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JUHA TURUNEN

Pain and Pain Management in Finnish General Population

Doctoral dissertation

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ABSTRACT

Pain is a very common symptom worldwide. The range of available treatment options is wide, and especially analgesics are often utilized in pain management. The objective of this study was to investigate the epidemiology of pain and the utilization of different pain management strategies, especially the use of analgesics, in the Finnish general population. The main focus was on chronic, long-lasting pain, which is often a cause of a persistent burden. Apart from assessing the different patterns of treating pain, the general public's information needs related to analgesics and pharmacological pain management were also described.

The research material included data ranging from a cross-sectional postal survey to a random representative sample of people aged 15–74 years and living permanently in Finland. In addition to the survey, the database of Kuopio Medicines Information Centre (KMIC) was retrospectively explored over two years time to gather data on what kind of information needs related to the use of analgesics lay people have. Traditional frequentistic bivariate (*t*-test, X^2-test) and multivariate (logistic regression) analyses were applied. The lower limit of the possibility interval was used when presenting the uncertainty caused by non-respondents. The absolute minimum values (at least -values) are calculated with an assumption that all the non-respondents would be non-cases.

The postal survey yielded a response rate of 71% (n=4542). The point prevalence of any pain was estimated to be 37.3% (at least 26.5%, or higher). The prevalence of any chronic (>3 months) pain was 35.1% (25.3%, or higher) and that of daily or continuous chronic pain was 14.3% (10.6%, or higher). Chronic pain was more common in the older age groups. No sex difference was detected. Poor self-rated health was strongly associated with having chronic pain. The population reported using a wide variety of pain management strategies. The choice of treatment was associated with the location and type of pain. In addition to analgesic usage and physician referrals, physical exercise was also frequently used for treating especially musculoskeletal pains. Overall, 8.5% (6.4%, or higher) reported using any analgesics daily, and 13.6% (9.8%, or higher) a few times a week. Prevalence of such frequent (daily or a few times a week) use of over-the-counter (OTC) analgesics was 8.8% (6.3% or higher). Prevalence of frequent use of prescribed (Rx) analgesics was 8.7 (6.5% or higher). In addition, 4.6% (3.4%, or higher) reported concomitant use of both OTC and Rx analgesics. Utilization of multiple pain management strategies and frequent analgesic use were associated especially with intense and frequent chronic pain.

During the two-year study period, KMIC received 2312 calls related to use of analgesics from lay people. The content and other information of these calls were retrospectively collected from KMIC's database. Altogether 2683 inquiries were categorized and analyzed. A large variety of information needs were observed. The inquiries were most frequently related to drug interactions, dosage, pain management, need for better pain relief, and effects and adverse effects of analgesics. The inquiries often pertained to paracetamol, ibuprofen, coxibs or naproxen. The contents of inquiries differed with regard to the different analgesic substances.

In conclusion, this study showed that chronic pain is a common condition in the Finnish general population. Individuals use multiple measures in attempt to control severe pain. The observed pattern of frequent concomitant use of OTC and Rx analgesics may lead to interactions, overdosage and serious adverse events. Unsupervised daily use of OTC analgesics may delay the proper diagnosis of the actual cause behind the pain. The general public has a need for drug information services that provide counseling related to analgesics and pharmacological pain management.

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Medical Subject Headings: Pharmacoepidemiology; Pain/epidemiology; Prevalence; Pain/therapy; Pain/drug therapy; Chronic Disease; Analgesia; Analgesics/therapeutic use; Drug Information Services; Cross-Sectional Studies; Finland

"We believe that a large epidemiological study about pain in the general population is essential and clearly necessary in every country."

E. Català et al. in European Journal of Pain, 2002

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Kuopio, February 2007

Juha Turunen

ABBREVIATIONS

ASA	Acetylsalicylic acid (Aspirin®)
ATC	Anatomic therapeutic chemical classification*
CI	Confidence interval
CMP	Chronic musculoskeletal pain
CWP	Chronic widepsread pain
DDD	Defined daily dose*
IASP	International Association for the Study of Pain
KMIC	Kuopio Medicines Information Centre
LRA	Logistic regression analysis
MSK	Musculoskeletal
NRS	Numeric rating scale; a pain measurement scale
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
OTC	Over-the-counter; non-prescription drug
PIL	Patient information leaflet; an instruction leaflet in a drug package
PRC	Finnish Population Register Centre
QoL	Quality of life; in this thesis QoL means especially health-related quality of life
Rx	Prescribed; prescription drug
SII	Social Insurance Institution, Kela
SPSS	Statistical Package for Social Sciences; software for statistical analyses
SRH	Self-rated health
VAS	Visual analogue scale; a pain measurement scale

* For details, see the website of WHO Collaborating Centre for Drug Statistics Methodology: http://www.whocc.no/atcddd/atcsystem.html

TERMINOLOGY

Analgesic
A pharmacological substance used for relieving pain; painkiller. In this study, the term 'analgesics' is used to refer to the ATC classes M01 (anti-inflammatory and anti-rheumatic products), M02 (topical products for joint and muscular pain), and N02 (analgesics, including opioids). Low-dose aspirin, specific antirheumatic agents, and anaesthetics are excluded.

Consumption of analgesics
The amount of analgesics sold in a country during a defined time period. Consumption can be measured e.g. as DDDs, money, or packages. Consumption is higher than actual utilization i.e. use of analgesics.

Coxibs
Selective cyclo-oxygenase-2 (COX-2) inhibitors; a group of analgesic drugs targeted especially to the COX-2 enzyme, which mediates inflammation and pain.

Drug
In this study, the term "drug" refers exclusively to legal medications, not to illicit drugs.

Epidemiology
Study of the distribution and determinants of health-related states in specific populations.

Pain
"An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (IASP).

Prevalence
The proportion (%) of a defined population with a defined condition at a designated time.

Utilization i.e. use of analgesics
The occurrence of actual use of analgesics, usually self-reported. Can be measured as the number of tablets taken, a period prevalence, and / or the frequency of use.

LIST OF ORIGINAL PUBLICATIONS

This doctoral thesis is based on the following original publications, which are referred to in the text by their Roman numerals **I–IV**.

I Mäntyselkä P, Turunen J, Ahonen R, Kumpusalo E. Chronic pain and poor self-rated health. JAMA 290: 2435–2442, 2003

II Turunen J, Mäntyselkä P, Kumpusalo E, Ahonen R. How do people ease their pain? A population-based study. J Pain 5: 498–504, 2004

III Turunen J, Mäntyselkä P, Kumpusalo E, Ahonen R. Frequent analgesic use at population level: prevalence and patterns of use. Pain 115: 374–381, 2005

IV Turunen J, Mäntyselkä P, Ojala R, Kröger P, Ahonen R. Public's information needs on analgesics: A descriptive study in a drug information centre. (Submitted for publication)

In addition, this thesis contains previously unpublished data, presented in chapter **7**.

CONTENTS

1 INTRODUCTION

Pain is a very prevalent symptom, and it can turn into a complex chronic disorder. It is one of the major reasons for seeking medical care, and it is often managed pharmacologically. However, there is a lack of comprehensive population-level data on the epidemiology and management of pain in Finland.

In this study, pain and pain management are approached from the general population's perspective. The review of earlier literature regarding the epidemiology of pain, the use of different pain management strategies, and the analgesic utilization patterns focuses on large population-level studies. In addition, different pain definitions, instruments for measuring pain, and the diverse consequences of pain are introduced.

The overall volume of international research literature related to pain is enormous. The methodologies, definitions and perspectives in pain research have developed and changed during the past decades. Hence, except for some classic papers, the literature review presented here has been limited to only relatively recent publications, mainly newer than ten years.

Most minor acute pain episodes are transient, but once an individual develops a chronic, long-lasting pain, the prognosis of the pain is poor and the consequences can be devastating. According to a large multinational telephone survey, approximately 19% of European adults suffer from chronic pain (Breivik et al. 2006). The vast amount of pain patients burdens the health care system. Pain management also comprises a substantial proportion of overall drug expenditure.

The use of analgesics and other potentially pain-relieving pharmacological substances is essential in pain management, both as prescribed by physicians and as self-care. All analgesics can cause serious adverse effects, especially when unintentionally misused. Therefore, it is important to study the different patterns of analgesic utilization, along with the needs for information and the problems related to analgesic use.

The general aim of the present study was to investigate the epidemiology of pain and the use of different pain management strategies in the Finnish general population. Data on the prevalence and epidemiological characteristics of pain can be useful for public decision makers planning the allocation of health care services, preventive programs, or health education campaigns. The selection of available ways to manage pain is wide. This study covers especially the general usage patterns of both prescribed and over-the-counter analgesics, as both are widely utilized and potentially harmful. The needs for information related to analgesics and pharmacological pain management are also described.

REVIEW OF THE LITERATURE

2 PAIN

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" (IASP 2006). In addition, IASP stresses that pain is always a subjective sensation and experience. It is also possible to see pain as a distinct descriptive diagnosis, independent of its cause (Smith et al. 2004a).

The established definitions of pain can be challenged with more philosophical argumentation. It has been suggested that, in many instances the word "pain" should be replaced by "people in pain" (Finer 2006). Finer argues as follows: People can usually point at least roughly the anatomical site(s) where the pain is. This can give the idea that pain is a material object, which has a place in a material space. If the pointed anatomical site is opened surgically, one can not identify something called "the pain". The patient may recover, but there has been no removal of a material object, called "the pain". Therefore, instead of saying "I have a pain there", it should be said "I am in pain and I feel it there".

Clinically, pain can be determined according to its physiological processes. The effects and consequences of pain can be reduced to the functioning of receptors, proteins, and neurotransmitters at the cellular and molecular levels (Holden and Pizzi 2003). Briefly, detection of pain begins with nociceptors that are expressed on primary afferent fibers distributed throughout the body (Dickenson et al. 2005). These afferent fibers transduce stimulus energy into electric signals, known as action potentials, which are conducted along neurones to the spinal cord and brain. The most famous pain theory, the gate control theory introduced by Melzack and Wall (1965), emphasizes the mechanisms in the nervous system that control the perception of noxious stimuli. Peripheral neural signals will increase or decrease the flow of pain impulses to higher processing centres in the central nervous system.

It must be kept in mind that there is no consistent relationship between the intensity of the pain-causing stimulus and the pain that is eventually perceived (Dickenson et al. 2005). In some pain conditions, no organic cause for pain can be found, and the verification of the existence of pain is made solely based on the subjective symptoms reported by the patient (Holden and Pizzi 2003). Regardless of physiological and linguistic definitions, pain is something real. When a patient reports pain, the health care professional's responsibility is to accept and respect that report and to proceed with appropriate assessment and treatment (McCaffery 1999). To better understand the

nature of each individual's pain, various specifying dimensions of pain, such as duration, intensity, localization, and pathophysiology, must be considered.

2.1 Classification of pain

Pain can be categorized in many ways. The temporal approach focuses on the duration and persistence of pain, i.e. how long the pain has lasted, and how frequent the symptoms are. The localization-based approach defines the site or the organ system where the pain is perceived. The biological approach concentrates on the different physiological mechanisms underlying the pain. In addition, the intensity of pain must also be considered. The key points and definitions related to each approach are presented below. However, all these classifications can be combined, e.g. a patient may be said to have a chronic intense benign daily occurring nociceptive pain in the knee.

2.1.1 Temporal characteristics of pain

Acute pain begins suddenly, usually has an obvious cause, and is alleviated relatively quickly. One way to differentiate between acute and chronic pain is to say that chronic pain is "pain that extends beyond the expected period of healing" (Turk and Okifuji 2001). In other words, acute pain remits when the underlying pathology resolves. This definition was originally suggested by Dr. John Bonica in 1950's (IASP 1994). Unfortunately, the duration of the healing process can be ambiguous in many conditions, such as rheumatoid arthritis.

In non-clinical study settings, it is more feasible to use duration-based definitions. The two common, although arbitrary, time markers used to define chronic pain are durations of over three or six months since the initiation of pain (Turk and Okifuji 2001). IASP has stated, without a specific rationale, that "with non-malignant pain, three months is the most convenient point of division between acute and chronic pain, but for research purposes six months will often be preferred" (IASP 1994). The limits of both three months (cf. Elliott et al. 1999, Andersson 2004) and six months (cf. Dunajcik 1999, Eriksen et al. 2003) have been used in epidemiological studies and textbooks.

In addition to duration, the temporal characteristics of pain include the pattern of occurrence of pain symptoms (IASP 1994). For example, pain can be continuous or nearly continuous and recur regularly or irregularly. The concept 'frequency of pain' has been commonly operationalized for different study settings (cf. Mäntyselkä et al. 2001b, Bajwa et al. 2004, Ståhl et al. 2004). Typically, categorizations of pain frequency include classes such as pain once a month or less often, pain less often than

four times a month, pain once a week, pain several times a week / almost daily, daily pain, or constant pain.

2.1.2 Classification of pain according to the site and organ system

Usually, pain complaints are described first in terms of the region and later in terms of the aetiology (IASP 1994). The main sites of pain listed by IASP include, for instance, head, face, and mouth; upper shoulder and upper limbs; thoracic region; abdominal region; low back and lower limbs. In surveys and other self-administered non-clinical study designs, the most convenient way to elicit further information about concurrent pain, in addition to its temporal characteristics, is to ask the people in pain: where do you feel it? This can be done by asking the respondent to mark the site(s) of pain into a drawing of a human body (cf. Hunt et al. 1999, Rustøen et al. 2004b). The presence of pain at pre-defined body sites can also be asked in postal surveys and telephone interviews (cf. Hagen et al. 1997). These methodologies result in definitions such as low back pain, pelvic pain, and headache. However, it must be kept in mind that referred pain can be localized to an area which is different than the actual site of e.g. injury or other noxious stimulus. Classic example of referred pain is pain in the left arm, caused by myocardial infarction.

The localization or origin of pain can be described according to the organ system, as gastrointestinal, genito-urinary, or other pain (IASP 1994). However, this classification may sometimes be very difficult to use in practice. For example, is migraine a disorder of the central nervous system or the vascular system? Therefore, the Headache Classification Committee of the International Headache Society (1988) has outlined definitions for migraine. Very briefly, migraine is a long-lasting headache (4 to 72 hours) that can be pulsating and get worse with activity. Symptoms of migraine include photophobia and phonophobia (sensitivity to light and sound), nausea, and vomiting. Migraine with aura additionally involves a visual aura (vision of spots, stars, lines, flashing lights, zigzag lines, visual loss, and blurry vision) or a sensorimotor aura (symptoms of numbness or tingling).

There are also other general ways to describe the origin of pain. The term ‘visceral pain’ means pain in an internal organ or in its covering (Russo and Brose 1998). Visceral pain can be difficult to localize (Pasero et al. 1999). The concept ‘somatic pain’ means pain which typically arises from joints, muscles, or skin. Both somatic and visceral pain are nociceptive pains (see **2.1.3**).

The division of pain into central pain and peripheral pain refers to the anatomical site of the noxious stimulus (Russo and Brose 1998). All stimulation outside the central

nervous system is referred to as “peripheral”. However, this site-based division is typically used only when talking about neuropathic pain (see **2.1.3**).

The main site of pain can be difficult to determine if the pain is widespread, and the patient has several tender points. Fibromyalgia can be considered a kind of soft tissue rheumatism with chronic widespread pain in joints, muscles, and spine (Geenen and Jacobs 2001). It is sometimes also called “fibromyalgia syndrome”, as the related symptoms include fatigue, morning stiffness, sleep disturbances, anxiety, and irritated bowel. Fibromyalgia pain responds poorly to analgesics. In epidemiological and other research, the most commonly applied definition of fibromyalgia is that by American College of Rheumatology (Wolfe et al. 1990). Very briefly, chronic (>3 months) widespread pain (pain in the axial and in the upper and lower plus left and right body segments) together with pain at 11 or more of 18 specific tender points can be called fibromyalgia. However, the pathogenesis and even the existence of fibromyalgia is still under debate (cf. Gordon 2003).

2.1.3 Classifications according to the pathophysiology of pain

Pain can be divided into two major types according to its pathology: nociceptive pain and neuropathic pain (Russo and Brose 1998, Pasero et al. 1999). Nociceptive pain is a normal reaction to a noxious mechanical, thermal, or chemical stimulus. It is transmitted from peripheral, central, or visceral nociceptors. Neuropathic pain is abnormal pain, initiated by a pathological change in the nervous system itself. Due to this change, the nerve signals the presence of a noxious stimulus, although no such stimulus actually exists.

Inflammation can cause pain. Injuries and irritation can lead to redness, heat, swelling, pain and dysfunction. This inflammation process is mediated by numerous transmitters (cf. Meyer et al. 2006). Inflammation must not be confused with infection, which is caused by an infecting organism. Typically these pathogenic organisms are bacteria, viruses, fungi and parasites. Also inflammation induced by infection can be painful.

Some pain types are named according to the cause of pain, e.g. labour pain, menstrual pain and post-operative pain. Pain caused by cancer or a tumor is called malignant pain, and it is often visceral nociceptive pain. Painful conditions which are not cancer-related are called non-malignant or benign pains.

It has occasionally been suggested that pain may be of psychological origin, i.e. it cannot be explained by examinations, imaging, or laboratory tests. Pain, for which no organic pathology can be found, has also been called idiopathic or psychogenic pain. The utility of such classifications has been questioned (Turk and Okifuji 2001).

2.1.4 Verbal descriptions of different pain types

Most patients can describe their pain verbally. These descriptions, together with information of the pain location, can help to assess whether the pain is of nociceptive or neuropathic origin (Siddall et al. 2000). Nociceptive pain located in musculoskeletal structures is usually characterized as dull, aching, and movement-related, and it is alleviated upon rest. Visceral pain, usually located in the abdominal region, can be described as dull or cramping. Neuropathic pain is usually described as sharp, shooting, burning and electric. See also chapter **2.2.5**.

2.2 Pain intensity scales and other measuring instruments

The most frequently assessed and essential dimension of pain is its intensity (Campbell 2003, Melzack and Katz 2006). As pain is a private internal event, its quantity must be measured through pain patients' own conversion of their subjective experience to a rating on a scale. The most commonly used rating scale types include visual, numeric and verbal scales and picture scales, such as rating scales with faces. Multidimensional pain scales and generic QoL measuring instruments with a pain dimension are also available. The prime examples of each pain-measuring tool type are described in this chapter.

2.2.1 Visual analogue scale

The visual analogue scale (VAS) has been used widely over the past decades in research associated with all types of pain (Chapman and Syrjala 2001, Campbell 2003). It has been shown to be reliable, valid, and internally consistent. The VAS was originally introduced in 1923 for educational purposes. It became more popular in pain research during the 1960s. The VAS consists of a 10–15 cm line labeled with the extremes of pain: no pain and the worst possibly imaginable pain, or similar verbal descriptors (Figure 1). The patient is asked to mark the point on the scale which best represents the intensity of his or her pain. Usually, a line of 10 cm is used, and the result is measured and recorded to the accuracy of one millimetre. The VAS score is sensitive to treatment effects and has qualities of ratio data.

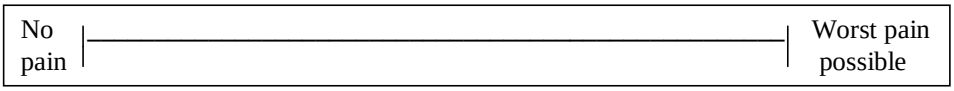

Figure 1. Visual analogue scale (VAS).

2.2.2 Numeric rating scale

The numeric rating scale (NRS) is a convenient way to determine pain intensity (Chapman and Syrjala 2001, Campbell 2003). The scale can include up to 101 points, but an 11-point version is convenient to use and accurate enough. NRS is like VAS, but instead of a line, there is a row of numbers: zero represents no pain and ten (or one hundred) represents the most intense pain possible (Figure 2). The patient is asked to choose the number that best represents his/her pain. Although VAS is used widely, NRS has been found to be equally good for pain assessment (Breivik et al. 2000, Lundeberg et al. 2001).

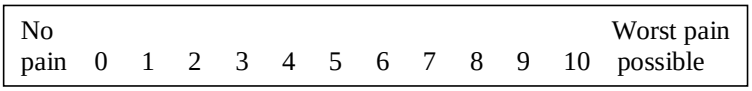

Figure 2. The 11-point numeric rating scale (NRS).

2.2.3 Verbal rating scales

A verbal rating scale (VRS) contains a list of adjectives describing various levels of pain intensity from no pain to the most intense pain possible (Chapman and Syrjala 2001, Campbell 2003). The patient is asked to read through a list of words or phrases and to choose the one that best describes his/her pain intensity (Von Korff et al. 2000). A simple VRS may include only four words: none, mild, moderate or severe pain. A typical seven-category VRS could be: none, weak, mild, moderate, severe, excruciating or unbearable pain. Other applied adjectives include discomforting, distressing and horrible. These qualitative adjectives do not possess any ratio properties and are not suitable for statistical analyses. In addition, patients may interpret the differences between any two adjectives differently. VRS can be combined with NRS, so that each number or some of the numbers on the scale are also described verbally.

2.2.4 Pictorial pain scales

Pictures-based pain intensity scales have been designed for children, illiterate persons, and older people unaccustomed to scaling their experience (Chapman and Syrjala 2001, Campbell 2003). The most frequently used pictorial pain scales use drawings of facial expressions (“smiley faces”) ranging from an appearance of being happy to extreme distress. Photograph-based scales, such as the Oucher scale, have also been developed

and validated for children of different ethnic backgrounds (Beyer et al. 2005). When using pictorial scales, patients are asked to indicate which facial expression best represents their pain experience.

2.2.5 McGill Pain Questionnaire

The McGill Pain Questionnaire (MPQ) has been extensively tested, and it is the simplest and frequently used multidimensional pain scale, which measures several components of pain in one questionnaire (Chapman and Syrjala 2001, Campbell 2003). It consists of 78 words describing pain in sensory, affective, and evaluative terms. Patients are asked to choose the words that best describe their current pain (Melzack and Katz 2006). Some of these words will be chosen with greater frequency than others for certain pain problems. In addition, MPQ includes a six point verbal rating scale for pain intensity. Patients are also asked to mark in drawings of a human body the areas where they feel pain, and whether the pain at each location is external or internal.

MPQ was first introduced in 1975 (Melzack 1975). The history of its development was recently revisited (Melzack 2005). Briefly, Dr. Melzack interviewed pain clinic's patients who described their pains vividly with rich vocabulary. He collected the descriptive words and realized that patients with different pain syndromes used different sets of descriptors, and more intense pains were described with more words. This led eventually, after other projects, such as the development of the gate control theory (Melzack and Wall 1965), and after years of clinical studies, to the publication of MPQ (Melzack 1975). MPQ has been translated into many languages, including Finnish (Ketovuori and Pöntinen 1981). Later, MPQ was considered too long and complex for use in some clinical settings. Thus, a short form of MPQ (SF-MPQ) was also produced (Melzack 1987). SF-MPQ has been applied especially in clinical trials of new therapies.

2.2.6 Examples of other pain measurement instruments

Profile of Chronic Pain: Extended Assessment Battery (PCP:EA) is a newly developed set of instruments to be administered to adults with chronic pain (Ruehlman et al. 2005). PCP:EA is an example of a pain question pattern that aspires to provide detailed and exhaustive information. It consists of 86 items concerning the location, severity and characteristics of pain, medication use, and the psychosocial aspects of adaptation to chronic pain. The validation of PCP:EA is in process.

Older pain measurement questionnaires are briefer. Von Korff's Chronic Pain Grade Questionnaire (CPG or CPQ), also known as the Graded Chronic Pain Scale (GCPS),

grades the severity of chronic pain as a function of pain intensity, and pain-related disability (Von Korff et al. 1992, Von Korff et al. 2000). The questionnaire consists of only seven items. Like CPG, Brief Pain Inventory (BPI) also measures both the intensity of pain and the disability that pain causes for activity, mood, work, sleep, and other functions (Chapman and Syrjala 2001). BPI has been applied especially in studies of cancer pain. Another relatively well known multidimensional instrument is (West Haven-Yale) Multidimensional Pain Inventory ((WHY)MPI), which also measures pain intensity and interference with activities (Kerns et al. 1985). The original version of MPI was recommended especially to be used together with behavioral and psychophysiological assessment instruments in clinical settings when evaluating chronic pain patients.

A variety of very specific measurement instruments for different painful conditions have been developed. For example, the two widely used measures Roland-Morris Low Back Pain Disability Questionnaire (RDQ) and Oswestry Disability Index (ODI) were designed to study disability due to low back pain (Roland and Fairbank 2000). Both instruments can be used in clinical trials as an outcome measure as well as in clinical practice to monitor patients. Both contain a list of claims about back pain and consequences of the pain. Based on the answers, a score or an index describing the disability and physical functioning is calculated.

