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Factors Affecting the Pharmacotherapeutic Management of Chronic Non-Malignant Pain in Ageing and Elderly Populations in Ireland

A thesis submitted to the University of Dublin, Trinity College, for the Degree of Doctor of Philosophy

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Summary

Chronic non-malignant pain (CNMP) has emerged as a global health priority due to the prevalence, complexity and presentation of the condition across all age-groups, social classes and ethnicities. There is a high prevalence of CNMP in ageing and elderly populations. The condition is associated with a range of negative physical, emotional, psychosocial and financial outcomes for patients, particularly when poorly managed. Pharmacotherapeutic, non-pharmacotherapeutic and surgical interventions may be used separately or in combination to provide pain relief for patients. The World Health Organisation (WHO) Analgesic Ladder (1986) provides a framework for the prescribing of analgesics and adjuvant agents for pain conditions arising from malignancy. This framework has also been applied to the pharmacotherapeutic management of CNMP. Opioids, which are included in Step 2 and Step 3 of the ladder, are valuable agents in the management of CNMP but have several drawbacks. Opioids may precipitate adverse outcomes in ageing and elderly patients which may limit their use. There are concerns also surrounding the addiction potential of these agents or implications of long-term use. These drawbacks are familiar to patients and to General Practitioners (GPs) alike and this may affect the manner in which these agents are used for the management of pain. A mixed methods approach was used to examine the pharmacotherapeutic management of ageing and elderly patients with CNMP and to describe the GP and patient factors that influence use of analgesics, particularly opioids.

A systematic review of guidelines directing the prescribing of opioids for CNMP in primary care evaluated the quality of development and clinical content of these guidelines. Eleven guidelines were included in the review; six were developed in the USA, two in Canada, one in the UK and two in Australia. The methodological rigour of guideline development, quality of presentation and clinical content of these 11 publications varied considerably. Since guidelines are frequently used by GPs to support prescribing decisions, poor quality guidelines may hamper effective decision making and ultimately impact upon the quality of pharmacotherapeutic management.

Examination of a national pharmacy claims database, the Health Service Executive-Primary Care Reimbursement Service (HSE-PCRS) database, identified the prevalence of analgesic use in the General Medical Scheme (GMS) eligible

population aged 55 years and older and also described trends in analgesic and concurrent medication use between 2003-2011. A cross-sectional analysis of The Irish Longitudinal Study of Ageing (TILDA) dataset provided a socio-demographic description of a nationally representative population aged 50 years and older with non-malignant pain. Approximately 36% reported a pain condition, 28% of whom reported an analgesic medication. Non-opioids, systemic non-selective NSAIDs, moderate opioids and adjuvant medications were the most commonly used analgesics according to the databases. The prevalence of sedating agent and opioid co-prescribing, an inappropriate prescribing practice, was greater than laxative and opioid co-prescribing, an appropriate prescribing practice, in both databases. Examination of the population reporting pain in TILDA identified that being female, taking ≥5 medications, being retired or unemployed/disabled/carer, having good/fair self-rated physical health, having moderate or severe pain, having pain that restricted daily activity, reporting ≥2 chronic diseases and being a current or past smoker were significant factors associated with analgesic use. Pain intensity was not identified as being associated with the use of a weak, moderate or strong opioids relative to a non-opioid/NSAID/ adjuvant medication.

Semi-structured interviews with members of Chronic Pain Ireland (CPI) and GPs investigated the influences upon analgesic use in CNMP. Clinical considerations such as the efficacy of analgesics, adverse effects and co-morbidities were key factors for GPs when constructing and managing an analgesic regimen. Similarly, beliefs about medications, pain severity, limitations on daily activity, adverse outcomes, implications of long-term use and access to non-pharmacological interventions were important considerations for individuals with CNMP. Both GPs and patients described the impact of organisational and structural barriers of the Irish healthcare system in the management of CNMP.

Changes in practice behaviours of healthcare professionals working in primary care coupled with health system reforms are required to improve the quality and consistency of pharmacotherapeutic management of CNMP in primary care. Publication of national guidelines with recommendations on the prescribing of analgesics, particularly opioids, for ageing and elderly patients with this condition may provide assistance and support to GPs. Enhanced provision of specialised pain management services in primary care may also improve patient outcomes.

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Table of Abbreviations

AGREE II (instrument)	Appraisal of Guidelines for Research and Evaluation (instrument)
AGS	American Geriatric Society
BNF	British National Formulary
BPS	British Pain Society
CASP-19	'Control', 'Autonomy', 'Self-realisation' and 'Pleasure'
CBT	Cognitive Behavioural Therapy
CES-D	Centre for Epidemiologic Studies Depression (Scale)
CNMP	Chronic Non-Malignant Pain
COX	Cyclooxygenase
CPG	Clinical Practice Guideline
CPI	Chronic Pain Ireland
DTSS	Dental Treatment Services Scheme
DPS	Drug Payment Scheme
DoHC	Department of Health and Children
ESRI	Economic and Social Research Institute
GMS	General Medical Scheme
GP	General Practitioner
HSE-PCRS	Health Services Executive - Primary Care Reimbursement Service
IASP	International Association for the Study of Pain
IMF	Irish Medicines Formulary
LTI	Long Term Illness Scheme
NM	Non Malignant (Pain)
NSAID	Non-Steroidal Anti-inflammatory
OBD	Opioid Induced Bowel Dysfunction
PHN	Public Health Nurse
PMPs	Pain Management Programmes
PSI	Pharmaceutical Society of Ireland
QoL	Quality of Life
RRR	Relative Risk Ratio
STOPP/START	Screening Tool of Older Person's Prescriptions /Screening Tool to Alert doctors to Right Treatment
SSRI	Selective Serotonin Reuptake Inhibitor
TCA	Tricyclic Antidepressant
TENS	Transcutaneous Electrical Nerve Stimulation
TILDA	The Irish Longitudinal Study on Ageing
VHI	Voluntary Health Insurance
WHO	World Health Organisation

Preface

This work was funded by the Health Research Board (HRB) in Ireland under Grant No. PHD/2007/16. I was a full-time PhD student in the HRB PhD Scholars programme in Health Services Research from September 2010 to September 2014. This is a four year structured PhD programme with taught modules in year 1 and the research project commencing in Year 2 and finishing in Year 4. The aim of the programme is to improve health through quality healthcare delivery and management in the Irish system. It is proposed that this will be achieved through the development a critical mass of HSR expertise through PhD scholars who will excel in research, policy evaluation and translation of evidence into practice. The HRB Scholars are required to submit a PhD research proposal for approval by the Steering Committee at the end of Year 1 of the programme. A comprehensive overview of the HRB PhD Scholars Programme is provided in *Appendix A*.

I qualified as a pharmacist from Trinity College Dublin in 2009 and registered with the Pharmaceutical Society of Ireland in 2010. Since registration, I have worked as a community pharmacist in a suburban pharmacy on evenings, weekends and holiday periods. This pharmacy serves a large ageing and elderly population. I initially developed an interest in the topic of chronic pain management based on a number of observations in practise. I noticed a heterogeneous approach to the prescribing of analgesic medications for ageing and elderly populations with chronic pain by the prescribers in the area. In particular, there was variation in the initiation and maintenance of patients on stronger opioid formulations. Furthermore, when discussing the issue of pain management with patients, a number described the challenges in gaining access to specialist consultation or additional services such as physiotherapy or occupational therapy.

Upon consultation with the literature on the subject, a number of recent publications from Ireland, Europe and the United States highlighted the prevalence, burden and complexity of chronic pain together with problems associated with effective analgesic management of the condition in ageing and elderly populations. This initial review of the literature on the area highlighted that this subject matter required additional attention and necessitated a literature review to identify the research gaps on this topic in Ireland and formulate a research question.

Chapter 1. Literature Review

Why are we weigh'd upon with heaviness,
And utterly consumed with sharp distress,
While all things else have rest from weariness?
All things have rest: why should we toil alone?

The Lotos Eaters from *Poems* (1832)
Alfred, Lord Tennyson (1809-1892)

1.1. The Concept of Pain

Pain is a ubiquitous human experience that affects behaviour and emotion (1). It is essential for human survival and evolution, acting as a mechanism for sensory detection which may trigger the fight-flight mechanism. The description and understanding of pain has evolved over time, along with our approach to management. Aristotle (384 BCE-322 BCE) thought pain to be an emotion arising from evil spirits entering the body following an injury. Hippocrates (460 BCE-370 BCE) described pain as an imbalance of the vital fluids. In recent decades, pain has been defined as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage' (2, 3). Pain is a global health priority due to the prevalence, complexity and presentation of the condition across all ethnicities, social classes and age groups (4). Such are the negative physical, emotional, economic and psychological impacts of pain that the Declaration of Montreal (2008) established that access to pain management is a fundamental human right. It is therefore incumbent upon governments and healthcare institutions to develop and implement policies and systems to ensure that this right is satisfied (5).

Pain may be categorised as acute or chronic (2, 5). Acute pain arises from activation of nociceptive transducers at the site of tissue damage. This is a normal, predicted, physiological response to an adverse chemical, thermal or mechanical stimulus associated with surgery, trauma and acute illness (6). Acute pain is an important biological function as it alerts the individual to the potential for further harm or informs the individual of the extent of the injury. This then activates protective reflexes in the individual to prevent further harm. Acute pain may precede the onset of chronic pain, and this transition beginning with the occurrence of pathophysiological and histopathological alterations (7).

Chronic pain of malignant or non-malignant origin differs from acute pain by the duration for which the condition exists (8). Chronic pain conditions are associated with significant physical and psychological morbidities that diminish the quality of life of the patient. Chronic pain is therefore a more significant public health burden than acute pain (4, 9). Chronic malignant pain, associated with a cancer diagnosis, may have inflammatory, neuropathic, ischaemic or compression features (10). A systematic review and meta-analysis of 52 studies investigating the prevalence of pain in patients with cancer has highlighted differing estimates of prevalence based on the stage of cancer or the use of anti-cancer treatments. Studies including patients after curative treatment identified a 33% prevalence of pain; a prevalence of 59% has been reported for patients while receiving anti-cancer treatment, while prevalence amongst patients with advanced or terminal disease was 64% (11). Approximately one-third of cancer patients report pain of moderate or severe intensity (11). The prevalence and severity of cancer pain is universally acknowledged by healthcare professionals and the provision of analgesia is a key consideration in palliative care plans (12).

Chronic non-malignant pain (CNMP) is defined as pain that exists beyond an expected timeframe for healing and is also referred to in the literature as intractable or persistent pain (13). The duration of pain which characterises it as chronic has been disputed by various sources. Bonica, a founding father of the study of pain management, defined CNMP as that which persists a month beyond the usual course of acute disease or beyond a reasonable time for any injury to heal. It may also be associated with chronic pathologic processes that causes continuous pain or pain at intervals for months or years (13). The American Society of Interventional Pain Medicine (ASIPP) defines CNMP as pain that persists for 6 months after an injury and beyond the usual course of an acute disease or a reasonable time for injury to heal (14). The International Association for the Study of Pain (IASP) define it as pain without apparent biological value, that has persisted beyond the normal tissue healing time and which persists for a period of 3 months or longer (15, 16). The differing definitions of duration for CNMP present challenges in presenting estimates of prevalence for the condition despite this information being an essential pre-requisite for the proper planning of health services for the condition (17).

Breakthrough pain is episodic in nature and produces a transient increase in pain to greater than moderate intensity (18). The concept of breakthrough pain was initially described in the context of cancer pain and then applied to CNMP (19). It commonly occurs in patients with advanced diseases or poor functional status. It can arise from pain originating in the vertebral column and to a lesser extent from other weight-bearing bones, or it could be pain originating from the nerve plexuses or nerve roots (20). Episodes of breakthrough pain may require the administration of short-acting medications to manage these transient increases in pain intensity (21).

Pain, therefore, is an inherent feature of the human experience and at times essential for survival. However, pain that extends beyond acute episodes may be debilitating for individuals and can produce negative physical, emotional, psychological and social outcomes, particularly when poorly managed (22).

1.2. Prevalence, Associated Factors and Impact of Chronic Non-Malignant Pain

Establishing the exact prevalence of CNMP in a population is challenging since pain is frequently a symptom arising from another condition and may be underreported by both healthcare professionals and patients for this reason. Furthermore, the differing definitions for the duration of the condition, greater than 3 or 6 months, may also produce differing estimates of prevalence (23). A variety of sociodemographic factors may produce a higher prevalence of CNMP in certain populations including, *inter alia* gender, age, educational status, mental health, marital status, health insurance and alcohol consumption (24-29).

The European Survey of Pain (Breivik et al) and the Prevalence, Impact and Cost of Chronic Pain (PRIME) study in Ireland provides the most recent approximations of the prevalence of CNMP in community dwelling adult European and Irish populations (30, 31). Breivik et al conducted a computer assisted telephone survey (n=46,934), with in-depth interviews with 4,839 respondents. Prevalence of chronic pain, which was defined as >6 months, was in the range 12-30%, most prevalent in Norway (30%), Poland (27%), Italy (26%), and least prevalent in Spain (12%), Ireland (13%) and the UK (13%) (31). These estimates

of prevalence do not differ greatly from national investigations of chronic pain prevalence within a number of these European countries. An epidemiological study of Norwegian adults aged 18 years and older, in which chronic pain is defined as a period of 3 months or longer, identified a prevalence of 30%, while a study of the adult Spanish population (n=5,039) identified a prevalence of 17% (32, 33). The PRIME study (n=1,204), which defined chronic pain as ≥3 months, reported a prevalence of 36% (30). The Pfizer Health Index, an annual survey of health perceptions, attitudes and behaviours in Ireland, reported a 4% incidence of chronic head or back pain for the period 2007-2014 based on a sample of 8,174 Irish respondents aged 16 years and older; of these, 40% reported moderate pain and 46% reported severe pain (34). These estimates of prevalence are comparable with the USA, where the Institute of Medicine (IOM) has reported that one third of the adult population have CNMP, with approximately 40% of that population reporting moderate to severe pain (35, 36).

The increased burden of chronic pain amongst ageing and elderly populations has been attributed to the development and progression of chronic degenerative conditions associated with the ageing process (37). CNMP may be particularly debilitating for ageing and elderly patients, as, in addition to the psychological and physical impairments of the condition, it may also produce gait disturbance, cognitive decline and result in accidents (23). Again, epidemiological studies have produced conflicting estimates of the prevalence of CNMP amongst ageing and elderly populations. A number of studies have identified a continued increase in pain prevalence with age. Elliott et al reported a prevalence of 30% amongst a population aged <50 years increasing to >60% for individuals aged ≥50 years, peaking in the seventh decade (n=2,184) (38). Results from the Jerusalem Longitudinal Study of Ageing (n=277) recorded a prevalence of chronic back pain of 44% amongst those aged 70 years and older, increasing to 58% at 77 years (39). A UK longitudinal study of joint pain (n=2,403) reported a prevalence of 83% amongst those aged >75 years, the prevalence being associated with age and female gender (40). However, several epidemiological studies have reported a decrease in prevalence with age. The North Staffordshire Osteoarthritis Project (NorStop) (n=11,230) identified an inverse relationship between age and prevalence of pain.

Similarly, Dionne et al indicated that there is a curvilinear association between chronic back pain and age, decreasing from 60 years onwards (41).

Finally, a number of studies have reported that chronic pain peaks in the seventh and early years of the eighth decade and decreases thereafter (42, 43). Helme et al postulated that this trend may be associated with selection bias of studies which focus primarily on the community dwelling elderly and omit the population in residential care settings. Stoicism of elderly patients and an increased tolerance towards painful conditions have also been suggested to explain these findings (42). Regardless of the precise estimates or trends amongst the ageing and elderly, it is apparent that CNMP is widespread amongst this population and constitutes appropriate recognition by healthcare professionals and policymakers.

CNMP has a substantial economic impact on society owing to its prevalence and the significant effects of the condition on patient's health and functionality (44). The condition may require that the individual accesses healthcare services more frequently, placing an increased burden on the resources of the healthcare system than before. This individual may also be unable to participate in the workforce, thereby diminishing their contribution through the taxation system. The direct and indirect costs for the individual with the CNMP are summarised in *Table 1-1*. Direct costs are those associated with medications, medical care, hospitals, pensions and benefits while indirect costs are considered to be those associated with loss of productivity and lost earnings. Productivity losses may be considered in terms of inability to work or premature retirement. Indirect costs can be difficult to estimate due to difficulties associated with measurement of costs associated with sick days, work disability, the impact of morbidity and loss of contributions towards insurance schemes and government welfare (30, 45). Poor management of CNMP conditions contributes to the economic impact, indicating that improved management of the condition may address the economic burden of the condition to the healthcare system and the wider economy (46).

Table 1-1: Typical classification of costs in health economics

Direct Costs	***Healthcare Utilisation:*** Treatment costs, diagnostic tests, inpatient stays, outpatient consultations
	Social Services: Home carers, day care provision
	Private Expenditure: Over-the-counter medications, private domestic care, purchase of goods and services
Indirect Costs	***Lost Productivity:*** Early retirement, part-time, not full-time work, absenteeism/compassionate leave
	Lost Earnings: Early retirement (patients and caregivers), part-time, not full-time work (patients and caregivers)
	Lost tax revenue: Direct taxes, indirect taxes
Intangible Costs	***Reduced quality of life:*** Lost leisure opportunities through reduced morbidity, lost social opportunities, stress, anxiety, depression

The condition has been estimated to cost the USA more than $600 billion per annum in direct medical treatment and lost productivity costs (47). The Australian National Pain Strategy Management recently estimated that pain affects one in five Australians in their lifetime, costing the Australian economy $34 billion per annum and making it the third most expensive healthcare problem in the country. Based on national prevalence estimates for the condition, it is calculated that CNMP costs €1.9 billion to the Irish economy from primary care management to the point of referral to a multidisciplinary pain clinic (48).

The National Health and Wellness Survey investigated the impact of chronic pain on the labour force and workforce status amongst individuals reporting pain from the United Kingdom, France, Spain, Italy and Germany. Moderate and severe daily pain was associated with a 10 and 20 point reduction respectively in participation in full time employment among this European workforce (49). The recent Survey of Pain in Europe (Breivik et al [n=46,934]) indicated that 60% of the European population with CNMP do not work outside the home; approximately 20% have become unemployed due to their chronic pain condition and those in employment were absent from work for 7.8 days in a 6 month period (31). Similarly, Blyth et al reported that 28.5% of the Australia population reporting pain were restricted in their work due to pain conditions, while 68.5% of these had reported absenteeism due to their pain condition (50). This evidence suggests that

chronic pain limits workforce participation to a substantial degree. Absenteeism and unemployment reduces the potential economic contribution of this individual, while the pain condition may also necessitate intensive management in the healthcare system; it is the combination of these two elements that results in the high cost to society of CNMP.

1.3. Physiological Models of Pain

Theory surrounding the physiological nature of pain and the neural mechanisms precipitating the condition have been hypothesised since the 19th century; these models include the specificity, intensity (or summation), pattern and gate control theories of pain (51, 52). Current models reflect the complex physiological transmission pathways involved in pain processing and the greater awareness of the implicit psychological and environmental factors associated with pain (52).

The specificity theory of pain proposed that injury activates the pain receptor which creates pain impulse in the spinal cord pathway to the brain where it is recovered by a pain centre (53). The theory postulated that a dedicated fibre leads to a pain pathway, connecting to the sensory compartment of the brain. The theory emanates from Descartes, a hypothesis which he published in the Treatise of Man (1602), that pain arose from a combination of neural phenomena and perceptual experiences (54). The intensity theory has been postulated at various points in the physiological examination of pain process although it was first conceptualised in the 4th century BCE by Plato. The theory proposed that stimulation of sensory input from the stimulation of nerve fibre occurred in the grey manner of the spinal cord. However, the theory did not indicate the role of the brain in the pain perception and modulation function and is at odds with the mechanism proposed by the specificity theory (54).

The Melzack Gate Control Theory (1965) proposed that the CNS participated in the perception of pain through an integrated efferent and afferent network that becomes activated through noxious stimuli (2). The gate control theory proposes that the transmission of nerve impulses from afferent fibres to the spinal cord is modulated by a spinal gating mechanism in the dorsal horn. The spinal gating mechanism is influenced by the amount of activity in large and small

diameter fibres and by nerve impulses that descend from the brain. A specialised system of large diameter rapidly conducting fibres activates selective cognitive processes that can influence the modulating properties of the spinal gating mechanism. When the output of the spinal cord transmission exceeds a critical level, the neural area that underlies the patterns of behaviour and experience characteristics of pain is activated. A development in the gate control theory proposed that excitatory amino acids may permanently alter spinal cord function producing chronic pain symptoms (53).

Sherrington initially proposed this model of nociception through primary afferent receptors that are activated by noxious stimuli (55). Primary afferent nociceptors respond to thermal, mechanical or chemical stimulation of nociceptors located throughout the body on skin, muscle, connective tissue, blood vessels and viscera (56). These activate nerve fibres which terminate in the dorsal horn, this acts as a gate regulating the flow of peripheral afferent activity. The dorsal horn is arranged as 10 lamina in somatotropic order, a spatial arrangement within the nervous system whereby the sensory information structure is maintained throughout the spinal cord and the brain. Aδ fibres are myelinated, thermal and mechano thermal fibres which are 2-5 μm in diameter. These fibres innervate Lamina I and II of the dorsal horn. C fibres are non-myelinated and are 0.4 -1.2 μm in diameter and terminate in Lamina I and II. The cell bodies of these primary afferent neurons are located in the trigeminal and dorsal root ganglia (DRG) (55). Neurotransmission in the dorsal horn requires excitatory transmitters are released from the primary afferent fibre to activate neurons within the spinal cord. Inhibitory transmitters are also released from interneurons of the spinal cord and supraspinal sources (56). A number of these substances activate T-fibres transmitting information to the thalamic and cortex centres of the brain, allowing the individual to plan an action removing the stimulus. Descending pathways from the midbrain and brainstem have an inhibitory effect on dorsal horn transmission, this process is mediated by enkephalins, inhibitory amino acids and amines. A summary of the types and activities of neurotransmitters is provided in *Table 1-2* (57).

Table 1-2: Chemical required for transmission of pain and comment on location and purpose

Amines	Noradrenaline; 5-HT (5-Hydroxytryptamine): Descending modulation of pain.
Endogenous Opioid Peptides	Enkephalins, B-Endorphins; Inhibitory effect by binding to opioid receptors.
Non-Opioid Peptides	Substance P, Galanin, Cholecystokinin and others: Within the dorsal root ganglion (DRG) of C-fibres. Associated with inflammation, antinociception and transmission in visceral pain respecitvely.
Excitatory Amino Acids	Glutamate; Active on NMDA and non-NMDA receptors: Required for development, memory and neuronal plasticity.
Inhibitory Amino Acids	GABA & Glycine: Regulates behaviour associated with non-noxious stimuli.
Others	Cannadinoid; involved in anti-nociception.
	Nitric Oxide: Peripheral and Central Sensitisation and associated NMDA activity.

Opioids exert an analgesic effect partly by activation of the descending inhibitory pathways. There are four types of opioid receptors involved in the transmission of pain; these receptors also act as targets for a number of analgesic medications (58). Receptors are located in five general areas of the CNS responsible for integrating pain information; these are the brainstem, the medial thalamus, the spinal cord, the hypothalamus and the limbic system, in addition to being found in the peripheral nervous system and immune cells. μ-opioid receptors (Mu), of which there are the subtypes μ1 and μ2, are found in the brain stem and the thalamus (59). Activation of μ opioid receptors may produce undesirable effects such as respiratory depression, euphoria, sedation, diminished GIT mobility and physical dependence. Kappa (κ) opioid receptors are located in the limbic and dineuphalic area of the brain and spinal cord. Activation of κ opioid receptors produces spinal analgesia, sedation, dependence and respiratory depression. δ (Delta) opioid receptors are located primarily in the brain; activation produces dysphoric and psychomimetic effects when activated (60).

In addition to the duration of the condition, pain can be further classified on the basis of the underlying pathophysiology and so may be neuropathic or

nociceptive (61). Nociception is the physiological process of transduction, transmission and modulation of neural signals arising from an external noxious-stimulus; it arises from activation of Aδ and C receptors by noxious stimuli and occurs in an otherwise healthy nervous system (62). Visceral pain arises from activation of nociceptors in the thoracic or abdominal viscera, while somatic pain arises from activation of peripheral nerve endings of nociceptive neurons which are located in structures such as tendons, bones, ligaments and blood vessels (63). Chronic nociceptive pain activates the central and peripheral nervous system causing allodynia (pain due to stimulus that does not normally provoke pain), hyperalgesia (increased pain sensitivity), and hyperpathia (abnormally exaggerated subjective response to painful stimuli that can diminish normal functioning) (7).

Neuropathic pain describes a variety of conditions affecting the peripheral or central nervous system and occurs when these systems become impaired (62). It may be caused by trauma, inflammation, metabolic diseases (e.g. diabetes), infections (e.g. herpes zoster) and primary neurological conditions. This type of pain becomes chronic when pathophysiological changes occur independently of the initial causative factor. Central sensitisation, a state of spinal neuron hyper-excitability, can then persist causing the pain to become chronic (64). Epidemiological studies estimate that neuropathic pain affects 1% of the UK population and 2% of the US population, although, these are proposed to be underestimates of the true prevalence of the condition owing to inadequate methods of detection of this type of pain (65).

1.4. Medical Models and Chronic Non-Malignant Pain

The biomedical model has traditionally been used as a framework for explaining disease processes. This model views the body as a biological entity in which disease emerges following a malfunction of a physiological process. The biopsychosocial model, proposed by Engel, offers a non-reductionist model for disease and considers the complex interaction of biological, psychological and social factors with health (51, 66, 67). An understanding of pain gained through the biopsychosocial model, as presented in *Figure 1-1*, provides an insight into the complex modalities of health and illness with the patient's medical or biological

circumstances interacting with their psychological well-being, which also relates to the social dimensions of that individual (66). The biopsychosocial model has been criticised for having an excessive individualistic focus, enforcing strict divisions between biology, psychology and society and allocating a central role to the biological mechanisms of the model (68-70). Nonetheless, it remains a starting point for understanding the complex matrix of the factors that contribute towards health. It highlights that pain is not limited to a nociceptive, physical experience but involves a number of human dimensions such as emotion, behaviour, cognition and socialisation (71).

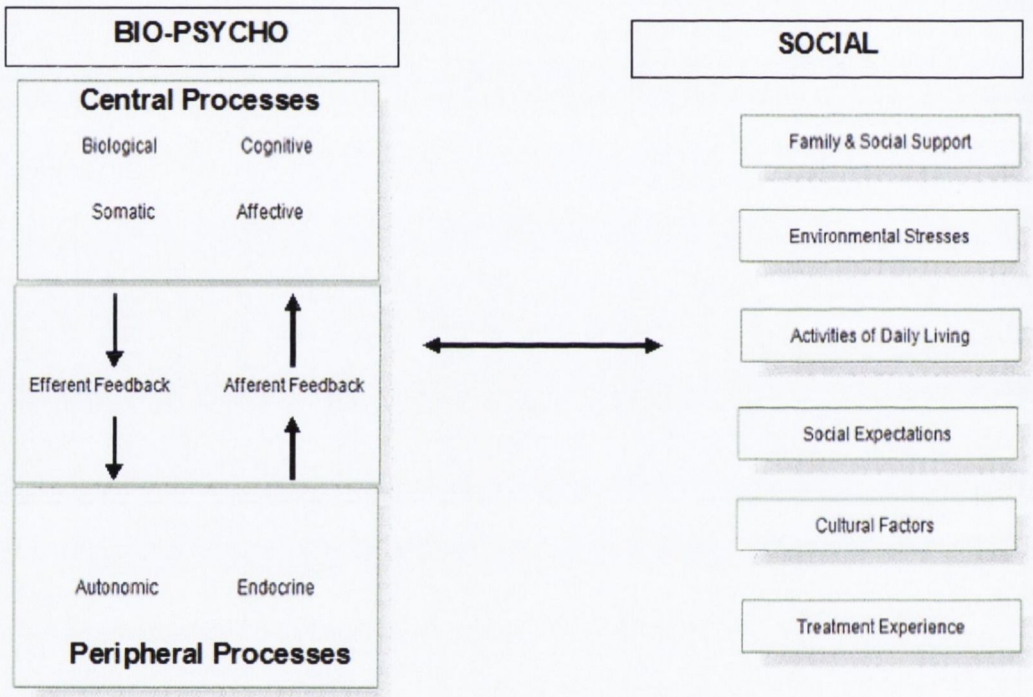


Figure 1-1: Biopsychosocial model of pain

Loeser's four component model of chronic pain (1982) represents another understanding of the condition in light of the inclusion of the added human dimensions of suffering and behaviour, as it relates to the physical features of the pain condition (*Figure 1-2).* The model places the clinical experience of pain at the centre, those which impact upon the individuals' behaviours. The model proposes that the hierarchy of nociception leading to behavioural and emotional disturbances may perpetuate a cycle of nociception, distress and disability for the patient (66). Although this model does not detail the clinical steps needed to effectively manage

the biopsychosocial domains of chronic pain, it depicts the enveloping layers of suffering, positive coping strategies and maladaptive behaviours that are often demonstrated by individuals with chronic pain (72).

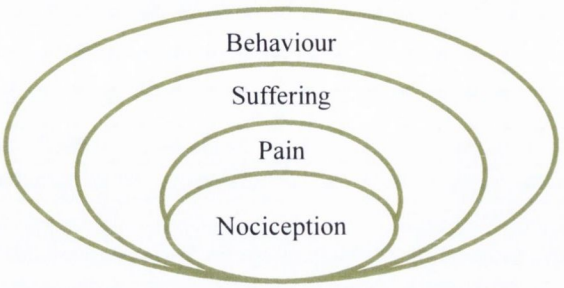


Figure 1-2: Loeser's model of pain (66)

Anxiety and depression are strongly associated with CNMP (73, 74). CNMP impacts upon an individual's ability to complete tasks and sometimes can affect cognitive function, this may lead to poor performance of tasks giving rise to frustration for the patient (75). It has been proposed that pain and depression interact bi-directionally, with worsening pain producing a negative impact on day-to-day functioning of the individual and yielding a diminished sense of self for the pain sufferer (76). The causal relationship between pain and depression has been long debated by clinicians; it has been argued that chronic pain is a variant of depression or that chronic pain and depression are both associated with an underlying affective spectrum disorder (77, 78). Von Korff et al described depression and pain as being 'reciprocal psychological and behavioural [...] involving both processes of illness expression and adaptation' (66, 79).

The IASP have reported a one in five prevalence of anxiety disorders amongst those with CNMP conditions (80). The WHO have reported that patients with chronic pain managed in primary care are four times more likely to have co-morbid anxiety or depressive disorder than pain-free primary care patients (81). The Midlife Development in the United States Survey (MIDUS) investigated associations between pain and psychiatric disorders in a large sample (n=3,032) representative of adults aged 25–74 in the United States population. They reported a prevalence of 35% for psychiatric disorders amongst CNMP sufferers compared to 18% in the general population.

Individuals with chronic pain also have a higher risk for suicide; a review of 12 studies investigating the association between suicide and chronic pain found that relative to controls, risk of death by suicide was double (82). The lifetime prevalence of suicide attempts was between 5% and 14% in individuals with chronic pain, while the prevalence of suicidal ideation was approximately 20% (83). In common with pain, anxiety and depression may be managed through a combination of pharmacological and non-pharmacological interventions. There is some degree of overlap between the pharmacotherapeutic interventions used for both conditions including, neuroleptics, benzodiazepines, anticonvulsants and antidepressants (80). Additional non-pharmacotherapeutic interventions, such as Cognitive Behavioural Therapy (CBT), may further equip the individual with the necessary skills to address both the psychological and physical implications of the condition (84).

1.5. Assessment of Pain Conditions

Pain may be assessed using self-report, observational or physiological measures. Observational measures require a third party to assess the patient's pain experience, while physiological measures assess clinical parameters such as heart rate, sweating, breathing and muscle tension indicating the stress response to the pain (85, 86). Self-report measures are considered the gold standard for assessment of patients given the subjective nature of pain. A number of self-report instruments have been developed and validated to assist clinicians in establishing pain severity, to determine progression of pain and to establish the efficacy of pain management interventions. These self-report measures may be single or multidimensional in their focus (87, 88). One-dimensional scales measure only pain intensity and are useful in acute pain when the aetiology is clear. Multidimensional scales measure the intensity, nature, and location of pain, as well as, in some cases, the impact that pain is having on a patient's activity or mood. Multidimensional scales are useful in complex or persistent acute or chronic pain. For such instruments to be of benefit to the healthcare professional they must be reliable, valid instruments and appropriate for implementation in the practice setting (89). Factors such as age, verbal fluency and the ability of the patient to understand the language in which the

scale is presented, all influence the type of pain assessment scale that may be used with a patient (90). For patients with cognitive impairment, or those resident in long-term care facilities, regular assessments combined with short direct-observation tools may provide the best assessment of the patient's pain level (87). Regular evaluation is required to take account of variations in the presentation and severity of symptoms and in the progression of the condition (87). *Table 1-3* provides an outline of a number of commonly used assessment instruments and presents information on their reliability, validity and target population.

Table 1-3: Examples of pain assessment instruments; description, reliability and validity

Instrument	Description	Validated Populations	Test-Retest Reliability	Construct Validity
Instruments to Assess Pain Level (91, 92)				
Visual Analogue Scale	Measures pain intensity using a number of values presented on a horizontal line, usually 100 mm in length. Requires 1 minute to administer.	Adults with pain	High test-retest reliability coefficient (r = 0.93) before and after a regular clinic visit. Illiterate patients had test-retest correlation coefficients of 0.71 (93).	Highly correlated with a 5-point verbal descriptive scale ("nil," "mild," "moderate," "severe," and "very severe") and numeric rating scale (with response options from "no pain" to "unbearable pain"), with correlations ranging from 0.71–0.78 and 0.62–0.91, respectively) (93).
Numeric Rating Scale	Scale labelled 0-10, 0 representing no pain, 5 representing moderate pain and 10 representing worst pain.	Adults with pain	High test–retest reliability has been observed in both literate and illiterate patients with rheumatoid arthritis (r = 0.96 and 0.95, respectively) before and after medical consultation (94).	Highly correlated to the VAS in patients with rheumatic and other chronic pain conditions (pain >6 months): correlations range from 0.86 to 0.95 (94).
(Wong Bake) Faces Pain Scale	Series of faces, each face representing increasing levels of pain. Faces pain scales are popular self-report measures of pain intensity in acute, procedural, and recurrent pain (95).	3 years and older	Test-retest reliability, $r > 0.5$ (95)	Correlation, $r > 0.7$, with another self-report pain scale given at the same time(95).

Assesses Dimensions of Pain (96)				
Brief Pain Inventory (BPI)	Measures intensity of pain and interference of pain with daily activities.	Adults with pain	Data collected from non-cancer pain patients was comparable to that reported in the literature for cancer patients (coefficient alphas were greater than 0.70) .	A confirmatory factor analysis study was completed in a sample of individuals diagnosed with HIV/AIDS and cancer patients. Two-factor and three-factor models (i.e., pain intensity, activity interference, and affective interference) were developed based on the hypothetical design of the instrument. The results of this study support a three-factor representation of the BPI, and the originally hypothesised two-factor structure (97)
McGill Pain Questionnaire	Measures qualities of pain; contains 20 subclasses of words divided into 4 subscales which describes the sensory, affective and evaluative aspects of pain and a 5-point intensity scale. Requires 5-15 minutes for administration	Adults with chronic pain	Cronbach's alpha of 0.74 for the sensory pain scale and 0.62 for the affective pain scale (98).	A study of 262 patients with chronic pain indicates a test-retest reliability of 0.62 - 0.93, and responsiveness to change, standardized response mean > 0.80 for patients with musculoskeletal and rheumatic pain (98).
West Haven-Yale Multidimensional Pain Inventory (WHYMPI)	Fifty-four item questionnaire that measures severity and interference of pain and the individual's response to pain and impact on daily activities. Consists of 12 subscales assessing: interference, support, pain severity, self-control, negative mood, punishing responses, solicitous responses, distracting responses, household chores, outdoor work, activities away from home and social activities. Requires 5-10 minutes to administer.	Adults with pain	Internal reliability coefficients ranges from 0.70 to 0.90. Test-retest reliabilities of these scales over a 2-week interval range from 0.62 to 0.91 (99).	Confirmatory and exploratory factor analytic procedures revealed that the WHYMPI scales significantly correlated with several criterion measures of anxiety, depression, marital satisfaction, pain severity, and health locus of control (99).

1.6. Management of Chronic Non-Malignant Pain

Pain management may be achieved through a variety of methods such as pharmacotherapeutic interventions, surgery, physiotherapy and a number of non-pharmacotherapeutic methods encompassing active and passive strategies (100).

1.6.1. Pharmacotherapeutic Management of Chronic Non-Malignant Pain

Analgesics are those pharmacological agents that alter the physiological pain pathway without requiring a loss in consciousness to produce the effect (101). The World Health Organisation (WHO) presented the Analgesic Ladder in 1986 as a framework for the management of pain associated with malignancy (102, 103). In the absence of an internationally available analgesic prescribing framework specific to CNMP, it remains the single-most comprehensive guideline for the pharmacotherapeutic management of pain available to non-specialists (104). It is widely used by healthcare professionals having been translated into 22 languages (105). The WHO Analgesic Ladder provides information on effective patient assessment and clinical considerations prior to and following introduction of an analgesic medication (105). The ladder responds to the intensity of pain symptoms, with analgesics increasing in potency across each step of the ladder (105).

There are, however, a number of limitations associated with the implementation of the WHO Analgesic Ladder. The most significant limitation relates to the specificity of the ladder to malignant pain, with, at present no adaptations published by the WHO for non-malignant or acute pain (106). Secondly, there has been debate as to the clinical usefulness of Step 2 opioids for mild to moderate pain. A meta-analysis and a systematic review of 6 randomised control trials on the efficacy of NSAIDs (Step 1) for cancer pain in comparison to Step 2 opioids has indicated that there is no difference in analgesia attained between these two steps of the ladder (107, 108). This has raised the question as to whether the ladder should be modified to a two-step model, with opioids for mild to moderate pain appearing in Step 1 of this revised model. Finally, Step 3 of the ladder which endorses the use of strong opioids for severe pain, does not differentiate between controlled release or fast-acting agents (106).

A proposed modification of the ladder to accommodate those with CNMP or contraindications to specific medications includes the addition of nerve blocks, epidurals, spinal stimulators as an additional Step 4 (102). This adapted ladder proposes that neuropathic pain should be considered distinct to that of nociceptive origin, with a separate treatment algorithm appropriate for effective management. There has also been a further proposal to modify the individual steps of the ladder to a platform, extending the concept of pain management from a linear approach to a three dimensional perspective of the patient, incorporating non-pharmacological interventions (105). Modification of the ladder in this way extends the concept of pain management to a holistic philosophy divergent from the one dimensional management offered by pharmacological interventions, one which incorporates emotional and cognitive domains related to pain (105). Such changes reflect the considerations presented within the biopsychosocial model and are distinct from the medical model of disease. The quality and efficacy of patient care may benefit from a non-reductionist, considered approach to pain management, which is not exclusively focused on pharmacotherapeutic interventions. The WHO Analgesic Ladder, including the proposed introduction of a Step 4 is presented in *Figure 1-3* (105, 106).

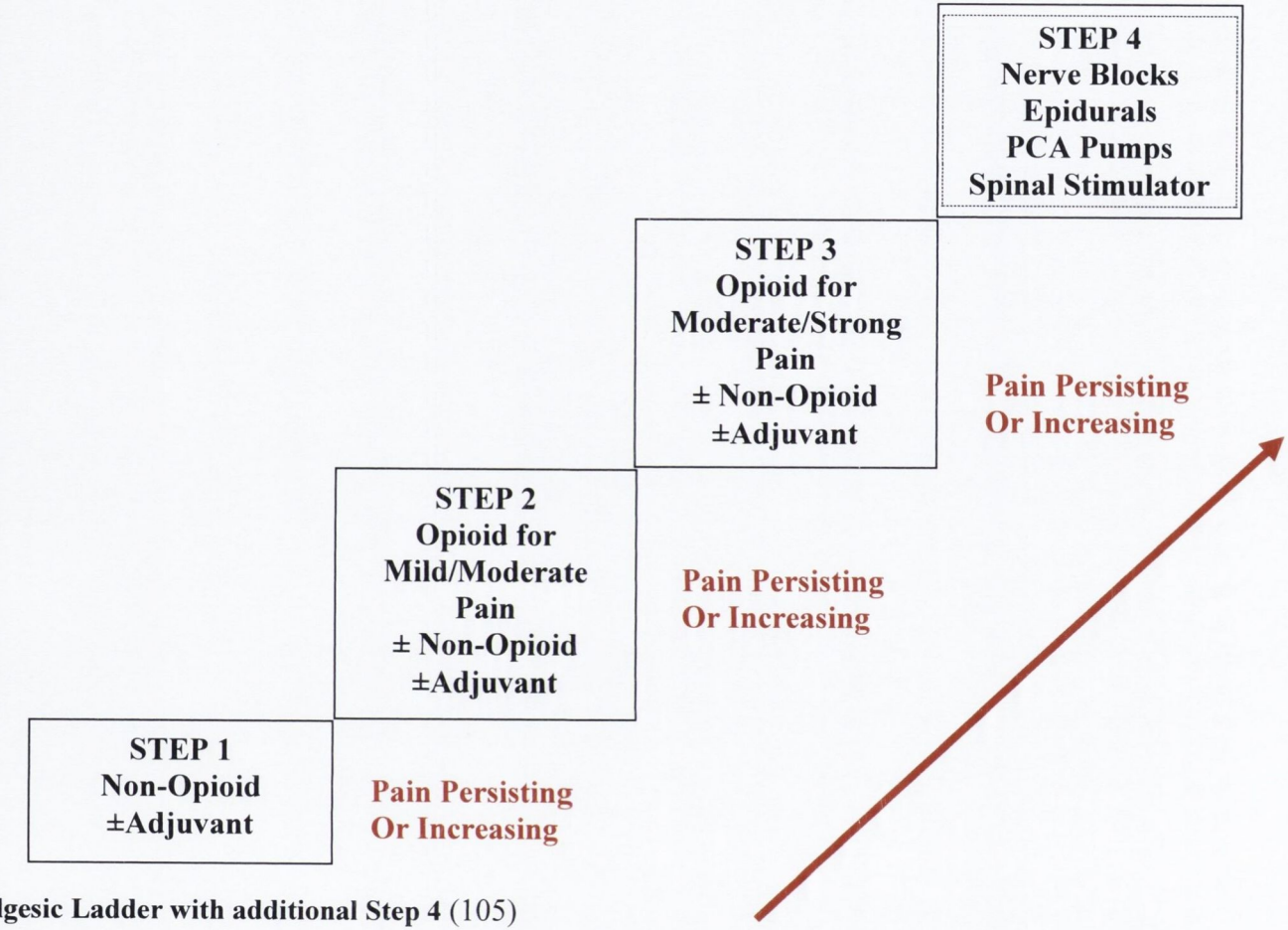


Figure 1-3: WHO Analgesic Ladder with additional Step 4 (105)

There are a variety of clinical factors that may inform a prescribing decision, particularly for ageing and elderly populations. Medicines should be used with caution in these populations, as physiological changes associated with ageing, such as a diminished ability to metabolise drugs and altered distribution patterns and cognitive impairments, can make elderly patients more susceptible to suffering adverse events (109). Decreased muscle mass, increased fat to non-fat tissues and decreased body water produces an alteration in the metabolism, distribution and elimination of analgesic medications. Diminished glomerular filtration and a potentially decreased hepatic function, alters the levels of drug metabolites eliminated by the patient but there is a potential for heightened adverse effects or toxicity (110). Enzymes responsible for the metabolism of certain medications may be affected by frailty associated with ageing. Dementia may also complicate effective pain management, as these patients have a diminished physiological response to painful stimuli (109, 111). The potential for drug interactions may be increased with elderly patients due to polypharmacy, this is associated with an increased morbidity and mortality in these patients (112-114). Analgesic regimens may therefore be difficult to construct for an elderly CNMP patient group due to the variability in drug deposition, co-morbidities and polypharmacy in this population.

While the prescribing of medications for ageing and elderly populations may be challenging due to the physiological reasons described above, health care professionals may access a variety of resources to aid with prescribing. The STOPP/START (Screening Tool of Older Persons' Prescriptions/Screening Tool to Alert doctors to Right Treatment) instrument (European) and the Beers (USA) Criteria are perhaps the most widely known of these prescribing resources. The STOPP instrument may be used for review of prescription medications for individuals aged 65 years and older. It is composed of 65 recommendations that should be reviewed by the prescribing physicians, with a view to discontinuing certain medications, as they may produce adverse outcomes for older adults. The START criteria is a list of 22 evidence based prescribing recommendations for conditions common to ageing and elderly populations. Initiation of these medications is in keeping with high quality care (115). The Beers Criteria, originally conceived in 1994, catalogue medications that may produce adverse

effects in patients aged 65 years and older (116). The criteria recommend only cessation of medication, while the STOPP/START recommend medications that should be introduced to ageing and elderly patients.

Safe and effective prescribing of analgesic medications for ageing and elderly populations with CNMP is therefore challenging due to the range of physiological complications presented by this patient group and the absence of internationally recognised guidelines to direct prescribing. At present, there are two publicly available international guidelines directing the prescribing of analgesics for ageing and elderly patients published by the American Geriatrics Society Panel and the British Geriatrics Society (117, 118). A search for resources providing information on the prescribing of analgesics in Ireland identifies four publicly available documents providing information on analgesic prescribing for non-malignant pain conditions; these are presented in *Table 1-4*. However, the applicability of these resources to the primary care management of patients with CNMP, and more specifically ageing and elderly patients with CNMP, is limited due to the focus and content of the document or the practice setting at which the guidance is directed. There may, however, be additional sources of information on this subject that are circulated to healthcare professionals through private organisations or professional groups which may not be publicly accessible.

Table 1-4: Types of publicly available documents directing the prescribing of analgesics in Ireland

Department of Social Protection; Chronic Pain Disorders and Fibromyalgia (2010) (119)	This document provides detailed information on the pharmacotherapeutic management of CNMP but does not specify the practice setting (primary or secondary) in which recommendations are to be implemented nor is there information provided on the development process of the document.
Mid-Western Regional Hospitals Complex; St. Camillus and St. Ita's Hospitals; Analgesic Policy (2009) (120)	The policy document does not specify the practice setting (primary or secondary) in which recommendations may to be implemented. The publisher of the document would indicate that the document has developed for use in secondary care. There is also no information provided on the development process of the policy document.
Pain in Primary Care 1: Non-Opioids; Pharmacological Management of Pain in Primary Care: Non-Opioids (2005) (121); Pain in Primary Care 2: Opioids; Pharmacological Management of Pain in Primary Care : Opioids (2005) (122)	These two documents are published by the National Medicines Information Centre associated with St. James's Hospital. These resources are publically available and are a useful tool for healthcare professionals to keep abreast of developments on the management of various conditions. These two publications, however, are not specific to CNMP.

1.6.1.1 Routes of Administration

Analgesics, similar to most other classes of medications, may be delivered through oral, transdermal, intranasal, rectal or parenteral formulations. The oral route of delivery represents a safe, effective, convenient and inexpensive method for drug delivery. Topical analgesia is advantageous as a delivery system as it can avoid the systemic side effects produced by a medication that may preclude the drug being used in a population and is beneficial in the management of localised pain symptoms (19, 123). Transdermal delivery in the form of adhesive patches are also appropriate for administration of analgesics. This form of drug delivery avoids the first pass effect of the liver which may prematurely metabolise medications, and is associated with enhanced adherence and reduced adverse effects (124, 125). However, there are some specific shortcomings with this form of delivery including poor adhesiveness which may lead to poor efficacy, poor dose titration flexibility, and the potential for inappropriate/incorrect use (126).

1.6.1.2 Non-Opioids

Non-opioids referenced in Step 1 of the WHO Analgesic Ladder *(Figure 1-3)* refers to a group of analgesics including paracetamol, selective and non-selective non-steroidal anti-inflammatories (NSAIDs).

Paracetamol

Paracetamol appears in Step 1 of the WHO Analgesic Ladder and is appropriate for mild to moderate pain conditions. Paracetamol is a weak inhibitor of prostaglandin synthesis of COX-1 and COX-2 (127). It has limited drug interactions and is therefore favoured as a first line analgesic for those on complex medication regimens, although it should be used with caution in individuals with established hepatic insufficiency. Paracetamol may be administered orally, rectally and intravenously with a maximum daily dose of 4 gr administered in four divided doses (128).

Non-Steroidal Anti-inflammatories

Cyclooxygenase (COX) or prostaglandin endoperoxide synthase is a membrane bound glycoprotein found in greatest quantities in the endoplasmic reticulum of

prostanoid forming cells (129). COX exists as two isoforms, COX-1 and COX-2. COX-1 exists under normal conditions in a number of tissues. It catalyses the formation of essential prostaglandins and does not contribute towards nociception or inflammation. COX-2 is induced in inflammatory tissues but is constitutively expressed in some tissues and organs, such as the kidney. COX-2 produces inflammatory prostaglandins within the damaged tissues (130). Prostaglandins are a group of ten lipid compounds. These act to produce a variety of physiological effects including aggregation of platelets, constriction of muscle and blood vessels, and induction of inflammatory responses (131).

NSAIDs act through the inhibition of COX and are utilised in the management of pain conditions (132). Non-selective NSAIDS inhibit both COX-1 and COX-2, while selective NSAIDs inhibit only COX-2. Non-selective and selective NSAIDs have anti-inflammatory, anti-pyretic and analgesic properties. Nociceptive pain conditions generally respond best to NSAIDS and regular paracetamol administration as a first line regimen; the doses can be titrated in response to pain severity in accordance with the WHO Analgesic Ladder. Topical and oral non-selective NSAIDs are available both on a prescription and non-prescription basis in Ireland.

The selection and use of NSAIDs should be clinically rational and consideration given to concomitant medication, medical history and risk factors. Patients with a high cardiovascular risk may increase their risk of a cardiovascular events due to platelet activation and COX inhibition by any NSAID (133). NSAIDs also act to inhibit platelet aggregation, which produces an increase in bleeding time that usually does not extend outside the normal range for most patients (134). Indeed, a number of selective NSAIDs were withdrawn in a number of countries because of their association with adverse cardiovascular outcomes (135). Rofecoxib was withdrawn by the Irish Medicines Board in 2004. The selective NSAIDs that remain available on a prescription basis in Ireland are contraindicated for use in patients with established ischaemic heart disease (136).

NSAIDs may also produce a range of negative outcomes on the kidneys including renal insufficiency, sodium and water retention and potentially acute renal failure (130). Advanced age, diuretics and ACE inhibitors increased the risk of developing these renal complications (137). Gastric erosion is also associated

with these non-selective NSAIDs, particularly in the absence of a protective agent such as a Proton-Pump Inhibitor (138). While COX-2 selective agents are less damaging to the GIT, their effects on renal function are similar to those of nonselective agents (130). Such are the risks associated with NSAIDs, their long-term use in ageing populations and individuals presenting with the co-morbidities described above, that both selective and non-selective NSAIDs are listed in the Beers and STOPP criteria (115, 116).

1.6.1.3 Adjuvant Medications

Adjuvant medications feature in all steps of the WHO Analgesic Ladder alongside non-opioid and opioid analgesics and for this reason are often termed 'co-analgesics'. These agents include anticonvulsants, antidepressants, ketamine, skeletal muscle relaxants and steroids (139).

Anticonvulsants have been used in the management of pain since the 1960s and are one of the most important classes of adjuvant medications (123). These agents act on a variety of neuro-receptors and are hypothesised to suppress electrical discharges in the Central Nervous System. Gabapentin, a GABA (γ-Aminobutyric Acid) analogue also displays anti-convulsant and analgesic effects (140). It is proposed that the anti-nociceptive action of gabapentin arises from its action on α_2 subunits of spinal Ca^{2+} channels. Pregabalin is a prodrug of gabapentin and was approved by the European Medicines Evaluation Agency in 2004 for the treatment of peripheral neuropathic pain (141). It displays a similar mechanism of action to gabapentin. Dizziness and somnolence are the most common adverse effects associated with gabapentin and pregabalin (142). Doses for both these agents must be titrated over a period of time, with pregabalin requiring a shorter period for dose titration. Elderly patients may require a lower dose of both agents due to decreased renal function. Carbamazepine is indicated for the relief of pain associated with trigeminal neuralgia. Elderly patients are particularly susceptible to the adverse outcomes of nystagmus, dizziness, lethargy and cognitive changes associated with this agent. It should therefore be considered as a second line therapy after gabapentin for the management of neuropathic pain conditions in these patients (137).

Antidepressants are effective in the management of chronic pain conditions when prescribed at doses lower than those required to achieve an anti-depressant effect. Animal studies demonstrate that antidepressants produce their analgesic effect in nociceptive, inflammatory and neuropathic pain conditions (62). Tricyclic antidepressants (TCAs) were traditionally considered to be a first line treatment for neuropathic pain conditions. They are thought to affect pain transmission in the spinal cord by inhibiting the reuptake of norepinephrine and serotonin, both of which influence descending pain pathways. TCAs are used predominantly in the management of pain associated with postherpetic neuralgia and diabetic neuropathy (143). Amitriptyline is the most commonly used TCA; doses of 10-20 mg are administered at night with a maximum daily dose of 75 mg (144). The elderly are particularly likely to experience adverse reactions from amitriptyline, especially agitation, confusion and postural hypotension. The selective serotonin reuptake inhibitors (SSRIs) family of antidepressants, including duloxetine and venlafaxine, are also used in diabetic neuropathy (143).

Ketamine is a fast-acting general anaesthetic for intravenous and intramuscular use; it produces analgesia in addition to sedation and amnesia. It should be considered when other agents including opioids and non-opioids are inappropriate for the patient or fail to provide adequate analgesia (145). Ketamine acts through antagonising the NMDA receptor (a ligand operated Ca^{2+} channel with glutamate the analgesic agonist) (146). Activation of the NMDA receptor is thought to be central to the pathogenesis of chronic pain states, therefore ketamine is particularly effective for chronic pain (147).

Muscle relaxants cover a wide range of medications including antispasmodics such as benzodiazepine and non-benzodiazepine medications (148). These agents are approved for muscle spasticity or musculoskeletal conditions and include baclofen, tizanidine and dantrolene. Cyclobenzaprine has been demonstrated to produce consistently better results than placebo medications when used for chronic pain states and would also appear to be the most advantageous of the skeletal muscle relaxants for chronic pain conditions (123).

Cannabinoids are a relatively new pharmacological option for the management of CNMP (149). A systematic review of RCTs investigating the use of cannabinoids in chronic pain states has demonstrated that cannabinoids are most

beneficial in chronic neuropathic pain states (150). Finally, steroids may be used to suppress neuro-immune reactions which manifest themselves in a variety of CNMP conditions. However, the adverse effects associated with oral steroid use, particularly long-term use, negate the advantages of use of this drug class on a continuous basis (151).

1.6.1.4 Opioids

The term "opioid" applies to any substance, whether endogenous or synthetic, that produces morphine-like effects, while "opiate" describes the natural alkaloids found in the poppy, *Papaver Somniferum* (152). Opioids are particularly effective at decreasing pain and improving functionality of patients, however, this class of analgesic is associated with adverse outcomes including undesirable side-effects, dependence, increasing misuse and mortality (153-155). Their role in CNMP has been controversial for a variety of reasons including the appropriateness of opioids for this pain condition and the implications of long-term use (156). Approximately 1% of those patients with CNMP use opioids in the management of their pain condition in the long term (118). Long-term use of opioids may pose a risk for tolerance, physical dependence and may cause aberrant drug behaviours in vulnerable patients (157). Tolerance is a state of adaptation to the drug which diminished the drug's effect over a period of time. Tolerance to the analgesic effects of opioids is variable between patients; there is no established upper limit to dosage of pure opioid agonists (158). Physical dependence is a predictable physiological response in which a drug class-specific withdrawal syndrome manifests upon cessation of the therapy (159). It is a consequence of long-term use of a range of medications including beta-blockers, corticosteroids and antidepressants. Patients taking opioids over a prolonged period may therefore require tapered dose reduction to avoid adverse effects associated with withdrawal. According to the Cochrane review of long-term opioid management for CNMP, correct management of opioids in appropriately selected patients with no history of drug or alcohol misuse is not associated with the development of addiction, misuse or serious side-effects, although these outcomes may occur in some instances. However, further studies are required to determine whether patients would benefit

from long-term use of these agents (160). *Table 1-5* outlines the opioid medications currently available on the Irish market (58, 128, 161).

Table 1-5: Summary of opioid analgesics

Drug	Indication & Mechanism of Action	Availability in Ireland & Routes of Administration
Codeine	Used in the management of mild to moderate pain (Step 2 of the WHO Analgesic Ladder) which cannot be adequately managed with non-opioid formulations (42). The capacity to metabolise codeine to morphine can vary considerably between individuals; there is a marked increase in morphine toxicity in patients who are ultra-rapid codeine metabolisers (CYP2D6 ultra-rapid metabolisers) and a reduced therapeutic effect in poor codeine metabolisers (162). Codeine is available in combination with paracetamol or ibuprofen in number of doses 8mg-30mg.	Prescription and non-prescription. Oral administration
Dihydrocodeine	Demonstrated to have an analgesic effect similar to that of codeine and is used in mild to moderate pain conditions. Demonstrates affinity for μ, ƙ and δ opioid receptors. Dihydrocodeine is available in combination with paracetamol. Higher doses may provide some additional pain relief but may cause nausea and vomiting.	Prescription only Oral administration
Tramadol	Tramadol is a centrally acting analgesic with at least two mechanisms of action; useful in the management of moderate pain conditions and appears on Step 2 of the analgesic ladder. It has a weak affinity for the μ-opioid receptor and also inhibits the re-uptake of adrenaline and serotonin. Potency of morphine to tramadol is 10:1 (137). It has been demonstrated to be effective in the management of pain associated with osteoarthritis, fibromyalgia and neuropathic pain conditions such as post-herpetic neuralgia and diabetic neuropathy (163). Tramadol is also available in combination with paracetamol as an oral formulation.	Prescription only Intravenous, intramuscular, subcutaneous or oral administration
Oxycodone	Oxycodone is a strong semi-synthetic opioid with μ-opioid receptor agonist activity and approximately one and a half times the potency of morphine (Step 3 agent). Oxycodone is available in formulations with naloxone, acting on local opioid receptors to reduce some of the adverse effects associated this opioid.	Prescription only Intravenous, subcutaneous or oral administration

Morphine	Morphine, a natural plant alkaloid was isolated in 1804. It is a μ-opioid receptor agonist and is used in severe pain conditions (Step 3 WHO Analgesic Ladder). Morphine is primarily reserved for post-operative and chronic malignant pain states but may also be used for CNMP. Prolonged release formulations are preferred in CNMP with breakthrough analgesia achieved through administration of one-fifth of the daily morphine dose.	Prescription only Intravenous, intramuscular, subcutaneous or oral administration
Hydromorphone	A μ1 opioid agonist used for severe pain conditions (Step 3 WHO Analgesic Ladder). The equianalgesic dose compared to morphine is 5:1 with some intra-individual variability (137). Produces analgesic, anxiolytic, antitussive and sedative effects.	Prescription only Intravenous, intramuscular, subcutaneous or oral administration
Fentanyl	A μ opioid and is used in severe pain conditions (Step 3 WHO Analgesic Ladder). Transdermal fentanyl formulations are popular amongst community dwelling patients, the ease of administration of this system enhancing compliance (137). Fentanyl is less constipating than morphine and produces less day time drowsiness for patients and may therefore be an appealing analgesic option for clinicians.	Prescription only Sublingual, intranasal, transdermal, intravenous, intrathecal and subcutaneous administration
Pethidine	Opioid with short-acting activity, less potent than morphine. Pethidine exerts its principal pharmacological actions on the CNS where produces analgesic and sedative effects. It provides pain relief for moderate to severe pain (Step 3 of the WHO Analgesic Ladder) and is used as an adjunct to anaesthesia, as a pre-operative medication or during labour.	Prescription only Intravenous, intramuscular, subcutaneous or oral administration
Pentazocine	Pentazocine is a potent analgesic and is used in severe pain conditions (Step 3 WHO Analgesic Ladder). Demonstrates agonist and antagonist action on opioid receptors. It demonstrates agonist activity at κ-receptors and antagonist effects on μ-receptors (164). Analgesia is achieved for 2-3 hours regardless of the route of administration By injection it is more potent than dihydrocodeine or codeine, but hallucinations and thought disturbances may occur.	Prescription only Intravenous, intramuscular, subcutaneous or oral administration
Methadone	Acts at the μ receptor and also has some agonist actions at the κ and σ receptors. Used as an adjunct treatment of opioid dependence and is also used in severe pain conditions (Step 3 WHO Analgesic Ladder). The analgesic activity of the racemate is almost entirely due to the l-isomer, which is at least 10 times more potent as an analgesic than the d-isomer.	Prescription only Intravenous, intramuscular or oral administration

Tapentadol	Produces analgesia by acting as an agonist at the μ-opioid-receptor and it also inhibits noradrenaline reuptake. Tapentadol is used in the management of acute pain of moderate to severe intensity (Step 2 and Step 3 of the WHO Analgesic Ladder) and has demonstrated efficacy in preclinical models of nociceptive, neuropathic, visceral and inflammatory pain.	Prescription only Oral administration
Meptazinol	A centrally acting analgesic belonging to the hexahydroazepine series, which demonstrates mixed agonist and antagonist activity at opioid receptors. Displays a low affinity for δ and κ receptor sites, it has a somewhat higher affinity for a subpopulation of μ sites. These binding sites also display a high affinity for the endogenous opioid peptides, and are thought to be responsible for, among other things, analgesia, but not for the mediation of respiratory depression. Indicated for the management of moderate pain conditions (Step 2 and Step 3 of the WHO Analgesic Ladder).	Prescription only Intravenous, intramuscular or oral administration
Buprenorphine	Buprenorphine is a partial μ-opioid receptor agonist and a weak antagonist at the κ receptor and is indicated for moderate to severe pain conditions (Step 3 WHO Analgesic Ladder) (165). It has a longer duration of action than morphine and sublingually is an effective analgesic for 6 to 8 hours. Non-oral administration is preferable as bioavailability is relatively poor through the oral route (166).	Prescription only Sublingual, buccal intranasal, transdermal, intravenous, intrathecal and subcutaneous dosage administration

Adverse Effects of Opioids

There are a number of adverse effects associated with the use of opioid analgesics such as gastrointestinal disturbances, sedation, respiratory depression, pruritus, immunologic effects, hormonal alterations and hyperalgesia. Development of these adverse effects is dependent on the type, strength and frequency of the opioid administered and the underlying clinical features of the patient (167). A meta-analysis of RCTs of non-cancer patients receiving opioids for moderate-to-severe pain indicated that approximately 80% of patients experienced at least one adverse effect, with constipation (41%) and nausea (32%) occurring most commonly (168).

Sedation

Sedation and decreased cognitive function are the primary CNS adverse effects associated with opioids mediated by μ-opioid receptors. Effects may be transient and diminish with prolonged use (169). Concurrent medications and patient co-morbidities may exacerbate severity of sedation. Sedation may arise from the additive effects of opioids taken concomitantly with other sedating agents such as benzodiazepines and non-benzodiazepine hypnotics (128). This outcome may be prevented through changes to these concurrent medications or by selection of an alternative analgesic regimen.

Gastrointestinal Effects

Opioid Induced Bowel Dysfunction (OBD) is the most common adverse effect arising from opioid therapy (170). Activation of μ-opioid receptors in the periphery of the CNS (i.e. in the GIT) reduces bowel motility, inhibits small and large intestinal propulsion, decreases gastric and intestinal secretions and increases anal sphincter tone; the occurrence of one or a combination of these effects will produce OBD (171). Constipation persists throughout the duration of therapy with opioids (171). The severity of OBD is influenced by opioid dose, formulation type, titration schedule and polypharmacy (172). Older patients are also more likely to develop OBD due to age-related physiological changes, polypharmacy, co-morbidities and inadequate physical activity (173).

Constipation arising from opioids has been demonstrated to have a negative impact upon health related quality of life. Results of a US and European survey of

individuals taking oral opioids for chronic pain (n=322) (PROBE 1) demonstrated that constipation reduced QoL, measured using the EuroQol five dimension questionnaire (EQ-5D), and diminished ability to undertake daily activities (174). A second study undertaken in the Netherlands (n=588) also found a lower median EQ-5D score in patients taking opioids presenting with constipation in comparison with those with no constipation (175).

Laxatives may be combined with non-pharmacological interventions e.g. changes to dietary fibre intake, fluid intake and daily activity to manage the onset and development of OBD (176). The British National Formulary (BNF) recommends that OBD should be prevented through administration of a stool softener or lactulose solution with a senna preparation at the commencement of opioid therapy (128). Stool softeners when used on their own may be ineffective if there is insufficient fluid intake and may necessitate use of another type of laxative such as a stimulant laxative (128). Patients who do not achieve an adequate response from this therapy may require another laxative such as a mild osmotic agent, a lubricant or a bulk forming laxative to attain normal bowel function (128). Methylnaltrexone is licensed specifically for the treatment of opioid induced constipation and is predominantly prescribed in palliative care (177). Prucalopride demonstrates pro-kinetic properties; it is however only appropriate for use in women with chronic constipation when other laxatives have produced insufficient response (128).

Respiratory Depression

Respiratory depression is one of the major limiting factors in the prescribing of opioid medications for patients, particularly ageing and elderly populations (113). Post-operative opioid-induced respiratory depression is estimated to occur in 1% of patients in the UK (178). Opioid induced respiratory depression is mediated by the μ-opioid receptor (179). Opioids have been demonstrated to produce antitussive effects through suppression of the cough reflex. Codeine containing cough formulations are sold in retail pharmacy businesses in Ireland on a prescription and non-prescription basis (180).

Pruritus

This adverse outcome is observed in 2-10% of patients and occurs following histamine release in a peripheral or central CNS process (169). It is also possible that pruritus occurs as an allergic reaction to the medication. Oral and topical antihistamines may be used to manage the adverse effect although opioid rotation and alternative pharmacological therapies should also be considered (169).

Immunologic suppression

Both acute and chronic opioid administration can produce immunosuppression by exerting inhibitory effects on antibody and cellular responses (167). Potential mechanisms include modulation of the hypothalamic pituitary axis, stimulation of the sympathetic nervous system or direct action via μ receptors on immune cells (181).

Hormonal Changes

Long-term use of opioids may produce opioid endocrinopathy which may impact upon a patient's sexual function, fertility and mood. It may also precipitate osteoporosis and osteopenia (182). Endocrinopathy results from the effects of opioids on two endocrine systems, the hypothalamic-pituitary-gonadal axis and the hypothalamic-pituitary-adrenal axis (183). Opioids diminish luteinising hormone (LH) production in females which may interrupt the menstrual cycle. In men, it may reduce testosterone secretion, with a subsequent reduction in testicular interstitial fluid production. Daily opioid use amongst chronic pain populations has also been demonstrated to diminish adrenal androgen production (182).

Opioid Induced Hyperalgesia

Opioid induced hyperalgesia (OIH) is a state of nociceptive sensitisation arising from exposure to opioids, which may occur when increasing doses of opioids fail to relieve pain or exacerbate pain in certain cases (184). The mechanism by which OIH arises is poorly understood although it is proposed that genetic factors may predispose patients to the development of this complication (185). When OIH has been confirmed, there are a variety of management strategies available to the prescriber including, the reduction or elimination of opioid medication, use of

NMDA receptor antagonists to negate hyperanalgesic effect, prescribing COX-2 inhibitor combination therapy due to their ability to inhibit prostaglandin synthesis e.g. parecoxib and rofecoxib or the introduction of α_2 receptor agonists (59).

1.6.1.5 Prescribing Policies for Opioids for CNMP

The prescribing and supply of opioid analgesics in Ireland is regulated by the Medicinal Products (Prescription and Control of Supply) Regulations 2003, while strong opioids are also regulated by the Misuse of Drugs Acts 1977 & 1984; prescribing and supply of opioids is therefore controlled at a national level by these regulations (186-188). Similarly, prescribing and supply of opioids is governed by the Controlled Substances Act implemented by the Drugs Enforcement Administration (DEA) in the USA (189). Opioid consumption in Ireland has increased from 253.6 morphine equivalence (ME) mg/capita in 2001, to 282.5 ME mg/capita 2011. By comparison, opioid consumption has increased in the USA from 542.8 ME mg/capita in 2001, to 749.8 ME mg/capita in 2011 (190, 191). Indeed, North American and Canada are the largest consumers of prescription opioid medications internationally; opioid prescribing has increased over the past two decades in the USA to a greater extent than any other country. Supply of these medications has become a point of debate amongst healthcare professionals due to the concurrent increase in prescription drug and mortality and morbidity amongst those misusing opioids (155, 192-194).

Following publication of the WHO Analgesic Ladder (1986), the US Public Health Agency endorsed the role of opioids in the management of moderate to severe pain in 1992 (195, 196). However, concerns were reported about the use of opioid agents relating to addiction, side-effects or compromised physical or psychological functioning of certain patients (197). The American Society of Anaesthesiology (1996) recommended that patients should be assessed to determine risk of aberrant opioid behaviour prior to receiving such therapies. In 1998, the Federation of State Medical Boards released model guidelines for the use of opioids in the management of acute and chronic pain; these guidelines were revised in 2005 (35, 198). Since publication of these model guidelines, numerous states have developed policies to enhance safe and effective prescribing within the

current regulations. Washington became the first US state to attempt to limit opioid doses prescribed for chronic pain, restricting the equi-analgesic morphine dose of an opioid that may be prescribed by a physician without referral to a pain consultant (199). New York has introduced further restrictions modelled on initiatives in Washington requiring that patients discharged from emergency care settings are prescribed low dose short acting opioids rather than long acting/extended release formulations (200). By 2007, it became incumbent on pharmaceutical companies to inform clinicians and patients of medication risks, and in 2010, these regulatory controls were tightened further following continued increases in opioid prescribing and a parallel increase in prescription opioid misuse, dependence and death rates (201).

There have been ongoing efforts in the USA to improve professional prescribing practices in an effort to minimise these adverse outcomes (202). These enhanced prescribing measures are cognisant of monitoring safety, efficacy and misuse of opioids balanced with a patient centric, multidisciplinary approach to pain management (153). Opioid contracts or urine testing have been proposed as mechanisms to improve patient adherence and minimise opioid related aberrant behaviours amongst patients (203). Proponents of the opioid contract suggest that it represents a useful clinical decision making framework which is transparent in its description of risks associated with the opioid regimen (203). Urine testing is also commonly used to assess a patient's compliance with a prescribed opioid regimen and is endorsed by most US and Canadian guidelines (204, 205). It is proposed that by improving both professional prescribing practices, and enhancing regulations directing the supply of opioids, it may curtail further increases in prescribing rates while also protecting patient safety and welfare (206).

Practices such as urine testing and opioid contracts are not yet commonplace in Ireland, with such measures enforced only for patients receiving opioid replacement therapy. The Pharmaceutical Society of Ireland (PSI) introduced guidance for pharmacists on the safe supply of non-prescription codeine containing products sold in retail pharmacy businesses in 2010. This measure was introduced following concerns about prolonged-use of these agents in the UK, Northern Ireland and Ireland. Pharmacists are now obliged to recommend an alternative non-opioid containing analgesic to the patient at the outset. If the patient has not experienced

pain relief from these non-opioid formulations, a codeine-containing product may be supplied. The pharmacist must counsel on the appropriate use of the codeine-containing formulation prior to supply of the product to the patient (207). This is perhaps the most significant policy relating to the supply of opioid containing formulations to have been implemented in Ireland in recent years.

1.6.1.6 Patient and Physician Factors in Prescription Medication Use

A variety of factors may influence the types of prescription and non-prescription medications used by patients in addition to the severity of the pain condition, co-morbidities and adverse effects as previously described. GP's prescribing decisions may be determined by a variety of 'fixed' factors such as the age and gender of the GP, age and gender of the practice population or the socioeconomic status of patients. Additional factors, including the regulations relating to prescribing of certain medications, cost of medications, continuing education, attitudes towards branded and generic medications and time pressures, may also alter approaches to prescribing (208, 209). The marketing practices of pharmaceutical companies have also been documented as influencing both patients and prescribers. Direct-to-consumer advertising, commonplace in the USA and New Zealand, has been shown to increase the volume of prescribed medication in these countries (210). However, this form of marketing has been criticised for being poorly regulated, misinforming patients and placing pressure on prescribers (210). Marketing literature, disseminated by pharmaceutical companies directly to healthcare professionals, has been cited as a valuable source of valuable information on prescription medications (211).

The manner in which patients use medications may be influenced by a range of internal and external factors. Internal factors are individual to the patient and include beliefs about medication and perceptions of pain, concerns about tolerance or addiction and side-effects (212-214). External factors describe sociocultural influences and the impact of the media or other sources of information available to patients (215). Similar to the physicians, both internal and external factors combine to determine the individual's perception and attitude towards prescribed medications which may affect the manner in which these agents are used.

The interaction between the GP and the patient during the prescribing process is of critical importance in determining the type of medication prescribed (216). The influence of the patient on this interaction is dependent on whether the GP opts for a paternalistic approach to decision-making or whether an informed choice model is incorporated into the consultation (216, 217). Shared decision is associated with improved patient adherence, increased interaction with the healthcare system and with enhanced cost-effectiveness of management strategies (218). Patients with pain may particularly benefit from such a shared decision making model, as, given the subjective nature of the condition, communication with healthcare professionals is essential to establishing and monitoring the efficacy of interventions.

1.6.2 Non-Pharmacotherapeutic Management of Chronic Non-Malignant Pain

Reference to the biopsychosocial model would suggest that addressing the psychosocial elements of CNMP may improve the quality of life of the individuals with the condition. Non-pharmacotherapeutic interventions may be classified as physical, psychological or clinical. Physical interventions include acupuncture, transcutaneous electrical stimulation (TENS), massage and exercise therapies. Psychological interventions include relaxation techniques, mindfulness, cognitive behaviours therapy and hypnosis. Finally, non-pharmacotherapeutic clinical processes describe education of the patient by healthcare professionals or self-education undertaken by the patient (219).

These non-pharmacotherapeutic interventions are in essence a method of self-care adopted by the individual to attain pain relief. Self-care is defined as 'the care of oneself without medical, professional or any assistance or oversight' (220). Self-management represents a type of self-care of long-term conditions whereby the individual aims to control the condition through the setting of goals with the aim of maintaining, changing and creating meaningful life roles in spite of the chronic pain condition (221). It therefore represents the ability of the individual to manage symptoms, treatment, physical and psychosocial consequences and life-style changes associated with the chronic condition (222, 223). Health education

forms a part of personal development and incorporates the role of healthcare professionals in the provision of information to patients in addition to the patient's own pursuit of information through personal education about their pain condition and through consultation with support groups and other patients with CNMP.

Cognitive behavioural therapy (CBT) is a psychological intervention for pain conditions which acknowledges that pain is not limited to a biomedical model but extends into the sensory and emotional domains of the patient (224). CBT requires the application of behavioural change such as positive reinforcement of desirable behaviour, modification of thought processes and goal setting. A systematic review conducted by Morley et al concluded that CBT is effective in altering the patient's pain experience, mood, cognitive coping and appraisal, pain behaviour and activity levels, but the quality of these outcomes is dependent upon waiting list conditions to access these services and the degree of follow-up with the patient (225). CBT interventions are optimal when delivered in conjunction with stress management and relaxation training as part of a psychological rehabilitation programme (226).

Physical interventions include exercise programmes and educating the patient on postural, motion and muscle balance to improve physical functionality. Passive physical interventions such as TENS; ultrasound and heat are promoted as secondary physical rehabilitation tools for patients with CNMP (226). TENS is based on the gate control theory of pain in which counter-stimulation of pain modifies the patient's perception of pain. More recent studies of TENS hypothesise that the technique stimulates the production of endorphins in the spinal fluid (227). A systematic review of TENS (1996) indicated that it is ineffective for relief of post-operative pain. A later Cochrane review (2007) assessing the role of TENS in severe pain concluded that insufficient RCTs on the intervention existed in order to conduct a meta-analysis (228).

While incorporating non-pharmacotherapeutic interventions into the management of CNMP is endorsed by the WHO and is referenced extensively in the literature, it would appear that these interventions are associated with varying degrees of success. Randomised control trials investigating the efficacy of these interventions are not as easily identified as those for pharmacotherapeutic

interventions suggesting that a sufficient evidence base does not yet exist to endorse a number of these interventions for pain management (229).

1.7 Healthcare Systems and the Management of Chronic Non-Malignant Pain

Healthcare systems have an important role in ensuring effective management of the condition thereby ameliorating outcomes for patients. At present, western healthcare systems are experiencing differing degrees of success in addressing the management of CNMP. Groups of healthcare professionals, state agencies and patients are responsible for altering the manner in which the healthcare system recognises and manages the condition in each country. However, direct comparison between countries is of limited value due to the differing structures and processes of care delivery, available resources and societal attitudes to health.

1.7.1 The Irish Healthcare System

Formalised health services in Ireland began in the 18th century through the voluntary, philanthropic and private sectors. By the mid-19th century, the hospital and health services were co-ordinated by religious orders and lay organisations (230). Health services formally became the responsibility of the state in 1970, with the implementation of the Health Boards Act. The Department of Health (DoH), under the direction of the Minister for Health is responsible for advising on the strategic development of the health system including policy and legislation, evaluating the performance of health and social services and working with other sectors to enhance people's health and well-being. The Health Service Executive (HSE), established by the Health Act 2004, is responsible for the delivery of health and personal social services (231).

Healthcare services are financed by public expenditure, health insurance payments and private payments by patients. Public finance of the healthcare system is gained through the taxation system and is administered by the DoH. The Voluntary Health Insurance (VHI) Board established in 1957 was a state operated health insurer that encouraged individuals to buy insurance to gain access to private hospital care and timely consultation with specialists. At present, there are 5 health insurers operating in Ireland, VHI, Aviva, Laya Healthcare (formally Quinn

Healthcare), GloHealth and HSF Health plan. The most recent statistics released by the Health Insurance Authority (HIA) indicate that 2,052,000 people are insured with inpatient health insurance plans, representing 45% of the population. In addition to those insured with inpatient plans, there were 99,000 insured with products solely providing outpatient benefits or health insurance cash plans (232). Those individuals who purchase health insurance are entitled to attend both public and private hospitals, where access to care may be more rapid than the public system. This system of public and private healthcare has created a two-tier healthcare system, with inequities in access to care for public patients, particularly specialist consultation. This issue is further compounded by differences in access to health care service between geographical regions of the country and differences in prescribing patterns between public and private patients (231).

Prescription medications are provided in primary care by retail pharmacy businesses. Prescriptions are financed through a number of state subsidised schemes or by private expenditure by the individual patient. The General Medical Services (GMS) Scheme provides medicines free of charge following an assessment of the patient's means. The Health (Amendment) Act 2010 introduced a prescription levy of €0.50 per item which increased to €2.50 in 2013. Payments are capped at €25.00 per month for a family unit receiving medications under the GMS Scheme. Prescriptions issued to GMS eligible patient by Dental Practitioners may be supplied under the Dental Treatment Services Scheme under similar provisions as the GMS Scheme. The Long Term Illness (LTI) Scheme provides medications free of charge to patients with one or more than 16 chronic conditions covered by this scheme e.g. Type I and Type II Diabetes, Epilepsy, Cystic Fibrosis and Multiple Sclerosis. The Drugs Payment Scheme (DPS) allows individuals and dependents under 18 years or dependents under 23 year who are in full time education to limit expenditure on prescription medications to €144.00 per month. All Irish citizens are eligible to register for the DPS regardless of means. The Health Amendment Act (HAA) Scheme (1996) provides medications without charge to persons who have contracted Hepatitis C directly or indirectly from the use of Human Immunoglobulin-Anti D or the receipt within the State of another blood product or blood transfusion. Eligibility for this scheme extends for the lifetime of affected patients. The High Tech Drugs Scheme facilitates supply and

dispensing of High Tech medicines through retail pharmacy businesses. These high cost medicines are generally only prescribed or initiated in hospital and include items such as anti-rejection drugs for transplant patients or medicines used in conjunction with chemotherapy or growth hormones. Patients must pay only the GMS levy or the DPS payment when receiving such High Tech medications, depending on which scheme the patient would ordinarily receive prescription medications (233). Methadone is dispensed for palliative purposes and opioid replacement therapy by retail pharmacy businesses. Methadone may be prescribed and dispensed by doctors and pharmacists for approved clients under the Methadone Treatment Scheme in the treatment of opioid drug addictions. The Central Treatment List is a register of all individuals receiving methadone for the purposes of opioid replacement. Patients receiving methadone for palliative purposes are not required to register with the Central Treatment List.

Access to health services delivered in primary, secondary or tertiary settings and receipt of prescription medications by patients with CNMP is therefore dependent on personal means or the medical condition which has precipitated CNMP. The range of state-subsidised schemes ensures that the majority of the population may secure financial assistance in obtaining the majority of prescription medicines. The limited resources of the public healthcare system may restrict rapid access to consultant level care which may impact negatively upon the individual. Those that finance their healthcare through private means may also be unable to access care due to the financial burden this places upon the individual.

1.7.1.1 Ageing and Elderly in Ireland: Chronic Conditions

A socially constructed definition of old age includes people aged 50 years and older who have completed their career in paid employment and/or child bearing. Individuals aged 65 years and older are described in the medical literature as elderly, primarily due to the altered physiological and metabolic features of this group, while individuals aged 65-79 years may be described as 'aged' (111). A further transition phase of ageing occurs between healthy active living and frailty, usually occurring in the 7th or 8th decade, the latter group sometimes described as the 'very aged' (23, 234). Advancements in preventative and curative medicines

combined with technological developments have contributed to lengthened life expectancy and improved quality of life of the ageing and elderly in developed countries over the past sixty years (235). At present, approximately 11% of the Irish population are aged 65 years and older. This is projected to increase to 14% by 2021, and 19% by 2031 (236). The greatest increase will occur in the group aged 80 years plus, this population is expected to treble in size by 2036 (237).

The increase in the number of ageing and elderly will produce a corresponding increase in chronic conditions (238). Chronic diseases are long-term conditions which can be treated and controlled but not cured and may involve some level of impaired function or disability (238). At present, over one third of the Irish population report a chronic condition including respiratory diseases, cancer and diabetes (239). The increasing focus on chronic conditions in Ireland is reflected by the publication of numerous policy documents addressing the management of chronic conditions in the Irish healthcare in recent years. 'A policy framework for the management of chronic diseases; Tackling chronic diseases' details the burden of chronic conditions and the contributors towards these conditions. This document outlines measures to aid the Irish healthcare system in adapting to the challenges of chronic conditions. It details the necessity for a cohesive model of collaborative care between primary and specialist services and describes the advantages associated with the introduction of disease management programmes with interdisciplinary collaboration (238). Following publication of this policy framework, a number of additional policy documents have been developed focusing on specific chronic conditions. 'A practice guide to integrated Type 2 Diabetes Care' addresses the delivery of care to patients with this condition through primary care, diabetes units and centres and was developed following an increase in the prevalence of diabetes in Ireland. The purpose of the guide is to improve the manner by which care is delivered to diabetics as, in the past, it had been unstructured and delivered in an opportunistic manner (240). Finally, one of the most recent policy documents, 'Changing Cardiovascular Health; National Cardiovascular Health Policy 2010-2019', provides a series of recommendations to improve the clinical management of cardiovascular diseases and stroke in all healthcare settings (241).

The publication of these policy documents highlights the recent development of national strategies to improve management of chronic disease in

Ireland. The IASP have proposed that national policies such as these are the cornerstone of implementation of any healthcare programme. They propose that an effective pain management strategy should be included in any national health plan to ensure optimal management of patients with CNMP (180). At present, Ireland has no such national strategy to manage CNMP conditions detailing for instance referral of a patient from a primary care setting to specialist management (242). There is also no national prescribing guideline for analgesics for CNMP (as highlighted in *Section 1.6.1*) nor is there a publically disseminated clinical practice guideline available to primary care practitioners detailing a management strategy for CNMP in the Irish healthcare system. Such national strategies have been developed or are in the process of development in many westernised countries such as the USA, England, Wales, Scotland, Australia and Canada (117, 243-246).

Specialised management of pain is provided in 28 out-patient pain clinics in Ireland with an average waiting time of waiting at least 12 weeks to access care (242). Emphasis is placed on providing comprehensive, holistic pain assessment, and if possible, providing patients with a diagnosis. The geographical location of the specialist clinics associated with public hospitals in Ireland are highlighted in *Figure 1-4*.

Pain management programmes are offered in St. Vincent's University Hospital, The Adelaide and Meath Hospital, Dublin and the Mercy University Hospital Cork, and provide a psychological based rehabilitation for individuals with chronic pain conditions. The aim of these programmes is to teach physical, psychological and practical skills to the patient to improve quality of life for the patient (247). Pain management programmes such as these have been demonstrated to reduce pain intensity, decrease emotional distress and reduce absenteeism (248).

