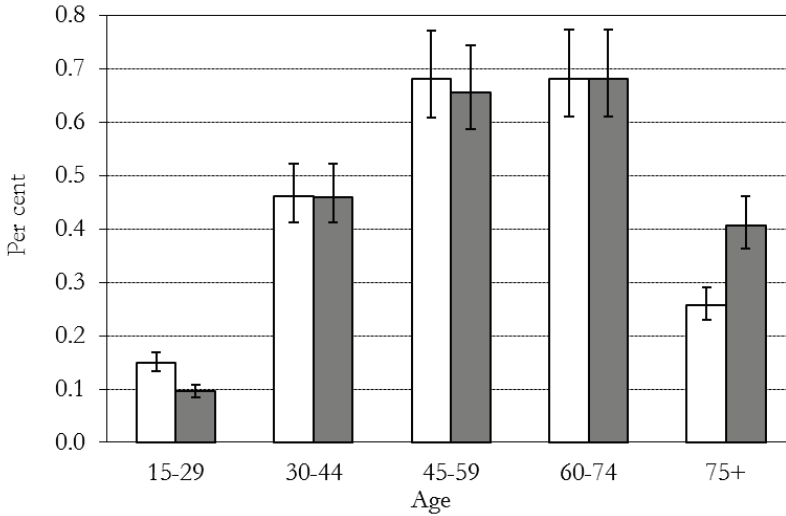


Figure 6. Prevalence of spondyloarthritis (ankylosing spondylitis, psoriatic arthritis, arthritis associated with inflammatory bowel disease, and undifferentiated spondyloarthritis) in Sweden. Error bars show the effect of the sensitivity analysis when adjusting the denominator from -5% to -25%. White bars: women; grey bars: men.

Table 7. The prevalence of SpA (that led to a doctor's consultation), and its component subgroups in southern Sweden by the end of 2007. Age 15 or older.

	Crude prevalence (%)		
	Women	Men	Total
Spondyloarthritis	0.45	0.45	0.45
AS	0.075	0.16	0.12
PsA	0.27	0.22	0.25
Aa-IBD	0.021	0.010	0.015
USpA	0.12	0.094	0.10

AS: ankylosing spondylitis; PsA: psoriatic arthritis; Aa-IBD: inflammatory arthritis associated with inflammatory bowel disease; USpA: undifferentiated spondyloarthritis.

The most frequent subgroup of SpA was PsA, with a prevalence of 0.25% (95% CI 0.24-0.26), followed by AS with a prevalence of 0.12% (95% CI 0.11-0.124) and USpA with a prevalence of 0.10% (95% CI 0.098-0.112). Aa-IBD was the least frequent subgroup, with a prevalence of 0.015% (95% CI 0.011-0.018) (Table 7).

Of the total number of SpA cases, 93.6% did not have a combination of SpA diagnoses in the register between 2003-2007. The remaining 6.4% (n=248) had some form of combination of SpA diagnoses. The most frequent combinations were AS and USpA (n=133), and PsA and USpA (n=52).

In a validation analysis, the accuracy of the diagnostic coding between the SHCR and a consecutive series of patients seen at an out-patient rheumatology clinic was evaluated. Medical records for 347 patients were reviewed with regard to the items included in classification criteria for AS, PsA, USpA, and Aa-IBD. A valid SpA diagnosis was found in 340 (98%) of the cases. In the remaining seven patients (2%), reactive arthritis (ReA) was found in two patients; otherwise, the cause was still an unclear rheumatic condition.

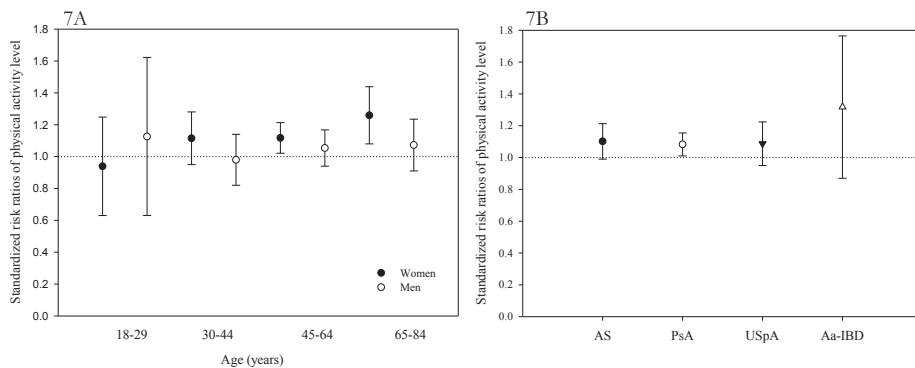
The three sensitivity analyses resulted in a crude prevalence ranging from 0.41% to 0.54%, i.e. marginally different from 0.45%. In the first analysis, a more liberal case definition was used where diagnosis was only required in the SHCR on one occasion, resulting in a prevalence of 0.54%. In the second analysis, the denominator was adjusted to simulate the loss of cases only seen in private health care and not forwarded to the SHCR, resulting in a prevalence between 0.41% and 0.51% shown by error bars in Figure 6, by gender and age. In the third analysis, the prevalence was estimated in a health-care district with no private rheumatologist and few private practices, without any adjustment to the denominator, resulting in a prevalence of 0.51%.

Differences in physical activity pattern (Paper II)

The patients with SpA overall met the WHO_{rec} to a higher degree than the Swedish population (RR 1.09; 95% CI 1.04-1.15). The age-adjusted RR for meeting the WHO_{rec} in women with SpA was 1.14 (95% CI 1.06-1.22) and in men it was 1.05 (95% CI 0.97-1.12). The lowest RR was found in young women with PsA (0.60; 95% CI 0.26-0.95). For men, the point estimates were above 1.0 for all age groups except those aged 30-44, where it was just below 1.0 (RR 0.98; 95% CI 0.82-1.14) (Figure 7A, page 52). The age and sex-adjusted RRs for all SpA subgroups, including AS, PsA, USpA, and Aa-IBD, showed higher rates than for the Swedish population (Figure 7B, page 52).

A total of 68% of all patients (n=1,470) met the WHO_{rec}, and more frequently in women (70% vs. 66%, p=0.007). When slitting WHO_{rec} into MI-PA_{rec} and VI-PA_{rec}, a total of 57% of patients (n=1,237) in the SpA group were exercising at a moderate intensity

(≥ 30 minutes, ≥ 5 days a week), more frequently in women (61% vs. 53%, $p < 0.001$). Thirty-two per cent ($n=697$) of the patients with SpA met the VI-PA_{rec} (exercising more vigorously for at least 30 minutes, 2-3 times a week), more frequently in men (35% vs. 29%, $p = 0.01$) (Table 8).



Age	18-29		30-44		45-64		65-84	
Women (W)	W	M	W	M	W	M	W	M
Men (M)								
Observed	36	20	172	140	389	342	185	174
Expected	38	18	154	143	348	326	147	162

Subgroup	AS	PsA	USpA	Aa-IBD
Observed	390	782	254	33
Expected	354	723	234	25

Figures 7A and 7B. A. Standardized risk ratios (RRs) and 95% CIs for meeting the WHO_{rec} in women and men in different age groups with spondyloarthritis. B. Age- and sex-standardized risk ratios (RRs) and 95% CIs for meeting the WHO_{rec} in the different subgroups of spondyloarthritis.

