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Back and neck pain

Patterns in healthcare consultations

Anna Jöud



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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 29 november 2013, kl. 09.00.

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Back and neck pain

Patterns in healthcare consultations

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Abbreviations and definitions

Aa-IBD	Inflammatory arthritis associated with inflammatory bowel disease
AS	Ankylosing spondylitis
ATC	Anatomic Therapeutic Chemical Classification
CI	Confidence interval
CiPCA	Consultation in Primary Care Archive
GP	General practitioner
IASP	International Association for the Study of Pain
ICD	International Classification of Disease and Related Health Problems system
ICD-10-SE	Swedish version of the International Classification of Diseases and Related Health Problems system, version 10
LBP	Low back pain
LISA	Longitudinal integration database for health insurance and labour market studies
MSD	Musculoskeletal disorders
NSAID	Non-steroidal anti-inflammatory drugs
OA	Osteoarthritis
OR	Odds ratio
PIN	Personal identification number
PsA	Psoriatic arthritis
RA	Rheumatoid arthritis
RR	Risk ratio
SD	Standard deviation
SHR	Skåne Healthcare Register
SMR	Standardised morbidity prevalence ratio
SPDR	Swedish Prescribed Drug Register
SpA	Spondyloarthritis
SSIA	Swedish Social Insurance Agency
USpA	Undifferentiated spondyloarthritis
WAD	Whiplash associated disorder
WHO	World Health Organization
YLDs	Years lived with disability

List of papers

This thesis is based on the following four publications. They will henceforth be referred to by their roman numerals (I–IV).

- I. Jöud A, Petersson IF, Englund M. Low back pain: epidemiology of consultations. *Arthritis Care Res (Hoboken)*. 2012 Jul;64(7):1084–8.
- II. Jordan KP, Jöud A, Bergknut C, Croft P, Edwards JJ, Peat G, Petersson IF, Turkiewicz A, Wilkie R, Englund M. International comparisons of the consultation prevalence of musculoskeletal conditions using population-based healthcare data from England and Sweden. *Ann Rheum Dis*. 2013 Jan 23. DOI:10.1136/annrheumdis-2012-202634.
- III. Jöud A, Stjerna J, Malmström EM, Westergren H, Petersson IF, Englund M. Healthcare consultation and sick leave before and after neck injury: a cohort study with matched population-based references. *BMJ Open*. 2013;3(8):e003172.
- IV. Jöud A, Petersson IF, Jordan KP, Grahn B, Löfvendahl S, Englund M. Socioeconomic status as a risk factor for being diagnosed with spondyloarthritis or chronic pain: a case-control study (Submitted).

Paper II. KPJ and AJ co-lead authorship.

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Abstract

Musculoskeletal disorders are very common and affects the individual by pain and functional impairment, and the society through work disability and healthcare utilisation. To what extent is less studied. Routinely collected healthcare registers is a potential resource for epidemiological studies of musculoskeletal disorders. Skåne region, as opposed to nationally in Sweden, has healthcare registers covering all care including primary care.

The overall aim of this thesis was to incorporate healthcare registers in the epidemiological research of consultation prevalence, healthcare consultation and sick leave patterns in patients with musculoskeletal disorders.

The thesis comprises four studies in which the Skåne Healthcare Register was linked with national registers on sick leave, prescribed drugs, and socioeconomic status. Additionally, the thesis include a comparative study between data from the Skåne Healthcare Register with that of an United Kingdom (UK) consultation database. The main variables under study are in Paper I–III disease, consultations, and sick leave and in Paper IV education, income, and work status.

The consultation prevalence of low back pain was estimated to 3–4% in the Skåne region while the figure was larger in the UK. People having low back pain had increased levels of healthcare consultations in general, and more pain diagnoses in particular. People diagnosed with whiplash associated neck injury had higher healthcare consultation rates already three years before the neck injury and the postinjury consultation level was associated with the preinjury consultation levels. Low socioeconomic status was associated with being diagnosed with chronic pain.

It was feasible to use routinely collected databases in the studies of the burden of disease from musculoskeletal disorders, thus potentially also for other public health disorders. While there are vast potentials with register data, it is also important to bear in mind limitations due to e.g., missing data and misclassification which may introduce bias. My main findings indicate a need for early interventions after initial pain and neck injury to prevent the pain to becoming chronic. Stratification-based management is especially suggested.

Background

Introduction

Musculoskeletal disorders (MSD) are common complaints when consulting healthcare.¹⁻⁴ Back and neck pain are especially common, 80% of the population are sometime during the lifespan affected.⁵⁻⁷ Living with musculoskeletal pain and especially persisting pain, affects the individual in terms of poor health related quality of life, and restrictions in daily living.⁸ The burden on society through high healthcare costs and sick leave episodes due to MSD is large.^{9,10}

The Swedish use of registers is renowned internationally and the ability to link different registers by the personal identification number (PIN) makes it unique. Nationally, we have valid healthcare registers covering all healthcare except primary care. However in Skåne region (population 2012, $n = 1,263,088$) the most southern part of Sweden, the healthcare registers are more complete covering all levels of healthcare including primary care thus enabling even more in debt studies. In this thesis I use this data and link it to national registers on sick leave, prescribed drugs, and socioeconomic status to analyse the occurrence, consequences for society, as well as risk factors for being diagnosed with MSD.

Health, public health and epidemiology

The definition of health has changed over time as more knowledge and comprehension on the aspects of health has been grasped. The current definition, and the definition I use in my thesis, is derived from the first International Conference on Health Promotion, held 1986. Here health promotion and health were defined as

*. . . the process of enabling people to increase control over, and to improve, their health. [. . .] Health is, therefore, seen as a resource for everyday life, not the objective of living. Health is a positive concept emphasizing social and personal resources, as well as physical capacities.*¹¹

This definition opens up to the knowledge that health is a resource that can and will change over time and that health promotion is not only the responsibility for the health sector. Thus, all important sectors of a society are dependent on health, and also on disease. While sickness, symptoms, and health are subjective, disease are more objective, assessed by external criteria.¹² Inevitably, disease is also a health determinant, but two people suffering from the same disease might and will assess their health differently depending on other determinants such as genetic predisposition, age, sex, socioeconomic factors, support, lifestyle, work environment, structures in society and more (Figure 1). Likewise, living with a disease will affect your health, the surrounding environment, and burden society through poor health related quality of life, work disability, and costs due to use of healthcare, prescribed drugs and sick leave.

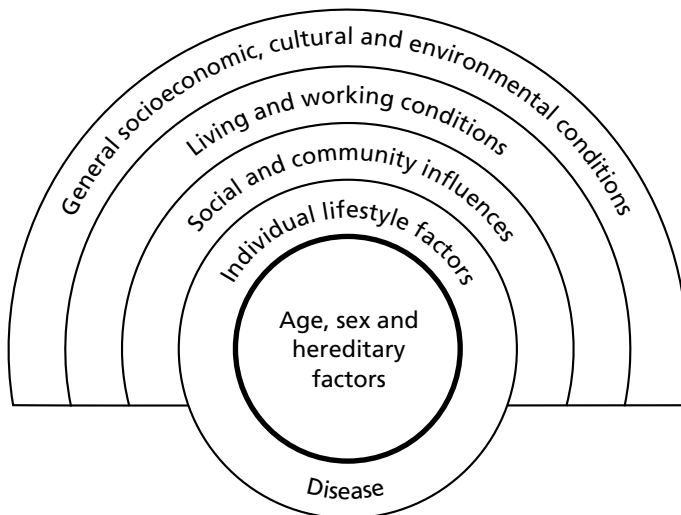


Figure 1 Determinants of health. Modified from Dahlgren and Whitehead, 1992 (ref. 13).

The level and distribution of all health in a population could be referred to as the level of the overall public health state.¹⁴ The science of public health aim at preventing disease, prolonging life, and promoting physical health through organised community efforts. Systematic surveillance of health and populations at risk is one important part of public health work and research. Through surveillance, potential health problems, needs, and demographic changes can be identified. This facilitate health promotion prioritising. Public health is very much linked to the context in which you are. In Sweden, health is strongly associated with i.e., a good working environment and equal healthcare, while the biggest public health interventions in most parts of the world is sanitary interventions and vaccine treatment.

The core methodology in public health is epidemiology, the science of the study of the distribution and determinants of health and disease frequency.¹⁵ Epidemiological studies are usually divided into descriptive, in which the state of a disease burden is described, or analytical where the occurrence or burden is analysed in relation to risk factors, outcomes and exposures.¹⁶ This thesis include both descriptive and analytical parts.

Musculoskeletal disorders

Regardless of how common a disease is the public health aspects focus on how much the society is affected by it. One disease group with great burden on the public health internationally is MSD. Within this group there are both common and less common diseases and symptoms involving the musculoskeletal system including muscles, joints and skeleton. For many of the complaints within the MSD group no specific disease diagnosis apply but rather symptom specific diagnoses since the cause of the complaint is unknown. From a public health perspective, if a person is affected by his or her problem to the extent that it renders high healthcare utilisation, reduced work productivity, and pharmaceutical use this is an important topic to study. Whether the person is defined as having a disease or suffer from a symptom or illness is less important. Thus, for legibility, within this thesis, the term disease is used for both disease specific and symptom specific disorders.

In this thesis the aim is to focus on the consequences of, and risk factor for, various MSD. However, a basic knowledge of the disease itself is important to have in order to understand the methodological applications. The following section provide a very brief introduction to the diseases under study regarding occurrence, manifestations and outcome. One important part of the MSD are the rheumatic diseases. One central aspect and shared feature of all included diseases is pain.

Pain

The International Association for the Study of Pain (IASP) defines pain as

*an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.*¹⁷

Pain is subjective, and can only be assessed by the affected. The pain can be regional, in many sites, widespread, acute, recurrent, or long standing (often referred to as chronic). An initial acute pain could transform to chronic and/or widespread pain, thus early intervention is important to halter this process.^{18,19} Pain is often divided into different types depending on the origin of the pain the

most common are here: nociceptive (caused by tissue irritation/damage), neuropathic (caused by disease or injury in nervous system or in peripheral nerves) or idiopathic pain (pain due to unknown cause).¹⁷ Regardless of the cause of the pain experienced, the pain is real for the individual and limits his/her everyday living.

Low back pain (LBP) is in this thesis referred to non-malignant LBP with no known cause, so called *non-specific* LBP. The prevalence of LBP varies drastically between 2–80% depending on different definitions and methods.^{5–7} In a recent systematic review, the point prevalence, after adjusting for methodological differences, was estimated to be 10–14%.⁶ During a lifetime 60–80% of the population is affected.^{20–23} LBP is somewhat more common in women than men⁶ and there is conflicting data as to whether the prevalence increases or decreases with age.^{24,25} Often it is stated that 90% of those suffering from acute LBP recovers within three months, however the results on fast recovery are conflicting, and very much dependent on how you define recovery.^{26,27} It is not uncommon that an initial acute regional pain transforms into a more chronic pain,¹⁸ it is also common that a somewhat regional pain area (such as LBP) is part of a widespread pain problem,^{19,28} in which the pain becomes more severe and disabling.²⁹

Chronic pain is usually referred to as pain lasting for more than three months. The term chronic imply that the pain is definite, hence the term longstanding might be more appropriate to use especially in clinical contexts with patients. Yet in epidemiological studies the term chronic is widely used. In this thesis the term chronic is used for longstanding pain, definite or not. The chronicity is proposed to come from sensitisation from initial nociceptive pain (so called centrally disturbed pain modulation).³⁰ The annual self-assessed prevalence of chronic pain is high, over 35%, with higher prevalence in women than in men.³¹ There is an uneven socioeconomic distribution within patients with chronic pain, with people defined as having a lower socioeconomic status being overrepresented.^{32,33} It is however less clear as to whether people suffering from chronic pain have a lower socioeconomic status due to problems caused by the pain or if an initial low socioeconomic status is a risk for developing pain and/or chronic pain.

Whiplash associated neck injury

Neck pain due to whiplash associated violence, what former used to be referred to as whiplash injury, is neck injury caused by violence. The trauma mechanism may result in tearing of several structures present in the neck e.g., facet joints.³⁴ stabilising muscles³⁵ and intervertebral discs^{36,37} The type of injury, and the outcome thereof, varies. In 1987, the Quebec task force launched a whole new terminology within the field, subdividing these injuries into five groups, Whiplash associated disorder WAD 0–IV, based on the severity of the pain, musculoskeletal as well

as neurological signs.³⁸ Although this subdivision has been questioned,^{39,40} it is reflected in the Swedish ICD-10-SE version where these types of neck injuries should be diagnosed according to the WAD scale.