Condition-specific outcome measures are also available for osteoarthritis and rheumatoid arthritis. The Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) is applicable for studying arthritic conditions in the lower extremities (Brazier et al. 1999, Salaffi et al. 2005). WOMAC is a 24-item questionnaire with three dimensions: pain, stiffness, and physical functioning. The Arthritis Impact Measurement Scales 2 (AIMS2) is a long questionnaire regarding pain related to articular disease, functioning, and QoL (Meenan et al. 1992). A Finnish version of AIMS2 is also available (Arkela-Kautiainen et al. 2003). The modified short-form version of Brief Pain Inventory (m-BPI-sf) has also been applied to repeated measurements of pain in patients with osteoarthritis (Mendoza et al. 2006).

The Migraine Disability Assessment Questionnaire (MIDAS) quantifies headache-related disability (Stewart et al. 2000, Stewart et al. 2001). The first five questions, based on which the MIDAS disability summary score is calculated, concern absences from work and reduced productivity in the household during the past three months. The following two questions inquire about the number of days with headache and the average pain intensity level measured with a version of 11-point NRS. These two additional questions are included in the questionnaire to provide the physician with clinically important information that may help to choose the best treatment.

2.2.7 Pain dimension in instruments measuring quality of life

Quality of life (QoL) instruments usually give a summarized index figure or an illustrative profile of the level of QoL in different areas of life and health. The indexes and profiles are based on series of questions regarding these areas. Pain is one health-related dimension in several generic (i.e. not disease-specific) QoL measuring instruments, such as Nottingham Health Profile, Dartmouth COOP Charts, Health Utilities Index mark III (HUI-3), EQ 5D, and 15D (Coons et al. 2000, Hawthorne et al. 2001). The 15D instrument has been developed in Finland (cf. Sintonen 2001). In addition to the aforementioned instruments, a health survey titled Short Form 36 (SF-36) also pays attention to pain (Brazier et al. 1992). It includes a two-item subscale concerning pain intensity and the interference of pain with normal activities during the past four weeks. This subscale, named the SF-36 Bodily Pain Scale can also be used alone for pain measurement purposes (Von Korff et al. 2000). The advantage of the Bodily Pain Scale is its short length, while its major disadvantage is the lack of assessment of the chronicity or persistence of pain. SF-36, like many other QoL instruments, is also available in Finnish (Hagman 1996).

In general, the pain-specific scales introduced in the preceding chapters are sensitive to changes in pain and therefore useful for health care professionals treating individual pain patients. On the contrary, generic QoL measuring instruments provide data for decision makers and enable comparison of different populations and different health states related to different diseases (Guyatt et al. 1993). If the focus is solely on pain intensity, generic QoL instruments may not adequately reflect small changes in pain status, as pain is only one dimension among others. Typical other dimensions in generic QoL instruments are: physical functioning and mobility, psychosocial functioning, eating, and sleeping.

2.3 Epidemiology of pain

During the past decade, the epidemiological characteristics of pain have been approached from several perspectives. The most commonly studied pain type is chronic pain. In practice, it often means chronic musculoskeletal (MSK) pain. The epidemiology of specific pain types, e.g. migraine and low back pain, has also been studied widely (cf. Andersson 1999, Manzoni and Torelli 2001). In addition, the epidemiology of different pains can be studied in various sub-populations defined by age, sex and race. This thesis focuses on the general adult population. Appendix table 1 introduces the major studies on the epidemiology of non-specific pain in the general

population published in international scientific journals over the past ten years. Studies conducted in primary care or other health care settings were excluded. The content of the table will be discussed throughout this chapter.

Pain states are dynamic, as an individual's pain status may change over time (Von Korff et al. 1990). Figure 3 depicts different possible pain states and pain dynamics in a population. For example, in the follow-up study by Papageorgiou et al. (2002), 44% of the followed up subjects experienced a change of pain status over a seven-year period. However, once chronic pain was established, it was likely to persist or recur. The poor recovery from and prognosis of chronic pain has been recently reported by McBeth et al. 2001, Bergman et al. 2002, Elliot et al. 2002 and Andersson 2004 (see Appendix table 1). Probably the most discouraging results were obtained by Elliott et al. (2002) who calculated the annual recovery rate from chronic pain to be only 5.4%. This can lead to unfortunate consequences, such as those reported by Breivik et al. (2006). Almost 60% of the study subjects with chronic pain had had pain for 2 to 15 years. In addition, 21% had suffered from pain for over 20 years. Rustøen et al. (2004b) reported similar findings from their postal survey. Of the respondents with chronic pain, 65% reported that they had experienced pain for over five years. The mean duration of chronic pain was 13.2 years.

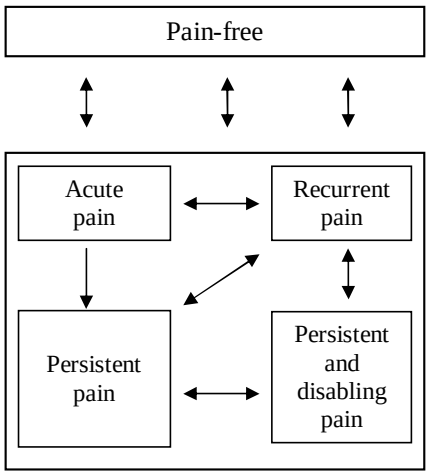

Figure 3. Pain in a dynamic population (Von Korff et al. 1990).

2.3.1 Prevalence of "any pain" and chronic pain in the general population

Epidemiological studies on pain in the general population often report a variety of observations. Many studies have a screening question to identify the subjects with any pain at the moment. For example, Gerdle et al. (2004) reported the overall point prevalence of pain to be 48.9% based on the question "Do you have pain anywhere in the body today?" Experiences of any pain over a longer period can also be inquired. Typically, questions that define a period prevalence of pain inquire about the presence of any pain during the previous week or month or year. For example, Hagen et al. (1997) observed the one-month prevalence of MSK pain to be 60.8%, and Ng et al. (2002) reported that 80.3% of their study subjects had had some pain in the past 12 months. However, the majority of studies focus especially on chronic, long-lasting pain. Compared to minor temporary pain episodes, chronic prolonged pain can be considered much more significant from both individuals' and society's point of view. The huge human and economic burden caused by especially chronic pain is discussed in detail in chapter **2.4**.

Von Korff et al. (1990) stated over 15 years ago that there is no agreement as to how chronic pain should be measured and classified in epidemiologic research. As discussed in chapter **2.1** no consensus has been reached to date. The prevalence of chronic pain has been studied in several countries and populations with a variety of methods and definitions. A widely cited review article by Verhaak et al. (1998) gathered information on studies published from 1984 to 1996 regarding the prevalence of chronic benign pain among adults. Similar studies published since then are included in the Appendix table 1.

The most commonly applied methodologies in the studies reviewed by Verhaak et al. (1998) were postal survey, telephone interview and face-to-face interview. The same methodologies have also been applied during the past ten years (Appendix table 1). The review concluded that the median prevalence of chronic pain was 15%, ranging between 2% and 40%. The differences in the results were assumed to be related to the study settings, the design of questions, and the different definitions of chronic pain.

A variety of chronic pain definitions have also been used in more recent studies. Some research groups have focused on MSK pains, sometimes combined with headache, whereas some studies have included all possible pains. Some studies have especially excluded pains related to cancer. The chosen limits on the duration of chronic pain, usually three or six months, can be specified in many ways. Blyth et al. (2001) inquired about pain experienced every day for three months during the six months prior to the interview. The prevalences were 17% for males and 20% for females. Breivik et al. (2006) were interested in individuals who had been suffering from pain for at least six

months, had experienced pain in the last month, experienced pain at least twice a week and rated their pain intensity when last experienced as 5 or higher on a 10-point rating scale. The study observed the overall prevalence of such pain to be 19%. In contrast, Elliott et al. (1999) kept their procedure simpler and asked about "pain or discomfort that persisted continuously or intermittently for longer than three months". They found an overall prevalence of 46.5%. Later, Smith et al. (2001) utilized the same data and reported prevalences of "significant chronic pain" (12.3% had pain due to which they used painkillers and sought treatment frequently) and "severe chronic pain" (5.7% had pain that had caused marked disability and severe limitations).

The association between the variation in reported prevalences of chronic pain and the limits, definitions, and recall periods is not very clear. Other factors possibly causing variation between studies may be related to differences in the populations and data collection methods. Sampling issues and poor participation rates may further explain part of the discrepancy. As a conclusion of the studies represented in Appendix table 1, and after the exclusion of the few studies with exceptionally high or low prevalence estimates, a clear majority resulted in a 17%–29% overall prevalence of chronic pain.

2.3.2 Prevalence of pain according to sex and age

In epidemiological studies, the distribution of pain is typically presented in multiple groups defined by sex and age. It is often suggested that females report suffering from pain more often than males. Verhaak et al. (1998) found some consensus in the reviewed studies about the characteristics of chronic pain patients: they are relatively often middle-aged females. A majority of the studies presented in Appendix table 1 also report a sex difference in the prevalence of pain: in 18 of the 20 original datasets the studied pain types were more common in females (follow-ups and multiple publications from same data are not included here). The magnitudes of the perceived prevalence differences vary greatly from study to study and depend on the definition of the studied pain type. For example, Buskila et al. (2000) observed a sex difference of 1 percentage point (14% females vs. 13% males) in the prevalence of chronic regional pain and a difference of 11 percentage points (pps) (14% vs. 3%) in chronic widespread pain. Typically, the sex difference in the prevalence of any pain experienced during a given period varied roughly from 12 pps to 17 pps (see studies by Bingefors and Isacson 2004, Bassols et al. 1999 and Català et al. 2002 in Appendix table 1). Comparison and generalization are difficult due to the different time periods and the different definitions used. However, estimated in the same manner, the differences in the prevalence of chronic pain seem to vary from 2.9 pps (Elliott et al. 1999, Blyth et al. 2001)

to 4–7.5 pps (Moulin et al. 2002, Eriksen et al. 2003, Bergman et al. 2001, Ohayon and Schatzberg 2003). Interestingly, exactly the same difference of 2.9 pps was reported by both Elliott et al. 1999 (51.8% vs. 48.9%) and Blyth et al. 2001 (20.0% vs. 17.1%) but the differences in actual prevalences between the studies were huge, presumably mainly due to different definitions of chronic pain. Therefore, comparisons of sex differences in percentages are not very rewarding. However, presenting the differences in relative percentages may also be confusing and misleading. For example, it could be stated that the probability of having chronic pain is 112% higher among females (31.4% vs. 14.8% in Català et al. 2002).

The possible reasons for the apparent general sex differences were recently summarized by Wijnhoven et al. (2006):

1) Females are, more than males, willing to report pain.
2) Females are more exposed to risk factors (e.g. static working postures) for pain.
3) Females are more vulnerable to develop pain, meaning that females react in a different way to risk factors of pain.

Wijnhoven and colleagues utilized the same dataset as Picavet and Schouten (2003), but selected only respondents aged 65 years and younger, as they wanted to study the effects of work status on sex differences in chronic musculoskeletal pain (CMP) in a general population. As reported by Picavet and Schouten, the prevalence of CMP was higher in females. Winjnhoven et al. tried to identify specific explanatory factors for this phenomenon. They concluded that having no work (paid job) partly explains the sex difference in CMP, as less females are working in paid jobs, and not having a paid job is associated with CMP. Females' vulnerability to different risk factors may also explain part of the difference. However, further research was considered warranted, as possible mechanisms of females' vulnerability may be related to hormones and physiology, differences in pain sensitivity, and differences in social and psychological factors. Bingefors and Isacson (2004) concluded that, in addition to biological factors, the sex differences in the prevalence of pain could be related to disparities in work, economy, and social life. In order to avoid oversimplification, we must also keep in mind that not all epidemiological studies have found sex differences in the prevalence of pain. For example, Brattberg et al. (1989), Andersson et al. (1993), and Hunt et al. (1999) observed no significant sex difference. The reason for this could be attributable to differences in the study subjects and the studied pain types; the higher pain frequency among females may be related to only pains at certain body sites.

Another slightly unclear issue is the distribution of pain according to age. In an editorial by Crombie et al. (1994), the age-related findings of epidemiological studies on pain published 1984–1991 were summarized in the following way: Some research

groups have reported that the prevalence of pain increases steadily with age, or that the prevalence is lower in the elderly. Others have shown that the change in prevalence with age depends on the site and the kind of pain investigated.

Indeed, the prevalence of some specific pain types such as myocardial complaints and visceral infection pains are less prevalent among the elderly (Gibson and Helme 2001). Also, the prevalences of headache, back pain, and neck-shoulder pain decrease with age, whereas pains in the arms, hips and legs increase (Picavet and Schouten 2003, Thomas et al. 2004, Bingefors and Isacson 2004). The complicated changes in pain experiences along with aging could be related to biological degeneration or other illnesses.

The review by Verhaak et al. (1998) concluded that the prevalence of chronic pain generally increased with age, with some studies reporting a peak prevalence between the ages of 45 and 65 years. Of the studies described in Appendix table 1, sixteen reported a positive association between increasing age and the prevalence of the studied pain type. These studies usually showed a continuous or even linear increase of especially chronic pain with age (cf. Figure 1 in Moulin et al. 2002 and Table 3 in Eriksen et al. 2003). Some studies reported a peak in prevalence at the approximate age of 55 to 69 years, depending on the selected cut-off points. A decrease following this peak is visible especially among males (cf. Figure 1 in Buskila et al. 2000, Figure 2 in Bergman et al. 2001 and Figure 1 in Blyth et al. 2001). Thus, it must be kept in mind that age and sex cannot be considered as totally independent variables related to pain. Some pains can be more common in younger females and vice versa. For example, younger females report more shoulder pain, but the difference decreases by advancing age (Bingefors and Isacson 2004). In contrast, pain in the extremities increases with age especially among females. Based on a rough estimate, the actual differences in sex-aggregated pain prevalences between the young and older age groups are typically around 15–25 percentage points. For example, Català et al. (2002) reported prevalences of 20.1% (18–29 years) and 41.7% (65 years and older) for any pain during the day preceding the telephone survey. Eriksen et al. (2003) reported 9% (16–24 years) and 29% (67 years and older) prevalences for chronic pain. However, there is also an exception. The study by Bassols et al. (1999) suggested that the prevalence of pain actually decreases slightly but almost linearly with age. The reported prevalences were 80.5% (20–30 years) and 73.6% (71–91 years). The difference was statistically significant even after adjustment for multiple background variables. The authors described the result as “unexpected”, but did not speculate about possible explanations. They asked their subjects about having any pain experience during the past six months. It might be that older people consider small transient pains as a normal part of life and

do not remember or report every minor pain sensation, whereas younger subjects may be more precise.

2.3.3 Distribution and epidemiology of different pain localizations and types

As discussed in chapter **2.1**, pain can be classified in many ways. This chapter presents basic information on the distribution of pain to bodily localizations and the epidemiology of the most common and distinct pain types.

Many epidemiological surveys report the prevalences of pains at different body sites either among all respondents or only among those with pain. Also, the total distributions of respondents' pains according to cause or body site have been reported. Once again, due to these big differences in methodologies and definitions, comparisons are difficult. However, some congruence can be detected in recent studies describing the most common painful body areas.

Rustøen et al. (2004b) displayed visually with a body outline diagram the pain locations of subjects with chronic pain. Of their patients, 52.4% had pain in the low back, 46% in the shoulder area, 40.7% in the neck, and 38.1% in the calf or foot. Bassols et al. (1999) stated that the most common pain locations were back (reported by 50.9%), head (42%) and leg (36.8%). The percentages can not be compared to other studies because it remained unclear whether the proportions had been calculated from all respondents or from those with any pain during the past six months. Bergman et al. (2001) reported the actual prevalences of chronic musculoskeletal pain in the different body regions by sex. Pain in the head was not included. The most common painful regions were the low back (26.4% among females; 19% among males), shoulder or upper arm (23.8%; 15.4%), neck (22.9%; 14.5%) and elbow or hand (21.4%; 11.4%). In the telephone survey by Català et al. (2002), the question regarding the site of pain was an open label. The results were reported as prevalences among the whole study population. Of all the respondents, 22.7% had experienced pain in their legs or feet during the day preceding the interview. Pains in head (20.3%), lower back (11.9%), and higher back (9.7%) were also relatively common. Ng et al. (2002) stated that the most common pain was headache, occurring in 48.6% of all respondents. Other overall prevalences were not reported, only the respondents' reports about the most severe pain type or location. Breivik et al. (2006) reported that the most common localizations of chronic pain were unspecified back (24% of subjects with chronic pain), low back (18%), knee (16%), head (15%), and leg (14%). In the study by Elliott et al. (1999), some respondents reported the actual cause behind the pain, whereas others reported the anatomical site of their symptoms. Of all respondents, 16% reported back pain, 15.8%

had arthritis, and 5.9% had sustained an injury. Based on the results of these different studies, it seems that back pain and headache are generally the most common pains, followed by pains in neck-shoulder area and legs.

The epidemiology of back pain, especially low back pain has been studied very widely. The back between the neck and the lowest rib is rarely the site of pain (Ehrlich 2003). Low back pain poses the most interesting and relevant challenge to the diagnostic and therapeutic skills of health care professionals, as only a minority of the patients presenting with low back pain will be found to have an underlying organic cause. The review by Andersson (1999) concluded that low back pain of at least moderate intensity and duration has an annual incidence of 10%–15% in the adult population and a point prevalence of 15%–30%. The prevalence rises with age up to 65 years, after which it drops for unknown reasons. A recent Canadian study on chronic back pain observed an overall prevalence of 9% in a general population aged 12 years and older (Currie and Wang 2004).

As summarized by Colás et al. (2004), approximately 4%–5% of the Americans and Europeans may suffer from daily or almost daily headache. The lifetime headache prevalence has been estimated to be 93% and the three-month prevalence 70% (Boardman et al. 2003). The prevalences clearly decline with age. Thomas and colleagues (2005) utilized the same data as Boardman et al. to test different hypotheses that could explain this decline. They ruled out several explanations related to e.g. retirement from stressful work and reduced self-reporting of headache. Suggested possible reasons included biochemical changes in the mechanism of pain and pain perception as well as the suggestion that older people may learn to avoid headache and to cope with it more quickly.

Migraine is a specific type of headache. See definitions of different migraine types in chapter **2.1.2**. In their review, Manzoni and Torelli (2001) estimated that the lifetime prevalence of migraine without aura is 6%–10% for males and 15%–26% for females. The corresponding one-year prevalences are 2%–15% and 4%–35%. The prevalence of migraine without aura increases up to about the age of 40 years and then gradually decreases. For migraine with aura, the lifetime prevalence is about 6% and the one-year prevalence 4%. A somewhat newer epidemiological study by Lipton et al. (2002) observed the overall prevalence of any kind of migraine to be 13% (males 6%; females 17.2%).

As summarized by Badcock et al. (2003), pain in the shoulder-neck region is very common with a point prevalence of 7%–34%. They carried out a postal survey and observed that 11.7% of their respondents had shoulder-neck pain.

Pain in legs or in lower extremities in general is a wide and unspecific concept. It can be divided into pains in either the hip or the knee. The prevalence of knee pain has been estimated to be 19% and that of hip pain 9% (Urwin et al. 1998). Pains in the lower extremities are often due to osteoarthritis (Kidd 2006) or rheumatoid arthritis (Roche et al. 2003). The aetiology of these diseases is unknown and, they are associated with inflammation and different pains in very complex ways.

2.3.4 Pain and co-morbidity

Pain is obviously associated with many chronic diseases, such as osteoarthritis, rheumatic diseases, and cancer. Acute infections and injuries can also cause inflammation and pain. In addition, pain has been associated with some other health conditions. The term "co-morbidity" means here the simultaneous presence of pain with one or more other diseases or disorders.

The co-morbidity of pain and depression is evident. The comprehensive review by Fishbain et al. (1997) concluded that depression is more common in chronic pain patients than in healthy controls. More recent studies have confirmed the association between chronic pain and depression (cf. Ohayon and Schatzberg 2003). However, it is difficult to say when pain causes depression and when depression manifests as somatic pain, because both scenarios are possible. Associations between pain and other psychological problems such as panic disorder (McWilliams et al. 2003), insomnia (Wilson et al. 2002, Ohayon 2005), and suicidal ideation (Smith et al. 2004b) have also been found. Pain-related depression can further cause memory problems (Muñoz and Esteve 2005).

Kadam et al. (2005) studied the associations between pain and a variety of symptoms. They found that especially chronic widespread pain independently predicted increased health care consultations due to dermatological, gastrointestinal and genitourinary disorders. The authors suggested as a possible explanation that pain triggers a propensity to seek health care services more frequently for different symptoms. Increased medical visits due to pain also provide physicians with more opportunities to detect and record more health problems. It is further possible that there are shared pathological mechanisms for pain and other symptoms and clinical conditions. Pain might also increase vulnerability to other health problems.

One interesting observation related to pain, morbidity, and mortality was presented by Macfarlane et al. (2001), who found an association between having pain and having an increased risk for dying from cancer after five years. The study was commented on by Crombie (2001), who speculated that pain may sometimes be an early symptom of

undiagnosed cancer. Smith et al. (2003) unsuccessfully attempted to corroborate these observations. The original research group soon published another study exploring the phenomenon in the same cohort, now after nine years of follow-up (McBeth et al. 2003). They still observed an association with widespread pain and subsequent increased incidence of cancer and reduced cancer survival, but the explanation remained unclear.

2.3.5 Factors associated with pain in population level studies

Most epidemiological studies attempt to find statistically significant and biologically or otherwise plausible associations between different possible explanatory factors and the presence of reported pain, especially chronic pain. As the designs of the majority of epidemiological studies on pain are cross-sectional, actual cause-effect relationships can not be proved with complete certainty. Age and sex are typically used as explanatory variables, as they remain unchanged regardless of whether or not the individual has pain. The associations between age, sex and pain were discussed in chapter **2.3.2**. This chapter introduces different sociodemographic factors found to have been statistically significantly associated with self-reported pain.

Rustøen et al. (2004b) found that, after controlling for the effects of other variables in a statistical model, chronic illnesses and low educational level were independently associated with having chronic pain. The reason for this could be that less educated people do not know sufficiently well how to take care of their health, or are not interested in their health. They also often have physically demanding jobs. Educational level is a typical sociodemographic indicator that reflects the individual's socioeconomic status, although the socioeconomic status is difficult both to define and to measure. Eriksen et al. (2003) similarly found an association between chronic pain and low education. They also showed that having a job that requires high physical strain is related to chronic pain. This seems logical and plausible. In addition, they showed that divorced or separated persons have a higher risk for chronic pain.

Besides education, the following socioeconomic factors are associated with having chronic or disabling pain: living in a council-rented house (Elliott et al. 1999), low income and unemployment (Portenoy et al. 2004), living in a socially compromised area, being a low level employee, and being an immigrant in Sweden (Bergman et al. 2001). The possible explanations for why such indicators of lower socioeconomic status are associated with increased reported pain have remained somewhat unclear. Possible related problems could be not having a health insurance or otherwise insufficient access to health care, having a heavy workload, and work dissatisfaction. People with different

ethnic backgrounds may have difficulties adjusting to new environments. Blyth et al. (2001) observed associations of ambiguous direction. In addition to a low educational level, they found that having chronic pain was strongly associated with poor self-rated health. It can be assumed that poor self-rated health is more likely a consequence than a cause of chronic pain. Their models of significantly associated variables included other variables, such as "being unemployed for health reasons", which could be a consequence rather than an antecedent of pain.

A variety of studies on more specific pains in different population groups have been conducted. For example, Chen et al. (2003) showed that severe pain in the lower extremities among elderly females was associated with heavy weight and high body mass index (BMI). The direction of this association is complex. Heavy body weight increases the pressure on the leg joints and muscles and may thereby cause pain. On the other hand, leg pain caused by rheumatoid arthritis, for instance, limits mobility and physical activities such as sports. This may lead to excessive weight gain. Scher et al. (2003) studied factors associated with chronic headache. They found, in line with the results of Eriksen et al. (2003) on chronic pain, that individuals with low educational level and those being divorced, separated, or widowed had an increased risk of chronic daily headache.

In addition to cross-sectional studies, follow-up studies have reported various factors related to the onset and continuity of pain. Andersson (2004) showed that working in bent positions increased the risk of developing a chronic pain, but having a close friend outside the family increased the odds for getting rid of pain problems. Bergman et al. (2002) also reported that personal social support could protect from pain. Interestingly, the habit of drinking alcohol weekly or daily was also found to be inversely associated with development of chronic widespread pain (CWP). The reasons behind this association were briefly discussed by the authors. There is a possible biological mechanism, but confounding is also possible, as those developing pain may have health problems that make them refrain from alcohol. Papageorgiou et al. (2002) analyzed factors that explain the persistence of CWP. The result was that "feeling too tired during the day to do what you want to do" and having a dry mouth or dry eyes were such predictors. Presumably, these are just surrogate measures related to some health conditions or medications. A new pilot case-control study in young adults aged 18–25 years suggested that there is an association between low birth weight and the risk for developing chronic musculoskeletal pain (Mallen et al. 2006).