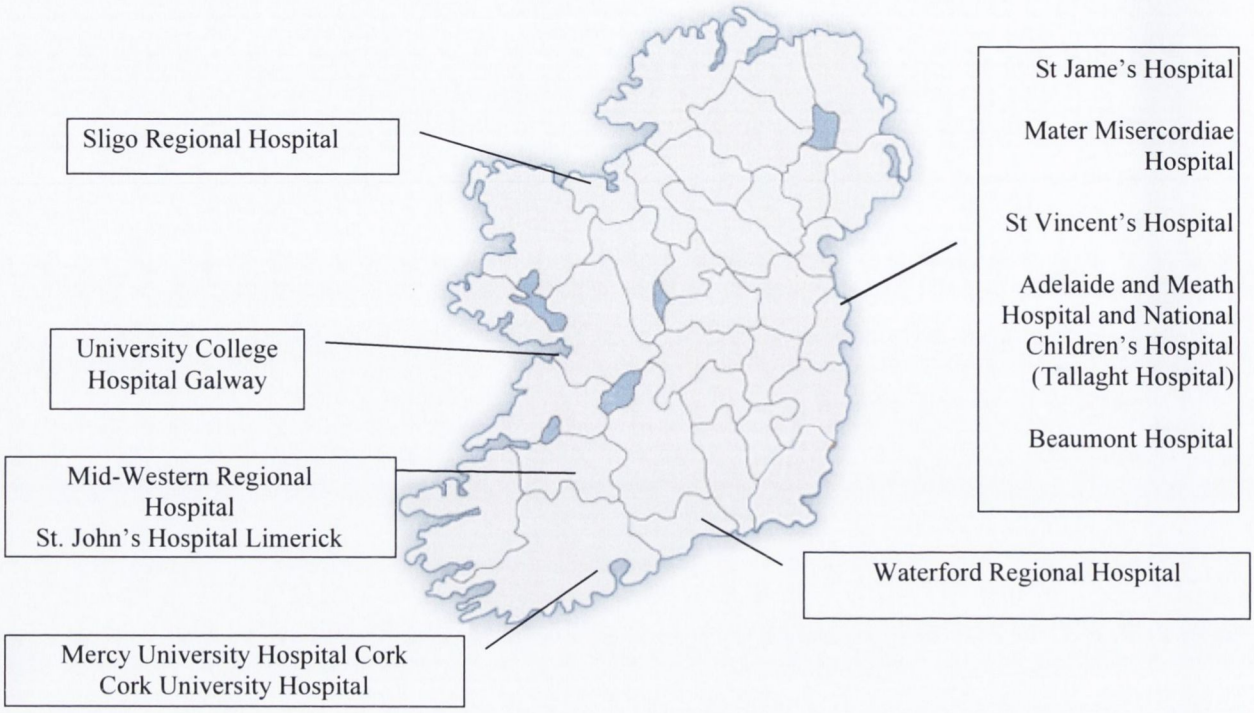


Figure 1-4: Location of specialist pain clinics in the Republic of Ireland

Patients with CNMP and healthcare professionals managing these patients may seek support from a number of sources. A number of patient support groups for individuals with CNMP have been established. The Irish Chronic Pain Association, also known as Chronic Pain Ireland (CPI), was founded in 1992. The organisation aims to provide information and support to those living with chronic pain conditions to provide support to their family and friends.

Research on the subject of CNMP is also active in Ireland, with academics from the fields of medicine, pharmacy, physiotherapy, occupational therapy, economics and psychology contributing to our knowledge of the condition. The Centre for Pain Research (CPR), founded in 2007, is an interdisciplinary pain research collaboration between National University of Ireland, Galway, the HSE and related health service agencies. The centre aims to improve the scientific understanding of pain from the basic sciences through to the population level. The CPR, in conjunction with researchers in the School of Psychology, NUIG, and the Centre for Health Policy and Management, Trinity College Dublin, and the Department of General Practice, NUIG, conducted the PRIME (Prevalence, Impact and Cost of Chronic Pain) study, which is the first national study in Ireland to

provide epidemiological information on the prevalence of pain in the Republic of Ireland, in addition to providing an estimate of the financial burden of chronic pain (30). This research study provides the most recent information on the national prevalence of CNMP in Ireland and information on healthcare utilisation of this population.

There is undoubtedly a growing interest in the problem of effective management of CNMP amongst researchers and healthcare professionals in Ireland and increasing representation of patients with the condition. However, the lack of a national strategy guiding management of these patients in the healthcare system, together with issues relating to access of specialised care, indicates that there are significant hurdles which must be overcome to improve on the current standard of care provided to this patient group.

1.7.2 International Comparisons of Healthcare Systems and Chronic Non-Malignant Pain

In response to the prevalence of CNMP and the negative economic and societal implications of the condition, a number of western healthcare systems have introduced strategies to improve the management of this patient group.

United Kingdom

The National Health Service (NHS) of the UK is a publicly funded health system and provides free at the point of use healthcare for individuals legally resident within the UK. Unlike the Irish healthcare system, access to primary care is free regardless of means. The British Pain Society (BPS) is the largest multidisciplinary professional organisation in the field of pain in the UK and is the British Chapter of the International Association for the Study of Pain (243). The BPS has recently contributed towards the development of the Pain Patient Pathways document. This is a set of management recommendations mapping progression of a patient through care pathways within the NHS system (249). At present, management maps are available for the initial assessment and management of spinal pain, pelvic pain, chronic widespread pain and neuropathic pain. These maps were developed on behalf of the BPS, following the publication of the NHS White Paper, 'Liberating

the NHS', in July 2010, of which one of the core recommendations was the initiation of GP led commissioning (249). The management map system places the GP at the centre of the pathway and also emphasises the necessity to consider self-management strategies to supplement pharmacological or surgical interventions.

United States of America

Healthcare in the USA is delivered through both public and private methods. There are two dominant public healthcare programmes, Medicare and Medicaid, the former serving the population aged 65 years and older, the latter designed to finance healthcare for those of limited means (250).

The 2010 Patient Protection and Affordable Care Act outlined the necessity to heighten national recognition of the condition, to engage public health strategies, to improve self-management and to evaluate the current system of care for patient. The Act required that the Department of Health and Human Services (HHS) sought the assistance of the Institute of Medicine (IOM) in the examination of pain as a public health priority (251). The report produced by the IOM, *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*, presents the study committee's findings and recommendations. Amongst the recommendations contained within the report was the necessity to address the deficiencies in knowledge about the condition, for both patients and healthcare professionals, to increase research into the condition and to remove health system barriers in the management of the condition (251).

Due to the highly privatised nature of the US healthcare system, hospital groups and insurance groups may develop health management strategies to improve patient outcomes; these are separate and distinct from national policies. The Kaiser Permanente Northwest Health Maintenance Organisations Pain Management programme is one such initiative operating in Oregon and Washington which advocates a multidisciplinary primary care oriented approach to pain management services. The programme delivers interventions in primary care through a management team composed of a GP, social worker, physiotherapist, pharmacist and nurse. This programme has succeeded in reducing emergency department visits by 43% amongst patients with CNMP (252).

Canada

Healthcare in Canada is delivered through a group of social health insurance plans that provides coverage to all citizens. It is publicly funded and administered on a provincial or territorial basis, within guidelines set by the federal government. Under the system, citizens are provided preventative healthcare and medical treatments from primary care physicians in addition to access to hospitals, dental surgery and additional medical services. With a few exceptions, all citizens qualify for health coverage regardless of medical history, personal income, or standard of living (253).

Currently, groupings of healthcare professionals and patient support groups are advocating for a National Pain Strategy for Canada, proposing a system whereby provincial and territorial governments of Canada would implement province-wide programs addressing awareness, prevention, health literacy and education of healthcare professionals and improving access to care and research into the condition (254).

Australia

Healthcare in Australia is delivered through public and private providers. Medicare, the state-run healthcare scheme, is available to all citizens, permanent residents and some temporary visitors. A key principle underlying Australia's health system is universal access to most health care regardless of ability to pay (255).

Australia were amongst the first westernised healthcare systems to introduce a national pain strategy. The National Pain Strategy Pain Management for all Australians (2010) documents the assessment and treatment approaches for all types of pain in the context of the Australian healthcare system; PainAustralia, a national not-for-profit body, was established to implement the policy (254). The strategy identifies pain as a national health priority and describe health systems structures that currently provide the highest quality of care for pain patients. The strategy aims to improve management of CNMP in Australia by proposing a new cost-effective, efficient multidisciplinary model of care.

In summary, it would appear that a number of western healthcare systems are making concerted efforts to provide a structured system of care to patients with CNMP. The prevalence of the condition within these countries and the burden this places on the healthcare system appears to be the primary impetus for these measures. Since, a number of these national strategies and healthcare initiatives have only recently been introduced to these countries, it is difficult at present to compare the efficacy of these measures.

1.8 Conclusion

Chronic non-malignant pain arises from an initial impairment of the central and peripheral nervous system that persists beyond a defined period during which resolution of the condition would be expected to occur. The condition is associated with a range of negative physical, social, emotional, psychological and financial outcomes for patients particularly when poorly managed. It is necessary for healthcare professionals charged with care of these patients to appreciate the complexity of the condition and consider these non-physical dimensions of the condition when constructing a pain management plan. Pharmacotherapeutic, non-pharmacotherapeutic and surgical interventions may be used separately or in combination to provide pain relief for patients. Prescription and non-prescription analgesics are important management tools available to healthcare professionals when developing a patient management plan. Analgesics prescribed for the patient may be dependent on the severity of the condition, the clinical appropriateness of the medication or the decision making process of the clinician. Physiological alterations associated with the ageing process, increased morbidities, cognitive decline and polypharmacy may limit the types of analgesics a clinician may use for pain management. This can lead to the under-treatment of CNMP in ageing and elderly patients, a problem which is further exacerbated by the under-reporting of pain by this population. Patients can also influence the nature and extent of pharmacotherapeutic use in the management of their condition. Patients may be reacting to personal perceptions of medication, beliefs about the condition or experiences of adverse outcomes arising from medication use. These individuals may also be motivated by external influences such as sociocultural perceptions of

medications or information obtained from the media. Patients that are not adequately managed in primary care may require referral to specialised pain clinics or benefit from pain management programmes. The two-tier nature of the Irish healthcare system may limit access of publicly and privately funded patients with CNMP to secondary or tertiary level care. These patients are therefore predominantly supervised by GPs in primary care in which pharmacotherapy is a key component of pain management.

Key points from literature review:	Chronic non-malignant pain is variously described as persistent pain continuing for a period of >3 or ≥6 months after injury. The International Association for the Study of Pain has defined the period as >3 months; this is the definition used for this thesis.
	Ageing and elderly is defined as a population aged 50 and older. Those aged 65-80 are termed 'ageing', while those aged 80 years and older are termed 'very aged'. This PhD thesis related to an ageing and elderly population, as it focuses on individuals aged 50 years and older with CNMP.
	Estimates of the prevalence of CNMP obtained from epidemiological studies vary according to the defintiion of CNMP used in the study and the population of interest. The prevalence of the condition has been estimated to be 13-35% in Ireland. Female gender, increasing age, lower socioeconomic status and poor mental health are amongst the key factors associated with CNMP.
	The non-reductionist Biopsychosocial Model facilitates interpretation of the complexity of CNMP. Incorporating this into patient management strategies may enhance the quality of care delivered by healthcare professionals.
	Management of CNMP in the context of the Irish healthcare system is influenced by the absence of a national pain strategy, a fragmented system of referral from primary to specialist care and the absence of publicly available analgesic prescribing guidelines for CNMP for primary care.
	Management of CNMP may be achieved by pharmacotherapeutic, non-pharmacotherapeutic and/or surgical interventions. The WHO Analgesic Ladder is an important framework directing the prescribing of analgesics. It was designed in 1986 for the prescribing of analgesics in malignant pain. Adaptations of the WHO Analgesic Ladder have been suggested for analgesic management of CNMP but have not yet been formally incorporated into a document by the WHO.
	Opioid analgesics appear in Steps 2 and 3 of the WHO Analgesic Ladder. Opioid medications are associated with issues of abuse and misuse in vulnerable populations in addition to being clinically inappropriate for particular patients. Aberrant opioid behaviors are particularly prevalent in the USA but such behaviours have not been observed to the same extent in European populations.

Chapter 2. PhD Thesis Overview

2.1 Background

The literature review presented in *Chapter 1* described the manner in which the development and delivery of an appropriate pharmacotherapeutic regimen for CNMP in primary care is influenced by the health system, the availability of guidelines combined with GP and patient factors. *Figure 2-1* presents a conceptual model proposing the manner in which these factors may interact to affect the management of CNMP.

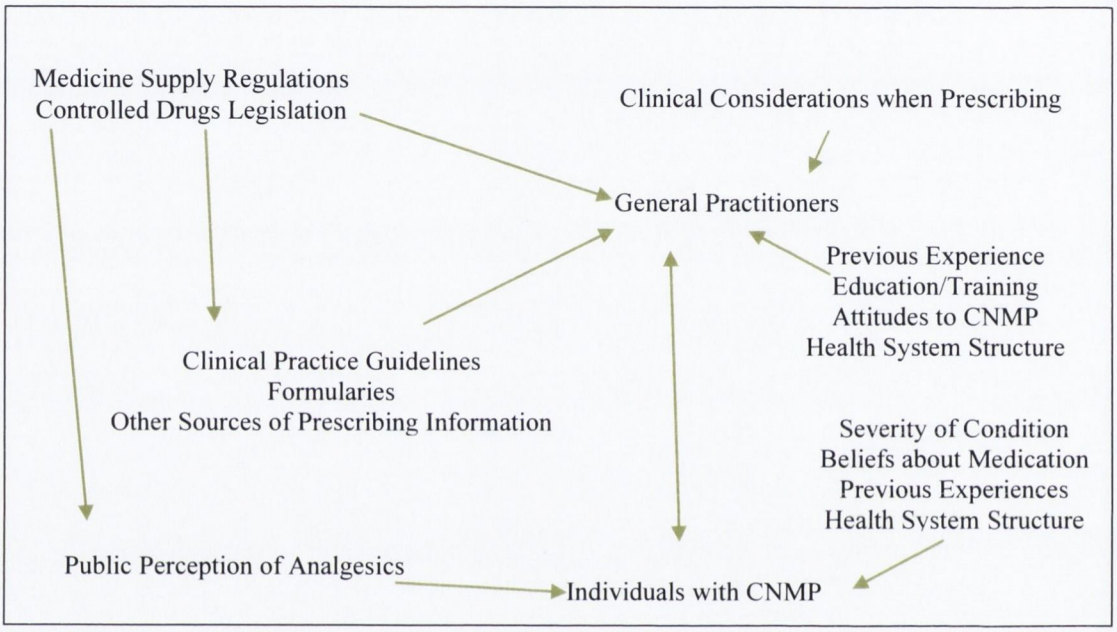


Figure 2-1: Conceptual model outlining factors influencing pharmacotherapeutic management of CNMP

The following aspects of the conceptual model contribute to the development of the research question:

1. Pharmacotherapeutic interventions are one branch of the biopsychosocial model of healthcare which also informs the management of CNMP (256). In the case of pain management, analgesic prescribing is based upon the 1986 WHO Analgesic Ladder; this framework is widely used in guiding pharmacotherapeutic prescribing in the absence of a distinct analgesic ladder for CNMP (257). At present, there is no national clinical practice guideline on the prescribing of analgesics publicly available to GPs, for the general population or ageing and elderly individuals, nor is there a national strategy

directing management of this condition. Therefore, elements of public policy and regulation of medication supply in Ireland, together with recommendations contained within formularies and similar documents, inform prescribing decisions (258). Furthermore, clinician factors may inadvertently create a framework of practice requirements that influence prescribing practices, for instance, perception of risk associated with analgesic medications, concerns about misuse of opioid analgesics and professional experience in the management of CNMP (259, 260). These issues may be compounded by a sense of scrutiny from professional authorities which may further influence the approach to practice (261).

2. A multidisciplinary approach in the delivery of pain management services, incorporating the elements of the biopsychosocial model of healthcare, is recommended for effective disease intervention (262, 263). To date, the delivery of healthcare to CNMP patients in Ireland has been characterised by a fragmented system with insufficient integration of medical disciplines, with no uniform structure to deliver shared care (264). General practice is frequently the first and only point of contact with the medical service for patients with CNMP, with approximately 2-5% of patients evaluated or treated by pain specialists (242, 265). Access to physiotherapy and specialised pain management is difficult for these patients and may cause them to be managed in primary care for prolonged periods (242).

3. Patient attitudes and beliefs about the condition and perspectives of clinical interventions are factors which may also have a significant impact upon disease management and progression (266, 267). This is especially true of opioids, since public knowledge of the negative aspects of opioids, particularly addiction and misuse of morphine and heroin, is widespread (268). Concordance with a prescribed medication regimen therefore centres on a patient's decision making process in which medication concerns are consciously or unconsciously balanced with the necessity for the medication, perceived risk-benefit ratio of therapy or previous experiences with the medication (212).

In summary, the type of medications prescribed and the manner in which these agents are taken is not merely a product of the interplay between the GP and the individuals presenting with CNMP. It is a complex dynamic process, responsive to a variety of external factors which are themselves in a state of flux.

2.2 Research Question

Based on the points presented in *Section 2.1*, this gives rise to the research question: How is chronic non-malignant pain managed with pharmacotherapeutic interventions in ageing and elderly populations in primary care, and what are the GP and patient factors that influence the use of these medications?

2.3 Aim & Objectives

The aim of this research is to describe the nature of, and factors affecting, the use of analgesics, particularly opioid analgesics, by individuals aged 50 years and older with chronic non-malignant pain conditions in Ireland.

This aim will be achieved by three objectives:

- **Objective 1:** To identify the type and quality of information that may be used by clinicians when prescribing opioids for CNMP;
- **Objective 2:** To describe the nature and extent of analgesic use by ageing and elderly populations with CNMP in the Republic of Ireland;
- **Objective 3:** To investigate the factors affecting the prescribing of analgesics for ageing and elderly populations by primary care physicians in the Republic of Ireland.

2.4 Thesis Outline

2.4.1 Overview of Studies

A systematic review of CPGs relating to opioids, combined with quantitative investigations, will establish the current theoretical and actual pharmacotherapeutic management of CNMP. It will provide an overview of the features of an ageing and elderly chronic pain population and describe the patterns

of analgesic use of the non-malignant pain population relative to the general ageing and elderly population. Having characterised the range and scope of the issues through these studies, qualitative research seeks to explore explanations for the patterns of analgesic use in the context of the Irish healthcare system.

Chapter 3 is a systematic literature review of international clinical practice guidelines directing the prescribing of opioid analgesics in CNMP. It provides an indication of both the quality and clinical content of these clinical practice guidelines, which will inform and facilitate interpretation of both qualitative and quantitative investigations. This chapter is intended to provide an overview of the specific issues associated with this class of medication and the measures which may be undertaken to minimise adverse outcomes for the patient, providing further understanding of the nature and extent of scientific evidence on this subject; this will contribute to an evaluation of the findings in the remainder of the studies.

Chapter 4 and *Chapter 5* describes the quantitative investigations of the Health Services Executive - Primary Care Reimbursement Service (HSE-PCRS) and The Longitudinal Study on Ageing (TILDA) respectively. The HSE-PCRS database provides an outline of national prevalence statistics for analgesic use amongst the general population aged 55 years and older, under the General Medical Scheme (GMS) in Ireland for the years 2003-2011. The TILDA research describes the demographic features and analgesic use through cross-sectional analysis of a nationally representative population reporting non-malignant pain.

Having presented a quantitative description of the phenomenon of analgesic use in the ageing and elderly Irish population, and more specifically in an ageing and elderly NM pain population, an explanation of these findings is sought in *Chapter 6* and *Chapter 7*. *Chapter 6* describes semi-structured interviews with GPs, key stakeholders in the provision of patient care in the Irish healthcare system. *Chapter 7* details the findings from semi-structured interviews with members of Chronic Pain Ireland (CPI). This study contextualises the findings from the quantitative investigations and provides an insight into the patient's perspective of CNMP management in the Irish healthcare setting. The qualitative research studies are the final phase of the PhD research and will provide a unique insight into the issues associated with pharmacotherapeutic management of CNMP specific to the Irish setting.

Chapter 8 discusses the findings of the thesis, describing the potential implications for health policy in Ireland. It is hoped that findings from this research will contribute to a growing body of knowledge of CNMP in Ireland and also improve the quality of pharmacotherapeutic management of ageing and elderly populations with this condition. *Figure 2-2* demonstrates how each of the research objectives described in *Section 2.3* maps onto each the studies described above to answer the research question.

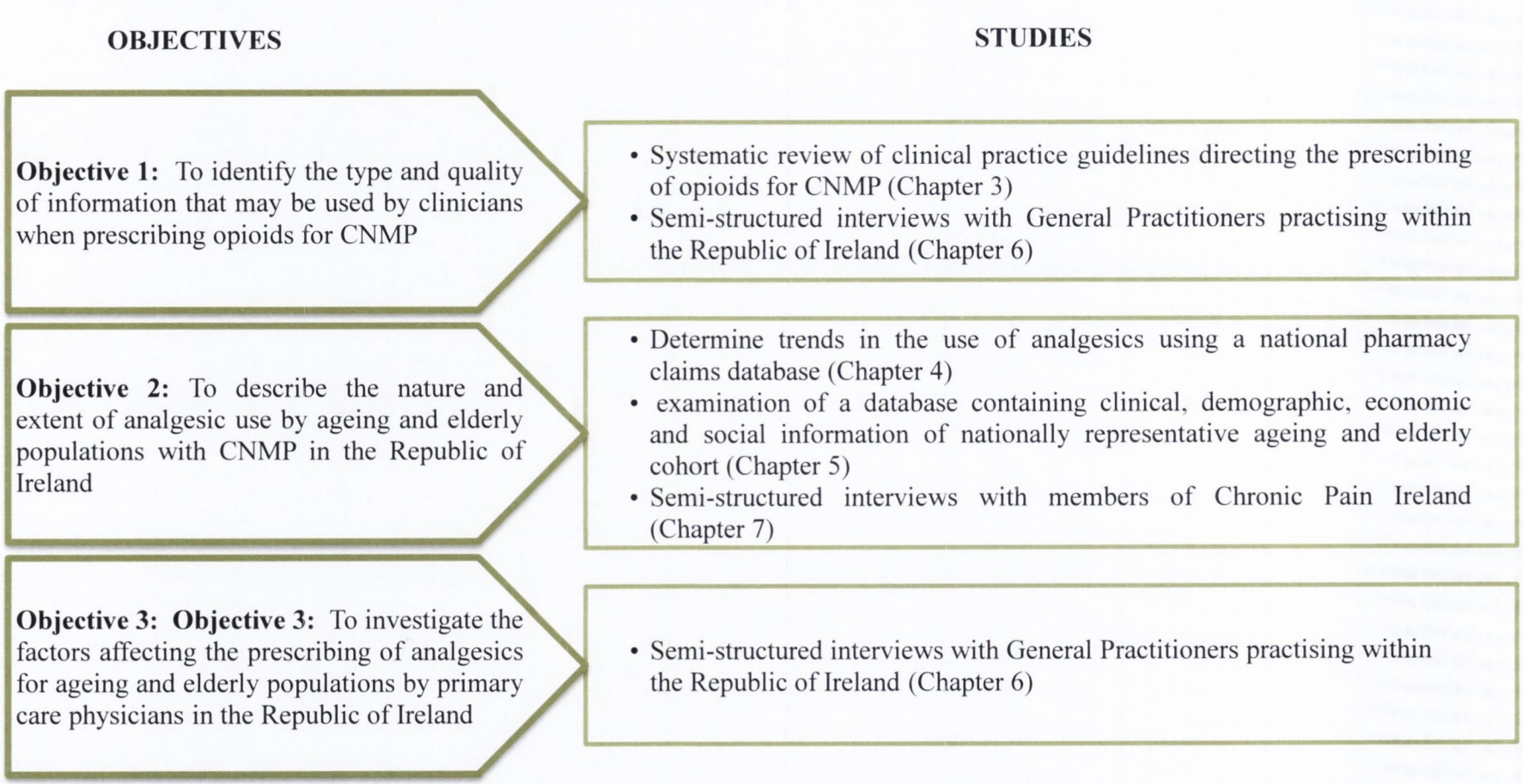


Figure 2-2: Mapping of objectives to the studies described in Chapters 3-7

2.4.2 Selection of Mixed Methods

Mixed methods research is acknowledged as the third major research paradigm in addition to qualitative and quantitative research methodologies (269). It is defined as 'research in which the investigator collects and analyses data, integrates the findings and draws inferences using both qualitative and quantitative approaches or methods in a single study'(270). This design approach originates from a belief that a combination of qualitative and quantitative approaches to answering a research question is feasible and preferable for some forms of social, behavioural and human sciences (269).

This study has mixed sequential design whereby the systematic review and quantitative studies were conducted to describe the extent and nature of the analgesic use by ageing and elderly populations with CNMP while the qualitative studies were used to aid in the interpretation quantitative output. Combining the findings from quantitative studies, grounded in the positivist paradigm, with the constructivist philosophy of qualitative research captures the complexity of the subject matter (269, 271). The methodology addresses the complexity of the research question and acknowledges that there are multiple factors affecting the process (272). The approach permits a rigorous interrogation of the various factors associated with the use of analgesics among individuals with CNMP and attempts to describe the manner in which stakeholders interact to produce the stated outcomes (272).

There are, however, a number of limitations with mixed methods research. This approach requires the researcher to become familiar with a variety of research techniques but specialise in none. Furthermore, the methods must be mixed appropriately and effectively to answer the research question. This research approach also places significant pressures on time and resources of the researcher (273). Finally, interpretation, appraisal and integration of results obtained from the methodologies may be challenging for the researcher (271).

Chapter 3. Systematic Review of Clinical Practice Guidelines Directing the Prescribing of Opioids for Chronic Non-Malignant Pain in Primary Care

3.1. Background

Clinical Practice Guidelines (CPGs) have been defined as 'recommendations intended to optimise patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative options' (274). They are a means of communicating scientific evidence in an accessible manner to healthcare professionals (275). Guidelines are designed to inform clinical decision-making with respect to diagnosis and management of patient groups, to act as a tool to assist in the delivery of a homogenous standard of care and to act as a possible guide to the allocation of economic resources (276). They are also viewed as instruments by which accountability for the delivery of healthcare services may be determined and assessed (277).

Recommendations contained within guidelines are 'actions that should be considered but may be performed depending on the patient, the circumstances, or other factors (258, 278). Recommendations may be derived from systematic reviews of available evidence on the subject or through a process of expert consensus (154, 276). The development of high quality guidelines is dependent therefore upon the rigour with which this evidence base is evaluated; this requires a systematic, transparent approach that may be audited by external parties (277). Implementation of guideline recommendations may be challenging due to constraints in the healthcare system or issues associated with the regulation of healthcare professionals at a regional or national level. Clinical practice guidelines, therefore, may need to be adapted for local applicability. At this interface between (inter)national recommendations and regional or local requirements, it is possible that the adaptation of recommendations may produce a divergence from the underlying scientific evidence; indeed in the absence of a systematic and rigorous approach, guideline adaptation for regional purposes may undermine the clinical intentions of the original guideline (278-280). Therefore, it is necessary to review guidelines prior to publication and dissemination to consider the clarity, applicability and acceptability to the target audience and the extent to which recommendations suit specific regional restrictions or limitations and patient circumstances (281).

Constructing guidelines for chronic non-malignant pain (CNMP) is challenging, perhaps more so than acute or chronic malignant pain, due to the

diversity of types and aetiologies of the condition and the intractable, progressive nature of the pain which frequently requires multi-faceted management (282). The subjective nature of pain requires the physician to interact with the patient to successfully determine the severity of pain or the efficacy of the analgesic intervention. Indeed, rational prescribing principles require that the patient is viewed in a wider context, considering not only the appropriateness of the medication but the initial evaluation and continued monitoring of the condition (283). Clinicians should therefore be cognisant of the clinical effectiveness of medication, minimisation of harm, avoiding waste of healthcare resources and patient preferences to ensure that medications are prescribed and managed in a patient-centric manner. The rational prescribing pathway outlined in *Figure 3-1* emphasises the necessity to focus on patient outcomes and not merely the clinical or therapeutic aspects of initiation of therapy (283). Such considerations should therefore be contained within any guideline aimed at physicians and be described in sufficient detail to permit clinicians to inform prescribing decisions.

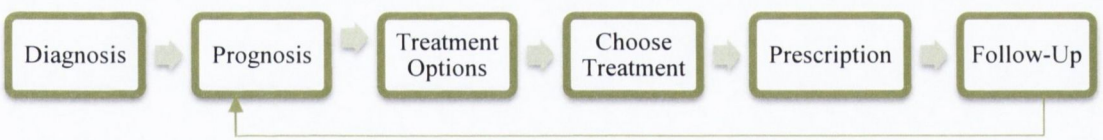


Figure 3-1: Rational prescribing pathway

The World Health Organisation (WHO) Analgesic Ladder provides a framework on which to base a rational prescribing approach for pain although it has been proposed that modifications are required for non-malignant pain, as previously discussed in *Chapter 1*. The ladder proposes that opioid analgesics, introduced in Step 2 and Step 3, should be considered in the management of moderate and severe pain conditions (284). However, the clinical appropriateness of opioids for individuals with CNMP should be reviewed at the point of prescribing taking into account the potential for adverse outcomes, medication interactions and the potential for aberrant drug behaviours (156, 160). The potential risks associated with opioid use for CNMP in the primary care setting may be addressed through

application of clinical judgement and the enforcement of recommendations on monitoring and review of patients contained within several evidence based guidelines (285).

A number of appraisal tools have been developed to review the transparency of guideline development and resultant quality of guidelines but these vary considerably in their quality and scope (286). The Institute of Medicine (IOM) was the first to develop an instrument that assessed the key features of quality guidelines, validity, reliability, clinical applicability, flexibility, clarity and patient review (287). Subsequent tools have sought to enhance the precision of assessment and quality assurance that can be derived from the application of the appraisal tool to a clinical guideline (287). An examination of the literature on the development and application of the appraisal tool indicates a disparity in the scope, validity and transparency of the instruments. However, critical appraisal tools are appropriate only for the evaluation of the methodological development and presentation of content within a guideline and do not evaluate the clinical content of the guideline nor do they evaluate the quality of the clinical evidence contributing toward the development of the guideline (287). *Table 3-1* provides an overview of a number of critical appraisal tools and the contribution of the instrument to the development of retrospective appraisal of the guideline.

Table 3-1: A selection of instruments for review of guidelines (all instruments are validated)

Name of Instrument	Description	Contribution to Development
Conference on Guideline Standardisation Checklist (COGS) (288)	Defines a standard for guideline identifying features such as quality and implementation facilitation. Checklist of 18 items defines the components necessary for evaluation of validity and usability of a guideline.	Prospective use to improve the guideline by improving documentation
Methods for Evaluating Research Guideline Evidence (MERGE) (289)	Used when reviewing the quality of studies for clinical or public interventions or when reviewing existing guidelines and recommendations. Consists of 5 checklists for reviewing quality of studies.	Prospective tool for guideline development or retrospective review instrument for users of a guideline
Grades of Recommendation Assessment Development and Evaluation (GRADE System) (290, 291)	System for grading clinical evidence and creating guidelines based on the underlying evidence. The GRADE approach provides guidance for rating quality of evidence and grading strength of recommendations in health care (292).	Prospective tool for guideline development or retrospective review instrument for users of a guideline
The Appraisal of Guidelines for Research and Evaluation Tool (AGREE II) (293)	Twenty-three item instrument that evaluates the development methodology and how well the process is reported Does not assess the clinical content of the guideline or the quality of evidence that underpins the recommendations (294).	Prospective tool for guideline development or retrospective review instrument for users of a guideline
Are guidelines following guidelines? (295)	Twenty-five item tool with questions on guideline format and development (10 items), identification and summary of evidence (10 items) and formulation of recommendations (5 items).	Retrospective review instrument for users of a guideline
Evaluation of guidelines developed by specialty societies (280)	Three items consisting of a description of the type of professional involved in developing the guideline, a description of the sources of information used to retrieve relevant evidence and grading of the evidence in support of recommendations.	Retrospective review instrument for users of a guideline

A critical approach to clinical practice guidelines (296)	Nine question instrument which examines quality relevance and effectiveness of the guideline. Questions are divided into those directed at consumers and those directed at guideline developers. Answers in a yes/no format.	Prospective tool for guideline development or retrospective review instrument for users of a guideline
Generic methodology to assess the quality of clinical guidelines (293)	Thirty-seven items across three dimensions rigour of development, clarity of presentation and implementation issues. Appraises the validity and content of guidelines and helps to establish a framework for systematic development of new guidelines (286).	Prospective tool for guideline development or retrospective review instrument for users of a guideline

3.2. Aim

To perform a comprehensive systematic search for, and evaluation of, clinical practice guidelines directing opioid analgesic prescribing for the management of CNMP in the primary care setting and to evaluate the quality of development and clinical content of these guidelines.

3.2.1. Study & PhD Research Objectives

This study was conducted to meet Objective 1 described in *Chapter 2, Section 2.3*: To identify the type and quality of information that may be used by clinicians when prescribing opioids for CNMP.

3.3. Methods

3.3.1. Search Strategy

Guidelines were identified by a systematic search through electronic resources and the application of the exclusion criteria to publications identified in the search. Pubmed, CINAHL, Embase and Web of Science were searched using standard Medical Subject Headings (MeSH) terms. The International Association for the Study of Pain (IASP) was also used as an initial reference point to amass a list of further websites of interest through which guidelines may be accessed. This resource provided links to a further 300 websites that referred to pain or focused on specific conditions in which pain is a symptom. The search was finally extended to include websites of (inter)national professional and patient groups, guideline repositories and guideline development bodies. The general search terms '*chronic pain*', and '*opioids*', were used in the search of the IASP and inter(national) websites to identify potentially relevant publications. The search was completed in March 2012. The search strategy of electronic databases and other websites is detailed in *Appendix B, Table B-1.*

3.3.2. Eligibility Criteria

Guidelines were included if they met the conditions outlined in *Table 3-2.*

Table 3-2: Inclusion and Exclusion Criteria

Inclusion Criteria	***Population***	Adult ≥18 years with CNMP
	Intervention	Opioids used in the management of CNMP
	Target Audience	Physicians licensed to prescribe in primary care setting
	Health Care Setting	Primary care
	Publication Type	Clinical Practice Guidelines
	Search Period	Earliest available in database(s)
	Language	English
Exclusion Criteria	• Guidelines referring to non-pharmacotherapeutic interventions • Guidelines superseded by a more recent version • Guidelines referring exclusively to secondary or tertiary care settings • Guidelines containing recommendations for pharmacotherapeutic management requiring specialist intervention	

3.4. Guideline Assessment

Those guidelines retained for review were evaluated with the AGREE II statement and a set of 16 clinical content criteria. Two appraisers (MCK & RG) conducted the assessment of the guidelines using the AGREE II instrument and the clinical content criteria using the method described in *Figure 3-2.*

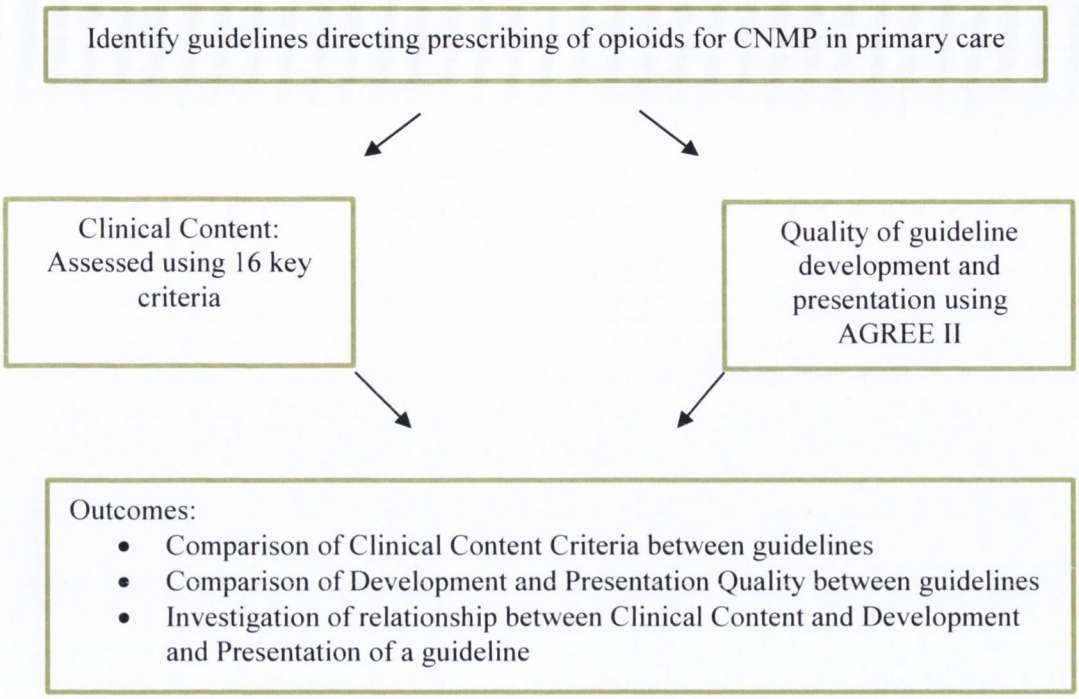


Figure 3-2: Overview of review process for guidelines

The AGREE II (Appraisal of Guidelines for Research & Evaluation II) instrument was chosen for this review of opioid guidelines (287). The instrument was selected as it is validated and may be applied prospectively or retrospectively to guidelines through the application of a numerical rating scale. Scoring of guidelines would facilitate comparison between the findings of the individuals reviewing the guidelines and allow for meaningful interpretation of differences or similarities between guidelines. Furthermore, this assessment instrument has been used extensively to complete similar studies, therefore references on the application and interpretation of the instrument were widely available.

Two appraisers (MCK & RG) reviewed the retained guidelines. Both appraisers completed the online training tools recommended by the AGREE collaboration prior to commencing the review process. The AGREE II assessment was conducted online and stored electronically in a password protected account. The instrument includes 23 statements across 6 domains; statements are rated from 1 (strongly disagree) to 7 (strongly agree). A seventh domain requires appraisers to determine if the guideline is recommended for use, with or without modifications, or not recommended for use. The AGREE II instrument is

accompanied by detailed instruction for the appraisers on the criteria to be considered for each of the 23 statements which aids interpretation of criteria and harmonisation of scoring (297). *Table 3-3* outlines the headings of each of the domains and the number of items within each domain.

Table 3-3: AGREE II instrument domain structure

	Domain	Number of Items	Description
1	Scope and Purpose	3	Aim of the guideline and identification of target group
2	Stakeholder Involvement	3	Extent to which appropriate stakeholders were involved in developing the guideline and represents the views of its intended users
3	Rigor of Development	8	Process of gathering and summarising the evidence, methods used to develop recommendations
4	Clarity of Presentation	3	Language, structure, format of guideline
5	Applicability	4	Barriers and facilitators to implementation, strategies to improve uptake, resources needed to implement the guideline
6	Editorial Independence	2	Biases due to competing interests
7	Overall Guideline Assessment	1	Recommended/recommended with changes/ not recommended

Following independent completion of the review process, the results were merged into the AGREE II rater concordance calculator spreadsheet (298). This spreadsheet contains formulae previously entered in certain cells such that the overall score for each question and each domain can be calculated. The standard deviation (SD) between the scores assigned by the appraisers across the domains can also be calculated. Scaled percentages are calculated on this spreadsheet to permit inter-domain comparison. *Appendix B, Table B-2* provides a template of the scoring sheet used when completing an assessment with AGREE II and an outline of the formula used to calculate the scaled percentage scores.

A rater concordance tool is also provided by the AGREE development team and indicates if more than two appraisers are required. The decision to add an additional appraiser is based on the concordance of the first two appraisers results.

A third appraiser is required if the item scores of two appraisers are greater or equal to 1.5 SDs (calculated from the mean of 3 of 5 domains) or if individual scores are greater or equal to 2 (calculated from the mean of 5 domains). If results remain discordant after evaluation by three appraisers, a fourth reviewer is sought. A third or fourth appraiser was not required for this study as there was concordance between the scores of MCK & RG.

Following discussion between the appraisers, it was decided that an 'Overall Outcome of Guideline Development' score in the range 0-3 would indicate that a guideline was not recommended for use, a score in the range 4-6 was recommended for use, but with modifications, while those scoring >6 were recommended for use without modification.

3.4.1. Evaluation of Clinical Content

A set of clinical content criteria was developed to define the key features of guidance for prescribed medications and also to identify the additional components that may be present in prescribing recommendations for opioid analgesics. A number of resources were accessed to develop the clinical content classification criteria including the British National Formulary (BNF), National Institute for Health and Care Excellence (NICE) guidance and electronic sources of information available to clinicians such as the American Medical Association (AMA) website. The BNF is a joint publication of the British Medical Association and the Royal Pharmaceutical Society and aims to provide healthcare professionals with up-to-date information on medications. Guidance relating to medications is contained within the monographs providing information on indication, dose, hepatic/renal impairments, side-effects, cautions, contraindications and pregnancy and lactation (*Figure 3-3)*. Medication interactions are considered as a separate section in an appendix of the BNF. The monograph therefore focuses particularly on the clinical appropriateness of the agent for the patient (128).

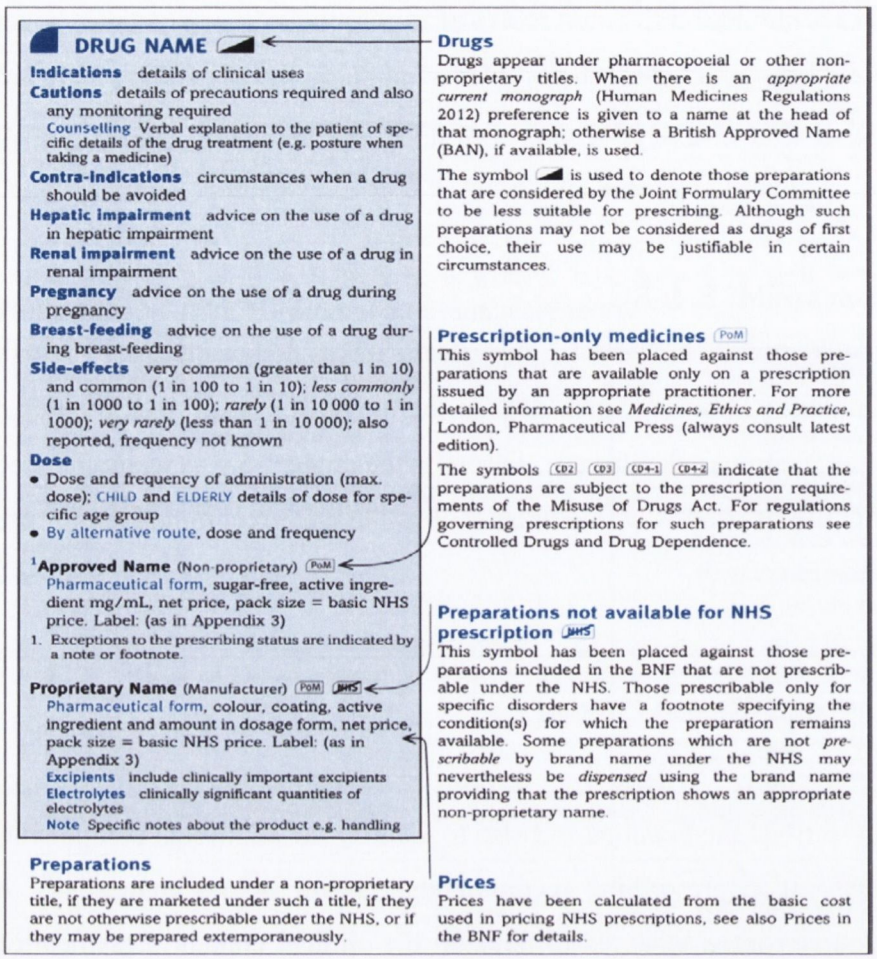


Figure 3-3: Extract from medication monograph from British National Formulary

The American Medical Association (AMA) has developed 8 principles for the safe prescribing of opioid medications which have been endorsed by the American Academy of Pain Medicine. They were developed in response to the increase in use of prescription opioids in the US which may be associated with physician led over-prescribing or misuse or abuse by patients or other individuals; negative patient outcomes may occur with overuse or unanticipated co-morbidities such as respiratory or cardiovascular issues (155, 299). The 8 principles are outlined in the right column of *Table 3-4,* (300). The principles relate in some cases to specific co-morbidities of the patient or concurrent medications. The left-hand column headings have been developed to summarise the themes emerging from these principals, merging some of the similar recommendations.

Table 3-4: Summary of themes and AMA principles of safe prescribing

Summary of themes	8 Principles of Safe Prescribing
Clinical Cautions or Contraindications	1) Respiratory
	2) Apnoea
	3) Co-Morbidities
	4) Long-Term Use
Patient-Oriented Cautions/Contraindications	5) Experience- assess biologic, social and psychiatric risk factors
Dose Reduction/Switching	6) Caution when Switching
Dose Initiation	7) Initiating Methadone
Medication Interactions	8) Benzodiazepines

Sixteen clinical criteria were developed independently by two researchers (MCK & RG) working together by combining the content considered in a BNF monograph and those proposed by the AMA; these are listed and defined in *Table 3-5*. These criteria also reflect those principles described in Passik's 'Four A's of Pain' which proposes a strategy for the physician to review a patient's analgesic regimen through monitoring pain relief, impact on activity levels, adverse effects and assessing for aberrant drug related behaviours (284). The two researchers initially agreed on 13 clinical content criteria. A third party (MH) then reviewed the three clinical criteria which were disputed by the two researchers, resulting in the finalisation of a 16 item list.

Table 3-5: Clinical Criteria for assessment of content of guidelines directing prescribing of opioids in CNMP

Domain	Items	Description
Condition & Severity	***Definition of CNMP Duration***	CNMP has been variously defined in the literature as lasting 3 or 6 months. For the purposes of this guideline, the presence of a definition of CNMP would be considered adequate if the authors attempted to define the condition, using any definition available in the literature.
	Pain Measurement Scale (Establish Severity)	A recommendation to evaluate the patient's current level of pain using a validated pain scale (285).
	Pain Measurement Scale (Monitoring Analgesia)	A recommendation to repeat the pain measurement scale or another similar scale following introduction of the drug therapy.
Pharmaco-therapeutic Details	***Indication***	A symptom that suggests certain medical treatment is necessary.
	Dosage	The measured quantity of a therapeutic agent to be taken at one time.
	Contraindication	Specific situation in which a medication, procedure, or surgery should not be used because it may be harmful to the patient.
	Cautions	Situation in which a medication may be used but at a modified dose or frequency and with active monitoring by the prescriber (128).
	Interactions	An interaction is said to occur when the effects of one drug are changed by the presence of another drug, herbal medicine, food, drink or by some environmental chemical agent (301).
	Pregnancy & Lactation	Reference to use of opioids in women who are pregnant or breast-feeding (128)
	Side-Effects	Undesirable pharmacological effect at recommended doses (302).
	Management of Side-Effects	Reference to pharmacotherapeutic or lifestyle management approaches to side-effects.
Risk Management : Guidance	***Dose Escalation***	Opioid analgesics may need to be gradually introduced to a patient; a process of dose titration is said to be required in this instance. Dose titration is the manner in which a medication dose may be progressively increased or decreased in response to the patient's status. Dose escalation or dose reduction should be discussed and a procedure outlined in the guideline to guide prescribers.
	Dose Reduction	
	Identifying/ Monitoring Addiction	Addiction, which can include physical dependence, is distinguished by compulsive drug seeking and drug use despite sometimes devastating consequences (303).
	Managing Addiction	Recommendations on managing a patient with opioid addiction e.g. referral to support services.
	Overdose	When a drug is eaten, inhaled, injected, or absorbed through the skin in excessive amounts and injures the body. Overdoses may be intentional or unintentional; if the person taking or giving a substance did not mean to cause harm, then it is unintentional (304).

A Microsoft Excel spreadsheet was developed containing, the names of each of the guidelines, the clinical content criteria and a drop down menu in each cell with the options of 'Present', 'Partially Present' or 'Absent'. The classification system is based upon an adaptation of the Cochrane Collaboration assessment for the risk of bias i.e. low, high and unclear (305). The presence, partial presence or absence of each recommendation within the guideline was determined independently by the same appraisers that completed the AGREE II assessment. Following this independent appraisal process, results were compared. Since the results obtained by the two appraisers were identical, it was not necessary to seek the opinion of a third appraiser. A score of 1, 0.5 and 0 was then apportioned to each of the clinical content criteria depending on the presence, partial presence or absence of the criteria respectively. Awarding of scores in this manner allowed an overall score to be calculated (addition of scores from absence, partial presence and presence) for the guideline which is reflective of the completeness of the clinical content of the guideline. This is summarised in *Table 3-* 6.

Table 3-6: Clinical Content Criteria

Criteria	Description	Symbol	Clinical Content Criteria Score
Present	Reference to the clinical criteria. Sufficient detail present to facilitate the clinician to support a prescribing decision.	+	1
Partially Present	Reference to the clinical criteria, however, insufficient detail to support the prescriber in managing the opioid regimen of the patient.	±	0.5
Absent	No reference to the clinical criteria in the guideline (including Appendices)	–	0

3.5. Results

Publications were identified and the title and abstract reviewed for eligibility. A core set of guidelines relating only to the prescribing of opioid analgesics for CNMP patients in the primary care setting was collated. A flow diagram of the search strategy is presented in *Figure 3-4*; 3,956 unique records were screened for

eligibility, 109 full text guidelines were assessed for eligibility, with 11 being identified as eligible for inclusion.

Six of the guidelines were developed in the USA, two in Canada, one in UK and two in Australia. *Table 3-7* provides a list of the full titles of guidelines included in this study, the abbreviation used when discussing analysis and results in this document and a brief description of the stated aims of the guidelines. Guidelines ranged from 12 pages to 181 pages in length, with the average length being 66 pages. Four guidelines were written by Health Service Providers (HEW; GSAGP; UCG; DVA/DOD), while the rest were produced by Professional/Representative Bodies. The earliest year of publication was 2002, with the most recent guideline published in 2010.

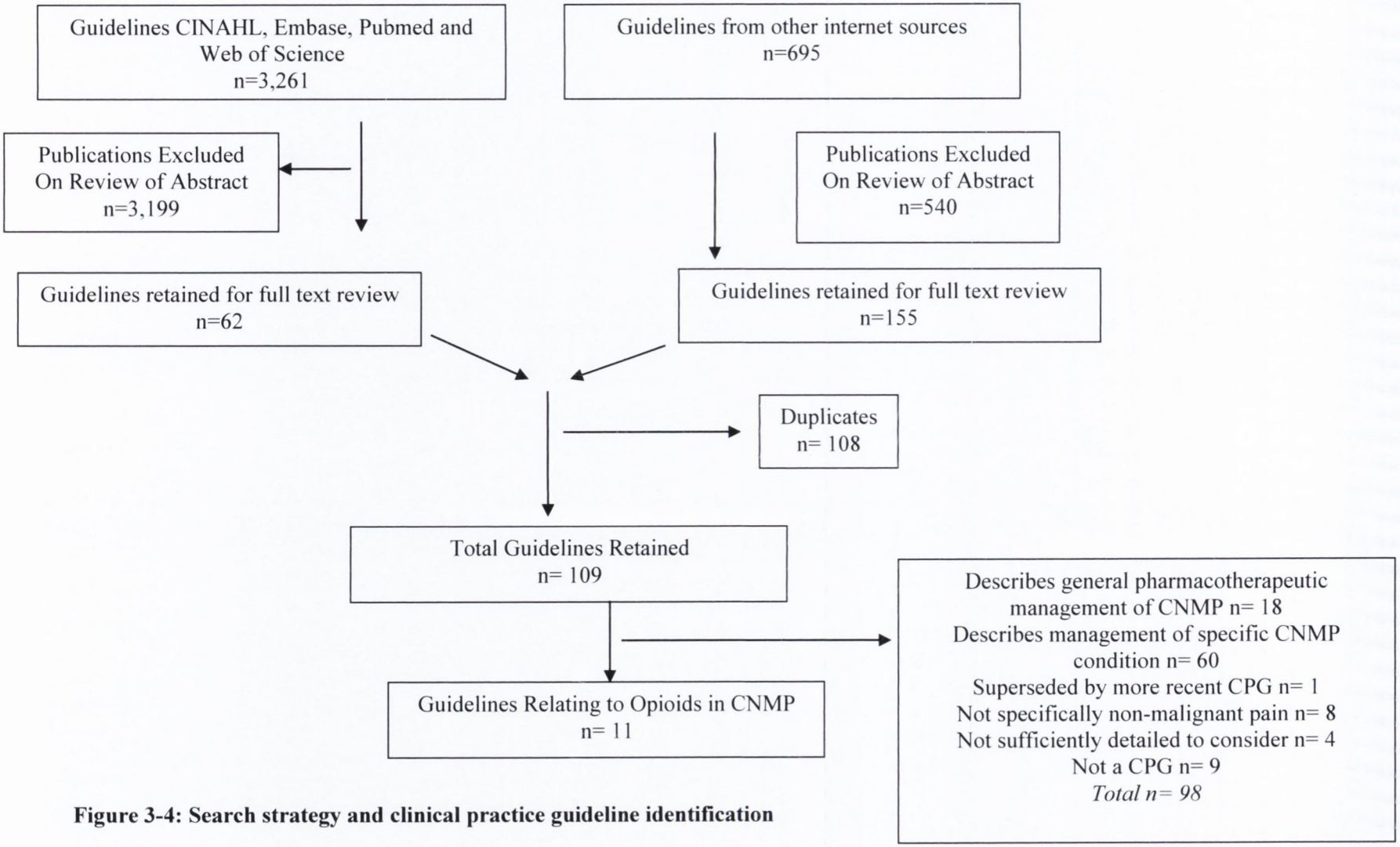


Figure 3-4: Search strategy and clinical practice guideline identification

Table 3-7: Clinical practice guidelines name, selected abbreviation, publication information and stated aim(s)

Clinical Practice Guideline Name	Abbrev	Country	Year	Length (Pages)	Stated Aim(s) & Development to Recommendations
Use of opioid analgesics for the treatment of chronic non-cancer pain – A Consensus statement and guidelines from the Canadian Pain Society (306)	CPS	Canada	2002	14	Educate both Canadian physicians and Canadian regulators in understanding the role of opioid analgesics in the treatment of CNMP. There is no statement provided in this guideline on the approach to development of recommendations.
Opioid Use in Persistent Pain Hunter New England New South Wales Health (307)	HEW	Australia	2007	12	Not clearly stated, however, the document provides an outline of the approach to prescribing and management of opioids based on a synthesis of current scientific evidence and recommendations from other guidelines. There is no statement provided in this guideline on the approach to development of recommendations.
Opioid Prescription in Chronic Pain Conditions Guidelines for South Australia General Practitioners Drug and Alcohol Services South Australia (308)	GSAGP	Australia	2008	55	Provide information to GPs about the medical treatment of chronic pain using opioid drugs; it includes recommendations on the prescribing of opioids for CNMP while minimising abuse, addiction, and diversion of these analgesics. There is no statement provided in this guideline on the approach to development of recommendations.
Guidelines for the Chronic Use of Opioids American College of Occupational and Environmental Medicine (309)	ACOP	USA	2008	25	Manage injured workers whose pain has not been controlled by more conservative means. Recommendations developed from the Evidence Based Practice Panel on Chronic Pain; the evidence used to inform recommendations is graded as A, B,C, or I.
Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain Recommendations for Practice National Opioid Use Guideline Group (310)	NOUGG	Canada	2010	126	Assist physicians with decisions to initiate appropriate trials of opioid therapy for patients with CNMP and provides guidance on monitoring long-term opioid therapy detect and management of patients presenting with opioid misuse.

					Recommendations were developed upon systematic review of evidence and graded using a system adapted from the Canadian Task Force on Preventative Health Care.
Opioids in the management of chronic non-cancer pain: an update of American Society of the Interventional Pain Physicians' (ASIPP) Guidelines (311)	ASIPP	USA	2008	181	Recommendations on the use of opioids for the treatment of CNMP and strategies reduce the incidence of abuse and drug diversion. Evidence was reviewed and assessed by ASIPP to develop recommendations. Evidence was graded using methods adapted from the U.S Preventative Services Taskforce.
Clinical Guidelines for the use of chronic opioid therapy in chronic non-cancer pain; American Pain Society/American Academy of Pain Medicines Opioids Guidelines Panel (312)	APS/AAPM	USA	2009	37	Provides guidance on patient selection and risk stratification; informed consent and opioid management plans; initiation and titration of chronic opioid therapy; use of methadone; monitoring of patients on chronic opioid therapy; recommendations on dose escalations, high-dose opioid therapy, opioid rotation, and indications for discontinuation of therapy; prevention and management of adverse effects. An evidence report developed following consultation with the literature on this subject. Recommendations were then developed and evaluated using the GRADE evaluation system.
Utah Clinical Guidelines on Prescribing Opioids for Treatment of Pain Utah Department of Health (313)	UCG	USA	2009	83	Provide guidance on the use of opioids in the prescribing of CNMP and the long-term use of these agents in the management of this condition. A rating scale developed by the guideline developers based on the quality of the research informing the evidence base was prepared prior to development of recommendations.
Interagency Guideline on Opioid Dosing for Chronic non-cancer Pain; Washington State Agency Medical Directors' Group (314)	WSAM	USA	2010	55	Resource for healthcare professionals in the primary care setting on the prescribing for patients with CNMP; provides recommendations on monitoring of treatment, identification and management of problems with opioids.

					Review of published meta-analyses of systematic reviews was used as evidence to develop recommendations which were finalised through following expert consensus.
The British Pain Society's Opioids for persistent pain: Good Practice; A consensus statement prepared on behalf of the British Pain Society, the Faculty of Pain Medicine of the Royal College of Anaesthetists, the Royal College of General Practitioners and the Faculty of Addictions of the Royal College of Psychiatrists (243)	BPS	UK	2010	36	Guidance on the management of patients with CNMP with opioid analgesics; provides recommendations on monitoring of treatment, identification and management of problems with opioids. There is no statement provided in this guideline on the approach to development of recommendations.
Management of Opioid Therapy for Chronic Pain Department of Veteran Affairs Department of Defence (315)	DVA-DOD	USA	2010	158	Provide education and guidance to primary care clinicians, researchers and other health professionals who encounter patients with chronic pain and the good practices in the prescribing of opioids for these persons. Evidence is graded using a system developed by the US Preventative Services Task Force (USPSTF) and recommendations were evaluated on the basis of the evidence used in their development.

3.5.1. AGREE II Guideline Quality Assessment

Table 3-8 provides a summary of the standardised percentage scores awarded by the appraisers for the 11 guidelines calculated using the Rater Concordance Tool; scores are provided by guideline and by domain. The SD between appraiser scores across all domains was between 0.00 and 1.41; this was classified as low by the AGREE scoring guidelines.

Overall assessment score ranged between 3.00 and 7.00. Scope and purpose scores were between 11-100%. Stakeholder involvement scores were between 0-100%, Rigour of development scores were between 17-100%, Clarity of presentation scores were 72-100%, Applicability scores were between 38-90% and Editorial independence scores were between 0-100%. The range for all domains was wide and reflects the fact that a number of guidelines had very low scores in comparison to others. The overall mean domain score was 69% (59-88%).

The ASIPP and ACOP guidelines jointly received the highest ratings; the ACOP guideline had the narrowest range of scores at 75-100%. HEW and CPS produced consistently low results across all domains with a score of < 4 in the overall guideline assessment and were not recommended for use. Those guidelines that averaged a mean score for all domains of ≤45% were not recommended, while the remainder were recommended or recommended with modifications. Six guidelines achieved an overall score of 6 to 7 and were recommended for use without modification. The remaining four guidelines scored between 4 and 5 and were recommended for use, provided modifications were applied to the existing guideline.

Clarity and Presentation produced the highest mean score of 88%, the range here was the narrowest, 72-100%, when compared to other domains, suggesting that all guidelines considered these criteria. This domain specifies that the recommendations are clear, concise and easily identifiable to the reader. This relatively high score suggests that the guidelines considered present recommendations in a clear, unambiguous manner. Scope & Purpose and Stakeholder Involvement attained mean domain scores of 79% and 71% respectively, both with a wide range of scores 0-100% and 11-100%. The mean standardised percentage score for Applicability was 61% (38-90%), the third lowest

score across all domains. This domain considers barriers and facilitators of implementation of recommendations, methods to enhance use by healthcare providers and resource considerations. The quality of this element of the guideline contributes directly towards the incorporation of recommendations in practice.

Table 3-8: Mean standardised scores (%) for guidelines by domain including standard deviations

	Domain 1 Scope & Purpose *(SD)*	Domain 2 Stakeholder Involvement *(SD)*	Domain 3 Rigour of Development *(SD)*	Domain 4 Clarity of Presentation *(SD)*	Domain 5 Applicability *(SD)*	Domain 6 Editorial Independence *(SD)*	Mean (Range %)	Mean Overall Guideline Assessment Score	Domain 7 Recommend Use
DVA/DOD	100% *(0.00)*	64% *(0.24)*	61% *(0.44)*	100% *(0.0(0)*	69% *(0.18)*	13% *(0.71)*	68% (13-100%)	6.5	Yes
CPS	78% *(0.94)*	58% *(0.71)*	28% *(0.62)*	72% *(0.47)*	44% *(0.53)*	0% *(0.00)*	47% (28-78%)	4.0	Yes with modifications
NOUGG	92% *(0.71)*	97% *(0.24)*	100% *(0.00)*	92% *(0.71)*	65% *(0.53)*	88% *(0.00)*	89% (65-100%)	7.0	Yes
ASIPP	100% *(0.00)*	89% *(0.00)*	89% *(0.44)*	100% *(0.00)*	71% *(0.71)*	100% *(0.00)*	92% (71-100%)	6.0	Yes
WSAM	56% *(1.41)*	53% *(0.71)*	29% *(0.53)*	86% *(0.71)*	67% *(0.35)*	21% *(0.71)*	52% (29-86%)	4.5	Yes with modifications
BPS	81% *(0.94)*	86% *(0.71)*	25% *(0.62)*	86% *(0.47)*	48% *(0.53)*	63% *(0.00)*	65% (25-86%)	4.5	Yes with modifications
GSAGP	97% *(0.24)*	83% *(0.47)*	40% *(0.53)*	67% *(0.94)*	54% *(0.35)*	8% *(0.71)*	58% (8-97%)	4.5	Yes with modifications
APS/AAPM	100% *(0.00)*	67% *(0.00)*	96% *(0.18)*	81% *(1.18)*	63% *(0.35)*	100% *(0.00)*	85% (63-100%)	7.0	Yes
UCG	83% *(0.94)*	83% *(0.47)*	74% *(0.62)*	94% *(0.47)*	67% *(0.00)*	75% *(0.71)*	79% (67-94%)	6.5	Yes
ACOP	75% *(0.24)*	100% *(0.00)*	92% *(0.71)*	97% *(0.24)*	90% *(0.88)*	100% *(1.41)*	92% (75-100%)	6.0	Yes
HEW	11% *(0.47)*	0% *(0.00)*	17% *(0.53)*	89% *(0.47)*	38% *(1.41)*	0% *(1.41)*	26% (0-89%)	3.0	No
Mean Domain Score (Range %)	79% (11-100%)	71% (0-100%)	59% (17-100%)	88% (72-100%)	61% (38-90%)	57% (0-100%)	69% (59-88%)	---------	---------

Rigour of Development produced a wide range of scaled domain scores, from 17-100%, and attained a mean score of 59%; the wide range of scores within this domain may be attributed to the large number of items (8 items) that were considered within the domain. The mean standardised percentage score for Editorial Independence was 57%, the lowest across all the domains, though it also had the widest range of values across the guidelines. This is perhaps associated with the fact that this domain relies upon a declaration by contributors to the guidelines as to a potential conflict of interest. In the instance, where such as reference was lacking in the guideline, the resultant score was quite low in comparison to those with such a reference. This domain produced the lowest percentages of all guidelines assessed, although, three guidelines scored 100% in this domain; eight scored under 50% however.

Figure 3-5 presents the Mean Overall AGREE II Assessment scores awarded by the two appraisers against the Mean AGREE II score (%) for each guideline. The Mean Overall Assessment was determined upon consideration of the overall quality of the guideline and whether the guideline would be recommended for use in practice. This score, therefore, is reflective of the sense gained by appraisers of the quality and utility of the guideline. By comparison, the Mean AGREE II score (%) is derived from the scoring of the guideline across each of the 6 Domains. While there was a positive relationship between the Mean Overall AGREE II Assessment score and the Mean AGREE II score (%), this relationship was not linear. Both NOUGG and APS/AAPM attained a Mean Overall Assessment Score of 7 but attained a Mean AGREE II score of 89% and 85% respectively. Both ACOP and ASIPP attained a lower Mean Overall Assessment score of 6.0 but had the highest Mean AGREE II scores of 92%. The BPS, GSAGP and WSAM guidelines each achieved a Mean Overall score of 4.5 but an overall domain score in the range 52-65%.

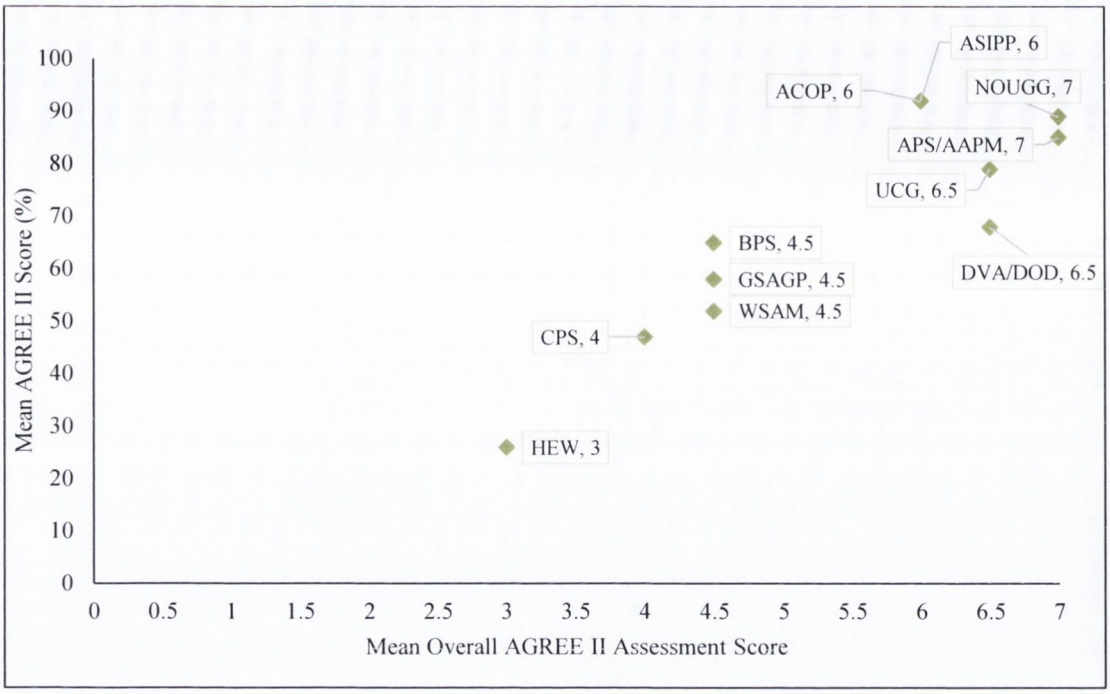


Figure 3-5: Mean Overall Scores for guideline and Mean Domain Score

3.5.2. Clinical Content Criteria

Table 3-9 provides a summary of the presence, partial presence or absence of the 16 clinical content criteria from the 11 guidelines. The resultant score from the present (1), partially present (0.5) and absent (0) criteria for each guideline was also calculated and is presented in the right-hand column. The clinical content scores awarded to each guideline are presented in *Figure 3-6* to aid interpretation, these scores range from 5.5/16 to 15/16. The HEW guideline emerged as the lowest scoring for Clinical Content Criteria, with 3 criteria present, 5 partially present and 8 absent. The CPS was the second lowest scoring of the guidelines, with 7 present, 6 partially present and 3 absent criteria. The HEW and CPS were also the shortest of the guidelines in terms of page length, with 12 and 16 pages respectively. The NOUGG and DVA/DOD guidelines both achieved a score of 15/16, both guidelines have 14 criteria present and 2 partially present. These two guidelines were also amongst the longest of those included in the review, with 126 and 158 pages respectively. There was no apparent relationship between the country within which the guideline was published and the resultant clinical focus of the guideline, as both

NOUGG and CPS were published in Canada but had markedly different scores according to this set of criteria.

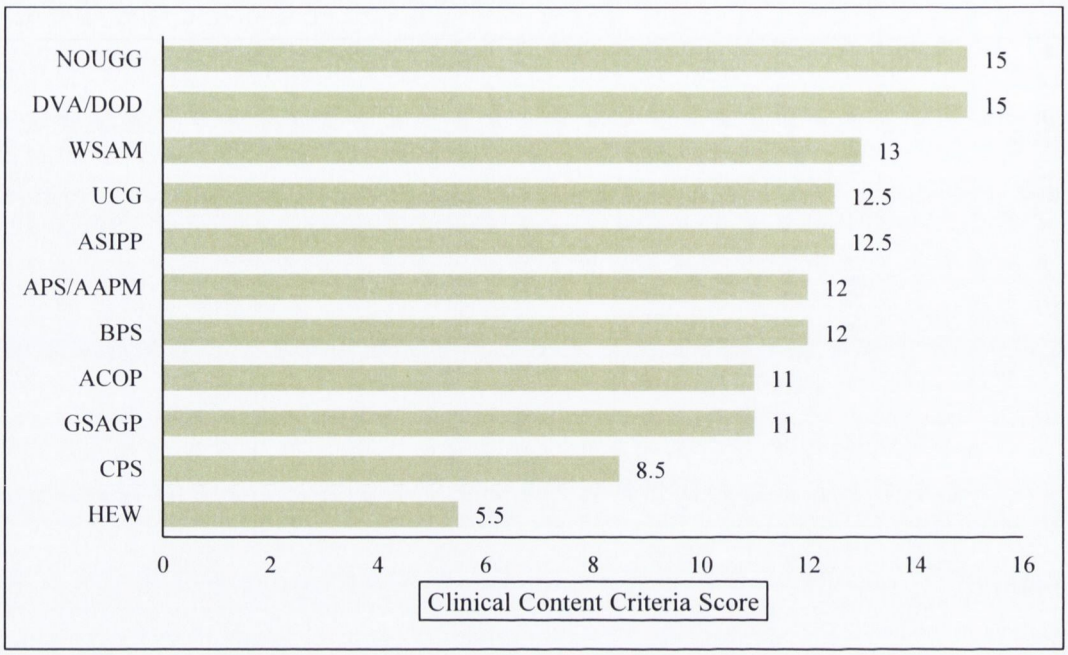


Figure 3-6: Clinical content criteria score for each guideline

Table 3-9: Clinical classification criteria for each clinical practice guideline (Present (+)=1, Partially Present (±)=0.5, Absent (—)=0)

	CNMP Duration	Pain Scale (Establish Severity)	Pain Scale (Monitoring Analgesia)	Indication	Dosage	Contraindication	Cautions	Interactions	Pregnancy/ Lactation	Side-Effects	Mgt Side-Effects	Dose Escalation	Dose Reduction	Identifying Addiction	Managing Addiction	Overdose	Score
DVA/ DOD	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	*15*
CPS	+ *(1)*	+ *(1)*	— *(0)*	+ *(1)*	± *(0.5)*	— *(0)*	— *(0)*	— *(0)*	— *(0)*	+ *(1)*	± *(0.5)*	+ *(1)*	± *(0.5)*	+ *(1)*	+ *(1)*	— *(0)*	*8.5*
NOUGG	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	*15*
ASIPP	+ *(1)*	— *(0)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	± *(0.5)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	*12.5*
WSAM	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	— *(0)*	+ *(1)*	± *(0.5)*	± *(0.5)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	*13*
BPS	— (0)	± *(0.5)*	± *(0.5)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	— *(0)*	*12*
GSAGP	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	+ *(1)*	— *(0)*	+ *(1)*	— *(0)*	— *(0)*	+ *(1)*	+ *(1)*	— *(0)*	+ *(1)*	+ *(1)*	+ *(1)*	± *(0.5)*	*11*

HEW	ACOP	UCG	APS/ AAPM	
(0) –	(0) –	(1) +	(1) +	CNMP Duration
(0) –	(0.5) ±	(1) +	(1) +	Pain Scale (Establish Severity)
(0) –	(0.5) ±	(1) +	(1) +	Pain Scale (Monitoring Analgesia)
(0.5) ±	(1) +	(0) –	(1) +	Indication
(1) +	(1) +	(1) +	(0.5) ±	Dosage
(0) –	(0.5) ±	(1) +	(0) –	Contraindication
(0.5) ±	(1) +	(1) +	(0.5) ±	Cautions
(0.5) ±	(0.5) ±	(1) +	(0) –	Interactions
(0) –	(1) +	(0) –	(1) +	Pregnancy/ Lactation
(1) +	(1) +	(1) +	(1) +	Side-Effects
(0.5) ±	(0) –	(0) –	(1) +	Mgt Side-Effects
(0.5) ±	(1) +	(1) +	(0.5) ±	Dose Escalation
(0) –	(1) +	(1) +	(1) +	Dose Reduction
(1) +	(1) +	(1) +	(1) +	Identifying Addiction
(0) –	(1) +	(1) +	(1) +	Managing Addiction
(0) –	(0) –	(0.5) ±	(0.5) ±	Overdose
5.5	11	12.5	12	Score

Figure 3-7 considers the presence, partial presence or absence of each of the 16 clinical content criteria. Identification of addiction and side-effects was addressed comprehensively in all guidelines included in the review, while overdose was addressed thoroughly by 1 and partially by a further 6 but is absent in 4 guidelines. Dose initiation, dose reduction and approaches to management of addiction were present in 9 guidelines and perhaps reflect the clinical challenges surrounding the cessation of opioid therapy. Similarly, the inclusion of a pain scale to both establish pain severity and monitor outcomes following introduction of an analgesic medication indicate that these two criteria were often considered simultaneously within guidelines.

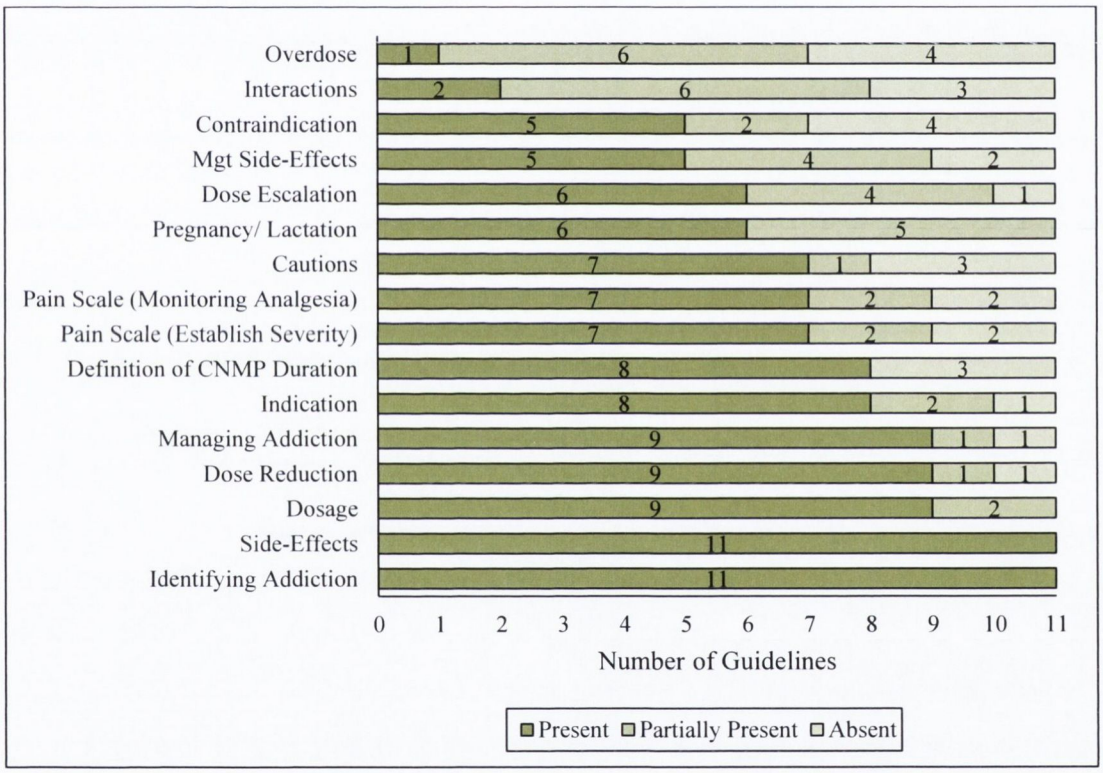


Figure 3-7: Number of guidelines containing each specified clinical content criterion

Guidelines were reviewed to identify those that referenced a definition of CNMP and approaches to assessment of pain severity. A definition for the duration of pain was provided by 8 guidelines; (DVA/DOD/CPS/NOUGG/ASIPP/WSAM/GSAGP/APS-AAPM/UCG). The cause and severity of pain should be established prior to consideration of analgesic

therapy which can then be selected according to the source and type of pain (316). *Table 3-10* considers the types of scales and instruments included in the guidelines used to assess pain, prior to and following, introduction of an opioid medication and the instruments used to detect or monitor opioid aberrant behaviours. Seven guidelines included a pain assessment scale to initially establish pain severity or recommended reassessment of pain intensity upon introduction of an opioid analgesic; two guidelines partially referenced a pain assessment scale in the document while two guidelines omitted this information completely. Several guidelines provided a detailed algorithm and description of the steps required in the assessment of patients with CNMP eligible for opioid therapy. Two guidelines did not suggest any pain assessment tools (BPS and CPS), while several suggested multiple instruments for such an assessment. The Brief Pain Inventory was recommended by 3 guidelines (HEW, NOUGG and UCG) but several other guidelines also recommended scales to evaluate quality of life in conjunction with pain severity (ACOP, UCG and WSAM).

The clinical content criteria included information on indication, dose, contraindications, cautions, interactions, pregnancy and lactation, and side-effects and management of side-effects. The 'Indication' or the circumstances under which a physician may consider initiation of an opioid is referenced in 10 guidelines. However, all guidelines referenced, to some extent, the selection of opioid formulations available to the practitioner and the dosage range in which these medications are available. All guidelines provided information on side-effects, however, only 5 guidelines provided detailed information on management of these side-effects (DVA/DOD/ASIPP/WSAM/BPS/APS-AAPM).

Management strategies included, suggestions of alternative analgesic regimens, additional assistance from healthcare professionals such as pain specialists, or the introduction of a medication to prevent or treat the particular side-effect. Eight guidelines specifically referenced the increased incidence of adverse effects in ageing and elderly populations (DVA/DOD/ACOP/GSAGP/UCG/NOUGG/WSAM/BPS/APS-AAPM).

Information was provided on indication and dosage recommendations including dose reduction by the majority of guidelines. Recommendations on the titration of opioid medications including dose escalation and dose reduction,

management of overdose and strategies for detecting, monitoring and managing addiction were considered to be essential clinical content criteria. Since dose reduction of opioids is clinically challenging, the majority of guidelines (9) provided detailed information on this aspect of opioid prescribing (DVA/DOD/NOUGG/ASIPP/WSAM/GSAGP/BPS/APS-AAPM/UCG/ACOP). However, fewer guidelines (6) provided comprehensive information on approaches to initiation and escalation of doses of an opioid regimen. Specific information was provided in 6 guidelines on the dose alterations for elderly populations (DVA/DOD/HEW/NOUGG/CPS/BPS/APS-AAPM/ACOP). These guidelines discussed the necessity to initiate elderly patients on lower doses of opioids than younger populations and to titrate the dose more slowly.

Seven guidelines highlighted cautions such as co-morbidities that should be considered when prescribing an opioid (DVA/DOD/NOUGG/ WSAM/BPS/GSAGP/UCG/ACOP). Five guidelines outlined absolute contraindications to their use in particular patients (DVA/DOD/ ASIPP/WSAM/BPS/NOUGG). These contraindications included hypersensitivity to opioids, renal insufficiency or current or past history of drug, alcohol or other substance misuse. These were referenced in detail in only 5 guidelines (DVA/DOD/ASIPP/WSAM/BPS/UCG). The potential for medications interactions with opioids was also detailed by only 2 guidelines (NOUGG/UCG), with 6 providing some reference to their potential for drug interactions with opioids (DVA/DOD/ASIPP/BPS/GSAGP/ACOP/HEW). Complete recommendations on the prescribing of opioids in pregnancy or lactation was provided by 6 guidelines (DVA/DOD/NOUGG/ASIPP/BPS/APS-AAPM/ACOP), however, the remaining 5 guidelines referenced these populations at least once.

Risk management guidance refers to those recommendations contained within guidelines which direct prescribers on methods to prevent or manage aberrant drug behaviours. Ten guidelines referenced the necessity to assess for aberrant drug behaviours, while several provided multiple assessment instruments; these are detailed in *Table 3-10*. Guidelines from the US and Canada provided multiple instruments for the detection and monitoring of such behaviour, ranging from the DSM-IV criteria for medication misuse (ACOP and DVA/DOD) to the Opioid Risk Tool (WSAM, UCG and APS/AAM). The Screen and Opioid

Assessment for Patients in Pain (SOAPP) was referenced by 4 guidelines (NOUGG, ASIPP, UCG and ACOP).

All guidelines detailed methods to identify addiction to opioid medications amongst patients but only 9 guidelines (DVA/DOD/CPS/NOUGG/ASIPP/WSAM/APS-AAPM/UCG/ACOP/HEW) provided information to the prescriber on strategies to manage addiction. This information was only partially available in the BPS guideline, published in the UK, and absent from the HEW guideline, published in Australia. Urine testing regimens and opioid contracts were amongst the most commonly referenced strategies for managing addiction. The 'overdose' criterion had the poorest inclusion across all guidelines included in the review, with a comprehensive reference to the criterion included only in the NOUGG guideline.

Table 3-10: Tools listed in guidelines for the evaluation of pain severity and assessment of the potential for opioid behaviours

	Evaluation of Pain Severity (Prior to and During Opioid Therapy)	Assessment for Potential for Opioid Aberrant Behaviours
DVA/DOD	Numeric Scale Rating Functional Assessment Tests	Substance Misuse Criteria DSM-IV Summary of Risks for Opioid Misuse of Opioid Therapy
CPS	No tools provided/recommended	Screening Instrument for Substance Abuse and Potential
NOUGG	Brief Pain Inventory	Current Opioid Misuse Measure Screener and Opioid Assessment for Patients in Pain
ASIPP	4 "A's" Recommended	Screening Questionnaire Recommended / Urine Testing following initiation
WSAM	Graded Chronic Pain Scale SF36 Brief Pain Inventory Quick Dash Quality of Life Scale Oswestry Disability Index Short Musculoskeletal Function Assessment Neck Disability Index	Opioid Risk Tool CAGE-AID Patient Health Questionnaire
BPS	No tool provided/recommended	Recommended tests on: Psychological state PTSD Other significant risk Depression
GSAGP	Structured Pain Questionnaire: Type of Pain Appropriate Modalities for Treatment	Red flags listed but no assessment tool provided/recommended

APS/AAPM	Pain Assessment and Documentation Tool	Current Opioid Misuse Measure Screener and Opioid Assessment for Patients in Pain Opioid Risk Tool
UCG	Pain Management Evaluation Tool & Medication Tracking Chart Sheehan Disability Scale Brief Pain Inventory SF-12	Current Opioid Misuse Measure Screener and Opioid Assessment for Patients in Pain Opioid Risk Tool
ACOP	Questions Concerning Activities of Daily Living	Substance Misuse Criteria DSM-IV Screener and Opioid Assessment for Patients in Pain
HEW	Hunter Integrated Pain Service (HIPS) Patient Screening Questionnaire Brief Pain Inventory	No tool provided/recommended

3.5.3. Comparison between AGREE II & Clinical Content Criteria

Figure 3-8 presents a scatterplot of the mean AGREE II score compared to the clinical content criteria score for all guidelines included in this review. The scatterplot points are annotated with the selected abbreviation of the guideline and associated scores of the AGREE II assessment and clinical content criteria assessment. As the mean AGREE II score increased so too did the clinical content criteria score, however, this relationship is not linear.

The HEW guideline emerged as the scoring rated guideline for both clinical content and AGREE II evaluations. The CPS guideline scored second lowest with both instruments, with 7 clinical content criteria present and 6 absent from this guideline (clinical criteria score =8.5/16) and an AGREE II score of 47%. The NOUGG and the DVA/DOD guidelines received the third and sixth highest mean score respectively using the AGREE II instrument (89% & 68%), however, both attained the highest score in clinical content criteria assessment (15/16). The ASIPP and UCG guidelines both scored 12.5/16 in the clinical content criteria assessment, however, their mean AGREE II scores were quite divergent, 92% and 79% respectively. The ACOP guideline, with the same mean AGREE II score as ASIPP (92%), had 9 clinical criteria present, and attained 11/16 in the clinical content criteria assessment; by comparison the ASIPP had 10 clinical criteria present and scored 12.5/16 in the clinical content criteria assessment. The WSAM guideline had the third lowest mean AGREE II score, but had eleven of the clinical criteria present, with only one absent; it scored 12/16 in the clinical content criteria assessment.

