`POSSIBLY THE MOST DIFFICULT THING YOU'LL DO'

A NURSE SUPPORTED PATHWAY TO ENABLE PRESCRIPTION OPIOID REDUCTION AND ENTRY TO TREATMENT FOR CHRONIC NON CANCER PAIN

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STATEMENT OF ORIGINALITY

I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision. The thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968 and any approved embargo. [Signature] [Kathie Nickerson]

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This thesis is the culmination of years of listening to people's stories about weaning opioids, their fears, anger and sense of abandonment, and wondering what could be done to support what is possibly the most difficult thing they will ever have to do.

Likewise writing this thesis for me has not only been the pinnacle of my academic achievement but also the hardest task I have ever set myself. I had gained a BA in the early 80's and had not had academic experience since.

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Abstract

Pain is a multidimensional sensory and emotional experience that, despite its protective mechanism, is aversive to most people. The quest to find a medication to alleviate this sensation led to the widespread use of prescription opioid medications. Although effective for acute and cancer pain opioids have proven to be less beneficial in the treatment of CNCP. Long term treatment is associated with adverse effects and limited benefit. Reduction and cessation of prescription opioids presents a challenge for both prescribers and patients due to the complex effect opioid medication has on the individual and the perceived lack of alternatives. Australia Legislation has sought to limit opioid prescription for CNCP precipitating the need for a dedicated treatment approach to support prescription opioid dose reduction and cessation.

The primary aim of this thesis was to evaluate if a nurse supported prescription opioid reduction pathway (NS-PORP) enabled participants with chronic non cancer pain (CNCP), attending a specialist multidisciplinary pain service, to reduce opioid dose and maintain engagement to continue on to group program pain treatment. Secondary aims were to determine if NS-PORP met participant's expectations in terms of satisfaction and to provide a cost estimation of NS-PORP compared to usual specialist pain medicine physician consultations. The rationale behind the need for an intervention to support opioid dose reduction, that of the complex behavioural issues associated with opioid use and opioid dose reduction, were explored in relation to participant experience and expectation of NS-PORP.

A scoping review of the literature described a wide array of intervention types for the purpose of prescription opioid reduction with limited evidence to indicate any specific treatment approach was more effective in promoting opioid dose reduction. This was due to the quality of studies that were conducted and in part to the characteristics of study participants. Barriers and facilitators to participation in interventions for prescription opioid reduction were identified in a small number of studies. Based conceptually on behavioural change theory a nurse supported pathway for prescription opioid reduction (NS-PORP) was developed to meet the needs of patients who had been referred to Hunter Integrated Pain Service (HIPS) and wanted to commence group program pain treatment but were taking a prescription opioid dose greater than the threshold for acceptance into the group program. As a two-step process that included an introduction and education session followed by ongoing telephone support,

NS-PORP was delivered through a flexible in person or telehealth approach. To evaluate NS-PORP a prospective cohort study was designed which compared two treatment arms with a comparator arm. The comparator group was made up of patients who participated in the same assessment process, received the same recommendations about medication reduction but chose not to participate in NS-PORP.

Univariable logistic regression demonstrated that there were significantly greater odds (OR > 1) of reducing prescription opioid dose to ≤40mg oMEDD when compared to the comparator group, OR 2.67, 95% CI1.12, 6.34, with a p-value of 0.027. Weighting with propensity scoring meant that the odds of achieving opioid reduction were greater again when compared to the comparator group 3.71(1.91, 7.21), p=< .001. Of the treatment group 57% compared with 33% of the comparator group reduced opioid dose to ≤ 40mg oMEDD. Satisfaction was explored with most participants reporting to be highly satisfied (72%) and modest economic savings were estimated from the implementation of NS-PORP. The clinical implications of the study were that NS-PORP provided a beneficial acceptable and cost effective means of supporting prescription opioid reduction which may have utility in primary care as well as specialist multidisciplinary settings. Changes to the intervention recommended by study participants will be considered for inclusion into prospective interventions. This knowledge adds to the evolving body of research compiled on prescription opioid reduction.

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List of Abbreviations

BCW - Behaviour Change Wheel

CASP - Critical Appraisal Skills Program

CDC - Centre for Disease Control and Prevention

CI - Confidence Interval

CNCP - Chronic Non Cancer Pain

CNS - Clinical Nurse Specialist

DASS-21 - Depression Anxiety and Stress Score (Short form21)

ED - Emergency Department

G.P. - General Practitioner

HIPS - Hunter Integrated Pain Service

HNELHD - Hunter New England Local Health District

IAPT - Introducing Active Pain Treatment

IASP - International Association for the Study of Pain

MES - Medication Education and Support Group

MORE - Mindfulness Oriented Recovery Enhancement

NS-PORP - Nurse Supported Prescription Opioid Reduction Pathway

oMEDD - Oral morphine equivalent daily dose

OIH - Opioid induced hyperalgesia

OR - Odds Ratio

PSEQ - Pain Self-Efficacy Questionnaire

STROBE- Strengthening the Reporting of Observational Studies in Epidemiology

Chapter 1: The Encumbrance of Prescription Opioid Use in Chronic Non Cancer Pain

1.1 Introduction

Chapter one presents the rationale for the study along with an exploration of the harm and complex behavioural issues associated with prescription opioid use. Scientific evidence has brought about a change in recommendations regarding the treatment of chronic non cancer pain (CNCP) with prescription opioid medication.

Sleep had a thousand sons, and of that number
He made the choice of waking Morpheus, ….Ovid Metamorphoses

Pain is part of human sentient experience which along with other sensory inputs keeps the human organism safe (Raffaeli & Arnaudo, 2017; Stack et al., 2020). Despite this utility, the compelling nature of pain has been described from earliest records in undesirable terms and people have sought ways to control and reduce the sensation (Gugsa, 2018). Opiates, first extracted from the opium poppy thousands of years ago, have been used for pain reduction since that time (Bandyopadhyay, 2019). In the last century opioids, (opiate like drugs) became the mainstay of pain management (Hodgson, 2001). The widespread release of oral prescription opioid formulations in the 1990s, led to the dramatic escalation of opioid prescribing including for CNCP (Rivat & Ballantyne, 2016). A previously little understood phenomenon, CNCP came to be treated in a similar way to acute pain (Crofford, 2015). The evidence to support the use of opioids for acute and cancer pain is well established unlike for chronic pain and in that context remains a topic that polarises opinion among health professionals and the general community (Rivat & Ballantyne, 2016; Rosenblum et al., 2008).

Key characteristics associated with prescription opioid use for CNCP are: escalating risk of harm with concurrent reduction in benefit associated with long term use (Dowell et al., 2016; Els et al., 2017; Sullivan & Howe, 2013), complex physical and psychological effects impeding capability to reduce reliance (Garland et al., 2017) and extensive continued prescribing (Blanch

et al., 2014; Lalic et al., 2019). Harm and lack of benefit evident with both misuse and compliant use becomes an encumbrance even if opioid treatment is perceived to be helpful for pain (Rosenblum et al., 2008). This dual negative effect is a compelling reason to stop opioid treatment with cessation supported by most expert specialist organisations and legislation (Blanch et al., 2014; Royal Australian College of General Practitioners, 2017; Dowell et al., 2016; Chou, 2009; NSW Health, n.d.; Therapeutic Goods Administration, 2021). Many prescribers and patients feeling they have no practical alternative to control pain continue to deliver and accept prescription opioid therapy (Dasgupta et al., 2018; Desveaux, et al., 2019; Holliday et al., 2013). As a consequence prescription opioid use has become a global health issue, and may be considered pandemic in the developed world (AIHW, 2018). Personal factors contribute to patient resistance to undertake dose reduction and include the complex effect opioids have on brain functions (Garland et al., 2017). Opioid dose reduction in people with entrenched opioid use entails a change in lifestyle and habits (Velasquez et al., 2016). The challenge in developing a prescription opioid reduction intervention is to facilitate this change in behaviour while remaining patient centred and cost effective.

1.2 Pain and Opioid Use

1.2.1 Differentiation between Acute and Chronic Pain

Pain is a protective multidimensional multisystem response originating in the central nervous system that encourages people to avoid or remove themselves from a dangerous situation (Raffaeli & Arnaudo, 2017; Stack et al., 2020). The International Association for the Study of Pain (IASP) defines pain as "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage," and followed with the accompanying key notes:

- "Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors.
- Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.
- Through their life experiences, individuals learn the concept of pain.
- A person's report of an experience as pain should be respected.
- Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being.

- Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or a non-human animal experiences pain" (Raja et al., 2020, p2).

The belief that painful stimuli is detected by pain receptors is a common misconception, as nociceptors detect only pressure, temperature and chemical changes (Schaefer et al., 2017). Through a complex process where messages are sent from the peripheries via the nervous system and spinal cord to the brain, information regarding the current situation is weighed up and interpreted in the context of multiple variables including past experience, knowledge and expectation. If the brain perceives that there is potential danger or threat, multiple areas of the brain constituting the 'pain neuromatrix' are activated culminating in a pain response. This is not a linear process but rather a highway of messages both ascending and descending that are processed in many areas of the central nervous system and brain and present in a complicated neurosignature (Butler & Moseley, 2003; Corder et al., 2018). These signals activate areas in the brain including the primary and secondary somatosensory areas, insular anterior cingulate, prefrontal cortices, thalamus, basal ganglia, cerebellum, amygdala, hippocampus and parietal and temporal cortices causing an individualised response to the circumstance (Tracey & Mantyh, 2007). Descending modulating signals originating in areas such as the periaqueductal grey (Pathan & Williams, 2012) can modify or reduce the pain response if the brain either determines that the experience does not pose a significant threat or that it is a safer option to respond to the threat before experiencing the sensation of pain (Butler & Moseley, 2003).

Acute and chronic pain is primarily differentiated by time of onset to recovery. Acute pain resolves within a three month timeframe which is the expected time of tissue healing (Merskey, 2007), and pain that continues beyond three months is considered to have become chronic (Treede, 2018). Cancer pain is categorised as a separate entity again and is treated with an acute focus. With improving treatment options and better survival rates, cancer pain may become chronic after active cancer treatment is complete. As such, chronic pain is labelled chronic non cancer pain (CNCP) for clarity (Schug et al, 2016). Pain types share common symptoms but have their own unique drivers and characteristics. Acute pain is a healthy adaptive response that warns about or deters the organism from continuing an activity that may cause harm. Chronic pain, also a mechanism for protection, is a maladaptive process that incorrectly perceives an ongoing threat when there is no immediate danger to the organism (Crofford, 2015). Acute pain usually occurs in response to an external stimulus such as injury or disease

and commonly the level of pain experienced reflects the level of danger or injury sustained. Chronic pain although frequently originating from tissue damage, continues after tissue healing has occurred and becomes less about the external stimulus and more about the individual's internal response to trauma. The nervous system becoming sensitised and sends out unnecessary warning messages resulting in pain (Crofford, 2015; Rosenblum et al., 2008).

Chronic pain, in different manifestations, had been reported in medical literature throughout the previous century, as clinicians struggled to understand and treat a phenomena that did not have specific symptoms and was resistant to most management (Crofford, 2015). Over 15% (3.2 million individuals) of the Australian population experience CNCP (Economics, D.A., 2019) with international prevalence reported as ranging from 10.8% to 53.7% (Henderson et al., 2013), and CNCP is described in almost every body part. For most, a precipitating physical event, either minor or significant and now healed is identifiable, however, for 17% of people experiencing CNCP no inciting health event is noted (Painaustralia, 2019). The experience of CNCP is usually out of proportion to the perceived causative event, is often migratory and may continue to increase over time rather than resolve (Crofford, 2015; Garland, 2012; Rosenblum et al., 2008). Pain and conditions where pain is a primary symptom are some of the most common contributors to the burden of disability and disease globally (Vos et al., 2012).

1.2.2 The Pain Relieving Mechanism of Opioids

Opioids are the common name for the family of medication that include opiates, the naturally occurring alkaline compounds morphine and codeine, semisynthetic formulations derived from these such as oxycodone and heroin and synthetic substitutes including fentanyl and methadone (Rummans et al., 2018). Originally described as opiates when only naturally occurring substances were available, the family of related compounds came to be known as opioids following the development of semisynthetic and synthetic versions. Opioids lock into specific G protein opioid receptors systems, mu opioid receptors (MOR), delta opioid receptors (DOR), kappa opioid receptors (KOR) and nociceptin opioid receptors (NOR) to produce effects, with opioid and MOR binding producing the strongest analgesic action (McDonald & Lambert, 2005). Analgesia results from the twin effect of lowering firing threshold in the neural cell and inhibition of neurotransmitter release (Chahl 1996; Pathan & Williams, 2012) which causes cognitive sedative and emotional detachment from reality (Corder et al., 2018; Ghelardini et al., 2015). Opioid receptors are recruited throughout most areas of the body with high numbers expressed in the central nervous system, including the brain (Trang et al., 2015). This wide

dissemination of receptors is responsible for the diverse range of opioid effects such as gut and respiratory inhibition. Modulation of the central and peripheral nervous system occurs through activation of neurotransmitters, including Dopamine and Gamma Aminobutyric Acid (GABA), by opioid and receptor coupling (Al-Hasani & Bruchas, 2011). Opioids readily cross the blood brain barrier (Schaefer et al., 2017) causing significant neurotransmitter activation in the brain. Messages travel to many areas of the brain including those responsible for attention, mood, emotion and reward and cause the complex and individual behavioural response that is evident with opioid use (Rivat & Ballantyne, 2016; Rosenblum et al., 2008).

Opiates have been used in some capacity for most of recorded history (Gugsa, 2018) with the first documented use by the Sumerians in Mesopotamia (Bandyopadhyay, 2019). The extraction of Morphine from opium poppies in the early 1800s was closely followed by the development of the hypodermic needle, facilitating rapid delivery of pain relieving treatment. This pairing of medication and administration by injection remains the gold standard of care for acute pain to the present day (Rosenblum et al., 2008). Opiates were used predominantly in a medicinal capacity for acute and surgical pain until oral opioid compounds were formulated in the early 1990s (Rosenblum et al., 2008).

Prescription opioids have clear benefits for treating acute and palliative pain. In 1680, Thomas Sydenham stated that "Among the remedies which it has pleased almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium" (Trang et al., 2015, p13885). Opioid analgesia used for acute pain disguises the impact of tissue damage, facilitates movement and function until tissue healing occurs, when opioid medication can be ceased and the individual continues back to a full life (Cisewski & Motov, 2019; Shug et al., 2016; Sinatra, 2010). In the case of palliation when death is imminent opioids reduce the awareness of damaged tissue and enable passing on peacefully (Shug et al., 2016).

Following this utility opioid medication was embraced for CNCP and has shown benefit in subjective pain reduction in a number of trials. Chou et al. (2015) reported there was insufficient evidence to demonstrate effectiveness from prescription opioid use in treating CNCP however subsequent systematic reviews have demonstrated benefit with caveats. Meske et al. (2018) looked at enriched RCTs of short duration and reported pain intensity reduction in CNCP. Busse et al. (2018) found opioid therapy compared to placebo, for CNCP, improved pain levels however the effect was less pronounced in longer trials and was similar to that from non-opioid alternatives. Bialus et al. (2020) determined that select pain types; chronic low back

pain, osteoarthritis and neuropathic pain reported benefit from long term opioid therapy however this did not extrapolate to all CNCP. Low quality trial methods and the prevalence of industry funding for studies maintains uncertainty regarding the benefit of opioid medication for CNCP.

1.2.3 Non Acute Reasons for Opioid Use

Illicit use has been associated with the development and distribution of opiates and opioids throughout most of its reported history. Soon after the discovery of morphine, dependence and addiction were recognised as possible effects of ongoing use. The search for a form of morphine that would provide equal benefit in managing pain without the negative consequence commenced. Heroin was synthesised in 1898 and described as a non-addictive form of morphine. Methadone again in 1946 was developed as the solution to heroin addiction (Hodgson, 2001). Opioid agonist therapy, although not within the scope of this thesis to detail, as part of a comprehensive management plan, is an accepted form of treatment for opioid addiction (McDonough, 2013).

Unrelieved acute pain resulting from inadequate management of nociceptive processes may lead to CNCP and long term opioid therapy. Prescription opioids acting as an unhelpful prop after the stress of sickness or injury become part of the pattern of increased pain and disability rather than the treatment (Sud et al., 2020). Opioid therapy that continues beyond the time of healing encourages and embeds the belief that damage has not resolved promoting continuation in the injured or sick role (Toye et al., 2017; McCrorie et al., 2015).

Just as opioids are used to cover the negative impact of tissue injury, unwanted and unpleasant feelings of stress, fear, anxiety and catastrophizing, can be inappropriately cloaked by opioid medication. This allows escape from the overwhelming constraints of reality which may also cause adverse pain sensations in the brain (Darnell, 2014; Dasgupta et al., 2018; Pecina et al., 2019; Rosenblum et al., 2008; Vowles et al., 2018). The emotional component of pain is recognised by IASP in its definition of pain (Raja et al., 2020).

Both prescribers and patients contribute to the problem of opioid overuse through their own individual characteristics. Unrealistic expectations of what opioid treatment can achieve and the challenge of managing a chronic and complex medical condition may influence patterns of opioid use and prescribing (Dasgupta et al., 2018). Despite the best clinical intentions regular

use of opioids even when taken appropriately can lead to dependence, adverse side effects, and death (Rosenblum et al., 2008).

1.2.4 The Emergence of Prescription Opioid Use

The liberation of prescription opioids came from a perfect storm that had a number of contributors. Encouraged by the new discipline of palliative care, pharmaceutical companies formulated oral opioid preparations to suit the specific needs of people during palliation. Formulations were developed that were easy to give as regular doses to frail patients and could be given as long and short acting preparations for flexible pain management (Rivat & Ballantyne, 2016). This created an opportune environment for the pharmaceutical industry which quickly realised the financial benefits that would come with the widespread use of easily administered oral opioids. Pharmaceutical companies set about ambitiously marketing oral opioid medications, (Rivat & Ballantyne, 2016) most notably OxyContin, developed in 1995 by Purdue, which was sold (as previous synthetic preparations had been) as a less addictive form of opioid (Van Zee, 2009). Recommendations from a simple letter in the New England Journal of Medicine in 1980 affirmed the ethical need to treat chronic pain with prescription opioids and significantly understated the risk of addiction for people with chronic pain (Porter & Jick, 1980). These recommendations have been quoted and followed since that time (Rummans et al., 2018). A brief study with small numbers supported these conclusions and stated that prescription opioid use in non-malignant pain was safe and humane (Portenoy & Foley, 1986; Rummans et al., 2018).

At the same time consumers were starting to believe that they could and should be pain free and the ‘Pain as the 5th vital sign’ campaign initiated by the American Pain Society supported this. (Jones et al., 2018; Tompkins, 2017). The campaign was directed at health professionals and encouraged regular monitoring of pain scores followed by pharmaceutical treatment of pain as would occur with any significant change in heart and respiratory rate, blood pressure or body temperature. World Health Organisation confirmed the importance of opioid treatment with the creation of the analgesic ladder, initially developed for use in palliative care, but soon used as the go-to tool for all pain management. The ladder encouraged escalating pharmacological treatment if pain continued, with opioids sitting at the top of the ladder as the optimum treatment (Ballantyne et al., 2016). Opioid therapy intrinsically became synonymous with pain relief for both health professionals and consumers (Dasgupta et al., 2018; Van Zee, 2009; Wegrzyn et al., 2018).

1.3 The Encumbrance of Prescription Opioid Use

Prescription opioid use for CNCP presents a health and social problem in all developed countries of the world including Australia. The complexity of this problem and the need for effective treatment to support the reduction of prescription opioids is highlighted by the following problems associated with use in CNCP. The connection between increasing harm with decreasing efficacy is well established in long term opioid use (Dowell et al., 2016; Els et al., 2017; Sullivan & Howe, 2013) and is evident in prescribed treatment as well as illicit use (Ballantyne & Shin, 2008; Kolodny et al., 2015). The impact of harm from opioids is borne by the individual, family, health care system and wider society. Lack of benefit from long term prescription opioid treatment (Ballantyne & Shin, 2008; Chou, 2009) contradicts earlier beliefs regarding safe use that were based on short term studies of opioid treatment (Portenoy & Foley, 1986). Current research indicates that rather than reducing pain in the long term, opioid use is likely to lead to increased pain through either or both tolerance and opioid induced hyperalgesia (Lee et al., 2011).

Opioid prescribing rates have remained high in many countries including Australia (Blanch et al., 2014; Lalic et al., 2019) with individual efforts to decrease use hampered by the complex effect this medication has on thinking and behaviour (Manhapra et al., 2018; Twillman et al., 2018). Concern about the lack of evidence in demonstrating benefit for CNCP and the obvious level of harm from regular prescription opioid use (Therapeutic Goods Administration, 2019), has led expert bodies to recommend opioid prescription not be continued beyond what is needed for acute pain treatment (Blanch et al., 2014; Royal Australian College of General Practitioners, 2017). These include the Centre for Disease Control and Prevention (CDC) in the US (Dowell et al., 2016), American Pain Society, American Academy of Pain Medicine (Chou, 2009), Australian and New Zealand College of Anaesthetists, Faculty of Pain Medicine (FPM, ANZCA). NSW Health. New South Wales legislation restricts opioid prescription for a dependent person (NSW Health, n.d.) and Australian federal legislation requires that prescription of opioids beyond three months requires a second opinion to support maintaining therapy (Therapeutic Goods Administration, 2021). Diagnosing dependence, which results from licit prescription opioid use as well as illicit use (Holliday et al., 2013) and prescribing appropriately in that circumstance is challenging and is often left to General Practitioners (GPs) with little experience in making that diagnosis (Holliday et al., 2018). Despite recommendations to avoid ongoing opioid prescribing clinicians may feel conflicted about

discontinuing therapy in patients who are perceived to have a legitimate need for pain relief if they believe there is no practical alternatives to offer. (Dasgupta et al., 2018; Desveaux, et al., 2019; Holliday et al., 2013).

1.3.1 Deaths from Opioids

Opioid overdose and death statistics provide the most visible and significant evidence of opioid related harm. Opioid poisoning results from taking a higher dose than that prescribed, combining prescription opioids with other medications, or simply ongoing use with deteriorating health status (Boyer, 2012; Australian Institute of Health and Wellbeing (AIHW), 2018). Opioid toxicity manifests in respiratory depression, decreased level of consciousness, and death if untreated (Boyer, 2012). Overdose fatality traditionally viewed as a consequence of taking illicit drugs has now been shown to be more closely associated with prescription medication use (AIHW, 2018). Data used to demonstrate adverse effects and events from opioid use is coded by the Australian Bureau of Statistics and the Centre for Disease Control in the United States to reflect opioid type rather than means of acquisition. Therefore, statistics reflecting both prescription and illicit use are frequently amalgamated. Despite toxicology analysis there is at times limitations to the determination of which opioid type has been used due to drug metabolism (Australian Bureau of Statistics, 2019). To illustrate the overall problem of opioid use, statistics combining all opioid use, have been presented and where possible identified as prescription or otherwise. This acknowledges the continuum of opioid use where there is increased likelihood of transition from prescribed opioids to illicit use of prescribed opioids and the use of illegal opioid drugs (Wilton et al., 2021).

In the United States (US) 130 people die each day from opioid overdose (National Institute on Drug Abuse, n.d.). President Trump announced in 2017 that the opioid crisis was a national public health emergency. This declaration was supported by members of the Commission on Combating Drug Addiction and the Opioid Crisis, with the commission pointing out that at that time more people were dying from opioid overdose than from the combined total of gun homicides and car crash fatalities and acknowledging that the majority (over 60%) of all opioid overdoses were from prescription opioid use (Madras, 2018). The number of deaths attributed to opioids was greater than that from the previously declared public health emergency in the US of Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) (DeWeerdt, 2019). The public health emergency of opioid overuse was predicted to

continue until active steps and interventions were undertaken to reverse the trend (Chen et al., 2019).

Recent Australian statistics reflect those from the US with three people dying every day from opioid related poisoning and 1123 of the 1740 drug use deaths in 2018 specifically attributed to opioid ingestion (Australian Bureau of Statistics, 2018a). This was comparable to the national death rate from motor vehicle accidents (MVA) for the same time period but while MVA fatality numbers had been creeping downward (Australian Bureau of Statistics, 2018b) opioid overdose numbers have increased by more than 60% over the past 15 years (AIHW, 2018) after a peak to 1,245 in 1999 due to the widespread use of heroin (AIHW, 2018). Significant action to reduce heroin availability reversed that public health danger with current statistics attributing 70% of opioid related deaths in Australia to prescription opioid use (Dunlop et al, 2021). This was fuelled by a jump in opioid prescribing from 10 million scripts written in 2009 (Penington Institute, 2019) to over 15 million in recent years (AIHW, 2018). Tragically, most opioid related overdose deaths are accidental rather than intentional (Roxburgh et al., 2019) with daily opioid dose a significant indicator of likelihood of overdose death (Bohnert et al., 2011). Opioid related deaths comprised nearly 1% of the total 158,493 Australian deaths in 2018, including those from age related pathology (Australian Bureau of Statistics, 2018a).

Death from drug related causes, on average, reduced an individual's life span by up to 33 years (Penington Institute, 2019) with 38 years being the median age of death for this group in 2016. This contrasts with 81 years for all other causes of death (AIHW, 2018).

1.3.2 Harm to the Individual

Morbidity associated with prescription opioid use although less confronting than mortality has significant long term physical, psychological and social impacts on individuals who continue to take prescription opioids. In 2011 the health burden from taking opioids was determined to be nearly 1% of the total cost of burden of disease and injury in Australia (AIHW, 2018). The encumbrance from prescription opioid use depends upon the dose and length of use (Shah &Hayes, 2017).

Side effects of prescription opioid use result from allergic reaction, hypersensitivity, idiosyncratic reaction, interaction with other drugs or simply ongoing therapy (AIHW, 2018). Well known adverse effects include itch, constipation, urinary retention, somnolence, and

cognitive impairment (Holliday et al., 2013). Less recognised sequelae of long term opioid use are immunosuppression (Boland & Pockley, 2018), endocrine dysfunction along with increased risk of falls, MVA and sudden death (Benyamin et al., 2008; Holliday et al., 2013). Risk of dependence or addiction is associated with both illicit and long term prescription opioid use. Dependence leads to withdrawal symptoms including increased pain on reduction or cessation (Kosten & George, 2002). Addiction is characterised by cravings, desire to continue taking opioids despite negative consequence, prioritisation of opioid use above other aspects of life and difficulty in reducing or even maintaining a steady dose (Kosten & George, 2002). Potential transition to illegal drugs (National Academies of Sciences et al., 2017) and inclination to smoke tobacco are associated with taking prescription opioids (Ekholm et al., 2009). Negative cognitive effects from opioid therapy may be significant (Dasgupta et al., 2018; van Steenbergen et al., 2019). Social estrangement, breakdown in family relationships, greater risk of harm from accident or misadventure and legal consequences may also result from prescription opioid use (AIHW, 2018; Dasgupta et al., 2018).

1.3.3 Harm to Others

Research on the effect that prescription opioid use has on family members or significant others is limited but it is apparent that spouse and parental opioid use leads to greater household instability (Dasgupta et al., 2018). Individuals reliant on prescription opioids have reduced capacity to work (Campbell et al., 2015), greater reliance on healthcare and social welfare support as well as increased mental health diagnoses (AIHW, 2018; Dasgupta et al., 2018). Prescription opioids are more likely to be used in lower socioeconomic households further driving the downward economic spiral (AIHW, 2018). Children are especially vulnerable when they reside with an adult who uses prescription opioid medication. Maternal opioid use may result in poor prenatal care and neonatal abstinence syndrome and there is a greater incidence of childhood death from either accidental overdose, or deliberate homicide if either parent takes opioids (Dirks, 2018). Children of opioid dependent parents are more likely themselves to have mental health problems such as attachment disorder and display avoidant behaviour (Dirks, 2018; Romanowicz et al., 2019). There is a greater risk of older children taking up drug use as well as the increased risk of their death from both experimentation and deliberate suicide when prescription opioid medication is available in a household (Gaither et al., 2018) with statistics from the US showing the death rate of children in this group has increased in recent years (Gaither et al., 2018). Most opioid medication accessed by children was intended for use by an adult in the house (Romanowics et al., 2019).

1.3.4 Cost to Society

The monetary cost of taking opioids is significant and is broken up into medication acquisition and the cost of treating adverse effects. In Australia the cost of treatment is borne primarily through the public health system and pharmaceutical benefit scheme (Whetten et al., 2020) and thereby with taxpayer money. In a report by Deloitte Access Economics, for Painaustralia, the breakdown of money spent in 2017-18 to support prescription opioid use was assessed at $60.2 million to purchase prescriptions and $13.4 million for hospital care associated with misuse treatment (Economics, D.A., 2019).

In Australia a significant component of the total cost of treatment for adverse outcomes associated with prescription opioid use comes from hospital presentations. In the 10 years from 2007–2017 hospital presentations increased and resulted predominantly from treatment for prescription opioid use rather than illicit opioids (AIHW, 2018). In 2016–17 there were 27,147 admissions resulting from opioid use. This comprised 9,636 hospitalisations or 26 admissions a day, 4,234 (44%) of which recorded opioid poisoning as the principal diagnosis, and 16,903 hospitalisations or 46 a day for opioid dependence. There were 608 hospitalisations or nearly two hospitalisations a day for mental health and behavioural disorders connected with opioid use. For the same period, there were 4232 presentations or 12 a day to an emergency department (ED), for opioid poisoning. A further 566 people presented to ED with dependence and 314 for other mental health and behavioural disorders associated with opioid use in that time period (AIHW, 2018).

In real terms this means that every day in Australia, there are 74 people hospitalised for opioid related causes, more than a third of whom are admitted for acute management of opioid poisoning and 14 present to ED each day with problems associated with opioid consumption. This is a 25 percent increase over this ten year period while the rate of hospitalisation with any diagnosis including opioid poisoning has increased by 38 percent in the same time period (AIHW, 2018). Although men in the 35–44 age group are more likely to die from opioid related causes (Australian Bureau of Statistics, 2018a), women have a higher representation in hospitalisation numbers related to opioid treatment (AIHW, 2018). This has significant implications for families in terms of primary wage earner and carer roles.

The total financial cost of opioid related deaths in Australia during 2017-18 was calculated at $4.7 billion. This comprises $3.7 billion in health and wellbeing related costs, and nearly 1

billion in potential lost earnings (Economics, D.A., 2019). Premature mortality was estimated to cost $1.04 billion or $1.3 million for each individual who died (Economics, D.A., 2019) with the total cost of loss of wellbeing reported as $3.7 billion (Economics, D.A., 2019, 2019). Australian data focused primarily on healthcare costs however loss of productivity in the workplace, and the cost of crime associated with opioid use were reported as substantial components of the total cost of prescription opioid use in the US (Economics, D.A., 2019).

1.4 Reducing Benefit with Long Term Prescription Opioid Use

The implications of long term prescription opioid use are significant. Continued opioid use may lead to a vicious cycle of increased pain and further opioid use through the mechanisms of tolerance and opioid induced hyperalgesia (OIH), rather than pain reduction (Fishbain & Pulilkal, 2019; Hayhurst & Durieux, 2016; Rivat & Ballantyne, 2016). Early studies of prescription opioid use for CNCP supported ongoing opioid treatment. Failure to detect or report lack of benefit with longer term use reflected brevity of study duration with no study going beyond four months (Chaparro et al., 2013). A seminal study conducted by Portenoy, (Portenoy & Foley, 1986) with study duration of 12 weeks, promoted opioid use for CNCP and has influenced prescribing attitudes from publication to present times. Recent research demonstrated that opioids are no better than other analgesic medication for CNCP (Chaparro et al., 2013; Krebs et al., 2018), that pain does not worsen with opioid cessation and may in fact improve (Mcpherson et al., 2018), and that the majority of people taking opioids do not experience objective improvement in pain as a result of ongoing use (Currow et al., 2016). Although study participants often self-report better pain relief and physical capacity with opioid treatment than with control treatments, this is not supported by objective data and may reflect expectation rather than actual experience (Goesling et al., 2018; Krebs et al., 2018).

1.4.1 Tolerance

Opioid tolerance stems from a process of desensitisation. This occurs more with opioid and receptor coupling than with any other feedback loop within the body (Hayhurst & Durieux, 2016). Traditionally overcome by increasing the dose, the variable effect on different opioid receptor sites means that tolerance is more pronounced for pain messaging than for effects such as respiratory depression, causing a mismatch in desired result versus possible harm when the opioid dose is titrated up (Boyer, 2012). Continuing to increase the opioid dose in response to

tolerance can lead to serious consequences, including altered level of consciousness and respiratory arrest (Boyer, 2012).

1.4.2 Opioid Induced Hyperalgesia

Opioid Induced Hyperalgesia (OIH) is a hyperalgesic state induced in the nervous system through sensitisation from continued or increased opioid dose and is characterised by increased pain and allodynia, or sensitivity to sensory stimuli which would not normally be perceived as painful (Hayhurst & Durieux, 2016; Rivat & Ballantyne, 2016). OIH is demonstrated with both high and low dose opioid treatment (Lee et al., 2011) and is associated with short and long acting preparations (Angst & Clark, 2006). Progression from acute to chronic pain may be associated with this mechanism (Rivat & Ballantyne, 2016). The brain, in a sensitised hyperprotective mode, urges that the message of danger be heard and acted upon, by an amplified pain response to override the cognitively dulling effect of the opioid medication (Rivat & Ballantyne, 2016).

Tolerance and OIH both lead to decreased opioid dose efficacy however they differ in how they need to be managed. Tolerance may require a dose increase to control the level of pain although adverse side effects dictate how high an increase can be made before harm outweighs benefit, whereas OIH resolves with opioid reduction and cessation (Hayhurst & Durieux, 2016). Despite knowledge of OIH for nearly one hundred years, worsening pain continues to be routinely treated by escalating opioid dose with little consideration to the causative mechanism (Hayhurst & Durieux 2016). Conceptually, comprehending that while each dose of opioid gives a degree of pain relief OIH will cause the baseline level of pain to continue climbing while ever they remain on opioid medication can be challenging for both opioid users and prescribers (Rivat & Ballantyne, 2016). Any perceived short term reduction in pain may reinforce the patient's insistence to maintain or increase the opioid dose (Manhapra et al., 2018).

1.5 Widespread Opioid Prescribing

Prescription opioid use is one of the most widespread health issues in the developed world (Bhadelia et al., 2018; Häuser et al., 2017). Paradoxically, developed countries have an abundant supply of opioid medication for CNCP whereas poorer countries struggle to maintain a sufficient supply of opioids to treat acute pain (Bhadelia et al., 2018). The United States are

world leaders in prescription opioid consumption accounting for 80% of the world's use (Rummans et al., 2018) and supplying 38% of their adult population with opioids (Lasser, 2017).

1.5.1 Prescription Opioid Use in Australia

In Australia opioid prescribing has grown 15 fold since the late 1990s (Blanch et al., 2014). More than three million Australians or 16% of the population take prescription opioids each year, dispensed from more than 15 million prescriptions written annually, with most prescribed by GPs for CNCP treatment. Oxycodone, codeine and Tramadol are the most commonly prescribed opioids (AIHW, 2018; Lalic et al., 2019). Australia is ranked eighth in the world in opioid prescribing prevalence. In Australia, opioid prescribing is more likely in regional areas than in cities or remote or very remote locations (AIHW, 2018). Women, older individuals people in lower socioeconomic groups (AIHW, 2018; Blanch et al., 2014) and indigenous populations (Osbourne et al., 2020) are more likely to be prescribed opioids. In contrast, individuals in higher socioeconomic groups and city dwellers are better able to be treated if they present requesting support with opioid problems (AIHW, 2018). Prescribing patterns show clusters with some regional areas having prescribing rates up to 10 times the number in other areas (Blanch et al., 2014; Campbell et al., 2015). Of the 13 specialist services providing chronic pain management in the state of New South Wales (NSW) ten are located in metropolitan areas (Painaustralia, n.d.). In Australia as in other countries there is a strong correlation between the number of prescriptions written and opioid related harm (Blanch et al.,2014; Mercadante, 2019).

A `lost generation' of people epitomised by Ballyntyne (2017), some of whom had been taking prescribed opioid medication for up to 30 years without aberrant use behaviours, have been strongly encouraged or compelled to comply with opioid reduction recommendations (Rose, 2018). These individuals, in the main, perceive they have a legitimate `need' to take opioid medication and see themselves as a distinctly separate group to those who misuse opioid drugs (Young et al., 2019). For that reason many are reluctant to accept recommendations to reduce or stop medication.

1.6. The Complex Effect of Opioids

Pharmaceutical opioids, like illicit opioids, exert a complex effect on the brain that alters function and supports continuation of opioid use making opioid dose reduction contentious and challenging for many individuals (DiMarco et al., 2019). Structural changes within the brain from prescription opioid use visible on imaging include volumetric changes in various regions of the brain (Upadhyay et al., 2010; Younger et al., 2011). Magnetic Resonance Imaging demonstrates changes to areas of the brain associated with reward processing, including reduced amygdala volume and a reduction in the support pathway structures that allow connectivity between these and other areas of the brain (Upadhyay et al., 2010; Younger et al., 2011). Anatomical changes noted on imaging after even short term prescription opioid use did not reverse at opioid cessation with the degree of damage being contingent on length of opioid use (Upadhyay et al., 2010; Younger et al., 2011).

1.6.1 The Endogenous Opioid System

The human body has an endogenous opioid system, consisting of, β-endorphins, enkephalins, dynorphins, and nociceptins/orphanins, which are intrinsic substances that recruit their own receptors to influence cognitive and motivational functions of the brain through neurotransmitter release (Benarroch, 2012). They are not opiates but have similar precursors to those of exogenous opioids and bind to the same neuroreceptors that exogenous opioids are able to access, allowing this mechanism to be shared. (Ghelardini et al., 2015). The primary function of this endogenous system is to enhance the desire to perform activities that support continuation of life. Activation of reward pathways by endogenous opioids occur in response to eating, drinking and sexual activity (Ting-A-Kee & van der Kooy, 2012).

