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**CHRONIC PAIN AND NEUROPATHIC PAIN AMONG  
COMMUNITY-DWELLING OLDER ADULTS  
IN PRIMARY HEALTH CARE SETTINGS**



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Doctoral Programme in Clinical Research  
University of Helsinki, Finland

# CHRONIC PAIN AND NEUROPATHIC PAIN AMONG COMMUNITY- DWELLING OLDER ADULTS IN PRIMARY HEALTH CARE SETTINGS

**Susanna Rapo-Pylkkö**

ACADEMIC DISSERTATION

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valot pimeyksien reunoilla  
ovat toisinaan himmeitä ja harvassa  
sulla on sisällä valtameren kokoinen voima, jonka sä voit oppaaksesi valjastaa  
Toni Wirtanen

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## Abbreviations

ACPA	American Association of Chronic Pain
AGS	American Geriatrics Society
BAI	Beck Anxiety Inventory
BPI	Brief Pain Inventory
CNS	Central nervous system
COX	Cyclo-oxygenase
CV	Cardiovascular
DN4	Douleur Neuropathique en 4 questions
EFIC	European Federation of International Association for the Study of Pain
GDS	Geriatric Depression Scale
GP	General practitioner
IASP	International Association for Study of Pain
IQR	Interquartile range
LANSS	Leeds Assessment of Neuropathic Symptoms and Signs
MMSE	Mini Mental State Examination
NeuPSIG	Special Interest Group on Neuropathic Pain
NICE	National Institute for Health and Care Excellence
NOPPAIN	Non-Communicative Patient's Pain Assessment Instrument
NP	Neuropathic pain
NRS	Numeric rating scale
NSAID	Non-steroidal anti-inflammatory drug
OA	Osteoarthritis
PAINAD	Pain Assessment IN Advanced Dementia Scale
RAI	Resident Assessment Instrument
RCT	Randomized controlled trial
SD	Standard deviation
SF-36	Medical Outcomes Survey Short Form
SNRI	Serotonin-norepinephrine reuptake inhibitor
START	Screening Tool to Alert doctors to Right Treatment
TCA	Tricyclic antidepressants
VAS	Visual Analogue Scale
VDS	Verbal Descriptor Scale

## List of original publications

This thesis is based on the following original publications referred to in the text by their Roman numerals:

I Rapo-Pylkkö S, Haanpää M, Liira H. Chronic pain among community-dwelling elderly: a population-based clinical study. *Scand J Prim Health Care* 2016; 34: 159-164.

II Rapo-Pylkkö S, Haanpää M, Liira H. Neuropathic pain among community-dwelling older people: a clinical study in Finland. *Drugs Aging* 2015; 32: 737-42.

III Rapo-Pylkkö S, Haanpää M, Liira H. Subjective easiness of pain assessment measures in older people. *Archives of Gerontology and Geriatrics* 2016; 65: 25-28.

IV Rapo-Pylkkö S, Haanpää M, Liira H. A one-year follow-up study of chronic pain in community-dwelling older adults with and without neuropathic pain. *BMC Geriatrics* 2017; 17: 152.

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# Abstract

## Background

Chronic pain is a common reason for primary care consultations in older community-dwelling adults. Chronic pain is often related with multimorbidity and may compromise patient's independency and quality of life. Neuropathic pain (NP) causes a more severe burden than nociceptive pain in patients. Diagnosis and pain assessment are challenging in older adults, and identification of pain among the other presenting health problems deserves more attention. Prognosis of chronic pain and NP in older adults is unknown. As the population is ageing, the cost and impact of chronic pain to both the individual as well as the community are becoming increasingly significant.

## Objective

The focus of this study was to map the occurrence, characteristics and consequences of chronic pain in community-dwelling older adults in three age groups (75, 80 and 85 year olds). The primary focus was on the presence, aetiology, diagnostic certainty and treatment of NP among older people. The study also investigated the easiness of use of two unidimensional scales Visual Analogue Scale (VAS) and Numeric rating scale (NRS); and two multidimensional scales Brief Pain Inventory (BPI) and PainDETECT pain scales in older adults. One-year follow-up was conducted via a postal survey investigating pain, mood and quality of life of the patients.

## Methods

Independently living older adults were screened for chronic pain during preventive home visits in 2009-2013 in Kirkkonummi, Finland. Patients with chronic pain (duration  $\geq 3$  months) with average pain intensity and / or interference of  $\geq 4$  on the NRS 0-10 scale during the week prior to the visit were invited to participate in the study. During the preventive home visits, 106 patients were recruited to the study. During the clinical study visit, a nurse interviewed the patients regarding their pain, and the patients rated their pain intensity on the VAS and filled in five questionnaires (Beck Anxiety Inventory (BAI), BPI, Geriatric Depression Scale (GDS-15), PainDETECT and Medical Outcomes Survey Short Form (SF-36)). The geriatrician then performed a clinical evaluation including assessment of pain intensity on the NRS. Based on the clinical examination, the geriatrician classified the type(s) of pain, if required, in consultation with a pain specialist. The diagnostic certainty of NP was then graded as definite, probable or possible according to the recommended criteria. In the end of the visit, the nurse asked patients to assess the ease of use for the pain scales (VAS, NRS, BPI and PainDETECT) using a 7-point verbal rating scale. One-year postal follow-up survey was conducted and patients were asked to fill out four questionnaires (BPI, GDS-15, BAI and SF-36) and answer questions about their current pain medication and any new pain states.

## Results

Based on the data collected during the preventive home visits, older adults with chronic pain rated their health and mobility worse, and felt sadder, lonelier and more tired than those living without chronic pain. However, older adults with chronic pain rated their life satisfaction similarly to those without chronic pain.

Most of the participants had more than one pain state (only 5 subjects had just one), and the worst pain in 83% was musculoskeletal. The worst pain was purely nociceptive in 58% and combined nociceptive and NP or purely NP in 40% of participants. The duration of worst pain was longer than five years in half of the patients and in 80% it occurred daily. Regular pain medication, most commonly paracetamol or NSAIDs, were used by 77%. Use of non-pharmacological treatments was also common; 75% named at least one non-pharmacological method to alleviate pain.

NP (either as the worst or second worst pain) was diagnosed in 51 (48%) participants. Forty-three participants rated NP as the worst pain. Diagnosis of NP was definite in 75% and probable in 25% of all NP pain states. The most common aetiology of NP was degenerative disease of spinal column causing radiculopathy. NP had higher pain intensity and interference in patients compared with non-NP pain. Only a fifth of the patients with NP were taking recommended medication.

Multidimensional pain scales (PainDETECT and BPI) were rated easier to use compared with the unidimensional NRS and VAS. On average, all four scales were assessed as “quite easy” to use.

Chronic pain did not compromise participant independence in the one-year follow-up. On average, no significant changes occurred in the pain intensity or interference, mood or quality of life in the follow-up, however, individual level changes were observed.

## Conclusions

Chronic pain is often a combination of multiple conditions in community-dwelling older adults. Subjective health and mobility are impacted and worsened in those with chronic pain, however life satisfaction remains similar to those without pain. NP is common in community-dwelling older adults and its intensity and interference are greater compared to non-NP. VAS, NRS, PainDETECT and BPI are quite easy to use for community-dwelling older adults. One-year follow-up study shows that on average, chronic pain remains unchanged. Population-based longitudinal studies of chronic pain among older adults are needed to outline the significance and treatment in the older adult population.

# Tiivistelmä

## Tausta

Krooninen kipu on yleinen vanhusten perusterveydenhuollon käyntisy. Krooninen kipu liittyy usein monisairastavuuteen ja uhkaa yksilön itsenäisyyttä ja elämänlaatua. Neuropaattinen kipu on vaikutuksiltaan vielä kroonista nosiseptiivista kipua vaikeampi. Kivun diagnosoiminen ja arviointi on haasteellisempaa vanhuksilla kuin nuoremmilla henkilöillä, ja kivun tunnistaminen useiden terveysongelmien joukosta haastaa klinikon. Kroonisen kivun ja neuropaattisen kivun ennustetta vanhuksilla ei tunneta. Kuitenkin vanhusten kroonisen kivun seuraukset ja sen aiheuttamat kustannukset kasvavat väestön ikääntymisen myötä.

## Tutkimuksen tavoitteet

Tämän tutkimuksen tavoitteena oli kartoittaa kroonisen kivun esiintyvyyttä, piirteitä ja seurauksia itsenäisillä 75-, 80- ja 85-vuotiailla vanhuksilla. Erityisenä kiinnostuksen kohteena oli neuropaattisen kivun esiintyminen, etiologia, diagnostinen varmuus ja hoito vanhuksilla. Lisäksi tutkittiin yksilöotteisten kipumittareiden (VAS ja NRS) sekä moniulotteisten mittareiden (BPI ja PainDETECT) käytön helppoutta. Vuoden kuluttua tutkimuskäynnistä tehtiin seuranta postikyselynä, jossa selvitettiin kipua, mielialaa ja elämänlaatua.

## Menetelmät

Ennaltaehkäisevillä kotikäynneillä selvitettiin itsenäisten vanhusten kroonista (vähintään 3 kk kestänyttä) kipua kysymällä heidän kipunsa voimakkuutta ja häiritsevyyttä. Jos henkilöllä oli ollut tutkimusta edeltäneen viikon aikana kipua, jonka keskimääräinen voimakkuus tai haittaavuus oli vähintään 4 NRS-asteikoilla, hänet kutsuttiin kipututkimukseen. Ennaltaehkäiseviltä kotikäynneiltä kerättiin potilaita tutkimukseen vuosina 2009-2013 Kirkkonummen kunnassa, ja kaikkiaan 106 henkilöä osallistui tutkimukseen. Tutkimuskäynnin alussa tutkimushoitaja kartoitti potilaiden kiputilannetta. Sen jälkeen potilaat arvioivat kipunsa käyttäen VAS-asteikkoa sekä viittä kyselylomaketta (BAI, BPI, GDS-15, painDETECT ja SF-36). Sen jälkeen geriatri tutki potilaat, ja he arvioivat kipunsa NRS-asteikolla. Kliinisen tutkimuksen perusteella geriatri luokitteli kivun ja konsultoi tarvittaessa kipuasiiantuntijaa. Neuropaattisen kivun diagnoosi luokiteltiin varmaksi, todennäköiseksi tai mahdolliseksi suositeltujen diagnostisten kriteerien mukaisesti. Tutkimuskäynnin lopuksi potilaita pyydettiin arvioimaan VAS- ja NRS-asteikkojen sekä BPI- ja PainDETECT-lomakkeiden käytön helppoutta 7-portaisella sanallisella asteikolla. Seuranta toteutettiin vuoden kuluttua tutkimuskäynnistä postikyselynä, jossa tiedusteltiin potilaiden kivun voimakkuutta, kipulääkitystä sekä mahdollisia uusia kiputiloja, ja lisäksi potilaita pyydettiin täyttämään neljä kyselylomaketta (BPI, GDS-15, BAI ja SF-36).

## **Tulokset**

Ennaltaehkäiseviltä kotikäynneiltä saatujen tietojen perusteella kroonista kipua raportoineet vanhukset kokivat terveydentilansa ja liikkumiskykynsä huonommaksi ja tunsivat itsensä surullisemmaksi, yksinäisemmäksi ja väsyneemmäksi kuin kivuttomat ikätoverinsa. Kuitenkin he olivat yhtä tyytyväisiä elämäänsä kuin kivuttomat vanhukset.

Suurimmalla osalla tutkimuspotilaista oli useampi kuin yksi kiputila (viidellä henkilöllä oli vain yksi kiputila), ja pahin kipu oli muskuloskeletaalista 83 prosentilla. Pahin kipu oli nosiseptiivista kipua 58 prosentilla potilaista ja sekamuotoista eli yhdistelmä nosiseptiivista ja neuropaattista kipua 40 prosentilla potilaista. Pahin kipu oli kestänyt vähintään viisi vuotta puolella potilaista, ja kipu oli päivittäistä 80 prosentilla potilaista. Säännöllistä kipulääkitystä käytti 77 prosenttia potilaista, suurin osa heistä parasetamolia tai tulehduskipulääkkeitä. Lääkkeettömien hoitojen käyttö oli yleistä; 75 prosenttia potilaista käytti ainakin yhtä lääkkeitöntä kivun hoitoa.

Neuropaattinen kipu (joko pahimpana tai toiseksi pahimpana kipuna) diagnosoitiin 51 (48 %) potilaalla, ja 43 potilasta arvioi neuropaattisen kivun vaikeimmaksi kivukseksi. Neuropaattisen kivun diagnoosi oli varma 75 prosentissa ja todennäköinen 25 prosentissa neuropaattisista kiputiloista. Neuropaattisen kivun yleisin etiologia oli selkärangan degeneratiivinen sairaus, johon liittyi radikulopatia. Neuropaattisen kivun voimakkuus ja haittaavuus olivat vaikeammat kuin nosiseptiivisen kivun. Hoitosuosituksen mukainen neuropaattisen kivun lääke oli käytössä vain viidesosalla neuropaattista kipua raportoineista potilaista.

Moniulotteiset kipumittarit (PainDETECT ja BPI) olivat potilaiden mielestä helpompia käyttää kuin yksiulotteiset (NRS ja VAS). Kaikki neljä kipumittaria olivat kuitenkin potilaiden mielestä kohtalaisen helppoja käyttää.

Krooninen kipu ei ollut heikentänyt potilaiden itsenäisyyttä vuoden seurannassa. Keskimäärin kivun voimakkuus ja haittaavuus, mieliala ja elämänlaatu eivät muuttuneet seurannan aikana. Muutoksia havaittiin kuitenkin yksilötasolla.

## **Johtopäätökset**

Itsenäisten vanhusten krooninen kipu koostui usein monista eri kiputiloista. Krooninen kipu heikensi koettua terveyttä ja liikuntakykyä, mutta tyytyväisyys elämään säilyi. Neuropaattinen kipu oli yleistä itsenäisillä vanhuksilla, ja sen voimakkuus sekä haittaavuus olivat suuremmat kuin muiden kroonisten kipujen. Itsenäiset vanhukset arvioivat, että VAS, NRS, PainDETECT ja BPI olivat kohtalaisen helppoja käyttää. Krooninen kipu pysyi keskimäärin samanlaisena vuoden seuranta-aikana. Väestöpohjaisia pitkäaikaistutkimuksia tarvitaan kuvaamaan kroonisen kivun merkitystä ja hoitoa vanhuksilla.

# 1. Introduction

Chronic pain is a common reason for primary care visits in community-dwelling older adults. Hasselström et al. (2002) reports, that approximately 30% of patients visited a general practitioner (GP) for pain, and that their primary pain was musculoskeletal. Most of these patients were older adults. A Finnish study by Mäntyselkä et al. (2001) finds that in a similar setting, up to 40% of patients saw a primary care physician for pain. The most common pain sites were the back and the joints. The prevalence of chronic pain among community-dwelling older adults aged 75 years and over was estimated at 49% in non-selected Finnish population, remaining consistent in three quarters of the patients in the two-year follow-up (Karttunen et al. 2015). According to epidemiological studies, the prevalence of neuropathic pain (NP) is estimated to be between 7 to 10 % in general population (van Hecke et al. 2014), however, its prevalence in people aged 75 years and over is unknown.

Chronic pain is more common among older adults because the prevalence of diseases causing pain (e.g., osteoarthritis (OA), degenerative spine conditions, atherosclerosis) increase with age (Rastogi and Meek 2013). Chronic pain deteriorates the physical performance (Bryant et al. 2007) and self-rated health in individuals (Mäntyselkä et al. 2003, EFIC 2012). NP tends to have even more devastating impact on sleep, mood and the quality of life (Jensen et al. 2007, Attal et al. 2011).

Physiologic changes with advancing age have influence on the pharmacodynamics and pharmacokinetics of drugs. This, in turn, complicates the pain management (van Hecke et al. 2013) as treatment options become more restricted and challenging (Haanpää et al. 2010).

There is a need for comprehensive recognition and assessment of pain among older adults. Multimorbidity, possible cognitive decline, disturbed sleep and patient's mood should be taken into account in patient's pain analysis (Hadjistavropoulos et al. 2007). Guidelines recommending tools for pain assessment in older adults are available (Hadjistavropoulos et al. 2007, Hadjistavropoulos et al. 2014, Crome et al. 2007), but only a few tools have been validated for use in community-dwelling older adults with most studies excluding patients aged 70 years and over (Paeck et al. 2014).

This study aimed to assess the prevalence and treatment of chronic pain, NP in particular, in a clinical setting in the community-dwelling population aged 75 to 85 years. Patients with NP were compared to patients with non-NP for their mood, pain intensity and interference, and quality of life. We also studied ease of use of unidimensional visual analogue scale (VAS) and numeric rating scale (NRS) and multidimensional pain assessment tools in our patients. Due to the lack of follow-up studies regarding pain in the elderly (Karttunen et al. 2015, Thielke et al. 2012), we carried out a one-year postal survey follow-up asking the participants about their current pain states, intensity and interference of pain, mood and quality of life.

## 2. Review of the literature

### 2.1. Definitions of chronic pain

The International Association for Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (IASP). The current IASP definition of chronic pain is persistent or recurrent pain lasting longer than 3 months (Treede et al. 2015). The definition of American Association of Chronic Pain (ACPA 2016) states that chronic or persistent pain can be described as ongoing or recurrent pain, lasting beyond the usual course of acute illness or injury healing, more than 3 to 6 months, and which adversely affects the individual's well-being. Chronic or persistent pain can also be defined as a pain that continues when it should have disappeared (Marcus 2009).

### 2.2. Chronic pain and ageing

The relationship between age and chronic pain is controversial (Abdulla et al. 2013). Although pain generally seems to increase with age, the oldest old (85 years and over) appear to suffer less from pain compared with their 64 to 75 year old peers (Carmaciu et al. 2007, Larsson et al. 2017). This could be explained by the survivor effect; oldest old are more robust. Another explanation to strengthen same effect is selection: those with multiple disease and more pain may die earlier (Nunes et al. 2016). Pain may also be the first sign of a severe disease (Kåreholt and Brattberg 1998). The oldest people may have adapted to living and coping with chronic pain (Sofaer et al 2005). A systematic review of the prevalence of low back pain shows that only the prevalence of severe pain conditions increase with age (Dionne et al. 2006).