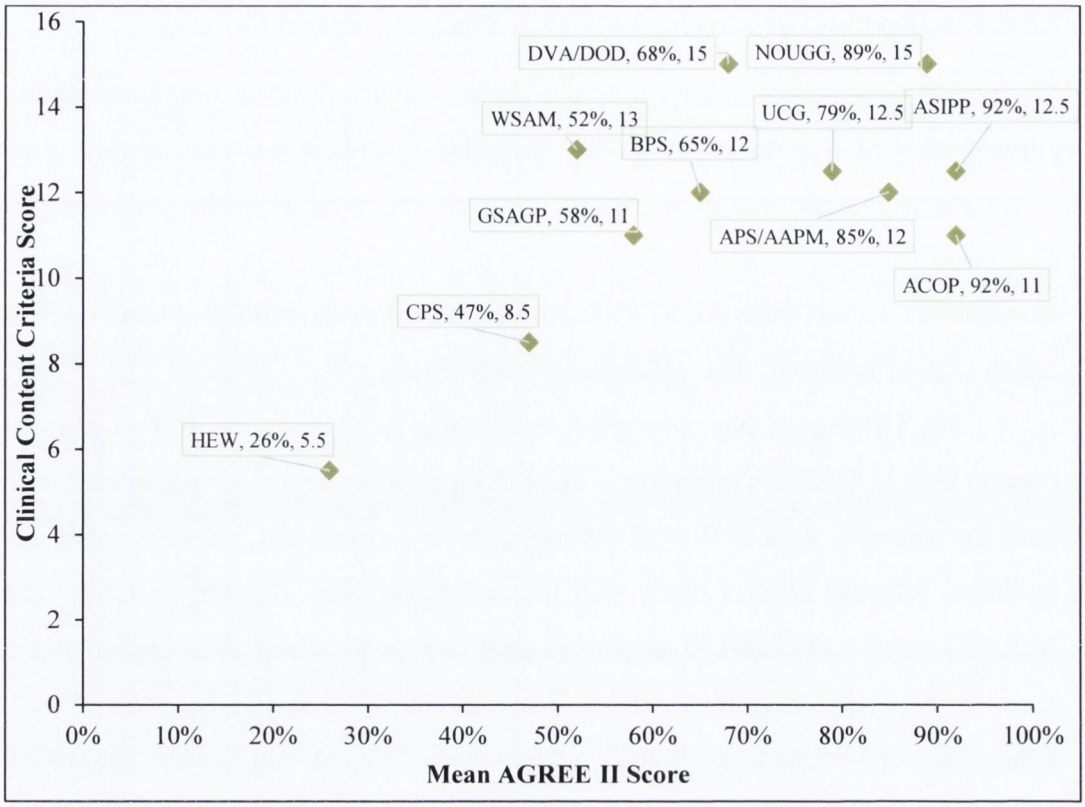


Figure 3-8: Mean AGREE II Score compared to Clinical Content Criteria Score for all guidelines

Figure 3-9 presents mean Overall Guideline Assessment AGREE II scores (maximum score is 7.0) compared to the clinical content criteria score for the guidelines. Again, the scatterplot points are annotated with the selected abbreviation for the guideline and scores awarded by appraisers. Since the Mean Overall Guideline Assessment score is the average score awarded by the appraisers upon consideration of the overall quality of the guideline, it is a more subjective measure than the mean AGREE II score, which is calculated from the domain scores.

According to this presentation of scores, the NOUGG guideline was the highest scoring for both assessment tools. The HEW and CPS guidelines were also the lowest and second lowest guidelines using these ratings. The DVA/DOD guideline, which had the sixth highest Mean AGREE II score (68%), has a Mean Overall Guideline Assessment score of 6.5, with a similarly high Clinical Content Criteria Score (15). The APS/AAPM guideline attained a score of 12 in the clinical content criteria assessment but attained 7.0 in the Mean Overall Assessment. The ACOP guideline had a Mean Overall Assessment AGREE II score of 6 and a

Clinical Content Criteria score of 12; this places the ACOP guideline below four guidelines, while it appeared as the second highest ranked guideline in *Figure 3-8*. Conversely, the UCG guideline, which had a mean AGREE II score of 79% and a Clinical Content Criteria score of 12.5, scored highly in the Overall Mean Assessment AGREE II score (6.5). GSAGP, BPS and WSAM each had a Mean Overall Assessment Score of 4.5, with Clinical Content Criteria Scores of 11, 12 and 13 respectively. When viewed in terms of the Mean AGREE II score, these guidelines scored in the range 52-65% and did not deviate considerably in their positions relative to each other in this scatterplot.

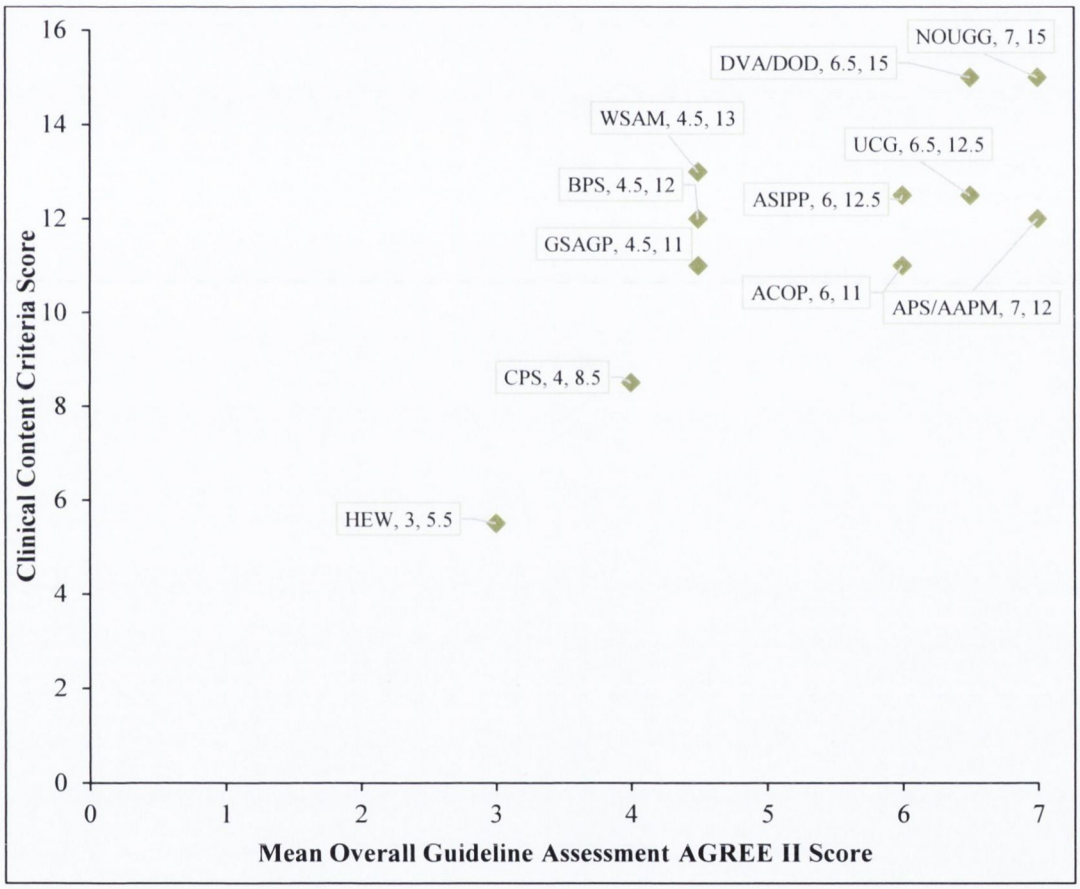


Figure 3-9: Mean Overall Guideline Assessment AGREE II Score compared to Clinical Content Criteria Score for all guidelines

3.6. Discussion

The aim of this review was to evaluate the quality and content of guidelines directing the prescribing of opioids in the management of CNMP in primary care.

The clinical content criteria selected for this review were designed to reflect prescribing recommendations relevant to an international audience and also to acknowledge the necessity to incorporate principals of prescribing with risk management strategies to optimise patient outcomes (317). The AGREE II instrument was used to assess the methodological rigour and transparency of the guideline development process (318). The clinical content criteria scores were compared to two outcomes of the AGREE II review, the mean AGREE II score (%) and the Mean Overall Assessment AGREE I score. Those guidelines that score poorly relative to others using the AGREE II instrument also have low scores for clinical content; those with higher AGREE II scores are more difficult to compare, as the relationships is not linear. While a guideline may have a high mean AGREE II score comparable to other guidelines, this does not automatically produce an equally high Mean Overall Assessment score which is based upon the considered reflections of the appraisers.

The increasing rate of opioid related morbidity and mortality in the USA has prompted policy makers and guideline developers to adopt a cautious approach to prescribing and maintaining a CNMP patient on an opioid regimen (155, 319, 320). The US are the biggest consumers of morphine, accounting for 55% of global morphine consumption, followed by Europe, 26%, and Canada, 6.2% (321). Prescriber guidance, therefore, places an emphasis on measures to minimise aberrant drug related behaviours, including opioid contracts and urine screening tools to assess for or detect misuse during patient-clinician consultations. Evidence suggests problematic opioid use has only recently emerged in Europe and remains behind the USA in terms of morphine consumption; there is therefore less emphasis on this aspect of opioids in European guidance aimed at clinicians and patients, focusing instead on the clinical aspects of drug administration such as dose titration and adverse effects (322, 323). Indeed, this is reflected by the focus on instruments to detect and monitor for opioid aberrant behaviours in guidelines published in the USA and Canada. The BPS guideline, published in the UK, briefly references approaches to management strategies, though not as thoroughly as US guidelines.

The variability in guideline quality, determined by using the AGREE II statement, is similar to that detected by a recent review of opioid guidelines, which demonstrated a variability in mean scores of 28-76%; although this review

produced a narrower range of 59-88% (324). However, Nuckols et al excluded two guidelines included in this review (BPS and HEW). These guidelines were omitted, as they failed to include an evidence grading system to support recommendations. These omitted guidelines provide direction on the prescribing of opioids in CNMP in primary care, the BPS was the only such English language guidance identified in this study that was published in Europe and the HEW was used to inform prescribing of opioids in an entire region of Australia. These guidelines were therefore included in this review as it is reasonable to assume that prescribers may access these documents regardless of the absence of an evidence grading system. Furthermore, assessment of these guidelines indicates whether there is a significant difference in quality or clinical content between those with and without an evidence grading system. HEW performs poorly across all assessment tools, however, BPS is comparable in clinical content and AGREE II scores to several evidence based guidelines.

The duration of CNMP has been variously defined as pain lasting for longer than 3 or 6 months (317, 325). The International Association for the Study of Pain (IASP) have also described it as pain persisting beyond the usual time for recovery of a tissue injury (29). The guidelines included in this review are also inconsistent in the definition of duration, and in some instances, no reference is made to duration or description of types of CNMP conditions. Neither is there agreement within guidelines originating from the same country; for instance the US guideline, DVA/DOD, defines it as pain lasting longer than 3-6 months while the WSAM specifies a 3 month duration. The lack of a consistent definition of duration, or the absence of it in some instances, presents difficulties for comparing guidelines, especially when duration and severity of pain conditions are considered central to prescribing decisions (300).

The aim of effective analgesia is to improve patient welfare by facilitating an increase in patient function (326). Outcome assessments should therefore incorporate an element of assessment of daily activities, prior, and subsequent, to the opioid regimen (284). The majority of guidelines reviewed refer to the necessity for such monitoring by the prescriber, with several providing specific assessment tools to monitor changes in patient activity. A variety of pain scales are suggested

for use prior to, and during, treatment with an opioid, with some permitting the user to establish the extent to which pain disrupts daily activity.

Opioids, unlike the majority of medications, do not have a dose ceiling nor do they achieve identical therapeutic plasma levels in each patient (327). The physiological response and subsequent analgesia gained from the initiation of an opioid and titration of the dose cannot be predicted and is dependent upon the individual patient's response to therapy. The occurrence of adverse drug events and the heightened probability of drug interactions, particularly in ageing and elderly populations, may curtail the extent of dose titration permitted for a patient (328). Indeed, the necessity to exercise caution in the dose initiation and titration for elderly patients is included in the majority of guidelines. Adverse effects include side-effects of sedation, dizziness, gastrointestinal effects such as nausea, vomiting and constipation, in addition to respiratory depression and physical dependence (329). While all guidelines refer to the types of adverse effects, many do not provide advice on the measures that should be taken for the physician-led management of the adverse effect. Those guidelines that reference medications that can be used to manage adverse drug effects refer to these agents according to the indication for the agent e.g. anti-emetic, but most do not discuss in detail the specific types of medications which may be appropriate.

Apart from the quality of guidelines, perhaps the most important consideration of guidelines in healthcare is the extent to which they are implemented in practice (330). Implementation of practice recommendations may be complicated by non-clinical considerations such as resource constraints or service deficiencies in particular geographical regions or at certain points in the healthcare system. For instance, the applicability of a recommendation within a guideline to a patient with significant co-morbidities or taking multiple medications may be unclear due to focus of a guideline on a general population.

The length of the guideline may also hinder the implementation of recommendations contained within the document by GPs (276, 331). The guidelines included in this review had an average length of 66 pages; this length of document may curtail the speed with which a GP may locate and assess the relevant information. However, those guidelines with fewer than 20 pages scored poorly in

both the AGREE II and clinical content criteria, indicating that a short guideline may impair the quality and content of the document.

3.6.1. Limitations

The search for guidelines was limited to electronic resources, a number of guidelines may therefore be absent if they exist only in hard copy or electronic resources with restricted access. The search for guidelines was limited to those in the English language, again causing some guidelines to be perhaps omitted from this review. The clinical content criteria are intended to capture the topics considered essential to a guideline advising on the use of opioids in CNMP. These criteria aim to examine the completeness of the recommendations and therefore its usefulness in directing the primary care prescriber. The criteria do not focus on differences in the detail of the recommendations, merely the presence of the criteria. The variability in the availability of prescription or non-prescription opioids is dictated by regulations surrounding the prescribing and supply of opioids specific to that jurisdiction; this is not examined in this review. Furthermore, differences in the education and training of clinicians or cultural variations in attitudes towards opioids are not considered in this review but may affect the manner in which opioids are prescribed (332, 333).

3.7. Conclusion

The systematic search through electronic databases and grey[1] literature has highlighted the absence of guidelines directing the prescribing of opioids for CNMP in Ireland. Guidelines directing the prescribing of opioids for CNMP from other countries differ in their quality and clinical content. A guideline should be reviewed using a variety of instruments so as to gain an understanding of the methodological rigour with which the guideline was developed but also to understand the extent to which essential clinical information is described in the text. There are many common features amongst guidelines; all documents make detailed reference to the

[1] Documents produced by government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers

risk-benefit considerations associated with opioid therapy, proposing strategies to minimise and manage the occurrence of adverse effects. Guidelines originating from USA or Canada in particular emphasise the assessment and monitoring procedures which should be employed by a GP when prescribing an opioid to CNMP patients so as to address the potential for aberrant drug behaviours. The necessity for similar assessment and monitoring procedures associated with the prescribing of opioids in Ireland may not be necessitated given the low levels of consumption of strong opioids relative to the USA (*Chapter 1; Section 1.7-1*). The topic of opioid prescribing for CNMP in Ireland will be examined in greater detail in the analysis of a national prescribing dataset, and through interviews with GPs managing CNMP in primary care.

What is already known about this topic:	Guidelines are reference tools or practice aids for clinicians in the prescribing of a wide variety of medications for a range of conditions. CNMP, however, is a symptom arising from an underlying aetiology and not viewed by the majority of clinicians as an independent condition.
	The content of guidelines directing the precribing of medications may vary according to the availability of certain medications or regulatory restrictions in the country or region.
	The quality of guidelines may also vary depending on the process by which the clinical practice guideline was produced and edited. Variation in the quality of clinical practice guidelines may emerge following adaptation of a document for regional purposes.
	The USA is the largest consumer of prescription opioids per capita globally. There is an increasing problem with the misuse and abuse of prescription opioid medications particularly with stronger opioid agents.

What this study adds:	There are a limited number of guidelines directing the prescribing of opioid analgesics for CNMP in primary care. The majority of these guidelines originate in the USA and Canada with only one clinical practice guideline published within Europe.
	Guidelines developed in the USA score highly when the AGREE II instrument is applied, in comparison to all other guidelines identified in this study.
	The clinical content of the recommendations differs in scope and focus according to the country of origin of the clinical practice guideline. US guidelines include risk minimisation measures to address the potential for aberrant opioid behaviours; such content is not discussed in detail for guidelines originating from EU and Australia.
	Those guidelines that scored poorly in the AGREE II assessment also performed poorly in the assessment of the clinical content of clinical practice guidelines. However, the relationship with the clinical content of guidelines and the quality of guideline development as determined by the AGREE II score is not linear, with those guidelines with high AGREE II scores not also producing the highest clinical content scores.

Chapter 4. Analgesic Dispensing Patterns for an Ageing and Elderly Population: A National Population Study

4.1 Background

Prescription and non-prescription analgesics are amongst the most commonly used classes of medications globally, with 20-30% of the ageing population in the developed world taking at least one analgesic daily (334). The World Health Organisation (WHO) Analgesic Ladder recommends a pain management approach that responds to pain severity, with the aim of providing the patient with optimal pain management using the most appropriate analgesic(s) (263). Careful selection of medications, used concurrently with analgesics, is required, particularly for those agents acting on the Central Nervous System (CNS). This is most important for ageing populations who have a higher risk of adverse outcomes with medications. Opioids can produce adverse effects in vulnerable patients, including respiratory depression, injury arising from sedation and gastrointestinal effects such as constipation and nausea (168, 335). This is due to a combination of a diminished ability to metabolise drugs, altered distribution patterns, polypharmacy and multi-morbidities present in this population (37, 113, 137, 336, 337). Opioid bowel dysfunction (OBD) is the term used to describe the range of gastrointestinal effects associated with opioid medications (171). The occurrence of OBD may be minimised through co-prescribing of laxatives with opioid analgesics (335, 338). Sedation associated with opioids may be exacerbated by the concomitant use of CNS medications such as anxiolytics, hypnotics and antidepressants (59).

At present, the Irish state supplements the payment of 80% of prescription medications; in the primary care setting patients may receive free or subsidised prescription medications under the General Medical Service (GMS) Scheme, the Drugs Payment Scheme (DPS), the Long-Term Illness (LTI) Scheme, the High Tech Scheme, The Health Amendment Act (1996) Scheme or the Dental Treatment Services Scheme (DTSS). The GMS scheme facilitates persons who are unable without undue hardship to arrange GP, medical and surgical services for themselves and/or their dependants. The scheme, introduced in 1972, provides free GP services to public patients and replaced the Dispensary System which dated from The Poor Patient (Ireland) Act 1951. The conditions for eligibility for the GMS have changed in recent years. Between July 2001 and December 2008, all persons aged 70 years and older were eligible for GMS services. All individuals under this age were also eligible for the scheme following an evaluation of means; 97% of this population

availed of the scheme during this time (339). From January 2009, automatic entitlement to the GMS for those aged 70 years and older was removed, with individuals required to undergo a means test to secure eligibility for the scheme; approximately 95% of the population aged 70 years and older remained registered with the scheme (339). From 1st October 2010-31st November 2012, a person dispensed a medicine or medical or surgical appliance from a prescription of a Registered Medical Practitioner, Registered Dentist or Registered Nurse Prescriber by a Community Pharmacy Contractor was charged €0.50 per item subject to a limit of €10 per family per month; this charge is recouped from payment to the pharmacist. This prescription charge was increased to €2.50 per item (December 2012) dispensed under the scheme, with a maximum monthly charge of €25.00 per family per month.

The Health Products Regulatory Authority (HPRA; formerly the Irish Medicines Board [IMB]) is responsible for the regulation of medicines, medical devices and other health products in Ireland to protect human and animal health. The HPRA grants licences to companies to make, distribute and market medicines after a review of their safety, quality and effectiveness; licences may be revoked if additional evidence on the medication becomes available. Withdrawal of a prescription medication in this manner, or the attachment of conditions or cautions to the prescribing of the medication, may affect the rates of dispensing of that product. Additional factors such as marketing by pharmaceutical companies, the availability of clinical guidance, education and training of physicians and patient preferences may also contribute to the types of medications dispensed (211, 340, 341). *Figure 4-1* provides an overview of some of the key changes to the healthcare system, the GMS scheme and the licensing status of analgesics in recent decades which may influence the results obtained in this study.

1995	The Irish Medicines Board (IMB) was established and replaced the National Drugs Advisory Board. The mission of the IMB is to 'to protect and enhance public and animal health through the regulation of medicines, medical devices and healthcare products'.
2002	Report of the Benzodiazpeine Committee examines prescribing practices for benzodiazepines in Ireland and makes a number of recommendations to clinicians to improve these practices. This report was published in companion with 'Good Practice Guidelines' to assist physicians in adopting best practice recommendations.
2004	The selective NSAID rofecoxib was removed from the market in 2004 following concerns about the cardiovascular toxicity of the medication.
2005	The Health Service Executive (HSE) was established following approval of The Health Act 2004. The Primary Care Reimbursement Service (PCRS) is part of the HSE and is responsible for providing reimbursement to primary care contractors for the provision of health services or medications. The PCRS is therefore responsible for overseeing the reimbursement of pharmacists for the provision of medications provided under the General Medical Card Scheme.
2006	Withdrawal of Dextropropoxyphene/Paracetamol formulations (Co-Proxamol-Distalgesic®) from the Irish market due to concerns about the safety and efficacy profile of the medication. Overdose with this medication had caused the deaths of 300-400 fatalities in the UK in 2005. The alternative medications recommended for use were paracetamol or NSAIDs as a first step followed by introduction of codeine containing analgesics.
2006	The Irish Medicines Board and the European Medicines Evaluation Agency (EMEA) introduced restrictions on the prescribing of the remaining selective NSAIDs on the market. EU reviews carried out in 2005 and 2006 concluded that NSAIDs were associated with a slight increased risk of arterial thromboembolic events.
2007	Nimesulide (Aulin®) is removed from the Irish market.
2008	National Institute for Clinical Excellence (NICE) published guidance on the treatment and management of patients with osteoarthritis. Topical NSAIDs should be a core treatment for knee and hand osteoarthritis. When offering treatment with an oral NSAID / COX-2 inhibitor, for a patient aged under 65 years with no increased GI risk factors, the first choice of treatment to offer the patient is a standard NSAID (not a COX-2 inhibitor), co-prescribed with a proton pump inhibitor.
2010	The Pharmaceutical Society of Ireland (PSI) published guidance directing the non-prescription supply of codeine-containing medicinal products. The guidance required the pharmacist to consult with patients seeking a codeine-containing agent and counsel on the correct use of these medications; Introduction of GMS prescription co-payment.

Figure 4-1: Timeline of health service changes, policy developments and medication withdrawals or introductions to the Irish market

4.2. Aim & Objectives

The aim of this study is to provide an overview of analgesic and concurrent medication use in Ireland, so as to contextualise findings for the remainder of the thesis. The primary objectives were to examine the prevalence of:

- Analgesics and adjuvant medications dispensed over a 9 year period, 2003-2011;
- Concurrent laxative and sedating agents dispensed with weak, moderate and strong opioid analgesics.

4.2.1. Study & PhD Research Objectives

This study was conducted to meet Objective 2 described in *Chapter 2, Section 2.3*: To describe the nature and extent of analgesic use by ageing and elderly populations with CNMP in the Republic of Ireland.

4.3. Methods

4.3.1. Study Population and Data Source

The HSE-PCRS database was used as the data source for this research study. This database records monthly pharmacy claims for dispensed medications by hospital and community pharmacy contractors in Ireland. Permission was gained from the data controller to use the GMS database if anonymised and analysed at group level.

At the outset of the study, the WHO ATC codes required by the researcher were provided to the data controller of the HSE-PCRS database at the HRB Centre for Primary Care, RCSI. Using the WHO ATC code as a method of identifying the dispensing records of interest from the HSE-PCRS database the following information was also retrieved by the data controller for each dispensing record: a 5-Digit Drug Code; prescriber information, defined daily dose, strength, quantity, method of administration, net ingredients and pharmacy dispensing fee per item. The gender and age-group of each patient are also recorded but no diagnosis or disease outcomes are recorded. Patients aged ≥55 years exposed to any analgesic or adjuvant medication during the period 2003-2011 were included in the study.

Concurrent dispensings of laxatives and sedating agents with weak, moderate and strong opioids were also extracted. Patients were categorised by gender and age group; 55-64, 65-69, 70-74 and ≥75 years. This data was then placed on a password protected encrypted computer for use by the researcher and accessed on site at the Health Research Board (HRB) Centre for Primary Care, Royal College of Surgeons in Ireland, Dublin (RCSI) for a 6 week period.

4.3.1.1. Classification of Analgesics

Consistent with the WHO Analgesic Ladder, analgesics were classified as, non-opioid, nonselective and selective NSAIDS and opioids. Opioid analgesics were further categorised as weak, moderate or strong according to their use for mild, moderate or severe pain. The Irish Medical Formulary (IMF) and British National Formulary (BNF) were consulted to support this approach to categorisation of the opioid analgesics. If the Summary of Product Characteristics (SPC) or the BNF/IMF monograph for the drug recommended the analgesic for mild pain, this was classified as a 'Weak Opioid'; mild to moderate pain was classified as a 'Moderate Opioid', while moderate to strong were classified as a 'Strong Opioid'. Additionally, consideration was given to the quantity of the opioid agents in the formulation; all weak opioids contained ≤20 mg codeine, while moderate opioids contained >20 mg codeine (342, 343). A list of the weak and moderate opioid formulations is provided in *Appendix C, Table C-1.*

The ATC code for all paracetamol/codeine formulations is the same regardless of the quantity of codeine in the product. To differentiate the higher strength paracetamol/codeine formulations from the non-prescription low dose formulations, these medications were identified using the Drug Code of the various products and assigned to weak or moderate opioid groups as appropriate. Drug codes were also used to identify strong opioids delivered through the transdermal route. The ATC Code N02BE51 is described by the WHO ATC directory as paracetamol combinations excluding psycholeptics. Upon consultation with the IMF, this ATC code is also used to represent a number of paracetamol formulations containing codeine as an active ingredient. For the purposes of this analysis, it was necessary to ensure that this ATC code correctly identified paracetamol formulations containing codeine and those containing a different adjunct

medication e.g. caffeine, pseudoephedrine. Those formulations containing codeine would be more correctly categorised as "Weak Opioids" or "Moderate Opioids", while those containing adjuvant, such as pseudoephedrine or caffeine, should not be categorised as opioid medications. The database was consulted to identify the drug codes represented by the ATC code "N02BE51"; upon completion of this process, all these agents were identified as being codeine-containing formulations combined with paracetamol. Therefore, the ATC code "N02BE51" was not included in the non-opioid category, instead, it was categorised in the opioid category for the purposes of this analysis.

Adjuvant medications were considered separately to analgesics. As this database does not provide a clinical indication for the medication, it is not possible to determine the reason for which these medications are prescribed; it is therefore not appropriate to classify them as analgesics. Sedating agents (benzodiazepines and Z drugs) and laxatives were also extracted for analysis, alongside weak, moderate and strong opioids.

Non-opioids, non-selective NSAIDs, selective NSAIDs, weak, moderate and strong opioids are listed in *Table 4-1*, while adjuvant medications, laxatives and sedating agents are listed in *Table 4-2*.

Table 4-1: Drug name and ATC code for analgesic medications by therapeutic class

Non-Opioids *(ATC Code)*	**Non-Selective NSAIDs** *(ATC Code)*		**Selective NSAIDS** *(ATC Code)*	**Weak Opioids** *(ATC Code)*	**Moderate Opioids** *(ATC Code)*	**Strong Opioids** *(ATC Code)*
Nefopam *(N02BG06)*	**Systemic Non-Selective**	**Topical Non-Selective**	Celecoxib *(M01AH01)*	Codeine Phosphate, Paracetamol Combinations *(N02BE51)*[†]	Tramadol *(N02AX02)*	Buprenorphine *(N02AE01)*
Paracetamol *(N02BE01)*	Benzydamine *(M01AX07)*	Benzydamine *(M02AA05)*	Etoricoxib *(M01AH05)*	Ibuprofen Codeine Combinations *(M01AE51)*	Tramadol, Paracetamol *(N02AX52)*	Fentanyl *(N02AB03)*
	Diclofenac Potassium *(M01AB05)*	Diclofenac Sodium *(M02AA15)*	Nimesulide *(M01AX17)*		Meptazinol *(N02AX05)*	Hydromorphone *(N02AA03)*
	Dexketoprofen *(M01AE17)*	Etofenamate *(M02AA06)*	Parecoxib *(M01AH04)*		Tapentadol *(N02AX06)*	Morphine Sulphate *(N02AA01)*
	Diclofenac Sodium /Misoprostal *(M01AB55)*	Felbinac *(M02AA08)*			Dihydrocodeine *(N02AA08)*	Morphine Tartrate
	Fenbufen *(M01AE05)*	Capsaicin *(N01BX04/M02AB01)*			Dihydrocodeine Combinations *(N02AA58)*	Cyclizine *(N02AA51)*
	Ibuprofen *(M01AE01)*	Ibuprofen *(M02AA13)*			Dihydrocodeine, Paracetamol Combinations *(N02BE51)*	Oxycodone *(N02AA05)*
	Mefenamic Acid *(M01AG01)*	Piroxicam *(M02AA07)*			Codeine Phosphate, Paracetamol Combinations *(N02BE51)*[‡]	Oxycodone, Naloxone *(N02AA55)*
	Meloxicam *(M01AC06)*	Ketoprofen *(M02AA10)*				
	Nabumetone *(M01AX01)*					
	Naproxen *(M01AE02)*					
	Piroxicam *(M01AC01)*					
	Aspirin (Analgesic) *(N02BA01)*					
	Ketoprofen *(M01AE03)*					

[†] Formulations containing ≤20 mg codeine
[‡] Formulations containing >20 mg codeine

Table 4-2: Drug name and ATC code for adjuvant medications, sedating agents and laxatives

Adjuvant Medications *(ATC Code)*	Sedating Agents *(ATC Code)*	Laxatives *(ATC Code)*
Duloxetine *(N06AX21)*	Alprazolam *(N05BA12)*	Isphaghula Husk/Isphaghula Husk Combinations *(A06AC01/A06AC51)*
Amitriptyline *(N06AA09)*	Bromazepam *(N05BA08)*	Methylcellulose *(A06AC06)*
Pregabalin *(N03AX16)*	Chlordiazepoxide *(N05BA02)*	Sterculia/Sterculia Combinations *(A06AC03/A06AC53)*
Gabapentin *(N03AX12)*	Clobazam *(N05BA09)*	Bisacodyl/Bisacodyl Combinations *(A06AB02/A06AG02/A06AB52)*
Carbamazepine *(N03AF01)*	Diazepam *(N05BA01)*	Dantron/Dantron Combinations/Dantron Incl Combinations *(A06AB03/A06AB53/A06AG03)*
Nortriptyline *(N06AA10)*	Lorazepam *(N05BA06)*	Docusate Sodium/Docusate Sodium Incl Combinations *(A06AA02/A06AG10)*
	Prazepam *(N05BA11)*	Glycerol *(A06AG04/A06AX01)*
	Flunitrazepam *(N05CD03)*	Senna/Senna Glycoside Combinations *(A06AB06/A06AB56)*
	Flurazepam *(N05CD01)*	Sodium Picosulfate/Sodium Picosulfate with Magnesium Citrate/Combinations (A06AB08/A06AB58)
	Lometazepam *(N05CD06)*	Liquid Paraffin/Liquid Paraffin Combinations *(A06AA01/A06AA51)*
	Nitrazepam *(N05CD02)*	Lactulose/Lactulose Combinations (A06AD11/A06AD61)
	Temazepam *(N05CD07)*	Macrogols/Macrogol Combinations *(A06AD15/A06AD65)*
	Triazolam *(N05CD05)*	Methylnaltrexone Bromide *(A06AH01)*
	Zaleplon *(N05CF03)*	Prucalopride *(A06AX05 /A03AE04)*
	Zolpidem *(N05CF02)*	Pyridostigmine *(N07AA02)*
	Zopiclone *(N05CF01)*	

4.3.2. Statistical Analysis

Dispensing rates refer to the number of adults aged ≥55 years, who are receiving at least one analgesic medication per 1,000 GMS eligible population; the term ≥1 dispensing indicates that the individual received at least one analgesic (or specific class of analgesic e.g. non-opioids) in that year. The number of people per 1,000 in receipt of >3 dispensings of an analgesic or adjunct medication was also calculated as a method of indicating recurrent use of that agent. Prevalence rates for dispensings (≥1 dispensing and >3 dispensings) for all classes of medications were calculated according to age group and gender for each year, while 95% Confidence Intervals (CI) were also calculated using the appropriate GMS eligible population for that year; these figures were obtained from Table 9.1 (GMS: Number of Eligible Persons by Gender within Age Groups) of the PCRS Annual Reports for 2003-2011. Data was analysed using Stata Version 13 (Stata Corp, College Station. Texas, USA). To allow for ease of reading of results presented in this chapter, the population numbers (n) underlying the results presented in the tables in the 'Results' section are provided in separate tables in *Appendix C*.

The following results are presented in Figures for classes of analgesic and adjuvant medications:

- Prevalence rate (per 1,000) of the particular class of analgesic or adjuvants dispensed (≥ 1 dispensing & >3 dispensings)
- Prevalence rate (per 1,000) of analgesics or adjuvants dispensed according to age-group and gender (>3 dispensings) to the GMS eligible population aged ≥55 years for the years 2009-2011. Given the level of detail presented in these Figures, the three most recent years are presented to capture the most recent trends for this data.

Concurrent use was defined as a co-prescription of a laxative or sedating agent and a weak, moderate or strong opioid dispensed in the same calendar month in a calendar year. The larger GMS database was initially searched to identify the individuals who had been dispensed a sedating agent and laxative in addition to an opioid medication for the years 2006-2011 (identified using WHO ATC code). This database of extracted sedating agents and laxatives was then combined with opioid medications in a single database, a total of 28,603,604 observations. Results are reported as the prevalence rate of individuals taking a laxative with a weak,

moderate or strong opioid or a sedating agent, with a weak, moderate or strong opioid per 1,000 of the population taking a weak, moderate or strong opioid respectively.

4.4. Results

4.4.1. General Analgesic Use

Table 4-3 presents the number of prescription analgesics dispensed for GMS patients aged ≥55 years, the number of patients dispensed ≥1 analgesic medication prescription and the total GMS eligible population. From January 2003 to December 2011, the number of individuals aged ≥55 years identified from the PCRS annual reports increased from 490,501 in 2003 to 592,348 in 2011. A total of 22,570,124 analgesic prescriptions were recorded between 2003 and 2011. There was a slight decrease in the number of prescription analgesics dispensed and the number of patients dispensed at least one analgesic in 2007. *Appendix C, Table C-2,* details the number of GMS eligible patients from 2003-2011 according to age-group and gender, while *Appendix C, Table C-3,* provides a comprehensive outline of the proportion of men and women according to age-group receiving an analgesic in each year of the database. For each of the nine years of the study, women consistently accounted for approximately 60% of analgesic use and men 40%.

Table 4-3: Number of analgesic prescriptions dispensed and number of patients dispensed ≥1 prescription analgesic medication under the GMS Scheme 2003-2011

Year	No. of Prescription Analgesics Dispensed	No. of Patients Dispensed ≥1 Analgesic Medication	Total GMS Population
2003	2,089,537	293,329	490,501
2004	2,113,762	293,355	500,390
2005	2,312,903	307,463	513,995
2006	2,371,552	316,186	530,100
2007	2,107,415	312,064	545,321
2008	2,688,993	336,551	555,917
2009	2,811,838	344,029	554,334
2010	2,946,413	356,334	578,561
2011	3,127,711	371,237	592,348

Figure 4-2 illustrates analgesic consumption per annum across genders and for the overall population. The highest use was detected in 2011, with 626.7 (625.5-628.0) dispensed ≥1 analgesic per 1,000 population. This is equivalent to two-thirds of the eligible GMS population receiving at least one analgesic per year.

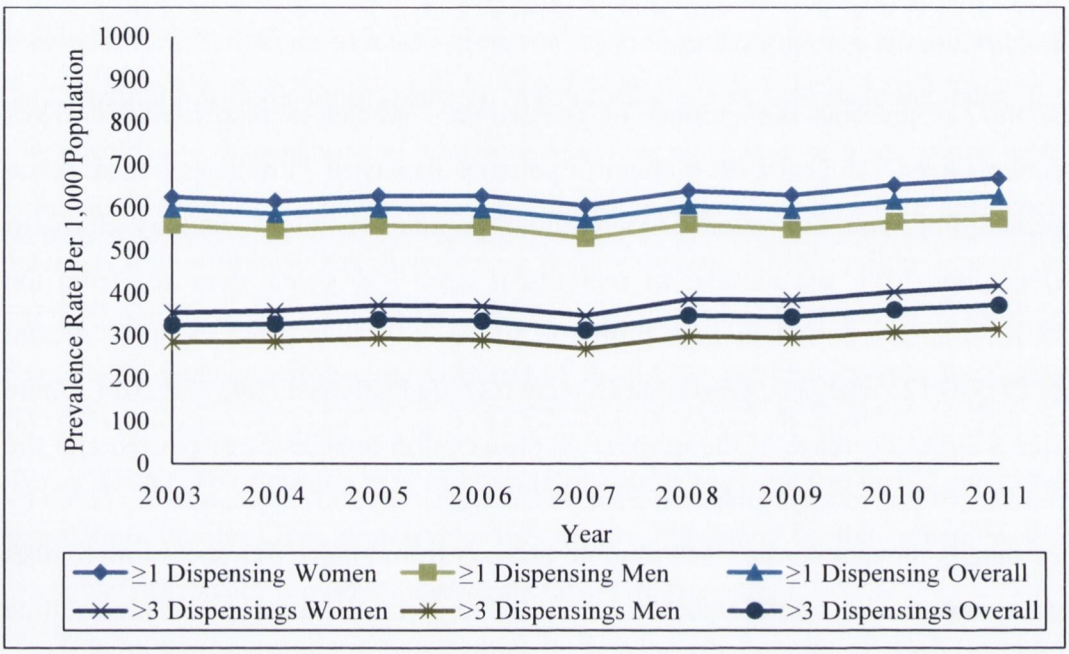


Figure 4-2: Prevalence rate (per 1,000) of analgesic prescribing (≥ 1 dispensing & >3 dispensings) for GMS eligible population aged ≥55 years

Table 4-4 provides an outline of the prevalence per 1,000 population of those receiving >3 dispensings of analgesics per annum by age-group. Approximately 30-40% of each age-group in the GMS eligible population were dispensed >3 analgesic medications in 2011. The oldest age-group, ≥75 years, accounted for the greatest proportion of analgesic dispensings per 1,000 population for all years. Those aged 65-69 years were the second most prevalent group in receipt of analgesics for the years 2003-2008 inclusive and in 2010, however, from 2009 the 70-74 years age-group became the second most prevalent group in receipt of this class of medications and again in 2011.

Table 4-4: Prevalence rate (per 1,000) of analgesic dispensed (>3 dispensings) to GMS eligible population aged ≥55 years according to age-group and gender

	Prevalence Rate per 1,000 population			
Year	55-64 Years (95% CI)	65-69 (95% CI)	70-74 Years (95% CI)	≥75 Years (95% CI)
2003	282.6 (280.0-285.1)	315.0 (311.5-318.6)	296.4 (293.8-299.1)	369.8 (367.7-372.0)
2004	287.2 (284.6-289.8)	318.4 (314.8-321.9)	293.2 (290.6-295.9)	374.4 (372.2-376.5)
2005	303.5 (300.9-306.1)	332.4 (328.9-336.0)	304.0 (301.4-306.6)	378.9 (376.8-380.9)
2006	296.5 (293.9-299.0	327.7 (324.2-331.2)	298.5 (295.9-301.1)	379.6 (376.0-381.7)
2007	278.9 (276.5-281.4)	304.8 (301.4-308.2)	279.7 (277.2-282.2)	354.8 (352.8-356.8)
2008	312.4 (309.9-314.9)	338.8 (335.3-342.2)	307.5 (305.0-310.1)	394.0 (392.0-396.0)
2009	293.0 (280.7-297.3)	310.1 (306.9-313.2)	329.2 (326.4-331.9)	398.6 (396.6-400.6)
2010	318.2 (315.9-320.6)	335.0 (331.0-338.2)	331.5 (328.7-334.2)	413.1 (411.1-415.1)
2011	327.5 (325.2-329.8)	342.0 (345.9-348.9)	343.0 (340.2-345.7)	427.2 (425.3-429.6)

Figure 4-3 illustrates the proportion of the analgesic taking population who were dispensed different analgesics within each year. This was calculated by identifying the proportion of the GMS analgesic-taking population who were dispensed a medication with a different ATC Code within the year. Approximately 40% of the population consistently received one analgesic medication each year (i.e. one ATC Code), approximately one quarter received 2 different analgesics, another quarter of the population received more than 3 or 4 different analgesics each year, while approximately 7-10% received 5 different analgesics (5 different ATC Codes).

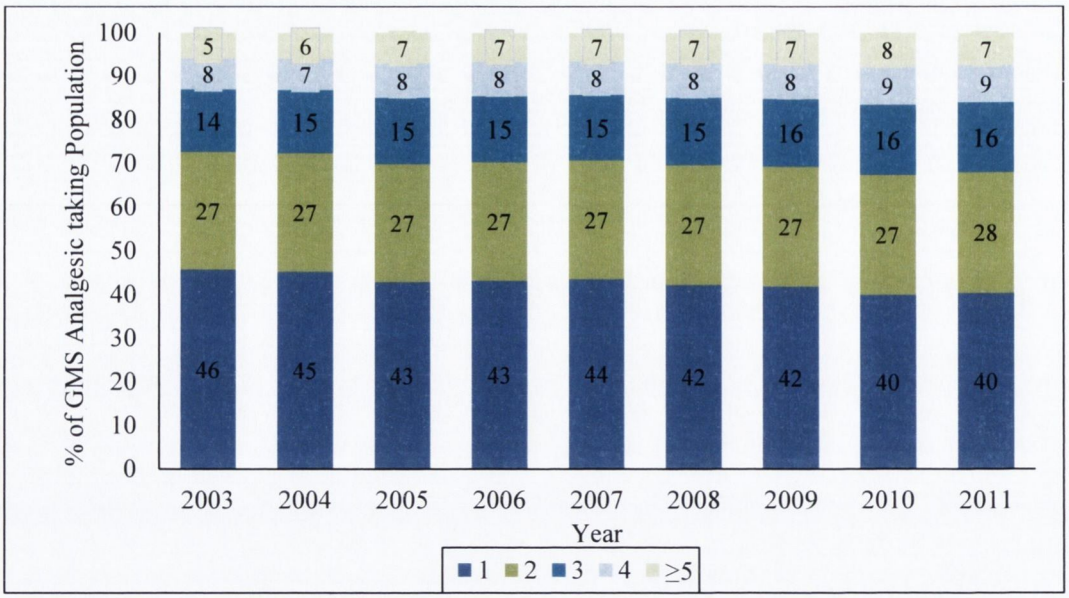


Figure 4-3: Percentage of GMS analgesic population dispensed ≥1 analgesic ATC Code each year

4.4.2. Non-Opioids

Paracetamol has a consistently high frequency of prescribing according to the HSE-PCRS Annual Reports. In 2011, it was the 4th most commonly prescribed medication and the 5th in 2010 (233, 344). *Table 4-5* presents the number of individuals receiving at least one dispensing of paracetamol or nefopam (non-opioids) during the years 2003-2011. The number of such individuals approximately doubled in this 9 year period and exceeded the number receiving any other medication when considering all other classes of analgesics and adjunct medications.

Table 4-5: Prevalence of non-opioid medications according to the number of GMS eligible patients aged ≥55 years receiving ≥1 dispensing

	Non-Opioids		
Year	**Drug Name**	**No. of GMS Eligible Patients Aged ≥55 Years Receiving ≥1 Dispensing**	**% of all Drugs in this Class**
2003	Paracetamol	64,250	99.7
	Nefopam	189	0.3
2004	Paracetamol	68,802	99.8
	Nefopam	167	0.2
2005	Paracetamol	87,518	99.8
	Nefopam	189	0.2
2006	Paracetamol	109,060	99.8
	Nefopam	200	0.2
2007	Paracetamol	114,150	99.9
	Nefopam	171	0.1
2008	Paracetamol	137,926	99.9
	Nefopam	176	0.1
2009	Paracetamol	149,535	99.9
	Nefopam	199	0.1
2010	Paracetamol	166,2253	99.9
	Nefopam	245	0.1
2011	Paracetamol	179,385	99.9
	Nefopam	232	0.1

Figure 4-4 presents prevalence per 1,000 eligible population dispensed ≥1 and >3 non-opioid medications. There was a general upward trend in the receipt of these medications, with 303.0 (301.8-304.2) per 1,000 population in 2011; the lowest prevalence occurred in 2003, with 131.4 (130.4-132.3) per 1,000 receiving at least one dispensing in this year. As per general analgesic dispensings, women

consistently had a higher prevalence rate per 1,000 population than their male counterparts.

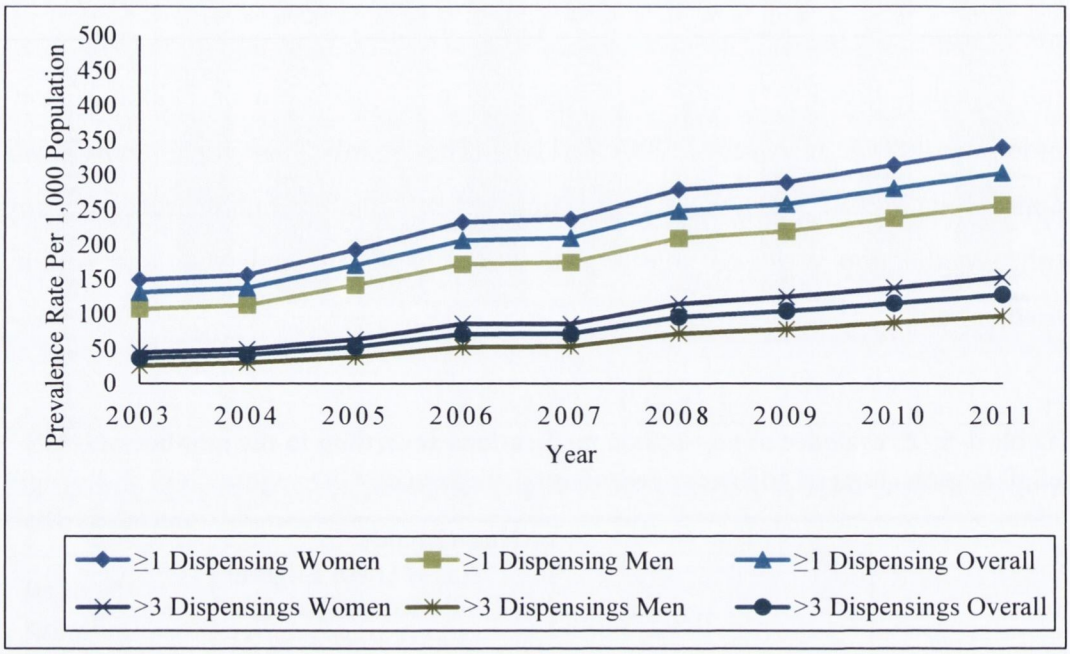


Figure 4-4: Prevalence rate (per 1,000) of non-opioids dispensed (≥ 1 dispensing & >3 dispensings) for GMS eligible population aged ≥55 years

Figure 4-5 considers >3 dispensings according to age-group and gender for the years 2009-2011. Women had a consistently higher prevalence rate per 1,000 population than their male counterparts across all age-groups. Prevalence increased across age-groups in each of the three years for both genders; the greatest difference between men and women was observed in the ≥75 year age-group, where the difference was approximately 70 individuals per 1,000 population in each of the three years.

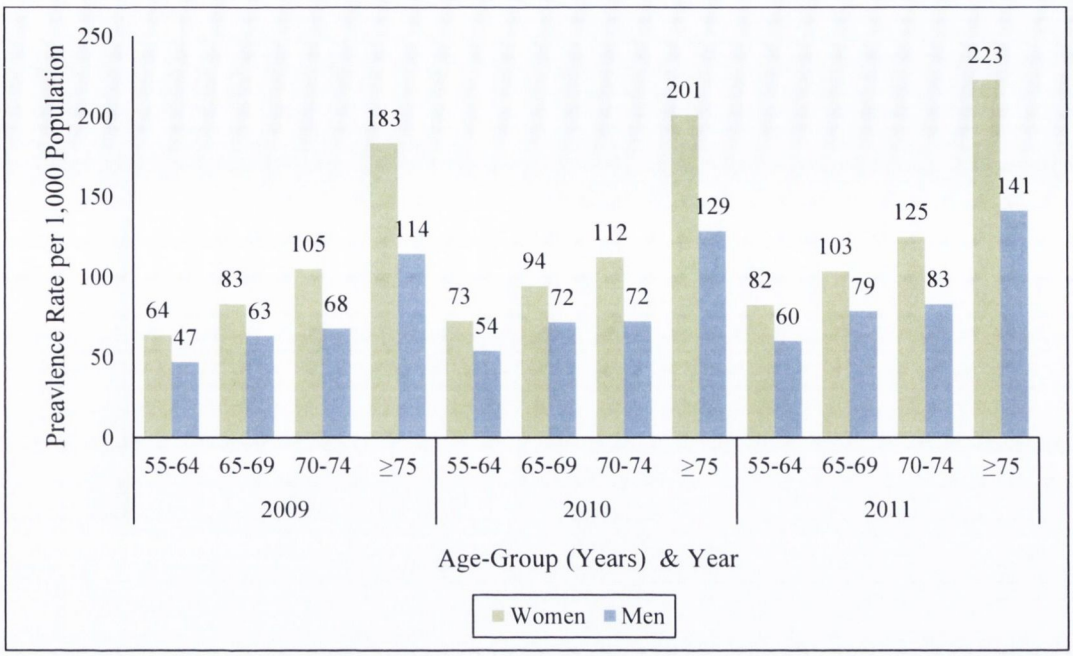


Figure 4-5: Prevalence rate (per 1,000) of non-opioids according to age-group for the years 2009-2011 (>3 dispensings)

4.4.3. Non-Selective NSAIDS

Non-selective NSAIDs have been classified as topical and systemic agents for the purposes of this analysis; this was considered necessary as the cautions, contraindications and interactions differ according to the route of administration of this class of analgesic. *Table 4-6* presents a summary of the prevalence of systemic and topical non-selective NSAIDs per 1,000 population. The extent of use of these agents is further evidenced by HSE-PCRS annual reports, where systemic diclofenac is positioned in the 20 most prescribed medications under the GMS scheme in 2010 and 2011. Similarly, topical diclofenac appears in the 45 medications most prescribed under the scheme in 2010 and 2011 (233, 344). Diclofenac is a single agent within this class, therefore, when additional agents were included, such as ibuprofen or mefenamic acid, the non-selective NSAIDs have a high prevalence rate of dispensings in the GMS population when compared to the other classes of analgesics.

Figure 4-6 and *Figure 4-7* presents prevalence per 1,000 eligible population dispensed ≥1 and >3 systemic and topical non-selective NSAID medications respectively. Women had a higher prevalence of dispensings per 1,000 population

of both systemic non-selective NSAIDs and topical non-selective NSAIDs than men each year. Furthermore, while the rate of topical non-selective NSAIDs continued to increase for both ≥1 dispensing and >3 dispensings, the rate of systemic non-selective NSAIDs decreased from 2008 onwards.

Table 4-6: Three most prevalent systemic and topical non-selective NSAIDS according to the number of GMS eligible patients aged ≥55 years (≥1 dispensing)

	Systemic Non-Selective NSAIDs			Topical Non-Selective NSAIDs		
	Drug Name	No. of GMS Eligible Patients Aged ≥55 Years receiving ≥1 Dispensing	% of all Drugs in this Class	Drug Name	No. of GMS Eligible Patients Aged ≥55 Years receiving ≥1 Dispensing	% of all Drugs in this Class
2003	Diclofenac	68,474	39.2	Diclofenac	42,067	56.3
	Mefenamic Acid	27,439	15.8	Ketoprofen	10,643	14.3
	Aspirin (Analgesic)	25,154	14.6	Felbinac	10,591	14.2
2004	Diclofenac	66,763	42.2	Diclofenac	45,199	56.96
	Mefenamic Acid	24,753	15.6	Ketoprofen	11,454	14.4
	Ibuprofen	22,918	14.5	Ibuprofen	11,018	13.9
2005	Diclofenac	82,567	44.8	Diclofenac	53,099	58.4
	Ibuprofen	27,215	14.8	Ketoprofen	12,968	14.3
	Mefenamic Acid	25,407	13.8	Ibuprofen	12,320	13.5
2006	Diclofenac	83,901	46.6	Diclofenac	58,213	59.5
	Mefenamic Acid	26,197	14.6	Ketoprofen	14,058	14.5
	Ibuprofen	25,720	14.3	Ibuprofen	12,502	12.8
2007	Diclofenac	88,514	44.9	Diclofenac	60,106	59.6
	Ibuprofen	27,997	14.2	Ketoprofen	13,783	13.7
	Mefenamic Acid	24,728	12.5	Ibuprofen	11,535	11.4

2008	Diclofenac	101,015	45.9	Diclofenac	75,959	60.7
	Ibuprofen	32,673	14.8	Ketoprofen	17,232	13.8
	Mefenamic Acid	27,215	12.4	Ibuprofen	13,396	10.7
2009	Diclofenac	97,223	45.9	Diclofenac	75,928	57.9
	Ibuprofen	33,577	15.9	Ketoprofen	18,637	14.2
	Mefenamic Acid	25243	11.9	Ibuprofen	12,304	9.4
2010	Diclofenac	96,828	44.9	Diclofenac	75,396	54.9
	Ibuprofen	35,925	16.7	Ketoprofen	21,372	15.6
	Mefenamic Acid	24,378	11.3	Etofenamate	17,485	12.7
2011	Diclofenac	93,330	43.8	Diclofenac	79,655	54.4
	Ibuprofen	38,229	17.9	Etofenamate	24,217	16.5
	Mefenamic Acid	23,475	11.0	Ketoprofen	20,285	15.5

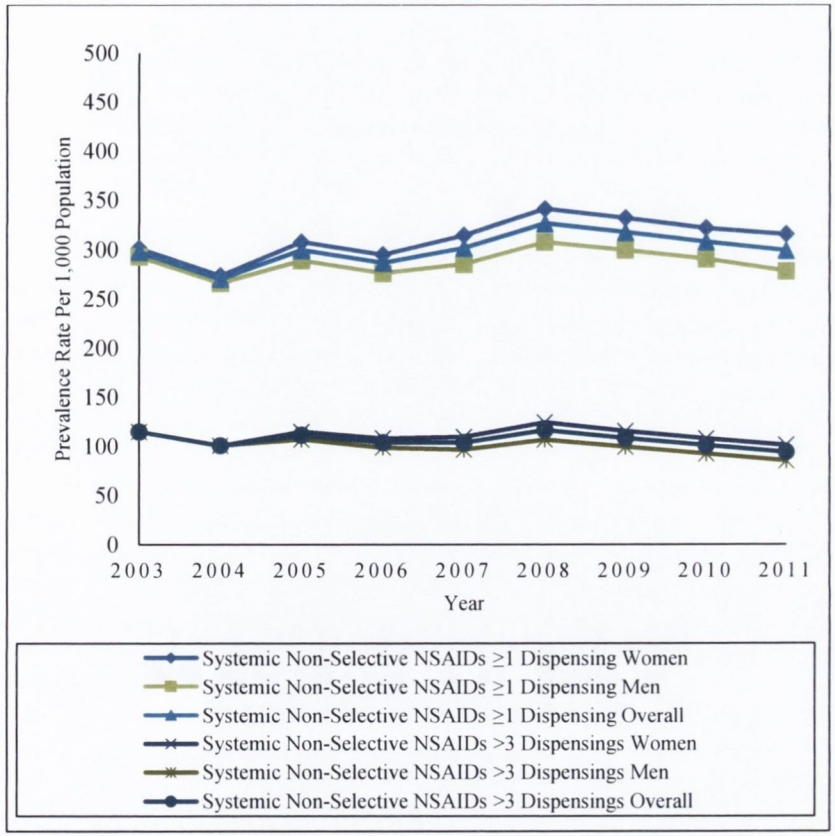


Figure 4-6: Prevalence rate (per 1,000) of systemic non-selective NSAIDs dispensed (≥ 1 dispensing & >3 dispensings) for GMS eligible population aged ≥55 years

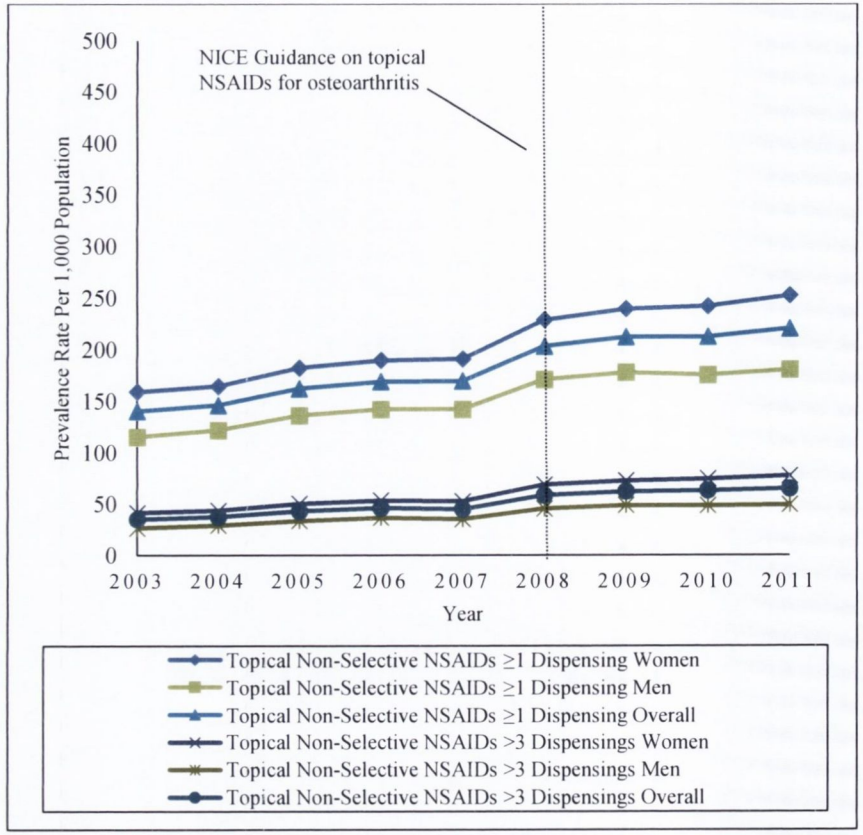


Figure 4-7: Prevalence rate (per 1,000) of topical non-selective NSAIDs dispensed (≥ 1 dispensing & >3 dispensings) for GMS eligible population aged ≥55 years

Table 4-7 presents the prevalence rate per 1,000 population of systematic and topical non-selective NSAIDs *(Table C-4, Appendix C presents the population numbers supporting this analysis).* Systemic non-selective NSAID dispensings peaked in 2008, with 326.5 (322.2-327.7) dispensed per 1,000 population, following the lowest prevalence in 2004 in which 270.4 (265.7-271.6) per 1,000 population were dispensed; the increase may be attributed to the withdrawal of a number of systemic selective NSAIDs from the market in the preceding years, as previously discussed. Approximately one third of the population receiving ≥1 dispensing of a systemic non-selective NSAID continued to receive >3 dispensings each year. The highest prevalence rate per 1,000 population for topical nonselective NSAIDs was recorded in 2011, with 220.6 (219.6-221.7) individuals per 1,000 receiving such a medication and 65.0 (64.4-65.7) individuals per 1,000 receiving >3 dispensings in that year.

Table 4-7: Prevalence rate (per 1,000) of systemic and topical non-selective NSAIDs (≥ 1 dispensing & >3 dispensings) to GMS eligible population aged ≥55years

	Systemic Non-Selective NSAIDs		Topical Non-Selective NSAIDs	
Year	**≥ 1 Dispensing (95% CI)**	**>3 Dispensings (95% CI)**	**≥ 1 Dispensing (95% CI)**	**>3 Dispensings (95% CI)**
2003	297.9 (293.2-299.2)	114.9 (109.6-115.5)	140.3 (139.4-141.3)	34.9 (34.4-35.5)
2004	270.4 (265.7-271.6)	100.8 (95.5-101.6)	146.2 (145.2-147.1)	37.3 (36.8-37.8)
2005	299.8 (295.2-301.0)	111.6 (106.4-112.4)	162.3 (161.3-163.3)	42.9 (42.4-43.5)
2006	286.8 (282.3-288.0)	104.1 (99.0-104.9)	169.0 (168.0-170.0)	46.1 (45.5-46.7)
2007	301.8 (297.4-303.0)	103.9 (98.9-104.7)	169.6 (168.6-170.6)	44.9 (44.4-45.5)
2008	326.5 (322.2-327.7)	116.7 (111.8-117.6)	203.4 (202.4-204.5)	58.4 (57.8-59.1)
2009	317.7 (313.3-318.9)	108.5 (103.5-109.3)	212.4 (211.3-213.5)	62.1 (61.5-62.7)
2010	308.0 (303.8-309.2)	101.1 (96.2-101.9)	212.7 (211.7-213.8)	63.0 (62.4-63.6)
2011	299.0 (294.7-300.2)	94.2 (89.3-94.9)	220.6 (219.6-221.7)	65.0 (64.4-65.7)

Figure 4-8 demonstrates the extent of the difference between age-groups in receipt of these agents; there was a slight increase observed in all age-groups in this period. As may be determined by observation of both *Table 4.4-5* and *Figure*

4-6, the rate of dispensing of systemic non-selective NSAIDs was higher than that of topical agents. Perhaps most notable, is the substantial decrease in >3 dispensings of systemic non-selective NSAIDs for the oldest age-group ≥75 years, from 101.1 (93.5-102.6) in 2009 to 82.6 (74.2-83.7) in 2011; this is matched by a slight increase in the number receiving >3 dispensings of topical agents.

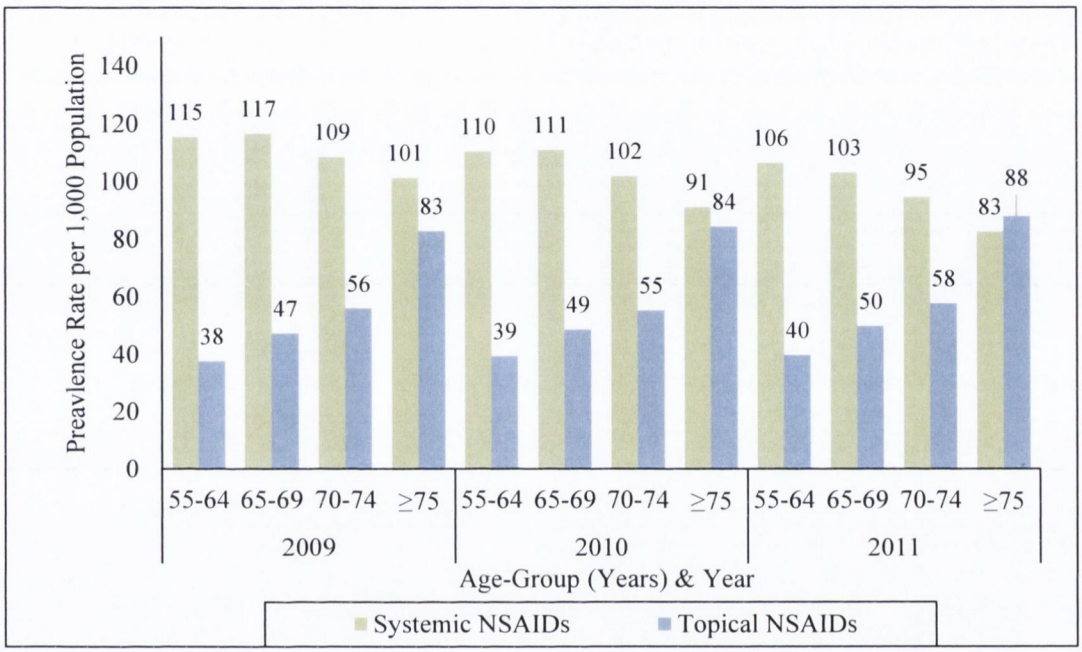


Figure 4-8: Prevalence rate (per 1,000) of systemic non-selective NSAIDs according to age-group for the years 2009-2011 (>3 dispensings)

4.4.4. Selective NSAIDS

Figure 4-1 highlights the concerns associated with the use of this class of medication which were initially highlighted in 2005. Over a two year period, a number of medications from this class were withdrawn from the Irish market, while the remaining medications in the class continued to be available but with specific cautions and contraindications associated with their use. *Table 4-8* captures the reduction in individuals receiving this group of medications, indeed, the systemic selective NSAIDs have a parity in terms of dispensings to the systemic non-selective NSAIDs. Following the withdrawal of nimesulide (2007) and the attachment of cautions and contraindications to the prescribing of remaining systematic selective NSAIDs, these agents were amongst the least prescribed

classes of analgesic medications in the most recent years of the database. The rate of selective NSAID dispensings is observed to have increased from 2009 onwards following the lowest rate in 2008, however, the most recent prevalence rate was considerably less than that observed in 2003-2006.

Table 4-8: Three most prevalent selective NSAIDS according to the number of GMS eligible patients aged ≥55 years receiving ≥1 dispensing

Year	Systemic Selective NSAIDs		
	Drug Name	No. of GMS Eligible Patients Aged ≥55 Years receiving ≥1 Dispensing	% of all Drugs in this Class
2003	Nimesulide	56,881	58.8
	Celecoxib	38,527	39.8
	Etoricoxib	12,815	1.3
2004	Nimesulide	54,510	49.8
	Celecoxib	43,460	39.7
	Etoricoxib	11,577	10.6
2005	Nimesulide	72,568	73.6
	Celecoxib	15,762	16.0
	Etoricoxib	10,243	10.4
2006	Nimesulide	81,617	84.9
	Etoricoxib	9,588	10.0
	Celecoxib	4,933	5.2
2007	Nimesulide	45,795	67.6
	Etoricoxib	16,683	24.6
	Celecoxib	5,253	7.8
2008	Etoricoxib	24,530	79.5
	Celecoxib	5,689	18.4
	Nimesulide	646	2.1
2009	Etoricoxib	27,619	84.7
	Celecoxib	4,993	15.3
2010	Etoricoxib	30,942	84.4
	Celecoxib	5,714	15.6
2011	Etoricoxib	33,268	80.1
	Celecoxib	8,243	19.9

Figure 4-9 presents the prevalence per 1,000 eligible population dispensed ≥1 and >3 selective NSAIDs for the GMS eligible population aged ≥55 years and reflects the contribution of changes in the licensing status of a number of medications in this class to the prevalence of dispensings. There was a reduction in the number of patients receiving ≥1 dispensing from a peak of 197.1 (196.0-198.1) per 1,000 population in 2004 to 54.2 (53.6-54.8) per 1,000 population in 2008, however, the rate of dispensing rises in the years following this minimum point, increasing to 68.2 (67.5-68.8) dispensings per 1,000 population in 2011.

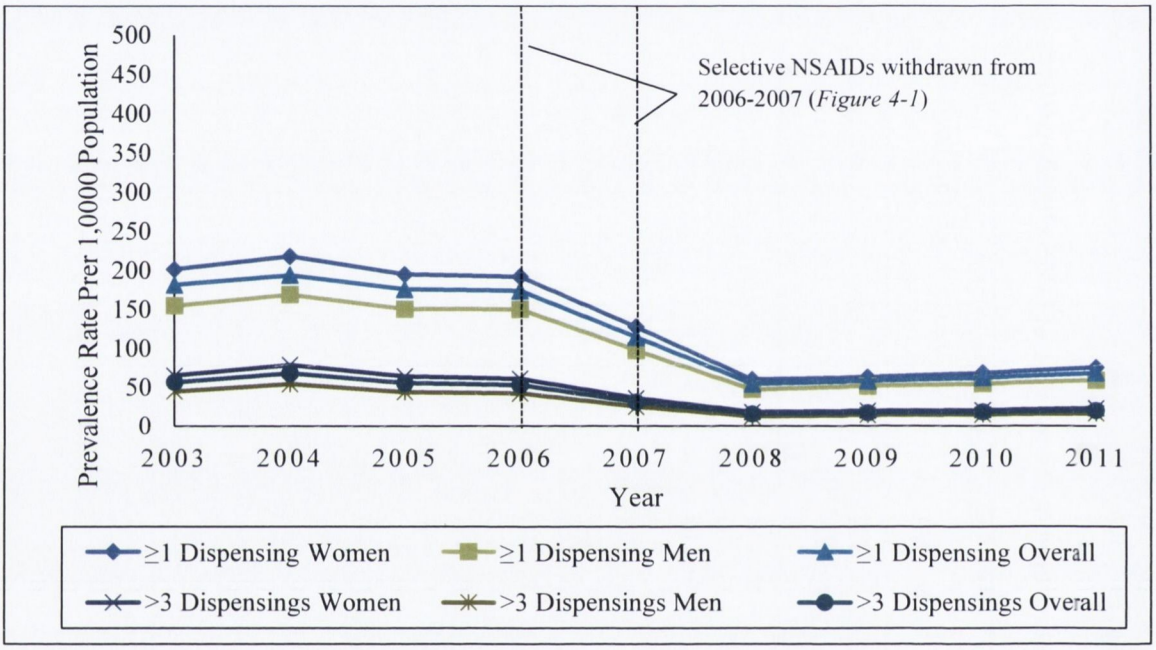


Figure 4-9: Prevalence rate (per 1,000) of selective NSAIDs dispensed (≥ 1 dispensing & >3 dispensings) to GMS eligible population aged ≥55 years

Figure 4-10 presents the prevalence of dispensing across age-group and gender for those receiving >3 dispensings of a selective NSAID in a year. There was no difference between men and women across all age-groups; those in the youngest age-groups, 55-64 years and 65-69 years, had a consistently higher prevalence in comparison to older populations, however, the difference here again is slight, being approximately 3 persons per 1,000.

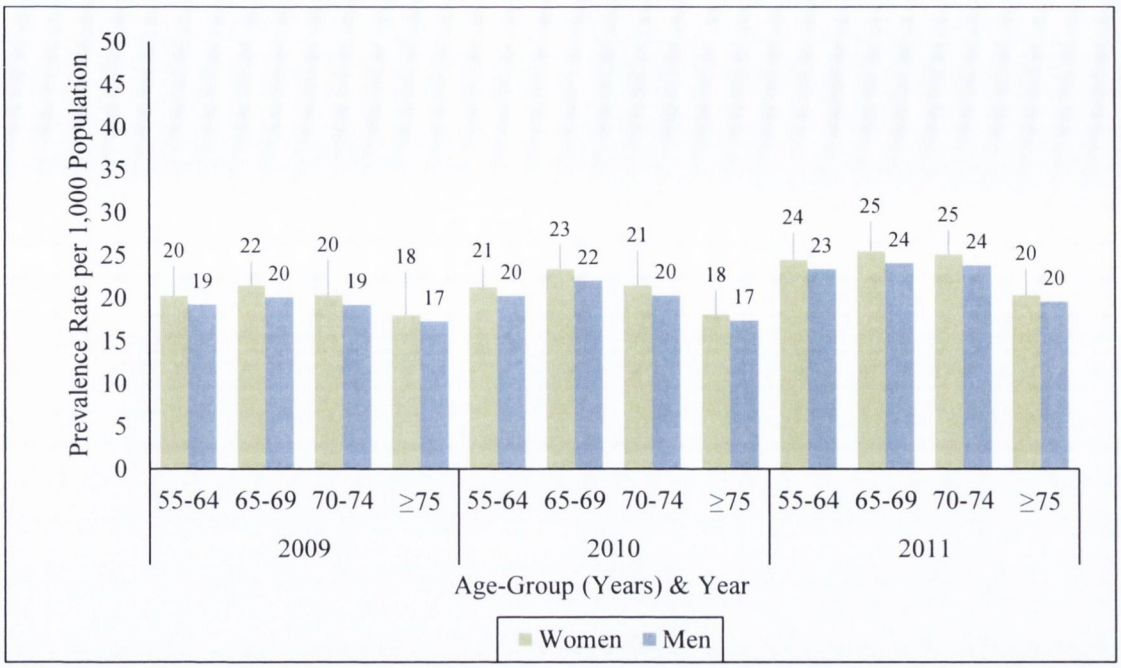


Figure 4-10: Prevalence rate (per 1,000) of selective NSAIDs according to age-group and gender for the years 2009-2011 (>3 dispensings)

4.4.5. Opioids

Table 4-9 presents the 3 most prevalent medications dispensed in each classification of opioids, weak, moderate and strong. The number of individuals who were dispensed a weak opioid approximately doubled during the period under investigation. The ibuprofen/codeine formulation included, during the years 2003-2006, was removed from the GMS scheme and therefore does not appear from this date onward. Dextropropoxyphene/paracetamol combinations were the most common type of moderate opioid dispensed for the period 2003-2005. Upon withdrawal of this formulation from the market in 2006, paracetamol/codeine and tramadol formulations increased in prevalence of dispensings. From this year onwards, there was a small difference between the numbers of individuals receiving a paracetamol/codeine formulation and tramadol; approximately 4,000 individuals each year. This corresponds with the PCRS Annual Reports which details the most commonly prescribed medications dispensed each year; paracetamol/codeine combinations appear approximately five to six places above tramadol in these listings (Paracetamol #34 and Tramadol #40 respectively in 2010, Paracetamol #37 and Tramadol #42 respectively in 2011) (233, 344). There has been a steady

increase in the number of individuals in receipt of a strong opioid since 2003. The emergence of buprenorphine as the most commonly dispensed agent can be observed from 2006 to 2011 when this medication has the highest rate of dispensing within this class.

Table 4-9: Three most dispensed opioids (weak, moderate and strong) according to the number of people receiving at least ≥ 1 dispensing

	Weak Opioids			Moderate Opioids			Strong Opioids		
	Drug Name	**n**	**%**	**Drug Name**	**n**	**%**	**Drug Name**	**n**	**%**
2003	Paracetamol/Codeine	23,522	94.0	Dextropropoxyphene/Paracetamol	73,950	47.9	Morphine Sulphate	5,870	34.8
	Ibuprofen/Codeine	1,474	5.9	Tramadol	37,829	25.4	Fentanyl	4,661	27.6
				Paracetamol/Codeine	18,453	11.7	Oxycodone	2,814	16.7
2004	Paracetamol/Codeine	22,662	95	Dextropropoxyphene/Paracetamol	72,327	47.8	Morphine Sulphate	5,745	33.1
	Ibuprofen/Codeine	1,266	5	Tramadol	37,708	24.9	Fentanyl	4,641	26.7
				Paracetamol/Codeine	30,181	19.9	Oxycodone	3,264	18.8
2005	Paracetamol/Codeine	27,025	96.3	Dextropropoxyphene/Paracetamol	63,815	40.8	Morphine Sulphate	5,954	29.8
	Ibuprofen/Codeine	1,044	3.7	Tramadol	44,183	24.9	Fentanyl	4,926	24.6
				Paracetamol/Codeine	35,804	19.9	Oxycodone	4,297	21.5
2006	Paracetamol/Codeine	39,955	99.7	Paracetamol/Codeine	55,715	40.4	Morphine Sulphate	5,887	24.98
	Ibuprofen/Codeine	128	0.3	Tramadol	52,276	37.9	Buprenorphine	5,731	24.3
				Paracetamol/Dihydrocodeine	21,564	15.7	Fentanyl	5,213	22.1
2007	Paracetamol/Codeine	40,188	100	Paracetamol/Codeine	50,789	42.8	Buprenorphine	7,247	28.4
				Tramadol	49,563	41.8	Morphine Sulphate	5,743	22.5
				Paracetamol/Dihydrocodeine	18,208	15.3	Fentanyl	5,620	21.98
2008	Paracetamol/Codeine	47,987	100	Paracetamol/Codeine	57,635	41.9	Buprenorphine	9,343	30.2
				Tramadol	54,962	39.9	Fentanyl	6,698	21.7
				Paracetamol/Dihydrocodeine	17,615	12.8	Morphine Sulphate	6,558	21.2
2009	Paracetamol/Codeine	49,772	100	Paracetamol/Codeine	57,406	39.9	Buprenorphine	11,297	33.5
				Tramadol	53,246	36.9	Oxycodone	7,101	21.0
				Paracetamol/Tramadol	17,216	12.0	Fentanyl	6,691	20.6
2010	Paracetamol/Codeine	52,356	100	Paracetamol/Codeine	57,288	38.2	Buprenorphine	12,354	34.1
				Tramadol	53,457	35.6	Oxycodone	7,899	21.8
				Paracetamol/Tramadol	23,525	15.7	Morphine Sulphate	7,056	19.5
2011	Paracetamol/Codeine	58,949	100	Paracetamol/Codeine	56,759	37.2	Buprenorphine	13,942	34.1
				Tramadol	52,826	34.6	Oxycodone	8,932	21.9
				Paracetamol/Tramadol	27,556	18.0	Morphine Sulphate	7,649	18.7

Figure 4-11 presents the prevalence rate per 1,000 population receiving an opioid medication on at least one occasion and on more than 3 occasions per year for the GMS eligible population aged ≥55 years. For completeness, the graph presents overall opioid dispensings with and without dextropropoxyphene/paracetamol in the years 2003-2006 (this single agent contributes significantly to the volume of dispensings in these years). Women again received more opioids per 1,000 populations (both ≥1 dispensing and >3 dispensings) for each year included in this analysis.

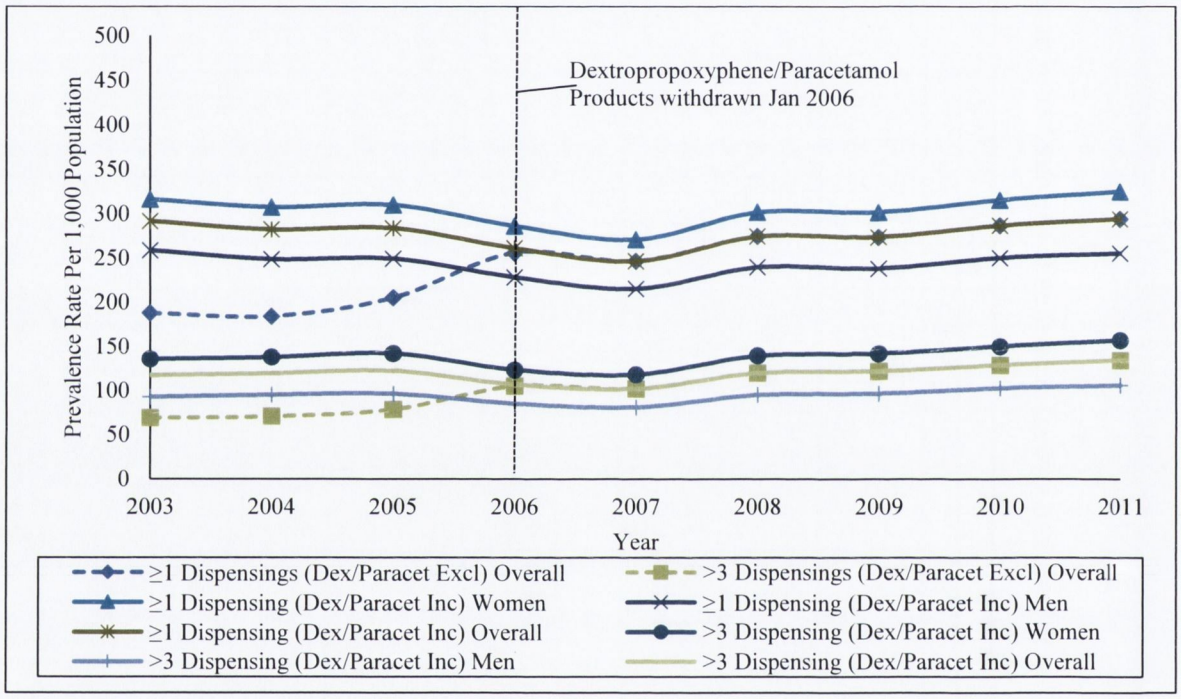


Figure 4-11: Prevalence rate (per 1,000) of opioids dispensed (≥ 1 dispensing & >3 dispensings) to GMS eligible population aged ≥55 years (Dex/Paracet= Dextropropoxyphene/Paracetamol)

Table 4-10 details the prevalence rate per 1,000 population receiving ≥1 dispensing and >3 dispensings of weak, moderate and strong opioids respectively *(Appendix C, Table C-5, provides the population numbers supporting this analysis).* Moderate opioids were the most prevalent class of opioids dispensed between 2003 and 2011. The highest rate was observed in 2003, 251.9 (250.7-253.1), this decreased steadily reaching the lowest point of 184.4 (183.5-185.5) in 2007, which is followed by a gradual increase to 212.0 (211.0-213.0) in 2011, considerably

lower than the highest point in 2003. Conversely, the prevalence rate per 1,000 population increases for both weak and strong opioids, with the exception of a slight reduction for weak opioids in 2007, although this differs only marginally to the prevalence rate in the previous year. Strong opioids have the lowest prevalence rate compared to weak and strong opioids, with the highest prevalence of 55.5 (54.9-56.6) per 1,000 eligible population observed in 2011.

Table 4-10: Prevalence rate (per 1,000) of weak, moderate and strong opioids dispensed (≥1 dispensing & >3 dispensings) to GMS eligible population aged ≥55 years 2009-2011

Year	Weak Opioids		Moderate Opioids		Strong Opioids	
	≥ 1 Dispensing (95% CI)	> 3 Dispensings (95% CI)	≥ 1 Dispensing (95% CI)	>3 Dispensings (95% CI)	≥ 1 Dispensing (95% CI)	>3 Dispensings (95% CI)
2003	49.2 (48.6-49.8)	15.9 (15.6-16.3)	251.9 (250.7-253.1)	91.5 (90.7-92.3)	27.6 (27.1-28.0)	11.5 (11.2-11.8)
2004	46.3 (45.7-46.9)	15.6 (15.3-15.9)	243.2 (242.0-244.4)	93.2 (92.4-94.0)	28.0 (27.5-28.4)	12.6 (12.3-12.9)
2005	52.1 (51.4-52.7)	17.2 (16.8-17.5)	240.5 (239.4-241.7)	93.7 (92.9-94.5)	31.4 (31.0-31.9)	14.3 (14.0-14.6)
2006	69.6 (68.9-70.3)	22.1 (21.7-22.5)	203.9 (202.8)	69.7 (69.0-70.4)	36.2 (35.7-36.7)	17.4 (17.1-17.8)
2007	68.1 (67.5-68.8)	21.9 (21.5-22.3)	184.4 (183.4-185.5)	63.2 (62.6-63.9)	38.8 (38.3-39.3)	19.0 (18.6-19.4)
2008	79.1 (78.4-79.8)	27.5 (27.1-27.9)	205.6 (204.5-206.0)	73.1 (72.5-73.8)	45.5 (44.9-46.0)	24.4 (24.0-24.8)
2009	81.2 (80.5-81.9)	28.2 (27.8-28.7)	204.5 (203.4-205.5)	74.4 (73.7-75.1)	50.1 (49.5-50.7)	27.4 (26.9-27.8)
2010	83.5 (82.8-84.2)	28.9 (28.5-29.4)	212.3 (211.3-213.4)	77.7 (77.0-78.4)	51.6 (51.0-52.2)	29.0 (28.5-29.4)
2011	91.6 (90.8-92.1)	31.5 (31.0-31.9)	212.0 (211.0-213.0)	78.8 (78.2-79.5)	55.5 (54.9-56.6)	31.2 (30.8-31.7)

Figure 4-12 presents the prevalence rate of weak, moderate and strong opioids dispensed according to age-group for the years 2009-2011. These were the most recent years of the database and therefore discount the popularity of dextropropoxyphene/paracetamol formulations. It may be important to consider the number of medications that were considered as moderate opioids for the purposes of this analysis. The approach to categorisation of weak, moderate or strong opioids may have introduced misclassification bias and may explain the difference between the weak and moderate categories prevalence rates. The ≥75 year age-group

accounted for the smallest prevalence rate for moderate opioids but the highest for both weak opioids and strong opioids, with the peak occurring for the latter in 2011.

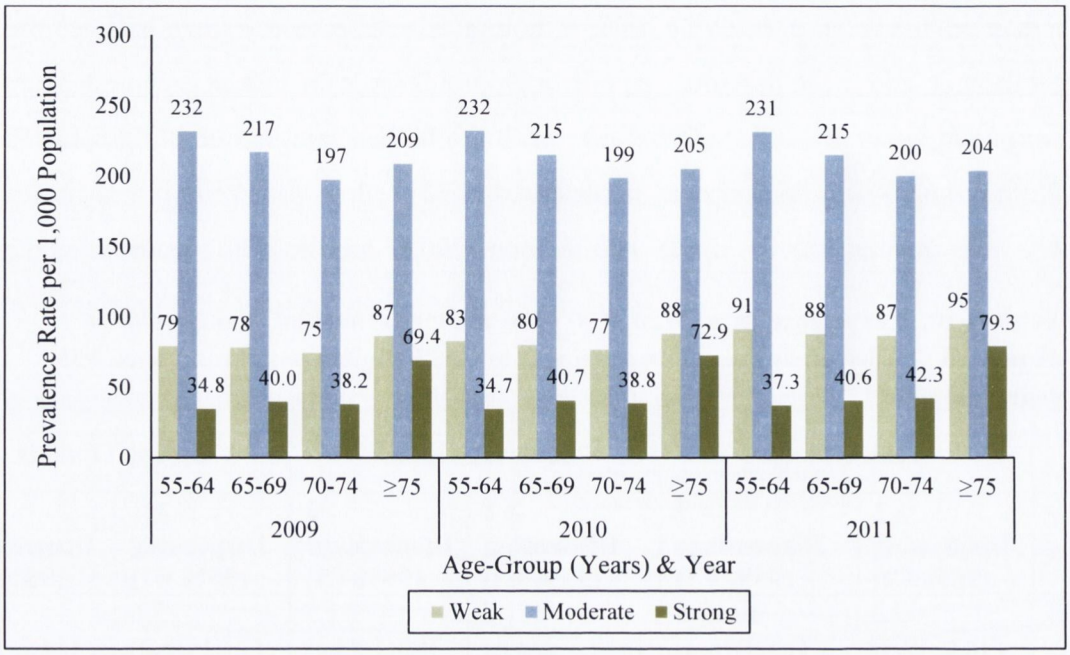


Figure 4-12: Prevalence rate (per 1,000) of weak, moderate and strong opioids dispensed (≥1 dispensing) to GMS eligible population aged ≥55 years according to age-group

Table 4-11 provides an additional description of dispensing patterns according to age-group and gender *(Appendix C, Table C-6, presents the population numbers supporting this analysis)*. When considering moderate opioids dispensed from 2009-2011, the prevalence rate per 1,000 population increased with increasing age for the female population and decreased with increasing age for the male population. The number receiving >3 dispensings of a moderate opioid has increased from 2009 to 2011. The weak and moderate opioids display similar trends, with prevalence rates per 1,000 population increasing with age and a higher rate of dispensing observed amongst women than among men.