1.6.2 Prescription Opioid Effect

Prescription opioids target and expropriate reward pathways in the brain (Garland et al., 2017) through interference with usual neurotransmitter function, influencing dopamine, glutamate and GABA release and uptake (Fields et al., 1991). This initially leads to feelings of euphoria and a sense of distancing from reality but with regular use causes a shift in the gratification response point (Garland et al., 2017). This means that pleasure from experiences that would otherwise have given joy is reduced and the `need' for more opioids to provide positive feelings is enforced (Garland et al., 2017). In addition, negative reinforcement to avoid withdrawal symptoms, promotes further opioid use (Kutlu & Gould, 2016). Executive brain functions connected with logical reasoning (van Steenburgen et al., 2019), attention (Allegri et al., 2019), and working memory (Baker et al., 2016) are disrupted by prescription opioid use resulting in

poor decision making, reduced impulse control and alteration in memory to reinforce positive feelings about the use of opioids (Borjkhani et al., 2018). Memory disruption may be a feature of chronic opioid use (Tolomeo et al., 2019) and contributes to alteration in self-identity (Garland et al., 2017). Opioid dependent individuals continue to medicate despite knowledge of harm with many expressing a desire to stop (Thielke et al., 2014). The entire maladaptive effect of prescription opioid use dampens endogenous opioid function and promotes continued use of exogenous opioids in a desire to feel normal (Hauser & Knapp, 2018; Le Merrer et al., 2009; Pecina et al., 2019; Riquino et al., 2018).

1.6.3 Vulnerable Populations on Prescription Opioids

Vulnerable individuals are more likely to be sensitive to the complex effect of opioid medication. Chronic pain itself causes changes to the brain, with areas responsible for cognitive and emotional modulation of pain demonstrating loss of grey matter, likely related to central reorganisation of neuroplastic brain tissue (Yang & Chang, 2019). These changes are compounded by opioid use (Crofford, 2015; Riquino et al., 2018; Yang & Chang, 2019). People of lower socioeconomic status with less resources and support are more likely to turn to prescription opioids to address pain and emotional distress (Campbell et al., 2015; Grol-Prokopczyk, 2018; Krashin et al., 2013). There is a strong connection between opioid use and depression with half of all people treated with opioids in the US having a concurrent diagnosis of depression (Campbell et al., 2015; Scherrer et al., 2018; Sullivan, 2018). Stress (Bershad et al., 2018) and functional disability (Lauer et al., 2019) may likewise be treated ineffectually with prescription opioids. The usual modulating effect that endogenous opioids have on mood is overwhelmed by the stronger message from prescription opioids which cause dysregulation of the natural system (Pecina et al., 2019; Toubia & Khalife, 2019). In an attempt to treat both pain and depression and regain life balance, prescription opioid medications are often inappropriately continued (Jamison et al., 2003; Martel et al., 2014; Sullivan & Sullivan, 2018). Depression results in a lack of motivation to change, low self-efficacy and poor coping and self-management skills (Sullivan, 2018). These in turn impede helpful change in behaviour and sabotage the capacity to reduce opioid medication.

Personal vulnerabilities along with alterations to perception and cognitive function contribute to the challenge of undertaking prescription opioid dose reduction. In order to change the lifestyle and habits which cause individuals to continue entrenched prescription opioid use, patient centred support during weaning is likely to facilitate better outcomes.

1.7 Conclusion

For the last 30 years prescription opioid medications have been the principal treatment for CNCP and extensive prescribing continues. Although efficacious in acute and cancer pain prescription opioids have not been demonstrated to have benefit when used for CNCP. The encumbrance of long term prescription opioid use, with increasing risk of harm in combination with decreasing benefit, provides a compelling argument to limit opioid use in CNCP. The complex effect opioids have on the brain, however, makes reduction a difficult and daunting task. Prescribers are informed by guidelines from expert bodies with many suggesting that the most current evidence based message is to deprescribe for most patients to cessation (Royal Australian College of General Practitioners, 2017; Dowell et al., 2016; Busse et al., 2018.; NSW Therapeutic Advisory Group Inc, 2015). Patients increasingly find themselves compelled to accept this recommendation as GPs comply with changing legislation directed at restricting prescription opioid use. To support opioid reduction, a dedicated, patient-centred, low-cost, intervention based on evidence should be implemented across all levels of healthcare service delivery as policy.

The next Chapter presents a scoping review of the literature to explore studies of interventions for the purpose of prescription opioid reduction. This knowledge will form the basis of evidence for the thesis and design of the study.

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Chapter 2: Review of Literature on interventions to support prescription opioid medication reduction for chronic non cancer pain

Chapter 1 presented the background and rationale for the thesis along with an exploration of the harm and complex behavioural issues associated with prescription opioid use. This chapter presents the findings from a scoping review on interventions for prescription opioid reduction. The review will discuss what interventions are used for prescription opioid reduction, and what evidence there is to support individual interventions. This knowledge will guide development and evaluation of an intervention to support prescription opioid reduction.

A scoping review protocol was developed to guide this review. This protocol, `**What characteristics does the literature reveal about outpatient interventions for prescription opioid reduction in a chronic non cancer pain population? Protocol for a scoping review'** is provided in Appendix 1. The Scoping review was not registered however the protocol is published online in Open Science Foundation DOI 10.17605/OSF.IO/UBJDS and provided in Appendix 1. The scoping review is published in Journal of Clinical Nursing DOI: 10.1111/jocn.16235. The review is reproduced below as published.

The key finding from this review was that there is an array of interventions used for prescription opioid reduction in both tertiary care and primary care settings facilitated by clinicians from a variety of specialties. Most show promise in supporting opioid dose reduction although only a small number have demonstrated a statistically significant reduction. Few barriers to participation in interventions were discussed however low recruitment numbers and high drop out rates meant that robust evidence of what facilitated prescription opioid reduction was difficult to demonstrate and further research is needed. Chapter Three will discuss the conceptual design and development of a nurse supported prescription opioid reduction pathway (NS-PORP) which evolved to maintain connection with patients reducing prescription opioid medication in order to commence group program pain treatment. The subsequent study design for the NS-PORP study is detailed in Chapter Four.

2.1 A scoping review of outpatient interventions for the reduction of prescription opioid medication for chronic non cancer pain

2.1.1 Abstract

Aim- This review aimed to examine and describe outpatient interventions that support the reduction of prescription opioid medication for chronic non cancer pain.

Introduction - Prescription opioid use is a global health issue. Previous systematic reviews have not identified that any specific intervention supports prescription opioid reduction effectively. In keeping with the nature of a scoping review, this review details an overview of the existing literature on this topic, with quality of evidence being discussed rather than formally analysed.

Methods and analysis – Following a structured review approach an electronic database search, of Medline, Embase, Cochrane, Cinahl, and Proquest and grey literature was undertaken. Search results were screened by title for relevance. Abstracts were reviewed against inclusion criteria, keywords and target concepts. Two reviewers adhering to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews checklist charted and assessed studies for quality using Critical Appraisal Skills Programme checklist assessment tools. Extracted data were collated and synthesised for presentation as a tabular and narrative review.

Results – From the initial search of 5089 papers, 19 underwent full-text review and quality appraisal. A variety of interventions were described to support reduction in prescription opioid use, however only one study of at least fair quality was able to demonstrate a demonstrated a statistically significant benefit in reducing measured opioid dose compared with a control group. Interventions were implemented in both specialist pain services and in primary care with multidisciplinary and interdisciplinary clinician care. Barriers and facilitators were observed in both settings.

Conclusion and implications for clinical practice – Further rigorous research needs to be conducted to conclusively answer the question of what outpatient interventions support opioid reduction in chronic non cancer pain. This scoping review is the first step of inquiry in the development of a nursing intervention to support reduction of prescription opioids.

Keywords: Chronic pain, persistent pain, prescription opioids, reduction, weaning, tapering, intervention, nurse led, nurse support.

What does this paper contribute to the wider global clinical community?

- The review contributes to the evolving body of knowledge surrounding interventions utilised to support prescription opioid reduction in the context of CNCP
- The review presents an overview of what is currently known about the various types of interventions used to support patients to reduce prescription opioids
- The literature demonstrates that in the context of chronic non cancer pain reduction can be achieved without increased level of pain and loss of functional capacity

2.2 Introduction

Opioid use and misuse is a global health issue. Prescription opioid treatment for chronic non cancer pain (CNCP) is characterised by the key elements of: escalating risk of harm with concurrent reduction in benefit, (Sullivan & Howe, 2013) high prescribing rates (Rivat & Ballantyne, 2016) and complex physical and psychoactive effects from the use of opioids (A. Rosenblum et al., 2008). Current evidence does not support the use of prescription opioids for CNCP (McPherson et al., 2018). Following the 2016 release of prescribing guidelines by the Centre for Disease Control in the United States (Dowell, Haegerich, & Chou, 2016) restricted opioid prescribing for CNCP was recommended by many peak expert bodies including those in Australia (Australian Institute of Health and Welfare, 2018).

Escalating risk of harm along with declining benefit are features of both aberrant and compliant prescription opioid use. Despite this dual negative effect, dose reduction is often challenging for patients and recommendations to reduce opioid dose may result in conflict with prescribers. Prescribers may be reluctant to deprescribe opioids for patients they perceive have a legitimate need for pain medications, particularly if they have limited access to practical and effective pain management alternatives (White et al., 2021). Over 15 million opioid prescriptions are written annually in Australia (Lalic et al., 2019) which has resulted in a 15 fold increase in the last 30 years (Blanch et al., 2014) with poor health outcomes from prolonged prescription opioid use leading to negative economic consequences for the individual and society (Kolodny et al., 2015). Opioids exert a complex effect on the brain that reinforces continuing use (Le Merrer et al., 2009). Reward pathways are expropriated by exogenous opioids, replacing pleasure from natural reward with the desire for opioid effect (Garland et al., 2013). Disruption to executive function in the brain from opioid use alters decision making and memory. This causes positive feelings about opioid use to be favoured and leads to the continued use of opioids against better judgement (van Steenbergen et al., 2019). Structural changes related to opioid use are visible on imaging in areas of the brain associated with emotional processing and connectivity (Younger et al., 2011).

Despite a wide array of interventions suggested for the purpose (Eccleston et al., 2017);(Frank et al., 2017) there is no standard approach to support prescription opioid reduction. Guidelines and protocols help prescribers make decisions about opioid management but are often not well received by individuals established on opioid therapy. Education alone has been demonstrated to be insufficient to bring about behavioural change (Traeger et al., 2018). Inpatient treatment for opioid reduction is costly and disconnects patients from their support systems,

responsibilities, and real-world concerns, creating an artificial environment, unable to be sustained upon discharge (The National Guidelines for Medically Assisted Treatment of Opioid Dependence 2018). Multidisciplinary pain treatment programs frequently incorporate opioid tapering, and demonstrate success in prescription opioid dose reduction, without identifying the particular component of the program that facilitates opioid reduction (Eccleston et al., 2017). Decreasing barriers to opioid reduction, through behavioural treatment, (Nicholas & Blyth, 2016) may help individuals accept and adhere to opioid reduction plans. For practical application an intervention to support prescription opioid reduction needs to be accessible and acceptable to people with CNCP, be cost effective, and easily integrated into a multidisciplinary pain service or primary care clinic. These criteria may be met by a nurse-led intervention.

Previous systematic reviews, conducted by Eccleston et al. (2017) and Frank et al. (2017) reported on interventions for the reduction of prescription opioid use. Meta-analyses were not performed in either review due to significant variability in intervention types, and outcomes along with small sample sizes. Both authors concluded there was insufficient quality of evidence to support the recommendation of any specific intervention for prescription opioid dose reduction. An evidence brief undertaken by Peterson et al., (2016) examined complementary interventions for prescription opioid reduction and described the evidence base as extremely limited. Recent systematic reviews of tapering methods by Mathieson et al., (2020) and Sud et al., (2020) comment on the heterogeneous nature of studies. Lieschke et al. (2020) performed a rapid realist review of evidence on prescription opioid tapering in the rural context, and White et al. (2021) conducted a systematic literature review of the feasibility of behavioural interventions to support prescription opioid tapering in CNCP, both found limited evidence to support approaches within these contexts. Further inquiry into what facilitates prescription opioid reduction in this dynamic and fast moving area of research (Frank et al., 2017) and in the context of harm and cost from long term opioid use, is warranted.

2.2.1 Aims

The aim of this scoping review is to examine and describe outpatient interventions for the primary purpose of reducing prescription opioid medication for CNCP by mapping the available literature and identifying the gaps in current knowledge.

2.3 Methods

The five-stage framework proposed by Arksey and O'Mallery (2005) was used to guide the scoping review. This framework consists of identifying the research question, identifying relevant studies, selecting eligible studies, charting the data and collating, summarizing and reporting the results. The sixth optional stage of the framework involving consumer consultation was not conducted due to time and cost constraints. The review adhered to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist (**PRISMA** extension for scoping reviews 2018). A protocol for this scoping review was developed and is available on Open Science Foundation (DOI 10.17605/OSF.IO/UBJDS).*(Appendix1)* A scoping review has a broader reach of the literature to overcome the paucity of evidence from study designs acceptable to other literature review types and address the complexities of reviewing evidence about human behaviour.

2.3.1 The research questions

The specific question of identifying which intervention(s) in the context of CNCP support prescription opioid reduction will not be answered by this review. Rather evidence gathered through the review process will guide new directions for evaluating if a nurse-led intervention, underpinned by behavioural change methodology, would be an effective approach to supporting prescription opioid reduction in patients with CNCP in both primary and specialist care settings.

To address the review aim, an investigative approach was developed to map the literature using the following questions. 1. What interventions are studied for the purpose of prescription opioid reduction? 2. Do they demonstrate effectiveness in reducing prescription opioids? .3. Where are these interventions undertaken and who delivers the interventions? 4. Have barriers and facilitators associated with provision of the interventions been identified? 5. What are the gaps in knowledge relating to this evidence?

2.3.2 Identifying relevant studies

Inclusion criteria - Papers included in the review were those that described an original study and included the following criteria: 1. The study population were adults, over the age of 18, with CNCP, defined as pain extending beyond three months (Treede et al., 2015) on prescription opioid medication; 2. The study was of a clinical intervention undertaken for the primary purpose of supporting the reduction of prescription opioid use; 3. The primary outcome for review was the reduction in prescription opioid use either measured as a dose or as an

intention to reduce opioid dose using a standardised tool. Secondary outcomes of interest were satisfaction with the intervention and cost of the intervention; and 4. The study was set in an outpatient setting in any country. All original research study designs were considered for inclusion.

Exclusion criteria - Review exclusions were: 1. Studies set in inpatient locations; 2. Studies of prescription opioid reduction for conditions other than CNCP; 3. Studies of chronic pain treatment; 4. Studies of opioid monitoring programs, opioid prescribing guidelines or legislative measures to restrict opioids; and 5. Studies of opioid substitution treatment or adjunct medication therapy to support opioid reduction. Although these are effective methods to limit prescription opioid use evaluating them was not the purpose of the review.

Search strategy - The literature search comprised of three stages: 1) Identification of relevant key words and MeSH terms related to the key concepts; 2) A complete search of selected databases, grey literature and trial registers using a search strategy developed from the key words and MeSH terms; and 3) Identification of key articles with an additional search of paper reference lists.

The search strategy was developed in consultation with a senior librarian using the key phrases of `prescription opioid treatment or therapy for CNCP, chronic pain or persistent pain' and `intervention, method or support for prescription opioid dose reduction, weaning or tapering'. Subject headings, keywords and keyword phrases were compiled for each of the search concepts and the concepts were combined using the 'AND' operator. The Cochrane Highly Sensitive Search Strategies for identifying randomized trials in MEDLINE (2008 rev.) validated search filter was applied to the Medline search. The search strategy was developed in Medline before being translated to the other databases. The search was limited to human studies and English language citations published after 1999. The date limit was applied in recognition of the timing of research into this topic which followed popularisation of opioid use for CNCP starting in the early 1990s (Holliday, Hayes, & Dunlop, 2013).

Sources of evidence - A systematic search of the Medline, Embase, Cochrane, Cinahl, and Proquest databases was conducted in August 2020, supplemented by a grey literature search of the following resources; Med Nar, Open Grey, PsycExtra, Science.gov, World Wide Science Org and Theses and Dissertations Guide. Trial registers including Cochrane Central Register of Clinical Trials (Central), ANZCTR-Australian New Zealand Trails Registry, Clinical

Trials.gov, ISRCTN Registry, Centerwatch, WHO International Clinical Trials Registry Platform and EU Clinical Trials Register were also examined for relevant studies.

The literature search comprised of three stages: 1) Identification of relevant key words and MeSH terms related to the key concepts; 2) Complete search of selected databases, grey literature and trial registers using a search strategy developed from the key words and MeSH terms; and 3). Identification of key articles with an additional search of paper reference lists. (*Appendix 2*)

Quality was appraised using the Critical Appraisal Skills Program (CASP) checklists for Randomised Control Trials (RCT), Cohort study and Qualitative study (Critical Appraisal Skills Programme (CASP) UK, n.d.). CASP appraisal tools were chosen over other quality appraisal tools to accommodate the variety of study designs to be reviewed. The studies were reviewed and appraised as poor, fair or good quality according to the number of key areas on the CASP checklist that were adequately met. For RCTs key areas included basic study design, methodological soundness, accuracy of results and application to local population. For cohort studies similar questions were asked in addition to whether possible confounders were addressed. Appraisal for qualitative design looked at study design, methodological soundness and accuracy, and value of results and included a question about ethics and the relationship between researcher and participant.

2.4 Results

2.4.1 Study selection

A total of 5088 articles were retrieved following the initial search, which reduced to 4032 with the removal of duplicates. Papers were initially screened by title looking for keywords and 69 were selected for a full text screening. A further paper was added that had been published after the search was completed, bringing the number of papers reviewed to 70. A total of 51 papers were then excluded with eight being systematic reviews, 10 were studies of pain management programs, five were of prescriber advice or guidelines, eight described trials set in acute or inpatient settings, 14 were trial registrations or protocols and six included populations not part of the entry criteria for this review (mainly of substance abuse treatment). The selection process for studies is shown in detail using the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram in **Figure 2.1** (Page et al., 2021).

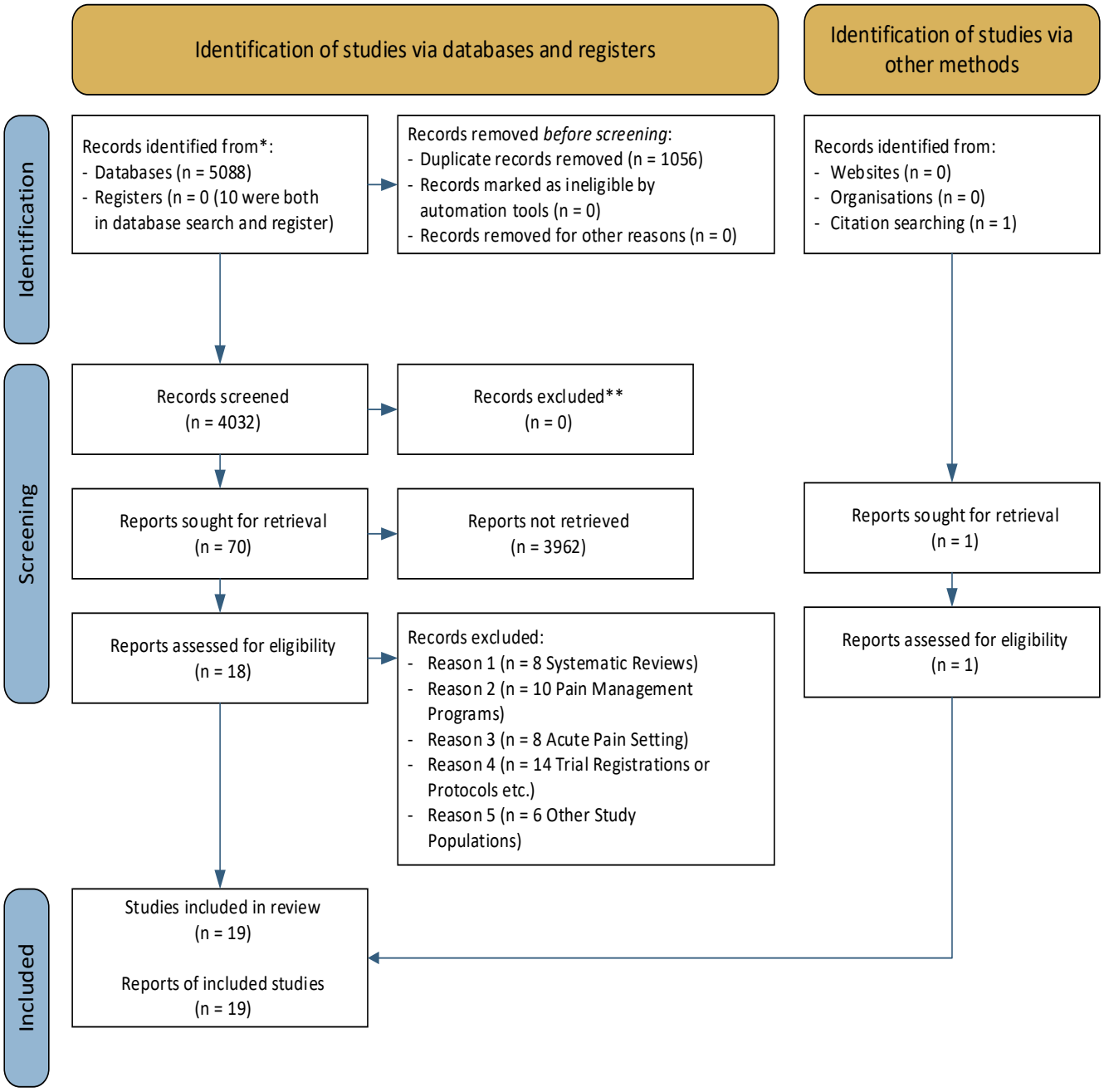

Figure 2.1. *Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram*

There were 19 papers that met the inclusion criteria and were independently screened by two reviewers, KN and KI, with the option of further input from HR and GL to resolve any disagreement. Study quality was found to be of moderate to low level and is displayed in **Table 2.1**. Randomised control studies and qualitative studies were found overall to be of a higher quality than observational studies. As observed in other reviews sample sizes were noted to be low with 667 study participants contributing data from 16 trials along with 32 individuals providing qualitative data. There was agreement between the review team

members to include all papers despite their variable quality, as their relative contributions to advancing knowledge toward the objective of the review was acknowledged. Two papers were based on the same trial with the second paper reporting outcomes three years after the original study and both were included in the review as new data was evaluated.

Table 2.1 *Quality Appraisal Table*

RCT Studies	Poor	Fair	Good
Garland et al 2014		✓	
Garland et al 2019		✓	
Guarino et al 2018		✓	
Jamison et al 2010		✓	
Kurita et al 2018		✓	
Naylor et al 2010		✓	
Sullivan et al 2017		✓	
Zheng et al 2007		✓	
Zheng et al 2019		✓	
Observational Studies			
Chang et al 2014		✓	
Darnell et al 2018	✓		
Doolin 2017	✓		
Goodman et al 2018	✓		
Mehl-Madrona et al 2016	✓		
Scott et al 2020		✓	
Ziadni et al 2020	✓		
Qualitative Studies			
Mathias et al 2017		✓	
Young et al 2017		✓	

2.4.2 Data charting

A standardised data extraction template based on the Joanna Briggs Institute data extraction template for scoping reviews (https://reviewersmanual.joannabriggs.org/display/MANUAL/Chapter+11%3A+Scoping+reviews, 2017) was used to collect data and followed the process outlined by the PRISMA-ScR checklist (Page et al., 2020). The template included details of author, publication date, country of study, study design, aims and purpose of the study, population studied and setting, sample size and completion numbers, intervention and clinician description, length of the intervention, primary outcomes, follow up time, key findings and study funding *(Appendix 3).* This information was then used to develop the Scoping Review Table **Table 2.2** Following charting by two independent reviewers and discussion with the

extended review team findings were corroborated and concepts were developed to answer the study questions and objective.

2.4.3 Data collation summary and reporting

The primary objective of the scoping review was to describe outpatient interventions that support prescription opioid reduction for CNCP. The evaluation questions provided the following information.

1. *Interventions for the purpose of prescription opioid reduction.*

   The scoping review examined a wide array of interventions described as being for the purpose of prescription opioid reduction. Most aimed to change participant behaviour in some way. Some used a structured program format most commonly based on psychological treatment, including Mindfulness Oriented Recovery Enhancement (MORE) (Garland et al., 2014; Garland et al., 2019) close monitoring and cognitive behavioural substance misuse counselling (Jamison et al., 2010), `Opioid taper support group' utilising motivational interviewing (Sullivan et al., 2017), group medical visits inclusive of complementary and alternative therapies, (Mehl-Madrona et al., 2016), cognitive behavioural therapy for codeine reduction (Nilsen et al., 2010) and motivational interviewing (Chang et al., 2015). All except one (Chang et al., 2015) were offered in specialist pain service settings. Less structured information and education was provided in a pain service setting where the goal was to sequentially stabilise opioid dose then taper (Kurita, et al.,2018) and patient-centred `Prescription Opioid Tapering' appointments, partnering with the prescribing physician (Darnall et al., 2018; Ziadni et al., 2020). A number of primary care settings also offered a more informal approach with physician-patient discussion of ethical principles and evidence-based practice (Goodman et al., 2018), communication about opioid management for chronic pain (Matthias et al., 2017) and holistic care using self-management principles through the South Gloucestershire pain review service (Scott et al., 2020). Two trials of electroacupuncture were conducted with pain reduction purported through the gate control theory described by (Melzack and Wall 1970) thereby reducing the need for opioids (Zheng et al., 2008; Zheng et al., 2019) and a core strengthening exercise program (Doolin, 2017). Utilising both psychological treatment and a self-management approach a web based program `Take Charge of Pain' (Guarino et al., 2018) and `Therapeutic Interactive Voice Response' (TIVR) opioid reduction counselling through a telephone service (Naylor et al., 2010) were included. The

Harnessing Online Peer Education (HOPE) intervention (S. D. Young & Heinzerling, 2017) using social media to support opioid reduction was the final study reviewed. In addition to the last three interventions, where participation was entirely self-directed, many of the structured interventions that encouraged behavioural change also integrated principles of self-management with home practice, journaling or self-directed activity included as a core element of the intervention (Chang et al., 2015; Doolin, 2017; Garland et al., 2014; Garland et al., 2019; Jamison et al., 2018; Naylor et al., 2010).

2. *Effectiveness of interventions in reducing prescription opioid*s.

The majority of studies included for review stated that the trialled intervention helped reduce prescription opioid use. The only study that did not make this claim was that of opioid stabilisation followed by tapering set in a Danish pain service (Kurita et al., 2018). The intervention was described as not feasible for reducing prescription opioids, after a high dropout rate of participants, with only one person from the tapering group providing follow up data. Of the 17 papers that provided quantitative data, nine reported a statistically significant reduction in opioid use in the intervention group, although not all studies included a control group (Chang et al., 2015; Darnall et al., 2018; Garland et al., 2014; Garland et al., 2019; Guarino et al., 2018; Naylor et al., 2010; Nilsen et al., 2010: Ziadni et al., 2020). Most studies that demonstrated a statistically significant benefit from the intervention used a psychological treatment approach (Garland et al., 2014; Garland et al., 2019; Guarino et al., 2018; Jamison et al., 2018; Naylor et al., 2010; Nilsen et al., 2010). Two studies reported statistically significant opioid reduction but noted a similar reduction was evident in the comparator group (Sullivan et al., 2017; Goodman et al., 2018) and a small number of studies showed statistically significant opioid reduction during the intervention period that was not maintained to the final study endpoint (Garland et al., 2014; Zheng et al., 2008; Zheng et al., 2019). Participants at specialist pain services started with higher opioid doses with the average starting dose reported as 193mg morphine equivalent dose (MED) (Gurino et al., 2018; Kurita et al 2018; Naylor et al., 2010; Sullivan et al., 2017; .Zheng et al., 2008; Zheng et al., 2019; Ziadni et al., 2020) in contrast to the average dose of 85mg MED reported in studies from primary care clinics (Doolin, 2017; Goodman et al., 2018; Mehl-Madrona et al., 2016; Scott et al., 2020).

3. *Setting and delivery of interventions for opioid reduction*.

Of the reviewed studies, data came from specialist pain services, (Darnell et al., 2018; Guarino et al., 2018; Jamison et al., 2010; Kurita et al., 2018; Naylor et al., 2010; Sullivan et al., 2017; Zheng et al., 2008; Ziadni et al.,2020) primary care clinics, (Goodman et al., 2018; Mathias et al., 2018; Mehl-Madrona et al., 2016; Scott et al., 2020; Young et al., 2017), a combination of both (Chang et al., 2015; Garland et al., 2008; Garland et al., 2019; Zheng et al., 2019) and one was conducted in a medical service of a correctional centre (Doolin et al., 2017). Structured psychological care was more likely to be undertaken in a specialist pain service (Garland et al., 2008; Garland et al., 2019; Jamison et al. 2010; Nilsen et al., 2010; Sullivan et al., 2017) as was the development of internet and telephone based techniques (Guarino et al., 2018; Naylor et al., 2010). The studies that used a RCT design were conducted in specialist pain services with only one including data collected in conjunction with a primary care clinic (Zheng et al., 2019). Most RCTs were conducted in services located in US cities with the exceptions of one study from Denmark (Kurita et al., 2018), one from Norway (Nilsen et al., 2010) and the two trials of electroacupuncture (Zheng et al., 2008; Zheng et al., 2019) in Australia. Structured psychological programs were all trialled in city locations (Garland et al., 2008; Garland et al., 2019; Jamison et al. 2010; Naylor et al., 2010; Nilsen et al., 2010; Sullivan et al., 2017). In contrast interventions trialled in primary care settings were studied in both city and non-metropolitan sites (Chang et al., 2015; Goodman et al., 2018; Mehl-Madrona et al., 2016; Scott et al., 2020).

Specialist pain services were able to provide care from a range of clinician specialties. `MORE' mindfulness training, cognitive reappraisal skills, and positive emotion regulation was delivered by a masters-level clinical social worker (Garland et al., 2008; Garland et al., 2019). `Take charge of Pain' was developed by pain specialist clinicians with help from chronic pain patient focus groups (Guarino et al., 2018). Close cognitive behavioural substance misuse counselling was run by a psychiatrist trained in pain and addiction medicine and a clinical psychologist trained in pain and behavioural medicine was utilised to monitor participants (Jamison et al. 2010). A pain specialist physician led the stabilisation and tapering intervention (Kurita et al., 2018) and a group therapist monitored participant use of `Therapeutic Interactive Voice Response', which followed eleven weeks of cognitive behavioural therapy treatment with a trained clinician (Naylor et al., 2010). A pain medicine/psychiatry physician provided weekly care using motivational interviewing for a taper support group (Sullivan et al., 2017) and registered acupuncturists provided

electroacupuncture for two trials (Zheng et al., 2008; Zheng et al., 2019). In contrast, primary care interventions were of an interdisciplinary nature, most commonly delivered by the primary care physician (Goodman et al., 2018; Mehl-Madrona et al., 2016; Scott et al., 2020) with two exceptions. Motivational interviewing (Chang et al., 2015) was conducted by two nurse practitioners specialising in psychiatric mental health. The nurse practitioners received training in the technique and were supported by a doctorally prepared researcher. Core strengthening exercises were supervised by a correctional service nurse (Doolin, 2017).

4. *Barriers and facilitators associated with provision of the interventions.*

Few barriers to intervention participation were noted in studies conducted in specialist pain services except for the sequential stabilisation and taper intervention (Kurita et al., 2018) where high dropout rates were reported in response to the mandated opioid taper. This was despite noting that those who progressed to the taper component of the intervention experienced better outcomes such as feeling more rested. Adverse effects resulting from the study were reported in two papers; one from the second electroacupuncture trial which was reported as mild (Zheng et al., 2019) and a severe drug reaction during the `Opioid Taper Support Group' which was unrelated to the intervention (Sullivan et al., 2017). Primary care studies noted that patients were often reluctant to reduce opioids and this affected their ongoing participation in the intervention (Goodman et al., 2018; Mehl-Madrona et al., 2016) and that primary care providers were fearful of losing patients if they stopped providing opioid prescriptions which influenced intervention provision (Goodman et al., 2018).

Intervention facilitation could be inferred from participant satisfaction. Satisfaction, engagement and benefit were reported from participation in a number of interventions, (Chang et al., 2015; Guarino et al., 2018; Jamison et al., 2018; Naylor et al., 2010; Sullivan et al., 2017) along with the agreement to recommend the intervention to others (Zheng et al., 2008). Incentives to remain in the intervention for the purpose of the study were provided to participants in a number of trials (Guarino et al., 2018; Jamison et al., 2010; Sullivan et al., 2017; Young et al., 2017) and the intervention itself was offered to the control arm of one trial after the study was completed (Zheng et al., 2019). Credibility of treatment was a secondary outcome in one study of psychological treatment (Garland et al., 2014). The cost benefit from utilising the intervention rather than regular treatment was reported in two studies (Mehl-Madrona et al., 2016; Doolin, 2017). The change in expert

recommendations regarding opioid prescribing caused primary care physicians to reduce opioid prescribing in one study, which led directly to increased patient participation in the opioid reduction intervention (Mehl-Madrona et al., 2016).

5. *Gaps in knowledge relating to this evidence.*

The gap in current knowledge regarding outpatient interventions to support prescription opioid reduction in CNCP is attributable to limited evidence and is linked to study heterogeneity and variable study quality. Of the nine RCTs (Garland et al., 2014); (Garland et al., 2019); Guarino et al., 2018; Jamison et al., 2010; Kurita et al., 2018; Naylor et al., 2010; Sullivan et al 2017; Zheng et al., 2008; Zheng et al., 2019) none were appraised as being of higher quality than fair, and of the seven observational trials (Garland et al., 2014) Nilsen et al., 2010; Scott et al., 2020; Ziadni et al., 2020) and two qualitative studies (Mathias et al., 2017; Young et al., 2017) four were rated as fair and two as low quality.

Although the study populations were uniformly described as individuals experiencing CNCP a number of studies restricted participant eligibility to specific criteria, such as aberrant medication use (Chang et al., 2015); Jamison et al., 2010, Young et al., 2017), and specific chronic pain conditions (Doolin, 2017; Naylor et al., 2010; Nilson et al., 2010) making aggregation of data more difficult. Only half of the studies used a control arm or comparator group in the study (Garland et al., 2008; Garland et al., 2019; Goodman et al., 2018; Guarino et al., 2018; Jamison et al. 2010; Kurita et al., 2018; Naylor et al., 2010; Sullivan et al., 2017, Zheng et al., 2008; Zheng et al., 2019) and outcome measures were of opioid use with nearly half of all studies not objectively measuring opioid dose (Garland et al., 2014); (Garland et al., 2019); Guarino et al., 2018; Jamison et al., 2010; Mathias et al., 2017; Young et al., 2017). In most studies where opioid dose was measured (Darnall et al., 2018; Doolin et al., 2017; Goodman et al., 2018; Kurita et al., 2018; Naylor et al., 2010; Nilsen et al., 2010: Scott et al., 2020; Sullivan et al 2017; Zheng et al., 2008; Zheng et al., 2019; Ziadni et al., 2020) data came from patient self-report with no documented corroboration. Sample sizes were low in all studies with numbers between 10 and 115 enrolled in each trial. Sample size calculations were provided in six studies only (Garland et al., 2014; Guarino et al., 2018; Jamison et al., 2010; Kurita et al., 2018; Sullivan et al 2017; Zheng et al., 2008) and most studies reported that validity of findings was hampered by low study numbers. One study assigned treatment and comparator groups retrospectively as participants moved from one group to the other (Goodman et al., 2018) and another modified the study design as participants were initially unwilling to join the

treatment intervention group (Mehl-Madrona et al., 2016). There were few external influences noted to bias study quality with only one study having received industry funding (Jamison et al., 2010).

2.5 Discussion

This scoping review aimed to examine and describe outpatient interventions for the primary purpose of reducing prescription opioid medication for CNCP. The wide array of treatment approaches indicated the diversity of prescription opioid effects and the lack of reported efficacy from any single treatment type. Although not all interventions included a component of psychological treatment, the objective of all was to bring about a change in behaviour. Most studies reported success in reducing prescription opioid use with studies of psychological treatment showing the most measurable benefit (Chang et al., 2015; Garland et al., 2014; Garland et al., 2019; Jamison et al., 2010; Naylor et al., 2010; Nilsen et al., 2010). However, only one study of at least fair quality was able to demonstrate a statistically significant reduction in measured prescription opioid dose compared to a control group (Naylor et al., 2010).

Interventions were trialled in both specialist pain service settings with multidisciplinary clinicians, and primary care clinics using an interdisciplinary approach. Studies set in specialist services were conducted using more rigorous study techniques (Garland et al., 2014; Garland et al., 2019; Guarino et al., Jamison et al., 2010; 2018; Kurita et al., 2018; Naylor et al., 2010; Sullivan et al., 2017; Zheng et al., 2008; Zheng et al., 2019), reported manualised or comprehensively described interventions (Garland et al., 2014; Garland et al., 2019; Guarino et al., Jamison et al., 2010; 2018; Kurita et al., 2018; Naylor et al., 2010; Sullivan et al., 2017; Zheng et al., 2008; Zheng et al., 2019) and demonstrated greater benefit in reducing prescribed opioid use (Garland et al., 2014; Garland et al., 2019; Guarino et al., Jamison et al., 2010; 2018; Naylor et al., 2010; Nilsen et al., 2010), than observational or qualitative studies which were mainly conducted in primary care clinics (Chang et al., 2015; Darnall et al., 2018; Ziadni et al., 2020). There was no reported advantage or disadvantage from the use of any clinician speciality in facilitating opioid reduction and the cost of care from specialist clinicians was not discussed. Of particular interest, the use of nurses to deliver motivational interviewing in primary care demonstrated statistically significant benefit in reducing opioid use (Chang et al., 2015) and

the provision of core strengthening exercises by correctional facility nursing staff reduced cost per patient compared with previous opioid treatment (Doolin et al., 2017).

