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NIINA KARTTUNEN

*Pain, Persistence of Pain
and Analgesic Use
in Community-Dwelling
Older Finns*

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NIINA KARTTUNEN

*Pain, Persistence of Pain and Analgesic Use
in Community-Dwelling Older Finns*

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ABSTRACT

People live longer and pain-related conditions become more common in old age. Since there are many confounding factors related to pain treatment in older people, concerns have been raised regarding the management of pain. Pharmacokinetic and pharmacodynamic changes that occur with normal ageing, common multimorbidity and polypharmacy may all increase the risk of inappropriate use of pain medication. A better understanding of pain and its treatment can assist in achieving the goals of optimizing pain management in this age group.

This study aimed to determine the pattern of analgesic use, the persistence of chronic pain, and factors related to mobility limitation in community-dwelling older Finns. In addition, older persons' perceptions of whether they hoped to receive more attention from the physician in the management of their pain were explored.

This study utilized the data collected in the population-based Geriatric Multidisciplinary Strategy for the Good Care of Elderly (GeMS). The GeMS was conducted in 2004–2007 and the participants (n=1000) aged ≥ 75 years and living in Kuopio, Finland, were randomly selected from the population register of Kuopio. The participants were randomized to intervention (n=500) and control (n=500) groups, and both groups were interviewed annually by study nurses to assess health status and drug use. Those subjects in the intervention group underwent an annual comprehensive geriatric assessment including physician's examination with medication assessment, physiotherapist's counselling and a nutritionist's appointment if needed.

Musculoskeletal chronic pain is often persistent, i.e. the majority of those participants with pain at baseline suffered from it also after two follow-up years. Almost half of the community-dwelling older participants were using analgesics and analgesic drugs were most commonly taken on an as needed rather than on a daily basis. Females were more commonly analgesic users than men, and paracetamol was the most commonly taken analgesic drug. The risk of mobility limitation was highest among analgesic users with pain and it was associated with older age, poor overall health, living alone, sedentary lifestyle and poor muscle strength. Almost half of older people with musculoskeletal chronic pain hoped that the physician would be paying more attention to the management of their pain.

This study showed that there is an evident need for better pain management in community-dwelling older people. Regular pain assessments, evaluation of the effectiveness of treatment, and developing new strategies to manage pain are needed to optimize pain treatment. In addition, adjuvant therapy with nonpharmacological approaches should be encouraged to supplement pharmacological pain management.

National Library of Medicine Classification: WL 704, WL 704.6, WT 500, QV 95, WE 103

Medical Subject Headings: Pain; Chronic Pain; Musculoskeletal Pain; Pain Management; Drug therapy; Analgesics; Acetaminophen; Mobility Limitation; Physician-Patient Relations; Independent Living; Aged; Aged, 80 and over; Finland

Karttunen, Niina

Kipu, kivun pysyvyys ja kipulääkkeiden käyttö kotona-asuvilla iäkkäillä suomalaisilla

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TIIIVISTELMÄ

Ihmiset elävät pidempään ja kipu ja sairaudet yleistyvät vanhuudessa. Monista sekoittavista tekijöistä johtuen kivun hoito iäkkäillä herättää huolta. Normaalin ikääntymisen seurauksena tapahtuvat farmakokineettiset ja farmakodynaamiset muutokset, sekä monet sairaudet ja lääkitykset lisäävät riskiä käyttää kipulääkkeitä epätarkoituksenmukaisesti. Tietämys kivusta ja sen nykyhoidosta voi auttaa saavuttamaan tavoitteen kivun hoidon optimoinnista tällä ikäryhmällä.

Tässä väitöstutkimuksessa tarkasteltiin kipulääkkeiden käyttöä, kroonisen kivun pysyvyyttä ja tekijöitä, jotka ovat yhteydessä liikuntakyvyn rajoittumiseen kotona-asuvilla iäkkäillä suomalaisilla. Lisäksi selvitettiin toivoisivatko iäkkäät kivun hoitoon enemmän huomiota lääkäriltä.

Tutkimuksessa analysoitiin aineistoa, joka kerättiin väestöpohjaisessa Hyvän Hoidon Strategia (HHS) -tutkimuksessa. HHS toteutettiin vuosina 2004–2007 ja yli 75-vuotiaat osallistujat (n=1000) oli satunnaisesti valittu kuopion väestörekisteristä. Osallistujat satunnaistettiin interventio (n=500) ja kontrolli (n=500) -ryhmiin, ja tutkimushoitaja haastatteli molemmat ryhmät vuosittain terveydentilan ja lääkkeiden käytön selvittämiseksi. Interventioryhmään kuuluville tehtiin vuosittain geriatrinen arviointi, johon kuului lääkärin tutkimus ja lääkehoidon arviointi sekä fysioterapeutin neuvonta ja ravitsemusterapeutin tapaaminen tarvittaessa.

Tutkimuksen mukaan krooninen tuki- ja liikuntaelinkipu on erittäin pysyvää luonteeltaan, sillä suurin osa lähtötilanteessa kipua kokevista iäkkäistä kärsi kivuista myös kahden seurantavuoden aikana. Lähes puolet kotona-asuvista iäkkäistä käytti kipulääkkeitä ja suurin osa käyttäjistä käytti kipulääkkeitä vain tarvittaessa. Naiset käyttivät kipulääkkeitä yleisemmin kuin miehet ja parasetamoli oli käytetyin kipulääke. Liikuntakyvyn rajoittumisen riski oli suurin kipulääkkeiden käyttäjillä, joilla oli kipuja ja se oli yhteydessä korkeampaan ikään, huonoksi koettuun terveyteen, yksin asumiseen, vähäiseen liikuntaan ja huonoon lihasvoimaan. Lähes puolet kroonista tuki- ja liikuntaelinkipua kokevista iäkkäistä toivoi, että lääkäri kiinnittäisi enemmän huomiota kivun hallintaan.

Tutkimus osoitti että kotona-asuvat iäkkäät tarvitsevat ja haluavat parempaa kivun hoitoa. Säännöllistä kivun ja hoidon tehon arviointia sekä uusien kivunhoitostrategioiden kehittämistä tarvitaan kivun hoidon optimoimiseksi kotona-asuvilla iäkkäillä. Lisäksi lääkkeettömien liitännäishoitojen käyttöä tulisi edistää lääkkeellisen kivun hoidon tukena.

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Yleinen suomalainen asiasanasto: kipu; krooninen kipu; kivunhoito; lääkehoito; kipulääkkeet; parasetamoli; liikuntarajoitteisuus; hoitosuhde; kotona asuminen; ikääntyneet; vanhukset; vanhuus; Kuopio; Suomi

“Educating the mind without educating
the heart is no education at all”

Aristotle (384 BC – 322 BC)

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Kuopio, September 2014

Niina Karttunen

List of the original publications

This dissertation is based on the following original publications:

- I Pokela N, Bell J S, Lihavainen K, Sulkava R, Hartikainen S. Analgesic use among community-dwelling people aged 75 years and older: a population based interview study. *The American Journal of Geriatric Pharmacotherapy* 8:233-244, 2010.
- II Karttunen N*, Lihavainen K*, Sipilä S, Rantanen T, Sulkava R, Hartikainen S. Musculoskeletal pain and use of analgesics in relation to mobility limitation among community-dwelling persons aged 75 years and older. *European Journal of Pain* 16:140-149, 2012.
*Authors contributed equally to this work
- III Karttunen N, Turunen J, Ahonen R, Hartikainen S. Persistence of nonmalignant musculoskeletal chronic pain among community-dwelling older people – a population based longitudinal study in Finland. *Clinical Journal of Pain*, Feb 25. [Epub ahead of print] doi: 10.1097/AJP.000000000000089, 2014.
- IV Karttunen N, Turunen J, Ahonen R, Hartikainen S. More attention to pain management in community-dwelling older persons with chronic musculoskeletal pain. *Age and Ageing*, May 9. [Epub ahead of print] doi: 10.1093/ageing/afu052, 2014.

The publications were adapted with the permission of the copyright owners. In addition, previously unpublished data are presented in chapter 5.

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Abbreviations

ADE	Adverse Drug Event
ADR	Adverse Drug Reaction
ASA	Acetylsalicylic acid
ATC	Anatomic Therapeutic Chemical Classification System
BMI	Body Mass Index
BPI	Brief Pain Inventory
CGA	Comprehensive Geriatric Assessment
CI	Confidence Interval
CNS	Central Nervous System
COPD	Chronic Obstructive Pulmonary Disease
COX	Cyclo-oxygenase enzyme
CVD	Cardiovascular disease
FCI	Functional Comorbidity Index
GDS	Geriatric Depression Scale
GeMS	Geriatric Multidisciplinary Strategy for the good care of the elderly
GI	Gastrointestinal
IADL	Intrumental Activities of Daily Living
MMSE	Mini Mental State Examination
MPQ	McGill Pain Questionnaire
NRS	Numeric Rating Scale
NSAID	Nonsteroidal Anti-inflammatory Drug
OR	Odds Ratio
SD	Standard Deviation
SF-36	Short Form Health Survey containing 36-items
SII	Social Insurance Institution
TUG	Timed Up and Go
VAS	Visual Analogue Scale
VDS	Verbal Descriptor Scale
WHO	World Health Organization
QoL	Quality of Life

Definitions of key terms

Analgesic drug

In this thesis, the term analgesic drug 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.

Chronic pain

The term chronic pain is used when referring to pain that persists uninterrupted for at least three months.

Community-Dwelling

The term community-dwelling refers to older people who are living at home or in circumstances comparable to home, not in assisted living facilities, nursing homes, long-term care facilities, hospitals or other types of institutional accommodation where they are assisted also at night-time.

Mobility limitation

In the literature review, the term mobility limitation refers to mobility restriction that has been determined with self-report or physical performance test. In the methods and results sections, the term refers to mobility difficulties measured with the Timed Up and Go test.

Older

In this thesis, the term older refers generally to persons aged ≥ 75 years, but the literature review includes some studies concerning younger people because of the limited number of studies focusing on older age groups.

Over-the-counter (OTC) drug

Drug that can be purchased from pharmacies without a prescription. The term non-prescription drug may also be used.

Prescription drug

Drug dispensed from pharmacy only on presentation of a prescription from a physician.

1 Introduction

Life expectancy is lengthening in most developed countries and the proportion of older people is growing rapidly. In 2010, approximately 17.5% of the Finnish population was aged ≥ 65 years and this share is estimated to increase to 26.2% by the year 2040 (Official Statistics of Finland, 2012). In demographics, the definition of an older person has been traditionally ≥ 65 years since this is the common retirement age, but the problems related to aging generally occur later in life. Morbidity, mortality and social problems increase rapidly after the age of 75 (American Geriatrics Society, 2009). Lengthened life expectancy and later onset of chronic diseases and disabilities support the proposal to alter the age limit of older people so that it should refer to individuals aged 75 years or more (Christensen et al., 2009).

Pain and pain associated co-morbidities, such as cancer, musculoskeletal conditions, neuropathies and vascular diseases, become more common as the individual approaches old age. Adaptation to painful stimuli and injury may be impaired with advancing age, resulting in a substantial vulnerability to suffer persistent pain (Gagliese and Melzack, 2013). Pain or its inadequate treatment exerts a number of adverse consequences on functional, cognitive, emotional and social well being of older people. In particular, restrictions in functional capacity and mobility threaten older persons' ability to live independently in the community (Guralnik et al., 1994, Sheppard et al., 2013). In addition, pain causes enormous economic costs for society. It is one of the most common reasons for seeking medical treatment and pain related restrictions in functioning and mobility increase the need for institutional care (Andersson et al., 1999, Lim et al., 2006, Von Korff et al., 1991, Coyte et al., 1998, Maniadakis and Gray, 2000). If one considers the individual and societal burden of pain, then its effective management should have a high priority. Pain and pain-related situations in older people have been studied widely in recent years, but there is lack of information concerning the persistence of pain in older people in a longitudinal setting.

Managing pain in older people requires a consideration of a variety of factors that influence the safety and efficacy of treatment. The assessment and management of pain may be confounded by multimorbidity, cognitive impairment and attitudes (both professionals' and patients'). Furthermore, polypharmacy and age-related changes in pharmacokinetics and pharmacodynamics complicate the provision of optimal drug therapy (Barber and Gibson, 2009, McLachlan et al., 2009). Older people are susceptible to suffering the adverse drug reactions (ADRs) associated with analgesic drugs, such as the adverse gastrointestinal and renal effects associated with NSAIDs and the central nervous system (CNS) effects encountered with opioids (Barber and Gibson, 2009, Hersh et al., 2007). Notwithstanding the potential for ADRs, with individually tailored therapeutic plan, analgesic drugs represent an important component of an effective pain management strategy (American Geriatrics Society, 2009). More research is needed into the use of analgesics among older people in order to reveal problems and to optimize pharmacotherapy in older patients with pain.

Pain is a complex and subjective experience, and there is conflicting evidence about possible age differences in pain experience. Older people may attribute pain symptoms to the normal aging process, especially if it is a case of mild aches (Helme and Gibson, 2001). They may adopt a stoical attitude and have a stringent noncomplaining response criterion resulting in an underreporting of mild or weak pain symptoms (Yong, 2006). Older person's attitudes and beliefs may also influence their help-seeking behaviour, expectations and the successfulness of pain treatment (Allcock et al., 2007, Cornally and McCarthy, 2011). However, few studies have focused on older persons' perception, their hopes and expectations concerning pain management.

The purpose of this thesis was to examine the epidemiology of pain and its management in the Finnish community-dwelling older population. This thesis explored the use of analgesics, the persistence of chronic pain and older persons' perception of whether they hoped to receive more attention from the physician for the management of their pain. In addition, the association of pain and analgesic use with mobility limitation was examined. Epidemiological information can help to develop preventive or educational programs and it is important for public decision makers planning the structure and allocation of the health care resources. Since the analyses of this study included only community-dwelling older people, also the literature review was limited to review mainly to non-institutionized older individuals. In addition, the literature concentrated on pain at musculoskeletal locations rather than other pain conditions because the pain data used in the studies included in this thesis focused on musculoskeletal pain. Furthermore, the other pain types (such as neuropathic pain, chest pain and abdominal pain) are often treated with different types of drugs to those investigated in this thesis. However, the literature was not strictly restricted because of the limited number of studies focusing on older age groups and certain topics.

2 Review of the Literature

2.1 PAIN IN COMMUNITY-DWELLING OLDER PEOPLE

2.1.1 Prevalence, types and sites of pain

The definitive prevalence of pain is difficult to determine in older people. Differences between studies lead to wide variations in prevalence, because the prevalence of pain is influenced by many factors e.g. country and population studied, type and methods of study, pain definitions, type and sites of pain, time period of pain examined, methods used etc. (Abdulla et al., 2013). In addition, since pain is a subjective experience, it is extremely difficult to measure it objectively. However, pain is highly prevalent among the aging population and many of the conditions that impact on general health and occurrence of pain are more common in older individuals. There are many epidemiological studies demonstrating that the prevalence of any pain complaints varies in a range between 33% and 74% in community-dwelling older people aged 70 years or more (Bassols et al., 1999, Bergh et al., 2003, Blay et al., 2007, Brattberg et al., 1996, Brochet et al., 1998, Jakobsson et al., 2003, Pitkälä et al., 2002, Reyes-Gibby et al., 2002, Thomas et al., 2004). The time window of pain complaints varied from the past two weeks to the past 12 months. Furthermore, the prevalence of chronic pain (duration of at least 3 months) varies from 24% to 62% in older populations (≥ 75 years) (Bergh et al., 2003, Blyth et al., 2001, Elliott et al., 1999, Jakobsson, 2010).

It is unclear whether the prevalence of pain increases or decreases with age, especially in old age. It has been suggested that there is a peak or plateau in the prevalence of pain by age 65 and a decline in reported pain in the age groups of 75–84 years and 85+ years (Helme and Gibson, 2001). However, in the study of Jakobsson, Klevsgard et al. (2003) the prevalence of pain increased among older people living in their own home, being 36% for those aged 75–84 years, 41% for those aged 85–89 years and 48% in the oldest age group (90+ years). Similar results were shown also in Jakobsson's later study (2010). Brattberg, Parker et al. (1996) reported that the prevalence of pain decreased among women in the older age groups (77–98 years) but did not substantially change among men. Contrasting results were reported by Blyth, March et al. (2001) and Thomas, Peat et al. (2004) since their studies detected an increase in pain prevalence among women and a decrease in men in the older age groups, but it should be noted that there were only two age categories with individuals aged 75 years or more in both studies and the oldest age groups contained fewer participants than younger age groups.

Most studies have demonstrated that pain is more prevalent and widespread among women than men late in life (Blay et al., 2007, Blyth et al., 2001, Brattberg et al., 1996, Brochet et al., 1998, Elliott et al., 1999, Helme and Gibson, 2001, Jakobsson, 2010, Leveille et al., 2005, Thomas et al., 2004, Urwin et al., 1998). In addition, older women tend to report more severe pain than men (Brattberg et al., 1996). The magnitude of sex differences in pain prevalence may depend on gender-related factors. For example, osteoarthritis and joint pain have been reported to be more prevalent in women than men (Brochet et al., 1998, Donald and Foy, 2004, Felson et al., 1997). There is also evidence that women are more willing to report pain than men (Greenspan and Traub, 2013). One possible reason for sex differences in pain reporting is that the older men represent a selected sample of survivors because the mortality of men is higher in the younger age groups (Official Statistics of Finland, 2012). It is important to recognize some confounding issues related to the pain reports of older people when evaluating pain prevalences. The very old are often survivors that may experience less pain-causing disease, or they may have a stoic attitude towards pain even misattributing pain symptoms to the aging process itself (Helme and Gibson, 2001).

The types and causes of pain change with age. It has been suggested that pain perception alters with increasing age and in particular the visceral pain sensation is impaired in older people. The sensation of visceral pain may change because of several reasons, including impaired A-Delta fiber nociceptive function, altered serotonin metabolism, and as may their response to analgesics e.g. increased responsiveness of older individuals to nonopioid analgesic pathways at the spinal cord level (Moore and Clinch, 2004). In addition, there may be a role for reduced nitric oxide responsiveness and slower central processing of noxious stimuli. Due to these changes, older patients are much more likely than younger patients to present with atypical types of visceral diseases; e.g. there may be an absence of pain in silent ulcerations and life-threatening GI-bleeding (Hilton et al., 2001). Furthermore, variations in chest pain complaints related to myocardial infarction occur more frequently in older people. In particular the incidence of silent or painless myocardial infarction increases and is estimated in a range of 35–42% in people older than 65 years (Gibson and Helme, 2001). These atypical presentations of pain increase the risk of delay in the diagnosis and treatment of underlying conditions. Furthermore, the prevalence of any headaches tends to decline with increasing age, particularly the prevalence of migraine headache decreases after the age of 40 (Lipton et al., 2001, Prencipe et al., 2001) (Figure 1). Despite a decline in headache prevalences with age, the tension-type headache continues to be relatively frequent in older populations. According to Prencipe, Casini et al. (2001), tension-type headache is the most common primary headache type in older people aged 65–96 years; the one year prevalence rate for tension-type headache was 45% as compared with 11% for migraine headache and 3% for other headaches.

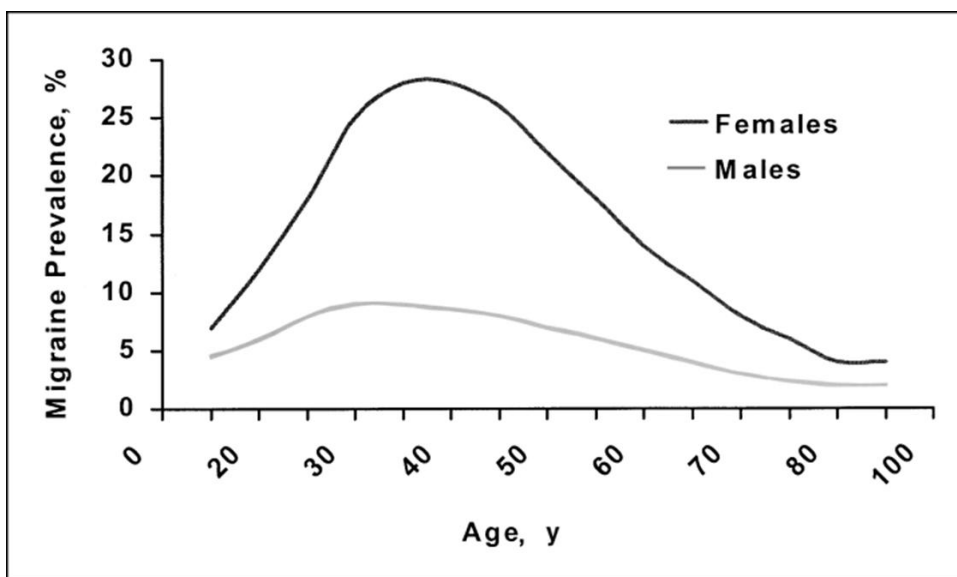


Figure 1. Adjusted age-specific prevalence of migraine by sex (Lipton et al., 2001).

Neuropathic pain (pain associated with the somatosensory system) becomes more common in old age, because the frequency of diseases evoking neuropathic pain, such as herpes zoster and diabetes, increases with age (Cruccu and Truini, 2010). It is difficult to diagnose neuropathic pain and especially distinguishing it from nociceptive pain is challenging often requiring analysing the exact quality of somatosensory abnormalities (Baron et al., 2010). Neuropathic pain involves heterogeneous mechanisms of pain and it is most commonly treated with drugs that decrease the sensitivity of nociceptive receptors or desensitize the pain transmitting C-fibers (e.g. anti-depressants and anti-epileptics). In addition to neuropathic pain, there is evidence that fibromyalgia becomes more prevalent with advancing age (Bannwarth et al., 2009, Santos et al., 2010). In the study of Branco, Bannwarth et al. (2010), the prevalence of fibromyalgia appeared to increase from approximately 2% to 7% between age groups 35–44

years and 74–85 years but subsequently the prevalence declined dramatically. However, in an other study the presence of fibromyalgia (based on the criteria of the American College of Rheumatology) was rather uncommon (0.3%) in community-dwelling older people (≥ 70 years), although higher tender point counts, multisite pain and widespread pain were relatively common (Eggermont et al., 2010).

Musculoskeletal conditions (such as osteoarthritis, rheumatoid arthritis, osteoporosis and low back pain) are the most common cause of severe long-term pain and the prevalence of these conditions increases markedly with age (Woolf and Pfleger, 2003). For example there is a report that the prevalence of musculoskeletal pain can be as high as 62% in older people (Grimby et al., 1999). The musculoskeletal pain in older patients is often degenerative in its nature and it is most commonly a consequence of osteoarthritis, a condition that increases substantially in old age (Palazzo et al., 2014, Yamada and Thomas, 2011) (Figure 2). Age has been shown to be the strongest predictor for osteoarthritis development; this is thought to be due to insufficient repair mechanisms, hormonal changes and the cumulative impacts of a variety of noxious environmental exposures (Pettersson and Jacobsson, 2002).

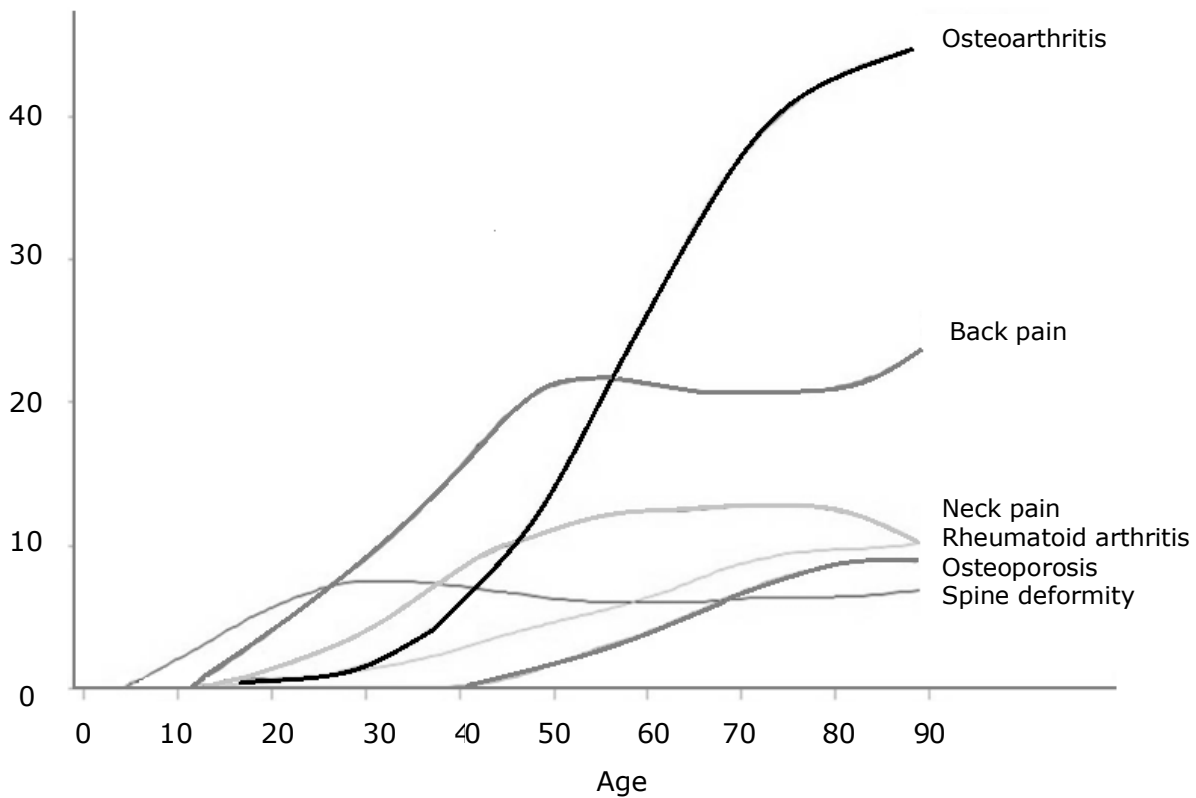


Figure 2. The changes in the prevalence of musculoskeletal conditions with age (Palazzo et al., 2014).

The knees are the most common pain site in community-dwelling older people (Lichtenstein et al., 1998, Thielke et al., 2012, Thomas et al., 2004, Urwin et al., 1998). It seems that with advancing age, pains and aches move from the upper body to lower body parts. A Finnish study that analyzed pain complaints in general practice clients revealed that the most common pain site in adults aged 20–39 years was the head (33%) whereas in older people (70+ years) the most common pain site was the lower limbs (41%) (Mäntyselkä, 1998). Pain in hips, knees, most joints and multiple areas seems to increase with age while in other areas there is only a minor change (Figure 3) (Urwin, Symmons et al 1998). In addition, the pain experience becomes more disabling with age, if this is measured by its interference with daily activities (Figure 4) (Thomas et al., 2004). The most common pain sites after the knees are back and shoulders, but the frequency order of neck, hip, foot and hand pain has varied in different studies (Lichtenstein et al., 1998, Thielke et al., 2012, Urwin et al., 1998).