Table 4-11: Prevalence rate (per 1,000) of weak, moderate and strong opioids dispensed (≥3 dispensings) to GMS eligible population aged ≥55 years according to age-group and gender 2009-2011

		>3 Dispensings Weak Opioid		>3 Dispensings Moderate Opioid		>3 Dispensings Strong Opioid	
Year	Age-Group	Women (95% CI)	Men (95% CI)	Women (95% CI)	Men (95% CI)	Women (95% CI)	Men (95% CI)
2009	55-64	45.1 (43.6-46.6)	16.7 (15.7-17.6)	81.4 (79.5-83.4)	65.3 (63.5-67.1)	19.8 (18.8-20.8)	18.1 (17.0-19.1)
	65-69	48.8 (46.8-50.9)	19.8 (18.4-21.3)	79.9 (77.4-82.4)	65.2 (62.7-67.8)	23.2 (21.7-24.6)	21.3 (19.8-22.9)
	70-74	49.4 (47.7-51.1)	17.7 (16.6-18.8)	80.3 (78.1-82.5)	54.6 (52.-56.5)	23.2 (22.0-24.4)	16.7 (15.6-17.8)
	≥75	54.3 (53.1-53.5)	22.0 (21.1-23.0)	90.9 (89.-92.5)	59.4 (57.9-61.0)	46.3 (45.2-47.4)	25.9 (24.9-26.9)
2010	55-64	32.3 (31.0-33.5)	17.7 (16.8-18.7)	86.7 (84.7-88.7)	69.9 (68.1-71.8)	21.2 (20.2-22.2)	17.6 (16.7-18.6)
	65-69	33.2 (31.6-34.8)	19.8 (18.3-21.2)	87.6 (85.1-90.2)	69.2 (66.6-71.8)	24.0 (22.6-25.4)	21.3 (19.8-22.8)
	70-74	50.4 (48.3-52.1)	17.9 (16.5-19.0)	81.6 (79.4-83.8)	57.1 (55.2-59.1)	25.1 (23.8-26.3)	17.2 (16.1-18.3)
	≥75	55.5 (54.3-56.7)	22.6 (21.6-23.5)	93.4 (91.8-94.9)	60.9 (59.4-62.5)	50.5 (49.4-51.7)	27.3 (26.2-28.3)
2011	55-64	35.3 (34.1-36.6)	19.2 (18.2-20.1)	87.9 (85.9-89.8)	71.7 (69.9-73.6)	22.1 (21.1-23.1)	19.1 (18.1-20.1)
	65-69	37.0 (35.5-38.6)	22.0 (20.5-23.5)	87.1 (84.6-89.6)	70.1 (67.6-72.7)	23.3 (22.0-24.7)	22.1 (20.7-23.6)
	70-74	37.8 (36.3-39.4)	20.4 (19.2-21.6)	83.3 (81.1-85.5)	59.6 (57.6-61.6)	26.6 25.3-27.9)	19.1 (17.9-20.2)
	≥75	43.5 (42.5-44.6)	26.5 (25.5-27.5)	94.9 (93.4-96.4)	60.5 (59.0-62.0)	55.9 (54.7-57.1)	29.6 (28.5-30.7)

Transdermal formulations containing strong opioids may be seen as a more favourable method of administration than oral formulations, as they may precipitate less adverse effects associated with first pass metabolism and also enhance patient compliance (these medications require rotation every 72 hours or once weekly) (124). *Figure 4-13* presents the prevalence of dispensings for strong opioid patches per 1,000 population for those individuals receiving >3 prescriptions each year by age-group between 2009 and 2011. Prevalence of strong opioid patches increased across both age-groups each year, with the largest increase observed in the oldest age group. Prevalence of dispensings of transdermal patches containing a strong opioid was considerably higher in the oldest population amongst women.

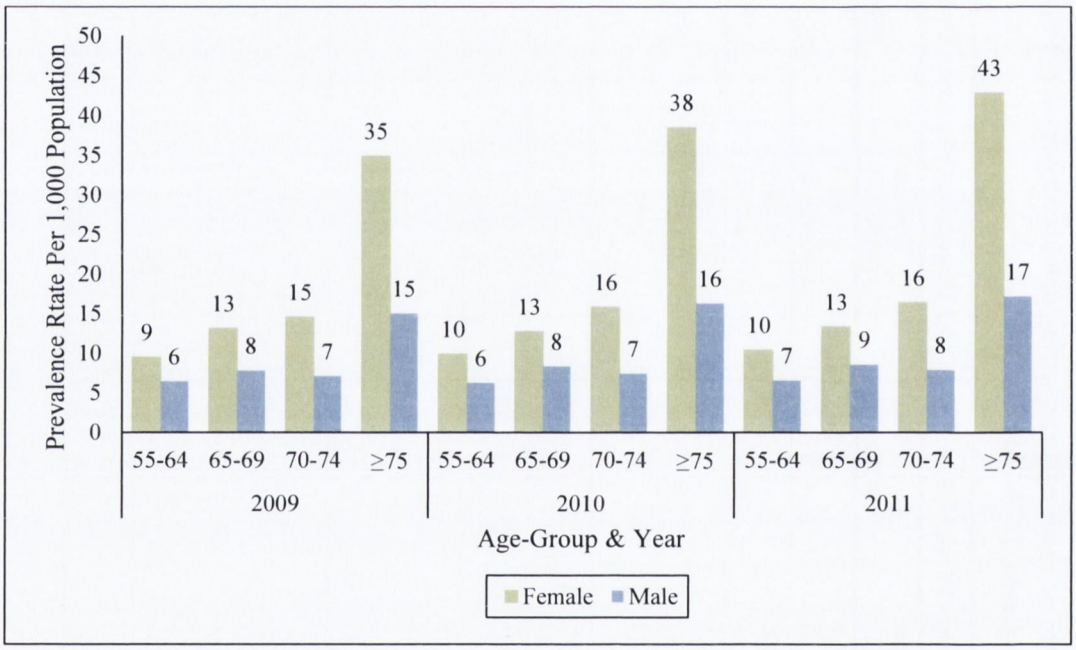


Figure 4-13: Prevalence rate (per 1,000) of strong opioid patches according to age-group for the years 2009-2011 (>3 dispensings)

4.4.5.1. Opioid Dispensing Patterns

The pattern of dispensings of opioid medications was examined in greater detail by determining whether an individual was dispensed a weak, moderate or strong opioid for a period of 1-7 months or ≥8 months. This allocation of months is based on the hypothesis that if an individual is dispensed medication for 8 months of a calendar year, at one point, the individual would have received that medication for 2 consecutive months; this is presented visually in *Figure 4-14*. However, this is an

arbitrary instrument to indicate duration of use of the medication since the quantity received upon each dispensing was not examined.

Jan	Feb	Mar	Apr	May	June	July	Aug	Sep	Oct	Nov	Dec
Disp1		Disp2		Disp3	Disp4	Disp5		Disp6		Disp7	Disp8

Figure 4-14: Demonstration of dispensing patterns for those dispensed medication for ≥8 months

Table 4-12 outlines the number of months a weak, moderate or strong opioid was dispensed per 1,000 population *(Appendix C, Table C-7, provides the population numbers supporting this analysis).* The prevalence per 1,000 population who were dispensed a weak, moderate or strong opioid respectively for 1-7 months was similar for each class when considering the prevalence rates on a yearly basis. There was an annual increase of prevalence per 1,000 who were dispensed a weak, moderate or strong opioid for an 8-12 month period, with a corresponding decrease in those who were dispensed these medications on a 1-7 month basis. The prevalence rate per 1,000 individuals dispensed a strong opioid for 8-12 months peaks in 2011 at 267.4 (262.6-272.2) per 1,000 receiving a strong opioid medication. This is a higher prevalence than weak or moderate opioids, 187.5 (184.2-190.8) and 92.5 (190.3-194.7) respectively, and may highlight a movement towards long-term use of strong opioids in the management of chronic malignant and chronic non-malignant pain conditions, as opposed to moderate and weak opioids, which are primarily prescribed for acute pain management.

Table 4-12: Number of months dispensed a weak, moderate or strong opioid analgesic dispensed (per 1,000 population receiving that class of opioid)

Year	Weak Opioid		Moderate Opioid		Strong Opioid	
	1-7 Months (95% CI)	8-12 Months (95% CI)	1-7 Months (95% CI)	8-12 Months (95% CI)	1-7 Months (95% CI)	8-12 Months (95% CI)
2003	846.2 (841.7-854.8)	153.8 (149.2-158.3)	836.8 (834-.8-838.9)	163.2 (161.1-165.2)	867.4 (861.7-873.1)	132.6 (126.9-138.3)
2004	842.8 (838.1-847.5)	157.2 (152.5-161.9)	825.6 (823.5-827.8)	174.4 (172.2-176.5)	846.5 (840.5-852.4)	153.5 (147.6-159.5)
2005	835.7 (831.2-840.1)	164.3 (159.9-168.8)	816.8 (814.7-819.0)	183.2 (181.0-185.3)	843.8 (838.2-849.5)	156.2 (150.6-161.8)
2006	848.5 (844.9-852.1)	151.5 (147.8-155.1)	848.6 (846.5-850.7)	151.4 (149.3-153.5)	820.8 (815.0-825.8)	179.6 (174.2-185.0)
2007	877.2 (873.9-880.5)	122.8 (119.5-126.1)	865.2 (863.0-867.3)	134.8 (132.7-137.0)	841.8 (836.9-846.7)	158.2 (153.3-163.1)
2008	818.4 (814.8-822.4)	181.6 (178.0-185.2)	824.8 (822.6-827.0)	175.2 (173.4-177.4)	772.6 (767.4-777.7)	227.4 (222.3-232.6)
2009	807.7 (804.4-811.3)	192.3 (188.7-196.0)	817.9 (815.7-820.1)	182.1 (179.9-184.3)	754.6 (749.9-759.6)	245.4 (240.3-250.4)
2010	815.8 (812.4-819.3)	184.2 (180.1-187.6)	814.1 (812.0-816.3)	185.9 (183.7-188.0)	735.9 (730.9-740.9)	264.1 (259.1-269.1)
2011	812.5 (809.2-818.8)	187.5 (184.2-190.8)	807.5 (805.3-809.7)	192.5 (190.3-194.7)	732.6 (727.8-737.4)	267.4 (262.6-272.2)

4.4.6. Adjuvant Medications

According to *Table 4-13*, adjuvant medications, similar to the other classes of medications, increased gradually over the 9 year period. Pregabalin appears in position 38 and Amitriptyline in position 65 of the most prescribed medications under the GMS scheme in 2011 (233, 344). In this analysis, there was a gradual reduction in prevalence of amitriptyline and an increase in dispensing of pregabalin and gabapentin, most notably from 2008 onwards. Pregabalin was first licensed for use in Ireland in 2004, which may account for the slow rise in prescribing trends following this date. Dispensing of duloxetine has also increased over the period of time exceeding the dispensing of gabapentin on the first occasion in 2011.

Table 4-13: most prevalent adjuvant medications according to the number of GMS eligible patients aged ≥55 years receiving ≥1 dispensing

	Adjuvant Medications		
	Drug Name	**No. of GMS Eligible Patients Aged ≥55 Years receiving ≥1 Dispensing**	**% of all Drugs in this Class**
2003	Amitriptyline	11,361	45.5
	Gabapentin	7,294	29.2
	Carbamazepine	6,335	25.4
2004	Amitriptyline	11,393	44.0
	Gabapentin	8,536	33.0
	Carbamazepine	5,979	23.1
2005	Amitriptyline	12,413	44.2
	Gabapentin	8,862	31.5
	Carbamazepine	5,940	29.1
2006	Amitriptyline	13,228	38.6
	Gabapentin	8,584	27.0
	Carbamazepine	5,841	17
2007	Amitriptyline	13,360	32.5
	Pregabalin	11,445	27.2
	Gabapentin	8,132	19.3
2008	Pregabalin	17,279	34.3
	Amitriptyline	15,073	29.9
	Gabapentin	8,441	16.7
2009	Pregabalin	23,672	20.9
	Amitriptyline	15,733	27.2
	Gabapentin	8,054	13.9
2010	Pregabalin	29,539	43.5
	Amitriptyline	18,558	27.3
	Gabapentin	7,836	11.5
2011	Pregabalin	35,838	45.7
	Amitriptyline	21,209	27
	Duloxetine	7,897	10.1

Figure 4-15 presents the prevalence rate of adjuvant medications per 1,000 populations receiving ≥1 dispensing and receiving >3 dispensings for the years 2003-2011. The highest prevalence rate occurred in 2011, with 113.5 (112.7-114.3) per 1,000 receiving an adjuvant medication on at least one occasion. The difference in prevalence rate per 1,000 receiving >3 dispensings and ≥ 1 dispensing was the least when considering all other classes of analgesics included in this study, with 74.0 (73.4-74.7) per 1,000 receiving >3 dispensings of this medication class in 2011. This may be associated with the necessity to titrate the doses of these medications gradually to achieve therapeutic efficacy and to taper the dose of the medication upon cessation.

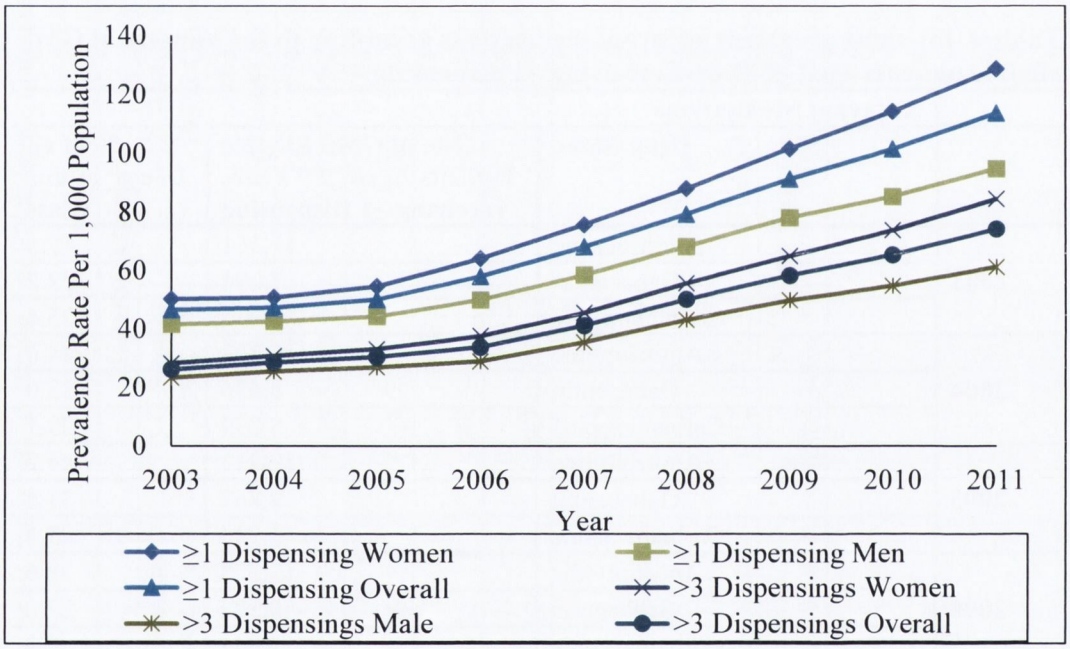


Figure 4-15: Prevalence rate (per 1,000) of adjuvant medication dispensed (≥ 1 dispensing & >3 dispensings) to GMS eligible population aged ≥55 years

Figure 4-16 demonstrates the prevalence rate per 1,000 population of those receiving >3 dispensings of an adjuvant medication, with the prevalence rate for this age-group increasing from 2009 to 2011; dispensings are consistently higher amongst women in each of the 3 years. Prevalence rates decreased with increasing age; those aged ≥75 years consistently had the lowest prevalence rate for these medications for women. The lowest rate of dispensing for men was observed in the 70-74 years age-group for the years 2009-2011 inclusive.

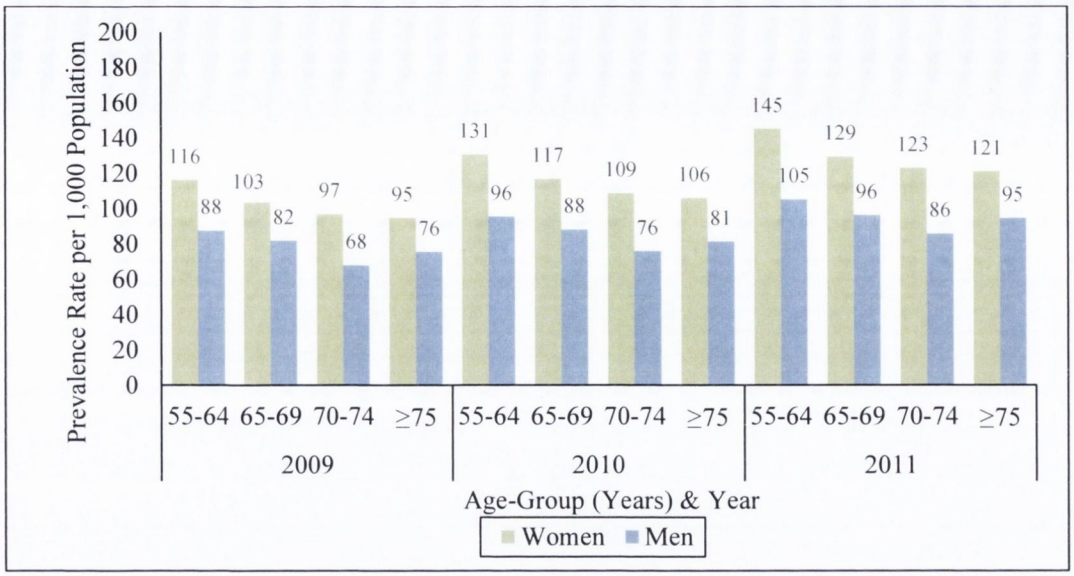


Figure 4-16: Prevalence rate (per 1,000) of adjuvant medication dispensed (>3 dispensings) to GMS eligible population aged ≥55 years according to age-group and gender

4.4.7. Recurrent Use of Analgesics and Adjuvant Medications

Figure 4-17 presents the prevalence rate per 1,000 population for those individuals in receipt of >3 dispensings of the various classes of analgesics for the three most recent years of the database 2009-2011. Presentation of the data in this manner seeks to place individuals on a step of the WHO Analgesic Ladder. Non-opioids (Step 1 WHO Analgesic Ladder) were the most prevalent class of medication dispensed for 2010 and 2011, with more systemic NSAIDs dispensed in 2009. The weak and moderate opioids introduced at Step 2 of the ladder had a lower prevalence than those agents recommended at Step 1 of the ladder, such as non-opioids and non-selective NSAIDs (but not selective NSAIDs). It is notable that dispensings of strong opioids were more prevalent for all three years presented here than selective NSAIDs, which were the least dispensed class for these years.

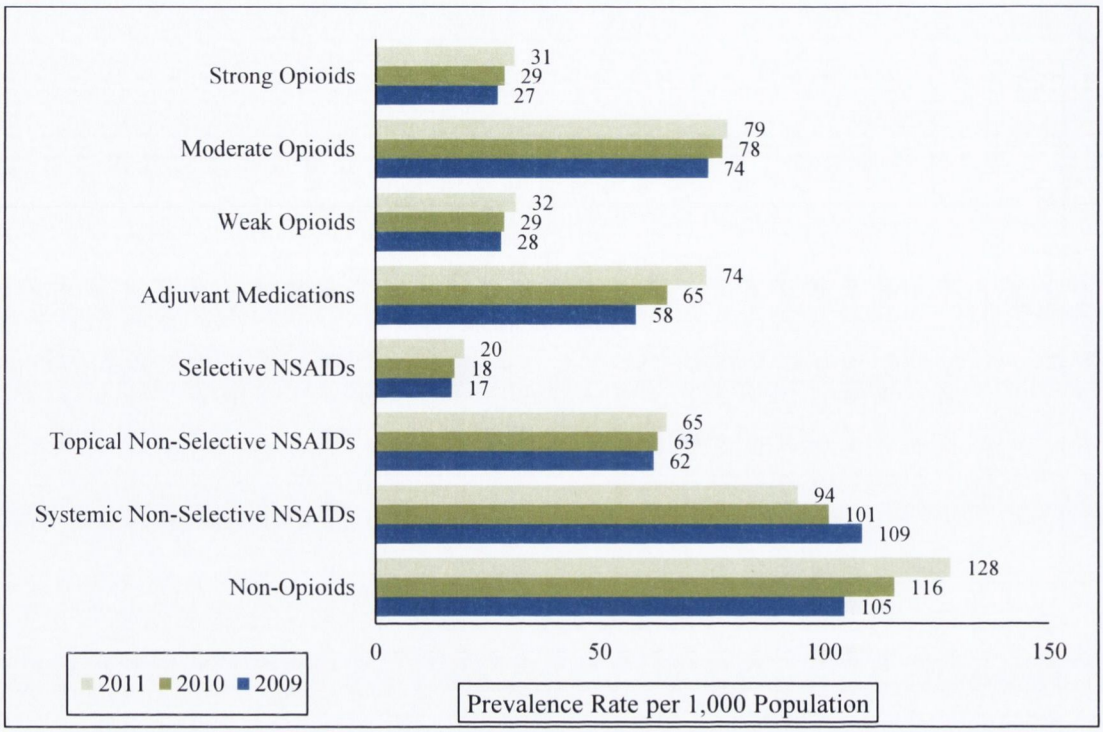


Figure 4-17: Prevalence rate (per 1,000) of analgesic and adjuvant medications dispensed (>3 dispensings) to GMS eligible population aged ≥55 years

4.4.8. Concurrent Prescriptions

Co-prescriptions of laxatives or sedating agents with weak, moderate and strong opioids analgesics were considered for the years 2006-2011, with the years 2003-2005 omitted in order to accommodate the contribution of dextropropoxyphene/paracetamol dispensings to opioids during the latter period. The contribution of this single agent to the dispensing of opioids during this period is best appreciated by the reduction in dispensings of opioids in 2007 (*Figure 4-11*), which may be attributed to the withdrawal of this agent from the market in 2006. In order to assess concurrency of laxatives and sedating agents accurately, it was decided that analysis may be most meaningful if it was conducted over a series of years where there was little deviation in the availability of opioids on the market i.e. no withdrawal of a significant medication. For this reason, the years 2006-2011 were included in the analysis for concurrency.

4.4.8.1 Sedating Agents and Opioid Analgesics

Figure 4-18 presents the prevalence rate of sedating agents per 1,000 population dispensed in the same calendar month as a weak, moderate or strong opioid (≥1 dispensing) *(Appendix C, Table C-8, provides the population numbers supporting this analysis).* The prevalence rate of concurrent dispensing of sedating agents and strong opioids, remained relatively constant for the 6 years considered in this analysis and higher than all other rates of concurrency.

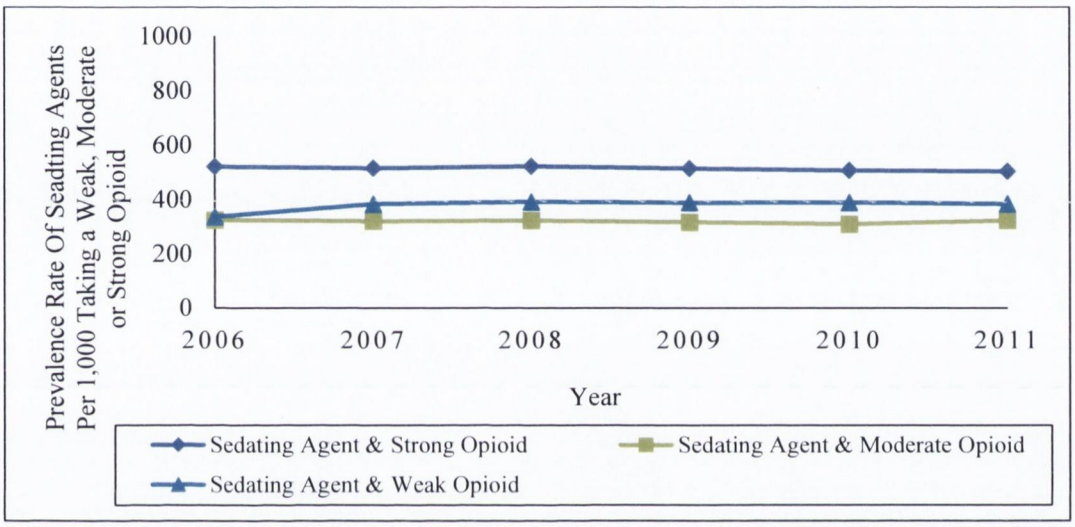


Figure 4-18: Prevalence rate of sedating agents per 1,000 population dispensed weak, moderate and strong opioids respectively (≥1 concurrent dispensing)

Table 4-14 presents the prevalence rate of individuals taking a sedating agent per 1,000 population who were dispensed a weak, moderate or strong opioid *(Appendix, Table C-9, provides the population numbers supporting this analysis).* Those in receipt of ≥1 dispensing of a strong opioid consistently received a higher prevalence of dispensings of sedating agents in the same month compared to weak or moderate opioids. The rate of concurrent dispensing remained consistently high for all years included in the analysis. The prevalence rate ranged from the lowest point of 503.0 (497.7-508.5) individual dispensed a sedating agents per 1,000 individuals dispensed ≥1 strong opioid in 2011 to 521.0 (513.9-528.1) individuals dispensed a sedating agent per 1,000 individuals dispensed ≥1 strong opioid in 2006.

The rate of concurrent dispensing of sedating agents per 1,000 population receiving a weak opioid (≥1 concurrent dispensing) was higher than that of

moderate opioids on a yearly basis. However, when recurrent prescribing is considered (>3 dispensings), those receiving a sedating agent with a weak opioids remained approximately the same as those receiving ≥1 dispensings. The rate of concurrent dispensings for moderate and strong opioids was approximately one third of those receiving at least one concurrent dispensing.

Table 4-14: Prevalence rate of sedating agents per 1,000 population dispensed weak, moderate and strong opioids respectively (≥ 1 concurrent dispensing & >3 concurrent dispensings)

	Weak Opioids		Moderate Opioids		Strong Opioids	
Year	≥ 1 Concurrent Dispensing (95% CI)	> 3 Concurrent Dispensings (95% CI)	≥ 1 Concurrent Dispensing (95% CI)	>3 Concurrent Dispensings (95% CI)	≥ 1 Concurrent Dispensing (95% CI)	>3 Concurrent Dispensings (95% CI)
2006	336.0 (331.2-340.8)	292.9 (284.6-301.1)	323.9 (321.0-326.7)	244.9 (240.4-249.3)	521.0 (513.9-528.1)	310.2 (300.7-319.6)
2007	382.9 (378.0-387.9)	329.1 (320.7-337.5)	319.9 (317.0-322.8)	231.8 (227.3-236.2)	515.2 (508.4-521.9)	304.7 (295.8-313.6)
2008	391.0 (386.4-395.5)	347.8 (340.2-355.3)	322.1 (319.4-324.8)	243.8 (239.6-248.0)	522.1 (516.0-528.3)	319.7 (311.8-327.5)
2009	388.2 (383.7-392.7)	355.5 (348.0-363.0)	315.6 (313.0-318.3)	232.9 (228.9-236.9)	514.0 (508.1-519.8)	339.8 (332.3-347.3)
2010	388.7 (384.3-393.0)	350.3 (343.1-357.5)	308.6 (306.0-311.2)	225.3 (221.4-229.1)	506.9 (501.2-512.6)	327.4 (320.3-334.7)
2011	383.6 (379.5-387.7)	351.6 (344.7-358.4)	322.2 (319.7-324.8)	237.1 (233.2-240.9)	503.0 (497.7-508.5)	324.6 (317.9-331.4)

Concurrent administration of sedating agents with an opioid analgesic may be particularly problematic for elderly populations who may be more likely to experience outcomes such as falls or cognitive impairment. *Figure 4-19* outlines the rate of concurrent prescribing of sedating agents per 1,000 population who were taking a strong opioid according to age-group and gender. The rate of concurrent dispensings remains consistent amongst all age-groups and genders in the years 2006-2011, with minor fluctuation observed within age-groups in these years. Women in the 55-64 and 65-74 years age-group consistently had the highest rate of prevalence of concurrent dispensings, while women in the ≥75 year age-group had the lowest. By comparison, the highest prevalence of concurrent dispensing for men was observed in the 65-69 and 70-74 years age-groups, and similar to their female counterparts, was lowest in the ≥75 years age-group.

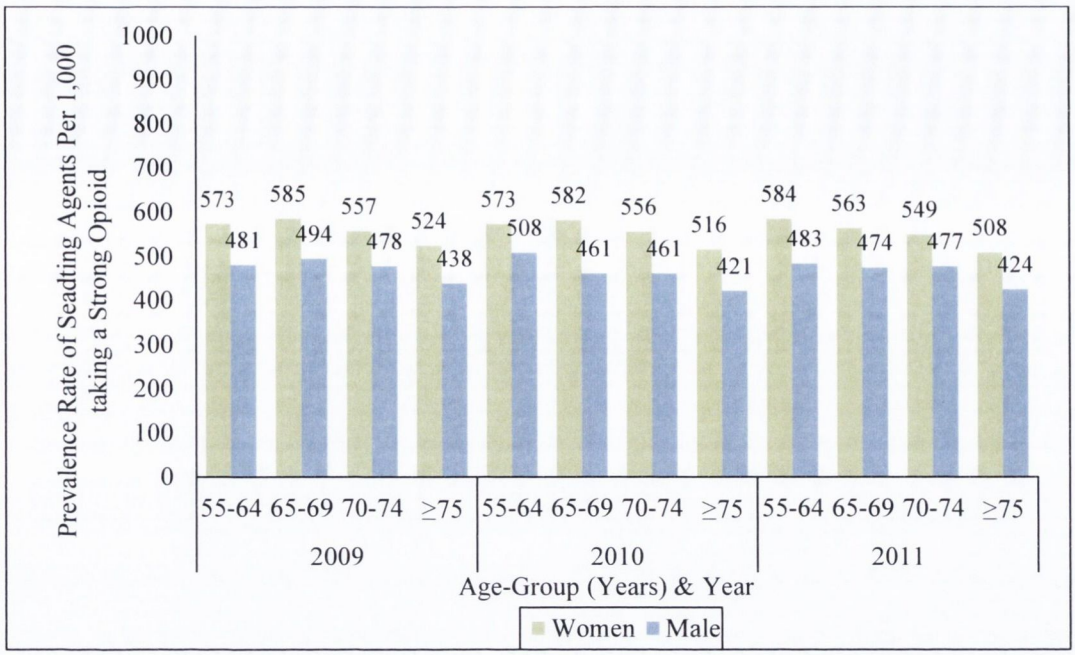


Figure 4-19: Prevalence rate of sedating agents per 1,000 population dispensed a strong opioid (≥1 concurrent dispensing)

4.4.8.2. Laxatives and Opioids

Figure 4-20 presents the prevalence rate of laxatives per 1,000 population dispensed in the same month as a weak, moderate or strong opioid (≥ 1 dispensing). Concurrency of laxatives with strong opioids was higher than that of either weak opioids or moderate opioids and increases from 2009 onwards.

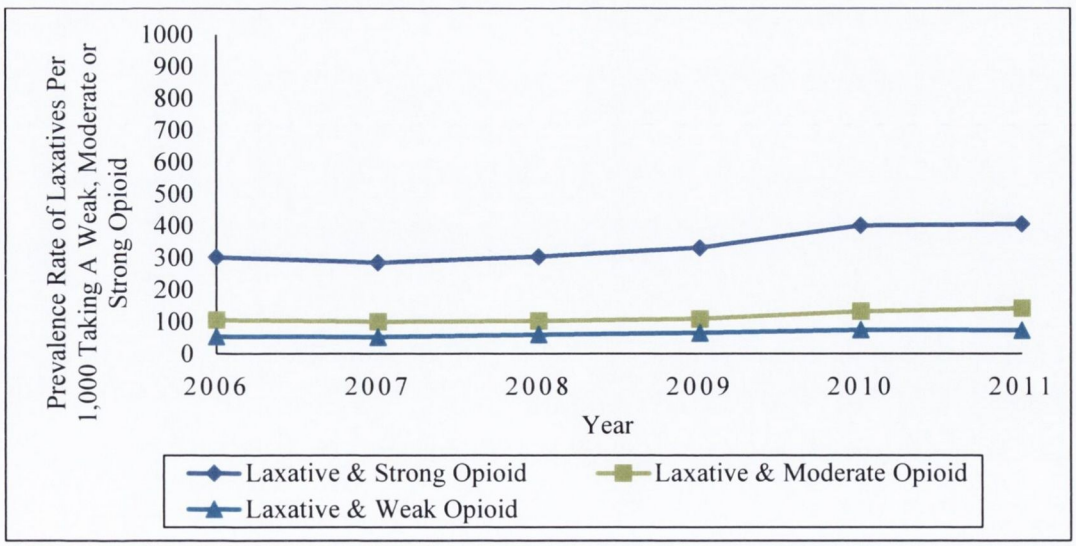


Figure 4-20: Prevalence rate of laxatives per 1,000 population dispensed weak, moderate and strong opioids respectively (≥1 concurrent dispensing)

Table 4-15 presents the prevalence rate of individuals taking a laxative per 1,000 population dispensed a weak, moderate or strong opioid (≥1 concurrent dispensing). There was an increase in concurrent dispensing of strong opioids and laxatives between 2009 and 2010 (both ≥ 1 dispensing and >3 dispensings). When this was investigated further there was found to be a notable increase in the dispensing of macrogol laxatives in this year, a larger increase than between any other year. The HSE-PCRS Annual Report 2008 does not include macrogol in the most frequently dispensed medications list, the agent appears in the report in 2009 and frequency of dispensing increased from 2010 onwards.

The highest rate of concurrent dispensings was that of strong opioids and laxatives. Indeed, the prevalence of those dispensed >3 concurrent laxative and strong opioids prescriptions exceeded the prevalence of those in receipt of at ≥1 concurrent dispensing of a laxative with a weak or moderate opioid. However, approximately 85% of those receiving >3 concurrent dispensings of a strong opioid did not receive a concurrent dispensing of a laxative in the same month.

Table 4-15: Prevalence rate of laxatives per 1,000 population taking weak, moderate and strong opioids respectively (≥ 1 concurrent dispensing & >3 concurrent dispensings)

	Weak Opioids		Moderate Opioids		Strong Opioids	
Year	**≥ 1 Concurrent Dispensing (95% CI)**	**> 3 Concurrent Dispensings (95% CI)**	**≥ 1 Concurrent Dispensing (95% CI)**	**>3 Concurrent Dispensings (95% CI)**	**≥ 1 Concurrent Dispensing (95% CI)**	**>3 Concurrent Dispensings (95% CI)**
2006	53.4 (51.1-55.7)	27.7 (24.8-30.7)	105.3 (103.4-107.1)	35.8 (33.8-37.7)	301.4 (294.9-307.9)	105.1 (98.8-111.3)
2007	51.5 (49.3-53.8)	25.7 (22.8-28.5)	100.4 (98.5-102.2)	30.8 (28.9-32.6)	284.7 (278.6-290.8)	93.0 (87.4-98.6)
2008	59.0 (56.8-61.3)	30.9 (28.2-33.7)	102.1 (100.4-103.9)	37.0 (35.2-38.8)	302.9 (297.2-308.5)	107.9 (102.7-113.1)
2009	64.7 (62.4-66.9)	33.2 (30.4-36.0)	109.0 (207.2-110.7)	35.4 (33.6-37.1)	330.9 (325.3-336.4)	116.7 (111.6-121.8)
2010	74.2 (71.9-76.5)	42.8 (30.4-36.0)	132.4 (130.5-134.3)	46.5 (44.6-48.5)	400.5 (395.0-406.1)	169.4 (163.7-175.1)
2011	72.6 (70.4-74.8)	43.7 (40.7-46.6)	141.1 (139.2-143.1)	51.4 (49.4-53.4)	404.6 (399.3-409.9)	173.0 (167.6-178.5)

As presented in *Figure 4-21*, those aged ≥75 years consistently received the highest rate of concurrent dispensings of strong opioids and laxatives in comparison to all other age-groups. Men consistently had a higher rate of concurrent dispensing

in comparison to their female counterparts across all age-groups and years. This is in direct contrast to the higher rate of concurrency observed amongst women in the concurrent sedating agents and strong opioid analysis.

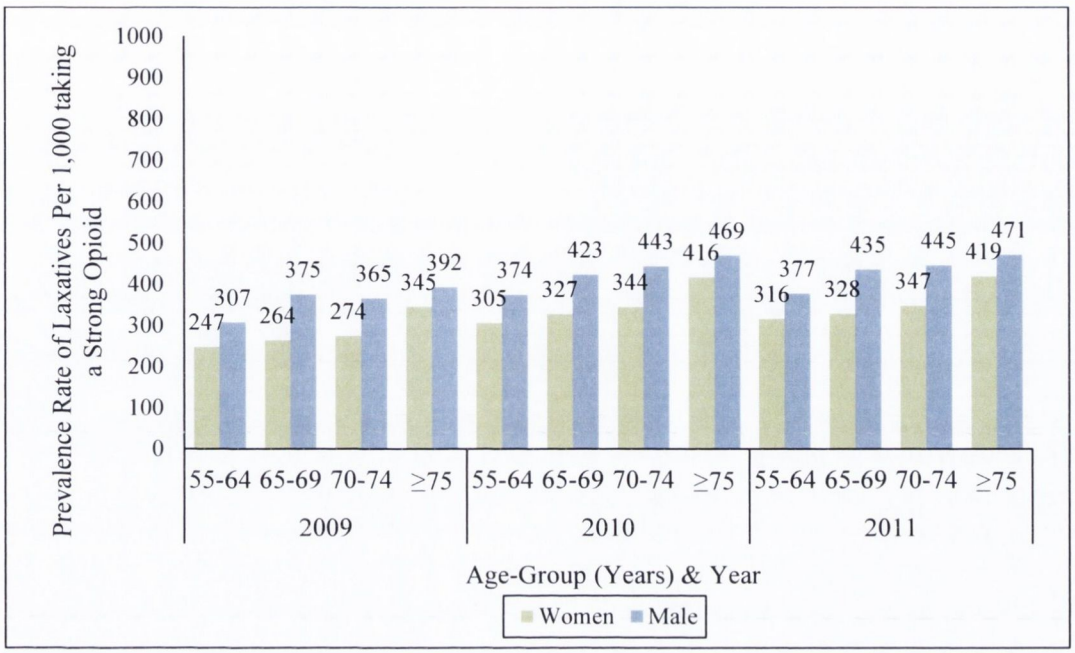


Figure 4-21: Prevalence rate of laxatives per 1,000 population dispensed a strong opioid (≥1 concurrent dispensing)

4.5. Discussion

This study aimed to provide an overview of analgesic use in Ireland amongst GMS eligible patients aged ≥55 years for the period 2003-2011 by describing the prevalence of dispensings of non-opioids, non-selective NSAIDs, selective NSAIDs, and weak, moderate and strong opioids. The prevalence of adjuvant agent dispensings and concurrent dispensings of sedating agents and laxatives with weak, moderate and strong opioids was also presented.

There was a modest increase in dispensings of analgesics in the nine year period, 2003-2011, from 626.0 to 668.8 per 1,000 population, with an increasing proportion of individuals receiving multiple analgesics, characterised by the receipt of different ATC codes within the year. The increase in analgesic use over time appears to be driven by the increase in dispensing of specific analgesic classes such

as non-opioids, opioids and non-selective NSAIDs, as the prevalence of dispensings of selective NSAIDs has decreased considerably since 2003.

Moderate opioid analgesics had a higher prevalence of dispensing (for both ≥1 dispensing and >3 dispensings) than weak or strong opioids but had a lower prevalence rate than both systematic non-selective NSAIDs and non-opioids. The greater prevalence of recurrent dispensings of systemic non-selective NSAIDs and non-opioids may highlight greater persistence in use of these agents for chronic pain conditions and may also be indicative of a reluctance amongst prescribers to reissue prescriptions for opioid containing formulations (333, 345).

Dispensing rates of analgesics within specific age-groups may also be reflective of the safety and appropriateness concerns with the use of specific medications in certain populations. For instance, systemic selective and non-selective NSAIDs should be used with caution amongst the ageing and elderly due to the cardiovascular concerns associated with both, and gastrointestinal effects associated with the latter. It is not surprising therefore that these classes of medications had the lowest prevalence of recurrent dispensings (>3 dispensings) in 2011; selective NSAIDs had a prevalence rate of 20.0(19.6-20.3) per 1,000 population in the ≥75 year age-group, while systemic nonselective had a prevalence of 94.2 (89.3-94.9) per 1,000 population compared to prevalence rate of 128.1 (127.2-128.9) for non-opioids and 134.5 (133.6-135.3) for opioid analgesics.

Adjuvant agents were placed alongside analgesic medications, as the WHO Analgesic Ladder proposes that these agents may also be used to provide pain relief. However, direct comparisons of use between analgesics and adjuvant agents is somewhat tenuous due to the lack of clinical information available in the HSE-PCRS database. Carbamazepine, gabapentin and pregabalin have an indication for seizure activity. If used for the management of epilepsy, it would be dispensed under the Long Term Illness (LTI) Scheme, thus, inclusion of these agents in the analysis is therefore appropriate. The prevalence rates for recurrent dispensings of adjunct medications exceed those of weak and strong opioids and selective NSAID and may reflect the necessity to reduce doses of these adjunct medications gradually, prior to cessation of therapy (128).

Worldwide prevalence of prescription opioid use has tripled since 1991 (346). The greatest increase in use has occurred the US and Canada (347, 348).

Fluctuations in the dispensing of opioids are observed since 2003 in this database, with an initial decrease in the prevalence of dispensings of opioids with the removal of co-proxamol from the market in 2006. Upon alteration of the licensing status of this medication, it would appear that there is a simultaneous increase in dispensings of paracetamol/codeine formulations. A similar phenomenon was observed in the UK following the withdrawal of co-proxamol from the market in 2004, when the number of prescriptions for the formulation decreased from 835 million to 121 million in 2007, with a concurrent increase in prescriptions for co-codamaol and paracetamol (349). The emerging popularity of other opioid containing formulations in response to these market withdrawals, similar to that identified in this analysis, was reported in England and Wales, with an increase in prescribing of paracetamol (+10%), codeine (+23%) and tramadol (+19%) during the years 2005-2010 (350).

Paracetamol/codeine containing formulations (both <20 mg codeine (weak) and ≥20 mg (moderate) codeine) are the most prevalent form of opioid analgesic dispensed in this population, followed by tramadol and tramadol/paracetamol formulations; these agents exceed the prevalence rates of dispensing of any of the strong opioids. This is similar to dispensing trends within European countries; a recent study of prescribing for a Scottish population (n=311,881) also identified codeine containing formulations as the most commonly dispensed opioid analgesic, followed by tramadol and dihydrocodeine formulations (351). The increasing use of tramadol containing analgesics reported in this study, second to paracetamol/codeine formulations, mirrors the trend identified by Ruscitto et al, who describe this as a 'tramadol epidemic' in Scotland, however, the prevalence of dispensings in this country does not indicate dramatically accelerated use of these tramadol analgesics at present (351).

The relatively small prevalence of dispensings of weak opioids (<20 mg codeine) detected in this study in comparison to moderate opioids may be associated with categorisation of the medication; a number of the agents included in this class are composed of 500 mg paracetamol and 8 or 12 mg codeine, since these agents are available as non-prescription medications and as such may be prescribed for mild pain. Individuals receiving a once-off prescription of an opioid

may be treating an acute pain condition where a moderate opioid may be more appropriate in the short-term.

While the prevalence of dispensing of strong opioids increased in the nine year period under investigation, this increase in dispensings of strong opioids does not match that of the increase in use of strong opioids in the USA and Canada, which has contributed to morbidity and mortality rates that are associated with use this class of medications (155, 244). However, when one considers dispensing per 1,000 population for 1-7 and 8-12 month periods, there appears to be a greater persistence amongst those in receipt of strong opioids than moderate or weak opioids, with a higher prevalence rate than those receiving these agents for 8-12 months, indicating that those who are initially started on strong opioids tend to use this class of opioid for prolonged periods.

The emerging trends in the type of strong opioids dispensed may be reflective of the variety of formulations available on the market in recent years. Dispensings of morphine sulphate have decreased since 2006 in comparison to buprenorphine, fentanyl and oxycodone. The diminishing use of morphine sulphate has been reported in Ireland since 2002, as pharmacies were seen to reduce quantities purchased from wholesalers over the course of a year (-11%), however, there was an increase in the purchasing of fentanyl (+25%) (346). The prevalence of morphine prescribing varies considerably between countries. An Australian study reported a decline from 38.3 to 30.7 per 1,000 population between 2003 and 2008, while a UK study of prescribing of strong opioids, by primary care physicians for the years 2000-2010, identified morphine as the most commonly prescribed strong opioid, followed by fentanyl, oxycodone and buprenorphine (352, 353). Amongst those dispensed strong opioids in this study, there is an increasing use of transdermal delivery systems with older age groups. For instance, in 2011, 79.3 individuals per 1,000 population aged ≥55 years received >3 dispensings of a strong opioid (either oral or transdermal), with 30 individuals per 1,000 population dispensed a transdermal formulation. The popularity of transdermal formulations for elderly populations may be due to several reasons: the ease of administration and subsequent increased compliance associated with this dosage form, and the diminution in adverse effects owing to the avoidance of first pass metabolism (124).

These pharmacokinetic and pharmacodynamic attributes may lead to less adverse outcomes associated with this class of medication.

Clinical practice guidelines recommend that laxatives should be concurrently prescribed with moderate and strong opioids to prevent constipation. Conversely, medications with a CNS depressant effect, such as anxiolytics and hypnotics, should be used cautiously due to exacerbation of the sedating and depressive respiratory effects of opioids (311, 354). Estimates of concurrent dispensings of laxatives and sedating agents with opioids in the literature provide a wide range of values of prevalence, depending on the population studied, the data source or the types of opioid medications included in the analysis. This study identified a higher prevalence of concurrent dispensing of sedating agents with moderate and strong opioids, rather than laxatives, for both ≥1 dispensing and >3 dispensings. Four hundred patients per 1,000 population dispensed a strong opioid were also dispensed a laxative; this is considerably higher than 1% concurrent use identified in a study of the Quebec Public Prescription Drug Insurance Plan, but similar to the 55% concurrency reported from a study of Medicaid patients (173, 335). Approximately 500 patients per 1,000 population dispensed a strong opioid were also dispensed a sedating agent (≥1 dispensing) and approximately 300 patients per 1,000 population received >3 concurrent dispensings. This is similar to that reported by the CONsortium to Study Opioid Risks and Trends (CONSORT) study, which reported that 30% of long-term opioid users also used sedative hypnotics, while Nielsen et al reported a 30% concurrency rate for buprenorphine and benzodiazepines (355, 356). Finally, the prevalence of concurrent dispensings of sedating agents decreased but that of laxatives increased with age, perhaps highlighting the increased vigilance associated with the use of strong opioids in older populations amongst prescribing physicians.

The prevalence of analgesic dispensings and trends associated with age and gender reported in this study may be associated with features of healthcare utilisation in these populations. In Ireland, increasing age has been demonstrated to be associated with increased use of healthcare services, with those aged ≥ 80 years attending the GP on average 5.7 times per year in comparison to 3.6 times for those aged 55-59 years. Those with poor self-rated physical health, ≥3 chronic diseases and in possession of a medical card are also more likely to utilise health

services (357). This demonstrates that there are factors in addition to age and gender contributing towards healthcare use and, consequently, dispensing of prescription medications. These factors in combination with factors influencing the nature and extent of analgesic use merit further investigation that is beyond the scope of this particular study.

Recent measures to reduce expenditure on health by the Department of Health and the HSE may also contribute to altered prescribing and dispensing patterns. The introduction of a co-payment for prescription medications to the GMS scheme may contribute to changes in the use of medication by patients. Studies undertaken in Ireland, following the introduction of this prescription levy, have demonstrated that the use of prescription medication may decrease, depending on the magnitude of the co-payment and the perceived necessity of the medication (358, 359). Furthermore, following review of the GMS scheme, the HSE has rescinded eligibility of a number of GMS patients for subsidised prescription medications or GP consultations or both (360). The impact of the prescription levies and changes in access to health services under the GMS scheme on prescription medication use, specifically analgesics, merits further investigation which is beyond the scope of this study.

4.5.1. Limitations

There are a number of limitations associated with this study. The data contained within the HSE-PCRS database may not be reflective of dispensings of prescription medications by retail pharmacy businesses in Ireland. A patient may provide a GMS prescription to a pharmacist but not require all items on the prescription. Depending on the operating procedures within the retail pharmacy business, that item may be allocated as 'Not Dispensed' or 'Owing' to the patient. The former is not recorded in the PCRS and the retail pharmacy business is not reimbursed for non-supply of the medication. Conversely, the pharmacy is reimbursed in the latter instance and the item is recorded in the PCRS database. This unique feature of the reimbursement scheme may lead to an over-estimation of analgesic use.

The HSE-PCRS database does not contain information on disease status or clinical indication for the prescribed medication. An effort has been made in differentiating between acute and chronic pain conditions by examining both ≥ 1

dispensings and >3 dispensings. Analgesics may be purchased over-the-counter, both within retail pharmacy businesses and in other retail settings. However, it is unlikely that patients would purchase analgesics when such medications may be covered under the GMS scheme. However, certain medications may be recommended or prescribed by GPs but may not be covered under the GMS scheme. In this study, this includes certain brands of analgesics including paracetamol/codeine, paracetamol/other and ibuprofen/codeine formulations and laxatives such as senna or fig based formulations. Indeed, the estimates of concurrency of laxatives and opioids may be an underestimate due to the absence of these laxative preparations from the available database

The introduction or withdrawal of a number of medicines from the Irish market, is summarised in the timeline in *Figure 4-1*. This timeline does not capture the withdrawal and introduction of all brands of analgesics, adjuvants, laxatives or sedating agents to the Irish market. It is also difficult to appreciate the marketing or advertisement of medications or certain brands of medications towards prescribers in addition to changes in clinical practice recommendations over this 9 year time period. This may account for fluctuations in the prescribing of certain analgesics, laxatives or sedating agents.

A number of strong opioids were not included in this analysis, most notably methadone and alfentanil. The BNF, IMF and summary of product characteristics of these agents indicate that they are used for the management of severe palliative pain and are not habitually used in the management of chronic pain in the primary care setting (128). The figures for strong opioid dispensings may therefore be an underestimation of the actual prevalence of prescriptions for strong opioids in Ireland during these years. An additional phase of analysis may contribute to our understanding of concurrent use of analgesic classes in the context of the WHO Analgesic Ladder, however, this is beyond the scope of this research. Finally, this study did not seek to infer a relationship between demographic variables and analgesic use, this was due to the limited time frame the researcher had for completion of this study. A negative binomial regression analysis may permit the identification of changes in prescription analgesic use with age-group and gender; this was beyond the scope of this study which was to provide a descriptive overview of analgesic use in this population.

4.6. Conclusion

Regulatory and safety concerns relating to certain classes of medications may cause fluctuations in the dispensing of specific classes of medications. The response by prescribers to changes in the licensing of pharmaceutical agents may be observed by both co-proxamol and the selective NSAIDs classes of medication. Non-opioids, systemic non-selective NSAIDs and moderate opioids are the most prevalent types of analgesics recurrently prescribed, perhaps demonstrating reliance upon analgesics on Step 1 and Step 2 of the WHO Analgesic Ladder. While strong opioid dispensings become more prevalent with age, perhaps due to palliative management, transdermal formulations appear to be a preferential delivery system. Despite this apparent cautious use of strong opioids, there appears to be a high rate of potentially inappropriate prescribing of sedating agent and a low rate of good practice prescribing of laxatives. This potentially inappropriate use of strong opioids is perhaps related to the absence of specific clinical practice guidelines directing the prescribing of these agents in primary care, as demonstrated in *Chapter 3*.

What is already known about this topic:	Analgesics are one of the most commonly prescribed medications in the primary care. The HSE-PCRS Annual Reports indicate that a number of these agents are consistently within the top 50 most frequently prescribed medications, paracetamol and diclofenac (systematic and topical).
	Analgesics, similar to other medications may be associated with cautions and contraindications for certain populations of patients e.g. those with comorbidities, concomitant medications or diminished cognitive function.
	Women access healthcare services more than their male counterparts, have a higher prevalence of pain conditions and are more likely to recieve multiple medications.

What this study adds:	Topical non-selective NSAIDs and systematic NSAIDS had amongst the highest prevalence of use per 1,000 population for both men and women. Systemic nonselective NSAIDs use diminished with increasing age and topical non-selective NSAIDs became more prevalent.
	Dextropropoxyphene/paracetamol, and a number of selective NSAIDs, accounted for a considerable proportion of analgesic use; removal of these agents from the market produced a slight drop in dispensings of analgesics which resumed their upward trends from 2008 onwards, as other products remaining on the market e.g tramadol, paracetamol/codeine formulations increased in popularity.
	Analysis of >3 dispensings provides an estimation of persistent use of analgesics; non-opioids, systemic NSAIDs and moderate opioids remained the most prevalent classes of analgesics dispensed in this analysis.
	Concurrent dispensings of sedating agents with strong opioids was greater than concurrent dispensings of laxatives with strong opioids. Women had a higher concurrency dispensing of sedating agents with strong opioids (≥1 dispensing) than their male counterparts across all age-groups and years. Men had a higher concurrency of laxative and strong opioids dispensed (≥1 dispensing) than their female counterparts across all age-groups and years.

Chapter 5. Non-Malignant Pain in a Community Dwelling Ageing and Elderly Population: A Description of Sociodemographic Characteristics and Analgesic Use

5.1. Background

Chronic non-malignant pain is a complex condition, as the occurrence, progression and approach to management of the condition is influenced by a range of physical, psychosocial and behavioural factors. Epidemiological studies have identified older age, female gender, lower educational level, unemployment, poor mental health and reliance on the public healthcare system as significant factors associated with chronic pain (27, 30, 361, 362). The greater prevalence of pain with age may be attributed to the heightened burden of pathology associated with the ageing process (263, 363). The cognitive, motivational, behavioural and physical components of chronic pain may impact negatively on quality of life (QoL) for individuals with the condition (46, 364, 365). QoL of individuals with CNMP may also be diminished as a result of under-treatment of the condition. However, QoL may also be diminished by adverse effects of medications in patients adequately managed with analgesics. Both under-treatment and adverse outcomes are particularly common amongst ageing and elderly populations (366, 367). Therefore, an analgesic regimen, which balances the specific risk-benefit factors is essential so as to not diminish, and perhaps improve, QoL for those with the condition (366).

The WHO Analgesic Ladder, the cornerstone of analgesic prescribing guidance, advocates a pain management approach that responds to pain severity with the aim of providing the patient with optimal pain management using the most appropriate analgesics (263). The dose and frequency of NSAIDs, opioids and adjuvant agents may have to be modified for ageing populations who have a higher risk of suffering adverse outcomes from medications, due to a combination of a diminished metabolic function, altered distribution patterns, polypharmacy and multi-morbidities (37, 130, 137, 336, 368). Opioids can produce adverse effects in elderly patients including, respiratory depression, injury arising from sedation and gastrointestinal effects such as constipation and nausea (168, 328, 335). This group of gastrointestinal effects termed Opioid Bowel Dysfunction (OBD) is particularly associated with moderate and strong opioids and should be prevented through co-prescribing laxatives with these medications (171). Sedation and respiratory depression associated with opioids may be exacerbated by the concomitant use of CNS medications such as anxiolytics, hypnotics and Z-drugs (59).

5.2. Aims

1. Determine the sociodemographic characteristics of a nationally representative sample of Irish adults aged 50 years and older (ageing and elderly), reporting non-malignant pain;
2. Determine the prevalence of analgesic use amongst the ageing and elderly population reporting non-malignant pain in comparison to those reporting no pain;
3. Examine pharmacotherapeutic management of an ageing and elderly population with non-malignant pain using the WHO Analgesic Ladder as a descriptive framework;
4. Describe the quality of opioid prescribing by examining concurrent use of laxative and sedating agents by the ageing and elderly population with non-malignant pain.

5.2.1. Study & PhD Research Objectives

This study was conducted to meet Objective 2 described in *Chapter 2, Section 2.3*: To describe the nature and extent of analgesic use by ageing and elderly populations with CNMP in the Republic of Ireland.

5.3. TILDA

The Irish Longitudinal Study on Ageing (TILDA) is an inter-institutional research project which aims to improve the quantity and quality of data available on the ageing and elderly in the Republic of Ireland (237). This is the first cohort study of ageing people of its kind in Ireland and is comparable to the English Longitudinal Study on Ageing (ELSA), the Survey of Health, Ageing and Retirement in Europe (SHARE) and the Health and Retirement Study (HRS) in the USA (236).

The study recruited a cohort of 8,175 eligible participants aged 50 years and older during the first wave of data collection. Recruitment for the study began in 2009, with fieldwork completed in February 2011;the cohort is reviewed on a two yearly basis (236). Information is collected from participants on a broad range of subjects *(Table 5-1)* including, economic (pensions, employment, living standard), health (physical, mental, service needs and usage) and social aspects (contact with friends and kin, formal and informal care, social participation The researcher gained consent to access and analyse the data from the TILDA Management Committee in September 2011.

Table 5-1: Summary of data collected in TILDA CAPI and Self-Completion Questionnaire

Demographic Data Education Childhood Health Migration Status Marital status and marriage history	**Physical Health** Self-Rated Health Limiting long-standing illness/disability Sensory Function Cardiovascular Disease Non-Cardiovascular Disease Falls/Fear of Falling/Steadiness Chronic pain Incontinence Medical Screening	**Transport** Transportation Driving
Retirement and Expectations Planning for Retirement Expectations	**Mental Health** Self-reported Mental Health Depression Life Satisfaction Anxiety Worry Loneliness Perceived Stress Stressful Life Events Quality of Life	**Ageing Perceptions**
Social Circumstances Transfers to (and from) children Transfers to (and from) parents (Instrumental) activities of daily living Helpers Social connectedness Participation in social/recreation activities Relationship Quality	**Cognitive Health** Self-rated Memory Orientation Word-list Learning (immediate and delayed recall) Verbal Fluency Prospective Memory	**Healthcare Utilisation** **Behavioural Health** Smoking Physical Activity Sleep Alcohol
Employment and Lifelong Learning Employment Situation Job History Lifelong Learning	**Income and Assets** Sources of Income Assets	**Medications**

5.3.1. TILDA Sample & Data Collection

The target population of TILDA are individuals aged 50 years and older with a residential address in the Republic of Ireland and their spouses or partners (of any age). The Irish Geodirectory, an up-to-date listing and mapping of residential postal addresses in the Republic of Ireland, compiled from the Irish Postal Services (An Post) and the Ordnance Survey, were the sampling frames for the TILDA study (236). The RANSAM sampling procedure, a computer based system designed by the Economic and Social Research Institute (ESRI), was used to derive an initial multi-stage probability sample (236, 369). The RANSAM system is updated each year by referencing the most recent Electoral Register; it facilitates the selection of a representative sample when conducting research on a regional or national basis (370).

Stratification is employed when data of specific precision is required from subdivisions; each of these subdivisions is treated as a separate population. This approach helps to address sampling problems associated with identifying certain groups within a population and allows greater precision in estimates of the entire population (371). A stratified random sampling approach was used to identify potential participants for the TILDA study. A probability sample allowed each member of the population to have a non-zero probability of selection for participation in the study (237).

All postal addresses in Ireland were assigned to one of 3,155 geographic clusters. These clusters are townlands or aggregations of townlands and range in size from 500 to 1,180 addresses. The addresses were divided into two groups, the first, a list of 25,600 addresses and a reserve list of 6,400 addresses. The required sample size for the study was recruited through the first group; the reserve list was not used for the study. A sample of 640 clusters was selected. Clusters were selected with a probability proportional to the number of individuals aged 50 and over in each cluster. Forty households were selected from each cluster. Households identified using this selection system were then approached to participate in the study. All residents of the household aged 50 years and older, and their spouses or partners of any age, were invited to participate in the study (236).

Wave 1 of the TILDA study included a face-to-face interview in the participants' home and a self-completion questionnaire, which was returned after

the visit. A total of 8,504 interviews were conducted with 6,282 households. The response rate to the self-completion questionnaire was 84% and the adjusted response rate to the study was 62%. Participants in the TILDA study were visited in their place of residence where the interview was conducted by trained professional social interviewers with the assistance of computer-assisted personal interviewing (CAPI) (237). Interviewers asked participants, "*to record all medications that you take on a regular basis, like every day or every week. This will include prescription and non-prescription medications, over-the-counter medicines, vitamins and herbal and alternative medicines.*" Data collectors were provided with medication packages by participants to copy down the correct medication names; assistance from relatives in this process was permitted. The Drug and Medical Appliances inventory from the Health Services Executive-Primary Care Reimbursement Service (HSE-PCRS) was used to capture medications taken by participants. This inventory system allowed interviewers to record all drugs included in the state subsidised community reimbursement schemes in Ireland (discussed in *Chapter 1*). Medications were recorded by the World Health Organisation (WHO) Anatomical Group Code (ATC), the international non-proprietary name (INN), brand name and drug code.

Information relating to pain conditions was elicited by asking participants, *"Are you often troubled with pain?"*. Participants were also asked to classify the severity of pain as mild, moderate or severe and indicate the location of the pain. Information relating to a cancer diagnosis was obtained from TILDA respondents by asking *"whether a doctor had ever told them that they have cancer or a malignant tumour"*.

The CASP-19 measure was selected to measure QoL in TILDA. CASP-19 measures the concepts of Control, Autonomy, Self-Realisation and Pleasure through 19 Likert Scales. QoL is interpreted through this model as the extent of satisfaction in each of these domains (6). The mean CASP-19 score for TILDA participants was 42.7, representing 75% of the total possible score of 57 (365). Depression was identified using The Centre for Epidemiological Studies Depression (CES-D) measure. This is a 20-item measure which requires individuals to rate how often they have experienced symptoms of depression in a week. A score of 16 or greater identifies individuals with clinical depression, with

good sensitivity and internal consistency (7). Physical health was evaluated using a single question with five response 'Excellent/Very Good/Good/Fair/Poor'. For the purpose of this analysis, the self-rated physical health categories were collapsed into Excellent, Very Good/Good, Fair/Poor.

5.4. Methods

The sociodemographic features and pharmacotherapeutic management of a population reporting non-malignant are of interest in this study. In order to ensure that the focus of the study was on a population with pain that does not arise from malignancy, those reporting a diagnosis of cancer were excluded. Throughout the course of this chapter, the participants with pain describe those with non-malignant pain. The nature of the question relating to the duration of pain does not permit characterisation as chronic according to the IASP's definition of ≥3 months. A diagnosis of epilepsy was not recorded during interviews with TILDA participants. It was therefore possible to identify those participants reporting anticonvulsant medications for the treatment of pain or the treatment of epilepsy.

Prescription and non-prescription medications were identified using ATC codes, the medication's International Non-Proprietary Name (INN)and brand names. Medications were identified using these three systems to ensure accuracy and reduce the risk of misclassification bias. Analgesic agents were classified according to the therapeutic subclasses outlined in the WHO ladder; non-opioid, adjuvant, NSAID (selective and non-selective) and opioid (weak, moderate and strong). The ATC codes included in this analysis were the same as those in the analysis of the HSE-PCRS dataset and are outlined in *Table 4-1.* As detailed previously in *Chapter 4*, the ATC code for all paracetamol/codeine formulations is the same regardless of the quantity of codeine in the product. To differentiate the higher strength paracetamol/codeine formulations from the non-prescription low dose formulations, these medications were identified using the brand name of the products and assigned to weak or moderate opioid groups as appropriate.

Duloxetine, amitriptyline, nortriptyline, pregabalin, gabapentin and carbamazepine were categorised as adjuvant medications and identified using ATC codes. Laxatives were identified using the ATC code, a drug name and a brand name to ensure that all laxatives were identified during the analysis. For the

purposes of this analysis, benzodiazepines (anxiolytics and hypnotics) were grouped with Z-drugs to create a single group called sedating agents and were identified by ATC code. The ATC codes for adjuvant medications, laxatives and sedating agents are presented in *Chapter 4, Table 4-2.*

5.5. Statistical Analysis

Descriptive and inferential statistical analyses were conducted to meet the aims of this study. All analyses were weighted with respect to age, gender and education. Descriptive demographic statistics are reported for participants reporting pain and no pain. Chi square analyses were used to examine the relationship between pain, demographic variables and analgesic use by therapeutic class. Listwise deletion was used to manage missing data.

Multinomial logistic regression was used to identify the factors associated with the use of any analgesic among participants reporting pain (n=2,655). In this model, the outcome variable had 5 possible outcomes in line with the WHO Analgesic Ladder (Step 0) No Analgesic, (Step 1) Non-opioid/NSAID/Adjuvant Medication, (Step 2) Opioid for Mild Pain ('Weak Opioid'), (Step 3) Opioid for Moderate Pain ('Moderate Opioid'), (Step 4) Opioid for Severe Pain ('Strong Opioid'). No analgesic use (Step 0) was used as the reference category for interpretation of results for a specific risk factor and is based on the Relative Risk Ratio (RRR) of using, for example, a strong opioid for pain relief rather than no analgesic (*Figure 5-1*). A second multinomial logistic regression model was used to identify the factors associated with the use of weak, moderate or strong opioids among participants reporting pain (n=736). This model had 4 different outcome variables, (Step 1) Non-Opioid/NSAID/Adjuvant Medication, (Step 2) Opioid for Mild Pain ('Weak Opioid'), (Step 3) Opioid for Moderate Pain ('Moderate Opioid'), (Step 4) Opioid for Severe Pain ('Strong Opioid'). Use of a non-opioid/NSAID/adjuvant medication (Step 1) was used as the reference category for this model; interpretation of results for a specific risk factor based on the RRR of using for example a strong opioid for pain relief rather than a non-opioid/NSAID/adjuvant medication. This regression model is presented in *Figure 5-2.*

For both models, weak, moderate and strong opioids were separated so as to represent distinct stages of an analgesic management strategy. Considering the original WHO Analgesic Ladder (presented in *Chapter 1, Figure 1-3*), opioids for weak to moderate pain appear in Step 2 while opioids for moderate to strong pain appear in Step 3 of the WHO Analgesic Ladder. In order to overcome the potential duplication associated with the 'moderate' opioids, which appear in both Step 2 and Step 3 of the model, opioids were categorised as weak, moderate or strong and were considered separately, thereby creating three distinct opioid groups. These three categories were created using the same method as described in *Chapter 4, 4.3.1.1.*

Univariate analysis was initially conducted to determine association between each of the covariates. Those covariates, which were significant at the $p \leq 0.05$ level, were included in the multinomial model. Results are reported as relative risk ratios (RRRs); a relative risk ratio >1 indicates that the event is more likely to occur in the group under examination than the reference group (372).

The factors associated with changes to the CASP-19 score for the population with pain were initially examined at a univariate level using linear regression analysis. Those factors that were statistically significant ($p \leq 0.05$) at a univariate level were incorporated into a multivariate linear regression model.

The behavioural model of health services use was used and adapted to identify factors potentially associated with multiple medicine use in our ageing population (373). In this model, the use of health services consists of predisposing, enabling and need factors. Candidate variables that were within our scope of analysis and were considered for inclusion in the regression models included in this analysis were;

- Predisposing variables; age, gender, marital status, severity of pain condition, marital status, depression, polypharmacy, pain location
- Enabling factors: healthcare utilisation, location of residence, employment status, smoking status, level of health insurance cover
- Need factors: self-rated physical health, pain limits daily activity, and number of conditions

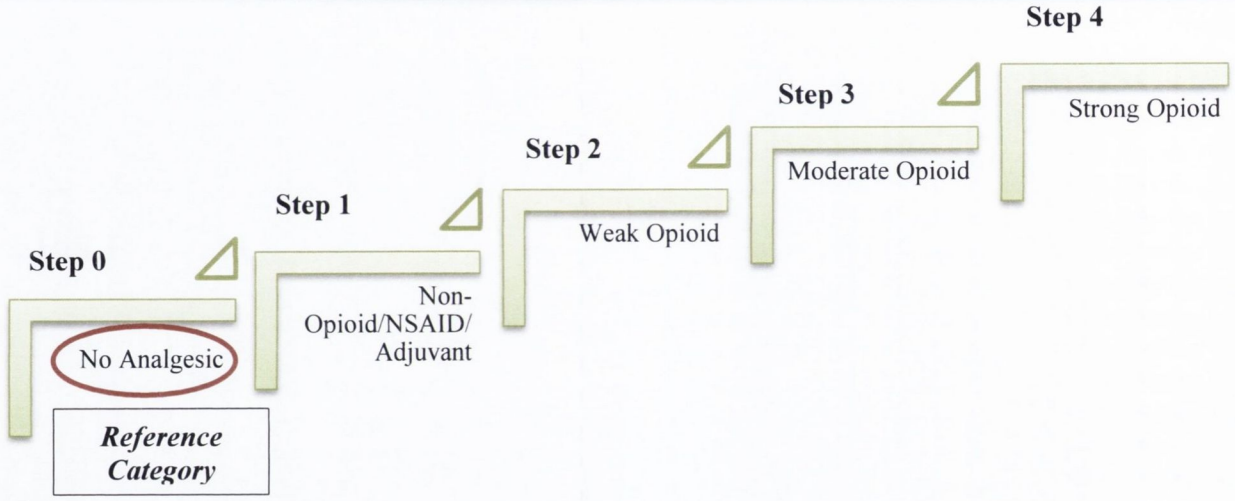


Figure 5-1: Adapted WHO Analgesic Ladder: factors associated with various steps of the ladder among patients reporting pain (Multinomial logistic regression model 1)

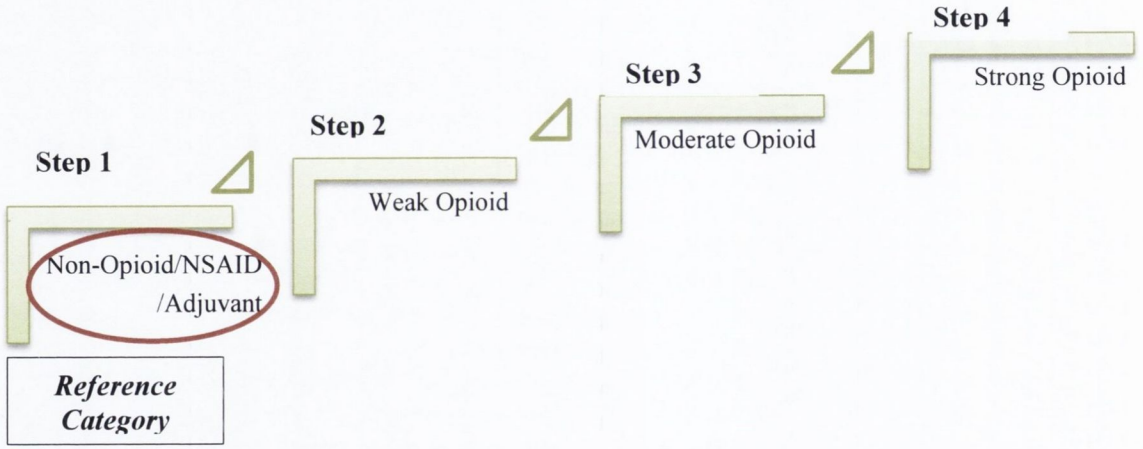


Figure 5-2: Adapted WHO Analgesic Ladder: factors associated with various steps of the ladder among patients reporting pain (Multinomial logistic regression model 2)

5.6. Results

The results of the analysis are described under the following headings:

1. Demographic features of participants with pain aged 50 years and older: this provides a sociodemographic description of those with pain in comparison to those with no pain.

2. Source/ location and severity of pain: this is an outline of the severity of pain reported by participants and an overview of the location of pain according to age-group and gender.

3. Analgesic use for participants aged 50 years and older reporting pain: this provides a description of the prevalence of analgesic use. This analysis also identifies the weak, moderate or strong opioid formulations reported by individuals with pain and the types of medications used concurrently with these opioid formulations. The regression models identify factors associated with positioning on the WHO Analgesic Ladder.

4. QoL (CASP-19) for those reporting pain aged 50 years and older: this is an assessment of factors influencing the QoL of participants with pain and the extent to which these factors alter the CASP-19 score.

5.6.1. Sociodemographic characteristics of TILDA Participants

TILDA collected information from 8,504 individuals, of which 8,093 (95%) participants provided information about their medication use. A total of 8,175 individuals were aged 50 years and older and 512 reported a diagnosis of cancer. Of the 512 participants with a cancer diagnosis, 39.3% (34.9-43.9%, n=199) reported pain. Upon excluding these 512 individuals from further analysis, 7,663 participants remained, of which 2,692 reported the presence of pain. There were 8 missing observations from the pain/no pain population aged 50 years and older. The number of participants at each stage of analysis is summarised in *Figure 5-3*.

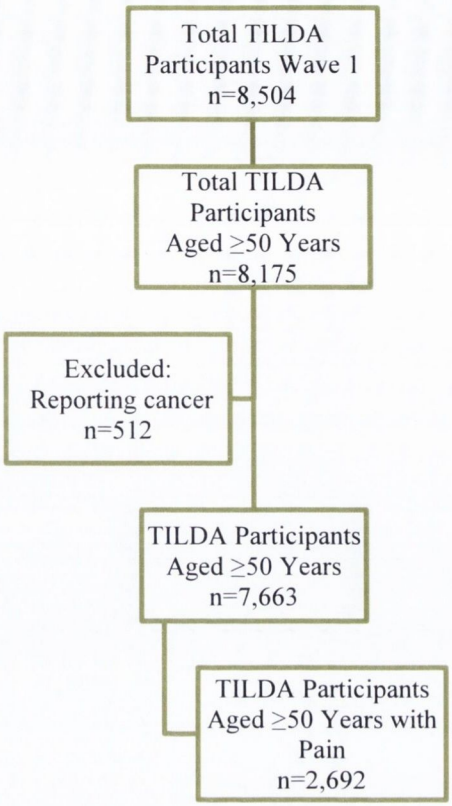


Figure 5-3: Number of TILDA participants at each stage of analysis

Table 5-2 provides a summary of characteristics of TILDA participants aged 50 years and older with and without pain. Thirty-six percent of participants reported pain, approximately, 40% of women and 31% of men ($p<0.001$). Of those reporting pain, approximately 58% were women and 42% were men. The mean age of those reporting mild pain was 63.3 (±9.7), moderate pain was 63.9 (±9.8) and severe pain was 64.7 (±10.0). Almost two thirds (58.9% (56.9-60.8%)) of the participants with pain had a medical card (i.e. GMS eligible) in comparison to 47.1% (45.7-48.6%) of the participants with no pain, however, there was a higher prevalence of medical insurance reported by the latter group, 41.0% (39.6-42.5%).

The highest prevalence of pain occurs in the 55-59 years age group (21.4% (19.7-23.3) followed by the 50-54 year olds, at 19.0% (17.4-20.7%). Considering participants with pain, 42.8% (40.8-44.8%) reported primary level education and 41.8% (39.8-43.7%) reported second level education. Third level education was reported by 20.4% (19.4-21.4%) of participants with no pain, in comparison to 15.5% (14.3-16.7%) of participants with pain. Forty per cent of participants with

no pain were employed at the time of the study in comparison to approximately 29% (27.2-30.9%) of those with pain. A larger proportion 36.2% (34.1-38.3%) of pain participants indicated that they are currently unemployed/ sick or disabled/ looking after a family member than the population reporting no pain (25.4% (23.9-26.8%). Approximately two thirds of those with and without pain were married, while a slightly higher proportion of those with pain were widowed, 17.9% (16.3-19.6%) in comparison to 14.5% (13.4-15.7%) of those with no pain.

A slightly higher proportion of those with no pain reported that they had never smoked, 45.2% (43.7-46.6%) in comparison to 39.6% (37.7-41.5%) and a higher proportion of those with pain are current smokers. Those with pain had a greater burden of chronic disease, with 38.3% (36.3-40.3%) reporting at least three chronic conditions, in comparison to 17.2% (16.1-18.3%) of participants with no pain. Indeed, the prevalence amongst those reporting 2 chronic conditions is also higher than the population with no pain (21.5% (20.3-22.7%)). Considering this alongside polypharmacy (≥5 medications), there is also a higher prevalence amongst those with pain (31.7% (29.9-33.6%)) relative to those not reporting pain, 14.4% (13.4-15.5%). There is a higher prevalence of clinical depression (≥CESD-16) detected in the pain sample 17.2% (15.7-18.8%) in comparison to 5.8% (5.1-6.6%) of the no pain population. Just over half of the population (54.7% (52.6-56.8%) reporting pain attended a GP on 4 or more occasions in the previous 12 months in comparison to one third (33.1% (31.6-34.5%) of participants reporting no pain. Finally, self-rated physical health is considered to be 'good/fair' by 63.7% (61.8-65.5%) of those with pain in comparison to 45% (43.6-46.5%) of the no pain sample; 10.5% (9.3-11.8%) of pain participants reported poor health in comparison to 2.0% (1.6-2.5%) of the no pain population.

Approximately 47% of participants with pain reported arthritis in comparison to 16% of participants with no pain. Considering participants with pain by age-group, 35.6% (33.1-38.2%) aged 50-64 years, 60.3% (56.2-64.2%) of those aged 65-74 years and 65.7% (60.8-70.3%) of those aged ≥75 years reported arthritis. The relationship between reporting pain and arthritis was found to be significant (Chi-squared, $p<0.001$). Considering those with arthritis who also reported pain, 20.6% (18.4-23.0%) reported mild pain, 48.7% (45.5-51.9%) reported moderate pain and 30.7% (27.9-33.6%) reported severe pain. There was a

significant association between pain severity and arthritis (Chi-Squared, p<0.001). Approximately 40% of participants who reported a diagnosis of diabetes also reported pain (42.2% (38.0-46.6%) of whom 28.8% (23.4-34.9%) reported mild pain, 40.8% (34.5-47.5%) reported moderate pain, and 30.3% (24.9-36.4%) reported severe pain. However, the association between pain severity and diabetes was not found to be significant (Chi-Squared, p=0.12). Finally, participants that reported pain had a lower quality of life score. The mean CASP-19 score for participants with pain was 41.5 (41.2-41.9), in comparison to 45.4 (45.1-45.7) for the population without pain.

Table 5-2: Characteristics of TILDA participants, according to whether participants reported pain

Characteristics	Pain (n =2,692)		No Pain(n= 4,963)		Chi-Sq P-value
	n	% (95% CI)	n	% (95% CI)	
Gender					
Male	1,076	42.1 (40.1-44.0)	2,457	51.9 (50.4-51.3)	<0.001
Female	1,616	57.9 (56.0-59.9)	2,506	48.1 (46.7-49.6)	
Age (Years)					
50-54	521	19.0 (17.4-20.7)	1,027	20.6 (19.3-21.9)	0.36
55-59	560	21.4 (19.7-23.3)	1,021	21.2 (19.9-22.6)	
60-64	468	18.0 (16.4-19.7)	838	17.8 (16.6-19.0)	
65-69	376	12.7 (11.4-14.4)	925	12.7 (11.7-13.7)	
70-74	302	9.8 (8.7-11.1)	570	10.3 (9.4-18.9)	
≥75	465	19.1 (17.3-21.1)	782	17.5 (16.2-18.9)	
Residence					
Urban	1,489	54.1 (52.1-56.1)	2,467	48.1(46.7-49.6)	<0.001
Rural	1,202	45.9 (43.9-47.9)	2,485	51.9 (50.4-53.3)	
Marital status					
Married	1,803	65.8 (63.8-67.6)	3,490	69.4 (67.99-70.7)	<0.001
Never Married	226	8.3 (7.3-9.5)	514	10.4 (9.7-11.3)	
Divorced/Separated	223	8.1 (7.0-9.2)	296	5.7 (5.1-6.4)	
Widowed	440	17.9 (16.3-19.6)	663	14.5 (13.5-15.6)	
Education level					
None/Primary level	945	42.8 (40.8-44.8)	1,389	35.4 (34.0-36.8)	<0.001
Secondary level	1,063	41.8 (39.8-43.7)	1,998	44.2 (42.8-45.7)	
Third level	684	15.5 (14.3-16.7)	1,572	20.4 (19.4-21.4)	
Employment Status					
Employed	792	29.0 (27.2-30.9)	2,019	40.5 (38.9-42.2)	<0.001
Retired	989	34.8 (32.8-36.9)	1,796	34.2 (32.5-35.9)	
Unemployed/ Sick Disabled/Carer	911	36.2 (34.1-38.3)	1,148	25.4 (23.9-26.8)	
Health Insurance					
Not Covered	270	10.5 (9.3-11.8)	551	11.8 (10.9-12.8)	<0.001
Medical Insurance	910	30.7 (28.9-32.4)	2,215	41.0 (39.6-42.5)	
Medical Card	1511	58.9 (56.95-60.8)	2,194	47.1 (45.7-48.6)	

Self-Rated Physical Health Status					
Excellent/Very Good	742	25.9 (24.1-27.7)	2,732	53.0 (51.5-54.4)	<0.001
Good/Fair	1,683	63.7 (61.8-65.5)	2,138	45.0 (43.6-46.5)	
Poor	266	10.5 (9.3-11.8)	93	2.0 (1.6-2.5)	
Polypharmacy					
<5 medications	1,831	68.3 (66.4-70.1)	4,220	85.6 (84.5-86.6)	<0.001
≥5 medications	829	31.7 (29.9-33.6)	693	14.4 (13.4-15.5)	
Depression (CES-D ≥16)					
Not Depressed	2194	82.8 (81.2-84.3)	4,618	94.2 (93.4-94.9)	<0.001
Depressed	278	17.2 (15.7-18.8)	440	5.8 (5.1-6.6)	
Smoking history					
Never smoker	1086	39.6 (37.7-41.5)	2,275	45.2 (43.7-46.6)	<0.001
Past smoker	1062	38.9 (37.0-40.9)	1,831	36.6 (35.2-38.4	
Current smoked	543	21.5 (19.8-23.4)	857	18.3 (17.1-19.4)	
Chronic Diseases					
0 Chronic Diseases	373	14.2 (12.8-15.8)	1,466	29.6 (28.1-31.0)	<0.001
1 Chronic Disease	620	22.7 (21.2-24.4)	1,578	31.8 (30.5-33.3)	
2 Chronic Diseases	677	24.8 (38.-40.3)	1,078	21.5 (20.3-22.7)	
≥3 Chronic Diseases	1,022	38.3 (36.3-40.3)	841	17.2 (16.1-18.3)	
No of GP Visits Per Year					
0 GP Visits	798	7.6 (6.5-8.9)	796	15.98 (14.8-17.2)	<0.001
1 GP Visits	294	10.7 (9.6-12.0)	1,009	20.0 (18.9-21.3)	
2 GP Visits	439	15.9 (14.5-17.4)	1,014	19.9(18.7-21.2)	
3 GP Visits	314	11.1 (9.9-12.4)	562	11.0 (10.1-11.9)	
≥4 GP Visits	1,441	54.7 (52.6-56.8)	1,578	33.1 (31.6-34.5)	
Arthritis					
No Arthritis	1,421	53.1(51.0-55.2)	4,140	83.6 (82.4-84.7)	<0.001
Arthritis	1271	46.9 (44.8-48.9)	823	16.4 (15.3-17.6)	
Diabetes					
No Diabetes	2,351	90.7 (90.4-92.6)	4,622	92.8 (92.0-93.5)	<0.01
Diabetes	246	9.3 (8.3-10.5)	341	7.2 (6.5-7.9)	

5.6.2. Severity, Source/Location & Type of Pain

Almost half of those reporting pain (46.4% (44.0-48.5%) reported moderate pain severity, followed by mild pain 28.4% (26.6-30.2%) and severe pain, 25.4% (23.5-27.4%). Women were significantly more likely to report pain than men at each pain threshold, as presented in *Table 5-3*. Almost two-thirds of participants reporting severe pain were female.

Table 5-3: Prevalence of pain according to pain intensity and gender and for the total population* (N= 2,692)

Pain Severity	Men		Women	
	n	% (95% CI)	n	% (95% CI)
Mild Pain	363	48.7 (45.2-52.3)	418	51.3 (47.7-54.8)
Moderate Pain	477	40.7 (38.1-43.4)	782	59.3 (56.6-61.9)
Severe Pain	236	37.1 (40.3-43.8)	416	62.9 (59.3-66.5)
Total	1,076	42.1 (40.3-43.8)	1,616	57.9 (56.2-59.7)

(Chi-Squared p < 0.001)

Approximately one third of each age-group reported pain with a higher proportion of those aged ≥75 years reporting pain, 38.5% (35.5-41.6%), than those in the 50-64 or the 65-74 year age-groups, 35.5% (33.8-37.2%) and 35.5% (33.1-37.8%) respectively (Chi-squared, $p<0.001$). *Figure 5-4* presents pain severity according to age-group. There was an increase in the prevalence of severe pain with increasing age with a prevalence of approximately 29% amongst those aged ≥75 years in comparison to 23% of those aged 50-64 years and 28% of those aged 65-74 years. The prevalence of moderate pain remains consistent across age-groups, while the prevalence of mild pain decreases with increasing age. However, the difference in reported intensity of pain between age-groups was not significant.

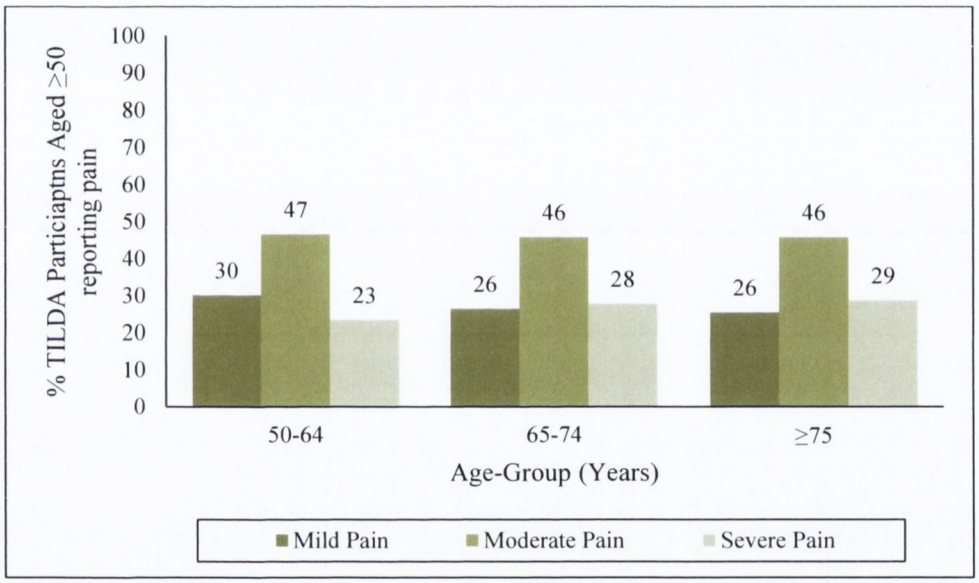


Figure 5-4: Pain severity by age-group (N=2,692)

Table 5-4 presents the prevalence of pain severity according to gender and age-group. Almost half of participants with pain reported that their pain was of moderate severity. The relationship between pain severity and age was not found to be significant for men or women. The highest prevalence of severe pain was reported by men aged 65-74 years, affecting 25.7% (20.4-31.8%) of this population, while the highest prevalence of severe pain occurred in women aged ≥75years occurring in 31.4% (25.8-37.6%) of this age-group.