The most typical manifestations after trauma is musculoskeletal symptoms and consequences such as neck pain, headache and stiffness in neck muscles with reduced mobility and sensitisation.^{41,42} Up to 50% report an incomplete recovery⁴³ and about 30% remain moderately or severely disabled.^{44,45} There is also evidence that initial whiplash injury might transform into widespread pain.⁴⁶

With prolonged problems, the work ability is negatively affected.^{47,48} For the society, reduced work ability is a greater problem than the actual healthcare cost following whiplash associated neck injury.⁴⁸ Research on the work ability following whiplash associated neck injury is conflicting as to how large proportion of patients having prolonged reduced work ability^{47,49,50} and what factors are affecting this.^{49,51–53} Given the burden on society from whiplash associated neck injury, prognostic factors are needed. Recently the notion about self-assessed preinjury health status being important not only for the prognosis but also for the risk of being involved in a car accident has emerged.⁵⁴

Osteoarthritis

Osteoarthritis (OA) is the most common non inflammatory rheumatic disease, with an overall prevalence of 5% that increases with age. OA is manifested through pain and decreased functioning in joints. OA is as common in women as in men, although the distribution of affected joints varies in men and women.⁵⁵ Since OA is increasing with age prognostic studies indicate that an increasing number of people will be affected in future years since we live longer,^{56,57} increasing the societal burden from work disability in patients with OA.⁵⁸

Rheumatoid arthritis

Rheumatoid arthritis (RA) is the most common rheumatic inflammatory disease with a prevalence of around 0.6–0.8% in Western countries.^{59,60} RA is more common in women than men and is typically manifested by symmetrical inflammation in peripheral joints, causing pain and stiffness.⁵⁵

RA has a negative influence on the affected, by low health related quality of life,⁶¹ extended work disability^{62,63} and restrictions in daily living.⁶⁴ The introduction of biologic treatment, targeting key pathogenic factors, have improved the life of many of the patients considerable,⁶⁵ however conflicting results over its beneficial effect on work productivity exists.^{66,67}

Spondyloarthritis

Spondyloarthritis (SpA) is in this thesis used as an umbrella term for four subtypes of inflammatory diseases with various degree of spine involvement: psoriatic arthritis (PsA), ankylosing spondylitis (AS), inflammatory arthritis associated with inflammatory bowel disease (Aa-IBD) and undifferentiated spondyloarthritis (USpA).⁶⁸ The prevalence figure for SpA varies in different populations,⁶⁹ in Sweden the prevalence has been estimated to be 0.45%.⁷⁰ The subtypes have the main clinical manifestations in common, inflammatory back pain, peripheral arthritis, enthesitis, and association with the HLA-B27 antigen.⁷¹ The most common subtypes are PsA (0.25%) and AS (0.12%). AS is more common in men than in women while data from Sweden suggest that PsA is more common in women.⁷⁰

As for RA, SpA is negatively affecting work productivity, functioning and health related quality of life,^{72–74} rendering high societal costs.⁷⁵ The introduction of biological treatments have improved quality of life and work ability.^{76,77}

Surveillance of burden of disease

Altogether, MSD are very common and the non-fatal consequences are substantial. In the latest ranking within the Global burden of disease study, MSD explain a great proportion of the burden and continues to be top ranked in terms of years lived with disability (YLDs).⁷⁸ This thesis will study the burden from MSD through health care consultation patterns, sick leave and use of prescribed pharmaceuticals. About 15–25% of the population seek physician healthcare due to MSD complaints annually,¹ and it is the most common cause of pain complaints presented to primary care.^{2–4} MSD are the dominant source of long lasting pain worldwide,³¹ and have a significant impact on individuals and health-care systems.⁷⁹ The society is also affected by MSD through sick leave episodes.⁹ However, there remain significant gaps in our understanding of the frequency and management of different MSD, and their variation within and between countries.

Socioeconomic status in relation to health and disease

Many variables influence your susceptibility to disease, including your health status (Figure 1, page 16). A poor general health increases your risk of many diseases. An indicator for health status could be healthcare utilisation, pharmaceutical use and work disability. Health inequality is a public health concern as is inequity in healthcare utilisation.^{80–82} The way this inequality and inequity works is still, to a great extent, unclear^{83,84} and disease specific.⁸⁵ There is a lack of

knowledge regarding the association between socioeconomic status and MSD.⁸⁶ Traditionally, socioeconomic status is measured by the individual's level of education, income, and occupation or work status, either separately or combined.⁸⁴ Socioeconomic status is important in studies of health and disease, and may also influence the management of the condition and of the patient. Studies have provided conflicting results concerning socioeconomic equity in primary care use,^{87,88} with pro-rich inequity in the use of specialist healthcare in most western countries,^{87,89–91} while the use of pharmaceuticals has been linked to low socioeconomic status.^{92,93} Lower socioeconomic status and manual work are related to poor health status in general and to chronic pain in particular.^{32,33,94} It is also suggested that low level of education and low socioeconomic position are associated with work disability due to non-inflammatory back pain, inflammatory back pain including SpA^{70,94} and chronic pain.^{33,95,96}

I hypothesised that your socioeconomic status is relevant when consulting healthcare. Doors can either open to referrals, specialist care, and expert assessments or be closed resulting in prolonged delay between pain initiation and treatment enabling the initial regional pain to become widespread and chronic. Could it be that socioeconomic status partly explain the status of the door? For SpA there are classification criteria that physicians can use when labelling SpA patients.⁹⁷ For chronic pain, similar established criteria are not available, hence, the two diseases could be hypothesised to be diagnosed and managed differently in the healthcare system which in turn could be partly explained by your socioeconomic status. It might be that the actual disease does not differ between socioeconomic groups but rather the way they are diagnosed.

Epidemiological opportunities in Swedish registers

Nationally, we have valid healthcare registers covering all healthcare except primary care. However in Region Skåne have more complete healthcare registers, Skåne Healthcare Register (SHR), covering all levels of healthcare including primary care. The SHR could be viewed upon as a large scale cohort of prospectively ascertained data of all healthcare provided in the Skåne region from 1998 and onwards. This data enables us to perform longitudinal studies: following individuals over many years retrospectively and prospectively in time (see section “Skåne Healthcare Register”, page 29). A unique feature for Sweden (and the Nordic countries) is the PIN assigned to all residents in Sweden.⁹⁸ The PIN is the key for linkage between different registers of importance in epidemiological studies. Routinely collected electronic healthcare data linked with sick leave, prescribed pharmaceuticals, and socioeconomic data provide a valuable source of information on trends and variation in the occurrence, determinants, consequences, and

22 Background

management of health problems. With falling response rates and under-representation of segments of the population in surveys, healthcare databases may be the most valid approach to use in morbidity surveillance.⁹⁹ The registers also enable us to study risk factors for certain diagnoses. Finally, the use of register data enable studies of important public health diseases and the complex interplay between health, disease and their determinants.

Aims

The overall aim of this thesis was to incorporate routinely collected healthcare data in the epidemiological research of consultation prevalence, health care consultation and sick leave patterns in patients with MSD.

The specific aims were

- Paper I To study the consultation prevalence of LBP and to among people consulting for low back pain study the patterns of healthcare consultations.
- Paper II To determine the feasibility of comparing prevalence figures between two European nations and to assess the consultation prevalence of MSD.
- Paper III To study healthcare consultation and sick leave patterns before and after being diagnosed with whiplash associated neck injury.
- Paper IV To study if, and in what direction, socioeconomic status is a risk factor for being diagnosed with SpA and chronic pain.

Methods

The following section starts with a brief introduction to epidemiological study designs, followed by a description of data sources and diagnostic groups that have been used in one or more of the included papers. The latter part of the section starts with paragraphs on the methods and statistical analyses used in Paper I–IV, respectively. The section ends with a discussion part.

Epidemiological study designs

Broadly, epidemiological studies can be divided in two types: experimental, where the researcher intervenes the natural process, and observational, where the researcher studies the natural course.¹⁰⁰ In this thesis all studies are of observational nature. The two most common observational study designs are cohort and case-control.

Cohort design

A cohort is here a group of patients with common exposures, i.e., a disease, which you follow over time, often forwards, but sometimes backwards, in terms of important outcomes (Figure 2, next page). In a cohort design you can also include a reference cohort. Commonly you compare the outcome, e.g., healthcare consultation, within the study cohort to that of the reference cohort over a sufficient period of time. The cohort could be closed or open. A closed cohort is in this thesis defined as a cohort where the exposures are measured once at the start of the study. The subjects are then followed over time and the number of exposed subject may decline due to e.g., deaths or relocation but no additional subjects are included. The open cohort design is more dynamic, subject can be added and excluded over time as can an exposed subject change to become unexposed during the study. Paper I and III are both cohort studies.

A cohort study is the best option to an experimental design for studying risk when the latter is not optional.¹⁰¹ The obvious drawback is when studying diseases with rare outcomes, hence you have to gather a very large cohort and then follow it for a long period of time in order not to miss the infrequent outcome. Here

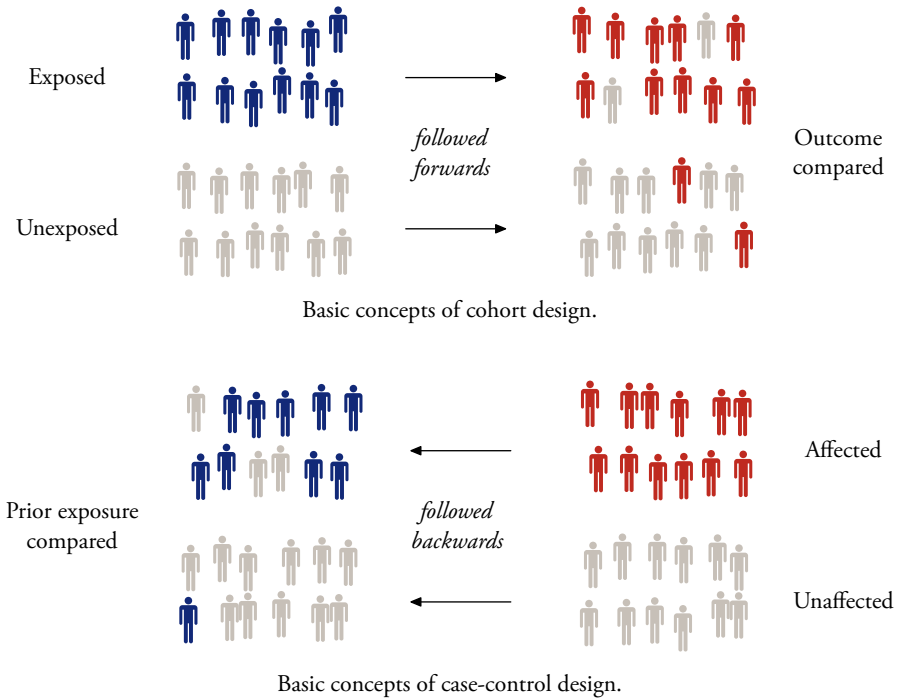


Figure 2 Illustration of epidemiological study designs.

the use of register data is prominent, even better is the routinely collected data that in a way could be regarded as a large prospectively collected cohort.

Case-control design

The case-control design is often considered the best option if you are to study a rare condition.¹⁰¹ In a population based case-control study, as in Paper IV, the cases are defined in the source population as those individuals that have the outcome of interest (prevalent cases), e.g. everyone with SpA, diagnosis in a specified time period. Then you select controls that do not have SpA, preferably random controls from the same source population (Figure 2).

In the ideal epidemiological world, the study design is fixed, however in real life, the design is often a mix between case-control and cohort and variations thereof.

Bias in observational studies

In all epidemiological study designs error can occur. While error that occur by chance is out of the researcher control, bias refer to systematic error that systematically influences the results. Bias can and should as much as possible be adjusted

or controlled for by the researcher, before or after the data has been collected. Especially important in this thesis are bias through misclassification, confounding, and selection bias. There are different techniques to handle bias before or after data collection. This section will particularly cover matching, standardisation and stratification.

Misclassification

Misclassification appears when the disease or exposure is classified as something it is not.¹⁶ It can occur when an individual is being classified as having a disease when in fact he or she is not having the disease. Another example is when an individual is classified as being treated with NSAID, when he or she is not. Differential misclassification as opposed to nondifferential misclassification is dependent on the exposure or outcome under study thus introducing bias either exaggerating or underestimate the results.¹⁶ In nondifferential misclassification of a dichotomous variable, in most cases, if the misclassification is independent from other error, the effect under study will be underestimated.¹⁶

Very much linked to misclassification is the concepts of sensitivity and specificity. Sensitivity refers to the ability to identify true cases, e.g., identifying people having LBP that are diagnosed with LBP. Specificity refers to the ability to rightfully not include patient that do not have the disease under study e.g., to not include patients with a diagnostic code that really do not meet the diagnostic criteria.¹⁶

Confounding

Confounding means that a third variable is interfering the association between an exposure (here a factor influencing another factor e.g., disease status, socio-economic status) and an outcome (here a factor of interest e.g., disease, number of consultations). To be defined as a confounding factor the third variable must independently be associated with both exposure and outcome. Let us say that we want to study the association between income (exposure) and OA (outcome), we find that high income is associated with the risk of OA. When looking closer, people with high income are likely to be older and also more likely to have an OA diagnosis. Therefore age is confounding the relation between income and OA diagnosis (Figure 3, next page).

In relation to confounding bias, the concept of effect modification needs to be explained. Effect modification occurs when an effect of one exposure is different between subgroups depending on another variable. This other variable is called an effect modifier. The theoretical difference is that the effect modifier is related to the outcome but not the exposure. Whereas effect modification often is identified and handle through stratification (as in Paper IV).

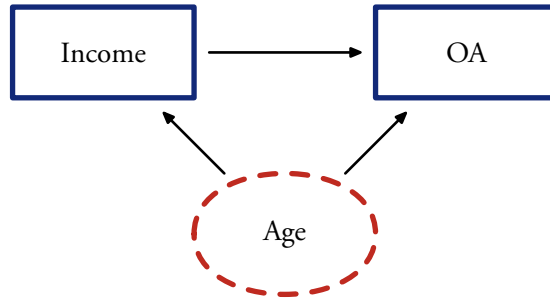


Figure 3 Illustration of confounding where a third variable (age) explain the association between exposure (income) and outcome (OA).

Matching

Controls can be matched to a case on known confounding factors. In a case-control design, this would increase the efficacy of the study by introducing a balance of important variables, hence the variance in the parameters of interest. This will, however, not eliminate the confounding effect. When matching is done on a factor that is a true confounder, the result can introduce selection bias. Although pushing the results toward the null since you make the case and controls more similar. Even if the matching variable is not a confounding factor this can happen. If the matching variable is related to the exposure this makes the exposure similar between case and control, rendering crude odds ratio (OR) close to 1. Therefore, the matching variable should be taken into account in the analysis.¹⁰² Finally, you want to avoid matching on a variable on the causal pathway, again causing the efficacy to decrease.^{16,103}

In a cohort design, the use of matched references can control for the confounding effect from the matched variables (Paper III). However, if the matching variable and the exposure is associated with the outcome or censoring (e.g., loss to follow up) then the initial balance created by the matching procedure is no longer applicable in the remaining cohort, thus there could be a need for controlling for the confounding factor in the analyses.¹⁰⁴

A cohort study can preferably also include references to be able to standardise your finding on the actual structure of e.g., age and gender in the population from which you select your references (Paper I). Finally you can include population references to help you determine to what extent an identified change over time in the case group actually has to do with structural changes in society (Paper III). An observed change in the study cohort while no change in the reference cohorts could mean that the change actually occur in the cases. An observed change both in cases and the references indicate more structural changes. This is especially important when you study healthcare utilisation and work disability which both are sensitive to structural and political change.

Stratification

Stratification is another way to control for confounding effects. By stratifying on the confounder variable you can study the effect under study in the different strata (Paper IV). Stratification can also help to identify confounding from the specific variable as in Paper III where stratification was used to control for potential underlying confounding effect. In real life epidemiology it is often not that simple that you analyses one factor at a time, one exposure and one outcome. Often your interest is not only one but many exposures and also different combinations of these. In that case a multivariate analysis is a better choice to adjust for potential confounding, this technique was used in Paper IV.