Back pain is the most prevalent musculoskeletal complaint in older adults in primary care (Mäntyselkä et al. 2001). In a recent German study of people aged 65 years or older, the top three pains for visiting a GP were relating to the back, the shoulders or the knee (Frese et al. 2016), highlighting the need for pain recognition and treatment in the elderly in general practice. Back pain in older adults is often accompanied by co-morbidities and disabilities in daily life (Scheele et al. 2014). Joint diseases present another common source of pain and are associated with pain more than any other pathology, with major impacts on everyday life in older adults (Carmaciu et al. 2007). Pain has significant impacts on increased health care utilization and costs. A large population-based Swedish study of people aged 64 years and over, showed that the more severe the chronic pain experienced by the patient is, the more extensive (and expensive) their health service utilisation (Bernfort et al. 2015).

Chronic pain is associated with multiple factors, including physical, psychological and social variables. Many of the risk factors are non-modifiable, such as age, sex, cultural and socio-economic determinants, history of trauma and genetic background. On the other hand, there are a number

of modifiable factors which can form a basis for preventive actions. Common modifiable variables include smoking, alcohol consumption, obesity, sleep, nutrition. (van Hecke et al. 2013 A) Determinants of chronic pain among older adults include smoking, obesity, depression, female gender and lower socio-economic status (Carmaciu et al. 2007, Shi et al. 2010). Evidence suggests that geographical and cultural variation have an impact on the prevalence of chronic pain (Breivik et al. 2006). Personal history of abuse or violence, and occupational risk factors can also increase the incidence of chronic pain (van Hecke et al. 2013 A). Older people have the highest risk of injury, hospitalization, surgical treatments, and diseases with high risk of pain. Chronic pain has strong links to mood disturbances, sleep problems, functional impairments, and reduced quality of life (Gibson et al. 2012).

### 2.3. Epidemiology and prevalence of pain in older adults

Chronic pain is a major global health problem. A large international survey found that the prevalence of chronic pain in adult population was between 12 to 30 per cent, and one fifth of the respondents with chronic pain had suffered from it for more than 20 years. More than half of those with chronic pain had suffered from it for 2 to 15 years. Chronic pain of moderate to severe intensity impacts 19% of adults in Europe. (Breivik et al. 2006) A large Finnish national study found that the prevalence of chronic pain in adults was 35%, and the prevalence of daily chronic pain was 14%. The older the participants were, the higher the prevalence of chronic pain. Over a quarter of those aged 70 years or older had daily chronic pain. (Mäntyselkä et al. 2003)

More than two thirds of painful states in the primary care patients locate in the musculoskeletal system (Hasselström et al. 2002). The three most common sites of pain in older people are the back, leg/knee or hip and other joints (Abdulla et al. 2013), suggesting that the most common causes of chronic pain among older people are degenerative back diseases and OA.

Based on the current literature, determining the definitive prevalence of chronic pain in older people is unattainable (Abdulla et al. 2013)

### 2.4. Types of chronic pain

Chronic pain can be classified by pathophysiology (the functional changes associated with or resulting from disease or injury) into three groups: nociceptive pain (due to ongoing tissue injury), neuropathic pain (resulting from damage to the brain, spinal cord, or peripheral nerves), or a mixture of both (ACPA 2016). Nociceptive pain is divided to somatic pain (mediated via somatosensory pain pathways) and visceral pain (mediated via visceral nociceptive pathways). Coexistence of nociceptive and NP is called mixed pain (Baron et al. 2010). In addition, a new main category, nociplastic pain (referring to pain conditions with altered nociceptive processing without presence of nociceptive or NP) has been suggested recently and is included in the IASP pain nomenclature (Kosek et al. 2016, IASP). The wide application of this concept in research has not been utilised.

### 2.4.1. Nociceptive pain

Nociception is the process of detection and transmission of pain signals from the site of injury to the central nervous system (CNS). The pain process can be categorised (Rastogi and Meek 2013, Farquhar-Smith 2008) into four stages: (1) Nociception – stimulation of the peripheral pain receptors; (2) Pain transmission – travelling of the pain signals from the periphery to the dorsal horn through C- and A-delta fibers, and ascending in the spinal tracts to the central level; (3) Pain modulation – modulation of pain signals along the neuraxial pain pathway; and (4) Pain perception – projection of the pain signal onto the somatosensory cortex. Nociceptive pain may result from mechanical, thermal or chemical damage to the tissue.

Nociceptive pain may be physiological (such as muscle cramps) or pathological (tissue injury). Figure 1 presents pain classification according to Bennett 2010 dividing pain to nociceptive and neuropathic origin.

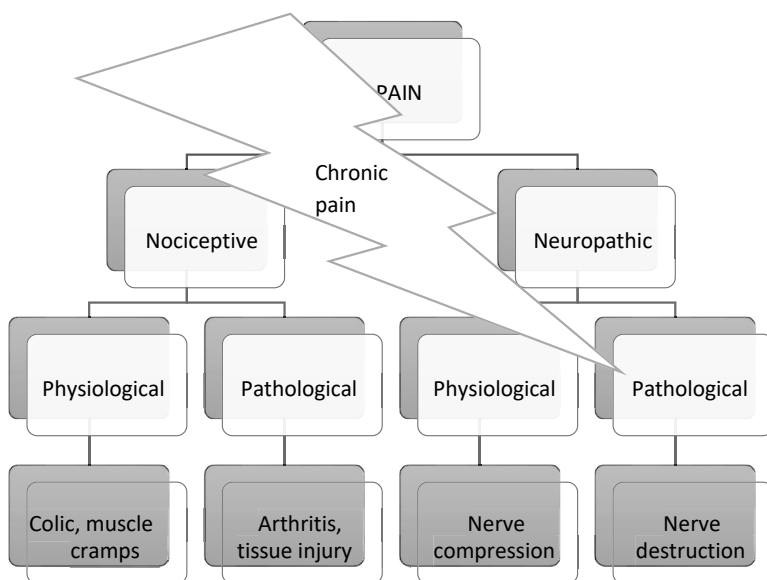


Figure 1. Three level classification of pain. Modified from Bennett MI 2010.

### 2.4.2. Neuropathic pain

NP is common, although the prevalence estimates in the general population vary (Smith and Torrance 2012). Based on data collected via postal surveys in France (Bouhassira et al. 2008) and the UK, (Torrance et al. 2006) the prevalence estimate of NP was between 6% and 8%, respectively. In a recent systematic review of epidemiological studies (van Hecke et al. 2014) the estimated population prevalence of NP was between 7% and 10%. NP is more common in older adults, as many



of its causes (eg. spinal degeneration, herpes zoster and stroke) increase in the population with age (Dieleman et al. 2008, Hall et al. 2006).

The first IASP definition of NP was “pain initiated or caused by a primary lesion, dysfunction, or transitory perturbation of the peripheral or central nervous system” (Merskey and Bogduk, 1994). In 2008, a more precise definition of NP was published by the Special Interest Group on Neuropathic Pain (NeuPSIG), together with a grading system of the certainty of NP (Treede et al. 2008, IASP). According to the new definition, NP is “pain arising as a direct consequence of a lesion or disease affecting the somatosensory system”. A slightly modified version of the definition was proposed and accepted by the IASP Taxonomy Committee: “pain caused by a lesion or disease of the somatosensory nervous system.” (IASP, Jensen et al. 2017). Certainty of NP diagnosis was classified as possible, probable and definite. The first criterion of the grading system relates to pain distribution, which for the diagnosis of NP is required to be neuroanatomically plausible. The second criterion is a history suggestive of a relevant lesion or disease affecting the peripheral or central somatosensory system. NP is possible when the first and second criteria are met. The third criterion relies on a clinical examination with demonstration of neurologic signs (negative or positive sensory signs) that support the presence of a lesion or disease, consistent with the distribution of pain. If the first three criteria are fulfilled, NP is probable. The fourth criterion relates to diagnostic tests to confirm the presence of a relevant disease or lesion affecting the somatosensory system. Examples of such tests include magnetic resonance imaging, electroneuromyography showing peripheral nerve lesion and a laboratory confirmation of multiple sclerosis. Meeting all of the four criteria confirms a definite diagnosis of NP. (Treede et al. 2008) Finnerup et al. (2016) presented a slightly revised grading system for NP following the classical clinical method of diagnosis. History, clinical examination, and stepwise diagnostic tests add to the diagnostic level of certainty of neuropathic pain. Annotation of terms was added to the grading system for improved clarity. The group also highlighted that while a definite diagnosis required for the pain to arise from disease or lesion of somatosensory nervous system, it did not explain causality. Figure 2 shows the updated grading chart for NP.

The main goal of a clinical examination of a pain patient is to identify the underlying disease and pain type(s). When NP is possible, the clinical examination focuses on verifying or rejecting the hypothesis of a lesion, or a disease of the somatosensory system. Therefore, a neurological examination (with the emphasis on sensory testing) is required. Bedside examination is the only approach able to exclude the presence of other types of pathological processes, which may also be causing the pain. It is also the only approach able to locate the pathology on the neuraxis generating NP. (Haanpää et al. 2009, Haanpää and Treede 2010, Haanpää et al. 2011).

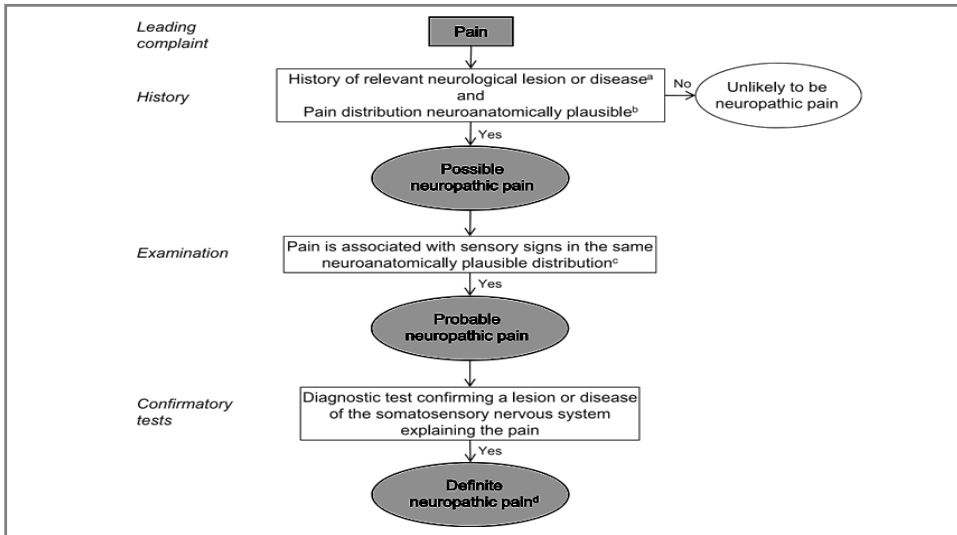


Figure 2. Flow chart of updated grading system for NP. (Finnerup et al. 2016)

With a suspected NP, the most important part of a clinical examination is sensory testing. Table 1 summarizes the different tests for sensory modalities (giving information of function of different sensory fiber types). The findings in the painful area are compared with findings in the contralateral area in unilateral pain, and in the other sites on the proximal-distal axis in bilateral pain.

Skin areas of abnormal sensation and hypersensitivity reveal *positive symptoms*. Mechanical and thermal hypersensitivity are typically present in NP; allodynia is a pain response to non-nociceptive stimulus such as light touch on skin, and hyperalgesia is an overreactive sensation to a nociceptive stimulus (as a pin prick, for example). Cold, heat and deep mechanical pressure can also evoke positive NP symptoms. *Negative symptoms* and signs include reduced sensation of non-painful stimuli (hypoesthesia, hypoalgesia), and reduced sensation to cold or warm stimuli (thermal hypoesthesia). *Spontaneous sensation or pain without stimuli* are the third type of symptoms in NP; nonpainful positive sensations like tingling (paraesthesias), shooting electrical attacks lasting for a few seconds (paroxysmal pain) and superficial pain similar to a burning sensation of the skin.

Table 1. Bedside sensory examination for NP according to Finnerup et. al 2016 and Haanpää and Treede 2010.

Sensation	Clinical testing	Fiber type
Touch	Cotton bud or ball, painter's brush, fingers	A-beta
Vibration	Tuning fork (64 or 128 Hz)	A-beta
Pinprick, sharp pain	Pin, toothpick, cocktail stick	A-delta
Cold	Cold metal (under 20 °C), tube with cold water, cloth with surgical spirit	A-delta
Warm	Warm metal, tube with warm water (over 40 °C)	C

### 2.4.3. Mixed pain; low back pain as the most common clinical manifestation

Low back pain is one of the most common chronic pain conditions (Scheele et al. 2014, Hasselström et al. 2002). Low back pain is localized below the costal margins and above the inferior gluteal folds, with or without referred leg pain (Airaksinen et al. 2006). Most individuals experience low back pain at some point during their lifetime, and it is considered chronic when it persists for 12 weeks or more. After an acute episode of low back pain, as many as two-thirds of the patients develop chronic pain (Itz et al. 2013), which is a costly and disabling condition.

Chronic low back pain is often a heterogeneous condition including components of mixed pain. Both nociceptive and NP mechanisms may be present. In low back pain, nociceptive pain results from activation of the nociceptors that innervate ligaments, joints, muscles and fascia as a response to a tissue injury or inflammation, and biomechanical stress. NP arising from injury or disease affects the nerve roots innervating the spine and lower limbs, and local pathological invasive innervation caused by damaged lumbar discs. (Baron et al. 2016). In primary care settings, the prevalence of NP in low back pain patients aged 55 years or over, was only 2% (Enthoven et al. 2013). Up to a third of patients with chronic low back pain have a NP component (Freyenhagen and Baron 2009, Fishbain et al. 2014). The neuropathic component of the back pain is often under-recognized and hence, undertreated.

There are three categories for practical classification of low back pain: specific spinal pathology, nerve root pain/ radicular pain, and nonspecific low back pain (Airaksinen et al. 2006). The first two can include a NP component (i.e. being either nociceptive or mixed pain), whereas the pathophysiology of the third category remains unknown.

Despite back pain being a common health problem among older adults, current research focuses mainly on the working-age population. It is not well understood, whether the back pain in the working-age people leads to a significant risk of developing back pain in the older age. Reid et al. (2005) found that older adults with back pain are more prone to developing disabilities.

In their BACE cohort study, Scheele et al. (2014) compared back pain between two age groups; one aged 55 to 74 years and another aged 75 years and over. Patients in the older cohort reported lower quality of life, more depressive symptoms and feelings of fear, more frequent avoidance behaviours, as well as had more negative thoughts about back pain compared with those aged 55-74 years. Older group had also several other health conditions and reported high blood pressure, heart diseases and osteoporosis more often. The use of pain medication and physical therapy were similar across the two age groups, despite the fact that the older cohort reported having more severe disabilities and co-morbidities.

#### 2.4.4. Nociplastic pain

Kosek et al. 2016 proposed the term nociplastic pain to describe chronic pain conditions with altered nociceptive processing, such as fibromyalgia, irritable bowel syndrome, complex regional pain syndrome and non-specific chronic low-back pain. Patients who initially suffer from nociceptive pain, such as pain typical to OA, may also develop alterations in nociceptive pain by inhibitory descending which is accompanied with hypersensitivity, and pain can then be a combination of nociceptive and nociplastic components. IASP Taxonomy 2017 (IASP) defined nociplastic pain as pain that (1) arises from altered nociception despite no (2) clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or (3) evidence for disease or lesion of the somatosensory system causing pain.

#### 2.5. Pain perception and ageing

Age related changes in somatosensory pain perception have been studied in healthy people for many years. According to a recent meta-analysis by El Tumi et al., the tolerance for pressure pain was lower in older adults compared with their younger counterparts, but found no difference in the heat pain threshold between the age groups (2017). Another meta-analysis, which combined findings of studies using pressure, thermal, and electrical stimuli, reported increased pain threshold with age, whereas pain tolerance thresholds did not show substantial age-related changes (Lautenbacher et al. 2017). Visceral pain perception in the aged population has been studied using rectal distension testing (Lagier et al. 1999) and graded intraesophageal balloon distension testing (Lasch et al. 1997). Both studies reported an increase in the sensory pain threshold in older participants. In the latter study, a third of the older participants felt no pain even when the balloon was inflated to its maximum volume (Lasch et al. 1997). These observations of impaired visceral pain sensation are in line with the clinical observations. In the ageing population, pain presents less frequently as a symptom in a variety of acute visceral crises. Approximately 40% of patients aged 65 years or over experience little or no pain during peritonitis, intestinal obstruction, or pneumonia. The “silent” or painless heart attack is so frequent in older persons, that it is recognized as an entirely separate clinical entity. (Gibson 2006)

Ageing is associated with global and spatially-localized changes to the brain structure, with similar brain changes found relating to chronic pain states (Cole and Franke 2017, Buckalew et al. 2008). A recent study using magnetic resonance imaging and brain-predicted age-difference analysis method showed that chronic pain was associated with additional “age-like” brain atrophy in relatively healthy, community-dwelling older adults (Cruz-Almeida et al. 2019).

## 2.6. Assessment of pain

### 2.6.1. Assessment of chronic pain

A comprehensive clinical assessment of pain is a key component in pain management. The assessment, including a detailed investigation of the pain and the patient's medical history, is used to identify the cause of the pain (Herr 2011). Additional diagnostic testing such as imaging, neurophysiological investigations or laboratory tests may also be undertaken.

Crome et al. (2007) emphasize the importance of assessing both the patient's cognitive and psychological functioning as well as their social situation and support network when diagnosing pain in older adults. The pain history assessment should include characterization of the current problem, including related features or secondary signs and symptoms. Patient's present pain complaint should be carefully localized. Drawings and maps of the pain are useful because they can also reveal any pain radiation. Different sensory complaints (numbness, hyperalgesia, allodynia) can also be marked in the maps. It is also important to assess what factors are relieving and what are aggravating the pain.