Table 5-4: Presence of pain and severity according to age-group and gender (N=2,692)

	Mild Pain		Moderate Pain		Severe Pain	
	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)
Men (n=1,076)†						
50-64	215	33.5 (30.0-37.3)	284	45.4 (41.4-49.4)	132	21.1 (17.9-47.1)
65-74	95	32.9 (27.5-28.7)	112	41.4 (35.2-47.9)	68	25.7 (20.4-31.8)
≥75	53	30.1 (22.7-38.8)	81	46.9 (39.5-54.5)	36	22.9 (17.1-30.0)
Total	363	32.9 (29.9-35.9)	477	44.8 (41.6-48.0)	236	22.4 (19.8-25.2)
Women (n=1,616)‡						
50-64	259	27.1 (24.2-30.3)	436	47.5 (44.1-51.0)	224	25.3 (22.5-28.4)
65-74	90	22.0 (1.3-26.3)	205	48.8 (43.7-53.9)	110	29.2 (24.6-34.2)
≥75	69	23.3 (18.7-28.7)	141	45.3 (39.4-53.9)	82	31.4 (25.8-37.6)
Total	418	25.1 (22.9-27.4)	782	47.3 (44.6-50.0)	416	27.6 (25.2-30.1)

†(Chi-Squared p=0.6) ‡ (Chi-Squared p=0.2)

Figure 5-5 illustrates the prevalence of pain according to location across each of the age-groups (Chi-squared, p<0.001). Back pain was the most prevalent pain across all age-groups, accounting for 36-44.3% of all pain. Joint pain increases with age and accounts for approximately one third of pain in the oldest age-group.

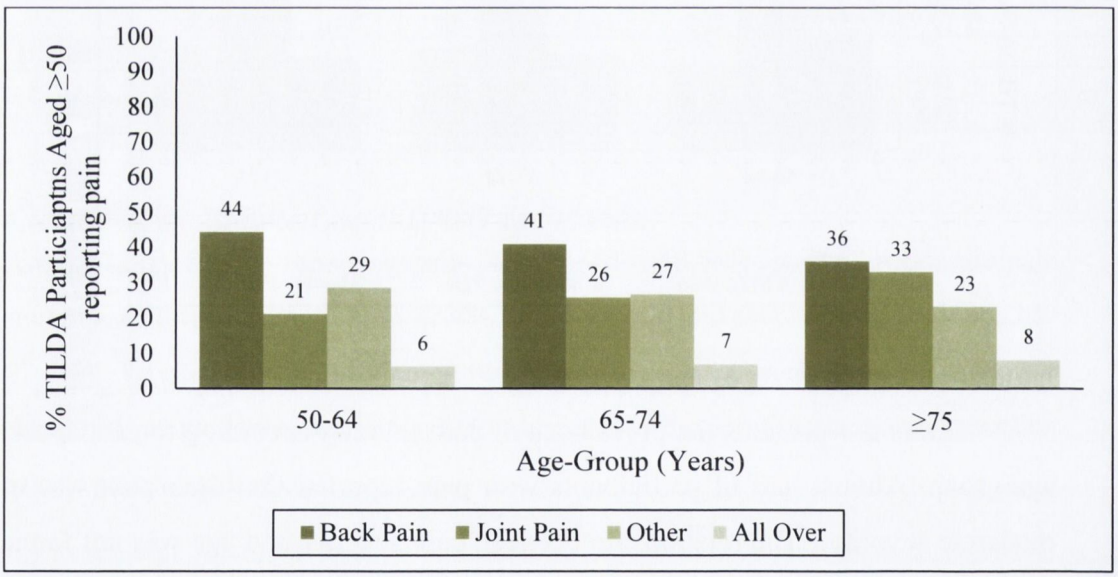


Figure 5-5: Presence and severity of pain according to age-group (N=2,692)

Women were more likely to report back pain (56.3% (53.4-59.2), joint pain (61.9% (57.9-65.7%), all over pain (65.8% (58.3-72.6%), and other pain (54.9% (51.4-58.3%), than men (Chi-squared, p<0.01). *Table 5-5* outlines the location of pain across gender and age-group. Women were significantly less likely to report

back pain with increasing age, however, there is instead an increasing prevalence of joint pain, a difference of approximately 15% between the youngest and oldest age-groups. There was a similar decrease in the prevalence of back pain with increasing age amongst men with a concurrent increase in the reporting of joint pain, however, the increase was not as large as that observed amongst female participants.

Table 5-5: Location of pain according to gender and age-group (N= 2,692)

	Back Pain		Joint Pain		All Over		Other	
	n	% (CI 95%)	n	% (CI 95%)	n	% (CI 95%)	n	% (CI 95%)
Male (n=1,076) †								
50-64	288	45.1 (41.1-49.1)	128	20.7 (17.7-24.0)	31	5.2 (3.6-7.3)	184	29.1 (25.5-33.0)
65-74	116	43.0 (37.0-49.3)	64	23.0 (18.3-28.5)	13	5.0 (2.9-8.4)	82	29.0 (23.5-35.1)
≥75	64	37.6 (30.3-45.6)	42	26.7 (20.3-34.3)	13	7.5 (4.4-12.5)	51	28.2 (22.0-35.5)
Total	468	43.5 (40.5-46.7)	234	22.1 (19.6-24.7)	57	5.5 (4.2-7.1)	317	29.0 (26.2-31.9)
Female (n=1,616)*								
50-64	395	43.6 (40.1-47.1)	195	21.4 (18.5-24.5)	63	7.2 (5.5-9.3)	266	27.9 (25.0-31.0)
65-74	162	39.4 (34.6-44.5)	111	27.5 (23.1-32.3)	33	8.1 (5.7-11.5)	99	25.0 (20.9-29.6)
≥75	107	35.2 (29.6-41.3)	99	35.9 (30.1-42.1)	25	8.2 (5.4-12.4)	61	20.6 (16.2-25.9)
Total	664	40.7 (38.2-43.4)	405	26.0 (23.6-28.6)	121	7.6 (6.3-9.2)	426	25.6 (23.4-28.0)

†*(Chi-Squared p=0.5)* **(Chi-squared, p<0.001)*

5.7. Pain & Analgesic Use

Approximately 5% of the population with no pain reported use of at least one analgesic, while 28% (26.1-29.9%) of participants with pain reported use of at least one analgesic medication (*Table 5-6*). Amongst those with pain, two-thirds of those reporting at least one analgesic were women (67.2% (63.6-70.6%)) in comparison to 55.2% (48.3-62.0%), of the no pain population, reporting at least one analgesics, who were women. Systemic non-selective NSAIDs were the most reported class of medication amongst participants with pain and the population not reporting pain, 11.7% (10.4-13.0%) and 1.8% (1.5-2.3%) respectively. Moderate opioids were the second most reported type of analgesics reported by participants with pain, 7.7% (6.7-8.8%), followed by adjuvant medications for participants, at 5.7% (2.6-6.7%).

By comparison, 0.7% (0.5-1.0%) of participants without pain reported a moderate opioid and 1.4% (1.1-1.8%) reported an adjuvant medication Weak and strong opioids were least reported by participants with pain, 1.4% (1.0-2.0%) and 1.6% (1.2-2.2%) respectively.

Table 5-6: Analgesic exposure by drug class amongst participants with pain and no pain* (N= 7,655)

Drug Category	Pain n=2,692		No Pain n=4,963	
	n	% (95% CI)	n	% (95% CI)
≥1 Analgesic	740	28.0 (26.1-29.9)	232	4.9 (4.4-5.7)
≥1 Non-Opioid	118	4.6 (1.8-2.6)	37	0.8 (0.6-1.2)
≥1 NSAID	388	14.5 (13.1-15.9)	104	2.2 (1.8-2.7)
≥1 Non-Selective NSAID	326	12.1 (10.8-13.5)	92	1.9 (1.5-2.4)
Systemic Non-Selective NSAID	314	11.7 (10.4-13.0)	88	1.8 (1.5-2.3)
Topical Non-Selective NSAIDs	19	0.7 (0.4-10.7)	5	0.1 (0.004-0.2)
Selective NSAID	71	2.7 (2.1-3.5)	13	0.3 (0.2-0.5)
≥1 Adjuvant Medication	156	5.7 (2.6-6.7)	63	1.4 (1.1-1.8)
≥1 Opioid	272	10.6 (9.4-11.9)	45	0.9 (0.7-12.8)
Weak Opioid	43	1.6 (1.2-2.2)	10	0.2 (0.0009-0.4)
Moderate Opioid	198	7.7 (6.7-8.8)	32	0.7 (0.5-1.0)
Strong Opioid	36	1.4 (1.0-2.0)	2	0.0004 (0.0001-0.02)

(Chi-Squared p < 0.001 for all)

The WHO Analgesic Ladder supports the use of multiple analgesics if pain is inadequately managed by a single agent. A number of participants with pain reported concurrent use of several classes of analgesics. The prevalence of concurrent use is presented in *Table 5-7*. One in four of those with pain, who were taking a non-opioid, also reported taking a non-selective NSAID or taking a selective NSAID with a moderate opioid. Approximately 20% of participants with pain concurrently reported an adjuvant agent with a moderate opioid, while approximately 10% reported concurrent use of a strong opioid. Thirteen per cent of those reporting a non-selective NSAID also concurrently reported a moderate opioid, while 9.4% (6.7-13.1%) also reported an adjuvant medication.

Table 5-7: Concurrent use of analgesic and adjuvant medications among participants with pain

	Non-Opioid % (95% CI) n	Non-Selective NSAID % (95% CI) n	Selective NSAID % (95% CI) n	Adjuvant Medication % (95% CI) n	Weak Opioid % (95% CI) n	Moderate Opioid % (95% CI) n	Strong Opioid % (95% CI) n
Non-Opioid	--------	--------	--------	--------	--------	--------	--------
Non-Selective NSAID	24.9 (7.8-33.6) n=30	--------	--------	--------	--------	--------	--------
Selective NSAID	2.1 (0.5-8.1) n=2	2.9 (1.4-6.0) n=9	--------	--------	--------	--------	--------
Adjuvant Medication	7.6 (3.9-14.2) n=10	9.4 (6.7-13.1) n=32	2.3 (0.5-9.3) n=16	--------	--------	--------	--------
Weak Opioid	2.1 (0.7-6.4) n=3	2.9 (1.5-5.6) n=9	3.8 (0.9-15.0) n=2	1.7 (0.6-4.5) n=4	--------	--------	--------
Moderate Opioid	6.8 (3.5-12.8) n=9	13.1 (9.6-17.7) n=42	23.6 (15.3-34.7) n=18	21.4 (15.5-28.8) n=32	1.3 (0.2-9.0) n=1	--------	--------
Strong Opioid	1.3 (0.2-8.9) n=1	4.3 (2.5-7.3) n=12	5.1 (1.6-14.9) n=3	10.3 (6.3-16.0) n=15	2.5 (0.3-15.9) n=1	1.5 (0.5-4.7) n=3	--------

Oral diclofenac was the most prevalent analgesic reported by participants with pain, with 5.6% (4.7-6.6%) indicated current use of this medication; 4.6% (3.8-5.5%) reported paracetamol and 1.9% (1.4-2.5%) reported ibuprofen. Considering opioid containing formulations, 4.1% (3.4-5.0%) reported a paracetamol/codeine (prescription only) containing formulation, 2.9% (2.3-3.7%) tramadol; pregabalin was the most prevalent adjuvant analgesic reported by the population (2.7% (2.1-3.7%)). *Figure 5-6* presents the proportion of men and women respectively reporting pain and also reporting at least one analgesic according to the therapeutic class. This indicates that similar to the HSE-PCRS dataset, women consistently report the greater prevalence of analgesic use across all classes of medications considered in this analysis ($p \leq 0.05$).

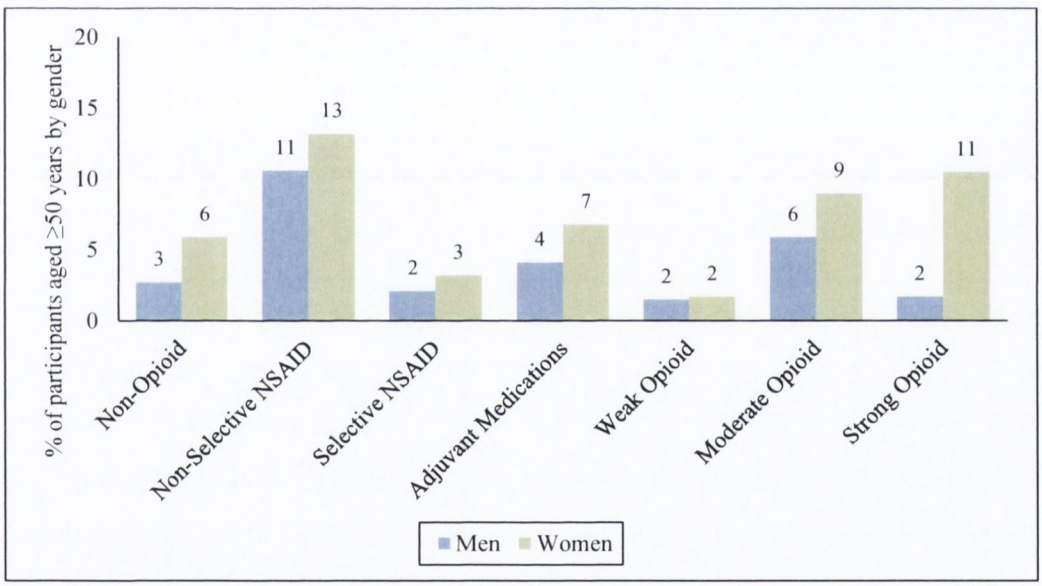


Figure 5-6: Prevalence of analgesics reported by class by men and women participants reporting pain (N=2,692)

Figure 5-7 presents the types of analgesic medications reported by those participants with pain, reporting at least one analgesic. Forty-three percent (39.3-46.9%) of those taking an analgesic with pain reported a non-selective NSAID. Moderate opioids were the second most prevalent class of analgesic reported, accounting for almost one third of all the analgesics reported (27.5%). Adjuvant medications are the third most prevalent medication reported by the population with

pain, indicating the probable use of agents with a neuropathic mechanism of action to supplement analgesic medications.

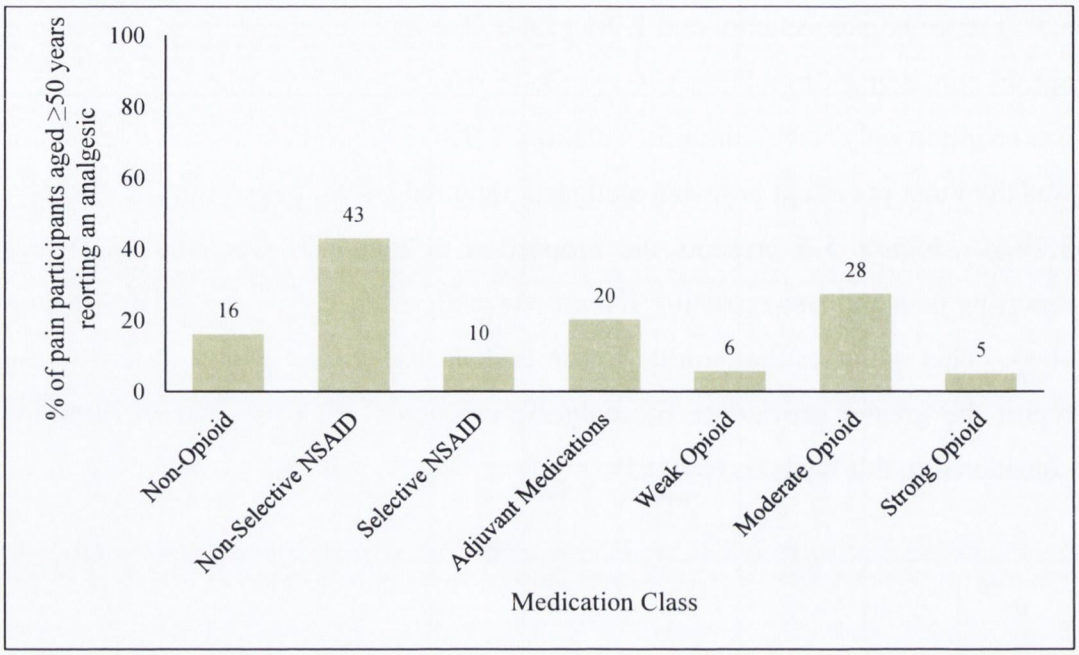


Figure 5-7: Class of analgesic reported by participants with pain taking ≥1 analgesic (N= 740)

Figure 5-8 presents the use of specific classes of medications by age-group from the participants with pain reporting at least one analgesic medication. Approximately 38% of participants with pain, taking an analgesic, aged 50-64 years, reported taking a non-selective NSAID, in contrast to 37% of those aged 65-74 years, and approximately 20% of the ≥75 year age-group. Adjuvant medications were reported by 16%, 17% and 15% of those with pain, reporting an analgesic; these were aged 50-64, 65-74 and ≥75 years respectively. Moderate opioids are reported by one in five participants with pain taking an analgesic aged 50-64 years and 65-74 years, in contrast to approximately one in four of those aged ≥75 years. Strong opioids were reported by 3% of those aged 50-64, 65-74 and 6% of those aged ≥75 years. Viewing this graph in light of the WHO Analgesic Ladder, it would appear that the oldest population have a higher prevalence of use of Step 2 and Step 3 agents than Step 1 agents when compared to the younger age-groups. However, there is a much lower prevalence of use of both selective and non-selective NSAIDs in the older population; this is possibly reflective of the cautions and

contraindications associated with the prescribing of these agents to elderly populations.

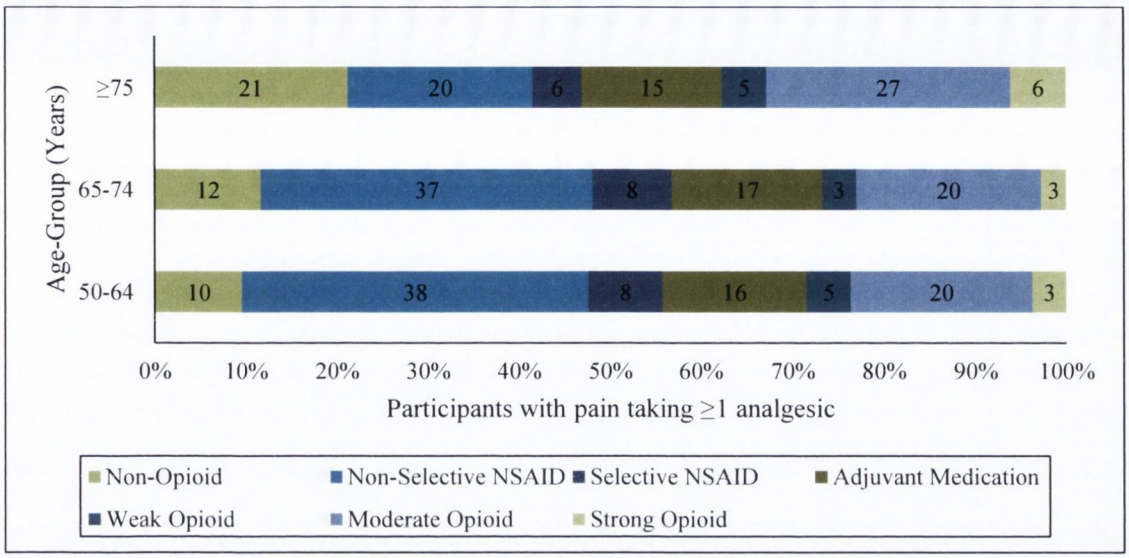


Figure 5-8: Percentage of participants with pain taking at least one analgesic by age-group reporting use of a specific class of analgesic (N=740)

Figure 5-9 presents the use of specific classes of analgesics according to pain severity. Non-opioids are used mostly by those reporting moderate pain. Non-selective anti-inflammatories are used by almost 50% of individuals with moderate pain conditions taking a non-selective NSAID. Half of those reporting taking a selective NSAID or moderate opioids had severe pain. Adjuvant medications were more prevalent amongst those with severe pain, although there were similarly high proportion with moderate pain reporting these agents. Finally, approximately 55% of those taking a strong opioid reported severe pain; this outcome is expected, as this class of opioid should be reserved for use with severe pain conditions.

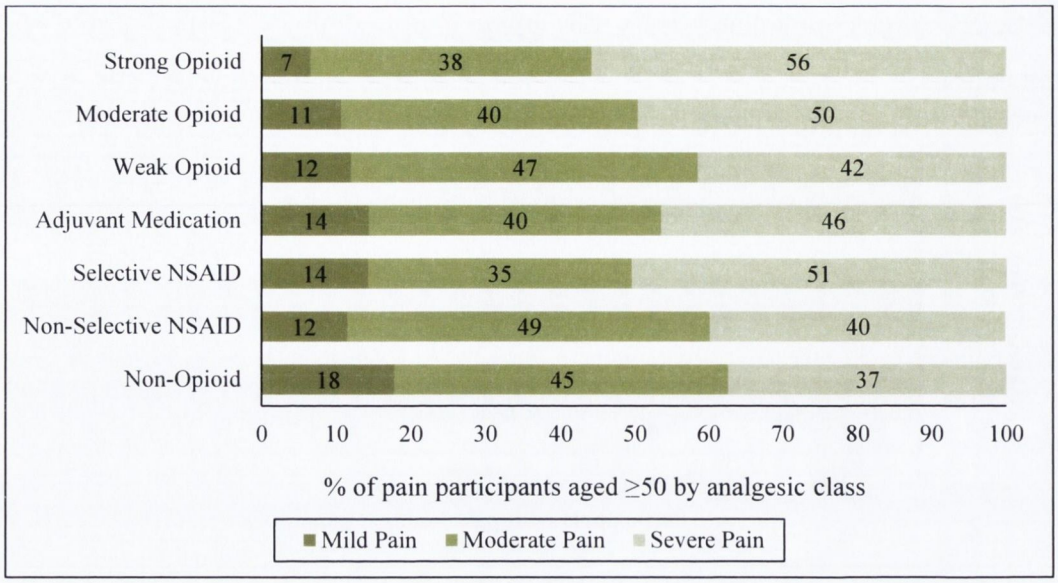


Figure 5-9: Analgesic use according to pain intensity for pain population aged ≥50 and older (N=740)

5.8. Opioid Analgesics and Concurrent Medications

Approximately 1% of participants with pain reported the use of a laxative. There was a low prevalence of concurrent use of laxatives with opioid analgesics, with 4.2% (2.1-8.4%) of those reporting a moderate opioid, and 6.9% (2.0-21.2%) of those reporting a strong opioid also reporting a laxative medication. No individual with pain reported concurrent use of a laxative with a weak opioid.

Figure 5-10 presents concurrent use of laxatives by those reporting a moderate or strong opioid by age-group. The highest rate of concurrent use was reported by the 65-74 year old group with pain group taking a strong opioid (25.3%). Concurrent reporting of a laxative with a moderate opioid for those aged 50-64 year olds was approximately one in twenty. No individuals in the oldest age-group reported a laxative alongside a strong opioid, while 4% reported concurrent use with a moderate opioid.

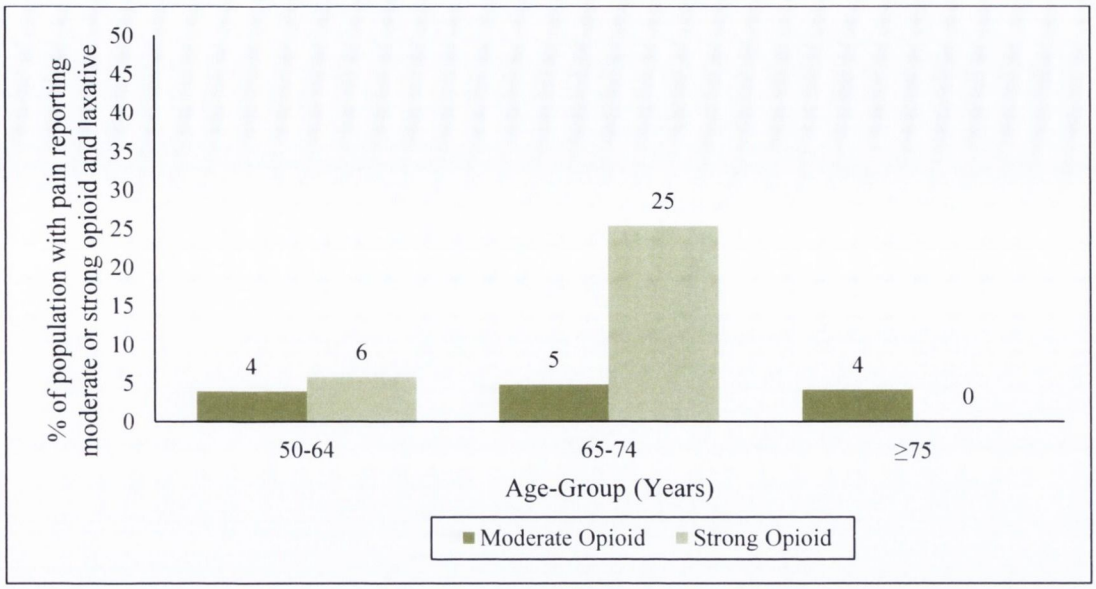


Figure 5-10: Concurrent laxative use amongst those reporting opioids (by class) according to age-group for participants with pain (N=11)

Approximately 10% of the participants with pain reported the use of a sedating agent. The concurrent use of sedating agents with a weak opioid was 10.9% (4.5-24.1%), however, concurrent use was higher with moderate and strong opioids, with 23.2% (17.7-29.8%) and 27.8% (14.3-43.3%) respectively reporting concurrent use.

Figure 5-11 presents concurrent use of a sedating agent by those reporting a weak, moderate or strong opioid by age-group. Concurrent use of a sedating agent with a weak opioid was least prevalent for all age-groups; concurrent reporting of a sedating agent with a moderate opioid was identified in approximately one-quarter of 50-64 and 65-74 years old and one-third of those aged ≥75 years (Chi-squared, $p<0.001$). Prevalence of concurrent use of a sedating agent with a strong opioid was highest in the 50-64 and 65-74 year age-groups, 27.1% and 42.9% respectively, with a prevalence of 18.7% detected for the oldest age-group ($p<0.001$).

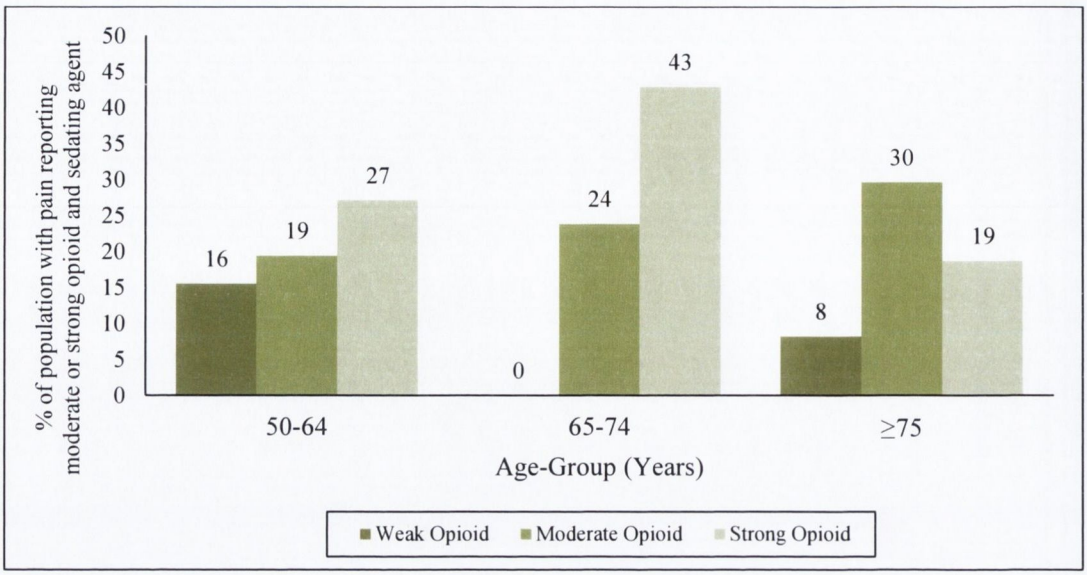


Figure 5-11: Concurrent sedating agent use amongst those reporting opioids (by class) according to age-group for participants with pain (N=60)

5.8.1. Multinomial Logistic Regression Model for WHO Analgesic Ladder

Table 5-8 presents the results for Model 1 *(as presented in Figure 5-1)* of the multinomial regression analysis to identify positioning of those with pain on the WHO Analgesic Ladder relative to those reporting pain but no analgesic (absence from ladder/Step 0). Gender, age-group, marital status, self-rated physical health, polypharmacy, educational level, employment status, pain severity, pain limiting daily activities, clinical depression (CES-D ≥16), number of chronic diseases and smoking status were all significant at a univariate level (*Appendix D, Table D-1*). The Relative Risk Ratios (RRRs) of the variables that remained significant at a multivariate level are highlighted in *Table 5-8*.

People classified as being on Step 1 (Non-Opioid/NSAID/Adjuvant) of the ladder were significantly more likely to: be female, take ≥5 medications, be retired or unemployed/disabled/carer, have good/fair self-rated physical health, have moderate or severe pain, have pain that restricted daily activity, and have ≥2 chronic diseases. People classified on Step 2 of the ladder (Weak Opioid) were significantly more likely to: report severe pain, take ≥5 medications, and be a current smoker. People classified as being on Step 3 (Moderate Opioid) of the ladder were significantly more likely to: report ≥5 medications, be unemployed/disabled/carer, have moderate or severe pain, have pain that restricted daily activity and be a past

or current smoker. Finally, people classified as being on Step 4 (Strong Opioid) of the ladder were significantly more likely to: report ≥5 medications and have pain that restricted daily activity. Receiving ≥5 medications is the only variable that remains significant across each step of the analgesic ladder.

Table 5-8: Model 1 Multinomial logistic model for WHO Analgesic Ladder for individuals with pain aged 50 years and older (N=2,655)*

	WHO ANALGESIC LADDER							
	No Analgesic (Step 0)/ Non-Opioid/NSAID/Adjuvant (Step 1)		No Analgesic (Step 0)/ Weak Opioid (Step 2)		No Analgesic (Step 0)/ Moderate Opioid (Step 3)		No Analgesic (Step 0)/ Strong Opioid (Step 4)	
	RRR(95% CI)	P-Val	RRR (95% CI)	P-Val	RRR (95% CI)	P-Val	RRR (95% CI)	P-Val
Gender								
Male	1		1		1		1	
Female	**1.44** (1.12-1.86)	0.005	1.48 (0.76-2.88)	0.25	1.39 (0.95-2.04)	0.09	1.34 (0.57-3.17)	0.50
Age-Group								
50-64	1		1		1		1	
65-74	0.90 (0.66-1.23)	0.51	0.57 (0.22-1.48)	0.25	0.80 (0.49-1.30)	0.36	0.80 (0.25-2.60)	0.71
≥75	0.77 (0.51-1.17)	0.22	1.01 (0.44-2.31)	0.99	0.95 (0.52-1.73)	0.87	1.50 (0.43-5.22)	0.53
Marital Status								
Married	1		1		1		1	
Never Married	1.06 (0.70-1.6)	0.78	2.21(0.88-5.54)	0.09	1.10(0.62-1.98)	0.75	0.91 (0.22-3.72)	0.89
Sep/divorced	1.13 (0.76-1.68)	0.53	1.34 (0.46-3.92)	0.59	0.86 (0.47-1.58)	0.63	0.5 (0.01-2.58)	0.41
Widowed	0.9 (0.7-1.43)	0.9	0.76 (0.24-2.43)	0.64	1.35 (0.84-2.18)	0.21	1.22 (0.453.31)	0.69
Self-Rated Physical Health								
Excellent/Very Good	1		1		1		1	
Good/Fair	**1.61** (1.17-2.20)	0.003	1.04 (0.4-2.66)	0.42	1.40 (0.83-2.37)	0.21	0.92 (0.24-3.61)	0.91
Poor	1.36 (0.84-2.02)	0.21	0.88 (0.22-3.62)	0.86	1.56 (0.77-3.16)	0.21	3.41 (0.80-14.57)	0.1
Polypharmacy								
<5 Medications	1		1		1		1	
≥5 Medications	**1.90** (1.46-2.47)	0.00	**5.79** (2.65-12.65)	0.00	**4.58** (3.08-6.81)	0.00	**5.60** (1.71-18.34)	0.004

Educational Level								
None/primary level	1		1		1		1	
Secondary level	1.11 (0.85-1.43)	0.45	1.00 (0.43-2.35)	0.99	1.33 (0.98-3.40)	0.14	0.62 (0.23-1.67)	0.34
Third level	1.28 (0.94-1.74)	0.11	1.1 (0.44-2.76)	0.84	1.16 (0.71-1.87)	0.55	0.82 (0.25-2.65)	0.74
Employment Status								
Employed	1			1	1		1	
Retired	**1.92** (1.35-2.73)	0.00	1.52 (0.55-4.23)	0.42	1.82 (0.98-3.40)	0.06	2.86 (0.26-32.27)	0.39
Unemployed/ Sick Disabled/Carer	**2.0** (1.44-2.79)	0.00	1.09 (0.41-2.94)	0.86	**2.01** (1.17-3.47)	0.01	6.88 (0.78-60.47)	0.08
Pain Severity								
Mild	1		1		1		1	
Moderate	**1.98** (1.45-2.72)	0.00	2.03 (0.73-5.6)	0.17	**2.17** (1.25-3.78)	0.006	2.07 (0.49-8.80)	0.32
Severe	**2.76** (1.96-3.89)	0.00	**3.30** (1.08-10.08)	0.04	**4.59** (2.57-8.19)	0.00	2.95 (0.74-11.84)	0.13
Pain Limits Daily Activity								
No Limitations	1		1		1		1	
Limitations	**1.47** (1.15-1.88)	0.002	2.11 (0.96-4.65)	0.07	**1.99** (1.31-3.05)	0.001	**3.91** (1.07-14.34)	0.04
Depression (CES-D ≥16)								
Not Depressed	1		1		1		1	
Depressed	1.05 (0.79-1.41)	0.74	0.93 (0.41-2.10)	0.87	1.13 (0.74-1.71)	0.58	1.24 (0.52-2.97)	0.63
Number of Chronic Diseases								
0 Chronic Diseases	1		1		1		1	
1 Chronic Disease	1.33 (0.83-2.13)	0.25	2.12 (0.53-8.6)	0.29	2.10 (0.94-4.70)	0.07	0.75 (0.06-8.83)	0.82
2 Chronic Diseases	**1.71** (1.06-2.76)	0.03	0.84(0.18-3.81)	0.82	1.84 (0.83-4.08)	0.14	2.39 (0.26-22.07)	0.44
≥ 3 Chronic Diseases	**1.71** (1.05-2.77)	0.03	0.84 (0.22-3.23)	0.8	1.27 (0.55-2.91)	0.58	0.84 (0.08-8.54)	0.88
Smoking Status								
Never Smoked	1		1		1		1	
Past Smoker	1.03 (0.79-1.34)	0.82	2.20 (0.89-5.44)	0.09	**1.55** (1.06-2.26)	0.02	1.21(0.55-2.65)	0.64
Current Smoker	1.03 (0.75-1.41)	0.86	**2.75** (1.01-7.47)	0.05	**1.87** (1.20-2.92)	0.006	0.83 (0.22-3.10)	0.79

(Prob > F = 0.005)

Model 2 takes into account only those participants with pain in the WHO Analgesic Ladder, excluding those who do not report an analgesic or adjuvant medication (as presented in *Figure 5-2*). This model permits further understanding of positioning on the WHO Analgesic Ladder by including only those individuals that reported an analgesic medication.

Marital status, educational level, self-rated physical health, pain severity, polypharmacy, pain limiting daily activities, clinical depression (CES-D ≥16), and smoking status were significant at a univariate level (*Appendix D, Table D-2*). Results from the multinomial regression model are presented in *Table 5-9,* with the RRRs of those variables that remained significant highlighted.

People classified as being on Step 2 (Weak Opioid) of the ladder were significantly more likely to: take ≥5 medications or be a current smoker. People classified on Step 3 of the ladder (Moderate Opioid) of the ladder were significantly more likely to: report taking ≥5 medications and be a past or current smoker. No variables remained significant on Step 4 (Strong Opioid) of the ladder.

Table 5-9: Model 2 Multinomial logistic model for WHO Analgesic Ladder for individuals with pain aged 50 years and older (N=736)*

	WHO ANALGESIC LADDER					
	Non-Opioid/NSAID/Adjuvant Agent (Step 1) / Weak Opioid (Step 2)		Non-Opioid/NSAID/Adjuvant Agent (Step 1) /Moderate Opioid (Step 3)		Non-Opioid/NSAID/Adjuvant Agent (Step 1)/ Strong Opioid (Step 4)	
	RRR	P-Value	RRR (95% CI)	P-Value	RRR (95% CI)	P-Value
Marital status						
Married	1		1		1	
Never Married	2.19 (0.78-6.11)	0.14	0.99 (0.50-1.93)	0.97	0.68 (0.14-3.2)	0.62
Sep/divorced	1.11 (0.37-3.39)	0.85	0.73 (0.37-1.42)	0.35	0.42 (0.77-2.27)	0.31
Widowed	0.78 (0.26-2.30)	0.65	1.35 (0.85-2.13)	0.20	1.32 (0.52-3.32)	0.56
Education level						
None/primary level	1		1		1	
Secondary level	0.96 (0.41-2.22)	0.92	1.17 (0.77-1.77)	0.89	0.44 (0.17-1.15)	0.09
Third level	0.94 (0.38-2.32)	0.89	0.89 (0.54-1.47)	0.65	0.47 (0.16-1.38)	0.17
Self-Rated Physical Health						
Excellent/Very Good	1		1		1	
Good/Fair	0.65 (0.2-1.66)	0.37	0.96 (0.55-1.67)	0.89	0.61 (0.16-2.32)	0.46
Poor	0.57 (0.14-2.31)	0.43	1.15 (0.53-2.48)	0.72	2.55 (0.60-10.79)	0.20
Pain Severity						
Mild Pain	1		1		1	
Moderate Pain	0.93 (00.3-2.61)	0.89	1.12 (1.40-2.91)	0.73	0.9(0.21-4.75)	0.08
Severe Pain	1.13 (0.34-3.73)	0.85	1.68 (0.87-3.24)	0.12	0.87 (0.19-4.01)	0.85
Polypharmacy						
<5 Medications	1		1		1	
≥5 Medications	**2.12** (1.05-4.29)	0.04	**2.02** (1.4-2.91)	0.00	2.75 (0.9-8.4)	0.08

Pain Limits Daily Activity						
No Limitations	1		1		1	
Limitations	1.46 (0.66-2.23)	0.36	1.36 (0.82-2.25)	0.24	2.42 (0.62-9.41)	0.2
Depression (CES-D ≥16)						
Not Depressed	1		1		1	
Depressed	0.73 (0.31-1.76)	0.49	1.0 (0.63-1.6)	0.9	1.36 (0.53-3.49)	0.52
Smoking Status						
Never Smoked	1		1		1	
Past Smoker	2.00 (0.78-5.1)	0.15	**1.56** (1.02-2.38)	0.04	1.12 (0.5-2.51)	0.79
Current Smoker	**3.03** (1.09-8.44)	0.03	**1.96** (1.2-3.22)	0.008	0.77 (0.24-2.49)	0.66

(Prob > F = 0.005)

5.9. Quality of Life and Pain

Significant predictors of CASP-19 score among this group of participants with pain included age-group, marital status, pain limiting daily activities, a CES-D score ≥16, self-rated physical health, the location of pain and smoking status. Polypharmacy, educational level, medical insurance, pain severity, type of analgesic reported, the number of chronic diseases and the number of GP visits in the previous 12 months did not significantly predict QoL scores but were significant at a univariate level (*Appendix D, Table D-3*). The results for this multivariate linear regression analysis are presented in *Table 5-10,* with those statistically significant scores highlighted in the table.

Self-rated physical health was a key predictor of QoL with participants who rated their health as 'Good/Fair', having a CASP-19 score that was 3.21 points lower than those who rated their health as Excellent/Very Good. Furthermore, those participants who reported their health as 'Poor' had CASP-19 score that was 7.37 points lower than those who rated their health as Excellent/Very Good. Pain which affects activities in daily living reduced the CASP-19 score by 2.33 points in comparison to those reporting no such limitation. Those participants with pain in the 65-74 years age-group had a score that was 1.42 points higher than individuals in the 50-64 years age-group. Those participants with pain who were separated or divorced had a CASP-19 score that was 1.33 points lower than those with pain that were married. Individuals reporting pain 'All Over' had a CASP-19 score that was 1.63 points lower than those reporting back pain. Current smokers who reported pain received a score that was 1.41 points lower than those participants with pain who reported never smoking. Finally, those individuals with pain with a CES-D score ≥16, indicating clinical depression, had a CASP-19 score that was 6.51 points lower than those without clinical depression.

Table 5-10: Multivariate linear regression for CASP-19 scores for participants with pain aged 50 years and older (N=1,837)

Characteristic	Beta Coeff (95% CI)	P-Val
Age-Group		
50-64	1	
65-74	**1.42** (0.48-2.36)	0.003
≥75	-0.53 (-1.73-0.67)	0.39
Marital Status		
Married	1	
Never Married	-1.0 (-2.31-0.30)	0.14
Separated/divorced	**-1.33** (-2.51-(-)0.15)	0.03
Widowed	0.76 (-0.27-1.79)	0.15
Employment Status		
Employed	1	
Retired	0.29 (-0.76-1.34)	0.59
Unemployed/ Sick Disabled/Carer	-0.69 (-1.62-0.265)	0.15
Self-Rated Physical Health		
Excellent/Very Good	1	
Good/Fair	**-3.21** (-3.96-(-)2.45)	0.00
Poor	**-7.37** (-8.90-(-)5.83)	0.00
Polypharmacy		
<5 Medications	1	
≥5 Medications	-0.12 (-1.07-0.30)	0.81
Educational Level		
None/primary level	1	
Secondary level	-0.34 (-0.88-0.81)	0.94
Third Level	0.23 (-0.68-1.14)	0.62
Pain Limits Daily Activities		
No Limitations	1	
Limitations	**-2.33** (-3.17-(-)1.61)	0.00
Depression (CES-D ≥16)		
Not Depressed	1	
Depressed	**-6.51** (-7.64-(-)5.38)	0.00
WHO Analgesic Ladder Position		
No Analgesic	1	
Non-Opioid/NSAID/Adjuvant	-0.47 (-1.37-0.43)	0.31
Weak Opioid	1.87 (-0.58-4.31)	0.13
Moderate Opioid	-1.03(-2.57-0.51)	0.09
Strong Opioid	-0.61 (-4.5-3.28)	0.76
No of GP Visits Per Year		
0 GP Visits	1	
1 GP Visit	-0.15 (-1.71-1.41)	0.85
2 GP Visits	-0.42 (-1.97-1.13)	0.60
3 GP Visits	-0.22 (-1.77-1.33)	0.78
≥4 GP Visits	-0.43 (-1.89-1.04)	0.57
Pain Severity		
Mild Pain	1	
Moderate Pain	-0.08 (-0.83-0.66)	0.83
Severe Pain	0.02 (-1.02-1.05)	0.98

Pain Location		
Back Pain	1	
Joint Pain	-0.32 (-1.19-0.55)	0.47
Other	-0.26 (-1.11-0.58)	0.54
All Over	**-1.63** (-3.1-(-)0.1)	0.04
Smoking Status		
Never Smoked	1	
Past Smoker	-0.22 (-0.90-0.47)	0.53
Current Smoker	**-1.41** (-2.37-(-)-0.45)	0.004
Medical Insurance		
Medical Card	1	
Other	0.66 (-0.575-1.86)	0.29
Not covered	-0.51 (-1.71-0.71)	0.42
Number of Chronic Diseases		
No Chronic Diseases	1	
1 Chronic Disease	0.79 (-0.32-1.91)	0.16
2 Chronic Disease	1.13 (-0.02-2.28)	0.06
≥3 Chronic Diseases	0.57 (-0.56-1.71)	0.32

5.10. Discussion

This study sought to describe the sociodemographic and clinical features of a population aged 50 years and older reporting pain from a nationally representative sample. Thirty-six percent of participants in this study reported pain. This estimate is similar to that obtained in the recent PRIME study (n=1,204) which reported a prevalence of 35.5% (32.8-38.2%) from a postal survey of community based adults (chronic pain defined as >3 months) (30). Both this study and the PRIME study have identified a higher prevalence of pain in Ireland compared to 13% reported in the European survey on chronic pain (≥6 months), which was conducted by Breivik et al (n=46,394). However, the European survey examined pain existing for a period of longer than 6 months and focused exclusively on the self-reporting of pain in an ageing and elderly population, which may produce higher estimates of prevalence (31).

Chronic pain has been demonstrated to be more prevalent among women, older populations, those of a lower educational level, individuals who are divorced or separated, living in rural areas or who are in receipt of a pension (32, 46, 374, 375). Similar to international epidemiological studies on gender differences in the prevalence of pain, this study identified a significant difference in prevalence across genders, with 40% of women and 31% of men reporting pain (24, 376, 377). Numerous studies have also demonstrated that the prevalence of chronic pain varies with age. Approximately one third of each age-group reported pain with a higher proportion of those aged ≥75 years reporting pain than any other age group (38.5%). Epidemiological studies have proposed that the increased prevalence of pain in the elderly is associated with the increased prevalence of chronic diseases (27). Back pain was the most prevalent site of pain for all age-groups, although prevalence of pain at this location decreases with increasing age with an increase in joint pain observed. This finding highlights the changing aetiology of pain according to age and the possible progression of articular degeneration (42). A number of studies investigating the prevalence and impact of back pain with age have identified a curvilinear association between back pain and age (41, 378). The heightened prevalence of joint pain is attributed by some sources to the greater prevalence of osteoarthritis amongst elderly populations (379, 380). This study also identified that among participants reporting pain, the highest prevalence of osteoarthritis was

reported in the ≥75 year age-group. These findings highlight the necessity for healthcare professionals to continuously assess the nature, cause and progression of pain for a patient with pain as they age and adapt the pain management strategy so as to remain responsive to the patient's changing needs over time.

Analgesics are widely used in the management of pain conditions in primary care. The WHO Analgesic Ladder advocates a pain management approach that responds to pain severity with the aim of providing the patient with optimal pain relief using the most appropriate analgesics (263). A low prevalence of analgesic use was detected in this study, with only 28% of participants with pain reporting the use of an analgesic medication at the time of data collection. This estimate of analgesic usage is lower than other studies of community dwelling individuals with pain conditions in which prevalence has been identified in the range of 45-75% (381, 382). The low estimate of analgesic use in this study may indicate that a proportion of individuals reporting pain do not regularly take an analgesic or may also highlight a sporadic use of the class of medications. A Danish study of community dwelling elderly (n=348) reported a disagreement between the medications prescribed by GPs and those reported by the study population, with approximately 24% of the elderly population not reporting taking medications that had been prescribed. Hypnotics, analgesics, bronchodilators and diuretics were among the most common medications not reported by patients (383). Another study of community dwelling elderly patients (n=100) with CNMP reported that 57% of patients did not take analgesics as prescribed but did not indicate if this was medication overuse or underuse (384). Therefore, while the estimate of analgesic use in this population with pain is undoubtedly an underestimate, it is difficult to determine whether this is associated with under-treatment or under-reporting by participants.

Two multinomial regression models were used to determine the factors associated with the use of analgesics medications by the ageing and elderly population reporting pain in this study. The first model which included all participants with pain indicated that being female, taking ≥5 medications, being retired or unemployed/disabled/carer, having good/fair self-rated physical health, having moderate or severe pain, having pain the restricted daily activity, ≥2 chronic diseases and being a current or past smoker, were significant factors associated with

analgesic use. The second model, which included only those participants with pain that reported an analgesic medication, identified that the likelihood of being in Step 2 (weak opioid) or Step 3 (moderate opioid) relative to Step 1 (non-opioid/NSAID/adjuvant) was associated with taking ≥5 medications or being a past or current smoker. The factors identified in this study as being associated with analgesic use are similar to those reported in other studies. A study of the Swedish Survey of Living Conditions (n=13,295) showed that poor self-rate physical health, lifestyle, sleeping problems, increased health care utilisation, poor levels of educational and marital status were associated with analgesic use (385). Another study of the Danish population (n=45,000) also identified poor self-rated health, increasing age, smoking, low level of education as contributory factors (386). This may indicate that regional differences in prescribing practices do not exclusively drive analgesic use; sociodemographic and disease specific factors are also associated with analgesic use.

According to the WHO Analgesic Ladder, pain severity is a key determinant of progression along the steps of the ladder i.e. there is a linear relationship between pain severity and the use of analgesics of increasing potency (103). This study identified that moderate or severe pain is associated with the use of a non-opioid/NSAID/adjuvant (Step 1), a weak opioid (Step 2) or a moderate opioid (Step 3) relative to no analgesic. There was no association identified between those reporting severe pain and those reporting a strong opioid medication, as would be expected by the guidance of the WHO Analgesic Ladder. However, it is plausible that the pain of the individuals taking a strong opioid is well controlled, therefore, these individuals are experiencing pain of a lesser intensity. Pain affecting daily activities was associated with the use of a strong opioid relative to no analgesic. This finding may provide further evidence that, while severe pain is controlled, the individual's physical functioning remains impaired. The second model did not identify pain intensity as being associated with use of a weak, moderate or strong opioid relative to a non-opioid/NSAID/adjuvant medication. A relationship between pain intensity and analgesic use would have been expected considering the WHO Analgesic Ladder framework. The significance of polypharmacy in both models may be indicative of the aetiology of the pain condition; pain may arise as

a symptom of another chronic condition for which other medications may be prescribed (387, 388).

This study identified that the prevalence of strong opioid use was highest among those with severe pain conditions, with 58% of those reporting a strong opioid also reporting severe pain. However, 652 participants reported severe pain yet only 36 indicated the use of a strong opioid. This perhaps highlights underuse of these agents for the management of pain conditions. Underuse may arise from a physician's unwillingness to prescribe this medication for this population but may also be indicative of a reluctance amongst patients to use strong opioids for pain management (260, 389). The term 'opiophobia' has been used to describe this unwillingness amongst prescribers to use a strong opioid (390, 391). This has been attributed to poor knowledge and experience of opioids, lack of education in pain management, fear of regulatory scrutiny or concerns about adverse outcomes in vulnerable populations (389, 392).

The adverse gastrointestinal effects associated with opioids are well established and can be managed through the concomitant use of a laxative. The START (Screening Tool to Alert Doctors to Right Treatment) criteria recommends that ageing and elderly patients prescribed an opioid should also take a laxative to prevent constipation (393). The concurrent use of an opioid and laxative medication was low in this study, less than 5% although this may be associated with the intermittent and undetected use of OTC laxatives but may also be associated with the underuse of laxatives. A similarly low concomitant use of laxative and opioid medications was reported by Williams et al (335). Allowing for the under-reporting of laxatives, this study outcome may indicate poor implementation of clinical practice recommendations supporting the prescribing of laxatives in patients taking opioids.

Concurrent use of opioids with sedating agents occurs in approximately 20% of this population, with approximately the same proportion reporting concurrent use with both moderate and strong opioids. The prevalence range for the use of opioids and other CNS depressants varies considerable in the literature primarily due to the heterogeneity of study designs, with estimates of 29-60% concurrency rates documented (356, 394, 395) Concomitant use of these medications has the potential to cause harm to the patient and is listed among the

STOPP criteria when prescribing for ageing and elderly populations (393). Exacerbation of the sedative effect of these agents when used with opioids has the potential to produce adverse events which may be further precipitated by a combination of physical and medical co-morbidities in this population. However, the significance of this interaction is difficult to predict given the absence of dosage information although analysis of patient outcomes in future waves of data may provide an insight as to the extent and gravity of adverse outcomes.

The inherent link between the CNMP condition and psychological issues requires that a non-reductionist perspective is taken of the condition (72). The prevalence of depression and anxiety amongst the CNMP condition has been demonstrated and the reciprocal nature of pain and these conditions has been frequently examined (79, 396-398). There was a statistically significant higher prevalence of clinical depression (CESD≥16) when compared to the general population, with a reduced quality of life (CASP-19) score detected for those individuals with pain and clinical depression.

Owing to the complex and subjective nature of pain, evaluation of the condition should extend beyond a one-dimensional assessment of pain severity (62). The QoL of individuals reporting pain may be affected by a multiplicity of psychosocial variables and not simply physical aspects of the condition (399). This study determined the specific features of pain that significantly alter the CASP-19 score for these individuals. Being separated/divorced, having 'Good/Fair' or 'Poor' self-rated physical health, pain limiting daily activities, a CES-D score ≥16, pain 'All Over', and being a current smoker, were identified as significant factors in reducing the quality of life of participants with pain (67). Interestingly, there was no relationship detected between taking specific classes of analgesic medications and QoL. The severity of pain also did not appear as significant in affecting QoL outcomes in this study.

The number of factors that were identified to be associated with QoL in this group of individuals with pain may reflect the complexity of pain conditions and the impact of the condition on the psychosocial dimensions of the affected individual and not merely the physical welfare of the individual. Anxiety, depression, and catastrophizing beliefs about pain are associated with chronic pain and with a poor prognosis in people with various pain conditions (400). This study

found that those individuals with pain with a CES-D≥16 have a CASP-19 score 6 points lower than those with a CES-D<16. Several epidemiological studies have reported an association between chronic pain and depression, indeed, a number of epidemiological studies have identified depression as a strong predictor of chronic pain (79, 401, 402). A study of patients, who were referred to a Danish multidisciplinary pain centre (n=150), reported a SF-36 score lower than the norm values of a Danish population of a similar age and gender distribution. Furthermore, results of the SF-36 measure were highly correlated with the HAD (Hospital Anxiety and Depression Scale) and Psychological General Well-Being Scale (PGWB) scales, correlation coefficients for depression, anxiety, mental health, (validity in the range 0.69-0.79 ($p<0.0001$). It is difficult to establish from this study the directionality of the factors associated with diminished QoL for individuals with pain and the extent to which these factors influence disease severity and prognosis. Nonetheless, the findings highlight the necessity to focus on the impact of the pain condition on the patient and not merely on clinical interventions.

5.10.1. Limitations

The TILDA study does not include individuals aged 50 years and older, who are nursing home residents or resident in another institution. Approximately 21,000 people are residents of such facilities (2008), of which approximately 90% are aged 65 years and older (237, 403). However, it could be said that the exclusion of such individuals is not critical to this research project, as the research question focuses on the management of chronic non-malignant pain patients in the primary care setting.

TILDA participants were asked *"Are you often troubled with pain?"* Those that responded in the affirmative were then recorded as having chronic pain in the TILDA dataset. Since there is no indication of duration in this question, either 3 or 6 months, it is not possible to identify individuals who are reporting chronic pain or acute pain. Furthermore, while those participants reporting pain with a concurrent cancer diagnosis were excluded, so as to ensure pain was of a non-malignant origin; it is possible that individuals did not report a cancer diagnosis to

interviewers. These considerations place limitations on our ability to compare the findings with other studies involving ageing and elderly individuals with CNMP.

There are also a number of limitations relating to the recording and classification of medications in this analysis. A group of medications were identified as adjuvant medications for the purposes of this analysis. However, it was not possible to establish the precise indication for which the medication was originally prescribed using this dataset, since epilepsy is not recorded for all participants in the study. Furthermore, due to the relatively low prevalence of analgesics reported by those with pain and indeed amongst those with no pain, there may be an issue with underreporting of medications that may be considered 'nonessential' or those medications that are used intermittently. It is possible that participants failed to report medications purchased OTC; this is especially relevant to paracetamol-only formulations, non-selective NSAIDs and laxatives examined in this study. In addition, dosage and frequency of use of medication is not recorded within the TILDA dataset; it is therefore not possible to attain information on medication posology. Finally, when considering the analysis of co-prescriptions and the conclusions arising from this phase of the analysis e.g. concurrent use of opioids and laxatives or sedating agents, it is not possible to conclude that such medications are taken concomitantly by patients and only concurrent use can be suspected.

A key limitation of the multinomial regression models is the assumption that individuals are taking one analgesic in the management of the pain condition (the analgesic on the highest step of the WHO Analgesic Ladder). The WHO Analgesic Ladder proposes that additional analgesics of a lesser potency may be added at each step of the ladder to achieve pain relief. For instance, it is possible that an individual reporting a moderate opioid is also taking a non-opioid such as paracetamol. Such possible combinations are not taken in to consideration in this adaptation of the WHO Analgesic Ladder that was constructed for this research. However, the multinomial models were constructed in this manner to avoid multiplicity/double-counting of participants. A second limitation of both regression models is the potential for multicollinearity among independent variables. This phenomenon occurs where the correlations among the independent variables are strong. It may also be described as "interdependence among explanatory variables"

(404). It may result in increased standard errors, and unreliable estimation results in regression models. Thus, it has the potential to make some variables statistically insignificant, while they should be otherwise significant. Further statistical analysis would indicate the extent of multicollinearity in the regression models presented in this study.

5.11. Conclusion

Approximately one third of the population aged 50 years and older reported experiencing pain, however, only a small proportion of these individuals indicated the use of an analgesic medication. This may be associated with under-reporting of analgesics but may also identify a proportion of the population in which pain is unrecognised or undertreated. Non-selective NSAIDs, which are available on a prescription and non-prescription basis, were the most commonly reported, followed by moderate opioids. Use of NSAIDs and opioids, particularly within ageing populations, is associated with the risk of adverse events associated with the often complex physiological and clinical features of this patient group. Guidelines emphasise the importance of physicians recognising and preventing adverse outcomes through prescribing and patient management interventions. OBD associated with opioids medications, for instance, requires a physician initiated laxative regimen. The reported laxative use amongst this opioid-taking population is very low, even when accounting for limitations associated with the data. Furthermore, medications which may precipitate adverse outcomes such as anxiolytics and hypnotics are reported concurrently with opioids, to a greater extent than laxative medications. These findings may highlight potentially inappropriate prescribing practices particularly relating to moderate and strong opioids amongst ageing and elderly populations reporting pain.

What is already known about this topic:	Analysis of the HSE-PCRS dataset has indicated that there is a higher consumption of non-opioids and systemic non-selective NSAIDs than opioids in the general population. This analysis has also indicated that there is a relatively low concurrency of use of laxatives with weak and moderate and strong opioids but a much higher concurrency with sedating agents.
	The WHO Analgesic Ladder suggests that pain patients should progress upwards through the analgesic ladder in accordance with pain severity. However, evaluation of the literature relating to prescribing in the elderly and the guidelines directing the management of opioid medications indicate that certain medications should be used with caution in the elderly. The ladder must therefore be adapted to meet the clinical needs of the indvidual pain patient.

What this Study adds:	The TILDA dataset facilitated detailed analysis of a variety of demographic, social and clinic descriptors of pain. There is a higher prevalence of analgesic use amongst those with pain in comparison to those who did not report pain. Non-selective NSAIDs, moderate opioids and non-opiods are amongst the most reported analgesics in this study.
	The two regression models contribute to our understanding of the factors associated with positioning on the analgesic ladder or absence from the ladder. Increasing pain severity is associated with use of an analgesic but this does not follow the linear pattern directed by the WHO Analgesic Ladder (increasing pain severity and the use of analgesics of increasing potency). There was no association identified between those reporting severe pain and reporting a strong opioid medication relative to no analgesic, as would be expected by the guidance of the WHO Analgesic Ladder.
	QoL has previously been demonstrated to be reduced by the presence of pain, this is suported by the findings of this study. QoL is influenced by a number of factors including age, martial status, pain limiting daily activities, a CES-D score $\geq$16, self-rated physical health, the location of pain and smoking status. A number of these factors relate to the social, behavioural and lifestyle dimensions of an individual with pain and are not exlusively features of the condition. It is notable that QoL is not affected by positioning on the WHO Analgesic Ladder according to this study.

Chapter 6. General Practitioner Perspectives and Experiences of the Pharmacotherapeutic Management of Chronic Non-Malignant Pain in the Irish Primary Care Setting

6.1. Background

Rational prescribing has been defined by the World Health Organisation (WHO) as the provision of medications to patients that are 'appropriate to their clinical needs, in doses that meet individual requirements, for a sufficient length of time with the lowest cost' (405). The prescribing process can therefore be complex, as it may require the physician to initiate, monitor, review and modify the pharmacotherapeutic regimen so as to reach a satisfactory clinical and cost-effective outcome (405). Painful conditions are one of the most common reasons for consultations in primary care (260, 406); there is consequently a high volume of analgesics prescribed by primary care physicians in the management of pain conditions (407-411). Chronic pain conditions may cause the patient to attend a physician on numerous occasions if an effective pharmacotherapeutic intervention is not initially identified or if the severity of the pain worsens (412, 413). It is important to consider also that due to the multifaceted nature of CNMP, satisfactory management of the condition with medications alone may not be possible. The physician may then have to identify supplementary or alternative interventions to assist the patient. These may include physiotherapy, occupational therapy, surgical interventions or self-management strategies (414). However, given the limited resources available in the Irish health system at present, particularly in the public system, these additional interventions may be difficult to access. It is reasonable, therefore, to focus on the manner in which CNMP is managed with analgesics in primary care and on the factors that influence the prescribing of these medications.

Previous studies investigating the prescribing process have described a hierarchy of factors that determine this decision making process (415, 416). These factors may be categorised as micro, meso, and macro, depending on whether they are specific to the physician-patient consultation (micro), reflective of regional requirements or practices in prescribing (meso), or arise from national or international influences (macro) (416).

Micro level factors are primarily concerned with the clinical aspects of patient management such as disease severity, concurrent medications and the comorbidities of the patient. The development of safe and effective analgesic regimens may be particularly challenging with ageing and elderly populations due to altered pharmacokinetics, pharmacodynamics, and sometimes, cognitive states

of patients. This population may also have a higher prevalence of frailty, co-morbidities and polypharmacy (333, 417). The prescribing of NSAIDs and opioids presents particular clinical challenges for prescribers because of the adverse effects and cautions associated with these drug classes. There is a risk that such concerns amongst prescribers, about the potential for adverse events with these medications, may cause suboptimal pain management in elderly populations (113, 418). However, such clinical concerns may be exaggerated and this may also contribute to under-treatment of pain in these populations (62). The confidence with which a physician prescribes these analgesics may be dependent on their knowledge of these clinical considerations. This is related to the individual's education and training in pain management during medical school, residency or participation in continuing professional development (419). Appropriate education and training has been demonstrated to be essential for safe and effective prescribing but additionally for medication management. CPD is also essential to keep abreast of developments in clinical practice to ensure optimal outcomes for patients (420). Furthermore, the physicians' attitudes and perceived goals of pain management or concerns about professional scrutiny in the prescribing of opioid analgesics may produce variability in the prescribing of certain medications for patients (260, 421).

Meso factors are intermediate variables that relate to the localised practice setting of the GP and describe the role of localised formularies, access to secondary or specialist care and the cultural role of healthcare professionals in relation to patients. Barriers to effective pain assessment and management in the healthcare system arise from poor or absent practice standards and failure to manage patients between primary, secondary and tertiary care (62). The issues associated with access to secondary and tertiary care in Ireland have been discussed at length in *Chapter 1*. The dynamic between the physician and patient may determine the outcome of the consultation and is largely informed by cultural and societal perspectives of the role of physicians in the delivery of care. There is an increasing desire for a shared decision making approach in which consensus is reached between in the development of an analgesic regimen (422). Such an approach would not have been considered under the traditional paternalistic model of physician management (216, 423). Shared care models are more common amongst

younger and better educated patients with certain ageing and elderly patients satisfied to allow the physician manage care independently (424).

Macro factors, describe those which are relevant to a national and international context, are common to most clinicians and not specific to the local primary care environment (416). These include, the information disseminated to physicians through guidelines, conferences, evidence-based journal articles or literature from pharmaceutical companies. Guidelines and evidence-based literature allow prescribers to make informed decisions on appropriate medications and analgesic regimens for a variety of populations in advance of a consultation with a patient. Guidelines have been demonstrated to improve the quality of patient care and improve the cost-effectiveness of healthcare interventions when incorporated into a patient management plan (295). Barriers to their use in practice include a lack of awareness and familiarity (425). There are currently no specific guidelines in Ireland directing the pharmacotherapeutic management of CNMP for the general population or elderly populations. It is therefore perhaps not an issue with an awareness of guidelines that produces variability in prescribing practice in Ireland, rather, it may be associated with the lack of any specific guidelines in this area at present (425). Pharmaceutical companies supply marketing material to physicians which provide information on a medication, but they also seek to promote its use. This also contributes towards the prescriber's knowledge of the medication and the perceived acceptability of a medication to the public. Studies of exposure of physicians to marketing literature demonstrates that they produce higher prescribing rates for the medication (211).

In summary, factors affecting the prescribing decision-making process extend beyond clinical considerations and include external influences associated with cultural practices, healthcare system limitations and information disseminated to prescribers (426). Since GPs are primarily responsible for daily management of CNMP patients in Ireland, an understanding of their approach to the prescribing of analgesic medications is an important focus of this research.

6.2. Aim & Objectives

The aim of this study is to describe the experiences and attitudes of GPs in relation to the prescribing of analgesic medications, particularly opioids, for ageing and

elderly patients with chronic non-malignant pain conditions. The primary objectives are to:

1. Describe the nature and extent of consultation with clinical practice guidelines or evidence based guidance in the management of ageing and elderly patients with CNMP.
2. Examine GP perceptions of the management of CNMP with analgesics, in particular, opioids.
3. Describe the current practices and perceptions of GPs in the use of concurrent medications particularly sedating agents and laxatives with opioid analgesics.

6.2.1. Study & PhD Objectives

This study was conducted to meet Objective 3 described in *Chapter 2*: To investigate the factors affecting the prescribing of analgesics for ageing and elderly populations by primary care physicians in the Republic of Ireland.

6.3. Methods

Qualitative research, grounded in the constructivist philosophy, seeks to examine social settings or groups of individuals that inhabit these settings (271). This method allows researchers to access and evaluate unquantifiable information based on the process of observation or interaction with the subjects of interest, acknowledging the complexity of people or the phenomenon under-investigation (427).

The consolidated criteria for reporting qualitative research (COREQ-32) is a checklist for reporting qualitative research studies. The criteria are listed in *Appendix E: E.1*. The framework is similar to the reporting criteria for quantitative research studies such as observational research or randomised control trials and may enhance the transparency of qualitative research studies. The checklist incorporates 32 items across the 3 domains of research team and reflexivity, study design and analysis of findings (428). The COREQ-32 criteria form the framework for reporting the qualitative research in this chapter, and in *Chapter 7*.

6.3.1. Ethical Approval

Ethical approval was gained from the Health Sciences Research and Ethics Committee, Trinity College Dublin, in March 2013. It was proposed that GPs in the study could seek Continuing Professional Development (CPD) credits for completing the interview process. The Irish College of General Practitioners (ICGP) had been approached prior to submission of the ethics application and had permitted that participating GPs could apply for CPD credits following completion of the interview. The Research Ethics Committee expressed reservations about awarding CPD credits to GPs for completing the study, indicating that it may be an unethical incentive for potential participants. This was disputed by the researcher as the inducement was neither a monetary reimbursement nor a gift, but instead, acknowledged the time spent by the GP reflecting on the topic and in discussion with the researcher. Furthermore, this group could not be considered to be a vulnerable population in relation to the researcher. This was a discussion between two healthcare professionals, with no information or power asymmetry between parties; there was therefore thought to be no threat of coercion for potential interviewees (429). Upon appeal by the researcher, the Research Ethics Committee TCD granted approval for the project but noted their concerns in the letter of approval (*Appendix E: E.2*).

6.3.2. Data Collection, Sampling & Recruitment

Interviews may be structured, unstructured or semi-structured depending on the rigidity of adherence to the interview guide. Structured interviews do not permit deviation from question order or wording, nor does it permit clarification of questions or answers about the interview questions by either the interviewer or the participant. By contrast, unstructured interviews do not possess a question order; clarifications of questions or answers are permitted and questions may be added on at the discretion of the interviewer (427, 430).

A semi-structured interview approach was selected for this qualitative research. The same questions were asked of all participants, however, the order and language of questions was adapted to suit the individual and probing questions were asked when interesting relevant information came to light. This approach was

selected as it ensured that all GPs were asked similar questions yet the tone or subject could be adapted to reflect the variability of the participant's responses (430, 431).

6.3.2.1. Sampling and Recruitment

A purposive sampling approach was initially used to recruit GPs for the study. The Irish Medical Directory (IMD), which contains a list of all registered medical practitioners in Ireland in general practice and hospital sectors, was the sampling frame for the selection process. This alphabetical list, which is updated annually, divides practitioners according to practice region at a county level. In addition to the name and practice area of the GP, the IMD provides the address of the GP practice, telephone number and e-mail address.

GPs were selected at random from the IMD from Leinster, Connaught and Munster regions. This was achieved by inputting all names in to an Excel file and generating random numbers which identified a number of potential GPs from the list. Having identified 50 GPs within these geographical regions, a letter of invitation, a consent form a participant information leaflet and a stamped addressed envelope were posted to all randomly selected GPs (*Appendix E: E.3, E.4, E.5*). As demonstrated in *Figure 6-1*, this initial approach to recruitment was unsuccessful and only recruited 3 interviewees (representing an uptake of 6%).

A chain referral or snowballing approach was then adopted to recruit the remainder of GPs until data saturation was achieved (432). There is no commonly accepted test for saturation in qualitative research (433). Francis et al proposed that data saturation could be identified based on an appropriately sized sample or by 'defining stopping criteria' e.g. number of additional interviews required before data saturation is reached (434). It was decided that at least 3 additional interviews would be completed once no new themes emerged from the preceding interviews.

Two GPs based in the Health Research Board (HRB) Centre for Primary Care Research, RCSI, a department which is affiliated with the HRB PhD Scholars Programme, were approached by the researcher requesting an interview for the study. One of these GPs suggested four former colleagues that might be interested in participating in the research. Two further participants were recruited having

contacted these GPs. One of these GPs suggested a former colleague who may also be interested in participating in the research. This GP was contacted and completed an interview with the researcher. This individual suggested a further five GPs to the researcher. The remaining four interviewees were recruited having contacted these individuals. A summary of this snowball method is presented alongside the purposive sampling approach initially selected by the researcher in *Figure 6-1*.

GPs were excluded from the study if they did not practice predominantly or exclusively in the primary care setting or if they did not treat patients aged 65 years and older with CNMP. The process of recruitment finished when data saturation was reached, i.e. no additional themes were raised during the interview process. Data saturation was achieved following 7 interviews, however, a commitment had been made to interview the remaining 5 GPs by this stage, and these interviews were duly conducted.

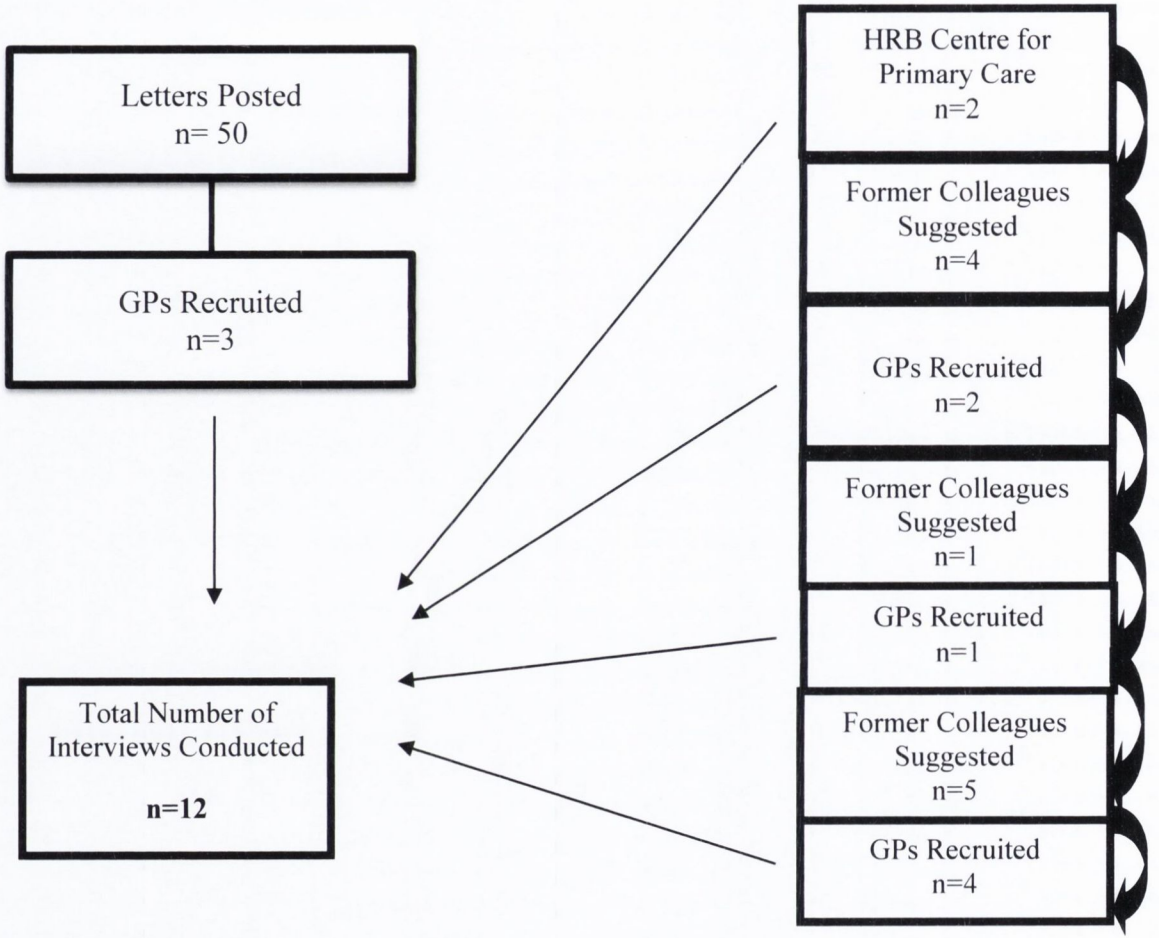


Figure 6-1: Purposive sampling (left) and snowballing approaches to recruitment of GPs (right)

According to ethics requirements sufficient information must be provided to potential participants and supplemental information should be made available upon request. This information is necessary to allow the individual to make an informed decision on participating in the research study (429). Requesting that participants sign a consent form increases the likelihood that the individual understands the risks and benefits of participation and their rights in terms of confidentiality and anonymity (429). In this instance, interviews were only conducted upon receipt of a signed consent form, in addition, a minimum of 5 days was allowed between signing the consent form and conducting the interview to allow participants time to reconsider participating in the study.

Five male and seven female GPs completed interviews with the researcher. GPs recruited into the study practised in both rural and urban settings and had been working as GPs in a time span ranging from 3 and 30 years. All GPs completed their undergraduate education in an Irish university.

The interview guide was developed following consultation with the literature and the questions raised from the findings of the systematic literature review (*Chapter 3*) and the TILDA study (*Chapter 5*). *Figure 6-2* provides an outline of the question themes, interview questions and provides an explanation for inclusion of this question(s) in the interviews with GPs.

Question Theme	Statements /Questions in Interview Guide	Reason for Inclusion of Statement/Question
Introduction and explanation of process	Thank you for agreeing to participate in this interview on the management of chronic non-malignant pain by General Practitioners. Chronic non-malignant pain is that which persists for a period of longer than 3 months and arises from several causes such as osteo and rheumatoid arthritis, lower back pain and neuropathic pain. Effective management of pain in this group of patients can be difficult. It might be even more difficult for ageing populations i.e. those aged 65 and older because of other medical problems in this patient group and the medications that these patients might be taking. We have very little information on the practices of GPs in the management of this population group for instance the experiences you have with the use of certain types of painkillers and the types of concerns you might have with prescribing painkillers for this patient group. I was hoping that we might be able to discuss your experiences with managing chronic pain conditions with your elderly patients and perhaps provide me with some insight as to how you approach pain management with prescription and non-prescription painkillers	Describes the aims and objectives of the study.
Experiences and Attitudes in the Prescribing of Analgesics	Do you treat many patients aged 65 and older for chronic pain conditions in your practice? What are the most common types of pain conditions you see on a day- to-day basis? What is your approach for managing patients aged 65 and older with chronic non-malignant pain conditions in your practice? How does this contrast with your management of pain in younger populations? ➢ Assessment? ➢ Initiation on painkillers? Do you feel confident managing these patients in the primary care setting? (*Prompt: access to specialist management*) Do you feel confident prescribing analgesics for these patients? At what point in the management of a patient's pain condition do you consider initiation of an opioid analgesic medication? How does this contrast with your management approach in you younger populations?	Gain understanding of practice setting, patient population and frequency of encounters with patients presenting with CNMP conditions
Support Available to GPs	What is your opinion of the support available to GPs in the management of CNMP patients i.e. referral to physiotherapists, occupational therapists, pain clinics etc? *(Prompts: Ease, Cost-Effectiveness)*	Discussion about the role of the GP in the management of patients with CNMP with a focus on referral pathways to

		allied healthcare professionals, pain specialists and pain management clinics.
Prescribing Analgesics for Ageing and Elderly Populations	Do you prescribe opioid type medications for patients with chronic pain conditions? Can you tell me about the circumstances under which you are more likely to prescribe an opioid analgesic? Some patients wish to continue taking opioids on a long-term basis. What are your thoughts on prescribing opioid analgesics on a continuous basis for your patients? At what point do you decide to change from one opioid formulation to another? *(Prompt: Is this a consistent approach for all patients?)* Are there any circumstances under which you would not prescribe an opioid analgesic to a patient? What is your approach to discontinuing a patient from an opioid analgesic?	Prescribing process undertaken by the GP investigating the clinical and patient factors that lead to the prescribing of certain analgesic medication
Patient-GP Interactions	Do you think that your patient's expectations of a doctor's visit influence your prescribing of analgesics?	Discussion on the interaction between the GP and patient and how it influences prescribing decisions.
Adverse Effects Associated with Opioids and Management of Adverse Effects	Are you concerned about the adverse effects such as constipation and nausea arising from opioid use? Do you take steps to prevent/manage such adverse effects? For instance do you prescribe laxatives when you prescribe opioids? Do you consider the sedative medications such as sleeping agents and benzodiazepines that the patient might be taking when you prescribe opioid medications?	Discussion on experiences with use of opioids in ageing and elderly populations and adverse outcomes associated with opioids.
Clinical Practice Guidelines and Prescribing Information	*In some countries such as the United States and Canada there are many clinical practice guidelines available. These clinical practice guidelines provide advice to physicians on the types of analgesics that are appropriate for the management of different types of pain conditions and the steps that should be taken to ensure optimal management whilst minimising risks associated with therapy* Do you consult guidance on prescribing such as the BNF or other guidance before selecting an opioid formulation for a patient? If so what guidance? Do you think that such guidance would be useful to you in your everyday practice? Who do you think should issue this guidance?	Discussion on the information sources accessed by GPs to gain more information on analgesics medications.

Closing statements for interview	Thank you again for taking the time to complete this interview. I will send you a copy of the interview transcript in the coming weeks. You will have an opportunity to remove any comments from this transcript. You may also still withdraw from this study if you are no longer willing to participate.	Provides information on supply of the transcript to the participant and their right to edit the transcript or remove themselves from the study.

Figure 6-2: Question themes, interview questions and reason for inclusion of question

Four interviews were conducted in person, with the remaining 8 interviews conducted by telephone. All interviews were completed by the research, Mary-Claire Kennedy and were audio-recorded using the free download software package Audacity® and also with the Olympus Digital Voice Recorder VN-712PC. All recordings on the Olympus recording device were also saved onto the researcher's password protected laptop. *Table 6-1* summarises the duration of interviews and information on transcripts edited by the participating GP. Interviews were then transcribed verbatim and disseminated to all participants for review and revision if appropriate. Passages of text that were to be removed prior to analysis were highlighted by the researcher. These passages of text revealed geographical location or the names of family members, or healthcare professionals associated with the participant. It was essential that these segments were removed from the transcripts; as the sensitivity of the topics discussed over the course of the interviews, confidentiality was of utmost importance. Any revisions made to the transcripts were applied by the researcher prior to beginning analysis.

Table 6-1: Interview duration and additional information relevant to interview transcripts

Participant Number	Interview Duration	Additional Comments
1	15min 20sec	Transcript Edited
2	21min 43sec	Transcript Edited
3	31min 00sec	Transcript Edited (Interviewed In-Person)
4	17min 22sec	Transcript Edited
5	48min 52sec	Transcript Edited
6	16min 04sec	Transcript Edited
7	17min 19sec	Transcript Edited
8	36min 09sec	Transcript Edited (Interviewed In-Person)
9	15min 08sec	Transcript Edited
10	26min 21sec	Transcript Edited (Interviewed In-Person)
11	33min 04sec	Transcript Edited
12	22min 57sec	Transcript Edited (Interviewed In-Person)

6.3.3. Data Management and Analytical Approach

Qualitative data, particularly semi-structured interviews, presents a large amount of information to the researcher. As such, analysis required a degree of abstraction and generalisation to produce a cohesive set of findings (8). The Framework Method of Data Management and Applied Thematic Analysis techniques were employed for management and analysis of data arising from interview with GPs. *Figure 6-3* summarises the various stages of data management and analysis.

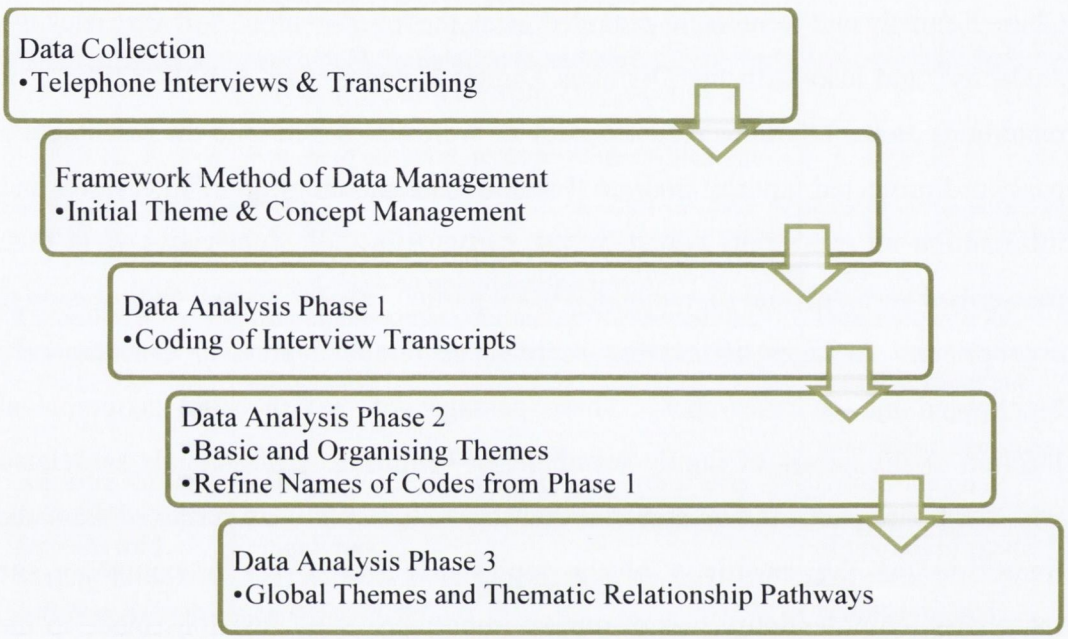


Figure 6-3: Collection, management and analysis of interview transcripts

6.3.3.1. The Framework Method of Data Management

The Framework Method of Data Management facilitates the condensing of data through summarisation and synthesis of categories. The approach was developed in the 1980s by the National Centre for Social Research (UK) (435). The NVivo® Version 10 software package has incorporated a facility to arrange the data using the Framework Method. The Framework Method requires that data arising from the interviews is summarised and entered into a document resembling an Excel file; each row of the spreadsheet represents an interviewee, while each column is a theme or concept relevant to the transcript. Upon inputting a summary of the information or a direct quote from the transcript into the spreadsheet, it is possible to maintain

a link to the original data source through electronically labelling and linking the data to the original transcripts that are uploaded on programme. The steps involved in the Framework Method are summarised in *Figure 6-4*, (436). The data management categories created for this research study are presented in *Table 6-2*.