Standardisation

Standardisation can also be used to control for the confounding effect when a variable is affecting the association under study. In studies of health care consultations it is believed that age and sex is important. Thus, if you compare the number of health care consultations between two groups that differ in age and sex it is likely that the potential differences is explained by the underlying age and sex distribution. You would then want to standardise your figures so that you can get the figures in relation to the true age and sex distribution in the population. This method was used in Paper I and II.

Data sources

Skåne Healthcare Register

In Sweden, the responsibility for all healthcare is decentralised to each county or region. Skåne region is located in southern Sweden and has a population of 1,263,088 (2012). In this region, Region Skåne has the responsibility for providing all healthcare. Although it is most common to first see a general practitioner (GP), patients can access secondary care directly. All healthcare provided in Skåne region renders data entries into the SHR, the basis for all analysis within this thesis (Paper I–IV). Thus the SHR contains routinely collected prospectively ascertained information on all health care within the region. The SHR includes, for example, data on type of consultation (e.g., public/private, primary, specialist or hospitalisations), type of health care professional (physician, nurse, physiotherapist etc.), date of consultation, diagnostic, surgical, and/or injury codes where relevant. Since 1997 diagnoses are classified according to the Swedish version of the International Classification of Diseases and Related Health Problems system, version 10 (ICD-10-SE), (up until 2011 referred to as KSH97, *Klassifikation av*

sjukdomar och hälsoproblem 1997). All diagnostic codes are transferred from medical records and administrative applications to the SHR. Diagnoses from private practitioners are not transferred to the SHR and therefore only cases diagnosed within the public care are included in this thesis.

All study groups are in this thesis defined by diagnostic codes. In doing so some important additional limitations need to be highlighted. The SHR was set up for reimbursement purposes not for research. This is reflected in how the database is constructed, what type of information is included and also the organisation around the register. There are guidelines as to what should be registered in the administrative applications as well as how this should be done, still there is inconsistency between different hospitals, clinics and practices. In Sweden free health care is provided by both public and private healthcare providers, through the same tax-based financing system. All healthcare can be divided into three groups providing data to the SHR to different extents:

- Public healthcare, the most common form of all healthcare within the Skåne region. All types of data concerning the consultation including diagnostic codes are being transferred to the SHR (83% of all physician healthcare in SHR 2012).
- “Private public” care, all private care provided by private practitioners organised within the public care. The co-payment for the patients are the same as at a public practice. The SHR include all consultation data except the diagnostic codes (17% of all physician healthcare in SHR 2012). In this thesis this type of care is referred to as private care, throughout.
- “Private private” care, for privately owned and organised practices, where the patients themselves pay for the healthcare provided. The SHR holds no information at all. I would estimate this to be a very small proportion of all care provided in Sweden. This type of care will not be discussed further in this thesis.

Social insurance register

In Sweden you are entitled to sickness benefit when you cannot work owing to disease or injury. The Swedish social insurance is administered by the Swedish Social Insurance Agency (SSIA). Sickness benefit is generally limited to one year but can be extended. You receive compensation from day two and if you are employed, your employer will pay sick pay day two–14 and from day 15 you receive sickness benefit. If your work ability is permanently reduced by at least 25% you can receive a disability pension. All sick leave periods exceeding 14 days and all disability pension payments are administered and registered by the SSIA.

The SSIA register includes dates, type and amount of sick leave and disability pension as well as diagnostic codes. For individuals only sick listed seven days or less no data exists in these registers. For those individuals with a work disability lasting 14 days and longer all data, from day one, are included in the register. If you are unemployed you will get compensation from day two from the SSIA. However, many people that are unemployed will not report sick days since the sickness benefit is typically lower than their usual allowance.

Both sick leave and disability pension can be granted for 100, 75, 50 or 25% of a working day depending on the extent to which your work ability is reduced.

Sick leave data was used in Paper III and IV. Sick leave was defined as days with sickness benefit registered by the SSIA and net sick days (Paper III). Net sick days are the total number of days for which sickness benefit or disability pension payment is received from the SSIA, multiplied by the extent of the sick leave or disability pension for each day (e.g., 20 sick days with 25% of a day extent are equal to five net sick days). Sick leave data in the form used here, is available since 2003.

Population register

In Sweden everyone is free to consult healthcare wherever they they choose. Therefore SHR data were linked by personal identification numbers with the Swedish population register (Paper I–IV) to exclude non-residents as appropriate per paper. The register is the civil registration of vital events (e.g., births, deaths, marriages, change of residential address), administered by the Swedish Tax Agency. The register was also used to define deaths and relocation.

LISA database

All data on socioeconomic exposures (Paper III–IV) were drawn from the Longitudinal integration database for health insurance and labour market studies (LISA by Swedish acronym), held by the National official statistics Sweden (<http://www.scb.se>). LISA holds annual data on e.g., country of birth (own and parents), education, type of work, work status and income for all residents aged >15 years from 1990 and onwards. LISA is an integrated database that overall is of very good quality, however LISA holds data from many different data sources with various degrees of coverage and data quality.

Swedish Prescribed Drug Register

The Swedish Prescribed Drug Register (SPDR) covers all prescribed drugs to Swedish residence excluding drugs given in hospitals.¹⁰⁵ Drugs given within nursing home are also not complete. The register goes back to June 2005, thus 2006

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is the first full year of data available. Prescribed pharmaceuticals are classified according to the Anatomic Therapeutic Chemical Classification (ATC). Data from the register was used in Paper IV and for additional analysis in Paper III.

All data was linked together using the PIN.⁹⁸

CiPCA

In Paper II data from the Consultation in Primary Care Archive (CiPCA) database was used. CiPCA is a database over routinely collected healthcare data from 14 general practices in the North Staffordshire area of mid-east UK.^{106,107} In this study data from 11 practices was used. The practices undergo an annual cycle of assessment, feedback and training in morbidity coding.¹⁰⁷ Approximately, 97% of all contacts with a GP have a morbidity code assigned. In primary care in the UK, morbidities are generally recorded using Read Codes¹⁰⁸ (see section “Defining patients by diagnoses”, page 39).

Diagnostic groups

In all included papers (Paper I–IV) the subjects are defined by ICD-10-SE diagnostic codes (Table 1). Consensus on which codes to use have been made through guidelines, and discussion with physicians in the specific fields. The exception is Paper II where a mapping procedure between ICD-10-SE codes and Read Codes was done.

Ethical statement

All papers included in the thesis were approved by the Regional Ethical Review Board in Lund; study II was also approved by North Staffordshire Local Research Ethics Committee. The use of the SHR for research purposes was also approved by the Region Skåne Quality registers, Healthcare registers and Bio bank ethics group (Samrådsgrupp för kvalitetsregister, vårddatabaser och biobank, S-KVB Swedish acronym).

Occurrence of LBP (Paper I)

Subjects

In the first paper all patients with a LBP diagnosis (Table 1) registered 2009 in the SHR was identified. The consultation prevalence was estimated as the proportion of residents diagnosed with LBP by a physician at least once during

Table 1 Disease groups included within each paper, defined by ICD-10-SE codes. The suffix P denotes codes specifically used within primary care.

Disease/disorder	ICD-10-SE code	Paper(s)
Low back pain		I
Low back pain with sciatica	M54.4	
Low back pain	M54.5	
Other dorsalgia	M54.8	
Dorsalgia unspecified	M54.9	
Dorsalgia not specified	M54.9P	
Osteoarthritis		II
Primary generalized (osteo)arthrosis	M15	
Primary coxarthrosis, bilateral	M16	
Gonarthrosis [arthrosis of knee]	M17	
Primary arthrosis of first carpometacarpal joints, bilateral	M18	
Other arthrosis	M19	
Joint pain		II
Pain in extremities, specified sites	M79.6B–H	
Myalgia in specified site	M79.1B–H	
Pain in joints	M25.5	
Disease in knee joint	M23.9P	
Enthesopathy	M77.9P	
Low back pain		II
Pain with sciatica	M54.4	
Low back pain	M54.5	
Other dorsalgia	M54.8	
Dorsalgia unspecified	M54.9	
Dorsalgia not specified	M54.9P	
Dorsopathy unspecified	M53.9	
Spinal instabilities	M53.2	
Rheumatoid Arthritis		II
Seropositive rheumatoid arthritis	M05	
Seronegative rheumatoid arthritis	M06	
Spondyloarthritis		II, IV
Ankylosing spondylitis	M45	
Psoriatic arthritis	L40.5, M07.0–3	
Inflammatory arthritis associated with inflammatory bowel disease	M07.4–5	
Undifferentiated spondyloarthritis	M46.0–1, M46.8–9	
Neck injury		III
Distortion of cervical spine (incl. Whiplash injury WAD 1–3)	S13.4	
Chronic pain		IV
Other chronic pain	R52.2	
Pain unspecified	R52.9	

2009. Additionally the new onset rate of LBP was determined as adults with a LBP diagnosis in 2009 that did not have a record of LBP the prior five calendar years (2004–2008). Finally, the proportion of all patients consulting with a MSD (ICD-10-SE chapter XIII) diagnosis that were diagnosed with LBP was calculated.

Analyses

To compare the healthcare consultation rate between the identified patients and the general population a standardised healthcare utilisation ratio (with 95% confidence interval [CI]) was calculated by dividing the observed number of healthcare consultation in 2009 by the expected number based on data from the general population, standardised for age and sex. Since the LBP patients had had at least one consultation with a physician (in order to be included in the LBP cohort) the number of observed contacts 2009 for LBP patients was reduced by one (1) per subject.

Finally, a standardised morbidity prevalence ratio (SMR), including 99% CI, was estimated by dividing the observed prevalence of a specific disease in the LBP cohort by the expected prevalence based on data from the general population seeking care, standardised for age and sex.

Comparative prevalence study (Paper II)

Subjects

Paper II was a collaborative work with Keele University, UK. All individuals diagnosed with any of the selected diagnoses, in 2010, and in 2004–2010, respectively were identified in the SHR and CiPCA. Consultation prevalence for primary care alone and for primary and secondary care together was calculated for the two time periods. The selection of the diagnostic codes used was based on previous work in Sweden and discussions within the research team (Table 1, previous page). The selected ICD-10-SE codes were then mapped to Read Codes. The exceptions were the codes for joint pain where previously derived Read Codes were used to which ICD-10-SE codes were mapped.

Analyses

Assessment of the feasibility of comparing prevalence between UK and Sweden was based on two criteria. First, whether the methodologies for deriving healthcare prevalence could be standardised between the two nations. Feasibility would not be shown if we were unable to translate any part of the methods between the

two nations (for example, standardisation between Read and ICD-10-SE codes). The second criterion was based on known differences between the healthcare systems and recording practices. Direct access to physiotherapy for back pain in Sweden (i.e. without referral from a general practitioner) is common but not routinely recorded in the SHR, and there is more complete recording of secondary care in the Swedish than in the UK database. Therefore, the expectation was that there would be a difference between the nations in prevalence of low back pain (higher in UK) and for all healthcare including primary and secondary care for inflammatory disorders (higher in Sweden). Less difference was expected in the consultation prevalence of OA, and primary care prevalence of inflammatory disorders.

Neck injury – consultation patterns (Paper III)

Subjects

The study cohort was defined as all adult (18 years or older) residents in Skåne region who had been diagnosed with neck injury, whiplash associated, by a physician in an acute setting in 2007–2008. Individuals with a previous record of an injury involving the head and/or neck (ICD-10-SE chapter S00–S19) since 1998—up until the month before diagnosis were excluded. The month before inclusion is referred to as the “screening” month. The screening month was used to allow patients with a somewhat delayed neck injury diagnosis to be included. The study cohort and a matched reference cohort were followed for six years (Figure 4). Sick leave was only studied three years before to two years after study inclusion. As a sensitivity analysis, three different reference cohorts were defined (Table 2, next page).

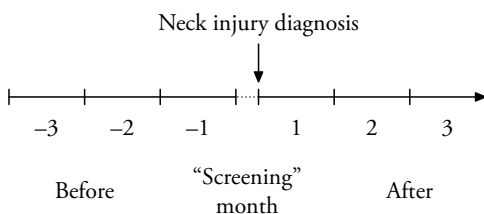


Figure 4 Schematic figure over the six-year study period; three years before until three years after neck-injury diagnosis.

Analyses

The overall number of consultations and the number of consultations to physicians and physiotherapists were derived, respectively. Based on the median (quartile 1 [Q1]; quartile 3 [Q3]) number of consultations in the reference cohort

Table 2 Matching variables for the different reference cohorts (Paper III).

	References 1 (primary)	References 2	References 3
Sex	✓	✓	✓
Age (± 5 years)	✓	✓	✓
Area of residence	✓	✓	✓
Observation time	✓	✓	✓
Educational level		✓	✓
Health care consultation the year of case inclusion			✓

(References 1) the three year period prior to the neck injury, cut-offs were specified to define low-frequent (= 1 consultation), frequent (2–8 consultations) and high-frequent consulters (≥ 9 consultations). The risk ratio (RR) and absolute portion of those neck injured who went from being a low-frequent to a high-frequent consulter due to the injury (attributable risk) was assessed. The proportion of cases assigned a diagnosis for MSD, dizziness, tinnitus, psychological distress (depression, anxiety and stress) was calculated by year.

Differences in number of consultations and sick days between the study cohort and the reference cohorts were determined by the Jonckheere-Terpstra test and Mann-Whitney *U*-test. Differences between subgroups (low-frequent/frequent/high-frequent consulters) were analysed by negative binominal regression, adjusting for age and sex. Student's *t*-test was used to analyse difference between groups regarding age, while χ^2 -analysis was used to compare categorical data. Pearson correlation coefficient (ρ) was computed for the association between number of sick leave days and number of consultations both pre- and postinjury. The Fisher's *z*-transformation was used to compute 99% CI around the correlation coefficient. Due to multiple tests performed, a *p*-value of 0.01 or less was considered to be statistically significant.

After publication of this article, I have made some additional analysis on the differences in proportion between cases and references with prescribed antidepressants and NSAID the year before inclusion until two years after.