Barriers and facilitators are recognised to play a significant role in engagement with behavioural treatment. Key barriers to intervention participation were reported to be the mandated reduction of prescription opioids which was characteristic of interventions that were delivered by prescribers. These interventions usually comprised information provision and education about opioid use and the studies reported difficulty recruiting participants and higher rates of attrition (Goodman et al., 2018; Kurita et al., 2018; Mehl-Madrona et al., 2016). Involving participants in their own treatment plans may improve satisfaction with less desirable interventions and enable mandated reductions to be better tolerated. This is borne out in qualitative interviews where participants indicated that they wanted information about planned opioid dose reduction and the capacity to negotiate about the regime, and feared abandonment if not included (Matthias et al., 2017). Having the choice to be able to continue prescription opioids during the intervention was a powerful facilitator and this was indicated by high satisfaction ratings and participant retention (Chang et al., 2015; Guarino et al., 2018; Jamison et al., 2010; Naylor et al., 2010; Sullivan et al., 2017; Zheng et al., 2008). Novel interventions, which were primarily offered by specialist pain services, were also noted to have high participation and study completion rates (Garland et al., 2008; Garland et al., 2019; Guarino et al., 2018; Jamison et al., 2010; Naylor et al., 2010; Zheng et al., 2008; Zheng et al., 2019) suggesting that choice and perceived benefit are significant factors in intervention acceptability. Perceived benefit toward participating in the intervention changed as participants became aware of the benefits that complementary therapies offered for pain reduction in lieu of opioid medication (Mehl-Madrona et al., 2016). Intervention credibility reported after participation in a randomised psychological treatment group was found to be no different to that of the comparator support group and was not predictive of treatment outcome (Garland et al., 2008) and qualitative data suggests that both formal and informal models of support were viewed as potentially being helpful (Young et al., 2017). The key to encouraging participation in prescription opioid reduction interventions may be through tailoring intervention type, duration, and location to meet the varied expectations of participants.

Barriers to treatment from distance, comorbidities or other commitments were not reported. Interventions involving structured treatment were predominantly conducted in specialist pain services which were located in cities (Garland et al., 2014; Garland et al., 2019 ; Guarino et al., 2018; Jamison et al., 2010; Kurita et al., 2018; Naylor et al., 2010; Zheng et al., 2008; Zheng

et al., 2019), providing a barrier to rural dwelling patients requiring specialist levels of care. The lack of health care services providing pain treatment in rural areas is well documented (Lieschke et al., 2020). Internet and phone-based treatment requires reliable infrastructures and participant motivation and if accessible, could be a feasible way of supporting patients in rural and remote locations through prescription opioid reduction.

Resource cost to conduct interventions in terms of development, clinician training and running costs, was not considered. Most structured psychological interventions required specialist clinician involvement (Garland et al., 2014; Garland et al., 2019; Guarino et al., 2018; Jamison et al., 2010; Kurita et al., 2018; Naylor et al., 2010; Sullivan et al., 2017; Zheng et al., 2008; Zheng et al., 2019) and were run over time frames of between six to twenty four weeks with the longest being six months of TIVR (Naylor et al., 2010), offered only after the completion of eleven weeks of cognitive behaviour therapy. This level of psychological support is unlikely to be feasible outside of a specialist pain service. In contrast primary care clinics set in both city and non-metropolitan areas adopted simple education and psychological strategies which could be offered in any primary care practice and provide possible financial benefit to the service from its implementation (Mehl-Madrona et al., 2016; Doolin., 2017). Partnering of tertiary and primary tier healthcare services to provide opioid reduction support is likely to mean that knowledge and resources, such as web-based programs, are shared. This would ensure a more equable and tailored approach to supporting complex and vulnerable individuals with CNCP during opioid reduction.

The gap in knowledge about what supports prescription opioid reduction results from the lack of endorsement for any particular intervention(s) and limited research into key determinants of intervention success including acceptability and accessibility. Previous systematic reviews on the topic have commented on low study quality and the quality appraisal generated from this review corroborates those reports. (Eccleston et al., 2017, Frank et al., 2017; White et al., 2020). Eccleston et al., (2017) identified sample size as the most significant factor affecting study quality, recommending that future studies have a sample number of at least 100 in both treatment and control arms. Further research with adequately powered studies over longer timelines, may provide a clearer view of this challenging topic.

2.5.1 Limitations of the review

This scoping review is limited by review type in which a wide range of study designs have been included. The aim of the review was to examine and synthesise evidence, rather than

provide a conclusive answer through meta-analysis of data, given the small number of studies available on prescription opioid reduction and study heterogeneity restricting interpretation of data. Most studies were conducted in the US and in large cities. This may not be indicative of the legislative restrictions that patients and clinicians experience in other countries nor does it adequately represent the experiences of rural populations with CNCP.

2.5.2 Implications of the review and recommendations for future practice

Barriers to participation in treatment for reducing prescription opioids could be minimised by active partnership from the primary care sector, with patients. This model of care could be offered with guidance and support from specialist pain services. Having primary care treatment as the first tier with support of specialist services as the second tier, would provide a range of interdisciplinary and multidisciplinary treatment options to support prescription opioid reduction and could be tailored to the individual's requirements. Specialist pain treatment, however, needs to be accessible to complex and vulnerable CNCP populations including those in rural and remote areas. For some this may be best served through internet-based applications and telehealth models. There is a need for further rigorous studies into interventions to support prescription opioid reduction either through adequately powered RCTs, or observational studies with a comparator arm. There are several clinical trials currently registered that aim to determine effective ways to reduce prescription opioid medications. These include the Improving Wellbeing of people with Opioid Treated Chronic Pain (I-WOTCH) study in Warwick, UK Clinical Trials Unit ISRCTN (Https://clinicaltrials.gov/show/nct03454555, 2019) and the Empower trial in Stanford, US (Https://clinicaltrials.gov/show/nct03308188, 2017).

2.6. Conclusion

This scoping review contributes to the evolving body of knowledge surrounding interventions utilised to support prescription opioid reduction in the context of CNCP. The review presents an overview of what is currently known about the various types of interventions used to support patients to reduce prescription opioids, the settings in which they are typically implemented, and the barriers and enablers often encountered by clinicians and researchers in this challenging area of practice and research. As previous reviews have found, demonstrating the efficacy of approaches used to support prescription opioid reduction, is hampered by challenges associated with recruitment and retention of participants in studies, the heterogeneity of the studies undertaken, and the variable quality of study designs available to review. The current body of

literature suggests the increased uptake of behavioural management approaches being utilised to support prescription opioid deprescribing, and the increasing engagement of nursing staff to help deliver these approaches are probable cost-effective alternatives, both within specialist pain services and primary care settings. The potential utility of these approaches could be explored in prospective well-designed studies.

2.6.1 Relevance to clinical practice

The lack of evidence regarding effective and acceptable treatment approaches to promote prescription opioid reduction leads to the quandary of what support can be offered to those on long term therapy who either elect to or are mandated by their prescriber to reduce or cease prescription opioids. Overcoming the challenges associated with reducing prescription opioids is complex. What is evident from the limited literature in the context of chronic non cancer pain is that reduction can be achieved without increased level of pain and loss of functional capacity. This is particularly evident when patients are well-supported, involved in the development of deprescribing plans and interventions are underpinned by behavioural change approaches. There is a burgeoning need for well-designed, adequately powered prospective implementation studies to evaluate novel models of care that seek to integrate treatment approaches, provide longitudinal data on patient outcome and examine cost-effectiveness.

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Table 2.2. *Characteristics of included studies Scoping Review Table*

Author Publication Year Country	Study Design Study Aim	Population, Setting Sample size / Number completed	Intervention Description including duration, staffing and follow-up	Primary Outcomes and Key findings for Opioid reduction Satisfaction / Cost	Funding Participant Incentives
Randomised Control Trials					
Garland et al. 2014 US	Double blinded RCT To demonstrate that Mindfulness Oriented recovery Enhancement (MORE) targets mechanisms underpinning chronic pain and opioid misuse	Chronic pain on prescription opioid medication Tallahassee FL from primary and tertiary clinics 115 randomised 70 completed treatment 52 completed follow up	`MORE' a novel multimodal intervention that integrates mindfulness training, cognitive reappraisal skills, and positive emotion regulation into a therapeutic approach versus Support group care 8 x 2hr weekly sessions + home practice and journaling Masters-level clinical social worker 3 month follow up	**Desire for opioids** (10 point scale) - MORE participants had significantly less desire for opioids post treatment than study group patients (β = 1.39, 95% CI [0.22, 2.56], *p* = .02), this was not sustained at follow up **Self-reported opioid misuse** Current Opioid Misuse Measure (COMM) – There was a 63% reduction in opioid use disorders in the MORE group, compared to 32% in the support group (SG), *p* = .05 **Treatment credibility** - No significant difference in credibility between treatment groups **Cost** - not evaluated	National Institute on Drug Abuse
Garland et al. 2019 US	Double blinded Stage 2 RCT To conduct a theory-driven mechanistic analysis of the linkage between	Chronic non cancer pain with prescription opioid use Salt Lake UT from primary care and pain clinic 95 randomised 70 completed treatment	Integrative therapy of mindfulness training, third-wave cognitive-behavioural therapy, and principles from positive psychology versus active support group care 8 x 2hr sessions weekly + home practice with CD and log	**Opioid misuse risk (COMM)**- Participation in MORE significantly reduced opioid misuse by enhancing positive psychological mechanisms and decreasing pain severity. Change in opioid misuse risk by 3-month follow-up (β = −.31, *p* = .027) **Satisfaction/cost -** not evaluated	Fahs Beck Fund for Research and Experimentation

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	positive psychological processes and proximal outcomes	48 completed follow up	journaling Masters-level clinical social worker 3 month follow up		
Guarino et al. 2018 US	Single blinded RCT To evaluate effectiveness of web based behavioural program in reducing aberrant drug related behaviours	Adults with CP on long term opioid therapy with misuse features New York City pain treatment practice 110 randomised, 97 completed	Take Charge of Pain program comprising 27 self-paced web based modules teaching a variety of cognitive-behavioural skills versus treatment as usual (no behavioural component) 12 week program developed by pain experts, pain medicine clinicians with CP patient focus groups consulted. Research staff had regular phone and email contact for technical assistance 3 month follow up	**Aberrant Drug Related Behaviours** (ADRB) - measured by COMM - Greater reductions in ADRB than patients receiving treatment as usual (6.96-point reduction in mean COMM vs a 2.55, $p = 0.001$) post intervention. Reductions sustained at 3 month follow-up. Reduction in COMM scores occurred in the treatment period by the four- and eight-week time points **Patient engagement** - Patients assigned to web-CBT were more likely to report engaging in and benefiting from the eight core CBT skills and activities **Cost** - Not evaluated	US National Institute on Drug Abuse (NIDA) Participants paid for completing assessments up to $250 ($50 for baseline assessment and $40 for each subsequent assessment)
Jamison et al. 2010 US	RCT, 3 arms To determine if close monitoring with cognitive behavioural substance misuse counselling increases compliance	Patients with back and neck pain on prescription opioids Pain Management Centre Boston 62 randomised 58 completed	Group education sessions with 5 components, monthly electronic diaries, urine screens, opioid compliance checklist, group education sessions and individual motivational compliance counselling + monthly counselling for high risk group versus usual care Treatment for up to 6 months monthly	**Percent with a positive Drug Misuse Index** (DMI) a composite score of self-reported drug misuse, (Prescription Drug Use Questionnaire), physician reported abuse behaviour (Addiction Behaviour Checklist), and abnormal urine toxicology results. 73.7% of high-risk v control patients demonstrated positive scores on DMI compared with 26.3% of high-risk experimental group and 25.0% of low-risk controls ($p<0.05$) **Satisfaction** - 71.6% satisfied with treatment and electronic diaries particularly helpful	Endo Pharmaceuticals National Institute on Drug Abuse (NIDA) Participants received $50 gift cards for completing baseline and

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	with opioid treatment		Led by a psychiatrist trained in pain and addiction medicine + individual motivational, compliance counselling led by a clinical psychologist trained in pain and behavioural medicine 6 month follow up	**Cost** - not evaluated	post-treatment measures
Kurita et al. 2018 Denmark	Phase 2, single-centre, non-blinded RCT To evaluate the efficacy of a program where sequentially opioid therapy was stabilized before tapering in patients at a pain clinic	Outpatients aged over 18 years with CNCP at least 7 years of schooling and pain for 6 months, opioid treatment for at least 3 months with daily dose at least 60mg Multidisciplinary Pain Centre of Rigshospitalet, Copenhagen University Hospital 75 consented 35 randomised 13 completed (1 in taper group)	2 phase intervention stabilisation – 2 assessments. Taper off Group – 7 assessments with planned 10% reduction weekly (or fortnightly) until cessation or 6 months, contact from research nurses for encouragement and reinforcement of dose reduction versus usual care 6 months (242 days mean timeframe of care) Certified pain specialist physicians certified by the Nordic Course in Advanced Pain Medicine and experienced clinical nurses. Psychologist, social worker and physiotherapist available if needed 6 month follow-up	**Equivalent dose in Morphine -** increased during the stabilization phase (**a**nalysis on first 4 assessments only) Differences between first and second assessments (prior to randomisation) in Opioid dose n=38 Mean= 29.5 SD=277.9, *p*=0.017. Opioid dose increased an average of 29.5 mg of oral morphine equivalents *p* = 0.446. Effect sizes were not calculated due to the reduced sample size **Satisfaction/cost -** not evaluated	Danish Agency for Science, Technology and Innovation and Hørslev-Fonden
Naylor et al.	RCT	Patients with CP on prescription opioids who had completed 11 weeks	Therapeutic Interactive Voice Response (TIVR) 4 components through phone interaction (via	**Self- reported medication intake -** Decrease in mean opioid dose at 4 month follow up (p=0.03), and 8 month follow up (*p*=0.05) in the experimental	National Institute of Drug Addiction,

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2010 US	To examine whether a telephone-based automated enhancement program can help to reduce opioid and NSAID use	of Cognative Behavioural Therapy (CBT) group coping pain skills MindBody Medicine Clinic, Vermon 51 (32 on opioids), randomised 51 completed	touch tone keypad) with a computer for 4 months – daily self-monitoring questionnaire didactic review of skills, guided behavioural rehearsal of skills, versus standard care Monthly therapist feedback message 8 month follow up	group. Increase in opioid dose at 8 month follow up in control group (p=0.045) **Satisfaction** -all subjects who used (TIVR) 50% or more reported the TIVR was useful. One felt four months was too long. **Cost -** not evaluated	National Institute of Arthritis, Musculoskeletal and Skin Diseases and National Institute on Alcohol Abuse and Alcoholism
Sullivan et al. 2017 United States	Pilot, non blinded RCT To demonstrate feasibility and effectiveness of a pilot prescription opioid taper support intervention for patients receiving moderate- or higher-dose long term opioid use (LtOT) for CNCP with no evidence of	Patients with CP on prescription opioids interested in tapering opioids Medicine Center for Pain Relief in Seattle, Washington 35 randomised 18 completed treatment (3 years to recruit) 32 completed follow up	Taper Support intervention using motivational interviewing assessment, education, identifying barriers and seeking commitment +17 weekly 30-minute sessions about different topics and x3 booster phone calls versus usual care Duration 22 weeks An experienced pain medicine/psychiatry physician evaluated patient for medication and supervised the study. A physician assistant (PA) trained by two clinical psychologists in motivational interviewing led intervention 34 week follow up	**Opioid dose Morphine Equivalent dose (MED) -** At 22 weeks, opioid dose reduced from baseline in both groups with no significant difference between groups (adjusted mean difference = −42.9 mg (MED); or in percent reduction from baseline in dose (mean, 43% vs 19%; adjusted mean difference = −0.25). At 34 weeks, opioid dose reduced from baseline with no significant difference between groups (adjusted mean difference = −26.7 mg (MED) or in percent reduction from baseline in daily dose **Satisfaction** – Of 16 participants in taper support at 22 week assessment - 13 (81%) rated the intervention as very or extremely helpful, 11 at 34 weeks **Cost** - not evaluated	National Institute on Drug Abuse Participants received $15 for completing baseline assessment, $30 for 22-week follow-up, and $50 for 34-week follow-up

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	current substance abuse				
Zheng et al. 2007 Australia	Pilot single blinded RCT To evaluate the effect of Electro acupuncture on consumption of opioid like medication	CP patients using prescription OLM Barbara Walker Centre for Pain Management, St. Vincent's Hospital, Melbourne 35 enrolled 23 completed follow up	Electro acupuncture (EA) twice a week for 6 weeks versus sham EA EA was provided by registered acupuncturists 3 month follow up	**Opioid dose in Morphine Equivalents** - From baseline to the 8th week, the opioid like medication (OLM) was significantly reduced in both treatment groups ($F(2, 66) = 18.4$, $p < 0.001$). The reduction was 39% in the real EA group, and greater than 25% in the sham EA group. The group difference in the changes over time was not statistically significant but indicated a trend toward a more rapid reduction of OLM in the REA group ($F(2, 66) = 3.0$, $p = 0.056$). Intervention group participants increased OLM dose more rapidly than sham group after 8 weeks **Satisfaction** - Over 90% of participants were willing to refer the treatment to others **Cost -** not evaluated	Faculty of Life Sciences and Australian Acupuncture and Chinese Medicine Association.
Zheng et al. 2019 Australia	Multicentre RCT with 3 arms, single blinded To evaluate the efficacy of EA in reducing opioid consumption	CP patients on prescription opioid medication Pain Services Unit, Royal Melbourne Hospital, Caulfield Pain Management and Research Centre, Caulfield Hospital, Sunshine Hospital, RMIT Clinical Trial Laboratory, and one site in Geelong	Electro acupuncture twice a week; 3 arms, EA vs sham with a battery-operated electroacupuncture instrument connected to the handles of four needles in the main acupuncture points in the extremities versus sham EA versus Pain and Medication Management Education (PMM) 10 weeks duration EA was provided by registered acupuncturists with at least three	**Opioid dose in morphine equivalents** - Opioid dosage, was reduced by 20.5% ($p < 0.05$) and 13.7% ($p < 0.01$) in the two acupuncture groups and by 4.5% in the education group at the end of the treatment phase, but without any group difference. Paired t tests showed a statistically significant reduction in opioid medication in the EA (20.5% reduction, mean reduction = 95.1 mg, 95% CI = [49.3, 140.8,],$t_{47} = 4.18$, $p < 0.001$) and the sham EA groups (13.7% reduction, mean reduction = 85.3 mg, 95% CI = [35.5,135.0], $t_{28} = 3.52$, $p < 0.002$), but not in the PMM group (4.5% reduction, mean reduction = 39.2 mg, 95% CI = [–34.3, 112.6], $t_{30} = 1.09$, P = 0.285). No statistically significant difference at 3	National Health and Medical Research council and Helen McPherson Smith trust PMM education group offered EA after study completion

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		108 randomised 90 finished treatment 67 followed up	years of clinical experience. PMM was delivered by pain specialists 3 month follow up	month follow up in the EA or SEA groups; PMM not included in analysis **Satisfaction/cost** - not evaluated	
Observational and Qualitative Studies					
Chang et al. 2015 US	Pre- and post-design To test the effect of office-based motivational interviewing (MI) on prescription opioid adherence in older adults with chronic pain	Patients on opioids for CNCP rated as at risk for prescription opioid misuse by Screener and Opioid Assessment for Patients with Pain (SOAPP; ≥7) A primary care office and a pain management clinic in Buffalo, New York. 33 recruited 30 completed	MI intervention consisted of one face-to-face session (15 to 20 min) in week 1 and three weekly phone sessions (each lasting 10–15 min) during weeks 2 to 4, using a manualized and client-centred, yet directive, motivation enhancement intervention followed by participant diarising pain and medication-taking Weekly phone call for 3 weeks One doctorally prepared researcher and two doctorally prepared nurse practitioners in psychiatric mental health with MI training and experience. 1 month follow up	**Self-efficacy for Appropriate Medication Use (SEAMS)** - Participants in MI intervention showed a significant reduction in the risk of prescription opioid misuse post-test ($p < .000$) and 1-month follow-up ($p < .000$). Satisfaction - Participants reported a high level of satisfaction post-test (mean = 10.1, SD = 4.1) regarding the usefulness of MI **Cost -** not evaluated	Patricia H. Garman Behavioral Health Nursing Endowment Fund Award, The State University of New York, and the University at Buffalo School of Nursing
Darnell et al. 2018 United States	Cohort study Evaluation of prescriber reduction of long-term opioid dosages in a setting without	CP patients on prescription opioids Community setting 82 enrolled 51 followed up	Education about the benefits of opioid reduction (reduced health risks without increased pain) by their prescribing physician who voluntarily partnered with patients to facilitate dose reduction Patients could control pace or discontinue reduction	**Opioid MEDD -** After 4 months, median MEDD was reduced to 150 (IQR, 54-248) mg ($p = .002$) **Satisfaction/cost** - not evaluated	National Institutes of Health, National Center for Complementary and Integrative Health

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	behavioural services		4 month follow up		
Doolin 2017 United States	Quasi-experimental design To track daily prescribed opioid dosage throughout intervention period.	Male inmates with chronic low back pain A California correctional facility 51 enrolled 41 followed up	Daily self use of core stabilization exercises from a WebMD Pain Coach application, with fortnightly checks that the exercises were correctly done. 2 month intervention Nursing staff from correctional service	**Opioid dose -** Core muscle strengthening exercises for chronic low back pain decreased opioid use (t=11.227, *p*= 0.000) over 60 days Opioid use was decreased by an average of 72% (95% CI , [59,85] **Satisfaction** - not evaluated **Cost-** from study intervention found to be less than from ongoing opioid treatment	None declared
Goodman et al. 2018 United States	Retrospective review of pre-test and post-test results with a comparator group To examine the efficacy of a primary-care intervention in reducing opioid use among patients who have chronic non-cancer pain	Participants with CNCP for at least 6 months and current use of opioid medication over 16 years of age Family practice 41 recruited 40 followed up	Initial discussion of ethical principles, evidence-based practice, and current published guidelines. Following discussion, patients self-selected to participate with their FP in a continuing tapering program versus medical pain clinic (MPC) care One off contact with ongoing appointments /family physician 6 month follow-up	**Medication level in Morphine Equivalents -** Paired t tests indicated significant differences between baseline and 6-month average daily narcotic doses in morphine equivalents for the Taper Group. No significant difference between baseline and 6-month daily morphine equivalents for the MPC group. Taper Mean=15.94 SD=30.79 [5.58.24.12] *p* =.003 MPC Mean=134.2 SD=155.11 SD=163.66 [-42.88, 120.368], *p* =.324 **Satisfaction/cost** - not evaluated	None declared

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Mathias et al. 2017 United States	Case study To understand communication processes related to opioid tapering, to identify best practices and opportunities for improvement	Patients at least 18 years of age with chronic musculoskeletal pain currently taking a prescribed opioid for pain. Participating primary care physicians (PCP) Conducted in 4 of the 9 primary care clinics at an academic, safety-net hospital serving primarily low-income patients 9 PCPs, 37 patients. 31 interviews analysed (9 PCP, 22 patient)	Patient and PCP communication. Duration not noted PCP appointments Up to 20 months	**Qualitative data** from patient and PCP interviews. Four themes revealed different aspects of patient–provider communication that appeared central to the tapering process: 1) explaining reasons for tapering, 2) negotiating the tapering plan, 3) managing difficult conversations, and 4) assuring patients that they will not be abandoned. **Satisfaction/cost -** not evaluated	Funded by the National Institute on Drug Abuse of the National Institute of Health
Mehl-Madrona et al. 2016 United States	Matched case controlled To determine if complementary or alternative therapies help opioid reduction in a rural setting	Patients attending Group medical visits (GMV) Medical practice in rural New England. 84 recruited 42 followed up Initially no one volunteered for treatment intervention and study had to be redesigned	GMV inclusive of complementary and alternative medicine therapies. Education about non-pharmacological methods for pain management including mindfulness techniques, movement, guided imagery, relaxation training, yoga, *qigong*, and *t'ai chi* versus conventional care Family doctor with training in behavioural health, a nurse, and a behavioural health specialist Up to 2 years	**Opioid MED** - Those who stayed in the practice did not increase dose. Patients who left GMVs before six months did not statistically significantly reduce opiate use. Eighteen people reduced their dose, and eight people stopped opiates altogether; average reduction was 0.19 95% CI [0.12,0.60], $p = 0.01$). In conventional care, no patients reduced opiate use and 48.5% increased dose over the two years of follow-up. **Satisfaction -** not evaluated **Cost** – Determined to be the same as usual care	Coyote Institute, Inc.

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Nilsen et al. 2010 Norway	Pre–post design (case series) To examine whether a brief CBT intervention helped to withdraw codeine in chronic non-malignant pain patients having problematic opioid use	CNCP patients aged 18-70 years, referred due to problematic opioid (codeine) use Multidisciplinary Pain Centre at St Olavs University Hospital in Trondheim or the Department of Physical Medicine and Rehabilitation at Aalesund Central Hospital 17 enrolled 11 followed up	CBT during an agreed gradual codeine taper 6 subsequent 1-hour sessions over 8 weeks. Two specifically trained physicians with 15 years of specific clinical experience with pain patients trained by CBT therapist 3 month follow-up	**Codeine dose in mg** - Mean (SD) codeine dose at pre-, mid- and post-treatment and follow-up assessment points were 237.3 (65.0), 120.0 (40.3), 45.0 (66.1) and 47.7 (64.6). There was a significant reduction from pre-treatment to follow-up (t 5 11.7, p <0.001). There was 80 % reduction at group level and six of the 11 patients ceased at 3 month follow up. At 3-month follow-up, five patients were not using codeine or other opioids, while one had started again with one tablet. Of the remaining five patients, none had increased the medication **Satisfaction/cost -** not evaluated	None declared
Scott et al. 2020 United Kingdom	Prospective cohort study To evaluate the service and its potential impact on opioid use, health and wellbeing outcomes, and quality of life	Patients eligible for inclusion had received ≥3 opioid painkiller prescriptions in a 3-month period, had taken opioids for ≥3 months (long-term opioid use), and were not using illicit drugs or receiving end-of-life care. Pain Review Service in 2 GP practices in South Gloucestershire 34 enrolled 18 followed up	A comprehensive and holistic assessment exploring medical and psychosocial factors involved in opioid use, with an individual pain management plan including setting daily goals, developing a relaxation plan, introducing gentle exercise, dealing with low mood, and improving sleep. Access to alternative care and support options available, including physiotherapy and relaxation groups Median duration 7.7 months / 6 appointments	**Opioid dose in daily morphine equivalent** - median prescribed opioid dose reduced from 90 mg (IQR 60, 240) at baseline to 72 mg (IQR 30, 160) at follow-up (p< 0.001). 15 service users (44%) reduced dose, 3 (8.8%) reduced to zero, 19 maintained the same dose (55.9%), and 0 increased dose. Of those prescribed > 120 mg per day at baseline, 4/14 (28.6%) dropped below 120 mg by follow-up. **Satisfaction/cost** – not evaluated	National Institute for Health Research Collaboration Health Protection Research Unit, British Heart Foundation, Cancer Research UK, Economic and Social Research Council, Medical Research

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			2 GP project workers		Council, the Welsh Government, and Wellcome Trust, under auspices of UK Clinical Research Collaboration
Young et al. 2017 United States	Qualitative interviews To determine the feasibility and acceptability of using social media to reduce complications of opioid use among patients experiencing chronic pain specifically in reducing addiction and overdose.	Adults ≥ 18 years with chronic pain who met DSM-IV criteria for opioid dependence being treated with buprenorphine 5 staff from UCLA clinic were also interviewed. University of California, Los Angeles (UCLA) Health System patients 10 recruited 10 completed	The Harnessing Online Peer Education (HOPE) intervention is a peer-led behavioural intervention delivered via social media Follow-up time not stated	**Qualitative data** from participant and clinician interviews. Three main themes were identified: 1) respondents saw online social support as important for reducing pain and improving outcomes; 2) offline social support interventions (e.g., alcoholics anonymous or narcotics anonymous) were seen as valuable but had notable limitations; and 3) a tailored, online peer support intervention would be desirable and might improve clinical outcomes. Participants asked how online peer-led communities might benefit them. **Satisfaction/cost** – not evaluated	National Institute on Drug Abuse. Participants received a $20 online gift card after completing the interview. Staff did not receive payment.
Ziadni et al. 2020	Prospective cohort study	Patients with CNCP taking long-term opioids	Education about the benefits of opioid reduction (reduced health risks without increased pain) by their prescribing physician who	**Opioid MEDD** - the reduction in MEDD from 4 months (mean = 147.04, SE = 25.86) to 2 to 3 years (mean = 66.59, SE = 19.94) was significant (p = 0.012). Since baseline, 20 of 21 (95%) reduced	National Institutes of Health, National

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United States	2-3 year follow up of data from a voluntary opioid tapering study	Community suburban and rural pain clinics in Colorado 82 enrolled 51 completed 23 followed up 21 in analysis	voluntarily partnered with patients to facilitate dose reduction Patients could control pace or discontinue reduction. 4-months duration and up to 3 year follow-up	MEDD by 3-year follow-up, and 15 of 21 (71%) further reduced MEDD at 3-year follow-up. **Satisfaction/cost -** not evaluated	Institute on Drug Abuse

CBT Cognitive behaviour therapy; CI: Confidence interval; CNCP: Chronic non-cancer pain; COMM: Current Opioid Misuse Measure; GP: General Practice; IQR: Inter Quartile Range; MEDD: Morphine Equivalent Daily Dose; MED: Morphine Equivalent Daily Dose; RCT: Randomised controlled Trial; SD: Standard deviation

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Chapter 3: The Rationale for and Challenge of Developing an Opioid Reduction Intervention

Chapter Two described a scoping review of the literature. Findings were that an array of interventions are used for prescription opioid reduction in both tertiary care and primary care settings facilitated by clinicians from a variety of specialties. Most show promise in supporting opioid dose reduction although only a small number have demonstrated a statistically significant opioid dose reduction. Few barriers to participation in the interventions were discussed however low recruitment numbers and high dropout rates meant that robust evidence of what facilitates prescription opioid reduction was difficult to demonstrate and further research is needed.

This Chapter provides the thesis aims along with discussing the development of a nurse supported prescription opioid reduction pathway (NS-PORP) developed to maintain connection with patients reducing prescription opioid medication in order to commence group program pain treatment.

3.1 Introduction

The use of prescription opioid medication as the primary treatment for CNCP encourages reliance on passive strategies (Becker et al., 2017; Cosio & Lin, 2018). Decreased motivation to change means that participation in active pain treatment is difficult. Typically pain treatment group programs focus on developing active non-pharmacological strategies to replace less helpful and unhealthy passive ones such as medication use. In order to maximise the therapeutic outcomes of active pain treatment groups delaying participation until opioid therapy is reduced to a certain level or completely ceased is a beneficial but complex policy to implement. Patients may feel abandoned or judged if they are not allowed to participate in active pain treatment groups due to their high opioid use. Supporting patients to reduce opioids by maintaining rapport and trust until pain treatment can commence is an important component of care. Discussions around recommendations to reduce opioids are often emotionally charged and can adversely impact patient-prescriber relationships. Providing a patient-centred intervention that supports the reduction of opioids, promotes active involvement of patients in their own healthcare and improves readiness to make positive changes, is hypothesised to promote

understanding and capacity to comply with opioid reduction recommendations. Underpinning the development of such an intervention by a robust conceptual behavioural change framework and evaluating the outcomes of the changed clinical approach through a study maintains an evidence based approach.

3.2 Study Aim

In order to determine if treatment with NS-PORP provided a beneficial change in clinical practice the Candidate committed to integrate the study of the pathway into a higher research degree.

The primary aims of the thesis were to evaluate if a nurse supported prescription opioid reduction pathway (NS-PORP) enabled participants with chronic non cancer pain (CNCP), attending a specialist multidisciplinary pain service, to reduce opioid dose and continue to group program pain treatment.

Secondary aims were to explore participant satisfaction with NS-PORP and to undertake a cost estimation of NS-PORP compared with specialist pain medicine physician care.

The thesis also explored the complex behavioural issues associated with opioid use and the difficulty of opioid dose reduction from the viewpoints of service providers and participants. The mixed method NS-PORP study followed a traditional format.

3.3 The Specialist Pain Service Experience

Hunter Integrated Pain Service (HIPS), a tertiary, multidisciplinary pain service, within NSW Health, treats people with CNCP. HIPS is located in the major metropolitan area within Hunter New England Local Health District (HNEHLHD), one of the largest local health districts in NSW, covering over 130 000 square kilometres. Utilising the skills of medical, psychiatry, psychology physiotherapy and nursing clinical specialities HIPS offers a cohesive multidisciplinary service to support pain management carried out in 38 widely scattered metropolitan and rural hospitals as well as that performed by over 1500 primary healthcare practitioners (White et al., 2019). HNELHD has a resident population of about 920,000 nearly 6% of whom identify as having Indigenous heritage (HNELHD, n.d.). About 1600 patients with CNCP are referred to HIPS every year. From these referrals each year over 500 individuals attend introductory HIPS appointments, nearly 400 progress to the assessment phase and about

80 commence group program treatment (HIPS, 2020). Patients referred to HIPS were likely to be older with a median age of 55 years, economically disadvantaged (demonstrated by postcode), more likely to identify as indigenous (11% of HIPS population) and having comorbid health problems. Over half reported coexisting mental health illness, a third reported cardiovascular disease and a third respiratory disease (ePPOC, 2020).

The primary pathway for adults referred to HIPS with CNCP are sequential group programs where education, multidisciplinary assessment and treatment are provided. Program content comprises information about chronic pain recovery using a whole person approach which integrates the five domains of pain treatment recommended by HIPS; biomedical, mindbody, connection, activity, and nutrition care (Rajappa et al., 2019).Age specific pathways cater to patients referred under the age of 20 years and those older than 80 years and provide similar content delivery.

The majority of people referred to HIPS take opioid medication at referral and a key service message directed at both patients and referrers is the benefit of reducing opioids for pain recovery and general health. A marker of opioid potency, oral Morphine Equivalent Daily Dose (oMEDD), allows dose comparison between different opioid medications using morphine as the baseline dose measure (Armstrong et al., 2020). In 2017 66% of individuals referred to HIPS were taking regular opioid medication, with an average dose of 77mg oMEDD (ePPOC, 2017). Specialist pain medicine physicians at HIPS provided opioid reduction recommendations on a consultative basis but the actual responsibility of acting upon these recommendations rested with the primary prescriber, usually the patients' GP. Despite strong messaging, many people were enrolled historically into HIPS treatment programs still taking large doses of opioid medication with no intention to stop. Their attendance at HIPS may have been prompted by a desire to comply with their GP's advice to engage with HIPS or to take the opportunity to personally argue their case for continuation of opioid therapy. In addition the landscape of increasing scrutiny and tightening legislation around ongoing opioid prescription for CNCP may have pushed otherwise reluctant patients with entrenched opioid use to attend HIPS group program pain treatment in order to satisfy authority conditions imposed upon their prescriber by the NSW Ministry of Health. This led to indifferent engagement with the active focus of the group program and disrupted treatment for other group participants.

Prescription opioid reduction was supported by specialist pain medicine physician recommendations and medication review appointments along with ad hoc telephone contact

from pain service nurses as requested. By consensus in 2018 HIPS clinicians decided to set entry criteria for active pain treatment group programs to patients who were taking an opioid dose of 40mg oMEDD or lower. Reduction in opioid dose facilitates a change in focus from passive to active means of controlling pain and often results in better functional outcomes (Tardiff et al., 2021). Opioid reduction either prior to group program enrolment or as an integral and mandated part of the group program is a policy employed by many multidisciplinary pain services (Huffman et al., 2013; Krumova et al., 2013; Townsend et al., 2008). This change meant that a cohort of people who chose group treatment as the next step of engagement after completing assessment at HIPS, were unable to proceed without reducing their opioid dose. There was concern that without robust timely support this group would feel abandoned or judged by the service and be lost to treatment. Cost-effective structured ways to provide this support were explored.

3.4 The Candidate's Role

Prior to commencing the role at HIPS, the Candidate had spent twenty years working and attaining clinical nurse specialist (CNS) status in a busy Intensive Care Unit (ICU) where an interest in pain and pain medications developed along with an understanding of the context that surrounds pain such as the distress of trauma, sickness and ICU admission. Looking for a professional change the Candidate joined the HIPS team twelve years ago as a CNS, developing the knowledge and skill base for a socio-psycho-biomedical approach to chronic pain treatment.

This interdisciplinary role included active participation in innovative pain treatment group programs, timely and appropriate patient triaging and troubleshooting difficult patient queries around opioid reduction recommendations made in outpatient clinic or group appointments. Clinicians in the service recognised that medication weaning support was needed on a more regular and lengthy basis. The Candidate's current role grew from this requirement and a medication education component in the treatment group program was developed. Harm from prescription opioid use coupled with the lack of benefit from long term therapy and the importance of opioid reduction for pain treatment and improved health was discussed. Patient participation in developing their own opioid reduction plans was promoted. Clinicians in other services were also supported to develop knowledge around opioid weaning and its support through formal presentations and ad-hoc phone interactions. Education about opioids helped patients understand that the side effects and lack of pain relief they frequently experienced were

related to their long term reliance on prescription opioids. Education alone, however, did not create the paradigm shift in patient's behaviour that would have enabled them to reduce opioid dose.