The painful area should be examined for signs of inflammation (redness, hyperhidrosis, warmth, oedema) or altered temperature (colder contralateral side of body referring to ischaemic limb or complex regional pain syndrome), motor functioning, atrophy of muscles, and sensory changes. Comorbidities such as cognitive impairment, depression, anxiety and sleep disturbances can impact patients' behaviour and how the pain is experienced and expressed. Comorbidities may also be at least partly consequences of the pain. It is important to take the patient's age into account when interpreting findings of a clinical examination. Muscle atrophy, impaired muscle strength or range of motion in the joints, as well as impaired peripheral vibration sensation are all common in the older cohort, and these symptoms can be unrelated to the patient's pain problem. The possible coexistence of different pain aetiologies can make clinical examination challenging (e.g., coexistence of lumbar radiculopathy and peripheral polyneuropathy in a patient with pain in lower extremities).

Table 2 lists suitable tools for pain measurement in older adults. Self-reported tools are an important component of the assessment (Herr and Garand 2001). Pain intensity is probably the most clinically relevant dimension of the pain experience regardless of the disease (Hjermstad et al. 2011). Pain intensity can be measured with three largely used tools: a unidimensional, 11-point Numeric Rating Scale (NRS), where 0=no pain and 10=worst possible pain, or a Visual Analogue Scale (VAS), which is a line where 0 cm represents no pain and 10 cm is worst possible pain, or a Verbal Descriptor Scale, (VDS), where the seven points representing the level of pain intensity are described as "no pain, slight pain, mild pain, moderate pain, severe pain, very severe pain, and the most intense pain imaginable" (Herr 2011). VAS and NRS are recommended for both daily medical practice and clinical trials (Dworkin et al 2005, Haanpää et al. 2011). They are considered suitable for cognitively intact older

people who are capable of self-reporting (Breivik et al. 2008, Hadjistavropoulos et al. 2007, Tiplady et al. 1998). NRS is believed to be easier to use than VAS for older adults (Dworkin et al. 2005, Hawker et al. 2011, Hjermsstad et al. 2011). It is also regarded as the most reliable tool for assessing effects of a treatment for chronic pain (Dworkin et al 2005). Hadjistavropoulos et al (2007) recommends VDS and NRS as the preferred brief assessment tools of pain intensity among cognitively normal older adults.

When assessing chronic pain, it is important to measure the subjective disability, i.e., the functional limitations associated with pain (Hadjistavropoulos et al. 2007). Functionality and quality of life are measured by multidimensional tools. A generic measure for these is an interference subscale, or the brief pain inventory (BPI) (Table 2) (Cleeland et al. 1994). The BPI is recommended for a number of pain conditions, whereas condition-specific measures are recommended for specific disease entities (e.g., Oswestry Disability Index for patients with low back pain). The BPI has been used widely and successfully among older adults, proven to be reliable and valid also in several languages, including Finnish. Pain Disability Index measuring general pain-related disability, and the Geriatric Pain Measure, are recommended to be used with the elderly, because the tools are short and easy to complete and provide information on the overall impact of pain for monitoring the effectiveness of treatments. (Breivik et al. 2008). A quality of life measurement tool, SF-36, is another tool for assessing physical functioning and role limitations on a physical composite scale (von Korff et al. 2000).

Table 2. Pain measurements suitable for older adults.

Name of the measure	Short description	Cut points
<i>Unidimensional measures</i>		
Numeric Rating Scale (NRS)	Numeric descriptors of pain from 0 to 10 (verbally).	0= no pain, 1-3= mild pain, 4-6= moderate pain, 7-10= severe pain
Visual Analogue Scale (VAS)	A horizontal (or vertical) 10 cm line anchored by descriptors, such as 'no pain', or 'worst possible pain'. Patient marks their pain intensity on the line.	0= no pain, 1-3= mild pain, 4-6= moderate pain, 7-10= severe pain
Verbal Descriptor Scale (VDS)	Verbal description of pain (5-7 options to choose from).	
Faces Pain Rating Scale	Scale shows six pictures of faces describing state of pain (0-10 options).	
<i>Multidimensional measures</i>		
Brief Pain Inventory (BPI)	Measures the intensity of pain (4 sections) and the interference of pain (7 sections).	≥4= moderate pain
<i>Measures of mood</i>		
Geriatric Depression Scale (GDS-15)	Short version of Geriatric Depression Scale, 15 questions with yes/ no options.	≥ 6/15= possible depression
Beck Anxiety Inventory (BAI)	Anxiety questionnaire, with 21 questions (score 0-3 points/ question).	22-35= moderate anxiety, > 36= severe anxiety
<b>Neuropathic pain (NP) measures</b>		
Douleur Neuropathique 4 (DN4)	Questionnaire containing four questions, with a total of 10 sub questions (yes/no): 7 related to the symptoms and 3 related to the clinical examination.	≥4 /10= likely NP
PainDETECT	Questionnaire with 9 sections: seven of which are sensory descriptor items and two are related to the spatial and temporal characteristics of the pain.	≤ 12= nociceptive pain, 13-18= unclear result, 29-38= likely NP
Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)	Questionnaire with seven yes/no questions: five relating to the symptoms and two relating to the clinical examination.	≥12/24= likely NP
<b>Measures for cognitively impaired individual</b>		
Pain Assessment IN Advanced Dementia Scale (PAINAD)	Scale with five descriptive items relating to: breathing, vocalization, facial expression, body language, consolability (0-2 points/item).	0=no pain, 10=severe pain
Doloplus 2	Questionnaire with 10 items: five relating to somatic reactions, two to psychomotor reactions and three to psychosocial reactions.	≥ 5/30= susceptible pain
Abbey Pain Scale	Six descriptive items (each 0-3 points). Additional question whether the pain is acute or chronic.	3-7= mild pain, 8-13= moderate pain, >14/18= severe pain

The BPI is a patient-completed numeric rating scale that assesses the severity of pain (Severity scale) and its impact on the patient's daily functioning (Interference scale). The BPI was originally

developed for cancer pain assessment, but it has since been validated also for use in assessing chronic pain (Tan et al. 2004). The Pain Interference Scale assesses the degree to which pain interferes with seven daily activities (mood, sleep, walking, general activity, normal work, relations with others, and enjoyment of life). The ratings are measured using a 11-point numeric rating scale ranging from 0 (does not interfere) to 10 (completely interferes). The mean of these seven ratings is used to indicate the patient's overall level of pain interference. Because chronic pain is likely to vary throughout the day and night, the BPI asks for four various pain intensity recordings over the past 24 hours.

The cut-off scores for the empirically derived BPI Interference subscale have not yet been established, but Jensen (2011) proposed that this scale could be similar to the intensity ratings: 4 and less representing a mild, 5-6 a moderate and 7-10 a severe level of interference. A meaningful positive response to treatment in most patients could be demonstrated as a 2-point decrease on the assessment scale (Jensen 2011).

In conclusion, several methods exist for pain assessment in older adults. Clinicians should select the most useful measures to their daily practice and use the same tools consistently in the follow-up (Herr 2011). The clinical guidelines recommended self-report procedures, most often NRS and VDS for intensity assessment and BPI for functional assessment (Hadjistavropoulos 2007).

## 2.6.2. Assessment of neuropathic pain

Recognizing that NP has a significant impact among older adults is important as many causes of NP increase in prevalence with age. The identification of NP is also essential for optimal management of the symptoms (Torrance et al. 2007).

The NP assessment guidelines (Cruccu et al. 2010, Haanpää et al. 2009, Haanpää et al. 2011) emphasize a stepwise procedure; a history of the pain according to the NP criteria and assessment of the possibility of NP using screening tools, the clinical examination and any further diagnostic testing, including but not limited to radiologic imaging, neurophysiologic tests or skin biopsy.

Pain drawing is recommended to document pain locations, using different colours for different pain components such as stabbing pain, burning pain, allodynia, hyperalgesia or numbness. Pain intensity can be evaluated primarily with NRS or a verbal rating scale. In recent years, several screening tools have been developed and validated for NP (Bennett et al. 2007). LANSS, Neuropathic Pain Questionnaire (NPQ), Douleur Neuropathique en 4 questions (DN4) and painDETECT are among the most used measures in the literature (Table 2).

The DN4 was developed in France for clinical use and patient interviews, and consists of 10 items. Seven of these items are sensory qualities described by the patient, and three sensory items are



recorded in the clinical examination (Bouhassira et al. 2005). Recently, the DN4 has been identified as one of the most precise measurement tools for NP in a Canadian systematic review (CADTH 2015).

The PainDETECT is available also in Finnish. It was originally developed to detect an NP component in lower back pain (Freyenhagen et al. 2006), but it has also been validated for other NP conditions. PainDETECT contains nine items. There are seven weighted sensory descriptor items, and a further two items relating to the spatial (radiating) and temporal characteristics of the individual pain pattern.

In clinical practice, screening tools are easy to use and provide timely information for further investigation as well as increase the reliability of decisions around diagnosis regarding NP. Nevertheless, they fail to identify approximately 10 to 20% of patients with clinically diagnosed NP, and thus the tools cannot replace clinical judgement (Mathieson et al. 2015). Their importance has been noted in the quality of epidemiological data as standardized measures as well as in treatment efficacy assessments.

The use of assessment tools in NP among older adults is yet to be validated, however, commonly accepted tools (such as the ones mentioned above) are recommended for self-reporting of pain as well as assessing cognitive capacity (Pickering et al. 2010).

### 2.6.3. Pain assessment in special situations: patients with cognitive impairment as an example

Cognitive problems tend to complicate the assessment and recognition of chronic pain. However, seniors with mild to moderate cognitive impairments (MMSE scores 18/30 or higher) are likely to be able to respond to unidimensional self-reported measures. Even patients with severe dementia (MMSE scores 12-13/30) may be able to use the NRS-scale 0-10 and the Verbal Descriptor Scale (Hadjistavropoulos et al. 2007, Chibnall and Tait 2001). It is worth noting that the use of multidimensional assessment tools becomes more difficult with the increasing severity of the cognitive impairment.

The most important steps in pain assessment among non-verbal older adults include observing the pain over time under consistent circumstances, assessing their behaviours during movement, verifying pain before and after therapy interventions and using standardised well-validated tools (Hadjistavropoulos 2014).

In advanced dementia, self-reporting is often unachievable due to the impaired cognitive, linguistic and social ability, and behavioural-observational pain assessment tools should be the primary instrument of choice. The most commonly used and recommended tool is the Abbey Pain Scale, which is endorsed by the Australian Pain Society. It was the most strongly supported tool in a systematic comparison of 24 instruments including the Doloplus 2 (originally developed in French),

the Non-Communicative Patient's Pain Assessment Instrument (NOPPAIN) and the Pain Assessment IN Advanced Dementia Scale (PAINAD) (Hadjistavropoulos 2014). These scales use the observation of pain behaviour as a measure: facial expressions, vocalisations, body movements, changes in interpersonal interactions (eg. not allowing to be touched), changes in activity patterns or routines (eg. sleep, decreased activity in daily routines) and changes in mental status. In the Abbey Pain Scale, facial expression, change in body language, vocalisation, changes in behaviour, as well as changes in physiology and physics are observed and rated. The NOPPAIN and PAINAD use similar ratings, and the PAINAD consists of five items with three response options scored from 0 to 2 points each. In Doloplus 2, there are two psychomotor, five somatic and three psychosocial items to be observed and rated. These scales are yet to be validated for clinical practice and further research is required for their validation, but systematic evaluation and algorithm have recently been proposed by Gisele Pickering et al. (2016).

In a Finnish study, the PAINAD-tool and a part of the pain assessment in the RAI-instrument (Resident Assessment Instrument) were compared among severely demented patients (Björkman et al. 2007). The PAINAD-measure was more accurate to recognize pain during treatment procedures compared with the RAI-instrument. A recent systematic review identifies the PAINAD as the most convenient tool to use in assessment of pain in long-term care patients (Ellis-Smith et al. 2016).

## 2.7. Management of chronic pain in older adults

Pain management in older adults is often insufficient. This is partly because the aetiology of pain may be difficult to diagnose due to restrictions in the individual's physical and cognitive capabilities, and because it is challenging to measure and monitor the effects of their pain treatment. A stepwise approach in diagnosing and treating chronic pain among older adults is recommended, although the construction algorithms may vary (AGS 2002, ACPA 2016).

Rastogi and Meek (2013) presented a simplified pain management model in frail older adults. The model contains four steps; assessment, diagnosis, management and pharmacology, and it includes aspects of personalized needs of the patient. The framework is useful for the assessment and management of chronic pain patients in clinic, especially in general practice. In optimizing pain treatment, the assessment and recognition of the pain as well as continuous re-evaluation of the results of therapy are required. In addition, the social aspects of chronic pain need to be monitored.

When the time spent with patients is limited, it is necessary to understand the many aspects of chronic pain – and to treat the person and not only the pain (Tauben 2012). David Tauben (2012) presented a 4-step model for chronic pain assessment, a measurement-based step pain care model. It includes measurement tools for mood, sleep, functional abilities (pain interference, intensity and daily functionality) and medical risk assessment for a substance use disorder. These steps are essential in the assessment of chronic pain as well as optimising the following pharmacotherapy.

Current geriatric guidelines recommend the use of combined pharmacological and non-pharmacological strategies (AGS 2002, Gibson 2006, AGS 2009, Gloth 2011, Abdulla et al. 2013, Tracy and Morrison 2013, Makris et al. 2014). A recent American study found that only one-third of older adults with persistent pain treated their pain according to the pain management strategies based on the current guidelines. Many older adults who have chronic pain use no pain therapies at all, especially the oldest old and those who have cognitive impairments or reside in assisted living or nursing homes (Stewart et al. 2012).

The recommended geriatric pharmacotherapy strategy “start low and go slow” is suitable for managing pain in older adults (AGS 2009). Due to the possible polypharmacy, sensitivity to side effects of drugs, frailty and slower metabolism of the ageing cohort, this strategy prioritizes safety with starting on low dosage of medications with a gradual increases to the doses. However, following this “golden strategy” can potentially lead to under-treatment of patients (Pickering 2012).

### 2.7.1. Non-pharmacological treatment

Of non-pharmacologic treatments, the following therapies have the strongest evidence in reducing pain in literature: self-management education programmes and acupuncture (Ia-level evidence from meta-analysis of randomized controlled trials), exercise, massage and mindfulness meditation (Ib-level evidence from at least 1 randomized controlled trial) (Makris et al.2014). Many of these treatment modalities require active participation from the patient, which can restrict the usefulness among the oldest old and those cognitively impaired. An exercise programme with professional guidance can be offered also for frailer older persons. Evidence suggests that the programme should include strengthening, flexibility, endurance and balance strategies. (AGS 2002, Makris et al. 2014)

Older adults appear to prefer non-pharmacological strategies over pharmacology for treatment of chronic pain (Abdulla et al. 2013, Stewart et al. 2012). Considering the complex and multiple origins of chronic pain, non-pharmacological approaches may have better results compared with drugs. Other reasons include the older adults’ dissatisfaction with conventional medicines, lack of knowledge of medical possibilities or concerns relating to medication side effects. The MOBILIZE Boston Study, which recruited over 700 subjects aged 65 years or older, reported that a quarter of the participants with moderate to severe chronic pain used non-pharmacological therapies as their only pain management. The most commonly used modalities in the study were exercise (50 %) nutritional supplements (17 %), ointments and local creams (14 %), heat (14 %) and massage (13 %). Fewer than 5 % reported the use of transcutaneous electrical nerve stimulation, chiropractic therapy, vitamins, herbal remedies, magnets and acupuncture. (Stewart et al. 2012)

There is increasing evidence that exercise and physical activity are effective for chronic joint pain management (Fransen et al. 2015). However, barriers for exercise among older adults with chronic pain consist of patient-related factors as well as factors relating to environmental and health care

delivery (Meeus et al. 2016). These factors need to be addressed in older patients by assessing the individual needs and identifying any restrictions with exercise. Fear-avoidance behaviour means that a patient starts to avoid activities due to their fear of pain, which leads to potential inactivity with reduced tolerance to exercise. A vicious circle of inactivity and fear of pain can develop easily, and graded exercise therapy approach is recommended for chronic pain patients.

Self-management of pain covers many techniques including relaxation, coping strategies, adaptation to activities and education about pain and its effects, as well as exercise. Self-management programmes are already being used in patients with arthritis and chronic pain (Abdulla et al. 2013, Arthritis Foundation 2018, Hadjistavropoulos et al. 2019). The effectiveness of non-pharmacological treatments vary. The Cochrane and other systematic reviews provide recommendations that mostly are based on the data from chronic low back pain studies (Toth and Moulin 2013). According to a randomised controlled trial (RCT), cognitive behavioural therapy-based pain self-management is more effective compared with exercises and is common in reducing disability among community-dwelling older adults with chronic pain both in short and long term (i.e. one-year follow-up) (Nicholas et al. 2013 and 2017).

A treatment goal may be the acceptance of chronic pain, which is not a pure coping strategy per se. A phenomenological study by Ojala et al. (2015) assessed different ways of coping with chronic pain. The patients used combination of coping and acceptance as their way to deal with chronic pain. The study covered a protracted process involving a complex mixture of unpleasant emotions and uncertainty, as well as humble optimism regarding living with chronic pain in the future. The authors also found that while the management of chronic pain was carried out with the aid of professionals, most importantly the support of family members and support groups were used, also among older adults.

## 2.7.2. Pharmacotherapy for nociceptive pain

Although the older adults are not often included in clinical trials, current research evidence supports the use of pharmacotherapies as an effective pain management tool in older adults. Table 3 summarises the results of the contemporary research on the topic as the current clinical guidelines (Abdulla et al. 2013, AGS 2009, Barber and Gibson S. 2009, McCarberg 2012, Makris et al. 2014, Fine 2012) for treatment of pain in older adults.