Socioeconomic status as a risk factor for MSD (Paper IV)

Subjects

Two working-age (20–66 years) case groups were identified through the SHR as 1) all patients diagnosed with SpA diagnosis (Table 1, page 33) in the period 2010–2012 at least once by a rheumatologist or internist, or at least twice by any physician in primary or secondary care. The cases were excluded if they had an

SpA diagnosis registered in the SHR between 2005–2009. 2) all patients diagnosed with chronic pain (Table 1, page 33) in the period 2010–2012, two times by any physician or at least once by a specialist in secondary care. Equivalently, the cases were excluded if they had a chronic pain diagnosis registered in the SHR between 2005–2009. To all cases we randomly assigned two controls from the general population, matched for age and sex. The controls also had to have at least one consultation (for any reason) to a physician in the period 2010–2012 but no SpA diagnosed between 2005–2012 (for SpA controls) or any chronic pain diagnosis registered between 2005–2012 (for chronic pain controls).

Analyses

Data on exposures (Table 3, next page) were defined year four before case inclusion (e.g., if included in 2010, data on socioeconomic status were defined as the current status 2006). Differences between groups regarding demographic characteristics was tested by χ^2 -test (categorical data), and Mann-Whitney *U*-test or Student's *t*-test for numerical data as appropriate. Potential factors associated with being diagnosed with SpA and chronic pain were tested by conditional logistic regression models. In the initial crude models all *a priori* hypothesised variables were tested separately. After this, an additional models including all variables of socioeconomic status adjusting also for geographic area. This was done for SpA and chronic pain separately.

Additionally for SpA, since the different prevalence by ethnicity of the HLA-B27 antigen which is strongly associated with SpA (AS in particular),¹⁰⁹ analyses stratified on country of origin Nordic/non-Nordic origin was done.

Finally, a comparative analysis, using negative binominal regression, between the SpA cases and chronic pain cases determined if they differed in number of healthcare consultations and numbers of NSAID prescriptions, adjusted for all other variables. A *p*-value less than 0.05 was considered as a significant difference.

All statistical analyses and data preparations was done using SAS, versions 9.1–9.3 (SAS Institute Inc., Cary, North Carolina).

Methods discussion

Consultation prevalence

Prevalence is the proportion of the population under study that have the disease in which you are interested, in a defined period of time. In this thesis consultation prevalence is a key term. Consultation prevalence is here, if not stated otherwise, defined as the prevalence of those consulting a physician and being diagnosed for a given disease. The consultation prevalence could be studied during e.g., one

Table 3 Description of exposure variables used in logistic regression models (Paper IV).

Exposure	Description
Country of origin	
Nordic origin	Subject and both parents born in the Nordic countries (Sweden, Norway, Denmark, Finland and Iceland)
Non-Nordic origin	Subject and/or both parents born outside the Nordic countries
Marital status	
Married	married/registered partner (same sex)
Unmarried	single, divorced/unregistered partner, widow/widowed
Education (highest achieved)	
Low	0–9 years
Moderate	10–12 years
High	>12 years
Work status	
Full time sick leave	Full-time sick leave/disability pension
Not working	Either unemployed, students etc.
Working	Worked in November the given year
Disposable income (tertiles)*	
Low	< \$19,700
Middle	\$19,701–29,400
High	> \$29,401
Geographic area	Municipality

* \$1 = 6.60 SEK 9 September 2012.

day, one year (Paper I and II), seven years (Paper II) or a lifetime. Prevalence is closely related to the incidence (the number of new cases within a period of time) and disease duration. Therefore, depending on disease and study period, the prevalence figures changes. In Paper I, I was interested in the incidence of LBP, or more correctly the consultation incidence. However, LBP is often recurrent and although the SHR covers many years (1998 and onwards) the patients consultations history prior to 1998 is unknown. Therefore the rate of new onset LBP was calculated by identifying all patients with a LBP diagnosis one year and excluding those patients with any LBP diagnosis the five previous years. The use of this type of wash-out periods can be an effective way of identifying new onset of disease. This method was also used in Paper III.

Defining patients by diagnoses

Self-assessed measures are often regarded as less valid in epidemiological research than objective measures. For example, self-assessed sick leave does not always correspond to actual sick leave as measured through registers over actual sick leave days. However, how you assess your pain is subjective, and a physician or a physiotherapist can not argue that the patient is not in pain while claiming so, thus self-assessed pain is often used in epidemiological studies on pain. Not all people with pain seek healthcare, there is a somewhat systematic selection (Figure 5). Once the pain affects the patient to the level that you seek healthcare, the pain is influencing your daily life and possibly family and work life. This group of patients is of special public health importance because their symptoms to a greater extent affect society, in terms of healthcare utilisation and sick leave.

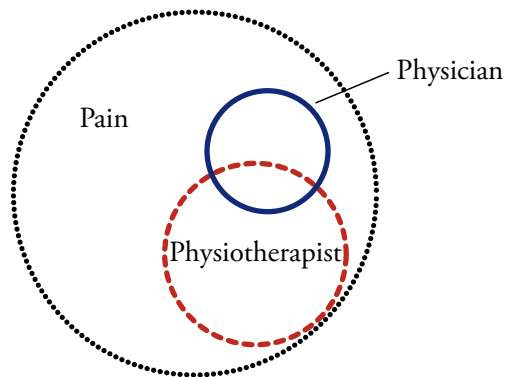


Figure 5 Schematic figure over all individuals with pain, illustrating that not all individuals with pain consult physician and/or physiotherapist, hence not included in the SHR.

Physicians use diagnostic codes differently. In Sweden, the diagnostic procedure is since 1997 based on the tenth version of the International Classification of Disease and Related Health Problems system (ICD-10). The ICD is the global health information standard for mortality and morbidity statistics governed by the World Health Organization and it is the international standard for defining and reporting diseases and health conditions in more than 100 countries (<http://www.who.int>). The ICD-10 includes 22 disease chapters, covering ten different areas of diseases and injuries. Within each chapter there are different numbers of blocks specifying different diseases/code groups. For example, most commonly unspecified back pain is recommended to be diagnosed within the ICD-10 diagnostic chapter (M), Diseases of the musculoskeletal system and connective tissue, block M40–M54 (dorsopathies) and code group M54 (dorsalgia). The Swedish version of the ICD-10 is referred to as ICD-10-SE. Additionally in

Sweden there is a specific diagnostic coding system labelled KSH97-P (P for primary care) that applies within primary care. In order to facilitate the diagnostic procedure within primary care, some diagnostic codes combine one or many diagnostic codes. M54.9P is used for M54.0 (panniculitis), M54.1 (radiculopathy), M54.8 (other dorsalgia), and M54.9 (dorsalgia unspecified) combined. However, a diagnosis such as chronic pain is found under the (R), Symptoms, signs and findings not elsewhere classified. Despite the use of the same coding system, deriving comparable estimates even within the same country can be difficult.^{106,110} While Swedish healthcare as mentioned uses ICD classification, primary care in England uses Read Codes.¹⁰⁸ The Read Code system is a hierarchical system structured into process of care and diagnostic chapters, which become more specific further down the hierarchy. For example, codes under Chapter N represent “Musculoskeletal and Connective Tissue Diseases”. There are complications introduced in cross-national comparisons.

The first challenge relates to differences in healthcare systems. The second challenge relates to the characteristics of data collected in healthcare databases. There may be differences in the extent of data collected (for example, every contact may be recorded in some systems but not in others), and in training and incentives given to healthcare professionals for morbidity recording. Databases may be based on different coding systems.

Comparing occurrence of musculoskeletal disorders presents further challenges, including obtaining valid and comparable case definitions when use of diagnostic labels such as OA that often varies between healthcare professionals.^{111,112} The inflexibility of coding systems also raises challenges. Although diagnoses have a clear coding system, symptoms such as joint pain and back pain may be spread across several chapters including the musculoskeletal, and symptoms and injury chapters.¹

Missing data

Apart from the missing data on diagnostic codes in the SHR due to loss of private physician care as explained in section “Skåne Healthcare Register” (page 29), the diagnostic coverage also differs depending on the year and level of care you study (Figure 6). Not only physicians can label a patient by a diagnosis, although not until around 2010 physiotherapists were encouraged to do so in the medical records. For the patients groups in this thesis physicians and physiotherapists are the two most common groups of healthcare personnel.

Three aspects on missing data are important to discuss here. Firstly, the diagnostic coverage as such has changed dramatically since 1998 when the SHR was shaped in its current form. Especially after 2004 the coverage has dramatically changed, this is because then the direct connection between reporting diagnosis

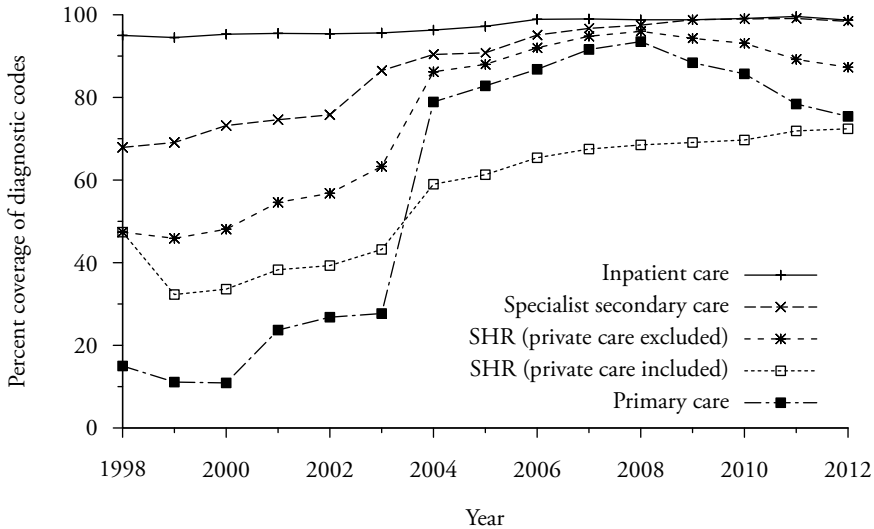


Figure 6 Diagnostic coverage in SHR depending on level of care.

in order to get compensation was introduced. We have, however, no reason to believe that codes registered prior to 2004 are less valid. Secondly, in all included studies patients are identified based on diagnosis as reported in the SHR. The SHR, thus far, only includes diagnostic codes set in the public healthcare (public as described previously in section “Skåne Healthcare Register”, page 29). This means that people only diagnosed by a private physician is not eligible to be included in any of my studies. As seen in Figure 6, the shape is somewhat changing around 2009 looking like the coverage is decreasing. This is explained by the introduction of the so called “Hälsoalet”. Hälsoalet meant that all residents had to register to one specific general practitioner of their choice. This also meant that all practices had to supply the same kind of services in terms of professionals, opening hours and such, in order to be qualified, hence given reimbursement from Region Skåne. Thus, before 2009 we did miss a lot of important information about those only consulting private care, after 2009 a great proportion of these practices became publicly organised thus transferring data to the SHR. Unfortunately, still their diagnostic codes do not end up in the SHR. Therefore the number of public practices has increased, but the diagnostic labels have not. This makes it look like the coverage now is lower than it used to be, but still the coverage within the former public organised practices (without the addition by Hälsoalet) is the same or even increasing.

Thirdly, although some diagnostic codes set by physiotherapists were included already 1998, they did not really start to appear in the SHR until 2009. In Sweden and in Skåne region it is common and recommended that people with back pain

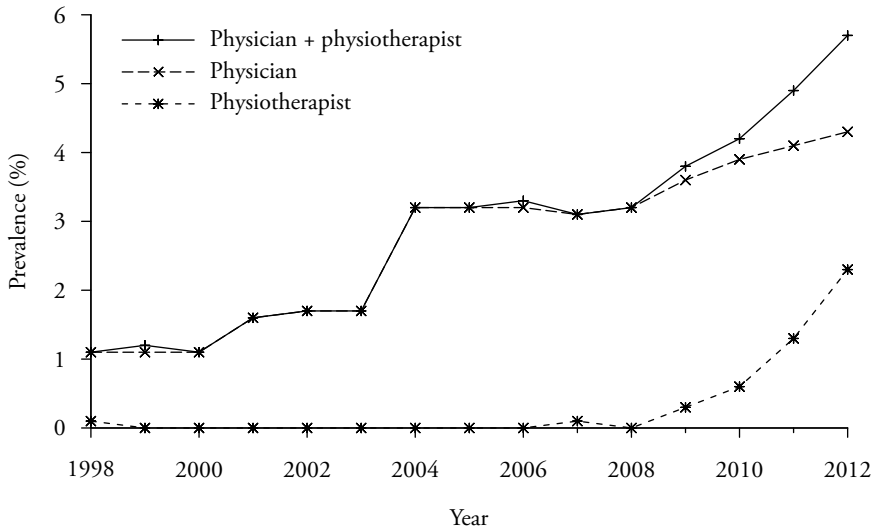



















































































Figure 7 Consultation prevalence of back and/or neck pain (ICD-10-SE code M54) in Skåne region depending on health care provider.

consult with physiotherapists via direct access as their initial healthcare contact. This is a large proportion of all people consulting: from a recent project called BackUp in the Skåne region, with the aim of facilitating a structured management around people seeking care due to LBP, 70% saw a physiotherapist as their first care giver (unpublished data). Starting from 2009, diagnostic codes from physiotherapists are transferred to the SHR although this data is still not complete. It is evident that this will effect consultation prevalence data, especially of pain conditions. The consultation prevalence of back and neck pain (ICD-10-SE code M54) changes when including only physician diagnoses or both physician and physiotherapist diagnoses (Figure 7).

These limitations have great impact on my studies. Regarding the overall loss to private care, there are evident problems with missing data on diagnostic codes and the problem might differ in size depending on the disease under study. In Paper I–II the denominator was reduced by 30% in primary care and 15% in the specialist secondary care. This assumption was based on 1) the proportion of consultations made in private care and 2) number of people that consult only within the private care sector. However, the vast majority seeking private care also seek public care, hence they would be identified in our studies. People seeking only private care seem to be adults primarily in the working ages (Table 4). Still selection bias in relation to the missing data is a concern.

Table 4 Age and gender description of proportion (%) of patients consulting different types of healthcare in Skåne region during 2012. The proportions are also illustrated by bar charts.