For many years the Candidate listened as patients shared their personal stories of disbelief, fear, frustration and anger, after being told they would have to reduce opioid medication. They expressed anger toward their GPs, the pain medicine specialists and the government. Many felt it was a cost saving measure from the government and some saw the medical fraternity as uncaring and unjust having started them on medication and now abandoning them (Mathias et al., 2017) once recommendations about prescribing had changed. Patients were usually at pains to distance themselves from any reference to substance abuse as many had been labelled in that way previously.

Fear of increasing pain without access to their usual opioid medication was a common concern. Although most were willing to work towards opioid reduction, some resisted reduction and either pressured their current prescriber to continue prescribing or changed providers. At times, feelings of anger were directed at the pain service for making such recommendations leading to complaints against the service and threats of harm toward medical clinicians. Most people, however, enjoyed the opportunity to discuss their concerns on one-to-one basis with the Candidate, away from the scrutiny of group participants many of whom were not using any medication. These discussions were open and provided a voice to patients including those who did not want ongoing engagement with the service.

These experiences led the Candidate to question how best to help patients, who were reliant on prescription opioid medication, to comply with opioid reduction recommendations. As legislation around opioid prescription tightened and opioid prescriber scrutiny increased, maintaining patient rapport and trust to facilitate good healthcare outcomes became more important. Having undertaken brief training in the patient centred style of communication, Motivational Interviewing (MI), (Resnicow & McMaster, 2012) the Candidate identified the utility of this non-judgemental method for discussing opioid reduction. Integrating MI technique into conversations allowed patients to draw their own conclusions about opioid use and reflect on the possibility of dose reduction.

3.5 Considerations for the Development of a Nurse Supported Prescription Opioid Reduction Pathway

Most patients receiving pain treatment with HIPS while taking prescription opioids stated to the Candidate that they did `not want' to be on opioid therapy but did not know what else they could do to control pain, stating that they `needed to' or `had to take' opioid medication. Knowing the service stance on opioid medication there was reluctance from some patients to request help and many disengaged. External influences that swayed patient use of opioids included the opinions of their GPs, family members and friends. GPs had a significant influence through their role as prescriber. Some family members advocated for the ongoing use of opioids out of a desire to see suffering eased, however, most patients related that their family members disagreed with their ongoing opioid use, many commenting after opioid cessation that their families felt they were back to being the person they had previously been.

Previous telephone contact may have been beneficial in helping patients to reduce opioid dose with anecdotal comments from patients indicating their appreciation of this contact, however, as contact was provided in an unstructured manner and was not evaluated the benefit was hard to quantify. Following discussions with the entire HIPS team the development of a cost-effective intervention to support opioid reduction, acceptable to both patients and clinicians, commenced. The objectives of care were in line with HNELHD patient care aims which are outlined in the HNELHD strategic plan (HNELHD, 2020). Providing a structured predictable support pathway seemed intuitively a better way to help people wean opioid medication than relying on ad hoc options.

The proposal of a nurse supported prescription opioid reduction pathway (NS-PORP) designed, written, and facilitated by the Candidate was put forward. Along with supported self-management principles, concepts from twelve step programs and stages of change treatment used by Drug and Alcohol services were incorporated into the pathway (Donovan et al., 2013.;Velasquez et al., 2016). This included utilising the benefit of group dynamics for supportive therapy, facilitating change talk to develop helpful strategies and goals that reflected personal values, and addressing barriers and reducing resistance to change. A non-judgemental clinician approach reduced stigma, and communication was facilitated through the use of Motivational Interviewing techniques.

3.5.1 Motivational Interviewing

Motivational Interviewing (MI) was a communication technique particularly suited to the purpose of supporting opioid dose reduction, as it was developed to overcome unhelpful behaviours related to substance use disorders, initially being used for the treatment of alcohol abuse (Emmons & Rollnick, 2001). MI could be delivered with modest training by a variety of clinical specialties including nurses (Brobeck et al., 2014; Dobber et al., 2019; Miller & Rose, 2009; Vallis et al., 2019). The technique was described by its developers as a `directive, client centred counselling style for eliciting behaviour change by helping clients to explore and resolve ambivalence' (Emmons & Rollnick, 2001, p69). Patient resistance seen as the reverse and a barrier to achieving change was addressed. Clinicians utilising non-judgemental reflective listening choose to 'roll with resistance' rather than create resistance by challenging patient thinking. Patients were encouraged to contrast their personal values and future goals with current behaviours, engage in 'change talk' and initiate their own behavioural change. (Emmons & Rollnick, 2001; Resnicow & McMaster, 2016; Rollnick & Miller, 1995). Rather than clinicians giving expert recommendations, patients were supported to find their own solutions (Emmons & Rollnick, 2001), and the quality of the interaction between the clinician and patient was key to the success of the intervention. Allowing the patient to have a voice and make their own commitment to change was the single most significant component of MI and their ownership of the statement of change meant that they were more likely to achieve the proposed change (Brobeck et al., 2019).

MI could be adapted for use as a brief intervention especially if the intervention was repeated and was suitable for use over the telephone (Emmons & Rollnick, 2001). A popular method of demonstrating readiness to change behaviour was to measure and reflect on how important it was for the individual to make the change and how confident they were of being able to achieve the change (Emmons & Rollnick, 2001; Resnicow & McMaster, 2012). This was scored using a Likert scale. High levels of both importance and confidence are prerequisites to self-driven change (Emmons & Rollnick, 2001). In most chronic condition treatment including opioid dose reduction, behavioural change is the initial outcome sought before clinical treatment goals can be met (Emmons & Rollnick, 2001).

3.5.2 Self-Management in Chronic Health Care

Self-management a shift from passively receiving treatment involved patients actively participating in all aspects of their own healthcare and treatment (Araújo-Soares et al., 2019).

Self-management strategies widely used in chronic care management involved a collaborative partnership between patient and clinician with the clinician providing expert knowledge and the patient taking a hands-on approach to manage day to day care of their own condition (Nicholas & Blyth, 2016). Nurses and allied health professionals with appropriate skills and knowledge, may best deliver self-management education to patients through a group process that included motivational counselling (Harris et al., 2008). Active self-management has proven to be particularly effective in improving patient outcomes in diabetes, heart disease and hypertension (Harris et al., 2008). Encouraging patient participation in aspects of decision making about opioid dose reduction promoted a degree of autonomy and may have led to better acceptance of dose reduction.

3.5.3 Nursing Leadership

Although there is paucity in the literature about nurse led interventions for opioid reduction the discipline of nursing seemed an obvious choice to run a clinical intervention that incorporated both psychological support and medication knowledge. Nurses work within a professional practice framework that includes promotion of safety, evidence-based practice, clinical competency, person centred care, and positive interpersonal communication (Oldland et al., 2019) are well positioned with their knowledge of medication use, effects and administration, to provide this care. Nursing expertise is used extensively in chronic disease management whereby nurses provide education and continuity of care over an extended timeframe developing strong therapeutic relationships (Young et al., 2016). Coming from a background in which compassion and empathy are firmly embedded, nurses are recognised for being approachable and willing to spend time listening to their patients (Young et al., 2016). This allowed patients the time to find their voice, build rapport and share concerns in an open manner while receiving practical and compassionate advice, in the confidence that they would not be judged. As in all chronic healthcare management, holistic, efficacious and low cost care could be provided to people reducing opioid medication by making the paradigm shift from traditional medical specialist driven models of care to greater utilisation of nursing support (Salmond & Echevarria, 2017). A recent Australian study undertaken to determine acceptability and feasibility of prescription opioid reduction in a primary care setting noted the integral role practice nurses played in supporting patients during opioid weaning (White et al., 2021).

3.5.4 Nursing Supported Prescription Opioid Reduction Pathway

With geographical constraints to participation in mind the Nursing Supported Prescription Opioid Reduction Pathway (NS-PORP), was developed to be a pragmatic flexible intervention responsive to the needs of all patients with chronic noncancer pain including those from rural and remote areas. NS-PORP was delivered through two methods. One method constituted a two hour face to face information program `Medication Education and Support group' (MES) held at the hospital campus, followed by scheduled phone-support (NS-PORP1). The other method in a dedicated telehealth format included an introductory phone call followed by scheduled phone support (NS-PORP 2). Both methods were facilitated by a clinical nurse specialist who worked exclusively in pain management. Provision of NS-PORP through both delivery models was expected to provide an adaptable approach, allowing face to face contact for participants who preferred this method, while reducing barriers of access related to distance, time, family commitments and transport issues to other participants.

The intervention consisted of two steps. The introduction at MES for NS-PORP1, or the initial 20-30 minute phone call for NS- PORP2, provided the opportunity to discuss the medication recommendations given previously at the assessment workshop or phone consultation and was a chance for patients to voice their thoughts and concerns. This was followed by scheduled monthly phone calls which provided the opportunity for ongoing weaning support, maintenance of clinical connection and promotion of patient accountability to the weaning regime. The use of MI for communication encouraged participants to explore issues relating to opioid medication reduction through decisional balance methods and promoted self-participation in care. As part of the self-management approach participants were supported to write or contribute to their own opioid reduction plans. Shame and guilt felt about opioid use was addressed while better decision making was facilitated. Physical and psychological withdrawals were discussed and a slow opioid dose reduction was encouraged. Readiness to wean was self-assessed, during the introduction step and at monthly phone contact, by determining how important opioid reduction was to the participant and how confident they were in continuing dose reduction (DiClemente et al., 2004; Rollnick, 1998). Regular importance and confidence scoring allowed participants to monitor their own level of readiness to wean.

Cost is a significant factor in health care provision and may affect availability of a service. It is estimated that about 20% of the Australian population experience CNCP with 16%

prescribed opioid medication each year (Deloitte Access Economics, 2019). There are limited numbers of qualified specialist pain medicine physicians in Australia to support this number of people through opioid deprescribing regimes. Multidisciplinary group programs have been noted to be cost effective compared with ongoing pain specialist consultation in treating pain (EconomicsD.A., 2019) and NS-PORP-1 used the cost saving approach of group program utilisation. In addition by providing brief regular telephone contact, opioid reduction support was able to be spread evenly over the entire twelve months rather than concentrating care into less frequent and more costly face to face appointments.

A pilot study comprising of 14 participants attending three MES groups was conducted, as part of the research study development. Promising results were demonstrated with over half of the participants (57%) reducing opioid dose and a third (36%) progressing to pain treatment group programs. A summary of results from the pilot study are shown in (*Appendix 3)*

3.6 Conceptual Behavioural Change Framework

In order to develop an appropriate intervention to support prescription opioid reduction an understanding of what underpinned the required behavioural change was important. After surveying the range of behavioural change theories relating to improved health care, the Behaviour Change Wheel (Michie et al., 2018) was chosen as the conceptual framework for developing the proposed pathway. The Behaviour Change Wheel showed in a clear and straightforward way the link between personal behaviours and external influences and processes.

Within the hub of the wheel were potential drivers of personal change, the product of an individual's capability, opportunity and motivation to change (Mitchie et al., 2018). These were encircled by a wheel of wider societal or interventional influences which are processes that have the potential to bring about small scale change in the individual. These are in turn enclosed by a circle of overarching policy and legislative measures which enforce change. **See Figure 3.1**.

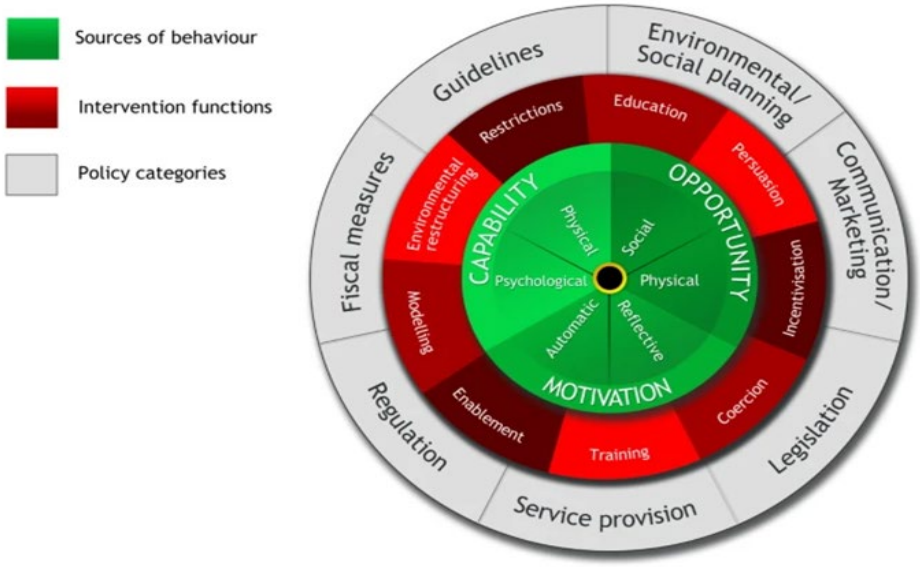
The Behaviour Change Wheel had been successfully tested for reliability on the English Tobacco Control Strategy and was evaluated by the National Institute for Health and Social Care Excellence (NICE) in the UK, (Mitchie et al., 2018). In Australia the underlying mechanisms demonstrated by the Behaviour Change Wheel were evident in policy changes

such as seat belt laws and smoking legislation. Supporting changes in patient behaviour had been a catalyst to improved clinical outcomes in chronic disease management (Araújo-Soares et al., 2019; Mitchie et al., 2018).

Behaviour change starts with pressure from institutions that develop policy, including legislation from state and federal governments, regarding opioid prescribing and dispensing, opioid use guidelines developed by peak expert bodies and the provision of services to monitor prescription opioid use and support prescription opioid reduction. This is represented on the outer wheel and exerts a significant influence on prescription opioid taking behaviour. Represented by the middle wheel, institutions and action at a local level, such as those provided by HIPS, reinforce these policies through recommendations to prescribers and patients. Prescribers were encouraged to restrict provision of prescribed opioids while at the same time education and support were offered to patients to enable the development of new behaviours to facilitate reduction.

The role of NS-PORP was to support personal behaviour change in the individual once laws and policies were enacted and is represented in the inner hub of the wheel (The World of Work Project, 2019). Motivation for the individual to change prescription opioid use was encouraged by information provision and the promotion of self-management. This frequently took the form of decisional balance activities. Capacity to change was facilitated by the delivery of practical information about how to commence prescription opioid reduction and what to expect during the reduction regime, along with ongoing support. The opportunity to change was promoted by the availability of support services and encouragement to develop strategies rather than medication use. NS-PORP utilised flexible delivery means and times which allowed most people including remote participants and those with other commitments to access the intervention and facilitated transition to the next step of pain treatment where active management was promoted.

Figure 3.1. *The Behaviour Change Wheel*



The Behaviour Change Wheel.

Mitchie et al., 2018

3.7 Translational Research Approach

The NS-PORP study utilised a translational research approach to determine if the change in clinical practise was beneficial. Translational research bridges the gap between research purely for the pursuit of knowledge and that targeted to meet a clinical need (Rubio et al., 2010). and is a prioritised form of research for healthcare provision (Mace & Critchfield, 2010). Research in this form encourages collaboration between researchers and clinical organisations, ensuring a more rapid and targeted progression from enquiry to outcome and integration into clinical practice. An observational study design provided a naturalistic rather than experimental view of outcomes (Paterson et al., 2003) by enabling observation of day to day facilitators and barriers to prescription opioid reduction.

3.8 Conclusion

The development of the Nurse Supported Prescription Opioid Reduction Pathway (NS-PORP) arose from the need to support and maintain connection with patients who had completed the assessment phase at HIPS, had chosen to progress to group program pain treatment but were unable to start due to their level of opioid use. The design process included consultation with members of the specialist multidisciplinary pain service (HIPS) team and was informed by current evidence surrounding the use of prescription opioids in the context of CNCP along with

a behavioural change framework. Incorporating a flexible delivery approach NS-PORP a structured nurse led pathway, utilising Motivational Interviewing communication technique, supported self-management principles to educate and support participants reducing prescription opioids. To maintain an evidence-based approach, evaluation of NS-PORP using a prospective cohort study design was the subject of this Higher Research Degree Thesis.

The next Chapter will detail the methods used to conduct the NS-PORP study. This study was a three armed prospective cohort study designed primarily to evaluate if a nurse supported prescription opioid reduction pathway (NS-PORP) enabled participants with chronic non cancer pain (CNCP), attending a specialist multidisciplinary pain service, to reduce opioid dose and continue on to group program pain treatment.

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Chapter 4: Methods for a Prospective Cohort Study

Evaluating the effectiveness of a nurse supported pathway that enables reduction of prescription opioids and entry to treatment for chronic non cancer pain: A prospective cohort study

Chapter Three discussed the development of NS-PORP an intervention designed to enable patients to reduce prescription opioid dose to the threshold needed to enter group program pain treatment. NS-PORP a nurse led intervention using a supported self-management approach and facilitated using motivational interviewing communication is based on behavioural change principles. This Chapter will detail the methods used to conduct a three armed prospective cohort study to evaluate NS-PORP.

4.1 Introduction

The use of prescription opioid medication for CNCP is no longer supported by the majority of clinical expert bodies given the risk of significant harm and lack of sustained benefit. (Dowell et al., 2016). Legislation in Australia reflect this growing body of evidence with opioid prescription restricted for use in this context (Australian Government Department of Health, 2020). While there is evidence to support reduction and cessation of prescription opioid medication, there is a gap in the evidence as to what comprises effective and acceptable support to facilitate opioid dose reduction in patients currently taking prescription opioids.

4.1.1. Aims

The primary aim of this study was to evaluate if a nurse supported prescription opioid reduction pathway (NS-PORP) enabled participants with chronic non cancer pain (CNCP), attending a specialist multidisciplinary pain service, to reduce opioid dose and continue on to group program pain treatment

Secondary aims were to explore participant satisfaction with NS-PORP and a cost estimation of NS-PORP compared to specialist pain medicine physician care.

4.2 Methods

The methods used in this research were reported using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cohort studies (Tricco et al., 2018). A study protocol was written to guide study fidelity, (*Appendix 4).* Currently submitted to Australia and New Zealand Clinical Trials Registry with submission number 382589 for retrospective registration.

4.2.1 Study Design

The study used a prospective cohort design to observe and compare the outcomes from three non-randomised study arms consisting of two treatment arms and one comparator arm. The choice of study design facilitated the observation of a number of outcomes and meant that patients were able to decide which arm they would participate in which ensured that all participants had access to a treatment pathway.

The two concurrent treatment arms consisted of:

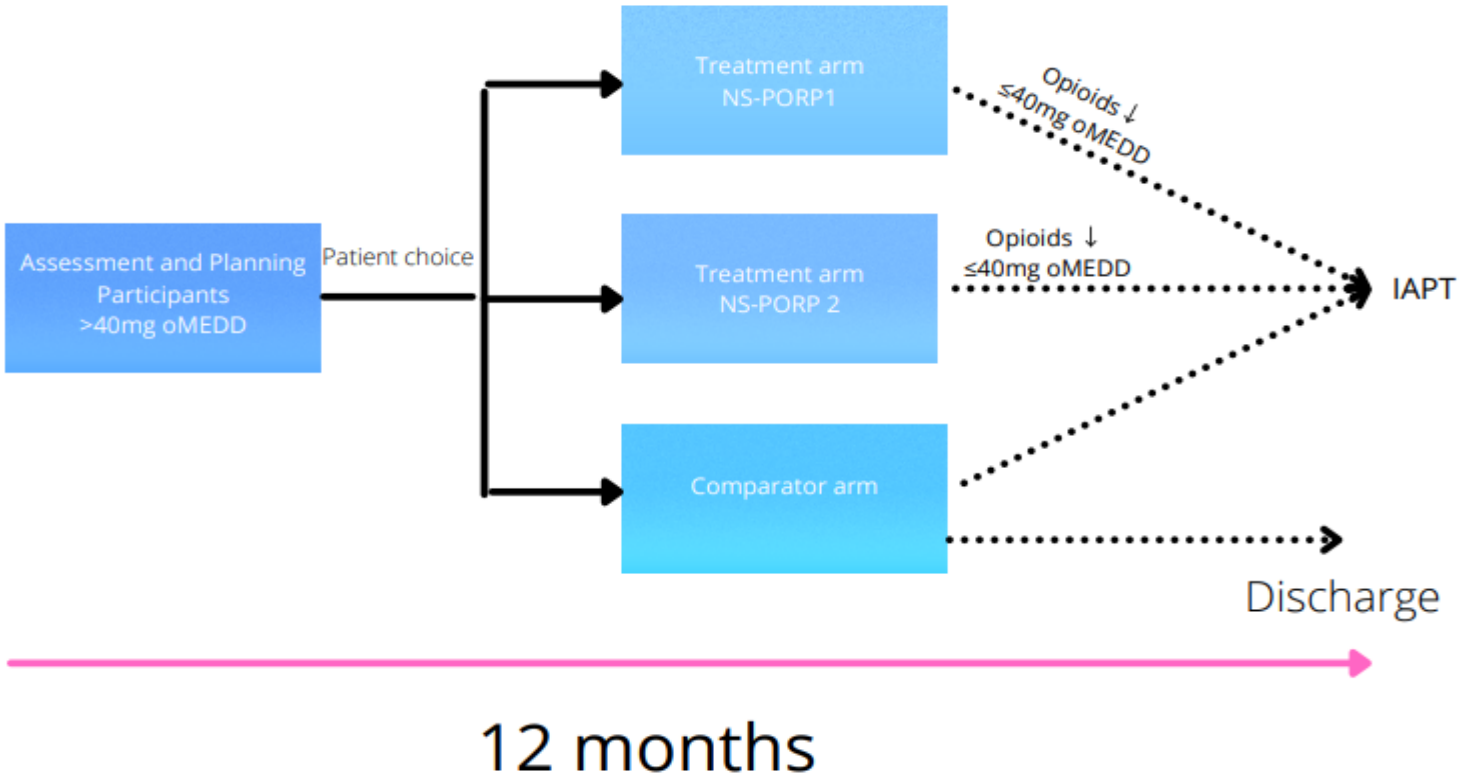
1) "Medication Education and Support (MES) Group" followed by scheduled phone support (NS-PORP-1), or

2) Phone support alone, (NS-PORP-2).

Patients who elected not to enrol in either treatment arm, but who met study eligibility were included in the comparator arm against which outcomes from both treatment arms were compared. The patients in the comparator arm were those who continued with usual treatment either with HIPS care or after discharge with their GP. The prospective cohort study design is illustrated in **Figure 4.1**.

Figure 4.1.

NS-PORP Study Design Diagram



IAPT = Introducing Active Pain Treatment

4.2.2 Study Population

Inclusion Criteria – The study cohort was made up of every consecutive patient aged over 20 years, who had participated in HIPS assessment phase and was identified as taking opioids with oMEDD more than 40mg during the study recruitment time frame.

The treatment arms comprised participants who after assessment, had chosen to progress to group program pain treatment with HIPS and consented to participate in the study.

The comparator arm was made up of participants who had completed the assessment phase and were eligible to participate in the treatment arm of the study by reason of opioid dose but chose not to.

Exclusion Criteria – Excluded from the study were people under the age of twenty years and those over the age of 80 years who ordinarily enter age-specific HIPS specialised pathways. Those concurrently enrolled in an opioid agonist and substitution treatment program were also excluded as HIPS does not provide medication recommendations for this group.

4.2.3 Ethical Considerations

Study approval was granted by Hunter New England Local Health District Human Research Ethics Committee (reference number 2019/ETH11763), and the University of Newcastle human ethics committee. The study was conducted in accordance with the National Statement on the ethical conduct of research involving humans (National Health and Medical Research Council, 2007).

Confidentiality was maintained throughout the study and treatment information including opioid dose was recorded in full only in participants' electronic health record through the password protected `Clinical Applications Portal '(CAP) which is available to authorised HNELHD clinicians. All patient data tabulated for analysis were de-identified and given a study number for use during analysis. De-identified data were stored electronically on a secure password protected HNELHD shared drive and on the University of Newcastle OwnCloud.

The observational nature of the study design meant that the risks associated with the study itself were inherently low. Withdrawal from prescription opioids can be unpleasant but is rarely dangerous (Glare et al., 2020) and information about the signs and symptoms of opioid withdrawal along with mitigation strategies to limit withdrawal symptoms were provided to study participants. Slow opioid reduction was recommended to GPs who were encouraged to contact HIPS for more discussion and support from specialist pain medicine physicians. Study data were primarily collected during clinical contact times to minimise unnecessary demands on research participants, with the exception of a phone call made at the end of the study to treatment and comparator group participants.

4.2.4 Study Setting

This single centre study was undertaken at HIPS, with data collected from September 2019 to June 2021. Referrals for adult patients with CNCP to HIPS were accepted from medical doctors. The primary pathway for adults referred to HIPS, was through three sequential group programs (Rajappa et al., 2019) with the focus of treatment to encourage psychological and

physical pain recovery by using a whole person approach (Rajappa et al., 2019) through behavioural change treatment (Rajappa et al., 2019).

The first group program of the sequential pathway a 90-minute introductory and education seminar `Understanding Pain', presents current knowledge on pain reduction strategies and sets the scene for subsequent education. `Understanding Pain' was directed at people who have been recently referred to HIPS and up to 30 participants were invited to attend each seminar. This was followed by `Assessment and Planning' a five-hour group assessment workshop, presented by a multidisciplinary team (consisting of specialist pain medicine physician, psychologist and physiotherapist), in which participants assessed contributors to their own pain experience and developed a `Whole Person Plan' to guide direction of future treatment. This was a small group program including up to ten participants. Core pain treatment commenced during `Active Pain Treatment', a multidisciplinary led small group program over eight weeks, in which group participants developed and consolidated active skills to aid recovery from chronic pain, through practice during group time. This program was run by a psychologist and physiotherapist with a nursing component to further explore medication use. Introducing `Active Pain Treatment' a one hour individual appointment was held before APT, and conducted by one of the clinicians who delivered the APT group, to discuss expectations and goals before commencing the eight week program. It was organised close to the start of APT and was a mandatary component of the program. If patients wished to continue treatment with HIPS after assessment, while taking an opioid dose over the admission threshold for participation in APT, they were first offered NS-PORP. **Figure 4.2** depicts HIPS Standard Group Program Pathway.

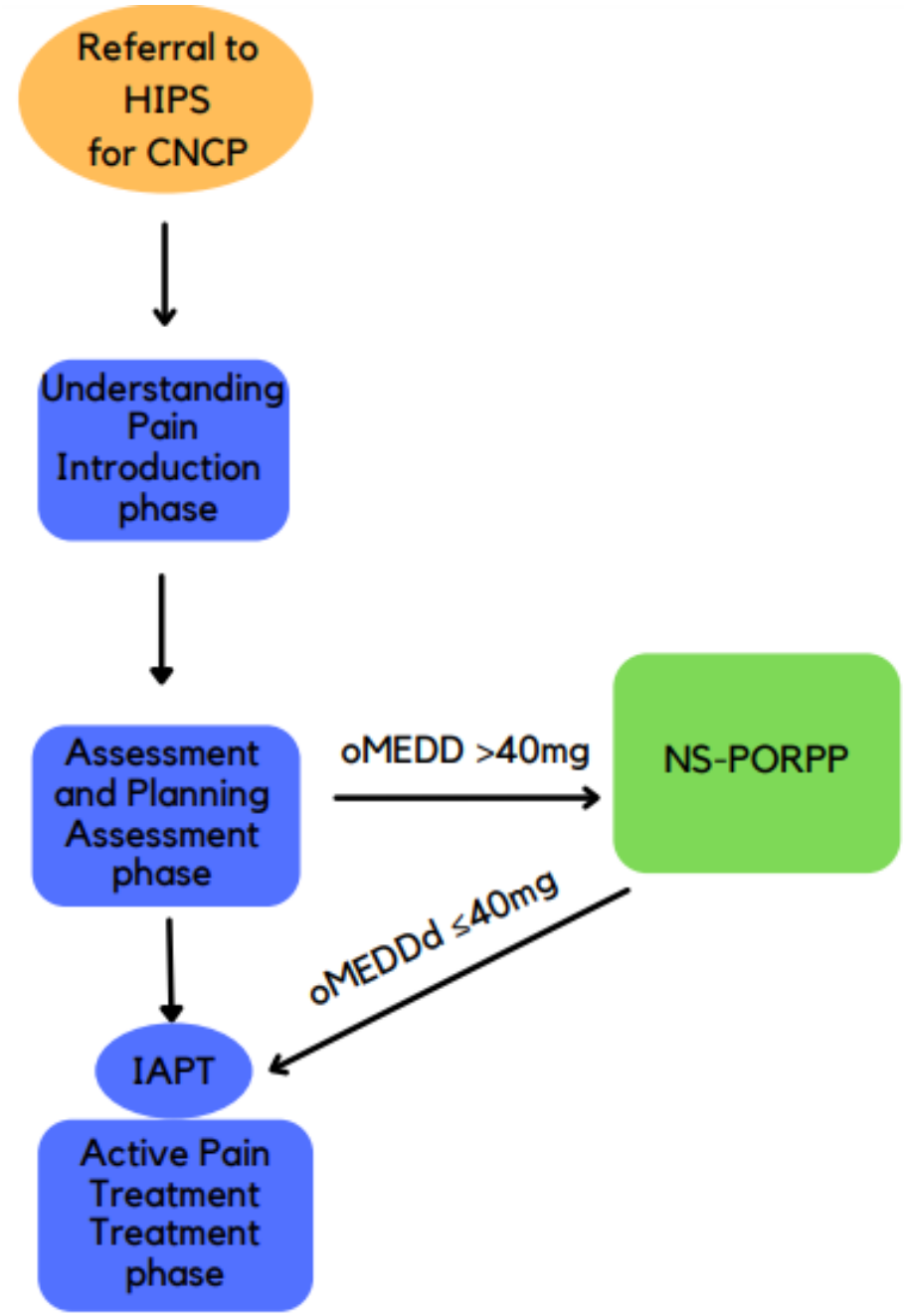
4.2.5 Recruitment and Consent

Participants were recruited during the assessment phase at HIPS. Study information was provided to all patients attending group assessment including those who did not meet the oMEDD criterion to avoid stigmatising or openly identifying patients on high dose opioids. Signed consent forms were collected from individuals participating in both treatment and comparator arms. Clinicians not involved in the pathway provided attendees with a participant information sheet (A*ppendix 6*), offered additional information if required, collected consent forms (*Appendix 7).* They made potential participants aware that aside from ongoing monthly phone contact in the treatment arms a phone call would be made twelve months after the start of the study to either obtain feedback regarding the experience of NS-PORP for those participating in treatment arms or to obtain current opioid dose from those in

the comparator arm. Attendees received standard information and recommendations about prescription opioid medication and their GPs received a letter with standard recommendations to commence a slow opioid dose reduction.

Figure 4.2.

HIPS Standard Group Program Pathway



4.2.6 Study Interventions

The treatment intervention NS-PORP was delivered through one of two methods, either a two hour information program `Medication Education and Support group' (MES) followed by regular phone-support (NS-PORP-1) or phone support alone (NS-PORP-2). Both methods were facilitated by a pain specialist registered nurse (the Candidate) and consisted of two steps. The first step was the introduction at MES (NS-PORP-1) or a 20 to 30 minute introductory telephone call (NS-PORP-2) both of which provided the opportunity for the patient to discuss medication recommendations given at the assessment phase and to provide opioid weaning advice. This was followed by the second step which comprised scheduled telephone calls for ongoing support to facilitate weaning and maintain accountability to the opioid reduction regime. The telephone calls were made monthly to each participant and usually took about fifteen minutes. A flexible approach to patient needs meant that some patients took longer to discuss their concerns, and some had more frequent contact than monthly if requested. The use of Motivational Interviewing (Miller & Rollnick, 2013; Miller & Rose, 2009) by the facilitator (the Candidate) during the face to face group program and phone calls, promoted self-reflection and facilitated supported self-management during the weaning regime.

MES group was broken into two interactive sessions with a brief break in the middle during which participants were able to chat with each other and share their experiences. The first session started with the reasons for HIPS recommendations regarding reduction of prescription opioid medications and information about legislative restrictions then continued with a detailed discussion on possible adverse side effects associated with ongoing opioid use, decreasing benefit as a result of opioid tolerance and opioid induced hyperalgesia. Discussion around the experience of opioid reduction, including withdrawals and how to ameliorate withdrawal symptoms, followed. Participants were encouraged to write notes, weigh up the benefits versus risks of prescription opioid use by using decisional balance methods and discuss any opioid related issues or concerns they had. During the second session participants were given the opportunity to write their own opioid reduction plan or write the next step if they had already commenced reducing opioid medication. Program facilitators assisted with the formulation of plans and participants were encouraged to take the written plan back to their GP for discussion. Importance and confidence scores were rated before and after the program to explore their readiness to wean. The final component of the program was a home task in which participants were encouraged to write a brief note about what their life would look like after ceasing opioid treatment.

The MES group program was manualised to ensure a standardised approach and the manual is included in *Appendix 5*. The telehealth method of introduction followed a similar format and was tailored to address the needs of the individual participant with the rationale for opioid dose reduction recommendations discussed along with the means to facilitate reduction. Participants were encouraged to contribute over the telephone to their own opioid reduction planning. Subsequent monthly phone calls covered general wellbeing, current opioid dose, any problems with the reduction regime including withdrawal symptoms, progress with reduction and importance and confidence levels related to weaning.

4.2.7 Study Variables

Demographics characteristics and clinical variables used as categorical variables for analysis included age, gender, marital status, employment status, distance in travel time from HIPS, and identity as an Aboriginal/Torres Strait Islander, mood measured by DASS (Lovibond & Lovibond, 1995), self-efficacy measured by Patient self-efficacy questionnaire (PSEQ) (Nicholas, 2007) and starting opioid dose. Continuous variables were age in years and opioid dose. A description and where relevant the categories for each of these variables was as follows:
1. Age was collected as a numerical variable at the time of recruitment.

2. Gender was collected as a binary categorical variable of ”Male” or ”Female”.

3. Dose at assessment was a numerical variable related to the patient’s opioid dose at assessment. This was then categorised as less than 40mg oMEDD or equal to greater than 40mg oMEDD

4. Distance from HIPS was a categorical variable of three levels ”Within 30 minutes of HIPS”, ”30-90 minutes from HIPS”, and ”Over 90 minutes from HIPS” and was related to how far away the participant lived in terms of travel (driving) time from HIPS.

5. Depression anxiety stress scale (DASS-21) (Lovibond & Lovibond, 1995) was a numerical variable related to the participant’s score on the DASS-21 scale. The DASS-21 rating measures the negative emotional states of depression, anxiety and stress. It comprises three components. For ease of use in this study the components have been added together into one score which is considered an acceptable way of using DASS-21 for research (UNSW, n.d.). DASS-21 scores greater than 43 are considered to show a moderately high negative emotional state, over 62 a

severely negative emotional state with greater than 85 considered extremely severe (*Appendix 10).*

6. Patient self-efficacy questionnaire (PSEQ) (Nicholas, 2007) was a numerical variable related to the participant's score on the patient self-efficacy questionnaire. PSEQ assesses the confidence an individual has to continue performing activities while in pain. Lower scores are associated with low levels of confidence in dealing with pain and a low functional state, with 20-30 considered a moderate score and lower than 20 severe. (*Appendix 11).*

Baseline demographics were collected from all study participants using data from electronic medical records. DASS 21 (Lovibond & Lovibond, 1995) and PSEQ (Nicholas, 2007) scores were obtained from a pre-assessment questionnaire filled in by all HIPS patients after the introduction seminar.

Further data were collected to explore participants' beliefs and expectations. Importance and confidence ratings were collected using a five point Likert scale, (see A*ppendix 13)* and were recorded for the majority of study participants at the assessment phase (this practice starting in November 2019), then by treatment arm participants at multiple time points when clinically appropriate, starting at the `Medication Education and Support' group or the introductory phone call. NS-PORP-1 participants, during participation in the MES group, were requested to complete a five point `Reduction Influence Questionnaire' which explored reasons for opioid dose reduction. An open ended question also asked them to describe their fears and concerns about stopping prescription opioid medication. These responses were to provide additional information about the study cohort (see *Appendix 14*).

4.2.8 Outcome Measures

The primary outcomes measured were:

1. Opioid dose reduction to ≤ 40mg measured in oMEDD

2. Entry into group program pain treatment

The first opioid dose data point was at attendance to the assessment phase for all study participants. Opioid dose was then collected at monthly intervals by telephone from treatment arm participants when possible. For comparator group participants the final opioid dose was

obtained twelve months after assessment by telephone if they had consented to a phone call or by chart audit. The study endpoint for all participants was when opioid dose reached 40mg oMEDD or under, or at 12 months, whichever came earlier. All opioid doses were converted

to oMEDD for consistency in comparing doses of different types of opioid medication.

Entry into group treatment was measured at entry to `Introducing Active Pain Treatment' (IAPT) which is the initial step of `Active Pain Treatment' (APT). This outcome was identified through an electronic patient record review.

Secondary outcomes measured were:

1. Participant satisfaction with NS-PORP
2. Cost estimation of NS-PORP compared with specialist pain medicine physician treatment

Satisfaction was rated by NS-PORP-1 participants at two time points, after attending the `Medication Education and Support' group, and at the end of the NS-PORP study. Due to time and functional constraints associated with the shorter introduction format, participants of NS-PORP-2 rated satisfaction at the end of the study only. A five point Likert scale was utilised to measure three patient perceptions relating to; the overall benefit or otherwise of NS-PORP in helping opioid dose reduction, how helpful or otherwise the information provided during NS-PORP was, and how helpful or otherwise was the manner of the facilitator delivering NS-PORP. Study participants were invited to respond to two open-ended questions (Questions A. and B.), following NS-PORP, which provided the opportunity to describe in their own words their experience of participating in the study intervention. One question asked how beneficial the participant had found NS-PORP in helping to wean opioid medication**,** and the other explored how the pathway could be improved (see *Appendix 15)*. Self-reported appraisals of the utility of the intervention (NS-PORP 1 and 2) in assisting with opioid dose reduction, as well as suggestions for improvement to the interventions were collected from participants at the completion of the study during individual phone interviews. All individual participant phone interviews were conducted by an independent, experienced researcher who was not otherwise involved in the study, nor responsible for the provision of any clinical services within HIPS. Qualitative data collected during the course of the interviews were transcribed verbatim

by the researcher, with opportunity at the completion of the interview given to participants to revise, edit or delete any responses they did not want recorded.