The World Health Organization's pain ladder, originally targeted for cancer pain, is now an internationally recognised stepwise approach to pain management in older adults (Tracy and Morrison 2013). The first recommended step in the management of mild pain is the use of non-opioid medications, such as paracetamol (acetaminophen) and non-steroidal anti-inflammatory drugs (NSAIDs). The second step, for patients with moderate pain, involves adding a weak opioid, with or without an adjuvant agent. The third step, used in severe pain, is a strong opioid combined with an adjuvant. (Crome et al. 2007)

Barriers to pharmacological management of persistent pain in geriatric populations include multimorbidity, age-related physiological changes, altered drug absorption and decreased renal excretion, sensory and cognitive impairments, polypharmacy causing risk of drug-drug interactions, physicians' concerns about treatment-based harm and the patient's negative attitude or fear of medication. In addition, accessibility of treatment options and availability of recommended treatments present limitations to the use of pharmacotherapy. Sometimes off-label use of medications and other alternative interventions become more prevalent in this population (Makris et al. 2014, Rastogi and Meek 2013).

Table 3. Contemporary guidelines for treatment of pain among older adults.

Guideline	Year	Pharmacological/ Non-pharmacological	Neuropathic pain treatment
American Geriatrics Society. The management of persistent pain in older persons.	2002	+/+	+
Ahmad and Goucke. Management strategies for the treatment of neuropathic pain in the elderly.	2002	+/+	+
American Geriatrics Society. Pharmacological management of persistent pain in older persons.	2009	+/-	+
Barber J, Gibson S. Treatment of chronic non-malignant pain in the elderly.	2009	+/-	+
Schmader et al. Treatment considerations for elderly and frail patients with neuropathic pain.	2010	+/+	+
Fine Perry. Treatment guidelines for the pharmacological management of pain in older persons.	2012	+/-	+
McCarberg et al. The management of neuropathic pain with a focus upon older adults.	2012	+/-	+
Abdulla et al. British Geriatric Society. Guidance on the management of pain in older people.	2013	+/+	+
Makris et al. Management of persistent pain in the older patient. A clinical review.	2014	+/+	+
Finnerup et al. Pharmacotherapy of neuropathic pain in adults: systematic review, meta-analysis and NeuPSIG recommendations.	2015	+/-	+
NICE. Neuropathic pain—pharmacological management guideline for adults.	2017	+/-	+

The tolerance to and the effectiveness of pharmacological treatments vary significantly among older adults. Age is not the only determinant; frail older adults are more prone to adverse drug reactions (ADR) and interactions than their fit counterparts. Shi et al. 2008 suggested dividing the elderly into three subgroups based on their age (e.g., 65-75, 75-85 and above 85 years) in order to better understand the process of ageing and the most typical decades for age-related physiological changes, as well as age-related changes in pharmacokinetics and pharmacodynamics.

Both polypharmacy and under-prescription of drugs are common in the treatment of chronic pain in older adults. A Dutch study on geriatric patients in general practice found polypharmacy (five or more drugs) in 61% and under-prescription in 31% of cases when prescribing of drugs was compared to the national guidelines (Kuijpers et al. 2007). Under-prescribing increased in the case of polypharmacy, and sequentially resulted in inappropriate medication according to the guidelines presenting a risk for achieving optimal pain medication.

Beers criteria, updated in 2015 by the AGS, represents a collection of potentially inappropriate medications for older adults (AGS 2015), and is one of the most frequently consulted references for safe prescribing of medications for older adults. Tables of clinically important drug-drug-interactions to be avoided, as well as the varying levels of drug dosages with adverse effects on the kidney functions (e.g. analgesics duloxetine, gabapentinoids and tramadol), were added in the updated versions of 2015 and 2019 (AGS 2015, AGS 2019). Table 4 summarizes the Beers criteria regarding older adults with normal kidney function for pain relieving drugs (AGS 2015, AGS 2019).

Table 4. Beers criteria for pain relieving drugs in older adults with normal kidney function.

Drug(s)	Rationale	Recommendation	Quality of evidence	Strength of recommendation
Amitriptyline* Nortriptyline*	Highly anticholinergic, sedating, and causes orthostatic hypotension	Avoid	High	Strong
Oral NSAIDs	Increases the risk of gastrointestinal bleeding and kidney injury, increases blood pressure	Avoid chronic use unless safer alternatives are ineffective and patient is unable to take a gastroprotective agent	Moderate	Strong
Carbamazepine ** Oxcarbazepine ** SNRIs * Tramadol	May exacerbate or cause hyponatremia or syndrome of inappropriate antidiuretic hormone secretion	Use with caution. Avoid SNRIs in patients with history of falls or fractures	High/ Moderate	Strong
Opioid receptor agonist (together with ≥2 other CNS-active drugs)	Increases the risk of falls	Avoid total of ≥3 CNS-active drugs#; minimize number of CNS drugs	High	Strong

\* first-line drugs for NP in non-elderly adults (Finnerup et al. 2015)

\*\* first-line drugs for trigeminal neuralgia (Cruccu et al. 2008)

# antipsychotics; benzodiazepines; hypnotics; tricyclic antidepressants; selective serotonin reuptake inhibitors

In addition, the European version of Medication Guidelines for Older Persons, Screening Tool of Older Persons` potentially inappropriate Prescriptions (STOP) and Screening Tool to Alert doctors to Right Treatment (START) represent the criteria that were first developed in 2008 updated in 2015 (O`Mahony et al. 2015). The main differences between the START and the Beers criteria are, that

the START also alerts to right treatment and includes a criteria for adverse drug effects in acutely ill older people. In Finland, the Meds75+ database of medication for the elderly has been available since 2010. It is maintained by the Finnish Medicines Agency and is accessible to all physicians and health care professionals online (Finnish Medicines Agency 2018). The database classifies medical substances into four categories based on their suitability for persons aged over 75 years.

### **Paracetamol**

Acetaminophen (paracetamol) is the most recommended non-opioid analgesic for treatment of chronic nociceptive mild-to-moderate pain such as OA and low back pain in older adults (AGS 2009, Abdulla et al. 2013, Barber and Gibson 2009). The exact mechanism of action of paracetamol remains undetermined, but central mechanisms, including effects on prostaglandin production, serotonergic, and cannabinoid pathways are likely involved (Sharma and Mehta 2014). Used according to recommended doses, paracetamol is a relatively safe choice. Paracetamol's absorption rate is rapid and efficient independently of the patient's age.

The recommended starting dose for older adults is 325 mg every 4 hours, and the maximum recommended daily dose ranges from 3.25 to 4 grams. However, in the case of hepatic insufficiency or a history of alcohol abuse, the maximum daily dose should be reduced by 50 to 75% (Makris et al 2014, AGS 2009). Another review by Rastogi and Meet (2013) recommends a maximum daily dose of 2 grams for the older adult cohort. Hepatotoxicity is reported mainly among younger patients, and the risks of overdose and toxic effects among older adults are predominantly associated with cognitive decline and combined use of different paracetamol-containing analgesics (Barber and Gibson 2009). Paracetamol-induced intoxication is treated with intravenous N-acetylcysteine, based on observed paracetamol levels, and treatment after 24 hours is indicated. (Barber and Gibson 2009)

A recent meta-analysis by da Costa et al. (2016) and Machado et al. (2014) concluded paracetamol, independently of treatment doses, to be clinically ineffective, and not to be recommended for symptomatic treatment of OA. The authors, however, found NSAIDs to be an effective treatment for OA pain. Due to the adverse effects of long-term use of NSAIDs, they are not suitable for the treatment of chronic pain.

### **Nonsteroidal anti-inflammatory drugs**

NSAIDs inhibit cyclo-oxygenase (COX), which reduces pain and inflammation through the inhibition of prostaglandins. Inhibition of COX explains both the therapeutic effects (inhibition of COX-2) and side effects (inhibition of COX-1) of NSAIDs. (Nissen et al. 2016)

Nociceptive pain in older adults is often treated with NSAIDs despite older subjects bearing considerable risks, which are further elevated with regular use. Up to 90% of all NSAID prescriptions

are for patients aged 65 years or over. Up to 10-35% of patients over 65 years of age use NSAIDs daily, and 70% use NSAIDs at least once a week (Lanas et al. 2007).

A Finnish cohort study (Hartikainen et al. 2005) on analgesic treatment in the home-dwelling elderly (aged over 75 years) found that every third subject experienced daily, interfering pain. The same study reported NSAIDs (51 %) and paracetamol (23 %) to be the most commonly used analgesics, however, regular use was uncommon (13 % with NSAIDs and 18 % with paracetamol).

The most recommended NSAID preparations include ibuprofen, diclofenac sodium and naproxen sodium. The AGS recommends lower dosages for persistent pain in older adults; ibuprofen 220 mg three times a day, naproxen sodium 220 mg twice daily and diclofenac sodium 50 mg twice daily or 75 mg as an extended release tablet, taken once daily (AGS 2009).

NSAIDs carry several risks, especially for the older adults. The risk of gastrointestinal toxicity (symptoms of dyspepsia, endoscopic ulcers, bleeding) is high with the prevalence increasing with age and regular use. All NSAIDs increase the risk of cardiovascular (CV) thrombotic events (myocardial infarction and stroke) especially with longer term NSAID use and previous history of CV disease (McCarberg 2013). It is probable that naproxen sodium possesses less CV toxicity (Curiel and Katz 2013).

Long-term use of NSAIDs can also result in renal toxicity and renal papillary necrosis in some patients, as well as dose-dependent renal blood flow deterioration and renal decompensation. Frail older patients, patients with heart failure, impaired renal or liver functions, and those using diuretics and angiotensin-converting enzyme inhibitors, are at higher risk of renal toxicity. The risks with NSAIDs are well-known by clinicians, yet these drugs are often used for their clinical efficacy, low cost, accessibility without prescription and minor risks of abuse problems. Appropriate gastrointestinal protective therapy needs to be added on when NSAIDs are prescribed in old age (over 60 years). Gastrointestinal bleeding represents the primary risk of NSAID use and a major risk with concurrent use of warfarin or novel anticoagulant agents, aspirin and corticosteroids (Lanas et al. 2007).

Discussion and new data on the risks of CV events associated with the use of both nonselective NSAIDs and selective COX-2 inhibitors have emerged recently. Selective COX-2 inhibitors are associated with a significantly lower incidence of gastrointestinal (but not CV) adverse effects (Curiel and Katz 2013). Therefore only a diminished selection of COX-2 inhibitors (celecoxib and etoricoxib) is available for musculoskeletal pain and (parenterally dosed) parecoxib for acute pain.

The PRECISION trial (2006-2014) showed the noninferiority of moderate doses of celecoxib, as compared with naproxen or ibuprofen, regarding to the primary CV events. Celecoxib treatment resulted in lower rates of gastrointestinal events compared with both comparator drugs and in lower rates of renal adverse events compared with ibuprofen (Nissen et al. 2016). In a recent systematic



review, naproxen was found less harmful in terms of CV safety than some older NSAIDs and even COX-2 inhibitors (Pirlamarla and Bond 2016). A 2017 review by Ross et al. found adverse CV outcomes to be associated with the use of both selective COX-2 and nonselective NSAIDs among patients with known cardiovascular disease. Risks are also emphasized in The American Heart Association guidelines in treating musculoskeletal pain specially among CV patients (Amsterdam et al. 2014).

In a recent meta-analysis diclofenac at the maximum daily dose 150 mg/day was the most effective for the treatment of pain and physical disability in OA and etoricoxib at the maximum dose of 60 mg/day was equally effective against pain. The authors emphasized the safe and cautious use of NSAIDs among elderly. (da Costa et al. 2016)

A Finnish study of the prevalence and pharmacotherapy of musculoskeletal pain in 1999 and in 2009 among 75-85-year-old people reported an increase of prescribed pain medication, a decrease of NSAID use and an increased use of paracetamol, COX-2 inhibitors and weak opioids. An increase in the use of gastro-protective drugs in NSAID users was also detected (Halla-aho et al. 2013).

Topical NSAIDs seem to be the safest choice of NSAIDs for localized pain. They are beneficial from both their therapeutical as well as adverse effects perspectives, and many guidelines recommend topical NSAIDs prior to starting oral NSAID therapy for OA of knee and hand, especially for patients aged 75 years or older (Abdulla et al. 2013, Makris et al. 2014). Evidence shows that topical formulations can achieve therapeutic concentrations locally while maintaining low serum levels and without systemic adverse effects or drug-drug interactions. Local skin irritation is the only disadvantage of topical NSAIDs (McPherson and Cimino 2013).

## **Opioids**

Opioids provide analgesia through action on opioid receptors that are present in the CNS as well as peripherally. Opioids are divided into three classes ranging from mild to moderate and strong opioids (Kalso et al. 2018). Codeine and tramadol represent mild opioids, and both are available in Finland (codeine is only available in combination with paracetamol or ibuprofen). Buprenorphine is a moderate opioid, and it is available for transdermal and sublingual use in Finland. Strong opioids, such as oxycodone, fentanyl, morphine, hydromorphone and methadone, are available for outpatient care in Finland. Oxycodone is the most frequently used drug in Finland out of the above opioids (Finnish Statistics on Medicines 2017).

Opioids are recommended for moderate-to-severe nociceptive pain when other treatments have failed to provide adequate pain relief, and the patient has substantial impairments in physical functioning and quality of life (Makris e al. 2014). Moderate to severe non-cancer related pain among old persons often arises from musculoskeletal diseases such as OA, osteoporosis, collapsed vertebrae and CV diseases such as peripheral vascular disease and coronary artery disease. There is

a growing evidence base on opioids to be efficacious in the treatment of non-cancer pain, however, there is a need for individual dose titration and the tolerability and effect of the medication should be considered (Dowell et al. 2016). The typical side effects of opioid use include constipation, nausea, vomiting, sedation, dizziness, and motor imbalance. In addition, there is an increased risk of falls with opioids in older adults (Dowell et al. 2016).

Strong opioids are accepted as first-line treatment for severe acute pain and chronic cancer-related pain or at the end of life, but their use for non-cancer chronic pain remains controversial. They are recommended for chronic non-cancer pain only if expected benefits for both pain and function are anticipated to outweigh the risks to the patient. A short-term opioid trial is recommended to evaluate efficacy and tolerability of strong opioids, and the treatment is to be continued only if they provide sufficient pain relief and are well tolerated (Papaleontiou et al. 2010). The US Centers for Disease Control and Prevention Guidelines for prescribing opioids for chronic pain recommends the lowest effective dose (maximum 50 morphine milligram equivalents) per day, and avoiding concurrent opioids and benzodiazepines whenever possible, as well as evaluating benefits and disbenefits of continued opioid therapy with patients at least quarterly (Dowell et al. 2016). In addition to the general side effects of opioids, the risk of respiratory depression needs to be considered in use of strong opioids (Dowell et al. 2016). Neurotoxicity presents another significant risk of opioid use in older adults, and can manifest as hallucinations, confusion or cognitive impairment. Central adverse effects can usually be managed by decreasing the dosages of opioids (Rastogi and Meek 2013).

Hartikainen et al. (2005) found 10% of home-dwelling elderly use opioids across all age groups, with 6% of 75-79 year-olds and 16% of those aged 85 years or more using the drugs. Most commonly prescribed opioids included a combination of codeine and paracetamol (68 %), tramadol (30%) and oxycodone (11 %). (Hartikainen et al. 2005)

The risk of addiction seems to be lower in older adults compared to their younger counterparts. The strongest predictive factor appears to relate to previous drug or alcohol abuse. Screening for addiction risks using a recommended tool is a cost-saving exercise (Chou et al. 2009).

An American retrospective cohort study found the risk of all-cause mortality, including deaths from causes other than overdose (especially CV deaths), to be significantly higher in patients using opioids for non-cancer chronic pain than among those who used anticonvulsants or cyclic antidepressants, although persons aged 75 years or older were excluded from the study. The potential increase of mortality in elderly opioid-users has not been studied thoroughly, but many adverse effects and medication risks bear considerable potential for that (Ray et al. 2016).

### 2.7.3. Pharmacotherapy for neuropathic pain

#### **Adjuvant drugs and drugs for NP**

Adjuvant drugs are agents that were originally developed for purposes other than pain treatment, and they first appeared in the cancer pain literature. They alter or attenuate the patient's pain perception in many pain-producing conditions without raising the pain threshold (AGS 2009, McCarberg et al. 2012). Adjuvant drugs may be used on their own, or they can be co-administered with non-opioid or opioid analgesics for the management of persistent pain conditions, primarily NP. The drug classes include antidepressants (tricyclic antidepressants or TCAs, such as amitriptyline, nortriptyline, desipramine) serotonin-norepinephrine reuptake inhibitors (or SNRIs, such as venlafaxine and duloxetine); and anticonvulsants (pregabalin and gabapentin being the most common). These drugs are used for both fibromyalgia and the various states of NP (Haanpää et al. 2010, Barber and Gibson 2009). Anticonvulsant oxcarbazepine is the recommended drug for trigeminal neuralgia for older adults, due to its better tolerance compared with carbamazepine (Crucchi et al. 2008).

Management of NP can be challenging and requires the evaluation of benefits and adverse effects of the drugs available, possible lifestyle interventions and treatment of the underlying cause, where applicable. It is important to account for comorbidities, such as anxiety and depression (Kalso et al. 2013), to avoid possible drug interactions and adverse drug events. There are serious risks involved with these conditions, especially when carbamazepine is prescribed. Kalso et al. (2013) emphasize low starting dose, slow titration and avoiding drugs with anticholinergic effects, especially for elderly patients with cognitive impairment, and patients who are prone to dizziness and falls. Duloxetine lacks anticholinergic effects and is hence preferable. As nearly three-quarters of preventable adverse drug events are due to errors in monitoring, close follow-up with new prescriptions of drugs for NP are essential (Schmader et al. 2010).

Chronic diseases are another aspect to be considered when prescribing pain medication for older patients. CV diseases, such as hypertension, coronary heart disease, and arrhythmia are common, and renal impairment and hepatic impairment may also limit the use of adjuvant medication. Polymorphism in the CYP2D6 isoenzyme, as well as its interactions must be noticed with antidepressants and tramadol. Serotonin syndrome is a well-established pharmacodynamic drug-drug interaction potentially present when using concomitantly several serotonergic drugs. New drugs should be trialled one by one, and in long-term use, the lowest effective dose of each drug should be prescribed (Haanpää et al. 2010).