	Age groups	Public and private	Public	Private
Women	All ages	36.9	48.7	14.4
	0–19	9.1 	37.5 	13.9 
	20–29	7.2 	15.2 	8.6 
	30–39	8.9 	12.0 	15.4 
	40–49	17.3 	6.9 	23.2 
	50–59	17.6 	7.4 	18.5 
	60–69	19.7 	6.9 	12.9 
	70–79	11.7 	8.0 	5.0 
	80–89	6.5 	5.3 	2.3 
	90–	2.0 	0.7 	0.3 
Men	All ages	21.8	67.2	11.0
	0–19	18.8 	33.1 	20.3 
	20–29	6.5 	11.5 	9.8 
	30–39	8.0 	12.0 	13.7 
	40–49	10.3 	11.6 	16.0 
	50–59	12.7 	11.8 	18.1 
	60–69	18.7 	11.0 	14.5 
	70–79	14.4 	6.2 	5.7 
	80–89	8.7 	2.6 	1.8 
	90–	1.7 	0.2 	0.1 
Total	All ages	30.1	57.1	12.8
	0–19	12.3 	35.2 	16.4 
	20–29	7.0 	13.2 	9.0 
	30–39	8.6 	12.0 	14.7 
	40–49	15.0 	9.4 	20.4 
	50–59	16.0 	9.7 	18.4 
	60–69	19.4 	9.1 	13.6 
	70–79	12.6 	7.0 	5.3 
	80–89	7.3 	3.9 	2.1 
	90–	1.9 	0.4 	0.2 

Misclassification

In this thesis misclassification of exposure could appear and potentially be a problem. Sick leave episodes as expressed in the SSIA only covers those with sick leave

episodes longer than 14 days, hence those on shorter sick leave periods are classified as not being on sick leave. There are reasons to believe that some diseases usually are connected to shorter sick leave episodes (LBP) while other is overrepresented in the longer sick leave periods (OA) (Hubertsson J et al.; unpublished, unreferenced). As for sick leave, there is also potential misclassification in the use of prescribed drugs especially concerning the use of non-steroidal anti-inflammatory drugs (NSAID). The prescribed drug register only covers prescribed, hence people using over the counter NSAID or patients receiving NSAID in hospitals are classified as non NSAID users.

In Paper I and II, since pain is subjective and the diagnostic code is more symptom related it could be assumed that a majority of the defined cases actually do have LBP, hence a high specificity. On the other hand the sensitivity might be low, partly because a great proportion of patients with LBP do not see a physician but rather only a physiotherapist or do not consult at all (Figure 5, page 39). For a disease like SpA (Paper II and IV), there could be lower specificity since not all patients with a registered diagnosis actually meet all medical criteria for SpA, and also possibly a lower sensitivity. Studies have shown that the period from initial symptom to diagnosis is long.^{113,114}

In Paper III and IV, more strict criteria of having the diagnosis registered once by a specialist or at least twice by any other physician in order to get a higher specificity was set up. Recent work from the SHR show high validity of diagnoses retrieved from the SHR and that identified in the medical records.^{70,115}

Generalisability

The generalisability, or to what extent the results can be applied to other settings, is essential in epidemiological studies. The main population used here is the population in Skåne region. In many aspects Skåne is representative for Sweden. Skåne region has a registered population of 1,263,088 (31 December 2012) people, which is about 13% of the total Swedish population. In terms of important socio-demographic variables, Skåne region is considered a miniature of Sweden (Table 5).

In Paper II, data from Sweden and SHR was compared to that of UK and CiPCA. CiPCA is a regional database and the area in which the data are collected is more deprived than UK as a whole, the age and gender distribution was similar between the two settings SHR and CiPCA (CiPCA mean age 41.5 years, women 50.8%). Age-adjusting the results to that of the standardised US population 2000 to validate our comparative results did not change the results.

Table 5 Demographics for Sweden and Skåne region, 2012.

	Sweden	Skåne
Registered population	9,555,893	1,263,088
Women (%)	50.1	50.4
Mean age (years)	40.7	40.4
Civil status people aged ≥ 25 (%)		
Non married	31.8	29.0
Married*	47.8	49.8
Divorced†	13.6	14.3
Widow/widower	6.9	6.9
Education (Highest achieved) people aged ≥ 16 (%)		
Low, (0–9 years)	23.1	23.2
Moderate, (10–12)	43.1	41.4
High, (>12)	30.9	31.6
High+, (PhD degree)	1.0	1.2
Missing	2.0	2.6
Country of origin (%)		
Born in Sweden, both parents born in Sweden	72.8	68.9
Born outside of Sweden	15.4	18.4
Born in Sweden, at least one parent born outside of Sweden	11.8	12.7
Employment people aged ≥ 16 , (%)	58	54

* Married or registered partner (same sex).

† Divorced or unregistered from partner.

Results

Occurrence of LBP (Paper I)

Prevalence

In 2009 24,949 individuals (57.3% women) 20 years or older were 1-year consultation prevalence of LBP in the adult population diagnosed with LBP. The mean (SD) age was 55.3 (18.3) years. The was 3.8% (4.3% for women and 3.3% for men) and increased with age. The rate of new onset consultation was 238 per 10,000 adults (women = 265, men = 209), thus 63% of those consulting for LBP was defined as having a new onset LBP. The age and gender distribution was similar for the overall consultation prevalence and the new onset prevalence rate (Figure 8).

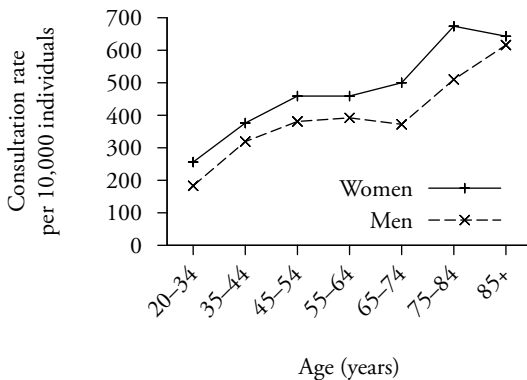


Figure 8 Rate of new onset physician consultations due to LBP in 2009 (new onset defined as no registered LBP diagnosis between 2004 and 2008) $n = 15,601$ (Paper I).

Consultation pattern

Among all consultations in 2009 13.2% was due to a MSD (ICD-10-SE chapter M (XIII)) among which LBP accounted for 17.7%. The group of patients consulting due to LBP had higher total consultation rates compared to the general population with a standardised healthcare utilisation ratio of 1.74 (95% CI 1.73–1.75) for women and 1.81 (95% CI 1.80–1.82) (Figure 9, next page).

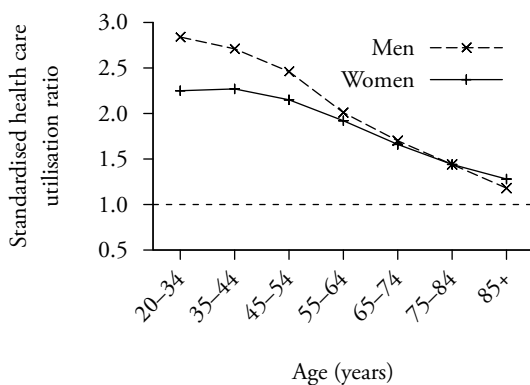


Figure 9 Standardised healthcare utilisation ratios for patients with LBP ($n = 24,949$) compared to the general population ($n = 938,397$) in 2009 in Skåne region. A value of 1.0 indicates no difference (Paper I).

The ratios declined with increasing age, reaching a ratio closer to 1 in the oldest men and women. Predominantly, the LBP patients consulted due to other pain problems (Table 6).

Table 6 Standardised morbidity prevalence ratio (SMR) (99% CI) for the 20 most common other causes for consultation in patients with LBP as compared to the general population (Paper I).

Diagnostic blocks (ICD-10-SE)	Women	Men
Other intervertebral disc disorders (M51)	8.93 (8.00–9.92)	8.71 (7.78–9.69)
Other spondylopathies (M48)	5.01 (4.43–5.63)	6.20 (5.34–7.13)
Pain not elsewhere classified (R52)	2.36 (2.15–2.57)	2.37 (2.10–2.66)
Other soft tissue disorder (M79)	1.91 (1.80–2.02)	1.83 (1.68–1.98)
Abdominal and pelvic pain (R10)	1.71 (1.60–1.83)	1.50 (1.35–1.65)
Pain in throat and chest (R07)	1.48 (1.33–1.64)	1.40 (1.24–1.57)
Other joint disorders, not elsewhere classified (M25)	1.47 (1.34–1.61)	1.36 (1.20–1.54)
Other anxiety disorders (F41)	1.38 (1.25–1.52)	1.26 (1.08–1.45)
Cystitis (N30)	1.34 (1.25–1.44)	1.16 (0.95–1.40)
Other chronic obstructive pulmonary disease (J44)	1.33 (1.17–1.50)	1.19 (1.01–1.39)
Dizziness and giddiness (R42)	1.31 (1.17–1.47)	1.26 (1.07–1.47)
Depressive episode (F32)	1.29 (1.18–1.40)	1.33 (1.17–1.51)
Acute upper respiratory infection of multiple sites (J06)	1.23 (1.14–1.33)	1.07 (0.95–1.19)
Unspecified acute lower respiratory infection (J22)	1.23 (1.09–1.38)	1.19 (1.02–1.39)
Chronic ischaemic heart disease (I25)	1.04 (0.91–1.18)	1.04 (0.93–1.16)
Non-insulin-dependent diabetes mellitus (E11)	0.99 (0.89–1.10)	1.01 (0.91–1.12)
Senile cataract (H25)	0.98 (0.88–1.10)	0.97 (0.83–1.12)
Atrial fibrillation and flutter (I48)	0.93 (0.81–1.05)	0.94 (0.83–1.06)
Essential (primary) hypertension (I10)	0.91 (0.86–0.96)	0.87 (0.81–0.93)
Disorders of lipoprotein metabolism (E78)	0.88 (0.78–1.00)	0.79 (0.69–0.90)

Comparative prevalence study (Paper II)

The mapping procedure between diagnostic codes based on Read codes used in the UK and ICD-10-SE used in Sweden was successful. Based on all healthcare, primary and secondary care, there were 2,143/10,000 persons in the English database and 1,610/10,000 persons in the Swedish database that had a record of consulting at least once in the year 2010 for MSD. This overall difference between UK and Sweden was apparent especially in the different prevalences for LBP (587 vs. 294/10,000). By contrast, RA, SpA, and PsA had slightly higher prevalences in the Swedish database. OA and AS prevalence figures were similar between the two nations (Table 7).

Table 7 Annual (2010) consultation prevalence of MSD (95% CI) per 10,000 registered population (Paper II).

	CiPCA, UK	SHR, Sweden
All health care		
Musculoskeletal (all)	2,143 (2,114–2,173)	1,610 (1,603–1,617)
Low back pain	587 (572–603)	294 (290–297)
Rheumatoid arthritis	40 (36–44)	59 (58–61)
Spondyloarthritis	13 (11–16)	30 (29–31)
Ankylosing spondylitis	5 (3–6)	6 (5–6)
Psoriatic arthritis	8 (6–10)	16 (15–17)
Osteoarthritis	211 (202–220)	269 (266–272)
All health care, ages 45+		
Osteoarthritis	447 (428–468)	578 (571–585)
Joint pain	875 (847–903)	631 (624–638)
Osteoarthritis or joint pain	1,192 (1,160–1,225)	1,094 (1,085–1,103)
Primary care consultations only		
Musculoskeletal (all)	1,967 (1,939–1,995)	1,354 (1,347–1,361)
Low back pain	543 (529–558)	290 (286–293)
Rheumatoid arthritis	25 (22–28)	26 (25–28)
Spondyloarthritis	8 (7–10)	8 (8–9)
Ankylosing spondylitis	3 (2–4)	0.2 (0.1–0.3)
Psoriatic arthritis	5 (3–6)	3 (3–4)
Osteoarthritis	176 (168–185)	196 (193–199)
Primary care consultations only, ages 45+		
Osteoarthritis	375 (357–393)	443 (436–449)
Joint pain	794 (768–821)	603 (596–610)
Osteoarthritis or joint pain	1,074 (1,044–1,106)	967 (958–977)

When the analysis was restricted to primary care consultations, the absolute difference in prevalence of MSD consultation changed somewhat, however the occurrence of AS was rarely recorded in Swedish primary care (Table 7, page 49). Similar cross-national patterns to the annual consultation prevalence figures were observed when assessing seven-year period prevalence. The prevalence of diagnosed OA in those aged 45 and older was reasonably consistent between UK and Sweden (Table 7, page 49). Including joint pain codes with OA increased these figures, although recorded joint pain prevalence was slightly higher for UK. The age-gender patterns were similar between UK and Sweden, with the exception that the higher prevalence of RA for women than for men was more marked in Sweden and that LBP showed a more constant increase by age in the Swedish data (Figure 10, page 51).

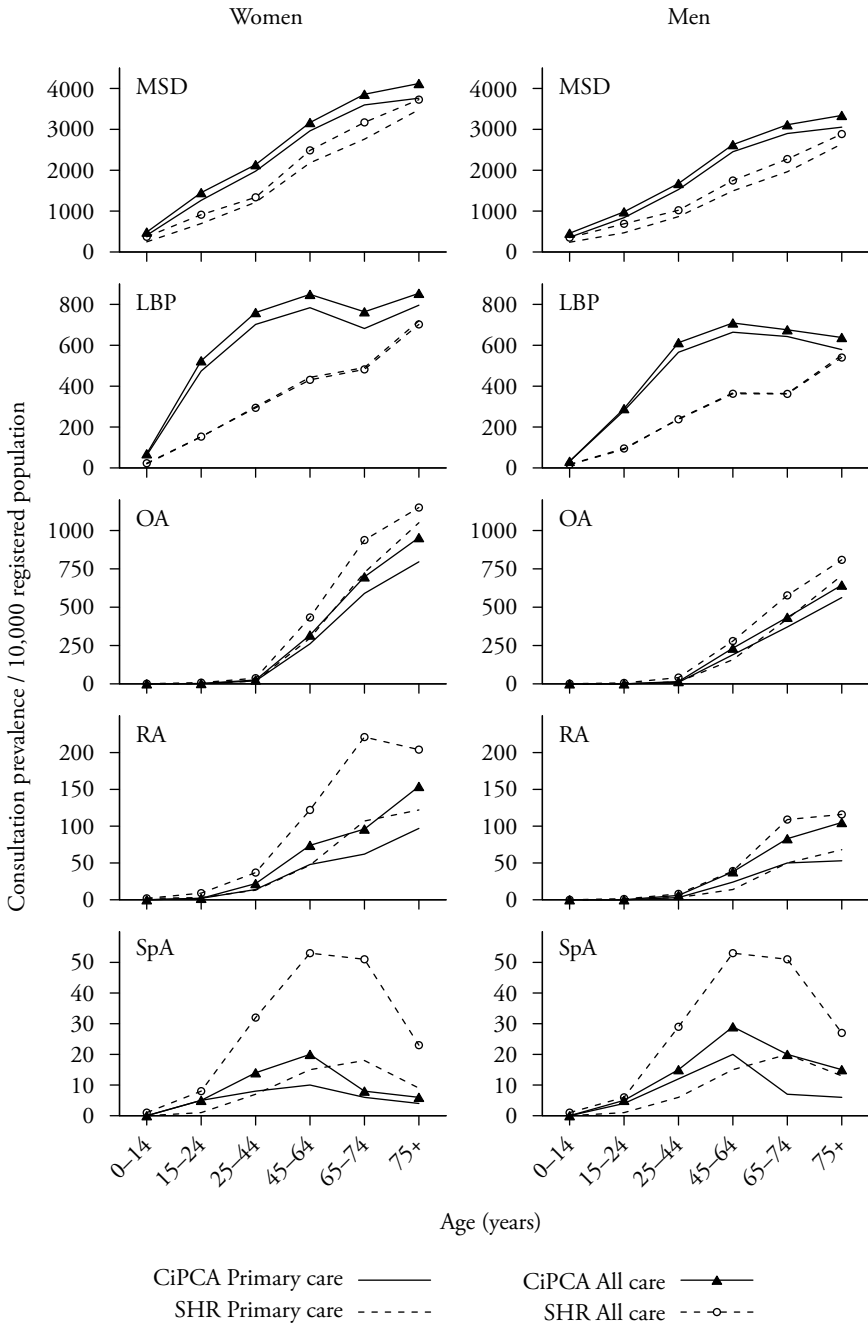


Figure 10 Annual (2010) consultation prevalence of MSD by age and sex. All care includes primary and secondary care.