The estimated cost of implementing NS-PORP-1 and 2 was compared to the estimated cost of biannual specialist pain medicine physician medication reviews which for the purpose of the study was also defined as a pathway. The outcome comprised the cost of the initial appointment and the cost of 12 monthly telephone calls or a subsequent specialist pain medicine physician medication consultation and the estimated cost of specific resources required for that appointment type. A cost estimate of clinician wages was made based on data obtained from the NSW Health website that details clinician remuneration and conditions (NSW Health, n.d.) and was combined with the cost of resources. Resources comprised manpower and stationary used to assemble NS-PORP-1 manuals and was obtained from HIPS administration staff who regularly purchase materials through NSW Health purchasing systems and the cost of telephone and internet usage for the appointments which were estimated by HIPS administration staff.

4.3 Potential Confounding Factors and Biases

Confounding factors, considered a priori, that were likely to influence the opportunity, capability and motivation of study participants to achieve prescription opioid dose reduction related to GPs' willingness to deprescribe and patient acceptance of reduction advice. The greatest leverage to GP deprescribing was likely to have been that of legislation. Changes to legislation in 2020 (Australian Government Department of Health, 2020) and support of this legislation through greater scrutiny of GP prescribing by the Pharmaceutical Regulatory Unit of NSW Health, would have promoted deprescribing during the study period and promoted prescribers' encouragement of patient participation in HIPS interventions. The relationship between prescriber attitude and the degree of opioid reduction was not measured in this study however one of the survey questions in the `Reduction Influence Questionnaire' asked NS-PORP1 participants to rate subjectively what influenced their dose reduction. One of the options they were able to choose was influence from their GP.

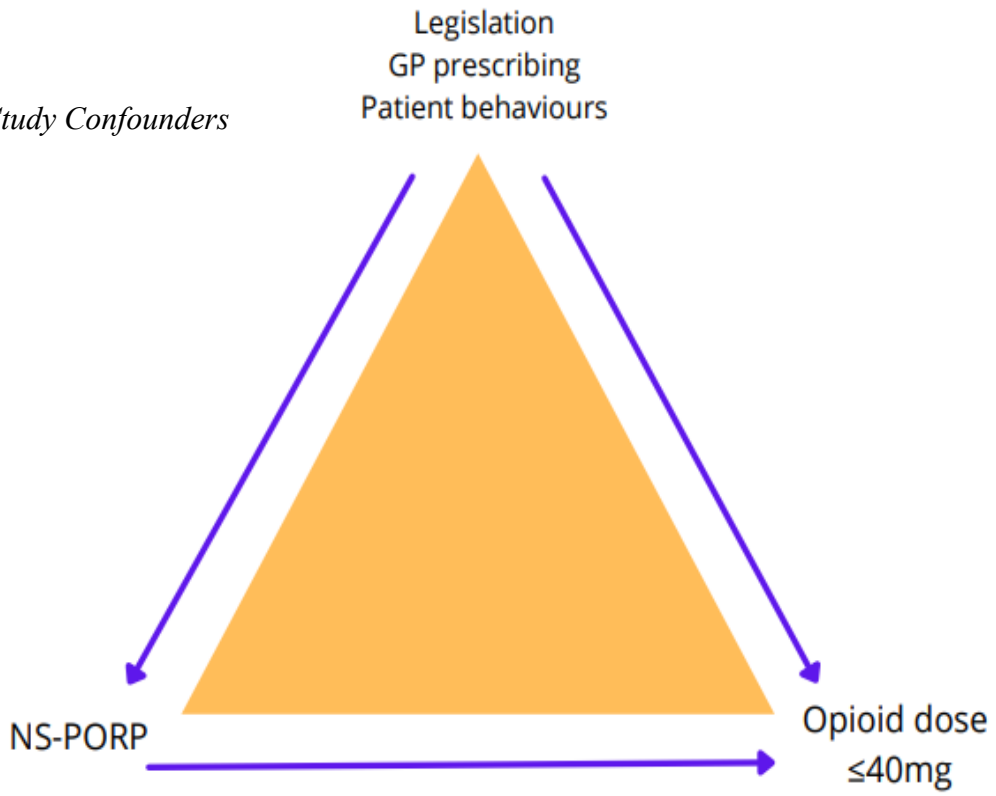
Participant acceptance or otherwise of prescription opioid reduction recommendations influenced whether individuals continued with treatment with HIPS and remained in the study. Individuals who consented to participate in the treatment arm of the study may have previously decided to reduce their opioid dose and this may have affected the generalisation of these

results to the source population. The knowledge of legislative changes may have brought about acceptance of opioid reduction recommendations in otherwise unwilling patients. Variables that potentially affected the study outcomes included confounders of gender, age, marital status, Aboriginal or Torres Strait Islander identity, employment, distance lived from the pain service, DASS-21 score, PSEQ score and opioid dose at assessment. Factors that were associated with possible confounding are highlighted in the discussion chapter. The role of the candidate as both researcher and clinician was a further source of possible bias. This was mitigated in part by utilisation of clinicians not involved with the study to recruit and collect subjective data. In addition the clinician candidate maintained awareness of this conflict and took care to reduce its effect on the study results.

General steps to reduce bias included adherence to STROBE guidelines and the study protocol. Documented variations to the protocol have been included in this chapter. Information bias was addressed by regularly corroborating participant self-report of opioid dose with electronic area health care notes. Loss to follow up was reduced by using telephone contact rather than mail or email communication and by making multiple attempts to telephone study participants.

Figure 4.3

NS-PORP Study Confounders



4.4 Sample Size

Determined a priori and based on the number of patients who were predicted to choose the NS-PORP pathway during the eighteen months of recruitment, the aim was to recruit a total of 120 people with CNCP, using opioid medication into the study. This consisted of 60 participants into one or other of the treatment arms and 60 participants into the comparator arm. Anticipating a 30% withdrawal rate, this number meant that at least 40 people would provide data in each arm.

4.5 Data Analysis Plan

Study data were analysed using both quantitative and qualitative methods. Numerical data were collected on a Microsoft Excel data base, where figures were checked for completeness and accuracy. Statistical analyses were programmed using SAS v9.4 (SAS v9.4 (SAS Institute, Cary, North Carolina, USA).

4.5.1 Primary Outcome Analysis

The association between achieving an opioid dosage of ≤ 40mg and treatment was modelled using univariable logistic regression. Results were reported as odds ratios (OR) and 95% confidence intervals (CIs). Statistically significant odds ratios were those where the 95% CI does not include 1. Propensity scores were then calculated based on the confounders of gender, age, marital status, Aboriginal or Torres Strait Islander identity, employment, distance lived from the pain service, DASS-21 score, PSEQ score and opioid dose at assessment. Propensity scores are a statistical methods approach that helps to reduce selection bias and confounding. Propensity scores in this study estimated the probability that a participant would have received NS-PORP based on their characteristics at commencement of the study

Descriptive statistics regarding participant demographics were created and covered two subset of participants; valid and omitted. Valid participants contributed data regarding opioid dose at two time points whereas omitted participants either did not provide data at the second time point or chose to withdraw from NS-PORP treatment or from the NS-PORP study. Categorical variables were described through frequencies (n (%)) and numerical variables were described through mean, median, min, max, and standard deviation (Mean (SD), Median (Min, Max)).

Opioid dosage reading ≤ 40mg: was a binary categorical variable of levels “Yes” or ”No”. Participants were labelled as ”No” if they did not achieve an opioid dosage reading ≤ 40mg by their last dosage record within the 12 month observation period, and ”Yes” if they did.

The predictors were: Treatment group: which was a binary categorical variable of levels “Control” or “Treatment”. Treatment encompassed the two treatments used in the study, which were combined due to insufficient sample size in one of the treatments.

Results were reported as odds ratios using a 95% confidence interval and with statistical significance set at $p<0.05$. Outlying values were excluded from the analysis as well as participant data which did not include a pre and post intervention opioid dose. In addition opioid dose reduction was reported as a percentage and opioid dose to cessation was reported separately.

Entry into group program pain treatment was measured as a percentage of NS-PORP participants attending IAPT. The number of group program participants ordinarily expected to transition from assessment to treatment groups at the pain service is less than 30%, therefore greater than 30% of study participants being able to start group program pain treatment was considered to be clinically significant.

4.5.2 Secondary Outcome Analysis

Satisfaction with NS-PORP participation was measured using an ordinal Likert scale satisfaction measure. Participants rated three components of the intervention with a score from one to five. Scores from each component were combined to provide an overall score out of a possible maximum of 15. Analysis of the overall score was broken into three categories with participants who scored between three and seven considered unsatisfied with the intervention, eight to 11 considered moderately satisfied and 12 - 15 highly satisfied.

Characteristics of participants who were both satisfied and unsatisfied were described along with the connection between the level of satisfaction and readiness to wean opioid dose.

Qualitative Satisfaction Analysis

Qualitative analysis of Questions A. and B. followed an inductive approach. Participant answers were summarised through a descriptive process. Key words and phrases were

identified and grouped. The grouped data were then organised into categories from which themes were drawn and highlighted. Themes were presented utilising a conceptual map in reference to participant characteristics and described in a narrative summary. Qualitative data related to patient satisfaction associated with NS-PORP pathways 1 and 2 were collated, and aggregated to provide a descriptive summary of responses that coalesced around two themes, perceived helpfulness and unhelpfulness associated with the respective pathways.

NS-PORP Cost Estimation

The cost estimate of NS-PORP-1 and 2 was compared to the cost estimate of biannual specialist pain medicine physician medication reviews. NS-PORP-1 and 2 comprised an initial appointment and 12 subsequent phone calls (one per month for 12 months). Pain medicine physician medication reviews comprised an initial appointment and a subsequent consultation and was defined as a pathway for this outcome. Both initial and subsequent appointments of the three interventions were shown as a separate cost then combined with the resources required for the appointment type and displayed as a pathway cost in a table and described in a narrative summary.

4.5.3 Missing Data

In keeping with the study design, participants were observed interacting with the treatment pathway rather than participating in a controlled experimental process. As such asking specific questions was inappropriate at times and at times participants chose not to respond to questions leaving data missing from some occasions of study contact. Reasons for missing data were reported.

4.6 Alterations to Study Process and Protocol

Due to changed service provision resulting from the COVID-19 pandemic the capacity to provide group program treatment and therefore continue the study as originally planned was significantly affected. Patients with SARS - CoV-2 were receiving care in the co-located tertiary referral hospital in 2020 and restrictions were placed on outpatients and visitors entering the building. Clinical staff working at the hospital were strongly encouraged to consider telehealth options rather than face to face healthcare provision whenever possible.

In keeping with the guidance of reducing risk, face to face group programs were put on hold. To continue service provision and accommodate changing restrictions in response to the evolving pandemic, the HIPS team redesigned the group program pathway to utilise telehealth options, deciding to maintain telehealth as default format of all service delivery until the end of 2020.

A webinar format allowed the introductory seminar to continue with the usual number of participants. The assessment phase was provided through a one hour, joint telephone appointment with two clinicians and the patient, using a modified format based on the usual assessment process. The resource efficiencies of running the assessment component with a number of patients in a group format was lost resulting in more clinician time needed to meet the demand. Clinicians who usually did not routinely participate in assessments were encouraged to undertake assessment phone calls to share the workload, leading to inconsistencies in content delivery and study recruitment. A trial of a video linked format of the treatment group was conducted. This was found to be difficult due to the challenge of implementing a new treatment process and further group treatment programs were postponed until 2021.

Although NS-PORP treatment continued with minimal disruption due to utilisation of the telehealth option, COVID 19 restrictions had a considerable impact on the NS-PORP study. Recruitment was disrupted as the practice of recruiting at the group assessment was affected. In addition observing the varying effect of the two treatment arms was not possible without the face to face component of NS-PORP nor was it possible to demonstrate that NS-PORP had benefit in facilitating entry to group program CNCP treatment. Study recruitment continued despite the change from face-to-face group program assessment to joint telephone consultations in April 2020, with clinicians explaining the study process over the phone using an information guide developed for the purpose (*Appendix 8*). The Participation Information Statement and consent form were mailed to the participant to sign and return after they agreed, over the telephone, to be in the study. Although many people verbally consented no consent forms were returned in a six month period. An amendment to the ethics application was made to obtain verbal consent over the phone rather than by a signed form with approval for this being granted in November 2020.

Up to this point in time only one person had signed a consent form to be included in the comparator group. As the information used in the study was routinely accessible to the

candidate through the electronic health record as part of her clinical role, a further amendment to ethics was submitted requesting that comparator group recruitment proceed without the need for a signed consent form. Approval for this change was obtained in May 2021, whereby, apart from the one participant who had previously consented, a chart audit provided the remaining data for the comparator group.

Group treatment programs recommenced in February 2021. After restarting face to face interventions patient attendance did not return to pre COVID-19 pandemic levels. Fear and uncertainty about contracting the Sars-Cov-2 virus remained, along with an increased familiarity with telehealth options which meant that patients were less willing to attend face to face appointments.

4.7. Study Strengths and Limitations

The advantage of the cohort study design was that a pragmatic real world view of the intervention effect was observed on variable factors and multiple outcomes resulting from the implementation of NS-PORP were measured and evaluated. In addition, all eligible participants who wished to engage with the treatment pathway were able to. The inclusion of both quantitative data and qualitative feedback data meant that not only were objective values measured but subjective participant views were heard. Propensity weighted analysis meant that selection bias and the effect of measured cofounders was reduced and allowed data from every participant to be used for analysis.

Limitations of the study included the inability to draw a causal conclusion that participation in NS-PORP had led to reduced opioid use and increased participation in the subsequent treatment group program although inference was possible. In this study multiple factors affected the power of the study thereby influencing the interpretation and generalisation of findings. These included the small sample size, restricted by the single study setting and the number of participants able to be recruited within the nominated time-frame along with reluctance of some participants to answer the telephone to provide data. Participant self-selection to study groups was another limitation of the study. Although self-selection was likely to decrease representation to the target population it meant that participants were able to choose their own treatment path. This bias was reduced by including all participants who attended the assessment phase at HIPS and met eligibility criteria in the study and the use of weighted propensity analysis to reduce confounding from participant characteristics. In the current legislative

climate where restrictions on opioid prescribing were coming into effect, GPs were likely to encourage all patients to engage with treatment. The characteristics of participants in the treatment groups were similar to those of the comparator group. Lack of blinding of participants or the researcher, a further limitation, was due to blinding being infeasible in a behavioural intervention study. Finally, all quantitative data were collected and stored by the candidate and then were analysed and interpreted by an independent statistician. Similarly, the qualitative data were collected and collated by an experienced researcher who had no responsibility for the provision or evaluation of HIPS clinical services, and all analysis and interpretations derived from the qualitative data were overseen and reviewed by the supervisory team that included experienced qualitative researchers.

4.8 Conclusion

This chapter documented the design and methods of an original, prospective cohort study to evaluate if a nurse supported prescription opioid reduction pathway (NS-PORP) enabled participants with chronic non cancer pain (CNCP), attending a specialist multidisciplinary pain service, to reduce opioid dose and continue on to group program pain treatment. The benefit of implementing NS-PORP was evaluated using the primary goals of prescription opioid reduction and progression to group program pain treatment and supplemented by an exploration of participant satisfaction and an estimation of the cost of NS-PORP in comparison with specialist pain medicine physician consultations

Chapter Four described the methods used in a prospective cohort study to evaluate if a nurse supported prescription opioid reduction pathway (NS-PORP) enabled opioid dose to be reduced sufficiently for participants with chronic non cancer pain (CNCP) to enter pain treatment programs in a multidisciplinary pain service. Participants self-selected either of two treatment arms or a comparator arm to participate in. Secondary outcomes that were evaluated included satisfaction with NS-PORP and a cost estimation of NS-PORP compared to usual treatment. The next Chapter will detail the results from the NS-PORP study including cohort characteristics and primary and secondary outcomes.

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Chapter 5: NS-PORP Study Results

5.1 Introduction

Chapter Four described the methods used to conduct a three armed prospective cohort study. The study evaluated if a nurse supported prescription opioid reduction pathway (NS-PORP) enabled participants with chronic non cancer pain (CNCP), attending a specialist multidisciplinary pain service, to reduce opioid dose to 40mg oMEDD or under and continue on to group program pain treatment. The secondary outcome of participant satisfaction with NS-PORP were explored and an estimation of cost savings described. This Chapter will detail results generated by the NS-PORP study.

5.1.1 Cohort Composition

The three study arms were made up of a cohort of 105 individuals who had attended the assessment phase of HIPS treatment and were identified as taking > 40mg oMEDD prescription opioid medication. A further 31 assessment participants provided consent but were ineligible to be in the study as they did not meet opioid dose eligibility criteria.

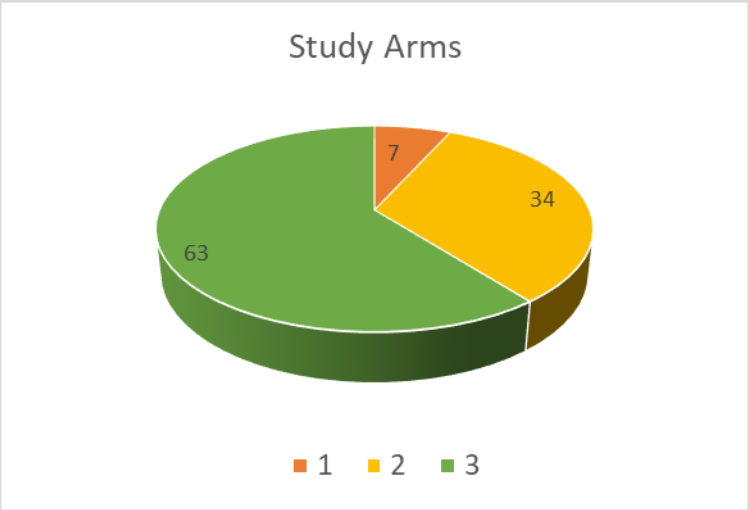
Of the 105 eligible participants who participated in the study cohort, seven participants were recruited into the first treatment arm NS-PORP-1 and 34 into the second treatment arm NS-PORP-2. One participant was recruited into the comparator group and a further 63 participants identified through a chart audit comprised the comparator arm**. Figure 5.1.** demonstrates the comparative sizes of the study arms.

From the treatment arms six participants were omitted from analysis after four withdrew and two were uncontactable despite at least four attempts to make telephone contact. Of the 64 comparator group participants there was insufficient data in the electronic health record to reliably report opioid dose for seven participants at the end of twelve months and these were omitted from analysis.

For the primary outcomes the two treatment arms were combined into one treatment group due to the small NS-PORP-1size. As a result, there were 35 in the treatment group and 57 in the comparator arm. This patient flow is demonstrated in **Figure 5.2**

Figure 5.1

Comparative NS-PORP Study Arm Sizes Diagram, n=104



1 = Treatment -1 arm
2 = Treatment -2 arm
3 = Comparator arm

5.1.2 Cohort Characteristics

Of the analysed cohort of 92, nearly half were female (48%) with 44% female in the comparator group and 54% in the treatment group. The average age was 56 years (SD 14) with the average being 57 years in the comparator group and 55 years in the treatment group, and an age range of 22-78 years. Just over half were married (54%) in both treatment and comparator groups. A significant number of participants identified as indigenous (14%), compared to 6% in the HNELHD population (HNELHD, n.d.) and this characteristic was equally represented in both treatment and comparator groups. A small number had part time employment (6.5%) with less holding full time employment (3.3%).Part time employment was held by 5.3% of comparator group participants with no one holding part time employment in the treatment group. Full time employment was held by 5.3% of the comparator group and 8.6% of the treatment group. In both treatment and comparator groups 54% of participants lived within 30 minutes of the pain service. There were 28% of participants living between 30-90 minutes from the pain service (29% from the treatment group) and 17% living further than 90 minutes from the pain service (18% in the comparator group).

Depression, Anxiety and Stress scores (Lovibond & Lovibond, 1995) indicated that most of the cohort experienced a moderate to highly negative emotional state (52 average and 52 median) with the average being 51 in the comparator group and 52 in the treatment group. Pain Self-Efficacy Questionnaire (Nicholas, 2007) scores were low indicating low self-efficacy (average 19 and median 17) with the average being 19 in the comparator group and 20 in the treatment group. The cohort's average starting opioid dose was 109mg oMEDD with a median dose of 89mg and a range from 42-400mg. In the comparator group the average was 108mg and in the treatment group 111mg. There were no statistically significant differences between groups for any baseline characteristic ($p>0.05$).Baseline socio-demographic and health characteristics of participants in treatment and comparator groups are presented in **Table 5.1.**

Figure 5.2

NS-PORP Study Participant Flow Diagram

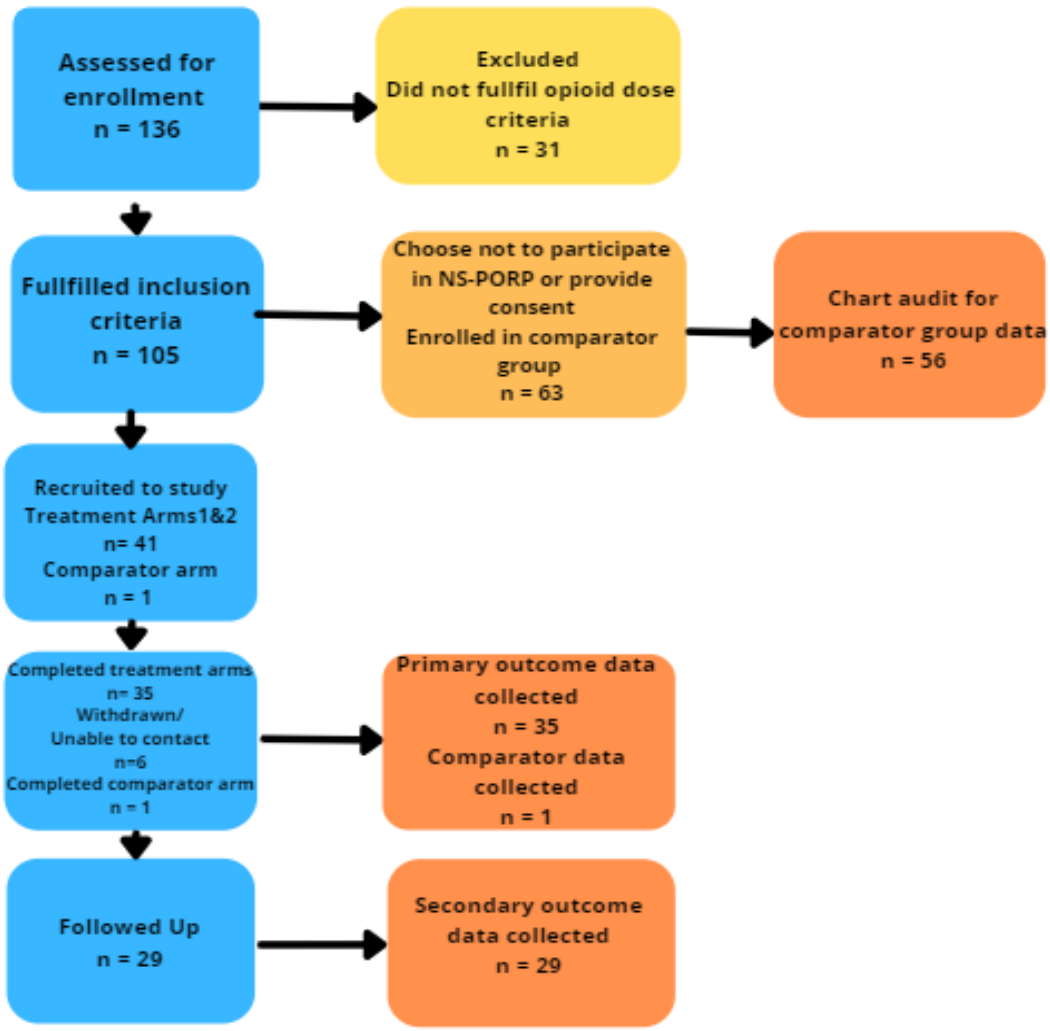


Table 5.1

Cohort Demographics and Clinical Information of study participants

Demographic	Response	Comparator n=57	Treatment n=35	Total n=92	*P* value
Gender	Female	25 (44%)	19 (54%)	44 (48%)	
	Male	32 (56%)	16 (46%)	48 (52%)	.331
Age	Mean (SD)	57 (13)	55 (15)	56 (14)	
	Median (Min, Max)	58 (24,77)	57 (22,78)	57 (22,78)	.501
Marital Status	Married	31 (54%)	19 (54%)	50 (54%)	
	Divorced	6 (11%)	6 (17%)	12 (13%)	
	Single	15 (26%)	7 (20%)	22 (24%)	
	Widowed	5 (8.8%)	3 (8.6%)	8 (8.7%)	.779
Aboriginal or Torres Strait Islander	Yes	8 (14%)	5 (14%)	13 (14%)	
	No	49 (86%)	30 (86%)	79 (86%)	.973
Employment	Part-time	3 (5.3%)	0	3 (3.3%)	
	Full-time	3 (5.3%)	3 (8.6%)	6 (6.5%)	
	Unemployed	51 (89%)	32 (91%)	83 (90%)	.721
Distance	<30 minutes from HIPS	31 (54%)	19 (54%)	50 (54%)	
	30-90 minutes from HIPS	16 (28%)	10 (29%)	26 (28%)	
	>90 minutes from HIPS	10 (18%)	6 (17%)	16 (17%)	.998
DASS 21	Mean (SD)	51 (32)	52 (31)	52 (31)	
	Median (Min,Max)	47 (4,124)	52 (0,116)	52 (0,124)	.883
PSEQ	Mean (SD)	19 (14)	20 (11)	19 (13)	
	Median (Min,Max)	15 (0,57)	18 (2,41)	17 (0,57)	.720
Opioid Dose at Assessment	Mean (SD)	108 (83)	111 (71)	109 (78)	
	Median (Min,Max)	80 (45,400)	101 (42,360)	89 (42,400)	.859

5.2.3 Characteristics of Participants Omitted from Analysis

Study participants who dropped out of study before data analysis (n=13) had a greater likelihood of being female (77%) and this was more pronounced in those omitted from the comparator group (86%). They were marginally younger than the analysed groups, average age 50 years and less than half were married (46%) with less again (29%) of those omitted from the comparator group being married. The number of people who identified as indigenous (85%) was significantly higher than the analysed group. Part time employment was held by similar numbers (14%,) with no omitted participants holding full-time employment.

The starting opioid dose was higher in the omitted population than those who contributed data (122mg oMEDD, SD 110, median 80 with a dose range of 50-420mg) and this was most pronounced in people omitted from the treatment group (135mg, SD 141, median 85 and dose range of 50-420). In both groups average DASS-21 scores indicated a moderate to highly negative emotional state (72, SD 33, median 76 with a range of 4-124) and PSEQ scores were low (17, SD 14, median 10 and range 1-47) indicating low self-efficacy. DASS-21 was more clinically significant in those omitted from the comparator group and PSEQ was more clinically significant in omitted treatment group members. The differences between gender, Indigenous status and DASS-21 scores were statistically significant. Baseline socio-demographic and health characteristics of both cohort and omitted participants in total and according to group are presented in **Table 5.2**

Table 5.2

Demographic and Clinical Information for Participants Omitted from Analysis compared to those included in the analysis

Demographic	Response	Total omitted n=13	Total included n=92	*p* value
Gender	Female	10 (77%)	44 (48%)	
	Male	3 (23%)	48 (52%)	.049
Age	Mean (SD)	50 (8)	56 (14)	
	Median (min, max)	50 (32,62)	57 (22,78)	.135
Marital Status	Married	6 (46%)	50 (54%)	
	Divorced	3 (23%)	12 (13%)	
	Single	4 (31%)	22 (24%)	
	Widowed	0	8 (8.7%)	.810
Aboriginal or Torres Strait Islander	Yes	11 (85%)	13 (14%)	
	No	2 (15%)	79 (86%)	.00001
Employment	Part-time	1 (7.7%)	3 (3.3%)	
	Fulltime	0	6 (6.5%)	
	Unemployed	12 (92%)	83 (90%)	.771
Distance	<30 minutes from HIPS	6 (46%)	50 (54%)	
	30-90 minutes from HIPS	3 (23%)	26 (28%)	
	>90 minutes from HIPS	4 (31%)	16 (17%)	.459
DASS 21	Mean (SD)	72 (33)	52 (31)	
	Median (min, max)	76 (8,124)	52 (0,124)	.033
PSEQ	Mean (SD)	17 (14)	19 (13)	
	Median (min, max)	10 (1,47)	17 (0,57)	.201
Opioid Dose at Assessment	Mean (SD)	122 (110)	109 (78)	
	Median (min, max)	80 (50,420)	89 (42,400)	.595

5.3 Primary Outcome Results

The two primary outcomes were:

1. Prescription Opioid dose reduction to ≤ 40mg oMEDD

2. Entry into pain treatment group program at `Introducing Active Pain Treatment' (IAPT)

5.3.1 Prescription Opioid Dose Reduction to ≤ 40mg Measured in oMEDD

Univariable logistic regression was used to demonstrate the odds of a participant achieving opioid dosage equal to or less than 40mg oMEDD after participating in NS-PORP. The odds ratio, 95% confidence interval and associated p-value, along with the number of observations used in the model are shown in **Table 5.3**

Table 5.3

Univariable Model

Effect	Response	Odds Ratio (95% confidence)		
Group	Comparator	Reference	p- value	Numbers of observations used
	Treatment	2.67 (1.12, 6.34)	0.027	92

The odds ratio represents the odds of NS-PORP treatment group participants achieving an opioid dosage of ≤ 40mg compared against not achieving the dosage level. These odds are compared with the odds of comparator group participants achieving the same level of opioid reduction. Participants in the NS-PORP treatment groups had 2.67 times higher odds of achieving an opioid dosage of ≤40mg when compared to the control group (OR > 1). This is statistically significant with a p-value of 0.027 and a 95% confidence interval of (1.12, 6.34).

Logistic regression with propensity weighting was used to demonstrate the odds of a participant achieving an opioid dosage equal to or less than 40mg oMEDD after participating in NS-PORP and is shown in **Table 5.4.**

Table 5.4 shows the results of the propensity weighted logistic regression on the variables described in the methods chapter and displayed in the previous table.

Table 5.4

Propensity Weighted Univariable Model

Effect	Response	Odds Ratio (95% confidence)		
Group	Comparator	Reference	p-value	Numbers of observations used
	Treatment	3.71 (1.91, 7.21)	<.001	79

Propensity weighting shows that when potential confounders of gender, age, marital status, Aboriginal or Torres Strait Islander identity, employment, distance lived from the pain service, DASS-21 score, PSEQ score and opioid dose at assessment were taken into account NS-PORP participants had an even greater odds of opioid reduction to ≤40mg oMEDD than comparator group participants. The odds of achieving an opioid dosage of ≤40mg is 3.71 with a p-value of <.001. To further contextualise these results, **Table 5.5** shows the proportions of participants who achieved opioid dose reduction to of ≤ 40mg.

Table 5.5

Proportions of Participants achieving opioid dose reduction to ≤ 40mg

Objective	Response	Comparator n=57	Treatment n=35	Total n=92
Opioid dose reduction to ≤ 40mg by the final reading	Did not achieve ≤ 40mg	38 (67%)	15 (43%)	53 (55%)
	Achieved ≤ 40mg	19 (33%)	20 (57%)	39 (42%)
	Missing	0	0	0

Percentage of Participants Reducing Opioid Dose to≤ 40mg oMEDD

Of the treatment group 57% (20) participants achieved the goal of reducing opioid dose to ≤ 40mg oMEDD. In the comparator group 33% (19) achieved the same level of opioid dose reduction.

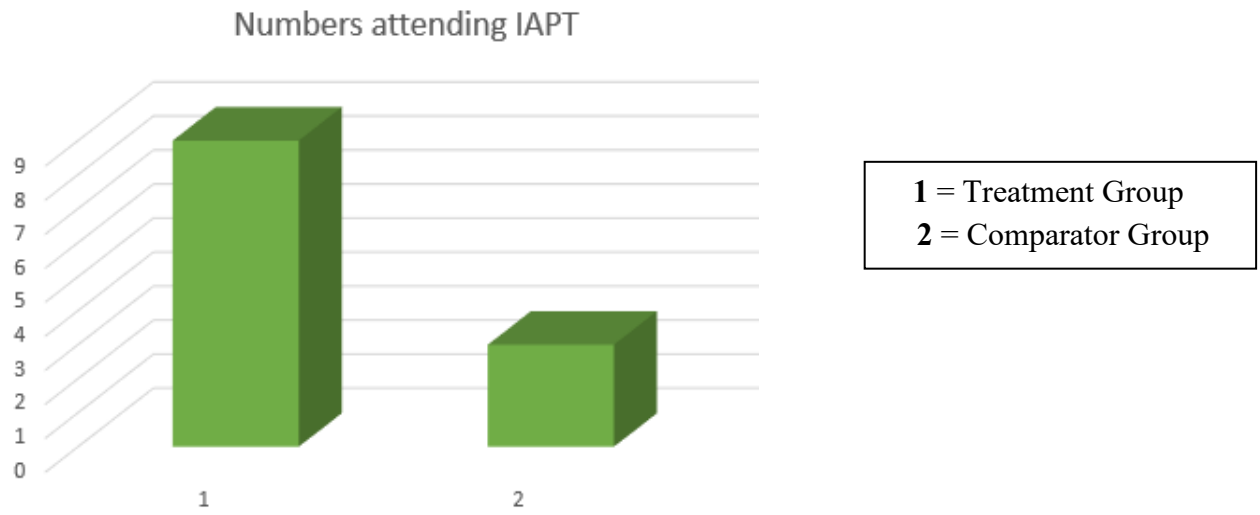
Opioid Reduction to Cessation

A review of the excel data base combined with a retrospective chart audit revealed that at the completion of the study 20% (n=7) of treatment group participants achieved cessation of opioids along with 10.5% (n=6) from the comparator group.

5.3.2 Entry into Pain Treatment Group Program

This was demonstrated by attendance at `Introducing Active Pain Treatment' (IAPT). Of the treatment group cohort nine (26%) attended IAPT. From the comparator group three (5%) commenced IAPT.

Figure 5.3 *Number of Study Participants attending IAPT after NS-PORP*



5.4. Secondary Outcome Results

The two secondary outcomes reported for this study were patient satisfaction and cost savings

1. Participant satisfaction with NS-PORP
2. Cost estimation of NS-PORP compared to specialist pain medicine physician treatment

5.4.1 Satisfaction with NS-PORP

Satisfaction ratings from ordinally ranked survey questions rated satisfaction with three components.

1. Overall helpfulness of NS-PORP in weaning opioid medication
2. Helpfulness of information provided
3. Helpfulness of presenter manner

Satisfaction with Medication Education and Support group was rated by the seven NS-PORP– 1 participants and satisfaction with the NS-PORP pathway was rated by all 29 contactable individuals who participated in both NS-PORP-1 and 2 pathways.

Six of the seven participants who attended the MES group rated the experience as highly satisfying (86% of participants) with the highest rated component being presenter manner. The seventh participant rated their experience as moderately satisfying.

At the end of the study the seven NS-PORP-1 participants remained highly satisfied with the pathway (86%) with the exception of the same individual who was again moderately satisfied. The component that was rated most highly was again presenter manner. On both occasions satisfaction with information received was rated higher than overall helpfulness of the intervention.

Of the remaining 22 NS-PORP-2 participants 68% rated involvement with NS-PORP as highly satisfactory, 18% moderately satisfactory and 14% were unsatisfied. Presenter manner was again the highest scoring component. Overall helpfulness and satisfaction with information were rated equally. Six participants were not able to be contacted after three attempts.