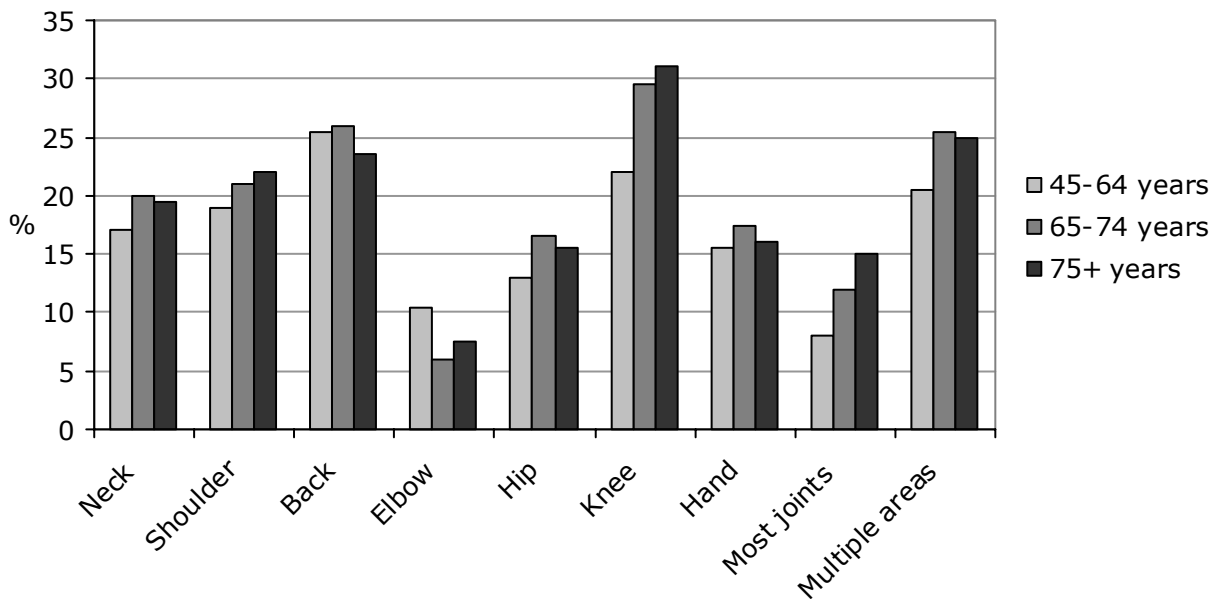


Figure 3. The prevalence of musculoskeletal pain symptoms (more than one week in the past month) according to age groups. Modified from the study of Urwin et al. (1998).

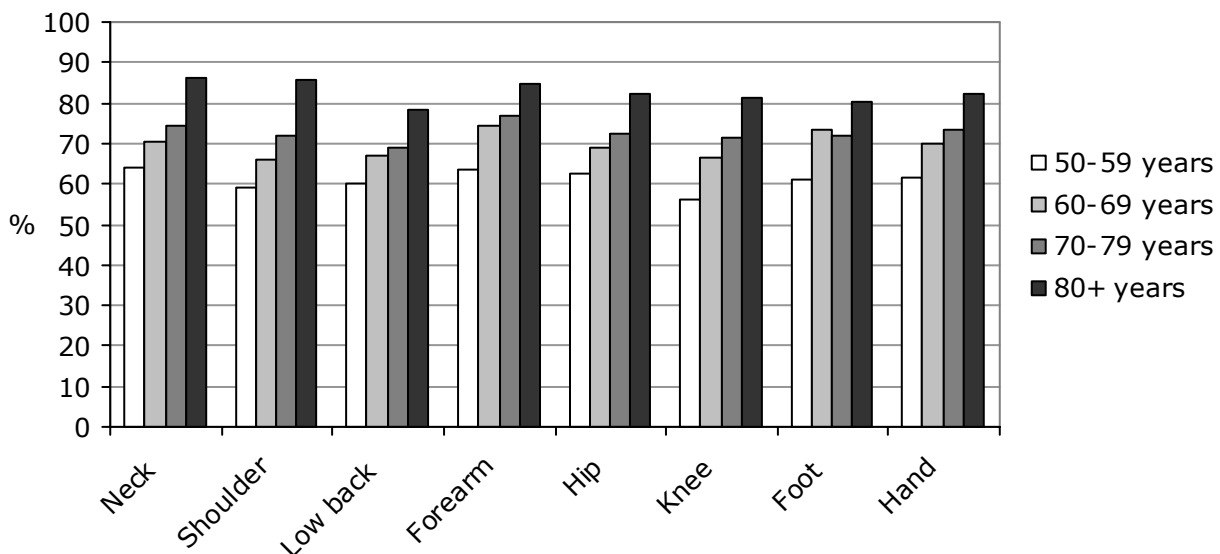


Figure 4. The proportion of regional pain sufferers (for one day or longer in the past 4 weeks) reporting pain interference subdivided into different age groups. Modified from the study of Thomas et al. (2004).

2.1.2 Persistent and chronic pain

Pathophysiologic processes causing chronic pain differ from those involved with acute pain. Repeated stimulation of pain pathways induces hypersensitization of the pain-sensing system due to physiochemical changes in neural pathways of the spinal cord and this causes a simultaneous increase in the resistance to intrinsic inhibitors of pain (Katz and Barkin, 2010). Older people are particularly vulnerable to suffer prolonged pain problems since the regenerative capacity of the body and adaptation to painful stimuli become impaired with advancing age (Gagliese and Melzack, 2013). The terms persistent pain and chronic pain are often used interchangeably in the literature to refer to a painful experience that continues longer than the expected healing time for an injury or illness, or if there is no injury or illness, but the pain persists uninterrupted for at least 3 to 6 months (American Geriatrics Society, 2002). The cut-off points of 3 and 6 months are most commonly used in research, but even a period as long as 12 months has been used (Main and Spanswick, 2001). The use of a longer period may be reasonable in some cases, for example to determine chronic pain after a surgical procedure.

However, the definitions differ when they are used to categorize certain pain syndromes. Persistent pain may refer to patients with neck or back pain who do not recover from the original acute pain but they exhibit none of the characteristics of chronic pain syndrome (Long, 2013). In other words, patients with persistent pain remain functional and they do not develop psychological abnormalities despite the pain symptoms remaining more or less constant for years. Chronic pain syndrome is characterized by the chronicity of pain complaints and it is often complicated and worsened by other comorbid conditions and psychological distress. Due to its multidimensional nature, chronic pain cannot be attributed simply by nociception because there might be also sociodemographic, genetic and affective factors influencing pain perception (van Hecke et al., 2013). Unfortunately, some older persons associate the term "chronic pain" with negative stereotypes associated with psychiatric problems, futility of treatment, malingering or drug-seeking behaviour and therefore the term "persistent pain" may be more advisable for use with older persons (American Geriatrics Society, 2002).

2.1.3 Pain assessment

The patient's self-report is the gold standard for assessing the existence of pain and its intensity since there are no objective biological markers or diagnostic tests that measure pain (American Geriatrics Society, 2002). Pain assessment tools, such as questionnaires and rating scales, have been developed to measure both the quantity and the dimensions of pain. It has been claimed that the commonly used pain assessment tools are valid and likely to work also in older patients, even in the presence of mild to moderate cognitive impairment (Bergh et al., 2000, Ferrell et al., 1995, Herr et al., 2004). However, sensory impairments (hearing or vision), dysphasia and aphasia should be noted as they can complicate the assessment of pain and their presence may require adopting modified methods with which to assess pain (Herr, 2011).

The use of common pain assessment tools requires language and cognitive skills that are often diminished in the presence of cognitive impairment. A number of pain assessment tools have been developed for patients with advanced cognitive impairment and an inability to self-report (Zwakhalen et al., 2006). However, tools based on observation of behaviour may not be unambiguous because behaviours associated with pain cues can also be signs of physiologic or emotional distress. The tools believed to have the strongest conceptual and psychometric support as well as clinical utility include The Assessment of Discomfort in Dementia Protocol, Checklist of Nonverbal Pain Indicators, The Doloplus 2, Nursing Assistant-Administered Instrument to Assess Pain in Demented Individuals, The Pain Assessment Scale for Seniors with Severe Dementia and The Pain Assessment in Advanced Dementia Scale (Herr et al., 2006). However, because the focus of this thesis was on community-dwelling older persons without severe cognitive impairment, these pain assessment tools will not be described further here.

Unidimensional pain scales

Unidimensional pain scales help to define the intensity of pain. The Visual Analogue Scale (VAS) consists of a 100mm horizontal or vertical line anchored by verbal descriptors such as 'no pain' and 'worst pain possible'; this scale has been widely used to measure pain intensity in younger patients, but it is probably not the best choice for older adults (Gagliese et al., 2005, Pesonen et al., 2008, Peters et al., 2007). VAS has a higher failure rate and it is less preferred by older people (Hadjistavropoulos et al., 2007).

Numeric Rating Scale (NRS) has both written and verbal forms and it can have variety of scale ranges (including 0–5, 0–10, 0–20 and 0–100). Patients rate their pain intensity e.g. on the scale of 0 to 10 where 0 indicates 'no pain' and 10 represents 'most intense pain imaginable'. NRS is suitable and often preferred by older people who are able to self-report, but some older adults may experience difficulties with the scale because it requires abstract thought (Hadjistavropoulos et al., 2007, Wood et al., 2010). It has been claimed that a verbally administered NRS can be a good choice if the patient's poor vision causes difficulties with visual scales and it is also believed to be more suitable for some cognitively impaired patients (Herr, 2011).

Faces Pain Scale (FPS) includes pictures of faces ranging from a neutral happy face (no pain) to a grimacing face (worse pain) and it may assess a broader construct of pain affect than pain intensity, but it requires abstract thinking and has been problematic for older people with cognitive impairment (Hadjistavropoulos et al., 2007).

Probably the most widely recommended tool for use with older people is the Verbal Descriptor Scale (VDS) (Herr et al., 2004, Pesonen et al., 2008). VDS is available in a variety of scale types, but the most simple version includes only four words to describe pain intensity; none, mild, moderate and severe. VDS has strong psychometric support, it is preferred, and able to be completed by most older patients, even those with impaired cognition (Herr et al., 2004, Peters et al., 2007, Taylor et al., 2005). However, VDS requires also abstract thinking and additionally it poses greater demands on language capabilities (Hadjistavropoulos et al., 2007).

Multidimensional pain tools

Unidimensional pain scales do not provide information about pain locations, interference or qualities, and therefore multidimensional methods have been developed to evaluate those aspects of pain. This is a reasonable approach because of the subjective, complex and multidimensional nature of pain. An interdisciplinary consensus statement has recommended for cognitively intact older adults that the assessment should be conducted with the Brief Pain Inventory (BPI) combined with the McGill Pain Questionnaire (MPQ) (Hadjistavropoulos et al., 2007).

BPI is a short, self-administered questionnaire designed to assess the severity of pain and how much it interferes with daily routines (Cleeland and Ryan, 1994). Respondents rate their worst, least, average, and current pain intensity and also rate the degree to which pain interferes with 7 domains of functioning (general activity, mood, walking ability, normal work, relations with other persons, sleep, and enjoyment of life) on a scale of 0 to 10. BPI has been validated in over 30 languages. Not only does it have good psychometric properties but it is also simple to administer and score; unfortunately it does not evaluate the affective dimension or qualitative aspects of pain (Hadjistavropoulos et al., 2007).

MPQ includes 20 categories of adjectives to describe the sensory, affective, evaluative and miscellaneous pain experiences (Melzack, 1975). Patients are asked to select those words that best describe their feelings and sensations at that moment. MPQ is valid and reliable for use in older people suffering chronic pain, but it is not recommended for illiterate and cognitively impaired persons (Gagliese and Melzack, 2003, Hadjistavropoulos et al., 2007). Short forms of both questionnaires have been developed and validated to simplify their use for clinical and research purposes (Melzack, 1987, Cleeland, 2009).

The comprehensive assessment of older persons with pain should also include measures of physical disability, interference of pain with daily life and psychological distress, since pain is modulated by psychological state and functional status (Gagliese and Melzack, 2013). Objective measures of these constructs are in frequent use; there are also pain assessment tools that include some of those dimensions, e.g. Functional Pain Scale (Gloth III et al., 2001), Pain Disability Index (Tait et al., 1990), Geriatric Pain Measure (Ferrell et al., 2000), Multidimensional Pain Inventory (Kerns et al., 1985), Western Ontario and McMaster Universities Osteoarthritis Index (Bellamy et al., 1988) and Arthritis Impact Measurement Scale (Meenan et al., 1980).

2.1.4 Older people's experience of pain and its treatment

Being old and suffering pain is a highly subjective experience. Older persons' attitudes (affective response to an object) and beliefs (ideas and ideals held by individuals) about pain, play an important role in influencing how a patient experiences pain, and these include pain intensity, psychological distress, coping strategies and functional impairment (Abdulla et al., 2013, Yong, 2006). It is a common belief among older adults that pain is a normal part of aging (Cornally and McCarthy, 2011). Furthermore, especially pain-related stoicism (adopting an indifferent attitude towards pain) seems to be particularly evident in the older population and it has been implicated in the underreporting of pain (Helme and Gibson, 2001). Thus, the association between age and self-reported pain may be mediated by stoic and cautious attitudes, which suggests that the lower report of pain severity commonly described in patients of advancing age is due more to attitudes than age per se (Yong, 2006). Inappropriate stoicism can be perceived when patients' self-reports of pain are incongruent with their behavior or with their reported need for (or consumption of) analgesic therapies (Spiers, 2006). This phenomenon may result in a conflict between professionals trying to alleviate suffering by ensuring that there is appropriate pain management and their desire to be supportive of patient's point of view, i.e. trying to convince patients that their experience is being understood and appreciated. In the light of previous studies, there seems to be a risk that these underlying attitudes and beliefs held by older people act as barriers to effective pain management.

On the other hand, a stoical attitude may help to cope with pain in daily life. The older age group (60–81 years) has reported better mood scores and a higher quality of life scores than younger age groups (18-39 or 40–59 years) although they had higher pain intensity scores, longer duration of pain and a higher percentage of chronic diseases. (Rustoen et al., 2005). In addition, it has been demonstrated that there are two types of older people experiencing pain that express greater satisfaction in life; these have been classified as 'confident and serene' and 'competent and proud' (Blomqvist and Edberg, 2002) Older people seem to assess the type of pain which restricts their daily living as a greater problem than the actual pain itself. They may conceptualise health as representing independence and being able to carry out everyday tasks rather than as the state of health of the body. Older persons may consider themselves as being healthy even though they have painful joints and the presence of symptoms may not compromise their sense of being well, as long as their brain remains functional and they can be as independent as possible (Grime et al., 2010). Unfortunately, older people's autonomy becomes threatened by restricted physical activity leading to impaired social participation; aspects which have been described as an inevitable consequence of pain in old age (Mackichan et al., 2013). Blomqvist and Edberg (2002) identified also two groups of older people in pain who expressed primarily dissatisfaction. Those who were called 'misunderstood and disappointed' and 'resigned and sad' felt dissatisfaction not only due to the pain itself but also because their significant others did not listen to or did not take seriously their complaints. Feeling that they were considered as a nuisance increased their suffering. Thus, it is important that older people's experiences of pain are acknowledged as a true problem and their pain and possible depressive emotions are identified and treated by multidimensional strategies.

Many older people normalizing pain probably choose not to seek treatment for their pain problems. There is a report that stoic older adults (≥ 60 years) who were not willing to disclose

their pain to others were also less likely to seek help from health care professionals (Cornally and McCarthy, 2011). They found that female sex, increasing age, severe pain, living alone and higher education were associated with higher levels of expressing a need for help for chronic pain. In addition, those who believed that their pain had an organic cause were more likely to seek help. These findings seem reasonable because women tend to use health-care services more than men and usually the number of diseases increases with age so that there may be also other reasons in addition to pain requiring help from a physician (Redondo-Sendino et al., 2006). Furthermore, people probably handle mild pain problems by themselves and a person living alone may lack the social support of a partner and thus may be more inclined to seek professional help. Previous studies have demonstrated that people with higher education are more likely to engage in healthy behavior which can partly explain why higher education was associated with help-seeking behavior related to pain (Boylan et al., 2011). To an older person, it may feel also more acceptable to seek care for pain problems for which there is an apparent reason in comparison to help for pain with no clear cause.

Older patients' expectations of pain treatment are often difficult for clinicians to determine, but there are some studies into this topic. Older patients with musculoskeletal pain often feel information on prognosis as important and therefore it may be worthwhile to ask during the consultation whether the patient wants to know about the likely course of his/her condition (Mallen and Peat, 2009). In a small-scale exploratory study including older and younger participants with pain, patients were asked to prioritize reasons for their pain treatment; the main reasons were physical or functional improvements, including less pain, pain-free periods, and being able to do more everyday activities (Allcock et al., 2007). Sometimes merely the opportunity to talk frankly about pain, its consequences and to alleviate patient concerns, can represent a useful therapeutic intervention for older people (Sofaer et al., 2005).

The value of hope should be noted in pain treatment, because it is claimed that hopefulness fosters coping strategies that increase participation in treatment regimens and strengthen the belief that difficulties can be overcome (Hammer et al., 2009). Pain patients often feel that the most discouraging outcome of clinic visit is to be told that nothing can be done to alleviate their pain problem (Petrie et al., 2005). This kind of outcome in the consultation situation may lead to unnecessary despair and suffering of the patient. Thus supportive interventions responding to the hopes of pain patients may be recommended as facilitating the management of pain. However, older people's hopes in relation to pain and pain treatment have rarely been studied.

2.2 EFFECT OF PAIN

Living with pain is a significant burden that negatively affects an older patient's psychosocial and physical well-being. The adverse consequences of pain include mobility and functional disability (Leveille et al., 2002, Shah et al., 2011), increased risk of falling (Stubbs et al., 2014), decreased cognitive function (Moriarty et al., 2011), increased anxiety and depression (Arola et al., 2010), poor self-rated health (Reyes-Gibby et al., 2002), loss of appetite (Bosley et al., 2004), sleep disturbances (Chen et al., 2011), disruptions in social relationships (Peat et al., 2004) and decreased quality of life (Hawkins et al., 2013). However, only pain-related mobility limitation, self-rated health and quality of life will be discussed here in more detail since those are crucial factors with respect to this thesis.

2.2.1 Mobility

Physical inactivity and poor mobility have been found to display an association with increased mortality risk in older people (Newman et al., 2006, Äijö et al., 2002). Musculoskeletal pain, especially in the lower extremities (hip, knee, calf, ankle, foot) and back, has a detrimental impact on postural balance and mobility (Leveille et al., 2002, Jones et al., 2012). Severe pain leads to a restriction of painful movements and changes in normal movement patterns (Hurwitz

et al., 1997). This can create a vicious circle, with compensations causing atrophy of the muscles which further increases pain and impaired balance resulting in even further mobility restrictions (Visser et al., 2005). The fear of pain has been described in patients suffering from pain and it may accentuate the avoidance cycle. This can enhance safety seeking behaviours such as avoidance and hypervigilance, which although these behaviours can be considered as beneficial in the acute pain stage, they paradoxically worsen the problem in the case of long-lasting pain (Leeuw et al., 2007). In addition to a distinct fear of pain, the fear may be directed to other pain related outcomes such as fear of movement (kinesiophobia) or of falling. A recent review provided evidence that pain was associated with fear of falling and avoidance of activities which could involve falling in community dwelling older adults (Stubbs et al., 2014). These underlying factors may result in a vicious circle which is hard to break.

Older persons represent a significant group of people at risk for suffering pain and mobility problems sufficiently severe to influence daily functioning. Previous studies have demonstrated that musculoskeletal pain is significantly associated with the development of mobility disabilities in community-dwelling older people (Buchman et al., 2010, Shah et al., 2011). Furthermore, limitations in mobility threaten the older person's ability to live independently in the community. Leveille et al. (2002) reported that pains in the lower extremities were the main causes of disabilities in lower extremity mobility tasks e.g. bathing, using the toilet, walking, and stair climbing. The results linking musculoskeletal pain to mobility limitations raise the possibility that treatments which successfully decrease musculoskeletal pain may prevent the development of mobility disabilities in older persons. However, the biological pathways between musculoskeletal pain and mobility disability are far from clear and further research is needed to confirm that effective pain management strategies are able to prevent or delay the development of mobility disabilities.

2.2.2 Self-rated health

Good perceived subjective health and well-being are important in everyday life as ways to promote successful ageing. It has been demonstrated that self-rated health is an important and independent predictor of morbidity and mortality (Bardage et al., 2005, Tamayo-Fonseca et al., 2013). This phenomenon has been reported also in the very old (90+ years) population (Tiainen et al., 2013). Self-rated health is typically assessed using a single item: Overall, how would you rate your general health status? and 5 response options from poor (1) to excellent (5) are possible (Eriksson et al., 2001). The study of Bardage, Pluijm et al. (2005) documented that those individuals with either fair or poor self-rated health were more than twice as likely to have musculoskeletal diseases. Furthermore, the adverse impact of pain on self-rated health is well documented in general and also in older populations, even when clinical health status, access to medical care, and sociodemographic characteristics have been taken into account (Mäntyselkä et al., 2003, Reyes-Gibby et al., 2002). In addition to those with pain, there was about the same risk in those individuals with functional limitations perceiving themselves to be in poor health (Reyes-Gibby et al., 2002). The strong association between pain and self-rated health, as well as with functional status found in the study of Reyes-Gibby et al. (2002) emphasizes the importance of treating and controlling pain even although self-rated health may be a multidimensional construct that includes pain as only one of its dimensions.

2.2.3 Quality of life

Quality of life (QoL) is an multidimensional indicator of everyday life and it is negatively affected by functional and health complaints. Overall QoL takes a broader view than the health-related QoL measure that concentrates on functioning, well-being and general health status and is most commonly used in health care contexts (Borglin et al., 2005). The Short Form Health Survey containing 36-items (SF-36) is the most commonly used health-related QOL measure, but there are several alternatives to the SF-36 (Coons et al., 2000). The choice of a suitable measure depends on a variety of factors including the characteristics of the population and the

environment in which the measurement will be done. A shorter and more practical version of SF-36 is the 12-item Short Form Health Survey (SF-12); this may be more suitable for older persons, because the instrument is easy to administer and does not contain questions that are related to work (Jakobsson et al., 2003, Resnick and Nahm, 2001).

Pain has been found to be the strongest musculoskeletal correlate in the health-related QoL in persons with osteoarthritis (Laslett et al., 2012). Those who suffer from pain are at high risk of decreased QoL and should they also need help to manage daily routine tasks (perhaps because of functional limitations or other complaints) then this may result in an even lower QoL (Jakobsson et al., 2007). In the study of Borglin, Jakobsson et al. (2005) pain was significantly associated with low overall present QoL as well as with low physical and mental health-related QoL. A mobility impairment was associated with low physical health-related QoL and low present QoL. This emphasizes the need to focus on pain in older people and to take actions to improve their QoL by preventing and controlling pain and the pain-related mobility limitations. However, it may not be possible to fully relieve pain and improve functional limitations and in such a situation the goal of treatment should be towards promoting health and helping to maintain, even improve, the older person's overall quality of life.

2.3 MANAGEMENT OF PAIN IN OLDER PEOPLE

2.3.1 Pharmacological pain management

Pharmacotherapy plays a central role in the control of pain and the World Health Organization has developed a recommendation in the form of a three-step ladder (Figure 5), for cancer pain relief (WHO, 1996). The use of this analgesic ladder has been extended to other kinds of pain, including persistent pain from noncancer causes. Its educational value and the benefits resulting from its worldwide dissemination are uncontested, although it can be debated whether the ladder form is relevant in all pain cases (Vargas-Schaffer, 2010). According to the steps on the analgesic ladder the treatment is adjusted in relation to pain intensity and the presence of adverse effects. Non-opioids are suitable alone for mild pain and in the case of moderate to severe pain they can be combined with weak (step 2) and strong (step 3) opioids. It is important to consider that there are several confounding factors associated with the pharmacotherapy of pain in older people. These complicating factors include the large inter-individual variation in the response to analgesics, the lack of clinical studies in older populations and the increasing prevalence of comorbidities, polypharmacy, cognitive impairment and frailty (Koponen et al., 2013, McLachlan et al., 2009). Age-related changes in physiology may alter the pharmacokinetics and pharmacodynamics of analgesic drugs (McLean and Le Couteur, 2004, Mitchell et al., 2009) (Table 1). Since pain often has both varied and multiple underlying physiological processes, it is important to consider the multimechanistic nature of pain in the treatment i.e. to attempt to match the analgesic's mechanism of action with the type of pain. Therefore, in some situations it is reasonable to treat pain according to a more generalized 'pain pyramid' that provides clinical flexibility and patient-individualized care strategy to achieve better pain management (Raffa and Pergolizzi, 2014). The pain pyramid consists of four mechanism-based steps and includes the possibility for analgesic switching on the same step, or movement down steps and initiating therapy with a step 4 agent because it has an appropriate mechanism of pain relief.

Many analgesic medications are included in lists of inappropriate medications compiled by expert consensus panels, for example the updated 'Beers criteria for potentially inappropriate medication use in older adults' includes multiple agents from the non-steroidal anti-inflammatory analgesic class (AGS, Beers Criteria Update Expert Panel, 2012). This is reasonable since older people are at increased risk of suffering adverse effects from analgesic medications. It is important to recognize the clinical pharmacology of ageing and analgesics

because an understanding of advantages and disadvantages of analgesic medications can help with drug and dose selection for older people. Some considerations and recommendations related to analgesics and older people will be described at the end of this section (Table 2).

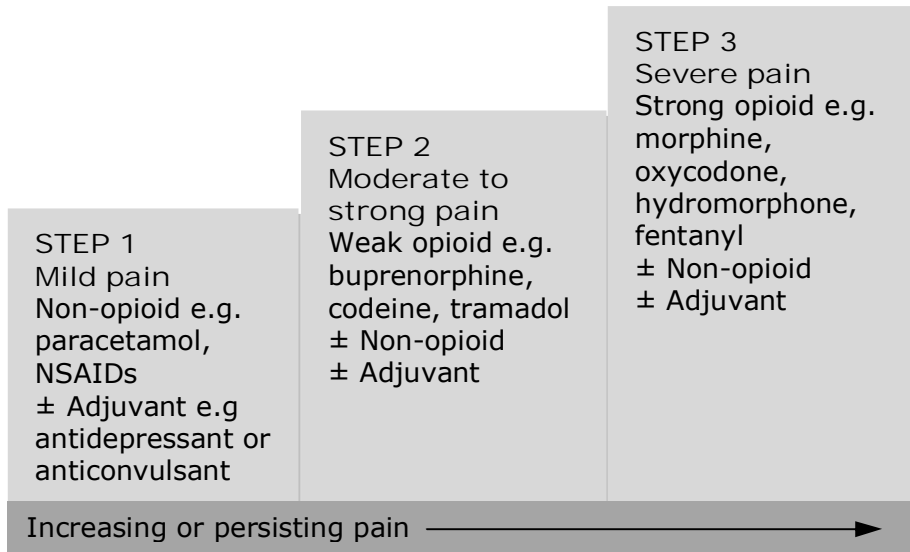


Figure 5. The World Health Organization analgesic ladder for treating cancer pain. Modified from WHO 1996.