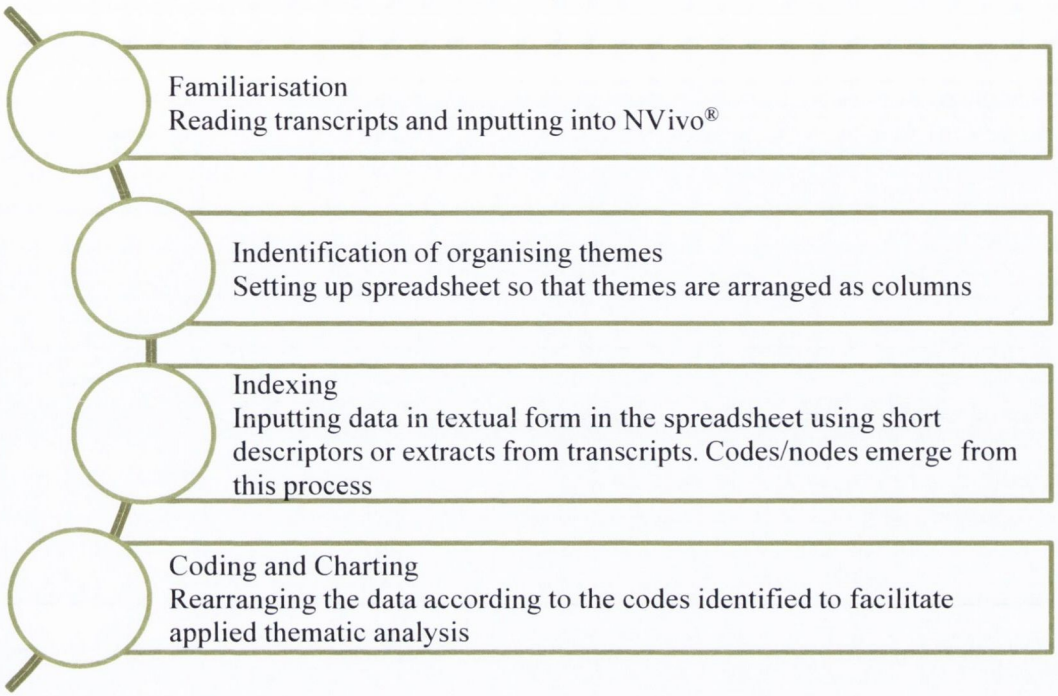


Figure 6-4: Description of phases of framework method of data management

There are several advantages in organising qualitative data in this manner at the outset of the research process. Firstly, the process of data management allows the researcher to come into contact with the data for the first time, themes, networks of themes and conceptual models may become apparent at this early stage. It is also possible to compare and contrast the responses of interviewees by observing the types of responses in each row and also the overall themes emerging from the data by comparison of the data contained in the columns. Finally, this approach facilitates the development of an audit trail for the researcher in organising and analysing the data thereby enhancing the integrity and credibility of the findings of the research.

Table 6-2: Framework data management categories

A : Types of CNMP	B : Description of Medical Practice	C : Assessment or Evaluation
D : Stepwise Approach WHO Model	E : Paracetamol	F : NSAIDS
G : Strong Opioids	H : Adjuvant Medications	I : Decision Making Process
J : Clinical Challenges in Prescribing	K : Access to Services for Patients	L : Use of Clinical Practice Guidelines or Literature
M : Personal Experiences with CNMP Management	N : Fellow Healthcare Professional Advice & Support	O : Additional Interventions
P : Comparing Primary Care with Other Settings	Q : Additional Comments	

6.3.3.2. Applied Thematic Data Analysis

Applied thematic analysis incorporates various qualitative approaches for data analysis and interpretation, including, grounded theory, positivism, interpretivism and phenomenology (437). This is an iterative approach which requires the researcher to reflect on the transcripts and consult with parties external to the analysis phase to ensure integrity of the process. It may be subdivided into three phases reflecting the evolution of analysis from descriptive codes to analytical themes. A theme is defined as 'an abstract entity that brings meaning and identity to a recurrent experience and its variant manifestations' (438). It is an important concept contained within the dataset and is a form of patterned response (439). Themes may be subcategorised as follows:

- Basic: Lowest order premise emerging from text
- Organising: Categories of basic themes combined producing an abstract principle
- Global: Represent principle metaphors of the dataset

This method of developing and categorising themes is also a helpful starting point to capture relationships between themes. This may be considered an inductive approach to analysis, as themes are identified at the lowest order and integrated to develop organising and global themes. It was applied to the thematic data analysis as follows (440):

Phase 1: Coding of dataset

Prior to beginning a broader thematic analysis of interview transcripts and elucidation of theories from the data, smaller groups of concepts or codes were identified from the transcripts. Codes identified in Phase 1 of data analysis should reflect the purpose of the research, be exhaustive, mutually exclusive and sensitive to category content (438, 441).

The term code is used interchangeably with node in the literature; the NVivo® software package refers to codes as nodes. Codes may be categories, themes or relationships of meaning contained within the transcripts (437). A code may be sub-divided into a parent and child node characterising a hierarchical relationship in defining a concept. Codes were refined into shorter names or

subdivided or merged until a finalised codebook was produced. The codes in this instance formed the basic themes in the analysis.

Phase 2: Identifying themes

Development of organising themes following completion of the coding phase imposes an additional hierarchical structure to the analysis and also permits the initial mapping of inter-relationships between codes. Themes were continuously refined throughout the exploratory phases of analysis, to an extent that they were discrete and non-repetitive. As the analysis progressed and themes became more defined, the hierarchical structure and the terms used to represent themes became more sophisticated.

Phase 3: Global themes and thematic networks

Global themes began to emerge following refinement of organising and basic themes and also through consultation with the existing literature. Global themes move beyond the semantic overview of the basic nodes and organising themes and make it possible to propose theoretical relationships between global themes; this was assisted by consultation with the supervisory team and informed also by an extensive review of the literature on the subject (439, 442). *Figure 6-5* provides an example of the organisation of themes into basic, organising and global. Upon completion of this phase of data analysis, a member of the supervisory team (MH) reviewed a sample of the transcripts to ensure that coding and thematic analysis was correct and exhaustive.

Healthcare System (Global Theme)
Primary Care (Organising Theme) Role of GP (Parent Node) *Advice* (Child Node)

Figure 6-5: Example of Global, Organising and Basic Themes (Parent & Child Nodes)

6.4. Results

Four global themes were identified following completion of data analysis:

1. Clinical Factors
2. Guidance & Information
3. Non-Clinical Factors
4. Non-GP Management

The results section presents an outline of the key parent and child nodes that informed the development of these organising and global themes, an overview of which is presented in *Figure 6-3*; these will be discussed in further detail in this section. A completed COREQ-32 checklist for this study is provided in *Appendix E, E.6*.

Table 6-3: Parent and child nodes, organising (horizontal) and global themes (vertical)

<table>
<tr>
<td>Analgesic Prescribing Approach
Adjuvant/Neuropathic Agents
NSAIDs (Selective & Non-Selective)
Paracetamol
Weak, Moderate and Strong Opioids
Evaluation & Assessment Pain Severity
Examination
Observation
Pain Scales
Patient Description
Re-Evaluation of Pain
Risk-Benefit Evaluation
Adverse Effects
Neuropathic Agents
NSAIDs
Opioids
Contraindications
Risk of Misuse</td>
<td rowspan="2">Clinical Factors</td>
<td>Non-GP Management
Additional Interventions
Improving CNMP Management
Pain Clinics
Pain Consultants
Pain Management Programmes
Secondary Care
Physiotherapy</td>
<td rowspan="2">Non-GP Management</td>
</tr>
<tr>
<td>Financial
Patient Perception of Drug Efficacy
Paracetamol
Engagement with Patients
Communication
Empathy</td>
<td>Non-Clinical Factors</td>
</tr>
<tr>
<td>National
Clinical Practice Guidelines
CPD Events
International
Clinical Practice Guidelines
Evidence Based Journals & Databases
Formularies
Pharmaceutical Companies
WHO Analgesic Ladder</td>
<td>Information & Guidance</td>
<td colspan="2"></td>
</tr>
</table>

6.4.1. Theme 1: Clinical Factors

Establishing pain aetiology, severity and progression, together with a consideration of the risk-benefit ratio of selected interventions, are key clinical factors contributing to the GP management plan for ageing and elderly patients with CNMP. Risk-benefits included efficacy of analgesia and the potential adverse outcomes associated with specific medications in ageing and elderly populations. The importance of gathering a patient history, particularly details of historical or current alcohol or drug misuse, is referenced in the context of prescribing strong opioids. Cautions and contraindications to a medication arising from co-morbidities or medical history contribute to the overall assessment conducted by the GP upon initial consultation and subsequent review of elderly patients with CNMP. Indeed, the process of consulting with the patient to establish the nature and severity of the pain may be considered as a cyclical process, as the GP reconsiders each of these factors with each consultation or prior to initiating a new analgesic. An overview of clinical factors associated with prescribing analgesics in primary care is presented in *Figure 6-6* and discussed in greater detail below.

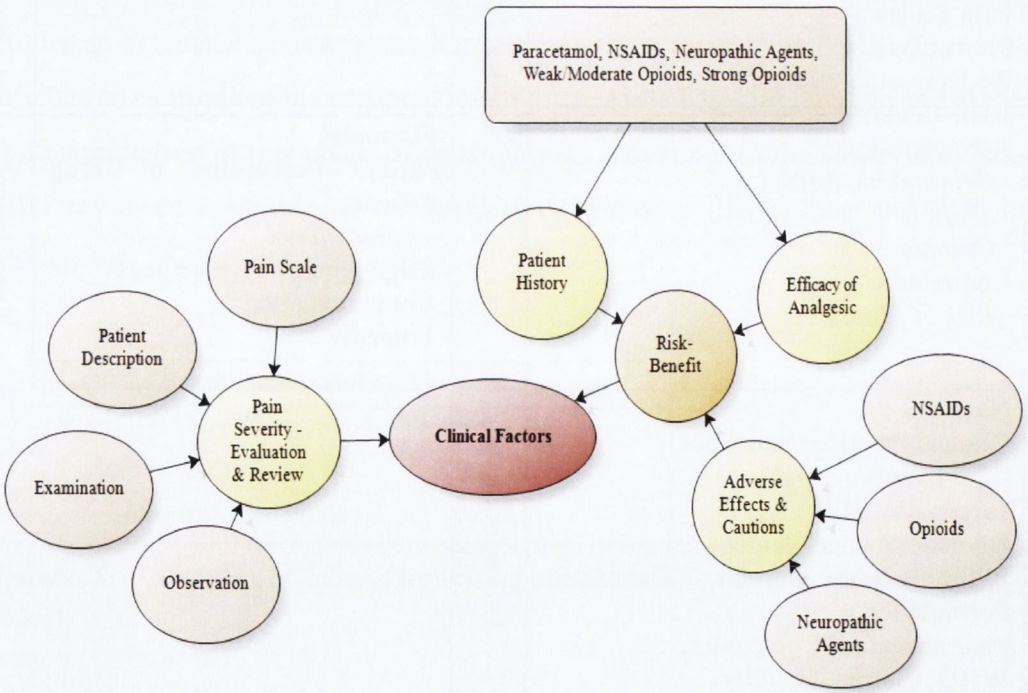


Figure 6-6: Clinical factors associated with prescribing analgesics in primary care

6.4.1.1. Pain Severity, Examination & Re-Evaluation

GPs were asked to describe their approach to assessment of a patient presenting with pain. The purpose of this question was to gain an understanding of the GP's general approach in determining pain intensity and the application of this information to the prescribing decision making process. A number of GPs described gaining an understanding of pain severity based on the extent to which pain impacts upon the patient's activities of daily living.

I'd be examining them, I'd have a fair idea about how much restriction this is giving rise to, I will want to know how bad it is and I will want to know are they having it at night... I will want to know are there any other associated features [pause] *is it radiating and all that kind of stuff.* (GP10)

The severity of the pain, the type of the pain and what has been done for the pain so far and I suppose ideally you would have to diagnose before you go for pain management, I suppose that is usually [pause] *is pretty evident but sometimes maybe not so.* (GP7)

When asked if a validated scale is used to calibrate pain intensity, several GPs reported they did not incorporate this into their everyday practice. Rather, nine GPs described gaining an understanding of the severity of the condition based on impact on daily activities and comparing this to a time in the past:

I don't use standardised scales for pain, it is often volunteered by the patient who comes and says they are in pain and then over time it gets to where a pattern is established where certain medication is being prescribed regularly. (GP9)

No, I don't use a scale, I probably should, but I don't. Generally, it's based on patient's symptomatology and how they can function, like you know, what they can't do anymore I guess; in terms of their day to day living. (GP12)

Those GPs that reported use of a scale described a simple zero to ten scale to rate pain:

A lot of the time I ask them to rate it on a scale of one to ten, ten being the worst pain they have ever had, it's not very sophisticated but that would be the usual one. (GP4)

One GP described using the pain scale as a method of explaining the stepwise approach to prescribing analgesics to patients.

I would explain to them that we would grade their pain 0 to 10 today and we would try something that's safe, assuming that it's going to be chronic pain relief, I would say to them, "Let's start simply and give you options." (GP 11)

According to all GPs interviewed, having established the nature and severity of pain and upon reaching a diagnosis, in most instances, an analgesic is prescribed. GPs then described regular reviews of patients either in person or over the telephone to determine the efficacy and suitability of the prescribed medication. The process of review and re-evaluation was described by GPs as a continuous and essential process in effective patient care:

I always review them, well I always give them a week or two, I don't necessarily need them to come to me, they can sometimes call me by telephone and tell me how they're getting on, but yes, I mean I wouldn't leave it any longer than a couple of weeks to see how they're doing and they know they can come back to me sooner than that if they are in trouble (GP12)

6.4.1.2. Risk-Benefits

GPs discussed the appropriateness of a selected therapy in terms of a risk-benefit assessment for that patient. As may be expected, the patient's medical history, psychosocial background, co-morbidities, concomitant or concurrent medications and adverse outcomes were central to the prescribing decision pathway, balanced with the pain relief achieved by the medication:

It's a very fine balancing act... you have to take into consideration that there are serious side effects, but on the other hand sometimes if their pain isn't well controlled then you have no choice but you know to step up the ladder and put them on stronger pain killers. (GP12)

Efficacy of Analgesia

Efficacy of analgesia is discussed in the context of the WHO Analgesic Ladder; if an adequate response is not attained by a selected medication, then the next step in the ladder is considered. However, GPs described their ardent efforts to maintain the patient on the lowest step of the ladder or attempt to step down from more potent medications once pain relief is attained or acute exacerbations are overcome. All GPs referred to starting on Step 1 of the WHO Analgesic Ladder and progressing to opioid containing formulations upon failure of these Step 1 agents:

Usually I would start with an NSAID if it's OA [osteoarthritis] *type pain or I usually do try to get people onto regular paracetamol 1gr tds ongoing but I find that people don't have much faith in it like and they have usually tried it and even if it's in conjunction with something else they will usually be not keen on starting it* [pause] *but ideally I would start them on paracetamol and move up to an NSAID and then onto something like tramadol* (GP2)

GPs described their conservative approach to prescribing opioid containing formulations and listed concerns about clinical appropriateness and the risk of tolerance and addiction as the reasons for reluctance in initiating opioid analgesics:

If I am needing to use something in the longer term then I would try to use a combination low dose, a paracetamol with a codeine. So I would probably step up to something like Solpadeine®§ to see if that would help and try to get them to come back and review in two weeks to see where they are at. (GP4)

§ Paracetamol 500mg/Codeine 8mg

There was a recurrent pattern amongst GPs describing the necessity to constantly review opioid formulations prescribed for patients so as to minimise long-term use and the potential for adverse outcomes. This is particularly the case with formulations containing opioid analgesics ranging from high doses of codeine to the more potent tramadol formulations or buprenorphine and fentanyl patches, Steps 2 and 3 of the WHO Analgesic Ladder respectively:

Battling to try and keep people on the lower end of the scale so you know encourage them to stay with regular paracetamol qds, or moving to Solpadeine®, so I would rarely move to something higher than that until you get into I guess what you are talking about, chronic pain patients. (GP9)

If pain relief cannot be attained by those analgesics in Step 2 of the ladder or with neuropathic/adjuvant agents, GPs described cautiously moving to the strong opioids upon consultation with the patient. However, four GPs indicated that they would refer the patient for management by a consultant at this point:

Yes for non-malignant chronic pain I would move up to tramadol and then I would add in probably at that point then amitriptyline or pregabalin. I generally [pause] *I wouldn't go much beyond* [pause] *in terms of me initiating the treatment I wouldn't go much beyond tramadol.* (GP6)

I would be quite cautious about starting patients on those, particularly for what appears to be [pause] *what is likely to be a chronic problem. I would definitely* [pause] *I do prescribe them but with a lot of reservations particularly Solpadol®** and Ixprim®†† things like that. Solpadeine® I would prescribe a bit more easily.* (GP6)

Another GP observed that while they were comfortable with prescribing a strong opioid such as buprenorphine for palliative patients, patients with severe non-malignant pain would only receive this type of medication following initiation

** Paracetamol 500mg/Codeine 30mg
†† Tramadol 37.5mg/Paracetamol 325mg

or review by a specialist, in this way stratifying patients according to the aetiology of their pain:

There are a few people who would be non-palliative but it would be mostly palliative [pause] *it is strange I almost stratify people* [pause] *like severe OA* [osteoarthritis], *I think I would be comfortable using some of the topical patches.* (GP9)

Opioid patches were referenced by six GPs as a preferred method of drug delivery, describing this as the drug administration system of choice when prescribing strong opioids for elderly patients. Indeed, GPs described being comfortable with maintaining the patient on this formulation, with continuous review for an indefinite period:

I would have been always very cautious in that sense and I did find the arrival of the opiate patches a huge relief to my stress over managing people who were going to have ongoing, continuous pain and we really have to put something significant in place on an ongoing basis (GP11)

If I've put somebody on a BuTrans®‡‡ patch, a low dose once a week and their pain is well controlled on that, I would leave them on that indefinitely. (GP12)

However, one GP described his reluctance in prescribing these agents and continuing the therapy for an indefinite period:

I'm certainly not a fan of using opiate patches. I know they are very commonly used, I am not a fan of them [pause] *certainly in people I have used them in it would be for an agreed period of time with a view to reviewing them and with a view to getting them on to the lowest dose that you possibly can I am always trying to get them to wean down to the step below, I certainly try not to leave people on patches long term.* (GP5)

‡‡ Buprenorphine

Patient History

As suggested by clinical practice guidelines a history of substance addiction or misuse is a contraindication to the use of certain analgesics such as opioids in patients presenting with pain; this is stated by some GPs as a key consideration when initiating analgesics:

You would want to be sure it was going to be short term and that you could do it [pause] *so you would want to know there is no history of any addiction.* (GP5)

One GP indicated that he had considered introducing opioid prescribing agreements with particular patients with whom he had concerns:

There are these new painkiller agreements out and you have an agreement that they will only go to such and such a pharmacist and low and behold when you go to their house you find that they have got those little red boxes that you buy as well as those that you prescribe so they do buy them and they can get them... (GP5)

Cautions & Adverse Effects

The potential for adverse effects and cautions particularly with opioids and NSAIDs are also considerations for GPs. At this point during the interviews, GPs tended to compare and contrast prescribing approaches based on the age and co-morbidities of patients. This provided an insight into the impact of these clinical issues associated with the ageing process and subsequently influenced the prescribing decision making process.

NSAIDs

NSAIDs should be used with caution in elderly populations due to the increased risk of adverse outcomes associated with the cardiovascular, gastrointestinal and renal effects of this class of analgesics. Unsurprisingly, therefore, GPs unanimously described their reservations in using systemically absorbed NSAIDs

in elderly populations. Those GPs that were willing to incorporate them into the analgesic regimen were content to do so only for short periods:

Depending on a few factors I try to avoid NSAIDs in the elderly except for very short periods of time obviously because of the risk of renal impairment and GI stuff but I will use them for short periods of time in people who don't have contraindications. (GP4)

However, such a cautious prescribing approach in relation to the systemically active NSAIDs is not reserved exclusively for elderly populations or those with specific cautions or contraindications. One GP described her concerns in prescribing this drug class for any age-group:

I would think I have been uniformly conservative about non-steroidal in any age group really. For most of my career, I don't know, I just always was. (GP11)

Neuropathic Agents/Adjuvants

GPs were prompted to discuss their perception of the role of adjuvant agents in an analgesic regimen. GPs reported incorporating them into the regimen if they identified pain of neuropathic origin but were selective about the type of adjunct agent that could be used amongst elderly patients.

I identify with amitriptyline being a potentially inappropriate drug in an older population [pause] *amitriptyline would be bad, so yeah, probably go with for neuropathic pain pregabalin or gabapentin.* (GP9)

One GP described prescribing lower doses of these agents for ageing and elderly populations so as to minimise the adverse effects associated with this class of drugs:

Problems are dry mouth and sedation and also urinary problems as well, you know particularly in men. You have to watch for it, okay. The amounts that I am using, I use very minuscule amounts a lot of the time. (GP10)

Opioids

Opioid containing formulations, particularly codeine based products, appear to be more acceptable amongst GPs, provided they are used for a short duration with regular review:

I tend to be careful with codeine based medicines really. I don't tend to use codeine a lot particularly in the elderly because it is nauseating and constipating and sedating and a lot of other things. (GP7)

The risks associated with NSAIDs are juxtaposed with those associated with opioid formulations particularly higher dose codeine containing formulations and tramadol:

So ideally we are trying to avoid any of the kind of dependency drugs, any of the opiates whether they be low or high dose and then even now trying to avoid anti-inflammatories because of the cardiovascular side effects. (GP9)

The practice of prescribing laxatives with opioids was probed by the interviewer, as GPs did not automatically refer to prescribing this medication for patients who were concurrently prescribed an opioid medication. There was a wide range of approaches to the co-prescribing of laxatives amongst the GPs interviewed. It would appear that GPs are aware that it is good practice to concurrently prescribe laxatives with opioids, particularly moderate and stronger opioids but readily admit to occasionally overlooking this when prescribing opioids.

I should and I know I should but yet I don't always. (GP9)

Another GP acknowledged that she frequently omits prescribing a laxative with a moderate opioid but will uniformly co-prescribe a laxative with a strong opioid:

I am probably not as good with the Tylex®[§§] though I should always prescribe lactulose but if I am moving somebody onto a patch at all they will always get a co-prescription for a laxative and if I remember it at all they will get a co-prescription when they are going on Tylex® but probably not as good at the co-prescribing for the laxative with the Tylex® to be honest. (GP4)

Upon questioning by the interviewer, all GPs were cautious about the concurrent prescribing of sedating agents with opioid medications for the elderly, citing the potential adverse outcomes that may arise from this combination of medications. However, all GPs also indicated that they were cautious about the prescribing of sedating agents for this population regardless of concurrent medications, therefore this type of medication interaction was rarely problematic in practice:

In so far as possible they are a no-no for the elderly population in general so unless they are on something for a long time and they absolutely refuse point blank to come off them we would tend to or hope to have minimal benzos. (GP7)

6.4.2. Theme 2: Information & Guidance

GPs were asked to comment on the types of resources that inform their approach to pain management in primary care. Despite the reported lack of specialised education and training on pain management at an undergraduate level in Ireland, GPs did not indicate that their learning or understanding of the topic was lacking. There was no apparent difference observed between awareness or use of guidance and the number of years the GP was in practice. Both recently qualified GPs and those practising for many years incorporated some form of guidance into the prescribing decision making process. Information and guidance published both within and outside of Ireland are referenced by all GPs and are illustrated in *Figure*

[§§] Paracetamol 500mg/Codeine 30mg

6-7. Resources used in multiple countries such as the WHO Analgesic Ladder feature strongly throughout the interviews and is considered as an international resource for the purposes of this analysis:

In terms of guidelines you know I always think about the WHO Analgesic Ladder. (GP2)

The absence of specific literature or guidelines on the subject of CNMP for the Irish primary care setting was acknowledged by a number of GPs. A number stated that guidelines would be useful but with the caveat that specific management strategies may vary according to access to the healthcare system and the specialist services provided therein:

It is not an area of practice that is guideline based of the minute. It probably wouldn't be a bad thing. (GP7)

Definitely a booklet on non-malignant pain would be fantastic but with the caveat that with the non-pharmacological stuff, your access will depend on where you work. (G4)

While guidelines might be a welcome tool for GPs, there was a desire that guidance is succinct and focused so that it is feasible for use in a primary care setting:

There are two problems, we are overloaded with information and paper and everything else in practice and then we want clarity. (GP3)

Furthermore, one GP acknowledged that since he felt confident in his approach to pain management, as distinct from the management of other pain conditions, he was less inclined to seek out specific guidance in the form of clinical practice guidelines as he might be for other chronic conditions:

I get to have an idea in my head as to what I might do. Well [pause] *I have a clear idea as to what I might do in pain. But maybe I need to be drilling down a little bit on that, maybe pulling out a guideline and just having a run through that, which I have not done specifically and I would have done for lots of other things, but not for that.* (GP 3)

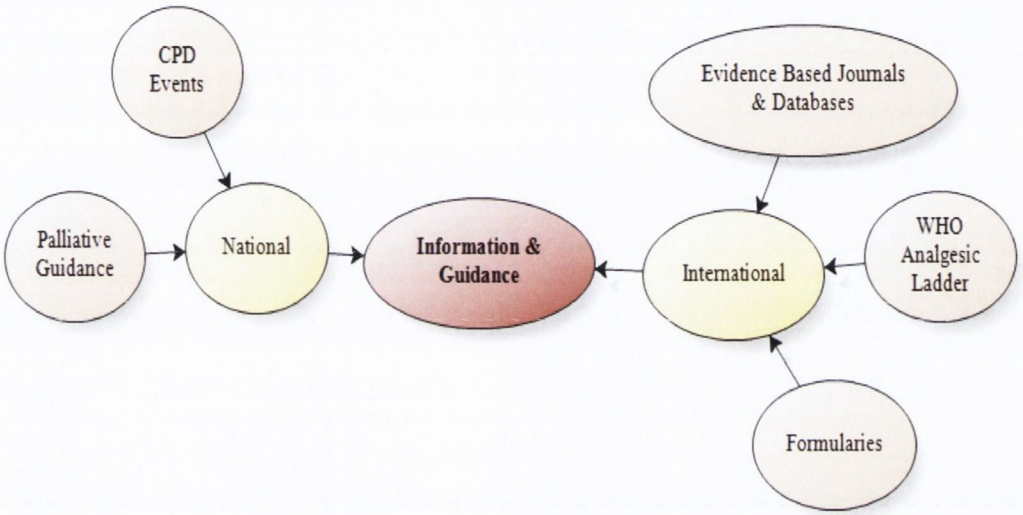


Figure 6-7: Information and guidance associated with prescribing analgesics in primary care

6.4.2.1. National

CPD Events

CPD events such as lectures, workshops and seminars provide GPs with the opportunity to enhance their knowledge on a range of topics. Some GPs reported attending lectures on the subject of pain as part of CPD while two mentioned completing annual CPD modules during which the subject of pain may be discussed:

I was at one last Friday on pain which was run by the Pain Society of Ireland and it was over two days and they had a number of speakers talking about managing pain in primary care. (GP4)

Palliative Clinical Practice Guidelines

Eight GPs reported accessing clinical practice guidelines on the topic of palliative pain management and adopting these recommendations for management of CNMP in primary care:

There is also palliative care produced guidelines [pause] *I know it's for cancer but they tend to be very good at producing guidelines if I am prescribing morphine in terms of what your equivalent dosing is for different types of morphines. So I would tend to use palliative guidelines if I am actually prescribing morphine just in terms of dosing and stepping up and stepping down. (*GP4)

6.4.2.2. International

WHO Analgesic Ladder

The WHO Analgesic Ladder guides was referred to extensively in all interviews as the basis for prescribing analgesics for pain conditions. Indeed, even when not mentioned in name by the GPs, the steps of the ladder were referenced when describing approaches to prescribing:

So the one that everyone refers to is the WHO Analgesic Ladder, so ideally we are trying to avoid any of the kind of dependency drugs. (GP9)

Yes, well, I would use the WHO pain ladder so starting off with a simple analgesic then moving up to NSAIDs. (GP6)

Formularies

The British National Formulary (BNF) was referenced as the primary guidance for GPs in day-to-day practice; this includes information on indications, dosage and frequency for medications currently marketed in the UK:

The BNF would be what I would go to first, you know in day to day practice. (GP6)

The Irish Medicines Formulary (IMF) was not mentioned by any GP, the Monthly Index of Medical Specialities (MIMs) was referenced by several although this is a prescribing reference containing limited information about licensed medications and is not as detailed as a the BNF or IMF.

Evidence Based Journals and Databases

Three GPs detailed their use of paper and electronic evidence based journals and websites to inform them on clinical and pharmacological developments. These were of UK and US origin and were used to enhance knowledge so as to improve management of the CNMP patient:

Another good website is The American Academy for Family Practitioners; they have tonnes of information on their website and another lot in California called Audiodigest. I download a lot and listen to it on my IPhone during my rounds. (GP5)

I would look up, there's various kind of websites, the NHS have a very good one, it used to be called PRODIGY Clinical Knowledge Summaries (GP10)

Pharmaceutical Companies

Literature provided by pharmaceutical companies was referenced by a number of GPs. Three spoke negatively about the focus and tone of this information, stating that it may be misinterpreted due to the way the data is presented. However, in the absence of other literature available on the medication, it appears that GPs access this material to support prescribing decisions:

I don't think you are supported at all except by the drug companies who are mad keen to support you (GP8)

I have reservations about pregabalin and Lyrica® because it seems in a way [pause] *it is just being pushed by pharmaceutical companies as super effective whereas, in reality, it isn't any more effective* (GP9)

6.4.3. Theme 3: Non-Clinical Factors

Non-clinical factors describing the psychosocial, communication and financial aspects of CNMP or medication management are presented in *Figure 6-8*. GPs referred extensively to communication and rapport with patients as a means of achieving a good patient-GP dynamic which may ameliorate management of the condition in primary care:

You would always appreciate that there is so much more to things than just physiological and then I think if you were worried that you are prescribing these heavy drugs to somebody on a regular basis and you think it is purely because they have a pain in their elbow, then you are completely missing the point, there is always more to everything. (GP9)

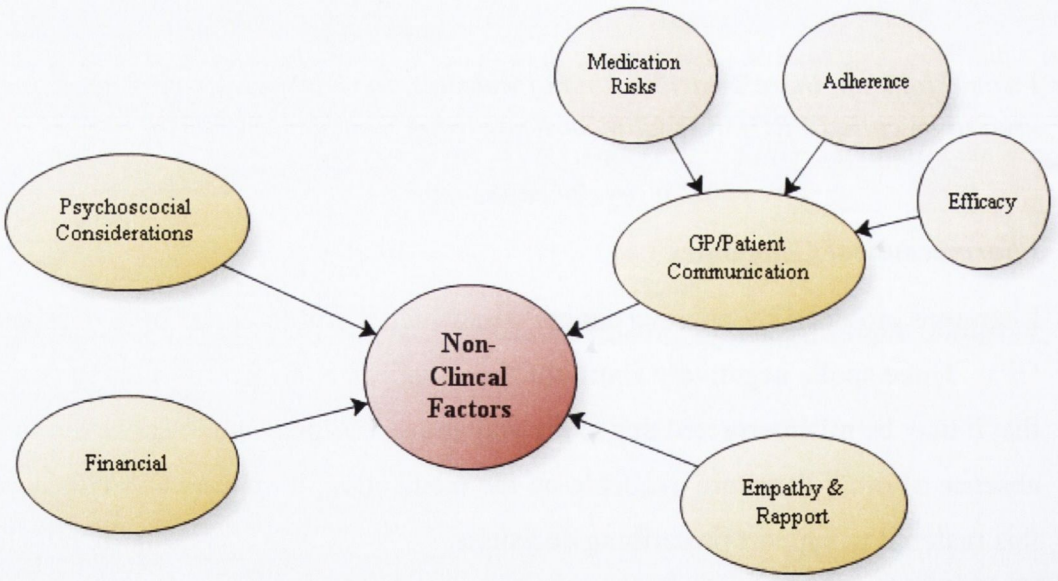


Figure 6-8: Non-clinical factors associated with prescribing analgesics in primary care

6.4.3.1. Psychosocial Considerations

A number of GPs acknowledged the implicit psychosocial complications of CNMP and the necessity to consider the patient as a whole, not merely prescribing medication for the condition. This echoes the non-reductionist model of patient management as distinct from the medical model:

Of course, the other point about pain is this, pain is not just pain, but it's also pain plus the anxiety and the whole preconception and all the social stuff, mood; a whole load of other things feed into pain. (GP10)

One GP considered physicians in the primary care setting well-placed to evaluate these aspects of the patient, given the GP's understanding of the individual's psychosocial and family background:

Usually, the psychosocial aspect of it is very relevant to pain and we tend to, in primary care, to know their background and their family situation and their other issues a lot more so than secondary care might and take those into account kind of almost as a given when we get them in the door. (GP7)

6.4.3.2. Financial

The cost of some medications particularly pregabalin and gabapentin and the burden this places upon privately funded patients, was highlighted by three GPs. Indeed it would appear that these GPs were reluctant to prescribe these agents for those patients paying privately and would consider them only if other analgesics are ineffective:

They are ridiculous [pause] *very expensive* [pause] *absolutely ridiculous price...* [pause] *and the lower dose tablets are as expensive as the higher dose ones.* (GP1)

I find them very expensive and, they're fine, you know what doesn't suit one, suits another, you have to be flexible too, but they are poisonously dear. (GP10)

6.4.3.3. GP/Patient Communication

GPs outlined the necessity to listen and understand the nature and severity of the pain condition through descriptions gained from the patient combined with clinical examination and observation. At the point of deciding on an appropriate intervention for the patient, whether pharmacological or non-pharmacological, GPs described the importance of engaging and consulting with the patient so as to determine their satisfaction with this outcome. Indeed, a number of GPs stated the importance of clearly communicating the risks associated with use of certain classes of medications and the challenges this can present, particularly when the patient has had a poor experience of the efficacy of certain analgesics such as paracetamol:

Patients usually don't like paracetamol regularly [pause] *they don't have any faith in it because you can buy it over the counter so you always have this conversation where they say that is no use and then you explain you have to try to take it regularly.* [pause] *It is interesting, definitely, in my experience patients perceptions of paracetamol* [pause] *they do not equate it with good pain relief.* (GP4)

The process of review of a patient's medications regimen, and the process of communication to discern the efficacy of the regimen, is described by all GPs as essential to an effective pain management strategy. However, it would also appear that elderly patients are often reluctant to have items removed from their prescription, regardless of their clinical necessity or efficacy:

Once you get people, particularly elderly people, on a medication, I have to tell you, you can roll up your sleeves to get them off and I don't care if it's a beta-blocker or a codeine, they get very set in their ways and you ask them, "Do we really need this?" "Oh, I most certainly do." (GP10)

6.4.3.4. Empathy & Rapport

Establishing a rapport with patients and having empathy for their pain condition was acknowledged by all GPs. The importance of displaying understanding as a component of effective GP-patient communication was described and appears to be particularly important when managing this patient group due to the persistent and sometimes progressive nature of the condition:

You know the medical model I suppose [pause] *well they need a good bit of empathy if they are in pain every day, they need to be understood.* (GP5)

I suppose there are the social issues of whether they are living alone and all those sort of things but with pain [pause] *I think pain just colours your life completely and does overwhelm you and take you, and it is only every so often when you get a pain yourself you suddenly realise what people are putting up with a lot of the time you know* [pause] *so they need time and that is what they don't get any more anywhere* (GP8)

6.4.4. Theme 4: Non-GP Management

All GPs discussed their experiences with referral of patients to other healthcare professionals in the primary care setting and also in gaining access to secondary and tertiary level care in the Irish context. The various domains of secondary and tertiary management are presented in *Figure 6-9*. Several GPs discussed the siloed*** nature of health services in Ireland as the key barrier to efficient and timely management of patients. There was a coherent sense of the fragmented nature of the Irish healthcare system and the difficulties associated with accessing services, particularly for patients dependent on care in the public system. This was emphasised in particular by GPs practising in rural areas. The opportunity to refer a patient to a multidisciplinary team with specialised knowledge of the condition in primary care would be a welcome development for GPs who currently almost exclusively oversee patient care in the community:

It's kind of silo medicine, but that's an awful lot of Irish medicine is silo medicine, and I think a lot of the primary care teams are only teams in name. (GP10)

We don't have primary care teams on the ground that are supposed to be there so, you know, it is very much you having to refer to different [pause] *I wish there was a team we could refer them to that would look after them, but there isn't. You can*

*** *system, process, department, etc. that operates in isolation from others*

do a Physio referral or you can get the PHN [public health nurse] *to call, it's very disjointed.* (GP12)

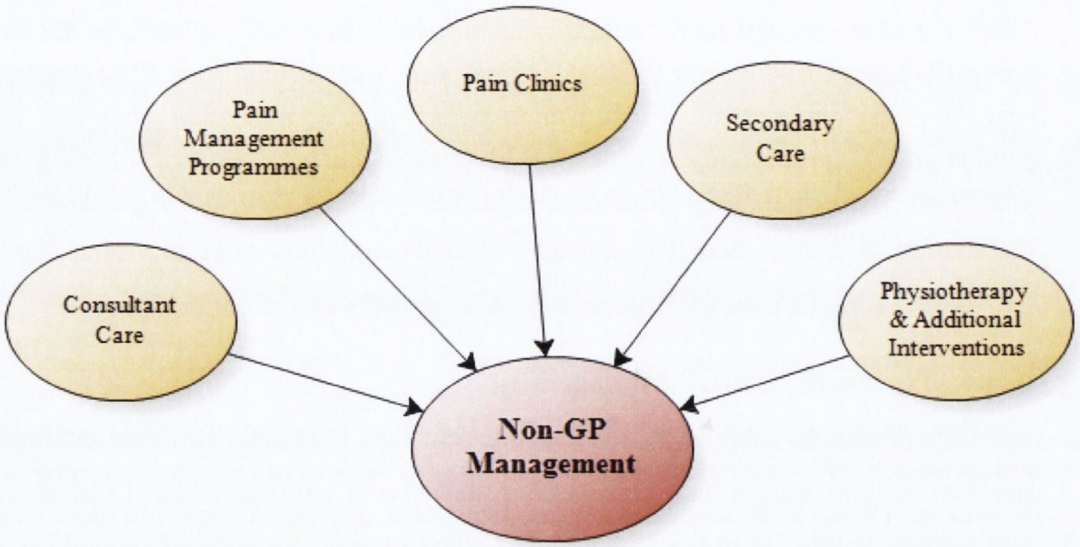


Figure 6-9: Non-GP factors associated with prescribing analgesics in primary care

6.4.4.1. Consultant Care, Pain Clinics & Pain Management Programmes

A number of interviewees described seeking assistance from pain specialists and pain clinics in cases where adequate analgesia cannot be attained or when a diagnosis is difficult to achieve in primary care. While it would appear that most GPs were satisfied with the quality of care delivered in this specialist setting, access to these services was described as difficult for public patients by seven GPs. Geographical proximity to a pain clinic also appeared to be a limiting factor in gaining access to such specialised interventions.

[Access is] *very bad unless you have a thing called money and you could easily be waiting a long long time if you have a medical card to see a pain specialist, it is a very under-staffed under resourced* [pause] *unless you have money in which case you can head to the Galway Clinic next week.. A very bad system and a very unfair system unless you can afford it.* (GP5)

However, GPs appeared to have positive experiences upon gaining access to pain management programmes or pain clinics:

So often if you can get the pain clinic on board as well they tend to have a good multidisciplinary approach. The pain nurse can often be quite good [pause] *just other alternative regimes and stuff can often work.* (GP4)

One GP described pain clinics as the point at which a patient management plan could be developed and implemented in a systematic and structured manner that is not always possible in primary care. Indeed, this GP appeared to welcome the intervention of the pain clinic, as it removed the patient from the spiral of continuous analgesic use that can develop when management is exclusively guided by the GP and also helped to manage patient expectations of the GP:

Things fall apart quite often with those patients and then they get into crisis and then you have to increase their painkillers and then [pause]*.and there is a lack of structure in terms of how we deal with them and what they expect as well. That is where the pain clinics are very useful that they give a structure and they get a plan.* (GP6)

However, one GP expressed concerns about the focus of care in pain clinics, in which patients may be initiated on strong medications such as opiates, which the GP is then obliged to manage in primary care upon discharge of the patient. This GP proposed that such an approach in the tertiary care setting is born from a lack of contextual understanding of the patient's psychosocial or other needs. This participant described the current management approach to CNMP conditions as unsatisfactory in both primary and specialist care settings but was unsure as to an effective solution to the problem:

What happens is the people who staff those pain clinics have no real connection to that person, they don't really care about them, they have standardised scales for pains, they have a clinic waiting list they have to get though and they will see them again in six months' time and they also have a book of medications that they use and they just throw them at them. (GP9)

6.4.4.2. Secondary Care

Several references were made to initiation of certain medications in the secondary care setting, in the Accident and Emergency (A & E) or in the post-surgical context. Three GPs expressed surprise at the types and combinations of analgesics prescribed for these patients upon discharge to the community, the appropriateness of such regimens, and the challenges presented in discontinuing the patient from the regimen:

I'm not a big fan of Tylex® and I'm just bemused at the volume and dosage that comes out of casualty in particular, I'm always bemused by that. (GP11)

Recently I had a lady discharged from hospital and she was sent out on Lyrica®††† and Palexia®‡‡‡ and Solpadeine®§§§ after one visit. It's hard to figure out the rationale sometimes and then you think she is on that medication now for months because she could [pause] *and yet she has not got any nociceptive pain that I can figure.* (GP5)

6.4.4.3. Physiotherapy & Additional Interventions

Finally, GPs were asked to comment on the extent to which physiotherapy or additional interventions, such as occupational therapy, are accessed in the community setting and their experiences with this process. GPs appeared to place such non-pharmacotherapeutic interventions at the centre of their patient management plan to aid attainment of analgesia in primary care. However, as was the case with tertiary care, access to physiotherapy is difficult due to the length of public waiting lists and expensive for private patients. All GPSs expressed the view that the limited access to such additional services in the primary care setting places the burden on the GP to manage the patient with analgesics whilst awaiting these services:

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††† Pregabalin
‡‡‡ Tapentadol
§§§ Paracetamol 500mg/Codeine 8mg

I use all the facilities I can, physiotherapy, some people will go to acupuncturists [pause] *there is a whole variety* [pause] *the patient will often decide themselves what they want.* (GP3)

If we had access to community occupational therapy and community physiotherapy I think we would prescribe way less, I strongly believe that. The big big issue is not having anything to offer anybody and having these huge waits for everything I definitely think if we had a more multidisciplinary input prescribing, would be way down. (GP4)

6.5. Discussion

This study aimed to describe the experiences and attitudes of GPs in relation to prescribing of analgesic medications, particularly opioids, for ageing and elderly patients with CNMP conditions. *Figure 6-10* provides an overview of the themes that emerged from interviews and the manner in which these themes interact to influence analgesic management of patients with CNMP in primary care. The themes identified from these GP interviews are similar to the micro, meso and macro hierarchy described previously as the determinants of prescribing in primary care (13). These are therefore annotated beside the global and organising themes in *Figure 6-10*.

The GPs interviewed in this study highlighted the challenges in delivering effective analgesia to ageing and elderly populations with CNMP. Indeed, these clinical considerations appear to be of central importance when making a prescribing decision. As this factor pertains to the individual patient, it may be considered a micro factor that influences prescribing. The selection of an analgesic regimen is informed by the pharmacokinetic and pharmacodynamic implications of the therapy for ageing and elderly populations; there is therefore a compromise between prevention of adverse outcomes and the attainment of optimal analgesia. Such clinical restrictions have been demonstrated to cause under-treatment of pain amongst ageing and elderly populations, a problem that these GPs readily acknowledged but appeared willing to accept, following a risk-benefit assessment of pharmacotherapy (113, 118).

Clinical issues arising from the suitability of NSAIDs and opioids act as barrier to the prescribing of these agents, particularly the addiction or dependence issues with the latter in patients with a history of substance abuse. These are similar concerns raised by American and Canadian physicians in surveys investigating attitudes towards prescribing (214, 261, 443). Recent graduation from medical school has shown to be predictive of a US or Canadian physicians' willingness to prescribe opioids. However, this was not identified in this Irish study, with both recently qualified GPs, and those in practice for several decades, equally willing or unwilling to prescribe strong opioids (444). It would appear that Irish GPs do not wish to adversely affect the patient's quality of life with the initiation of opioids due to the high propensity of adverse effects with the regimen. Instead, they would rather have additional interventions from specialists or allied healthcare professionals in primary care to supplement analgesic management.

Professional and regulatory scrutiny have been identified as barriers to the prescribing of opioids in North America and Canada (265, 444, 445). Such concerns were not raised specifically by this Irish group of GPs nor were regulations relating to the prescribing of opioid analgesics referenced as a barrier to their use. Indeed, there was an apparent willingness to prescribe buprenorphine and fentanyl patches for this population when other forms of analgesia were ineffective. This correlates with the findings of the study on prescribing trends in *Chapter 4* in which dispensings of strong opioid patches were found to be most prevalent amongst patients aged 75 years and older. Furthermore, this study also identified an under-prescribing of laxatives with strong opioids, with several GPs admitting that they frequently omit to co-prescribe. This again is supported by the low prevalence of concurrency with strong opioids detected in *Chapter 4* and *Chapter 5* and is similar to trends of underuse of laxatives in the literature (335, 446).

The approach to determining pain severity is individual to the prescriber and may be responsive to the subjective nature of pain. The GPs appeared to use an adaptation of WILDA approach (Words, Intensity, Location, Duration, Aggravating and Alleviating Factors), requesting that patients describe pain in terms of limitations on daily activity (447). However, GPs do not appear to incorporate this approach to pain assessment in a systematic manner into the consultation. This highlights the challenges in gaining an objective understanding

of the condition to facilitate comparison between patients, as consultations are based on the personal experience of the patient. Furthermore, the lack of a formal pain assessment approach may introduce disparity between the understanding of pain intensity of both patient and GP, which may contribute towards inadequately controlled pain (62).

All GPs described the necessity for an empathetic and understanding relationship with the patient in order to gain a complete understanding of the pain condition and the impact of the condition on the individual's daily life. Indeed, several suggested that this was central to the consultation with the patient such that psychosocial issues associated with the pain condition could be identified and addressed. The dialogue between GPs and patients demonstrates a degree of shared decision making with the goal of devising a strategy of managing the pain on a daily basis. This approach to prescribing decisions has been demonstrated to improve patient adherence to a prescribed medication regimen, which consequently ameliorates patient outcomes (448).

The poor availability of national guidance on the prescribing of analgesics for CNMP patients was universally acknowledged by GPs in this study. This is considered to be relevant to both macro and meso influences, since guidance may be produced by international and national bodies. Several described accessing such information on international websites or in evidence based journals which aided in the prescribing decision making process. Consulting additional resources is therefore demonstrated to interact with clinical factors in *Figure 6-10.* While several welcome the prospect of guidelines on prescribing medications for this condition, the problems associated with implementation of guideline recommendations in primary care were raised. GPs in this study echoed the evidence in the literature on this subject, which suggests that lengthy, paper guidelines are difficult to review and implement in practice (331). GPs also indicated that literature obtained from pharmaceutical companies was one of their primary sources of information when prescribing some medications. However, several GPs spoke sceptically of the manner in which evidence was presented in this literature. It was not possible to determine from this study the extent to which this literature promoted the prescribing of these medications, although studies

demonstrate that it is associated with increased prescribing which may not be cost-effective (211).

A number of GPs highlighted the cost of certain medications as a significant barrier in prescribing, particularly the cost of pregabalin and gabapentin. A number described the cheaper medication amitriptyline as a cost saving measure. This concern may be a reaction to increasing numbers of ageing and elderly patient becoming ineligible for the GMS scheme. The response of GPs to cost in this manner, while in keeping with the tenents of the WHO rational prescribing model of cost-effective prescribing, appears to restrict their choices when prescribing these medications (405).

Access to services offered by allied healthcare professionals and specialist care also influence GP prescribing practices and appears to be one of the key barriers to effective patient management. This issue is reflective of the health system approach to management of CNMP and has been classified as a meso factor. Access to physiotherapy and occupational therapy in primary care, and pain specialists including pain management programmes provided in tertiary care, are associated with better quality of life and pain management outcomes for patients and are viewed as essential in delivering optimal care (414, 449). It would appear that the extent to which the GP is required to pursue pharmacotherapy as a method of management is dependent on their ability to gain timely access to additional assistance in primary, secondary or tertiary care, particularly in instances of more severe pain. The non-GP management domain is therefore considered to interact with the clinical factors influencing analgesic management in primary care in *Figure 6-10*. There is an apparent frustration with access to the healthcare system and a sense that the disjointed nature of the current system places heightened pressure on GPs to act as gatekeepers in the provision of care to the patient with CNMP. Indeed, it was highlighted several times throughout the interviews that prescribing practices for CNMP patients should be considered in light of the health system barriers to pain management; addressing system barriers may improve the quality of care delivered to these patients.

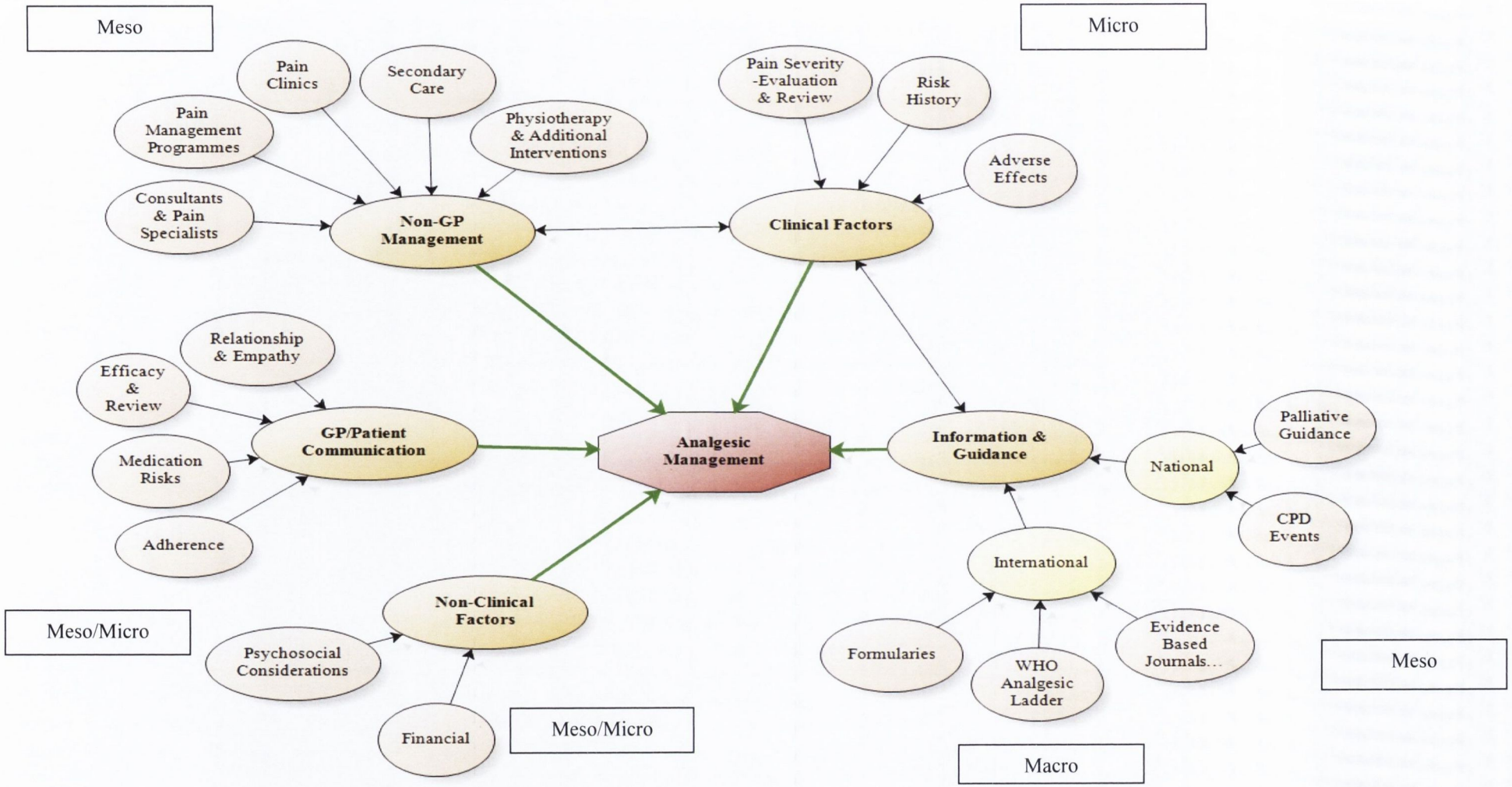


Figure 6-10: Summary of factors and interaction of factors hypothesised to influence analgesic prescribing in primary care

6.5.1. Strengths & Limitations

Quantitative purists may view qualitative methods as scientifically inadequate, as the validity, objectivity and reliability cannot be guaranteed owing to the nature and design of research studies in which internal and external validity may be difficult to demonstrate (450, 451). Sample sizes in qualitative research may not be representative of the population of interest under the quantitative definition (452). Furthermore, sampling and recruitment approaches may be difficult to replicate by other researchers, while the method of recruitment of participants may introduce selection bias to the study, which further contributes towards the perceived weaknesses of qualitative studies (451). Ethical issues may arise at each phase of a qualitative research project in the recruitment of candidates, the researcher-participant relationship during the course of the interview, and through the researcher's analysis and interpretation of interview data (453). The combined sampling approach used to recruit GPs in this study was not ideal and would be difficult to replicate following completion of the research process. The chain referral sampling method (snowballing method) introduces selection bias, as individuals included in the study may originate from a similar point e.g. same university or training programme. Furthermore, as some GPs were recruited into the study following the recommendation of a colleague, they may have felt duty-bound to participate in the research (454).

Interviewing fellow healthcare professionals, as a pharmacist interviewing a GP in this instance, can be advantageous as technical terms are easily communicated and it removes the occurrences of misinterpretation or misunderstanding, as both have a common experience with the healthcare system. However, interviewees may feel unable to deviate from the socially or professionally acceptable responses that might be anticipated by the interviewer therefore introducing bias into the results (432).

Telephone interviews are an inexpensive and efficient method of conducting semi-structured interviews (455, 456). The main disadvantage is the loss of nonverbal cues gained from face-to-face interaction and the opportunity to use visible aids during the course of the discussion. The interviewee may be unable to retain or interpret lengthy or complex questions, a reaction which may not be understood by the interviewer (455). However, the relative anonymity of telephone

interviews may be appealing to some GPs, particularly when discussing sensitive issues. Furthermore, this approach may facilitate recruitment of individuals who are difficult to access or who are unable to schedule a face-to-face meeting with an interviewer (457).

Finally, analysis of qualitative data may introduce bias into the study as the researcher may approach the topic with pre-formed opinions and ideas. This limitation may be addressed through extensive documentation, auditing and recording of recruitment and analytical strategies allowing external parties to review the reflexivity of the research process. Research reflexivity addresses this analytical bias arising from examination of qualitative data as the researcher aims to critically self-reflect and declare potential biases or preconceptions to the research question or research process (451).

6.6. Conclusion

Semi-structured interviews were an effective method of gaining an understanding the prescribing and dispensing findings in *Chapters 4 and 5*. The GPs interviewed in this study were familiar both with the challenges of the pharmacotherapeutic management of CNMP but also the limitations of the Irish healthcare system in this regard. This study particularly provides an insight into the factors influencing the pharmacotherapeutic management of ageing and elderly patients with CNMP that could not be identified from quantitative research. The selection of an analgesic regimen is dependent on a broad of micro, meso and macro factors relating to the prescribing physician, the patient, and influences emanating from external sources, such as guidelines and literature on the subject. Clinical considerations including patient history, comorbidities, co-prescriptions and pain severity are key factors informing the development of an analgesic regimen. The remaining factors such as access to prescribing information, interaction with the patient and health system are barriers which also inform the approach to management adopted by the GP. However, these factors appear to be weaker motivators in the prescribing process than the clinical considerations but nonetheless contribute to shaping the pharmacotherapeutic management of the patient in the primary care setting.

What is already known about this topic:	Micro, meso and macro factors influence the clinician's approach to prescribing in the primary care setting.
	Pain may be under-reported by ageing and elderly populations, with some individuals believing it to be part of the natural ageing process, while others are unwilling to highlight it in case it is a sign of disease progression. Under-reporting by patients and poor detection by clinicians may lead to inadequate pain management.
	Variability may also emerge in approaches to pain management owing to the education and training, differences in attitudes towards analgesic medications, or concerns about regulatory scrutiny.
	There are currently no clinical practice guidelines specific to the pharmacotherapeutic management of CNMP in ageing and elderly populations available to primary care physicians in Ireland; the BNF and IMF are commonly used references for information on prescription and non-prescription medications.

What this study adds:	GPs reference the WHO Analgesic Ladder as the primary tool to guide the prescribing of analgesics. A number of GPs referenced additional resources such as the BNF and palliative guidance, while others accessed articles in international journals. GPs acknowledged the potential benefits of clincal practice guidelines for the pharmacotherapeutic management of CNMP in Ireland.
	GPs appear to tailor their approach to analgesic prescribing based on the clinical profile of the patient e.g taking into account the pharmacokinetic and pharmacodynamic features of elderly patients and concomitant prescription medications.
	GPs emphasise the necessity to establish an empathetic relationship with patients. Several interviewes referenced the necessity to consider the psychosocial aspects of the patient and to take these into consideration when constructing a management plan for the patient. This reflects the tenants of the biopsychosocial model of patient. A shared decision making approach to prescribing was also described by several GPs.
	GPs described access to additional services such as physiotherapy or occupational therapy and to specialist management such as pain consultants as limited at present, particularly for patients receiving care through the GMS system and those in geographically remote areas. Many GPs proposed that access to specialised multidisciplinary pain teams through tertiary or primary care would enhance the quality of care for patients with CNMP.

Chapter 7 Ageing and Elderly Individuals with Chronic Non-Malignant Pain: Approaches to Analgesia and the Role of Pharmacotherapeutic Agents

7.1 Background

The Common Sense Model of Health Regulation, developed by Leventhal et al, proposes that mental representations of illness provide a framework for understanding and coping with the illness. The theory postulates that patients appraise the physical and emotional elements of the condition and adopt coping strategies determined to be appropriate for the condition or symptom (266, 458). Socio-cultural, emotional and psychological factors also inform the manner in which the patient appraises and selects interventions to manage the condition (459). The efficacy of these interventions in alleviating the symptom is appraised by the patient and additional interventions identified if necessary. The combination of pharmacological and non-pharmacological interventions frequently used to achieve pain relief indicate that patients with CNMP adopt a dynamic approach to disease management, in keeping with the common sense model of self-regulation.

Since analgesics are a commonly used intervention tool to cope with pain, it is necessary to consider the manner in which these agents are used by patients. The pattern and extent of medication use evolves through a combination of the perceived need for, efficacy of, and concerns about the medication (460, 461). A closer examination of the factors that influence a patient's use of a prescribed regimen suggests that combinations of internal and external factors influence a patient's approach to taking medications, as proposed in Horne's model of adherence presented in *Figure 7-1*. Internal factors are those beliefs and experiences of the patient, including beliefs about disease and medications, the perception of the role of medications in disease management, and the ability to take medication. External factors contribute towards the patient's internal appraisal system and include the sources from which patients gain information about medications including healthcare professionals, family, friends, the wider public and media (462, 463). The Horne model describes the factors that influence adherence to a prescribed medication regimen. While adherence is not the focus of this research study, the model identifies the range of factors that contribute to the patient's perception of medication and is therefore of some use as a method of framing our understanding the factors that inform medication use. The internal/external dimensions of this model mirror closely the micro, meso and macro factors that influence analgesic prescribing by physicians.

Non-pharmacological interventions may be viewed as a self-management strategy undertaken by the patient to supplement analgesic use or to prevent the use of these medications. The use of these non-pharmacological strategies may also inform the nature and extent of analgesic use by patients in addition to the internal and external factors previously described. It is therefore necessary to consider these non-pharmacological interventions alongside medications. The 20th century has seen patients increasingly incorporating self-management skills into their approach to disease management, supported and encouraged by knowledge gained from healthcare professionals, electronic media and printed literature (464). Indeed, the WHO has highlighted the importance of non-pharmacological interventions such as self-care and self-management strategies by incorporating these dimensions into recommendations for healthcare policy and healthcare delivery since 1998 (465). Self-management may therefore be considered as coping behaviours adopted by the patient (100). A variety of these interventions such as cognitive behavioural therapy, mindfulness and relaxation techniques may allow the individual to regulate their emotional response to the condition or their reaction to the illness (466).

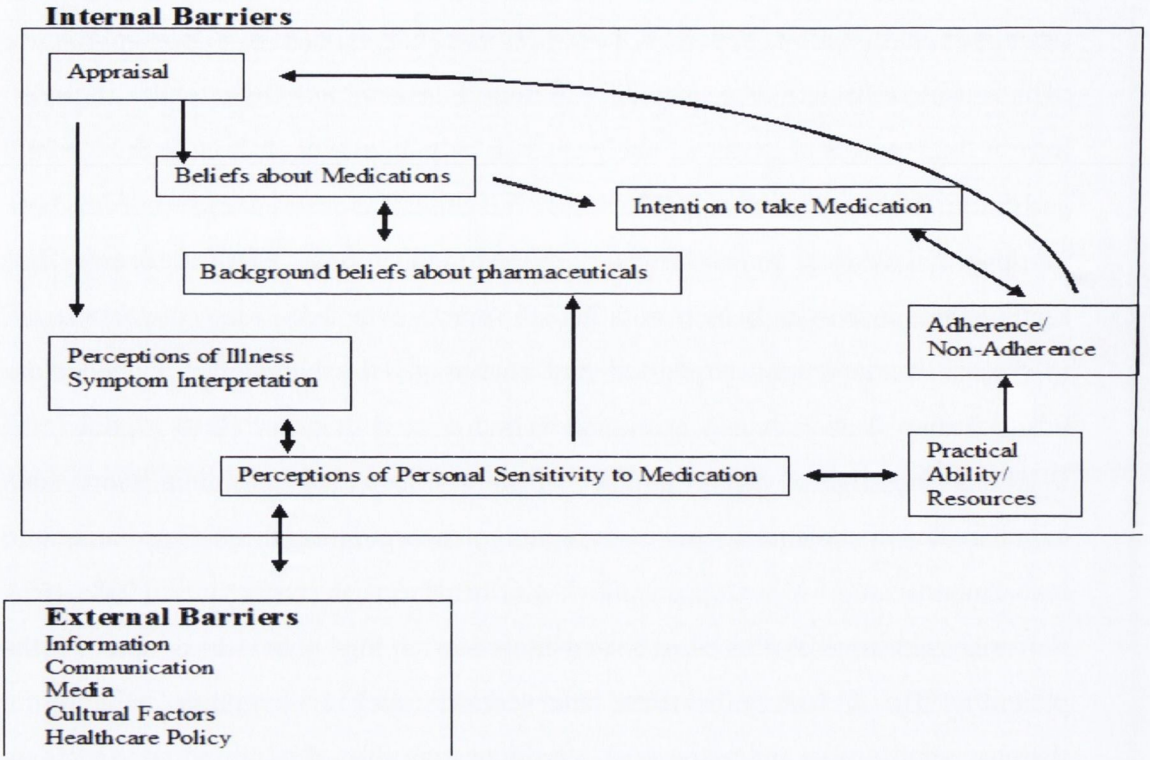


Figure 7-1: Internal and external barriers to adherence adapted from model of adherence proposed by Horne et al (462)

The manner in which an individual seeks to manage their condition is a dynamic process involving subjective, third party and health system factors. While analgesics are the mainstay of CNMP management in primary care, a patient may undertake a variety of strategies to supplement pharmacotherapy in an effort to attain pain relief. Adopting a regimen of multiple interventions in this manner acknowledges that pain is a complex matrix of psychological, emotional and sociological factors and does not merely encompass the physical wellbeing of the individual (467).

7.2 Aim and Objectives

This study aimed to examine the attitudes of individuals with CNMP, aged 50 years and older, towards analgesic medications and to assess the manner in which these medications are consumed by these patients.

The objectives were:

1. To identify the types of analgesics and adjuvant medications prescribed for individuals with CNMP;

2. To examine the relationship between reported pain intensity, types of medications used and frequency of use;
3. To examine patterns of use of prescription and non-prescription analgesics and adjunct medications;
4. To determine the nature of patient concerns relating to analgesics, particularly opioid analgesics.

7.2.1 Study and PhD Objectives

This study was conducted to meet Objective 2 described in *Chapter 2, Section 2.3*: To describe the nature and extent of analgesic use by ageing and elderly populations with CNMP in the Republic of Ireland.

7.3 Methods

A number of methodologies were considered by the researcher when planning this study. The Beliefs about Medication Questionnaire (BMQ) was initially proposed as an efficient and effective method of achieving the aims and objectives of this project (468). However, it was decided that the number of participants required to produce an adequately powered study, approximately >82 people with CNMP, would be difficult to recruit even with the assistance of Chronic Pain Ireland (CPI) (267). A qualitative approach would allow the researcher to investigate the more subtle aspects of CNMP management in Ireland by incorporating questions about the healthcare system, relationships with healthcare professionals, societal influences, and financial circumstances; such detailed information could not be captured using the BMQ.

7.3.1 Ethical Approval

Ethics approval for the research project was gained from the Health Sciences Research Ethics Committee Trinity College Dublin (TCD) in May 2013, *Appendix F: F.1*. Ethics approval had been granted for this project prior to this but the initial application proposed a focus group approach to the research project. Following consultation with CPI in April 2013, it was decided that semi-structured telephone interviews were to be completed with participants. The CPI suggested that due to the age-group of interest in the study and the physical disability of potential

participants, recruitment to the study would be more successful and equitable if telephone interviews were used to complete the research.

7.3.2 Sampling and Recruitment

A non-probability sampling approach was used to recruit CPI members into the study, using the CPI's 2013 membership list as the sampling frame. The secretary of the CPI emailed an invitation to all members of the association and posted the advertisement on the social networking site, Facebook®. An invitation was also posted to Twitter® which provided a link to a Survey Monkey webpage; this contained the full text of the advertisement e-mailed to potential participants. Finally, the advertisement was placed in the CPI quarterly newsletter which is circulated to all members. The text of these advertisements are included in *Appendix F: F.2.*

According to ethics requirements sufficient information must be provided to potential participants and supplemental information should be provided upon request. This information is necessary to allow the individual to make an informed decision on participating in the research study (429). Signing of consent forms is viewed as an important opt-in component of the consent process. Requesting that participants sign a consent form increases the likelihood that the individual understands the risks and benefits of participation and their rights in terms of confidentiality and anonymity (429). In this instance, interviews were only conducted upon receipt of a signed consent form, in addition, a minimum of 5 days was allowed between signing the consent form and conducting the telephone interview to allow participants time to reconsider participating in the study. Respondents to the advertisement communicated interest to the secretary of the CPI. The secretary of the CPI, therefore, acted as a gatekeeper to recruitment into the study. Gatekeepers ensure that vulnerable individuals or their families are protected and are free from coercion by the research team (469).

Men and women were eligible to be a participant in the research if they had a CNMP condition and were 50 years and older. Individuals could not participate in the study if they were not a current member of CPI, were unwilling participate in an audio-recorded telephone interview, had a terminal illness, or had been diagnosed with dementia or any other memory impairment.

Thirty-six members of CPI initially responded to the advertisements through the gatekeeper in the CPI. Prior to dissemination of the letters of invitation and information leaflets, one individual withdrew interest from the study due to poor health. Two members were younger than 50 years and therefore did not meet the inclusion criteria. Letters of invitation, information leaflets and consent forms were posted to 33 CPI members (*Appendix F: F.3, F.4 and F.5*). A calendar outlining a series of dates between June and August 2013 was also provided, representing the researcher's availability to conduct interviews. Prospective participants were requested to indicate on the calendar a date and time for interview. Upon receipt of a signed consent form and the calendar, all participants received a letter confirming the time and date of the telephone interview.

Twenty-eight consent forms were signed and returned. The 5 individuals that initially expressed interest in the research study, but had not returned the consent form to the CPI secretary, were issued with another invitation, a consent form and an additional questionnaire to determine why they had chosen not to participate in the research. The researcher did not receive any further correspondence from these individuals; it is not known why these individuals were lost to follow-up. *Figure 7-2* summarises the recruitment process, detailing the loss of interested individuals at various stages of the research. Twenty-seven transcripts were retained for data management and analysis.

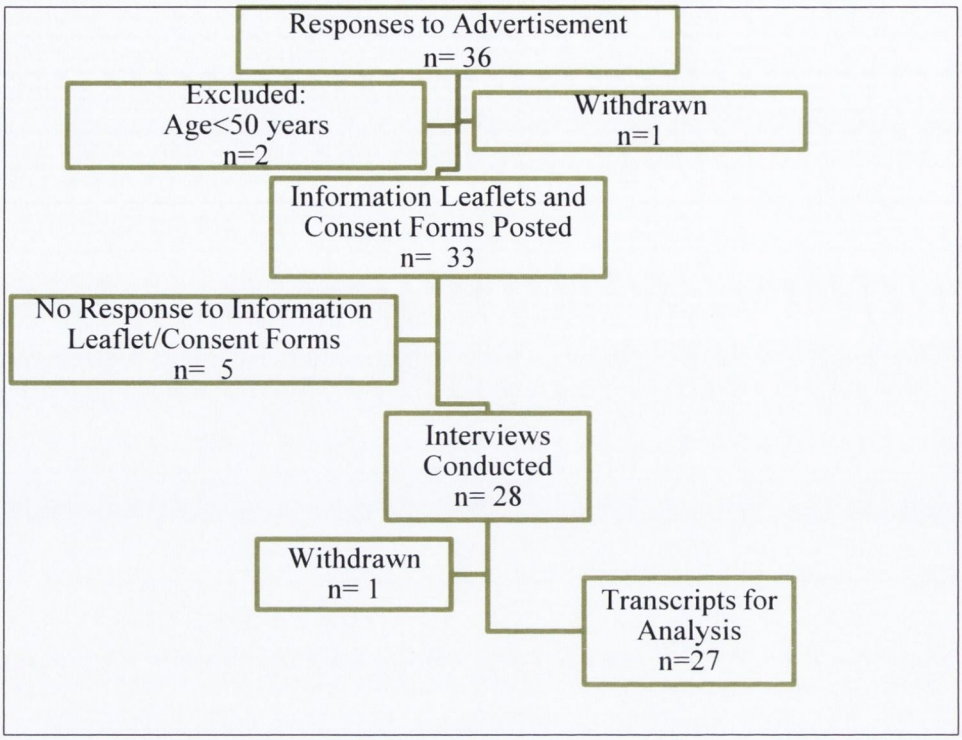


Figure 7-2: Recruitment of participants

The interview guide for semi-structured interviews with CPI members was constructed in such a way that it contained a number of similar question themes as the interview guide used with the GPs. The language of the questions was altered slightly such that clinical terms were included only in those questions directed at GPs. In addition, the question relating to clinical practice guidelines was excluded from interviews with CPI members. These interview guides were developed by the researcher and reviewed by the supervisory team on several occasions prior to the first interview. A number of questions were also included following consideration of the internal/external barrier framework discussed in the introduction section (462). Additional questions about analgesics were also added to the interview guide based on the researcher's findings from the literature review and results of the TILDA study. The themes of the questions contained in the interview guide are outlined in *Figure 7-3*.

Question Theme	Statements /Questions in Interview Guide	Reason for Inclusion of Statement/Question
Introduction and information for participants	Hello, my name is Mary-Claire Kennedy, I am a researcher with the School of Pharmacy, Trinity College Dublin. I am contacting you about the telephone interview on painkiller medications. The title of this study is 'An investigation of the use of painkillers and beliefs about painkillers with members of Chronic Pain Ireland aged 50 and older.' This study is being conducted by Mary-Claire Kennedy within the Health Research Board PhD Scholars Programme in Health Services Research and is a collaboration led by the School of Pharmacy, TCD, with the HRB Centre for Primary Care Research, RCSI Medical School. Are you still willing to participate in this research? Do you have any questions about the research project before we begin? Thank you. This interview will take approximately 20-25 minutes. Is now a convenient time for you to complete the interview or should I contact you another time? Do I have your permission to record this interview? All recordings will be held securely and accessible only to myself and my research supervisor. If you want to stop the interview at any time or you do not wish to answer a question please let me know.	Describes the aims and objectives of the study.
Demographic information and background on pain condition	Can you tell me what is the cause of your chronic pain? ➢ Duration of pain? ➢ Pain intensity/severity? ➢ Impact of pain on activities of daily living?	Background information on the nature of the pain condition including information on cause, progression and severity of pain condition on a daily basis.
Impact of pain and pain medications	Would you be able to name the painkillers that you take for your pain? *(Prompt frequency)* Can you describe when you take prescribed pain medications (triggers)? Are there certain times when you take more painkillers than others? Do you get satisfactory pain relief from the prescribed pain medications you are currently taking? Have you ever avoided taking prescribed painkillers? (*Prompts – no perceived benefit/ cost/ side-effects/ overuse*) *(if necessary follow-up)*	Discussion on the use of analgesics, including the use of prescription or non-prescription medications. Information on the use of analgesics during periods of pain exacerbations, and factors such as adverse effects that may alter analgesic use and efficacy of analgesic regimen.

	Do you ever reduce the number of tablets you take or avoid taking medication	
Management of analgesic regimen	Have you ever stopped taking a painkiller prescribed for you? What was the reason? Do you forget to the pain medications prescribed for you? Do you use any tools to help you remember to take your medications e.g. pill boxes, diary?	Discussion on adherence to the analgesic regimen, including the use of aids such as blister packed medications or diaries to record analgesic use.
Perceived barriers to management of CNMP with analgesics	Do you feel that you can discuss your pain medications with your doctor? Do you think there is more negativity surrounding the use of painkillers than other medications? Do you think that pain medications are more addictive or equally as addictive when compared with other types of pain medications? Did you try these treatments in addition to medications or as an alternative to medications?	Questions relating to the perceived efficacy of pain management focusing primarily on the efficacy of analgesics, however, questions also included personal perceptions of analgesics and external influences such as relationships with healthcare professionals and attitudes of friends and family members.
Supports available to patients in the healthcare system	What is your opinion of the support available to chronic pain patients in the management of their condition for instance your access to: ➢ physiotherapists ➢ occupational therapists ➢ pain clinics and specialist?	Discussion on the management of CNMP in the context of the Irish healthcare system including access to assistance from allied healthcare professionals and pain consultants.
Closing statements for interview	Thank you again for taking the time to complete this interview. I will send you a copy of the interview transcript in the coming weeks. You will have an opportunity to remove any comments from this transcript. You may also still withdraw from this study if you are no longer willing to participate. If you wish to discuss further any of the issues discussed today, please do not hesitate to contact me or the secretary of Chronic Pain Ireland.	Information on supply of the transcript to the participant and their right to edit the transcript or remove themselves from the study.

Figure 7-3: Question themes, interview questions and reason for inclusion of question

Interviews were completed over a 3 month period, from June to August 2013. Interviews were 20 minutes to 90 minutes in duration, with an average

duration of 35 minutes 30 seconds. All interviews were conducted by Mary-Claire Kennedy using teleconferencing facilities in a private meeting room in the School of Pharmacy, TCD and were audio-recorded using the free download software package Audacity® and also with the Olympus Digital Voice Recorder VN-712PC. All recordings on the Olympus recording device were also saved onto the researcher's password protected laptop. The interviews were transcribed verbatim by the researcher over a number of weeks. A copy of the transcript was posted to participants who were invited to amend or edit the transcript; two blank pages were also provided for additional comments or clarifications (*Appendix F: F.7*). Passages of text that were to be removed prior to analysis were highlighted by the researcher. These passages of text revealed geographical location or the names of family members, or healthcare professionals associated with the participant. It was essential that these segments were removed from the transcripts; as the sensitivity of the topics discussed over the course of the interviews, confidentiality was of utmost importance. Following application of these revisions an electronic copy of the transcript was transferred to NVivo ® Version 10. *Table 7-1* summarises the duration of each interview and the number of transcripts edited upon review by participants.

Table 7-1: Interview duration and requested revisions to transcripts

Participant Number	Interview Duration	Additional Comments
1	21min 59sec	
2	48min 52sec	Transcript Edited
3	25min 31sec	Transcript Edited
4	23min 41sec	
5	36min 50sec	
6	23min 44sec	
7	23min 16sec	
8	26min 32sec	
9	35min 42sec	
10	34min 18sec	
11	37min 51sec	
12	36min 28sec	Transcript Edited
13	58min 16sec	Transcript Edited
14	32min 01sec	
15	35min 17sec	Transcript Edited
16	21min 24sec	Transcript Edited
17	49min 37sec	Transcript Edited
18	41min 42sec	
19	25min 14sec	
20	34min 37sec	
21	22min 35sec	
22	32min 39sec	Transcript Edited
23	91min 01sec	
24	30min 40sec	
25	27min 15sec	Transcript Edited and Withdrawn
26	28min 11sec	Transcript Edited
27	24min 58sec	
28	64min 37sec	Transcript Edited

7.3.3 Data Management and Analysis

Analysis of the interview transcripts was conducted using the Framework Data Management approach and applied thematic analysis, as described in *Chapter 6*. *Table 7-2* lists the Framework Data Management categories used to initially organise the data obtained from the interview transcripts.

Table 7-2: Framework data management categories

A :Condition Type	B : Year or Date of Diagnosis	C : Description of Day to Day Pain	D : Impact on Activities of Daily Living
E : Medications Reported by Participant	F : Efficacy of Analgesic Regimen	G : Attitude towards Analgesic Medications	H : Side-Effects Arising from Analgesic Medications
I : Management of Side-Effects Arising from Analgesic Medication	J : Relationship with GP	K : Relationship with Pharmacist	L : Access to Services
M : Additional Comments relating to Pain Condition or Management of Condition	N :Alternative Approaches to Pain Management	O : Comment on Primary Care Management of Pain Condition	P : Concern about Addiction or Tolerance to Analgesic Regimen
Q : Minimising or Maximising Analgesic Use	R : Role of Consultant Level Care in Disease Management	S : Public Private Healthcare	

7.4 Results

Twenty-seven transcripts were retained for data management and analysis. These transcripts were from interviews with 10 men and 17 women. Participants were aged between 50 and 69 years. Participants reported pain arising from a variety of causes with differing severity and location. Six reported a diagnosis of fibromyalgia, 7 reported back pain, 4 reported neuropathic pain conditions, 1 reported chronic leg pain of unknown origin, 3 reported neck pain, while the remaining 6 reported pain of various aetiologies or causes including, chronic migraine, endometriosis, vulvovaginal pain and spina bifida.

There are a number of points which should be noted prior to presentation of the findings for this research.

- Interviews were conducted over a 3 month period from June to August 2013. During this period, the weather was unusually warm and sunny. Several participants described diminished pain and improved mood associated with the fine weather.

- The cost of medication was a point of discussion amongst interviewees. This topic was receiving substantial coverage in the media around this time, particularly the cost of medications in Ireland in comparison to other European countries and the substitution of branded medications with generic equivalents.
- Finally, this research was conducted during a time of international and national economic recession. Concerns such as the cost of healthcare and access to services were common to all interviewees and discussed extensively.

7.4.1 Overview of Emerging Themes

Four global themes were identified following completion of data analysis:

1. Clinical Factors
2. Non-Clinical Patient Factors
3. Health System Factors
4. Self-Management

Table 7-3 outlines the key child and parent nodes that informed the development of organising and global themes. A completed COREQ-32 checklist for this study is provided in *Appendix F, F.7.*

Table 7-3: Parent and child nodes (horizontal) and organising themes (vertical)

Healthcare Professional Management Connectedness or Cohesiveness **Primary Care** Role of GP *Advice* *Empathy* *Knowledge* Medication Management *Prescribing Approach* Role of Pharmacist *Pharmacist Assistance or Understanding* *Pharmacist Not Helpful* *Role of Pharmacist in Disease Management* **Secondary Care** Role of Consultant *Empathy* Pain Clinics *Experience of Pain Clinics* *Medication Management* **Healthcare System** Public Private *Access* *Experience* *Financial* *Geographical* *Waiting Time*	**Healthcare System**	**Active Behaviour Strategies** Classes Exercise Modified Posture Tai Chi Yoga or Pilates **Active Cognitive Strategies** CBT or other Cognitive Interventions Mindfulness Pain Management Programme Social Interests **Passive Behavioural Strategies** Aromatherapy Heat or Cold Therapy Massage Rest **Passive Conventional Medicine** Acupuncture Chiropractor Hydrotherapy Physiotherapy TENS **Self-Education and Support**	**Self-Management**
Third Party Influences Family Other Patients Public or Other *Internet* *Public* **Personal Perception of Pain Condition** Isolation Subjectivity of Pain Condition Understanding or Acceptance **Financial** **Beliefs about Medications**	**Non-Clinical**	**Medications Reported by Participant** **Efficacy** Attainment of Analgesia *Opioids* Non-Attainment of Analgesia *Opioids* Self-Management of Analgesic Regimen *Maximising/ Minimising Analgesic Regimen* **Long-Term Use** Availability of Additional Analgesia Benefits of Long-Term Use Health Outcomes with Long-Term Use **OTC Reported by Patient** **Rx Reported by Patient** **Side-Effects** Description of Side-Effects Management of Side-Effects **Addiction** **Pain Condition Related** Causative factor Impact on Daily Activities	**Clinical Aspects**

7.4.2 Theme 1: Clinical Factors

7.4.2.1 CNMP Condition

At the start of the interview, participants were invited to discuss the aetiology and progression of their condition. Some individuals provided a succinct clinical description of their condition, while others contextualised the condition in terms of alterations in physical activity or social, occupational and economic challenges arising from the condition. The researcher did not interrupt the interviewees during this segment of the interview, as it allowed the participant to vocalise their own understanding and management of the condition and developed a rapport with the interviewer. This also allowed the interviewer to tailor the remaining questions on analgesic management and interaction with the health system based on the participants' opening comments. Discussion about the CNMP condition could then be divided into two broad organising themes: impact on daily activity, and condition severity and progression. The interview guide then required participants to discuss the merits and disadvantages of the analgesic regimen in the management of the condition. *Figure 7-4* indicates that efficacy, adverse effects, addiction and implications of long-term use; these were the key themes raised during the discussion about analgesic and adjunct medications.

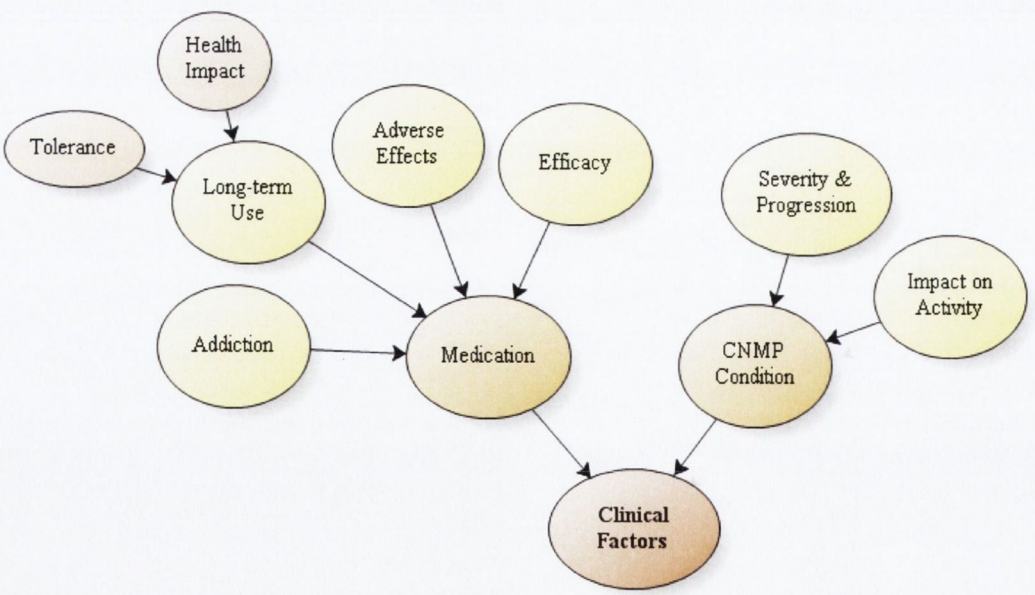


Figure 7-4: Clinical factors influencing medication use

7.4.2.2 Impact on Daily Activity

Pain affected participants in a variety of ways; some were restricted from completing daily activities such a washing and dressing, while others were limited only when they sought to undertake additional activities such as walking distances or driving. The more severe the pain condition, the less mobile and active the participant. Twenty-six interviewees contrasted previous activity levels with current abilities to contextualise current pain severity or to describe disease progression.

The pain was inhibiting me from doing other things. I do as much as I can while I am fit. That is the other thing, my stamina isn't nearly what it was. I could do a full day's work and do three meetings back to back whereas if I can do one expedition out of the house now in one day it is about as much as I can manage. (P28)

Despite the intensity of pain, several interviewees appeared determined to maintain a level of activity:

I wouldn't be able to walk now a lot anyway. It depends, there'd be times I might get a couple of days and I'd get away, and maybe I'd be able to walk a certain amount. Now when I say walking it'd be maybe walking 200 or 300 yards at a time. (P7)

For some interviewees, pain progressed during the course of the day thereby limiting the individual's functionality by the evening. This placed a limitation on the individual's ability to engage in social or leisure activities:

Getting dressed in the morning is okay, and I sort of manage a way around doing things, but I would say now, in the evening now... if I was to go out say, to do something I just couldn't go out, I wouldn't be able to sit, I wouldn't be able to manage even if I go to a play or something like that, it would just be, the pain would be too intolerable. (P19)

7.4.2.3 Condition Severity & Progression

Similar to the limitations placed on an individual's ability to engage in daily activities, pain severity is a subjective variable. Pain severity varied on daily basis for most participants depending on the level of physical exertion or compliance to

the prescribed analgesic regimen. However, a number of interviewees described being in severe pain, which was not alleviated by self-management strategies or analgesic interventions:

It's a 10 every day, and I have a pretty high pain threshold but this is unbearable. (P10)

For one interviewee, the pain was so severe on occasion that it appeared to be unmanageable, debilitating and intrusive on everyday activities:

It's a type of signal that it's all over [pause] *there is nothing you can do, you can only feel the pain, you can only think about the pain, you can't even eat because the pain is too bad.* (P14)

7.4.2.4 Medication

Questions based on analgesics and adjuvant agents were the primary focus of the interview. Participants spent considerable time discussing their perception and knowledge of the risk-benefit ratio of analgesics and also contextualised the role of these medicines in the overall management of their condition. Analysis of the dataset yields organising themes and global themes reflecting this debate on the relative advantages and disadvantages of medications.