Neck injury – consultation patterns (Paper III)

In all, 1,443 adult residents (54% women) diagnosed with whiplash associated neck injury between 2007–2008 were identified as the study cohort. To each case four references was drawn from the general population (Figure 11 and Table 2, page 36). The mean (SD) age at diagnosis was 38 (14.6) years.

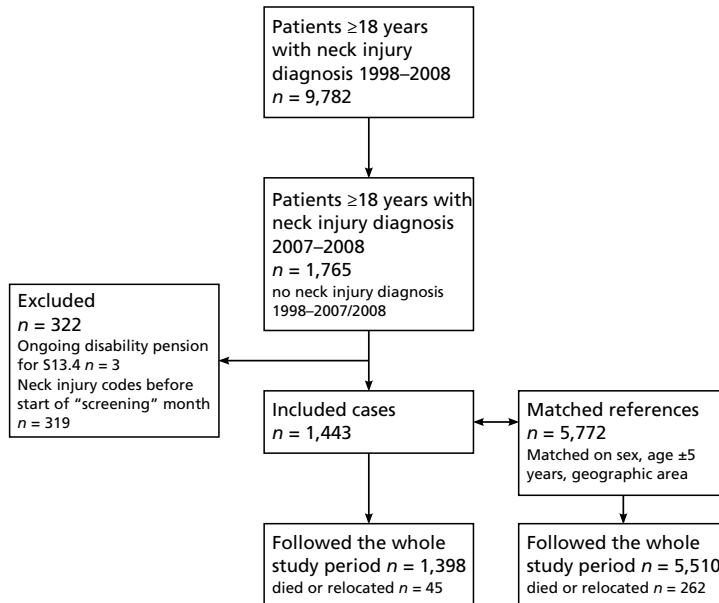


Figure 11 Flow chart of study inclusion (Paper III).

Healthcare consultation pattern

Over the six-year study period, the study cohort had significantly more healthcare consultations than each of the three different reference cohorts ($p < 0.0001$, Figure 12).

After stratification based on preinjury consultation levels, the three subgroups (preinjury consultation level: low-frequent, frequent, and high-frequent consulters), differed in terms of age and sex (older and more women in high frequent group, $p < 0.0001$). There was a similar shape of their consultation frequency curves and they remained separated from each other also after the injury. When studying mean number of consultations by month after injury diagnosis, a clear increase in consultations to a physiotherapist was seen in the period after injury (Figure 13, page 54). Number of consultations differed between the subgroups, pre and postinjury, after adjusting for age and gender ($p < 0.0001$).

The risk for changing from low to high-frequent consulter one year after injury was 2.27 (99% CI 1.63–3.15) and the attributable risk was 11%. The increased

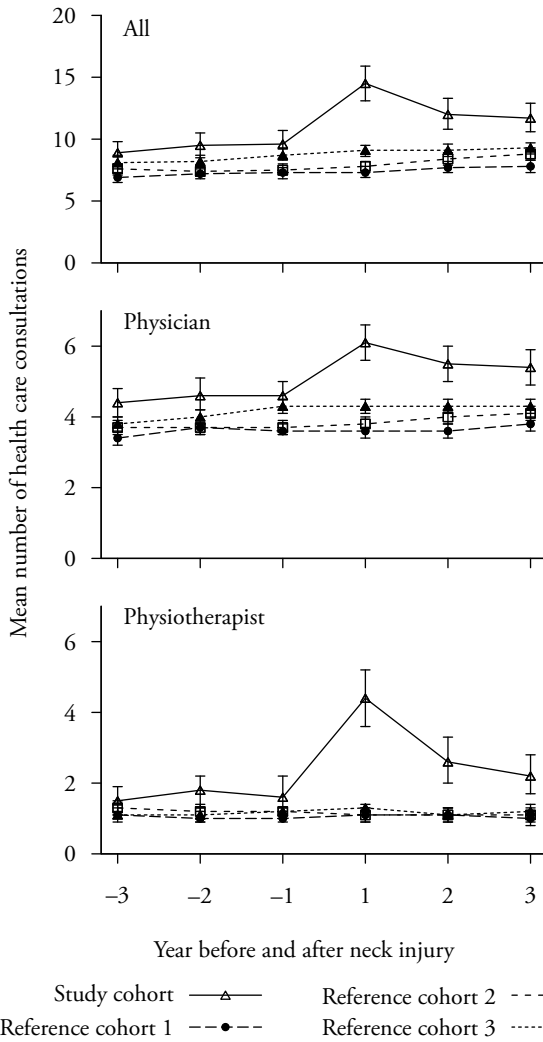


Figure 12 Mean number of healthcare consultations for all types of healthcare, physician and physiotherapist care in the study cohort and the three different reference cohorts.

risk was seen over the three year period following neck injury. Diseases that have been shown to be common after neck injury such as headache and dizziness increased in all subgroups. The proportion of cases consulting due to both MSD and psychological distress were higher among all study subgroups as compared to the reference subgroups already before the injury (Table 8, page 55). In all, the proportion of cases diagnosed with psychological distress or MSD increased ($p < 0.0001$) after the trauma although in the high frequent group no major change in the proportion consulting for MSD and psychological distress was seen.

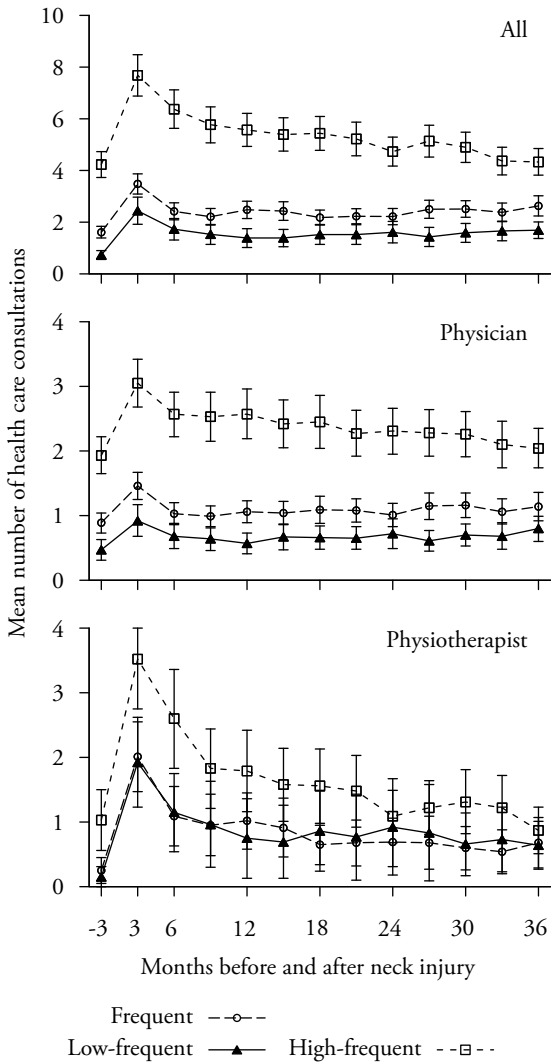


Figure 13 Mean number (99% CI) of healthcare consultations after neck injury for all types of healthcare, physician care and physiotherapist care in the study cohort stratified by preinjury consultation level; low-frequent ($n = 384$), frequent ($n = 583$) and high-frequent ($n = 476$).

The mean number of consultations due to psychological distress decreased preinjury while the mean number of consultations due to MSD increased.

Work disability

At the day of the neck injury diagnosis, 6.7% were on disability pension, primarily connected to musculoskeletal disorders (51%) and mental disorders (30%). Four per cent was on sick leave. The number of net sick days (sick leave and disability pension) correlated to the number of healthcare consultations before ($\rho = 0.47$; 99% CI 0.38–0.49) and after injury ($\rho = 0.32$; 99% CI 0.25–0.37).

Table 8 Proportion (%) that consulted a physician due to different diagnoses (ICD-10-SE) before and after neck injury diagnosis. For the study cohort the proportions are also illustrated by bar charts (Paper III).

Year	Low-frequent		Frequent		High-frequent	
	Cases	References	Cases	References	Cases	References
<i>n</i>	384	2,001	583	2,287	476	1,477
Diseases of the musculoskeletal system and connective tissue*						
Year -3	7.0	3.9	11.7	7.9	27.1	16.7
Year -2	1.3	0.8	10.5	9.1	33.8	22.7
Year -1	5.5	5.8	10.6	11.2	26.9	21.4
Year 1	13.8	4.1	18.2	10.0	35.5	20.4
Year 2	13.0	5.3	14.8	9.0	28.8	18.6
Year 3	10.7	6.3	17.8	12.0	29.8	21.5
Psychological distress†						
Year -3	1.6	0.5	2.9	2.7	13.4	10.1
Year -2	0.8	0.0	3.4	2.5	14.9	11.4
Year -1	1.0	0.5	4.6	2.0	13.4	10.7
Year 1	3.1	1.1	5.7	1.6	13.9	7.9
Year 2	4.7	0.9	4.8	2.6	14.5	8.5
Year 3	4.7	1.7	6.5	4.0	10.3	8.6
Headache, dizziness and tinnitus‡						
Year -3	1.0	0.1	0.7	0.7	4.0	2.8
Year -2	0.3	0.0	1.7	0.5	4.4	3.3
Year -1	0.8	0.8	1.0	0.8	4.2	2.8
Year 1	2.6	0.4	1.9	1.5	5.3	2.6
Year 2	2.6	0.6	1.9	1.5	6.5	3.2
Year 3	2.1	0.4	2.7	1.2	5.5	2.9

* ICD-10-SE chapter XIII.

† ICD-10-SE blocks F32, F41, F43.

‡ ICD-10-SE codes M53.1, G44.0, G44.3, F45.4, G44.2, R51, G44.1, H81.0-4, H81.8-9, R42.9, F40.0, H93.

The correlation was seen all three years after the neck injury. The number of sick days before neck injury was different; lower in low frequent and higher in high frequent consulters after adjusting for age and sex ($p < 0.0001$).

Use of prescribed drugs

In an additional analysis, after publication, I analysed the proportion of cases and references that used prescribed drugs the year before inclusion until two years after

inclusion. The proportion of cases on prescribed antidepressants was larger than among the reference group the whole study period (non-significant difference for men the year before injury). The use of prescribed NSAID was also larger among the cases before injury, although the sex difference, the year before neck injury, seen for antidepressants was not seen for NSAID. As expected the use of NSAID increased after the injury diagnosis to return to the same level as before the diagnosis after two years (Figure 14).

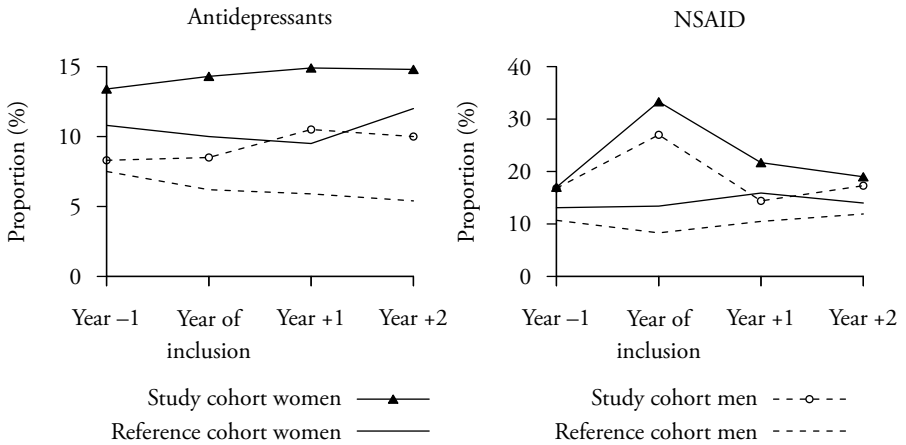


Figure 14 Proportion (%) in study cohort and reference cohort with prescribed antidepressants and NSAID one year before to two years after inclusion, unpublished data (Paper III).

Socioeconomic status as a risk factor for MSD (Paper IV)

SpA

A total of 1,194 patients diagnosed with a new SpA diagnosis 2010–2012 were identified. To each case, two controls matched for age and sex were enrolled (Figure 15). The mean (SD) age at diagnosis was 46 (12) years (Table 9, page 59).