Table 8. Physical activity and exercise level of the patients, by gender, and in different spondyloarthritis subgroups

		SpA total	Women	Men	p-value
SpA total	Physical activity level, %	57%	61%	53%	$p < 0.001$
	Exercise level, %	32%	29%	35%	$p = 0.011$
AS	Physical activity level, %	55%	65%	50%	$p < 0.001$
	Exercise level, %	36%	42%	34%	$p = 0.041$
PsA	Physical activity level, %	58%	60%	56%	$p = 0.078$
	Exercise level, %	28%	24%	34%	$p < 0.001$
USpA	Physical activity level, %	57%	62%	49%	$p = 0.011$
	Exercise level, %	38%	36%	42%	$p = 0.172$
Aa-IBD	Physical activity level, %	66%	71%	54%	$p = 0.269$
	Exercise level, %	44%	39%	54%	$p = 0.555$

Physical activity level: percentage who achieved a level of physical activity of moderate intensity for ≥ 30 minutes, ≥ 5 days a week. Exercise level: percentage who reached a vigorous level of exercise ≥ 30 minutes, 2-3 times a week.

In the multivariate logistic regression analyses, female gender and higher age were associated with meeting the MI-PA_{rec}, with OR ranging from 1.56 to 1.79 (for gender), and OR 1.02 for age per year. Also, a better HRQoL (EQ-5D) was positively associated with the outcome (OR 2.10), while patients with lower physical function (BASFI) (OR 0.93), higher self-reported disease activity (BASDAI) (OR 0.95), and higher score in anxiety (HAD anxiety) (OR 0.97) and depression (HAD depression) (OR 0.94) were less likely to meet the MI-PA_{rec} (significance level ≤ 0.05) (Table 9).

Table 9. Results of multiple logistic regression analysis with meeting the MI-PA_{rec} (physical activity performed ≥ 5 days a week at moderate intensity for ≥ 30 minutes) as the dependent variable

Variables	MI-PA _{rec}									
	BASFI ¹ n=2,018		BASDAI ¹ n=1,474		EQ-5D ¹ n=1,973		HAD anxiety ¹ n=2,046		HAD depression ¹ n=2,047	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Men	1		1		1		1		1	
Women	1.64 (1.36;1.99)	<0.001	1.79 (1.43;2.24)	<0.001	1.61 (1.33;1.95)	<0.001	1.57 (1.31;1.87)	<0.001	1.56 (1.30;1.88)	<0.001
Age (per 1 year)	1.02 (1.01;1.03)	<0.001	1.02 (1.01;1.03)	<0.001	1.02 (1.01;1.03)	<0.001	1.02 (1.01;1.02)	<0.001	1.02 (1.01;1.02)	<0.001
Non-smokers	1		1		1		1		1	
Smokers	0.94 (0.78;1.13)	0.50	0.87 (0.70;1.09)	0.23	0.92 (0.76;1.11)	0.37	0.93 (0.77;1.12)	0.44	0.94 (0.78;1.34)	0.54
Low education level ²	1		1		1		1		1	
High education level	1.03 (0.85;1.25)	0.78	1.00 (0.80;1.26)	0.99	1.07 (0.88;1.30)	0.51	1.03 (0.85;1.25)	0.74	1.03 (0.85;1.25)	0.76
Subgroup										
AS	1		1		1		1		1	
PsA	1.00 (0.80;1.24)	0.97	1.08 (0.84;1.39)	0.57	1.00 (0.80;1.24)	0.98	1.02 (0.82;1.27)	0.86	1.03 (0.83;1.28)	0.79
USpA	1.00 (0.76;1.33)	0.98	0.95 (0.70;1.28)	0.72	0.93 (0.70;1.24)	0.62	1.01 (0.76;1.33)	0.95	1.01 (0.77;1.34)	0.93
Aa-IBD	1.13 (0.57-2.24)	0.73	1.28 (0.57;2.84)	0.55	1.30 (0.65;2.61)	0.46	1.27 (0.64;2.49)	0.50	1.23 (0.62;2.42)	0.55
BASFI, 0-10 ³	0.93 (0.90;0.97)	<0.001								
BASDAI, 0-10 ³			0.95 (0.90;0.997)	0.04						
EQ-5D, 0-1 ³					2.10 (1.78;5.38)	<0.001				
HAD anxiety, 0-21 ³							0.97 (0.95;0.99)	0.01		
HAD depression, 0-21 ³									0.94 (0.92;0.97)	<0.001

¹The variables were included separately in the multiple logistic regression analysis together with the other independent variables according to high correlation. ²Low education level (≤ 12 years) ³Per unit increase.

Repeating the same multivariate logistic regression analyses using meeting the VI-PA_{rec} as a dependent variable, negative associations were found with higher age (OR 0.99), the diagnosis subgroup PsA (ORs ranging from 0.72 to 0.79), smoking (OR ranging from 0.67 to 0.74), lower physical function BASFI scores (OR 0.87), higher BASDAI scores (OR 0.92), and higher score in the HAD depression scale (OR 0.92). There was a positive association between better HRQoL and the outcome (OR 5.95) (Table 10, page 54).

Table 10. Results of multiple logistic regression analysis with meeting the VI-PA_{rec} (exercising 2-3 times a week at a vigorous level for ≥30 minutes) as the dependent variable

VI-PA _{rec}										
Variables	BASFI ¹ n=1,689		BASDAI ¹ n=1,257		EQ-5D ¹ n=1,653		HAD anxiety ¹ n=1,709		HAD depression ¹ n=1,709	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Men	1		1		1		1		1	
Women	0.87 (0.71;1.08)	0.21	0.84 (0.66;1.07)	0.16	0.79 (0.64;0.97)	0.02	0.77 (0.63;0.94)	0.01	0.77 (0.62;0.94)	0.01
Age (per 1 year)	0.99 (0.98;1.00)	0.05	0.99 (0.98;0.997)	0.01	0.99 (0.98;0.996)	0.002	0.99 (0.98;0.99)	<0.001	0.99 (0.98;0.99)	<0.001
Non-smokers	1		1		1		1		1	
Smokers	0.68 (0.55;0.84)	<0.001	0.69 (0.54;0.88)	0.002	0.74 (0.60;0.91)	0.005	0.67 (0.55;0.83)	<0.001	0.68 (0.56;0.84)	<0.001
Low education level ²										
High education level	1.07 (0.86;1.32)	0.55	1.06 (0.83;1.35)	0.65	1.12 (0.91;1.38)	0.30	1.14 (0.931;1.41)	0.21	1.12 (0.91;1.38)	0.29
Subgroup										
AS	1		1		1		1		1	
PsA	0.72 (0.57;0.92)	0.009	0.79 (0.60;1.05)	0.10	0.78 (0.61;0.997)	0.05	0.79 (0.62;0.999)	0.05	0.78 (0.61;0.99)	0.04
USpA	0.91 (0.67;1.23)	0.53	0.89 (0.64;1.22)	0.46	0.95 (0.70;1.29)	0.75	0.97 (0.72;1.30)	0.82	0.94 (0.69;1.27)	0.68
Aa-IBD	1.40 (0.68-2.88)	0.36	1.60 (0.71;3.60)	0.26	1.35 (0.66;2.77)	0.42	1.61 (0.80;3.24)	0.18	1.50 (0.74;3.04)	0.26
BASFI, 0-10 ³	0.87 (0.83;0.91)	<0.001								
BASDAI, 0-10 ³			0.92 (0.87;0.97)	0.002						
EQ-5D, 0-1 ³					5.95 (3.01;11.8)	<0.001				
HAD anxiety, 0-21 ³							0.98 (0.96;1.00)	0.10		
HAD depression, 0-21 ³									0.92 (0.90;0.95)	<0.001

¹The variables were included separately in the multiple logistic regression analysis together with the other independent variables according to high correlation. ²Low education level (≤12 years) ³Per unit increase.