A recent systematic review concluded SNRIs (duloxetine and venlafaxine), gabapentinoids (gabapentin and pregabalin) and TCAs as the first-line drugs for NP, and they also come highly recommended in the Grading Recommendations Assessment, Development and Evaluation classification. The second-line options are tramadol, capsaicin 8 % patch and lidocaine patch in low doses. Tramadol can be used for both peripheral and central NP, whereas topical agents are suitable

only for peripheral NP. Strong opioids and botulinum toxin A are the third-line options for NP (botulinum toxin being suitable only for localized peripheral NP) (Finnerup et al. 2015).

Capsaicin 8 % patch and pregabalin were compared for peripheral NP in a European 8-week multi-centre study. Capsaicin patch was found non-inferior to an optimized dose of pregabalin, however, it provided a faster onset of pain relief, higher level of satisfaction and fewer systemic side effects. Older subjects (up to age 80 years) were also included in the study. (Haanpää et al. 2016)

## 2.8. Burden of chronic pain

### 2.8.1. Activities and everyday life with chronic pain

The functional capacity of older adults is one of the most important predictive factors to independent living. Chronic pain affects daily activities in many ways. In the case of persistent pain, limiting activity because of pain exacerbation, may lead to cycle of limiting activities, decreased participation and even greater disability (Molton and Terrill 2014).

A study of community-dwelling Hispanic and non-Hispanic elderly from Colorado found that chronic pain has an independent association with worsening physical performance, regardless of ethnicity or specific condition (Bryant et al. 2007). The presence of chronic pain more than doubled the likelihood of worsened performance, but the intensity of pain did not elevate an additional risk. Multiple comorbidities also doubled the risk of worsened physical performance, and vascular disease and diabetes contributed to worsened performance on their own. Chronic conditions seem to present a significant risk of diminishing activity and mobility and increased frailty in older adults.

Frailty is a geriatric health condition with multicomponent risk factor for impaired functionality. It is a long-established clinical expression that expresses concerns for an elderly person's vulnerability and outlook. A gradual decrease in physiological reserve occurs with normal ageing but in frailty, the decrease is accelerated and homeostatic mechanisms start to fail (Clegg et al. 2013). A cross-sectional Canadian study of community-dwelling older adults showed that moderate or greater pain was independently associated with frailty. Although a cross-sectional study cannot establish causality, the authors interpreted that presence of persistent pain might reduce physiological reserves and predispose patients to developing frailty. The authors concluded that frailty might also cause the pain. (Shega et al. 2012)

An American cross-sectional study of over 18 000 participants found the presence of moderate or severe pain to be associated with higher rates of functional limitations regarding mobility, stair climbing, upper extremity tasks and activities of daily living. Patients with pain developed functional decline up to two to three decades before subjects without pain. (Covinsky et al. 2009)

## 2.8.2. Quality of life with chronic pain

Chronic pain is one of the major causes to affect quality of life. A Finnish postal survey including 6500 subjects aged 15-74 years found that the prevalence of poor subjective health was eight times higher among those with chronic daily pain. Daily chronic pain is found to have a stronger link to poor health compared with chronic disease or age. Frequent chronic pain and chronic diseases had a bigger impact on self-rated health in young individuals compared with their older counterparts (Mäntyselkä et al. 2003).

A systematic literature report by European Pain Federation (EFIC) on chronic pain in people aged over 50 years, confirmed that the prevalence of chronic pain in Europe increases with age and is associated with reduced quality of life. No significant association with pain and social relationships was detected. (EFIC 2012)

Patients who feel that they have no control over chronic pain are at higher risk of psychologic and functional impairment. A perceived control over pain and its consequences has a strong influence on behavioural adaptation, the choice of coping strategies, and the emotional effects of pain. (Hadjistavropoulos et al. 2007)

According to earlier epidemiological studies, neuropathic pain is more severe compared to nociceptive pain, has more detrimental effect on perceived health, functionality and quality of life, and is associated with more frequent use of health care facilities (Smith and Torrance 2012).

A large Swedish study of people aged over 64 years, collected data from registers and postal surveys to clarify the association with chronic pain, health care service use and quality of life. As the severity of chronic pain increase, so did the use of health care services increase while quality of life decreased (Bernfort et al. 2015).

## 2.8.3. Mental impacts of chronic pain

The link between depression and chronic pain has been identified in many studies. In the BACE-study on back pain in older adults in primary care (Scheele et al. 2013), subjects over 75 years old reported slightly more depressive symptoms and lower quality of life compared to their younger counterparts, aged from 55 to 75 years.

A British cohort survey, which studied the extent to which older people experience pain and the interrelationship between the presence of the pain, functional ability and depression, showed that those with pain over the previous month had slightly high prevalence of depression and reported poorer health compared to those without pain. Subjects with pain had also multiple functional limitations compared with the pain-free cohort. (Carmaciu et al. 2007)

The relationship between chronic pain and depression remains unclear, however it is probable that the pain causes poor mental health and vice versa (von Hecke et al. 2013 B). This dependence provides a rationale to treat both pain and mental suffering together in order to achieve better clinical results.

NP is reported to relate to a noticeable burden of psychiatric symptoms. A French cohort study recruiting patients for neurology practices and pain departments, studied the prevalence of psychiatric co-morbidities in patients with peripheral NP. Lifetime and current prevalence of anxiety disorder were at 39 % and 20 %, respectively, and the prevalence of mood disorder were 47 % and 30 %, respectively. (Radat et al. 2013)

As chronic pain is associated with symptoms of psychosocial distress and psychiatric disorders, the assessment for depression is recommended in pain studies using measures such as Beck's Depression Inventory and the Profile of Mood States (Dworkin et al. 2005).

## 2.9. Prognosis of chronic pain

Chronic pain among older adults may take different courses. Chronic pain does not necessarily only deteriorate or remain constant in older age. An American six-year longitudinal study of community-based large cohort of subjects aged over 65 years, revealed the dynamic nature of musculoskeletal pain. One fifth remained without pain, one third had chronic pain (during over 3 sequential years), one third had intermittent pain (more than once during follow-up time) and the rest reported pain every year. Pain in a specific location in the body was mostly of intermittent nature (Thielke et al. 2012).

Some researchers conclude, that chronic pain tends to continue and even deteriorate along with ageing (EFIC 2012, Shi et al. 2010, van Hecke et al. 2013 A). Karttunen et al. (2015) studied the high persistence of chronic pain among community-dwelling older adults over time. During a 2-year follow-up the pain remained consistent in three quarters of the study population. Persistent chronic pain was significantly associated with poor self-rated health, walking difficulties and deteriorated quality of life.

Insomnia is associated with increased chronic pain, particularly with OA, and improved sleep has a beneficial effect on pain (Vitiello et al. 2014). The treatment of mood disorders associated with pain potentially alleviate the burden of pain and increase the patients' functional capacity and quality of life.

Multimorbidity is the presence of two or more long-term health conditions. Chronic pain drives a significant part of the multimorbidity among older adults. Current guidelines for treatment options in clinical practice for multimorbidity have been established (NICE 2016, van der Heide et al. 2017).

## 2.10. Prevention of neuropathic pain

The recognition of risk factors of NP provide potential preventive strategies. Optimal diabetic and blood pressure control, as well as reducing risk factors such as smoking, overweight, and hypercholesterolemia are recommended to prevent diabetic polyneuropathy. A small study found that dietary management and an exercise program resulted in an improvement of painful symptoms and intraepidermal nerve fiber density in patients with impaired glucose tolerance and small fiber neuropathy (Smith et al. 2006).

Prevention of herpes zoster virus prevents postherpetic neuralgia. Vaccination of children against varicella is currently included in national vaccination program, and vaccination of older adults to prevent herpes zoster is considered (THL, Vesikari 2017). The prevention of strokes, HIV-infection, and prolonged back pain are all important factors in reducing the burden of NP in the future (Smith et al. 2012).

### 3. Aims of the study

This study aims to investigate the occurrence of chronic pain and neuropathic pain among community-dwelling older adults over 75 years of age.

The specific aims were:

- 1) To present the occurrence, characteristics, etiology, interference, and treatment of chronic pain among community-dwelling older adults.
- 2) To assess the occurrence, diagnostic certainty, aetiology and treatment of neuropathic pain among community-dwelling older adults with chronic pain.
- 3) To assess the subjective ease of use of self-reporting tools for pain among older home-dwelling adults.
- 4) To establish how chronic pain changes in time and whether there is a difference between chronic pain patients with and without neuropathic pain during a one-year follow-up regarding the intensity and interference of pain, mental health and quality of life.



## 4. Study participants and methods

### 4.1. Participants

Patients were recruited into the study during preventive home visits organized by the municipality of Kirkkonummi (2012 population, 37 600) for older adults aged 75, 80 and 85 years who were living independently. The visits were recommended by the Association of Finnish Local and Regional Authorities and were widely used in a number of Finnish municipalities in the recent years. The participants were recruited from three age groups: 75-year-olds (born 1933–1935), 80-year-olds (born 1931–1932) and 85-year-olds (born 1924–1925) between 2009 and 2013. Altogether 684 subjects (of the total target population of 802) were eligible for a home visit by a nurse, and 460 of them consented the visit (Figure 3).

During the visit, the participants were interviewed using the standardized preventive home visit questionnaire consisting of 48 items (Häkkinen and Holma 2004). In addition, they filled in a one-page questionnaire with questions on the occurrence and intensity of chronic pain (defined as pain with duration  $\geq 3$  months), the expected causes of pain, the interference of pain in their daily life, and current pain medications. Those having pain with an average daily intensity of  $\geq 4$  on NRS scale during the previous week, or with at least moderate interference (or  $\geq 4$  on NRS) in daily life, were offered a consultation with a geriatrician (SR-P). The exclusion criteria were impaired cognitive function (MMSE  $< 23$ ) or impaired communication skills (aphasia, insufficient ability to speak Finnish or Swedish). Out of all participants, 175 fulfilled the inclusion criteria, five were excluded and 64 did not agree to a geriatric consultation (Figure 3).

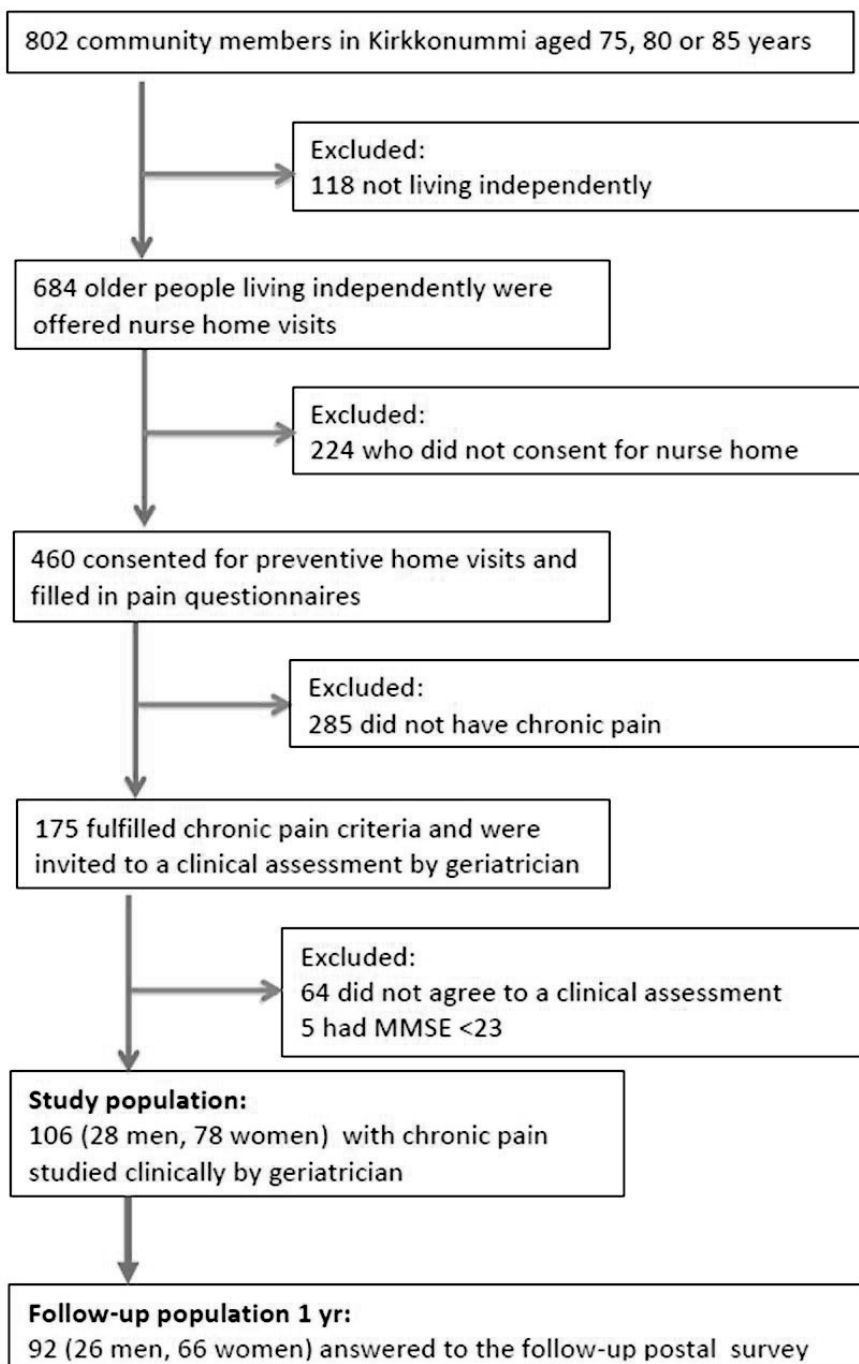


Figure 3. Population of the study

## 4.2. Study protocol

### 4.2.1. Preventive home visits

Data collected in the 6-item questionnaires using the standardized preventive home visit questionnaire (consisting of all together 48 items) during the preventive home visits were analysed: item 1 (living conditions; alone or not), item 12 (subjective health; good, satisfactory or poor), item 14 (doctor diagnosed conditions; an open question), item 16 (quality of life: feeling lonely, sad, tired, satisfied with life; often, seldom or never), item 21 (mobility; good, satisfactory or poor) and 38 (subjective income for daily expenses; good, satisfactory or insufficient). Data from those with chronic pain were compared the pain-free cohort.

### 4.2.2. Study visit to the geriatrician and the nurse

The consenting patients who fulfilled the inclusion criteria for this study, received an appointment to be examined by the research nurse and geriatrician. First, the research nurse instructed the patient to fill in the pain drawing. Secondly, the patient evaluated the average and maximum intensity of their worst pain during the previous week on the VAS. Finally, the patient was asked to fill in five validated questionnaires (BAI, BPI, GDS-15, PainDETECT and SF-36).

The BAI (Beck et al. 1988) is a 21-item screening instrument designed as a general measure of anxiety and to differentiate symptoms of anxiety from symptoms of depression. The questions are rated on a 4-point Likert-type scale ranging from 0 (no abdominal pain at all) to 3 (severe, I could barely stand it). The responses are summarized to provide a total score ranging from 0 to 63, higher scores indicating higher levels of anxiety. A total of 0 – 21 indicates very low levels of anxiety, a total of 22 – 35 indicates moderate levels of anxiety and a total of 36 or more indicates a clinical concern.

The BPI (Cleeland and Ryan 1994) is a patient-completed numeric rating scale that assesses the severity of pain (Severity scale) and its impact on daily functioning (Interference scale). The Pain Interference Scale assesses the degree to which pain interferes with seven daily activities (mood, sleep, walking, general activity, normal work, relations with others and enjoyment of life). The answers are measured using 11-point NRS ranging from 0 (no interference) to 10 (completely interferes). The mean of the seven ratings represents the patient's overall level of pain interference.

The GDS-15 was designed as a self- or interviewer-administered screening instrument and consists of questions addressing various depressive symptoms. A 15-item version has been developed by Sheikh and Yesavage (1986) and is particularly valuable with older patients due to its simple yes/no format and non-reliance on somatic symptoms that may be part of the normal ageing process or related to a diagnosed physical illness. Scores of 6 points or more are considered indicative of possible depression.

The PainDETECT (Freyenhagen et al. 2006) contains nine items; seven weighted sensory descriptor items and two items relating to the spatial (radiating) and temporal characteristics of the individual

pain pattern. It is used for screening presence of the neuropathic component of pain and divided into nociceptive (score <12), unclear (score 13-18) and likely NP (score 19–38).

The SF-36 is a short questionnaire with 36 items, which measure eight multi-item variables: physical functioning (10 items), social functioning (two items), role limitations due to physical problems (four items), role limitations due to emotional problems (three items), mental health (five items), energy and vitality (four items), pain (two items), and general perception of health (five items) (Jenkison et al. 1993). There is an additional unscaled item on changes in respondents' health over the past 12 months. For each variable item scores are coded, summarized, and transformed on to a scale from 0 (worst possible health state measured by the questionnaire) to 100 (best possible health state).

After filling in the questionnaires, the patients underwent a clinical examination by the geriatrician. The examination took 1-1,5 hours and assessed the pain states and their intensity, duration, etiology (if known), and pain-relieving methods (both pharmacotherapy and non-pharmacological treatments) and their benefit were assessed. The patients evaluated the average intensity and maximum intensity of their worst pain during the preceding week on the NRS. Presence of the worst pain was classified as “all the time”, “every day but not all the time”, “every day but appears only by certain provoking factor”, “on several days a week” and “occasional”. Finally, the geriatrician performed a clinical examination in order to diagnose the etiology of the pain states, and the type(s) of pain (nociceptive, neuropathic, combination of them, or neither of them classifying it as idiopathic pain). Where clinically required, the geriatrician had the opportunity to refer patients to pathology tests and/or imaging studies, or for a consultation with another specialist (e.g., neurologist, orthopedic surgeon). Certainty of NP was graded as definite, probable or possible according to the recommended criteria (Treede et al. 2008).

Where appropriate, the geriatrician modified the pain treatment (e.g., recommendation of dose escalation, trialing a different pain relief drug, or a non-pharmacological treatments).