Paracetamol

According to the WHO analgesic ladder, the administration of analgesics should start with nonopioids, most frequently paracetamol (WHO, 1996). Paracetamol represents the first line analgesic drug therapy for nonmalignant pain in older people. It is an effective drug particularly for musculoskeletal pain and it is well tolerated causing few ADRs when recommended limits are followed (a maximum dose of 4g in 24 hours for patients with no impairments of renal or hepatic function and no history of alcohol abuse) (Abdulla et al., 2013, American Geriatrics Society, 2009). It should be noted that older people are more likely than younger adults to use concomitant medications which can induce drug-metabolizing enzymes and are more likely to be frail (both conditions can cause an accumulation of the toxic metabolite of paracetamol), therefore it is reasonable to use less than 4 grams in this subgroup (O'Neil et al., 2012). The Finnish expert consensus recommendation for older people is no more than 3 grams in 24 hours in continuous use, and a maximum dose of 4 grams is acceptable only for short-term use (Fimea, 2014). This reduction in recommended maximum daily dose is reasonable since a recent Finnish study found that the administration of paracetamol resulted in higher exposure to the drug in older people due to the lower clearance and reduced apparent volume of distribution (Liukas et al., 2011).

Despite being one of the most widely used analgesics, the analgesic mechanism of paracetamol is still unclear. Paracetamol is not a peripheral anti-inflammatory agent but instead it is centrally acting. It is well absorbed after oral administration (Davis and Srivastava, 2003, Smith, 2009). Furthermore, it has few drug interactions because it is metabolized via glucuronidation. Although paracetamol is a relatively safe drug, it has a fairly narrow therapeutic index; in fact the major limitation of paracetamol is that it has an upper dosing limit (Mitchell et al., 2009). Paracetamol overdoses are associated with hepatotoxicity and the risk factors for paracetamol overdose include older age, malnutrition, alcohol abuse and underlying liver disease (Myers et al., 2008). It has been demonstrated that the proportion of accidental paracetamol overdoses increases with older age (Myers et al., 2007). There may be several reasons for paracetamol hospitalizations of which accidental overdose is one important cause, especially in the older patients. Thus 50% of all over 70 years olds requiring hospitalization for paracetamol-related

Table 1. Physiological changes and clinical consequences in older people. Data gathered from Abdulla, Adams et al. 2013, AGS 2009, Christo, Li et al. 2011, and Mitchell Hilmer et al. 2009.

PHYSIOLOGICAL CHANGE WITH NORMAL AGEING	CLINICAL CONSEQUENCE	EFFECT ON PAIN PHARMACOTHERAPY
GI-Absorption Delayed gastric emptying GI tract peristalsis ↓ GI tract blood flow ↓	Alteration of drug absorption has little clinical significance Risk for GI-related ADRs ↑ Effect of continuous release enteral agents ↑	Bioavailability of morphine ↑ Opioid related gut mobility disturbance ↑
Distribution Body water ↓ from 15% to 10% Body fat ↑ from 20% to 40% Plasma proteins ↓	Concentration of water soluble drugs ↑ Accumulation and half-life of lipid soluble drugs ↑ Free fraction of drugs that are highly bound to proteins ↑ Drug-drug interaction risk ↑	Free fraction of highly protein-bound drugs such as acetylsalicylic acid, celecoxib and fentanyl ↑ In older people the AUC of paracetamol ↑
Metabolism Liver mass ↓ Hepatic blood flow ↓ Functioning liver cells ↓	First pass metabolism ↓ Oxidative reactions (phase I) ↓ Prolonged half-life Conjugation (phase II) usually preserved Activity of acetylsalicylic acid esterase ↓ Difficult to predict precise effect in an individual	In frail patients: Phase I and II metabolism of paracetamol ↓ paracetamol hepatotoxicity ↑ Metabolism of morphine (II), fentanyl (I), codeine (I) and celecoxib (I?) ↓
Renal excretion Renal blood flow ↓ Glomerular filtration ↓ Tubular secretion ↓	Excretion of drugs and metabolites ↓ Accumulation and prolonged effects ↑	Reduced clearance and increased t _{1/2} of paracetamol and its metabolites, ASA, ibuprofen, celecoxib, oxycodone, fentanyl, morphine metabolites and codeine metabolites
Pharmacodynamic changes μ-opioid receptor density ↓ and affinity ↑	Sensitivity to the therapeutic effects but also to ADEs ↑	Risk and severity of ADEs ↑ in people using e.g. NSAIDs or opioids Lower opioid doses may be adequate

problems were admitted due to accidental overdose. This is more than three times higher than the figure in general population (15%). One should adopt strategies to reduce the risk of unintentional overdose with paracetamol in the management of pain in older people. Nonetheless, owing to paracetamol's advantages in relation to other analgesic drugs, it is likely that its use will remain at the top of the recommended analgesic drugs for administration to older people.

Non-steroidal anti-inflammatory drugs

NSAIDs are analgesics with anti-inflammatory and antipyretic properties and they are one of the most widely prescribed classes of drugs for pain and inflammation (Abdulla et al., 2013). NSAIDs have a major role in the management of acute and chronic pain syndromes, particularly for somatic or visceral nociceptive pain (Davis and Srivastava, 2003). These drugs inhibit the cyclo-oxygenase enzyme (COX) but they differ in their selectivity toward the two isoenzymes COX-1 and COX-2 (Mitchell et al., 2009). It has been claimed that NSAIDs provide better efficacy than paracetamol for relief of chronic inflammatory pain (such as the pain associated with rheumatoid arthritis) and for short-term relief (6 weeks) of osteoarthritis pain (American Geriatrics Society, 2009). Analgesia with NSAIDs occurs within 4 hours, much sooner than the anti-inflammatory effects which may take several days even weeks to appear (Davis and Srivastava, 2003).

Despite their great efficacy to relieve pain associated with many conditions, significant contraindications and adverse effects, that increase with age, limit their usefulness (Davis and Srivastava, 2003, Franceschi et al., 2008). NSAIDs have been associated with the risks of GI, renal, cardiovascular, haematological and hepatic adverse effects (Hippisley-Cox et al., 2005, Antman et al., 2007, Barkin and Buvanendran, 2004, Kearney et al., 2006, Rostom et al., 2005). Previous studies have shown that there is a significant association between the use of NSAIDs and unplanned hospitalization and deaths in older patients (Griffin, 1998, Price et al., 2014). With advancing age, particularly the risk for dangerous upper GI hemorrhages and perforations seems to multiply (Figure 6). The concomitant use of NSAIDs with low-dose acetylsalicylic acid (ASA) or with the common anticoagulant drug, warfarin, increases the risk of serious GI-bleedings (de Abajo and Garcia-Rodriguez, 2008). In addition, the combination of NSAIDs with corticosteroids, SSRIs (selective serotonin reuptake inhibitors) or paracetamol may be contraindicated due to increased GI-bleeding risk (American Geriatrics Society, 2009, Buescher and Meadows, 2004).

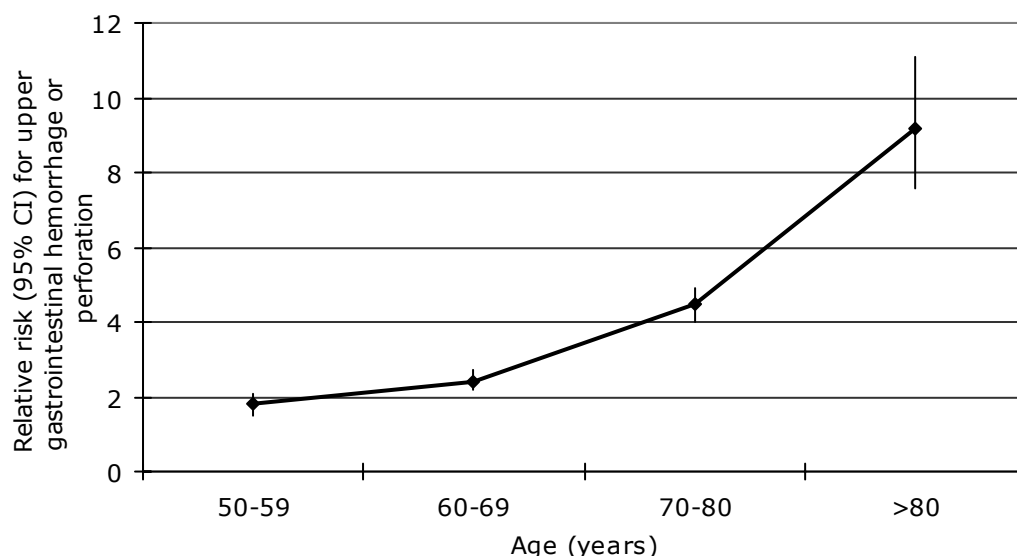


Figure 6. The effect of age on the relative risk of upper gastrointestinal hemorrhage or perforation (Hernández-Díaz and García Rodríguez, 2000, McLean and Le Couteur, 2004).

The renal adverse effects are mediated by COX-1 and COX-2 as both forms are constitutively expressed in the kidney. Therefore both nonselective and COX-2 selective NSAIDs are associated with renal adverse effects including decrease in renal blood flow leading to a reversible renal insufficiency, sodium and water retention, hyperkalemia, interstitial nephritis even acute renal failure (Barkin and Buvanendran, 2004, Barkin et al., 2010). The renal effects of NSAIDs are mechanism-based, dose-related and all of the drugs exert similar renal function effects. The concomitant use of diuretics, ACE inhibitors, as well as dehydration and older age are additional risk factors for their renal toxicity (Barkin and Buvanendran, 2004, Davis and Srivastava, 2003). The cardiovascular risk associated with NSAIDs (traditional and COX-2 selective) is particularly significant in older persons and therefore the use of NSAIDs for the management of persistent pain in older people demands individualized attention (American Geriatrics Society, 2009). NSAIDs, especially COX-2 selective compounds, have been associated with an increased risk of serious cardiovascular thrombotic events, myocardial infarction and stroke, and thus it is not recommended that NSAIDs should be used in patients with a high risk for suffering those events (Katz and Barkin, 2010).

When NSAIDs are used in the management of pain in older people, they should be used at the lowest effective dose and their use limited to the short-term use (< 2 weeks) only (O'Neil et al., 2012, Fimea, 2014). Thus, as-needed administration of NSAIDs is preferred, particularly for intermittent pain. Extended-release NSAIDs are often preferred for chronic pain for the sake of compliance although they increase the risk of upper GI-bleeding and renal dysfunction as compared with the short-acting NSAIDs (Davis and Srivastava, 2003, de Abajo and Garcia-Rodriguez, 2008). Furthermore, NSAIDs should be used one at a time and they should not be combined with other similar drugs that increase the risk for GI-toxicity, therapeutic redundancy or cause renal toxicity (Barkin et al., 2010, Davis and Srivastava, 2003). However, it seems that there are inconsistencies between guidelines and practice, because the study of Johnell, Fastbom et al. (2008) revealed that the most common potentially serious drug-drug interaction encountered in older people is concurrent use of ASA with an NSAID.

COX-2 selective NSAIDs were introduced in the hope of reducing NSAID-related adverse effects, but they failed due to an increased risk of cardiovascular events and pharmacokinetic ADRs (Mitchell et al., 2009). In addition, there is mixed evidence showing that COX-2 selective analgesics may be associated also with adverse GI effects (O'Neil et al., 2012). Two COX-2 inhibitors, rofecoxib and valdecoxib, had to be withdrawn from the market due to concerns about unacceptable risks of adverse cardiovascular events and celecoxib, that is still available, has a black-box warning about the increased risk of cardiovascular events (Katz and Barkin, 2010, Nurminen, 2011). According to guideline recommendations, COX-2 selective inhibitors should be considered only rarely, and with extreme caution, in highly selected older individuals (American Geriatrics Society, 2009).

A recommended strategy to reduce the risk of potential GI-toxicity of NSAIDs is co-administration with gastroprotective agents, such as misoprostol or a proton pump inhibitor (American Geriatrics Society, 2009). Older people should use a gastroprotective agent with traditional NSAIDs and with COX-2 selective NSAIDs when they are using low-dose ASA concurrently (Barkin et al., 2010). Despite the guidelines recommending preventive strategies in high-risk patients, most patients do not receive co-therapy (Abraham et al., 2005, Laine et al., 2009). In the study of Abraham et al. only 27% of high risk NSAID users had been provided with a strategy to decrease upper GI risk and the minority, 42%, of patients with three risk factors were receiving protective therapy. Furthermore, incomplete adherence (< 80%) to protective co-therapy significantly increases the risk of developing upper GI ulcers or bleeding in patients taking NSAIDs (Goldstein et al., 2006). There is a report that clinicians can reduce the risk of NSAID-related upper GI events by adhering to recommended guidelines for safer NSAID prescribing, although the risk can never be entirely eliminated (Abraham et al., 2008). Nonetheless, the systemic effects of NSAIDs should be noted regardless of gastroprotective co-therapy, because the above-mentioned agents do not protect from lower GI-damage or

bleedings (Nagata et al., 2014, Sostres et al., 2013). One useful way to avoid the ADRs associated with oral NSAIDs is to administer NSAIDs in a topical preparation (Altman and Barthel, 2011, Zhang et al., 2007, Zhang et al., 2007).

Topical analgesics

The topical analgesic products marketed in Finland include mainly NSAIDs (diclofenac, ketoprofen or piroxicam) and salicylate derivatives formulated as gels, creams or solutions. Topical NSAIDs provide analgesia by the same mechanism of action as oral NSAIDs, but due to their local application and localized site of action, the systemic NSAID exposure is substantially lower than with oral products (Altman and Barthel, 2011). The precise mechanisms of action of salicylate derivatives are unclear and their efficacy in pain management has been modest (Mason et al., 2004). The current Finnish care guidelines recommend topical NSAIDs for osteoarthritis pain alone or as an adjuvant therapy, because there is evidence that they reduce pain and increase patient's ability to function more than placebo (Barthel et al., 2009, Knee and Hip Osteoarthritis: Current Care Summary, 2012). Clinical trial data published to date support the analgesic efficacy of topical diclofenac and ketoprofen in patients with osteoarthritis affecting one or more superficial joints such as those in knees or hands but the data concerning piroxicam suggests that it has only modest efficacy (Altman and Barthel, 2011). According to some studies, one topical NSAID, diclofenac, provides effective analgesia for osteoarthritis even when compared to the oral diclofenac, but because insufficient numbers of older persons have participated in clinical trials, the risks of this type of therapy remain unclear (Derry et al., 2012, Fine, 2012, Simon et al., 2009). However, the safety studies have indicated that the most common ADEs are application-site reactions while serious adverse events are rare and almost always unrelated to treatment (Altman and Barthel, 2011). Therefore, topical NSAIDs have a potential role in the treatment of localized non-neuropathic pain in older patients since they minimize systemic exposure to NSAIDs. However, topical salicylates have not been recommended in recent guidelines for the management of osteoarthritis since they have shown less efficacy and are still associated with substantial systemic salicylate exposure and toxicity (Altman and Barthel, 2011).

Opioids

Opioid analgesics may represent the drugs of choice for older patients who do not respond to paracetamol or NSAIDs or who cannot tolerate the side effect profiles of these agents. Opioids inhibit pain pathways by binding to and activating the μ -opioid receptors in the CNS and they are recommended in the treatment of moderate to severe pain (O'Neil et al., 2012). Opioids are available for various routes of administration, such as oral, rectal, sublingual, transdermal, spinal and intravenous (Davis and Srivastava, 2003). Many guidelines recommend that opioid therapy should be considered for all patients with moderate-to-severe pain, pain-related functional impairment, or diminished quality of life due to pain (Gloth, 2011). However, opioids are not appropriate for all patients and the initiation and selection of an opioid for an older patient needs to take into consideration on the basis of the pain intensity, age-related alterations in liver and renal function, comorbid conditions, current medications and the patient's ability to take the preparation (O'Neil et al., 2012). The lack of a ceiling dose and possibility for titration of dose are advantages of most opioids but age-related changes in the CNS and GI-tract increase the sensitivity to both the therapeutic and toxic effects of opioids (Mitchell et al., 2009). For an older patient, it is recommended that prescribers should initiate opioid therapy at a low dose, titrate slowly, and monitor drug concentrations and adverse events. Due to their common mechanism of action, opioids share similar adverse effects, including sedation, drowsiness, dizziness, nausea, vomiting and constipation. Many of these effects are worse at the time of opioid initiation or at dose escalation, and may resolve later on, but constipation often need to be managed with laxative therapy or provision of a peripheral opioid antagonist (Abdulla et al., 2013).

Opioid therapy seems to have no effect on mood or to increase the risk of respiratory depression in older persons as long as low starting doses and proper titration are used (Podichetty et al., 2003). However, respiratory depression is a particular concern in very old and frail patients, as well as in individuals with underlying pulmonary conditions such as chronic bronchitis, multiple sclerosis, chronic obstructive pulmonary disease, etc. or in patients being treated other CNS drugs that affect ventilation (Pergolizzi et al., 2008). It is uncommon to note any decline in cognitive function in patients taking stable opioid doses, but this symptom may appear for one week after a dose increase (Abdulla et al., 2013). However, opioid CNS toxicity is a significant issue in older patients, where it can present as hallucinations, confusion and problems with cognition and these symptoms may occur when opioids are given over the long-term at high doses, particularly in dehydrated, severely ill patients with renal impairment (Pergolizzi et al., 2008). This is particularly detrimental for older persons who are at the increased risk of falling and suffering serious fractures. A higher fracture risk has been observed in older people who start to receive opioid analgesic therapy or who use high doses or short-acting opioid preparations (Miller et al., 2011, Saunders et al., 2010). In contrast, the risk of addiction or opioid abuse is probably not a major concern in the older population. Drug-seeking behaviour and 'doctor-shopping' to obtain multiple opioid prescriptions i.e. opioid abuse is not commonly encountered in older persons with nonmalignant pain (Neutel et al., 2013). There was an increase in the number of prescribers and in defined daily doses of opioids in cancer/palliative patients, but these patients typically represent a population needing larger amounts of opioids.

According to the WHO analgesic ladder, weak opioids (such as codeine, tramadol and buprenorphine) are the second-line option after non-opioids (Figure 5). However, codeine and tramadol are not the best options for older people (Arnstein 2010). In Finland, codeine is marketed only in fixed combination products including paracetamol or ibuprofen and those ingredients are associated with the previously mentioned risks and daily dose limits. In the case of tramadol which is a drug that displays also serotonin and noradrenaline reuptake inhibitory effects, drug-drug interactions with agents affecting noradrenaline and serotonin levels and the risk for seizures at high doses are problematic in the treatment of older patients (Arnstein, 2010). In addition, it has been claimed that codeine and tramadol may cause more nausea and constipation than other opioids (Mitchell et al., 2009). Furthermore, codeine and tramadol are prodrugs that are activated by the enzyme CYP2A6 to morphine and inherent genetic differences or consumption of medications influencing CYP2A6 may cause large variations in the efficacy of those drugs (Davis and Srivastava, 2003). The pharmacokinetics of both agents may change, with age-related alterations leading to accumulation of active metabolites (Katz and Barkin, 2010).

Buprenorphine has mixed agonist-antagonist properties but at low doses analgesia is the main property (Mitchell et al., 2009). Buprenorphine is often classified in the available literature as a strong opioid, but due to the fact that it possesses only partial opioid receptor activating properties and it has a ceiling effect, it is included into the group of weak opioids in this thesis. In addition, in clinical use, buprenorphine is often prescribed for the same indications as the other weak opioids, especially its transdermal formulation can be recommended for patients experiencing pain of moderate intensity (step 2) (Gatti et al. 2010). Transdermal buprenorphine may offer advantages over other weak opioids when used in older patients. It has been found to be effective against chronic noncancer pain and because of its mainly biliary excretion into the feces, there is no risk of accumulation even in cases of serious renal failure which is single most important common organ deficit found in older people (Gianni et al., 2011). In addition, transdermal buprenorphine has been well tolerated without evoking serious ADRs in older patients (>70 years).

Strong opioids represent the third step in the WHO analgesic ladder (Figure 5). The opioids of first choice in this group are morphine, oxycodone, hydromorphone and fentanyl (van Ojik et al., 2012). Morphine is widely considered to be a first line strong opioid, but its toxic metabolites

for those with high dose requirements or renal insufficiency may limit its usefulness. The less harmful choices are those opioids which do not form toxic metabolites and for whom the doses can be adjusted in conditions of reduced hepatic or renal function. Oxycodone may be a better oral opioid choice in older persons because of its high flexibility and tailoring possibilities (Arnstein, 2010). It is almost totally metabolized in the liver and therefore active metabolites do not accumulate in patients with renal failure (Mitchell et al., 2009). The oral bioavailability of oxycodone is significantly higher than morphine and there is less interindividual variation. Oxycodone is metabolised by the CYP2D6 enzyme and drugs that block that enzyme prolong its effects by delaying its elimination (Davis and Srivastava, 2003). Even though oxycodone has some favourable aspects, there are some pitfalls to be taken into account. Several case reports have been published in recent years showing synergism of oxycodone with serotonergic agents leading the appearance of the serotonin syndrome (Rastogi et al., 2011).

Hydromorphone and fentanyl are typically reserved for patients with severe pain. Hydromorphone is often administered in immediate release formulations whereas fentanyl is most commonly administered as a long-acting transdermal patch applied to the skin (Arnstein, 2010). Fentanyl is a highly potent opioid and it has a rapid onset of action due to its lipophilic properties (Davis and Srivastava, 2003). Long-acting transdermal fentanyl is indicated for chronic pain only but it may be better tolerated in older people than oral morphine because it is less constipating, produces less daytime drowsiness and less disruption of daily life, and can be used for patients with renal or hepatic dysfunction (Arnstein, 2010, Davis and Srivastava, 2003). However, it should not be used in opioid naïve patients because fentanyl is 100 times more potent than morphine and the fentanyl transdermal patch is an inflexible system; furthermore, it may require several days to achieve steady-state drug level and subsequently the drug can be released from skin deposits for as long as 24 hours after removal of the patch, this time may even be extended in older patients since absorption is often delayed (Davis and Srivastava, 2003). In Finland, the prevalence of transdermal fentanyl use seems to be higher than that of morphine, oxycodone, and hydromorphone among older people (≥ 80 years) even though the Finnish National Agency for Medicines has recommended that oral opioids should be considered as the first-line treatment when a strong opioid is required to relieve severe pain (Bell et al., 2009).

Table 2. Considerations and recommendations related to analgesics in the management of pain in older people. Data gathered from Abdulla, Adams et al. 2013, AGS 2009, Arnstein 2010, Davis, Srivastava 2003, Mitchell, Hilmer et al. 2009, O'Neil, Hanlon et al. 2012, Ong, Lirk et al. 2007 and Pergolizzi, Boger et al. 2008.

DRUG	CONSIDERATIONS	RECOMMENDATION
Paracetamol	Renal and hepatic toxicity at doses > 4g in 24 h, at lower doses if dehydration, malnutrition, alcohol abuse or renal or hepatic failure. Efficacy varies in different pain conditions.	First-line analgesic drug, well-tolerated and relatively safe, recommended daily dose, short-term use 4g/24h or continuous use 3g/24h must not be exceeded. Efficacy should be checked.
NSAIDs, Nonselective Acetylsalicylic acid	Increased risk for GI-bleeding, renal failure, cardiovascular events Plays a role in preventing cardiovascular diseases, but not in pain management	Considered with caution, avoid if high GI-bleeding risk, renal or heart failure, or concomitant drugs that increase GI toxicity. Short-term use (<2 weeks) recommended. Concomitant gastroprotective agent can reduce the risk of upper GI-bleedings. Topical products recommendable for localized pain.
Ibuprofen	The lowest GI risk among nonselective NSAIDs, inhibits platelet effects of low-dose ASA	Ibuprofen should not be used with low-dose ASA
Diclofenac, Naproxen	Intermediate risk for GI bleeding when compared to ibuprofen, diclofenac carries a higher cardiovascular risk than naproxen	Naproxen recommended after ibuprofen
Ketoprofen, Ketorolac and Piroxicam	High GI risk	Should be avoided due to high GI risk
Indomethacin	Many fatal events involving older people, serious GI risk, CNS effects	Indomethacin should not be used at all
NSAIDs, COX-2 selective Celecoxib Etoricoxib	Lower GI risk, equal renal risk and elevated cardiovascular risk when compared to nonselective NSAIDs Metabolized mainly via CYP2C9, drug-drug interactions Metabolized mainly via CYP3A4, drug-drug interactions	The smallest effective dose for the shortest duration should be used to minimize the cardiovascular risk. Contraindicated in ischemic heart disease, cerebrovascular disease or renal failure. Considered with caution if CVD risk factors (hypertension, hyperlipidemia, smoking, diabetes).
Weak opioids Codeine Tramadol	Prodrug, activated by CYP2D6, common side-effect: constipation Prodrug, activated by CYP2D6, accumulates in renal impairment, may cause confusion and seizures in older persons, drug-drug interactions with serotonergic drugs	Should be considered individually, codeine and tramadol generally are not the best options for older patients. Codeine should be avoided in renal failure and tramadol in hepatic failure.
Buprenorphine	No accumulation in renal impairment, effective and well-tolerated but as a partial agonist has a ceiling effect	Buprenorphine is relatively safe in older patients, its half-life is not changed in renal insufficiency.
Strong opioids Morphine Hydromorphone Oxycodone	Sedation, confusion, hallucination, constipation, nausea Relatively safe in hepatic failure but sensitive to renal function Prolonged half-life in hepatic failure but can be used in renal failure	Considered with caution, concurrent laxative recommended. Lower doses are usually adequate due to decreased clearance. Controlled-release formulations recommended. Morphine and oxycodone are usually the first choices, but renal and hepatic function must be considered before initiation.
Fentanyl	Almost exclusively metabolized by CYP2D6, accumulated significantly in hepatic failure but relatively safe in renal failure	Fentanyl should not be used for opioid initiation. Can be used for patients with mild to moderate renal or hepatic dysfunction.
Methadone	100 times more potent than morphine, transdermal fentanyl causes less constipation than oral opioids Long and variable half-life, prolonged effects in older people	Methadone should be avoided due to unfavourable pharmacokinetic properties and risk of accumulation.

2.3.2 Nonpharmacological pain management

Nonpharmacological pain management includes variety of strategies that help pain patients by releasing endogenous opioids, increasing blood flow in the treatment area, changing the mental focus away from pain or improving functional capacity. Given the numerous complicating factors (such as pharmacokinetic changes, multimorbidity, polypharmacy and susceptibility to ADRs) associated with the pharmacotherapy of pain in older people, the importance of nonpharmacological treatment should not be overlooked in the treatment of older patients with chronic pain problems. Nonpharmacological pain management reduces the risk of polypharmacy and ADRs. In addition, active nonpharmacologic self-management strategies to reduce pain have been associated with lower levels of pain-related disability and reduced health care use (Blyth et al., 2005). Therefore, nonpharmacologic therapies should be considered not just as a complementary or alternative adjunct to medications, but as an indispensable component in treating older patients with pain. Older people's willingness to try nonpharmacological pain management approaches is often good i.e. more than two out of every three chronic pain patients have reported a willingness to participate for non-pharmacological therapies for managing pain (Austrian et al., 2005). The nonpharmacologic pain alleviating methods include physical exercise, psychosocial interventions, body-based strategies, relaxation, electrotherapy, cold or hot treatment and alternative medicine or strategies (Table 3).

Physical exercise is the most commonly used self-care method for pain management after drug medication (Kemp et al., 2005, Turunen et al., 2004). More than 40% of older people (≥ 65 years) found that regular exercise was moderately or extremely helpful for their persistent pain (Kemp et al., 2005). The improved strength in older adults had a positive effect on the perception of pain and significantly diminished the quality of the pain after an eight-week training period (Knutzen et al., 2007). Physical exercise, training and rehabilitation have an important role in reducing pain related mobility limitation and participation restrictions in older people (Thomas et al., 2004). It has also been reported that the functional decline among older people can be minimized or delayed if the subjects take physical exercise. Since physical exercise is an effective intervention for improving physical functioning in older people and it can significantly improve pain management and pain related limitations, it should be considered as a part of the care for all older individuals with chronic pain (American Geriatrics Society 1998, Liu and Latham 2009).