These results are reported in **Table 5.6.** The distribution ratings of satisfaction with NS-

PORP-1 and 2 are represented **Figure 5.4.**

Figure 5.4

NS-PORP Satisfaction Rating Distribution, n=29

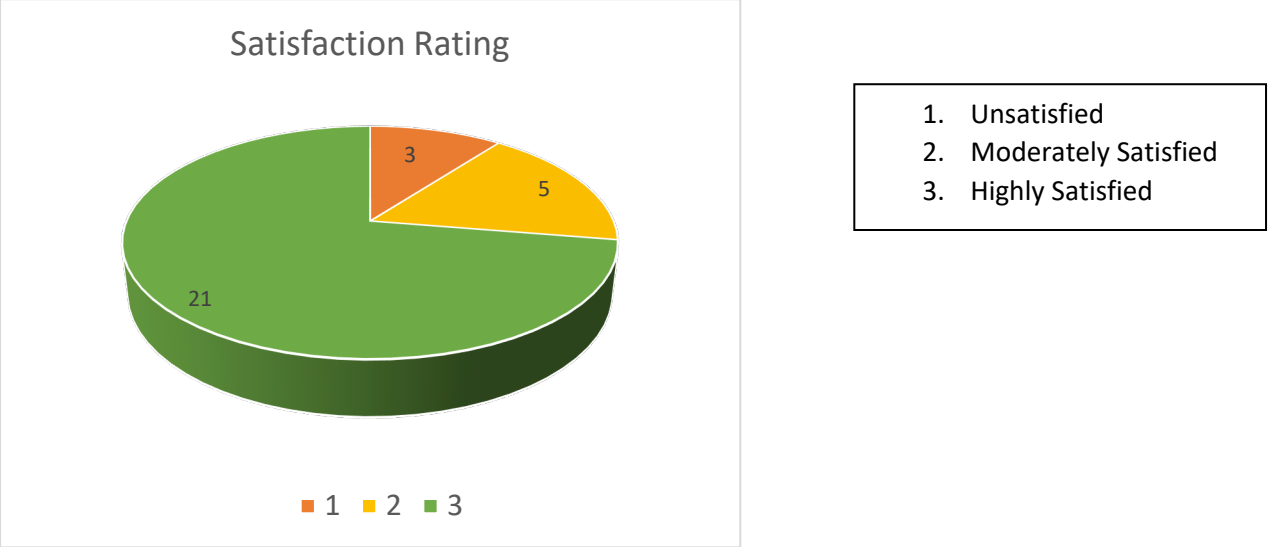


Table 5.6

Participant Satisfaction Ratings following MES group, n=7

Participant ID.	Rating of Helpfulness	Rating of Information	Rating of Presenters	Overall Score
3.	3	4	4	11
6.	5	5	5	15
7.	4	4	4	12
10.	4	4	5	13
12.	5	5	5	15
15.	5	5	5	15
36.	4	4	4	12
Mean Score	4.3	4.4	4.6	13.3

Table 5.7

Participant Satisfaction Ratings following NS-PORP, n=29

Participant No.	Rating of Helpfulness	Rating of Information	Rating of Presenters	Overall Score
3.	1	4	4	9
6.	5	5	5	15
7.	4	4	5	13
10.	5	5	5	15
12.	4	4	4	12
15.	4	4	5	13
36.	5	5	5	15
Average Score	4	4.4	4.7	13.1
1.	1	1	1	3
2.	2	3	5	10
4.	1	1	1	3
8.	5	3	5	13
9.	5	5	5	15
11.	4	5	5	14
13.	5	4	5	14
14.	4	5	5	14
15.	4	4	5	13
17.	1	4	2	7
19.	2	2	4	8
20.	3	3	5	11
21.	4	5	5	14
24.	5	5	5	15
27.	4	4	4	12
28.	5	5	5	15
30.	5	5	5	15
33.	3	5	5	13
34.	4	4	5	13
37	4	5	4	13
39.	5	5	5	15
42	2	4	5	11
Average Score	3.9	3.9	4.1	11.9

Characteristics of Participants Less Satisfied with NS-PORP

Of the eight individuals who reported being unsatisfied or moderately satisfied with NS-PORP-1 and 2, five were female (62.5%), and six were unmarried (75%). Their average DASS-21 score was 60 (median 72) and their average PSEQ score was 16 (median 11.5). Despite being less satisfied with the pathway five of the eight (62.5%) did achieve the primary goal of reducing their opioid dose to ≤ 40mg oMEDD with only one unable to reduce opioid dose at all. Two out of these eight participants then progressed to the next treatment step (25%). This is demonstrated in **Table 5.8.**

In comparison, of the highly satisfied participants (n=21), 15 (79%) were married, DaSS 21 was 44 on average (median 41) indicating better mood than the less satisfied group and PSEQ was on average 23 (median 22) indicating higher self-efficacy than the less satisfied group (2 missing of both DASS-21 and PSEQ scores). Of this group 15 achieved the primary goal of reducing opioid dose to 40mg oMEDD (71.5%) and only one was unable to reduce opioid dose at all. Six individuals progressed to the next treatment step (28.5%).

Table 5.8

Characteristics of Participants Less Satisfied with NS-PORP

Study ID	Gender	Marital Status	DASS-21	PSEQ	Opioid starting dose in oMEDD	Overall Satisfaction Score
1	Male	Single	104	38	105	3
2	Female	Single	98	2	105	10
3	Male	Married	0	No data	300	9
4	Female	Married	46	13	45	3
17	Female	Widowed	72	11	159	7
19	Female	Single	74	7	50	8
20	Male	Single	52	29	60	11
42	Female	Widowed	36	12	60	11

5.4.2 Connection between Satisfaction and Readiness to Wean

Of the 21 participants who rated NS-PORP-1 and 2 as highly satisfactory 13 (62%) reported an increase in importance and confidence scores over the course of their study involvement. Of this group reporting both high satisfaction rating and increased importance and confidence levels eight, (62%) achieved the primary goal of opioid dose reduction to 40mg oMEDD or less with the remaining five participants achieving opioid dose reduction to some level in comparison to starting dose. This is shown in **Table 5.9.**

Table 5.9 *Satisfaction and Importance and Confidence Connection Table*

Study ID	Satisfaction score	Importance score at start	Confidence score at start	Importance score at end	Confidence score at end	Opioid dose reduction
1	3	3	2	4	4	Yes
2	10	Not taken	Not taken	Not taken	Not taken	<40mg
3	9	4	4	4	4	Remained the same
4	3	1	1	5	5	<40mg
6	15	5	5	1	3	<40mg
7	13	2	2	4	3	<40mg
8	13	5	5	3	5	Yes
9	15	Not taken	Not taken	Not taken	Not taken	<40mg
10	15	2	3	1	2	<40mg
11	14	3	3	5	5	Increased
12	12	1	2	1	1	<40mg
13	14	4	5	4	5	<40mg
14	14	2	1	Not taken	Not taken	<40mg
15	13	2	4	5	5	Yes
16	13	1	4	1	2	<40mg
17	7	1	4	4	2	<40mg
19	8	2	2	2	4	<40mg
20	11	2	2	3	2	<40mg
21	14	1	5	2	3	Yes
24	15	3	3	1	2	<40mg
27	12	2	2	2	1	<40mg
28	15	2	2	1	1	Yes
30	15	3	4	1	2	<40mg
33	13	1	2	3	3	<40mg
34	13	2	4	1	1	Yes
36	15	5	5	2	5	<40mg
37	13	3	2	2	2	Yes
39	15	2	3	3	3	Yes
42	11	1	4	3	3	Yes

Highlighted are participants who rated both high satisfaction scores and increased Importance and Confidence levels at completion of NS-PORP

5.4.3 Qualitative Satisfaction Results

Two open ended questions asking what was helpful about NS-PORP and what could be improved in NS-PORP completed the satisfaction assessment. Individual phone interviews were conducted with 29/35 (83%) of participants at the completion of the study. Qualitative responses to the open ended questions were transcribed and categorised utilising an inductive approach to provide insights into what aspects of the treatment pathways participants reported helpful, or otherwise in assisting them to wean opioid. An aggregated descriptive account of participants responses are presented below after responses were transcribed and categorised.

5.4.4 Descriptive Summary

Question A:

Please describe how MES group and phone calls support have helped or not helped with weaning opioid medication.

Data generated from this question about helpfulness were grouped under two headings: helpful and not helpful. Most information collected in response to the question indicated the pathway was helpful in supporting prescription opioid reduction.

Helpful

Support during prescription opioid reduction through NS-PORP was a theme noted to be a helpful factor.

> *Found it helpful, kind, understanding. It was slow and steady but encouraging. Provided a sense of hope that (she) was on the right track ... support helpful* (participant 13)

> *Gave somebody to bounce off. Opportunity to unload – (which he found) helpful* (participant 16)

> *Moral support was helpful* (participant 24)

Support was then broken into subgroups which included the helpfulness of facilitator support specifically and facilitator acknowledgement of other factors in participant's lives when offering opioid reduction support.

> *(The facilitator) – ...fantastic. Anytime called for help, always answered or called back. Understood personnel pressures. Presenters - Couldn't fault, felt understood* (participant 8)

> *(The facilitator*) *was open supportive and friendly* (participant 28)

> *(The facilitator's*) *support was the main thing that was most helpful* (participant 30)

> *Very nice/lovely manner. Just being able to talk to someone was helpful knowing there was someone on my side* (participant 39)

> *Individualised understanding and took into consideration mood and other factors and adapted accordingly* (participant 24)

> *...supportive of mental health as well as pain. Currently facing difficult mental health problems which are the main focus at the moment (*participant 11)

> *It was more than just reduction of medication, there was an understanding that there are more factors at play which may impact ability to decrease medication (*participant 24)

Having individualised support, and maintaining accountability were described as helpful.

> *Individualised understanding and took into consideration mood and other factors and adapted accordingly* (participant 24)

> *Accountability, the accountability helped motivate to stay on track* (participant 42)

The quality and value of the information and recommendations provided was found helpful during prescription opioid reduction as was discussing and developing strategies to reduce pain and support weaning. The benefit of attending MES was noted.

> *MES group education was very helpful as presented in not too technical terms and in a group. Learned about the effects of opioids and other meds on your body and mind (negative side effects especially with long term use. E.g.,. `opioid and function on brain and other organs' – personality etc. Liked `holistic' approach to pain management offered in group session. Positives – Paperwork and notes given helped as not too*

technical – basic info. In group and phone calls (x4), nailed questions asked and offered strategies and support (participant 6)

MES – education, why it's (opioid reduction) important. Wasn't aware/didn't know and found this very helpful. Gained understanding and helped to wean (participant 10)

Also reassurance that more support strategies would be added to compensate (for) the reduction (fearful that wouldn't be given alternative strategies to `cope' but the reassurance decreases this fear) (participant 28)

(The facilitator) had an answer for every question, informative, would go and find the information. Everything was spot on – 10/10 (participant 30)

Also knowing what to expect and how to get to the end of the process (participant 36)

Also given good advice that (she) was happy with (participant 39)

A number of participants reported that they had started to develop strategies based on the recommendations.

Tries everything that is suggested in MES phone calls (participant 33)

Was having bad withdrawals while completing MES and phone support got (him) through. That was the biggest help (participant 36)

Linking the GP with HIPS and into the opioid reduction process was noted as helpful by a number of participants.

Has learnt to negotiate with GP (participant 8)

GP very supportive, proactive and involved, continued the step down .GP – one that put plan in place, and had nil issues with weaning (participant 10)

All good, own doctor more encouraged from participating (participant 12)

Provided feedback to GP (participant 30).

Two participants reported the pathway was helpful but described falling back to taking

medication as a strategy.

Not going too well after steroid injection last week. Has been given additional pain medication. Reluctant to take them but pain is `too bad' (participant 34)

However still had some bad days where he takes some medication (participant 37)

Not helpful

Two participants found that the intervention was not helpful one commented negatively on the regularity of contact and the other preferred support from her own GP during prescription opioid reduction.

... ring regularly, very repetitive. Has reduced medications and improved other lifestyle habits, weight, diabetes but that wasn't enough to be considered for additional support constantly told to decrease Panadeine forte before (she) could consider other options (participant 4)

Hasn't been helpful. Prefers face to face. Doctor taking on this and supporting… (participant 17)

Participants who reported an equivocal appraisal of the intervention where either; still seeking alternative approaches to help manage their pain concerned about the lack of available alternatives offered to manage pain once opioids ceased, or challenged by extraneous issue that precluded them from being able to engage in the intervention.

Several participants described having achieved reduction by themselves without the support of the pathway.

Not sure how to answer. ... been weaning. Previous patient and was weaning then. Time in HIPS much longer than the support phone calls (participant 15)

Had already weaned Targin by the time received phone calls. Did it on own, by herself (participant 2)

Some participants reported ambivalence toward the pathway due to their inability to reduce opioid dose or their hope for an alternate medication treatment.

> *Hard to say one way or the other, good relief going to Sydney for back injections. Difficult to say for sure in terms of what worked or didn't work* (participant 7)

> *Thought about it and realised I was taking too much (opioids). Trying to find something to help. Going to Royal North Shore. Needs to have hope. Looking at medicinal cannabis (has some but hasn't taken it yet). Too expensive through GP but was able to access elsewhere for free (*participant 14)

> *Grateful to be off Targin … that's a good (thing). There's nothing anyone can provide that will help with pain and not be harmful. So yes helped to reduce medication, but no alternative offered or available* (participant 27)

One participant described that external issues led to her ambivalent answer.

> *Issues related to system with healthcare system. GPs etc. HIPS good programs but barriers outside (her) control. Impeded (her) ability to progress with MES* (participant 19)

***Question B*:**

What do you think would improve MES group and phone support?

This second question about improvement revealed whether participants felt NS-PORP could be changed to improve participant benefit. Most responses fell into the categories of those who suggested change, and those who reported change was not necessary.

Suggested changes

A number of participants felt the pathway would benefit from change. Several commented on the benefit that face to face contact would have.

> *COVID, face to face preferred but understand situation. Didn't want to sit at computer on Skype so phone calls were good* (participant 12)

> *Hard to say because COVID-19 interrupted what would have been face to face session. Felt that the pathway was run as best it could be under the circumstances. Ideally would like combination of face to face and phone support* (participant 28)

One hoped alternative (natural) pharmaceutical options would be researched and offered.

> *More research into natural things so people have something that might help. Something to help deal with pain. All doctors against cannabis. Can't afford but if (she) can access, (she) would use it. More open minded to natural therapies… pain specialists and GPs* (participant 10)

Another hoped for better liaison between HIPS and their GP.

> *No. Would be good to have better communication/understanding between HIPS and*
>
> *GP – make things easier…* (participant 33)

The final comment suggesting change was directed at improving communication from the facilitator.

> *Listen, be more considerate and open with options available. Take notes and reflect before calling to prevent going in circles* (participant 4)

No change

The majority of respondents expressed that there was no need to change the pathway with a number reiterating the benefit they experienced from participating in the pathway or affirming satisfaction with the pathway.

> *…was sceptical at first but now convinced and living better life and improved function without opioids. No improvements needed for MES or phone contact* (participant 6)
>
> *Not off top of head was helpful, pretty happy with all. (The facilitator) was very good* (participant 7)
>
> *No everything was great* (participant 8)
>
> *No (The facilitator) has been really good* (participant 15)

> *Advise was given in a gentle encouraging way rather than a directive way. Appreciated ability to adapt style and approach based on how he was feeling at the time of the calls* (participant 24)

> *It was all very straightforward and helpful. Big thank you* (participant 36)

Several participants reiterated the benefit of the flexible delivery approach.

> *No – it was good not having to continually travel to Newcastle* (participant 30)

> *Wants to come to HIPS face to face after COVID (from Dubbo). Feels that would be helpful* (participant 33)

> *No- everything was fine. Does prefer phone as it saves a trip to the hospital. Participating in face to face groups is difficult so sitting and talking is easier to do at home* (participant 37)

Participant 17 reported the pathway was unhelpful in first question but responded to this question by saying that she *appreciates support* (from HIPS).

Several participants were unable to clearly describe whether they felt the pathway would benefit from change or not and a further group of participants suggested no change with ambiguous language. *No, not really, nothing really* (participant 1), *No not really* (participant 3), *No not really* (participant16), *No not really. Not interested at this stage* (participant 17), and *No - it was helpful but still in a lot of pain. Specialist appointment 6/7 for bulging disc and queried hip injury* (participant 27).

> *Nothing that was unhelpful* (participant 19)

> *No not really, can't think off the top of (her) head* (participant11)

5.4.4 Unrelated Responses

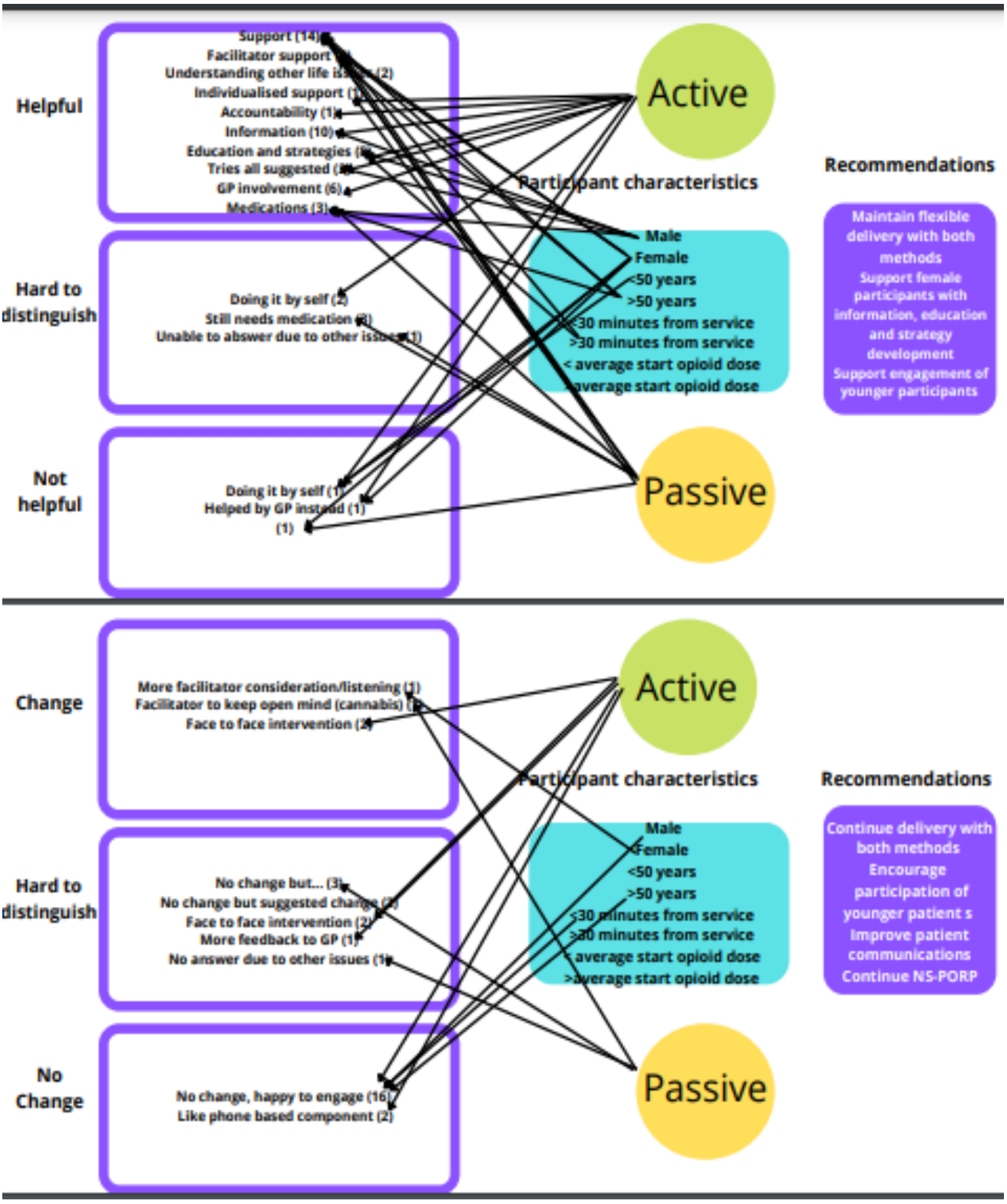
A number of participants related concern about issues other than the question topics. The most common unrelated issue that came up in the interviews, was that of difficulty with, or of accessing other health services. This was reported by four participants and comprised concerns

such as not being believed, insensitivity of clinicians as well as lack of support and provision of services in non-metropolitan areas.

The responses to the questions asked were tabled alongside participant characteristics and common themes in the data were noted. (*Appendix 14).* Key ideas and themes were mapped to show association. **Figure 5.5**

Figure 5.5

Qualitative Data Categorisation Map



5.4.5 Helpfulness of NS-PORP and Suggestions for Change

The multidimensional nature of patient experience and expectation meant that participants had many thoughts regarding the benefit of NS-PORP along with suggestions for change. Many participants expressed multiple ideas which were coded as separate themes. Although the sample size was small and limited interpretation could be made from the findings, trends did emerge.

The majority of responses rating support as a helpful component of the pathway came from females (9 out of 14 responses), those over 50 years of age (12 out of 14 responses) and those living more than 30 minutes from the pain service (9 out of 14 responses). Facilitator support was rated as helpful predominantly in responses by females (6 out of 9), those over 50 years of age (9 out of 9 responses), and those participants on higher than average starting opioid dose (6 out of 9 responses). Information provision on the other hand was more likely to be found helpful by males (6 out of 9 responses) and from participants with a lower than average starting opioid dose (8 out of 9 responses). The discussion and development of strategies to replace opioid medication was rated more helpful by participants who lived more than 30 minutes from the pain service (5 out of 8 responses). The two participants who reported having already used the opioid reduction strategies suggested during NS-PORP were both male, over the age of 50 who lived more than 90 min from the pain service.

Participants who described the pathway as helpful but expressed the need for additional medication or alternate forms of medication were all male (3 out of 3 responses) and over the age of 50 (3 out of 3 responses). In contrast participants who reported that the pathway was not helpful were all female (3 out of 3 responses) and most were younger than 50 years (2 out of 3 responses) and lived within 90 minutes of the pain service (3 out of 3 responses).

The majority of responses suggesting that the pathway did not need to change came from males (10 out of 16 responses), most were over the age of 50 (14 out of 16 responses) and most lived more than 30 minutes from the pain service (10 out of 16 responses). Responses to change the pathway came mostly from females (2 out of 3).

A large number of participants did not actually give an answer that could be categorised as indicating helpfulness or not from NS-PORP or suggesting change or not to NS-PORP (8 respondents to each question), and a number of answers to the second question contained language or sentence structure that indicated hesitancy or reluctance to answer the question.

5.4.6 Active and Passive Thinking

Participants offering ideas of what was helpful or otherwise from NS-PORP included both active and passive thoughts. Active thinking was around what a participant could take on themselves whereas passive thinking was around what another person or element could facilitate.

An active focus included finding information provided to be helpful, noting benefit from group programs, attempting strategies themselves, taking on accountability, finding individualised support useful and reporting GP involvement as helpful. The distinguishing characteristics of participants making these responses were that most were males (20 out of 31) and on a lower than average opioid dose (24 out of 32 responses).

A passive focus on the other hand included finding support alone helpful, including specifically facilitator support and hoping for additional or alternate medication. The distinguishing characteristics of this group were that the majority of responses came from participants over the age of 50 years (28 out of 31 responses) and most response came from participants who lived more than 30 minutes from the pain service (18 out of 22 responses).

Changes to NS-PORP that included active suggestions were the provision of face to face appointments as well as telephone options designed to make engagement and attendance easier and GP involvement with the reduction pathway.

Responses that reported NS-PORP did not require change and indicated willingness to engage with the pathway or appreciation with what was offered were considered to demonstrate an active focus. Most responses came from males (12 out of 19 responses), participants who were older than 50 (17 out of 19 responses) and most responses were from individuals on less than average opioid dose (13 out of 19 responses).

Looking at individual participant data showed that ten individuals were more likely to find active strategies helpful and to suggest active changes, rather than passive. These participants were more likely to rate feeling highly satisfied with the intervention (9 out of 10 participants) and more likely to achieve the goal of opioid reduction to 40mg oMEDD (9 out of 10 participants). A larger number of these participants were male (7 out of 10 participants), had a lower starting opioid dose (7 out of 10 participants) and were over 50 years of age (7 out of 10 participants).

Table 5.10 shows the number of active and passive strategies that participants reported as helpful and suggested as changes to NS-PORP.

Table 5.10

Connection between Active and Passive Focus and Satisfaction

Study ID	Gender	Distance < / > 30 minutes	Starting Opioid Dose < / > Average	< / > 50 Years	Number of Active Suggestions	Number of Passive Suggestions	Satisfaction	Opioid Dose Reduction Goal
1	M	>	<	>	0	2	3	No
2	F	<	<	>	1	2	10	Yes
3	M	>	>	>	0	2	9	No
4	F	<	<	<	1	4	3	Yes
6	M	>	<	>	3	1	15	Yes
7	M	>	<	>	1	1	13	Yes
8	M	>	>	>	4	1	13	No
9	F	<	<	<	3	1	15	Yes
10	F	<	<	<	3	2	15	Yes
11	F	>	<	>	1	3	14	No
12	M	<	<	>	3	0	12	Yes
13	F	<	<	<	1	1	14	Yes
14	F	>	>	>	0	2	14	Yes
15	M	<	>	<	2	0	13	No
16	M	>	>	>	0	3	13	Yes
17	F	>	>	>	1	1	7	Yes
19	F	>	<	<	0	2	8	Yes
20	M	<	>	<	2	0	11	Yes
21	F	>	>	>	2	2	14	No
24	M	<	<	>	2	1	15	Yes
27	M	>	<	>	0	2	12	Yes
28	F	<	>	>	2	2	15	No
30	F	>	>	>	3	2	15	Yes
33	M	>	<	>	5	1	13	Yes
34	M	>	>	>	2	3	13	No
36	M	>	<	>	4	0	15	Yes
37	M	<	<	>	1	2	13	No
39	F	<	<	>	2	2	15	Yes
42	F	>	<	>	2	2	11	No

Shaded areas demonstrate participants who responded with greater numbers of active strategies than passive.

5.5 Cost Estimation of NS-PORP

The estimated cost of NS-PORP-1 and 2 pathways were compared with the estimated cost of biannual specialist medicine pain physician appointments which was defined as a pathway for the study.

NS-PORP-1 comprised MES group which was held for two hours and had a minimum of 4 participants, followed by x12, 15minute telephone calls plus the resources (stationary telephone and internet use) to facilitate all appointment in the pathway and cost $172.90 for the year.

NS-PORP-2 cost marginally less for an initial 30 minute phone followed by x12, 15minute telephone calls and the resources for both at $170.60 for the year.

The cost of x 2 one hour consultations either face to face or through telehealth with a specialist pain medicine physician plus resources to facilitate appointments cost $197.44 for the year.

The cost of the pathways were measured in Australian dollars and are demonstrated in **Table 5.11**

Table 5.11
Cost Comparison Table (costs in Australian dollars)

	Hourly clinician pay rate	**Number of participants possible in initial appointment**	**Cost of resources**	**Cost of initial appointment**	**Cost of subsequent appointments**	**Cost per pathway**
NS-PORP 1	48.40/hr	4	4.50	24.20/person	12.10	173.90/ Person
NS- PORP 2	48.40/hr	1	2.00	24.20	12.10	171.60
Specialist Pain Medicine Physician appointment	98.72/hr	1	1.00	98.44	98.44	197.44

(Wage Data Source: NSW Health, n.d.)

5.6 Reduction Influence Summary

This data revealed factors that participants felt influenced their individual opioid dose reduction. A total of nine participants completed the reduction influence survey. Seven were NS-PORP-1 participants providing the information during MES groups. Two were NS-PORP-2 participants who were canvassed for information during the initial telephone call. For most participants it was felt that collecting this amount of extra data over the telephone would interfere with the clinical application of the telephone call as it was time consuming and challenging to administer over the phone.

All but one participant surveyed reported long standing chronic pain over at least five years duration. Over half (5) described having increased their prescription opioid dose in that time and four reported a decrease in dose. Most (7) participants described their current opioid dose reduction as being for health or personal reasons and all reported significant involvement in that decision. Varying levels of support during the reduction were reported with the majority (5) reporting considerable amounts of support. These results are shown in **Table 5.12**

Table 5.12

Reduction Influences

Study ID.	Length of time I have taken opioid medication	In that time the dose I am taking has	My reason for weaning or considering weaning	How involved am I in the decision to wean	How much support I have in weaning
3.	>10 years	Increased moderately	Government regulations	A fair amount	A fair amount
6.	>10 years	Increased moderately	Personnel	Very much	Moderate amount
7.	>10 years	Reduced	Personnel	Very much	Considerable amount
10.	>10 years	Increased moderately	Not answered	A fair amount	A little
12.	>10 years	Reduced	Health	Very much	Considerable amount
15.	>10 years	Reduced	Health	Very much	Considerable amount
36.	5-10 years	Increased moderately	Health	Very much	Considerable amount
24.	1-2 years	Reduced	Health	A fair amount	A fair amount
28.	5-10 years	Increased moderately	Health	A fair amount	Considerable amount

This group of participants were also asked the open-ended question

What are your fears and concerns about getting off opioid medication?

***** One participant (28) felt she had nothing to say about concerns and declined to answer the question. A number responded with concern about increased pain without opioid medication including:

`That I can live with no pain' (participant 3.)

`Pain. Life not being liveable. Not being able to function' (participant 10)

`Increasing pain' (participant 15)

More than half the group, however, either rejected this concern or indicated they were not getting benefit from the medication anyway.

`No fear if there is a better method of controlling the pain, I will use opioid medications if needed. The side effects are of major concerns as they are disproportionate.' (participant 6)

`None' (participant 7)

`At the start if the pain would persist. However, the pain appears to be the same as when I was on the large dose' (participant 12)

`I am taking a pragmatic approach to opiate meds. My opiates started with L1/L2 displacement. I am now in a better situation with no Endone and only Fentanyl. I am optimistic to be free of any meds hopefully by the end of the year' (participant 24)

Concern about both staying on and reducing opioid medication was nominated by one participant who simply wrote:

`Withdrawal symptoms. Dependency'(participant 36)

5.7 Conclusion

Chapter Five described the results from the NS-PORP Study. Propensity analysis weighting demonstrated that NS-PORP participants had a greater odds of reducing prescription opioid dose to the threshold for participation in group program pain treatment than the comparator group (OR 2.67, 95% CI1.12,6.34,with a p-value of 0.27.) Weighting with propensity scoring meant that the odds of achieving opioid reduction were greater again when compared to the comparator group (OR 3.71C1.91,7.21, p=< .001.) This meant that 57% of the treatment group compared with 33% of the comparator group reduced opioid dose to ≤ 40mg oMEDD. A

greater number of study participants (26%) commenced group program pain treatment following NS-PORP participation than from the comparator group (5%). Satisfaction with NS-PORP was explored with most participants reporting they were highly satisfied (73%), most found NS-PORP helpful and did not suggest changing the pathway. Satisfaction with NS-PORP appeared to be linked with the development of active and passive participant thinking regarding opioid dose reduction. The estimated cost of conducting NS-PORP was less than usual treatment with specialist pain medicine physician consultations.

The next Chapter discusses the results from Chapter 5 with reference to the findings of previous studies, reviews the study limitations and provides recommendations for future research, policy and clinical practice

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Chapter 6: Discussion

Chapter Five described the results from the NS-PORP study including propensity weighted analysis which demonstrated that participants of NS-PORP had higher odds of achieving the primary outcomes. Of the treatment group 57% reduced opioid dose to ≤ 40mg oMEDD, compared with 33% of the comparator group (p=.001). A higher percentage of participants in the treatment group compared to the comparator group entered group program pain treatment (26% vs 5%). Most participants in the treatment group reported high satisfaction (73%) and the multidimensional nature of patient experiences were explored in detail. Potential cost savings in terms of clinician and resource usage was estimated.

6.1 Introduction

This Chapter will discuss emerging evidence from the results with reference to previous studies. Along with study benefits and limitations, and the implications of the findings and recommendations for clinical practice policy development and future research will be discussed.

6.2 Nurse Supported Prescription Opioid Reduction Pathway

6.2.1 NS-PORP Development

Conceived through a specialist multidisciplinary pain team consultation process, behavioural change was identified as an effective means of achieving opioid dose reduction along with Motivational Interviewing as a method of engaging participants in their own self-care. The two-step process of introduction followed by regular brief supportive telephone contact provided the opportunity to develop rapport and trust before commencing a longer therapeutic relationship. The pathway continued for 12 months in order to support the recommendation for a slow reduction. This encouraged amelioration of withdrawals and associated discomfort and promoted success in dose reduction. Patients who may otherwise have become disconnected from HIPS were facilitated to remain engaged as was enablement of participants who ordinarily would be unable to attend treatment due to distance, personnel commitments, or ill health.

6.2.2 NS-PORP Evaluation

The study aimed to evaluate if NS-PORP enabled participants with chronic non cancer pain (CNCP), attending a specialist multidisciplinary pain service, to reduce opioid dose and continue on to group program pain treatment. Participant acceptability and economic feasibility, pivotal to the potential implementation of NS-PORP in either a specialist multidisciplinary pain service or primary care setting was explored. The study aims were addressed using a prospective cohort design with outcomes that met service treatment goals while remaining relevant to the patient. The complex behavioural presentation that is associated with prescription opioid use and its reduction drove the need for a patient centred intervention to support prescription opioid reduction. An observational study design provided the opportunity for study participants to engage in treatment if they wished.

6.3 Complex Patient and Prescriber Behaviours with Prescription Opioid Use and Reduction

The need for a patient-centred flexible intervention to support prescription opioid reduction is best understood in the context of the complexities of chronic opioid use and the significant challenges associated with opioid dose reduction. Fear of unresolved long term pain is a powerful driver (Crofford, 2015) and leads many people experiencing CNCP to explore every option of potential pain relief including opioids. The use of prescription opioids may start as a way to treat pain associated with tissue damage but, if pain continues beyond the tissue healing time of three months, may become chronic, and opioids then become a way to numb uncomfortable emotions such as fear, despair and grief (Darnall, 2014). Acknowledging and explaining these emotions to others is often difficult and stigmatising, (Barney et al., 2006; Yokoya et al.,2018). Discussing bodily discomfort and pain may be easier and provides a legitimate reason to continue taking opioid medication (Sheng et al., 2017). The use of regular medication to manage daily CNCP may correspond with patient and societal expectations. These include the use of medical modalities to resolve health issues (El-Haddad et al., 2020; Hart, 1998; " Sharma et al., 2021) even those best addressed through lifestyle choices (Australian Journal for General Practitioners, 2016) and the hope that pain will be abolished entirely by a biomedical means (Tompkins, Hobelmann, & Compton, 2017). Many patients cling to the ongoing prescription of opioids not just to avoid the physical and psychological

effects of withdrawal but because they are unable to envisage any other way to deal with unrelenting pain that cannot be explained after tissue healing.

GPs may continue prescribing opioids for CNCP despite the poor evidence base. This is related to multiple factors including pressure from patients, perceived difficulty in accessing alternative treatments and their own beliefs around potential worsening of pain with opioid reduction. A study of GP attitudes to prescribing opioids for CNCP suggested that most (nearly 80%) GPs surveyed in a local health district in Australia were reluctant to deprescribe when they perceived alternate treatments were lacking and many were influenced in their decision by patient factors such as fear of weaning (White et al., 2020).

6.3.1 Influence of Legislative Changes to Prescribing

In Australia, legislation at both state and federal levels has restricted the prescription of opioid medication. Recent federal legislative reforms included upscheduling codeine, (Therapeutic Goods Administration, 2018), reducing the amount of rapid release opioid formulations per prescription and mandating a second medical opinion for ongoing opioid prescription beyond three months for CNCP (Therapeutic Goods Administration, 2021). Authority to prescribe may also be required by NSW Health (NSW Health, n.d.). The full implication of these recent changes on GP prescribing decisions, is not yet evident but will be challenging as was evident in the US (Kroenke et al., 2019) after the release of opioid prescribing guidelines by the Centre for Disease Control and Prevention (Dowell et al., 2016). The impact of overarching legislation decisions as theorised by Mitchie, (2018) was likely to have influenced local prescriber decisions regarding provision or otherwise of opioids and would have forced patients to consider their own personal drivers of capability and motivation to make behavioural changes regarding opioid use. Preventing the initiation of opioid prescription would likely have been more accepted and led to greater societal behavioural change than reducing prescribing to existing patients.

6.3.2 Sense of Injustice about Forced Reduction

Many patients already established on prescription opioid treatment felt a sense of injustice regarding the change in legislation and recommendations, having had prescription opioids sanctioned and provided through legal prescription from a medical practitioner, some for many years. GPs also, conflicted about their role in deprescribing, (Kroenke et al., 2019) may have

continued to prescribe opioids while inadvertently adding to patients feelings of being judged as drug seeking through discussions about opioid safety and the need for reduction (Mathias et al., 2017). Identifying the primary problem of opioid dependence and transitioning to a drug and alcohol pathway and treatment with opioid agonist treatment (Nosyk et al., 2015) would have provided secure opioid prescription but was usually considered unacceptable to people with CNCP who saw themselves as distinctly different to illegal opioids users. Concern with stigma, (Ghosh et al., 2021) contact with illicit drug users, cost and difficulty accessing these services were cited as reasons to continue obtaining prescriptions from their GP (Jones et al., 2021; Prathivadi et al., 2021). Whether prescribers elected to commence a reduction regime or supported patients to transition to alternate opioid treatments, seeking consent and involving patients in planning was likely to have caused less apprehension and led to better tolerance of the proposed changes.

6.4. The Study Cohort

The baseline characteristics of NS-PORP study participants including age, gender, marital status and employment rates were similar to those reported in previous studies (Kurita et al., 2018; Zheng et al., 2007; Goodman et al., 2018). Of the NS-PORP study cohort a small number of notable differences were observed between NS-PORP study participants and those whose data was excluded from the final analysis due to incomplete participation. Of the omitted group many were female (77% versus 48%) and most identified as Indigenous (85% versus 14%). This highlighted the need to provide culturally sensitive prescription opioid support to achieve and maintain engagement along with flexible delivery methods to facilitate female participation.

The starting dose of opioids was reported in eight previous studies (Guarino et al.,2018; Kurita et al., 2018, Naylor et al.,2010; Zheng et al., 2007, Darnell et al., 2018; Mehl-Madrona et al.,2016; Nilsen et al., 2010; Scott et al., 2020) with the average dose ranging from 30 – 370mg. The starting dose of NS-PORP participants fell into the middle of this range with an average reported dose of 108mg. Mood was rated as moderate in NS-PORP study participants (52 average, median 52) while lower baseline self-efficacy evident from PSEQ scores (19 average, median 17) and low mood and self-efficacy was more obvious amongst omitted study participants.

The NS-PORP study examined in particular, the association between the outcome of opioid reduction and the travel distance for treatment at the specialist multidisciplinary pain service. Although the use of internet and telephonic formats was the subject of a number of studies (Guarino et al., 2018; Naylor et al., 2010; S. D. Young & Heinzerling, 2017) the issue of distance was not highlighted despite most studies being undertaken in metropolitan settings (Garland et al., 2014; Garland et al., 2019; Guarino et al., 2018; Jamison et al., 2010; Kurita et al., 2018; Naylor et al., 2010; Zheng et al., 2008; Zheng et al., 2019). More than a quarter of NS-PORP participants lived more than 30minutes drive away from the service and 17% lived more than 90minutes away. It is likely that the option of telehealth reduced the barrier of distance and enabled participation throughout the twelve months of the study.