A syntax-error was recognized in the calculations of the HAD score when the manuscript had been published and a report on errata was submitted. The HAD values in the demographics were recalculated (Table 5, page 46). Due to high correlation with BASFI, BASDAI and EQ5D the HAD anxiety and depression scores should not be included in the logistic regressions as a covariate and all values in the logistic regressions have been recalculated. The new calculations were based on separate inclusions of the HAD in the multiple logistic regression analysis together with the other covariates (Table 9, 10). However, this error does not affect the conclusion.

Work productivity (Paper III)

Fifty-five per cent (n=802) of the patients who answered the question concerning reduced productivity (n=1,447) reported no reduction in productivity at work. For those who reported reduced productivity, the mean reduction was 20% (95% CI 18–21). Women reported a statistically significantly higher degree of reduced productivity at work than men (mean reduction 23% vs. 17%, $p<0.001$). No statistically significant differences were found between the SpA subgroups AS, PsA, and USpA ($p=0.174$) (Figure 8).

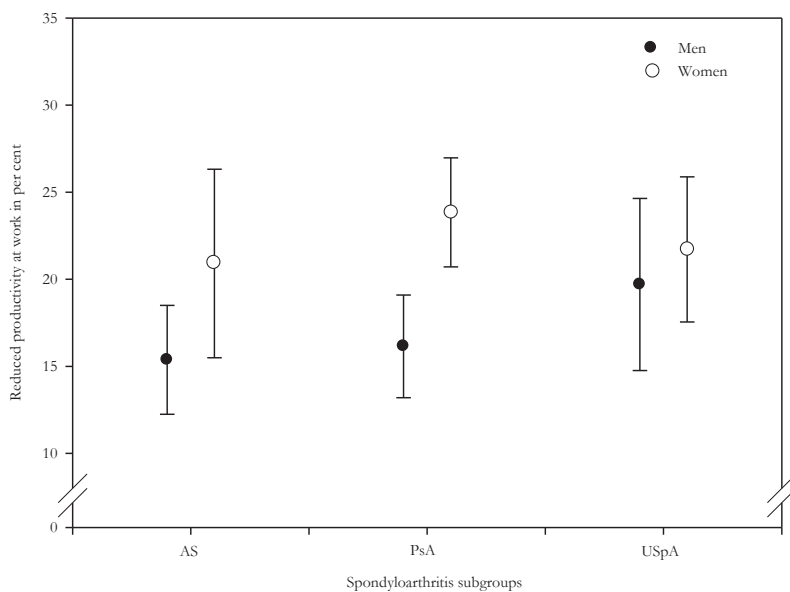


Figure 8. Productivity at work in women and men in different subgroups of spondyloarthritis: AS, PsA, and USpA. Presented as mean and 95% CI.

Sick-leave (absenteeism >14 days) ranged from 0-91 days per three months with a mean of 19 days (95% CI 17-20). A large proportion (72%) had no sick-leave at all (>14 days). The remaining patients, 28% (n=504/1,773), were registered for sick-leave, with 66 mean net days (95% CI 63-68). Fifteen per cent (n=263/1,773) had full register-based sick-leave, meaning absenteeism of ≥ 91 days per three months.

Reduced productivity at work was associated with higher disease activity (BASDAI) (β -est 7.8, $p<0.001$) (a β -est of 7.8 means that the productivity is reduced by 7.8% when the BASDAI score increases by one step), lower physical function (BASFI) (β -est 7.3, $p<0.001$), reduced HRQoL (EQ-5D) (β -est -9.6, $p<0.001$), lower self-efficacy in the ASES pain and symptom scale (β -est -0.5, $p<0.001$), higher anxiety scores (HAD anxiety) (β -est 2.3 $p<0.001$) or higher depression scores (HAD depression) (β -est 3.4, $p<0.001$), and an education level of less than 12 years (β -est 3.9, $p=0.013$) in patients with SpA (Table 11, page 56).

Table 11. Univariate ANCOVA. Associations between reduced productivity at work and disease variables, health-related quality of life, and personal variables in patients with spondyloarthritis (n=1,054-1,439)

Potential associations	All β -est	95% CI	p-value	R-square %
BASDAI ¹	7.8	(7.1;8.5)	<0.001	31
BASFI	7.3	(6.8;7.9)	<0.001	32
EQ-5D ²	-9.6	(-10.5;-8.8)	<0.001	27
ASES pain	-0.5	(-0.6;-0.4)	<0.001	13
ASES symptom	-0.5	(-0.6;-0.5)	<0.001	15
HAD anxiety	2.3	(1.9;2.6)	<0.001	11
HAD depression	3.4	(3.0;3.8)	<0.001	17
Disease duration	-0.1	(-0.3;0.07)	0.248	0
Physical activity ³				
Not meeting rec	2.9	(-0.3;6.2)	0.078	0
Meeting rec	0			
Education level				
≤12 years	3.9			
>12 years	0	(0.8;7.0)	0.013	0

¹n=1,054. ²EQ-5D 0.1 unit. ³Meeting or not meeting the WHO recommendations for physical activity. Bold text means a significance level of <0.05.

Predictors of presenteeism (Paper IV)

In the 2011 SSQ, the self-reported mean score of presenteeism was 24.9% (95% CI 23-27%). Women reported a statistically significantly higher degree of presenteeism than men (mean 28% vs. 22%, p<0.001) while no statistically significant differences were found between the SpA subgroups AS, PsA, and USpA (p=0.73).

In the multivariate logistic regression analyses, the dependent variable presenteeism at the 2.5-year follow-up was predicted by presenteeism at baseline (OR 1.04; 95% CI 1.03-1.05) controlled for gender, age, SpA subgroups, and the other possible predictors. Other statistically significant predictors of presenteeism at follow-up were reduced HRQoL (EQ-5D) (OR 0.68), higher disease activity (BASDAI) (OR 1.47), lower physical function (BASFI) (OR 1.42), lower self-efficacy (ASES) pain (OR 0.97) and symptoms (OR 0.97), higher score for anxiety (HAD anxiety) (OR 1.09) and depression (HAD depression) (OR 1.15), smoking (OR 1.73), and having a low level of education (OR 2.14). These variables were added separately in the analysis and were controlled for gender, age, SpA subgroup, and presenteeism at baseline. Disease duration, physical activity level, and sick-leave (also controlled for gender, age, SpA subgroup, and presenteeism at baseline) did not significantly predict presenteeism at follow-up (Table 12).

Table 12. Results of multivariate logistic regression analyses with presenteeism in 2011 as the dependent variable, expressed as OR with 95% CI (n=499-691)

Variables	OR	95% CI	p-value
Men	1		
Women	1.36	0.97;1.91	0.07
Age (per 1 year)	1.01	0.996;1.03	0.14
Subgroup			
AS	1		
PsA	0.94	0.63;1.42	0.77
USpA	0.76	0.46;1.24	0.27
Productivity in 2009	1.04	1.03;1.05	<0.001
EQ-5D, 0-1 ¹	0.68	0.57;0.82	<0.001
BASDAI (0–10) ²	1.47	1.29;1.67	<0.001
BASFI (0–10) ²	1.42	1.27;1.58	<0.001
ASES pain (10–100) ³	0.97	0.97;0.98	<0.001
ASES symptom (10–100) ³	0.97	0.96;0.98	<0.001
HAD anxiety (0–21) ²	1.09	1.05;1.14	<0.001
HAD depression (0–21) ²	1.15	1.08;1.22	<0.001
Non-smoker	1		
Previous smoker/smoker	1.73	1.22;2.45	0.002
Disease duration (per 1 year)	1.00	0.98;1.03	0.75
High education level (≥12 years)	1		
Low education level (≤12 years)	2.14	1.51;3.04	<0.001
Meeting physical activity rec ⁴	1		
Not meeting physical activity rec ⁴	1.19	0.83;1.70	0.36
Sick-leave ⁵	1.00	0.99;1.00	0.33

Gender, age, spondyloarthritis subgroups, and productivity at baseline in 2009 were analysed first. The other predictors were added separately, all controlled for gender, age, spondyloarthritis subgroups, and productivity in 2009. ¹Per 0.1 unit increase, 0 = worst health ² Per unit increase, best-worst ³ Per unit increase, 0 = worst ⁴ Meeting or not meeting the WHO recommendations for physical activity. ⁵ Sick-leave >14 days (0–91 days).