After the appointment with the geriatrician, the study nurse asked the patient to assess the ease of use of the pain scales (VAS, NRS, BPI and PainDETECT) using a 7-point verbal rating scale (1=very easy, 2=easy, 3=quite easy, 4=not easy, not difficult, 5=quite difficult, 6=difficult, 7=very difficult).

### 4.2.3. Follow-up

A follow-up questionnaire was sent to the patients one year after the visit to the geriatrician. Change of pain compared to the previous visit (much improved, partially improved, no change, worse), appearance of possible new pain and the expected cause of it, pain medication, and usefulness of participation in the study were studied. In addition, a pain drawing, the BPI, the GDS-15, the BAI and the SF-36 were enclosed. Information about the diagnostic procedures and treatment of pain during the follow-up period were collected from patient files.

Figure 4 represents the flow of the study and the assessment methods of the study are summarized in Table 5.

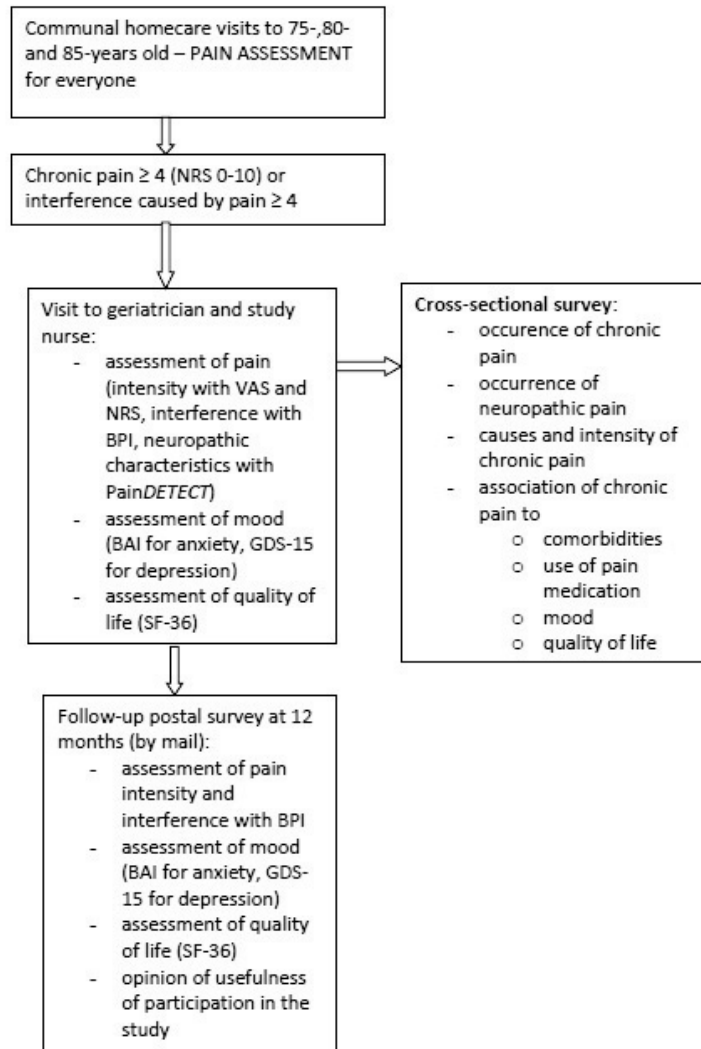


Figure 4. Flow chart of the study.

Table 5. Assessment methods and questionnaires.

Measure	Nurse at homecare visit	Study nurse	Geriatrician	Postal survey after 12 months
Standardized preventive home visit questionnaire	x	partly (questions 1, 12, 14, 16, 21 and 38)		
MMSE	x			
One-page pain questionnaire	x			
Pain drawing		x		x
VAS		x		
NRS			x	
BAI		x		x
BPI		x		x
GDS-15		x		x
PainDETECT		x		
SF-36		x		x
Questionnaire about ease of use VAS, NRS and the questionnaires		x		

### 4.3. Statistical analyses

#### The first aim (publication I)

The data is presented as means with standard deviations (SD), or as medians with interquartile range (IQR), or as counts with percentages. Statistical comparisons between the groups were performed with the  $\chi^2$  test, or Fisher–Freeman–Halton test, or Mann–Whitney test. Statistical significance for hypotheses of linearity was evaluated by a bootstrap-type analysis of variance (ANOVA). The normality of the variables was tested using the Shapiro-Wilk W test.

#### The second aim (publication II)

The data is presented as means with standard deviations (SD) or as counts with percentages. Statistical comparisons were made using the  $\chi^2$  test, Fisher’s exact test, t test or bootstrap-type t

test. Logistic regression was used to produce an age-adjusted odds ratio. The normality of the variables was tested using the Shapiro-Wilk W test.

The third aim (publication III)

The repeated measures were analyzed using generalizing estimating equation models with an unstructured correlation structure. Multivariate linear regression analyses with standardized regression coefficients beta ( $\beta$ ) were used to identify the predictors of ease of using the measures. Cohen's standard for Beta values above 0.10, 0.30 and 0.50 represent small, moderate and large relationships, respectively. Hochberg's procedure and Sidak's adjustment were used to correct multiplicity. The bootstrap method was used when the theoretical distribution of the test statistics were unknown, or in the event of a violation of the assumptions (e.g., non-normality). Partial correlations were calculated between ease of use of the measures, adjusted for age, gender and MMSE. The normality of the variables was tested using the Shapiro-Wilk W test.

The fourth aim (publication IV)

The data is presented as means with standard deviations (SD) or as counts with percentages. Statistical significance between groups was verified by the t-test, Mann-Whitney test, permutation test or  $\chi^2$  test, and the changes were compared using a bootstrap-type ANCOVA with the baseline measurement as a covariate. Correlation coefficients were calculated by the Pearson method. The normality of the variables was tested using the Shapiro-Wilk W test.

All statistical analyses were performed using STATA softwares, and the StataCorp LP (College Station, TX, USA) statistical package was used for the analyses.

#### 4.4. Ethical aspects

The study protocol was approved by the Ethics Committee of the Helsinki University Central Hospital (permission 128/13/03/00/09), and a written informed consent was obtained from all participants.

## 5. Results

### 5.1. Characteristics of patients

A total of 106 patients (28 males, 78 females) consented to participate in this study. Out of the participants, sixty-five were 75 years, twenty-eight were 80 and thirteen were 85 years of age. Data of preventive home visits of those without chronic pain was available on 220 subjects. The comparative results between those living with chronic pain and their pain-free counterparts are presented in Table 6. Chronic pain was significantly more prevalent in female participants. Patients with chronic pain rated their health and mobility significantly worse than those without chronic pain. Those with chronic pain felt significantly sadder, lonelier and more tired compared to the pain-free cohort. Subjective income for daily expenses was rated good by 30% and satisfactory by 61% of those with chronic pain and good by 35% and satisfactory by 56% by the pain-free cohort, and insufficient by 9% in both groups. There were no significant differences between the groups regarding income. Patients with chronic pain were not any less satisfied with their lives than those without chronic pain (often satisfied 87% and 91%, respectively).

Most of the 106 pain patients examined by the geriatrician had multiple chronic pain states. Only five (5%) patients had one pain condition, 35 (33%) had two and 66 (62%) patients had three pain conditions.



Table 6. Comparison of participants living with chronic pain and their pain-free comparators.

	Subjects with chronic pain (N=175)	Subjects without chronic pain (N=220)	p-value
Age, n (%)			0.57
75	102(58)	139 (63)	
80	40 (23)	42 (19)	
85	33 (19)	39 (18)	
Women, n (%)	129 (74)	110 (50)	<0.001
Living alone, n (%)	83 (48)	82 (38)	0.051
Subjective health, n (%)			<0.001
Good	55 (32)	127 (58)	
Satisfactory	85 (49)	82 (37)	
Poor	33 (19)	11 (5)	
Subjective mobility, n (%)			<0.001
Good	52 (30)	127 (58)	
Satisfactory	64 (36)	74 (33)	
Poor	59 (34)	19 (9)	
Feeling lonely, n (%)			0.011
Often	25 (14)	14 (6)	
Seldom	55 (32)	62 (28)	
Never	93 (54)	144 (66)	
Feeling sad, n (%)			0.005
Often	19 (11)	8 (4)	
Seldom	76 (44)	88 (40)	
Never	77 (45)	124 (56)	
Feeling tired, n (%)			<0.001
Often	75 (43)	51 (23)	
Seldom	76 (44)	110 (50)	
Never	22 (13)	59 (27)	
Satisfied with life, n (%)			0.39
Often	150 (87)	200 (91)	
Seldom	21 (12)	19 (9)	
Never	2 (1)	1 (<1)	

In the patients who participated in preventive home visits, median (IQR) number of chronic diseases was 3 (2,3) in those with chronic pain and 2 (1,3) in those without chronic pain ( $p<0.001$ ). Frequency of chronic diseases in those with chronic pain and in those without chronic pain is presented in Table 7. The differences between the groups was significant only regarding musculoskeletal diseases ( $p<0.001$ ) and respiratory diseases ( $p=0.02$ ).

Table 7. Chronic diseases in patients receiving home visits living with chronic pain and the pain-free patients.

	With chronic pain N (%)	Without chronic pain N (%)
Cardiovascular diseases	123 (70)	134 (61)
Musculoskeletal diseases	107 (61)	72 (33)
Endocrine diseases	73 (42)	84 (38)
Respiratory diseases	42 (24)	27 (12)
Neoplasms	15 (9)	18 (8)
Psychiatric diseases	11 (6)	13 (6)
Diseases of the nervous system	11 (6)	11 (5)

## 5.2. Characteristics of pain

The worst pain was located primarily in the torso in 44 (42%) patients, in lower limb(s) in 40 (38%), in upper limb(s) in 13 (12%) and in the head or neck in 9 (8%) patients (Figure 5).

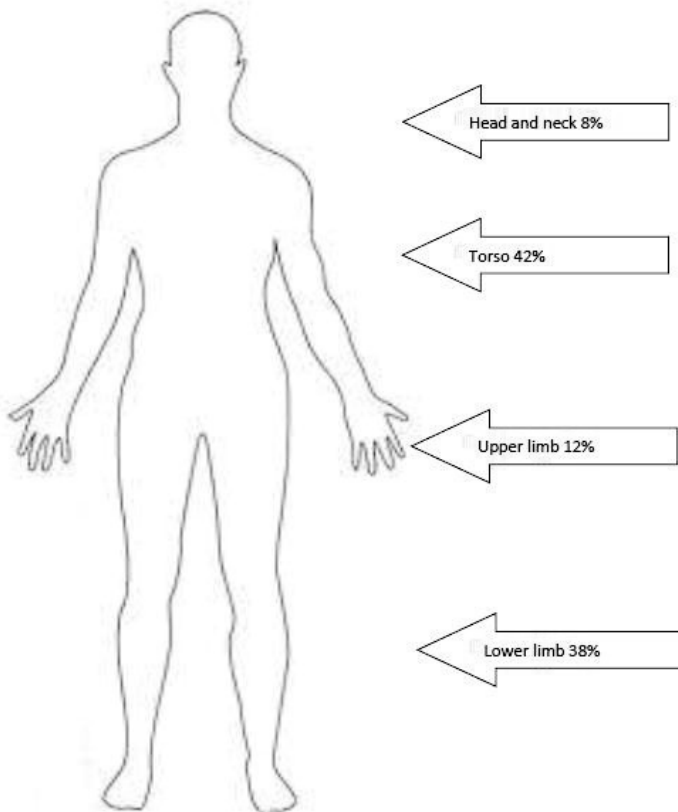


Figure 5. Location of the pain.

The largest diagnostic group of musculoskeletal pain was the spinal disorders (48 patients, 45%), of whom 43 had lumbar and five had cervical spine problems. The second most common cause of musculoskeletal pain was osteoarthritis of the hip (11) or the knee (11) (total of 21%). The remaining musculoskeletal diseases as cause of the worst pain were other OA (five patients), shoulder lesions (five patients), soft tissue disorders (four patients), sequelae of fracture of limb (two patients), gout (one patient) and polymyalgia rheumatica (one patient). The worst pain was classified as pure nociceptive pain in 61 (58%) patients, pure NP in nine (8%), combined nociceptive and NP in 34 (32%) and idiopathic in two (2%) patients. The worst pain by type and age group is presented in Table 8.

Table 8. Different pain types as the worst pain by age group.

	Aged 75 years, N (%)	Aged 80 years, N (%)	Aged 85 years, N (%)	All N (%)
<b>Type of pain</b>				
Nociceptive	39 (60)	14 (50)	8 (62)	61 (58)
Neuropathic	5 (8)	2 (7)	2 (15)	9 (8)
Combination	20 (31)	11 (39)	3 (23)	34 (32)
Idiopathic	1 (1)	1 (4)	0 (0)	2 (2)
N (%)	65 (100)	28 (100)	13 (100)	106 (100)

The average intensity (SD) of the worst pain on the NRS 0-10 during the preceding week was 5.7 (1.6), intensity of the maximal pain 7.7 (1.6) and interference of pain 5.9 (1.9). The intensity and interference of the worst pain by age group is presented in Table 9. The average pain intensity and the maximal pain decreased by age. Linearity was statistically significant for average pain intensity (p for linearity 0.008) and for maximal pain intensity (p for linearity 0.004).

Table 9. Intensity and interference of the worst pain by age group.

	Age group		
	75 mean (SD)	80 mean (SD)	85 mean (SD)
Average pain intensity	6.1 (1.6)	4.9 (1.5)	4.3 (1.2)
Maximal pain intensity	8.1 (1.4)	7.3 (1.5)	6.6 (1.9)
Pain interference	6.1 (1.9)	5.4 (2.2)	5.5 (1.4)

Figure 6 represents the duration of the worst pain, which was longer than 5 years in 51 (48%) patients.

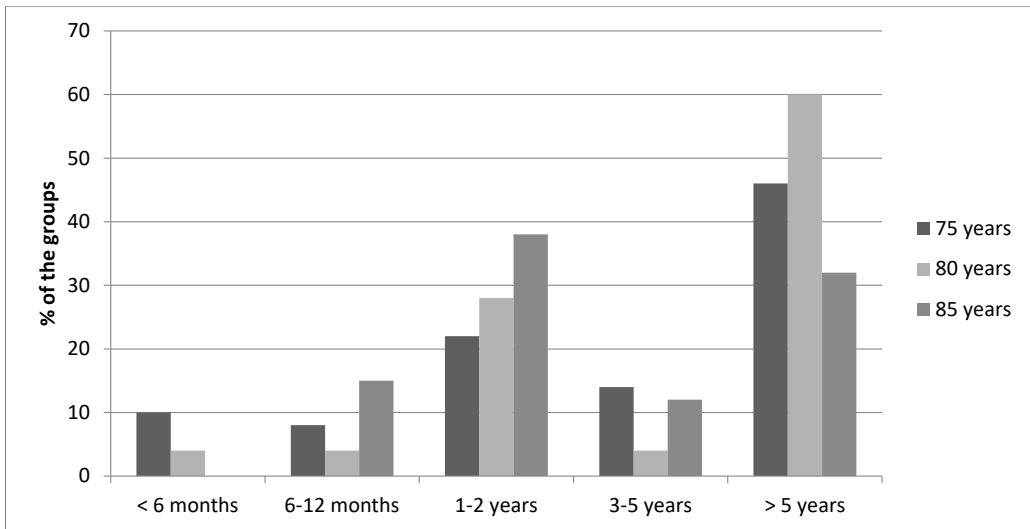


Figure 6. Duration of the worst pain by age group.

The occurrence of the worst pain is presented in Figure 7. The worst pain was present daily in 85 (80%) patients. The pain was provoked by some activity in almost half of the patients (40, 47%). Typical triggers include getting up, walking and doing housework.

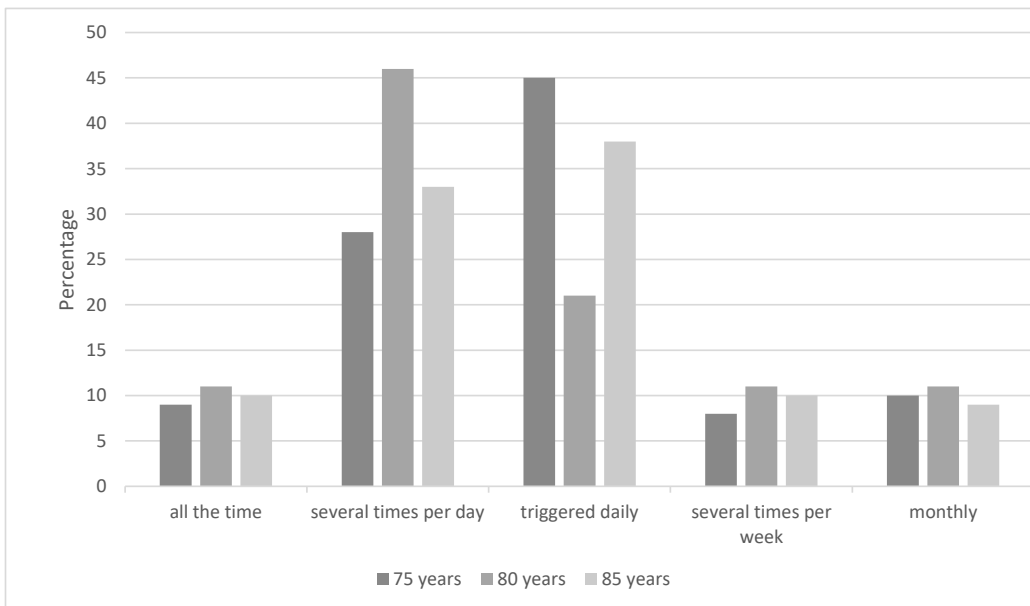


Figure 7. The occurrence of the worst pain.