The Pain and Opioids IN Treatment (POINT) study, which included 1514 Australian participants and was one of the largest and most comprehensive studies to describe patterns of opioid prescribing and individual outcomes for participants with CNCP, reported similar characteristics in their cohort including opioid dose. In addition they reported that 50%, only, of the cohort lived in a major city (Degenhardt et al., 2021). This suggested that patients in rural locations have similar characteristics to their city counterparts, along with similar requirements for prescription opioid reduction support and that application of NS-PORP in these settings may be possible and beneficial.

6.5 Opioid Dose Reduction to ≤ 40mg measured in oMEDD

The primary outcome evaluated by the study was opioid reduction to 40mg oMEDD or under within a 12 month time frame and the results demonstrated the utility of NS-PORP in supporting this goal. As noted in previous studies engaging participants on long term opioid therapy in dose reduction is challenging. Three prior studies had reported statistically significant opioid dose reduction of measured opioid dose compared with a comparator or control group (Mehl-Madrona et al., 2016; Goodman et al., 2018; Naylor et al., 2010) with one only (Naylor et al., 2010) rated to be of fair or better quality using the Critical Appraisal Skills Program (CASP) checklists (Critical Appraisal Skills Programme (CASP) UK, n.d.).

The capacity to reduce prescription opioid dose was influenced by many personal facilitators and barriers providing each study participant with a unique and individual weaning pathway. An unexpected feature that emerged during the data collection for this study which further highlighted these differences was the advent of the COVID-19 global pandemic in Australia.

Significant changes to healthcare delivery occurred in primary care to reduce the potential risk of COVID -19 transmission. GPs utilised telehealth to consult with patients whenever possible and were reluctant to make major changes to medications until face to face interaction was possible, especially in the context of potentially difficult interactions recommending opioid dose reduction. The uncertainty of those time frames meant that sometimes opioid prescription continued longer than was recommended. A number of study participants from this period who did start reducing opioid dose and noted the health benefits were quite proactive in requesting medication reduction with their GP despite the challenge of accessing appointments (participants 28, 30 and 33), with one participant even requesting that HIPS advocate on their behalf to the GP to commence reduction. A previous primary care study had similarly noted that as patients participated in the intervention and reduced opioid medication their attitudes changed and they became aware of the benefits that pain treatments other than opioids conferred (Mehl-Madrona et al., 2016).

Many study participants who failed to reach the goal of opioid dose reduction to ≤ 40mg oMEDD did attempt the reduction but found it arduous to continue, with their GP's often agreeing to hold the dose steady or another new GP taking over care. HIPS did not mandate opioid dose reduction but their recommendations along with tightening legislation did encourage most GPs to deprescribe. Of the four participants who withdrew from the study all indicated non-acceptance of recommendation to reduce opioids as the reason. Opposition to opioid dose reduction and subsequent withdrawal from study participation had been reported previously in studies and was most common where prescriber led interventions mandated dose reduction (Kurita et al., 2018; Goodman et al., 2018; Mehl-Madrona et al., 2016). One study concluded that for this reason the intervention was not feasible to continue (Kurita et al., 2018). Difficulty in recruiting participants into these interventions was also reported. A number of studies avoided the complex process of negotiating opioid reduction by measuring misuse and the expressed intention to reduce rather than actual opioid dose (Garland et al., 2014; Garland et al., 2019; Guarino et al., 2018).

During the NS-PORP study recruitment 31 additional patients consented to participate in the study despite being ineligible as they were already on a low opioid dose while 64 eligible participants chose not to participate in the treatment arm and eventually made up the comparator group. Low recruitment numbers had been identified in previous studies (Goodman et al., 2018; Sullivan et al., 2017; Kurita et al., 2018) with participants more willing to

participate in control groups than in the treatment option (Mehl-Madrona et al., 2016; Goodman et al., 2018). Long term prescription opioid consumers in Australia tend to be older, have multiple vulnerabilities including economic and educational disadvantage, multiple medical comorbidities and polypharmacy (Gisev et al., 2016; Kerr et al., 2004). Study participation may have been viewed as a lower priority than other health care and life concerns. Polypharmacy may have effected cognition, motivation and other higher order functions that impacted on participation in the study. Participant beliefs, expectations and possible resistance to pain service recommendations regarding opioid dose reduction may likewise have influenced their decision to participate in the study or to continue providing data for the entire study timeframe

From the NS-PORP cohort a number of participants experienced mitigating circumstances that made reduction during the study timeline challenging. Some endured significant health issues. Three had major surgery (participants 4, 11, 2,) one was involved in a serious motor vehicle accident (participant 27) and one participant was palliated and died during the course of the study (participant 5). Others experienced social upheaval. One moved from a domestic violence situation during the course of the study (participant 30) and one who had been residing in an aged care facility was facilitated through community resources to transition into independent accommodation (participant 2) while one was diagnosed with dementia (participant14). In addition, two participants identified themselves as having had a significant intravenous drug use history (participants 8 and 16) and one overdosed on opioid medication during the study (participant 11).

Despite these barriers the majority of the above group achieved the primary outcome of opioid dose reduction to ≤ 40mg oMEDD within the twelve month time frame and of those who did not achieve this goal all but two were able to reduce opioid dose to a level lower than their starting dose. Some participants were recruited late in the study and therefore were not able to be followed up for the full 12 months. These participants all reduced opioid dose to various extents and appeared to be on a reduction trajectory. The mean follow-up time of these participants was 5.75 months (range 3 to 10months).

The reasons study participants gave for accepting recommendations to reduce opioid dose were varied with a snapshot of nine participants following MES group reporting health benefit as the main reason for reduction. One participant indicated that legislative restrictions were the drivers for reduction, whilst another suggested their GP was the primary reason. Most felt involved in the decision to commence opioid reduction. These responses were supported by

answers to a question which asked what fears and concerns they had regarding coming off opioid medication. About half suggested they were fearful of opioid reduction with the other half indicating a willingness to reduce dose due to concerns about side effects and the lack of benefit from opioids.

There are few studies which looked specifically at which pain medicine discipline (medical/nursing/allied health) was best suited to promote opioid dose reduction, however, in facilitating NS-PORP the nursing role was well accepted by participants who frankly discussed concerns about prescription opioid use as well as accepting recommendations to alleviate difficulties associated with opioid dose reduction. A nursing role had empowered prescription opioid reduction utilising both Motivational interviewing and exercise based strategies in previous studies (Chang et al., 2015; Doolin et al., 2017).

The threshold of 40mg oMEDD for entry to group program pain treatment at HIPS was nominated by clinical consensus and was based on the Faculty of Pain Australian and New Zealand College of Anaesthetist opioid calculator mobile application which used a "traffic light" warning system to indicate the risk of dose-related harm. An opioid dose of 40mg oMEDD and under received a green light (Therapeutic Goods Administration, 2021). Although this allowed admission to group program pain treatment HIPS usual recommendations were to continue opioid dose reduction until cessation.

Opioid dose data from consented participants were self-reported and corroborated with hospital electronic record. Data collected for the comparator group, with the exception of the sole participant who provided consent and was contacted by telephone, were triangulated from hospital electronic record which is also linked to NSW HealtheNet records.

6.6 Pain Treatment

The second primary outcome evaluated by the NS-PORP study was entry to group program pain treatment. A larger percentage of NS-PORP participants achieved this than from the comparator group (26% versus 5%) however the clinical goal of at least 30% continuing to treatment was not reached and this percentage was slightly lower than observed during the pilot study of MES where the 36% of participants entered group program pain treatment. Entry to group program pain treatment was the study component most significantly affected by COVID-19 restrictions during the study period. HIPS attempted to continue group program treatment

but was forced to respond to the unfolding public health situation by cancelling all face to face appointments. An initial attempt to run active group treatment program by telehealth (videoconferencing) was abandoned due to technological difficulties. This meant that rather than 18 treatment group programs being conducted over the 21 months of study recruitment only 7 were held. Although IAPT as an individual appointment could have continued with a telephone option, with nowhere for patient flow to be directed after IAPT the decision was made to cancel these appointments. Of the nine study participants who completed IAPT seven did so before March 2020. Despite difficulties three participants from the treatment group went on to complete the entire pain treatment group program as did two participants from the comparator group. A number of the remaining participants were offered the group program beyond the study end point and most did not accept the offer possibly due to the significant time lag.

Despite the possibility of better engagement with active treatment after prescription opioid reduction, research thus far had not studied the link between opioid dose reduction interventions and progression to active nonpharmacological treatment. Most opioid reduction interventions in the published literature were stand-alone interventions in contrast to NS-PORP which was a component of a structured group program pathway at HIPS. Integration with other pain treatment was reported in two studies, however neither treatment was contingent on completing the opioid reduction intervention. One featured CBT preceding the studied intervention (Naylor et al., 2010) and the other offered concurrent pain treatment modalities during opioid dose reduction (Kurita et al., 2020).

6.7. Participant Satisfaction

Person-centred care is well recognised as a corner stone to safe, high-quality, cost-effective healthcare promoting trust and open communication between healthcare consumers and healthcare providers. Recognising the value of the consumer voice, data on participant experience was actively sought in this study. Clinician facilitators for the MES group, in the NS-PORP-1 arm generally gauged the participant audience to be reasonably satisfied with their experience in each of the groups run. This was substantiated by the satisfaction ratings with the majority of NS-PORP 1 participants (86%) reporting high satisfaction at both time points. The one NS-PORP-1 participant who rated being moderately satisfied at both time points, was also unable to make any dose reduction. NS-PORP-2, was rated by most (68%) as highly

satisfactory. Reviewing the subcomponents of the satisfaction score, manner of presenter was rated highest followed by content. It is possible that the use of Motivational Interviewing, in which a key component is the quality of interaction with the facilitator, meant that participants rated NS-PORP in this way and were receptive to the content provided.

Most previous studies that incorporated satisfaction rating allowed participants the choice to continue prescription opioid use during the study and all were rated with high satisfaction (Chang et al., 2015; Guarino et al., 2018; Jamison et al., 2018; Naylor et al., 2010; Sullivan et al., 2017). Novel interventions such as electroacupuncture, and internet and telephone based treatment (Guarino et al., 2018; Naylor et al., 2010; Zheng et al., 2008) were rated highly, with some participants (Zheng et al., 2008) agreeing to recommend the intervention to others. Of significance, studies with mandatory opioid reduction as a primary component did not look at patient experience or satisfaction (Kurita et al., 2018; Goodman et al., 2018; Mehl-Madrona et al., 2016).

Of interest were participant characteristics of those who reported low or moderate satisfaction. Most were unmarried and reported lower self-efficacy (PSEQ scores). They were also less likely to reduce opioid dose compared to those who reported higher satisfaction and were probably better engaged with the content. These findings were supported by conclusions from the MORE study which suggested modulating positive psychological processes to improve affect through an integrated treatment of Mindfulness Oriented Recovery Enhancement would reduce the risk of prescription opioid misuse and facilitate opioid dose reduction (Garland et al., 2013; Garland et al., 2019).

Allowing participants to have a voice in planning their own opioid reduction regime was likely to be associated with improved satisfaction and better acceptance of recommendations around opioid reduction. The desire to be included in planning and the sense of abandonment when excluded feature in qualitative interviews about prescription opioid reduction (Matthias et al., 2017).

The final component of the satisfaction rating of NS-PORP was a short telephone interview with participants, exploring the role of NS-PORP in supporting the reduction of prescription opioid medication and how it could be improved. The majority of study participants reported that the intervention had been helpful in a number of different ways and few minor refinements were suggested with most supporting the current intervention to continue unchanged.

In order to explore the connection between satisfaction with NS-PORP and the capacity to engage with behavioural change a number of components were examined. Of respondents that rated NS-PORP as highly satisfactory, the majority (62%) also had improvement in their importance and confidence ratings and most importantly were more likely to (62%) achieve the desired opioid reduction goal. Participant responses were surveyed for comments that indcated active or passive ideation. The number of active and passive responses from each individual were counted and it was observed that the group of participants who responded with more active than passive ideas also rated NS-PORP as being highly satisfactory and all but one had achieved the target goal of opioid dose reduction. This qualitative data suggested that satisfaction, and being able to formulate active strategies may be connected and that developing higher levels of these desirable attributes may promote readiness to wean and ultimately prescription opioid dose reduction.

Although the majority of respondents found the pathway helpful and needed little change it was clear from both positive and negative responses that there was still room for improvement, including maintaining a flexible service provision and facilitating NS-PORP with a considerate, non-judgemental approach. In general females appeared to appreciate the supportive nature of the pathway while males found the information they were given helpful. People who lived a considerable distance from the pain service were still likely to participate and were appreciative of the opportunity to join through telehealth options. Participants who had the capacity to envision active ideas and strategies were likely to employ them in achieving the desired outcomes of opioid dose reduction and continuing on to active pain treatment.

6.8 Cost Estimation of NS-PORP

Designed as part of a collaborative and cost saving approach to supporting prescription opioid reduction in patients referred to HIPS, NS-PORP followed specialist pain medicine physician recommendations, to both patients and prescribers, at the assessment phase. NS-PORP was developed to be the next step for patient contact rather than further medical appointments and freed up the resource of specialist pain medicine physician time to support the prescriber. Specialist pain medicine physician clinical time is an expensive and restricted commodity in chronic pain management services with only a small number of specialists available for consultation in Australia. NS-PORP provided an accessible, inexpensive and timely, option with regular specialist nurse contact over the course of the opioid reduction regime. Mehl-Madrona likewise found in a primary care study that opioid reduction strategies taught by

multidisciplinary clinicians in a group format in the primary care practise were cost effective in comparison with practice medical appointments (et al., 2016).

Not all individuals using prescription opioid medication need referral to a pain service with most requiring care at a lower cost in the community. Given the potential for cost savings and easier access to nursing staff, NS-PORP in either form, could be an effective default option in primary care as well as remaining a useful adjunctive option in a specialist multidisciplinary pain service.

6.9 Study Strengths and Limitations

The study demonstrated that a brief intervention focused on behavioural change facilitated prescription opioid reduction in participants, many of whom had been on long term opioid therapy, and enabled continuation to CNCP treatment. The study methods were designed to promote internal and external validity. The strengths of the study included the application of a pilot study to demonstrate feasibility prior to the study commencement and the development of a study protocol to maintain fidelity. Every HIPS patient who attended the assessment phase during the recruitment timeframe was either enlisted into one of the study arms or included in the comparator group. By including all possible participants not merely those who volunteered selection bias was reduced and there was greater representation to the target population .The development of specific and strategic aims along with objective quantitative measures and a prospective focus enhanced study vigour. The issue of compounding factors were reduced by propensity weighting regression analysis while the mixed method approach retained the view of consumer expectation and experience. The length of study enabled a more detailed view of the problems associated with opioid reduction as well as longer term participant outcomes.

There were limitations, however, in what the study could achieve. The single setting and smaller than hoped for sample size reduced representation. In addition the observational nature of the study design meant that the study environment was more difficult to control. This was most apparent during COVID restriction times when recruitment was difficult and study cohort members were unable to participate in group program treatment. The intention to employ NS-PORP-1 as the prime intervention and NS-PORP-2 as a lesser secondary option was reversed with the advent of restrictions on face to face appointments. NS-PORP-1 as the main pathway had been provided with more extensive development and MES alone had been the subject of the pilot trial. As well as reducing the opportunity to build a therapeutic alliance in the face to

face MES component this meant that parts of the planned data collection were unable to go ahead due to the inherent difficulties of explaining questionnaires over the telephone. The Candidate was both researcher and the principal NS-PORP clinician. This was a further source of possible bias. Although there were advantages to performing the dual role it was possible that participants were motivated to provide less objective data to someone they had developed a therapeutic relationship with. On the positive side the Candidate was able to utilise their knowledge having developed the intervention and prior clinical skills in delivering the intervention along with insider knowledge and awareness of insights when looking at the data. Bias from this source was reduced by using people not involved with the study to recruit, collect subjective data and perform analysis of the primary outcome. The clinician candidate maintained awareness of this potential conflict and took care to reduce its effect on the study results.

6.10 Implications for Clinical Practice

The utility of NS-PORP in improving multiple outcomes was suggested by the study. Against the environment of tightening opioid reduction recommendations participation in the study provided a timely opportunity for patients to engage with a simple method to support opioid weaning. The development of a partnership between nursing staff and participants may have helped to reduce feelings of abandonment and injustice that many patients felt regarding mandated opioid reduction. In addition withdrawals, psychological distress and aberrant medication use behaviours may have been lessened with empathetic regular professional support through a structured pathway. The nursing leadership role extended the nursing scope of practice within a specialist multidisciplinary pain service as well as providing professional development opportunities. Despite having a long duration, NS-PORP was a low cost intervention and liberated more costly specialist pain medicine physician time to support prescribers. Participant motivation and capacity to make change was specifically targeted and monitored with importance and confidence scoring.

6.11 Implications for Policy Development

Changes in legislation and expert recommendations have brought about a unique set of challenges for both clinicians and policy developers. GPs at risk of contravening legal requirements by continuing to prescribe opioid medication for CNCP may feel compelled to cease opioids abruptly leading to significant distress for many patients. Along with opioid

prescription guidelines, there needs to be a policy of well-funded, structured non-judgmental support systems for patients undertaking opioid reduction. Given that opioids are prescribed in multiple healthcare settings with no geographical specificity, it is important that the patient support for opioid reduction be widely available and easily accessible.

6.12 Future Directions

This study provided additional evidence to the knowledge base already available regarding prescription opioid reduction treatment. Further studies comprising larger numbers and with greater focus on the role of participant characteristics that enable opioid dose reduction would bring greater clarity to this perplexing health issue. This could be done either as an RCT or as a prospective observational study referenced against a control arm and should include measured opioid dose as an outcome. Exploring the connection between participant satisfaction self-efficacy and capacity to envision active means of problem solving may prove to be significant in facilitating the outcome aim of prescription opioid reductions. Longer follow up times may provide a better view of the characteristics and behaviours of participants as well as giving a longer opportunity to observe for changes in outcomes.

Although NS-PORP was developed for the specific purpose of supporting HIPS patients waiting for the opportunity to commence active group program pain treatment, it is likely to have utility in providing support to the wider population on long term opioid therapy in the context of CNCP. NS-PORP or components could be integrated into primary health care processes. Partnering between tertiary and primary tier healthcare services to share knowledge and resources would enable a more equable, tailored and accessible approach to supporting complex and vulnerable individuals with CNCP during prescription opioid reduction.

6.13 Conclusion

This aim of this study was to evaluate if a nurse supported prescription opioid reduction pathway (NS-PORP) enabled participants with chronic non cancer pain (CNCP), attending a specialist multidisciplinary pain service, to reduce opioid dose and continue on to group program pain treatment. Exploring the multifaceted issues around prescription opioid use for CNCP and the complex behavioural responses that challenge prescription opioid reduction led

to identifying personal characteristics that may have either promoted or limited opioid dose reduction in the individuals.

NS-PORP was developed out of a specific need to provide support during prescription opioid reduction to patients who were transitioning from assessment to pain treatment in a specialist multidisciplinary pain service. A scoping review of the literature identified features of previously reported interventions for prescription opioid reduction and formed the basis of enquiry for the NS-PORP study. A conceptual model of behaviour change provided the framework for NS-PORP development in which were incorporated elements of supported self-management communicated though motivational interviewing technique. The pathway was developed and facilitated as a nurse-led project.

A clinical trial to evaluate NS-PORP utilised a three armed prospective cohort study design and evaluated the primary aims along with exploring participant satisfaction and estimating cost benefit. The study outcomes were reported from a service delivery and patient perspective. Analysis demonstrated the advantage treatment with NS-PORP offered in the study aims of opioid dose reduction and entry to group program pain treatment. Participant satisfaction was shown to be high and there was estimated cost savings compared to specialist pain medicine physician consultations. The additional knowledge determined from this study adds to the evolving body of research being conducted on prescription opioid reduction. This thesis comprises the clinical study of NS-PORP along with a greater understanding of the complex background of prescription opioid use for CNCP.

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Appendices

Appendix 1. Literature Review Protocol

Title – What characteristics does the literature reveal about outpatient interventions for prescription opioid reduction in a chronic non cancer pain population? Protocol for a scoping review.

Masters in Philosophy Research Thesis
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Abstract

Introduction - Prescription opioid use and misuse is a global health issue. Escalating risk of harm with concurrent reduction in efficacy limits benefit with long term opioid use. Despite this paradoxical outcome, extensive prescribing continues. Opioids exert a complex physical and psychological effect that impedes reduction and can lead to conflict between prescribers and patients. Along with legislation and guidelines to limit prescribing, behavioural support for individuals on reducing regimes is likely to be beneficial. Previous systematic reviews of methods for prescription opioid reduction have not identified evidence for any specific intervention and have deemed meta-analyses of study data was not possible. This protocol outlines the scoping review that will add evidence, through a broader view, to the existing body of knowledge on this topic. In keeping with the nature of a scoping review, quality of evidence will be discussed rather than formally analysed.

Methods and analysis–The aim of the review will be to examine key characteristics about outpatient clinical interventions to support opioid reduction in an adult population with chronic non cancer pain on long term opioid therapy. The review will follow the staged framework proposed by Arksey and O'Mallery. An electronic database search, of Medline, Embase, Cochrane, Cinahl, and Proquest along with grey literature will locate relevant studies. Independent screening by two reviewers will examine title, key word and target concept for inclusion. Data analysis will adhere to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist. After findings are charted and assessed for quality using Critical Appraisal Skills Programme checklist assessment tools they will be collated and information synthesised for presentation as a narrative review.

Ethics and Dissemination - The scoping review will retrieve information from published studies precluding the need for ethical approval. Primary study reporting will be through a Research Masters thesis dissertation with key findings published in a peer reviewed journal, and presented at local and national clinical and research meetings.

Keywords: Chronic pain, persistent pain, prescription opioids, reduction, weaning, tapering, intervention, treatment, nurse led, nurse support.

Introduction

Opioid use and misuse is a global health issue. Opioid treatment for chronic non-cancer pain (CNCP) is characterised by three key elements which are escalating risk of harm with concurrent reduction in benefit, [1,2,3,4] extensive prescribing [5,6,7,8] and complex physical and psychological drug effect impeding reduction. [9,10] Prescribing guidelines released in 2016 [11] by the Centre of Disease Control in the US designed to restrict opioid prescribing and encourage deprescribing for existing opioid use, are now accepted by most expert bodies in Australia who recommend similar management. Australian legislation supports this through restriction of ongoing opioid prescriptions to people who are opioid dependent[12].

Harm and lack of benefit is a feature of both misuse and compliant opioid use and is associated with adverse health impact and economic cost to the individual and society.[13,14] Despite this dual negative effect, opioid reduction is often challenging to patients and prescribers and recommendations to reduce dose may cause conflict. Prescribers may be reluctant to deprescribe for patients they perceive have a legitimate need for pain medications, if they have few practical alternatives to offer. [15, 16] Over 15 million opioid prescriptions are written annually in Australia. [7] This has increased 15 fold in the last 30 years [6].

Opioids exert a complex effect on the brain that supports continuation of their use. By expropriating reward pathways pleasure from natural reward is replaced by the desire for opioid effect [17]. Decision making is disrupted leading to continuation of opioids against better judgement [18], and memory is altered to favour positive feelings about opioid use [19]. Structural changes related to opioid use are visible on imaging in areas of the brain associated with emotional processing and connectivity [20].

There is currently no standard approach to support prescription opioid reduction, and a wide array of clinical interventions are suggested for the purpose. [21,22,23]. Guidelines and protocols help prescribers make decisions about opioid management but are often not well received by patients. Reducing potential barriers through behavioural treatment [24] may help patients adhere to opioid dose reduction plans. Education alone seems unlikely to lead to reduction[25]. Inpatient treatment for opioid reduction is costly and removes patients from their support systems, responsibilities and real world concerns, creating an artificial environment, which is unable to be sustained on discharge [26]. Multidisciplinary pain management programs frequently incorporate opioid tapering and demonstrate dose reduction without identifying which

component of the program supports that outcome[27,28]. For real world application an opioid reduction support intervention would need to be viable in terms of accessibility, cost and acceptability to patients for whom it is designed. This criteria may be met by a nurse run intervention.

Previous systematic reviews, including a Cochrane review by Eccleston et al., 2017 [21] and one by Frank et al., 2017 [22] examined interventions for the purpose of opioid reduction. Meta analyses were not performed in either review due to significant variability in types of intervention, measured outcomes and small sample sizes, with the authors concluding there was not sufficient quality of evidence to support any specific intervention for opioid dose reduction. A further evidence brief by Peterson et al., 2016 examined complementary interventions for opioid reduction [29] and described the evidence base as extremely limited. Recent systematic reviews of tapering methods by Mathieson et al 2020 [30] and Sud 2020 [24] comment on the heterogeneous nature of studies. Lieschke et al 2020 [31] performed a rapid realist review of evidence on opioid tapering in the rural context. White et al 2021 [32] wrote a systematic literature review of feasibility of behavioural interventions to support opioid tapering and both found the evidence base was limited.

In light of previous findings, a scoping review is planned to take in a broader view of the literature. This protocol outlines the proposed scoping review. The scoping review will focus on interventions that a patient may undertake to enable change in behaviour leading to opioid dose reduction, rather than examine opioid reduction strategies from a joint prescriber and patient perspective. The review will encompass data from observational studies which would not ordinarily be included in a systematic review. This wider array of data will be used to elucidate and synthesise a more comprehensive evidence base.

As meta-analysis of existing data in not possible the single question of which intervention facilitates prescription opioid reduction will not be answered, however the review will strive to aggregate information about the topic, evaluate past and current clinical practice and identify the current knowledge gap in the literature. Nursing involvement has not been commented on in previous literature reviews and will be a focus of the review if noted. This is a dynamic and fast moving area of research [22] and the potential for harm when opioids are used ineffectively for CNCP, means that further review of the evidence is warranted.

Method

This scoping review will follow the five-stage framework proposed by Arksey and O'Mallery [33] which comprises identifying the research question, identifying relevant studies, selecting eligible studies, charting the data and collating, summarizing and reporting the results. The sixth optional stage of the framework which involves consumer consultation will not be included due to time constraints. Data analysis will adhere to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist [34] and study appraisal will follow Critical Appraisal Skills Program (CASP) checklists for Randomised Control Trials (RCT), Cohort study and Qualitative study (Critical Appraisal Skills Programme (CASP) [35].

Identifying the search Question

The purpose of the review is to systematically examine, from an array of research types, characteristics of outpatient clinical interventions that support opioid reduction in an adult population with chronic non cancer pain on long term opioid therapy.

Review questions are: 1.What interventions are characterised in the literature as being for the purpose of opioid reduction? 2. Do they demonstrate efficacy in reduction? 3. What outpatient settings and clinician group provide these interventions? 4. What barriers and facilitators are associated with provision of each intervention? 5. What are the gaps in knowledge relating to this evidence?

Identifying relevant studies

Inclusion Criteria - Studies considered for inclusion will contain pre-determined criteria related to participant characteristics, concept, outcomes and context. The scoping review will focus on adult study participants with CNCP, defined as pain extending beyond three months (IASP ref), taking LTOT or opioid therapy prescribed for longer than three months [22] who undertake opioid dose reduction.

The concept for review is any clinical intervention or method that is clearly defined for the primary purpose of prescription opioid reduction or cessation in an outpatient setting that can be replicated for this purpose. This may range from a single treatment modality or occasion

through to multidisciplinary management over a longer period of time delivered by any health clinician.

The primary outcome of interest is opioid dose reduction or cessation. Surrogate measures such as intention to reduce will be considered if actual opioid dose has not been measured. Secondary outcomes for evaluation will comprise aspects of therapy and service provision that promote the primary outcome of opioid reduction. These may be measures of readiness to make dose reduction or patient satisfaction with the intervention. The cost and resource use of the intervention will be considered.

The context of the review will be that of studies undertaken in outpatient settings including those in multidisciplinary pain clinics, from any country. All study designs will be considered for inclusion with observational data being added to analysis and synthesis to provide a comprehensive review of the topic.

Exclusion criteria - Review exclusions include studies set in inpatient locations, studies of prescription opioid reduction for acute or cancer pain, studies of general chronic pain management, studies of opioid monitoring programs, opioid prescribing guidelines or legislative measures to restrict opioids, studies of opioid substitution treatment or adjunct medication treatment to support opioid reduction. Although these are effective methods to limit opioid prescription and use they are outside the purpose of this review. Specific studies of children and adolescents under 18 and elderly individuals over 80 years will also be excluded as these patient subgroups often follow a specialised treatment pathway.

Search Strategy - The literature search will comprise three stages: 1) Identification of relevant key words and MeSH terms related to the key concepts; 2) Complete search of selected data bases, grey literature and trial registers using a search strategy developed from the key words and MeSH terms; and 3) Identification of key articles with additional search of their reference lists.

The search strategy will be developed in consultation with a senior librarian using the key phrases of `prescription opioid treatment or therapy for CNCP, chronic pain or persistent pain' and `intervention, method or support for prescription opioid dose reduction'. Subject headings, keywords and keyword phrases will be compiled for each of the search concepts. The concepts will be combined using the 'AND' operator. The Cochrane Highly Sensitive

Search Strategies for identifying randomized trials in MEDLINE (2008 rev.) validated search filter will be applied to the Medline search. The search strategy will be developed in Medline before being translated to the other databases. The search will be limited to human studies and English language citations published since 1999. The date limit is applied in recognition of timing of research which followed popularisation of opioid use for CNCP starting in the early 1990s [9,3,6].

Sources of evidence - A systematic search of the Medline, Embase, Cochrane, Cinahl, and Proquest databases will be conducted. This will be supplemented by a grey literature search of the following resources; Med Nar, Open Grey, PsycExtra, Science.gov, World Wide Science Org and Theses and Dissertations Guide. Trial registers including; Cochrane Central Register of Clinical Trials (Central), ANZCTR-Australian New Zealand Trails Registry, Clinical Trials.gov, ISRCTN Registry, Centerwatch, WHO International Clinical Trials Registry Platform and EU Clinical Trials Register will also be inspected.

Data Management - The results of the search strategy will be uploaded to Endnote where duplicated articles will be identified and removed, results will be screened and a reference list created. Where multiple articles are available on a single trial, publication of the main findings will be used.

Study Selection

Due to the breadth of the search a large number of articles may be identified and a two stage screening process will be employed. Studies will be initially screened by title for relevance, looking for terms identified in the first stage of the review strategy. If there is ambiguity around the title meaning, the abstract will be reviewed. Articles that are deemed to include target concepts, identified either by title or abstract, will be obtained in entirety and screened independently by two reviewers. Disagreement about paper inclusion will be resolved by discussion or consultation with a third reviewer if necessary and the reason for exclusion will be noted.

Search strategy results will be provided including information about source databases. A Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram [37] will be generated to show the number of studies retrieved and reviewed. Reasons for exclusion at each step will be documented in the diagram.

Data Charting

Information will be charted on a standardised purpose developed data extraction template based on the JBI data extraction template for scoping reviews[38] and include data information suggested by the PRISMA-ScR checklist [34] .The template will set out the following details: author, publication details, country of study, study design, aims and purpose of the study, population studied and setting, sample size and numbers lost to follow up, intervention description, length of intervention, measured outcomes, length of follow up, key findings and study funding.

Two independent reviewers will chart results using the template. Findings will then be corroborated and concepts developed based on the study objectives and questions.

Data Collation, Summary and Reporting

Analysis and synthesis will be in three stages. Critical Appraisal Skills Programme UK. **CASP** checklists [35] will be used to assess individual study quality and a tabular summary of studies will be generated. Study data will then be combined to develop themes. A discussion of their relevance to the review objective and questions will follow. The synthesis of key findings will form a critical appraisal of the literature and be presented as a narrative review to provide an overall survey of what interventions support opioid reduction, how effective they are, their setting and which clinicians are involved, what difficulties or facilitation is experienced in their provision and what further research is needed to provide a more comprehensive view of this area.

Ethics and Dissemination

Information will be gathered from published studies, precluding the need for ethical approval. The Scoping Review will form part of a Research Masters thesis dissertation with key findings to be published in a peer reviewed journal, and presented at local and national clinical and research meetings. The review will inform development of a study to observe a behavioural treatment pathway for supporting opioid dose reduction.

Discussion

Previous literature reviews have been unable to demonstrate conclusive benefit from any single clinical intervention for opioid reduction. This is not due to a lack of clinical modalities currently in use for this purpose but is indicative of the limited quality of studies available. Inclusion of observational data will enhance the range of information being captured and evaluated. The limitations of this review relate to the review type and the large volume of studies that may need to be reviewed. In addition a conclusive answer to the question of what intervention leads to opioid reduction cannot be made. The variable quality of studies eligible for inclusion will be dealt with by a quality assessment process and justification for inclusion of each study will be noted. The review is expected to highlight factors associated with successful prescription opioid reduction which could be used in both specialist pain services and primary health care settings and pave the way for future research.

Conclusion

Opioid medications continues to be prescribed for CNCP despite known association with harm and lack of benefit. Research has led to changing recommendations about opioid use, which may be challenging to both patient and prescriber. Support through behavioural therapy during reduction may lead to better individual outcomes.

Previous systematic reviews to determine what interventions promote opioid reduction have deemed that meta-analyses of study data is not possible. In keeping with scoping review type, quality of evidence will be discussed rather than formally assessed, allowing the body of research to be examined in a new light. Synthesis of evidence from the scoping review will add to the existing body of research on this topic and provide guidance to clinicians in developing and implementing effective clinical interventions for supporting prescription opioid reduction.