As a conclusion, low socioeconomic status, indicated by low educational level, seems to be associated with pain. Social support from a spouse or friends may have a protective effect against pain. The evidence and plausibility of the effects of the other

variables described here are sparser. It must be kept in mind that a significant statistical association can be observed even when the association is confounded or otherwise false.

2.3.6 Overview of earlier Finnish studies on pain

A large number of pain-related papers and books have been published in Finland during the past decades. Population-level basic data about the epidemiology of especially musculoskeletal (MSK) symptoms in Finland have been gathered in several health surveys and interviews. The methodologies, study settings, pain types studied, and population groups have varied greatly. Typically, the main focus in the study design and data collection phases has not been on pain. Especially studies with large samples of subjects have included only a few pain-related questions. Typically pain has been measured as periodic prevalences without collecting data on the persistence, frequency, or intensity of pain. This chapter introduces some earlier main findings on pain in Finland.

National Social Insurance Institution (SII) conducted a series of interview surveys in the years 1964, 1968, 1976 and 1987. The results related to the MSK disorders were collated and reported by Sievers et al. (1991). International publications from same data also exist (cf. Sievers and Klaukka 1991). The sample size varied from 17,500 in 1968 to 13,100 in 1987. The participation rate was highest (97%) in 1968 and lowest (85%) in 1987. In the 1964 study, 8.8% of adults reported having a chronic MSK disease. By 1987 this percentage had almost doubled to 17.3%. Back pain was the most common pain type, but soft tissue pain had increased most rapidly through the years. Osteoarthritis was also a common condition. Sievers et al. (1991) postulated that due to the changes in age structure, the prevalence of MSK disorders will continue to increase in Finland. These four surveys were followed by a fifth in 1995–1996. The main findings were reported by Arinen et al. (1998). The prevalence of MSK diseases had indeed increased to about 20%. Pain types other than toothache were not reported. Of the respondents, 25% had had toothache or other dental problems during the past five months.

The North Karelia Project aimed to lower the coronary mortality rates in North Karelia, Finland. During the project, five comparable cross-sectional surveys were conducted every five years from 1972 to 1992 in the North Karelia and Kuopio provinces (Heistaro et al. 1998). The respondents were inquired about the presence of back pain and headache during the preceding month. The one-month prevalence of back pain varied between 46% and 50% in males and 46% to 51% in females. The monograph by Salonen (1984) summarized the headache-related results from 1972 and

1977 surveys. The one-month prevalence of headache was 65% in 1972 and 60% in 1977. The corresponding prevalences of frequent headache were 16% and 11%. The term ‘frequent’ was not defined; the Finnish word used in the questionnaire was “usein”.

During the years 1977–1980, SII conducted a health survey titled “Mini-Finland Health Survey”. A representative sample of 8000 Finns aged 30 and over was drawn and 7217 (90.2%) of them participated. The subjects were interviewed and clinically examined. The study yielded several international publications, many of which were related to different pains and MSK conditions, including low back pain (Heliövaara et al. 1989), fibromyalgia (Mäkelä and Heliövaara 1991), sciatica (Heliövaara et al. 1991), neck pain (Mäkelä et al. 1991), MSK disorders in general (Mäkelä et al. 1993) and shoulder joint impairment (Mäkelä et al. 1999). The main results of these papers combined with previously unpublished data were published in a book by Heliövaara et al. (1993). Briefly, 76.3% of males and 73.3% of females had experienced at least one back pain episode during their life. Almost every tenth reported suffering regularly from back pain. The self-reported one-month periodic prevalence of back pain was 19.4% among males and 23.3% among females. The corresponding figures for neck pain were 26.8% and 34.7% and those for shoulder pain 22.1% and 32.7%, respectively. In addition to self-reporting, different pains were also verified by a clinician, based on his objective observations together with patients’ own reports. Overall, approximately 17% of the participants to the examinations had some back pain and over 10% had neck-shoulder pain. Some impairment of a shoulder joint was observed in 8.8%. The prevalence of fibromyalgia was 0.75%. In general, the prevalence of most pain types was highest at the age of 55–64 years. A kind of continuation of the Mini-Finland study, titled “Health 2000 Health Examination Survey”, was conducted by National Public Health Institute. Similar methodology was applied. The main results were published in a book edited by Aromaa and Koskinen (2002). The participation rate was 87% in home interviews and 79% in clinical examinations. The prevalence of back pain syndrome had decreased to about 11%, but the one-month prevalence of back pain had increased to 25.8% in males and 35.9% in females. Also, the prevalence of neck pain syndrome had decreased to 6%. However, the prevalences of self-reported neck and shoulder pains had increased slightly, especially among older females.

The National Public Health Institute of Finland has conducted annual postal population surveys of health since 1978 in a random sample of 5000 Finns aged 15–64 years. The most recent results from this time-series study titled “Health Behaviour and Health among the Finnish Adult Population” were reported by Helakorpi et al. (2005). The response rate after three reminders was 66%. The response rate has decreased

steadily since 1978, when it was 84%. The questionnaire includes questions about experiences of toothache, back pain and joint pain during the past month. In addition to annual reports, an international paper related to back and joint pains in 1988–1990 was published based on this data (Leino-Arjas et al. 1998). The pooled results from 1988–1990 (respondents aged 20–64 years were included) showed the one-month prevalence of back pain to be 33.5% and that of joint pain 14.7%. In 2005, the overall one-month prevalence of back pain was 33.6% and that of joint pain 20.2% among subjects aged 15–64 years (Helakorpi et al. 2005). The one-month prevalence of toothache was 10% in 2005.

Pain studies have also been conducted in Finnish primary health care. Rekola et al. (1993) carried out a study in six health centres in 1988. They observed that patients with MSK symptoms accounted for 21% of all the patients. Another study on pain in general practice patients was conducted in 1996 (Mäntyselkä 1998). Pain turned out to be a reason for 40% of health centre visits in Finland. Pains were most commonly located in the low back, abdomen and chest (Mäntyselkä et al. 2001b).

The epidemiology of different pains in children has been studied in Finland by Mikkelsson, Salminen, El-Metwally and colleagues. For example, Mikkelsson et al. (1997) studied MSK pain in preadolescents. Pain at least once a week was reported by 32.1%. After one-year follow-up, 30.0% had pain at least once a week. Especially neck pain was persistent. Pain was still prevalent at four-year follow-up (El-Metwally et al. 2004). Mikkelsson et al. (2001) also conducted a study on widespread MSK pain in 11-year-old twin pairs. The prevalence of widespread pain was 9.9%, with no sex difference. It was concluded that environmental family-related factors are more important than genetic factors in the epidemiology of pain. Children's back pain, neck pain and lower limb pain have also been studied (cf. Salminen et al. 1999, Ståhl et al. 2004, El-Metwally et al. 2005).

Many Finnish studies on pain among adolescents have utilized data from the Adolescent Health and Lifestyle Survey of Finland. It is a biennial time series postal survey. Using that data, Vikat et al. (2000) reported that neck-shoulder pain is perceived at least once a week by 15% and low back pain by 8% of adolescents aged 12–18 years. The prevalence of pain in back and neck was higher in the 1990s than in the 1980s and increased steadily from 1993 to 1997 (Hakala et al. 2002).

Some occupation-related pain studies have also been conducted in Finland. Manninen et al. (1996) reported that the one-year prevalence of MSK pain has decreased from 1979 to 1992 among farmers. More recently, the prevalence of different pains was studied among ageing employees of the city of Helsinki (Saastamoinen et al. 2005). A postal survey among 13,374 subjects was conducted in 2000–2002. The response rate

was 67%. Acute pain was reported by 15% of females and 12% of males. Chronic (>3 months) pain was reported by 29% and 24%, and chronic disabling pain by 7% and 5% respectively.

A study on the associations between chronic back pain and depression was conducted in Finland by Kuusinen (2004). He studied 786 consecutive chronic back pain inpatients admitted to multidisciplinary rehabilitation and concluded that chronic pain and depression are not parts of the same psychic problem entity but separate phenomena, although they correlate. The study suggested that the relationship between pain and depression is mediated by perceived life interference.

2.4 Impact of pain

The overall impact of pain at the individual and societal levels is substantial. The effects and consequences of chronic pain can be overwhelming, as pain limits mobility, hobbies, and social interaction and thereby impairs the person's overall QoL. In addition, the monetary costs of health care services and pain medications are considerable. As an extreme example of the extensive impacts of pain, even its effect on car driving performance has been demonstrated. The study by Veldhuijzen et al. (2006) showed that pain patients' driving quality, compared to matched healthy controls, was significantly poorer due to weaving of the vehicle. The diminished driving skills corresponded to a blood alcohol level of 0.8‰. Other more widely studied types of burden and suffering associated with pain are summarized in this chapter.

2.4.1 Pain and limited mobility: impact on everyday life

Especially musculoskeletal pain in the lower extremities and low back can limit mobility and interfere with everyday activities, hobbies and social life. Gradually, due to fear of pain and avoidance of mobility and activities, the initial pain episode may develop into chronic pain syndrome. The history of this fear-avoidance model was summarized in the review by Vlaeyen and Linton (2000). Figure 4 depicts a simplified version of the model. Briefly, confrontation of the fear of pain may lead to a reduction of pain. Avoidance of moving maintains the fear and leads to disability and other consequences of chronic pain. For example, Swinkels-Meewisse et al. (2006) conducted a prospective six-month cohort study of 555 patients with acute low back pain. Fear of movement at the baseline predicted future disability and low participation in work, home activities, sports, and other leisure time and family activities.

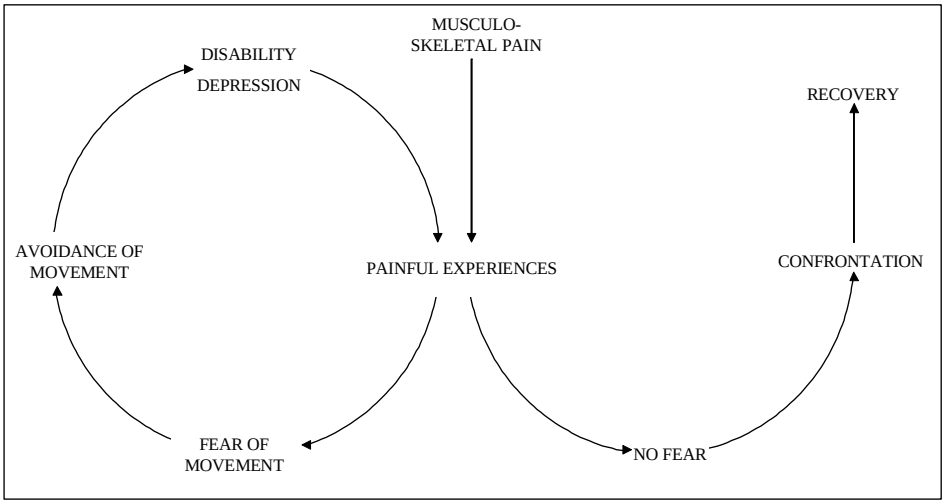

Figure 4. The fear-avoidance model (adapted and modified from Vlaeyen and Linton 2000, Main and Williams 2002).

Indeed, pain combined with fear of movement and mobility limitations affect all aspects of everyday life. The problems and limitations caused by pain have been inquired in several surveys and telephone interview studies in various populations and settings. For example, Strunin and Boden (2004) showed that there were commonly reported limitations related to housework, leisure time, and outdoor activities. In the multinational survey by Breivik et al. (2006), up to 54% of the subjects with chronic pain were less able to do housework. The study illustrates clearly how chronic pain in a majority of the sufferers severely limits their ability to exercise (reported by 73%), walk (47%) and drive a car (47%). Chronic pain also limited their participation in social activities (48%) and the maintenance of an independent lifestyle (30%). In a clinical setting, four out of five patients attending primary care due to pain reported some activity limitations (Mäntyselkä et al. 2001b). Pain hindered work in 25% of cases, hobbies in 16%, and home activities in 13%.

2.4.2 Pain and family dynamics

Pain and the related limitation of mobility may affect all aspects of family life from marital interaction and sexual functioning to parental roles and raising children. Smith and Friedemann (1999) conducted a qualitative study of persons with chronic pain. Pain patients felt excluded from many family activities and often from the family itself, mainly due to their pain-related mobility limitations. Evans et al. (2005) compared mothers with chronic pain to healthy controls. Mothers with pain reported significantly more conflicts in family. Chronic back pain patients interviewed by Strunin and Boden (2004) told that pain limited their ability to take part in raising children and to engage in leisure activities with their spouses. The limitations resulted in restructuring of the family roles, relationships and self-identities, as spouses and children took over the family responsibilities once carried out by the one now in pain. Söderberg et al. (2003) interviewed husbands of females with fibromyalgia pain. They observed similar changes in family dynamics as described above: increasing responsibility and work at home, changing relationship between spouses, changing relationships between friends and relatives, and deepening relationships with the children.

One very serious and multidimensional consequence of pain itself or pain treatment is the change in sexual desire and functioning. According to Ambler et al. (2001), up to 73% of chronic pain patients participating a pain treatment program reported pain-related difficulty with sexual activity. Problems were related to arousal, position, low confidence, performance worries and relationship problems. Kwan et al. (2005) found in their questionnaire survey of patients with non-cancer pain that those with high pain levels had greater sexual dysfunction. In the survey by Breivik et al. (2006), 24% of those with chronic pain reported being less able to have sexual relations, and 19% were no longer able to have any sexual relations. As summarized by Paice (2003), changes in family dynamics may cause a feeling that the pain patient is not contributing to the family. As the patient's self-esteem diminishes, sexual feelings and desirability also diminish. If pain is due to an injury or surgery, it may involve sexual dysfunctioning due to nerve damage. Some medicines used in pain management, such as opioids and tricyclic antidepressants, can also diminish libido.

2.4.3 Pain, quality of life and self-rated health

As discussed in chapter **2.2.7**, a pain dimension is included in several instruments measuring quality of life (QoL). Logically, when an index score instrument is used, overall QoL scores are lower among those with pain because the report of having pain

decreases the pain dimension score and thereby the index score. Häkkinen et al. (2005) applied 15D, which includes a "discomfort" dimension measuring the intensity of pains, aches, and other symptoms (see Sintonen (2001) for the details of 15D). Häkkinen and colleagues showed that the overall 15D score correlates with changes in pain. However, a lower score on the pain dimension is not the only reason to explain the lower QoL scores among people in pain. For example, Becker et al. (1997) applied the SF-36 profile measurement tool to chronic pain patients. Compared to the normal population, pain patients reported lower scores on all dimensions (e.g. social functioning, physical functioning, general health and mental health) of QoL. Dysvik et al. (2004) and Lee et al. (2005) also utilized SF-36 and obtained similar results: all SF-36 subscale scores (i.e. dimensions) of pain patients were lower than those of the local general population. Thus, these studies on pain and QoL confirm the multidimensional impact of pain.

The impact of pain on self-rated health (SRH) has also been studied. Compared to QoL instruments, the measures of SRH are cruder: "In general, would you say your health is Excellent, Very good, Good, Fair or Poor?" (Reyes-Gibby et al. 2002, Perruccio et al. 2005). The response options applied in WHO studies are "Very good, Good, Moderate, Bad, Very bad" (Daniilidou et al. 2004). Reyes-Gibby and colleagues examined the impact of pain on SRH in older adults aged 70 years or more. In a multivariate analysis, those who often had pain were 2.63 times more likely to report poor SRH. The study by Perruccio et al. was longitudinal. They collected data with two surveys and compared changes over two years time. As suggested by Reyes-Gibby et al., pain really predicted poor SRH. Worsening pain explained the changes in SRH. A portion of this effect of worsening SRH was mediated by the development of activity limitations.

2.4.4 Impact of pain on primary health care

In a Swedish study, 28% of the patients treated at a primary care practice had a medically defined pain problem (Hasselström et al. 2002). According to a collaborative study in 14 countries, 21.5% of primary care patients reported persistent pain for a period of 6 months or more during the previous year (Gureje et al. 1998). Among hospitalized patients in Italy, the 24-hour prevalence of pain has been shown to be up to 56.6% and point prevalence 43.1% (Costantini et al. 2002). Of course, especially individuals with the most serious pains usually seek health care services. According to the study of individuals with chronic pain by Blyth et al. (2004), there is a strong association between more severe pain-related disability and greater use of services. Eriksen et al. (2004) reported similar results: considerably more frequent use of both

primary and secondary health care services was observed among those with chronic pain. Andersson et al. (1999b) followed diagnoses in a primary health care registry. They observed that an increasing number of people with pain-related diagnoses are seeking primary care services. The increase was mainly due to an increased number of individuals with headaches and pains in soft tissues. It remained unclear whether this is due to an increase in morbidity or changes in care-seeking behavior. As a conclusion, pain is a very prevalent and possibly even increasing complaint in health care.

2.4.5 Economic impact of pain

In addition to the burden on the health-care system, pain has many other economic consequences. Pain patients, insurance companies, tax payers, and national social insurance systems spend huge amounts of money on analgesics. Sick leaves due to pain impair productivity. It is very challenging to do solid and comprehensive studies on all possible costs of all possible pains. Therefore, most studies focus on the costs of some specific pain type or on some specific economic consequence of pain. This chapter introduces some examples of the relatively scarce literature on the economic impacts of pain. The use of different currencies, changes in the value of money, and variations in the size of study populations make it difficult to draw conclusions or to compare studies conducted at different times in different countries.

Mäntyselkä et al. (2002) estimated that the mean costs of the investigations, therapies, referrals, and sick leaves related to one MSK pain patient's single visit in primary health care were around 530 euros per visit in 1996. On an average, follow-up visits were more costly than primary visits. The costs per visit decreased when pain became chronic, as most examinations and treatment options had already been tried out by then.

A new review tried to gather information on the costs of chronic pain (Phillips 2006). Exact figures, regarding chronic pain in general, were missing due to lack of appropriate studies. Thus, Phillips contented himself with a statement that the impact of pain on economies is enormous. He emphasized that the direct costs (drugs, health care visits, travel costs) are minor when comparing to the indirect economic consequences, such as productivity losses, caused by pain.

Meerding et al. (1998) compared the healthcare costs of different illnesses. Pain was not considered an independent diagnosis, but MSK diseases in general were the second most costly condition after mental retardation in The Netherlands. Another Dutch research group has published cost-of-illness studies of back pain (van Tulder et al. 1995) and neck pain (Borghouts et al. 1999). They estimated that the direct medical costs of back pain, particularly the costs of hospital care, general practice care, specialist

care, and paramedical care in the year 1991 were 368 million U.S. dollars ($). The total costs of absenteeism due to back pain were $3.1 billion and disability pensions accounted for $1.3 billion. The total costs of neck pain were estimated to be $686 million. Direct non-medical costs, such as travel and time expenses, were not included in these figures.

A cost-of-illness study of back pain was conducted also in UK (Maniadakis and Gray 2000). They estimated the direct healthcare costs of back pain in 1998 to be £1632 million. This figure included both prescribed and OTC analgesics. The costs of informal care by family members, and the related production losses totalled £10 668 million. Sleed et al. (2005) conducted a preliminary cost-of-illness study of adolescent chronic pain in UK. They sent a self-report retrospective questionnaire to 52 families of adolescents with chronic pain. The mean cost per adolescent with chronic pain was £8000 per year.

A recent review by Parthan et al. (2006) summarized the research on the economic burden of chronic low back pain in the USA. They concluded that annual healthcare costs due to back pain patients were at least $17.7 billion dollars. Stewart et al. (2003) conducted a large telephone survey to estimate the amount of lost productive time and costs due to any pain in the USA. Of the total active workforce, 13% had experienced loss of productive time during the two-week study period due to pain. Among pain sufferers, the mean lost productive time was 4.6 hours per week. Three fourths of the lost productive time was explained by reduced performance at work, not absence. The cost of the reported loss among all active workers was estimated to be $61.2 billion per year. Similar research was conducted in Australia by van Leeuwen et al. (2006), who studied the impact of chronic pain on absenteeism and the effectiveness of work. They estimated that 9.9 million workdays are lost annually due to chronic pain. In addition, due to reduced effectiveness, an equivalent of up to 36.5 million workdays is lost. Together, these equate a total cost of 6.5 billion Australian dollars annually.

All these huge figures expressed in different currencies and measured with different methodologies can be confounding. However, also the individual-level financial losses and tragedies behind the high figures must be kept in mind. Walker et al. (2006) conducted a qualitative interview study of 20 chronic pain patients and described how chronic pain can create a series of stressful economic life situations. All the participants of working age had lost their jobs after one long or several short periods of sick leave. This caused many of them to speak of having “lost everything”. The sense of loss was exacerbated by a lack of understanding or sympathy on the part of employers. The interviewees described their descent into poverty and social marginalization. They had sold their houses and were using second-hand clothes and furniture. In addition, one of

them was even unable to afford his prescribed analgesics. Such events can lead to despair, hopelessness, and mental problems such as depression. Thus, economic consequences can make the prognosis of pain even worse.

2.4.6 Pain and human suffering

Based on the preceding paragraphs, it is obvious that pain causes human tragedies of many kinds. Qualitative and descriptive studies of pain patients' experiences and perceptions give us a chance to hear the individuals behind p-values, odds ratios, dollars, pounds, and euros. Chapman and Gavrin (1999) published a brief review of suffering and the role of pain in it. According to them, the concepts of pain and suffering are frequently mixed, confused and used synonymously. However, pain and suffering are distinct phenomena. Suffering is a broader condition that includes more dimensions than pain. Suffering has many potential causes, of which pain is only one. A serious disruption of human life, such as the onset of uncontrollable pain, can cause suffering. When pain patients are asked to tell their life story, those who suffer tend to express discontinuity and breakdown in their personal narrative.

Carson and Mitchell (1998) used open-ended questions to collect pain patients' narratives in a descriptive exploratory interview study. The 17 participants had been living with persistent pain for at least six months. Twelve of them lived in a long-term care setting in a hospital. All the participants told about how pain changed their lives. They described the difficulties of living with terrible and relentless pain. The pain was described as a screwdriver, a cloud, and a destroyer. Living with pain was said to be nerve-racking and frustrating. The participants emphasized that, despite of medications, non-medical therapies, and time with a caring family, the pain never went away completely. All participants said they hoped for relief from pain, even if just for brief moments.

Paulson et al. (2002) conducted narrative interviews with 14 Swedish males with fibromyalgia. The authors constructed the following themes from their analysis of the interviews: fear of being considered a whiner, feeling like a guinea pig, feeling hopeful yet neglected, and having no prospects of recovery. Briefly, the subjects first endured a lot of pain before they sought health care. Sometimes the wife persuaded her husband to contact the health centre due to his troublesome pain. The feelings regarding treatments were ambiguous because the subjects wanted a thorough examination on the other hand, while on the other hand they simultaneously felt themselves exposed to numerous treatments like guinea pigs. The subjects were hopeful about being cured, but they also

felt neglected. All of them felt enormously alone with their pain. Time after time they received prescriptions without having a proper conversation with the physician.

Miles et al. (2005) interviewed 29 chronic pain sufferers at an outpatient pain clinic. Pain imposed several constraints on the subjects. Pain affected even their ability to do simple things like reaching out for something, because activities often resulted in pain flare-ups. However, some subjects focused their coping efforts on maintaining their pre-pain activities despite increased pain. As a conclusion, pain poses fundamental challenges to people's everyday reality by altering some taken-for-granted aspects of their lives. Such disruptive changes as the onset of severe pain can lead to stress, disability and suffering. As Chapman and Gavrin (1999) pointed out, physicians should make every effort to prevent pain and to relieve pain promptly and effectively when it does occur.

3 REACTING TO AND MANAGING PAIN

3.1 Process model of reacting to pain

An individual feeling pain must choose a course of action. Figure 5 presents a simplified process model of some possible scenarios after the detection of pain. The dashed arrows represent the individual's personal decisions to return back to the stage of choosing the course of action, after possibly unsatisfactory experiences.