### 5.3. Neuropathic pain

NP was diagnosed in 51 (48%) patients, and in 43 patients, NP was the worst type of pain. Nine patients had two separate NP conditions, and a total of 60 NP conditions were diagnosed in this study. Forty-five conditions were definite and 15 probable NP states. Unexpectedly, the occurrence of NP did not increase with age; NP presented in 33 (65%) of the patients aged 75, in 13 (25%) of the patients aged 80, and in five (10%) patients aged 85 years. NP presented in 71% of males and 40% of females. The age-adjusted odds ratio was 3.89 (1.51 to 10.03), where  $p=0.005$ . Mean (SD) intensity of NP was 4.7 (1.8) in males and 5.9 (1.7) in females ( $p=0.021$ ). The duration of NP was less than 6 months in one patient, 6 – 12 months in four patients, 1 – 2 years in 10 patients, 3-5 years in six patients and over 5 years in most, or 27 patients.

The etiology of NP is presented in Table 10. The most common diagnosis was the degenerative disease of the spinal column causing radiculopathy ( $n=36$ ). These patients had mixed pain, i.e. they had both axial (nociceptive) and radicular (neuropathic) pain. NP was caused by peripheral nerve trauma in eight, by peripheral nerve entrapment in seven, by polyneuropathy in five and by other conditions in five patients.

Table 10. The etiology of neuropathic pain.

Diagnosis	N (number of patients)
Degenerative disease of the spinal column	
Lumbar radiculopathy	28
Cervical radiculopathy	8
Peripheral nerve trauma	
Primary nerve trauma	5
Postsurgical nerve trauma	3
Peripheral nerve entrapment	7
Painful polyneuropathy	5
Postherpetic neuralgia	3
Diabetic mononeuropathy	1
Central post-stroke pain	1

The results of the validated pain and mood questionnaires in chronic pain patients with and without NP are presented in Table 11.

Table 11. Results of the PainDETECT, BPI, GDS-15 and the BAI in patients with and without neuropathic pain.

Variable	NP (N=51) mean (SD)	Without NP (N=55), mean (SD)	p value
PainDETECT	13.3 (6.8)	7.7 (5.2)	<0.001
BPI Intensity Scale	5.2 (1.9)	4.1 (1.9)	0.006
BPI Interference Scale	4.5 (2.4)	3.3. (2.4)	0.014
General activity	5.4 (3.4)	3.1 (3.3)	0.021
Mood	4.5 (3.1)	3.0 (3.0)	0.020
Housework	4.8 (3.4)	3.7 (3.4)	0.11
Walking	5.7 (3.3)	4.6 (3.4)	0.091
Relations with others	2.4 (3.2)	2.1 (3.1)	0.67
Sleep	5.1 (3.6)	3.5 (3.4)	0.019
Enjoyment of life	3.3 (3.4)	2.4 (3.2)	0.10
GDS	4.0 (3.2)	2.9 (2.4)	0.041
BAI	14.9 (12.5)	12.1 (8.0)	0.18

#### 5.4. Non-pharmacological management of pain

The patients were interviewed about their use of non-pharmacological treatments during the geriatrician appointment. Eighty patients named at least one non-pharmacological method to alleviate their pain. One non-pharmacological treatment was named by 44, two treatments by 28 and three different treatments by eight patients. A certain position to relieve pain was mentioned by 27 patients, rest by 22, physical activity by 22, warmth by 18, movement by nine, cold by eight and other methods, e.g., use of assistive device by a further five patients. The most popular forms of physical activity were hydrotherapy exercises (i.e., swimming or pool running), group exercise, gym exercises and walking.

#### 5.5. Pharmacotherapy of pain

The patients' pain medications were analysed in the primary examination. Majority of the patients (n=82, or 77%) took pain medication regularly and 12 (or 11%) only occasionally (i.e., as required) (Figure 8), whereas 12 patients (11%) did not take any pain medication. About one third (n=38, or 36%) managed their condition with one type of medication, whereas 45 patients (42%) were taking

at least two different drugs. Figure 9 represents the number of pain drugs (including drugs taken as required and topical drugs) by age groups.

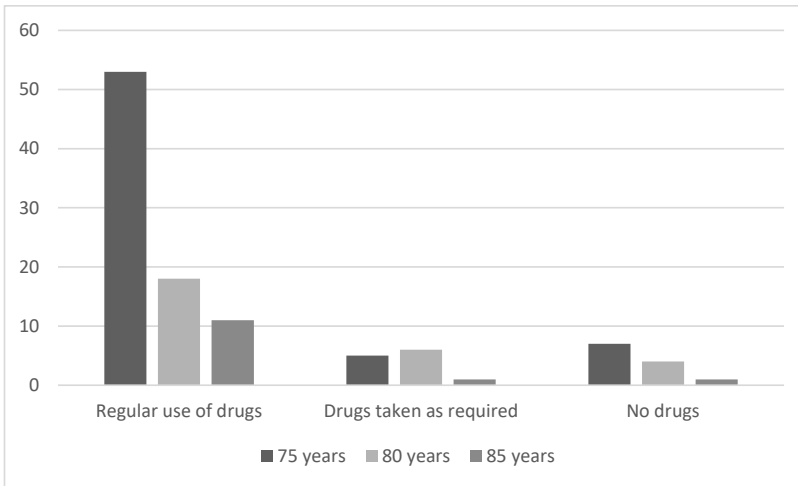


Figure 8. Regular and only on demand users (number) of pain drugs by age group.

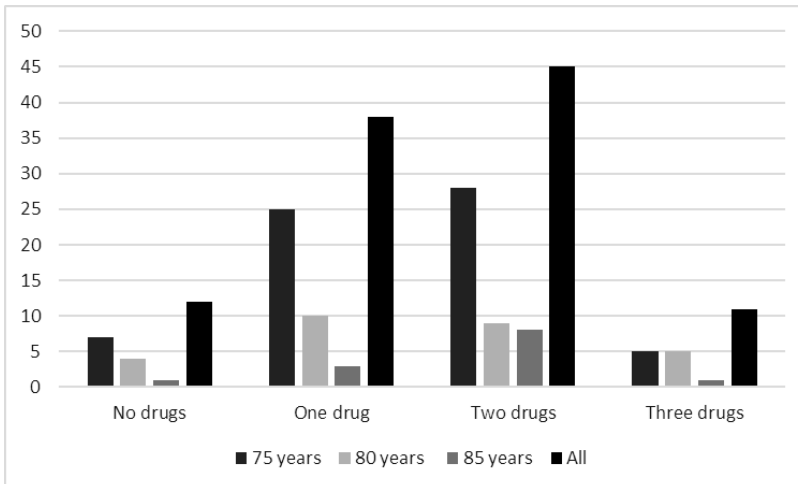


Figure 9. Number of pain drugs by age group.

Paracetamol (used by 62 subjects) and NSAIDs (used by 46 subjects) were the most common pain medications used by the study participants. Traditional NSAIDs were preferred by 38 and COX-2 inhibitors by eight patients. Although NP was common, only a minority (9 patients, or 8%) of our patients used drugs specifically for NP (i.e., TCA, SNRI or antiepileptic drugs). Eighteen patients (17 %) used weak opioids (either for nociceptive pain or combined nociceptive and NP). One patient used metamizole for abdominal pain when needed. In addition to systemic medication, 19 patients used a topical medication (topical NSAID was used by 18 and topical lidocaine by one patient). Table 12 presents use of different pain medications.

Table 12. The use of pain medication in the primary pain examination.

Type of pain medication	75 years N (% of age cohort)	80 years N (% of age cohort)	85 years N (% of age cohort)	All N (%)
Paracetamol	39 (60)	14 (50)	9 (69)	62 (59)
Traditional NSAID	27 (42)	9 (32)	2 (15)	38 (36)
COX-2 inhibitors	5 (8)	2 (7)	1 (8)	8 (8)
Weak opioids	9 (14)	6 (21)	3 (23)	18 (17)
NP drugs	6 (9)	1 (4)	2 (15)	9 (9)
Metamizole	1 (2)	-	-	1 (1)
Topical medication	8 (12)	8 (29)	3 (23)	19 (18)

Eleven patients with NP were on medication specially recommended for NP (Finnerup et al. 2015). Six patients were on tramadol (dose 50 – 375 mg/day), three on amitriptyline (dose 10 – 20 mg/day) and two on pregabalin (dose 150 – 300 mg/day). One patient also used a topical lidocaine cream (5 %) regularly in combination with pregabalin.

In addition, ten patients had previously trialed medication recommended for NP: five patients had trialed TCA, four had trialed gabapentinoid and one had trialed tramadol. Six patients had ceased taking their former medication due to the side effects (even where the medication had provided at least some pain relief), one patient had ceased former medication due to lack of pain relief and two patients had ceased former medication due to side effects and lack of pain relief. One patient could not define the reason for cessation of their former NP medication.

During the study visit, the geriatrician recommended a trial of new NP medication for 17 patients. Four of the patients did not start the recommended medication and seven patients trialed the suggested drugs but ceased taking them due to the side effects or insufficient pain relief. Six patients continued their new medication: two patients were taking gabapentin (dose 300 mg at bedtime), two patients took pregabalin (dose 25-75 mg/day), one took tramadol (dose 200 mg/day) and one took transdermal buprenorphine (dose 20 ug/hour).



## 5.6. The benefits of pain management

At the baseline visit, the benefits of pain treatment methods as a whole was rated as excellent by six patients, good by 21 patients, moderate by 34 patients, poor by 17 patients and negligible by 2 patients.

## 5.7. Ease of use of the pain assessment tools

Subjective ease of use of the VAS, NRS, BPI and PainDETECT was measured with a 7-point scale (1 = very easy, 7 = very difficult to use). The NRS was difficult or very difficult to use for 46% of the participants. Thirty-six percent found the VAS difficult or very difficult to use. The BPI and PainDETECT were regarded as difficult or very difficult to use by 31% and 23% of the subjects, respectively. The ease of use of all four measures is presented in Figure 10. There was a significant difference between the measures ( $p < 0.001$  after adjusting for age and gender). The PainDETECT was regarded as the easiest to use, and the difference was significant (compared with the VAS and with NRS;  $p < 0.001$  and compared with the BPI  $p = 0.009$ ). The intraclass correlation between ease of use of the measures was 0.84 (95% CI: 0.78 to 0.89).

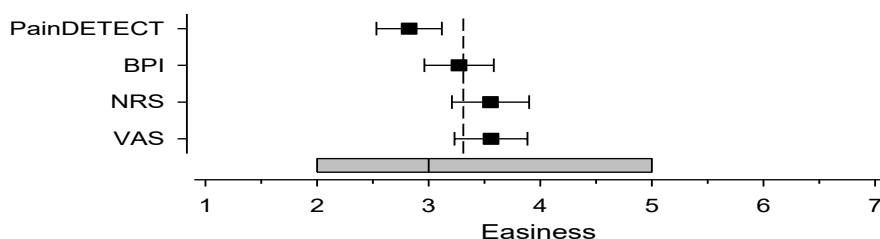


Figure 10. Mean easiness of use (1 = very easy to use, 7= extremely difficult) of four measures with 95% confidence intervals. Note: dashed line represents the mean of all ratings of the measures, and the box-plot represents medians and inter-quartile ranges.

The correlations between the ease of use of the measures (after adjusting for MMSE result, age and gender) are presented in Table 13. Adjusted correlations varied from 0.49 to 0.73, with the strongest correlation (0.73) found between difficulty of using the NRS and the BPI (Interference subscale).

Table 13. Correlation between subjective ease of use of the measures after adjusting for MMSE result, age and gender.

	NRS	BPI inter	PainDETECT
VAS	0.53 (0.31 to 0.72)***	0.60 (0.40 to 0.75) ***	0.49 (0.28 to 0.65) ***
NRS		0.73 (0.58 to 0.83) ***	0.55 (0.33 to 0.69) ***
BPI inter			0.54 (0.34 to 0.70) ***

Note: Sidak-adjusted probabilities: \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$

The PainDETECT was found relatively easy to use. However, the PainDETECT was not able to accurately classify the presence of NP at an individual level. Of those patients with NP (N = 51), the PainDETECT classified 12 patients as positive (score  $\geq 19$ , “a NP component is likely”), 17 as unclear (score between 13 to 18, “the result is ambiguous, however a NP component can be present”) and 22 as negative (score  $\leq 12$ , “a neuropathic component is unlikely”) for NP. Of those without NP (N = 55), the PainDETECT classified 47 as negative, five as unclear and three as positive for NP.

## 5.8. Pain in the one-year follow-up

Follow-up questionnaires at 12 months from the baseline visit were returned by 92 (26 men and 66 women) of the original 106 patients, representing 87% of the baseline. All patients from the original cohort continued to live independently at home at the time of the survey according to patient files. None of the patients in the baseline cohort had died. The reasons for non-response to the follow-up questionnaire are unknown.

Of those who replied to the follow-up postal survey, four patients had one pain state and 88 (96 %) patients had two or more different pain states at baseline. Nociceptive pain on its own was present in 48 patients, with a further 44 patients having both NP and nociceptive pain. None of the patients had NP alone. The causes of nociceptive pain ranged from spine disorders (n=55), OA of limb joints (n=38), soft tissue disorders (n=28, with shoulder pain in 16), sequelae of injuries (n=9), inflammatory polyarthropathies (n=5), visceral pain (n=5) and primary headache (n=2). NP was caused by degenerative disease of the spine causing radiculopathy (n=25), peripheral nerve trauma (n=7), peripheral nerve entrapment (n=4), painful polyneuropathy (n=4), postherpetic neuralgia (n=3) and central post-stroke pain (n=1).

The baseline characteristics of patients who replied to the follow-up postal survey are presented in table 14 by comparing those with NP (n=44) and those without NP (n=48). The only significant difference between the groups was the gender of the patients (NP was less common in women). Mean (SD) intensity of pain was 4.1 (2.0) in patients without NP and 5.1 (1.8) in patients with NP ( $p=0.003$ , adjusted for age and gender). Mean (SD) interference of pain was 3.4 (2.4) in patients without NP and 4.5 (2.3) in patients with NP ( $p=0.007$ , adjusted for age and gender). Median (IQR) follow-up time was 12 (8, 14) months in patients without NP and 12 (8, 16) months in those with NP.

Compared to the baseline, patients medication was changed at the follow-up in 30 cases: a new drug was prescribed for 22 patients, and the dose was modified for eight patients. Physiotherapy was recommended for 27 patients and assistive devices (orthosis, orthotic insoles, orthotic vest or collar) for eight. Twelve patients were referred to a specialist consultation (eleven to a surgeon and one to a neurologist). There were no significant differences between the groups regarding their treatments. Nine patients underwent surgery due to chronic pain (total hip replacement for 5 patients, total knee replacement for 1, lumbar decompression for 2 and nerve entrapment decompression to 1), and the procedure provided noticeable pain relief to the patients.

Table 14. Baseline characteristics of patients without NP and with NP.

Variable	NP- (N=48)	NP+ (N=44)	P-value*
Number of women, (%)	41 (85)	25 (57)	0.002
Age group, years, N (%)			0.87
75	30 (62)	29 (66)	
80	12 (25)	11 (25)	
85	6 (13)	4 (9)	
Living alone, N (%)	25 (53)	18 (41)	0.24
Duration of pain in years, (%)			0.72
<1	8 (17)	8 (18)	
1-2	15 (31)	10 (23)	
≥3	25 (52)	26 (59)	
MMSE, mean (SD)	28 (2)	27 (2)	0.44
Subjective health, N (%)			0.97
Good	17 (37)	16 (36)	
Satisfactory	21 (46)	21 (48)	
Insufficient	8 (17)	7 (16)	
Subjective mobility, n (%)			0.76
Good	16 (33)	15 (34)	
Satisfactory	18 (38)	19 (43)	
Insufficient	14 (29)	10 (23)	
Comorbidities			
Cardiovascular diseases	35 (73)	29 (66)	0.47
Musculoskeletal diseases	31 (65)	21 (48)	0.10
Endocrine diseases	22 (46)	18 (41)	0.63
Respiratory diseases	13 (27)	8 (18)	0.31
Neoplasms	6 (13)	4 (9)	0.60
Psychiatric diseases	2 (4)	0 (0)	0.49
Diseases of the nervous system	1 (2)	3 (7)	0.35
BAI, mean (SD)	12.6 (8.1)	13.5 (11.6)	0.68
GDS-15, mean (SD)	3.04 (2.50)	3.84 (3.02)	0.18
SF-36, mean (SD)			
Summary of Physical Component	34 (12)	33 (11)	0.63
Summary of Mental Component Summary	53 (10)	52 (11)	0.57
Systemic pain medication, N (%)	36 (75)	36 (82)	0.43
Paracetamol	29 (60)	24 (55)	0.57
NSAID	14 (29)	19 (43)	0.16
Mild opioid	5 (10)	7 (16)	0.54
NP drug #	3 (6)	4 (9)	0.71

NP-, without neuropathic pain, NP+, with NP

BAI, Beck Anxiety Inventory, GDS-15, Geriatric Depression Scale,

SF-36, Medical Outcomes Survey Short Form

\* Adjusted age and gender

# Antidepressant drug, antiepileptic drug or topical lidocaine for pain

At the follow-up, 13 patients reported experiencing a new type of pain. The diagnosis was OA of limb joints in five, visceral pain in two, painful polyneuropathy in two, bone fracture in two, spinal disorder in one, and a recent herpes zoster in one patient.

During the follow-up, there were no significant changes to the pain intensity in either group. The change in the intensity of pain (NRS 0 – 10) in those without NP was -0.01 (95% CI: -0.49 to 0.48),  $p=0.97$  and in those with NP it was -0.11 (95% CI: -0.79 to 0.58),  $p=0.65$ . The changes did not vary significantly between the study groups ( $p=0.22$ , adjusted at baseline). The change in the interference of pain (NRS 0 - 10) in those without NP was 0.76 (95% CI: 0.18 to 1.34),  $p=0.011$  and it was 0.09 (95% CI: -0.54 to 0.73),  $p=0.77$ , in patients with NP. The change in pain interference did not significantly vary between the groups ( $p=0.59$ , adjusted at baseline). Both intensity and interference had a negative correlation with the baseline value.

Change in pain, depression, anxiety and quality of life during the follow-up is presented in Table 15. No significant variation was observed within or between the groups.

Table 15. Change during follow-up in pain, depressive symptoms, anxiety and quality of life.