There were no interactions between gender and SpA subgroups with regard to the outcome ($p \geq 0.39$). When controlling for interactions by disease duration, lower education predicted a greater reduction in productivity (presenteeism) at follow-up in patients with longer disease duration than in those with a shorter disease duration (OR 3.43, $p < 0.001$ vs. 1.23, $p = 0.44$). For all other variables, there were no interactions with regard to disease duration.

The mean score for activity impairment outside work was 32.7% (95% CI 31–35). Women reported a statistically significantly higher degree of mean impairment of activity than men (mean 39% vs. 27%, $p < 0.001$). Small but non-significant differences ($p = 0.07$) in degree of mean values in activity impairment outside work were found between the SpA subgroups AS (30%), PsA (32%), and USpA (37%).

A strong association (OR 16.7; 95% CI 11.6–24.3; $p < 0.001$) was found between presenteeism and activity impairment outside work, with both variables dichotomized on the mean values. Having both presenteeism and activity impairment outside work was reported by 33% of the patients, also more commonly in women than in men (39% vs. 26%, $p < 0.001$). Women reported impaired activity outside work without a report of presenteeism to a larger extent (12%) than men (6%) (Figure 9). There were no differences between the three different subgroups AS, PsA, and USpA regarding activity impairment ($p = 0.37$).

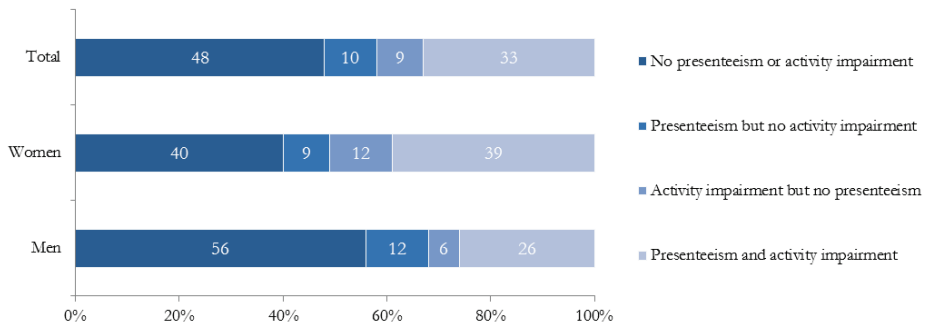


Figure 9. N=718. Distribution of presenteeism and/or activity impairment outside work in patients with spondyloarthritis who answered the SpAScania questionnaire in 2011. All proportions are expressed as percentages.

General discussion

The purpose of this thesis was to study the occurrence of SpA and its subgroups in the general population, and to describe the consequences, especially in relation to physical activity and work, for the individual and for society using a population-based cohort of patients.

SpA, with its different subgroups, is much less well studied than some other inflammatory rheumatic joint disorders such as RA. Even though a change in the consequences of chronic arthritis has been described recently in terms of reduced use of the health-care system and more effective pharmacological treatment (Hagel *et al.* 2013), the basic epidemiology of SpA has hardly been studied. To explore the consequences of SpA for the individual and for society as a whole, this thesis deals with the occurrence of SpA and its subgroups together with physical activity, and work productivity in a population-based cohort of patients with SpA. It also investigates associated and predictive factors for physical activity patterns and work productivity. A more developed understanding of these consequences will be valuable, and useful in clinical practice, when encouraging patients to achieve a healthy level of physical activity and work capacity. The occurrence of SpA reported in this thesis is based on an entire population in a well-defined region of Sweden, and provides a more robust overview than anything already published. A set of PROMs was found to be associated with patients with SpA who were at risk of having a worse prognosis both in terms of reduced level of physical activity and reduced productivity at work: HRQoL, disease activity, physical function, self-efficacy, and mental health status. These PROMs can help health professionals to identify patients at an early stage who are in need of more extensive care and individualized coaching.

Prevalence of spondyloarthritis

Up-to-date estimates of disease occurrence are highly valued and improve the possibility of better health-care planning and use of resources, but there are very few data concerning SpA. In southern Sweden, the prevalence of SpA leading to a consultation with a doctor was found to be 0.45% (study I), which is in line with some other population-based studies in Europe that have also found a prevalence of about 0.5% (Saraux *et al.* 1999; Andrianakos *et al.* 2003; Trontzas *et al.* 2005). In other European studies, the prevalence of SpA has fluctuated between 0.3% and 1.9%, which could be due to different study designs, genetic factors such as the frequency of HLA-B27 in different populations, and different classification criteria (Braun *et al.* 1998; Bruges-Armas *et al.* 2002; Saraux *et al.* 2005; De Angelis *et al.* 2007; Adomaviciute *et al.* 2008). AS and PsA were found to be the two most prevalent subgroups of SpA, representing 80% of the cases, which also is in line with earlier data (Saraux *et al.* 2005). The prevalence of AS (0.12%) was higher in Sweden than in other parts of the world, which can in part be

explained by a different distribution of the HLA-B27 phenotype (Hukuda *et al.* 2001; Helmick *et al.* 2008). PsA, the most frequent subgroup of SpA, had a prevalence of 0.25%, whereas earlier reports have varied from about 0.06% to 0.29% (Braun *et al.* 1998; Shbeeb *et al.* 2000; Andrianakos *et al.* 2003; Saraux *et al.* 2005; Nossent *et al.* 2009; Wilson *et al.* 2009). The sex distribution in SpA was found to be equal in women and men, which agrees with some other studies (Boyer *et al.* 1994; Saraux *et al.* 1999; Saraux *et al.* 2005; Adomaviciute *et al.* 2008) but contradicts others (Braun *et al.* 1998; Andrianakos *et al.* 2003). The inconsistent patterns can be explained by differences when identifying the cases, where earlier studies included a larger proportion of individuals from specialized care or mostly HLA-B27-positive blood donors with AS while the current study was based on the entire population, thereby also including cases with less severe disease (Braun *et al.* 1998; Hukuda *et al.* 2001; Trontzas *et al.* 2005).

The European Standard Population was selected as the reference population in study I, as the article was published in a European journal, to enable comparisons with other countries and put the results in a broader context. This reference population is commonly used when comparisons are made between European countries, and it is considered to be trustworthy (Waterhouse *et al.* 1976).

Disease consequences

To gain a better understanding of prognosis of the disease in clinical practice, earlier studies have concentrated on traditional observational outcome measures, such as disease activity (van der Heijde *et al.* 1999). In recent years, it has been more acceptable to use PROMs; this has also been suggested by the ASAS and OMERACT in order to provide a broader view of the patient's situation (Boonen *et al.* 2010a; Braun *et al.* 2011).

Disease consequences for physical activity

Physical activity and exercise have become of great importance in improvement of health, and attention to the value of physical activity has frequently been suggested as an important intervention (WHO 2002; Blair *et al.* 2009; Alford 2010; Lee *et al.* 2010; Sieverdes *et al.* 2010) and a cost-effective way of maintaining health (WHO 2002). Compliance to physical activity regimes to promote and maintain health, as recommended by the WHO, has hardly been studied, and an increased knowledge in this area can guide health professionals in their everyday work. In the SpAScania cohort, these recommendations on physical activity were successfully adopted by more than two-thirds of the patients with SpA. The patients were more physically active (68%) than the general Swedish population (65%) (study II), a phenomenon that was also found in an earlier Swedish report on RA patients (Eurenius *et al.* 2005), but the opposite has also been reported in patients with self-reported arthritis (Hootman *et al.* 2003; Fontaine *et al.* 2004; Halvorsen *et al.* 2012). The discrepancy may be explained by methodological differences,

both due to differences in identifying the patients and to different ways of assessing physical activity. Regular exercise is an established part of non-pharmacological care in the AS subgroup (Zochling *et al.* 2006a), which may in part explain why the SpA cohort reported a somewhat higher level of physical activity than in the general population. According to a recently published article, these recommendations are useful for all patients, irrespective of disease stage, and should be started as soon as possible (Ozgocmen *et al.* 2012).