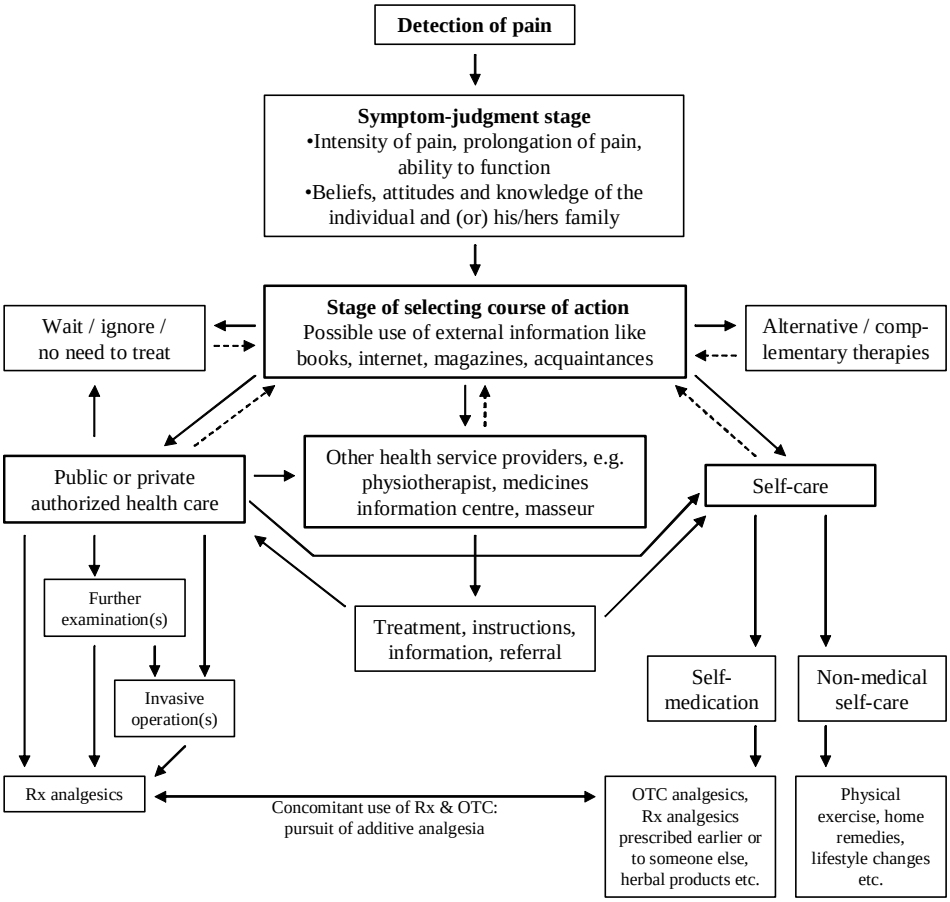

Figure 5. General model of reacting to and managing pain symptoms.
Compiled, adapted and constructed from Lilja (1988), Kokko (1988) and Sihvo (2000).

This process chart describes many different ways of reacting to pain. A vast selection of different pain management strategies are needed, as people with pain are not a homogenous group. Standardized “one size fits all” treatments cannot be applied (Brown 2004).

3.2 Iceberg model of pain management strategies

The selection and use of different pain management strategies can be visualized as an “iceberg”. The old metaphor of an iceberg has been often used to describe the proportion of illnesses that reach medical attention (Last 1963). The tip of the iceberg represents the disease cases or symptoms due to which patients contact a physician. The actions taken due to a symptom, e.g. pain, can also be categorized and illustrated as an iceberg. For example, a ranking of “no referral”, “informal or lay referral” and “formal or professional referral” has been used when studying the reactions to different symptoms at the population level (Hannay 1980). The concept of “lay referral” includes referrals to a relative, friend, or acquaintance, which do not primarily involve a professional role. Figure 6 depicts an iceberg of pain management strategies. The tip of the iceberg above the waterline represents the people referred to professional health care. Under the waterline lie the cases which are “invisible” to health care professionals. The grey zone around the waterline includes people utilising interventions which are not widely taught in Western medical schools. It is difficult to draw a straight line between lay and professional referrals, since some intervention providers can be considered as laypeople. Therefore, the waterline is wavering in the grey zone.

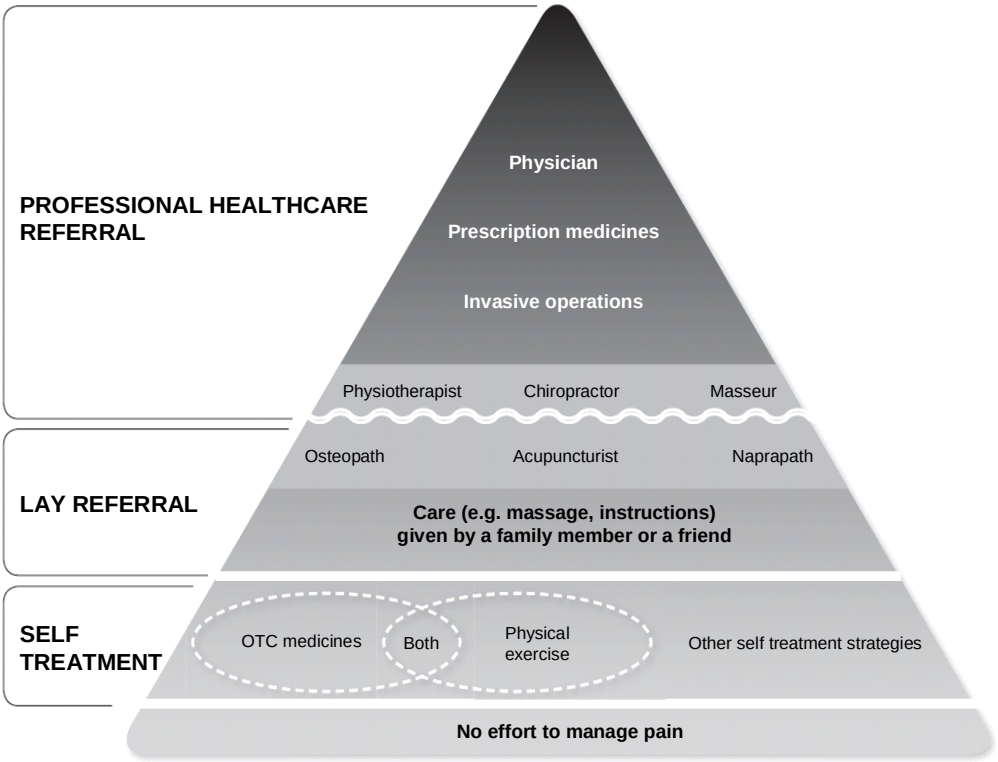

Figure 6. Iceberg model of pain management strategies.

The iceberg illustrates only some examples of the possible ways to manage pain. In real life, the selection of existing methods used to treat pain is large, as described in the next chapter.

3.3 Overview of the use of different pain management strategies

Bassols et al. (2002) surveyed the pain management strategies of the general Spanish population. They utilized the same data, collected in 1994, as in their paper on the epidemiology of pain (Bassols et al. 1999, see Appendix table 1). Of those with pain, 66.3% had visited a physician due to it. Self-medication (27.6%), complementary therapies (20.5%), and physical therapy (13.8%) were also commonly used. Physicians prescribed often analgesics, mainly paracetamol and diclofenac. Physiotherapy and surgery were also utilized. Self-medication consisted of ASA and paracetamol, whereas complementary therapies included herbal medicines, massage, heat, acupuncture, folk remedies, and homeopathy. On an average, people with pain had used 1.4 strategies. The authors did not report how long the time was about which the utilization of different therapeutic strategies was inquired.

The study by Blyth et al. (2005) reported the population's self-management strategies. They focused especially on how people treat their chronic pains without consulting health professionals. Telephone interviews reached 474 adults with chronic (>3 months) pain. Taking medication (47%), resting (31.5%), exercising (25.8%), using hot/cold packs (23.4%), and massage (18.0%) were reported most often. Less frequently reported ways to manage pain included relaxation techniques, meditation and chiropractic treatment. On an average, people reported the use of 2.0 strategies.

Andersson et al. (1999a) studied how chronic pain is treated in the general population. In addition to self-care, they also paid attention to health care seeking and medication by utilizing older research data (cf. Andersson et al. 1993). Of those with chronic pain, 45.7% had consulted a physician and 7.2% a physiotherapist during the preceding three months. Alternative therapies, such as chiropractic, acupuncture, homeopathy, and zone therapy had been used by altogether 5.9%. At least one self-care method, excluding self-medication, had been used by 58.2%. The most common steps to alleviate pain were heat (34%), rest (32%), and physical exercise (21%). One per cent had increased their alcohol and tobacco consumption for pain relief. Analgesics were used by 62.4% within the past two weeks. The authors also reported an obvious overlap between use of conventional and alternative care

Haetzman et al. (2003) studied the consultation habits and medicine choices of chronic pain patients. Of the 840 participating chronic pain patients, 67% had visited a general practitioner, 34% a hospital specialist, 26% a physical therapist, and 18% an alternative therapist during the preceding year. Rx medicines had been taken by 58%, OTCs by 57%, and alternative medicines by 16%. Alternative treatments had typically been used in addition to conventional health care.

Barry et al. (2004) studied how older (65–90 years old) persons cope with chronic pain. They asked 245 participants with non-cancer chronic pain the following question in a telephone interview: “Please tell me about all of the various methods you have used to cope or deal with your pain?” and after each response prompted: “Do you use any other methods to cope with pain?”. During the previous month, the most commonly used coping strategies included the use of analgesics (78%), exercise (35%), cognitive behavioral methods (27%), religious activities (21%), activity restriction (20%), and hot or cold modalities (15%). The use of two strategies was reported by 29%, and 52% had used three or more coping strategies in the past month. As a general conclusion based on all the studies reviewed in this chapter, the use of several very different pain management strategies, often concomitantly and overlapping with each other, is common.

3.4 Different ways to categorize pain management strategies

The above listed methods to treat pain can be classified in many ways. The iceberg model categorizes pain management strategies according to the different levels of referral. Andersson et al. (1999a) divided the reported strategies into conventional medicine, alternative care, and self-care. Medications were divided into Rx analgesics, OTC analgesics, herbal remedies, and ointments. Blyth et al. (2005) categorized self-management strategies into active and passive behavioral methods, cognitive methods, and conventional medicine. Bassols et al. (2002) applied such classifications as self-medication, complementary medicine, and physical therapy. These categorizations are partly overlapping and often imprecisely defined. For example, exercise has been variably included in the categories of active behavioral self-management (Blyth et al.), physical therapy (Bassols et al.), and self-care (Andersson et al.). Acupuncture has been regarded as passive conventional medicine (Blyth et al.), complementary medicine (Bassols et al.), and alternative care (Andersson et al.). Massage has been labeled as either passive behavioral strategy (Blyth et al.) or complementary medicine (Bassols et al.).

A relatively unambiguous way to classify the ways to manage pain to divide pain management into pharmacological and non-pharmacological strategies. The selection of different non-pharmacological pain treatments, appliances, exercise programs, and therapies available to patients is immense. The levels of evidence on the effectiveness of such pain management modalities vary greatly. The attitudes of health care professionals similarly do vary. Berman and Bausell (2000) sent a postal survey to a random sample of the physician members of the IASP. Of the respondents, 80% or

more considered treatments like psychotherapy, exercise, transcutaneous electrical nerve stimulation (TENS), behavioral medicine, and acupuncture to be part of the legitimate medical practice. On the other hand, less than one third considered aromatherapy, art therapy, Tai Chi, or prayers to be legitimate. Other examples of non-pharmacological ways to treat pain include surgery, hot and cold treatments, spinal cord stimulators, meditation, and hypnosis (cf. Ashburn and Staats 1999, Vallerand 2003, Cuellar 2005, Turk and McCarberg 2005).

The focus of this study is on pharmacological pain management, especially analgesics. The following chapter presents an overview of analgesic consumption and usage mainly at the population level.

4 PHARMACOLOGICAL PAIN MANAGEMENT

Pharmacological treatment of pain has its origins in herbal medicine. As summarized in the review by Borsook (2003), the first NSAIDs were refined from salicylic acid present in willow, whereas the opium of poppies is the predecessor of opioids. Today, different synthetic drugs are important tools in pain management. According to a study conducted in Finnish health centres, 67.3% of pain patients received a prescription (Mäntyselkä et al. 2001a). The most commonly prescribed drugs were NSAID preparations, such as ibuprofen, naproxen, topical piroxicam, diclofenac, and ketoprofen. Paracetamol, opioids, muscle relaxants, and antidepressants were also prescribed for pain. The review by Fishbain (2000) summarized the current, relatively consistent evidence on the analgesic effects of different antidepressants in various pain conditions. In addition, some anti-epileptic drugs such as gabapentin can be prescribed for neuropathic pain (Borsook 2003). The antiviral drugs acyclovir and valacyclovir can be used for the alleviation of very painful postherpetic neuralgia, which is a complication of herpes zoster infection (Quan et al. 2006). Anti-microbial drugs can alleviate the pain induced by acute infections.

Self-medication of pain is usually done with OTC analgesics; in Finland, these include NSAIDs and paracetamol (National Agency for Medicines and Social Insurance Institution 2006). The selection and availability of OTC analgesics as well as their utilization patterns vary between countries. Despite the advances in medical technology, alternative medicines, such as herbs and homeopathic products, are also still utilized by Western people to manage pain (cf. Eisenberg et al. 1998, Haetzman et al. 2003).

Although a variety of different pharmacological entities, including muscle relaxants, anti-epileptics, antidepressants, antibiotics, and herbal and homeopathic products, can be used for pain relief, the focus of this thesis is on conventional analgesics, as defined in Terminology. This chapter introduces the key issues and observations of statistics, population surveys, and other epidemiological studies regarding the use analgesics in Finland and other Western societies.

4.1 Consumption of analgesics in Finland

The consumption of analgesics, mainly NSAIDs, has been increasing in Finland for decades. Ahonen et al. (1991a) reported that the total consumption of all analgesics increased by 34% in 10 years since 1978, being slightly over 60 DDDs in 1988. In 2005 the corresponding figure was way over 100 DDDs (National Agency for Medicines and Social Insurance Institution 2006). Thus, theoretically, more than every tenth Finn uses one DDD of some analgesic every single day. In real life, analgesic use, especially the use of OTCs, is often sporadic, and daily intake can be lower than the DDD. Therefore, the proportion of people using analgesic at least occasionally is higher than 10%. Actually, over 17% of Finns annually received reimbursement for prescribed NSAIDs during the years 1997–2000 (Helin-Salmivaara et al. 2003). Due to recent changes in the social insurance system, even small and cheap prescribed packages are now reimbursable. Official statistics have not been published yet, but the proportion of Finnish people receiving reimbursement for NSAIDs and other analgesics has increased remarkably during the past year. In 2006, exactly 1,323,665 Finns (over 25% of the whole population) received reimbursement for analgesics at least once (Jaana Martikainen / Social Insurance Institution of Finland, personal communication on February 15th 2007). Majority (78.6%) of those receiving reimbursement, purchased only NSAIDs (ATC code M01A in SII's registry). Other reimbursable analgesics (ATC N02) were purchased by 10.2%. In addition, 11.2% purchased both NSAIDs and other analgesics in 2006. These figures do not include the sales of OTC analgesics.

Figure 7 shows the current distribution of OTC and Rx analgesics sales between different drugs and drug groups in Finland, measured in DDDs. Ibuprofen is evidently the best-selling analgesic drug. Slightly over half of all ibuprofen is sold over-the-counter. Paracetamol is also prescribed relatively commonly. Opioid sales consist mainly of tramadol, and codeine in combination with paracetamol. The group of other Rx NSAIDs includes diclofenac, naproxen, meloxicam and piroxicam. The market share of coxibs is constantly changing due to marketing withdrawals.

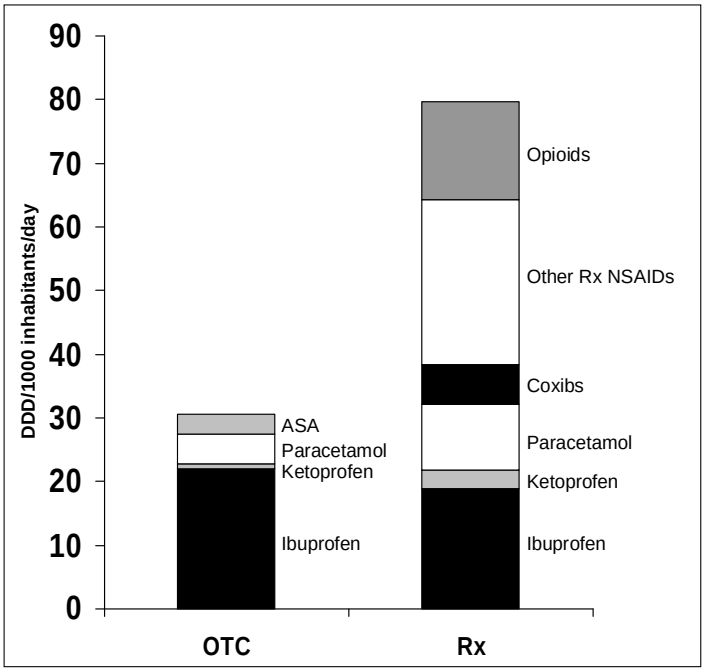

Figure 7. Sales of over-the-counter (OTC) and prescribed (Rx) analgesics in Finland in 2005. Gathered and calculated from Finnish Statistics on Medicines (National Agency for Medicines and Social Insurance Institution 2006).

Figure 8 displays a comparison of analgesic sales in the Nordic countries. The overall consumption of analgesics is the second lowest in Finland. The biggest difference can be seen in the consumption of paracetamol, which is used frequently in the other Nordic countries. Instead, mainly NSAIDs are consumed in Finland.

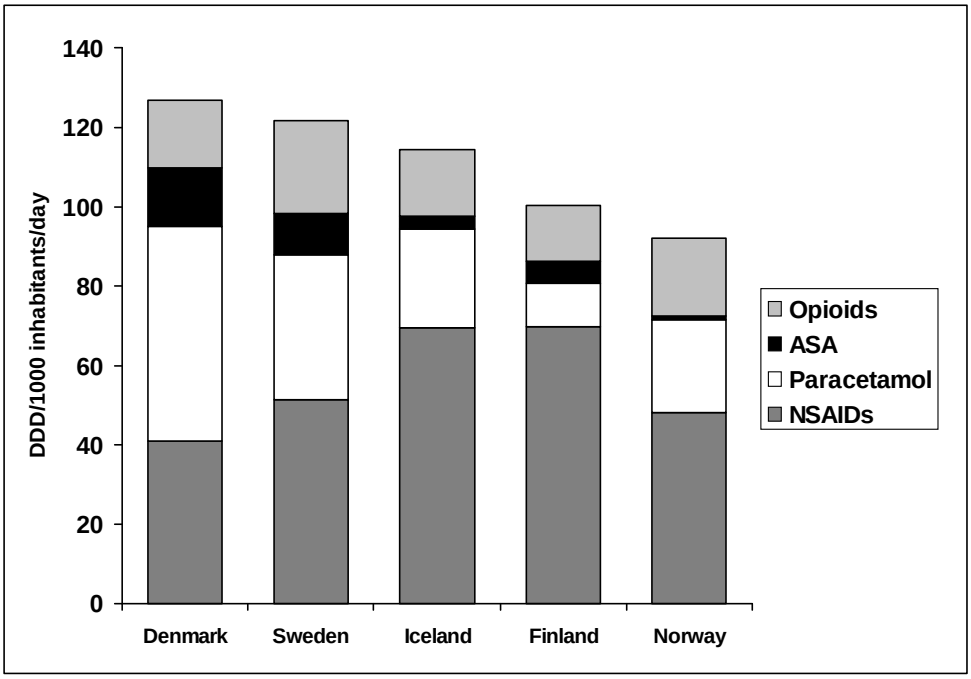

Figure 8. Sales of different analgesic groups in the Nordic countries in 2003. Gathered from Medicines Consumption in the Nordic Countries 1999–2003 (NOMESCO 2004).

Finnish Statistics on Medicines 2005 displays the changes in the consumption of different analgesics during the past 16 years (National Agency for Medicines and Social Insurance Institution 2006, pages 294–297). In addition to the steady increase of ibuprofen consumption, the use of paracetamol has also increased in Finland recently. There is a parallel increasing trend in the use of opioids. ASA is nowadays rarely utilized for pain management. Coxibs were quickly adopted as standard Rx NSAIDs for wide patient groups (Helin-Salmivaara et al. 2005a), but the sales dropped after withdrawals due to adverse events (Klaukka et al. 2005). This has increased the prescribing of ibuprofen.

4.1.1 Examples of registry studies on analgesic consumption

Helin-Salmivaara et al. (2003) explored the Finnish national prescription database to describe the epidemiology and intensity of NSAID consumption. “Low use” of analgesics was defined as purchased prescriptions for 30 or less DDDs per year and

"moderate" between 31 and 181 DDDs. "Heavy use" of NSAIDs was defined as over 181 DDDs of analgesics purchased during a year. In the year 2000 the prevalences of low, moderate and heavy use were 7.6%, 8.0% and 1.5% respectively. Females consumed more NSAIDs than males did. The prevalence of NSAID consumption increased with age. As the study covered only reimbursable Rx NSAIDs, the actual proportion of analgesic users is higher in reality. Clinical or other reasons for the consumption of NSAIDs could not be elicited from the registry. The consumption of opioids or paracetamol was not studied.

Leufkens et al. (1990) studied Rx NSAID consumption (excluding salicylates) in The Netherlands in 1987. They utilized computerized pharmacy records to identify different consumption patterns and to characterize the patients consuming Rx NSAIDs. Those receiving NSAID prescription(s) for 1–30 days during one year were categorized as "incidental users", whereas "regular users" had prescription(s) for 31–210 days, and "heavy users" for more than 210 days. The numbers of days illustrate possible exposure times and the theoretical use of NSAIDs. A total of 8.6% of the general study population had "used" one or more NSAIDs in 1987. Consumption was more common among females and the older age groups. The median number of prescriptions per patients was two. Of the users, 74% were incidental, 21.2% were regular and 4.8% were heavy users.

One limitation of database studies on the consumption of analgesics, such as described above, is the lack of information on the actual utilization of the analgesics. Even though most consumption studies report "analgesic use", it remains unknown whether the individual who purchased the analgesics from the pharmacy, actually used them. Therefore information on the actual analgesic utilization habits is collected also directly from people themselves.

4.2 Utilization of analgesics and factors associated with it

In addition to sales statistics, insurance registries and pharmacy registries, information on analgesic consumption and utilization can be gathered by conducting surveys and interviews. Methods and definitions related to the occurrence, periodic prevalence, frequency, and intensity of analgesic use vary from study to study. There are also differences in the availability of relevant background information on possible explanatory factors for the use of analgesics. Thus, it is difficult to summarize the results or to draw definite conclusions. This chapter introduces the key results of different studies in response to the questions of how common analgesic use is, which factors are associated with analgesic use, and what are the characteristics of users.

4.2.1 Major surveys on analgesic use

Results from cross-sectional studies on the use of analgesics especially in the Nordic countries have been published during the past two decades. The methodological limitations of these studies are discussed in the introduction of paper **III**. Briefly, data is usually derived from some big health survey, which has included some question(s) related to the use of analgesics. Both the frequency and the intensity of analgesic use and the characteristics of related pain are typically measured inadequately. Instead, the use of analgesics is often measured as periodic prevalence. The pain-related background information has often also been scarce.

Ahonen et al. (1991b) reported results on analgesic use from a large survey conducted in 1979, concerning farmers' occupational health (n=12,056). The use of Rx analgesics was determined by asking which medicines were currently in use. The use of OTCs over the past 7 days for headache, pains in joints, or other pains was inquired. Of the responders, 11% (8.7% of males, 13.2% of females) had used at least one Rx analgesic. Use of OTC analgesics was reported by 20.8% (18% males, 25% females). The proportion of analgesic users was higher among the older age groups. The use of Rx analgesics was associated especially with painful conditions and chronic morbidity.

Ahonen et al. (1993) also studied changes in analgesic use between the years 1976 and 1987 in Finland, based on data from two health interviews by National Social Insurance Institution (see chapter **2.3.6**). The use of OTC analgesics was determined as the use of drugs for headache or other pains during the two days prior to the interview. The overall prevalence of any analgesic use was 17.2% in 1976 and 23.3% in 1987. The rates were higher among females. The best predictors of Rx analgesic use were the occurrence of pain, chronic morbidity, and psychoneurotic symptoms.

In the health survey conducted in Norway in 1986/87, representatives of the general population aged 12 to 56 years were asked about the use of analgesics during the preceding 14 days (Eggen 1993). On an average, 28% of females and 13% of males had used analgesics. Menstrual pain explained part of the sex difference. The most significant factors having an impact on analgesic use were headache, infections, back ache, and neck ache.