Psychosocial interventions focus on the interactions between the mind, body and behavior and they emphasize knowledge and self-management strategies. Cognitive behavioural therapy, relaxation, hypnosis, visual imagery, meditation, and spirituality are examples of this type of therapy (Bruckenthal, 2010). Cognitive behavioural therapy is a widely utilized method for teaching chronic pain self-management and there are an increasing number of studies confirming its utility for pain management in individuals aged 65 years or more (Keefe et al., 2013, Nicholas et al., 2013). Its target is to alter pain-relevant thoughts, emotions and behaviours during 6-12 sessions the subjects learn and practice pain-management skills (Keefe et al., 2013). In the study of Nicholas, Asghari et al. (2013) cognitive behavioural therapy achieved a clinically significant improvement on pain disability and on a short-term scale it was more effective than exercises and usual care. Emotional disclosure, where the patients write or speak for several 15–20 min sessions about their deepest thoughts and feelings related to a stressful experience, may also have a role in pain management although the research results in the literature are mixed (Keefe et al., 2013). Furthermore, there is a growing interest in the use of mind-body interventions, such as mindfulness meditation and yoga with group discussions, evidence that these approaches may be helpful and in fact preliminary research appears promising. Mindfulness seems to increase well-being by improving sleep, attention skills as well as emotional processing and the acceptance of pain (Morone et al., 2008). The mind-body intervention may reduce mean pain scores even during a relatively short-term intervention conducted over the Internet (Berman et al., 2009). However, it should be noted that these

methods have been studied often with a small number of participants and therefore the conclusions drawn may be questionable.

Manipulative and body-based strategies include chiropractic techniques, osteopathic medicine, massage and acupuncture (Bruckenthal 2010). These strategies focus on body unity issues, enhance homeostatic mechanisms and structure-function interrelationships that may alleviate pain and discomfort for example in bones, joints and soft tissues. The use of manipulative therapies is relatively common among the general population especially for back-related pain problems, but there is little research concerning older populations (Ong et al., 2004, Xue et al., 2008). Cold and warmth are common physical methods used to alleviate pain and given the high benefit to risk ratio of such interventions and noting that each may lead to the release of endogenous opioids, it may be worth while considering these kinds of nonpharmacologic measures when appropriate. Dietary supplements such as vitamins, herbs, fatty acids and probiotics comprise a mixed group of products that can be used to help in self-management of pain. For example, correction of moderate vitamin D deficiency may be beneficial in older people with knee or hip pain (Laslett et al., 2012). Glucosamine sulphate and chondroitin sulphate are two of the most widely studied supplements and although there are claims that they may of benefit in the treatment of osteoarthritis the evidence is controversial (Bruckenthal, 2010, Wandel et al., 2010).

Unrelieved persistent pain often causes patients to seek relief from alternative practitioners utilizing homeopathy, naturopathy, spiritual healing etc. Although there is little scientific evidence for their efficacy, it is clear that alternative and complementary strategies are practiced with or without the knowledge of the treating physician. Nonetheless, they should be recognized as possible options for certain patients. The personal attention and physical contact provided by practitioners of these alternative therapies may provide some degree of relief to patients with persistent pain. However, many alternative interventions are costly and some even may represent health risks (Smith and Dillon, 2009, Tovar and Petzel, 2009). Often the physician is the only source of objective information on such options and for this reason, it seems reasonable that clinicians should be aware of the growing field of alternative medicine (especially in pain management).

Table 3. Examples of nonpharmacological pain management strategies. Gathered from Bruckenthal 2010; Kemp, Ersek et al. 2005; Shin and Kolanowski 2010 and Tsai, Liu et al. 2010.

NONPHARMACOLOGICAL PAIN MANAGEMENT STRATEGIES	
Physical exercise	Improving overall physical functioning, muscle strength and joint mobility, physiotherapy, gym training, stretching, swimming
Psychosocial interventions	Cognitive behavioural therapy, hypnosis, meditation, spirituality, yoga
Rest and relaxation	Sit/lie down, sleep, listen to music, read a magazine, watch TV, avoid painful movements
Body-based strategies	Massage, chiropractice, osteopathy, acupuncture
Electrotherapy	Transcutaneous Electrical Nerve Stimulation (TENS)
Thermal stimulation	Cold/hot pad or bath, warming ultrasound
Assistive device	Walker, walking stick, joint support
Dietary supplements and lifestyle	Vitamins, herbs, fatty acids, probiotics, glucosamine, chondroitin, vegetarianism, losing weight
Alternative strategies	Homeopathy, naturopathy, spiritual healing, energy healing, aromatherapy
Education	Arthritis self-management program, educational booklets

2.4 SUMMARY OF THE LITERATURE

Pain is highly prevalent in community-dwelling older people with musculoskeletal pain in the limbs being the most common type and site of pain. Both ageing and pain are very subjective experiences and therefore recognizing and assessing pain and its effect on daily life in older persons plays an important role in achieving appropriate management of pain and pain-related problems. Older people and even healthcare professionals may view pain as an inevitable consequence of aging but this “wear and tear” attitude can have devastating consequences. It worsens overall quality of life and may mean that older people limit their physical activity in order to avoid further ‘wearing’ of painful limbs. The restriction of painful movements results in atrophy of muscles which increases further the mobility limitation and additionally the fear of pain accentuates the avoidance cycle. In the long run, this vicious circle increases pain and its related functional restrictions. It seems that there is a complex mesh of factors influencing each other and therefore it is extremely difficult to determine accurately which are the causes and what are the consequences.

The early identification of people at high risk of pain-related mobility restriction and chronic disability may allow preventive strategies, more intensive management, better use of resources, all leading to a reduction in disability. It is important to combine both pharmacological and nonpharmacological pain management strategies to achieve a multidimensional intervention to help with an older person’s pain problems. However, there are significant challenges in this kind of implementation and more research is needed to determine the most effective interventions for older people. Although evidence about the effectiveness of improving pain management and the prevention of the functional decline in older people is limited, it does seem that more and more interest has arisen during the last decade. There are still many research gaps that need to be filled in order to improve pain management in older people. For example, little is known about the long-term pharmacokinetics, safety and efficacy of commonly prescribed nonopioids and opioids, nor have the properties of specific medication classes in older people been adequately compared. It is also important to identify those patient-level and medication-level factors that influence the likelihood of experiencing positive or negative treatment outcomes. Optimal nonpharmacological approaches combined with pharmacological treatment should be examined and supplemented into pain management guidelines. Furthermore, beliefs, attitudes and hopes of older pain patients and health care professionals are important issues that need to be taken into account when developing new interventions. There is a clear need to clarify the crucial factors that negatively impact on pain management.

3 Aims of the Study

The overall objective of this study was to investigate pain, analgesic use and the mobility limitation associated with pain among community-dwelling older people (≥ 75 years) in Finland.

The specific aims of this study were:

1. To assess the prevalence and the pattern of analgesic use.
2. To investigate the relationship between pain, analgesic use and mobility limitation and to identify factors associated with the mobility limitation.
3. To determine the persistence of musculoskeletal chronic pain and factors related to this condition.
4. To clarify whether older persons with musculoskeletal chronic pain hope for more attention to pain management from their physician and to investigate the persistence of those hopes.

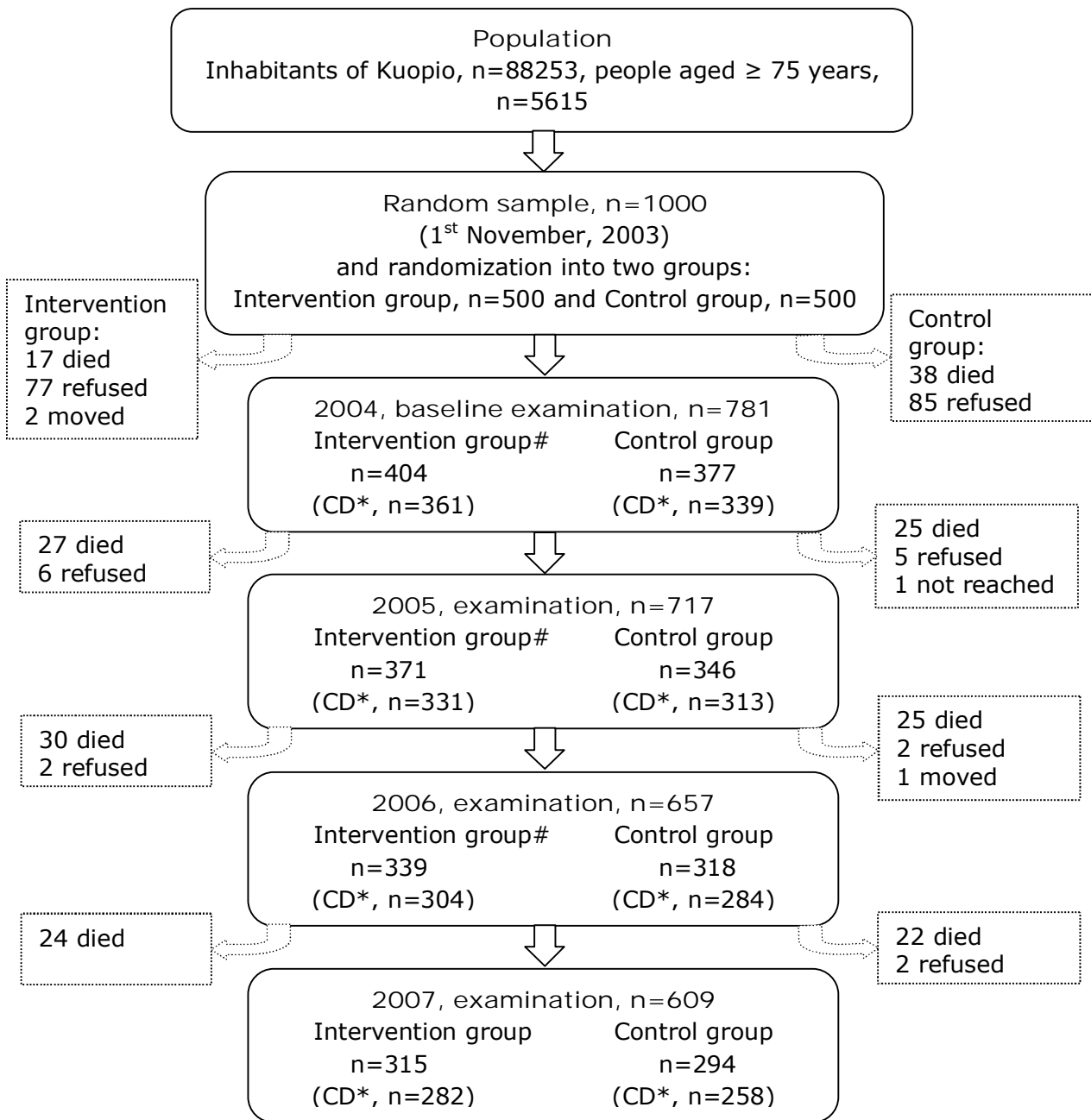
4 *Materials and Methods*

4.1 GEMS STUDY

This thesis is based on the population-based GeMS study (Geriatric Multidisciplinary Strategy for the Good Care of the Elderly). The GeMS is a multi-disciplinary health intervention study that was conducted in the City of Kuopio, Eastern Finland, between 2004 and 2007. The study was designed to evaluate the effects of annual Comprehensive Geriatric Assessment (CGA) based interventions on health and nutritional status, functional capacity, drug use and hospitalization in older persons.

4.1.1 Population

A random sample of 1000 persons aged ≥ 75 years was drawn from the population register of the City of Kuopio, Finland, on 1st November 2003 (88 253 inhabitants, 5615 aged ≥ 75 years) (Figure 7). These individuals were randomized into intervention (n=500) and control (n=500) groups. Of those invited to participate to the study, 162 declined to attend, 55 died before the examination and 2 moved to a different municipality. Thus, a total of 781 persons (78% of the initial sample, 404 in the intervention group and 377 in the control group), provided written consent to participate. The baseline examination was performed in 2004 and the study continued with annual examinations conducted in 2005, 2006 and 2007. Of the study participants at baseline, 233 (30%) were men and 548 (70%) women with a mean age 81.7 years (range 75.3–99.0). The majority were community-dwelling (n=700) with 81 living in institutional care. The attrition during the follow-up was mainly due to deaths. The details of the populations examined in studies I–IV are presented in Table 4.



#) Intervention group underwent a CGA and multiple interventions
 *) CD=Community-Dwelling

Figure 7. Flow chart of the GeMS study.

Table 4. The community-dwelling participants in the studies included in this thesis.

STUDY	POPULATION	DESIGN	MAIN OUTCOME
I	All community-dwelling participants in 2004, n=700	Observational Cross-sectional Additional data in the thesis: Longitudinal	The use of analgesics
II	All participants in 2004 fulfilling the inclusion criteria, n=622 1) did not have moderate or severe cognitive impairment (MMSE score >18) 2) participated in the mobility assessment 3) provided pain information	Observational Cross-sectional	Mobility limitation
III	Control group participants in 2005 fulfilling the inclusion criteria, n=272 1) did not have cancer 2) did not have moderate or severe cognitive impairment (MMSE score >18) 3) did not drop out before follow-up	Observational Cross-sectional and longitudinal	The course of chronic pain
IV	All participants in 2005 fulfilling the inclusion criteria below, n=270 1) did not have cancer 2) did not have moderate or severe cognitive impairment (MMSE score >18) 3) had chronic pain (≥ 3 months)	Observational Cross-sectional and longitudinal	A hope to receive more attention to pain management

4.1.2 Study protocol

The study protocol included an annual examination conducted in the years from 2004 to 2007 for all study participants. The participants were examined and interviewed annually by three study nurses, who were committed to follow written guidelines of the study. During the examinations and interviews, information was collected on demographic characteristics, living conditions, health status, functional capacity and drug use. The protocol also included some laboratory tests in the years 2004 and 2006. All participants had normal access to primary and specialized health care during the study period. In the GeMS study, several interventions were performed, but in this thesis the purpose was not to investigate their impact, because pain and pain medication was not on the focus of interventions.

Interventions

After the baseline examination, the participants in the intervention group underwent an annual CGA that included a clinical examination, medication assessment and interventions to improve nutritional status and functional capacity. The CGA was performed by a team of two physicians (trainees in geriatrics), three study nurses, two physiotherapists and a nutritionist. One of the original physicians left the study after the first baseline assessments and was replaced by another physician. The physician interviewed and examined the participants in the intervention group generally within two weeks after the nurse's interview. The physician undertook a critical drug assessment and referred the patient to a specialist when necessary. Each participant in the intervention group was supplied with a tailored training program (eg. supervised muscle strength and balancing training once a week in the gym) compiled by a

physiotherapist to improve functional capacity and mobility. Those who were at risk of malnutrition (short Mini Nutritional Assessment score ≤ 11), received a nutritional intervention. The nutritionist met the participant in the years 2005 and 2006, and spoke with the participants at least every two months during the intervention helping participants with meal plans, dietary issues etc. In addition, two experienced dentists performed an oral health assessment in the participants in the intervention group and an oral intervention was carried out if needed.

4.1.3 Data collection

Annual interviews and examinations were performed in the municipal health centre or in the participants' current residence. The study nurses used a structured questionnaire during the interview and when examining the participants. If the participant was unable to answer the questions (e.g. due to dementia), a caregiver or home nursing staff responded instead. The data collecting personnel had also access to medical records from the municipal health centre, home nursing service, local hospitals and Kuopio University Hospital to verify the accuracy of information collected during the interviews.

Participants were asked questions on living situation during the interview and they were categorized as either community-dwelling (living in own home or in sheltered accommodation) or under institutional care (nursing home, residential care home, long-term hospital care). They were also asked if they were living alone or with some other person. The total length of education was enquired and in this thesis it was dichotomized into two groups: 1) 6 years or less (compulsory primary education in Finland before the Second World War) and 2) more than 6 years (including additional and vocational education).

Pain and the use of analgesics

Annual interviews and examinations included the assessment of pain containing structured questions about the presence, location, frequency and severity of pain. Eighteen community-dwelling participants (2.5%) did not provide any information about the presence of pain at baseline in 2004. The study nurses interviewed the participants with regard to their prescriptions and OTC drug use. To reduce the possibility of recall error, the participants were asked to bring along their prescription forms and medication packages to the interview. Definitions of pain and analgesic drugs are described in more detail in chapter 4.2.

Mobility

The mobility of the participants was assessed with Timed Up and Go test (TUG) (study II). In the TUG, the participant rises from a standard chair with armrests, using arms for support if needed, walks three meters as quickly as possible, turns around and walks back to return to a fully seated position in the same chair. During the test, the participants wore their regular footwear and were allowed to use any mobility aids that they would normally require. The time taken to complete the test was measured with a stopwatch and participants were considered to have a mobility limitation if the time exceeded 13.5 seconds or if they were unable to perform the test. The cut-off point was based on the study of Shumway-Cook et al. (2000), in which the longer times were associated with an increased risk of falling among people aged 65–95 years.

In addition, self-rated mobility was asked by the question: "Are you able to walk 400 meters?" (studies I, III and IV). Participants chose one option from four alternatives: 1) yes, without difficulties 2) with difficulties, but independently 3) not without the help of some other person 4) no. In the study I groups 3–4 were combined into group "not independently". In studies III and IV groups 2–4 were considered to have mobility difficulties and they were compared to the subjects in group 1

Health and functional characteristics

Participants' body weight and height were measured and the Body Mass Index (BMI) calculated to reveal obesity. Information of chronic diseases was collected from the Finnish Social

Insurance Institution (SII) Special Reimbursement Register, interviews, medical records and lab tests. The question evaluating self-rated health included 5 response options and the subcategories 1–2 (good and fairly good) and 4–5 (fairly poor and poor) were combined in the analyses conducted in study I. The middle category 3 (moderate) was combined with categories 1–2 in study II and with categories 4–5 in studies III-IV to create a two class variable.

During the interviews, Mini Mental State Examination (MMSE) (Folstein et al., 1975) was performed to define the participants' cognitive performance and the 15-item Geriatric Depression Scale (GDS-15) (Sheikh and Yesavage, 1986) to assess depressive symptoms. In addition to mobility tests, functional status of the participants was determined with Instrumental Activities of Daily Living score (IADL) (Lawton and Brody, 1969), Barthel index (Mahoney and Barthel, 1965), muscle strength and self-reported physical activity. Detailed definitions concerning health and functional characteristics are presented in chapter 4.2.

4.1.4 Ethical issues

The GeMS study protocol was approved by the Research Ethics Committee of the Hospital District of Northern Savo as required by Finnish legislation. All the participants were informed about the study and they or their caregivers signed a written informed consent form.

4.1.5 Data management and statistical analyses

All the data collected in the GeMS study were entered into the SPSS statistical software for Windows (SPSS Inc., Chicago, USA) and all the statistical tests and analyses were performed with this software. In the analyses different versions of the software were used (I–II: 15.0, III: 17.0 and 19.0, IV: 19.0). In addition, Microsoft Excel 2007 was used to create bar graphs (I and II).

The characteristics of participants at baseline were compared using Pearson's χ^2 -test for categorical variables and Mann-Whitney U-test for continuous variables. Logistic regression models were used to determine Odds Ratios and 95% Confidence Intervals. P-values <0.05 were considered statistically significant.

4.2 DEFINITIONS

4.2.1 Pain

Musculoskeletal pain was defined as pain experienced in the shoulders, neck, back, hips, knees, or other sites in the upper or lower body. Headache and persistent pain with symptoms resembling "electric shocks, pressure-evoked pain, numbness, stabbing or tingling" (suggestive of neuropathic pain) were also asked. The frequency of pain was assessed with the question "For how long have you had pain?" and three response options were given: less than 1 month, 1–3 months, more than 3 months. Pain was defined as chronic, if pain duration was more than 3 months. The severity of pain was assessed with a 10-point Numeric Rating Scale (NRS), which had the numbers 1–10 written from left to right; the participant circled the number that corresponded best to his/her pain. Pain rated with numbers 2–4 was categorized as mild and pain rated with numbers 5–10 as moderate to severe. Unfortunately, due to a misunderstanding in the data collecting process, the pain data from the control group was incomplete at the baseline in year 2004. Detailed pain definitions in the studies included in this thesis are presented in Table 5.

Table 5. The definitions of pain in the studies I–IV.

STUDY	PAIN DEFINITION
I	Any pain Any pain during the previous month, e.g. pain in the shoulders, neck, back, hips, knees, or other sites in the upper or lower body. Headache and persistent pain with symptoms resembling “electric shocks, pressure-evoked pain, numbness, stabbing or tingling” (suggestive of neuropathic pain) were also included.
II	Musculoskeletal pain Pain experienced in the shoulders, neck, back, hips, knees or other sites in the upper or lower body for at least 7 days during the month immediately preceding the assessment.
III–IV	Chronic musculoskeletal pain Pain experienced in the shoulders, neck, back, hips, knees or other sites in the upper or lower body for at least 3 months immediately preceding the assessment.

4.2.2 Analgesic drugs

Analgesic drugs were categorized into four groups according to the Anatomical Therapeutic Classification System recommended by the World Health Organization (WHO, 2014). Detailed analgesic groups and subgroups are presented in Table 6. Low-dose acetylsalicylic acid (≤ 250 mg daily) was excluded i.e. it was being used as an antithrombotic agent. Acetylsalicylic acid, with caffeine and vitamin C powder (marketed for flu) and orphenadrine in combination with paracetamol (marketed as a muscle relaxant) were excluded from the list of analgesic drugs. Analgesic use was classified as either daily or as needed (less frequent than daily). Those participants who were analgesic users at the time of all four annual interviews were defined as frequent users.

Table 6. The classification of analgesic drugs. The table includes only drugs available on the market in 2004–2007.

ANALGESIC GROUP	ATC-CODE	CHEMICAL NAMES
Paracetamol	N02BE01	Paracetamol (acetaminophen)
NSAIDs		
Traditional	N02BA01	Acetylsalicylic acid
	M01AB	Indomethacin, diclofenac, etodolac, ketorolac
	M01AC	Piroxicam, tenoxicam, meloxicam
	M01AE	Ibuprofen, naproxen, ketoprofen, tiaprofenic acid, dexibuprofen, dexketoprofen
	M01AG	Mefenamic acid, tolfenamic acid
	M01AX01	Nabumetone
COX-2 selective	M01AH	Celecoxib, rofecoxib, valdecoxib, parecoxib, etoricoxib, lumiracoxib
Opioids		
Mild	N02AA59	Codeine
	N02AE01	Buprenorphine
	N02AX02	Tramadol
Strong	N02AA	Morphine, hydromorphone, oxycodone
	N02AB03	Fentanyl
Topical analgesics	M02AA	Piroxicam, ketoprofen, diclofenac
	M02AC	Preparations with salicylic acid derivatives

4.2.3 Health and functional characteristics

Definitions of the factors indicating the health and functioning of the participants are compiled in Table 7. Comorbid conditions influencing physical function were determined with the modified version of Functional Comorbidity Index (FCI) (Groll et al., 2005). The modified FCI was calculated by a simple sum score of 13 diseases found in the data of GeMS study: 1) rheumatoid arthritis and other connective tissue diseases, 2) osteoporosis, 3) asthma or chronic obstructive pulmonary disease (COPD), 4) coronary artery disease, 5) heart failure, 6) myocardial infarction, 7) multiple sclerosis or Parkinson's disease, 8) stroke, 9) diabetes type I or II, 10) depression, 11) visual impairment, 12) hearing impairment and 13) obesity (BMI < 30.0).

Patient diagnoses were obtained from registers maintained by the Social Insurance Institution (SII) of Finland, self-report and medical records. Finnish National Prescription and Special Reimbursement Registers maintained by the SII were used to screen for the presence of rheumatoid arthritis and other inflammatory connective tissue diseases (the data did not include osteoarthritis), chronic asthma or COPD, Parkinson's disease, or multiple sclerosis. Other conditions of the FCI were ascertained either from participant self-report or the medical records. Depressive symptoms were assessed with the GDS-15 (scores of 5 or more were considered as being indicative of depression) or any of the depression types defined by DSM-IV criteria (major depression, dysthymia, other depression, or depression episode of bipolar disease). The presence of each of the 13 conditions listed previously included in the FCI resulted in a score of one and thus a higher FCI sum score represented greater comorbidity.

Table 7. Definitions of the health and functional characteristics of the study participants.

	FACTOR	DEFINITION
STATE OF HEALTH	BMI	The Body Mass Index: body weight (kg) divided by body height squared in meters, score ≥ 30 indicating obesity.
	FCI (scale 0–13)	The modified Functional Comorbidity Index (Groll <i>et al.</i> , 2005) revealing the participants' comorbid conditions with a sum score of 13 diseases (detailed description in the text).
	GDS-15 (scale 0–15)	The 15-item Geriatric Depression Scale to screen for depressive symptoms (Sheikh and Yesavage, 1986), score ≥ 5 indicating depressive mood.
	MMSE (scale 0–30)	The Mini Mental State Examination scale to screen for cognitive performance (Folstein <i>et al.</i> , 1975), score < 18 indicating moderate to severe cognitive impairment.
	Self-rated health	Subjective health assessed by the question "How would you describe your present health?" with five options: 1) good 2) fairly good 3) moderate 4) fairly poor 5) poor. (Cousins, 1997)
	Diseases	
	Arthritis	Included rheumatoid and osteoarthritis. Rheumatoid arthritis was confirmed from the SII Special Reimbursement Register. Assessment of osteoarthritis was based on the baseline clinical examination and medical records.
	Asthma/COPD	Based on the SII Special Reimbursement Register code indicative of chronic asthma or COPD.
	CVD	Cardiovascular disease included coronary artery disease, heart failure and myocardial infarction. The presence of CVD was based on the SII Special Reimbursement Register codes (studies I–II) and the information was complemented from the interview and medical records (studies III–IV).
	Diabetes	Included types I and II. The presence of diabetes was based on the SII Special Reimbursement Register codes (Studies I–II) and the information was complemented from the interview, medical records and lab tests (studies III–IV).
Stroke	Included verified (from medical records) brain infarction due to thromboembolism, ICH, subarachnoidal bleeding or unclassified reason.	
FUNCTIONAL STATUS	IADL (scale 0–8)	The Instrumental Activities of Daily Living scale (Lawton and Brody, 1969) estimating functional capacity, score < 6 indicating reduced daily function.
	Barthel Index (scale 0–100)	Standardized tool for measuring functional status (Mahoney and Barthel, 1965), score < 80 indicating reduced independence.
	Muscle strength	Maximal isometric knee extension strength in a sitting position using an adjustable dynamometer chair (Good Strength, Metitur Oy, Palokka Finland). The results were categorized and divided by age and sex into tertiles. The highest tertile was compared to the lower tertiles.
	Physical activity	Assessed with a modified version of the scale of Grimby (Grimby, 1986). Categorization on the basis of self-reported physical activity into a sedentary group (no exercise, or at most light walking 1–2 times a week) and more active group.