There were some differences between men and women, as women were more physically active than men (study II), which contrasts with an earlier finding in the arthritis- and general populations, where men and younger individuals were more physically active (Hootman *et al.* 2003; Fontaine *et al.* 2004; Hurkmans *et al.* 2010). The explanation for this is not obvious, but could be due in part to the fact that men have more severe disease than women, with more radiographic abnormalities (Rudwaleit *et al.* 2009a). Women may also be more inclined to follow recommendations regarding health-related behaviour (Gavin *et al.* 2011), and advice about exercise has been offered to these patients for a long time. It was found that women were more prone to perform physical activity at a moderate level while men preferred vigorous physical activity. Women reported poorer perceived health, which has also been reported by others (Dagfinrud *et al.* 2004; Roussou *et al.* 2011) and could explain why female patients prefer to be only moderately physically active. This could also be explained by different preferences for exercise between genders, whereby women prefer walking and gardening while men prefer more intensive sports (Sundstrom *et al.* 2002). Interestingly, young women (18-29 years) with SpA had a tendency to be less physically active than women of corresponding age in the general population. This was the case despite that the young women had better disease activity scores and physical function scores, lower body mass index, and despite the fact that there were fewer smokers in this group as compared with the older age groups (study II). A larger proportion of the patients in this young group have PsA, and the lower levels of physical activity can partly be explained by the different clinical picture for this subgroup. PsA patients suffer more from inflammation of peripheral joints than patients in the other SpA subgroups (Roussou *et al.* 2012), which could lead to imprecise treatment recommendations by health professionals in clinical practice.

Even though the cross-sectional design leaves the causality unresolved, the findings indicate that poorer self-reported HRQoL, higher disease activity, and lower physical function were associated with and can partly explain, the reduced level of physical activity (study II). However, no association was found between achieving the recommended level of physical activity and reduced productivity (studies III and IV) in patients with SpA, which was a hypothesis since work in most cases presupposes a certain level of physical function. It is known that an adaptation to the disease occurs gradually (Ward *et al.* 2013), which could partly explain why there were no associations. Regardless of the cause, there should be general awareness that exercise at a more vigorous level may be more important from a cardiovascular point of view (Sassen *et al.* 2009). The benefits of physical activity are probably already apparent at an earlier stage of the disease, and in

recent studies the mean disease duration was between 10 and 20 years in the four different SpA subgroups. Low levels of exercise have been found to be predictive of disability in patients with low back pain and neck pain (Enthoven *et al.* 2006; Carroll *et al.* 2008), while the relationship between physical activity and work in patients with arthritis is complex (Kaptein *et al.* 2013) and hardly studied. To further explore a possible link, there may be a need for other ways of measuring physical activity, as with the International Physical Activity Questionnaire (IPAQ) or with observed measurements (aerobic capacity, accelerometer), which more clearly exemplifies what the individuals actually do.

The National Board of Health and Welfare in Sweden (Socialstyrelsen) recommends that all health professionals should work actively to support patients in achieving a healthy lifestyle (National Board of Health and Welfare 2011). Coaching of these patients involves giving advice on “how to live with the disease”, the overall objective being to suffer as few consequences of the disease as possible. The most important take-home clinical message is that one should make the recommendation irrespective of SpA subgroup, and also at an early stage of the disease. To offer opportunities for physical activity but also to coach the patients and motivate them will be the key in future treatment and care.

Disease consequences for work productivity

SpA has a relatively low prevalence as compared to low back pain, but due to the early onset, it affects patients for most of their working lives. This is important to understand in the context of work productivity. However, SpA as a whole, and also certain subgroups, have not been sufficiently studied regarding work productivity, and there is a gap in our knowledge.

Presenteeism

An influence of reduction on work productivity has previously been reported in RA patients (Filipovic *et al.* 2011), in those with other forms of arthritis (Burton *et al.* 2006; McDonald *et al.* 2011), and in AS patients (Kobelt *et al.* 2004; Healey *et al.* 2011; Rafia *et al.* 2012). Work productivity was also found to be reduced in the SpAScandia cohort, and 45% reported a reduction to some extent (study III). This figure is in agreement with data from patients with osteoarthritis (44%) (Zhang *et al.* 2010), but it is lower than what has been reported in patients with AS (53%) (Boonen *et al.* 2010b). The Dutch AS cohort (Boonen *et al.* 2010b) came from specialist rheumatology clinical settings, which differ from the SpAScandia cohort as patients were included from both specialist care and primary health care. Consistent with the results regarding mean reduction of productivity (20%) in study III, researchers in the United Kingdom found a mean reduction of productivity at work of 19% (Healey *et al.* 2011). In a study from Canada on patients with AS, a higher degree of reduced productivity (42%) was found, probably also due to methodological differences when drawing up the cohort (Maksymowych *et al.* 2010).

The findings from studies III and IV support the previous literature in general, but have added information about gender differences and about similarities and differences between the SpA subgroups. Women reported lower productivity than men (studies III and IV), which may in part be related to worse self-reported outcomes in women. It is well known that women have worse reports in PROMs on physical function, psychosocial health, pain, and disease activity (Keefe *et al.* 2000; Zink *et al.* 2000; Dagfinrud *et al.* 2005a).

When factors tentatively contributing to reduced productivity at work (presenteeism) were studied, associations (cross-sectional, study III) and predictors (longitudinal, study IV) agreed to a great extent. Reduced HRQoL (EQ-5D), higher disease activity (BASDAI), lower physical function (BASFI), lower self-efficacy (ASES), and higher score for depression (HAD depression) were all associated with (study III) and predictive of (study IV) reduced productivity at work in patients with SpA. Presenteeism could also be predicted by presenteeism two and a half years earlier, by higher score for anxiety (HAD anxiety), by smoking, and by having a low level of education (≤ 12 years) (study IV). A previous study has indicated that patients with the most severe disease are at greatest risk of developing presenteeism (Rohekar *et al.* 2010), which was also confirmed in the current study. It appears that several aspects of the patient's life situation affect his or her ability to be productive at work, and there is a need to take these considerations into account in order to maintain work productivity in all patients with SpA.

According to the results presented in study IV, limitation of activities during leisure time (activity outside work) and presenteeism go hand in hand. A comparable proportion of patients with SpA were affected in presenteeism and activity impairment, and to a somewhat greater extent in women. Men prioritize their leisure time activity to a greater extent than women, while women first reduce their activity outside work before letting a worse health affect their working life. Impaired activity outside work could indicate problems at work, and these issues need to be addressed and used as a basis for actions in the clinical situation. It is important to be aware that if health professionals in the clinic encounter a patient with reduced activity in leisure time, there will be a high probability that there is also reduced productivity at work (presenteeism). Several PROMs were shown to be associated with presenteeism, and as there is a high correlation between several of these variables, it is perhaps less important which factor is measured and more important to find those patients with worse scores, regardless of the PROMs chosen. By using relatively simple and common self-reported instruments, health-care providers can receive indications of whether the patients are at risk of reduced productivity at work and they can help by giving an appropriate treatment regime and provide individualized counseling.