Antonov and Isacson (1996) utilized data from the Swedish survey of living conditions conducted in 1988/89. Of the respondents, 35% had used analgesics at least once during the preceding two weeks. Six per cent reported regular analgesic use. The term "regular" was not operationalized. "Any analgesic use" was higher among females. Use of analgesics increased with age. The existence of pains in various locations was assessed, but the frequency or chronicity of pain was not determined. Poor self-rated

health, headache or migraine, and pains in shoulders, back, and joints were all independently associated with the use of analgesics. The same authors published another paper from the same data, reporting the use of Rx and OTC analgesics separately (Antonov and Isacson 1998). Rx analgesics had been used by 12.2% of females and 7.2% of males over the past two weeks. The corresponding figures for OTC analgesics were 30.4% and 20.0%.

Isacson and Bingefors (2002) utilized data from a health survey carried out in Sweden in 1995. The use of analgesics during the preceding two weeks was asked. 34.8% of females and 21.4% of males reported analgesic use. Aches and pains correlated strongly with the use of analgesics. After controlling for a variety of variables, female sex still explained a small part of the analgesic use.

Paulose-Ram et al. (2003) utilized data from the National Health and Nutrition Examination Survey conducted in the USA during 1988–1994. The participants were asked about any Rx analgesic use within the past month, and how long they had been taking the drug. No information was gathered on the frequency of use. The one-month prevalence of Rx analgesic use was 9%. The median number of days of Rx analgesic use was 340. One quarter of Rx analgesic users reported use for approximately three years, and 10% for more than six years. Use of OTCs was examined by reading a list of brand names of OTC analgesics. Participants also reported how often they took OTC analgesics. 76% of the population reported OTC analgesic use within the past month. The median days of use per month were three for ibuprofen and paracetamol and four for ASA. Females were more likely to use both Rx and OTC analgesics. Increasing age correlated positively with Rx analgesic use. No data on possible pains behind analgesic use was reported.

In addition to period prevalence data on analgesic use, Motola et al. (2004) gathered interesting data on the frequency and duration of NSAID use. They mailed a postal questionnaire regarding illnesses and drug use to a random sample of Italians in 2002. The subjects were asked to list all preparations (trade names) taken at least once during the previous week. The duration, frequency and indication of NSAID use were also asked. Of all the respondents, 23% had used NSAIDs during the past week. Prevalence was higher among females. According to age, prevalence was highest among the participants aged 35–49 years. Of the NSAID users, 18% reported daily or frequent use for more than six months (chronic use). The prevalence of chronic use was highest in the age group of 50–64 years among males and 65 years or older among females. More than 50% of all NSAIDs were prescribed, and 44% were taken as self-treatment. The different dimensions of pain were poorly measured, but having suffered from MSK disease or unspecified pain during the previous six months was significantly associated

with NSAID use. Headache, osteoarticular pain, and pain in general were the most commonly reported symptomatic reasons for NSAID use.

The Health 2000 Health Examination Survey collected some data on analgesic use in Finland. According to the report by Klaukka (2006), 38% of the Finns aged 18 or over were using some Rx NSAID at the moment of interview. The proportion of users was highest among females aged 35–54 years.

The annual postal survey "Health Behaviour and Health among the Finnish Adult Population" by National Public Health Institute asked the participants about their use of medicines over the past 7 days. According to the latest report by Helakorpi et al. (2005), 31.2% of the population had used some medication for headache and 18.0% medication for other aches during the preceding week. Medication use for both symptom categories was higher among females. Medicine use for headache decreased by age, whereas medication for other aches was more common in the older age groups. As discussed in chapter **2.3.3**, headaches are less common among the elderly, but the overall prevalence of pain increases with age (**2.3.2**).

The studies introduced in this chapter have been conducted over a long time span in different populations with a variety of methodologies and definitions. Still, the use of analgesics is obviously very common in the general population, especially in the older age groups. Heavy or chronic use also seems to increase by age. Very roughly, 20%–30% of the general population report analgesic use at least once within the preceding 7–14 days. It seems that overall analgesic use is increasing. At least as regards Finland, this is also supported by consumption statistics (National Agency for Medicines and Social Insurance Institution 2006). Use of analgesics seems to be more common among females. This is possibly related to sex differences in the epidemiology and perception of pain or differences in reporting behavior.

Different pain symptoms or the presence of painful conditions are logically strongly associated with analgesic use. Studies by Ahonen et al. (1991b and 1993) showed that the occurrence of psychoneurotic symptoms (e.g. insomnia, anxiety, non-specific fear, depression) was also independently related to the use of analgesics. It was suggested that this could mean that analgesics are sometimes used as substitutes for psychotropic medicines. In other studies, too, sleeplessness (Eggen 1993, Antonov and Isacson 1996) and depression (Eggen 1993) were associated with analgesic use. As discussed earlier in chapter **2.3.4**, pain can also be of psychological origin.

4.3 Problems related to pharmacological pain management

Pharmacotherapy with analgesics is prone to many problems. Like all medicines, analgesics can cause serious adverse effects. All NSAIDs increase the risk for gastrointestinal (GI) bleeding (cf. Hernández-Díaz and Rodríguez 2000) and myocardial infarction (cf. Helin-Salmivaara et al. 2006). Excessive doses of paracetamol may lead to liver failure (cf. Sheen et al. 2002). Most analgesics can also affect renal function (cf. Gambaro and Perazella 2003). Frequent use of paracetamol, ASA, or other NSAIDs has been observed to increase the risk of hypertension at least among males (Forman et al. 2007).

Patients with some chronic pain, such as chronic daily headache, frequently overuse analgesics (Fuh et al. 2005). Unlike their effect on other pain syndromes, analgesics may paradoxically increase headache frequency and chronicity. Fuh and colleagues recruited over 1800 patients with chronic daily headache. Almost half of the subjects were diagnosed with medication overuse headache. According to Colás et al. (2004), the prevalence of chronic daily headache, related to overuse of analgesics, is 1.4% in Spain (females 2.6%; males 0.2%).

The study by Bergman et al. (2000) in three European countries suggested that factors other than evidence-based medicine, such as marketing, have an impact on the patterns of prescribing NSAIDs. Especially in Italy, substances with a relatively high risk for GI complications, such as ketoprofen and piroxicam, were often prescribed. In addition to prescribing analgesics with lower a risk for adverse effects, pain patients' other medications must also be considered. Helin-Salmivaara et al. (2005b) estimated that, in Finland, during a three-month period, over 11,000 individuals received prescriptions for a NSAID together with prescription(s) for corticosteroids, anticoagulants, or selective serotonin re-uptake inhibitors. Such combinations increase significantly the risk for GI bleeding.

Nilsson et al. (2000) studied the frequency of drug-related therapy problems (an aspect of drug therapy that may interfere with the therapeutic objective) among patients using medicines for pain. The study was carried out in pharmacies, and 1840 subjects were involved. Up to 35% of patients with analgesic prescriptions reported drug-related therapy problems, such as GI adverse effects and opioid-induced constipation. A lack of effect was sometimes also reported.

Hanlon et al. (1996) studied sub-optimal analgesic use among 3973 randomly selected elderly subjects aged 65 years or older. The term "sub-optimal" referred to the practice of taking two or more analgesics from the same class, using three or more analgesics simultaneously, or using an analgesic that had a major interaction with another drug in

use. Analgesics were used by 60.4% of the participants. Sub-optimal use, most commonly therapeutic duplication or use of multiple analgesics, was detected in 9.2% of the analgesic users.

Lay people have various negative attitudes and misconceptions about analgesics, which can hinder effective pain management. Bostrom (1997) reported the results of a telephone survey involving over 1000 Americans. Of the participants, only 30% stated that when they last felt fairly severe pain, they acted quickly to relieve it. 66% said that they just withstood the pain. Furthermore, only 18% said that they are likely to take medication fairly quickly to stop pain, while 46% would try to avoid medication unless the pain "gets bad", and 35% would wait until the pain is unbearable. People avoided analgesics due to fears of becoming dependent on drugs. 87% agreed that "it is easy to become too reliant on pain medication", and 72% agreed with the proposition "if you take medication when you don't really need it, then when you need it, it won't work".

As a conclusion, effective and safe pharmacological pain management has many threats. Serious adverse effects, interactions, therapeutic duplication with different NSAIDs, overdosage, irrational prescribing patterns and lay people's misconceptions must be considered when managing pain.

4.3.1 Role and risks of OTC analgesics in pain management

As described in the chapters **4.1** and **4.2.1**, the consumption and utilization of OTC analgesics is very common among the general population. OTC analgesics are truly important medicines in self-care. Proper self-medication of especially acute and temporary pain episodes can help to maintain the individual's capability to function. Quick management of pain is reasonable in order to prevent the pain from becoming chronic. As summarized in the dissertation by Sihvo (2000), higher educational level, better access to information, and people's interest in their personal health have enabled an increase in self-care and a consequent increase in individual autonomy in health problem management. In Finland, analgesics are the best-selling group of OTC medicines in Finland, measured in euros (Pharmaceutical Information Centre / Finnish Pharmaceutical Data 2006). However, the good availability and prevalent use of OTC analgesics also bring risks.

Sihvo et al. (2000) reported that, of the Finns using OTC drugs, four per cent were exposed to potentially clinically significant interactions, most commonly caused by ketoprofen, ibuprofen, and ASA. Such interactions may lead to changes in the therapeutic effects of other medicines, such as antihypertensives, or result in adverse events. In addition, of the subjects using Rx analgesics, up to 10% reported also using

OTC analgesics continuously. Concomitant use of OTC and Rx NSAIDs is a serious risk for gastrointestinal problems. Simultaneous intake of both Rx and OTC products containing paracetamol may lead to overdosage and toxic or even fatal damages of the liver and kidneys. Cox et al. (2004) studied a group of coxib users in the United States. They also found a significant amount of co-medication with OTC analgesics.

Porteous et al. (2005) studied inappropriate use of OTC analgesics in Scotland. Altogether 21% of OTC analgesic users were found to have possibly inappropriate usage patterns. The authors found evidence of potential interactions, use of multiple analgesics (including several cases of subjects using more than one paracetamol-containing products), and use of OTC analgesics by risk groups (e.g. patients with allergies, asthma, ulcer, and renal or hepatic impairment).

Thomas III et al. (2002) conducted a case-control telephone survey among OTC NSAID users (use on 4 days or more often during the previous 7 days) and matched non-users (no NSAIDs within the past 30 days). The users of OTC NSAIDs were twice as likely to report gastrointestinal (GI) adverse effects. Thus, OTC NSAIDs, even at low doses, must not be assumed completely harmless and safe.

Whitaker et al. (1995) distributed 1500 questionnaires in UK pharmacies to non-selected customers. Of the 766 respondents, 96% reported buying OTC analgesics. Their use of Rx drugs was also asked. Over ten per cent of the subjects were considered to be in danger due to interactions or toxicity. Some four per cent of the participants were exposed to overdosage of OTC analgesics. Especially the elderly were at risk, as they took analgesics more often, for longer periods, and in combination with a greater number of Rx drugs.

Good availability of OTC analgesics and quick treatment of acute pains are important, as it is not reasonable to burden the health care system with minor self-manageable complaints. Although OTC analgesics are meant to be used only temporarily, Granås et al. (2006) observed that one out of five Norwegian pharmacy customers purchasing OTC analgesics reported using them daily. The researchers also found a reason why people use multiple analgesic products containing the same active substance: three out of four pharmacy customers using OTC paracetamol or ibuprofen did not know that Rx analgesics might contain the same substance.

4.3.2 Information needs related to the use of analgesics

Due to the large proportion of the population using analgesics, it can be assumed that a substantial number of individuals may be in need of information and advice on pain management and the use of analgesics. However, an observational study has shown that

fewer than half of pharmacy customers purchasing prescribed analgesics received any directions on the use of their medicines (Vainio et al. 2002). Further, only 19% received information on the mode of action and only 17% on adverse effects. In general, neither physicians nor pharmacists seem to counsel patients sufficiently on the various aspects related to correct use of drugs (Morris et al. 1997). For better availability of drug information, different information services have been established in many countries (cf. Raynor et al. 2000, Maywald et al. 2004). It has been shown that telephone drug information services lead to positive patient outcomes (Melnyk et al. 2000). Finland's first small-scale drug information service for nurses and physicians was started in 1982 at Kuopio University Hospital Pharmacy (Ojala 2005). Eventually, in 2001, this led to the establishment of Kuopio Medicines Information Centre (KMIC) which provides drug information to both health care professionals and lay people. The study by Bouvy et al. (2002) demonstrated that the lay people who contact a drug information service today have a wide variety of questions about their medicines. Over 10% of the inquiries addressed to KMIC are related to drugs for musculoskeletal system, i.e. mainly NSAIDs (Ojala 2005). The corresponding figure is 7.2% in Germany (Maywald et al. 2004). However, no detailed data is available on what kind of information about analgesics people contacting drug information services actually have.

EMPIRICAL STUDY

5 AIMS OF THE STUDY

The general aim of the present study was to investigate the epidemiology of pain and the use of different pain management strategies, with a special focus on analgesics, among the Finnish general population. The specific objectives were:

1. To determine the prevalence of frequent chronic pain and to assess its impact on health.

2. To describe and evaluate the pain management strategies used by the Finnish adult population.

3. To study analgesic use patterns at the population level.

4. To characterize lay people's information needs concerning analgesics and pharmacological pain management.

6 MATERIALS AND METHODS

This thesis is based on two datasets. Firstly, a postal survey was carried out in order to obtain comprehensive epidemiological data on:

a) the prevalence and characteristics of pain
b) the use of analgesics and other pain management strategies
c) relevant individual-level background information

Secondly, in order to obtain data on the kind of information needs analgesic users have, a retrospective database study was conducted in a drug information centre.

6.1 Design of the postal survey

To attain the aims 1–3 of the study, information was obtained from a large representative random sample of the Finnish general population. Compared to an interview survey, a postal survey is cheaper and faster (Tolonen 2006). Although postal surveys have lower response rates than home interview studies, the differences in the results are small (Picavet 2001). As our goal was to obtain generalizable results, the response rate in our survey had to be relatively high. The average response rates of the postal surveys published in medical journals in the 1990's have been around 60% (Asch et al. 1997).

When choosing relevant questions and measures for inclusion into the questionnaire, one aim was to keep the questionnaire short and easy to answer. Bergman et al. (2001) conducted a pain survey and afterwards contacted and interviewed a sample of non-respondents. Of them, 7.8% said they did not respond because the questionnaire was too long. The questionnaire of Bergman et al. included 52 questions and the SF-36 Health Survey (see chapter **2.2.7**). Thus, after pilot testing, only 25 relevant questions, measuring instruments and essential background inquiries were chosen into our study, as we limited the questionnaire to be only four A4 pages long (one folded A3-sheet). The study was conducted with Finnish and Swedish questionnaires, as those are the official languages of Finland, and at least one of them is spoken by virtually every permanent resident.

6.1.1 Content of the questionnaire and operationalization of the variables

As presented in the review of the literature, pain can be approached, defined and measured in various ways. In epidemiological studies, the most practical and most commonly investigated dimensions of pain are its temporal characteristics (duration,

frequency) as well as its localization and intensity. We designed the first part of the questionnaire based on this information. A non-validated English translation of the questionnaire is given in Appendix 2. The key variables and their operationalization are described in this chapter.

The first question in the questionnaire was a screening question, intended to identify those with a recent pain experience (any pain during the past week). The painful locations were determined with a list of pain sites together with space for answering open-ended questions. Also the most problematic (the most severe) pain was inquired. For paper **II**, answers were re-grouped in the following way: the location of the (worst) pain is either a) head, b) neck-shoulder or upper extremities, c) back or d) hip or lower extremities. The duration of pain was categorized with six options. In line with several earlier studies (cf. Appendix table 1), the papers **I–III** classified the respondents reporting that their pain had lasted for longer than three months as subjects with chronic pain. The frequency of pain was also measured with pre-defined alternatives. The following categories of pain: a) daily or continuously, b) several times a week and c) at most once a week, were applied in the papers **I–III**.

The intensity of pain was measured with an 11-point NRS (see chapter **2.2.2**). It is a valid, responsive and reliable pain intensity measure (Lundeberg et al. 2001). NRS was chosen as the pain intensity measure in this survey because it is easy to use and score (Bolton and Wilkinson 1998). In NRS, the response "zero" means no pain. In the papers **II** and **III** the NRS values from 1 to 10 were categorized into "mild pain" (1–3), "average pain" (4–6) and "severe pain" (7–10).

Self-rated health was measured as described in chapter **2.4.4**. The Finnish phrasing was the same as that used in Finnish Health Survey (Arinen et al. 1998). In paper **I**, the categories "good" and "quite good" health were combined into "good health", and "rather poor" and "poor" were re-categorized as "poor health". This was done in order to avoid excessively small sub-groups in the analysis, as especially the option "poor" was infrequently selected. Similar methodology was applied by Arinen et al. (1998).

Information on the subjects' chronic illnesses was considered important. It is not possible to make proper diagnoses in a postal survey, and the reliability of self-reporting can be questionable. Therefore the respondents were inquired about the disease number codes they had on their personal sickness insurance card (Kela card). This methodology is described in detail in paper **I**, see the chapter titled "Other Covariates". Those reporting disease code(s) were considered to have a chronic disease diagnosed by a physician (papers **I** and **III**).

The respondent's age was calculated from the year of birth. Prevalence results were reported in five-year clusters (papers **I**–**III**, and this thesis). Age categories of 15–44

years and 45–74 years (paper **I**), and 15–29, 30–44, 45–59 and 60–74 years (papers **II** and **III**, and this thesis) were applied. Age was also used as a continuous co-variable (paper **I**).

Educational level was measured with eight pre-defined options, and with space for open answers. In order to keep the analyses simple, the years of education were dichotomized into primary school (9 years or less) or more than primary school in all cases. Employment status was also dichotomized from six options to those working, studying or taking care of children and to those being unemployed, retired or on sick leave.

The questionnaire included the Depression Scale (DEPS). It is a short and validated depression screening instrument applicable to the general population (Salokangas et al. 1995). Those scoring more than 8 points out of a maximum of 30 were assumed to have depressive symptoms. With this cut-off point, the sensitivity of DEPS is 74% and specificity 85%, compared to the results of the Present State Examination interview (9^{th} version) conducted by trained interviewers.

6.1.2 Study population and sampling

The target population consisted of the people aged 15–74 years and permanently resident in Finland. This age group was considered to represent the majority of Finnish general adult population. We were also slightly concerned about the ability of the ageing people to fill in the questionnaire. In addition, the population aged 75 years or older was already actively studied by the geriatrics of the University of Kuopio. The sample size and the sampling method were chosen after consulting a biostatistician. Briefly, the method of random stratified sampling applied here guaranteed sufficient samples by sex and age from each in five-year subgroup. The age frame from 15 to 74 years includes 12 groups of both sexes. Each of the 24 sub-groups included 270 or 271 subjects, giving a total of 6500 individuals who were sent the questionnaire. This sample size was considered sufficient to give reliable and precise results about the target population. The actual random stratified sampling was conducted by the Finnish Population Register Centre (PRC) from their database, which is very comprehensive and up-to-date.

6.1.3 Mailing procedures

In the first round, 6500 questionnaires, each with a cover letter and a pre-paid return envelope, were mailed. The first round included only Finnish-language questionnaires.

The recipients who contacted us via telephone or mail to request a Swedish questionnaire were sent a Swedish-language questionnaire and cover letter. Written reminders, especially with a re-sent questionnaire, have been found to increase the response rate (Asch et al. 1997). Thus, two reminders were sent at approximately two weeks' intervals. In both reminder rounds, in addition to a Finnish questionnaire, a Finnish reminder letter and a return envelope, a Swedish questionnaire and a cover letter were manually added to the envelopes addressed to Åland or the western coast of Finland, as the majority of Swedish-speaking people live in those areas. Recipients with a Swedish first or last name or a Swedish-language town name in the address also received the questionnaire and cover letter in both languages.

6.1.4 Ethics and privacy protection in mailing and reminder procedures

Actual permission from the local ethics board was not obtained, as it was not required for postal surveys directed to non-institutionalized adults at the time of conducting this work. This study was not a clinical or otherwise intervening or invasive trial. Returning the filled questionnaire after reading the cover letter and the questions was considered as an informed consent for participating the survey.

The PRC delivered the randomly sampled names and addresses in an Excel datasheet. Each recipient was afterwards designated a code number. The corresponding number was printed on the return envelopes. After that, a list of code numbers together with the corresponding postal area codes was printed. When a questionnaire was returned, the code was checked from the envelope and marked as returned to the printed list, which contained no names or street addresses of the recipients. When the envelope was opened, the recipient's postal code was read from the list and written on the questionnaire. Neither name nor any other identifying data was available or attached to the filled-in questionnaires. After marking the postal area code, the questionnaires were taken out and the envelopes were disposed of. It thus became impossible to connect the questionnaires with the recipients' information at any later stage. Before the reminder rounds, the codes marked in the list as returned were removed from the list of recipients. In this way, the responders were not sent undue reminders. Complete anonymity of the respondents was ensured throughout the study. The postal area code information was considered important when evaluating the geographic representativeness of the respondents (paper **I**). This approach was chosen as it was assumed that, if the postal area code was inquired in the questionnaire, people might have ungrounded fears of endangered anonymity, which could impair the response rate.

6.2 KMIC database study

This study explored the general public's information needs related to analgesics and pain management. Kuopio Medicines Information Centre (KMIC) records the content of every inquiry into their database. Analgesic-related inquiries were retrieved from the database for further analyses. The flow of data collection is presented in Figure 1 of paper **IV**. The database and the applied methodology are described in the Methods section of that paper.

6.3 Data processing and statistical methods

All the available data from both the postal survey and the KMIC database were entered into the SPSS statistical software. Statistical tests and analyses were performed with SPSS. The latest available version (from 9.0.1 to 14.0.1) was always utilized. In addition, Microsoft Excel was utilized when calculating age- and sex-adjusted prevalences and possibility intervals. The proportions are given as percentages (%). As age- and sex-specific sub-groups were randomly sampled, the proportions were simply calculated by dividing the number of cases with the total number of participants in each group. As a consequence of stratified sampling, small age groups are over-represented in the total sample. Thus, when calculating overall prevalences, the results were adjusted for age and sex with a direct standardization method, using the actual age and sex distribution in 2002, provided by PRC, as the standard.

In bivariate analysis *Chi-square* test and *t*-test were applied with a limit of statistical significance of $p<0.05$. The significances of age-adjusted sex differences were tested with the standard test for two binomial proportions. In multivariate analysis, binary and multinomial logistic regression analyses were applied, with 95% confidence intervals. The methodologies are described in the original publications.

In this thesis, the Figures 10a-d display pain prevalences with the lower limit of the possibility interval (PI). Based on the studies by Papageorgiou et al. (1995), Bergman et al. (2001) and Picavet and Schouten (2003), the prevalence of pain is lower among non-respondents. The lower limit of PI represents the lowest possible prevalence, assuming that none of the non-respondents had pain. The real prevalence of pain is very likely between the respondent-based estimate and the minimum possible level. This PI methodology has been described in the abstract by Turunen and Soini (2006).

7 RESULTS

Of the 6500 questionnaires initially mailed, 68 were returned because the recipient was not reached due to various reasons: the address had expired, or the relatives returned an empty questionnaire with a notification that the recipient had moved abroad, was demented, institutionalized or had died very recently. Altogether 4542 of the 6432 eligible individuals responded to the postal survey (papers **I**–**III**), the final response rate being 71% (females 77.4%; males 62.3%, $p<0.001$). The flow of the survey is shown in Figure 9. The papers **I** and **III** utilized the whole collected set of data, whereas paper **II** focused on the individuals who had experienced pain within one week before completing the questionnaire.