Efficacy

All participants indicated that analgesics were an important element of their daily pain management. In cases where medications provide effective analgesia, interviewees described the importance of adherence to the prescribed regimen as pain may recur upon omission of a dose. Analgesics were taken according to the 'by the clock' and 'by the ladder' methods of pharmacotherapeutic management (470). Participants highlighted that omission of a dose may give rise to pain and discomfort:

If I happen to forget taking them or maybe went off by mistake, and I wouldn't have taken them, I'd know that evening that it would be much, much more painful anyway. (P8)

The Targin[****] *I am on at the moment, I take two they are slow release now I have no breakthrough one as they would call it. I would take one every twelve hours.* (P17)

Participants appeared to become frustrated when analgesics failed to adequately manage their pain condition; this is sometimes expressed in terms of the burden of purchasing the medication and the frustration in not attaining the expected analgesia:

And they were quite expensive and I didn't really find a huge difference. But I feel really frustrated to be spending money and not really getting any benefit from it. (P3)

For 13 participants, regardless of whether medications were successful in attaining analgesia, there appeared to be a reluctance to take analgesics either due to frustration with the chronicity of the condition or the perceived ineffectiveness of pharmacotherapeutic interventions:

I suppose for a person who never took a tablet for anything and now I am in a situation for the past number of years where it's a box full of tablets and you look at them and you think, what concoction will I take today to try and get relief and I still don't get that relief. (P18)

Participants described the internal conflict they experience when taking analgesics, acknowledging that they are an effective enabler, allowing the individual to complete daily activities, however, they oftentimes counteract the individual's inherent beliefs or preferences about medication use:

It is a terrible vicious circle that you get into [pause] *you are taking the medication, you know it is not going to cure it and at the same time you keep taking it in the hope of just bringing it down a few levels.* (P18)

Adverse Effects

Adverse effects associated with pharmacotherapy may also alter an individual's adherence to a prescribed regimen (471). Adherence may be associated with the

[****] Oxycodone/Naloxone combination

patient's perception of the necessity for the medication, misconception about the medication and benefits or side-effects of the medication (460). Adverse effects were described for NSAIDs, opioids and adjunct agents, however, adverse effects arising from opioids appeared to cause most distress for interviewees. An overview of adverse effects described by participants is provided in *Figure 7-5*. All participants reported adverse effects and were able to attribute the adverse effects to the correct analgesic. The nature and severity of some adverse effects caused some participants to comment that the condition was preferable to taking the medication:

Really all the time I felt the cure was worse than the disease. (P24)

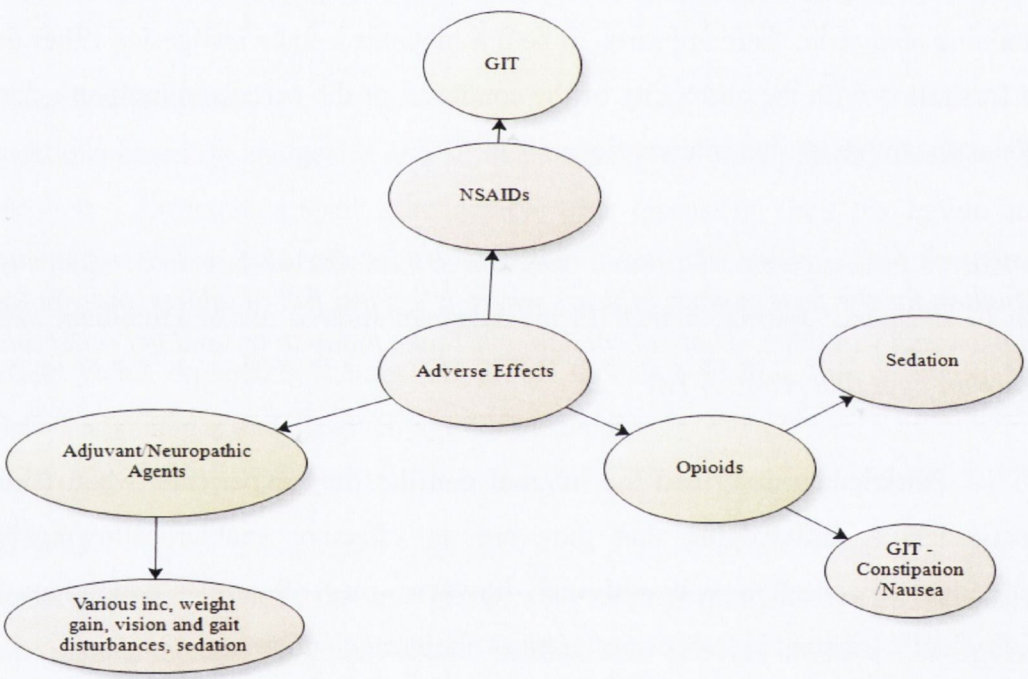


Figure 7-5: Medications referenced by CPI members that caused adverse effects

NSAIDs

Participants appeared to be aware of the adverse gastrointestinal effects of NSAIDs, however, no one discussed the potential adverse cardiovascular effects of this medication. One participant described the development of a stomach ulcer which he stated was caused by diclofenac:

I have osteoarthritis...then eventually I got a stomach ulcer from taking Difene®.[††††] *They say that it may have been stress but it may have been Difene®. Yeah, they found a stomach ulcer and they said the Difene® probably caused it.* (P27)

One participant mentioned that she had recently been prescribed a naproxyn/omeprazole formulation so that she would no longer have to take a separate PPI concurrently with an NSAID to minimise GIT effects:

I'm on the Vimovo®[‡‡‡‡] *because my tummy was full of damage from Difene® and things like that.* (P7)

Adjunct/Neuropathic Agents

Adjunct medications including pregabalin, gabapentin, amitriptyline and duloxetine were described as causing adverse effects amongst participants. All participants that reported present or past use of gabapentin or pregabalin also described adverse effects arising from these medications. Weight gain was a commonly reported adverse effect associated with pregabalin:

The other side effect that I have too which is a side effect of the medication, is that I am overweight, and that is because of the increased appetite... cravings for sweet foods because of medication (P9)

Lyrica® put on a huge amount of weight. (P15)

Eight participants reported taking amitriptyline at the time of the study or at some time in the past. A number of individuals described ceasing this medication due to the associated sedation:

I was told to try amitriptyline or something, an anti-depressant. I remember taking that from the first doctor [pause] *now that* [pause] *even the smallest amount of that would have me asleep for 24 hours..* (P10)

[††††] Diclofenac
[‡‡‡‡] Napoxen/Omeprazole

One participant described a serious outcome arising from sedation with this medication which prompted her to discontinue its use:

The amitriptyline I found quite effective except for sedation, I took it in combination with everything else for a while and I found that was a good concoction, but I had a car crash which was purely because I fell asleep with three kids in the car. (P26)

Opioids

Two participants referenced the use of a weak opioid (low dose codeine containing formulations on Step 2 WHO Analgesic Ladder), 6 referenced use of a moderate opioid (high dose codeine formulations and other opioids on Step 2 WHO Analgesic Ladder) and 9 referenced use of a strong opioid medication (Step 3 WHO Analgesic Ladder). Four participants reported the use of a patch containing a strong opioid. Strong opioids in particular were reported to cause sedation and GIT side-effects amongst those participants who were currently taking a strong opioid or had previously taken this medications. The adverse effects and potential substance dependence problems of opioids are widely known by the general public. It is therefore unsurprising that interviewees referenced such concerns in the interviews. For some participants, these adverse effects necessitated discontinuation of the medication, even if this medication was effective in providing pain relief:

I tried this other one that came out a few years ago, in 2010, Palexia®, and I was very excited about it, but I couldn't take it at all, I actually fainted after taking it, within an hour of taking one [pause] *I was sick with them, and weak you know, well I was taking them for the two weeks and that's it... it sort of helped with the pain but I couldn't* [pause] *you see I am trying to balance.* (P11)

One participant described the sense of detachment associated with opioids as impacting on her ability to function on a daily basis:

I found that I was too sedated [pause] *not so much sedated more that I felt maybe a detached, like feeling like the world was going on around me. Even the children were saying that my favourite hobby was sleeping!* (P26)

Constipation was reported by 8 participants when prompted by the researcher. The prompt was perhaps necessary, as some individuals may have been embarrassed to discuss this issue with an unknown individual. Four participants reported use of a prescription or non-prescription laxative to the researcher:

Constipation is a continuous problem, it's just that it has become very, very severe in the last month. I have been taking laxatives for many years. (P16)

One participant had developed an exercise and stretching routine to alleviate constipation and to supplement laxative use.

I manage the constipation using exercises, there's a particular yoga exercise that I use to activate peristalsis, it's a kind of rippling exercise... of the stomach muscles which helps, but also... I would have...bisacodyl,. (P13)

Addiction is a particular concern for a number of participants and referenced only by those interviewees taking an opioid containing formulation. However, there did not appear to be a consensus in opinion relating to the potential of addiction or tolerance to opioids, a number of participants described it as a serious concern, while a number of individuals did not think that the issues of addiction was applicable to them:

What I have learned is the opiates are only [pause] *I understand people take them for a long time but there should be something that stops you, because you eventually reach the stage where you need more and more to get the same effect* (P23)

Despite the efficacy of the medication, it appears that respondents are aware of its addiction potential and the difficulties associated with discontinuing this medication:

Addiction would be of a concern for me and with the family here and you're concerned about things like this. And they are very much aware of what they do. And they're concerned that I might be dependent too much on them. (P16)

Some interviewees feel that they are obliged to adhere to the regimen as the medications effectively manage their pain and contribute towards physical functionality:

I have to take them, I have no choice, I can't live, I tried and I'm also very conscious of the nature of quitting and the addictive nature. (P21)

Two participants described overcoming their concerns about addiction and tolerance through discussion with the GP or pain specialist responsible for prescribing the medication:

All the medicines I have I use them in the proportions that they are required. For the simple reason that I know if I misuse them [pause] *my GP acknowledge very early on that I don't have an addictive personality* (P13)

Again [name of consultant] is very good at explaining it and saying that once your body needs it you don't have to worry about becoming addicted to it. (P26)

Long-Term Use

Participants discussed the long-term health implications of taking analgesics and also the potential problems with the extended use of analgesics. These were distinct concerns and included impact of medication on their physical health, tolerance to the analgesic effect of the medication and the implications for the long-term pain condition. The concept of tolerance to the analgesic effect of certain medications necessitating elevated doses after a certain period, while discussed as a long-term consequence of medication use, is consciously separated from the problem of addiction to analgesics when discussed by participants:

I didn't want to be [pause] *for the rest of my life, that wasn't going to do* [pause] *it was going to relieve me of my pain, but really the end result would be that it would damage my system.* (P24)

I worry, it is kind of an irrational worry, but it is a worry all the same, I kind of realise if I was landed on a desert island in the morning and I didn't have access to these things how would I function [pause] *like I know my functioning is* [pause] *well*

I am functioning [pause] *it is totally dependent on a 'substance' and that's really scary. And yet I know I can't function without it or if my pain increased where do I go from there?* (P 26)

However, one participant balanced these concerns with the prospect of enduring pain for a prolonged period:

I was speaking to a colleague at work about the very same thing, we were sitting on night duty talking about it and she said, now you might die younger, but at least you won't be in as much pain. [Laughter] (P 21)

7.4.3 Theme 2: Non-Clinical Patient Factors

Interviewees also described a range of additional factors that influence analgesic use which were not directly related to the pharmacological aspects of medication; these are presented in *Figure 7-6*. Some of these relate to the individual's perception of the condition or beliefs about allopathic interventions including medications which inform the individual's interaction with the health system and internal appraisal of management strategies. Practical aspects of healthcare such as the financial burden of purchasing regular medications, or financing access to healthcare through private channels, are also considered.

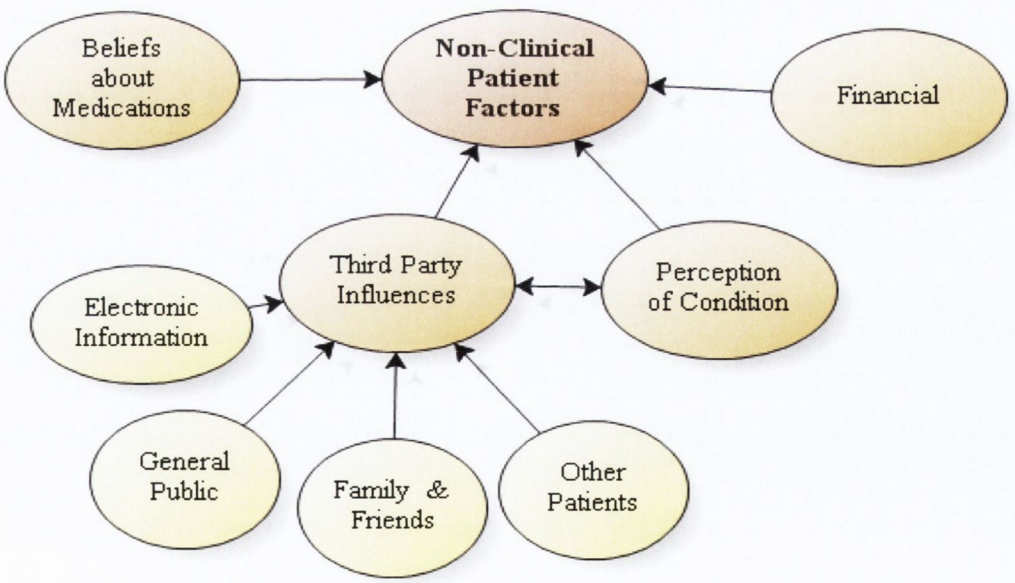


Figure 7-6: Non-clinical patient factors influencing medication use

7.4.3.1 Beliefs about Medications

A number of participants have a positive outlook on analgesics, their role in management of pain and as a facilitator for participating in daily activities and interacting with family and friends.

My perception of it is that it's essential for the maintenance of my health and wellbeing. It also assists in maintaining my relationship with my wife, my children and my grandchildren. (P13)

It appears that such participants, while not pleased about taking medications consistently, have reflected on the relative merits of continuing on a prescribed regimen:

No you know, I know we need them, I know that and a lot of people wouldn't be alive without them. (P1)

Contrast this with those participants with a negative outlook on analgesics, who viewed them as perpetuating a negative cycle of use which they are unable to stop:

And you know it is a terrible vicious circle that you get into, you are taking the medication, you know it is not going to cure it and at the same time you keep taking it in the hope of just bringing it down a few levels and that is [pause] *I think if I was dealing with somebody else, I would be telling them for God's sake* [sic] *come off that medication, and here I am. I am caught up in it.* (P18)

7.4.3.2 Perception of Condition

Depending on the severity of the pain condition, participants described differing perceptions of the condition. A number of patients had a negative outlook owing to the inevitable progression of the condition and the development of co-morbidities with advancing age:

It is part and parcel of my every day you know. I dream of the day that it won't be, but you know it is an ongoing dream, you know maybe it is good to think maybe it is possible but you know I am getting older, and you know, and I don't know what is going to happen. (P11)

Despite the severity of pain, one participant emphasised the need to adopt a positive outlook despite the chronic, intractable nature of the condition:

Just laugh because there's no sense [pause] *I honestly believe this, I can't do anything about it so, there's no sense in worrying about it.* (P16)

7.4.3.3 Financial

The cost of healthcare, particularly medications and private specialist care, was a concern for a number of participants, particularly those seeking healthcare through private means. This is contrasted with difficulties associated with access to similar services in the public system. Participants appear to factor the cost of management of their condition as a barrier to effective intervention:

But there is a drain, I mean there is no point in saying there isn't, but I'm very practical to say well, you know what, they're keeping me going so, I'll pay it. (P14)

Similar to the discussion on adverse effects, participants appear to consider the benefit-burden implications when spending money on healthcare:

The way I have sort of gone because paying, not that I can afford it, but paying you will get in somewhere much quicker anyway and you sort of have to weigh up things. (P1)

One participant described seeking a loan from a family member to meet the cost of consultant care:

But the only thing about that is, you know, I've had so many MRI scans, consultants, going to see people, whatever, and you have to pay everything up front. So, I've had to borrow money [pause] *I've had to ask my mother for money, you know.* (P4)

7.4.3.4 Third Party Influences

Participants have developed an understanding or perception of their CNMP condition through personal experience and observation of other patients or

interaction with family members. Interviewees described how they have reflected on these observations and altered their outlook on the condition or medication use.

Family

Family members were universally concerned about the pain of interviewees and were more accepting or encouraging of analgesic use than the general public. The support received from family members appears to dispel some of the reservations interviewees may have about taking analgesics:

Probably my family would be different because they've actually seen me and seen me in pain and they would be very much inclined to say look you know you're going to end up taking it, why don't you just take it now instead of in 4 hours time when you're much worse'. They would try to encourage me to take it much more. (P7)

However, it is apparent that the condition and the role of analgesics can at times place strain on these personal relationships. This participant described her husband's support of the use of the medication, as it permits the individual to undertake shared family activities:

My husband is the worst, he says I self-medicate [pause] *He doesn't understand why I don't take them all the time...he wants me to be better...And he wants me to do things, you know, as a couple, as a family.* (P4)

Other Patients with CNMP

Participants described how information on the condition and medications may also be gathered through interaction with other patients. However, this does not appear to be as popular as receiving information through sources such as patient support groups, healthcare professionals or through independent research:

And somebody said last Tuesday, I was in a meeting, and they said, 'Have you thought it might be the tablets that you are taking, have you changed tablets lately?' And I said 'Yeah'. 'Well that could be it and you ought to investigate that'. (P22)

General Public

Previous research has identified the perceived lack of understanding experienced by individuals with CNMP by society, which contributes to low self-esteem and

social isolation (472). Participants in this study unanimously described a feeling of isolation and misunderstanding from the general public. Indeed some interviewees described a sense of stigmatisation whereby an individual described back pain as being perceived by members of his local community as a term to disguise a psychiatric illness:

With this type of problem people think, well you know, years ago all the back problems [pause] *wink, wink, you know.* (P3)

I suppose what I would find about the community in general is that nobody understands the word chronic...By my nature I am always smiling, I suppose always in good humour and never let on what I am suffering underneath. So when people see you and you are looking well and tanned and say god you are looking great you must be great, you must be better. (P18)

Some interviewees believed that if their condition was physically apparent they may experience more understanding and acceptance from the public:

Unless people can see you're on crutches, people would be concerned about you. Some people [pause] *like some people, when you sit on the wall to have a rest. People just look at you, 'jeez* [sic] *he's too lazy even to walk. But unless they can see a reason for the pain, they don't believe it.* (P16)

Electronic Information

Electronic resources are an easily accessible and inexpensive source of health and medication information for patients to supplement counselling received from healthcare professionals (473). Several participants described accessing information on the internet and described the contribution of this information towards their personal appraisal of their medication regimen or their consultation with the prescribing physician:

If I go to somebody and they prescribe something, the first thing I do is go to the internet and look it up. And, what tends to be on the internet, to be honest with you, is quite a lot of negative stuff. And again you're starting off with a negative base about something. You know, even before you've tried it [pause] *But there's some people you know, in fact would say the internet, it's not a great thing, but then you pretty much have to be, keep yourself aware of what's in these products.* (P3)

One participant described engaging with other patients through online fora where they learned of potentially inappropriate analgesic use from other users. It appears that the participant in this way compared her own analgesic regimen to that of other CNMP patients:

I am part of a forum and I have seen people take medications that would just scare you, you know, and they would be doubling up on the same medications. (P11)

7.4.4 Theme 3: Self-Management

Twenty participants referred to number of different self-management strategies throughout the course of the interviews. These strategies appeared to supplement therapeutic (i.e. pharmacological and surgical) interventions and were sometimes the patient's initial response in addressing a pain complaint. It is important to note that the population interviewed were a self-recruited population and were members of CPI; this cohort may be more empowered than other CNMP patients and they may also be experts in aspects of their own illness. Blyth et al considered self-management strategies as active or passive interventions undertaken by the patient to alleviate pain (100). These strategies are summarised in *Table 7-4*.

Table 7-4: Active and Passive Strategies undertaken by CNMP patient during self-management

Active Strategies		**Passive Strategies**	
Active Behaviour	***Active Cognitive***	***Passive Behaviour***	***Conventional Medical***
Corrective Posture	Relaxation	Diet	Medication
Exercise	Distraction	Avoiding Activity	Physiotherapy
Social Activation	Prayer	Rest	TENS
Work	Meditation	Hot baths/showers	Acupuncture
Usual Tasks	Reduce Stress	Hot/cold packs	Chiropractor
		Smoking/Alcohol	
		Massage	

Without prompting or direct questioning by the interviewer on the subject, participants referred to a variety of active and passive approaches, some using these strategies in isolation, some in conjunction with other strategies or to supplement conventional therapeutic interventions; these are presented in *Figure 7-7*. The

model, consisting of nodes and organising themes, has been developed under the global theme of self-management and has been developed to incorporate the concept of active and passive strategies. There did not appear to be a disparity between genders when discussing the inclusion of self-management approaches with both men and women alluding to these strategies. All participants acknowledged the complexity of CNMP and stated that these self-management strategies were a method of addressing the psychological and emotional elements of the condition:

More than just the meds to deal with chronic pain....Absolutely there's so much psychology involved in pain that it's unreal. (P24)

One participant highlighted the importance of a self-management strategies including self-education and a patient centred management plan:

You don't get better or you don't change, and this is my looking at it... if you can't be involved in your own treatment as such [pause] *you have to have hope like you know.* (P17)

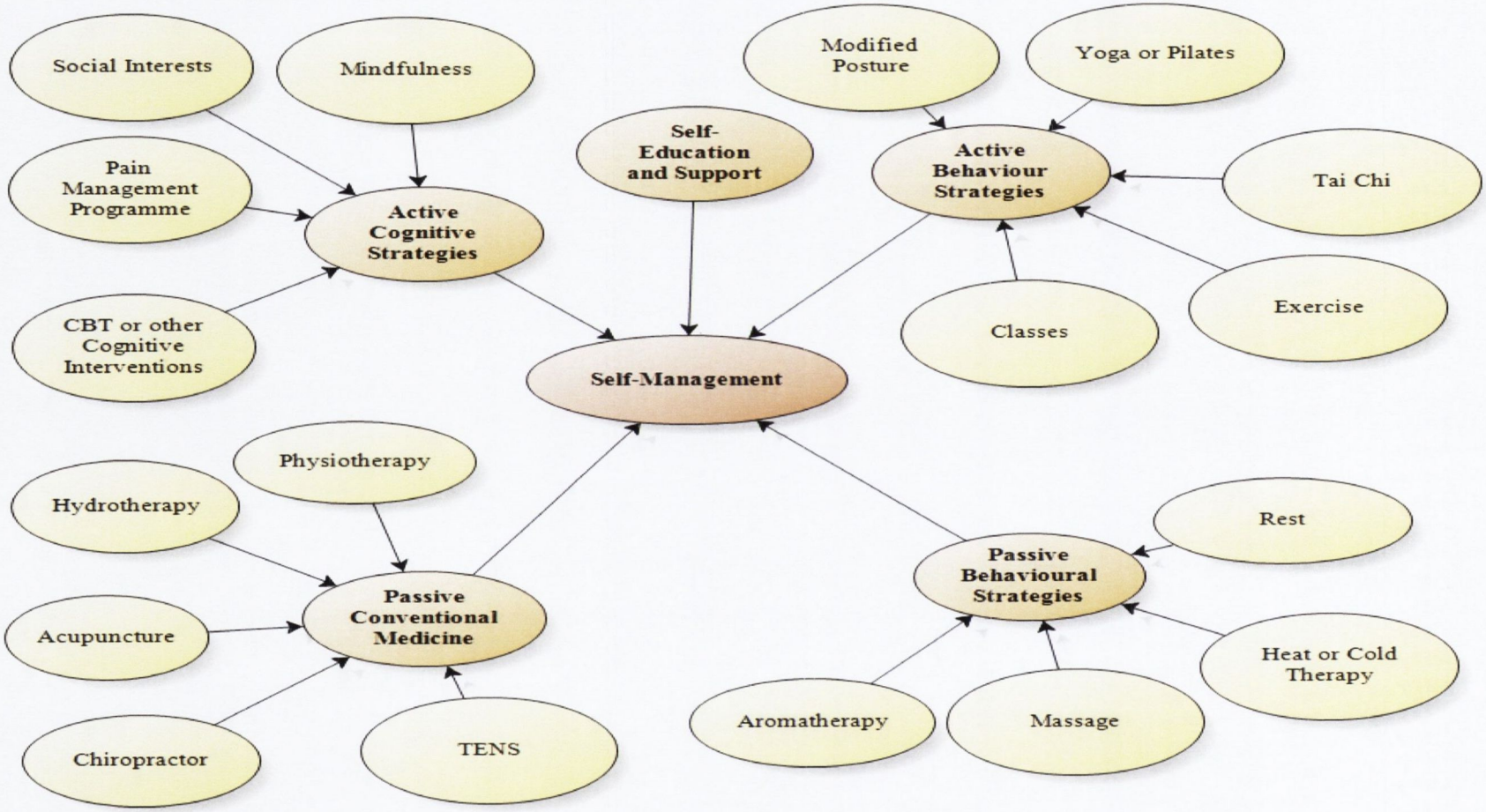


Figure 7-7: Self-care approaches reported by interview participants

7.4.4.1 Self-Education and Support

The role of patient support groups and self-education undertaken by interviewees is not considered as a singular activity in the active and passive strategies proposed by Blyth et al, but nonetheless, it represents an important self-management strategy to this cohort; it has therefore been considered as an adjunct to this organising theme. Interviewees referenced access and use of support groups such as CPI and Arthritis Ireland and have incorporated measures discussed in workshops and meetings into their every-day routine:

One of the great benefits of Chronic Pain Ireland is the fact that you're in a forum where people take you as you are [pause]. *They understand how difficult it can be to be in pain and to not be believed.* (P13)

Attending the workshops offered by CPI also offered a social outlet for some participants, allowing them to form relationships with other members thereby perpetuating the self-management techniques learned in workshops and seminars:

Well what I do get great pleasure out of, it was through Chronic Pain Ireland that I heard about you doing this research and I find their quarterly newsletters brilliant and I try to go to as many meetings as possible and I find that a great source of information. (P18)

An interviewee with fibromyalgia stated that receiving a definitive diagnosis for her condition was one of the most important steps in self-management. The diagnosis enabled the patient to access educational literature on the condition and develop a personalised regimen to effectively manage the condition:

The best day ever was when I got my diagnosis, I was able to go home look it up learn about it and you know, that was great in itself. Then eventually to get a bit of ease through the night, that I could sleep a bit, and you know allowing myself if I needed to have a break in the afternoon just to put my head down for even for a half an hour even acknowledge that I needed that. (P17)

This participant considers herself to be central to the patient-healthcare professional management equation, as any adverse events arising from analgesic interventions would impact only on the participant:

And living with a pain condition...you realise a big part of it is your mind set and your attitude. I mean my own attitude is that really I have to be part of the picture, I have to involve myself, I have to find out, I have to educate myself, I have to know what works for me and what doesn't, I have to know, I can't be a guinea pig like you know, because at the end of the day every time it is I that will suffer if things go wrong. (P17)

7.4.4.2 Active Strategies

Pain Management Programmes

Pain management programmes are based on cognitive behavioural principles and are a treatment for people with persistent pain which is adversely affecting their quality of life (247). The programmes are designed to recognise the biopsychosocial nature of CNMP conditions and examine the effects of CNMP on the individual's physical and psychological wellbeing. Pain management programmes are demonstrated to be advantageous for patients with CNMP when compared with no treatment or usual treatments (474). The outcomes following participation in a pain management programme range from pain relief, improvement in the function and emotional status of the patient or a return to work or diminished healthcare use (475).

Those participants (9 participants) that discussed attending a pain management programme outlined the improvements the programme had made to management of their condition. The programmes appeared to provide patients with skills that could be incorporated into their daily lives while also acting as a stimulus to seek further information on the condition:

The pain management course for 3 weeks, that helped me. (P14)

So I just finished a pain management programme and that has sort of given me more education [pause] *Well, it is multidisciplinary, you know physio, OT* [occupational therapy], *some* [pause] *not really education on medicines really, which is something they just wouldn't put into that model I suppose, and then there*

is psychology, and a lot of things about mindfulness and relaxation, you know, a lot of education about chronic pain, you know living with it, managing it, coping with it, flare ups, pacing, all that kind of thing. (P11)

The pain management programme also informed participants on the management of their analgesic regimens, thereby supplementing the role of the GP or prescribing physician:

But if, now one thing I was doing which was wrong, I was watching the clock and saying, oh I can take another tramadol, you know what I mean, I'd say every 4 hours. [pause] *With the pain programme I stopped doing that.* (P14)

Exercise

Some participants were severely debilitated by the pain condition and in some instances unable to leave the house for prolonged periods of time. However, six participants reported that exercise was an important component of their self-management approach, maintaining mobility and strength; any exercise undertaken by participants was beneficial, provided that it was not excessive:

I try to continue to be active in as far as that's possible, I exercise quite regularly, I have a variety of exercises that I do to keep my system supple. (P13)

I like to be active anyway but it can be hard but that doesn't stop me. I might go for a walk but I don't go for a long long walk I find that is counterproductive. (P17)

Mindfulness

Mindfulness is a technique developed in Eastern meditation practice and is described as "paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally" (476). Only one participant described formally incorporating the technique into a self-management programme:

I use Jon Kabat Zinns CDs. I have found with people on pain management courses that people seem to be getting little segments from his series but they are not advised to use the full series. They are not aware of it actually. You know mindfulness is fine provided when it is taught or learned fully and practised fully and it is a huge help. (P15)

Social Activation

Isolation may arise from an inability to engage with social activities and is compounded by a sense that members of the community lack empathy for their condition. The concept of legitimation of CNMP is a recurring theme in the literature and is supported by the sense of isolation which becomes apparent when participants discuss their personal experience of CNMP in the context of friends and wider society (477). One participant advocated a social interest outside of the home as this prevented him from focusing on the pain:

I would encourage people in this same situation as myself to have an interest outside the home [pause] *it's an outlet. It keeps me from thinking about my pains and I get benefit from this activity.* (P16)

Pain management programmes, previously described, are doubly advantageous to patients equipping the individual with a self-care skill set, while also providing them with a support network of patients with CNMP. One participant outlined how this group of attendees at a pain management programme discussed pain intensity in a social setting:

I've met two people at the pain management programme and there's a few of us kind of meet every now and again for coffee [pause] *and the way we weighted it, the pain goes from one to ten. Anything from one to five you'll manage yourself with painkillers, a little bit of psychology in the head, a little bit of walking...Anything that's goes six, seven, eight, nine you cannot block it out.* (P14)

7.4.4.3 Passive Strategies

Rest

Relaxation techniques reduce anxiety and may be beneficial for some CNMP patients (478). However, since this intervention is usually practised by the patient in the home setting, it is difficult to capture the nature and extent of this activity. Several participants acknowledged the physical limitations that pain placed upon achieving daily activities and described that a restful period may be required to

recuperate from such exertions. One participant described their own relaxation technique employed during winter periods when the pain condition was most severe:

Most evenings here during the winter I have relaxing time we will say between 5 o'clock and 6 o' clock. I throw on the television, I have Andrew Rieu tapes or something like that, I can sit down [pause] *just relaxing ... but once say I get back into normal things again the pain comes back.* (P2)

Acupuncture, Aromatherapy and Massage

Massage and aromatherapy are popular passive behavioural strategies reported by many participants. Massage has been demonstrated to be effective for a variety of CNMP conditions and is more effective than acupuncture, self-care educational materials or muscle relaxation exercises (479):

[I] go for an occasional massage, which is lovely at the time, but there is no long term benefit from it. It is literally just the hour I am there, it is nice but from a financial point of view, I find it hard to justify, just an hour relief as opposed to getting a week's relief or whatever [pause] *so finances would be one thing as to why I don't do other things.* (P26)

While most interviewees acknowledged the benefits that are derived from incorporating one or multiple active or passive interventions, some refered to the financial burden associated with these additional strategies. Passive behavioural strategies such as aromatherapy, massage and acupuncture were referred to as a luxury for a number of participants, as it is not financially sustainable:

I used to go for a massage, an aromatherapy massage, once a week, em, but it was just lavender oil that was used nothing else, and it would be something that I would really love to do again but I just can't afford to do it. (P9)

The acupuncture I find very, very good but I probably need to be going more frequently, but because I am not able to work because of the pain, it makes it difficult financially to do that. (P7)

Hot/Cold Packs

Application of hot or cold packs to the site of pain was reported by almost all participants reporting pain of a non-neuropathic origin. Hot and cold packs were used as an intervention to minimise use of more or stronger analgesic medication:

For a long time I wouldn't have taken more than that for a long time, because I just find lying down with a heat pack really nearly does it, with two ibuprofen is quite effective. (P12)

Transcutaneous Electrical Nerve Stimulation (TENS)

Five participants referred to using TENS; some indicated that they failed to experience adequate analgesia with the use of the machine. Those that found TENS effective also reported that additional methods were employed to supplement the pain relief delivered by TENS:

I got the TENS machine and I do find the heat, we have a thing that you stick in the microwave, that helps. (P6)

This captures the stepwise pattern that many interviewees described in approaching their pain management, moving from a non-pharmacological strategy to medication; although frequently, participants described this approach exclusively in terms of analgesic medications:

Well, I'd normally start with one and hope it works, but I do usually end up having to take a second one and, um, I kind of, try and use heat or a TENS machine or something else rather than take anymore, but often I'd need four. (P7)

Hydrotherapy

Hydrotherapy is frequently undertaken in the context of rehabilitation facilities and/or pain management programmes. Several participants described an informal approach to hydrotherapy, attending a swimming pool or aqua-aerobics classes as a method of diminishing pain and improving mobility:

In the swimming pool there is a sauna and a steam room so all things help. None of them cure but they all [pause] *when they are used help to ease the pain.* (P28)

7.4.4.4 Experiences with Self-Management

While many participants reported experimenting with self-management interventions, not all found these strategies advantageous to their condition. One participant described a frustrating experience with group sessions of cognitive behavioural therapy (CBT). This demonstrates that additional interventions undertaken by CNMP patients are frequently tailored by the patient to suit their own preferences and needs, based on experiencing and experimenting various self-management approaches:

I did cognitive behavioural therapy for maybe six or eight weeks or whatever, and I found it so frustrating. I can cope with my own illness, I can cope with work and can be very patient with people who are unwell, but I found that in my own time at 8 o'clock in the evening, when it was such an effort to get from [name of town] *to* [name of another town] *and then sit for an hour with other people some of them were taking over and going on and on and just focus on the detail of their own stories, interrupting etc.* (P26)

However, negative experiences were not restricted to self-management or alternative interventions, as several interviewees indicated that they failed to achieve satisfactory outcomes from conventional medical interventions demonstrating that allopathic strategies are not necessarily superior management techniques:

I saw physiotherapists, I've seen acupuncturists, I've seen oh, I don't know who else I've seen, I've seen a good few osteopaths. (P21)

Finally, not all participants were equally accepting of non-therapeutic interventions; these patients would not consider incorporating such techniques into a self-management strategy:

People are very good with coming up with suggestions for different things, between Reiki, now I am not that kind of person. Now I am not going to go against it but in my mind it is not for me. (P 23)

7.4.5 Theme 4: Health System Factors

The ongoing daily management of chronic conditions is conducted in primary care through GPs and allied healthcare professionals such as pharmacists, community nurses and physiotherapists (3, 480). Patients also received secondary and tertiary care from hospital doctors and consultants from a variety of medical disciplines, pain clinics and pain management programmes. Referral to a pain management programme may occur from primary or secondary care, with the programmes then delivered in an out-patient hospital setting. The significance of pain management programmes in providing the patient with self-management approaches to pain has previously been discussed. Pain management programmes are considered in this section in terms of gaining access to programmes and the referral pathway into PMPs. *Figure 7-8* presents an overview of the primary, secondary and tertiary care dimensions involved in CNMP management and the proposed interaction between these levels of the healthcare system.

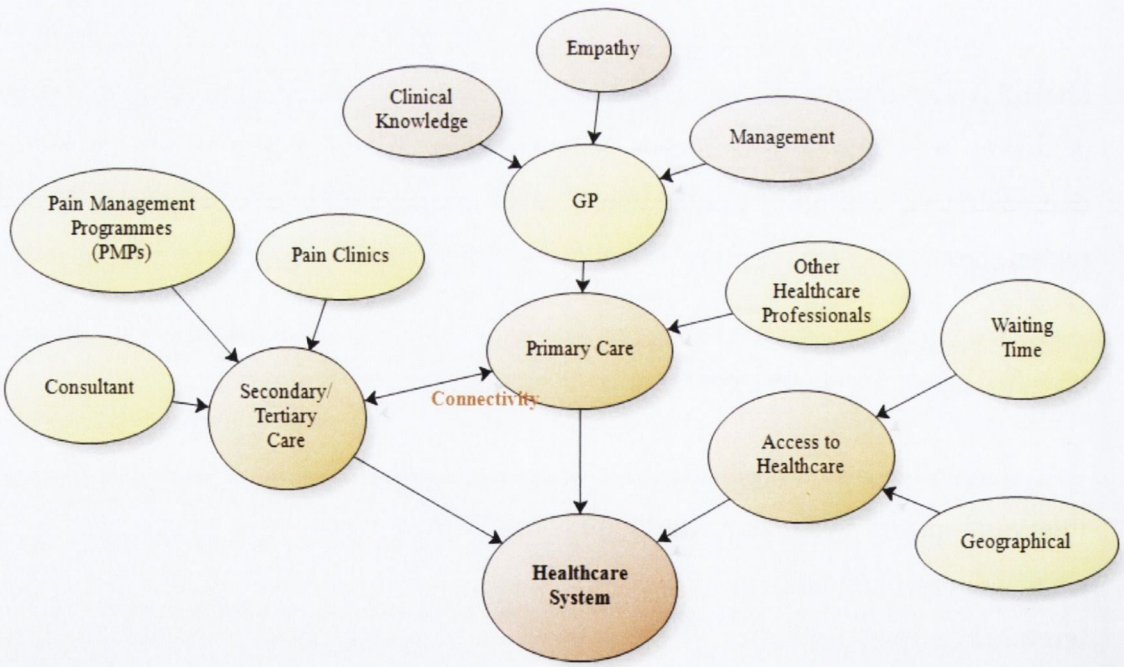


Figure 7-8: Health system factors associated with management of CNMP

7.4.5.1 Primary Care

GPs

All participants discussed the care received from their GP, with the majority speaking positively of the care received in this setting. Interviewees considered, the clinical knowledge, approach to management, in the context of the wider healthcare system, and the personal experience of interacting with their GP, as the most important topics when discussing GP care.

Clinical Knowledge

Some of the most negative comments relating to GP care referred to the perceived insufficiency of clinical knowledge of CNMP to ensure effective diagnosis and management. While some participants were satisfied with the management received from their GP, some did express the opinion that GPs had not received adequate specialised training in the area of CNMP:

The GPs there is a real need for more training and up-skilling in the area with me they just don't know what to do anymore and they haven't known what to do for a good while really. (P12)

A number of participants indicated that in the event of pharmacotherapeutic interventions being ineffective, the GP was unable to intervene further in the condition. Despite the perceived limitations imposed by a GP's clinical knowledge of CNMP, participants spoke warmly of their relationship with their physician. They understood that GPs wished to help and oftentimes independently and proactively researched the topic to aid their patient. One participant expressed the opinion that GPs become frustrated when allopathic interventions are unsuccessful:

Doctors [pause] *when there isn't an answer after a certain length of time, they have no medical training to cope with that because Western medicine is all about curing, fixing, the correcting of that issue, and right okay, we are onto the next issue.* (P11)

Empathy

Despite the perceived limitations in clinical knowledge or management options available to GPs, patients consider GPs to be empathetic to their condition. Twenty-three participants referenced this aspect of their relationship with their GP:

I mean there is a lot more understanding of chronic pain now than when I started out... I still think for doctors it seems so frustrating. I mean they want to help and we want to be helped and there is just no definitive answer. (P11)

Patient Management

Although GPs may sometimes be limited in their management options for CNMP in primary care, several participants reported that they also relied on the GP to ensure that the care received from the various healthcare professionals was harmonised in primary care, thereby entrusting the GP with overall supervision of management of their condition:

My doctor, I would give her... top marks. She is excellent you know, and she kept going until she got a diagnosis, and she is proactive in looking up new medication and trying to get it right you know get it sorted, and as I said I always get her to check what the hospital say. (P2)

GPs appear to proactively engage with interviewees to optimally manage the condition despite the limitations of the health service or clinical interventions. However, some patients spoke critically of this approach, perceiving the GP to be unwilling or unable to make changes to therapies initiated in secondary care:

Well they put me on it in [name of hospital], and he says 'Oh I better leave you on it' So they won't stop anything in case I really needed it, so I am taking all sorts of stuff that I am really not too sure about. (P22)

Finally, a small number of interviewees described their GPs as a conduit for prescriptions, with no active role in management of their conditions:

Lately I kind of got the feeling, you know, that it's kind of like, I can't really do anything else for you, you know, except give you this prescription, you know. (P3)

Pharmacists

Participants were specifically asked to discuss their interaction with their regular pharmacist and their perception of the role of the pharmacist in managing their condition. However, interviewees did not discuss in great detail their relationship with the pharmacist. Those that did, described the pharmacist as being helpful and knowledgeable about analgesics. One participant suggested that there is potential for pharmacists to adopt a more significant role in primary care in co-operation with GPs, particularly in advising on prescription medications:

There is a huge amount of health damage being done out there and pharmacists can't help what is being prescribed, and a lot of the time advice isn't wanted, people regard it as interfering. (P15)

7.4.5.2 Secondary Care & Tertiary Care

Interventions delivered in the secondary and tertiary care settings are generally more invasive than primary care and include nerve blocks, epidurals and surgical interventions. Analgesics were not frequently discussed in the context of secondary or tertiary care. Participants referred to the financial and geographical restrictions affecting access to this part of the healthcare system. References to financial barriers related primarily to the inequity of the public-private system currently in operation in the Irish healthcare system. Health insurance or private payments enabled the patient to bypass public waiting lists, gaining faster access to consultant level care, however, this placed considerable financial burden on most particpiants (231):

I was in private insurance, I would say it was through the medical card system which I have, I wouldn't be able to get anywhere (P8)

The participants' interaction with the public system was described in both a positive and negative manner and was informed by their personal experience of the system:

Like in some ways, I can't fault the public system, I think they are trying to do their utmost in a very limited situation, with very limited resources there, now what I did

find fantastic and again it was through the public system was I did a 3 week pain management course. (P18)

7.4.5.3 Connectivity of Care

Interviewees were asked to comment on their experience of interdisciplinary co-operation in the management of their CNMP condition. While participants tended to praise the care received in primary care, and acknowledged the expertise of secondary care, the connectivity of these domains remains an issue:

I had doctors who were writing out stuff. I know there were doctors who were writing out things but no one was paying any attention to what the other fella was doing. (P23)

One participant observed that healthcare professionals in Ireland appeared siloed (*defined in Chapter 6, Section 6.4.4*) and unable to work together:

Well I reckon this country is very lacking in joined up thinking between all the different sectors....There is no level playing field, everybody tends to do their own thing and follow their own interests. (P28)

Interviewees described the experience of receiving care from multiple healthcare professionals, who were predominantly acting in isolation, as a frustrating and sometimes frightening experience:

It is so frightening and then you go from doctor to doctor, and surgeons to consultants, and all the different specialities and all trying to look at you from this angle and that angle .... (P11)

7.5 Discussion

The aim of this research was to examine the attitudes of members of Chronic Pain Ireland towards analgesic and adjuvant medications and to determine the manner in which these medications are consumed. Four global themes emerged following applied thematic analysis of 27 CPI member interviews. These themes interact to produce a network of factors that influence the appraisal system of patients, which in turn influences the role of pharmacotherapeutic agents in the management of

CNMP. The model, illustrated in *Figure 7-9*, demonstrates the manner in which an individual's evaluation and inclusion of medications in an analgesic regimen is influenced by a complex hierarchy of factors. Some of these factors are derived from the patient's experience or concerns about the use of analgesics, while others are associated with the CNMP condition such as the severity and progression of the disease. Practical issues may also feature in the appraisal system such as the financial burden of healthcare and access to services. The model mirrors that proposed by Horne et al (*Figure 7-1*) whereby internal and external factors combine to affect acceptance of a prescribed regimen. However, this derived model also proposes a number of additional factors, such as self-management strategies, which contribute to analgesic use in a patient with CNMP. These factors may capture the experiences of patients with CNMP in the Irish healthcare setting where unique health system and financial influences may alter the affect the approach to CNMP management.

Clinical considerations appear to be the most important factors driving the use of analgesic medications. Previous studies have demonstrated that use of analgesics, in accordance with a prescribed regimen, is best amongst older populations, women, and in patients who perceive a necessity for the medication (481). While it is not possible to determine from this study an association between gender and drug use, it is possible to describe the perceived necessity of analgesics for individuals with CNMP. Analgesics were not only acknowledged by interviewees as providing pain relief but also as improving physical function. Ability to undertake daily activities or engage in social or leisure pursuits appears to be an implicit measure employed by patients to establish the efficacy of the analgesic regimen (482). The appraisal of medication efficacy in this manner is in keeping with the common sense model of self-regulation (482). The extent to which the medication regimen delivers the outcomes anticipated by the patient informs continued use of the medication or causes the individual to seen an alternative intervention.

These perceived benefits of pharmacotherapy are balanced with the risks associated with the medication. A number of participants described experiencing adverse effects from adjuvant medications, NSAIDs and opioids which caused them to cease use of the medication or to change the frequency with which the medication

was used. Indeed, adverse effects appear to be the most significant barrier to analgesic use or impede adherence to the prescribed regimen. This finding is similar to that of quantitative investigations of opioid adherence which have indicated that adverse effects such as gastrointestinal effects or sedation are key determinants in the cessation of this drug class (483). Addiction or dependence issues did not appear to concern participants to the same effect as other adverse effects and reflects the findings of the interviews with GPs (*Chapter 6*). The GPs interviewed appeared to be similarly motivated by adverse effects such as sedation, nausea and cognitive impairments and to a much lesser extent the potential for addiction or misuse of the analgesic in ageing and elderly patients.

The external dimension of third party perceptions of CNMP and the use of analgesic medication, particularly concerns relating to opioids, appear to influence some patients. Family members generally appear supportive of analgesics; patients describing their enhanced ability to participate in daily activities and family events in addition to family members concerns for patient welfare as the motivating factors for endorsing use of analgesics for the patient. Supportive personal relationships, such as those with family members, legitimate the individual's pain condition and has been demonstrated to improve activity levels and minimise maladaptive coping behaviours (484). Conversely the general public, friends and contributors to online may highlight the negative aspects or deficiencies of pharmacotherapy.

Healthcare professionals, particularly those clinicians responsible for prescribing medications, contribute to a patient's understanding and acceptance of pharmacotherapeutic interventions. A positive patient-physician relationship such as this has been demonstrated to reduce patient concerns and reduce negative perceptions of pharmacotherapeutic interventions (485). A period of trial and error is typically required by patients to identify a regimen that yields satisfactory analgesia with minimal negative outcomes. The extent to which the patient can communicate with the prescribing physician during this process enhances the relationship with the GP and also strengthens the role of the patient in the appraisal of medications. This consultation process with GPs surrounding medicines provides further evidence of the shared decision making approach to prescribing, which is described in the interviews with GPs. Shared decision making models such as these are associated with enhanced compliance to the prescribed regimen, with patients

also reporting a greater reduction in pain than those managed through the paternalistic model (486). The GP-patient relationships described in this study were therefore largely positive; patients are managed with empathy and respect. This finding is contrary to that of similar qualitative studies in which patients have described the feeling of being a burden to the GP or viewed as a drug seeker by healthcare professionals (419).

Patients are becoming an increasingly empowered group with access to information about healthcare that is independent of healthcare professionals, as the information is now freely available and more easily accessible (487). Accessing information on the condition and management approaches provides evidence of the self-management strategies undertaken with this population. Interviewees discussed their knowledge of medications gained from accessing electronic and published material. Self-management such as these have been associated with positive health outcomes for chronic pain condition including fewer GP and hospital visits and improved health behaviours (488). The perceived ease of access, non-invasiveness and relative efficacy of these interventions contributes in an important way to the patient appraisal system. Active and passive strategies were used by interviewees to supplement the pain relief attained from analgesics and in some instances to reduce the frequency with which analgesics were consumed. Self-management strategies and clinical factors are therefore interconnected in *Figure 7-1*. A key barrier to the use of active or passive self-management strategies were limited financial resources necessary to employ these interventions. Similarly, Bair et al reported that limited time, financial resources or poor family support impeded implementation of self-management strategies (489). The emphasis placed by interviewees on independent research into medications and CNMP may not however reflect that of the general CNMP population, given that these interviewees are members of a patient support organisation and are a self-motivated group of individuals. These participants may therefore be more informed and have well-formed opinions on analgesics and the role of medications in their condition.

The healthcare setting is of particular relevance to this research; most patients with CNMP interact with the secondary and tertiary level care, either through consultants, or pain clinics, or both, in their path to diagnosis and management of the condition. The model acknowledges also the challenges

associated with the two-tier healthcare system currently in operation in Ireland and the manner in which the patient manoeuvres through the system to optimise management of the condition. The public-private healthcare system permits those with health insurance, or who are in a position to pay, the opportunity to access consultant level care faster than those in the public system (490). Geographical issues also influence an individual's ability to access secondary or tertiary level care as some counties in Ireland under-resourced and under-served in the area of pain management (242). These barriers to access were referenced by all patients receiving care through the public system in this study. Furthermore, the frequency with which the patient may visit a pain specialist influences the intensity with which the patient accesses primary care in the form of their GP and allied healthcare professionals such as physiotherapists. The level at which the patient accesses the healthcare system and their satisfaction with the care received has a significant influence on the patient's appraisal of their condition and consequently on their decision to use analgesics. Negative experiences in tertiary level care or suboptimal analgesia achieved by clinical interventions in this setting may cause the patient to return to primary care seeking further interventions.

In summary, it appears that the patient's appraisal pathway is formed from a complex confluence of themes which are themselves formed from multiple subthemes. This complexity of themes was evident within all participant interviews to a greater or lesser extent. Both internal and external factors influence an individual's perception of analgesics and the role of these agents in the management of their chronic pain condition.

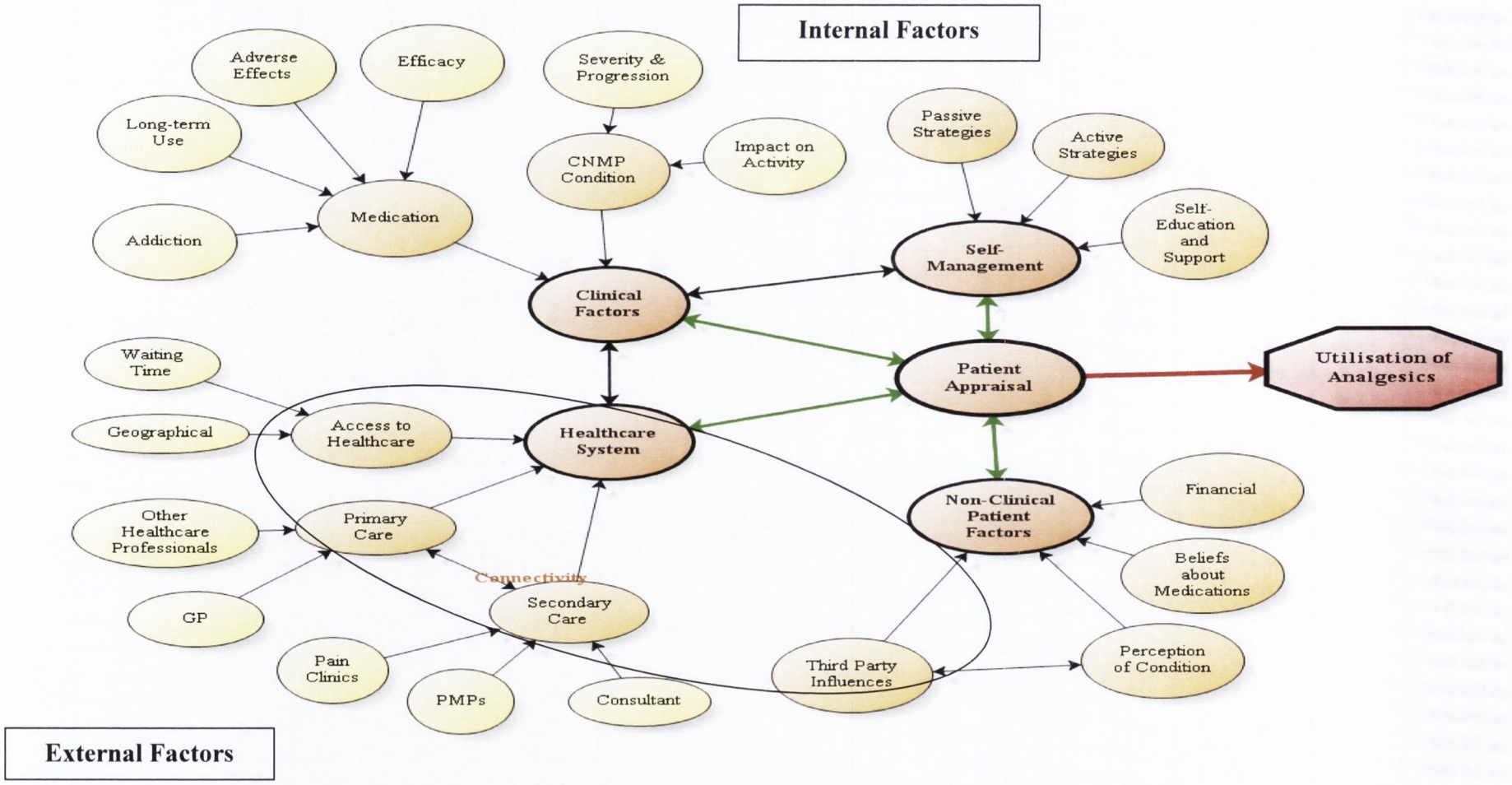


Figure 7-9: Proposed interaction of factors influencing analgesic use by CPI members

7.5.1 Limitations

The challenges relating to the use of telephone interviews and analysis of qualitative data are similar to those outlined in *Chapter 6*. There are also a number of additional limitations that are specific to this study.

Participants who are members of patient support organisations such as CPI may have a degree of assumed responsibility for management of their condition (491). These individuals have already demonstrated a degree of self-empowerment and interest in their condition by becoming a member of a CPI and undertaking the interview with the researcher. This group of interviewees may therefore not be representative of the general ageing and elderly population with CNMP. Comparison of findings from an analysis of individual transcripts is also challenging due to the diversity of the pain conditions that affected interviewees and the complexity of the psychological and social factors that influence the condition. Psychometric assessment of participants would be required to gain an understanding of these psychosocial factors; this was beyond the scope of this study. Finally, it is difficult to determine the severity of pain based only on the description gained from participants. This description is subjective and may be influenced by the individual's illness perception and coping strategies. Inclusion of a standardised pain scale would have allowed an objective understanding of pain severity, however, this was beyond the scope of the objectives of this study.

7.6 Conclusion

Individuals with CNMP commonly use analgesics and adjuvant medications to achieve pain relief. Internal factors including clinical considerations, self-management strategies and beliefs about medication are specific to the patient and may influence the nature and extent of analgesic use. Effective analgesia permits the individual to undertake daily activities and social pursuits. These benefits of analgesic medications are balanced with an individual's experience of adverse outcomes associated with the drug class. GIT effects and CNS depression resulting in sedation are the most commonly described adverse effects, which sometimes necessitate discontinuation of therapy. Concerns about opioid addiction and implications of long-term use also inform the role of these agents in the patient's pain management plan. Non-pharmacotherapeutic interventions incorporated into

the pain management strategy, when effective, mean that the individual may lessen the frequency of use of analgesics. External factors, such as poor access to pain consultants, physiotherapists or occupational therapists, affect the quality of management of the condition. GPs are responsible for the daily management of a patient with CNMP and frequently play an important role in harmonising and reviewing interventions received from other healthcare professionals.

What is already known about this topic:	CNMP emerges as a condition following the entension of an acute pain beyond a defined period. An individual's perception and attitude towards the condition and consequently, management of the condition is influenced by interaction with healthcare professionals and family and friends. Social inactivation and isolation have been described as the consequences of delegitmation of the condition by society, outcomes which have a negative impact on illness perception.
	Internal and external factors may affect acceptance and adherence of a prescribed medication regimen; central to this also, is the patient's illness perception. This confluence of factors contributes to the patients internal appraisal system which is dynamic and changing throughout the management cycle of the condition.
	Patients with CNMP are not restricted to allopatic interventions but may incorporate a variety of holistic and self-management approaches when seeking effective analgesia.

What this study adds:	Participants acknowledged the importance of pharmacotherapeutic interventions in the attainment of analgesia and their role as an enabler for the patient. There were, however, particular concerns associated with adverse effects, long-term use and addiction that may prevent the patient from remaining adherent to a prescribed regimen.
	A range of passive and active behavioural strategies were described by participants. These strategies supplemented analgesic and surgical interventions and were favoured by participants as a method of curtailing engagement with allopathic interventions.
	The expense of pharmacotherapeutic and surgical interventions and indeed self-managment strategies was one of the key limiting factors described by participants. This factor is perhaps a consequence of the current economic climate in Ireland but may also be associated with the public-private divide in the Irish healthcare system.
	Ultimately, the patient's internal apprisal system determines attitudes towards and perceptions of pharmacotherapeutic interventions. This is a highly subjective process influenced by external societal, health system and economic forces that are constantly in a state of flux.

Chapter 8. Discussion & Conclusion

8.1 Introduction

The research studies presented in this thesis seek to answer the research question: 'How is chronic non-malignant pain managed with pharmacotherapeutic interventions in ageing and elderly populations in primary care, and what are the GP and patient factors that influence the use of these medications?' An overview of the key findings of each of the five studies, and the challenges of these studies, is presented in *Section 8.2*.

8.2 PhD Objectives, Key Findings, & Challenges

Objective: To identify the type and quality of information that may be used by clinicians when prescribing opioids for CNMP.

- The systematic literature review of clinical practice guidelines directing the prescribing of opioid analgesics in primary care, described in *Chapter 3,* sought to achieve this objective.

Key findings: The clinical content and AGREE II assessment of guidelines demonstrated that there were significant differences between the quality and content of these documents. Following assessment of all guidelines, using the AGREE II instrument, the Rigour of Development, Editorial Independence, and Applicability domains scored the lowest of the six domains considered by the instrument. However, these are mean domain scores and, thus, may be affected by those guidelines that scored poorly in these areas. In terms of clinical content, all guidelines referred to side-effects and addiction, while information on medication interactions and management of overdose were considered by few guidelines.

Those guidelines that scored poorly using the AGREE II instrument also had low scores for clinical content criteria score. However, those with higher AGREE II domain scores were more difficult to compare with the clinical content criteria score, as the relationship was not linear. Furthermore, while a guideline may have had a high AGREE II score comparable to other guidelines, this did not automatically produce an equally high mean Overall AGREE II Assessment Score, a score apportioned by appraisers following consideration of the quality of the guideline as a whole.

Challenges encountered: While a systematic search was used to identify guidelines available through electronic databases, it may not have been possible to identify guidelines that are not publicly available. This review was also restricted to English language documents. Finally, it is possible that the clinical content criteria, used to evaluate guidelines, was not inclusive of all clinical considerations required when prescribing opioids.

Objective: To describe the nature and extent of analgesic use by ageing and elderly populations with CNMP in the Republic of Ireland.

- *Chapter 4* and *Chapter 5* described the quantitative investigations of the HSE-PCRS database and data from TILDA respectively. These studies sought to meet the objective by providing a quantitative understanding of the nature and extent of analgesic use in an ageing and elderly population with CNMP, relative to populations without the condition.

Key findings: The prevalence of pain among those aged 50 years and older in 2010, according to the TILDA database, was 36% (n=2,692), of whom 57.9% (56.2-59.7%, n=1,616) were women and 42.1% (40.3-43.8%, n=1,076) were men. Almost half of those reporting pain, indicated that it was of moderate intensity, followed by mild intensity, at 28.4% (26.6-30.2%), and severe intensity, at 25.4% (23.5-27.4%). According to the HSE-PCRS database, approximately 61.6% of individuals aged ≥55 years had received at least one dispensing of an analgesic medication 2010 and at least 35% received >3 dispensings of an analgesic. By comparison, however, 13.7% (12.8-14.5%) of TILDA participants with pain reported at least one analgesic. Systemic non-selective NSAIDs were the most reported class of medication, followed by moderate opioids and adjuvant medications for TILDA participants reporting pain. Considering recurrent dispensing (>3 dispensings) in the HSE-PCRS database, non-opioids, systemic non-selective NSAIDs and moderate opioids were the most commonly dispensed medications.

Multinomial regression analysis of TILDA participants reporting pain indicated that polypharmacy (≥5 medications), and being a past or current smoker, were associated with reporting a weak or moderate opioid rather than a non-

opioid/NSAID/adjuvant medication. Pain intensity was not identified as being associated with the use of weak, moderate or strong opioids relative to a non-opioid/NSAID/adjuvant medication.

Challenges encountered: The HSE-PCRS database provided information on gender and age-group but did not provide information on diagnosis or disease outcomes. It was not possible to establish from the TILDA dataset whether the low prevalence of analgesic use was associated with under-reporting by study participants or arose from under-prescribing.

Objective: To investigate the factors affecting the prescribing of analgesics for ageing and elderly populations by primary care physicians in the Republic of Ireland.

- *Chapter 6* presented semi-structured interviews with GPs (n=12), a key stakeholder in the provision of care to patients with CNMP in the Irish healthcare system.

Key findings: The development of an analgesic regimen appeared to be related to four key themes: clinical, non-clinical, health service and non-GP management. Clinical factors related to specific prescribing considerations such as disease severity, co-morbidities, adverse effects and medication interactions and were at the core of the prescribing decision making process. Clinical practice guidelines, formularies, literature disseminated from pharmaceutical companies, learning arising from continuing professional development or educational workshops were cited as informing prescribing decisions. All GPs stated that the WHO Analgesic Ladder remains the primary framework guiding the prescribing of analgesic medications for patients with CNMP. The lack of clinical practice guidelines on analgesic management for CNMP in Ireland, particularly guidelines directing opioid prescribing, initially described in *Chapter 3,* was again highlighted in this study.

Challenges encountered: Both purposive and snowball sampling approaches were required to gain an adequate sample to reach data saturation. Interviews were

conducted by telephone which may diminish the quality of interaction between interviewer and participant due to the loss of non-verbal cues. The framework method of data management and applied thematic analysis were used to ensure that data was organised and analysed in a systematic, transparent and auditable manner. However, qualitative data analysis may be subject to bias, as the researcher imposes pre-formed thoughts or opinions on the data.

Objective: To describe the nature and extent of analgesic use by ageing and elderly populations with CNMP in the Republic of Ireland.

- *Chapter 7* details the findings from semi-structured interviews with members of Chronic Pain Ireland (CPI) (n=27) which sought to achieve this research objective. This study seeks to provide greater understanding of the findings from *Chapter 4* and *Chapter 5*.

Key findings: Four key themes were identified upon completion of applied thematic analysis of interview transcripts and included, clinical, non-clinical, self-management strategies and health system factors. Illness perceptions, beliefs about medications, and psychosocial attributes were identified subjective factors that interacted with clinical factors such as disease severity, co-prescriptions and adverse effects to determine the nature and extent of analgesic use. A shared decision making approach with GPs was described by a number of these interviewees in the construction of a pharmacotherapeutic management plan in primary care. Individuals with CNMP also described undertaking self-management strategies to provide pain relief or improve physical functionality. The extent to which self-management was incorporated into the individuals daily regimen appeared to influence the extent to which analgesics were used. CPI members also described the limitations of the healthcare system in the management of CNMP, highlighting in particular, challenges in gaining access to services through the public system.

Challenges encountered: Members of CPI may represent a particularly self-motivated, informed and empowered group of individuals. The findings of this study may therefore not be relevant to the members of the general population with

CNMP. Challenges relating to the method of data collection and data analysis are similar to the GP study.

8.3 Discussion

Figure 8-1 demonstrates how each of the research objectives map onto each of the studies described, contributing towards a revised conceptual model which seeks to answer the thesis research question. The conceptual model, presented in *Figure 8-2*, which has been derived from the initial conceptual model presented in *Chapter 2, Figure 2-1*, incorporates additional dimensions based on the findings of this PhD research. Clinical considerations relating to disease aetiology, progression and severity, combined with the physiological characteristics of the patient, are of greatest importance in constructing an analgesic regimen for an ageing or elderly individual with CNMP. The remaining factors further shape the role of pharmacotherapy in pain management and are often a product of the sociocultural perspectives of CNMP and healthcare professional or health system approaches to management.

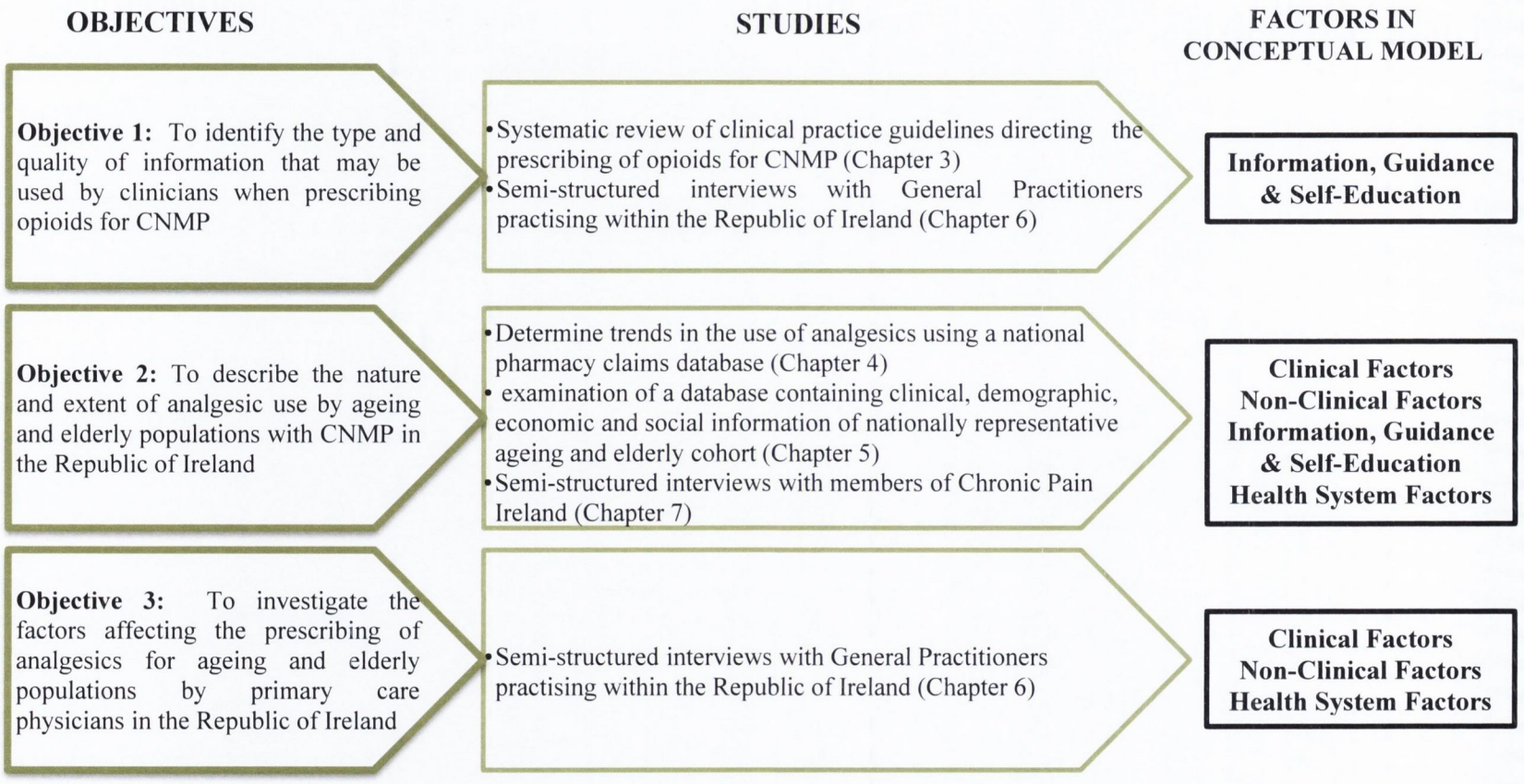


Figure 8-1: Mapping of objectives to the studies (described in Chapters 3-7) and contribution to themes in conceptual model

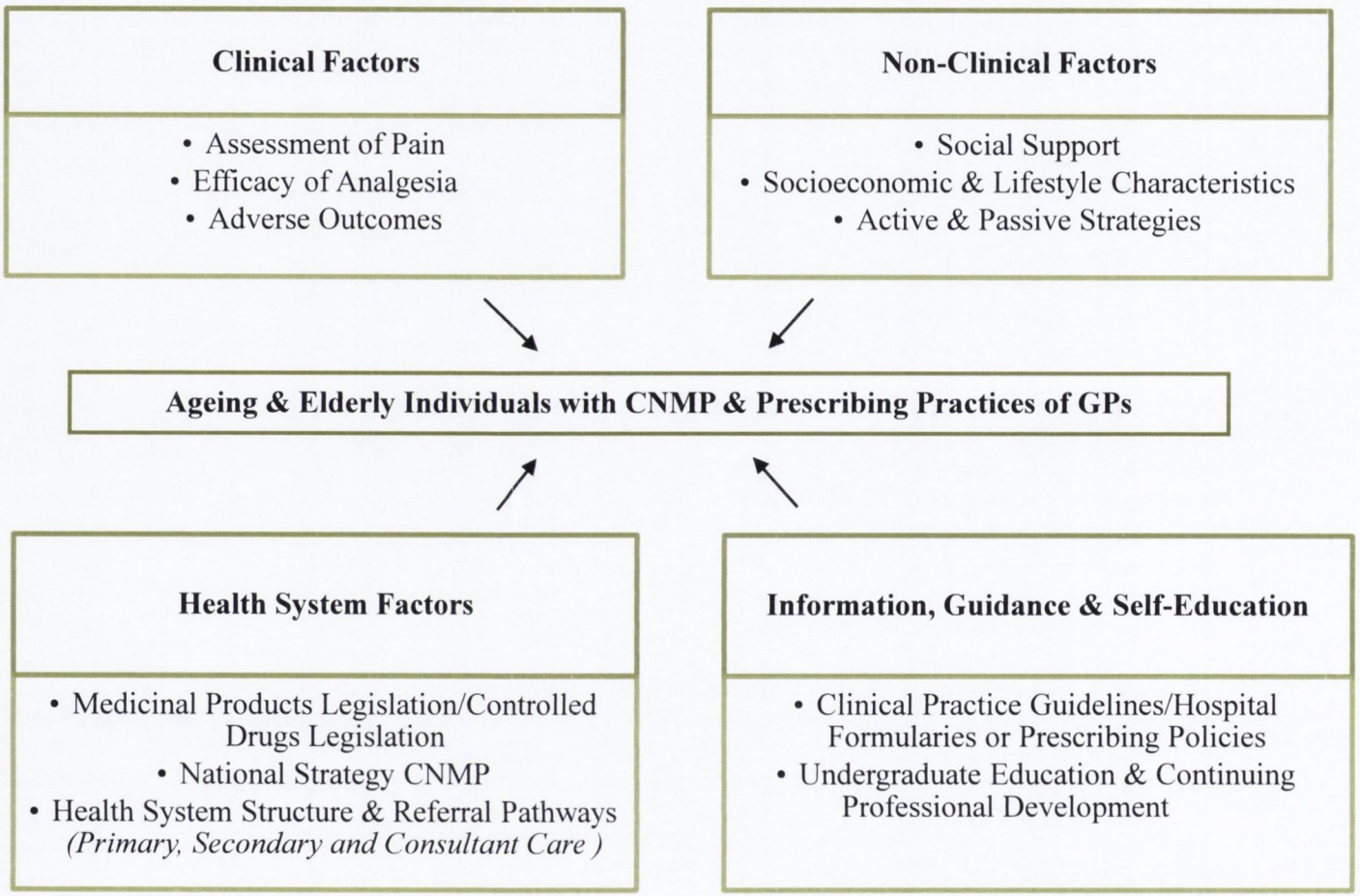


Figure 8-2: Conceptual model presenting factors affecting the prescribing of analgesics and their use by ageing and elderly individuals with CNMP

8.3.1 Clinical

Contribution to Research Question

The aetiology, severity, progression and prognosis of the pain condition, combined with aspects of pharmacotherapy, such as efficacy, adverse effects, cautions, contraindications, and, in the case of opioids, potential for tolerance and addiction, are some of the clinical factors that inform the analgesic regimen for an ageing or elderly patient.

Assessment of pain

Unlike other chronic conditions, such as epilepsy and diabetes, pain cannot be objectively quantified using clinical tests, although validated pain measurement scales can provide some insight into the severity of the condition (72, 492, 493). This complicates assessment of pain severity and evaluation of the efficacy of pharmacotherapeutic interventions, particularly in time-pressurised primary care consultations (89). This study described a heterogeneous approach to the assessment and description of pain by both GPs and patients. This may lead to under-diagnosis of pain, poor recognition of pain severity and may contribute to suboptimal pain relief (113, 494, 495).

Few GPs reported the use of a standardised pain scale such as a visual analogue scale to determine pain severity. Rather, both GPs and CPI members described the severity of the condition in terms of functional impairment and the consequent impact on activities of daily living. This understanding of pain can be of use and may provide adequate information to direct analgesic management. Indeed, Turk et al described this manifestation of pain severity as a key consideration when prescribing analgesics, particularly opioids, for patients with pain (496). The findings of the TILDA study highlighted the importance of physical functionality for patients with pain. Those that reported pain as limiting daily activity had a lower QoL score. Individuals with pain were 1.5 times more likely to receive a non-opioid/NSAID/adjuvant agent, nearly twice as likely to receive a moderate opioid and four times more likely to receive a strong opioid than no analgesic medication. It is difficult to determine from this analysis, however, whether use of an analgesic improves daily functionality. Several CPI members

described analgesics as an important pain management tool which enabled them to complete daily activities and engage in social and leisure pursuits.

These findings highlight the manner in which pain is understood and described by both healthcare professionals and patients and how efficacy of interventions are quantified. While validated pain assessment instruments would help to homogenise consultations with individuals presenting with pain, a review of the role of analgesics in the context of facilitating activities of daily living would appear to provide an equally important assessment of pain severity and efficacy of management strategies.

Nature and extent of analgesic use

Considering the prevalence of analgesics identified from both TILDA and the HSE-PCRS databases, there is an emphasis on analgesics on Step 1 and Step 2 of the WHO Analgesic Ladder over strong opioids (Step 3). Results of the multinomial regression model (*Model 2 in Chapter 5*) provides further evidence of the non-linear association between pain intensity and the steps of the WHO Analgesic Ladder, as there was no association between pain intensity and the use of weak, moderate or strong opioids relative to non-opioids/NSAIDs/adjuvants. However, this lack of association, between pain intensity and analgesics, has been reported in other studies. Tonies et al also demonstrated no association between the reported pain intensity and the type of analgesic prescribed from an analysis of 7,248 GP consultations and 1,083 analgesic prescriptions (497).

According to the interviews with CPI members, individuals with CNMP do not appear to consider those analgesics at Step 1 of the WHO Analgesic Ladder, particularly paracetamol, sufficiently potent medications and wished to advance to the next step of the ladder. If patients then failed to attain adequate analgesia with Step 2 analgesics, additional strategies such as physiotherapy or specialist interventions are incorporated into the regimen. These additional interventions appear to be employed preferentially to continuing to Step 3 analgesics (i.e. strong opioids).

Opioid Prescribing

The WHO Analgesic Ladder and clinical practice guidelines describe the aim of prescribing medications for pain as the delivery of optimal analgesia appropriate for the pain severity with minimal invasiveness or adverse outcomes for the patient (103). The GPs in this study advocated a conservative approach to analgesic use, attempting to remain on the lowest step of the analgesic ladder for the longest possible duration. Further assessment of behaviours surrounding opioid prescribing through the GP interviews, indicated that several would not initiate an opioid without consultation with a pain specialist. Those who were confident to prescribe strong opioids without consultation with specialists primarily used opioid patches, containing buprenorphine and fentanyl, preferentially over oral agents for ageing and elderly patients. This preference in drug delivery systems is detected in the HSE-PCRS analysis with recurrent dispensings (>3 dispensings) of transdermal strong opioids peaking in those aged ≥75 years.

The low prevalence rate of at least one dispensing and recurrent dispensings (>3 dispensings) of strong opioid medications detected in the HSE-PCRS and TILDA databases indicate that the prescribing of strong opioids has not reached the epidemic proportions described in the USA, which continues despite the widespread publication of clinical practice guidelines and increasing regulatory controls (195, 498). Several reasons may exist for this apparent limited use of opioids in Ireland. It may be reflective of the legal controls relating to the prescribing of these agents. However, the relevance of regulatory restrictions in Ireland was not referenced as a barrier to prescribing of opioids by Irish GPs.

It is more likely that these low prevalence rates highlight the conservative prescribing practices of GPs in Ireland, termed 'opiophobia' in the literature (391, 499, 500). This has been described as a customary underuse of opioid analgesics based on irrational and undocumented fears (391). The 'opiophobia' in the Irish context may be primarily associated with concerns relating to adverse effects of opioids and not from professional or regulatory scrutiny, which has been cited as a concern of American physicians (501). The negative consequences of opioids, such as sedation, cognitive impairment and GIT effects, were extensively discussed by both GPs and CPI members appeared to act as barrier to the initiation of opioids.

Opioids & Adverse Outcome

CPI members were particularly apprehensive about addiction and tolerance to opioids, focusing on the issue particularly when moderate or strong opioids were discussed. Such concerns have previously been cited as a reason for poor adherence to prescribed medications which may contribute to inadequate management of the condition (502, 503). GPs, while acknowledging the potential for misuse of opioids amongst vulnerable patients with a history of drug or alcohol abuse, focused on the clinical appropriateness of this class of analgesics for ageing and elderly population.

Good prescribing practice would suggest that laxatives should be co-prescribed with strong opioids especially for ageing and elderly patients who are particularly predisposed to developing opioid bowel disorder (504). The rate of laxative use detected in TILDA is perhaps too low to develop a meaningful comparison with the HSE-PCRS data. It is apparent however, that there is an unacceptably low level of reported concurrent use of laxatives and strong opioids estimated from either database; approximately 7% of the TILDA population and 40% of the HSE-PCRS population were co-prescribed a strong opioid and a laxative. This is supported by interviews with GPs who suggested that there is poor concurrent prescribing of laxatives with weak or moderate opioids but greater co-prescribing with stronger opioids, although co-prescribing did not consistently occur with every consultation. However, these low estimates of concurrent prescribing have been reported in international research studies. A Danish study, which examined dispensing records from 26 community pharmacies, reported a similarly low concurrent prescribing of opioids and laxatives, with 37% of patients prescribed a laxative within 5 days of receiving a prescription for an opioid (505). Similarly, Williams et al, from their analysis of the Quebec Public Prescription Drug Insurance Plan database, reported that less than 1% of patients receiving an opioid were also in dispensed a concurrent laxative (335).

Approximately 27% of TILDA participants with pain and 50% of patients in the HSE-PCRS database were identified as taking a sedating agent concurrently with a strong opioid medication. Regardless of the disagreement between these figures, there is a consistency in the fact that concurrent use of sedating agents with opioids, particularly strong opioids, is higher than that of laxatives. Again, this finding of potentially inappropriate prescribing is not unique to the Irish context.

The CONSORT study (Consortium to Study Opioid Risk and Trends) reported a prevalence of concurrent sedating agent and opioid use of 33% and 25% for women and men respectively (506).

These potentially inappropriate prescribing practices may be related to inadequacies in the prescribing guidance available to GPs. Only two guidelines included in the systematic review discussed the potential for opioid interactions, while five provided information on the management of adverse effects such as opioid bowel dysfunction. Both concurrent prescribing of sedating agents or omission of laxatives from a prescription with strong opioids are inappropriate prescribing practices with deleterious outcomes for patients. Both guidance providing information on concurrent prescribing and current prescribing behaviours should therefore be improved to minimise harmful outcomes.

8.3.2 Non-Clinical

Contribution to Research Question

Socio-economic and lifestyle factors both inform the manner in which analgesics are used to manage pain or may be affected by the pain condition, particularly when analgesia is inadequate. Interpersonal relationships with family members and healthcare professionals may enhance an individual's perception of the condition and clinical management strategies. An individal may also incorporate passive and active management strategies which may lessen the use of medicines.

Interpersonal Relationships

Interpersonal relationships and social supports emerge from CPI and GP interviews as important features in accepting and managing CNMP. The GP-patient relationship is described by both GPs and CPI members as central in establishing a sense of trust and confidence in the care delivered to the patient. GPs described it as a necessary aspect of the patient consultation, so as to gain an understanding of the psychosocial circumstances of the individual. This aspect of the GP-patient dynamic is referenced extensively by both populations as an acknowledgement of the necessity to view the patient in the context of the biopsychosocial model. This approach is distinct from the reductionist medical model whereby the patient is viewed in the context of the condition and disease progression (70). Recognition

of the complexity of CNMP and the various strata of the condition, at the centre of which is a biomedical issue, encourages both GPs and patients to consider and discuss management strategies using a shared decision making model (507). Incorporating shared decision making in the development of a regimen consisting of both pharmacotherapeutic and non-pharmacotherapeutic interventions may represent one solution to under-reporting and under-treatment of pain (216).

Family members, friends and members of the public contribute to the perception and understanding of the condition for several CPI members, encouraging and enabling adherence to a prescribed analgesic regimen. Supportive relationships with family, friends, fellow patients and healthcare professionals may legitimate the pain complaint by removing the stigma and disbelief that frequently surrounds this condition (508, 509). QoL analysis with TILDA indicates that those individuals reporting pain who are separated or divorced have a lower QoL score than those who are married. A number of CPI members indicated that family members were supportive of ongoing analgesic use, as it enabled the individual to engage in social and leisure activities as a family unit. This aligns with research by DiMatteo, which indicated that family support promotes adherence to medication by promoting optimism and self-esteem in the patient (510, 511).

Active & Passive Pain Management Strategies

The inclusion of active and passive self-management strategies was referenced extensively by CPI members and reported by several as a mechanism to offset the everyday use of analgesics or reduce the necessity for additional medications. It is perhaps of concern the extent to which some interviewees individualised their analgesic regimen, deviating from the prescriber's recommendations, based on the efficacy of these self-management approaches. However, this finding is perhaps not reflective of all ageing and elderly patients with CNMP, as this group are self-motivated, empowered and possibly had higher levels of education, demonstrated by their association with a patient support group and their ability to seek information through electronic media and educational workshops.

Employment & CNMP

The findings of the TILDA study indicated that those who were retired or unemployed/disabled/carer were more likely to be in receipt of an analgesic medication. This perhaps reflects the debilitating nature of pain conditions and the higher rate of absenteeism and unemployment amongst those with chronic pain (28, 512). High rates of unemployment have previously been detected at a European level, with severe pain being associated with a high probability of unemployment (31, 49). Indeed, a number of CPI members reported taking early retirement or reducing work commitments because of impaired physical functionality associated with the pain condition. Therefore, employment status appears to be an outcome of pain which affects functionality and which is therefore associated with analgesic use.

8.3.3 Information, Guidance & Self-Education

Contribution to Research Question

Information, guidance and self-education describe the range of approaches undertaken by GPs or individuals with CNMP to improve the management of the condition. Both GPs and CPI members reported employing a range of measures to improve their understanding and knowledge of the pharmacotherapeutic management of CNMP.

Information & Education for Individuals with CNMP

Information on the pain condition and management strategies may be gained by patients from a variety of sources including healthcare professionals, health related websites, the media and family and friends (513, 514). A number of individuals described accessing electronic literature and on-line discussion fora to supplement their knowledge of medications, however, the quality and reliability of the information gained from these sources is unknown. Accessing information in this manner can give rise to two outcomes, according to CPI members. A number of CPI members described the negative impact of reading this material on their perception of analgesic medications and consequently were often disinclined to take a prescribed medication regimen. However, a number described this information as an instrument enabling them to partake in shared decision making with the

prescriber. Shared-decision making in this context may not be evenly balanced between the physician and the patient. McMullen et al. postulate that healthcare professionals may become defensive when faced with an active, self-educated patient and respond by asserting their 'expert opinion'. Equally, the patient may attempt to assert excessive control on the decision making process. A balance between these two outcomes is optimal for effective shared decision making (515, 516).

Several CPI members also described using knowledge and skills gained from pain management programmes. The benefits of these interventions for patients with CNMP have been acknowledged for many years. A meta-analysis of 65 studies, reviewing patient outcomes from pain management programmes, has indicated that this approach to treatment is superior to single-discipline treatments such as medical treatment or physical therapy (517). An 8 year review of the efficacy of the Ulysses pain management programme offered by the Meath and Adelaide Hospital (Tallaght Hospital), Dublin, has also demonstrated positive physical and psychological outcomes for patients attending the programme (247). However, while these programmes are undoubtedly beneficial for patients, they appear to be difficult to access; at present only three institutions currently offer pain management programmes to public patients, all of which are in the Dublin region. Both GPs and CPI members described the inequities in accessing pain management programmes; these inequities were perceived to be worst for patients dwelling in geographically remote areas of Ireland.

Information, Education & Guidance for GPs

Fullen at al. have argued that there is insufficient education on the topic pain provided to medical students in undergraduate and postgraduate institutions in Ireland (242). Medical schools provide an average of 17 hours undergraduate training on pain management (242). GPs interviewed in the course of this research did not suggest that they possessed insufficient knowledge of pain management and indicated that any deficiencies in their knowledge were addressed by accessing guidance and information through a variety of sources such as CPD events, formularies and evidence-based literature. These resources allowed GPs to keep

abreast of pharmacological management approaches or recent developments in alternative management strategies.