Absenteeism

Little is known about sick-leave and work status, measured as absenteeism in patients with SpA, while several studies have investigated the impact of AS (Ward *et al.* 2001). As a previous study has shown recall bias and low compliance between self-reported and

register-based data for sciatica (Grovle *et al.* 2012; Strombeck *et al.* 2009; Boonen *et al.* 2010b; Rafia *et al.* 2012), only sick-leave data from a register is reported in Paper III. A large proportion of SpA patients with no sick-leave were found (study III): only 28% were recorded to have any sick-leave (AS 25%, PsA 31%, and USpA 26%), which is lower than reported in three European countries: the Netherlands (52%), France (48%), and Belgium (47%) (Boonen *et al.* 2002). In the study by Boonen, a larger proportion of patients were men, mean age was lower, and there was worse HRQoL and a lower degree of physical function than in the patients in study IV, which could have amplified the differences. However, there are major difficulties in comparing work productivity status and sick-leave data between countries, which has implications for the generalizability of the results. In the study by Boonen, the sick-leave was measured per year, but in study III the sick-leave was based on the previous three months, which would certainly have affected the comparability of the results (Boonen *et al.* 2002).

There was no association between presenteeism (reduced productivity at work) and absenteeism (register-based sick-leave) (study III), which may have been related to different assessment methods for these two outcomes. Yet another explanation might be that the patients who reported reduced productivity at work at a certain level passed on to absenteeism and were then no longer included in the analysis. Although it is difficult to draw conclusions about the results due to the variation in social security systems in different countries, the impact of AS on work status has consistently been substantial in all reports, and Paper III shows that this is applicable also to the SpA group as a whole. When we studied the relationship between self-reported data for presenteeism and register-based measures of sick-leave, no correlation was found. It appears that presenteeism and register-based sick-leave reflect and measure different dimensions of work disability, and thus represent two incomparable outcomes which justifies more studies on absenteeism. In the current analysis, only presenteeism was studied in greater depth.

SpAScania Questionnaire

The majority of the questionnaires used in the SSQ for assessment of patients in the SpAScania cohort have been validated for patients with AS or for other rheumatic diseases, and were considered trustworthy. The questions about physical activity used in study II can be considered to be generic measures. To date, there have as yet been no publications concerning their validity, but they were based on the WHO recommendations on how to measure self-reported physical activity in 2009. Since the questions used in study II have also been used in other Swedish surveys and were similar to the questions used in the national health survey, the methodological problems seem marginal. Observed and self-reported measures (accelerometer vs. questionnaires) of physical activity are not comparable (Hagstromer *et al.* 2010), why results in study II have only been compared with other studies based on self-reported data. At the time of planning for the SSQ in 2008, the national recommendations for physical activity were

used and they did not include measurements of muscle strength, which have now been added to the recommendations (Demmelmaier *et al.* 2013). In the follow-up SSQ in 2011, the validated IPAQ was used (IPAQ group 2005). The IPAQ makes it possible to study sedentary leisure time behaviour and we know that this behaviour has a negative effect on other chronic diseases (Dunstan *et al.* 2010). Questions about strength training were not included, in the follow-up 2011 but it would be best to also include validated questions on strength training in future studies or upon further follow-ups.

The question about work productivity (in study III), which was separated from the complete but valid questionnaire WPAI, has not been validated when used separately, but it was used after a face and content validation procedure. Extracting this question from a wider perspective of work productivity could have affected the results. The full WPAI was inserted in the follow-up, and in the future it should be used in its entirety.

Strengths and limitations

Strengths

The strengths of the design of these epidemiological studies were that they were based on the entire health-care seeking population of a well-defined geographic region (Skåne) with approximately 1.3 million inhabitants. All the patients who fulfilled the inclusion criteria were included in the analysis. The recruitment of the SpAScandia cohort covered a long time period (5 years), which increased the chances of identifying and including patients who had less frequent visits to the health-care system. The SpAScandia cohort included different subgroups of SpA and captured patients from both primary and secondary care, therefore also representing cases with less severe disease (in contrast to several other studies, which were solely based on patients identified at rheumatology clinics). Another strength was that all the patients had been identified with the same method. The large sample size of the SpAScandia cohort made it possible to study rather detailed age and sex characteristics of the different subgroups.

Limitations

There were also some limitations in the design. Firstly, since cases were found from the ICD-10 codes in a register, the validity of the diagnoses might be questioned. To compensate for this, validation of the diagnosis was done by reading the medical records, resulting in a high level of accuracy regarding the diagnoses in the register (ICD-10). Secondly, as there are no formal guidelines for diagnosis setting of SpA, the prevalence is based on patient-driven clinic visits and on the judgement of the physician. Thirdly, the diagnosis of patients seen only in private practice was not listed in the register that the estimates were based on, but the sensitivity analyses showed only marginal effects on the prevalence. Fourthly, the heterogeneity of the SpA group makes interpretation and

implementation of the findings difficult. The SpAScandia cohort was not recruited as a traditional clinical patient cohort, which could make comparisons of disease activity and disease severity more difficult. The population-based SpAScandia cohort is therefore not fully comparable to other SpA cohorts. Different ways of identifying cohorts are needed, but we must be aware of the difficulties in comparing them. Furthermore, the non-response to the questionnaires of approximately 30–40% is a limitation and may have introduced response bias affecting the generalizability, even though the response rate was similar to that in other questionnaire-based population studies (Swedish State Institute of Public Health 2010; Healey *et al.* 2011; Rafia *et al.* 2012). Lastly, the time between the 2009 SSQ and 2011 SSQ is short when studying patients with a lifelong disease, and in futures studies it would be interesting to see if the found predictors are stable also in a longer perspective.

Clinical implications

I have found that the results from this thesis could have certain clinical implications in the care and treatment of patients with SpA.

The findings presented show that the prevalence of SpA is 0.45% and the time between first symptoms and diagnosis is about six years. As the disease is life-long, often with an early onset, and has an effect on several dimensions of life, the consequences for the individual and society are significant. The main challenges in routine practice will be to reduce the time between onset of symptoms and diagnosis, and to identify individuals with possible disease at an early stage and start with the treatment. With greater awareness and knowledge, this time could be reduced. This presupposes knowledge of characteristic symptoms, classification criteria, and management when health professionals meet these patients in the early stages. It is often the general practitioners, the primary nurse, or the PT who meet the patient with back pain first. Regardless of whom, it is important to identify possible SpA patients early on and if necessary refer them to specialist care, which calls for education. A PT specialist in rheumatology could then serve as a help to the primary health-care team and contribute to a first screening through examination, to sort out possible SpA patients. Considering PROMs and with good insight into the differences between mechanical and inflammatory symptoms, PTs can assist rheumatologists in identifying individuals with SpA.

Approximately one-third of all patients with SpA do not meet the minimum requirements for physical activity. It is therefore important to provide recommendations on physical activity (regardless of SpA subgroup) at an early stage of the disease. Patients should be offered opportunities for physical activity, and also coaching strategies and encouragement to exercise. Exercise and physical activity are still key factors in the treatment and care, and PTs have the education and training needed to take a lead in this area.

Several factors including lower physical function, higher disease activity, reduced HRQoL, and impaired mental health were found to influence the levels of physical activity and work productivity. By using a relatively simple self-reported instrument common in clinical practice, health professionals can get indications of whether the patients are at risk of reduced physical activity level and/or reduced work productivity. These considerations should be examined by the health professionals when meeting an SpA patient, and the results from these PROMs can be used in clinical practice to individualize care.

Patients with reduced productivity at work were to a large extent also affected regarding their activity outside work. Activity impairment outside work could then reflect reduced work productivity, and a question about leisure time activity is probably more useful than questions about work productivity when patients visit different health professionals. The strong association suggests that a simple question about activity impairment outside work could be important in clinical practice to detect also the risk of having or developing a

reduced productivity at work.