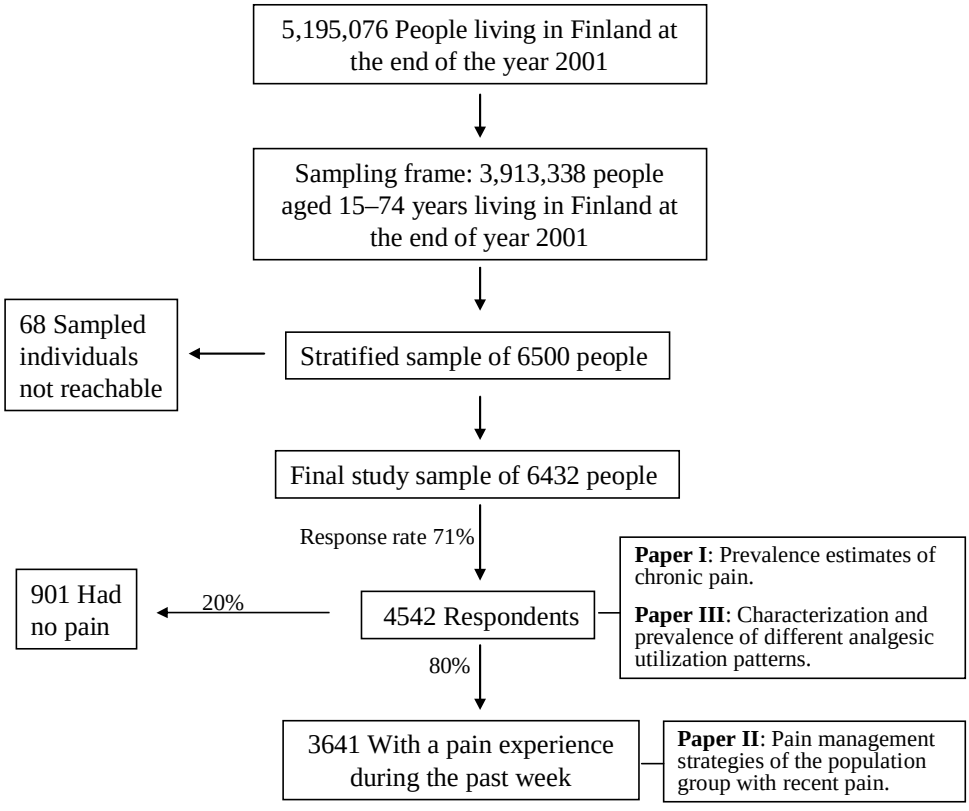

Figure 9. The flow chart of the postal survey process and publication data selection.

The response rate was 45.6% after the first mailing round, 62.8% after the first reminder and 70.6% after the second reminder. The response rates were highest in the oldest age groups. The increasing trend was almost linear. The rate was lowest among the 20- to 24-year-old males (45.0%) and highest among the females aged 70–74 years (92.3%). The data collection from the KMIC database covered two years and yielded data on 2683 analgesic-related inquiries. The sex distribution of the callers, together with other basic data, is presented in Figure 1 of paper **IV**.

7.1 Prevalence of pain according to different definitions (paper I and unpublished)

Figure 10a–d presents the proportion of people with any pain during the past week, the point prevalence of any pain and the prevalences of chronic and daily or continuous chronic pain. Of all the 4542 respondents, 3641 individuals had felt some pain during the preceding week (Figure 10a). This group was analyzed in more detail in the papers **II** and **III**. After adjusting for age and sex, the overall prevalence of any pain during the preceding one-week period was 79.5% (females 84.0%; males 75.0%, $p<0.001$). The possibility intervals illustrate the uncertainty caused by non-respondents, especially young males. There was no age trend.

7.1.1 Point prevalence of any pain

The age- and sex-adjusted point prevalence (any pain at the very moment) was 37.3% among Finns aged 15–74 years (Figure 10b). The point prevalence was higher among female respondents (females 43.0%; males 35.8%, $p<0.001$). The age-adjusted prevalences were 41.5% for females and 33.1% for males ($p<0.001$). When non-respondents were also included, the point prevalence of any pain turned out to be at least 26.5% among 15- to 74-year-old Finns (see the lower limit of the possibility interval in the “total” column, Figure 10b). In other words, the “true” value can be assumed to be between 26.5% and 37.3%.

7.1.2 Prevalence of any chronic and daily or continuous chronic pain

The adjusted overall prevalence of any chronic (>3 months) pain was 35.3%, including the respondents who did not report the frequency of their chronic pain (Figure 10c). Thus, this differs slightly from the figure reported in paper **I** (35.1%), which included only those with chronic pain categorized according to frequency. There was no sex difference among the respondents (females 37.6%; males 37.4%, p=0.89). After adjusting for age, the sex difference remained insignificant (females 36.1%; males 34.5%, p<0.26). Nor was there any sex difference for daily or continuous chronic pain among the respondents (females 15.5%; males 17.2%, p=0.11). After adjusting for age, the overall prevalence of daily or continuous chronic pain was 14.3% (females 14.1%; males 14.5%, p=0.70). The prevalences of both any chronic pain and daily or continuous chronic pain were clearly higher in the older age groups (Figures 10c and 10d). When the non-responders were also taken into account, the prevalence of any chronic pain was 25.3%–35.1%, and that of daily or continuous chronic pain 10.6%–14.3% (see the possibility intervals in Figures 10c and 10d).

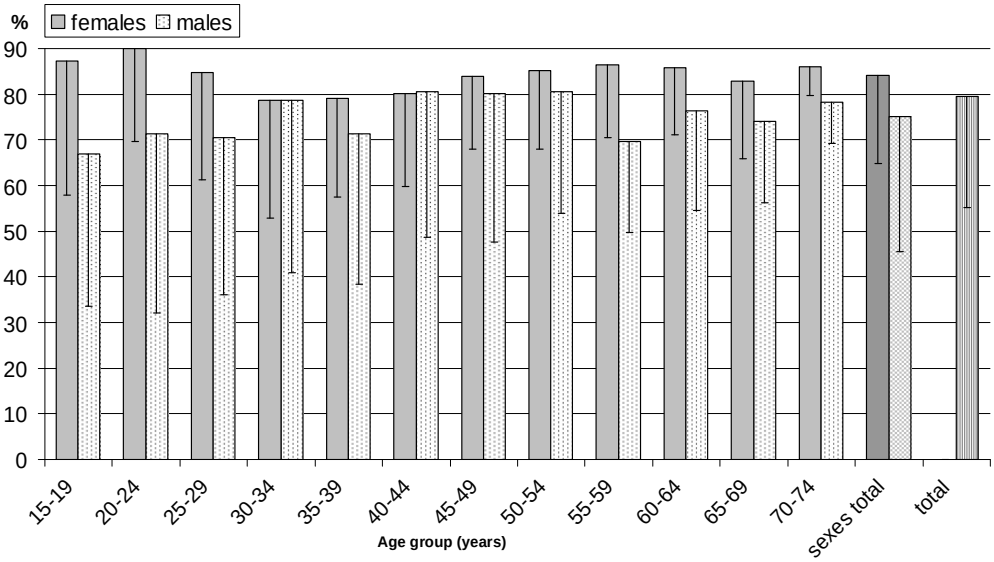

Figure 10a. Prevalence of any pain during the past week (3641 cases out of 4542 respondents). The lower limit of the possibility interval reflects the uncertainty caused by non-respondents.

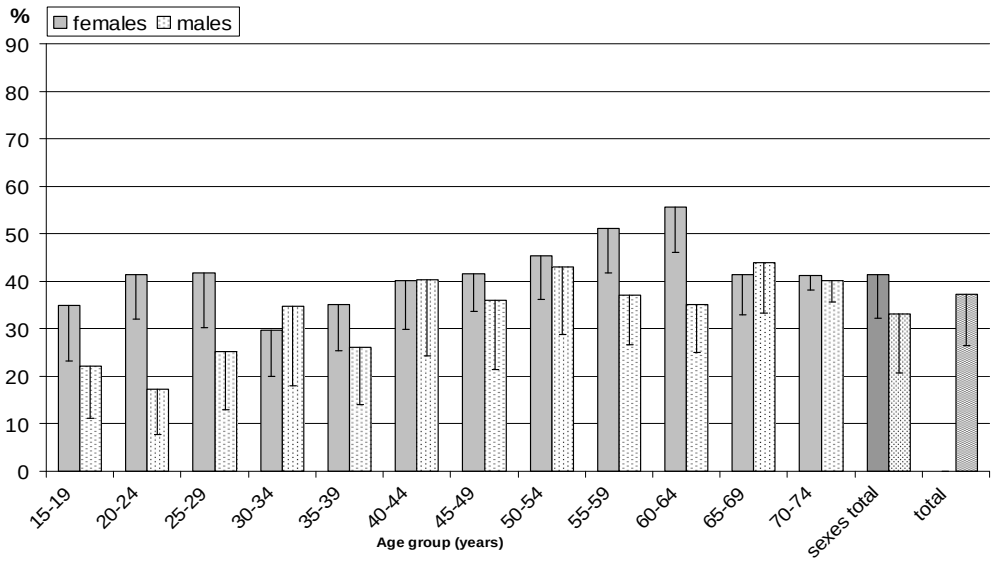

Figure 10b. Point prevalence of any pain (1759 cases out of 4542 respondents). The lower limit of the possibility interval reflects the uncertainty caused by non-respondents.

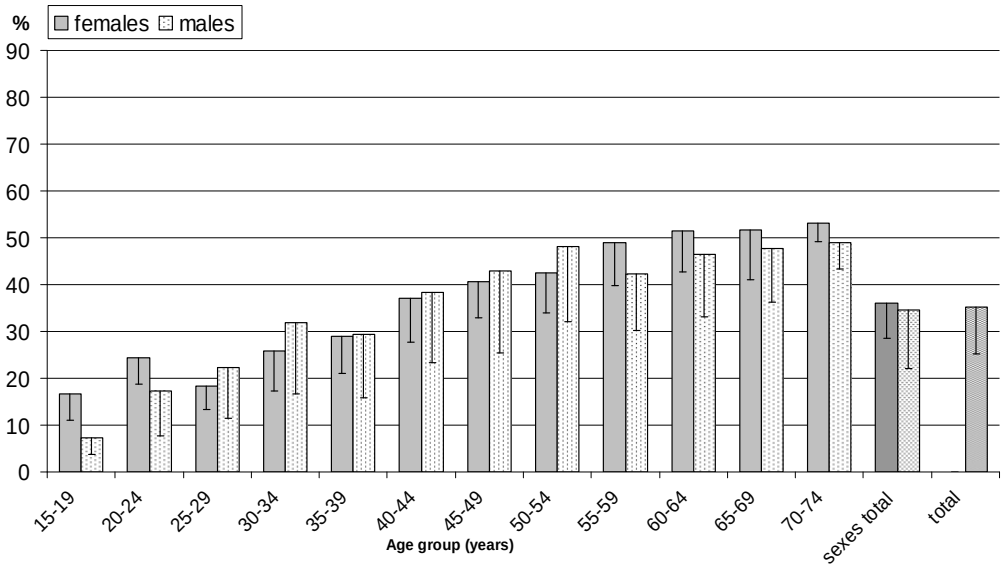

Figure 10c. Prevalence of chronic (>3 months) pain (1702 cases out of 4542 respondents). The lower limit of the possibility interval reflects the uncertainty caused by non-respondents.

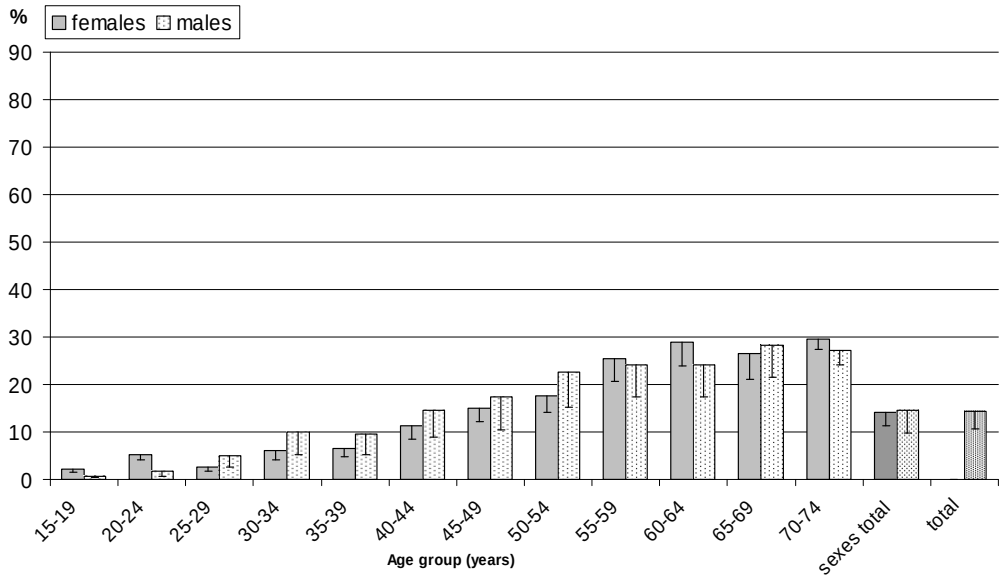

Figure 10d. Prevalence of daily or continuous chronic (>3 months) pain (738 cases out of 4542 respondents). The lower limit of the possibility interval reflects the uncertainty caused by non-respondents.

7.1.3 Factors associated with chronic pain (paper I and unpublished)

Chronic pain was used as an explanatory variable for self-rated health in paper **I**. The association between pain and poor health was evident. The possible explanatory variables for having chronic pain were explored with binary logistic regression analyses (Table 1). Depressed mood and especially older age were clearly associated with pain. There was also a weak association with having at least one chronic disease and chronic pain. Socioeconomic factors were not clearly associated with having chronic pain. Educational level and working status were weakly, yet statistically significantly, associated with daily or continuous chronic pain.

Table 1. Adjusted odds ratios for having chronic pain or daily/continuous chronic pain.

Explanatory variables	**Chronic pain (>3 months) (n=1687*) OR (95% CI)**	**Daily or continuous chronic pain (n=731*) OR (95% CI)**
Sex		
Male	1	1
Female	1.04 (0.92–1.18)	0.90 (0.76–1.06)
Age, years		
15–29	1	1
30–44	2.11 (1.71–2.61)	3.38 (2.21–5.16)
45–49	3.26 (2.66–4.00)	7.00 (4.71–10.40)
60–74	3.51 (2.74–4.49)	7.46 (4.86–11.46)
Education		
More than primary school	1	1
Primary school (9 y) or less	1.09 (0.95–1.26)	1.33 (1.11–1.60)
Working status		
Working (incl. studying)	1	1
Not working (incl. retired)	1.17 (0.98–1.40)	1.38 (1.09–1.74)
Mood		
Normal (DEPS** ≤ 8)	1	1
Low (DEPS** > 8)	2.27 (1.95–2.64)	2.79 (2.33–3.34)
Any chronic disease(s)		
No	1	1
Yes	1.34 (1.15–1.57)	1.41 (1.17–1.70)

* Those with a missing value in any of the variables were excluded from the models.
** DEPS; The Depression Scale (Salokangas et al. 1995).

7.2 The most common localizations of pain (paper II and unpublished)

The respondents of the postal survey were asked to report all the bodily localizations they had felt pain in within the past week. On average, among all the 4542 respondents, males reported pain in 2.20 and females in 2.82 localizations ($p<0.001$). Among those 3641 individuals with some pain experience within the past week, males reported on average pain in 2.93 and females in 3.35 localizations ($p<0.001$). Table 2 shows the most commonly reported pain localizations among all the respondents. Pains in neck, head and back were experienced most frequently. Females reported all the different pains, except knee pain, more frequently. Some sex differences were very significant.

Table 2. The most common localizations of pains experienced within the preceding week (n=4542).

Pain localization	Total n	% of all the respondents (n=4542)	% of all male respondents (n=2025)	% of all female respondents (n=2515)	Significance of sex difference (p-value)
Neck	1817	40.0	32.1	46.4	<0.001
Head	1666	36.7	28.5	43.3	<0.001
Back	1303	28.7	28.6	28.8	0.885
Shoulder / upper arm	890	19.6	19.1	20.0	0.409
Knee	741	16.3	16.7	16.0	0.545
Ankle / foot	728	16.0	14.1	17.6	0.002
Abdomen	620	13.7	9.8	16.7	<0.001
Wrist / hand	596	13.1	10.6	15.1	<0.001
Hip	504	11.1	10.3	11.7	0.141

Figure 11 displays the prevalences of five common complaints experienced within the past week, according to age. It can be clearly seen that the prevalences of certain pains, for instance knee pain, increase with age, whereas headache decreases substantially.

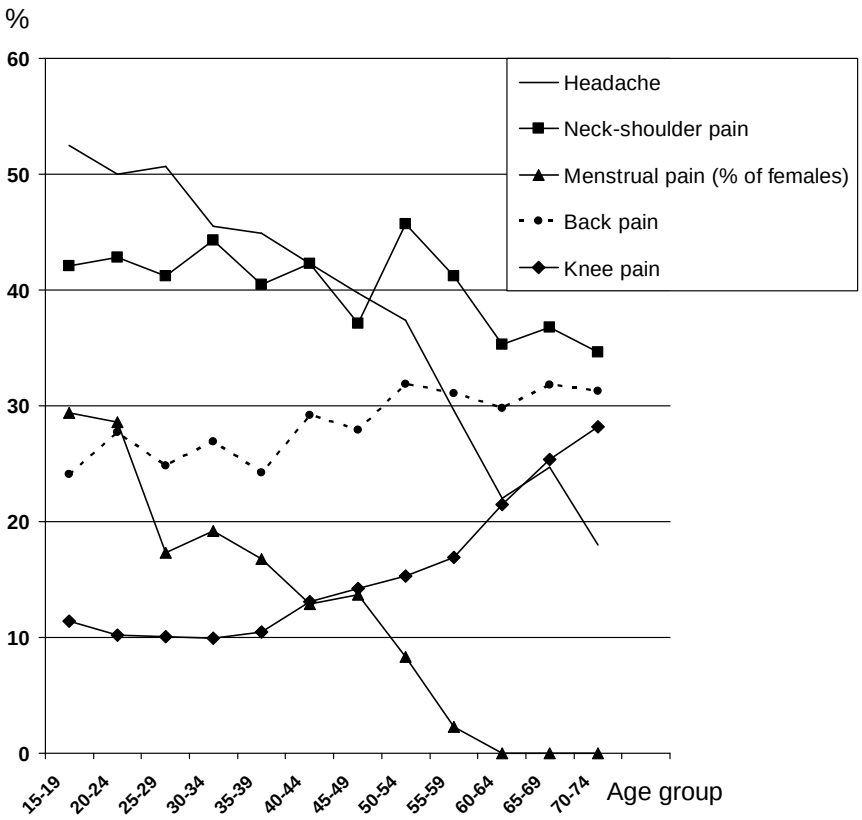

Figure 11. Prevalences of five commonly reported pains experienced within past week according to age (n=4542).

In addition to all the painful localizations, the respondents were asked to report which one is their most bothersome pain. Neck was most frequently reported to be the location of the most bothersome pain, followed by head, back and knee (see Table 3 of paper **II**).

7.2.1 The pain localizations of those suffering from chronic pain (unpublished)

Among the 1702 respondents with chronic (>3 months) pain, males reported on average pain in 3.45 and females in 3.92 bodily localizations within past week ($p<0.001$). Table 3 shows the most commonly reported pain localizations among those suffering from chronic pain. Pains in neck, back, and head were experienced most frequently within the preceding week. Males reported pains in back and shoulder upper arm more frequently, but those differences were not significant. Pains in e.g. neck and head were significantly more frequently reported by females with chronic pain.

Table 3. The most common localizations of pains experienced within the preceding week by those reporting some chronic (>3 months) pain (n=1702).

Pain localization	Total n	% of all the respondents with chronic pain (n=1702)	% of males with chronic pain (n=757)	% of females with chronic pain (n=945)	Significance of sex difference (p-value)
Neck	936	55.0	49.1	59.7	<0.001
Back	770	45.2	45.8	44.8	0.657
Head	695	40.8	35.1	45.4	<0.001
Shoulder / upper arm	573	33.7	34.1	33.3	0.745
Knee	465	27.3	27.2	27.4	0.929
Ankle / foot	452	26.6	23.4	29.1	0.008
Hip	362	21.3	19.8	22.4	0.190
Wrist / hand	354	20.8	16.6	24.1	<0.001
Abdomen	321	18.9	15.1	21.9	<0.001

When asking those with chronic pain, which is their most bothersome bodily localization of pain, the most frequent responses were: back (n=381), neck (358), knee (204), head (185), shoulder or upper arm (181), ankle or foot (177), and hip (156). Thus, back pain and neck pain seem to be the chronic painful conditions which bother Finnish adults most commonly.

7.3 General view of the population's pain management strategies (paper II and unpublished)

One key observation in paper **II** was the diversity of the ways to manage pain. Females were more active in utilizing different pain management strategies. The choice of treatment was rationally related to the location of pain. Physical exercise was used especially for mild musculoskeletal pains. It was also often found to be helpful (Table 4).

Table 4. Treatments found to be beneficial by the respondents.

Pain management strategy	Found the treatment most helpful (n)	% of the users of each treatment
OTC medicines (n=1930)	945	49
Physical exercise (n=1887)	853	45
Prescription medicines (n=1266)	611	48
Massage given by a family member or a friend (n=834)	274	33
Massage by a professional masseur / masseuse (n=686)	253	37
Treatment by a physiotherapist (n=386)	136	35
Rest, sleep (n=130)	91	70
Treatment by a chiropractor / naprapath / osteopath (n=183)	62	34
Acupuncture (n=77)	15	19
Absence from work / school (n=351)	16	5
Less housework (n=379)	11	3

7.3.1 Iceberg model of pain management (unpublished)

The iceberg model was introduced in chapter **3.2**. Below you will see an iceberg diagram completed with data from this study (Figure 12). The overall characteristics of pain management by those suffering from any pain were included. Bivariate analyses were conducted to estimate how the intensity and chronic nature of pain were related to the strategies chosen for pain management.

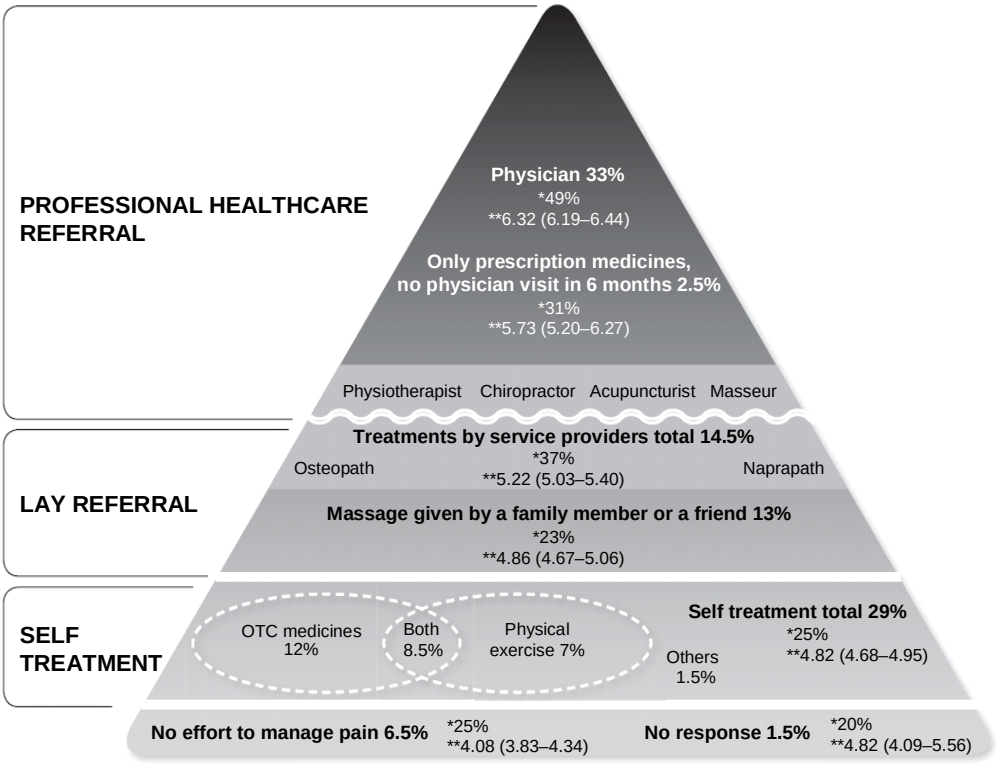

Figure 12. Iceberg model of pain management. The model includes all the 3641 respondents who reported having experienced any pain within past week. Only the highest level of referral from each individual is included in the picture.

* Percentage of chronic pain sufferers in each subgroup.
** Mean of pain intensity (95% CI) in each group (measured with NRS).

Chronic pain is more common at the top of the iceberg. The mean intensity of pain also clearly increases towards the tip. Almost one third of the people with pain relied exclusively on self treatment. However, 6.5% (females 3.9%; males 10.2%, $p<0.001$) of those with some pain had not attempted to manage it.

7.4 Frequent and concomitant use of OTC and Rx analgesics (paper III and unpublished)

Use of analgesics daily or a few times a week (frequent use) was common (see paper **III**). When the non-respondents were included in the calculations, the overall prevalences ranged as follows: daily use of any analgesics 6.4%–8.5%, use of any analgesics a few times a week 9.8%–13.6%, frequent use of only OTC analgesics 6.3%–8.8%, and frequent use of only Rx analgesics 6.5%–8.7%. In addition, concomitant frequent use of both OTC and Rx analgesics was reported by 4.6% (3.4%, or higher). Especially high pain intensity was associated with frequent and concomitant analgesic use. No sex difference was detected.