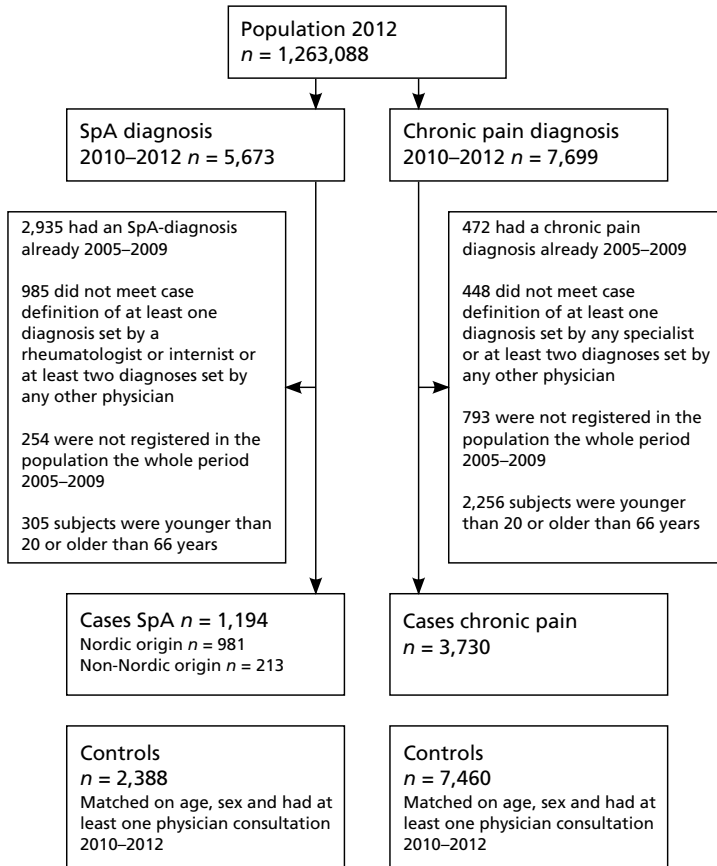


Figure 15 Flow chart of study inclusion (Paper IV).

Nordic origin was equally common in all subgroups around (80%) and more common in cases than in controls ($p < 0.0001$). Non-Nordics were to a lower extent on full time sick leave (5% vs. 8%) and to a greater extent not-working (27% vs. 16%) than cases with a Nordic origin rendering a greater proportion of non-Nordics with a low income, below the lowest tertile (49% vs. 33%). The proportion of cases with back and/or neck pain year four before diagnosis was

greater in the non-Nordics as compared to the cases with Nordic origin (9% vs. 4%)

In the regression analyses, the adjusted model was very similar to the crude, non-Nordic origin was significantly associated (OR = 1.44; 95% CI 1.20–1.73) with increased risk of being diagnosed with SpA (Table 10, page 60). After excluding the SpA cases with non-Nordic origin, the adjusted model showed that being on full time sick leave was an important factor associated with being diagnosed with SpA (OR = 2.09; 95% CI 1.46–2.98) (Table 10, page 60), implying that origin is an effect modifier in the model.

Chronic pain

Between 2010–2012, 3,730 patients with a diagnosis of chronic pain diagnosis were identified. To each case, two controls matched for age and sex were enrolled (Figure 15, previous page). The mean (SD) age at diagnosis was 47 (12) years and the proportion of women was 61%. Patients diagnosed with chronic pain differed from that of the controls regarding socioeconomic and healthcare consultation measures (Table 9). In the adjusted logistic regression model, all socioeconomic variables except marital status were significantly associated with being diagnosed with chronic pain (Table 11, page 61).

Comparative analysis SpA–chronic pain

In a comparative sub analysis, chronic pain cases had more consultations to GPs ($p = 0.0002$) and to specialist physicians in secondary care ($p < 0.0001$) than the SpA cases, while SpA cases used more prescribed NSAID ($p < 0.0001$) than the chronic pain cases did (results from adjusted model).

Table 9 Socioeconomic characteristics and consultation data including NSAID use among cases and controls (Paper IV).

	Spondyloarthritis		Chronic pain	
	Case	Control	Case	Control
<i>n</i>	1,194	2,388	3,730	7,460
Age (mean, SD)	46 (12)	46 (12)	47 (12)	47 (12)
Women (%)	53	53	61	61
Country of origin, [*] <i>n</i> (%)				
Nordic country	981 (82)	1,817 (76)	2,621 (70)	5,607 (75)
Non Nordic country	213 (18)	571 (24)	1,109 (30)	1,853 (25)
Marital status, [†] <i>n</i> (%)				
Married	532 (45)	1,103 (46)	1,725 (46)	3,515 (47)
Unmarried	662 (55)	1,284 (54)	2,005 (54)	3,944 (53)
Missing	1		1	
Education, [‡] <i>n</i> (%)				
High (>12 years)	382 (32)	807 (34)	932 (25)	2,539 (34)
Moderate (10–12 years)	574 (48)	1,104 (46)	1,861 (50)	3,453 (46)
Low (≤9 years)	238 (20)	477 (20)	937 (25)	1,468 (20)
Work-status, <i>n</i> (%)				
Working	892 (75)	1,789 (75)	2,375 (64)	5,657 (76)
Not working	216 (18)	471 (20)	911 (24)	1,431 (19)
Full-time sick leave/Disability pension	86 (7)	128 (5)	444 (12)	372 (5)
Income individualized, <i>n</i> (%)				
Tertile 3 (High)	315 (26)	701 (29)	807 (22)	2,051 (27)
Tertile 2 (Middle)	450 (38)	807 (34)	1,245 (33)	2,507 (34)
Tertile 1 (Low)	429 (36)	880 (37)	1,678 (45)	2,902 (39)
Physician consultations [§] , mean (SD)				
Primary care	1.1 (1.6)	0.8 (1.4)	1.4 (2.2)	0.9 (1.5)
Specialist care	1.5 (2.8)	1.1 (3.7)	2.5 (8.1)	1.1 (3.0)
Back and/or neck pain, <i>n</i> (%)	57 (5.0)	73 (3.0)	287 (7.7)	226 (3.0)
Psoriasis, [¶] <i>n</i> (%)	92 (8.0)	21 (0.9)	38 (1.0)	39 (0.5)
Prescribed NSAID, ^{**} <i>n</i> (%)	342 (29)	370 (15)	1007 (27)	1170 (16)

* Born in Nordic country by parents born in Nordic country.

† Married: married or registered partner (same sex). Unmarried: divorced from wife/husband/partner or widow/widower from wife/husband/partner.

‡ Highest achieved level.

§ Mean number of consultations year four before inclusion.

|| ICD-10-SE block M54* year four before inclusion.

¶ ICD-10-SE block L40* (not including L40.5) year four before inclusion.

** Prescribed NSAID year four before inclusion.

60 Results

Table 10 Logistic regression models over association between socioeconomic status and being diagnosed with SpA (Paper IV).

	All		Nordic origin		Non-Nordic origin			
	Crude model		Adjusted Model		Adjusted model		Adjusted model	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Country of origin								
Non Nordic country	1		1		–		–	
Nordic country*	1.45	1.22–1.73	1.44	1.20–1.73	–	–	–	–
Marital status [†]								
Married	1		1		1		1	
Unmarried	1.08	0.93–1.26	1.06	0.91–1.24	1.01	0.85–1.21	1.02	0.72–1.44
Education [‡]								
High (>12 years)	1		1		1		1	
Moderate (10–12 years)	1.10	0.94–1.30	1.04	0.88–1.23	1.04	0.87–1.25	0.86	0.58–1.28
Low (0–9 years)	1.06	0.86–1.32	1.02	0.81–1.27	1.07	0.83–1.37	0.98	0.59–1.63
Work status								
Working	1		1		1		1	
Not working	0.89	0.73–1.09	0.94	0.76–1.17	1.02	0.79–1.31	0.64	0.41–0.98
Full-time sick leave [§]	1.37	1.02–1.84	1.30	0.96–1.77	2.09	1.46–2.98	0.76	0.35–1.63
Income individualized								
Tertile 3 (High)	1		1		1		1	
Tertile 2 (Middle)	1.25	1.04–1.50	1.25	1.04–1.50	1.27	1.04–1.55	1.08	0.65–1.77
Tertile 1 (Low)	1.10	0.90–1.33	1.17	0.95–1.44	1.21	0.97–1.52	1.00	0.59–1.69

* Born in Nordic country by parents born in Nordic country.

[†] Married: married or registered partner (same sex). Unmarried: divorced from wife/husband/partner or widow/widower from wife/husband/partner.

[‡] Highest achieved level.

[§] Sick leave or disability pension.

Table 11 Logistic regression models over association between socioeconomic status and being diagnosed with chronic pain (Paper IV).

	Crude model		Adjusted model	
	OR	95% CI	OR	95% CI
Country of origin				
Nordic country*	1		1	
Non Nordic country	1.28	1.17–1.40	1.13	1.03–1.24
Marital status†				
Married	1		1	
Unmarried	1.04	0.96–1.13	0.99	0.90–1.08
Education‡				
High (>12 years)	1		1	
Moderate (10–12 years)	1.48	1.35–1.62	1.39	1.26–1.53
Low (0–9 years)	1.85	1.64–2.08	1.53	1.35–1.73
Work status				
Working	1		1	
Not working	1.57	1.41–1.74	1.40	1.25–1.57
Full-time sick leave§	2.95	2.53–3.43	2.59	2.21–3.04
Income individualized				
Tertile 3 (High)	1		1	
Tertile 2 (Middle)	1.32	1.18–1.47	1.15	1.03–1.29
Tertile 1 (Low)	1.59	1.42–1.77	1.18	1.04–1.33

* Born in Nordic country by parents born in Nordic country.

† Married: married or registered partner (same sex). Unmarried: divorced from wife/husband/partner or widow/widower from wife/husband/partner.

‡ Highest achieved level.

§ Sick leave or disability pension.

Discussion

The overall aim of this thesis was to incorporate routinely collected healthcare data in the epidemiological research of consultation prevalence, healthcare consultation and sick leave patterns in patients with MSD. The importance of doing so is related to the main findings of the thesis that MSD are affecting society, and structures therein, directly and indirectly by the individuals affected. I found that the occurrence of MSD varies between disease and, although fairly consistent, but to some extent, between European countries. Additionally, I find that patients diagnosed with pain in back and neck consult more healthcare, use more pharmaceuticals, and have more sick leave episodes than the references, as measured through different registers. I also find that socioeconomic status is associated with being diagnosed with chronic pain.

Occurrence

In previous reports, over 30% of the population have been reported to suffer from varying degrees of self-reported LBP.^{6,116,117} However, the pain does not necessarily lead to consultation. Studies on consultation patterns suggest that people with more severe pain seek healthcare more frequently than others.¹¹⁸⁻¹²⁰ Recent research on LBP suggests that elderly persons suffer from more severe pain.^{24,121} The finding that the older population is overrepresented, both in consultation prevalence and rate of new onset consultation, corroborates these findings and warrants concern in a steadily ageing population. The new onset rate of LBP was similar to the overall consultation prevalence, meaning that you often only consult once per episode or only the first time you suffer from LBP. Explanation for this could be that you get reassured the first time about whether it is likely that your pain is due to a specific severe cause or not and/or that you get sufficient self-management advice. It could also indicate that the diagnosis becomes more specific with time. However, it could also be explained by the missing data from physiotherapists, which are more likely to see the patients on a more regular basis.

Few studies on LBP consultation prevalence or equivalent measures of occurrence have been published. However, our rate of new onset consultations were

lower than those reported from the United Kingdom and the Netherlands.^{1,122} This could be explained by the definition of LBP. To be able to compare figures properly I did however, in Paper II try to study the occurrence of common MSD within two different European countries, using two different coding systems. The conclusions are that it is feasible to compare data given that you are aware of important differences. Still, in all epidemiologic work one crucial part is to put your result in the perspective of those already published. The results in Paper II highlights how difficult this is. This is also recognised in studies of the burden of disease,^{78,123} one can only compare results with those published and sometimes it is hard to know what it is that you compare given poor explanations in articles. In the studies of LBP for example self-assessed pain is pain, it is nevertheless not always specified what is defined as low back from study to study or what recurrent as compared to acute pain is. Consensus on this would facilitate comparisons.^{124–126} From our regional perspective in the SHR, the introduction of physiotherapist diagnostic codes will bring more light on the actual burden from especially pain diagnosis.

Reliable comparisons of routine healthcare data between countries and healthcare systems give opportunities to study causes and differences in management and outcome of morbidities. All databases using routine morbidity coding will incorporate variation by clinicians in using diagnostic criteria and in recording of morbidities. This can potentially lead to variation in recorded prevalence. Between countries, such variations may be exacerbated by differences in coding systems and contrasting components of the healthcare systems which may affect how morbidity data is recorded and collected. There may also be underlying differences in the occurrence of different conditions between countries. However, we observed a general consistency in healthcare prevalence of rheumatic disorders between UK and Swedish databases despite their dissimilar healthcare systems and recording practices. The identified contrasts in more unspecific pain conditions may be partially explained by the two known differences; direct access to physiotherapy and the direct transfer of morbidity data to the SHR from secondary care in Sweden. Patients who directly access physiotherapy tend to be younger, more educated and more likely to have unspecified symptoms or diseases.¹²⁷ Approximately 70% of LBP patients have their initial contact with a physiotherapist in Skåne (unpublished data). The healthcare figures for UK all care (primary and secondary care) are likely to underestimate prevalence for the inflammatory conditions, mostly handled in specialist secondary care, and the true prevalence is likely to be closer to the figures derived for Sweden where the coverage from secondary care is higher.

One challenge in comparing prevalence figures is in deciding on what constitutes “similar” prevalence. For example, Swedish annual healthcare prevalence of

PsA is twice that for UK but the absolute difference is low (8 extra people consulting per 10,000), whereas for a more prevalent condition like LBP, a similar relative ratio constitutes a larger absolute difference (293 extra people consulting in UK per 10,000).