It has been proposed that the culture of 'opiophobia' may be best addressed through further education of healthcare professionals (518). Educational interventions may also enhance knowledge of pain management strategies, provide information on effective pain assessment procedures and allay concerns about adverse outcomes arising from pharmacotherapy (519). Roth et al. reported that educational workshops, directed at medical residents, succeeded in minimising the barriers to opioid prescribing by reducing concerns about adverse outcomes, concerns about criticism from other healthcare professionals and concerns about regulatory scrutiny (520).

The absence of guidelines specific to pharmacotherapeutic management, with a focus on opioids, of CNMP in Ireland and the ongoing use of the WHO Analgesic Ladder for malignant pain amongst GPs, is one of the key findings of this research. It would appear that when this approach does not achieve an optimal outcome for the patient the prescriber is then motivated to seek out guidance to inform the next phase of management. A number of GPs stated that CNMP specific guidance may be beneficial for management in primary care. However, the necessity for such guidelines to be succinct and relevant to the healthcare setting, so as to be of practical assistance to GPs was frequently highlighted. This aligns with the literature which suggests that lengthy guidelines which are poorly adapted for the practice setting impair implementation (425, 521).

8.3.4 Health System

Contribution to Research Question

It is proposed that the healthcare system does not directly influence the manner in which medications are prescribed to or taken by ageing and elderly patients presenting with CNMP to the same extent as clinical factors or the availability of guidance on this subject. Rather, factors relating to the healthcare system describe the structure and quality of the framework in which care is delivered to patients with CNMP.

Public/Private Healthcare

At present, healthcare in Ireland is delivered through a combination of public and private systems. In recent years, healthcare delivered through the public system in Ireland has become synonymous with waiting lists for elective medical interventions. There are also geographical inequities in the availability of services and in prescribing patterns in comparison to private healthcare recipients (231, 490, 522). The altered economic environment in recent years has reduced family income and expenditure on private healthcare; this has transferred additional demand to the public healthcare system which then must deliver increased levels of care with diminished financial resources (523).

It is in this context that the discussion on management of CNMP in the primary care system is framed, with an inevitable focus on the current limitations of healthcare delivered in Ireland at present. Statistical analysis of TILDA did not identify significantly different QoL for individuals with pain receiving care through the public or private Irish healthcare system nor was this found to be associated with use of specific classes of analgesics. However, the perceived inadequacies of the Irish healthcare system were discussed at length by both CPI members and GPs. Access to additional services in primary care, such as physiotherapy or occupational therapy for public patients, was problematic. Lengthy waiting lists and poor availability of specialists or access to pain management programmes may require the patient to remain in the primary care setting for prolonged and inappropriate periods, with pharmacotherapeutic interventions being the most frequent intervention available to the GP (242). It would appear that those within the greater Dublin area benefit from a shorter waiting list period, as there are less options for specialist services in other regions of the country. Meanwhile, patients receiving care through private channels described the expense of physiotherapy and specialist care which was met through health insurance or private financing thereby identifying cost as a barrier to accessing services within the healthcare system.

GPs and CPI members described their satisfaction with the care received from pain consultants and within pain clinics upon gaining access to the service. One GP expressed reservations about the nature of care within pain clinics, stating that the emphasis on pharmacological management of pain with potent analgesics and the absence of a strong patient-physician relationship is deleterious to vulnerable

patients. This view is espoused by a number of CPI members who describe specialist care interventions as lacking patient-centeredness and subjectivity. However, it is difficult to determine if these views are borne from frustration with the system by which care is accessed or the quality of care received.

Multidisciplinary Care

A multidisciplinary primary care team, consisting of GPs, physiotherapists, occupational therapists and public health nurses, was described by many GPs and CPI members as a possible solution to the current challenges in accessing specialised care. Multidisciplinary primary care management has been demonstrated to improve clinical outcomes for patient with CNMP (524). Such a specialised team in primary care would allow patients to gain more rapid access to a group of physicians and allied healthcare professionals for the day-to-day management of the condition. Primary care teams such as these were initially described in 2001 in the health strategy document, 'Quality and Fairness: A Health System for You' (525). It was proposed that these teams would be composed of health and social care professionals who would deliver health and social services to the general population. At present, approximately 58% of GPs are members of primary care teams (526). Given the poor success of this health strategy thus far, and the reduced resources available to the Department of Health and HSE, it is unlikely that a primary care team capable of managing patients with CNMP will come to fruition in the near future.

8.4 Recommendations for Policy and Practice

A number of recommendations follow from this appraisal of research findings and are relevant to both GPs and policy makers involved in the delivery of care for ageing and elderly patients with CNMP.

1. Development and dissemination of international or national guidelines on the pharmacotherapeutic management of CNMP

This research has further identified the necessity for a pain management ladder specific to non-malignant pain conditions. A revised framework should provide specific recommendations to address pharmacotherapeutic concerns associated

with the use of analgesics and adjuvant medications in patients with CNMP. The WHO has sought to address the limitations of this ladder by the publication of a Scoping Document for Treatment Guidelines on CNMP in 2008 (229). This document presents pharmacotherapeutic and non-pharmacotherapeutic management strategies for patients with CNMP. However, there has been no additional publications on this subject by the WHO and no indication of a publication date for such a guideline. The Scottish Intercollegiate Guideline Network (SIGN) have recently produced a national clincal guideline on the management of chronic pain. This evidence based guideline provides information on pharmacotherapeutic management of CNMP directed at physicians who are operating in the primary care setting and it outlines recommendations on the prescribing of opioids for the condition (104). This is an important development in the availability of an English language guideline on this subject matter in Europe.

In the absence of guidance emanating from an international source, national guidance may be provided in the interim. An evidence based clinical practice guideline, specific to CNMP management in Ireland, and detailing the clinical considerations for prescribing analgesics, may be a useful reference tool for GPs. Recommendations on the pharmacotherapeutic management of nociceptive and neuropathic CNMP conditions may help to harmonise the approach to the prescribing of analgesics by GPs. Such a document would be particularly beneficial if it provided guidance on the risk-benefit considerations of the use of opioids in ageing and elderly population which appears to be a particular source of contention amongst prescribers. Indeed, such a guideline should not be limited to conventional therapeutic interventions but take into consideration the contribution of allied healthcare professionals such as physiotherapists and occupational therapists and the role of self-management strategies in pain prevention and management. This would help to meet the needs of GPs which were described in the interview process: to have access to succinct evidence-based prescribing recommendations and guidance on referral procedures. Such a document should be cognisant of the current limitations of the Irish healthcare system and include recommendations for patient management that are realisable in the present system. The recent SIGN guideline may be an appropriate starting point for the development of an Irish guideline. While such a document would be undoubtedly advantageous in directing

management of CNMP, it is difficult to determine the extent to which physicians would incorporate recommendations in the prescribing decision-making process, given the widespread use of the current WHO Analgesic Ladder highlighted during interviews with GPs.

2. Consistency in assessment of pain intensity

The findings from the interviews with GPs and analysis of the TILDA and PCRS datasets highlight that a number of changes may be applied to professional practice that may improve the quality and consistency of pharmacotherapeutic management of patients with CNMP. The method of assessment employed by clinicians to determine pain severity is inconsistent and not standardised. Discussion with CPI members indicates that patients understand pain severity in the context of activities of daily living, describing their ability to undertake household chores or leisure activities. An activities of daily living scale, used in conjunction with a validated tool to assess pain intensity, used in GP consultations, may assist a shared decision making approach to prescribing that meets the needs of patients. Indeed, assessment of pain using a multi-dimensional model was endorsed by many guidelines included in the systematic review (492, 527). Introduction of such an instrument into patient-GP consultations may bring clarity to pain assessment and homogeneity to prescribing practices. An interactive approach to pain evaluation and monitoring such as this may be particularly helpful for elderly patients, as this patient group both under-report pain and are under-treated with analgesics (528).

3. Additional education in the prescribing and use of certain classes of analgesics

The low prevalence of strong opioid prescribing detected in the quantitative arm of the research indicates that Ireland does not presently have a problem with over prescribing of this analgesic class. As previously described, these low prescribing rates are somewhat explained by findings of the interviews with GPs who described reserving opioids for palliative care, highlighted concerns about adverse outcomes and cited fears of addiction and tolerance as barriers to use of opioids. The provision of further education on pharmacotherapeutic management approaches for CNMP directed at GPs may address concerns about opioid prescribing. However,

rather than reforming undergraduate medical education to include a greater focus on pain management as proposed by Fullen et al., the provision of continuing medical education on this subject would allow GPs to keep abreast of developments in pharmacotherapeutic management, equipping GPs with the necessary confidence to alter their approach to prescribing (242).

Patients with CNMP may also benefit from educational interventions from reliable sources such as healthcare professionals and patient support groups. Such educational interventions should provide the individual with accurate information on the benefits and risks of pharmacotherapy thereby enhancing appropriate analgesic use by addressing concerns about medications (529).

4. Additional supports in the prescribing of certain classes of analgesics

The willingness of GPs to use stronger opioids may also be enhanced through shared care with the pain management clinics, particularly when considering the patient for long-term opioid use (530). However, prior the implementation of such a model of care further investigations into the outcomes associated with shared care models are required. A systematic review of shared care in chronic disease management indicates that there is, at present, insufficient evidence to demonstrate significant benefits from shared care apart from improved prescribing (531). The nature and extent of improved prescribing practices for analgesics in CNMP management specifically necessitates further investigation.

Pharmacists may also contribute to this shared care continuum by providing medication reviews and intervening in instances of potentially inappropriate prescribing e.g. identifying drug interactions (sedating agents and opioids) or preventing prescribing omissions (laxatives and strong opioids). Community pharmacists' involvement in prescribing has been demonstrated to improve the quality of care for ageing and elderly populations and for those prescribed opioid medications (505, 532). A recent randomised control trial which compared the effectiveness of pharmacist medication review, with or without pharmacist prescribing, with standard care, for patients with chronic pain indicated that there may be improved patient outcomes when receiving care from a pharmacist prescriber (533).

5. Reforms in health system management of patients with CNMP focused on primary care and specialised pain management

The GP and CPI member interviews highlight the urgent need for reform of the management of these patients in the context of the healthcare system. The reliance on GPs to manage the patient independently or navigate the patient through the system to a pain specialist is a point of concern for clinicians and patients alike. The increasing burden of chronic conditions, attributed in part to an ageing population, has prompted the development of a number of national management strategies for a variety of chronic conditions in Ireland. However, a national strategy document alone would not address the current limitations of the healthcare system, particularly for public patients. Fundamental changes are required in the health system approach to the management of CNMP.

A variety of models have been developed and adapted for health systems to address CNMP management. Wagner's chronic care model is increasingly referenced as a framework on which to base management of long-term conditions (534). This model is referenced in a number of strategy documents for chronic pain, including CNMP (246, 535, 536). Wagner's model proposes that the quality of care received by individuals with long-term conditions may be improved through enhancing community resources thereby facilitating the delivery of safe, high quality care. Patients are also encouraged to manage their healthcare through self-management, with support from healthcare professionals.

The Kaiser Permanente model is based upon Wagner's framework and proposes a method of integration of primary, secondary and specialist interventions in the mangement of chronic conditions (537). The Kaiser Permanente model was recently adapted by the NHS Scotland and incorporated into a framework to address management of chronic conditions, including chronic pain in 2010 (538). This model, acknowledges that GPs are primarily responsible for CNMP management and seeks to supplement care delivered by GPs with management by other healthcare professionals such as nurses, psychologists, physiotherapists, pharmacists and occupational therapists. The inclusion of self-management strategies in the model also emphasises the necessity for the inclusion of non-medical interventions which appear to be already commonly used by patients. At present, there is no information available on the outcomes from this revised care

approach, it is not possible to determine if it is associated with improved quality of care or outcomes for patients. However, if successful, elements of this model may be appropriate for the Irish healthcare setting, given the similarities in population demographics, prevalence of CNMP and the centrality of primary care physcians in the management of CNMP in both countries.

8.5 Future Research

Each of the chapters in this thesis presented the methodological, ethical and analytical limitations associated with the separate studies. This was an exploratory research study which sought to describe this issue from both a quantitative and qualitative perspective. The empirical nature of the studies requires that additional work should be undertaken to validate the findings or identify different outcomes than those described in this thesis.

The data on analgesic use in this PhD originated from two secondary data sources. The HSE-PCRS database records dispensing of medication while TILDA relied on self-reporting by participants or carers. Permission was gained from one third of TILDA participants to link their data with the HSE-PCRS database. This linkage may be used to determine agreement between self-reported medications and those recorded as dispensed in the pharmacy claims database. Richardson et al. identified the agreement between anti-inflammatory and analgesic medications recorded in the TILDA and HSE-PCRS databases as moderate to poor ($\hat{k}$= 0.54 and 0.5 respectively) (539). Nielsen et al. also demonstrated a difference between self-reported use of analgesics and opioid medications with prescription records; the kappa agreement between these records was 0.46 (0.4-0.51) and 0.49 (0.430.55) respectively (540). A further assessment of agreement between these two databases according to drug class (non-opioid, non-selective NSAID, selective NSAID, adjuvant medication, weak, moderate or strong opioid) would highlight those particular classes of analgesics that were under-reported by participants.

Collection and examination of primary data would be the most accurate method to determine the extent of analgesic and concurrent medication use. This may be undertaken through patient surveys or interviews, although this may also fail to detect non-adherence to a prescribed regimen as patient recall has been demonstrated to inaccurately measure medication adherence. Assessment of

biological markers, pill counts and electronic monitoring devices are the most accurate methods to examine medication use (541). This type of study would require that patients with CNMP are recruited at a primary care level and that medication use be monitored using one of these methods (542). However, given the nature of pain, which is characterised by periods of exacerbation or relief, an understanding of medication use alone is uninformative. Pain intensity, daily functionality, number of chronic diseases and QoL should also be considered to provide a complete understanding of the role of pharmacotherapy in the context of the condition.

The interviews with members of CPI provided a valuable insight into the use of analgesics by an ageing population with CNMP. However, as addressed in the chapter, this is a self-motivated group who actively participate in the management of their condition. The extent to which this population undertakes self-education and self-management may differ to members of the general population and may also alter the physician-patient dynamic to a greater extent (515). A similar concern is applicable also to the GP population that participated in this research study. These individuals were willing to participate in interviews sharing information on prescribing practices and attitudes towards CNMP management in primary care.

Interviews with ageing and elderly patients who are not members of CPI, recruited from primary care may provide a different insight into the use of analgesics for this condition. The views of individuals with CNMP recuited through a primary care setting (e.g. recruitment through GP practices) may provide a more representative viewpoint on the pharmacotherapeutic management of the condition. Furthermore, additional studies may be undertaken to identify the generalisability of results arising from the GP interviews to the wider population of GPs practising in Ireland. This again would require recruitment of greater numbers of GPs into a study perhaps through the purposive sampling approach attempted in this research study. This may substantiate the finding of 'opioiphobia' presented in this discussion and may also indicate whether reform of education or the provision of training supports for GPs is required.

Since completion of this PhD, Wave 2 TILDA data was published in 2014 and Wave 3 data is currently being collected with a view to publication in 2015/2016. Further analysis of these additional waves of data would transform this

cross-sectional analysis into a cohort study, providing a comprehensive insight into progression of pain amongst participants, resultant changes in QoL and analgesic use during this period. In particular, this work would capture persistent use of analgesic medications and long-term use of inappropriate medications with opioids.

The search for clinical practice guidelines was completed in March 2012, as this formed the basis for a number of research questions in the qualitative arm of the research. Upon renewal of the search strategy in August 2014, an additional two guidelines were identified: the West of Scotland Chronic Non Malignant Pain Opioid Prescribing Guideline, and South African guideline for the use of chronic opioid therapy for chronic non-cancer pain (543, 544). Future phases of this research would seek to incorporate these guidelines. This would be an interesting and useful addition to the research, as both of these guidelines are external to the USA and Canada and may therefore provide a different perspective than the majority of guidelines currently included in the review. The Scottish guideline in particular has been developed during a period of changing management of CNMP conditions in the NHS system and may offer valuable guidance on pharmacotherapeutic management in the context of primary care.

One of the key recommendations emerging from this research is the necessity for development and publication of high quality clinical practice guidelines to direct the prescribing of anagesics, particularly opioid analgesics for patients with CNMP in primary care. Such guidelines should also include recommendations on the pharmacotherapeutic management of ageing and elderly populations. Further research to determine outcomes associated with implementation of such recommendations may be conducted through assessment of the practices of those healthcare professionals engaging with the documents and subsequent outcomes for patients with CNMP. For instance, an intervention providing guidance to healthcare professionals on the prescribing of opioid analgesics, encompassing initiation and maintenance of opioids and co-prescribing, may lead to improved pain mangement and reduce potentially inapproporiate prescribing.

8.6 Conclusion

At present, in Ireland, delivery of care to patients with CNMP is focused in the community setting and managed predominantly by GPs. Pharmacotherapeutic

interventions are one of the cornerstones of pain management in this setting. Use of pharmacotherapeutic interventions in the management of this condition is dependent on those factors that inform the decision making process of the GP prescribing the medication and those influencing the patient taking the medication. These barriers and facilitators of pharmacotherapeutic management are informed by personal and sociocultural perspectives of pain and pharmacotherapy and are also influenced by the healthcare system.

From the GP's viewpoint, there are challenges in balancing evidence-based medicine with patient-centred medicine when prescribing medications for this condition. The findings of this PhD research propose that, while GPs strive to deliver optimal care to patients, additional guidance may be required to improve the quality, consistency and homogeneity of prescribing approaches. Guidance should be cognisant of the heterogeneity of CNMP and the specific clinical and psychosocial needs of ageing and elderly patients. While educational interventions may also be of some benefit to GPs, the provision of prescribing supports through clinical practice guidelines and enhanced consultation with pain specialists in a model of shared care may produce a more significant impact on prescribing behaviours.

Individuals with CNMP must balance beliefs and perceptions of medications and the potential for adverse outcomes with the benefits that may be derived from medications. Education on the role of medications in pain management delivered by healthcare professionals, including GPs and pharmacists, and organisations such as patient support groups may empower patients to partake in shared decision making when constructing a pain management plan. Educational interventions should endeavour to support a holistic approach to pain management by also informing individuals of the important role of self-management strategies which may address the psychosocial dimensions of the condition.

Reform of the healthcare system is required to ensure that care is delivered in an equitable, timely and efficient manner to individuals with CNMP, prioritising those in greatest need. Improved primary care management delivered by a multidisciplinary team, combined with an emphasis on self-management strategies, would complement pharmacotherapeutic interventions when striving to attain pain relief for this patient group.

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Appendices

Appendix A. Background on Health Research Board PhD Scholars Programme in Health Services Research

Programme Structure

Scholars are provided with a structured PhD training programme, consisting of 4 training strands with strand 1 completed in Year 1 and strands 2-4 extending over 4 years. The training in strand one is equivalent to a Masters level programme in health services research. The training in strands 2-4 addresses specialist research skills related to the scholar's research project, professional development and career development skills. A particular feature of the planned training is the determination to ensure that graduates of the programme are part of a network of HSR specialists that will provide mutual support and facilitate collaborations over their careers.

The four formal training strands are:

1. One year intensive course in Health Services Research
2. Specialist research skills training (related to research project)
3. Professional skills including time and project management, grant application skills, scientific paper writing, team-working, communication skills (written and oral, including media and advocacy training) and presentation skills
4. Career development skills (CV and interview skills, seminars with experts and leaders in relevant career settings)

Overview of Year 1 Intensive Course in Health Services Research

The Year 1 programme includes classroom, online and self-directed learning, workshops and seminars and a placement in a research organisation to provide understanding of how research is carried out, how data is collected and accessed, and how research is disseminated and put into policy and practice. A significant element of self-directed e-learning is required and the programme avails of RCSI's well-established e-learning infrastructure. By the end of Year 1, students develop a draft PhD proposal (including literature review, methods and feasibility issues addressed).

Core Modules

Modules are listed below covering contextual knowledge (particularly on health systems and population health), information systems and sources, generic research skills such as reviewing evidence, introductory material covering the main HSR disciplines and courses in discipline based research skills.

Module 1: Population and Individual Health

Module 2: Health Systems, Policies and Health Informatics

Module 3: Evidence synthesis and clinical trials

Module 4: Applying research methods

Module 5: Data Analysis with STATA

Module 6: Health economics and econometrics

Years 2 – 4

There is ongoing evaluation, peer support and course seminars for scholars. At the end of year 2 and year 3 the scholar and the supervisor submit evaluation reports. These are assessed with reference to the PhD proposal and feedback is given by the Steering Sub-Group to the PhD scholar and the supervisor.

Appendix B. Search Strategy and AGREE II Assessment Information

B.1. Search Strategy for Systematic Review of Clinical Practice Guidelines

Electronic Databases

Electronic Databases	Search Terms	No. Retrieved	No. Retained
CINAHL	(MH "Chronic Pain/DT/PA/PP/PC/LJ/SS/TH/TD/EP/ED") OR (MH "Practice Guidelines") OR (MH "Chronic Pain (NANDA)") OR (MH "Medical Technologists") OR (MH "Chronic Pain Control (Saba CCC)")	131	2
	(MM "Chronic Pain") AND (MM "Chronic Pain Control (Saba CCC)") AND (MM "Pain Clinics") AND (MM "Practice Guidelines") AND (MM "Chronic Disease") AND (MM "Guideline Adherence") AND (MM "Pain") AND (MM "Analgesia")	136	0
Embase	(pain AND 'clinical protocol'/de AND ([adult]/lim OR [aged]/lim OR [middle aged]/lim OR [very elderly]/lim)	173	14
Pubmed	(("chronic pain"[MeSH Terms] OR ("chronic"[All Fields] AND "pain"[All Fields]) OR "chronic pain"[All Fields]) AND ("organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "management"[All Fields] OR "disease management"[MeSH Terms] OR ("disease"[All Fields] AND "management"[All Fields]) OR "disease management"[All Fields])) AND ((Practice Guideline[ptyp] OR Review[ptyp]) AND English[lang] AND ("adult"[MeSH Terms:noexp] OR "middle aged"[MeSH Terms] OR ("middle aged"[MeSH Terms] OR "aged"[MeSH Terms]) OR "aged"[MeSH Terms] OR "aged, 80 and over"[MeSH Terms]))	520	5
	("chronic pain"[MeSH Terms] OR ("chronic"[All Fields] AND "pain"[All Fields]) OR "chronic pain"[All Fields]) AND ("organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND	526	44

	"administration"[All Fields]) OR "organization and administration"[All Fields] OR "management"[All Fields] OR "disease management"[MeSH Terms] OR ("disease"[All Fields] AND "management"[All Fields]) OR "disease management"[All Fields]) AND ("guideline"[Publication Type] OR "guidelines as topic"[MeSH Terms] OR "guideline"[All Fields])		
	chronic pain management AND ((Practice Guideline[ptyp] OR Review[ptyp]) AND English[lang] AND (adult[MeSH:noexp] OR middle age[MeSH] OR (middle age[MeSH] OR aged[MeSH]) OR aged[MeSH] OR aged, 80 and over[MeSH]))	313	0
Web of Science	Topic=(chronic pain) AND Topic=(guideline) AND Topic=(medication) Refined by: Languages=(ENGLISH) Timespan=1990-2012. Databases=SCI-EXPANDED, SSCI, A&HCI.	180	0
ScienceDirect	Chronic non-malignant pain clinical guidelines medication	989	12
TRIP database	Chronic pain, Persistent, Non-malignant, Guideline(s), Pain	293	5

Healthcare Professional Websites & Guideline Databases

Source	Country	Website	No. Retrieved On Search	No. CPGs taken for inclusion in review process
National Guideline Clearinghouse	USA	www.guidelines.gov	323	6
American College of Physician Guidelines	USA	http://www.acponline.org/clinical_information/guidelines/	3	3
Guidelines International Network Library	USA	http://www.g-i-n.net/library/international-guidelines-library	11	2
Ontario Guidelines Advisory Committee	Canada	www.gacguidelines.ca	1	1
Canadian Agency for Drugs and Technology in Health	Canada	www.cadth.ca/	51	2
National Electronic Library for Medicines - Guidelines Finder	UK	www.nelh.nhs.uk/guidelinesfinder	204	2
National Electronic Library for Medicines Evidence - Guidelines	UK	http://www.nelm.nhs.uk/en/NeLM-Area/Evidence/Guidelines/?category=4473	26	1

Royal College of Physicians Guideline and Audit Database leading to National Clinical Guideline Centre	UK	http://www.rcplondon.ac.uk/resources/clinical/guidelines http://www.ncgc.ac.uk/	See Results For Nice Guideline Search	N/A
E-Guidelines	UK	http://www.eguidelines.co.uk/	5	4
National Institute for Health and Excellence	UK	www.nice.org.uk	16	3
National Health and Medical Research Council	Aus	www.nhmrc.gov.au	9	0
New Zealand Guidelines Group	New Zealand	www.nzgg.org.nz	11	0
Scottish Intercollegiate Guidelines Network	UK	www.sign.ac.uk/guidelines	0	0
Faculty of Pain Medicine ANZA (Australia and New Zealand)	Aus/ New Zealand	http://www.anzca.edu.au/fpm	0	0
Centre for Studies in Aging & Health at Providence Care	Canada	http://www.sagelink.ca/content/best-practices-guidelines	3	2
National Pain Centre McMaster University	Canada	http://nationalpaincentre.mcmaster.ca/opioid/	1	1
American Geriatrics Society	USA	http://www.americangeriatrics.org/health_care_professionals/clinical_practice/clinical_guidelines_recommendations/	1	1
British Geriatrics Society	UK	http://www.bgs.org.uk/	1	1
The British Pain Society	UK	http://www.britishpainsociety.org/pub_professional.htm	20	1
American Pain Society	USA	http://www.ampainsoc.org/library/principles.htm	3	3
Australian Pain Society	Aus	http://www.apsoc.org.au/index.php	4	1
Canadian Pain Society	Canada	http://www.canadianpainsociety.ca/en/	0	0
American Chronic Pain Association	USA	http://www.theacpa.org/default.aspx	1	1
American Academy of Pain Medicine	USA	http://www.painmed.org/Library/Clinical_Guidelines.aspx	2	1

B.2. AGREE II Scoring Sheet and Associated Calculations

	Appraiser			
	1	*2*	*3*	*4*
Domain 1 - Scope and Purpose				
Q1 - The overall objective(s) of the guideline is (are) specifically described.				
Q2 - The health question(s) covered by the guideline is (are) specifically described.				
Q3 - The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.				
Domain 2 - Stakeholder Involvement				
Q4 - The guideline development group includes individuals from all relevant professional groups.				
Q5 - The views and preferences of the target population (patients, public, etc.) have been sought.				
Q6 - The target users of the guideline are clearly defined.				
Domain 3 - Rigour of Development				
Q7 - Systematic methods were used to search for evidence.				
Q8 - The criteria for selecting the evidence are clearly described.				
Q9 - The strengths and limitations of the body of evidence are clearly described.				
Q10 - The methods for formulating the recommendations are clearly described.				
Q11 - The health benefits, side effects, and risks have been considered in formulating the recommendations.				
Q12 - There is an explicit link between the recommendations and the supporting evidence.				
Q13 - The guideline has been externally reviewed by experts prior to its publication.				
Q14 - A procedure for updating the guideline is provided.				

Domain 4 - Clarity of Presentation				
Q15 - The recommendations are specific and unambiguous.				
Q16 - The different options for management of the condition or health issue are clearly presented.				
Q17 - Key recommendations are easily identifiable				
Domain 5 - Applicability				
Q18 - The guideline describes facilitators and barriers to its application.				
Q19 - The guideline provides advice and/or tools on how the recommendations can be put into practice.				
Q20 - The potential resource implications of applying the recommendations have been considered.				
Q21 - The guideline presents monitoring and/or auditing criteria.				
Domain 6 - Editorial Independence				
Q22 - The views of the funding body have not influenced the content of the guideline.				
Q23 - Competing interests of guideline development group members have been recorded and addressed.				
Overall Guideline Assessment				
1. Rate the overall quality of this guideline. *Scoring: 1(Least Quality) - 7(Highest Quality)*				
2. I would recommend this guideline for use. *Scoring: "Yes", "Yes, with modifications", "No"*				

Example for Domain 1 Scope & Purpose)

	Item 1	Item 2	Item 3	Total
Appraiser 1				
Appraiser 2				
Total				

Maximum Possible Score: 7(Strongly Agree) x 3(Items) x 2(Appraisers)
Maximum Possible Score: 1(Strongly Disagree) x 3(Items) x 2(Appraisers)
Scaled Domain Score:
(Obtained Score- Minimum Possible Score) ÷ (Maximum Possible Score - Minimum
Possible score)

Appendix C Tables Supporting Data Presented in Chapter 4

Table C-1: Classification of weak and moderate opioids according to brand name

Brand Name and Ingredients
Nurofen Plus® (Ibuprofen 200mg/ Codeine 12.8mg)
Solpadeine® (Paracetamol 500mg/Codeine 8mg)
Maxilief® (Paracetamol 500mg/Codeine 8mg)
Syndol® (Paracetamol 500mg/Codeine 10mg)
Panadeine® (Paracetamol 500mg/Codeine 8mg)
Migraleve® Yellow/Pink (Paracetamol 500mg/Codeine 8mg)
Co-Codaprin® (Aspirin 500mg/Codeine 8mg)
Codis® (Aspirin 500mg/Codeine 8mg)
Veganin® (Paracetamol 500mg/Codeine 8mg)
Paracodol® (Paracetamol 500mg/Codeine 8mg)
Codipar® (Paracetamol 500mg/Codeine 15mg)
Codafen Continuus® (Ibuprofen 300mg/Codeine 20mg)
Moderate Opioids in PCRS Analysis
Solpadol® (Paracetamol 500mg/Codeine 30mg)
Kapake® (Paracetamol 500mg/Codeine 30mg)
Tylex® (Paracetamol 500mg/Codeine 30mg)
Paramol® (Paracetamol 500mg/Dihydrocodeine 10mg)
Tramadol (various strengths)
Tramadol/Paracetamol (37.5mg Tramadol/325mg Paracetamol)
Meptazinol (various strengths)
Tapentadol (various strengths)
Co-Codamol® (Paracetamol 500mg/Codeine 30mg)
Co-Proxamol/Distalgesic® (Paracetamol 325mg/Dextropropoxyphene 32.5mg)

Table C-2: Number of GMS eligible patients 2003-2011 according to age-group and gender

	Age-Group	Women	Men	Total
2003	**55-64**	62,708	53,125	115,833
	65-69	36,766	28,572	65,338
	70-74	59,111	51,779	110,890
	≥75	122,685	75,755	198,440
	Total Population	**281,270**	**209,231**	**490,501**
2004	**55-64**	63,335	54,059	117,394
	65-69	36,814	29,244	66,058
	70-74	60,175	53,626	113,801
	≥75	125,122	78,015	203,137
	Total Population	**285,446**	**214,944**	**500,390**
2005	**55-64**	64,413	55,122	119,535
	65-69	37,096	29,926	67,022
	70-74	61,104	55,114	116,218
	≥75	129,222	81,998	211,220
	Total Population	**291,835**	**222,160**	**513,995**
2006	**55-64**	67,827	57,932	125,759
	65-69	37,489	30,649	68,138
	70-74	62,698	56,776	119,474
	≥75	131,964	84,765	216,729
	Total Population	**299,978**	**230,122**	**530,100**
2007	**55-64**	69,527	59,901	129,428
	65-69	38,642	31,759	70,401
	70-74	63,677	58,040	121,717
	≥75	135,284	88,491	223,775
	Total Population	**307,130**	**238,191**	**545,321**
2008	**55-64**	70,765	62,051	132,816
	65-69	39,182	32,066	71,248
	70-74	64,760	59,523	124,283
	≥75	136,736	90,834	227,570
	Total Population	**311,443**	**244,474**	**555,917**
2009	**55-64**	74,137	66,612	140,749
	65-69	42,457	33,459	75,916
	70-74	60,350	54,609	114,959
	≥75	133,550	89,160	222,710
	Total Population	**310,494**	**243,840**	**554,334**
2010	**55-64**	78,694	71,595	150,289
	65-69	46,390	36,076	82,466
	70-74	60,453	54,430	114,883
	≥75	137,648	93,275	230,923
	Total Population	**323,185**	**255,376**	**578,561**
2011	**55-64**	81,314	75,006	156,320
	65-69	49,261	38,249	87,510
	70-74	59,317	52,868	112,185
	≥75	139,913	96,420	236,333
	Total Population	**329,805**	**262,543**	**592,348**

Table C-3: Number of GMS eligible patients 2003-2011 taking ≥1 analgesics according to age-group and gender

		Women		Men		Overall	
Year	Age-Group	n	%	n	%	n	%
2003	**55-64**	39,294	22.3	29,232	24.9	68,527	23.4
	65-69	22,493	12.8	16,224	13.8	38,717	13.2
	70-74	35,015	19.9	27,007	23.0	62,022	21.1
	≥75	79,283	45.5	44,780	38.2	124,063	42.3
2004	**55-64**	38,754	22.0	28,885	24.6	67,639	23.1
	65-69	22,404	12.7	16,074	13.7	38,478	13.1
	70-74	34,662	16.7	26,882	22.9	61,504	20.97
	≥75	80,048	45.5	45,686	38.9	125,734	42.9
2005	**55-64**	40,564	22.1	30,383	24.5	70,947	23.1
	65-69	23,283	12.7	168,286	13.6	40,109	13.1
	70-74	36,143	19.7	28,704	23.1	64,847	21.1
	≥75	83,398	45.5	48,162	38.8	131,560	42.8
2006	**55-64**	42,342	22.5	31,688	24.8	74,030	23.4
	65-69	23,442	12.4	16,962	13.3	40,404	12.8
	70-74	36,764	19.5	29,221	22.9	65,985	20.9
	≥75	85,855	45.6	49,912	39.1	135,767	42.9
2007	**55-64**	42,489	22.8	31,562	25.0	74,051	23.7
	65-69	23,299	12.5	16,967	13.5	40,266	12.9
	70-74	36,122	19.4	28,591	22.7	64,713	20.7
	≥75	84,108	45.2	48,926	38.8	133,034	42.6

2008	**55-64**	45,821	23.0	34,554	25.2	80,375	23.9
	65-69	24,665	12.4	18,146	13.2	42,811	12.7
	70-74	38,559	19.4	30,851	22.5	69,410	20.6
	≥75	90,190	45.3	53,765	39.2	143,955	42.8
2009	**55-64**	47,904	23.5	36,680	26.1	85,584	24.6
	65-69	26,411	12.97	18,749	13.4	45,160	13.1
	70-74	37,722	18.5	29,929	21.3	67,651	19.7
	≥75	91,628	4.9	55,006	39.2	146,634	42.6
2010	**55-64**	51,377	24.3	39,958	27.5	91,335	25.6
	65-69	28,740	13.6	19,964	13.8	48,704	13.7
	70-74	37,480	17.7	29,373	20.3	66,853	18.8
	≥75	93,671	44.3	55,771	38.5	149,442	41.9
2011	**55-64**	53,924	24.5	42,088	27.9	96,012	25.9
	65-69	31,000	14.1	21,354	14.2	52,354	14.1
	70-74	37,684	17.1	29,181	19.4	66,865	18.0
	≥75	97,954	44.4	58,052	38.5	156,006	42.0

Table C-4: Number of GMS eligible population aged ≥55years dispensed systemic and topical non-selective NSAIDs (≥ 1 dispensing & >3 dispensings)

	Systemic Non-Selective NSAIDs		Topical Non-Selective NSAIDs	
Year	**≥ 1 Dispensing**	**>3 Dispensings**	**≥ 1 Dispensing**	**>3 Dispensings**
2003	146,119	56,361	68,829	17,139
2004	165,300	50,417	73,132	18,675
2005	154,078	57,337	93,418	22,084
2006	152,044	55,177	89,582	24,430
2007	164,575	56,660	92,506	24,512
2008	181,510	64,889	113,090	32,487
2009	176,104	60,139	117,739	34,420
2010	178,221	58,489	123,068	36,447
2011	177,119	55,773	130,685	38,521

Table C-5: Number of GMS eligible population aged ≥55years dispensed weak, moderate and strong opioids (≥1 dispensing & >3 dispensings)

	Weak Opioids		Moderate Opioids		Strong Opioids	
	≥ 1 Dispensing	> 3 Dispensings	≥ 1 Dispensing	>3 Dispensings	≥ 1 Dispensing	>3 Dispensings
2003	24,140	7,811	123,542	44,876	13,515	5,619
2004	23,182	7,803	121,677	46,633	13,997	6,299
2005	26,754	8,820	126,630	48,168	16,158	7,348
2006	36,879	11,722	108,063	36,963	19,192	9,240
2007	37,153	11,929	100,574	34,471	21,164	10,364
2008	43,891	15,292	114,278	40,662	25,272	13,576
2009	44,995	15,653	118,302	43,035	27,775	15,168
2010	48,295	16,745	122,853	44,470	29,850	16,761
2011	54,281	18,643	125,597	46,699	32,876	18,489

Table C-6: Number of GMS eligible population aged ≥55years dispensed weak, moderate and strong opioids (≥3 dispensings) according to age-group and gender 2009-2011

		>3 Dispensings Weak Opioid		>3 Dispensings Moderate Opioid		>3 Dispensings Strong Opioid	
Year	Age-Group	Women	Men	Women	Men	Women	Men
2009	55-64	2,232	1,110	7,145	5,379	1,465	1,203
	65-69	1,409	664	4,289	2,685	9,83	714
	70-74	2,016	966	4,639	3,152	1,401	912
	≥75	5,291	1,965	13,276	5,837	6,181	2,309
2010	55-64	2,540	1,230	6,824	5,007	1,670	1,262
	65-69	1,340	713	4,065	2,498	1,112	769
	70-74	2,073	973	4,434	3,108	1,516	936
	≥75	5,527	2,107	12,852	5,682	6,953	2,543
2011	55-64	2,873	1,437	6,409	4,678	1,795	1,432
	65-69	1,821	842	3,707	2,535	1,149	847
	70-74	2,245	1,074	4,855	2,971	1,580	1,008
	≥75	6,091	2,555	12,517	5,545	7,824	2,854

Table C-7: Number of GMS eligible population aged ≥55years dispensed weak, moderate and strong opioids (1-7 months & 8-12 months)

Year	Weak Opioid		Moderate Opioid		Strong Opioid	
	1-7 Months	8-12 Months	1-7 Months	8-12 Months	1-7 Months	8-12 Months
2003	20,428	3,712	100,383	20,189	11,723	1,792
2004	19,537	3,645	100,462	21,125	11,848	2,149
2005	22,358	4,369	100,984	22,646	13,634	2,524
2006	31,293	5,589	91,703	16,360	15,745	3,447
2007	32,591	4,562	87,012	13,562	17,816	3,348
2008	35,995	7,956	96,254	20,024	19,524	5,748
2009	36,341	8,654	96,761	21,541	20,960	6,815
2010	39,401	8,894	100,019	22,834	21,967	7,883
2011	44,076	10,172	101,416	24,181	24,085	8,791

Table C-8: Number of GMS eligible population aged ≥55years dispensed a sedating agent with a weak, moderate or strong opioids (≥ 1 dispensing & >3 dispensings)

	Weak Opioids		Moderate Opioids		Strong Opioids	
	≥ 1 Dispensing	> 3 Dispensings	≥ 1 Dispensing	>3 Dispensings	≥ 1 Dispensing	>3 Dispensings
2006	12,391	11,722	33,851	8,798	9,999	2,866
2007	14,227	11,929	32,149	7,988	10,903	3,158
2008	17,196	15,292	36,808	9,913	13,195	4,340
2009	17,467	15,353	37,338	10,024	14,275	5,154
2010	18,771	16,743	37,910	10,131	15,131	5,487
2011	24,809	18,643	40,473	11,070	16,541	6,002

Table C-9: Number of GMS eligible population aged ≥55years dispensed a laxative with a weak, moderate or strong opioids (≥ 1 dispensing & >3 dispensings)

	Weak Opioids		Moderate Opioids		Strong Opioids	
	≥ 1 Dispensing	> 3 Dispensings	≥ 1 Dispensing	>3 Dispensings	≥ 1 Dispensing	>3 Dispensings
2006	1,969	325	11,002	1,285	5,784	9,240
2007	1,914	306	10,087	1,060	6,026	10,364
2008	2,597	473	11,669	1,808	7,654	13,576
2009	2,909	519	12,891	1,522	9,190	15,168
2010	3,583	717	16,256	2,092	11,956	16,761
2011	3,939	814	17,128	2,402	13,303	18,489

Appendix D. Tables Supporting Data Presented in Chapter 5

Table D-1: Univariate Regression Model for WHO Analgesic Ladder for participants with pain (Model 1)

	WHO ANALGESIC LADDER							
	No Analgesic (Step 0)/ Non-Opioid/NSAID/Adjuvant (Step 1)		No Analgesic (Step 0)/ Weak Opioid (Step 2)		No Analgesic (Step 0)/ Moderate Opioid (Step 3)		No Analgesic (Step 0)/ Strong Opioid (Step 4)	
	RRR (95% CI)	P-Val	RRR (95% CI)	P-Val	RRR (95% CI)	P-Val	RRR (95% CI)	P-Val
Gender								
Male	1		1		1		1	
Female	1.73 (1.38-2.17)	0.00	1.22 (0.63-2.36)	0.55	1.79 (1.28-2.49)	0.001	2.12 (0.99-4.53)	0.05
Age-Group								
50-64	1		1		1			
65-74	1.46 (1.15-1.87)	0.002	0.99 (0.44-2.24)	0.99	1.29 (0.89-1.87)	0.18	1.18 (0.44-3.1)	0.74
≥75	1.37 (1.02-1.84)	0.035	1.61 (0.73-3.56)	0.24	2.07 (1.41-3.03)	0.00	3.15 (1.32-7.5)	0.01
Marital Status								
Married	1		1		1			
Never Married	1.21 (0.83-1.77)	0.32	2.46 (0.95-6.35)	0.06	1.25 (0.72-2.17)	0.43	1.15 (0.26-5.0)	0.86
Sep/divorced	1.46 (1.02-2.09)	0.04	1.88 (0.68-5.17)	0.22	1.23 (0.7-2.18)	0.47	0.75 (0.16-3.59)	0.72
Widowed	1.34 (0.99-1.81)	0.05	1.13 (0.42-3.08)	0.8	2.12 (1.47-3.06)	0.00	2.47 (1.05-5.78)	0.04
Self-Rated Physical Health								
Excellent/Very Good	1		1		1		1	
Good/Fair	2.64 (1.98-3.51)	0.00	2.28 (0.97-5.36)	0.06	3.06 (1.88-4.98)	0.00	2.35 (0.72-7.72)	0.16
Poor	4.29 (2.85-6.47)	0.00	4.18 (1.34-13.41)	0.02	8.69 (5.02-15.06)	0.00	21.38 (6.51-70.23)	0.00
Polypharmacy								
<5 Medications	1		1		1			
≥5 Medications	2.99 (2.41-3.7)	0.00	5.75 (2.91-11.34)	0.00	6.63 (4.86-9.04)	0.00	12.41 (4.42-34.89)	0.00

Educational Level								
None/primary level	1		1		1		1	
Secondary level	0.77 (0.61-0.96)	0.02	0.67 (0.32-1.41)	0.29	0.77 (0.56-1.07)	0.12	0.32 (0.13-0.74)	0.008
Third level	0.8 (0.61-1.05)	0.1	0.69 (0.32-1.46)	0.33	0.52 (0.34-0.79)	0.002	0.30 (0.11-0.85)	0.02
Employment Status								
Employed	1			1	1		1	
Retired	2.55 (1.91-3.41)	0.00	2.33 (0.95-5.7)	0.06	3.29 (2.03-5.34)	0.00	9.4 (1.16-75.46)	0.04
Unemployed/ Sick Disabled/Carer	3.04 (2.27-4.07)	0.00	1.89 (0.77-4.63)	0.16	4.32 (2.74-6.81)	0.00	20.6 (2.71-157.36)	0.004
Health Insurance								
Not covered	1		1		1		1	
Medical insurance	1.49 (0.98-2.29)	0.07	0.76 (0.24-2.44)	0.64	0.68 (0.35-1.32)	0.25	2.36 (2.01-2.95)	0.08
Medical Card	2.29 (1.52-3.34)	0.08	1.51 (0.52-4.36)	0.45	2.62 (1.46-4.69)	0.07	2.61 (2.30-3.05)	0.09
Residence								
Urban	1		1		1		1	
Rural	0.97 (0.78-1.21)	0.8	1.0 (0.52-1.96)	0.99	0.84 (0.61-1.15)	0.26	1.71 (0.81-3.62)	0.16
Pain Severity								
Mild	1		1		1		1	
Moderate	2.56 (1.89-3.46)	0.00	2.81 (1.00-7.83)	0.05	2.71 (1.61-4.57)	0.00	3.84 (1.02-14.55)	0.05
Severe	4.53 (3.29-6.24)	0.00	5.89 (1.99-17.51)	0.001	8.28 (4.95-13.85)	0.00	13.12 (3.56-48.36)	0.00
Pain Location								
All Over/Other	1		1		1		1	
Joint Pain	1.04 (0.79-1.37)	0.79	1.09 (0.43-2.73)	0.86	0.80 (0.5-1.27)	0.34	0.25 (0.5-1.18)	0.08
Back Pain	0.94 (0.73-1.21)	0.64	1.16 (0.54-2.51)	0.71	1.24 (0.89-1.75)	0.20	1.46 (0.64-3.31)	0.37
Pain Limits Daily Activity								
No Limitations	1		1		1		1	
Limitations	2.38 (1.89-2.99)	0.00	2.91 (1.39-6.24)	0.006	3.89 (2.69-5.64)	0.00	8.75 (2.81-27.26)	0.00
Depression (CES-D ≥16)								
Not Depressed		1	1		1		1	
Depressed	1.63 (1.24-2.14)	0.00	1.67 (0.77-3.63)	0.19	2.18 (1.50-3.16)	0.00	3.56 (1.68-7.56)	0.001

Number of Chronic Diseases								
No Chronic Diseases	1		1		1		1	
1 Chronic Disease	1.68 (1.07-2.66)	0.03	2.85 (0.74-10.92)	0.13	2.67 (1.27-5.58)	0.009	1.30 (0.12-14.6)	0.83
2 Chronic Diseases	2.51 (1.61-3.91)	0.00	1.56 (0.37-6.51)	0.54	3.35 (1.65-6.83)	0.001	7.52 (0.95-59.44)	0.06
≥3 Chronic Diseases	3.69 (2.45-5.59)	0.00	3.12 (0.83-11.61)	0.09	5.11 (2.56-10.21)	0.00	7.95 (1.03-61.19)	0.05
Smoking Status								
Never Smoked	1		1		1		1	
Past Smoker	1.0 (0.79-1.27)	0.99	2.17 (0.87-5.39)	0.096	1.38 (0.98-1.94)	0.06	1.05 (0.49-2.24)	0.9
Current Smoker	1.08 (0.81-1.44)	0.62	2.77 (1.04-7.36)	0.04	1.76 (1.2-2.58)	0.04	0.87 (0.9-2.55)	0.8
No of GP Visits Per Year								
0 GP Visits	1		1		1		1	
1 GP Visits	1.85 (0.91-3.81)	0.09	0.70 (0.98-5.04)	0.73	1.41 (0.25-7.76)	0.69	1.09 (0.95-1.21)	0.69
2 GP Visits	2.12 (1.08-4.19)	0.06	1.74 (0.36-8.46)	0.49	4.22 (0.97-18.48)	0.06	0.94 (0.85-1.2_	0.06
3 GP Visits	3.81 (1.94-7.49)	0.07	0.7 (0.11-5.47)	0.79	5.72 (1.29-25.3)	0.08	0.2 (0.07-0.3)	0.08
≥4 GP Visits	5.99 (3.22-11.17)	0.06	2.85 (0.67-12.1)	0.16	15.77 (3.88-64.2)	0.09	0.56 (0.34-0.71)	0.09

Table D-2: Univariate Regression Model for WHO Analgesic Ladder for participants with pain (Model 2)

	WHO ANALGESIC LADDER					
	Non-Opioid/NSAID/Adjuvant Agent (Step 1) / Weak Opioid (Step 2)		Non-Opioid/NSAID/Adjuvant Agent (Step 1) /Moderate Opioid (Step 3)		Non-Opioid/NSAID/Adjuvant Agent (Step 1) /Strong Opioid (Step 4)	
	RRR(95% CI)	P-Value	RRR (95% CI)	P-Value	RRR (95% CI)	P-Value
Gender						
Male	1		1		1	
Female	0.71 (0.35-1.41)	0.32	1.03 (0.71-1.5)	0.87	1.23 (0.55-2.71)	0.62
Age-Group						
50-64	1		1		1	
65-74	0.68 (0.29-1.57)	0.37	0.88 (0.58-1.33)	0.54	0.80 (029-2.19)	0.67
≥75	1.17 (0.51-2.69)	0.71	1.51 (0.96-2.37)	0.07	2.29 (0.92-5.71)	0.07
Marital Status						
Married	1		1		1	
Never Married	2.03 (0.76-5.42)	0.16	1.03 (0.54-1.97)	0.93	0.95 (0.21-4.34)	0.94
Sep/divorced	1.29 (0.45-3.7)	0.64	0.85 (0.45-1.60)	0.61	0.52 (0.099-2.66)	0.43
Widowed	0.85 (0.31-2.34)	0.75	1.58 (1.03-2.43)	0.04	1.84 (0.75-4.51)	0.18
Self-Rated Physical Health						
Excellent/Very Good	1		1		1	
Good/Fair	0.86 (0.35-2.15)	0.75	1.16(0.68-1.98)	0.59	0.89 (0.26-3.06)	0.86
Poor	0.97 (0.29-3.27)	0.97	2.02(1.07-3.82)	0.03	4.98 (1.44-17.22)	0.01
Polypharmacy						
<5 Medications	1		1		1	
≥5 Medications	1.92 (0.96-3.85)	0.07	2.22(1.58-3.12)	0.00	4.16(1.43-12.07)	0.009
Educational Level						
None/primary level	1		1		1	
Secondary level	0.88 (0.41-1.87)	0.74	1.01 (0.69-1.47)	0.95	0.41(.17-0.99)	0.05
Third level	0.89 (0.39-1.87)	0.7	0.65 (0.40-1.04)	0.07	0.38 (0.13-1.07)	0.07
Employment Status						
Employed	1		1		1	

Retired	0.91 (0.36-2.28)	0.84	1.29 (0.75-2.21)	0.36	3.67 (0.47-28.54)	0.21
Other	0.62 (0.25-1.55)	0.31	1.42 (0.84-2.39)	0.19	6.79 (0.92-50.14)	0.06
Health Insurance						
Not covered	1		1		1	
Medical insurance	0.51 (0.15-1.7)	0.3	0.45(0.21-0.97)	0.06	2.89 (2.11-3.1)	0.98
Medical Card	0.66 (0.22-2.02)	0.47	1.1 (0.58-2.27)	0.69	2.09 (1.97-2.21)	0.98
Residence						
Urban	1		1		1	
Rural	1.03 (0.52-2.06)	0.93	0.86 (0.6-1.22)	0.39	1.76 (0.81-3.79)	0.15
Pain Severity						
Mild	1		1		1	
Moderate	1.09 (0.39-3.13)	0.86	1.06(0.58-1.94)	0.84	1.50 (0.37-6.11)	0.57
Severe	1.30 (0.43-3.91)	0.64	1.83 (1.01-3.29)	0.05	2.89 (0.74-11.33)	0.13
Pain Location						
All Over/Other Pain	1		1		1	
Joint Pain	1.05 (0.40-2.73)0.92	0.92	0.77 0.46-1.27)	0.3	0.24 (0.05-1.12)	0.07
Back Pain	1.23 (0.5-2.74)	0.61	1.33 (0.9-1.95)	0.16	1.54 (0.68-3.52)	0.3
Pain Limits Daily Activity						
No Limitations	1		1		1	
Limitations	1.22 (0.56-2.67)	0.61	1.63 (1.05-254)	0.03	3.67 (1.17-11.49)	0.026
Depression (CES-D ≥16)						
Not Depressed	1		1		1	
Depressed	1.03 (0.46-2.27)	0.95	1.34 (0.89-2.02)	0.16	2.19 (0.99-4.82)	0.05
Number of Chronic Diseases						
No Chronic Diseases	1		1		1	
1 Chronic Disease	1.69 (0.42-6.74)	0.46	1.58 (0.69-3.64)	0.28	0.77 (0.064-9.31)	0.84
2 Chronic Disease	0.62 (0.14-2.73)	0.53	1.34 (0.58-3.06)	0.49	2.99 (0.36-25.21)	0.31
≥3 Chronic Diseases	0.84 (0.22-3.23)	0.8	1.38 (0.64-3.00)	0.41	2.15 (0.26-17.66)	0.48

Smoking Status						
Never Smoked	1		1		1	
Past Smoker	2.14 (0.84-5.49)	0.12	1.37 (0.93-2.04)	0.14	1.04 (0.47-2.31)	0.93
Current Smoker	2.82 (1.03-7.76)	0.04	1.80 (1.12-2.89)	0.02	0.81 (0.29-2.70)	0.84
No of GP Visits Per Year						
0 GP Visits	1		1		1	
1 GP Visits	0.38(0.05-3.03)	0.36	0.76 (0.12-4.75)	0.77	0.95 (0.89-1.2)	0.71
2 GP Visits	0.82 (0.15-4.49)	0.82	1.99(0.39-9.90)	0.40	1.02(0.98-1.08)	0.9
3 GP Visits	0.19 (0.025-1.57)	0.13	1.49 (0.29-7.51)	0.62	4.36 (4.25-4.52)	0.62
≥4 GP Visits	0.48 (0.1-2.25)	0.35	2.63 (0.57-12.01)	0.21	2.15 (2.09-2.18)	0.9

Table D-3: Univariate linear regression for CASP-19 Scores for participants with pain aged 50 years and older

Characteristic	Beta Coefficient	P-Val
Gender		
Male	1	
Female	0.70(-0.05-1.45)	0.07
Age-Group		
50-64	1	
65-74	1.57 (0.66-2.48)	0.00
≥75	-0.98(-2.07-0.11)	0.08
Marital Status		
Married	1	
Never Married	-2.50(-4.22-(-)0.77)	0.01
Sep/divorced	-3.32(-4.81-1.83)	0.00
Widowed	-0.78(-1.92-0.36)	0.18
Employment Status		
Employed	1	
Retired	-1.06 (-1.98-0.14)	0.02
Other	-3.61(-4.57--2.66)	0.00
Educational Level		
None/primary Level	1	
Secondary Level	1.47 (0.52-2.42)	0.00
Third Level	2.55 (1.56-3.54)	0.00
Self-Rated Physical Health		
Excellent/Very good	1	
Good/Fair	-5.00(-5.75-(-)4.25)	0.00
Poor	-11.9 (-13.43-10.49)	0.00
Polypharmacy		
<5 Medications	1	
≥5 Medications	-2.89(-3.76-(-)2.02)	0.00
Depression (CES-D ≥16)		
Not Depressed	1	
Depressed	-9.13(-10.27-(-)7.98)	0.00
Pain Severity		
Mild Pain	1	
Moderate Pain	-1.93 (-2.75--1.10)	0.00
Severe Pain	-4.66 (-5.78-3.54)	0.00
WHO Analgesic Ladder Position		
No Analgesic	1	1
Non-Opioid/NSAID/Adjuvant	-2.49 (-3.51-(-)1.46)	0.00
Weak Opioid	-1.39 (-4.46-1.68)	0.38
Moderate Opioid	-4.85 (-6.49-(-)3.22)	0.00
Strong Opioid	-5.42 (-9.89-(-)0.95	0.02
Residence		
Urban	1	
Rural	0.11 (-0.68-0.90)	0.79

Health Insurance		
Medical Card	1	
Other	2.69 (1.33-4.05)	0.00
Not covered	-1.02(-2.31-0.28)	0.12
Pain Limits Daily Activities		
No Limitations	1	
Limitations	-4.70(-5.44-(-)3.96)	0.00
Number of Chronic Diseases		
No Chronic Diseases	**1**	
1 Chronic Disease	-0.40(-1.66-0.85)	0.53
2 Chronic Disease	-0.82(-20.4-0.39)	0.18
≥3 Chronic Diseases	-2.69 (-3.85-(-)1.52)	0.00
Smoking Status		
Never Smoked	1	
Past Smoker	-0.49 (-1.32-0.35)	0.25
Current Smoker	-3.06 (-4.18-1.94)	0.00
Pain Location		
Back Pain	1	
Joint Pain	0.42 (-0.55-1.40)	0.39
Other	0.21 (-0.75-1.16)	0.67
All Over	-3.23(-5.05-(-)1.41)	0.00
No of GP Visits Per Year		
0 GP Visits	1	
1 GP Visits	-0.15 (-1.88-1.58)	0.87
2 GP Visits	-1.2 (-2.94-0.54)	0.18
3 GP Visits	-1.84 (-3.63-(-)0.05)	0.04
≥4 GP Visits	-4.12 (-5.65-(-)2.59)	0.00

Appendix E. Supporting Documents for Semi-Structured interviews with GPs

E.1. Consolidated Criteria for Reporting Qualitative Studies (COREQ): 32-Item Checklist

No. Item	Guide questions/description	Reported on Page #
Domain 1: Research team and reflexivity		
Personal Characteristics		
1. Interviewer/facilitator	Which author/s conducted the interview or focus group?	
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	
3. Occupation	What was their occupation at the time of the study?	
4. Gender	Was the researcher male or female?	
5. Experience and training	What experience or training did the researcher have?	
Relationship with participants		
6. Relationship established	Was a relationship established prior to study commencement?	
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	
Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	
12. Sample size	How many participants were in the study?	
13. Non-participation	How many people refused to participate or dropped out? Reasons?	
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	

15. Presence of non-participants	Was anyone else present besides the participants and researchers?	
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	
20. Field notes	Were field notes made during and/or after the interview or focus group?	
21. Duration	What was the duration of the inter views or focus group?	
22. Data saturation	Was data saturation discussed?	
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	
25. Description of the coding tree	Did authors provide a description of the coding tree?	
26. Derivation of themes	Were themes identified in advance or derived from the data?	
27. Software	What software, if applicable, was used to manage the data?	
28. Participant checking	Did participants provide feedback on the findings?	
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	
30. Data and findings consistent	Was there consistency between the data presented and the findings?	
31. Clarity of major themes	Were major themes clearly presented in the findings?	
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	

E.2. Letter of Approval from Health Science Research Ethics Committee Trinity College Dublin for GP study

COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH

Dámh na nEolaíochtaí Slainte,
Foirgneamh na Ceimice
Colaiste na Tríonóide,
Baile Átha Cliath 2, Éire.

TRINITY COLLEGE DUBLIN

Faculty of Health Sciences,
Chemistry Building,
Trinity College,
Dublin 2, Ireland.
T:- +353 (0)1 8964255

Mary Claire-Kennedy
School of Pharmacy and Pharmaceutical Sciences,
Panoz Institute,
Trinity College, Dublin
Dublin 2

06 March 2013
Study: Qualitative investigation of primary care physicians to determine attitudes and opinions on the management of chronic non-malignant pain conditions

Dear Applicant(s)
Further to a meeting of the Faculty of Health Sciences Ethics Committee held in October 2012, we are pleased to inform you that the above project (as amended) has been approved without further audit.

Please note however that the FREC does not condone the use of inducement in research, albeit to a non-vulnerable population of potential participants, as it may interfere with good research practice by potentially biasing selection and risking clarity in consent.
Yours sincerely,

p.p. Caroline Rooney

Dr. Ruth Pilkington
Chairperson
Faculty Research Ethics Committee

Supervisor: Dr Martin Henman

E.3. Letter of Invitation to Prospective Participants for GP Study

COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH | TRINITY COLLEGE DUBLIN
Ollscoil Átha Cliath | The University of Dublin

School of Pharmacy and Pharmaceutical Sciences,
Panoz Institute,
Trinity College Dublin,
Dublin 2

Invitation to Participate in Research on Chronic Non-Malignant Pain in the Elderly

Dear General Practitioner

We would like to invite you to participate in a qualitative study on the management of chronic non-malignant pain in older adults in primary care. This study is being conducted within the Health Research Board (HRB) PhD Scholars Programme in Health Services Research and is a collaboration led by the School of Pharmacy, TCD, with the HRB Centre for Primary Care Research, RCSI Medical School.

The aim of the study is to learn about Irish GPs experiences in managing older adults with chronic non-malignant pain, particularly in relation to pharmacological treatment. This patient group frequently present with a variety of medical, psychological and social problems and GPs have to take account of many factors before a suitable approach to management can be finalised. We are particularly interested in hearing your attitudes and opinions on the use of analgesics in this population.

The interviews will be conducted by telephone and will take 20-25 minutes. All information collected during the interviews will be anonymised so that it cannot be linked to you in anyway. The Irish College of General Practitioners (ICGP) have indicated that GPs may seek Internal Continuing Professional Development credits for participation in this research.

A participant information leaflet and a document with further information provided with this letter will give further background on the research study. If you have any questions in the meantime, please contact Mary-Claire Kennedy (PhD Scholar) or Prof. Martin Henman or Dr. Gráinne Cousins using the contact details below.

Kind Regards,

E.4. Consent Form for GPs



COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH | TRINITY COLLEGE DUBLIN
Ollscoil Átha Cliath | The University of Dublin

PROJECT TITLE: Qualitative investigation of primary care physicians to determine attitudes and opinions on the management of chronic non-malignant pain conditions

PRINCIPAL INVESTIGATORS:
Researcher: Mary-Claire Kennedy*
Research Supervisors: Associate Prof. Martin Henman, School of Pharmacy and Pharmaceutical Sciences, Trinity College, Dublin 2.
Dr. Grainne Cousins, HRB Centre for Primary Care Research, RCSI

Address:
School of Pharmacy and Pharmaceutical Sciences, Panoz Institute, Trinity College, Dublin 2

* *Corresponding Researcher*
E-mail: kennedm1@tcd.ie Tel no: 01-8962762/087-xxxxxxxxxxxxx [provided in original document])

BACKGROUND
The aim of this study is to gain an insight into the attitudes and behaviours of GPs in the prescribing of analgesic medications, in particular opioid analgesics, to chronic non-malignant pain patients.

The interview is digitally recorded on a laptop and also audio-recorded using a cassette device. A recording is necessary so that I can accurately reflect on our discussion. The recording will only be reviewed by myself and my research supervisor, Dr. Martin Henman, such that it may be transcribed and analysed. All recordings will then be erased.

Participants will be provided with a full transcript of the interview in addition to any additional field notes made during the interview process. Contributors are free to change or withdraw any information supplied to them.

All recordings and subsequent transcripts will be anonymously labelled and will not be used for any purpose other than that of this study. The data will be

confidential and stored in a secure manner in keeping with the requirements of the Health Research Ethics Committee, Trinity College Dublin.

All views shared by the contributors will be treated confidentially and any comments reported in publications arising from the research will be anonymous. The information gathered in the course of this study will not be used in future studies without your specific permission.

DECLARATION:

I have had the opportunity to ask questions and all my questions have been answered to my satisfaction. I freely and voluntarily agree to be part of this research study, though without prejudice to my legal and ethical rights. I understand that I may withdraw from the study at any time and I have received a copy of this agreement.

PARTICIPANT'S NAME:
.....

CONTACT DETAILS:.....

PARTICIPANT'S SIGNATURE:.....

Date:.....

Statement of investigator's responsibility: I have explained the nature and purpose of this research study, the procedures to be undertaken and any risks that may be involved. I have offered to answer any questions and fully answered such questions. I believe that the participant understands my explanation and has freely given informed consent.

INVESTIGATOR' SIGNATURE:.....

DATE:.....

E.5. Participant Information Leaflet for GPs



COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH | TRINITY COLLEGE DUBLIN
Ollscoil Átha Cliath | The University of Dublin

Title of study

Qualitative investigation of primary care physicians to determine attitudes and opinions on the management of chronic non-malignant pain conditions.

This study is being undertaken in part fulfilment of the PhD thesis entitled 'Factors Affecting Pharmacotherapeutic Management of Chronic Non-Malignant Pain Conditions in Adults Aged 65 and Older in the Republic of Ireland'.

Introduction

The chronic non-malignant pain (CNMP) population represent a particularly challenging patient group due to the physical and psychosocial complexities of this condition (84). CNMP patients are often managed in the primary care setting using a combination of pharmacological and non-pharmacological interventions. Physicians may face the task of developing a patient appropriate analgesic regimen that delivers satisfactory analgesia whilst minimising adverse outcomes. This may be more difficult to achieve with elderly patients in whom age-related pharmacokinetic and pharmacodynamic changes may lead to a less predictable drug response, increased drug sensitivity or potential harmful drug effects (113). Such clinical restrictions may present a challenge to clinicians wishing to prescribe analgesic medications for this patient group. Referral to a pain clinic or a pain specialist may also be required for those patients that cannot be managed satisfactorily in the primary care setting. However, gaining access to specialist pain services is difficult in Ireland with a waiting time of at least 12 weeks for CNMP patients (242).

Aim

The aim of this study is to gain an insight into the attitudes and behaviours of GPs in the prescribing of analgesic medications, in particular opioid analgesics, for CNMP patients in the context of the clinical problems associated with ageing patients and the current health service limitations.

Procedures

GPs who express an interest in participating in the research will be asked to complete a telephone interview with the researcher although interviews may be conducted in person if necessary. It is anticipated that the interview will be 20-25 minutes in duration. GPs are recruited through a non-probability convenience sampling method.

Benefits

You may find that your discussion with the researcher will provide a forum to highlight your concerns and opinions on the prescribing of pain medications in adults aged 65 and older with CNMP. You will also contribute towards a growing body of research on physician's attitudes and opinions towards the use of analgesic medications in ageing populations.

Risks

Some participants may find it difficult to discuss aspects of their professional practice with a third party. However, the participant will not discuss individual patients during the course of the interview but only refer in general terms to your professional practices and perceptions. The researcher will also refer you to resources relating to the prescribing of analgesic medications for ageing populations and regulations directing the prescribing of controlled drugs in Ireland which you may find helpful.

Exclusion from participation

You cannot participate in this study if any of the following are true:

- You do not treat patients aged 65 and older with a chronic non-malignant pain condition;
- You do not practice primarily or exclusively in the primary care setting.

Confidentiality

Your identity will remain confidential. Your name will not be published and will not be disclosed to anyone outside the study group.

Compensation

This study is covered by standard institutional indemnity insurance. Nothing in this document restricts or curtails your rights.

Voluntary Participation

If you decide to volunteer to participate in this study, you may withdraw at any time. If you decide not to participate, or if you withdraw, you will not be penalised and will not give up any benefits that you had before entering the study.

Stopping the study

You understand that the investigators may withdraw your participation in the study at any time without your consent.

Information shared during the study

A transcript of the interview will be made available to all participants. You may amend or withdraw any information shared in the questionnaire or interview stages of the study. This

information will be immediately removed from the study and will not be included in further data analysis.

What we intend to do with this information

The information gathered in this study will be anonymised and secured in Trinity College Dublin in accordance with the data protection policy. The identity of the study participants will remain anonymous and confidential. It is proposed that the findings arising from analysis of the interview transcripts will be published.

Who is involved?

This research is being co-ordinated by the School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin under direction of PhD candidate Mary-Claire Kennedy. Associate Professor Martin Henman, School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin and Dr. Grainne Cousins, School of Pharmacy, Royal College of Surgeons in Ireland are responsible for supervising the completion of the study.

Permission

Ethical approval for completion of this study has been gained from the Research Ethics Committee, Trinity College Dublin.

Further information

You can get more information or answers to your questions about the study, your participation in the study, and your rights, from Mary-Claire Kennedy, who can be telephoned at 01-8962762/087-xxxxxxxxxxxxx [provided in original document]or e-mail your query to kennedm1@tcd.ie. Mary-Claire Kennedy is a PhD candidate with the School of Pharmacy and Pharmaceutical Science, Trinity College Dublin and is also affiliated with the Health Research Board PhD Scholars Programme in Health Services Research. If the study team learns of important new information that might affect your desire to remain in the study, you will be informed at once.

E.6. Consolidated Criteria for Reporting Qualitative Studies (COREQ): 32-Item Checklist for Semi-Structured Interviews with General Practitioners

No. Item	Guide questions/description	Section
Domain 1: Research team and reflexivity		
Personal Characteristics		
1.Interviewer/facilitator	Which author/s conducted the interview or focus group?	Section 6.3.2
2. Credentials	What were the researcher's credentials?	Title Page & Preface
3. Occupation	What was their occupation at the time of the study?	Title Page & Preface
4. Gender	Was the researcher male or female?	Title Page & Preface
5. Experience and training	What experience or training did the researcher have?	Title Page & Preface
Relationship with participants		
6.Relationship established	Was a relationship established prior to study commencement?	Section 6.3.2.1
7.Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	Appendix E.3
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	Section 6.5.1
Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Section 6.3.3.1 & Section 6.3.3.2
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	Section 6.3.2.1
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	Section 6.3.2.1 & Appendix E.1/E.2/E.3
12. Sample size	How many participants were in the study?	Section 6.3.2.1
13. Non-participation	How many people refused to participate or dropped out? Reasons?	Section 6.3.2.1
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	Section 6.3.2.1
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	Section 6.3.2.1
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	Section 6.3.2.1
Data collection		

17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Section 6.3.2.1
18. Repeat interviews	Were repeat interviews carried out? If yes, how many?	No & N/A
19.Audio/visual recording	Did the research use audio or visual recording to collect the data?	Section 6.3.2.1
20. Field notes	Were field notes made during and/or after the interview or focus group?	Section 6.3.2.1
21. Duration	What was the duration of the interviews or focus group?	Table 6-1
22. Data saturation	Was data saturation discussed?	Section 6.3.2.1
23.Transcripts returned	Were transcripts returned to participants for comment and/or correction?	Section 6.3.2.1
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	Section 6.3.3.2
25. Description of the coding tree	Did authors provide a description of the coding tree?	Section 6.3.3.2
26. Derivation of themes	Were themes identified in advance or derived from the data?	Section 6.3.3.2
27. Software	What software, if applicable, was used to manage the data?	Section 6.3.3.1
28. Participant checking	Did participants provide feedback on the findings?	Section 6.3-2
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	Section 6.4
30. Data and findings consistent	Was there consistency between the data presented and the findings?	Section 6.4
31. Clarity of major themes	Were major themes clearly presented in the findings?	Section 6.4
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Section 6.4

Appendix F. Supporting Documents for Semi-Structured Interviews with CPI Members

F.1. Letter from Health Sciences Research Ethics Committee Trinity College Dublin for CPI Members Study

COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH TRINITY COLLEGE DUBLIN
Ollscoil Átha Cliath The University of Dublin

Dámh na nEolaíochtaí Slainte,
An Chéad Urlar, Foirgneamh na Ceimice (an sineadh)
Colaiste na Tríonóide,
Baile Átha Cliath 2, Éire.

Faculty of Health Sciences,
1st Floor, Chemistry Building
Extension,
Trinity College,
Dublin 2, Ireland.
T:- +353 (0)1 8964255

Ms. Mary-Claire Kennedy
School of Pharmacy and Pharmaceutical Sciences,
Panoz Institute,
Trinity College, Dublin.

13 January 2012

Study: An investigation of the use of medicines and beliefs about medicines with members of the Chronic Pain Association of Ireland.

Dear Applicant(s),

Further to a meeting of the Faculty of Health Sciences Ethics Committee held in September 2011, we are pleased to inform you that the above project has been approved without further audit.

Yours sincerely,

Prof. Orla Sheils
Chairperson
Faculty Research Ethics Committee

Supervisor:

Dr. Martin Henman

F.2. Text of Advertisement to Recruit CPI Members

Title of Study

An investigation of the use of painkillers and beliefs about painkillers with members of Chronic Pain Ireland aged 50 and older.

This study is being conducted by Mary-Claire Kennedy within the Health Research Board PhD Scholars Programme in Health Services Research and is a collaboration led by the School of Pharmacy, TCD, with the HRB Centre for Primary Care Research, RCSI Medical School.

Aim

To examine patient's (aged 50 and older) use and attitudes towards the use of painkillers for chronic pain conditions.

Objectives

1. To identify the types of prescription and non-prescription painkillers used by patients aged 50 and older with chronic pain conditions.
2. To understand the relationship between pain intensity and types of painkillers used by patients.
3. To investigate patient concerns about the use of painkillers.

Telephone Interviews

Members of Chronic Pain Ireland will be asked to participate in a private 15-20 minute telephone interview with the researcher, Mary-Claire Kennedy, a practising pharmacist. The researcher will ask for your consent to record the telephone interview. These recordings will be stored securely and accessible only to the researcher and the research supervisors. Your identity will remain confidential. Your name will not be published and will not be disclosed to anyone outside the research team.

F.3. Letter of Invitation to Prospective Participants (CPI Members)



COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH | TRINITY COLLEGE DUBLIN
Ollscoil Átha Cliath | The University of Dublin

School of Pharmacy and Pharmaceutical Sciences,
Panoz Institute,
Trinity College Dublin,
Dublin 2
[INSERT DATE]
[PARTICIPANT ADDRESS]

Chronic Pain Research at Trinity College Dublin

Dear [INSERT NAME],

Thank you for replying to my recent advertisement with Chronic Pain Ireland. Before you agree to take part in this research, I wish to provide you with a brief description of the study.

This study is being undertaken as part of a larger research project entitled '*Chronic non-malignant pain; influences on medication use*'. The aim of this study is to increase our understanding of the factors that influence the use of painkillers in chronic pain in patients aged 50 and older to help improve their use. I also want to understand the relationship between pain intensity and the types of painkillers used and to determine the patient's experience of and concerns about the use of painkillers.

Please find enclosed a Participant Consent Form, a copy of the Participant Information Leaflet and a calendar for July, August and September.

If you wish to participate in this research study, please sign the Participant Consent Form. I would also appreciate if you could indicate on the calendar provided the time and date that would be most convenient for you for interview. I would expect the interviews to take approximately 15-20 minutes.

I have enclosed a stamped addressed envelope for return of the Participant Consent Form and the calendar.

Please do not hesitate to contact me with any queries about this study. Thank you again for taking the time to read this letter and your interest in this research project.

Yours Sincerely,

Mary-Claire Kennedy, PhD Scholar in Health Services Research, TCD
(01-8962762/087-xxxxxxxxxxxx [provided in original document])
Professor Martin Henman, School of Pharmacy and Pharmaceutical Sciences, TCD
(01-8962826)
Dr. Gráinne Cousins, HRB Centre for Primary Care Research, RCSI (01-4022480)

F.4. Participant Information Leaflet for CPI members



COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH | TRINITY COLLEGE DUBLIN
Ollscoil Átha Cliath | The University of Dublin

Title of Study
An investigation into the use of painkillers and beliefs about painkillers with members of Chronic Pain Ireland aged 50 and older. *This study is being undertaken in part fulfilment of the PhD preliminary entitled: 'Chronic non-malignant pain; influences on medication use.'*

Introduction

This study seeks to recruit current members of Chronic Pain Ireland to participate in a study co-ordinated by researchers of the School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin. The purpose of this study is to gather information on the types of painkillers taken by individuals with chronic pain conditions and to investigate the attitudes and opinions of patients relating to the use of these medications.

Procedures

The aim of this study is to determine the types of prescription and non-prescription painkillers used by patients in the management of chronic pain conditions. Members of Chronic Pain Ireland will be asked to participate in a telephone interview with the researcher. The researcher will ask for your consent to record the telephone interview. These recordings will be stored securely and accessible only to the researcher and the research supervisor.

Benefits
You may find that your telephone discussion with the researcher will provide a forum to highlight your concerns and opinions in relation to pain medications. You will also contribute towards a growing body of research on patient attitudes towards painkillers used in the management of chronic pain conditions.

Risks

Some participants may find it difficult to discuss problems relating to medication use, particularly when these problems relate to overuse or dependence on certain medications. The researcher will help you find support if you wish to address any problems such as these.

Exclusion from participation

You cannot participate in this study if any of the following are true:

- You are not a current member of Chronic Pain Ireland.
- You do not have a chronic pain condition.
- You are under 50 years of age.

- You are not willing to participate in an audio-recorded telephone discussion.
- You have a terminal illness.
- You have been diagnosed with dementia or any other memory impairment.

Confidentiality

Your identity will remain confidential. Your name will not be published and will not be known to anyone except for the researcher, Mary-Claire Kennedy. The only circumstance under which confidentiality will be breached is if information emerges relating to inappropriate medication use that places the participant's health at risk; if this occurs the researcher will contact the prescribing general practitioner to ensure that the participant receives the necessary help with medication management.

Compensation

This study is covered by standard institutional indemnity insurance. Nothing in this document restricts or curtails your rights.

Voluntary Participation

If you decide to volunteer to participate in this study, you may withdraw at any time. If you decide not to participate, or if you withdraw, you will not be penalised and will not give up any benefits that you had before entering the study.

Stopping the study

You understand that the investigators may withdraw your participation in the study at any time without your consent.

Information shared during the study

A transcript of the telephone interview will be made available to all participants. You may amend or withdraw any information shared in the interview. This information will be immediately removed from the study and will not be included in further data analysis or publications arising from the research.

What we intend to do with this information

The information gathered in this study will be anonymised and secured in Trinity College Dublin in accordance with data protection policy. The identity of the study participants will remain anonymous and entirely confidential. It is proposed that findings of the study will be published, however all results in this publication will remain anonymised.

Who is involved?

This research is co-ordinated by PhD candidate Mary-Claire Kennedy. Associate Professor Martin Henman, School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin and Dr. Grainne Cousins, HRB Centre for Primary Care Research, RCSI are responsible for supervising the completion of the study.

Permission

Ethics approval has been gained from the Research Ethics Committee, Trinity College Dublin.

Further information

You can get more information or answers to your questions about the study, your participation in the study and your rights from Mary-Claire Kennedy who can be telephoned on 01-8962762 or email your query to kennedm1@tcd.ie or correspond with Mary-Claire Kennedy, School of Pharmacy and Pharmaceutical Sciences, Panoz Institute, Trinity College, Dublin 2. If the study team learns of important new information that might affect your desire to remain in the study, you will be informed.

F.5. Consent Form for CPI Members



COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH | TRINITY COLLEGE DUBLIN
Ollscoil Átha Cliath | The University of Dublin

PROJECT TITLE
An investigation of the use of painkillers and beliefs about painkillers with members of Chronic Pain Ireland aged 50 and older.

PRINCIPAL INVESTIGATORS

Mary-Claire Kennedy, School of Pharmacy and Pharmaceutical Sciences, Panoz Institute, Trinity College, Dublin 2*

Research Supervisors:

Professor Martin Henman, School of Pharmacy and Pharmaceutical Sciences, TCD

Dr. Gráinne Cousins, HRB Centre for Primary Care Research, RCSI

* *Corresponding Researcher*
E-mail: kennedm1@tcd.ie Tel no: 01-8962762/087-xxxxxxxxxxxxx [provided in original document])

BACKGROUND
The purpose of this study is to gather information on the types of prescription and non-prescription painkillers taken by individuals with chronic pain conditions in addition to investigating the attitudes and opinions of patients relating to the use of these medications.

Members of Chronic Pain Ireland will be asked to participate in a telephone interview with the researcher. In order to protect the integrity of the research process all interviews will be dealt with in the following way:

- The telephone interviews will be digitally recorded using recording software on the researcher's laptop and using a portable recording device. All audio recordings will be stored securely on the researcher's password protected laptop. The recording will only be reviewed by myself and the research supervisors Dr Martin Henman and Dr. Grainne Cousins, such that they may be transcribed and analysed. All recording will then be destroyed.

- Participants will be provided with a full transcript of the telephone interview and are free to change or withdraw any information shared during the course of the discussion.

- All recordings and subsequent transcripts will be anonymously labelled and will not be used for any purpose other than that of this study. The data will be confidential and stored in a secure manner in keeping with the requirements of the Ethics Committee of Trinity College.

- All views shared by contributors will be treated confidentially and all comments will be reported anonymously. The information gained during the study will not be used in future unrelated studies without your specific permission.

DECLARATION:

I have read, or had read to me, the information leaflet for this project and I understand the contents. I have had the opportunity to ask questions and all my questions have been answered to my satisfaction. I freely and voluntarily agree to be part of this research study, though without prejudice to my legal and ethical rights. I understand that I may withdraw from the study at any time and I have received a copy of this agreement.

PARTICIPANT'S NAME:.....

CONTACT DETAILS:.....

DATE:.....

PARTICIPANT'S SIGNATURE:

.....

Statement of investigator's responsibility: I have explained the nature and purpose of this research study, the procedures to be undertaken and any risks that may be involved. I have offered to answer any questions and fully answered such questions. I believe that the participant understands my explanation and has freely given informed consent.

INVESTIGATOR'S SIGNATURE:.....

DATE:.....

F.6. Invitation to Review Interview Transcripts sent to CPI Members



COLÁISTE NA TRÍONÓIDE, BAILE ÁTHA CLIATH | TRINITY COLLEGE DUBLIN
Ollscoil Átha Cliath | The University of Dublin

School of Pharmacy and Pharmaceutical Sciences,
Panoz Institute,
Trinity College Dublin,
Dublin 2
[PARTICIPANT ADDRESS]

Chronic Pain Research at Trinity College Dublin: Interview Transcript

Dear [INSERT NAME],

Further to our interview on [INSERT DATE] please find enclosed the transcript of our conversation.

You are invited to review the transcript and edit or withdraw any statements if necessary. I have provided space in the margin of the transcripts for revisions and two blank pages for additional comments or observations.

During the course of the interview you referred in name to various healthcare professionals, locations, and institutions. I have highlighted these in grey in the transcript and I will remove all reference to these in any published quotes such that you cannot be identified.

If you have any changes you wish to make to the transcript, please return the transcript marked with the changes using the stamped addressed envelope provided. If you are happy with the transcript you do not need to return the document but you may keep it for your own records.

I would like to take this opportunity to thank you again for your interest in this research. If you have any queries about this study please do not hesitate to contact me.

Kind Regards,

Mary-Claire Kennedy, PhD Scholar in Health Services Research, TCD
(01-8962762/087-xxxxxxxxxxxx [provided in original document])
Professor Martin Henman, School of Pharmacy and Pharmaceutical Sciences, TCD
(01-8962826)
Dr. Gráinne Cousins, HRB Centre for Primary Care Research, RCSI
(01-4022480)

F.7. Consolidated Criteria for Reporting Qualitative Studies (COREQ): 32-Item Checklist for Semi-Structured Interviews with CPI Members

No. Item	Guide questions/description	Section
Domain 1: Research team and reflexivity		
Personal Characteristics		
1.Interviewer/facilitator	Which author/s conducted the interviews?	Section 7.3.2
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	Title Page & Preface
3. Occupation	What was their occupation at the time of the study?	Title Page & Preface
4. Gender	Was the researcher male or female?	Title Page & Preface
5. Experience and training	What experience or training did the researcher have?	Title Page & Preface
Relationship with participants		
6.Relationship established	Was a relationship established prior to study commencement?	Section 7.3.2
7.Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	Section 7.3.2 & Appendix F.3/F.4
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	Section 7.3.2 & 7.5.1
Domain 2: study design		
Theoretical framework		
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	Section 6.3.3 & 7.3.3
Participant selection		
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	Section 7.3.2
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	Section 7.3.2
12. Sample size	How many participants were in the study?	Figure 7-2
13. Non-participation	How many people refused to participate or dropped out? Reasons?	Figure 7-2 & Section 7.3.2
Setting		
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	Section 7.3.2
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	Section 7.3.2
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	Section 7.4
Data collection		
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Section 7.3.2
18. Repeat interviews	Were repeat interviews carried out? If yes,	No & N/A

	how many?	
19.Audio/visual recording	Did the research use audio or visual recording to collect the data?	Section 7.3.2
20. Field notes	Were field notes made during and/or after the interview or focus group?	Section 7.4
21. Duration	What was the duration of the inter views or focus group?	Table 7-1
22. Data saturation	Was data saturation discussed?	Section 6.3.2.1
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	Section 7.3.2
Domain 3: analysis and findings		
Data analysis		
24. Number of data coders	How many data coders coded the data?	Section 6.3.3.2
25. Description of the coding tree	Did authors provide a description of the coding tree?	Section 7.3.3 & 6.3.3.2
26. Derivation of themes	Were themes identified in advance or derived from the data?	Section 7.3.3
27. Software	What software, if applicable, was used to manage the data?	Section 7.3.2
28. Participant checking	Did participants provide feedback on the findings?	Section 7.3.2
Reporting		
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	Section 7.4
30. Data and findings consistent	Was there consistency between the data presented and the findings?	Section 7.4 & 7.5
31. Clarity of major themes	Were major themes clearly presented in the findings?	Section 7.4 & 7.5
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Section 7.4 & 7.5

Appendix G. Dissemination of Research Findings

Poster Presentations

1. 'A review of clinical practice guidelines for the use of opioids in chronic non-malignant pain in primary care'; Pharmaceutical Care Network of Europe; Berlin; Feb 2013

2. 'Analgesic utilisation among ageing adults with chronic non-malignant pain'; Scientific Advisory Board Meeting of the Irish Longitudinal Study on Ageing; Dublin May 2013

Oral Presentations

1. 'Factors affecting pharmacotherapeutic management of chronic non-malignant pain in adults aged 65 and older in Ireland' Irish Gerontological Post-graduate Study Day at Our Lady's Hospice & Care Services, Harold's Cross, Dublin, May 2014

2. 'Analgesic and concurrent medication utilisation amongst adults aged 65 years and older: a cross-sectional study in the Irish population'; Irish Gerontological Society Scientific Meeting; Dublin; Sept 2013

3. An Investigation of the Use And Beliefs About Painkillers with Members of Chronic Pain Ireland Aged 50 And Older; Irish Pain Society Conference; Dublin; Nov 2013

Other Publications

1. Kennedy MC; Chronic pain and medication use: an overview of a research study with members of Chronic Pain Ireland; Chronic Pain Ireland Newsletter March 2015