5 Results

5.1 THE BASELINE CHARACTERISTICS OF THE STUDY PARTICIPANTS

The age of the community-dwelling participants' (n=700) ranged from 75.3 to 99.0 years with mean age of 81.3 ± 4.6 years. The majority of participants were women (n=486, 69.4%) (Table 8). The most common medical conditions suffered by the participants were cardiovascular diseases (n=455, 65.0%) and arthritis (n=278, 39.7%). Almost half of the participants (n=318, 45.4%) were users of daily or as-needed analgesics.

Slightly over half (51.7%, n=362) of the participants were without any pain but almost as many did have pain (45.7%, n=320). Those participants experiencing pain were more often women, had depressive symptoms, diabetes and a sedentary lifestyle (Tables 8 and 9). High BMI, arthritis, mobility limitation, poor self-rated health and daily use of analgesics were significantly more common among participants with pain than in those without pain. In addition, they were taking a higher total number of drugs (excluding analgesics) and had a higher FCI score.

Analgesic users were more often female and living alone than analgesic non-users, irrespective of the presence of pain ($p < 0.05$). Users experiencing any pain had depressive symptoms, poor self-rated health, asthma/COPD, diabetes, arthritis and daily analgesics more commonly than those without pain. Painfree analgesic users had lower functional statuses than their painfree non-user counterparts. In participants with any pain, the analgesic users had more often depressive symptoms and rated their health as poorer than non-users. In addition, they had more commonly cardiovascular disease, arthritis, a low IADL score and mobility limitations.

Table 8. The baseline (2004) Characteristics of the community-dwelling participants (n=700) according to the presence of any pain and the use of analgesics.

Variable (n=missing)	Without any pain n=362		With any pain n=320		No pain data, n=18	
	Number of missings	Non-user, n (%)	User, n (%)	Non-user, n (%)		User, n (%)
Age, 75–79		149 (54.6)	41 (46.1)	50 (51.0)	98 (44.1)	8
80–84		82 (30.0)	29 (32.6)	32 (32.7)	70 (31.5)	2
≥85		42 (15.4)	19 (21.3)	16 (16.3)	54 (24.3)	8
Sex, female		166 (60.8)	69 (77.5)	65 (66.3)	177 (79.7)	9
Education, 0–6 years	18	121 (45.7)	45 (51.7)	46 (47.4)	118 (54.9)	12
Living alone		138 (50.5)	63 (70.8)	48 (49.0)	143 (64.4)	10
Depressive symptoms, GDS-15 score 5–15	11	17 (6.3)	4 (4.5)	5 (5.3)	28 (12.9)	0
MMSE score 0–24	1	62 (22.8)	26 (29.2)	21 (21.4)	56 (25.2)	9
BMI ≥ 30	10	38 (14.0)	17 (19.8)	23 (24.0)	65 (29.3)	3
Poor self-rated health	2	132 (48.4)	43 (48.3)	52 (53.1)	163 (73.4)	7
FCI score, mean±SD		2.1±1.6		2.93±1.7		
		2.0±1.5	2.2±1.7	2.5±1.7	3.1±1.7	
Asthma/COPD		26 (9.5)	3 (3.4)	10 (10.2)	27 (12.2)	0
Cardiovascular disease		166 (60.8)	61 (68.5)	58 (59.2)	158 (71.2)	12
Diabetes	4	38 (14.0)	10 (11.2)	15 (15.3)	49 (22.2)	2
Stroke	9	35 (13.0)	11 (12.5)	10 (10.3)	36 (16.4)	2
Arthritis	34	61 (23.4)	34 (41.5)	46 (48.9)	134 (62.9)	1
Number of drugs, mean±SD		5.0±3.2	5.4±3.4	6.9±3.4	7.7±4.0	8.7±3.9
Use of analgesics,						
As needed		-	75 (84.3)	-	163 (73.4)	6
Daily		-	14 (15.7)	-	59 (26.6)	1
<i>Functional status</i>						
IADL score 0–6	2	93 (34.1)	32 (36.4)	23 (23.5)	91 (41.2)	13
Barthel index 0–80	5	10 (3.7)	12 (13.5)	4 (4.1)	23 (10.4)	2
Self-rated mobility, not able to walk 400m without help		22 (8.1)	15 (16.9)	5 (5.1)	35 (15.8)	2
Sedentary	50	81 (31.0)	36 (44.4)	36 (38.3)	102 (48.1)	missing data
Poor muscle strength	48	116 (44.4)	35 (42.7)	39 (41.5)	108 (50.7)	missing data
Mobility limitation, TUG > 13,5s	78	57 (22.4)	25 (33.8)	24 (26.1)	93 (46.3)	missing data

Table 9. Significant differences ($p < 0.05$) between participants with or without pain and users or non-users of analgesic drugs as assessed with chi-square test.

	with pain vs. without pain	painfree users vs. non-users	painful users vs. non-users	users with pain vs. without pain
Sex, female	0.002	0.004	0.010	
Living alone		0.001	0.009	
Depressive symptoms	0.023		0.043	0.029
BMI ≥ 30	<0.001			
Poor self-rated health	<0.001		<0.001	<0.001
Asthma/COPD				0.018
Cardiovascular disease			0.035	
Diabetes	0.018			0.026
Arthritis	<0.001	0.001	0.022	0.001
Daily use of analgesics	<0.001			0.041
IADL score 0–6			0.002	
Barthel index 0–80		0.001		
Not able to walk 400m without help		0.017	0.008	
Sedentary	0.005	0.026		
Mobility limitation (TUG)	<0.001	0.047	0.001	
FCI score	<0.001		<0.001	<0.001
Total number of drugs	<0.001	<0.001	<0.001	<0.001

5.2 THE PREVALENCE AND LONGITUDINAL COURSE OF ANALGESIC USE

The prevalence of analgesic use among community-dwelling people aged ≥ 75 years ($n=700$) was 45.4% ($n=318$) in 2004 (Study I). The use of analgesics according to gender and age group is presented in Figure 8. The prevalence of analgesic use on a daily or on an as needed basis was higher among female participants (females, 51.5%; males, 31.7%; $p<0.001$) and in those in the older age groups (aged 75 to 79, 41.3%; 80 to 84, 46.5%; over 85, 54.0%; $p<0.05$).

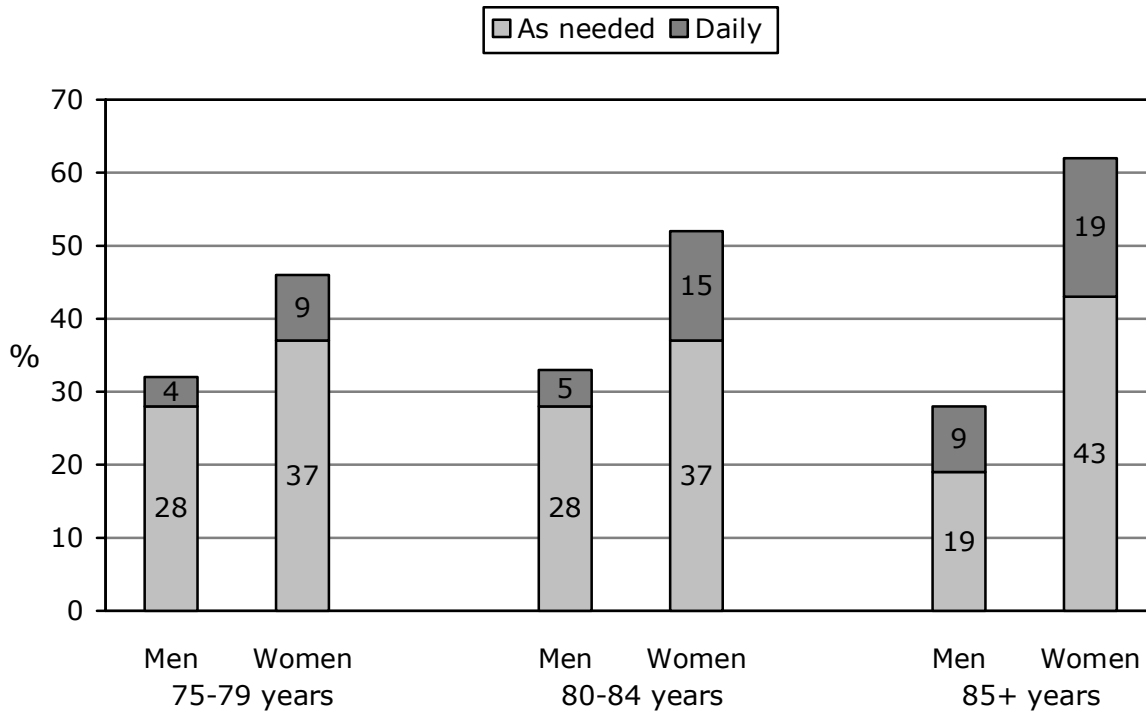


Figure 8. The prevalence (%) of daily and as needed analgesic use in 2004 according to sex and age group ($n=700$).

The longitudinal course of analgesic use in the control and in the intervention group in 2004–2007 is shown in the Table 10. The overall prevalence of analgesic use increased from 45.4% to 54.9% during the study years. Of all analgesic users at baseline ($n=318$), 52.2% ($n=166$) reported use in all three follow-up years and only 16.7% ($n=53$) had discontinued the use of analgesics during the follow-up period. Conversely, those participants who were analgesic nonusers at baseline ($n=382$), only 42.1% ($n=161$) remained as nonusers also over the next three years whereas 31.4% ($n=120$) had started to use analgesics on a daily or on an as needed basis. In addition, 11.6% ($n=37$) of baseline users and 11.5% ($n=44$) of baseline nonusers fluctuated between user and nonuser status. The loss due to deaths ($n=100$), refusals ($n=18$) and contact problems ($n=1$) was 19.5% ($n=62$) among the baseline analgesic users compared to 14.9% ($n=57$) among the baseline nonusers.

If the study groups are considered separately, the overall prevalence of analgesic use increased by 15% in the control group whereas the increase was only 10% in the intervention group during the study years. The proportion of frequent users and nonusers was almost the same in both groups. There were slightly more new incident cases and discontinuous cases in the intervention group, but the differences were not statistically significant ($p=0,22$; $p=0,18$). Fluctuating between user and nonuser status was twice as common in the control group as in the intervention group ($p=0.008$). The attrition due to deaths, refusals and other reasons did not differ in statistical terms between the groups ($p=0.50$).

Table 10. Use of analgesics among community-dwelling GeMS-study participants in control and intervention groups in 2004–2007.

	2004 (n=700) Users 46%, n=318	2005 (n=656) Users 51%, n=335	2006 (n=621) Users 55%, n=340	2007 (n=581) Users 55%, n=319	
CONTROL GROUP n=339 at baseline	User, n=159 (7 died, 2 refused before next examination)	User, n=124 (11 died, 2 refused)	User, n= 94 (5 died, 1 refused) Non-user, n=17 (3 died)	User, n=79 Non-user, n=9 User, n=8 Non-user, n=6	
		Non-user, n=26 (1 died)	User, n=11 Non-user, n=14	User, n=8 Non-user, n=3 User, n=8 Non-user, n=6	
	Non-user, n=180 (6 died, 3 refused, 1 could not be contacted before next examination)	User, n=41 (1 died)	User, n=32 (3 died) Non-user, n=8	User, n=19 Non-user, n=10 User, n=2 Non-user, n=6	
		Non-user, n=129 (6 died, 1 moved)	User, n=27 (3 died, 1 refused) Non-user, n=95 (4 died)	User, n=15 Non-user, n=8 User, n=18 Non-user, n=73	
	Users 41% (159/339)	Users 52% (165/320)	Users 55% (164/298)	Users 56% (157/278)	
	INTERVENTION GROUP n=361 at baseline	User, n=159 (9 died, 2 refused before next examination)	User, n=127 (4 died, 1 refused)	User, n=111 (9 died) Non-user, n=11 (1 died)	User, n=87 Non-user, n= 15 User, n=2 Non-user, n=8
			Non-user, n=21 (2 died)	User, n=5 (1 died) Non-user, n=14 (1 died)	User, n=1 Non-user, n=3 User, n=4 Non-user, n=9
		Non-user, n=202 (10 died, 4 refused before next examination)	User, n=43 (3 died, 1 refused)	User, n=31 (2 died) Non-user, n=8	User, n=25 Non-user, n=4 User, n=0 Non-user, n=8
			Non-user, n=145 (2 died)	User, n=29 (4 died) Non-user, n=114 (2 died)	User, n=19 Non-user, n=6 User, n=24 Non-user, n=88
		Users 44% (159/361)	Users 51% (170/336)	Users 54% (176/323)	Users 53% (162/303)

SUMMARY	All participants n=700 % (n)	Control group n=339 % (n)	Intervention group n=361 % (n)
Frequent users	24% (166)	23% (79)	24% (87)
Non-users	23% (161)	22% (73)	24% (88)
New incident cases	17% (120)	15% (52)	19% (68)
Discontinuous cases	8% (53)	6% (21)	9% (32)
Fluctuating cases	11% (81)	16% (53)	8% (28)
Deaths	14% (100)	15% (50)	14% (50)
Lost to follow up	3% (19)	3% (11)	2% (8)

5.3 PAIN AND THE USE OF ANALGESICS IN RELATION TO MOBILITY LIMITATION

Of the 622 participants in study II (Table 4), 199 (32.0%) had some degree of mobility limitation as estimated in the TUG test. Forty percent (n=251) reported musculoskeletal pain and 61.8% (n=155) of them rated their pain as either severe or moderate. In addition, in this group of participants 44.2% (n=275) were daily (n=58) or as needed (n=217) analgesic users. The percentage of mobility limitation was higher in the persons who also reported musculoskeletal pain (43.8%, n=110) in comparison to those without musculoskeletal pain (24.0%, n=89) and also in analgesic users (42.9%, n=118) as compared analgesic nonusers (23.3%, n=81).

The mobility limitation was most common among participants with pain using paracetamol only (72.2%, n=39), followed by users of opioids in combination with other drugs, (52.9%, n=27) (Figure 9). In the participants without musculoskeletal pain, a mobility limitation was most prevalent among users of paracetamol only (44.4%, n=4) and paracetamol with NSAIDs (43.5%, n=4), but due to the small number of cases, these results should be considered with caution.

The results concerning the factors associated with mobility limitation in older persons having musculoskeletal pain and using analgesic drugs are presented in Table 11. In the unadjusted regression model, participants with higher age, female sex and living alone exhibited a 2–3 times higher risk for mobility limitation than younger and male participants or those living with somebody. In addition, poor self-rated health, cardiovascular disease, depressive symptoms, poor muscle strength and sedentary lifestyle were associated with a mobility limitation in the unadjusted model.

After adjustments for age, sex, BMI, living alone, self-rated health, cardiovascular disease, chronic pulmonary disease, diabetes, depression, arthritis, physical activity and muscle strength, the association between mobility limitation and higher age, living alone, poor self-rated health, sedentary lifestyle and poor muscle strength was somewhat attenuated but nonetheless remained statistically significant. The association between mobility limitation and female sex, cardiovascular disease and depressive mood was not statistically significant in the adjusted regression model.

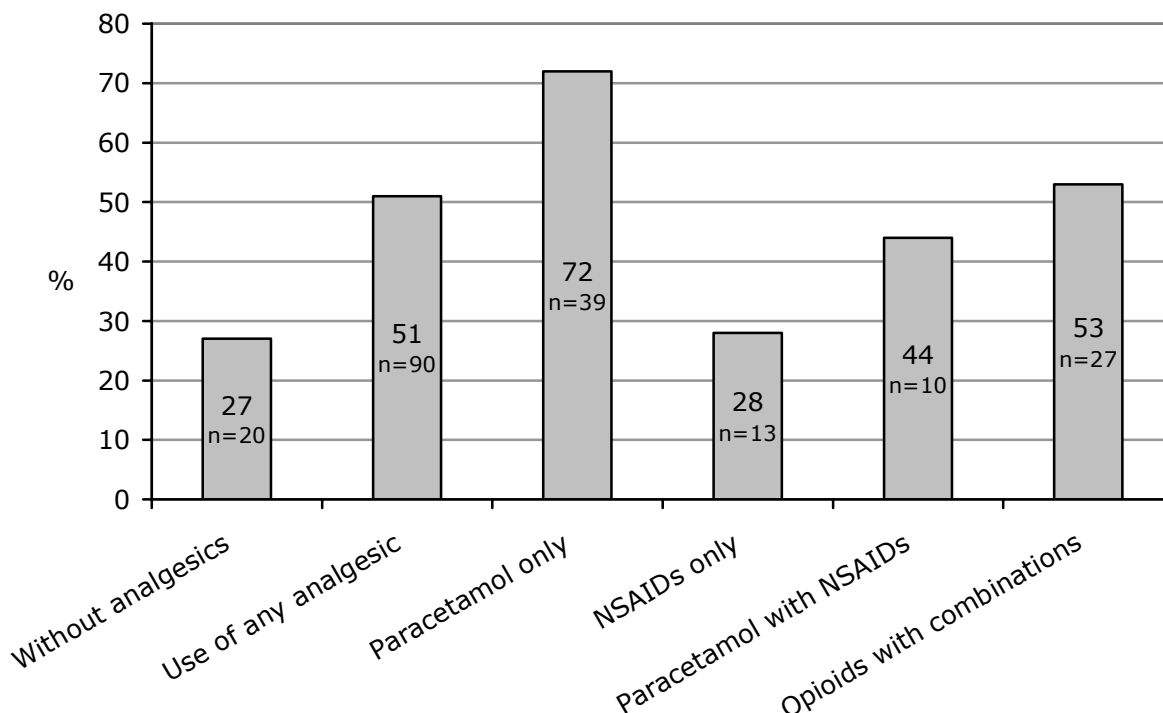


Figure 9. The percentage of participants with mobility limitation (TUG <13.5s) in those subjects with musculoskeletal pain (n=251) subdivided according to their use of analgesics.

Table 11. Sociodemographic and health characteristics associated with mobility limitation among analgesic users with musculoskeletal pain.

		Analgesic users with musculoskeletal pain n=177				Unadjusted	Adjusted
Variable		Mobility limitation				OR (CI 95%) [†]	OR (CI 95%) ^{†§}
		No (n= 87)	Yes (n=90)	n	%		
		n	%	n	%		
Age, y	≥80	29	33.3	58	64.4	3.63 (1.95-6.74)	2.54 (1.18-5.50)
Sex	Female	65	74.7	78	86.7	2.20 (1.01-4.78)	1.73 (0.64-4.66)
Body Mass Index	≥30	26	29.9	29	32.2	1.12 (0.59-2.11)	0.61 (0.26-1.45)
Living alone	Yes	44	50.6	68	75.6	3.02 (1.60-5.72)	2.37 (1.03-5.47)
Self-rated Health	Poor	8	9.2	36	40.0	6.58 (2.84-15.26)	6.40 (2.16-18.96)
Concomitant disease	Cardiovascular	59	67.8	74	82.2	2.20 (1.09-4.43)	2.40 (0.97-5.91)
	Asthma/COPD	9	10.3	15	16.7	1.73 (0.72-4.20)	1.40 (0.47-4.15)
	Diabetes	15	17.2	23	25.6	1.65 (0.79-3.42)	1.87 (0.71-4.96)
	Arthritis	60	69.0	61	67.8	0.95 (0.50-1.78)	0.74 (0.33-1.66)
Depressive symptoms	GDS-15 ≥5	7	8.0	20	22.2	3.27 (1.30-8.18)	0.79 (0.24-2.59)
Physical activity	Sedentary	28	32.2	61	67.8	4.43 (2.36-8.33)	2.77 (1.28-6.02)
Muscle strength	Poor	25	28.7	60	66.7	4.96 (2.62-9.39)	3.45 (1.53-7.81)
Want more attention to pain	Yes	37	42.5	46	51.1	1.41 (0.78-2.56)	1.53 (0.70-3.37)

** p < 0.001, * p < 0.05

†OR=Odds Ratio; 95% CI=95% Confidence Interval

§Adjusted for age, sex, BMI, living alone, SRH, CVD, COPD, diabetes, depression, arthritis, physical activity and muscle strength

5.4 PERSISTENCE OF CHRONIC PAIN

Of the 272 participants examined in study III (Table 4), in 2005 almost half (48.9%, n=133) reported nonmalignant chronic pain at baseline. After the two follow-up years, 99 were persistent cases reporting chronic pain every year, 45 were incident cases starting to report chronic pain and 36 were discontinuous cases ceasing to experience chronic pain during the follow-up. The no chronic pain group consisted of those participants, who did not report chronic pain in any of the study years.

The use of analgesic drugs was most common in the persistent chronic pain group (Figure 10). During the study years 2005–2007, the prevalence of analgesic use increased in persistent and incident chronic pain groups, fluctuated in the discontinuous chronic pain group but it remained almost the same in no chronic pain group. Most participants with persistent chronic pain rated their pain either as moderate or severe in all of the study years, although the percentage of moderate or severe pain decreased slightly (Figure 11).

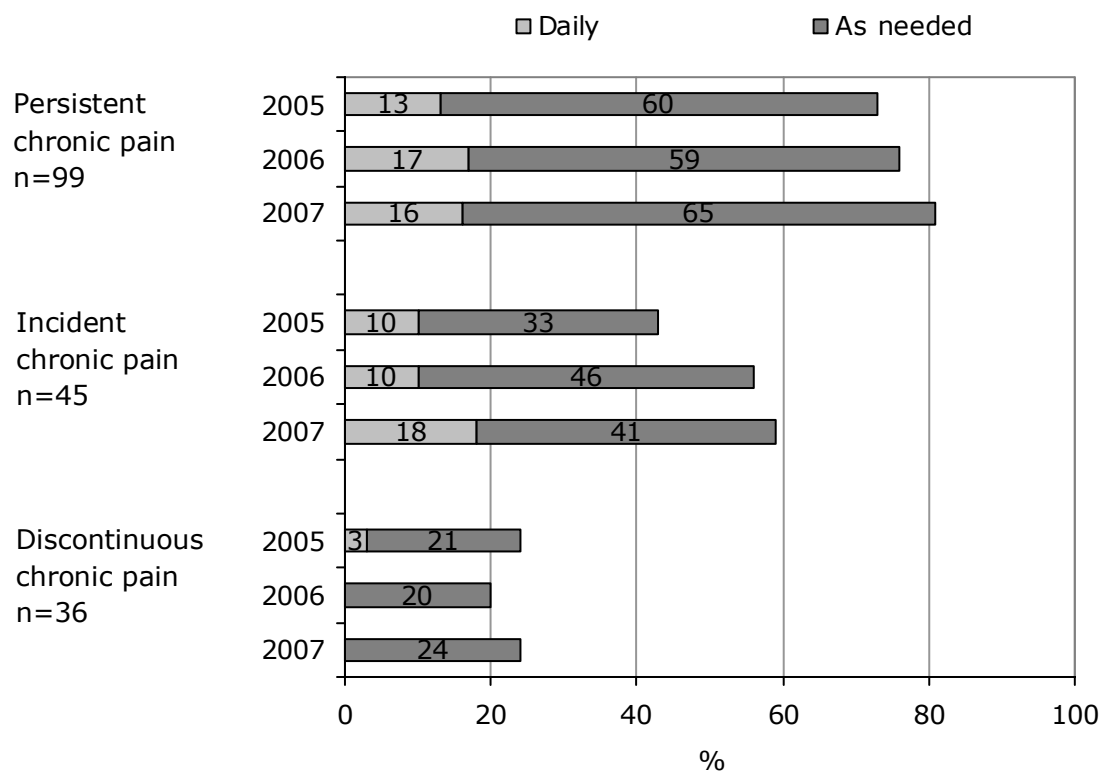


Figure 10. Percentages of daily and as needed analgesic use in 2005-2007 in participants with persistent, incident or discontinuous chronic pain and in participants not having chronic pain during the study period.

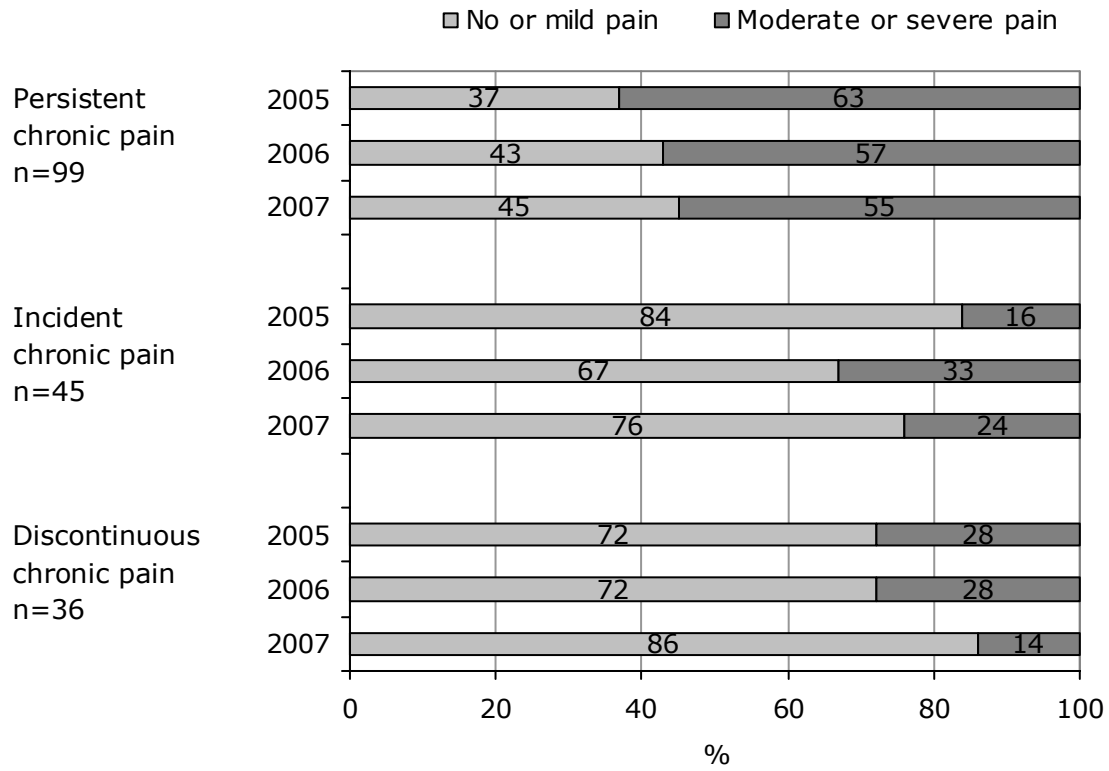


Figure 11. Percentages of dichotomized pain intensity according to chronic pain group in 2005-2007

5.5 HOPE FOR MORE ATTENTION TO BE PAID TO PAIN MANAGEMENT

At baseline in 2005, 41% of community-dwelling participants who experienced chronic musculoskeletal pain were hoping that the physician would be paying more attention to the management of their pain. This hope was most common among women (41.9%, n=85 vs. men 37.3%, n=25) and in the youngest age group (76–79 years 47.5%, n=47; 80–84 years 36.6%, n=37; ≥85 years 37.1%, n=26). At baseline, half (n=49) of those with persistent chronic pain (n=99) in the study III hoped that the physician would be paying more attention to their pain management. However, this hope, as well as the pain intensity decreased during the next two years (Figure 12). In addition, the use of analgesics increased from 73.7% to 81.8% during the study period.