Healthcare consultation patterns

The patients consulting with LBP consumed substantially more healthcare than the general population. The total excess healthcare utilisation was about two-fold for both women and men. The LBP patients who consumed the most in relative measures were those in the lower ages. For both women and men, the healthcare utilisation decreased with increasing age. This finding is probably explained by an increase in the healthcare consultation in the general population by age, more so than a decrease in the LBP patient group. With older age the consultation frequency is likely to increase due to comorbid diseases. It is plausible that many of these LBP diagnoses reflect pain from more specific conditions such as osteoporosis-related vertebral fractures and spinal stenosis not yet diagnosed. The most notable other common diagnostic code recorded for the patients with LBP included as expected specific back pain diagnoses such as intervertebral disc disorders. However, I also noted more frequent diagnostic codes for more widespread pain, e.g., from soft tissues and other sites. Previous data have shown that regional pain such as a LBP and also whiplash injury is a future risk factor for developing widespread and or chronic pain.^{18,19,26,31,46} Our finding strengthens the knowledge that a regional pain site often is part of a more widespread problem which in turn is a risk factor to developing chronic pain.¹⁸

All MSD should be studied from a bio-psychosocial perspective.²⁸ A disease affects your health, but your health also affects the disease and the outcome thereof. An initial poor self-assessed health status has been shown to have a negative effect on recovery and prognosis after whiplash.^{43,46,128} My findings of a clear association between pre and postinjury consultation level strengthens this further. There was also an association between number of consultations and number of sick days. It is not the number of consultations as such that is of importance, but rather what the number represents. Previous data have shown that number of consultations as a predictor for future consultations is strong.¹²⁹ I believe that number of consultations, regardless of cause, is correlated with your health, thus your health status. Thus it intrigues me to view number of consultations as a proxy for health and health status. An important player in the overall health status is your mental health and depression has been suggested to be a risk factor for neck pain.^{130,131} This was supported by high initial consultation rates due to psychological disorders among the neck injured. Among the neck injured who were

low-frequent consulters, the proportion diagnosed by a physician with psychological distress or dizziness before the neck injury was in line with their reference individuals. However, post-neck injury this subgroup increased their consultation rates due to these conditions, corroborating prior reports.¹³²

The proportion of patients with a physician diagnosis with psychological distress rose relatively more post-injury than musculoskeletal disorders did. This should be taken into account in treatment and rehabilitation based on the bio-psychosocial model.¹³¹ Interestingly, in the high-frequent group, the mean number of consultations due to psychological distress decreased while the mean number of consultations due to musculoskeletal disorders increased. One hypothesis would be that the former underlying cause of stress, anxiety or depression could be diverted to consultations regarding musculoskeletal symptoms after the injury. Our results indicate that psychological distress is a common reason for physician healthcare consultations already before an acute neck injury diagnosis as previously shown.¹³² One hypothesis is that poor health status actually increases your risk of being in an accident due to prescribed antidepressants.^{133,134} Data retrieved from the SPDR showed that the proportion of neck injury cases with an ongoing treatment of antidepressant the year before the injury was high. It is clear that the cases consumed antidepressants to a higher extent already before the injury while the corresponding proportion for use of NSAID is a bit different and perhaps more in accordance with the actual neck injury as such.

Patients diagnosed with neck injury are thus a heterogeneous group of patients, and it is important to recognise the different subsets within this patient group. In a recent study, Kasch et al. have presented a way of early stratification of acute neck injured patients based on a risk score in relation to chronic pain and work disability.⁵¹ Prior consultation frequency may serve as an additional variable for risk assessment of patients diagnosed with neck injury, as a proxy for health status. Stratification based management^{135,136} and early intervention can have a positive influence on prognosis after initial regional pain,¹³⁷ and can be cost effective.¹³⁸

Socioeconomic status in relation to health and disease

There is an established relationship between poor socioeconomic status and poor health and disease in general.^{81,82} Also studies show that your socioeconomic status influences the physician in the diagnostic decision making.^{139,140} In all included papers, socioeconomic status add a relevant aspect. In Paper I and II diagnostic differences and healthcare utilisation pattern might to an extents be explain by differences in socioeconomic status. Although in large Skåne region is fairly representative of Sweden, studies show that CiPCA covers one area of UK that is more deprived (lower socioeconomic status) than UK as a whole, still it

has been shown to give comparable prevalence figures to national databases.¹⁰⁶ However, it is fair to say that the differences seen in Paper II could partly be explained by bias because of the relative deprivation between the area covered by CiPCA and Skåne. On the other hand, the practices within the CiPCA network undergo annual cycle of assessment including diagnostic coding, thus it could be assumed that the physicians are more prone to diagnose correctly and might also be more perceptive on MSD.

In Paper III, some of the differences in number of healthcare consultations between cases and references are explained by level of education. The cases had significantly lower education than the references. After stratification on pre-injury consultation level, level of education did not significantly differ between the sub groups. Paper IV show that socioeconomic status is an important factor associated with chronic pain. In SpA no significant association was identified in the adjusted analysis for any of the included variables on socioeconomic status. However, the effect from work status seems to differ depending on the patient's origin. In Nordic-born cases, being on full time sick leave is associated with being diagnosed with SpA. A protective association was seen among the non-Nordic cases. The relation between origin and SpA, as such, is partly explained by the HLA-B27 antigen, which has an unequal ethnic distributions.¹⁰⁹ However, the genetic factor is not believed to increase your risk of being on full time sick leave, hence origin as a genetic factor is not considered a confounder but rather an effect modifier. If we look at origin as measuring something else, it could be that origin, here non-Nordic, actually does increase the risk of not being on sick leave (due to unemployment, unwillingness from physicians to apply for sick leave compensation etc.) and also decrease the risk of being diagnosed with SpA. From this perspective, origin could be defined as a confounder variable. In the initial adjusted analysis, origin is treated as a confounder, while it is treated as an effect modifier in the latter stratified analysis. I believe that both genetic and surrounding associated factors play a role in the relation between origin, sick leave and SpA although from the analyses the latter is more supported.

Many prior studies have shown the association between socioeconomic status and chronic pain.^{32,33,94} Although, to our knowledge no study has investigated the risk associated with poor socioeconomic status and being diagnosed with chronic pain. My initial hypothesis was based around the belief that your socioeconomic status plays a role when you first see your GP complaining about e.g., LBP. I hypothesised that two people consulting due to the same complaint might get different examinations, referrals and ultimately different diagnosis. Studies have provided conflicting results concerning socioeconomic equity in primary care use,^{87,88} with pro-rich inequity in the use of specialist healthcare in most western countries,^{87,89-91}

When you study risk factors, ideally you want to identify exposure happening prior to disease onset. However, both regarding SpA and chronic pain it is hard to identify when the disease actually started. I studied the association between exposures measured four years before initial diagnosis. I found that both SpA cases and chronic pain cases had increased levels of consultation and increased mean levels of daily doses of NSAID already four years before diagnosis. Increased use of NSAID and healthcare could partly be explained by the fact that the disease onset has already started; it has been shown that the time between onset of symptoms started and diagnosis of SpA is long, over 10 years,^{113,114} although a recent Danish study indicate that this time has considerably shortened during the recent years to only be months.¹⁴¹ In both the SpA cases and the chronic pain cases many of them had been diagnosed with back and/or neck pain four years earlier, again possibly related to general health status. Chronic pain typically starts with regional pain, often in the spine.^{19,33} Depending on healthcare system about 3–6% of the population are diagnosed with LBP by a physician annually (Paper II). This makes it important to clarify the relation with socioeconomic status in this group to better facilitate the care and to ensure patients are managed equally independent of their socioeconomic status but dependent on their needs. Also, patients with SpA might suffer from chronic pain and vice versa,¹⁴² although this was true in only 22 (0.6%) patients in our study i.e., cases identified as both SpA and chronic pain cases.

This study was designed to study the risk of being diagnosed with SpA or chronic pain. This is not necessarily the same as the risk of actually having the disease. Given the results, I would speculate that socioeconomic status plays a bigger role in actually getting chronic pain than a specific long lasting inflammatory disease like SpA. All MSD are influenced not only by the disease pathogenesis but also the environment, opportunities, and lifestyle.¹³¹ It is plausible that this complex interplay has an even bigger role in a more unspecific condition like chronic pain, but also LBP and neck injury, more so than a relatively well-defined group of related diseases such as SpA. If the actual disease does not differ between socioeconomic groups but rather the way you are diagnosed, then it is crucial to incorporate this knowledge in daily work by healthcare personnel.

Final comments and future perspectives

The present detailed studies on occurrence, consultation patterns and potential risk factors warrant concern given the great impact on important social structures from MSD. In light of the ageing population, this is even more important and we could benefit from benchmarking studies between different countries and systems.

There is a complex association between health, illness, disease, healthcare consultation, work disability, and use of pharmaceuticals. Our routinely collected healthcare databases and quality registers in the Nordic countries enable us to analyse these associations in detail. However, more research is needed to improve the usage of healthcare data further, especially to be able to use this type of data in outcome studies. Routinely collected databases are the present and the future for population based public health research aiming at studying the occurrence and societal impact of MSD and other public health disorders. While there are tremendous possibilities, it's also important to bear in mind potential limitations with register data due to e.g., missing data and misclassification which may introduce bias, ultimately affecting the results. To enhance the use even further, standardisation of both definitions and procedures are welcomed, as are clearer regulation on what to be registered, how and by whom.

Conclusions

The main conclusion drawn from the results of this thesis underscore MSD and especially LBP as a public health concern that warrants more awareness and structured management that inhibit longstanding pain (Paper I).

Routinely collected healthcare data offers potential for comparative studies of variations in occurrence and outcome of MSD between European nations. However due to different healthcare systems, more specified diagnoses seems more feasible to compare (Paper II).

Patients with whiplash associated neck injury is a heterogeneous group in terms of preinjury consultation rates and possibly health states. Given the clear association between pre- and postinjury consultation rates, I propose that taking consultation history and health status into account could facilitate for health care professionals to further improve the treatment and rehabilitation of patients with neck injury, reducing the risk of longstanding problems (Paper III).

Socioeconomic status is a risk factor for being diagnosed with chronic pain. It is important to clarify this association further in this group of patients to better facilitate the care and to ensure patients are managed equally independent of their socioeconomic status but dependent on their need (Paper IV).

Summary in Swedish – Svensk populärvetenskaplig sammanfattning

Denna avhandling är skriven inom ämnet folkhälsovetenskap med inriktning epidemiologi. Folkhälsa handlar i stort om hälsotillståndet i en befolkning, både vilken nivå hälsotillståndet ligger på och hur fördelningen av hälsa ser ut i befolkningen med avseende på kön, ålder och andra socioekonomiska faktorer. Hälsa är något mer än enbart frånvaro av sjukdom. Även andra faktorer så som boendemiljö, arbetsliv, social trygghet och jämlikhet spelar en stor roll.

Epidemiologi är vetenskapen om att studera sjukdomars utbredning i samhället samt riskfaktorer för olika sjukdomar och ohälsa.

Att ha ont i kroppen, eller delar av den, påverkar den drabbade i dennes liv; smärta under en längre period påverkar den drabbade ännu mer. Smärta i det vi kallar rörelseorganen, inbegripet muskler, leder och skelett är en av de vanligaste orsakerna till att vi söker vård i Sverige. I de allra flesta fall är smärtan ospecifik, d.v.s. den beror inte på någon känd bakomliggande orsak. Den vanligaste formen av smärta är smärta i ryggen och då oftast i ländryggen där ca 80% av befolkningen upplever smärta någon gång under sin livstid. Även smärta i nacke och skuldror är mycket vanligt. Både vanliga och mer ovanliga sjukdomar i rörelseorganen ger stor påverkan på vårt samhälle genom hög vårdkonsumtion, stor och relativt dyr läkemedelanvändning och negativ påverkan på arbetsförmågan. Det finns en stark koppling mellan vårdsökande, sjukskrivning och nedsatt produktivitet vilket gör att sjukdomar i rörelseorganen är en av vår tids stora utmaningar för folkhälsan. Prognoser för hur befolkningsutvecklingen kommer att se ut i framtiden tyder på att detta problem kommer att bli allt mer påtagligt framöver.

Sverige har unika resurser gällande registerdata och användningsområdena för dessa data är många. Bland annat utgör de en ovärderlig resurs inom området epidemiologi och då framför allt för longitudinella studier, d.v.s. studier över längre tidsperioder.

Avhandlingen består av fyra delarbeten som på olika sätt använder befintliga nationella och regionala register över vårdkonsumtion och sjukskrivning för att

studera förekomst av sjukdomar i rörelseorganen samt vårdsökarmönster och sjukskrivning hos dessa individer jämfört med hela Skånes befolkning.

I delarbete I studerade jag hur vanligt det är att söka vård för ländryggssmärta och hur den gruppen av patienter ser ut jämfört med befolkningen. Resultaten visade att ca 4% av den vuxna befolkningen i Skåne söker läkarvård varje år pga. ospecifik smärta i ländryggen. Dessa individer konsumerar också mer övrig vård jämfört med den övriga befolkningen, framförallt män i yngre ålder hade dubbelt så många vårdkontakter som män i samma ålder i befolkningen. Vanligt var att söka vård för smärta i andra delar av kroppen.

I delarbete II jämförde jag data från Region Skånes vårddatabaser med en regional vårddatabas som kallas CiPCA (Consultation in Primary Care Archive) i Storbritannien. Syftet var att studera möjligheten att jämföra siffror över förekomst av ospecifika och specifika sjukdomar i rörelseorganen. Resultaten visar att möjligheten att jämföra siffror mellan länder är lättare vid mer specifika diagnoser där diagnosättning kan tänkas mer lika i länderna, medan mer ospecifika symtomdiagnoser är svårare att jämföra då variationer i vårdsystemen påverkar diagnosättning. I framtiden kan en möjlighet vara att använda flera länders datakällor, för att studera vårdsökarmönstret efter olika vårdätgärder, i internationella studier.

I delarbete III studerade jag hur vårdsökarmönstret och sjukskrivningsmönstret ser ut bland individer som diagnostiserats med nackskada (s.k. whiplash), både före och efter skada. Mina resultat visade att gruppen patienter som diagnostiserades med nackskada har en högre vårdkonsumtion både före och efter diagnos jämfört med referensgruppen. Det visade sig också att det fanns ett samband mellan antalet vårdkontakter före och efter nackskada, d.v.s. de individer som hade många vårdkontakter före nackskadan också var de med högst antal kontakter efter. Mina resultat visar att det är viktigt att ta hänsyn till hälsostatus, mätt som vårdkonsumtion, före nackskada i behandling och rehabilitering.

I mitt fjärde delarbete studerade jag om socioekonomisk status, d.v.s. utbildningsnivå, arbetsstatus och inkomst var riskfaktorer för att diagnostiseras med den reumatiska sjukdomsgruppen spondylartrit SpA och kronisk smärta. Mina resultat visade att en låg socioekonomisk status var en riskfaktor för att diagnostiseras med kronisk smärta.

Sammantaget visar mina studier att longitudinella vårddatabaser är en bra datakälla vid epidemiologiska studier av förekomst av sjukdomar i rörelseorganen samt deras påverkan på viktiga samhällsfunktioner. De möjliggör olika typer av studieupplägg och frågeställningar. Mitt avhandling belyser också svårigheter och begränsningar i denna typ av studier.

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