Coaching is about meeting the patients “at their own level”, trying to motivate them, and helping them to overcome obstacles and see opportunities. All of the health-care team can and should support the patient in his/her effort to achieve a healthy lifestyle, including physical activity, activity outside work, and activity at work. The PT could serve as the expert for alternative physical activities, adapting activities and customizing exercises so that every patient has the opportunity to perform them.

The findings presented in this thesis could present a challenge to health professionals to identify possible diagnoses at an early stage, and to tailor activities, treatment, and care for patients with SpA. Furthermore, it is important for both patients and society to be able to identify those at risk of a worse prognosis by using simple clinical questions in routine practice.

Summary in English

Spondyloarthritis (SpA) is an inflammatory rheumatic disease consisting of several sub-diagnoses, e.g. ankylosing spondylitis (AS), psoriatic arthritis (PsA), arthritis associated with inflammatory bowel disease (Aa-IBD), undifferentiated spondyloarthritis (USpA), reactive arthritis (ReA), and juvenile idiopathic arthritis (JIA). The chronic forms (subgroups) of SpA are AS, PsA, Aa-IBD, and USpA where stiffness and pain are key symptoms. Insidious onset back pain, morning stiffness, waking up at night, and improvement from exercise are common characteristics. The disease is life-long, often with early onset, and can cause limitations in physical function and activity, affects the ability to work, and has a negative effect on health-related quality of life. However, little has been published on prevalence and we need to know more about the consequences of the disease to be able to identify patients at an early stage and to advise patients who are likely to have a poor prognosis. The overall aim of the present work was to determine the prevalence of SpA and to study the consequences for the individual and society in a population-based cohort of patients with the disease.

The four studies included in the thesis are based on a cohort of patients with SpA, identified through the Skåne Health Care Register. By searching for 12 ICD-10 codes for SpA that had led to a doctor's consultation during 2003-2007, the prevalence of SpA could be estimated in study I (n=3,852). The prevalence was 0.45% in adults (≥ 15 years), and SpA was equally common in women and men. The prevalence in different subgroups was 0.12% in AS, 0.25% in PsA, 0.0015% in Aa-IBD, and 0.10% in USpA with different sex distribution patterns.

In May 2009, a questionnaire was sent to all the patients in the cohort who were 18 years or older. The response rate was 58%, and data from the patients who had answered the survey formed the basis of Studies II and III.

Study II (n=2,167) dealt with the proportion who met the recommendations for physical activity, in comparison with the Swedish population. Seven out of 10 patients with SpA met the recommendations, more often in women than in men. The proportion was somewhat higher in the SpA cohort than in the Swedish population.

Study III examined reduced work productivity and associated factors in those of working age (n=1,773). Analyses showed that reduced productivity at work was associated with reduced health-related quality of life, higher disease activity, lower physical function, lower self-efficacy, worse mental health, and low education level.

Study IV was longitudinal, and in addition to data from the 2009 survey, data from a follow-up postal survey in November 2011 were used. Predictors of presenteeism (reduced productivity at work) and association between presenteeism and activity impairment outside work were assessed in all patients of working age who had answered both surveys (n=1,253). Analysis showed that presenteeism could be predicted from

several patient-reported outcome measures (PROMs): reduced health-related quality of life (HRQoL), higher disease activity, lower physical function, lower self-efficacy, anxiety, depression, smoking, and low education level. A clear association between presenteeism and activity impairment outside work was found and 33% of patients reported both presenteeism and activity impairment.

To conclude, the occurrence of SpA in the population is rather low as compared to low back pain. Affected individuals have a life-long disease that has significant consequences for the individual and for society. Several PROMs including reduced HRQoL, higher disease activity, lower physical function, and impaired mental health were found to be associated with and predictive of both reduced level of physical activity and reduced productivity at work in patients with SpA who were at risk of a poor prognosis. This knowledge is important and can help clinicians to identify patients at an early stage who are at risk of a worse prognosis. This information will also be valuable when coaching SpA patients to maintain a healthy level of physical activity and work ability. Together with the patient, the entire health-care team should promote a sustainable and healthy lifestyle regarding, for example, physical activity and work, but the physiotherapist should assume the role of expert regarding patient-specific physical activity and exercise.

Summary in Swedish – Sammanfattning på Svenska

Spondylartrit (SpA) som betyder ”inflammation i ryggradens kotor” är ett paraplybegrepp för flera olika reumatiska sjukdomar t ex ankyloserande spondylit (AS), psoriasisartrit (PsA), artrit vid samtidig förekomst av inflammatorisk tarmsjukdom (Aa-IBD, Crohns sjukdom eller ulcerös kolit), odifferentierad spondylartrit (USpA), reaktiv artrit (ReA) och juvenil idiopatisk artrit (JIA). Sjukdomen kan delas in i två varianter; ”axiell SpA” med besvär i huvudsak från ryggskelettet och ”perifer SpA” med besvär framförallt i och kring övriga leder. Smygande debut av lågt sittande ryggsmärta, störd nattsömn och morgonstelhet kännetecknar den axiella SpA-sjukdomen. Symtomen lindras av rörelse medan stillasittande oftast förstärker besvären. Andra vanliga besvär är smärtor från rygg och nacke med omkringliggande mjukdelar, ledsmärtor, besvär från muskelfästen runt leder, trötthet, ögoninflammation, hudsjukdomen psoriasis, inflammation i tarmen, vilket är besvär som kan förekomma i olika utsträckning och i varierad grad. Underdiagnosen PsA kan ge besvär från ryggen men ger först och främst besvär från andra leder i kroppen. Oftast är färre leder engagerade jämfört med tex besvären vid klassisk ledgångsreumatism (RA).

Sjukdomen är livslång och debuterar ofta tidigt i livet vilket medför konsekvenser för såväl den fysiska funktionen, arbetsförmågan och möjligheten till att ha ett aktivt liv. Dessutom medför ofta sjukdomen en negativ påverkan på den hälsorelaterade livskvaliteten. Det finns behov av dokumentation kring förekomst, dvs hur många som är drabbade, men också kring vilka konsekvenser sjukdomen ger. Denna kunskap är viktig och kan bidra till att tidigt identifiera och stödja de individer som har sämst prognos. Det övergripande syftet med avhandlingen och de fyra ingående studierna var att undersöka förekomst av och de konsekvenser som SpA medför för individen och samhället.

Individerna till den aktuella avhandlingen är identifierade genom Region Skånes vård-databas. I detta register finns information om alla vårdbesök som görs i regionen. Alla besök hos läkare i offentlig vård registreras även med en diagnoskod. Individerna till de fyra studierna som ingår i avhandlingen identifierades genom en sökning i registret av 12 olika diagnoskoder (ICD-10 koder) för SpA. I studie I beräknades förekomst i form av prevalens utifrån alla de 3852 individer som besökt en läkare och registrerats med en SpA diagnos mellan åren 2003-2007, vilka utgör SpA gruppen. Prevalensen var 0,45 % av den vuxna befolkningen (≥ 15 år). Sjukdomsförekomsten för gruppen som helhet var samma bland kvinnor som bland män. Prevalensen för respektive undergrupp var 0,12 % för AS, 0,25 % för PsA, 0,0015 % för Aa-IBD och 0,10 % för USpA.

En enkät skickades via post i maj 2009, till alla individer som identifierats i registret och som utformade SpA gruppen. Svarsfrekvensen var 58 % och data från de individer som återsände en besvarad enkät ligger till grund för studierna II-IV.