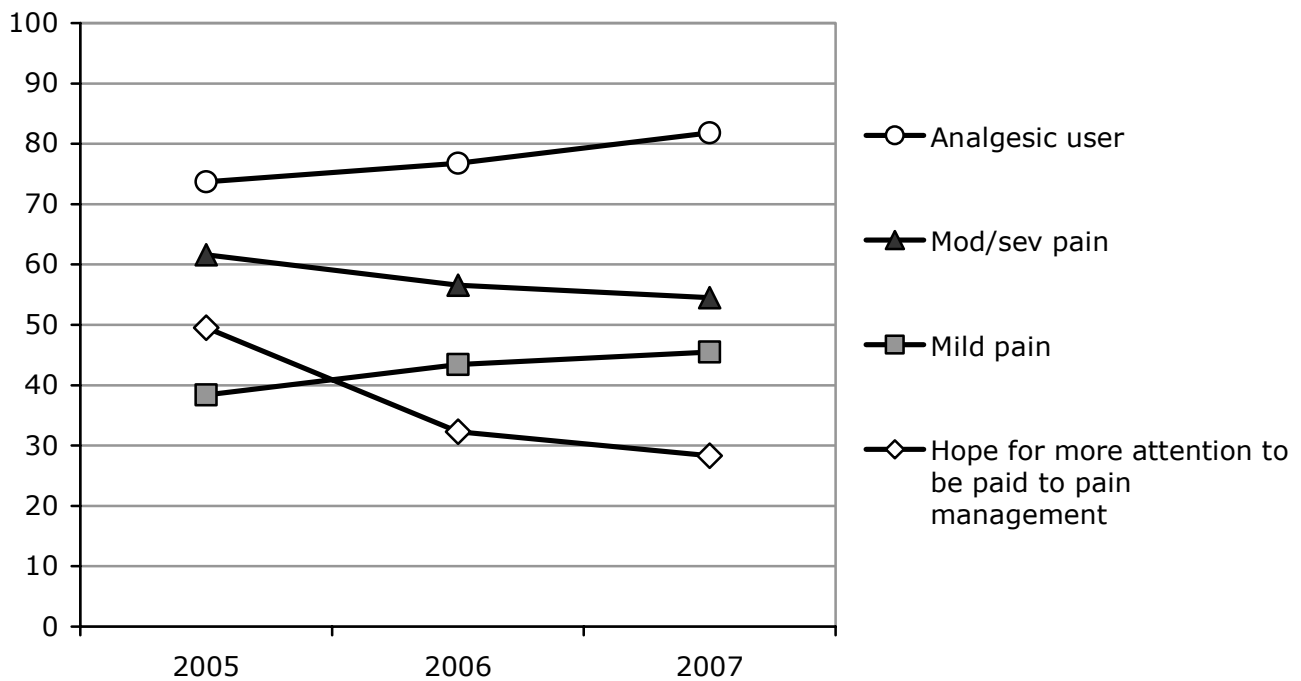


Figure 12. The percentages of pain intensity, analgesic use and the hope for more attention to be paid to pain management during years 2005-2007 in participants with persistent chronic pain (n=99).

6 Discussion

6.1 DISCUSSION OF THE RESULTS

This study revealed that almost half of the community-dwelling older participants were experiencing musculoskeletal chronic pain at baseline and it was highly persistent in its nature. The use of analgesics was common especially among women, and analgesics were most commonly used on an as needed basis. In addition, both the musculoskeletal pain and the use of analgesics were associated with mobility limitations. An important finding was that 40% of those with chronic musculoskeletal pain expressed a hope that the physician would be paying more attention to the pain management, i.e. clear evidence of a need for better pain management.

6.1.1 Pattern of analgesic use

This study showed that almost half of the community-dwelling older participants were analgesic users, most commonly analgesic drugs were being taken on an as needed rather than on a daily basis. The prevalence of daily analgesic use among all study participants was almost similar to that described in a previous Finnish study, conducted in 1998 in the same municipality with same sampling strategy (Hartikainen et al., 2005). There are some possible reasons why the daily use was relatively low, even in those individuals experiencing pain. It may be that the people only experienced mild pain or that they had either experienced or were at least concerned about the possible ADEs associated with daily use. The proportion of analgesic users that were taking analgesics on a daily basis was slightly higher in 2004 than 1998. This difference results from a lower overall analgesic use in the present study. Another Finnish study revealed a higher prevalence of regular analgesic use in 1999, but it should be noted that regular use was defined as weekly not daily use as was conducted in the present study (Pitkälä et al., 2002). In a recent study, every second older (aged >74 years) person with symptomatic radiographic knee osteoarthritis was a frequent user (i.e. on more than half of the days in the month prior to the assessment) of prescription or OTC analgesics (Kingsbury et al., 2013). The results of the present study may point to inadequate pharmacological treatment of pain in community-dwelling older persons because one third of those experiencing pain were nonetheless nonusers of analgesics. The reasons may include poor communication with health care providers, hesitation to take medicines for three possible reasons, fear of addiction, adverse side-effects or drug-drug interactions as well as the common belief that pain is a normal part of aging (Cornally and McCarthy, 2011, Davis et al., 2002).

In the present study the prevalence of analgesic use on a daily or an as needed basis doubled from those in the youngest age group to oldest age group. There were gender-related differences, i.e. the prevalence increased significantly among women with age whereas it remained almost the same or even decreased slightly among men. This is in line with the studies of Blyth, March et al. (2001) and Kingsbury, Hensor et al. (2013) although their investigations included a relatively small number of older individuals aged 75 or more. The finding that the overall and daily use of analgesics was more common among women than men was expected because according to most reports, pain is more prevalent and widespread in women than men (Blyth et al., 2001, Jakobsson, 2010, Leveille et al., 2005, Thomas et al., 2004). In addition, older women may be more willing to report pain and seek help than men (Greenspan, Traub 2013). The result is consistent with previous studies demonstrating the higher prevalence of analgesic use in older women in comparison to similar aged men (Kingsbury et al., 2013, Paulose-Ram et al., 2003, Sadowski et al., 2009). Living alone was more common among the

analgesic users than nonusers; this same trend was found by Sawyer, Bodner et al. (2006) who reported that an unmarried status was associated with prescription analgesic use.

This study revealed also the results of longitudinal course of analgesic use among community-dwelling older people. The overall prevalence of analgesic use increased almost 10% between years 2004–2007. The increase was similar in the intervention and control groups and therefore the medication interventions concerning persons in intervention group did not account for this in ceased analgesic use. In a longitudinal setting, the frequent use of analgesics was more common than that of being a stable nonuser status during the 4-year study period. However, we did not analyse the medication types used by individuals and whether they discontinued the use of certain analgesic and changed some alternative. The initiation of analgesic use was almost twice as common as the discontinuation of the analgesic use. There might have been higher pain levels that have increased the use of analgesics, but unfortunately it was not possible to determine the intensity of pain in relation to analgesic use in this study setting.

The present finding that paracetamol was the most commonly used analgesic drug among older people, was encouraging in the light of guidelines, where paracetamol is recommended as the step 1 analgesic drug in the treatment of pain (WHO, 1996) and it is recognized as the first line treatment for older people (Abdulla et al., 2013, American Geriatrics Society, 2009). In the previous Finnish study (Hartikainen et al., 2005), conducted in 1998 in the same municipality with a similar sampling strategy, NSAIDs were more frequently used among Finns aged ≥ 75 years and thus the present result reflects a shift away from their use. This change may have been promoted by Finnish care guidelines that have warned about ADRs, such as the high risk of gastrointestinal and renal toxicity associated with NSAIDs (Non-Steroidal Anti-inflammatory Drugs: Current Care Summary, 2009).

The use of opioids, especially strong opioids, was low in the present study, although during the last decade the use of strong opioids has increased rapidly in Europe and North America (Bell et al., 2009, Garcia del Pozo et al., 2008, Hamunen et al., 2008, Thielke et al., 2010). Some infrequent opioid use has been found previously in older people with osteoarthritis (Kingsbury et al., 2013). Opioids are often reserved for patients with pain which is refractory to treatment with other medications and/or non-pharmacologic interventions and the low extent of opioid use in this study may reflect the relatively low intensity and the less advanced nature of the pain symptoms. Previously it has been stated that opioids are underutilized in older people due to the negative attitudes towards this class of drugs; this might be the reason here for the low prevalence of opioid use (Nwokeji et al., 2007, Sale et al., 2006). In addition, the role of opioids in the management of nonmalignant chronic musculoskeletal pain may be an area of both controversy and uncertainty which may result in the infrequent use of opioids (American College of Rheumatology Pain Management Task Force, 2010). However, opioids are in steps 2 and 3 of the WHO analgesic ladder and they may be safer and more effective than NSAIDs in those older people who have a high risk of suffering gastrointestinal, cardiovascular and renal ADEs (American Geriatrics Society, 2009).

Despite the fact that the consumption of paracetamol and opioids increased substantially between the years 1998–2005 in Finland (Finnish Medicines Agency and Social Insurance Institution, 2013), this trend was not detected in the present study when compared to the study of Hartikainen, Mäntyselkä et al. (2005). While the prevalence of NSAID use decreased, the overall prevalence of paracetamol and opioid use remained static. This might be a cause of concern, because it seems that there was no shift towards replacing NSAIDs with either paracetamol or opioids although many participants stated that they were in pain in both studies. The avoidance of ADRs or potential interactions should not be a reason to neglect the treatment of pain. Although the growing trend in opioid consumption was not reflected in these results, it maybe that the upswing of opioid use has occurred after the present study. However, in Finland there has been undesirable feature of using transdermal fentanyl in preference to morphine, oxycodone and hydromorphone for nonmalignant pain in community-dwelling

older people (Bell et al., 2009). Several reasons may have influenced this trend, e.g. fentanyl may be favoured due to its easier administration since it is mostly dispensed as a transdermal patch, and there may also be commercial pressure, or fear of using morphine (Chinellato et al., 2003).

Choosing the appropriate pain treatment strategy involves assessing currently used medications for existing illnesses and deciding on appropriate pharmacological pain management according to the type and severity of pain. In this study, the assessment of pain was based on self-report and thus it was not possible to distinguish the mechanisms behind the painful symptoms. Thus, it is not possible to exclude the involvement of neuropathic pain in those participants reporting pain especially because chronic pain is often caused by a mixture of neuropathic and nociceptive components. For example, the participants reporting musculoskeletal back or leg pain may have had a mixed pain involving the irritation of the sciatic nerve, even though those participants did not report symptoms typical of neuropathic pain during their interviews. It is possible, that those participants may have taken nonanalgesic drugs (e.g. anticonvulsants or antidepressants) to alleviate their pain and this may have caused some overestimation of the level of inadequate treatment of pain.

6.1.2 Pain-related mobility limitation

The finding that the risk of mobility limitations related to musculoskeletal pain was highest among persons who used analgesics may also be a reflection of inadequate pain control. The pattern of analgesic use may have influenced the result, since older people often use extremely low doses of analgesics and the frequency of use is occasional rather than daily (Hartikainen et al., 2005, Pahor et al., 1999, Sale et al., 2006). However, this is a potential mediator that has rarely been examined and further studies will be needed to determine the role of analgesic use in the risk of pain related mobility limitation. The fact that mobility limitations were most common among those participants reporting musculoskeletal pain and using paracetamol when compared to the other analgesic groups may reflect the poor efficacy of paracetamol to relieve pain in some chronic diseases, such as severe osteoarthritis. It has been claimed that paracetamol may be less effective than NSAIDs in the treatment of hip or knee pain resulting from osteoarthritis (Towheed et al., 2006). Paracetamol is a suitable option as a step 1 drug for mild pain, but in view of its upper dosing limit and limited efficacy, it is often insufficient in cases of moderate or severe pain, particularly when used alone. According to the WHO analgesic ladder (1996) combination therapy or step 2 or step 3 analgesics should be considered in those cases where paracetamol does not result in the desired response.

When analgesic users with musculoskeletal pain were examined then the mobility limitation was associated with living alone, poor self-rated health, sedentary lifestyle and poor muscle strength. Previous findings have indicated that a walking disability and poor self-rated health are associated with a higher risk of death (Nuesch et al., 2011). These findings support the proposal that it is important to combine pharmacological and nonpharmacological pain treatment to promote the overall health of older individuals and improve their functional abilities. The goal of the management of pain in older people should be at least to reduce it down to a tolerable level so that the individual can maintain some mobility capabilities and perform routine daily activities. In severe osteoarthritis-related pain there is often no effective remedy except joint replacement, but this should be considered as a potential treatment option if an older person's mobility is threatened (Limnell, Jämsen et al. 2012). Older people often cope with tolerable pain problems and even in these situations they may consider themselves being as healthy as long as they have functioning cognition and they can remain as independent as possible (Grime et al., 2010). It is important to treat pain effectively and at as early a stage as possible to prevent functional and mobility restrictions that threaten autonomy, because once the subject enters vicious cycle driven by chronic musculoskeletal pain, it is difficult to break out of the downward spiral of muscle weakness and more and more functional and mobility limitations.

A multidimensional individualized approach based on both pharmacological and nonpharmacological strategies to manage pain might be the best way to improve pain control and help to prevent mobility-related disability in older people. Physical exercise could potentially confer benefits in pain management because it has been reported to enhance functional mobility and relieve pain in older patients (Tse et al., 2011). In addition, sufficient attention to comprehensive pain management could potentially increase the quality of life in older people since pain and mobility problems often threaten physical and mental well-being and lead to social isolation in daily life (Arola et al., 2010, Hawkins et al., 2013, Mackichan et al., 2013). Since older people are at a high risk for pain and mobility decline (Gagliese and Melzack, 2013, Gill et al., 2012), it is important to develop new strategies for alleviating pain and preventing mobility problems. In particular, randomized trials determining which approaches to pain relief achieve the greatest advantages in relation to maintaining and promoting daily functioning and mobility could help to optimize pain management in older people.

6.1.3 Persistent chronic pain

The prognosis of musculoskeletal chronic pain in community-dwelling older people seems discouraging in the light of these present results. Chronic pain seems to be very persistent in its nature since 74% of those community-dwelling older persons having chronic pain at baseline also reported it during the two following years. This is a particularly alarming finding because severe chronic pain is associated with increased mortality (Torrance et al., 2010). A high persistence of chronic pain has been found also in the general population (≥ 25 years), since one study revealed 79% persistence for chronic pain after an interval of 4 years (Elliott et al., 2002). That study included only one follow-up point and the fluctuation between different pain statuses was not identified. In contrast, another study has suggested that despite its high prevalence, musculoskeletal pain in community-dwelling older adults (≥ 65 years) was mainly intermittent (Thielke et al., 2012). However, that study included younger participants and the pain was estimated by a single question (Have you had pain in your bones or joints in the last year?) that did not reveal either the duration or the chronicity of pain. Furthermore, the intensity of pain or the use of analgesics was not determined. In addition to the high persistence of chronic pain noted here, 55–63% of individuals with persistent chronic pain rated their pain as either moderate or severe. This differed from the results of Elliott, Smith et al. (2002) since the prevalence of high intensity chronic pain grades was approximately 40% in their study. It is evident that the different definitions of pain intensity may account for this apparent discrepancy. Furthermore, the severity of chronic pain tended to be relatively static but in the present study the percentage of high pain intensity decreased slightly during the follow-up period. This may result from age differences in study populations, because older people tend to take a more stoical attitude and they may be unwilling to complain even though they have pain or they may claim to have a high pain tolerance (Helme and Gibson, 2001, Sale et al., 2006). In addition, memory disorders may lead to an inability to describe the qualitative aspects of pain and these are more common in older populations (Oosterman et al., 2014).

Despite the high persistence and intensity of pain, even those participants with chronic pain were using analgesics on an as needed rather than a daily basis and more than 20% did not use analgesics at all. This finding is in line with the earlier reports revealing that analgesic use on an as needed basis was common even in participants suffering daily pain severe enough to interfere with their daily routines (Hartikainen et al., 2005). There seems to be a discrepancy between the trend that older people do not use the maximum analgesic doses allowed or prescribed, and the finding that older persons may choose not take analgesic drugs because they feel that analgesic drugs are not effective enough to relieve their pain (Sale et al., 2006). The tendency of older people to minimise their perception of pain may result in poor adherence to analgesic therapy. The patients may be reluctant to take analgesics, because drugs while viewed as being important are often considered as a last resort for managing pain (Ross et al., 2001). In addition, fear of adverse effects, addiction or drug interactions may lead to avoidance of

analgesic use and reluctance to use analgesics often leads to activity restrictions and initiates the spiral of mobility decline (Sale et al., 2006).

However, in the present study there was a trend that overall prevalence of analgesic use increased among participants with persistent chronic pain whereas the pain intensity decreased. Analgesia may not always achieve complete relief of relieve pain, but the goal should be on reducing pain to the lowest level as possible and maintaining a good quality of life in spite of the presence of pain (American Geriatrics Society, 2009). It is important to recognize that the multiple dimensions of persistent chronic pain cannot be explained simply by nociception i.e. there may well be sociodemographic, clinical, genetic and affective factors as well as attitudes which influence pain perception (Gagliese and Melzack, 2013, van Hecke et al., 2013). The use of analgesics is not the only option to manage chronic pain e.g. the present study did not identify if participants were utilizing nonpharmacological pain management strategies to alleviate their pain. Even though the adoption of nonpharmacological methods is less frequent than the use of analgesics, these methods may have provided significant benefits for some individuals (Barry et al., 2005). Nonetheless, in the light of the present results it seems that persistent chronic pain was being insufficiently treated because a significant proportion of community-dwelling participants were suffering from persistent chronic pain of high intensity.

Various pain assessment methods and treatment guidelines have been developed, but it seems that they are not being systematically used in clinical practice. This may be a consequence of a gap in knowledge translation from research to clinical practice or it may be due to the diminished resources and current hectic nature of health care services. Clinicians should be more proactive to avoid situations where pain in older patients is being inadequately recognized and treated. It has been reported that the most common way to determine pain is to allow the patient to explain to the physician how they experience pain (Breivik et al., 2006). However, this is not necessarily a practical method for use with an older patient, because older age is associated with lower tendency to report pain and to express the need for pain treatment and there is a significant risk that persistent pain will remain unrecognized or inadequately treated (Cornally and McCarthy, 2011, Helme and Gibson, 2001). Comprehensive assessment of pain may be a challenge in clinical practice because there is often a limited time to carry out all the needed examinations and older people tend to have numerous health problems at the same time. However, objective assessment methods should be used systematically and the results should be documented sufficiently, because inadequate pain assessment and documentation represents a risk that there will be poor pain management.

The management of chronic pain should be considered as a time-dependent dynamic process, and therefore it is essential to create an individual plan for pain treatment and then to evaluate pain and the effectiveness of treatment at regular intervals. If desired response is not obtained or the patient suffers intolerable adverse effects related to analgesics, it is important to try other options or move on to the next step according to the guidelines. The selection of the appropriate analgesic should be based on a carefully assessment of individual benefits and risks. The regular evaluation should include estimates of physical activity and how much the pain interferences with the routines of daily life, because activity restrictions may be a marker for inadequate pain treatment or patient's poor adherence (Sale et al., 2006). By asking older patients about activity restrictions, clinicians may be able to identify those individuals who are not managing with their pain. In order to avoid nonadherence to pain treatment, it is important to discuss with their older patients about their hopes, fears and preconceptions towards analgesics and to explain the appropriate use of analgesics as aids to preventing activity restrictions.

In addition, the preventive perspective should be taken into account more effectively in the treatment of pain. It is well known that acute pain may become transformed into chronic pain, although the mechanisms involved of the chronification process are incompletely understood. Induction of central sensitization in the somatosensory pathways appears to be a common pathophysiologic mechanism in the transition from acute to chronic pain (Pergolizzi et al.,

2014). A central nervous system amplification occurs with increases in synaptic efficacy and reductions in inhibition pathways such that the response to noxious stimuli becomes enhanced in amplitude, duration and spatial extent. In addition, a low-threshold sensory input can activate the pain sensation, because low-threshold mechanoreceptors converge with nociceptors. Since older people are particularly vulnerable to suffering prolonged pain due to impaired adaptation to painful stimuli and an inadequate regenerative capacity, efforts must be undertaken to treat acute pain effectively to avoid its transition from acute to chronic pain (Gagliese and Melzack, 2013).

6.1.4 Older persons' hopes concerning the management of chronic pain

The present study revealed that almost every other community-dwelling older person with chronic musculoskeletal pain hoped that the physician would be paying more attention towards his/her pain management. Not surprisingly, the percentage of those who would like to receive more attention from the physician to their pain problems was highest among women and in the youngest age group. A previous study with an outpatient setting found that older patients with pain tended to receive a poorer quality of pain management than younger patients (Federman et al., 2006). Physicians may underestimate their patients' pain, especially in situations where the patient is suffering chronic pain as well as when there is severe pain (Mäntyselkä et al., 2001). This study did not investigate the treatment related expectations of those participants who hoped for more attention towards their pain management. Some participants may have had unrealistic expectations towards pain treatment, for example in those situations when the pain cannot be eliminated but only alleviated. It is also possible that some persons feared or even suffered from the adverse effects of analgesic drugs and they were not taking the drugs according to instructions (Sale et al., 2006).

As previously mentioned, many older people have a tendency to take a pain diminishing attitude. This may complicate the open communication with the physician making it difficult to appreciate the severity of pain, or the patient's hopes for pain treatment, particularly when there are multiple illnesses requiring therapy. In the current study older participants were actively asked about their pain and hopes concerning pain management, which may partly explain why a significant proportion of them hoped that more attention would be paid to their pain management. However, it was encouraging that the percentages of moderate to severe pain as well as the hope for more attention to be paid to pain management decreased during the study years in the participants with persistent chronic pain. In addition, the proportion of mild pain and analgesic use increased simultaneously in the same participants. This is a trend towards a modest step in the right direction in the management of pain in this challenging group of older people with persistent chronic pain.

Unfortunately, it was not possible to determine the reasons behind these hopes concerning pain management and further research will be needed into this topic. In the light of the results, it seems that the physicians need to take a more active role in the assessment of pain and to discuss openly the hopes and concerns expressed by older people with respect to their pain and its treatment (e.g. prognosis of pain, efficacy of treatment, and fear of addiction, adverse effects or interactions). It has been reported that open-ended pain questions and the use of follow-up questions will significantly increase the amount of important pain-related information provided by older adults with osteoarthritis pain and thus adopting a narrative approach along with a standardized pain assessment tool could prove useful (McDonald et al., 2009). However, older patients should be given time to describe their pain before asking them further questions or interrupting them in other ways, because it has been claimed that the interruptions might result in loss of important information needed for appropriate pain management (McDonald and Fedo, 2009). In addition, there is a report that educational seminars, in-service training and handout materials may help to improve the safe and effective management of persistent pain among older patients (Corrado-McKeon et al., 2013).

6.2 METHODOLOGICAL CONSIDERATIONS

This thesis was based on data from the population-based Geriatric Multidisciplinary Strategy for the Good Care of the Elderly (GeMS) study conducted in 2004–2007. The extensive data gathered for the GeMS study was appropriate for investigating the research questions examined in this PhD study. This randomly selected population-based sample was large enough (one sixth of those in the target population) to provide good representativeness of the target population (Eaton 1998). Since age was the only inclusion criterion for participation in the GeMS, the participants represented the full spectrum of the population aged 75 years or more. The participation rate was 78.1% which can be considered as acceptable for a face-to-face health survey (Greg 2002). Thus, the results are likely to be generalizable to older persons living in the Kuopio area. However, the characteristics of older population and prescribing culture may differ between geographical regions and therefore the results of this present study may not be generalizable to other countries or even to other parts of Finland.

The attrition of participants occurred mainly due to death and it was similar in the intervention and control groups. Death is a rather natural form of attrition since the individuals attending the GeMS study were old. Non-death attrition during the study period was relatively uncommon (3% among community-dwelling study participants) and it did not differ significantly between groups. In general, non-death attrition is potentially a greater source of bias than death in longitudinal studies concerning older people (Brilleman et al. 2010). Thus, it is unlikely that attrition conferred any significant bias in this study.

An important strength of the study was the data collection procedure that gathered diverse information annually from the same population providing an opportunity to examine the course of chronic pain, analgesic use and related issues in a longitudinal setting. Data on prescription and OTC drug use was collected during interviews and the self-reported information was verified from multiple sources (e.g. prescriptions, drug containers and medical records) to minimize recall bias. It has been demonstrated that asking the respondents to name the medicines they have been using is a reliable way to collect information about the prevalence of drug use (Ademi et al., 2007). This data collection method meant that it was possible to collect data on both prescription and OTC analgesic use which is an important strength of the present study since many analgesic drugs are available for purchase without prescription or reimbursement in Finland. It has been reported that OTC analgesics are frequently used medications by individuals more than 75-years old (Kingsbury et al., 2013). However, the OTC and prescription analgesics were not separated from each other in the data collection process and thus it was not possible to analyse if there were differences in the patterns of OTC and prescription analgesic use. This kind of data collection allowed taking nonadherence of analgesic use into consideration and thus the data reflected actual analgesic use rather than the dispensing or prescribing of analgesics. There have been some changes in the marketed analgesics which occurred after the data collection, for example rofecoxib and tiaprofenic acid are no longer marketed in Finland. However, the fact that it was not possible to investigate whether non analgesic drugs (e.g. tricyclic antidepressants or anticonvulsants) were being used for pain relief is a limitation of this study. An additional limitation is that the doses or effectiveness of analgesic drugs used by the study participants were not evaluated.

The data collecting procedure included multiple previously used questions about presence, sites, duration and intensity of pain enabling a good perspective of the pain. However, the fact that the pain assessment was not based on a standardized pain questionnaire can be considered as a limitation. In addition, due to a human error in the data collecting process at baseline in 2004, detailed pain information was not collected from participants in the control group. Therefore the data for the year 2004 had to be excluded from the studies investigating chronic musculoskeletal pain (III–IV). Participants were asked whether their symptoms resembled “electric shocks, pressure-evoked pain, numbness, stabbing or tingling” suggestive of neuropathic pain, but it was not possible to confirm the clinically important characteristics of

pain types or causes. Therefore, possible occurrence of false classifications concerning pain experiences should be noted. Furthermore, the successful treatment of chronic pain according to the guideline definition achieves about a 30% improvement in pain symptoms (Abdulla et al., 2013), but here it was not possible to determine minor changes in pain intensity, since moderate and severe pain categories were pooled. However, even small decreases in the pain score, (eg. 8 to 6 when pain intensity would still be categorized as moderate to severe) may lower the pain to a tolerable level and be significant at the individual level.

The internal validity of the study may have been influenced by several reasons. The fact that the study population was relatively small in studies III and IV is a limitation and it may have increased the probability of Type II errors (non-significant findings, when the null hypothesis is actually false) due to a lack of power (Lane 2014). On the other hand, when analyzing large data and several associations, there might be a risk for finding false positive results (type I error). Despite the relatively small population size, the results provide an important overview of this topic and a springboard for future studies. Unlike more specialized prescription drugs with well-defined indications, analgesics are used universally for a broad and often nonspecific array of complaints. Therefore confounding by indication cannot be totally excluded in this kind of observational study, although morbidity was taken into account in the analyses. Although the pre-analyses confirmed the similarity of the characteristics between the intervention and the control group, the fact that the intervention group was included in the fourth study may have influenced the results. Participants in the intervention group may have developed differently with regard to hope for more attention to pain management, even although pain was not on a focus of the interventions.