7.5 General public's needs for information on analgesics (paper IV)

During the two-year study period, 2312 calls to KMIC were related to analgesics. Altogether these calls comprised 2683 questions. Of the actual users of the analgesics in question, a clear majority were females. Tables 1–3 of paper **IV** display the numeric results of the KMIC data. Over 35% of the calls were related to interactions. Also dosing of analgesics (15%), instructions for pain management and enhancement of analgesia (9%), analgesics' effects (8%) and adverse effects (7%) were asked about. Some inquiries suggested that prescribed pain control may not always be sufficient. The questions were related to the most commonly used analgesics: paracetamol (mentioned in 24% of the 2312 calls), ibuprofen (23%), coxibs (15%), naproxen (14%), codeine in combinations (9%) and tramadol (8%). The content of questions differed a bit between the drugs. Inquiries related to adverse effects were relatively common with strong opioids. The actions and effects of coxibs were also discussed. The next chapter gives concrete examples that illustrate the actual questions behind the numbers and percentages.

7.5.1 Quotation-based description of analgesic-related inquiries (unpublished)

Interactions

In many interaction inquiries related to antibiotics, the caller had received a prescription for an antimicrobial drug and had later started wondering whether it was safe also to relieve the pain symptoms of infection or fever with analgesics:

> *"I'm taking penicillin for an infected tooth. Can I also take ibuprofen?"*

Of the interaction inquiries, 10.8% were related to the use of alcohol. Questions about interactions between alcohol and coxibs (n=21), ibuprofen (n=17) and paracetamol (n=16) were most commonly asked:

> *"I'm taking a course of valdecoxib. Is it OK to have a glass of wine?"*

Better analgesia and pain management

Questions related to analgesia enhancement were also addressed to KMIC:

> *"My back hurts so badly. I have taken 200 mg of celecoxib. Can I take another 200 mg tablet, and can I also take 600 mg of ibuprofen in addition?"*

Inquiries about how to manage pain were often related to self-care and OTC analgesics. The most commonly discussed analgesic was ibuprofen:

> *"I fell and hurt my back earlier this week [the call came in on Friday]. Is there any drug available without prescription? ... My back hurts when I lie down. My neighbour gave me 400 mg of ibuprofen."*

Effects and adverse effects of analgesics

Callers were interested in the mechanisms of action, pharmacokinetic properties and effectiveness of different analgesics:

> *"How quickly does rofecoxib 50 mg start to take effect?"*

"What is the active substance in this brand name [valdecoxib] product? What is the route of action? I hope it does not affect the central nervous system."

Questions were also asked about subjective adverse effects:

"I have used codeine+paracetamol for several years. Can it do something to kidneys, as my kidneys are hurting now?"
"I have been taking 40 mg valdecoxib a day for two weeks. Now I have diarrhoea. Can it be caused by this drug?"
"Can I continue taking diclofenac? It is the only drug that helps my hip pain, but it has made my ulcer bleed again."

Suitability and use of analgesics

Allergies, pregnancy or lactation and young age of the actual user of the drug led to questions about whether the planned use of analgesics was suitable:

"Does this etoricoxib product contain sulfa?" [The caller was allergic to sulfa.]

In addition, some callers wanted to confirm whether an analgesic was suitable for their current pain:

"The doctor gave me naproxen for back pain. At home I noticed that I have used the same product for migraine. Can the same drug really be used for such different purposes?"

The actual use, correct dosage and scheduling of the drug were not always simple and straightforward:

"Is this tablet containing acetylsalicylic acid meant to be swallowed or dissolved in the mouth?"
"I have severe pains. Today I bought some rofecoxib 50mg and paracetamol+codeine tablets. Am I supposed to use all the rofecoxib tablets first? Or can I also take paracetamol+codeine for the night, as I already took rofecoxib earlier today?"
"I was prescribed a course of ibuprofen for an inflamed tendon. Do I have to take it continuously or only when it hurts?"

Fears, beliefs and misconceptions

Ten callers were afraid of addiction to opioids. A telephone service can be a good place to talk about awkward matters:

> *"I have been taking codeine+paracetamol daily for a long time for headache. Can I get hooked on it? Should I quit gradually by decreasing the dose? I don't want to talk about my analgesic use with doctors."*

Less reasonable fears and beliefs were also revealed in inquiries related to adverse effects:

> *"Does naproxen induce yeast infections?" [the caller was also taking penicillin]*
> *"Can tramadol cause baldness?"*
> *"My sister had heard that oncologists say that ibuprofen is a horrible drug. It damages one's blood count and may cause cancer. Is it safe to take it occasionally for my rheumatism?"*

The patient information leaflet (PIL) included in the package may occasionally also cause a user to call to KMIC:

> *"I was prescribed meloxicam for pain caused by shingles. The PIL says that this drug is for arthrosis. But I don't have arthrosis!"*
> *"Can I take trimethoprim with meloxicam, as the PIL says it should not be used with methotrexate?"*
> *"I was prescribed nabumetone for shoulder pain. I'm afraid of taking it, because it has so many adverse effects. How do I dare to start that medication? Should I ask for a prescription for some other drug?"*
> *"I was dispensed a new generic tramadol product. The PIL says that even small doses may cause addiction. The original product's PIL didn't say so!"*

The data included several cases involving a misunderstanding. The difference between the strength and size of a tablet and between the different dosages of different substances can be confusing:

“I’m now at home and I have been taking generic paracetamol tablets, which are very big. The tablets I had in hospital were smaller. Have I been taking too much medicine, as these tablets are so big?”

“The doctor gave me a free sample of ketoprofen 50 mg tablets. How do I use it? Did I receive accidentally some children’s drug, as my ibuprofen product contains 400 mg per tablet?”

8 DISCUSSION

Each original publication contains a detailed subject-specific discussion. The methodology of the KMIC study is critically appraised in paper **IV**. This chapter complements especially the methodological discussion of the postal survey. In addition, the main results of this thesis are compared to those of other studies in this field.

8.1 Methodological considerations of the postal survey

The achieved response rate of 71% can be considered relatively good but not excellent, compared to the postal pain surveys presented in Appendix table 1. The average response rate of the eight original postal surveys was 63.4% (range: 46.9%–76.7%). According to the methodological dissertation by Tolonen (2006), based on current literature, the response rate should be 60%–75%. However, due to possible differences between the respondents and non-respondents, she suggested that the general recommendation for the response rate should be closer to 90% than 70%. Especially the males' response rate (62.3%) fell short of this. The response rate increased with age. Thus, the initial concern about the ability of the ageing people to fill in the questionnaire seems now ungrounded.

It has been shown that pain is more prevalent among the respondents of pain surveys (Papageorgiou et al. 1995, Bergman et al. 2001, Picavet and Schouten 2003). This is supported by the fact that, in this study, the prevalence of chronic pain was lower among those responding after the reminders had been sent (data not shown). The effect of non-respondents is difficult to control, as the only information available is age group and sex. All the multivariate analyses were controlled for age and sex, but this does not reduce the uncertainty caused by non-respondents. The prevalences of pain and analgesic use patterns were presented in this thesis with the lower limits of possibility intervals, which show the absolute minimum prevalences of e.g. each pain type according to age and sex (Figures 10a–d). The use of these minimum prevalences ensures that no over-estimation of prevalences is possible. However, in international journals, it is common to present only the point estimates from the actual data. It must be kept in mind, that the reported absolute minimum values very likely do not illustrate the exact "truth" either. It can be assumed that, in addition to pain-free individuals, the group of non-respondents includes also people with impaired health and pains causing activity limitations. Thus, the population's real values are assumingly somewhere within the possibility interval. This is supported by the studies that followed-up the non-respondents (Papageorgiou et al. 1995, Bergman et al. 2001, Picavet and Schouten

2003). The non-respondents also had pains, although slightly less likely than the initial participants.

Tolonen (2006) stated that the length of the questionnaire is directly reflected in the respondents' burden and, consequently, in the response rate and the reliability of the responses. However, Asch et al. (1997) found no association between the response rate and the length of the questionnaire measured as the number of questions. Surprisingly, of the surveys reviewed by Asch et al., those with more pages had higher response rates. However, the results of their bivariate analysis may be confounded by e.g. the topics of the surveys analyzed. In this study, the decision to keep the questionnaire short seems justified, as almost all the necessary data could be collected. Questions on the duration of reported frequent use of OTC and/or Rx analgesics should have been included in the questionnaire. Another minor fault of the questionnaire was that all the pensioners were included into a single category without information on the reason for retirement. This means that younger individuals with chronic illnesses and working disability were not differentiated from old but healthy retirees.

8.2 Epidemiology of pain

This study showed that pain is a very common complaint in Finland. Up to one third of Finnish people aged 15–74 years reported a pain that had lasted longer than three months. The pains were mainly of musculoskeletal origin, but headache was also common especially among the younger age groups.

When comparing the one-week prevalence of any pain (79.5%) to earlier studies, similar prevalences have been reported from such initial screening questions, but with longer recall periods: 78.6% during six months (Bassols et al. 1999), 80.3% and 74.5% for some pain in the past 12 months (Ng et al. 2002, and Picavet and Schouten 2003 respectively). Bingefors and Isacson (2004) observed a prevalence of 44.5% for any MSK pain or headache during the past two weeks.

Our results regarding the point prevalence of pain (37.3%) are relatively congruent with the earlier studies. For example, 44% had pain on the day of the interview in the study by Buskila et al. (2000). Other roughly comparable results are 29.6% (Català et al. 2002) and 48.9% (Gerdle et al. 2004).

As concluded in the review of the literature, a majority of the recent studies found the overall prevalence of chronic pain to be 17%–29%. The current results show the impact of different definitions. Long-lasting but infrequent pain is more common than daily or continuous chronic pain. Overall, the present results seem plausible: when the non-

respondents were also included, the prevalence of any chronic pain was between 25.3% and 35.1% and that of daily or continuous chronic pain between 10.6% and 14.3%.

This study did not find a sex difference in the prevalence of chronic pain. As described in chapter **2.3.2**, the evidence is inconclusive, although the majority of earlier studies have reported higher prevalences of different pains in females. In this study, females reported on average approximately 0.5 painful bodily localizations more than males did. The prevalences of certain pains, especially neck pain and headache, were higher in females. Some possible explanations for the sex differences were suggested in chapter **2.3.2**. Even if this study failed, due to the moderate response rate of males or some other flaw, to detect some sex difference in the prevalence of chronic pain that actually would exist in Finland, that does not necessarily have any particular practical implications at the population level. However, health care professionals must keep in mind the possible sex differences in pain thresholds and reactions to analgesics (Bradbury 2003).

The most common pain localizations (neck, head, back and knee) reported in this study are virtually identical to those found to be the most common in earlier studies, although the order may vary (see chapter **2.3.3**). The prevalences of different pains varied between the age groups, which is in accordance with other studies. Any detailed comparison of these results is difficult due to the different methodologies and ways to report the results, as discussed in chapter **2.3.3**. Possible national changes in the epidemiology of different pain types, caused by e.g. increased computer work, are difficult to detect, because Finnish health surveys have not reported detailed information of pain locations. For example, Arinen et al. (1998) reported only prevalences of MSK disorders and toothache from the Finnish Health Care Survey 95/96 data. Comparisons with the annual postal population surveys conducted by The National Public Health Institute of Finland are also difficult, as data is collected only on self-reported toothache, back pain and joint pain (cf. Helakorpi et al. 2005).

Paper **I** reported a strong association between chronic pain and poor self-rated health (SRH). Although this was a cross-sectional study, other studies have shown that pain is an antecedent and predictor of poor SRH (see chapter **2.4.3**). The effect of worsening SRH is assumed to be partly mediated by the development of activity limitation. Overall, the epidemiological results obtained from the postal survey seem solid and plausible, especially when the uncertainty in prevalences due to the non-respondents is recognized.

8.3 Use of analgesics and other pain management strategies

This study showed that frequent use of both OTC and Rx analgesics is relatively common. The duration of this frequent use was not measured. However, OTCs are intended only for temporal use. Frequent use of OTC analgesics without examinations and diagnosis of the cause of pain can hide possibly serious pathology. Generally speaking, however, the population's overall selection of different treatment strategies for different pains seemed rational.

Excessive unsupervised use of OTC analgesics, especially concomitantly with several Rx medicines, can be a serious hazard to health. The risk of adverse events, as described in chapter **4.3,** is similar with Rx and OTC analgesics. The risk increases if an OTC NSAID (in Finland: ibuprofen, ketoprofen or ASA) is utilized simultaneously with Rx NSAID, or if various OTC and/or Rx paracetamol preparations are utilized at the same time. In addition, use of two or more different Rx NSAIDs simultaneously increases the risk of adverse events.

The concomitant use of OTC and Rx analgesics (overall prevalence of 3.4%–4.6%) observed in this study is not a new phenomenon. Ahonen et al. (1989) analyzed the analgesic use patterns of 12,056 Finnish farmers. Of them, 375 (3.1%) reported the use of both OTC and Rx analgesics. The prevalence of concomitant use increased with age. It was most strongly associated with the occurrence of pain and psychoneurotic symptoms. The authors speculated that OTCs could be used in order to improve the inadequate pain relief provided by Rx analgesics. The results of Paper **IV** also suggested that OTCs are utilized in addition to Rx analgesics in order to enhance the analgetic effect. As the data utilized by Ahonen et al. (1989) was collected in 1979, not much has changed in over 20 years. A careful interpretation seems to suggest that concomitant use could be increasing. Signs of such development can be found from the other study by Ahonen et al. (1993), which indicated that the prevalence of concomitant use was 1.7% in 1976 and 3.0% in 1987. Naturally, all these results are not directly comparable due to differences in methodologies and study populations. This study did not collect substance level data on which Rx and OTC analgesics were utilized concomitantly. Therefore the actual amount of individuals with excessive risk for adverse events can not be calculated.

In general, the chosen treatments differed logically between pains. Due to cultural differences (e.g. use of herbs or homeopathic products) and differences in the availability of health care services, it is not easy to compare the results to those from other countries. However, based on the earlier studies, it was not surprising that analgesic utilization and medical appointments were common reactions to pain. Possible

implications related to the popularity of physical exercise in pain management are discussed in chapter **9.1**.

The iceberg model (Figure 12) suggested that, quite logically, mild pains are treated independently. Lay referral was also relatively common. Those visiting a physician had chronic intense pain more frequently. However, the results illustrated in the iceberg model must not be considered as a treatment guideline or a recommendation, as it is a description of the current situation. In addition to those trying to manage pain, there was also a group of individuals with pain (6.5% of those with any pain within the past week) who had not attempted to treat their pains within the past six months. On average, their pains were milder compared to those on other levels of referral, yet a quarter of them had chronic pain. Reports of similar results can be found over the decades. For example, in an American telephone survey conducted in 1985, those who had pain but had not consulted any professional, thought that no-one could help their pain (Sternbach 1986). In the study by Breivik et al. (2006) the reported reasons for having untreated chronic pain included: “pain not bad enough”, “nothing more can be done” and “just live with the pain”.

8.4 The KMIC study and information needs related to analgesics

The study conducted in Kuopio Medicines Information Centre revealed the wide range of information needs related to the use of analgesics and pharmacological pain management. Compared to earlier studies, the magnitude of the sample can be considered sufficient for descriptive analyses. For example, Bouvy et al. (2002) analyzed only 488 inquiries related to patients’ overall drug information needs. Maywald et al. (2004) recorded information on 2049 telephone calls during 24 months. However, their data included all the calls, not just those related to analgesics.

Interactions were the most common topic of inquiry. This may be a particularly Finnish phenomenon. The situation may have changed now, but a survey carried out in 84 drug information centres in 16 European countries in 1996, observed that interactions were the most frequent topic of inquiries in only two drug information centres (Müllerová and Vlcek, 1998). A brief review of the questions asked in a Dutch toll-free telephone service showed that interaction questions constituted only 9.2% of the inquiries (Bouvy et al., 2002). In our study, the interaction inquiries were not often related to pain, as analgesics were usually only mentioned as part of the drug regimen. Overall, the results from the KMIC study cannot be considered very generalizable, but they still provide a unique view to problems related to analgesic use.

All analgesic products are accompanied by patient information leaflets (PILs) in packages, and they caused confusion for some study subjects. It has been shown that there are great inconsistencies between the PILs of different brands of generically identical products (Bjerrum and Foged 2003). More attention should be paid to making PILs more comprehensive, and a proposal for producing better PILs has been made (Jones and Seager 2001). PILs should be clear, truthful, based on evidence, and still brief. However, the content and structure of PILs is strictly regulated by the authorities' document templates. European authorities are currently taking steps to improve the readability of PILs and to harmonize the content of the PILs of generic products. Finally, it must be kept in mind that written information cannot replace good communication and counselling. Patients should be fully informed about their medicines (Raynor and Britten 2001).

It might be considered useful to compile structured instructions concerning the information that physicians and pharmacists should provide to people using analgesics. However, this study showed that the range of information needs is very wide, and the type of information needed depends on the analgesic in question. Other factors affecting the content of optimal information might include the characteristics of the patient's pain, related diseases and beliefs, attitudes and fears. Patient counselling could be customized by ensuring that there is sufficient discussion with the patient. Patients should feel free to speak and ask questions about whatever is important or of concern to them.

9 CONCLUSIONS AND IMPLICATIONS

Based on the present results, the following conclusions can be made:

1. Pain is a very common complaint in Finland. The prevalence of daily or continuous chronic pain increases with age, being 10.6%–14.3% among the population aged 15–74 years. Chronic pain, especially daily or continuous chronic pain, is independently and very significantly associated with poor self-rated health.

2. The selection of pain management strategies at the population level is wide. Treatments vary according to the location and type of pain. Use of analgesics, physical exercise and health care referral are the most common reactions to pain. Frequent and intense pain and pain in multiple locations are associated with the use of multiple treatments.

3. Frequent use of both Rx and OTC analgesics is common in Finland. Concomitant use of both also occurs in a notable proportion of the adult population.

4. The general public has diverse needs for information on analgesics. The inquiries addressed to KMIC are frequently related to interactions, dosage and adverse effects. In addition, people also ask questions about how to treat pain pharmacologically.

9.1 Practical implications and future prospects

The relatively high prevalence of chronic pain, especially that of daily or continuous chronic pain, implicates a need for actions to prevent and minimize painful conditions. Unfortunately, there are no easy solutions available. Active and effective treatment of acute pains is one way to prevent chronic pain. As the review of the literature showed, once a chronic pain has developed, the prognosis of pain is poor. Possible interventions at the population level (e.g. education campaigns about safe and effective pain management) or in primary health care (e.g. intensive multidisciplinary treatment programs) are challenging and resource-consuming to execute. Verification of the possible long-term outcomes of such interventions, with sufficient statistical power, can also be difficult. The topical review by Smith et al. (2007) summarized that so far community-based psychosocial interventions and physical therapies have been found, at best, to be of a marginal benefit in reducing pain. To date, interventions have been most effective in highly selected secondary care samples of people with pain. There have also been some population-based interventions in some countries that have improved attitudes towards pain. In my opinion, some actions are needed in Finland to reduce the prevalence of chronic pain. Health care personnel and decision makers should bear in their mind how prevalent and persistent problem pain really is.

Although the consequences of pain were not studied in this thesis, based on the review of the literature it can be assumed that the subjective and economic burden caused by pain is immense also in Finland. The negative effect of pain on the quality of life is obvious, but up-to-date data on the economic impact of pain is needed. Cost-of-illness studies could be done on specific pains, such as low back pain or neck-shoulder pain. In addition to direct costs due to health care visits, examinations and drug costs, the indirect costs of absenteeism from work and disability pensions should also be calculated. Cost-effectiveness studies of different pain-specific management strategies could help decision makers. Further, comparison of the costs of untreated or under-treated pain to the costs of effective pain management could also lead to more efficient allocation of the scarce financial resources.

Smith et al. (2007) recently suggested that the scope of the epidemiological research of pain should be broadened to the biological mechanisms of chronic pain. They proposed that there will be some biological markers, such as genes, found for specific pain conditions. Therefore epidemiologists will need new tools for taking biological samples for e.g. DNA testing. Also the use of brain imaging techniques should be considered. However, this requires expensive prospective cohort studies, before new understanding of the chronic pain, its prevention and treatments can be achieved.

The most delightful result of this study was that Finns use physical exercise for treating MSK pains. A big proportion of people seem to consider physical exercise as a way to manage pain. This could result in good outcomes, if more systematic exercises were widely offered to people visiting health care services due to different pains. Various active training programs have already been developed. For example, Ylinen et al. (2003) studied the effects of neck muscle training in the treatment of chronic non-specific neck pain. Participation in a one-year strength training program considerably reduced neck pain and disability compared to a control group. Coping with headache can also be improved by light daily resistance training at the workplace (Sjögren et al. 2005). Van Baar et al. (1999) conducted a systematic review of the literature and concluded that there is evidence of the beneficial effects of exercise on pain in patients with osteoarthritis of hip and knee. Even a simple home-based exercise programme with elastic bands has been found to significantly reduce knee pain (Thomas et al. 2002). The review by Winett and Carpinelli (2001) stated that resistance training reduces the incidence of back injuries and reduces low back pain. Yoga has also been found to alleviate chronic low back pain (Sherman et al. 2005). In addition to improving muscle strength, physical exercise may have an indirect route of action by reducing body weight. As summarized by Nevitt and Lane (1999), weight loss can reduce the painful symptoms of osteoarthritis of knee and hip.

This study showed that frequent use of OTC analgesics, sometimes together with Rx analgesics, is relatively common in Finland. Therefore, both the dispensers and the prescribers of analgesics and other medication should routinely ask the patients about their use of OTC analgesics and inform them about possible interactions and other risks when necessary. As demonstrated by the results of the KMIC study (paper **IV**), people need information and counselling related to analgesic use. The great challenge for pharmacy personnel is to identify those with irrational and possibly harmful analgesic use patterns from the constant flow of customers. Placement of OTC analgesics behind the counter could possibly lead to better communication between pharmacists and customers. However, this could be impractical in real life due to the large number of customers purchasing OTCs. Still, it must be kept in mind that OTC analgesics contain same active substances as Rx analgesics, and no such thing as a “simple” or “mild” analgesic exists.

At the end of 2006, Finland’s National Agency for Medicines was campaigning in television, internet, newspapers and magazines for more rational use of analgesics. Hopefully, this will have some long-term effects and encourage people purchasing OTC analgesics to consult their pharmacists more actively. Pharmacies must ensure that their customers always have an opportunity to discuss their choice of OTC analgesic and the

use of other drugs with a licensed pharmacist. Counselling and referral to a physician as needed contribute to good pharmacological pain management and prevention of adverse events. In addition, physicians' good follow-up of pain patients might lead to more efficient, rational and safe analgesic utilization habits.

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APPENDICES

Appendix 1 (Table).
Major studies on the epidemiology and prevalence of non-specific pain in the general population published after the year 1996.

Appendix 2.
The questionnaire in English.

Appendix table 1. Major studies on the epidemiology and prevalence of non-specific pain in the general population published after the year 1996.

Reference	Country / area and target population	Data collection method	Studied pain type(s)	Prevalence of studied pain type(s)	Comments
Andersson 2004 (a 12-year follow-up of the studies by Andersson et al. 1993 and Andersson et al. 1996)	Sweden / Skåne. A cohort recruited from the general rural population aged 25 to 74 yr.	A postal questionnaire was sent to 183 eligible members of the original cohort (n=214) in the spring 2000.	Chronic pain, defined as pain with duration for over 3 months.	71% had chronic pain, compared to 63% 12 yr ago. After 12 yr, 34% of the individuals initially without chronic pain reported such pain. When the analysis was limited to the eligible individuals who responded, 85% of those who reported chronic pain 12 yr ago still had chronic pain.	Response rate at follow-up was 77% after excluding dead and unreachable individuals. Prevalence figures cannot be widely generalized due to a compromise in cohort structure: those without chronic pain were underrepresented.
Bassols et al. 1999	Spain / Catalonia. Population of 6,000,000.	Telephone interview in the year 1994 for a representative sample of the 1964 respondents aged 18 and over.	Any pain experienced during the past 6 months.	Overall prevalence 78.6% (females 85.6%; males 71.5%). Decreasing trend with aging.	High participation rate of 91.7%. Long recall period for any pain. No way to distinguish between severe and minor pains.
Bergman et al. 2001	Sweden / Halmstad and Laholm. Altogether 70,704 inhabitants aged 20-74 yr.	Postal survey in the year 1995 to a random sample of 3928 subjects aged 20 to 74 yr. Two reminders, the 2nd with an opportunity to fill in a short simple form.	Persistent or regularly recurrent musculoskeletal pain for more than 3 months during the past 12 months.	Any chronic musculoskeletal pain 34.5%; minimum possible prevalence 24.7%; estimated prevalence in the whole sample, based on an analysis of nonrespondents 31.4%. Prevalence was higher among females than males (38.3% vs. 30.9%). Increasing trend with aging up to 69 yr.	A moderate response rate of 61.7%, in addition to which 8.4% returned the simple form. Only musculoskeletal symptoms were included. Long recall period. A sample of nonrespondents was interviewed via telephone.
Bergman et al. 2002 (A 3-year follow-up of the above described study.)	Sweden / Halmstad and Laholm. 2425 individuals who completed the extensive questionnaire in the earlier survey were now followed up.	A 3-year follow-up from 1995 to 1998 with a postal questionnaire.	Original respondents were categorized as having no chronic pain, chronic regional pain (CRP), or chronic widespread pain (CWP).	There was no significant change in the overall prevalence over 3 yr. However, 16.4% of the subjects with initial CRP had developed CWP, and 56.9% of those with initial CWP still had it.	Follow-up reached 79% of the original respondents. Only 16.3% of the subjects with CWP did not have any chronic pain after 3 yr.

cont.