I studie II undersöktes i vilken grad de 2167 individerna uppnådde rekommendationen för en hälsosam fysisk aktivitet. Detta innebär 150 minuters fysisk aktivitet på måttlig ansträngningsnivå eller 75 minuter på mer ansträngande nivå varje vecka. Genom data hämtad från folkhälsoinstitutet gjordes en jämförelse mellan den fysiska aktivitetsnivån i SpA gruppen och den svenska befolkningen. Sju av 10 individer med SpA uppnådde rekommenderad nivå för en hälsosam fysisk aktivitet. Kvinnorna uppnådde rekommendationen i något högre grad och vid jämförelse med befolkningen visade det sig att individer med SpA något oftare uppnådde rekommendationen för fysisk aktivitet.

I studie III undersöktes i vilken grad individerna var nedsatta i sin självrapporterade produktivitet när de var på arbetet, men också vilka faktorer som utmärkte de med en nedsatt produktivitet. Analyser gjordes av data från de 1773 individer som var i arbetsför ålder. Resultatet visade att sämre hälsorelaterad livskvalitet, högre sjukdomsaktivitet, sämre fysisk funktion, sämre tilltro till sin egen förmåga och att rapportera mer depressiva besvär associerade med en nedsatt produktivitet i arbetet.

I studie IV användes förutom data från 2009 års enkät, även data från en uppföljningsenkät som skickades ut i november 2011. Denna studie baserades på data från två separata tidpunkter vilket innebär att den är longitudinell. Graden av nedsatt produktivitet i arbetet undersöktes hos alla 1253 individer i arbetsför ålder som besvarat de båda enkäterna. Nästan hälften av individerna (45 %) rapporterade någon grad av nedsatt produktivitet. Analyserna visade att graden av nedsatt produktivitet i arbetet kunde förutsägas av flera faktorer, såsom nedsatt hälsorelaterad livskvalitet, högre sjukdomsaktivitet, sämre fysisk funktion, sämre tilltro till sin egen förmåga och nedsatt mental hälsa i ångest och depressionstest, rökning och låg utbildningsnivå. Samband mellan nedsatt produktivitet i arbetet och aktivitet på fritiden studerades också, där resultatet visade ett starkt samband mellan dessa båda faktorer. Tre fjärdedelar av dem med påverkan på produktiviteten rapporterade även minskad fritidsaktivitet och 33 % rapporterade både nedsatt produktivitet och minskad aktivitet på fritiden.

Förekomsten av ryggsmärta utlöst av SpA är förhållandevis liten i befolkningen i förhållande till ryggsmärta av annan orsak, men för de individer som insjuknar i en kronisk och livslång sjukdom, innebär det negativa konsekvenser både för den som drabbas och för samhället. Ett flertal frågeformulär kring hälsorelaterad livskvalitet, sjukdomsaktivitet och fysisk och psykisk funktion som används i den kliniska vardagen, visade sig kunna förutsäga vilka individer som har störst risk för sämre prognos både avseende fysisk aktivitetsnivå och avseende produktivitet i arbetet. Kunskapen har betydelse för kliniskt verksam vårdpersonal, i arbetet med att tidigt identifiera de med störst risk för ett sämre mående. En ökad förståelse kring dessa prognostiska faktorer i vården är värdefull, för att underlätta arbetet med att vägleda individen till en hälsosam livsstil, t ex med regelbunden fysisk aktivitet, och till att fortsätta kunna arbeta. Tillsammans med individen själv bör all vårdpersonal som samverkar i teamet stödja och i dialog med individen diskutera förutsättningar för en hållbar hälsosam livsstil, men sjukgymnasten bör inta rollen som expert avseende den specifikt anpassade träningen.

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Fysisk aktivitet är all aktivitet som får Ditt hjärta att slå snabbare och som gör dig andfädd och varm. Fysisk aktivitet kan man hålla på med i idrottssammanhang, på fritiden, eller i vardagen. Några exempel på fysisk aktivitet är att promenera, cykla, dansa men också dammsuga eller arbeta i trädgården. När Du svarar på nedanstående frågor, **lägg ihop all tid som Du är fysiskt aktiv varje dag**. Sätt ett kryss i rutan för det alternativ som du tycker stämmer in bäst på dig.

2.5 Hur många dagar under en vanlig typisk vecka är du fysiskt aktiv sammanlagt minst 30 minuter om dagen?

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
0	1	2	3	4	5	6	7	dag/dagar

Träning är en form av fysisk aktivitet som är planerad och strukturerad. Träning utförs för att förbättra valda aspekter av hälsa, så som kondition eller styrka. Några exempel på träning är löpning, raska promenader, åka skidor, simma eller gymnastisera. Sätt ett kryss i rutan för det alternativ som du tycker stämmer in bäst på dig.

2.6 Hur ofta brukar du vanligtvis träna så att du blir andfädd eller svettas?

Varje dag	<input type="checkbox"/>
4-5 gånger i veckan	<input type="checkbox"/>
2-3 gånger i veckan	<input type="checkbox"/>
En gång i veckan	<input type="checkbox"/>
1-2 gånger i mån	<input type="checkbox"/>
Mindre än 1 gång/mån	<input type="checkbox"/>
Aldrig	<input type="checkbox"/>

2.7 Om du tränar, i genomsnitt hur länge brukar du vanligtvis träna varje gång?

Mindre än 15 minuter	<input type="checkbox"/>
15-30 minuter	<input type="checkbox"/>
31-60 minuter	<input type="checkbox"/>
Mer än 1 timme	<input type="checkbox"/>

1.11 Har du under den **senaste veckan** upplevt dig vara mindre produktiv på arbetet än du brukar vara pga värk eller trötthet?

Ja

Nej

Om Ja,

1.11.1 Under den senaste veckan, i vilken utsträckning påverkade din reumatiska ryggsjukdom din produktivitet medan du arbetade? Tänk på de dagar då det fanns begränsningar i den mängd eller typ av arbete du kunde utföra, dagar då du utträttade mindre än du önskade eller dagar då du inte kunde göra ditt arbete så noggrant som vanligt. Om din reumatiska ryggsjukdom påverkade ditt arbete i endast mindre grad väljer du att nedan ringa in ett lågt procenttal. Ringa in ett högt procenttal om din reumatiska ryggsjukdom påverkade ditt arbete avsevärt.

Ta bara hänsyn till i vilken utsträckning din reumatiska ryggsjukdom påverkade din produktivitet medan du arbetade

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100% _____

Min reumatiska ryggsjukdom hade
ingen påverkan på mitt arbete

Min reumatiska ryggsjukdom hindrade
mig fullständigt från att arbeta

Emma Haglund

From a physiotherapist's perspective Emma Haglund has an interest in inflammatory rheumatic diseases with a focus on patients with inflammatory back pain; spondyloarthritis. In her PhD-thesis she describes the prevalence of spondyloarthritis and explores the consequences of the disease for the individual and for society regarding physical activity and work productivity.

The four studies included in the thesis are based on a large cohort of patients with spondyloarthritis in Skåne. The findings provide valuable epidemiological information on prevalence rates of spondyloarthritis and its subgroups, and physical activity patterns also in comparison with the general Swedish population. The thesis gives a useful insight in predictive factors for reduced productivity at work by using simple clinical questionnaires in routine practice.

Emma Haglund has a background as a physiotherapist specialized in rheumatology, and works at Spenshult Hospital, Halmstad. As a practicing physiotherapist with regular contact with this group of patients, she highlights the need of better knowledge of characteristic symptoms for an early diagnose. She also emphasizes the importance of the insight in factors for a better or worse prognosis. Her main interest for the future is how to coach these patients to a better health-related quality of life in order to maintain a healthy level of physical activity and work ability. This PhD-thesis presents the results from her research education in rheumatology at the Department of Clinical Sciences, Lund, Faculty of Medicine, Lund University.