Variable	NP- (N=48) Change (95 % CI)	NP+ (N=44) Change (95 % CI)	P-value*
BPI			
Pain intensity	-0.01 (-0.49 to 0.48)	-0.11 (-0.79 to 0.58)	0.22
Pain interference	0.76 (0.18 to 1.34)	0.09 (-0.54 to 0.73)	0.59
GDS-15	0.5 (-0.3 to 1.3)	0.2 (-0.5 to 0.9)	0.93
BAI	-2.0 (-4.3 to 0.4)	-0.5 (-2.4 to 1.7)	0.15
SF-36			
Summary of Physical Component	-2 (-4 to 1)	-2 (-4 to 1)	0.75
Summary of Mental Component	-3 (-6 to 1)	-2 (-4 to 1)	0.78

NP-, without neuropathic pain, NP+, with NP

BPI= Brief Pain Inventory

BAI = Beck Anxiety Inventory, GDS-15 = Geriatric Depression Scale,

SF-36 = Medical Outcomes Survey Short Form

\*Baseline adjusted

## 6. Discussion

### 6.1. The main findings

As expected, those who reported presence of chronic pain at preventive home visits, reported deteriorated subjective health and mobility ratings and more feelings of sadness, tiredness and loneliness compared to those without chronic pain. However, the satisfaction with life among patients with chronic pain did not differ significantly from those without chronic pain, which possibly reflects good coping skills living with pain and acceptance of one's health state (Eccleston et al. 2016).

Most patients in the study population had several pain states with only 5% reporting one pain condition. The findings are in line with observations by others (Scherer et al. 2016). In the study participants, chronic pain had been present at least five years in about half of the cases and occurred daily in 80 %. Pain was provoked by some activity in nearly half of the patients, and is consistent with the reported deteriorated subjective health and mobility.

The most common reason for chronic pain was musculoskeletal pain with 83% of the patients reporting it to be their worst pain. The most common pain type was nociceptive pain, but NP was surprisingly common, and was present in 48% of patients. It is worth noting, that nine patients (8%) had two different NP states. Two patients had only NP, however, in most cases neuropathic and nociceptive pain occurred simultaneously. Radicular pain due to spine disease was the most common cause (60%) of NP. Both the pain intensity and interference were significantly higher in those with NP compared to those without NP, confirming previous observations of French and English population-based studies (Bouhassira et al. 2008, Torrance et al. 2006).

The VAS, NRS, BPI, and the PainDETECT were found suitable to use in independently living older adults. The use of multidimensional scales, such as the BPI and PainDETECT, was found easier compared to the NRS and VAS. There are several reasons that possibly explain this: multidimensional scales are generally better in describing the various pain dimensions (Doventas et al. 2011), the pain variation with time, and the relation between pain and provoking factors. As participants with cognitive impairment were excluded, the study population represents elderly people with good cognitive function, and they found these broadly used multidimensional pain scales relatively easy to use.

The results showed that chronic pain was persistent in the study participants in the one-year follow-up. However, both the relief and the exacerbation of pain were observed at an individual level. The study participants continued to live independently at the time of follow-up.

## 6.2. Further aspects of neuropathic pain

NP was unexpectedly prevalent in the study cohort. Older people are at higher risk of NP because the incidence of many diseases causing NP increases as the population ages. A possibility of a selection bias regarding the study population also exists; those with frequent, disturbing and/or disabling pain may have been more interested in participating in the study. Finally, a meticulous clinical examination of the patients revealed a neuropathic component in patients with a combination of nociceptive and NP (Haanpää et al. 2009).

Although screening tools for NP may be useful to alert the clinician to consider the possibility of NP, its diagnosis requires a clinical examination (Haanpää et al. 2011). The controversial role of NP screening tools is confirmed by this study, as the PainDETECT did not show clear positive result for NP even in the NP group. This finding further supports Mathieson et al. (2015) who highlighted the pivotal role of adequate clinical examination in diagnosing NP.

The most common cause for NP was degenerative disease of the spinal column causing mixed pain with nociceptive and neuropathic components. Entrapments and peripheral nerve traumas were also quite common in the study cohort. Only one patient had central NP. Two patients had post-surgical sciatic nerve lesion caused by total hip replacement, i.e. their chronic nociceptive pain due to OA was replaced by postsurgical NP. On the other hand, surgery provided good relief of NP for four patients (two of them had peripheral nerve entrapment and two had compression of neural tissue at low back level). These findings emphasize the importance of diagnosis of the cause of NP in older people, as well as the individual planning of their treatment. Referral to a surgeon needs to be considered in the case of older patients (Ahmad and Goucke 2002). The cause of pain should be treated wherever possible.

The pain interference measured on the BPI interference scale was significantly higher in those with NP in the following three domains: mood, sleep and general activity. This finding reflects the multifaceted burden of NP. Although the GDS scores were low across the participants, those with NP had significantly higher score in GDS compared to those without NP.

## 6.3. Non-pharmacological management of pain

Since chronic pain impairs the well-being and functional capacity of patients, it deserves special attention in general practice. According to the Finnish Current Care Guidelines, non-pharmaceutical interventions form the basics of the treatment (Pain, Current Care Guidelines Abstract, 2016). Optimal treatment strategies may include counselling, self-management of the pain, physical therapies and group interventions. Multi-professional teams that include physicians, nurses, physiotherapists, psychologists and other health professionals may be helpful in finding ways to manage the different aspects of chronic pain in the elderly. Despite of the strong clinical recommendation to prescribe non-pharmacological pain management, the primary approach of

many doctors is to prescribe pharmaceuticals in the first instance (von Spangenberg et al. 2012). Chronic pain management dominated by analgesic medication simply fails to notice the importance of the modifiable factors of chronic pain treatment, such as supporting physical activity, psychological factors and social aspects of pain (van Hecke et al. 2013 A, Toth and Moulin 2013).

The study participants listed the non-pharmacological pain relief methods used for their worst pain at the baseline visit. At least one non-pharmacological pain relief method was named by 80 patients (75 %). Although the wide use of non-pharmacological therapies among older adults is well known, the evidence for it is sparse. Most of the clinical studies and RCTs exclude patients older than 65 years of age (Paeck et al. 2014).

A Norwegian population-based cross-sectional HUNT 3 study found, that recreational exercise taking into account its duration, intensity and frequency were associated with lower prevalence of chronic pain especially among older participants (those aged over 65 years). However, the cross-sectional nature of the study limits conclusions of the possible causality between exercise and pain. (Landmark et al. 2011).

#### 6.4. Pharmacotherapy of pain

In this study, pain medication was commonly used among the participants. The frequent use of pain killers may be explained by the selection criteria of the patients; patients with chronic pain of at least moderate intensity or interference were included. A Finnish study which included a random sample of adults aged over 75 years reported that about half of the participants had chronic pain, and only 15% of them with chronic pain reported regular use of pain medication and 60% used analgesics as needed (Karttunen et al. 2015).

The most commonly used drugs among the study participants were paracetamol and NSAIDs. As anticipated, and also recommended to the patients by their clinician, paracetamol was the most frequently used (59% of patients). In line with the findings by Kemp et al. (2005), both paracetamol and non-pharmacological methods were the most common pain management methods in the study patients. Despite of their risks and possible interactions, NSAIDs were also used quite commonly (38% of patients). Both paracetamol and many traditional NSAIDs are available over-the-counter in Finland, possibly explaining their common use. We did not analyse the origin of the drug (i.e., whether it was over-the-counter or prescribed medication). The use of COX-2 inhibitors was uncommon, possibly due to their expensive nature and cautious prescription policy.

Current clinical guidelines suggest paracetamol as the first-line choice for the treatment of chronic nociceptive pain among older adults (AGS 2009, Abdulla et al. 2013), although the risks of the narrow safe therapeutic dosage have to be considered (Barber and Gibson 2009). There is also controversial evidence of the efficacy and use of paracetamol in the treatment of OA or low back

pain (Machado et al. 2014, da Costa et al. 2016, Saragiotto et al. 2016) and no evidence to support the use for NP (Wiffen et al. 2016).

Although NP was common in the study participants, the use of NP medication was uncommon; only a fifth of NP sufferers were taking an evidence-based medication for their pain. Challenges in the recognition of NP in clinical settings possibly impacts the rate appropriate medications are prescribed for the elderly (Rastogi and Meek 2013, AGS 2009). However, one fifth of the patients had previously tried NP medication, but had ceased taking it due to side effects and/or a lack of positive results. The attempts to try alternative drugs also proved disappointing; only one third of patients continued their new medication, even though the treatment was started at a low dose with slow titration. This is reflective of an unsatisfactory armamentarium of drugs especially for older patients with NP, who are more prone to side effects and whose comorbidities may limit the choice of safe drug treatment (Schmader et al. 2010). A few of the patients did not start the recommended alternative drug for NP, which potentially reflects their fear of side effects, the ability to cope well with their pain, or a tolerable intensity of pain. Poor tolerance of centrally acting drugs is quite common among older adults (Rastogi and Meek 2013, AGS 2009, Makris et al. 2014).

Only one of the study patients used a topical treatment (lidocaine cream) for NP. Lidocaine patch (recommended especially for old and frail patients) (Finnerup et al. 2015, Sawynok 2014) is not available in Finland, and at the time of the study, capsaicin 8% dermal patch was not readily available either. According to the clinical recommendations, topical treatments are a valuable choice for peripheral NP because of their positive local effects and minimized adverse effects in patients (Malec and Shega 2015).

The use of weak opioids was unexpectedly low in the study cohort (17% used them regularly or as required). A Finnish study by Hartikainen et al. (2005), which included a random sample of adults aged over 75 years, 10% of the subjects had an opioid prescription, and opioid treatment was nearly three times higher in the age group over 85 years (16%) compared to the younger cohort of 75-79 years (6%). Our study excluded patients with cancer, which is the most common indication for opioid treatment in Finland, and this possibly explains the low use of opioids in this study. In addition, the intensity of pain in the study participants was moderate (or even mild) rather than severe. Opioids are the last choice for those with severe pain refractory to other drugs (Pergolizzi et al. 2015).

None of the patients used strong opioids in this study. This finding is in line with the current recommendations to prescribe opioids in the second or third line drugs only, or for a posttraumatic or postsurgery use for a limited time or as needed in severe breakthrough pain (Abdulla et al. 2013, AGS 2002, Makris et al. 2014, Ray et al. 2016).

Pharmacotherapy should be tailored individually considering the pain type, comorbidities and their treatment, and preferences of the patient (Mills et al. 2016). Drug interactions and any potentially inappropriate medications for older people should be avoided (Makris et al. 2014, Kersten et al.



2015). Furthermore, all evidence-based systemic drugs for NP are classified either unsuitable (class D, e.g., amitriptyline, nortriptyline, pregabalin) or suitable with specific cautions (class C, e.g., duloxetine, oxycodone, tramadol and venlafaxine) for elderly patients by Finnish Medicines Agency Fimea (Finnish Medicines Agency 2018). This is descriptive of the challenge clinicians face in the provision of safe treatment options for older adults with chronic pain.

## 6.5. The use of assessment tools

Assessment tools are an important part of a comprehensive pain evaluation (Herr 2011, Hadjistavropoulos 2007), but their usefulness among older adults has mostly been studied comparing their usefulness in the light of the patients' cognitive capabilities (Hadjistavropoulos 2014). The present study evaluated the subjective ease of use of the following four pain measures (VAS, NRS, BPI and PainDETECT). The NRS and the VAS are primarily used to assess acute and postsurgical pain (Gagliese and Katz 2003) as well as measuring pain in an outpatient primary health care setting. The VAS measurement is difficult to use among older adults, and these patients should be provided assistance in the use of the VAS scale, if the recommended NRS scale cannot be used (Gagliese et al. 2005). The BPI is recommended for evaluation of pain intensity and interference both in research and clinical practice (Dworkin et al. 2005). The PainDETECT was originally developed to detect an NP component in low back pain (CLBP) (Freynhagen et al. 2006), however, since its validation for other NP conditions, it is being used more widely.

Only subjects with well-preserved cognitive function were included in our study. We used a similar cut-point as Thielke et al. (2012). In general, our patients rated all measures "quite easy" to use on average. Somewhat surprisingly, the subjects rated the use of the multidimensional scales (PainDETECT and BPI) easier to use compared with the unidimensional measures (VAS and NRS). Multidimensional scales consist of several easy-to-reply items and cover multiple dimensions of chronic pain better (Doventas et al. 2011). In line with our results, McDonald et al. (2008) found the BPI to be easy to use by the elderly. However, the higher the pain rating was, the more difficult the scale was to use subjectively.

This study did not assess the reliability or validity of the measures and merely evaluated the subjective ease of use of the tools. The measures were used during one visit, enabling the comparison of them. The patient cohort was recruited from the general population and included a broad spectrum of various pain states, providing a representative sample of older people with pain in primary health care.

## 6.6. Follow-up

On average, the one-year follow-up did not show any significant changes in the intensity or interference of the chronic pain among older adults. In a recent Swedish population-based study of chronic pain in people aged 65 years or older, the prevalence of pain remained unchanged in the one-

and two-year follow-ups. (Larsson et al. 2017). Another Finnish study of pain in community-dwelling older adults found, that three-quarters of those with pain at baseline had similar pain at one-year and two-year follow-ups (Karttunen et al. 2015).

Both relief from pain and worsening of the pain were observed at an individual level. Our findings are in line with Larsson et al. (2017): the authors detected both recovery from pain and the appearance of new pain states with an incidence of 5,4% per year during the follow-up. In a US study of community-based six-year follow-up study including subjects aged 65 years or older, a third of the subjects reported intermittent musculoskeletal pain, and another third reported their pain to have lasted for three or more consecutive years (Thielke et al. 2012). This supports our findings; some patients experienced pain relief at the follow-up, while others suffered new pain conditions. In our study, the appearance of new pain conditions had no significant impacts on the patients' quality of life. Our relatively small sample size may be the reason for this.

Our study found that there was a regression towards the mean in both the intensity and interference of the pain. The variables that were scored in the extreme end of the scale in the first measurement, showed a tendency of being closer to the average in the second measurement. In both the NP and nociceptive groups, patients with more severe pain reported a decrease and those with milder pain reported an increase in their pain intensity.

In a recent systematic review with the follow-ups ranging from three to eight years, the participants with persistent pain at the baseline had a 2-fold risk of developing frailty during the follow-up. The presence of pain potentially contributes to the process of frailty through the reduction of mobility and nutritional intake, and the increased rate of depression and social isolation. (Saraiva et al. 2018) Frailty was not measured in our study, and the relatively short follow-up time in our study would likely have limited the ability to detect a meaningful change in frailty in any case.

Regardless of their multiple pain states and comorbidities, all of the patients in our study continued living independently at follow-up time. This mitigates the view of Duffield et al (2017) that chronic pain with multimorbidity is likely to lead to a spiral of decline in the self-management in everyday life and pose a threat to the patients' independency.

Our patients with chronic pain did not have any major mental health problems, and their anxiety and depression scores remained low at the follow-up. The finding is likely to reflect the patients' ability to cope with their pain and adapt to any limitations arising from their conditions causing pain (Mackichan et al. 2013, Sofaer et al. 2005).

The management of chronic pain rarely relieves the pain completely, although it partially alleviates the pain (AGS 2002, Herr 2011, Fine 2013). Our findings correspond with the latter.

## 6.7. Strengths and limitations of the study

The study population was identified using a structured questionnaire for older adults living independently at home who consented to preventive home visits. The approach allowed us to recruit a representative sample of independent older adults with chronic pain. Unfortunately, one third (33%) of those who were offered a nurse home visit declined due to unknown reason(s), and only approximately two thirds (62%) of those who fulfilled the inclusion criteria of this study, participated. The study population is potentially biased; we presume that those with health problems were more likely to consent to nurse home visits, and those with more troublesome pain or other health problems were more motivated to consent to the geriatrician visit. Another potential weakness of this study is the limited size of our study group. This limitation decreases the possibility to generalize our results across the population.

The study protocol included a structured interview; a detailed clinical examination of the subjects; and the use of validated questionnaires to assess intensity and interference of pain, neuropathic characteristics of pain, mood and quality of life of the subjects. All of these processes provided multifaceted data of the patients. An experienced pain specialist (MH) was consulted as required for a reliable diagnosis of NP. We also studied the ease of use of the questionnaires to confirm their suitability to this type of studies.

The same questionnaire was used at the baseline and in the follow-up. The follow-up did not cover the whole study population, as 13 % of the patients did not reply to the postal follow-up. In addition to the postal survey, a review of the patient files was used as a source of data to get a more complete view of the patients' current health status. It is also worth noting, that the follow-up time was relatively short.

Our study was not designed to assess the effects of different pain management options. Instead, we observed the use of pain treatments by GPs and by a geriatrician as required. The pain treatments were planned during the study visit according to the current clinical guidelines. The GPs were responsible for the follow-up of the treatments.

## 7. Conclusions

In conclusion, the following observations were found in this clinical study on chronic pain in older adults:

1. A neuropathic component was surprisingly common in community-dwelling older adults with chronic pain, and presents a likely reason for the challenges in treating their pain.
2. Chronic pain impaired both mobility and subjective health of the community-dwelling older adults, however, it did not deteriorate their satisfaction of life.
3. Multidimensional assessment tools were easy to use for older adults. The PainDETECT did not accurately classify the presence of neuropathic pain at an individual level, but multidimensional tools can be used to describe the varying dimensions of chronic pain.
4. One-year follow up did not show any significant changes in pain, mood or quality of life on average, although at an individual level both relief and exacerbation of pain were observed. The mental wellbeing of the patients remained high, and they were able to continue living independently regardless of their pain.

## 8. Implications for practice and future requirements in the field

This study emphasized the need of a careful assessment of pain patients, including a clinical examination and discussion of their pain history, to be able to recognize the different components of pain. A stepwise model of care is recommended to support and improve functionality in older adults, especially with multimorbidity. Pharmacotherapy of chronic pain, especially neuropathic pain, was found not to provide complete relief from pain, and new therapies are required. Population-based longitudinal studies of chronic pain and its treatment among older adults are also required.

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