7 Conclusions

Based on the findings of the four studies included in this thesis, the following conclusions can be drawn:

1. Almost half of the community-dwelling older participants used analgesics and the majority of analgesic drugs were taken on an as needed rather than on a daily basis. Women used more commonly analgesics than men, and paracetamol was the most commonly used analgesic drug.
2. The risk of mobility limitation was highest among analgesic users experiencing pain. In addition, the mobility limitation was associated with many factors including older age, poor overall health, living alone, sedentary lifestyle and poor muscle strength.
3. Musculoskeletal chronic pain showed high persistence and intensity, since the majority of those individuals with pain at baseline were still suffering from it also after two follow-up years and the pain was rated mostly as moderate to severe. Persistent chronic pain was significantly associated with poor health, mobility difficulties and joint complaints.
4. The finding that almost half of community-dwelling older people with musculoskeletal chronic pain hoped that the physician would be paying more attention to their pain management emphasizes that there is a clear need for better strategies to manage pain in this population. The persistent hope for more attention to pain management was related to high pain intensity, daily analgesic use and poor health.

8 Implications for the Future

8.1 CLINICAL IMPLICATIONS

1. A more comprehensive approach to pain assessment and management in older people. The vicious circle where older people experiencing acute pain reduce their activity and are threatened with disabling mobility limitations and the chronification of pain should be interrupted by multidimensional pain management including nonpharmacological and pharmacological strategies, and additional physical rehabilitation.
2. A more active role of clinicians to assess and manage pain. Currently, clinical instruments with well established psychometric properties are available for the purpose of assessing pain and how pain affects bodily function. Pain in older patients and the effectiveness of their treatment need to be evaluated regularly. Furthermore, the hopes and concerns of these patients regarding their pain and its treatment should be discussed at length during the clinical consultation.
3. The availability of comprehensive pain assessment and management strategies. Training of health care professionals in primary health care should include approaches to promote the safe and effective management of pain. Better trained health professionals may also be better at identifying those older patients needing to be referred to a specialist before their pain has become persistent debilitating, even life-threatening.

8.2 SUGGESTIONS FOR FURTHER RESEARCH

1. A more detailed research is needed to explore whether the pattern of analgesic use (drug type, frequency of use), is appropriate in relation to the pain (quality and intensity) and its interference with daily routines in community-dwelling older people.
2. The effectiveness of pharmacological and nonpharmacological pain management strategies should be investigated and the possible reasons behind unsuccessful pain management should be determined.
3. The relationship between pain and pain management strategies with mobility limitations should be observed in a longitudinal setting and with interventions intended to prevent the persistence of pain and pain related mobility limitation; these approaches should be developed and piloted in practice.
4. It is important to widen investigations to determine hopes and expectations of older people with respect to pain assessment and management.

With more detailed information, better pain assessment and management strategies could be developed and new guidelines provided to prevent and reduce pain and unnecessary suffering among community-dwelling older people. In addition, more effective approaches to the management of pain and the prevention of mobility limitations would be anticipated

to prolong the time of independent living at home and thus to reduce the costs associated with the institutional care.

9 References

- Abdulla A, Adams N, Bone M, Elliott AM, Gaffin J, Jones D, Knaggs R, Martin D, Sampson L, Schofield P. Guidance on the management of pain in older people. *Age and Ageing*, 42: S1, i1–57, 2013.
- Abraham NS, El-Serag, HB, Johnson ML, Hartman C, Richardson P, Ray WA and Smalley W. National adherence to evidence-based guidelines for the prescription of nonsteroidal anti-inflammatory drugs. *Gastroenterology*, 129(4): 1171–1178, 2005.
- Abraham NS, Hartman C, Castillo D, Richardson P, Smalley W. Effectiveness of national provider prescription of PPI gastroprotection among elderly NSAID users. *The American Journal of Gastroenterology*, 103(2): 323–332, 2008.
- Ademi Z, Turunen JH, Kauhanen J, Enlund H. A comparison of three questionnaire-based measures of analgesic use over 11 years in adult males: a retrospective analysis of data from a prospective, population-based cohort study. *Clinical therapeutics*, 29(3): 529–534, 2007.
- AGS, Beers criteria update expert panel. American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*, 60(4): 616–631, 2012.
- Allcock N, Elkan R, Williams J. Patients referred to a pain management clinic: Beliefs, expectations and priorities. *Journal of advanced nursing*, 60(3): 248–256, 2007.
- Altman RD, Barthel HR. Topical therapies for osteoarthritis. *Drugs*, 71(10): 1259–1279, 2011
- American College of Rheumatology Pain Management Task Force. Report of the American College of Rheumatology Pain Management Task Force. *Arthritis care & research*, 62(5): 590–599, 2010.
- American Geriatrics Society. (AGS) Panel on the pharmacological management of persistent pain in older persons; pharmacological management of persistent pain in older persons. *Pain medicine*, 10(6): 1062–1083, 2009.
- American Geriatrics Society. (AGS) Panel on persistent pain in older persons; the management of persistent pain in older persons. *Journal of the American Geriatrics Society*, 50(6): S205–224, 2002.
- Andersson HI, Ejlertsson G, Leden I, Schersten B. Impact of chronic pain on health care seeking, self care, and medication. Results from a population-based Swedish study. *Journal of epidemiology and community health*, 53(8): 503–509, 1999.
- Antman EM, Bennett JS, Daugherty A, Furberg C, Roberts H, Taubert KA, American Heart Association. Use of nonsteroidal anti-inflammatory drugs: An update for clinicians: A scientific statement from the American Heart Association. *Circulation*, 115(12): 1634–1642, 2007.
- Arnstein P. Balancing analgesic efficacy with safety concerns in the older patient. *Pain management nursing*, 11(2): S11-22, 2010.

- Arola H, Nicholls E, Mallen C, Thomas E. Self-reported pain interference and symptoms of anxiety and depression in community-dwelling older adults: Can a temporal relationship be determined? *European Journal of Pain*, 14(9): 966–971, 2010.
- Austrian JS, Kerns RD, Reid MC. Perceived barriers to trying self-management approaches for chronic pain in older persons. *Journal of the American Geriatrics Society*, 53(5): 856–861, 2005.
- Bannwarth B, Blotman F, Roue-Le Lay K, Caubere JP, Andre E, Taieb C. Fibromyalgia syndrome in the general population of France: a prevalence study. *Joint, bone, spine*, 76(2): 184–187, 2009.
- Barber JB, Gibson SJ. Treatment of chronic non-malignant pain in the elderly: safety considerations. *Drug safety: an international journal of medical toxicology and drug experience*, 32(6): 457–474, 2009.
- Bardage C, Pluijm SM, Pedersen NL, Deeg DJ, Jylhä M, Noale M, Blumstein T, Otero A. Self-rated health among older adults: A cross-national comparison. *European Journal of Ageing*, 2(2): 149–158, 2005.
- Barkin RL, Beckerman M, Blum SL, Clark FM, Koh EK, Wu DS. Should nonsteroidal anti-inflammatory drugs (NSAIDs) be prescribed to the older adult? *Drugs & aging*, 27(10): 775–789, 2010.
- Barkin RL, Buvanendran A. Focus on the COX-1 and COX-2 agents: renal events of nonsteroidal and anti-inflammatory drugs-NSAIDs. *American Journal of Therapeutics*, 11(2): 124–129, 2004.
- Baron R, Binder A, Wasner G. Neuropathic pain: diagnosis, pathophysiological mechanisms, and treatment. *Lancet neurology*, 9(8): 807–819, 2010.
- Barry LC, Gill TM, Kerns RD, Reid MC. Identification of pain-reduction strategies used by community-dwelling older persons. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 60(12): 1569–1575, 2005.
- Barthel HR, Haselwood D, Longley S 3rd, Gold MS, Altman RD. Randomized controlled trial of diclofenac sodium gel in knee osteoarthritis. *Seminars in arthritis and rheumatism*, 39(3): 203–212, 2009.
- Bassols A, Bosch F, Campillo M, Cañellas M, Baños J. An epidemiological comparison of pain complaints in the general population of Catalonia (Spain). *Pain*, 83(1): 9–16, 1999.
- Bedson J, Mottram S, Thomas E, Peat G. Knee pain and osteoarthritis in the general population: what influences patients to consult? *Family practice*, 24(5): 443–453, 2007.
- Bell JS, Klaukka T, Ahonen J, Hartikainen S. National utilization of transdermal fentanyl among community-dwelling older people in Finland. *The American journal of geriatric pharmacotherapy*, 7(6): 355–361, 2009.
- Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: A health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *Journal of Rheumatology*, 15(12): 1833–1840, 1988.

- Bergh I, Sjostrom B, Oden A, Steen B. An application of pain rating scales in geriatric patients. *Aging Clinical and Experimental Research*, 12(5): 380–387, 2000.
- Bergh I, Steen G, Waern M, Johansson B, Oden A, Sjostrom B, Steen B. Pain and its relation to cognitive function and depressive symptoms: a Swedish population study of 70-year-old men and women. *Journal of pain and symptom management*, 26(4): 903–912, 2003.
- Berman RL, Iris MA, Bode R, Drengenberg C. The effectiveness of an online mind-body intervention for older adults with chronic pain. *The journal of pain*, 10(1): 68–79, 2009.
- Blay SL, Andreoli SB, Dewey ME, Gastal FL. Co-occurrence of chronic physical pain and psychiatric morbidity in a community sample of older people. *International journal of geriatric psychiatry*, 22(9): 902–908, 2007.
- Blomqvist K, Edberg AK. Living with persistent pain: experiences of older people receiving home care. *Journal of advanced nursing*, 40(3): 297–306, 2002.
- Blyth FM, March LM, Brnabic AJ, Jorm LR, Williamson M, Cousins MJ. Chronic pain in Australia: a prevalence study. *Pain*, 89(2-3): 127–134, 2001.
- Blyth FM, March LM, Nicholas MK, Cousins MJ. Self-management of chronic pain: a population-based study. *Pain*, 113(3): 285–292, 2005.
- Borglin G, Jakobsson U, Edberg AK, Hallberg IR. Self-reported health complaints and their prediction of overall and health-related quality of life among elderly people. *International journal of nursing studies*, 42(2): 147–158, 2005.
- Bosley BN, Weiner DK, Rudy TE, Granieri E. Is chronic nonmalignant pain associated with decreased appetite in older adults? Preliminary evidence. *Journal of the American Geriatrics Society*, 52(2): 247–251, 2004.
- Boylan S, Lallukka T, Lahelma E, Pikhart H, Malyutina S, Pajak A, Kubinova R, Bragina O, Stepaniak U, Gillis-Januszewska A, Simonova G, Peasey A, Bobak M. Socio-economic circumstances and food habits in Eastern, Central and Western European populations. *Public health nutrition*, 14(4): 678–687, 2011.
- Branco JC, Bannwarth B, Failde I, Abello Carbonell J, Blotman F, Spaeth M, Saraiva F, Nacci F, Thomas E, Caubere JP, Le Lay K, Taieb C, Matucci-Cerinic M. Prevalence of fibromyalgia: a survey in five European countries. *Seminars in Arthritis and rheumatism*, 39(6): 448–453, 2010.
- Brattberg G, Parker MG, Thorslund M. The prevalence of pain among the oldest old in Sweden. *Pain*, 67(1): 29–34, 1996.
- Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *European journal of pain* 10(4): 287–333, 2006.
- Brilleman S, Pachana N, Dobson A. The impact of attrition on the representativeness of cohort studies of older people. *BMC Medical Research Methodology* 10:71, 2010.
- Brochet B, Michel P, Barberger-Gateau P, Dartigues J. Population-based study of pain in elderly people: A descriptive survey. *Age and Ageing*, 27(3): 279–284, 1998.

- Bruckenthal P. Integrating nonpharmacologic and alternative strategies into a comprehensive management approach for older adults with pain. *Pain management nursing*, 11(2): S23-31, 2010.
- Buchman AS, Shah RC, Leurgans SE, Boyle PA, Wilson RS, Bennett DA. Musculoskeletal pain and incident disability in community-dwelling older adults. *Arthritis care & research*, 62(9): 1287–1293, 2010.
- Buescher J, Meadows S. Do acetaminophen and an NSAID combined relieve osteoarthritis pain better than either alone? Clinical inquiries from the family practice inquiries network. *The Journal of Family Practice*, 53(6): 501–502, 2004.
- Chen Q, Hayman LL, Shmerling RH, Bean JF, Leveille SG. Characteristics of chronic pain associated with sleep difficulty in older adults: The maintenance of balance, independent living, intellect, and zest in the elderly (MOBILIZE) Boston study. *Journal of the American Geriatrics Society*, 59(8): 1385–1392, 2011.
- Chinellato A, Terrazzani G, Walley T, Giusti P. Opioids in Italy: is marketing more powerful than the law? *Lancet*, 362(9377): 78, 2003.
- Christensen K, Doblhammer G, Rau R, Vaupel JW. Ageing populations: the challenges ahead. *The Lancet*, 374(9696): 1196–1208, 2009.
- Cleeland CS. The Brief Pain Inventory, User Guide. Available online at www.mdanderson.org/departments/prg > Assessment Tools > Brief Pain Inventory for more information. Last update 2009.
- Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Annals of the Academy of Medicine Singapore*, 23(2): 129–138, 1994.
- Coons SJ, Rao S, Keininger DL, Hays RD. A comparative review of generic quality-of-life instruments. *Pharmacoeconomics*, 17(1): 13–35, 2000.
- Cornally N, McCarthy G. Chronic pain: the help-seeking behavior, attitudes, and beliefs of older adults living in the community. *Pain management nursing*, 12(4): 206-217, 2011.
- Corrado-McKeon L, Saad M, Mir T, Liberman T, Cleary T, Lu C. Treating persistent pain in the elderly: how do we proceed? *The Consultant pharmacist*, 28(8): 509–514, 2013.
- Cousins SO. Validity and reliability of self-reported health of persons aged 70 and older. *Health care for women international*, 18(2): 165–174, 1997.
- Coyte PC, Asche CV, Croxford R, Chan B. The economic cost of musculoskeletal disorders in Canada. *Arthritis Care and Research*, 11(5): 315–325, 1998.
- Cruccu G, Truini A. Neuropathic pain and its assessment. *Surgical oncology*, 19(3): 149–154, 2010.
- Davis GC, Hiemenz ML, White TL. Barriers to managing chronic pain of older adults with arthritis. *Journal of nursing scholarship*, 34(2): 121–126, 2002.
- Davis MP, Srivastava M. Demographics, assessment and management of pain in the elderly. *Drugs & aging*, 20(1): 23–57, 2003.

- De Abajo FJ, Garcia-Rodriguez LA. Risk of upper gastrointestinal tract bleeding associated with selective serotonin reuptake inhibitors and venlafaxine therapy: interaction with nonsteroidal anti-inflammatory drugs and effect of acid-suppressing agents. *Archives of General Psychiatry*, 65(7): 795–803, 2008.
- Derry S, Moore RA, Rabbie R. Topical NSAIDs for chronic musculoskeletal pain in adults. *The Cochrane database of systematic reviews*, 9: CD007400, 2012.
- Donald IP, Foy C. A longitudinal study of joint pain in older people. *Rheumatology*, 43(10): 1256–1260, 2004.
- Eggermont LH, Shmerling RH, Leveille SG. Tender point count, pain, and mobility in the older population: the mobilize Boston study. *The journal of pain*, 11(1): 62–70, 2010.
- Elliott AM, Smith BH, Hannaford PC, Smith WC, Chambers WA. The course of chronic pain in the community: results of a 4-year follow-up study. *Pain*, 99(1-2): 299–307, 2002.
- Elliott AM, Smith BH, Penny KI, Smith WC, Chambers WA. The epidemiology of chronic pain in the community. *Lancet*, 354(9186): 1248–1252, 1999.
- Eriksson I, Unden AL, Elofsson S. Self-rated health. Comparisons between three different measures. Results from a population study. *International journal of epidemiology*, 30(2): 326–333, 2001.
- Federman AD, Litke A, Morrison RS. Association of age with analgesic use for back and joint disorders in outpatient settings. *The American journal of geriatric pharmacotherapy*, 4(4): 306–315, 2006.
- Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman B, Aliabadi P, Levy D. Risk factors for incident radiographic knee osteoarthritis in the elderly. *Arthritis and Rheumatism*, 40(4): 728–733, 1997.
- Ferrell BA, Ferrell BR, Rivera L. Pain in cognitively impaired nursing home patients. *Journal of pain and symptom management*, 10(8): 591–598, 1995.
- Ferrell BA, Stein WM, Beck JC. The Geriatric Pain Measure: Validity, Reliability and Factor Analysis. *Journal of the American Geriatrics Society*, 48(12): 1669–1673, 2000.
- FIMEA. läkkäiden lääkityksen tietokanta. Database of medications for older people. Last update 2014. Available online (accessed in April 16, 2014) at http://www.fimea.fi/kehittaminen/laakeinformaation_kehittaminen/iakkaiden_laakityksen_tietokanta
- Fine PG. Treatment guidelines for the pharmacological management of pain in older persons. *Pain medicine*, 13(2): S57–66, 2012.
- Finnish Medicines Agency and Social Insurance Institution. Finnish statistics on medicines 2012. Edita prima oy, Helsinki, 2013. Available online at http://www.kela.fi/web/en/statistical-publications_finnish-statistics-on-medicines
- Folstein MF, Folstein SE, Mchugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of psychiatric research*, 12(3): 189–198, 1975.

- Franceschi M, Scarcelli C, Niro V, Seripa D, Paziienza AM, Pepe G, Colusso AM, Pacilli L, Pilotto A. Prevalence, clinical features and avoidability of adverse drug reactions as cause of admission to a geriatric unit: a prospective study of 1756 patients. *Drug safety* 31(6): 545–556, 2008.
- Gagliese L, Melzack R. Pain In Older Persons. In: Wall and Melzack's Textbook of pain. Editors McMahon S, Koltzenburg M, Tracey I and Turk D. 6th edition. Philadelphia: Elsevier Saunders, pp. 315, 2013.
- Gagliese L, Melzack R. Age-related differences in the qualities but not the intensity of chronic pain. *Pain*, 104(3): 597–608, 2003.
- Gagliese L, Weizblit N, Ellis W, Chan VW. The measurement of postoperative pain: A comparison of intensity scales in younger and older surgical patients. *Pain*, 117(3): 412–420, 2005.
- Garcia Del Pozo J, Carvajal A, Vilorio JM, Velasco A, Garcia Del Pozo V. Trends in the consumption of opioid analgesics in Spain. Higher increases as fentanyl replaces morphine. *European journal of clinical pharmacology*, 64(4): 411–415, 2008.
- Gatti A, Dauri M, Leonardi F, Longo G, Marinangeli F, Mammucari M, Sabato AF. Transdermal buprenorphine in non-oncological moderate-to-severe chronic pain. *Clin Drug Investig*. 30(S2):31–38, 2010.
- Gianni W, Madaio AR, Ceci M, Benincasa E, Conati G, Franchi F, Galetti G, Nieddu A, Salani B, Zuccaro SM. Transdermal buprenorphine for the treatment of chronic noncancer pain in the oldest old. *Journal of pain and symptom management*, 41(4): 707-714, 2011.
- Gibson SJ, Helme RD. Age-related differences in pain perception and report. *Clinics in geriatric medicine*, 17(3): 433–456, 2001.
- Gill TM, Gahbauer EA, Murphy TE, Han L, Allore HG. Risk factors and precipitants of long-term disability in community mobility: a cohort study of older persons. *Annals of Internal Medicine*, 156(2): 131–140, 2012.
- Gloth FM 3rd, Scheve AA, Stober CV, Chow S, Prosser J. The Functional Pain Scale: Reliability, validity, and responsiveness in an elderly population. *Journal of the American Medical Directors Association*, 2(3): 110–114, 2001.
- Gloth FM 3rd. Pharmacological management of persistent pain in older persons: focus on opioids and nonopioids. *The journal of pain*, 12(3): S14–20, 2011.
- Goldstein JL, Howard KB, Walton SM, McLaughlin TP, Kruzikas DT. Impact of adherence to concomitant gastroprotective therapy on nonsteroidal-related gastroduodenal ulcer complications. *Clinical gastroenterology and hepatology*, 4(11): 1337–1345, 2006.
- Greenspan JD, Traub RJ. Gender Differences In Pain And Its Relief. In: Wall and Melzack's Textbook of pain. Editors McMahon S, Koltzenburg M, Tracey I and Turk D. 6th edition. Philadelphia: Elsevier Saunders, pp. 221–231. 2013.
- Griffin MR. Epidemiology of nonsteroidal anti-inflammatory drug-associated gastrointestinal injury. *The American Journal of Medicine*, 104(3): 23S–29S; discussion 41S–42S, 1998.

- Grimby C, Fastbom J, Forsell Y, Thorslund M, Claesson CB, Winblad B. Musculoskeletal pain and analgesic therapy in a very old population. *Archives of Gerontology and Geriatrics*, 29(1): 29–43, 1999.
- Grimby G. Physical activity and muscle training in the elderly. *Acta medica Scandinavica, Supplementum*, 711: 233–237, 1986.
- Grime J, Richardson JC, Ong BN. Perceptions of joint pain and feeling well in older people who reported being healthy: a qualitative study. *The British journal of general practice*, 60(577): 597–603, 2010.
- Groll DL, To T, Bombardier C, Wright JG. The development of a comorbidity index with physical function as the outcome. *Journal of clinical epidemiology*, 58(6): 595–602, 2005.
- Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, Scherr PA, Wallace RB. A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *Journals of Gerontology*, 49(2): M85–M94, 1994.
- Hadjistavropoulos T, Herr K, Turk DC, Fine PG, Dworkin RH, Helme R, Jackson K, Parmelee PA, Rudy TE, Beattie BL, Chibnall JT, Craig KD, Ferrell B, Ferrell B, Fillingim RB, Gagliese L, Gallagher R, Gibson SJ, Harrison EL, Katz B, Keefe FJ, Lieber SJ, Lussier D, Schmader KE, Tait RC, Weiner DK, Williams J. An interdisciplinary expert consensus statement on assessment of pain in older persons. *Clinical Journal of Pain*, 23(1): S1–S43, 2007.
- Hammer K, Mogensen O, Hall EO. The meaning of hope in nursing research: A meta-synthesis. *Scandinavian Journal of Caring Sciences*, 23(3): 549–557, 2009.
- Hamunen K, Paakkari P, Kalso E. Trends in opioid consumption in the Nordic countries 2002–2006. *European journal of pain*, 12(6):705-715, 2008.
- Hartikainen SA, Mäntyselkä PT, Louhivuori-Laako KA, Sulkava RO. Balancing pain and analgesic treatment in the home-dwelling elderly. *The Annals of Pharmacotherapy*, 39(1): 11–16, 2005.
- Hawkins K, Musich S, Bottone Jr FG, Ozminkowski RJ, Cheng Y, Rush S, Carcione Jr J, Migliori R, Yeh S. The impact of pain on physical and mental quality of life in adults 65 and older. *Journal of gerontological nursing*, 39(6): 32–44, 2013.
- Helme RD, Gibson SJ. The epidemiology of pain in elderly people. *Clinics in geriatric medicine*, 17(3): 417–431, 2001.
- Hernández-Díaz S, García Rodríguez LA. Association between nonsteroidal anti-inflammatory drugs and upper gastrointestinal tract bleeding/perforation an overview of epidemiologic studies published in the 1990s. *Archives of Internal Medicine*, 160(14): 2093–2099, 2000.
- Herr K. Pain assessment strategies in older patients. *The journal of pain*, 12(3): S3–S13, 2011.
- Herr K, Coyne PJ, Key T, Manworren R, Mccaffery M, Merkel S, Pelosi-Kelly J, Wild L. Pain Assessment in the Nonverbal Patient: Position Statement with Clinical Practice Recommendations. *Pain Management Nursing*, 7(2): 44–52, 2006.

- Herr KA, Spratt K, Mobily PR, Richardson G. Pain intensity assessment in older adults: Use of experimental pain to compare psychometric properties and usability of selected pain scales with younger adults. *Clinical Journal of Pain*, 20(4): 207–219, 2004.
- Hersh EV, Pinto A, Moore PA. Adverse drug interactions involving common prescription and over-the-counter analgesic agents. *Clinical therapeutics*, 29S: 2477–2497, 2007.
- Hilton D, Iman N, Burke GJ, Moore A, O'mara G, Signorini D, Lyons D, Banerjee AK, Clinch D. Absence of abdominal pain in older persons with endoscopic ulcers: a prospective study. *The American Journal of Gastroenterology*, 96(2): 380–384, 2001.
- Hippisley-Cox J, Coupland C, Logan R. Risk of adverse gastrointestinal outcomes in patients taking cyclo-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs: population based nested case-control analysis. *BMJ*, 331(7528): 1310–1316, 2005.
- Hurwitz DE, Hulet CH, Andriacchi TP, Rosenberg AG, Galante JO. Gait compensations in patients with osteoarthritis of the hip and their relationship to pain and passive hip motion. *Journal of orthopaedic research*, 15(4): 629–635, 1997.
- Jakobsson U. The epidemiology of chronic pain in a general population: results of a survey in southern Sweden. *Scandinavian journal of rheumatology*, 39(5): 421–429, 2010.
- Jakobsson U, Hallberg IR, Westergren A. Exploring determinants for quality of life among older people in pain and in need of help for daily living. *Journal of Clinical Nursing*, 16(3): 95–104, 2007.
- Jakobsson U, Kleivsgard R, Westergren A, Hallberg IR. Old people in pain: a comparative study. *Journal of pain and symptom management*, 26(1): 625–636, 2003.
- Johnell K, Fastbom J. Concomitant use of gastroprotective drugs among elderly NSAID/COX-2 selective inhibitor users: a nationwide register-based study. *Clinical drug investigation*, 28(11): 687–695, 2008.
- Jones SL, Henry SM, Raasch CC, Hitt JR, Bunn JY. Individuals with non-specific low back pain use a trunk stiffening strategy to maintain upright posture. *Journal of electromyography and kinesiology*, 22(1): 13–20, 2012.
- Katz WA, Barkin RL. Dilemmas in chronic/persistent pain management. *Disease-a-month*, 56(4):233-250, 2010.
- Kearney PM, Baigent C, Godwin J, Halls H, Emberson JR, Patrono C. Do selective cyclo-oxygenase-2 inhibitors and traditional non-steroidal anti-inflammatory drugs increase the risk of atherothrombosis? Meta-analysis of randomised trials. *BMJ*, 332(7553): 1302–1308, 2006.
- Keefe FJ, Porter L, Somers T, Shelby R, Wren AV. Psychosocial interventions for managing pain in older adults: outcomes and clinical implications. *British journal of anaesthesia*, 111(1): 89–94, 2013.
- Kemp CA, Ersek M, Turner JA. A descriptive study of older adults with persistent pain: use and perceived effectiveness of pain management strategies. *BMC geriatrics*, 5: 12, 2005.