Appendix table 1. Major studies on the epidemiology and prevalence of non-specific pain in the general population published after the year 1996 (cont).

Reference	Country / area and target population	Data collection method	Studied pain type(s)	Prevalence of studied pain type(s)	Comments
Bingefors and Isacson 2004	Sweden / Uppland county. Approx. 290,000 inhabitants in 1995.	A postal survey in 1995 to a random sample of 8000 persons aged 20 to 84 yr. Of the 5404 respondents, 4506 working-aged (20-64 y) individuals were selected for this study.	Musculoskeletal pain or headache during the 2 weeks prior to filling out the questionnaire.	Any musculoskeletal pain or headache 44.5% (Females 50.0%; Males 38%).	Initial response rate was 68%.
Blyth et al. 2001	Australia / New South Wales. Population of over 6,000,000 people.	Telephone interview using randomly generated numbers, in the year 1997. 17,543 completed interviews with subjects aged 16 yr or older.	Chronic pain, defined as "pain experienced every day for 3 months in the 6 months prior to interview".	The prevalence of chronic pain was 20.0% among females and 17.1% among males. Having chronic pain was significantly associated with older age and female sex.	Participation rate was 70.8%. Overall prevalence was not reported.
Breivik et al. 2006	Adult population of 15 European countries (including Finland) and Israel.	Large (n=46,394, of whom 2004 Finns) telephone interview in the summer 2003 to screen for subjects 18 yr and older with chronic pain. Additional in-depth interviews of 4839 screened subjects, of whom 303 were Finns.	Chronic pain, defined as pain that the subject had suffered from for 6 months or longer, pain in the last month and several times during the last week, and the pain intensity that was moderate or worse.	19% of the 46,394 respondents willing to participate had chronic pain (Spain 12%; Norway 30%; Finland 19%). Of the subjects with chronic pain, 56% were females. 41- to 60-yr-old subjects had most likely chronic pain.	Industry-driven project. Respondents to in-depth interview were offered money for their participation. Only people listed in phone directories were included. Participation rate was 54% (Germany 38%; Finland 80%).
Buskila et al. 2000	Israel / Negev, town of Yeruham. 4643 inhabitants aged 18 yr or older.	Sample of 2322 (fraction of 50%) was contacted by phone in the year 1997. 2210 agreed to participate in a face-to-face interview.	Any pain on the day of the interview. Chronic regional pain (CRP), chronic widespread pain (CWP). Chronic was defined as pain that had been present for at least 3 months.	44% of participants had pain on the day of the interview. 13.8% had CRP (females 14%, males 13%) and 9.9% had CWP (females 14%; males 3%). The subjects with no pain were the youngest, and those with CWP were the oldest.	High participation rate of 95.2%. Authors described the town of Yeruham as being representative of other towns in Negev, and referred to their study subjects as a general population.

Català et al. 2002	Spain / continent, Balearic Islands and Canary Islands. Whole adult population.	Telephone interview in 1998 to 5000 subjects aged 18 to 95 yr.	Any pain on the previous day and any pain during the week preceding the interview. Chronicity of pain (duration longer than 3 months).	29.6% had had pain on the previous day (females 37.6%; males 20.9%). 43.2% had had pain during the preceding week. The prevalence of chronic pain was 23.4% (females 31.4%; males 14.8%). The prevalences of both any pain and chronic pain were higher in the older age groups.	42% of initial contacts led to an interview.
Elliott et al. 1999	United Kingdom / Scotland, Grampian region. Grampian adult population.	Postal survey to a random sample of 5036 subjects aged 25 yr and older, drawn from general practice databases.	Chronic pain, defined as pain which had lasted longer than 3 months.	50.4% of the respondents had chronic pain (females 51.8%; males 48.9%). Significant increase with age. After standardization, the overall prevalence of chronic pain in the general population was estimated to be 46.5%.	The actually reported response rate was 82.3%. However, only 3605 subjects (71.5%) of the initial sample responded. The year of the study was not reported.
Elliott et al. 2002 (A 4-year follow-up of above described study.)	3605 individuals who returned the questionnaire in the earlier survey were now followed up.	A 4-yr follow-up from 1996 to 2000 with a postal questionnaire presented to the 2422 individuals willing to participate.	Chronic pain, defined as pain which had lasted longer than 3 months.	Of the individuals reached for follow-up, 45.5% had chronic pain at baseline. After 4yr the prevalence was 53.8%. The increase was larger among females and the youngest subjects (25-34yr at baseline). 78.5% of those with chronic pain at baseline still had it. Average annual incidence was 8.3% and annual recovery rate was 5.4%.	The actually reported corrected response rate was 83.0% because only 1937 questionnaires were successfully delivered. However, only 2422 (67.2%) of the 3605 original respondents were willing to participate in further research, and 1608 (44.6%) really responded.
Eriksen et al. 2003	Denmark. The whole adult population.	Face-to-face interviews of 12,333 participants from a random sample of 16,684 Danes aged over 16 yr in the year 2000. In addition, a postal survey was used to collect more data.	Chronic non-malignant pain (pain lasting for 6 months or more).	Overall prevalence of chronic pain was 19% (females 21%; males 16%). Prevalence of chronic pain increased with age.	The original sample comprised 16,684 subjects. 74% were interviewed. After excluding those who did not return the completed postal survey and those with cancer, 10,066 (60.3%) were included in this study.

cont.

Appendix table 1. Major studies on the epidemiology and prevalence of non-specific pain in the general population published after the year 1996 (cont).

Reference	Country / area and target population	Data collection method	Studied pain type(s)	Prevalence of studied pain type(s)	Comments
Gerdle et al. 2004	Sweden / Östergötland county. 284,073 people aged 18 to 74 yr.	A postal survey in 1999 to a representative sample of 9952 subjects aged 18 to 74yr.	Any pain today, any pain during the previous month, recurring pain during the previous 3 months. How long had the pain lasted? Over 3 months was considered chronic.	Overall point prevalence (any pain today) was 48.9%. One-month period prevalence was 63.0% and that of recurring pain during 3 months 61.3%. The prevalence of chronic pain was 53.7%. Prevalences were higher among females and associated with aging.	Response rate after two reminders was good, 76.7%.
Hagen et al. 1997 Hagen et al. 2000	Norway / Oslo and Nordland counties. The whole adult population.	A postal survey to 20,000 randomly selected subjects aged 20 to 79yr.	Any musculoskeletal (MSK) pain during the past month. Any non-inflammatory MSK pain during the past month. Regional or widespread non-inflammatory MSK pain during the past month. ('Non-inflammatory defined as pain without a report of inflammatory rheumatic diagnosis. 'Widespread' defined as pain in both the upper and the lower parts of the body.)	Prevalences of differently, but not exclusively defined MSK pains during the past month: any pain 60.8%; any non-inflammatory pain 54%; regional non-inflammatory pain 37%; widespread non-inflammatory pain 17%. The highest prevalence of widespread pain was found among females aged 50-64 yr.	Response rate after one reminder was moderate, 58.9%. The year of data collection was not reported. Basic results reported separately in two papers.

Hunt et al. 1999	United Kingdom / England, Greater Manchester area. Adult population registered at general practice.	Postal survey to 3004 randomly sampled individuals aged 18-65 yr.	Any pain lasting for at least 24 hrs during the previous month. Chronic widespread pain according to both the American College of Rheumatology definition: Pain present in at least 2 contralateral body quadrants and the axial skeleton for at least 3 months, and the Manchester definition: Pain in at least 2 sections of 2 contralateral limbs and in the axial skeleton for at least 3 months.	The crude prevalence of any pain lasting for 24 hrs during the past month was 57%. The American College of Rheumatology definition of chronic widespread pain was satisfied by 12.9% (n=252), and the Manchester definition was satisfied by 4.7%. After adjustments, the prevalence according to the Manchester definition was estimated to be 4.3% in the population. No statistically significant difference between the sexes, but the prevalence increased with age.	402 subjects did not receive the questionnaire. Two reminders were sent. Of those who actually received the questionnaire, 1953 (75%) responded. The differences in prevalences between the two definitions of chronic widespread pain were related to the fact that limb pains were localized rather than diffuse. The year of the data collection was not reported.
Jensen et al. 2004	Denmark. The whole adult population.	Face-to-face interviews of 4667 participants from a random sample of 6000 Danes aged over 16 yr in the year 1994. In addition, a postal survey was used to collect more data.	Intensity of pain during a 4-week recall period rated on a verbal pain rating scale: No pain; very mild or mild pain (low pain group) or moderate, severe, or very severe pain (high pain group).	Overall prevalence of “high pain” was 14% and that of “low pain” 43%. Female sex and older age were found to be important determinants of belonging to “high pain group”.	The original sample comprised 6000 subjects. 77.8% were interviewed. After excluding those who did not return the completed postal survey and those with cancer, 3992 (66.5%) were included in this study. No data on the duration or frequency of the pain.

cont.

Appendix table 1. Major studies on the epidemiology and prevalence of non-specific pain in the general population published after the year 1996 (cont).

Reference	Country / area and target population	Data collection method	Studied pain type(s)	Prevalence of studied pain type(s)	Comments
Leroux et al. 2005	Canada / province of Quebec. 7,246,896 inhabitants.	Initial face-to-face interview and questionnaire in 1998 to one member of each of the sampled 11,986 households representing 30,386 individuals. Then a second questionnaire to every individual in these households. Participants aged 18 and over were included in this study.	Short-term (within 2 weeks) and long-term (not defined) activity limitations due to musculoskeletal disorders (MSD) such as osteoarthritis, back disorders, rheumatism, and strains.	Within the previous 2 weeks, 2.3% had had short-term activity limitations related to MSD. 3.8% had had long-term activity limitations due to MSD. Both were more common among females and increased with age.	Initial participation rate in the interview was 82.1% and the response rate to the second questionnaire was 84.0%, the total completion rate of individuals being 69%. This includes those aged 15 yr to 17 yr, who were excluded. Real participation rate of the actual study group was not reported. Actual pain was not measured, just activity limitations.
McBeth et al. 2001 (A follow-up of the study by Hunt et al. 1999, see above)	The 252 subjects in the study by Hunt et al. who were classified as having a chronic widespread pain (CWP).	A 1-year follow-up of the patients with CWP with a postal questionnaire.	Chronic widespread pain according to the American College of Rheumatology definition: Pain present in at least 2 contralateral body quadrants and the axial skeleton for at least 3 months.	Of the respondents, 11% reported no pain at follow-up. 56% still reported CWP. 33% had some other pains that did not satisfy the criteria for CWP.	246 subjects were still living in the same address. Of them, 91% participated in follow-up.

Moulin et al. 2002	Canada. The whole adult population.	Telephone interview using randomly generated numbers, in the year 2001. 2012 completed interviews of subjects aged 18 to 75 yr.	Chronic pain, defined as “continuous or intermittent pain for at least 6 months”.	Chronic non-cancer pain was reported by 29% of the respondents (females 31%; males 27%). The prevalence of pain increased in the older age groups.	Participation rate was low 19.1%
Ng et al. 2002	China / Hong Kong. The whole adult population of 5.1 million inhabitants.	Telephone interview of 1051 subjects aged over 18 yr. The numbers were randomly selected from telephone directories.	Any pain in the past 12 months. Chronic pain, defined as “pain persisting for more than 3 months.”	80.3% of the respondents had had some pain in the past 12 months. The prevalence of chronic pain was 10.8%. Chronic pain was associated with female sex (adjusted OR 1.5) and age higher than 60 yr (OR 2.2).	Non-Caucasian studies on the epidemiology of pain are rarely published in Western journals. Only those speaking Cantonese were included. Participation rate was moderate 47.7%. Long recall period.
Ohayon and Schatzberg 2003, Ohayon 2004	The adult population of five European countries with a total of over 205 million inhabitants: Germany, Italy, Portugal, Spain and United Kingdom.	A telephone interview during the years 1994 to 1999, using randomly selected phone numbers. The 18,980 participants were aged 15 yr or older, except in Portugal 18 yr or older.	A chronic painful physical condition that had lasted for at least 6 months and had consequences on daily functioning or required medication (or required a health specialist consultation).	A total of 17.1% of the participants reported having a chronic painful physical condition (females 20.7%; males 13.2%). The prevalence increased linearly with age.	The overall participation rate was 80.4% (68.1% in Germany, 89.4% in Italy). The description of methods and definitions differed slightly between the two papers on the same data.

cont.

Appendix table 1. Major studies on the epidemiology and prevalence of non-specific pain in the general population published after the year 1996 (cont).

Reference	Country / area and target population	Data collection method	Studied pain type(s)	Prevalence of studied pain type(s)	Comments
Papageorgiou et al. 2002 (A follow-up of study by Croft et al. 1993)	United Kingdom / England, Cheshire area. Population originally aged 20-85 yr, who participated in surveys during 1991-1992.	A follow-up postal survey in 1998 to 1588 subjects who participated in the original surveys and were still alive, born after 1916 and were still registered with the same practice.	Chronic widespread pain according to American College of Rheumatology definition: Pain present in at least 2 contralateral body quadrants and the axial skeleton for at least 3 months.	The crude prevalence of CWP among the participants of the follow-up was 11% at baseline and 10% at follow-up. 34.1% of those with CWP at baseline had it after approximately 7 years and 51% still had other pain. Only 15% of the original CWP patients were free of pain. By comparison, 2% of the original subjects with no pain had developed CWP.	Baseline data was collected in two sets. Original paper by Croft et al. (1993) reported results from only the first data set. The original samples included a total of 3195 subjects. Of them, 2334 (73%) responded. Of them, 1588 (68%) were attempted to reach for follow-up. Of them, 1386 (87%) responded. Thus, actually 59% of the original respondents participated in the follow-up.
Picavet and Schouten 2003	Netherlands. The population aged 25 yr and older of over 10 million inhabitants.	Postal survey to a random stratified sample of 8000 subjects aged 25 yr or over.	Any musculoskeletal pain during the past 12 months. Any pain during the survey (point prevalence). Chronic pain lasting longer than 3 months.	The prevalence of any pain during 12 months was 74.5% and that of any pain during the survey 53.9%; 44.4% reporterd chronic pain. Women had higher prevalences.	The response rate after two reminders was moderate 46.9%. The year of data collection was not reported. Long recall period for any pain.
Portenoy et al. 2004	U.S.A. / Continent. The whole Hispanic / Latino, non-Hispanic African American and non-Hispanic white adult populations.	Telephone interview in the year 2002, using randomly generated phone numbers, to subjects aged 18 or older. According to inclusion criteria, only the aforesaid ethnic groups were asked about existence of chronic pain.	Frequent or persistent pain for at least 3 consecutive months during the past year (=chronic pain).	Among the contacted subjects, the prevalence of chronic pain was 28% in Hispanic, 35% in white, and 39% in African American subjects.	Initial participation rate not reported. Those with chronic pain were asked to participate in a further interview. 94.4% co-operated.

Rustøen et al. 2004a, Rustøen et al. 2004b Rustøen et al. 2005	Norway. The whole Norwegian adult population.	A postal survey in the year 2000 to a random sample of 4000 Norwegians aged 19 to 81yr.	Any pain in general. Chronic pain, defined as lasting longer than 3 months.	Of the respondents, 28.3% reported pain in general. The prevalence of chronic pain was 24.4%. More females than males reported chronic pain. Prevalence increased with age.	Response rate was moderate 48.5%. One reminder was sent. The main findings of the same survey have been separated into 3 articles.
Smith et al. 2001 (Same data as in the study by Elliott et al. 1999, see above)	United Kingdom / Scotland, Grampian region. Grampian adult population.	Postal survey to a random sample of 5036 subjects aged 25 yr and older, drawn from general practice databases.	Significant chronic (over 3 months) pain: painkillers had been taken and treatment sought recently and frequenly. Severe chronic pain: had resulted in high disability and severe limitation.	Of the respondents, 14.1% had significant chronic pain (females 15.8%; males 12.3%). 6.3% had severe chronic pain (females 6.9%; males 5.7%). After adjustments, overall prevalences were estimated to be 12.3% and 5.7% respectively. The prevalences increased with age.	This paper reports the prevalence of the most severe and incapacitating chronic pain, using the same data as Elliott et al. 1999.

Appendix 2.

The questionnaire in English. This study was conducted with Finnish and Swedish questionnaires. The English translation has not been validated or used in the study.

Answer the questions by circling the number of the reply alternative you find most suitable, or by writing your answer in the available space.

PART I Experiences of pain

1. Have you felt any pain or ache during the past week (7 days)?

1 No. **Proceed to question #5.**

2 Yes. **Circle all the pains you have experienced during the past week.**

1 Headache
2 Pain in the ear
3 Tooth pain
4 Sore throat
5 Neck pain
6 Pain in the shoulder or upper arm
7 Pain in the elbow or forearm
8 Pain in the wrist, hand or fingers
9 Chest pain
10 Back pain
11 Abdominal pain
12 Menstrual pain
13 Pain in the groins or genitals
14 Hip pain
15 Pain in the thigh
16 Knee pain
17 Leg pain
18 Pain in the ankle, foot or toes
19 Some other pain(s). **Which pain(s)?**

_____

_____

_____

_____

2. If you selected more than one pain, which one of them bothers you most, i.e. which is your worst pain?

_____

3. How long has this worst pain continued?

1 Less than a week
2 1 - 4 weeks
3 Over 1 month - 3 months
4 Over 3 months - 6 months
5 Over 6 months

4. By using the scale below, rate how <u>intense</u> your pain has been. Circle the number which best describes the intensity of your pain. (0 = no pain, 10 = the worst imaginable pain)

No Pain — Worst Possible Pain

0 1 2 3 4 5 6 7 8 9 10

5. How <u>frequently</u> have different pains bothered you?

1 Never. **Proceed to question #9.**

2 Less frequently than once a month
3 Approximately once a month
4 Approximately once a week
5 Several times a week
6 Every day or night
7 Several times a day
8 Pain is continuous

6. Does your pain interfere with your normal everyday life?

1 No. **Proceed to question #7.**

2 Yes. **How? You can select multiple answers.**

1 Pain limits mobility
2 Pain interferes with eating
3 Pain interferes with urinating and / or defecation
4 Pain disturbs sleeping
5 Pain depresses
6 Pain disturbs work or studying
7 Pain disturbs hobbies and leisure activities
8 Pain interferes with sexual functioning
9 Pain disturbs housework
10 Pain disturbs human relationships
11 Pain causes some other disturbance. **What kind of disturbance?**

_____

_____

_____

TURN THE PAGE

PART II Experiences of pain management

7. How have you treated your pain(s) during the past six months? You can select multiple answers.

1 I have not done anything. **Proceed to question #9.**

2 I have used over-the-counter (non-prescription) analgesics
3 I have visited a physician
4 I have used prescribed analgesics
5 I have done exercise / stretching / sports (e.g. Nordic walking, swimming)
6 A friend or a family member has massaged
7 I have visited a masseur / masseuse
8 I have visited a physiotherapist
9 I have visited a chiropractor / osteopath / naprapath
10 I have received acupuncture treatment
11 I have stayed out of work / school
12 I have abstained from doing housework
13 I have treated pain in some other way. **How?**

_____

_____

_____

_____

_____

8. Which treatment has helped you best?

_____

_____

_____

_____

9. How often do you use analgesics <u>prescribed by a physician?</u>

1 Daily
2 A few times a week
3 A few times a month or less frequently
4 I do not use analgesics prescribed by a physician

10. How often do you use <u>over-the-counter (non-prescription) analgesics?</u>

1 Daily
2 A few times a week
3 A few times a month or less frequently
4 I do not use over-the-counter (non-prescription) analgesics

11. If you have treated your pain(s) with medicines, which medicine(s) do you think have helped you most? Write the name(s) of the medicines on the lines below.

_____

_____

_____

_____

12. Due to your pain(s), have you had to take higher doses of medicines than prescribed or instructed on the package?

1 I have not treated pain with medicines
2 I have not been forced to take higher doses than instructed
3 Yes, I have been forced to take medicines in higher doses than prescribed or instructed on the package.
Which medicines and how high doses have you had to take?

_____

_____

_____

_____

_____

_____

_____

_____

PART III Your health status

13. How would you rate your current health?

1 Good
2 Quite good
3 Moderate
4 Rather poor
5 Poor

14. Have you been on sick leave due to pain during the past six months?

1 No.
2 Yes. **How many days altogether?**

_____

15. Do you feel any pain or ache right now, at this very moment?

1 No.
2 yes. **What kind of pain or ache?**

_____

_____

16. Do you have any chronic illnesses?

1 No.
2 Yes. **Which illnesses?**

_____

_____

_____

_____

_____

_____

17. Please check the section "insurance data" from the reverse side of your personal sickness insurance card. If there are any 3-digit reimbursement numbers (e.g. 103, 201, 205 etc.) please write the numbers down:

_____

18. Below are ten statements describing your mood during the past month. There are four reply alternatives to each statement. Circle the number which best corresponds your personal feelings.

During the last month, I have	Not at all	A little	Quite a lot	Extre-mely
Suffered from insomnia	0	1	2	3
Felt blue	0	1	2	3
Felt everything was an effort	0	1	2	3
Felt low in energy or slowed down	0	1	2	3
Felt lonely	0	1	2	3
Felt hopeless about the future	0	1	2	3
Not got any fun out of life	0	1	2	3
Had feelings of worthlessness	0	1	2	3
Felt all pleasure and joy has gone from life	0	1	2	3
Felt that I can not shake off the blues even with help from family and friends	0	1	2	3

TURN THE PAGE

PART IV Your background information

This information is very important for the success of the study.

19. Your year of birth _____

20. Your sex

1 Male
2 Female

21. Circle from the list every schooling and degree you have completed:

1 Elementary school 6 years
2 Elementary + secondary school 4+5 years
3 Modern comprehensive school 9 years
4 Vocational school
5 Vocational institute
6 Senior secondary school
7 Polytechnic degree
8 Academic degree, including post-graduate studies
9 None of the above mentioned
10 Some other education. **What?**

_____

22. What is your <u>current</u> employment status?

1 I'm working
2 I'm a student
3 I'm temporarily not working (due to e.g. maternity leave, or child care leave)
4 I'm on sick leave / sickness benefit
5 I'm laid off or unemployed
6 I'm retired

23. If you are working, temporarily not working, or retired, what is or was your level of profession?

1 Entrepreneur
2 Agricultural entrepreneur (farmer)
3 Higher administrative employee (e.g. manager, researcher, designer, teacher)
4 Lower administrative employee (e.g. foreman, office worker)
5 Laborer (e.g. industry work, manufacturing, working in delivery or services)
6 Something else. **What?**

_____

24. How would you rate your current economic status?

1 Good
2 Quite good
3 Moderate
4 Rather poor
5 Poor

25. Please, list <u>all</u> the medicines you are currently taking (also non-analgesic medicines) and natural products etc. (e.g. vitamins, cold gels). Write down the product name (e.g. Lisipril) and the treatment indication (e.g. hypertension).

Product name	Indication
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

Thank you for your thoroughness. If you wish, you can write on a separate sheet or on the back of the cover letter your experiences of pain and its management.

LIST OF ORIGINAL PUBLICATIONS

I Mäntyselkä P, Turunen J, Ahonen R, Kumpusalo E. Chronic pain and poor self-rated health. JAMA 290: 2435–2442, 2003

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2006. 115 p. Acad. Diss.

A 96. Haapalinna, Antti. The Effects of Atipamezole on Brain Neurochemistry and Behaviour in Laboratory Rodents – Possible Implications for the Treatment of Neurodegenerative Diseases with an Alpha2-adrenoceptor Antagonist.
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A 98. Jarho, Elina. Synthesis, Structure-Activity Relationships and Physico-Chemical Properties of Novel Prolyl Oligopeptidase Inhibitors.
2007. 121 p. Acad. Diss.