- Kerns RD, Turk DC, Rudy TE. The West Haven-Yale Multidimensional Pain Inventory (WHYMPI). *Pain*, 23(4): 345–356, 1985.
- Kingsbury SR, Hensor EM, Walsh CA, Hochberg MC, Conaghan PG. How do people with knee osteoarthritis use osteoarthritis pain medications and does this change over time? Data from the Osteoarthritis Initiative. *Arthritis research & therapy*, 15(5): R106, 1–12, 2013.
- Knee and hip osteoarthritis: current care summary. *Knee and Hip Osteoarthritis* (online). Current Care guideline. Working group set up by the Finnish Medical Society Duodecim and the Finnish Orthopaedic Association. Helsinki: Finnish Medical Society Duodecim, 2007 (updated 22 Oct 2012). Available online at: www.kaypahoito.fi.
- Knutzen KM, Pendergrast BA, Lindsey B, Brilla LR. The effect of high resistance weight training on reported pain in older adults. *Journal of sports science & medicine*, 6(4): 455–460, 2007.
- Koponen MP, Bell JS, Karttunen NM, Nykanen IA, Desplenter FA, Hartikainen SA. Analgesic use and frailty among community-dwelling older people: a population-based study. *Drugs & aging*, 30(2): 129–136, 2013.
- Laine L, Connors L, Griffin MR, Curtis SP, Kaur A, Cannon CP. Prescription rates of protective co-therapy for NSAID users at high GI risk and results of attempts to improve adherence to guidelines. *Alimentary Pharmacology and Therapeutics*, 30(7): 767–774, 2009.
- Lane D. *Introduction to Statistics*. Online edition. Rice University, Houston. Available at: http://onlinestatbook.com/Online_Statistics_Education.pdf (Accessed 26 August 2014)
- Laslett LL, Quinn SJ, Winzenberg TM, Sanderson K, Cicuttini F, Jones G. A prospective study of the impact of musculoskeletal pain and radiographic osteoarthritis on health related quality of life in community dwelling older people. *BMC Musculoskeletal Disorders*, 13: 168, 2012.
- Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist*, 9(3): 179–186, 1969.
- Leeuw M, Goossens ME, Linton SJ, Crombez G, Boersma K, Vlaeyen JW. The fear-avoidance model of musculoskeletal pain: Current state of scientific evidence. *Journal of Behavioral Medicine*, 30(1): 77–94, 2007.
- Leveille SG, Fried L, Guralnik JM. Disabling symptoms: What do older women report? *Journal of General Internal Medicine*, 17(10): 766–773, 2002.
- Leveille SG, Zhang Y, McMullen W, Kelly-Hayes M, Felson DT. Sex Differences in musculoskeletal pain in older adults. *Pain*, 116(3): 332–338, 2005.
- Lichtenstein MJ, Dhanda R, Cornell JE, Escalante A, Hazuda HP. Disaggregating pain and its effect on physical functional limitations. *The journals of gerontology. Series A, Biological sciences and medical sciences*, 53(5): M361–371, 1998.
- Lim KL, Jacobs P, Klarenbach S. A population-based analysis of healthcare utilization of persons with back disorders: results from the Canadian Community Health Survey 2000–2001. *Spine*, 31(2): 212–218, 2006.

- Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*, 41(7): 646–657, 2001.
- Liu CJ, Latham NK. Progressive resistance strength training for improving physical function in older adults. *The Cochrane database of systematic reviews*, 8(3): CD002759, 2009.
- Liukas A, Kuusniemi K, Aantaa R, Virolainen P, Niemi M, Neuvonen PJ, Oikola KT. Pharmacokinetics of intravenous paracetamol in elderly patients. *Clinical pharmacokinetics*, 50(2): 121–129, 2011.
- Long, D., 2013. Surgery For Back And Neck Pain (Including Radiculopathies). In: Wall and Melzack's Textbook of pain. Editors McMahon S, Koltzenburg M, Tracey I and Turk D. 6th edition. Philadelphia: Elsevier Saunders, pp. 1012, 2013
- Mackichan F, Adamson J, Goberman-Hill R. 'Living within your limits': activity restriction in older people experiencing chronic pain. *Age and Ageing*, 42(6): 702–708, 2013.
- Mahoney FI, Barthel DW. Functional Evaluation: the Barthel Index. *Maryland state medical journal*, 14: 61–65, 1965.
- Main CJ, Spanswick CC. Pain management: an interdisciplinary approach. Edinburgh: Elsevier, p. 93. 2001.
- Mallen CD, Peat G. Discussing prognosis with older people with musculoskeletal pain: a cross-sectional study in general practice. *BMC family practice*, 10: 50, 2009.
- Maniadakis N, Gray A. The economic burden of back pain in the UK. *Pain*, 84(1): 95–103, 2000.
- Mason L, Moore RA, Edwards JE, Mcquay HJ, Derry S, Wiffen PJ. Systematic review of efficacy of topical rubefacients containing salicylates for the treatment of acute and chronic pain. *BMJ*, 328(7446): 995, 2004.
- McDonald DD, Fedo J. Older adults' pain communication: the effect of interruption. *Pain management nursing*, 10(3): 149–153. 2009
- McDonald DD, Shea M, Rose L, Fedo J. The effect of pain question phrasing on older adult pain information. *Journal of pain and symptom management*, 37(6): 1050–1060, 2009.
- Mclachlan AJ, Hilmer SN, Le Couteur DG. Variability in response to medicines in older people: phenotypic and genotypic factors. *Clinical pharmacology and therapeutics*, 85(4): 431–433, 2009.
- McLean AJ, Le Couteur DG. Aging biology and geriatric clinical pharmacology. *Pharmacological reviews*, 56(2): 163–184, 2004.
- Meenan RF, Gertman PM, Mason JH. Measuring health status in arthritis: The arthritis impact measurement scales. *Arthritis and Rheumatism*, 23(2): 146–152, 1980.
- Melzack R. The short-form McGill pain questionnaire. *Pain*, 30(2): 191–197, 1987.
- Melzack R. The McGill pain questionnaire: major properties and scoring methods. *Pain*, 1(3): 277–299, 1975.

- Miller M, Sturmer T, Azrael D, Levin R, Solomon DH. Opioid analgesics and the risk of fractures in older adults with arthritis. *Journal of the American Geriatrics Society*, 59(3): 430–438, 2011.
- Mitchell S, Hilmer S, McLachlan A. Clinical pharmacology of analgesics in old age and frailty. *Reviews in Clinical Gerontology* 19:103–118, 2009.
- Moore AR, Clinch D. Underlying mechanisms of impaired visceral pain perception in older people. *Journal of the American Geriatrics Society*, 52(1): 132–136, 2004.
- Moriarty O, Mcguire BE, Finn DP. The effect of pain on cognitive function: A review of clinical and preclinical research. *Progress in neurobiology*, 93(3): 385–404, 2011.
- Morone NE, Lynch CS, Greco CM, Tindle HA, Weiner DK. "I felt like a new person." the effects of mindfulness meditation on older adults with chronic pain: qualitative narrative analysis of diary entries. *The journal of pain*, 9(9): 841–848, 2008.
- Myers RP, Li B, Fong A, Shaheen AA, Quan H. Hospitalizations for acetaminophen overdose: a Canadian population-based study from 1995 to 2004. *BMC public health*, 7: 143, 2007.
- Myers RP, Shaheen AA, Li B, Dean S, Quan H. Impact of liver disease, alcohol abuse, and unintentional ingestions on the outcomes of acetaminophen overdose. *Clinical gastroenterology and hepatology*, 6(8): 918-925, 2008.
- Mäntyselkä P. Kipupotilas terveyseskukuksessa. Patient Pain in General Practise. Doctoral thesis in finnish. Kuopio University Publications D. Medical sciences 165. 1998. 163p. ISBN 951-781-685-5, 1998.
- Mäntyselkä P, Kumpusalo E, Ahonen R, Takala J. Patients' versus general practitioners' assessments of pain intensity in primary care patients with non-cancer pain. *The British journal of general practice*, 51(473): 995–997, 2001.
- Mäntyselkä PT, Turunen JH, Ahonen RS, Kumpusalo EA. Chronic pain and poor self-rated health. *The journal of the American Medical Association*, 290(18): 2435–2442, 2003.
- Nagata N, Niikura R, Aoki T, Shimbo T, Kishida Y, Sekine K, Tanaka S, Watanebe K, Sakurai T, Yokoi C, Akiyama J, Yanase M, Mizokami M, Uemura N. Colonic diverticular hemorrhage associated with the use of NSAIDs, low-dose aspirin, antiplatelet drugs, and dual therapy. *J Gastroenterol Hepatol*. Apr 10 Epub ahead of print. 2014.
- Neutel CI, Skurtveit S, Berg C, Sakshaug S. Multiple prescribers in older frequent opioid users – does it mean abuse? *Journal of population therapeutics and clinical pharmacology*, 20(3): e397–405, 2013.
- Newman AB, Simonsick EM, Naydeck BL, Boudreau RM, Kritchevsky SB, Nevitt MC, Pahor M, Satterfield S, Brach JS, Studenski SA, Harris TB. Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. *The journal of the American Medical Association*, 295(17): 2018-2026, 2006.
- Nicholas MK, Asghari A, Blyth FM, Wood BM, Murray R, McCabe R, Brnabic A, Beeston L, Corbett M, Sherrington C, Overton S. Self-management intervention for chronic pain in older adults: a randomised controlled trial. *Pain*, 154(6): 824–835, 2013.

- Non-Steroidal Anti-Inflammatory Drugs: Current Care Summary. Non-Steroidal Anti-inflammatory Drugs (online). Current Care guideline. Working group set up by the Finnish Medical Society Duodecim and the Finnish Society of Gastroenterology and the Finnish Rheumatology Society. Helsinki: Finnish Medical Society Duodecim, 2009. Available online at: www.kaypahoito.fi.
- Nuesch E, Dieppe P, Reichenbach S, Williams S, Iff S, Juni P. All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. *BMJ*, 342: d1165, 2011.
- Nurminen M. 2011. Vanhakin lääke voi yllättää - haittavaikutusten vuoksi markkinoilta pois vedetyt lääkkeet. Sic! In Finnish. Available online at: http://sic.fimea.fi/vanhakin_laake_voi_yllattaa.aspx. (Accessed 18 March 2014)
- Nwokeji ED, Rascati KL, Brown CM, Eisenberg A. Influences of attitudes on family physicians' willingness to prescribe long-acting opioid analgesics for patients with chronic nonmalignant pain. *Clinical therapeutics*, 29: 2589–2602, 2007.
- Official Statistics of Finland. Deaths [e-publication]. ISSN=1798-2545. 2012, Appendix figure 1. Deaths by age group and sex 2012. Helsinki: Statistics Finland. Available at: http://www.tilastokeskus.fi/til/kuol/2012/kuol_2012_2013-04-12_kuv_001_en.html. (Accessed 26 March 2014).
- Official Statistics of Finland. 2012-last update, Population projection [e-publication]. ISSN 1798-5153. 2012, Appendix table 1. Population by age 1900–2060 (years 2020 to 2060: projection). Helsinki: Statistics Finland. Available at: http://www.tilastokeskus.fi/til/vaenn/2012/vaenn_2012_2012-09-28_tau_001_en.html (Accessed 11 Feb 2014).
- O'neil CK, Hanlon JT, Marcum ZA. Adverse effects of analgesics commonly used by older adults with osteoarthritis: focus on non-opioid and opioid analgesics. *The American journal of geriatric pharmacotherapy*, 10(6): 331–342, 2012.
- Ong CK, Doll H, Bodeker G, Stewart-Brown S. Use of osteopathic or chiropractic services among people with back pain: a UK population survey. *Health & social care in the community*, 12(3): 265–273, 2004.
- Oosterman JM, Hendriks H, Scott S, Lord K, White N, Sampson EL. When pain memories are lost: a pilot study of semantic knowledge of pain in dementia. *Pain medicine*, 15(5): 751–757, 2014.
- Pahor M, Guralnik JM, Wan JY, Ferrucci L, Penninx BW, Lyles A, Ling S, Fried LP. Lower body osteoarticular pain and dose of analgesic medications in older disabled women: the Women's Health and Aging Study. *American Journal of Public Health*, 89(6): 930–934, 1999.
- Palazzo C, Ravaud J, Papelard A, Ravaud P, Poiraudreau S. The Burden of Musculoskeletal Conditions. *PLoS ONE* 9(3): e90633, 2014.
- Paulose-Ram R, Hirsch R, Dillon C, Losonczy K, Cooper M, Ostchega Y. Prescription and non-prescription analgesic use among the US adult population: results from the third National Health and Nutrition Examination Survey (NHANES III). *Pharmacoepidemiology and drug safety*, 12(4): 315–326, 2003.

- Peat G, Thomas E, Handy J, Croft P. Social networks and pain interference with daily activities in middle and old age. *Pain*, 112(3): 397–405, 2004.
- Pergolizzi J, Boger RH, Budd K, Dahan A, Erdine S, Hans G, Kress HG, Langford R, Likar R, Raffa RB, Sacerdote P. Opioids and the management of chronic severe pain in the elderly: consensus statement of an International Expert Panel with focus on the six clinically most often used World Health Organization Step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). *Pain practice*, 8(4): 287–313, 2008.
- Pergolizzi JV Jr, Raffa RB, Taylor R Jr. Treating acute pain in light of the chronification of pain. *Pain management nursing*, 15(1): 380–390, 2014.
- Pesonen A, Suojaranta-Ylinen R, Tarkkila P, Rosenberg PH. Applicability of tools to assess pain in elderly patients after cardiac surgery. *Acta Anaesthesiologica Scandinavica*, 52(2): 267–273, 2008.
- Peters ML, Patijn J, Lame I. Pain assessment in younger and older pain patients: psychometric properties and patient preference of five commonly used measures of pain intensity. *Pain medicine*, 8(7): 601–610, 2007.
- Petersson IF, Jacobsson LT. Osteoarthritis of the peripheral joints. Best practice & research. *Clinical rheumatology*, 16(5): 741-760, 2002.
- Petrie KJ, Frampton T, Large RG, Moss-Morris R, Johnson M, Meechan G. What do patients expect from their first visit to a pain clinic? *The Clinical journal of pain*, 21(4): 297–301, 2005.
- Pitkälä KH, Strandberg TE, Tilvis RS. Management of nonmalignant pain in home-dwelling older people: a population-based survey. *Journal of the American Geriatrics Society*, 50(11): 1861–1865, 2002.
- Podichetty VK, Mazanec DJ, Biscup RS. Chronic non-malignant musculoskeletal pain in older adults: clinical issues and opioid intervention. *Postgraduate medical journal*, 79(937): 627–633, 2003.
- Prencipe M, Casini AR, Ferretti C, Santini M, Pezzella F, Scaldaferrri N, Culasso F. Prevalence of headache in an elderly population: attack frequency, disability, and use of medication. *Journal of neurology, neurosurgery, and psychiatry*, 70(3): 377–381, 2001.
- Price SD, Holman CD, Sanfilippo FM, Emery JD. Association Between Potentially Inappropriate Medications From the Beers Criteria and the Risk of Unplanned Hospitalization in Elderly Patients. *Annals of Pharmacotherapy*, 48(1): 6–16, 2014.
- Raffa RB, Pergolizzi JV Jr. A modern analgesics pain 'pyramid'. *Journal of clinical pharmacy and therapeutics*, 39(1): 4–6, 2014.
- Rastogi R, Swarm RA, Patel TA. Case scenario: opioid association with serotonin syndrome: implications to the practitioners. *Anesthesiology*, 115(6): 1291–1298, 2011.
- Redondo-Sendino A, Guallar-Castillon P, Banegas JR, Rodriguez-Artalejo F. Gender differences in the utilization of health-care services among the older adult population of Spain. *BMC public health*, 6: 155, 2006.
- Resnick B, Nahm ES. Reliability and validity testing of the revised 12-item Short-Form Health Survey in older adults. *Journal of nursing measurement*, 9(2): 151–161, 2001.

- Reyes-Gibby CC, Aday L, Cleeland C. Impact of pain on self-rated health in the community-dwelling older adults. *Pain*, 95(1-2): 75–82, 2002.
- Ross MM, Carswell A, Hing M, Hollingworth G, Dalziel WB. Seniors' decision making about pain management. *Journal of advanced nursing*, 35(3): 442–451, 2001.
- Rostom A, Goldkind L, Laine L. Nonsteroidal anti-inflammatory drugs and hepatic toxicity: a systematic review of randomized controlled trials in arthritis patients. *Clinical gastroenterology and hepatology*, 3(5): 489–498, 2005.
- Rustoen T, Wahl AK, Hanestad BR, Lerdal A, Paul S, Miaskowski C. Age and the experience of chronic pain: differences in health and quality of life among younger, middle-aged, and older adults. *The Clinical journal of pain*, 21(6): 513–523, 2005.
- Sadowski CA, Carrie AG, Grymonpre RE, Metge CJ, St John P. Access and intensity of use of prescription analgesics among older Manitobans. *The Canadian journal of clinical pharmacology*, 16(2): e322–330, 2009.
- Sale JE, Gignac M, Hawker G. How "bad" does the pain have to be? A qualitative study examining adherence to pain medication in older adults with osteoarthritis. *Arthritis and Rheumatism*, 55(2): 272–278, 2006.
- Santos AM, Burti JS, Lopes JB, Scazufca M, Marques AP, Pereira RM. Prevalence of fibromyalgia and chronic widespread pain in community-dwelling elderly subjects living in Sao Paulo, Brazil. *Maturitas*, 67(3): 251–255, 2010.
- Saunders KW, Dunn KM, Merrill JO, Sullivan M, Weisner C, Braden JB, Psaty BM, Von Korff M. Relationship of opioid use and dosage levels to fractures in older chronic pain patients. *Journal of general internal medicine*, 25(4): 310-315, 2010.
- Sawyer P, Bodner EV, Ritchie CS, Allman RM. Pain and pain medication use in community-dwelling older adults. *The American journal of geriatric pharmacotherapy*, 4(4): 316–324, 2006.
- Shah RC, Buchman AS, Boyle PA, Leurgans SE, Wilson RS, Andersson GB, Bennett DA. Musculoskeletal pain is associated with incident mobility disability in community-dwelling elders. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 66 A(1): 82–88, 2011.
- Sheikh J, Yesavage J. Geriatric Depression Scale (GDS) Recent evidence and development of a shorter version. In: Brink TL, editor. *Clinical Gerontology: A Guide to Assessment and Intervention*. New York: The Haworth Press, pp. 165–173. 1986.
- Sheppard KD, Sawyer P, Ritchie CS, Allman RM, Brown CJ. Life-space mobility predicts nursing home admission over 6 years. *Journal of aging and health*, 25(6): 907–920, 2013.
- Shin SY, Kolanowski AM. Best evidence of psychosocially focused nonpharmacologic therapies for symptom management in older adults with osteoarthritis. *Pain management nursing*, 11(4): 234–244, 2010.
- Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the timed up and go test. *Physical Therapy*, 80(9): 896–903, 2000.

- Simon LS, Grierson LM, Naseer Z, Bookman AA, Zev Shainhouse J. Efficacy and safety of topical diclofenac containing dimethyl sulfoxide (DMSO) compared with those of topical placebo, DMSO vehicle and oral diclofenac for knee osteoarthritis. *Pain*, 143(3): 238–245, 2009.
- Smith A, Dillon J. Acute liver injury associated with the use of herbal preparations containing glucosamine: three case studies. *BMJ case reports*, Epub 2 Sep 2009: bcr02.2009.16032009, 2009.
- Smith HS. Potential analgesic mechanisms of acetaminophen. *Pain physician*, 12(1): 269–280, 2009.
- Sofaer B, Moore AP, Holloway I, Lamberty JM, Thorp TA, O'dwyer J. Chronic pain as perceived by older people: a qualitative study. *Age and Ageing*, 34(5): 462–466, 2005.
- Sostres C, Gargallo CJ, Lanás A. Nonsteroidal anti-inflammatory drugs and upper and lower gastrointestinal mucosal damage. *Arthritis research & therapy*, 15(3): S3. 2013.
- Spiers J. Expressing and responding to pain and stoicism in home-care nurse-patient interactions. *Scandinavian Journal of Caring Sciences*, 20(3): 293–301, 2006.
- Stubbs B, Binnekade T, Eggermont L, Sepehry AA, Patchay S, Schofield P. Pain and the risk for falls in community-dwelling older adults: Systematic review and meta-analysis. *Archives of Physical Medicine and Rehabilitation*, 95(1): 175–187, 2014.
- Stubbs B, West E, Patchay S, Schofield P. Is there a relationship between pain and psychological concerns related to falling in community dwelling older adults? A systematic review. *Disability and rehabilitation*, Epub ahead of print (doi:10.3109/09638288.2014.882419), 2014.
- Tait RC, Chibnall JT, Krause S. The Pain Disability Index: Psychometric properties. *Pain*, 40(2): 171–182, 1990.
- Tamayo-Fonseca N, Quesada JA, Nolasco A, Melchor I, Moncho J, Pereyra-Zamora P, López R, Calabuig J, Barber X. Self-rated health and mortality: A follow-up study of a Spanish population. *Public health*, 127(12): 1097–1104, 2013.
- Taylor LJ, Harris J, Epps CD, Herr K. Psychometric evaluation of selected pain intensity scales for use with cognitively impaired and cognitively intact older adults. *Rehabilitation nursing*, 30(2): 55–61, 2005.
- Thielke SM, Simoni-Wastila L, Edlund MJ, Devries A, Martin BC, Braden JB, Fan MY, Sullivan MD. Age and sex trends in long-term opioid use in two large American health systems between 2000 and 2005. *Pain medicine*, 11(2): 248–256, 2010.
- Thielke SM, Whitson H, Diehr P, O'hare A, Kearney PM, Chaudhry SI, Zakai NA, Kim D, Sekaran N, Sale JE, Arnold AM, Chaves P, Newman A. Persistence and remission of musculoskeletal pain in community-dwelling older adults: Results from the Cardiovascular Health Study. *Journal of the American Geriatrics Society*, 60(8): 1393–1400, 2012.
- Thomas E, Peat G, Harris L, Wilkie R, Croft PR. The prevalence of pain and pain interference in a general population of older adults: cross-sectional findings from the North Staffordshire Osteoarthritis Project (NorStOP). *Pain*, 110(1-2): 361–368, 2004.

- Tiainen K, Luukkaala T, Hervonen A, Jylhä M. Predictors of mortality in men and women aged 90 and older: A nine-year follow-up study in the Vitality 90+ study. *Age and Ageing*, 42(4): 468–475, 2013.
- Torrance N, Elliott AM, Lee AJ, Smith BH. Severe chronic pain is associated with increased 10 year mortality. A cohort record linkage study. *European journal of pain*, 14(4): 380–386, 2010.
- Tovar RT, Petzel RM. Herbal toxicity. *Disease-a-month*, 55(10): 592-641, 2009.
- Towheed TE, Maxwell L, Judd MG, Catton M, Hochberg MC, Wells G. Acetaminophen for osteoarthritis. *Cochrane database of systematic reviews* 25(1): CD004257, 2006.
- Tsai YF, Liu LL, Chung SC. Pain prevalence, experiences, and self-care management strategies among the community-dwelling elderly in Taiwan. *Journal of pain and symptom management*, 40(4): 575–581, 2010.
- Tse MM, Wan VT, Ho SS. Physical exercise: does it help in relieving pain and increasing mobility among older adults with chronic pain? *Journal of Clinical Nursing*, 20(5-6): 635–644, 2011.
- Turunen JH, Mäntyselkä PT, Kumpusalo EA, Ahonen RS. How do people ease their pain? A population-based study. *The journal of pain*, 5(9): 498–504, 2004.
- Urwin M, Symmons D, Allison T, Brammah T, Busby H, Roxby M, Simmons A, Williams G. Estimating the burden of musculoskeletal disorders in the community: The comparative prevalence of symptoms at different anatomical sites, and the relation to social deprivation. *Annals of the Rheumatic Diseases*, 57(11): 649–655, 1998.
- Van Hecke O, Torrance N, Smith BH. Chronic pain epidemiology and its clinical relevance. *British journal of anaesthesia*, 111(1): 13–18, 2013.
- Van Ojik AL, Jansen PA, Brouwers JR, Van Roon EN. Treatment of chronic pain in older people: evidence-based choice of strong-acting opioids. *Drugs & aging*, 29(8): 615–625, 2012.
- Visser M, Simonsick EM, Colbert LH, Brach J, Rubin SM, Kritchevsky SB, Newman AB, Harris TB, Health Abc Study. Type and intensity of activity and risk of mobility limitation: the mediating role of muscle parameters. *Journal of the American Geriatrics Society*, 53(5): 762–770, 2005.
- Von Korff M, Wagner EH, Dworkin SF, Saunders KW. Chronic pain and use of ambulatory health care. *Psychosomatic medicine*, 53(1): 61–79, 1991.
- Wandel S, Juni P, Tendal B, Nuesch E, Villiger PM, Welton NJ, Reichenbach S, Trelle S. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. *BMJ*, 341: c4675, 2010.
- WHO, World Health Organization, Collaborating Centre for Drug Statistics Methodology. Norwegian Institute of Public Health. The Anatomical Therapeutic Chemical Classification System. Last update 2014. <http://www.whocc.no/atcddd/> (Accessed 15 Jan 2014)

- WHO, World Health Organization: Cancer Pain Relief. Second Edition. With a guide to opioid availability. Singapore 1996. Available online in English at: <http://whqlibdoc.who.int/publications/9241544821.pdf>.
- Wood BM, Nicholas MK, Blyth F, Asghari A, Gibson S. Assessing pain in older people with persistent pain: the NRS is valid but only provides part of the picture. *The journal of pain*, 11(12): 1259–1266, 2010.
- Woolf A, Pfleger B. Burden of major musculoskeletal conditions. Special Theme - Bone and Joint Decade 2000-2010. *Bulletin of the World Health Organization* 81:646–656, 2003.
- Xue CC, Zhang AL, Lin V, Myers R, Polus B, Story DF. Acupuncture, chiropractic and osteopathy use in Australia: a national population survey. *BMC public health*, 1(8):105, 2008.
- Yamada E, Thomas DC. Common musculoskeletal diagnoses of upper and lower extremities in older patients. *The Mount Sinai journal of medicine, New York*, 78(4): 546-557, 2011.
- Yong H. Can attitudes of stoicism and cautiousness explain observed age-related variation in levels of self-rated pain, mood disturbance and functional interference in chronic pain patients? *European Journal of Pain*, 10(5): 399–407, 2006.
- Zhang W, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW, Dincer F, Dziedzic K, Hauselmann HJ, Herrero-Beaumont G, Kaklamani P, Lohmander S, Maheu E, Martin-Mola E, Pavelka K, Punzi L, Reiter S, Sautner J, Smolen J, Verbruggen G, Zimmermann-Gorska I. EULAR evidence based recommendations for the management of hand osteoarthritis: report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Annals of the Rheumatic Diseases*, 66(3): 377–388, 2007.
- Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, Dougados M, Hochberg M, Hunter DJ, Kwoh K, Lohmander LS, Tugwell P. OARSI recommendations for the management of hip and knee osteoarthritis, part I: critical appraisal of existing treatment guidelines and systematic review of current research evidence. *Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society*, 15(9): 981–1000, 2007.
- Zwakhlen SM, Hamers JP, Abu-Saad HH, Berger MP. Pain in elderly people with severe dementia: A systematic review of behavioural pain assessment tools. *BMC Geriatrics*, 27(6):3, 2006.
- Äijö M, Heikkinen E, Schroll M, Steen B. Physical activity and mortality of 75-year-old people in three Nordic localities: a five-year follow-up. *Aging clinical and experimental research*, 14(3): 83–89, 2002.

NIINA KARTTUNEN
*Pain, Persistence of Pain
and Analgesic Use
in Community-Dwelling
Older Finns*

There are many confounding factors related to pain treatment in older people and concerns have been raised regarding the management of pain. This study aimed to determine the pattern of analgesic use, the persistence of chronic pain, and factors related to mobility limitation in community-dwelling older Finns. In addition, older persons' perceptions of whether they hoped to receive more attention from the physician in the management of their pain were explored. It was shown that musculoskeletal chronic pain is often persistent in its nature and there is an evident need for better pain management in community-dwelling older people.



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