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38. 11.2 Development of a scoping review protocol https://wiki.jbi.global/display/MANUAL/11.2+Development+of+a+scoping+review+protocol

Appendix 2. Data Base Search Strategy

Medline Search Strategy

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily <1946 to March 06, 2019>

Search Strategy:

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1 Chronic Pain/ (11353)

2 Pain, Intractable/ (6091)

3 Back pain/ or Low back pain/ or Headache/ or Musculoskeletal pain/ or Neck pain/ or Neuralgia/ or Pelvic pain/ (85794)

4 Sciatica/ (4873)

5 Arthritis/ or Arthritis, rheumatoid/ or Osteoarthritis/ (147511)

6 Fibromyalgia/ (7889)

7 ((chronic or persistent or intractable or noncancer or non-cancer) adj3 pain*).ti,ab,kw,kf. (68578)

8 1 or 2 or 3 or 4 or 5 or 6 or 7 (298719)

9 exp Analgesics, Opioid/ (109059)

10 (opioid* or opiate* or papaver).ti,ab,kw,kf. (98669)

11 (morphine or meperidine or methadone or buprenorphine or fetanyl or hydrocodone or oxycodone or codeine).ti,ab,kw,kf. (71004)

12 9 or 10 or 11 (177281)

13 exp Psychotherapy/ (184909)

14 ((psychotherap* or cogniti* or behavio?r* or family or psychosocial* or psycho-social*) adj5 (therap* or intervention*)).ti,ab,kw,kf. (84644)

15 (counsel* or cope or coping).ti,ab,kw,kf. (172328)

16 exp Physical Therapy Modalities/ (141451)

17 exp Mind-Body Therapies/ (48089)

18 ((physical adj therap*) or physiotherap*).ti,ab,kw,kf. (44552)

19 (multidisciplinary or multi-disciplinary or interdisciplinary or inter-disciplinary).ti,ab,kw,kf. (109165)

20 (biofeedback* or massage or acupuncture or electroacupuncture or "therapeutic interactive voice response").ti,ab,kw,kf. (37746)

21 (effluerage or anma or aquatic bodywork or bowen technique or craniosacral therapy or lomilomi or manual lymphatic drainage or myofascial release or postural integration or reflexology or shiatsu or structural integration or tui na or watsu).ti,ab,kw,kf. (1346)

22 (tai chi or taichi or tai ji or taiji or taijiquan or shadow boxing).ti,ab,kw,kf. (1646)

23 yoga.ti,ab,kw,kf. (4082)

24 Pastoral care/ or Spirituality/ (9726)

25 Adaptation, Psychological/ (89410)

26 (wellbeing or well-being or relax* or accept* or meditat* or spiritual*).ti,ab,kw,kf. (662435)

27 exp Rehabilitation/ (283395)
28 rehabilitat*.fs. (188600)
29 (wean* or cessation or cease* or taper* or reduc* or stop* or abstain* or abstinen* or withdraw* or discontinue* or detox* or terminat* or remove* or substit*).ti,ab,kw,kf. (3990690)
30 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 (5257210)
31 Randomized controlled trial.pt. (477139)
32 Controlled clinical trial.pt. (92944)
33 random*.ti,ab. (1031829)
34 placebo.ti,ab. (201098)
35 drug therapy.fs. (2087825)
36 trial.ti,ab. (533855)
37 groups.ti,ab. (1911649)
38 31 or 32 or 33 or 34 or 35 or 36 or 37 (4639466)
39 8 and 12 and 30 and 38 (3783)
40 exp animals/ not humans.sh. (4553712)
41 39 not 40 (3361)
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43 limit 42 to (case reports or clinical conference or comment or editorial or letter or news) (165)
44 42 not 43 (1925)

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2 intractable pain/ (5080)
3 exp musculoskeletal pain/ (138498)
4 pelvic pain/ (5368)
5 headache/ (206932)
6 neuralgia/ (9629)
7 sciatica/ (1813)
8 arthritis/ or osteoarthritis/ or rheumatoid arthritis/ (317679)
9 fibromyalgia/ (18685)
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15 12 or 13 or 14 (376044)
16 exp psychotherapy/ (255854)
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18 (counsel* or cope or coping).ti,ab,kw. (239130)
19 physiotherapy/ (86555)
20 ((physical adj therap*) or physiotherap*).ti,ab,kw. (76574)
21 alternative medicine/ (41439)
22 (biofeedback* or massage or acupuncture or "therapeutic interactive voice response").ti,ab,kw. (52751)
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24 (tai chi or taichi or tai ji or taiji or taijiquan or shadow boxing).ti,ab,kw. (2378)
25 yoga.ti,ab,kw. (5954)
26 (multi-disciplinary or multidisciplinary or inter-disciplinary or interdisciplinary).ti,ab,kw. (172062)
27 pastoral care/ (236)
28 spirituality/ (64687)
29 adaptive behavior/ (53836)
30 exp rehabilitation/ (378825)
31 (wellbeing or well-being or relax* or accept* or meditat* or spiritual*).ti,ab,kw. (864376)
32 (wean* or cessation* or ceas* or taper* or reduc* or stop* or abstain* or abstinen* or withdraw* or discontinue* or detox* or terminat* or remove* or substitu*).ti,ab,kw. (5350095)
33 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 (6968011)
34 crossover-procedure/ or double-blind procedure/ or randomized controlled trial/ or single-blind procedure/ or (random* or factorial* or crossover* or cross over* or placebo* or (doubl* adj blind*) or (singl* adj blind*) or assign* or allocat* or volunteer*).tw. (2142398)
35 11 and 15 and 33 and 34 (3919)
36 (animal/ or nonhuman/) not human/ (5742265)
37 35 not 36 (3852)
38 limit 37 to (english language and yr="2008 -Current") (2703)
39 limit 38 to (books or chapter or conference abstract or conference paper or "conference review" or editorial or letter or note) (856)
40 38 not 39 (1847)

Cochrane
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Date Run: 08/03/2019 06:08:04

Comment:

ID	Search	Hits
#1	MeSH descriptor: [Chronic Pain] this term only	1759
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#3	MeSH descriptor: [Back Pain] this term only	1703
#4	MeSH descriptor: [Low Back Pain] this term only	3186
#5	MeSH descriptor: [Headache] this term only	2137
#6	MeSH descriptor: [Musculoskeletal Pain] this term only	363
#7	MeSH descriptor: [Neck Pain] this term only	1003
#8	MeSH descriptor: [Neuralgia] this term only	973
#9	MeSH descriptor: [Pelvic Pain] this term only	446
#10	MeSH descriptor: [Sciatica] this term only	279
#11	MeSH descriptor: [Arthritis] this term only	1356
#12	MeSH descriptor: [Arthritis, Rheumatoid] this term only	5130
#13	MeSH descriptor: [Osteoarthritis] this term only	3289
#14	MeSH descriptor: [Fibromyalgia] this term only	1124
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#19	(morphine or meperidine or methadone or buprenorphine or fetanyl or hydrocodone or oxycodone or codeine):ti,ab	15439
#20	#17 or #18 or #19	25897
#21	MeSH descriptor: [Psychotherapy] explode all trees	21288
#22	((psychotherap* or cogniti* or behavior* or behaviour* or family or psychosocial* or psycho-social*) Next/5 (therap* or intervention*)):ti,ab	22269
#23	(counsel* or cope or coping):ti,ab	18932
#24	MeSH descriptor: [Physical Therapy Modalities] explode all trees	22256
#25	MeSH descriptor: [Mind-Body Therapies] explode all trees	5645
#26	(physical therap* or physiotherap*):ti,ab	19822
#27	(multidisciplinary or multi-disciplinary or interdisciplinary or inter-disciplinary):ti,ab	4884
#28	(biofeedback* or massage or acupuncture or electroacupuncture or "therapeutic interactive voice response"):ti,ab	14706
#29	(effluerage or anma or aquatic bodywork or bowen technique or craniosacral therapy or lomilomi or manual lymphatic drainage or myofascial release or postural integration or reflexology or shiatsu or structural integration or tui na or watsu):ti,ab	661
#30	(tai chi or taichi or tai ji or taiji or taijiquan or shadow boxing or yoga):ti,ab	2666

#31 MeSH descriptor: [Pastoral Care] this term only 12
#32 MeSH descriptor: [Spiritualism] explode all trees 5
#33 MeSH descriptor: [Adaptation, Psychological] this term only 3916
#34 (wellbeing or well-being or relax* or accept* or meditat* or spiritual*):ti,ab 51875
#35 MeSH descriptor: [Rehabilitation] explode all trees 31398
#36 (wean* or cessation or cease* or taper* or reduc* or stop* or abstain* or abstinen* or withdraw* or discontinue* or detox* or terminat* or remove* or substit*):ti,ab 336389
#37 #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 431950
#38 #16 and #20 and #37 with Cochrane Library publication date Between Jan 2008 and Feb 2019, in Cochrane Reviews, Cochrane Protocols, Trials 1102

S1	mesh(Chronic pain) OR mesh(Pain, Intractable) OR ti("chronic pain" OR "persistent pain" OR "intractable pain" OR "noncancer pain" OR "non-cancer pain") OR ab("chronic pain" OR "persistent pain" OR "intractable pain" OR "noncancer pain" OR "non-cancer pain")	Nursing & Allied Health Database	11019
S2	mesh(Analgesics, Opiod) OR ti(opioid* OR opiate* OR methadone OR buprenorphine OR fentanyl OR hydrocodone OR oxycodone OR codeine) OR ab(opioid* OR opiate* OR methadone OR buprenorphine OR fentanyl OR hydrocodone OR oxycodone OR codeine)	Nursing & Allied Health Database	26806
S3	ti(wean* OR cessation OR cease* OR taper* OR reduc* OR stop* OR abstain* OR abstinenc* OR withdraw* OR discontinue* OR detox* OR terminat* OR remove* OR substit*) OR ab(wean* OR cessation OR cease* OR taper* OR reduc* OR stop* OR abstain* OR abstinenc* OR withdraw* OR discontinue* OR detox* OR terminat* OR remove* OR substit*)	Nursing & Allied Health Database	689391
S4	mesh(Randomized controlled trial) OR mesh(Controlled clinical trials) OR ti(random* OR placebo OR trial OR groups) OR ab(random* OR placebo OR trial OR groups)	Nursing & Allied Health Database	924311
S5	S1 AND S2 AND S3 AND S4	Nursing & Allied Health Database These databases are searched for part of your query.	213

Appendix 3. Study Appraisal Table

RCT Design	Is the basic study design valid for a randomised controlled trial?			Was the study methodologically sound?			What are the results?			Will the results help locally?	
	Did the study address a clearly focused research question?	Was the assignment of participants to interventions randomised	Were all participants who entered the study accounted for at its conclusion?	Were the participants 'blind' Investigators 'blind' Assessers/analysts 'blinded'?	Were the study groups similar at the start of the randomised controlled trial	Apart from the experimental intervention, did each study group receive the same level of care (that is, were they treated equally)	Were the effects of intervention reported comprehensively?	. Was the precision of the estimate of the intervention or treatment effect reported?	Do the benefits of the experimental intervention outweigh the harms and costs?	Can the results be applied to your local population /in your context?	Would the experimental intervention provide greater value to the people in your care than any of the existing interventions?
Garland 2014	Yes	Yes	Yes	Partially	Yes	Yes	Yes	Yes	Can't tell	Partially	No
Garland 2019	Yes	Yes	Yes	Partially	Yes	Yes	Yes	Yes	Can't tell	Partially	No
Guarino 2018	Yes	Yes	Yes	Partially	Yes	Yes	Yes	No	Partially	Partially	Yes
Jamison 2010	Yes	Yes	Yes	Partially	Yes	Yes	Yes	No	Partially	Partially	Partially
Kurita 2018	Yes	Yes	Yes	Partially	Yes	Yes	Yes	No	No	Partially	No
Naylor 2010	Yes	Yes	Yes	No	Partially	Yes	Yes	No	Partially	Partially	No
Sullivan 2017	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Partially	Partially
Zheng 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No
Zheng 2019	Yes	Yes	Yes	Yes	Partially	Yes	Yes	Yes	No	Partially	No

Cohort Design	Are the results of the study valid?	Was the cohort recruited in an acceptable way?	Was the exposure accurately measured to minimise bias?	Was the outcome accurately measured to minimise bias?	Have the authors identified all important confounding factors taken account of the confounding factors in the design and/or analysis?	Was the follow up of subjects complete enough? Was the follow up of subjects long enough?	What are the results of this study	How precise are the results?	Do you believe the results?	Can the results be applied to the local population?	Do the results of this study fit with other available evidence	What are the implications of this study for practice?
Chang 2014	Yes	Partially	Yes	Yes	No/No	Yes/No	Positive	No	Can't tell	Yes	Can't tell	Can't tell
Darnell 2018	Partially	Can't tell	Can't tell	Yes	No/No	Can't tell/Yes	Positive	No	Can't tell	Partially	Partially	Can't tell
Doolin 2017	Yes	Can't tell	Partially	Can't tell	No/No	Can't tell/No	Positive	No	Can't tell	No	Can't tell	Can't tell
Goodman 2018	Partially	Can't tell	Partially	Yes	No/No	No/Yes	Positive	Yes	No	Can't tell	Can't tell	Can't tell
Mehl Madrona 2016	Partially	Can't tell	Yes	Can't tell	No/No	Can't tell/Yes	Positive	No	Can't tell	Can't tell	Can't tell	Can't tell
Nilsen 2009	Yes	Can't tell	Yes	Yes	No/No	Can't tell/Can't tell	Positive	No	Yes	Partially	Yes	Can't tell
Scott 2020	Yes	Partially	Partially	Yes	No/No	Can't tell/Can't tell	Neither	No	Yes	Partially	Yes	Can't tell
Ziadni 2020	Yes	Can't tell	Partially	Yes	Partially/No	Yes/Yes	Positive	No	Can't tell	Partially	Can't tell	Can't tell

Qualitative Design	Was there a clear statement of the aims of the research?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Was the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	Is the research of value?
Mathias 2017	Yes	Yes	Partially	Partially	Yes	No	Partially	Yes	Yes	Yes
Young 2017	Yes	Yes	Yes	Can't tell	Yes	No	No	Yes	Yes	Yes

Appendix 4. Data Extraction Template

Study Funding	
Article Author	
Publication Year Country	
Study Design Aims and Purpose of study	
Population Setting	
Study Size Numbers lost to follow up	
Intervention Description Intervention Length/staffing	
Outcomes Opioid reduction Satisfaction with intervention Outcome measurements Follow up time	

Key Findings	
Study Funding	

Appendix 5. Medication Education and Support Group Pilot Results

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n=14

Outcomes	Change	N	%
Opioid dose	Reduced	8	57
	Unchanged	1	7
	Increased	2	14
	Unknown	3	22
Progression to treatment group program	Progress to APT/ waitlist	5	36
	Ongoing phone support	3	21
	Individual HIPS appointments	1	7
	Discharged/Lost to follow up	5	36

Appendix 6. Research Study Methods Protocol

Title: Evaluating the effectiveness of a nurse supported pathway for prescription opioid reduction that enables progression to treatment of chronic non cancer pain: Protocol for a prospective cohort study

Version 1
Masters in Philosophy Research Thesis
Student Researcher: Kathie Nickerson
School of Nursing
University of Newcastle
KATHIE.NICKERSON@HEALTH.NSW.GOV.AU

Study Investigators

Name	Role/Details
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Dr Gena Lieschke Clinical Academic/Research Fellow-Pain, Surgical Service, John Hunter Hospital Hunter New England Health Service E: Gena.Lieschke@health.nsw.gov.au	Co-Supervisor/ Associate Investigator

Abstract

Background – Opioid medication in oral formulation has been prescribed for chronic non cancer pain (CNCP) since the early 1990s. Recent research questions the benefit, and clinical guidelines no longer recommend this use. The question of how best to support people taking prescription opioids to reduce and cease needs further research.

Study Aims – This observational study will examine if a nurse supported prescription opioid reduction pathway (NS-PORP) enables adults with chronic non-cancer pain to reduce opioid

dose and progress to pain treatment. Secondary aims are to evaluate within person opioid dose variation from start, participant satisfaction and healthcare savings.

Method and Analysis - A single centre, prospective cohort design will observe the outcomes of two outpatient treatment arms, a medication education and support group followed by regular phone support (NS-PORP 1) or regular phone support alone (NS-PORP2), compared to a treatment as usual comparator group. Adults with chronic non-cancer pain choosing to progress to pain treatment following assessment, while remaining on prescription opioid medication, make up the treatment population. Adults with chronic non-cancer pain on a similar opioid dose who choose not to enter the treatment arms after assessment, will comprise the comparator group. Logistic regression analysis will identify the association between covariates and the primary outcomes of opioid dose reduction and progression to pain treatment, reported as odds ratios with 95% confidence intervals. The study endpoint is when opioid dose is reduced to 40mg oMEDD, allowing participation in pain treatment programs, or at twelve months. Participant satisfaction will be explored through an ordinally ranked survey and a thematic narrative description. A simple economic evaluation will compare NS-PORP cost to usual treatment.

Discussion – Current research indicates there is insufficient evidence to identify a specific clinical intervention that supports prescription opioid reduction. Pilot study results suggest that an intervention incorporating behavioural change strategies does support opioid reduction.

Trial registration – Retrospectively registered

Keywords (3-10)

Chronic pain, persistent pain, prescription opioids, reduction, weaning, tapering, nurse led, nurse support.

Introduction

The use of prescription opioids for CNCP is no longer supported by many peak clinical bodies. A lack of evidence regarding effective and acceptable treatment approaches to support prescription opioid reduction leads to the quandary of what can be offered to individuals on long term opioids who either elect to, or are mandated by their prescriber to reduce or cease prescription opioid therapy.

Background and Current Knowledge

At present there is no standard approach to support opioid dose reduction and a wide array of clinical interventions are suggested for the purpose. Despite a number of systematic reviews meta-analysis of data has not been attempted due to intervention and measurement variability and small sample sizes [1,2,3] . While guidelines and protocols inform prescribing decisions, improving patient compliance through interventions that target patient behaviour may help with adherence to weaning plans.

There are no nurse-led interventions for opioid reduction described in the literature despite the obvious advantages of using nurses including relative ease of staffing and reduced cost in comparison with other clinical specialties. A recent Australian study undertaken to determine acceptability and feasibility of prescription opioid reduction in a primary care setting noted the integral role practice nurses played in supporting patients through opioid weaning [4].

Aims - The primary aim of this study is to observe if a nurse supported prescription opioid reduction pathway (NS-PORP) enables opioid dose to be reduced sufficiently, for participants with chronic non cancer pain (CNCP), to progress to further pain treatment programs in a multidisciplinary pain service. Secondary outcomes of interest include participant satisfaction with NS-PORP and economic evaluation of running NS-PORP in a multidisciplinary pain service. The study results will extend current knowledge on what facilitates prescription opioid reduction.

Methods

The methods used in this research will be reported using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cohort studies [5].

Study Design

A prospective cohort study design will observe and compare outcomes from two concurrently run treatment arms comprising 1) "Medication Education and Support (MES) Group" followed by scheduled phone support, NL-PORP 1, or 2) phone support alone, NL-PORP 2, with a comparator arm of patients eligible to participate in the treatment arm of the study but choosing not to. Participants who elect to enter the treatment arms of the study will self-select one of the pathways NS-PORP1 or NS-PORP 2. The study design ensures that all participants who wish to participate in the study have access to either treatment pathway.

Study Setting

The single centre study will be undertaken at Hunter Integrated Pain Service (HIPS), a multidisciplinary specialist pain service located at John Hunter Hospital, Newcastle, Australia with data collected from September 2019 to June 2021. The primary pathway for adults referred to HIPS for chronic pain treatment, includes three sequential group programs [24] with the focus being to encourage psychological and physical pain recovery by using a whole person approach underpinned by behavioural change theory [6]. A strong key message of opioid reduction to cessation is communicated at each patient and prescriber interaction. The majority of people referred to HIPS take prescribed opioid medication. Data collected by HIPS indicates that 65.4% of the nearly1600 individuals referred to HIPS in 2018/9 were on regular opioid therapy, with an average dose of 63.3mg[7]. Clinicians at the service noted that patients failed to engage well in pain reduction programs if they remained on moderate to high doses of opioid medication. To promote their active participation, clinical consensus in 2018, led to withholding pain treatment group programs until their opioid use were reduced to a low dose. Patient support for opioid reduction had previously been through ad hoc unscheduled phone contact if requested by the patient or general practitioner (GP). To improve the level of support provided for opioid weaning and to maintain connection with patients who had expressed interest in continuing on to group pain treatment programs but were unable to participate yet, a nurse supported pathway was developed. A pilot study of three exploratory group programs run at HIPS for the purpose of supporting opioid reduction by utilising behaviour change principles, showed promising results with over half of the participants reducing opioid dose and a third progressing to pain treatment programs. A summary of results of the pilot are shown in *Table 1.*

The first group program of the sequential pathway is a 90 minute group introductory and education seminar `Understanding Pain', which presents current knowledge of pain reduction strategies and sets the scene for subsequent education. This is followed by `Assessment and Planning' a five hour group assessment process, presented by a multidisciplinary team, in which participants assess contributors to their own pain experience and develop a pain recovery plan to guide direction of future treatment. Participants who choose to move along the group program pathway to the treatment phase while remaining on an oral morphine equivalent daily dose (oMEDD, which is a conversion of different types of opioid medication to a single comparable amount) of greater than 40mg, are offered NS-PORP to support opioid reduction prior to treatment. Core pain treatment commences in `Active Pain Treatment', a multidisciplinary led group program run over eight weeks, in which participants develop and consolidate through practice, active skills to aid recovery from chronic pain.

Study Interventions

NS-PORP is delivered through two techniques, either a two hour information program `Medication Education and Support group' (MES) followed by phone-support (NS-PORP1) or phone support alone (NS-PORP 2). Both NS-PORP1 and NS-PORP2 are facilitated by a pain specialist registered nurse and consist of two steps. Firstly the introduction at MES (NS-PORP 1) or the initial 20-30 minute phone call (NS-PORP 2) provides the opportunity to discuss medication recommendations given previously at the assessment workshop. This is followed by the second step of scheduled monthly phone calls for ongoing weaning support.

The use of Motivational Interviewing by the facilitator promotes self-management principles with participants encouraged to explore issues using decisional balance methods and write or contribute to their own reduction plans. Readiness to wean is self-assessed, during MES and at phone contact, by determining how important opioid reduction is to the participant and how confident they are in continuing dose reduction.

Study Population

Treatment Group – This will consist of adults over 20 years of age referred to HIPS with CNCP, who remain on a prescription opioid dose over 40mg oMEDD at the assessment group and choose to engage with further group treatment. Excluded from the study cohort are people under the age of twenty years who are currently treated through an `Adolescent and Young Adults' care model participants over the age of 80 years who are on an elderly

pathway and those concurrently enrolled in opioid agonist and substitution treatment programs for whom HIPS does not provide medication recommendations.

Comparator Group -- The treatment as usual comparator group will be group assessment participants who are eligible to participate in the treatment arm of the study but choose not to. They may continue to have care with HIPS or may elect to be discharged and have opioid management from their GP prescribers after having received the same recommendations about opioid reduction as treatment group participants. Their GPs will have received a similar letter to prescribers of treatment group participants recommending a slow opioid reduction.

Recruitment and Consent Process

All patients attending assessment workshops will be offered participation in the study to avoid publicly identifying eligible patients. Assessment workshop facilitators, (not involved in the delivery of intervention arms), will provide attendees with a participant information sheet, offer any additional information required, and collect consent forms from those expressing interest in study participation.

Workshop attendees, not interested in enrolling in the opioid reduction study arms will be invited to participate in the comparator arm by consenting to receive a follow-up phone call at 12 months post A&P workshop for the purpose of checking their progress and recording their current opioid medication dose at the time of contact.

Ethical Considerations

Study approval has been granted by Hunter New England Local Health District Human Research Ethics Committee with reference number 2019/ETH11763 along withUON ethical approval, and the study will be conducted in accordance with the National Statement on the ethical conduct of Research involving humans [8].

Due to the observational nature of the study design, the risks associated with enrolling in the study are inherently low. However, it is possible that participants entering the study may experience physical and psychological withdrawal symptoms. Withdrawal from prescription opioids may be unpleasant but is rarely dangerous [9]. Participants will be informed about the signs and symptoms of opioid withdrawal and mitigation strategies to limit withdrawal symptoms will include slow tapering recommendations, psychological support for participants and pain medicine physician support for prescribers. Participation in the study is voluntary and subsequent treatment with HIPS will not be affected by the choice to participate or not. Data will be collected during clinical contact times to minimise

unnecessary research demands with the exception of a phone call at the end of the study to both study and comparator group participants.

Confidentiality, imperative to both study integrity and ongoing treatment, will be maintained. Treatment information including opioid dose will be recorded in participants electronic health record through `Clinical Applications Portal '(CAP) accessible only by other authorised health professionals. All patient data tabulated for analysis will be de-identified. A study number will identify individual data for use outside of the clinical team and raw data with identifying information will not be available outside the research team. Electronically held data will be on secure password protected HNELHD shared drive and University of Newcastle OwnCloud. Study participants who choose to leave the study can request that their data be excluded from analysis.

Variables

Characteristics of study participants will be gathered from a number of sources. Baseline demographics of age, sex, indigenous status, marital status, employment and postcode are routinely provided by people referred to HIPS will be collected from the person's medical records. Depression anxiety and Stress Score (DASS 21) [10] and Pain Self Efficacy Questionnaire (PSEQ) [11] data are collected from all patients after the introductory seminar. Importance and Confidence will be scored using a 5 point Likert scale. These scores will be recorded, by treatment arm participants at multiple time points when appropriate, starting at the `Medication Education and Support' group or the introductory phone call. MES participants (NS-PORP1 pathway) will fill in a 5 point Reduction Influence Questionnaire in Likert scale form, developed by the student researcher, which explores barriers and facilitators to opioid medication reduction along with responding to a question to describe fears and concerns regarding opioid dose reduction.

Outcome Measures

The primary outcomes will be:

1. Reduction of opioid dose 40mg or less

2. Entry into the first stage of the pain treatment group program

The study start point will be at either `Medication Education and Support' group for NS-PORP1 participants or the initial phone call for those in the NS-PORP2 group and the assessment group for comparator group participants, where the initial opioid dose will be

recorded. For consistency and ease of measuring the variety of opioid medications used by study participants, all dosages will be converted to oMEDD. Opioid dose information will be collected from treatment arm participants at scheduled monthly phone calls and after 12 months for comparator group participants. The study endpoint for participants in both treatment arms and the comparator group will be when their opioid dose is less than 40mg oMEDD.

Secondary outcomes will include rating satisfaction with the treatment intervention and a brief economic evaluation. Satisfaction will be rated by treatment group participants at two time points, after attending the `Medication Education and Support ‘ group, and at the end of the study time frame. A five point Likert scale will be utilised to measure patients perceptions related to; the overall benefit or otherwise of the intervention in supporting opioid dose reduction, how helpful the information provided during the pathway was, and how supportive the facilitator was in delivering the intervention. Treatment group participants will be given an opportunity to describe in words their experience of participating in the study intervention by answering 2 open-ended questions exploring how beneficial the pathway was to their weaning experience and how the pathway could be improved. The cost of implementing NS-PORP will be compared with the cost of specialist pain medicine physician appointments which is the usual approach to supporting prescription opioid reduction.

Potential Confounding Factors and Biases

A priori knowledge indicates that confounding factors that may influence prescription opioid dose reduction relate to GPs’ willingness to deprescribe and patient acceptance of reduction advice. The greatest leverage to changing GP prescribing is legislation. Changes to NSW opioid prescription legislation are planned to be implemented in 2020 and support of this legislation through greater scrutiny of GP prescribing by the Pharmaceutical Regulatory Unit of NSW Health, are likely to result in increased deprescribing. The relationship between prescriber attitude and degree of reduction will not be measured objectively in this study however one of the survey questions in the `Reduction Influence Questionnaire’ asks NS-PORP1 participants to rate subjectively what influenced their dose reduction. One of the options they may choose is influence from their GP.

The response of patients to recommendations to reduce opioid dose depends on many factors. Individuals who consent to participate in the study may have already decided to reduce opioid dose and this may affect the generalisation of results to the source population. Legislative

changes and their implementation by GPs may encourage patients who would otherwise be reluctant to participate in an opioid reduction pathway, to agree to accessing support and study participation. Factors that are associated with improved opioid reduction compliance will be highlighted in the discussion.

General steps to reduce bias will include adhering to STROBE guidelines and study protocol along with reporting any variation from the study protocol. Information bias will be addressed by corroborating participant self-report of opioid dose with health care notes. Loss to follow up will be reduced by using phone contact rather than by mail and if necessary making up to four contact attempts.

Sample Size

Estimating a sample size to power this study is difficult due to the small number of previous studies of a similar nature. Determined a priori and based on the number of potential patients who will be treated with NS-PORP within a twenty four month time frame, the study aims to recruit 120 people with CNCP into the total cohort. This will consist of 60 participants in the two treatment pathways. Anticipating a 30% withdrawal rate this will mean that at least 40 people provide data.

Study Analysis Plan

Study data will be analysed using both quantitative and qualitative methods and will be collected on a Microsoft Excel data base and checked for completeness and accuracy. Baseline cohort characteristics will be reported.

Quantitative Analysis – This will be conducted using the statistical analysis package Stata. Primary outcome analysis will examine the difference between the three study arms in opioid dose reduction to 40mg oMEDD and progression to pain treatment, and will be reported as an odds ratio with a 95% confidence interval and statistical significance set at $p<0.05$. Within person opioid dose variance between both study groups and the comparator group will be analysed using paired t testing, and opioid dose cessation will be reported. A 30% opioid dose reduction, determined through expert consultation, will be considered to be clinically meaningful.

Univariable logistic regression with propensity weighting will determine the association between the primary outcomes of opioid dose reduction enabling progression to pain treatment. Variables will include age, sex, indigenous status, marital status, employment, DASS-21 and PSEQ distance. The number of group program participants at the pain service

ordinarily expected to transition from assessment to treatment groups is less than 30%. A statistically significance effect size determined a priori is that greater than 30% of study participants able to reduce opioid dose and progress to pain treatment.

Secondary outcome analysis will include analysis of ordinal data taken from Likert scale satisfaction measures indicating percentage of participants who were very satisfied, moderately satisfied and not satisfied with NS-PORP.

A simple economic evaluation of the implementation cost of each treatment intervention will be undertaken and will be compared to the cost of usual treatment for opioid reduction support with pain physician consultations. A full economic benefit analysis is beyond the scope of this project, however, cost is a prime concern when determining the feasibility of including an intervention into existing service provision. Outlying values will not be included for analysis and participant data which does not include pre and post opioid dose for all study arms will not be included in the final analysis. Reasons for missing data will be noted and will be included for discussion

Qualitative Analysis -Data gathered from two open ended questions will explore the participant's experience of NS-PORP by asking what was beneficial about the intervention and what could be changed and will generate a descriptive summary followed by the extraction of key words and themes .The questions enquire how helpful NS-PORP was and what could be changed to improve it. This will provide a more comprehensive view of intervention acceptability to the population for whom NS-PORP is designed.

Discussion

The evidence base for nonreliance on prescription opioids has been growing, however, there is a gap in the literature regarding what clinical interventions enable dose reduction and cessation. Treatment that enables change in patient behaviour may improve compliance with opioid reduction recommendations. This study will provide valuable insights into the efficacy, acceptability and costs associated with implementing a nurse-led approach to supporting patients during prescription opioid reduction in the context of CNCP.

Reducing opioid medication not only promotes recovery from chronic pain and improved health generally but also has the potential to reduce health care utilization and encourage reconnection with family and society. Potential factors associated with successful opioid

reduction will be highlighted, and as such could inform future research and clinical practice within specialist pain services and across primary health care.

Study strengths and limitations - The advantage of a cohort study design is that it shows a pragmatic real world view of the intervention effect, and allows consideration of multiple outcomes that result from exposure to NS-PORP. In addition all eligible participants who wish to engage with the treatment pathway are able to. Limitations of the cohort design include the inability to draw a causal conclusion that the pathway itself led to reduced opioid use although inference is possible. In this study the small sample size, restricted by the single study setting and the number of possible participants within the nominated time-frame will limit interpretation of the findings. Potential difficulty retaining participants in the study and data collection in both treatment and comparator arms may relate to the subject population

Dissemination of findings - Primary study reporting will be through a Research Masters thesis dissertation, publication in peer reviewed journals, and presentations at local and national clinical and research meetings. A summary of study results will be presented to the pain service staff and offered to participants. The study sits alongside other projects currently being undertaken by HIPS clinicians regarding opioid reduction.

Conclusion

This protocol sets out the components of a prospective observational cohort study to evaluate if a nurse led pathway supports prescription opioid reduction in adults and enables them to progress to group program treatment of chronic non cancer pain. Analysis will determine if the intervention provides statistically significant outcomes to usual treatment. Satisfaction and economic viability will be measured and qualitative analysis will add information regarding participant satisfaction and experience. The results will augment the collective body of work addressing the need for an effective and acceptable means of supporting patients through prescription opioid medication reduction.

Footnote

Table 1. Medication Education Support MES program pilot result; n=14

Outcomes	Change	n	%
Opioid dose at last contact	Reduced	8	57
	Unchanged	1	7
	Increased	2	14
	Unknown	3	22
Progression to further groups	Progress to APT/ waitlist	4+1*	36
	Ongoing phone support	3	21
	Other HIPS appointment	1	7
	Discharged/Lost to follow up	3+2*	36

* Indicates people who had further HIPS appointments but not in the pain treatment group pathway.

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Appendix 7. Medication and Education Support Group Manual

MEDICATION EDUCATION
AND SUPPORT GROUP
(MES)

Name_____

Hunter Integrated Pain Service (HIPS)
www.hnehealth.nsw.gov.au/pain
Phone: (02) 49223435

Deciding to wean medication can mean be a big change in how you deal with pain.
You are more likely to have success weaning medication if it is important to you to stop and you feel confident about doing so.
This form may indicate to you if you are ready to make that change.

How important is it to you to wean medication: please circle the answer that feels the most correct.

Very Important	Important	Neither	Not Important	Not at all Important

How confident do you feel about weaning medication: please circle the answer that feels the most correct.

Very Confident	Confident	Neither	Not Confident	Not at all Confident

Name_____

Why wean medication?

All medications have benefit and harm.

Long-term use of medication for chronic pain leads to reduced benefit and increased harm. Opioids, benzodiazepines and cannabis are all a problem to health.

HIPS recommends stopping all medications used for chronic pain.

Legislation governing prescribing of opioids has recently changed. This may have altered your GP's ability to prescribe opioids for you.

Research shows that not only do opioids loose effect and have increased harm when taken for longer than 3 months they may actually increase pain. This is due to the nervous system becoming more sensitive.

If you continue to take opioids for longer than 3 months, you may find yourself wanting to take larger doses. This cycle is **tolerance**. The answer is to wean the dose and stop. Depression and anxiety make weaning more difficult. Discuss this with your GP.

For success, stopping needs to be important to you and you need to feel confident about the process.

Activity

Are you concerned about taking medication?– write down 2 reasons to consider stopping

Sticking with weaning

Taking some types of medication for more than a few weeks can lead to **dependence.**

Withdrawal symptoms occur when you stop taking the medication you are usually on, or when you have taken it for a long time and get used to it.

Opioid and cannabis withdrawals are very uncomfortable but are not harmful. Your body may feel sped up or different. Weaning slowly will reduce the severity of symptoms. You can develop a plan for this with your GP or a doctor from HIPS.

Withdrawal from anti-depressants, anti-convulsant or benzodiazepines can be dangerous. If you are considering stopping talk to your GP about a slow weaning program.

Take care of yourself when you wean. Eat good food, drink plenty of fluids and take a daily walk. Get support. Try not to put yourself under too much pressure.

Remind yourself that you can do this.

Are you worried withdrawing will cause you to start taking medications again?

Activity

What can I do to prepare to wean-write down 2 ideas

Name Of OPIOID medication	Medication Strength	How Many do you take per day?	Information	
Name of OTHER Medication	**Medication Strength**	**How Many do you take per day?**	**Type**	**Information**

Weaning Plan

Date	Name of Medication	Morning Dose	Midday Dose	Evening Dose
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Weaning Plan

Date	Name of Medication	Morning Dose	Midday Dose	Evening Dose
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Date	Name of Medication	Morning Dose	Midday Dose	Evening Dose
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Learning more about medication for pain

Type of medicine	**Side effects - if you keep taking it**	**Withdrawal or effect of stopping - if you stop quickly**
Paracetamol Panadol Panamax	**liver failure** airway spasm low platelet count allergic reaction	Return of pain experience
Non-steroidal anti-inflammatory drugs (NSAIDS) Ibuprofen – Nurofen, Brufen Naproxen Voltaren Indomethacin – Indocid, Celecoxib – Celebrex Meloxicam - Mobic Aspirin – Aspro	**stomach upset** including gastric ulcers **kidney failure** **cardiac problems** including infarct, stroke, heart failure, high BP, fluid retention **worsening of asthma** rash (Stevens Johnson Syndrome) headache, dizziness sensitivity to light erectile dysfunction	inflammation swelling pain anxiety due to swelling & pain

Type of medicine	Side effects - if you keep taking it	Withdrawal or effect of stopping – if you stop quickly
Opioids Morphine - MS Contin, Ordine Hydromophone – Jurnista, Dilaudid Fentanyl - Durogesic Oxycodone – Oxycontin, Targin, Endone Methadone - Physeptone Tramadol - Tramal Tapentadol- Palexia Codeine – also found in Panadeine Forte, Panadeine Co Buprenorphine – Norspan	**nausea, vomiting, constipation** **drowsiness, dizziness, difficulty concentrating** **headache** confusion, hallucinations **itchiness**, dry mouth **constipation** difficulty urinating, stiff muscles **immune system suppression** **endocrine function effected** (decreased sex drive and testosterone levels) physical & psychological dependence, addiction **decreased driving capacity, risk of falls** **hyperalgesia** (increased pain) **increased risk of death**	flu-like symptoms nausea, vomiting abdominal cramps, diarrhoea sleeplessness anxiety, agitation, restlessness muscle & joint aches watering eyes & runny nose sweating & chills yawning dilated pupils goose bumps (cold turkey)
Benzodiazepines Diazepam – Valium, Ducene Oxazepam – Serapax, Murelax, Alepam Nitrazepam – Mogadon, Aloderm Temazaaepam – Euhypnos, Normison Alprazolam – Xanax, Kalma, Alprax	**dizziness** **drowsiness** later difficulty sleeping decreased coordination **difficulty concentrating** **memory loss** nightmares blurred vision, slurred speech nausea & vomiting **constipation** dry mouth headache decreased motivation **increased risk of falls / car accidents** **depression & increased suicide risk**	sleeplessness panic attacks tremors, agitation fearfulness muscle spasm irritability sweating depression psychosis suicidal behaviour seizures

Type of medicine	Side effects - if you keep taking it	Withdrawal or effect of stopping-if you stop quickly

Antidepressants Amitriptyline - Endep Citalopram – Cipramil Mirtazipine – Avanza Sertraline – Zoloft Fluvoxamine - Luvox	**sleepiness** **weight gain** dizziness decreased sex drive , constipation or diarrhoea dry mouth, sweating difficulty passing urine **anxiety**	Sleeplessness /tiredness anxiety, agitation & restlessness tremor, palpitations, headache dizziness dreams restless legs nausea muscle & joint pain increased sensitivity return of depression

Anticonvulsants Sodium Valproate – Epilim Gabapentin - Neurontin Pregabalin - Lyrica	**dizziness, sleepiness** unsteadiness , hand shaking **difficulty concentrating** blurred vision nausea, vomiting **constipation** dry mouth **weight gain** , fluid retention reduced platelet count increased suicide risk	agitation & restlessness sleeplessness anxiety nausea & vomiting stomach cramps, diarrhoea, muscle & joint aches seizures

Home Task

Please complete/attempt sometime today

Use your imagination.

If you were no longer taking medication, what would some of the positives be? (e.g. stop weekly Dr visits, be able to travel more easily, feel less tired)

Health
Hunter New England
Local Health District

Reconsidering opioid therapy

Summarised from Health Professional Resources
Hunter Integrated Pain Service
March 2013

A Hunter New England Perspective

Existing evidence does not support the long term efficacy and safety of opioid therapy for chronic non-cancer pain

1. Opioid therapy is **not** indicated for long term use in chronic non-cancer pain based on current evidence. There is a lot of evidence that opioids in the long term provide poor analgesia, lack of physical improvement or improvement in quality of life and give greater risk of harm to both individuals and society than previously recognised.
2. **Indications:** Current evidence based indications for opioid medication use are
    i. Acute pain
    ii. Cancer pain or Palliative or "comfort" care
    iii. Opioid dependency/addiction
3. **Efficacy:** The positive benefit of opioids is supported by strong evidence from randomised controlled trials in acute pain only. The development of tolerance is the major limiting factor in regard to longer term use. Population studies show that patients on long term opioid therapy continue to experience troublesome pain and high levels of functional interference.
4. **Harm:** There is growing evidence of **harm** from **long term opioid use**. The most commonly known problems are constipation, biliary dyskinesia and cognitive impairment. Additional adverse effects include increased risk of death, sleep apnoea, sexual and other endocrine dysfunction, immunosuppression, opioid induced hyperalgesia, driving impairment, the use of opioids to manage psychological distress, misuse, addiction and diversion of drugs. Dependence can make it hard to wean and cease opioids even when there is little analgesic benefit. The use of over-the-counter opioids such as codeine also has little pain relieving benefit and significant risk of harm. A focus on using medication can distract both patient and prescriber from active management strategies which have stronger evidence for long term pain reduction.
5. **Pain Assessment:**
    i. **General:** Multidisciplinary assessment is recommended for pain leading to a broad, whole person management approach.
    ii. **Opioid risk:** Misuse of opioids should be assessed and monitored with the support of government bodies established for this purpose.
6. **Opioid therapy for acute pain:** When opioids are used for acute pain (e.g. post-operative or post trauma pain) the time limited nature of treatment needs to be clearly stated.

   i. Opioid therapy should not be continued beyond **90 days** unless discussed with a pain medicine or addiction medicine specialist.
   ii. A daily oral morphine equivalent dose of **100mg** should not be exceeded unless discussed with a pain medicine or addiction medicine specialist.
   iii. A treatment agreement (verbal or written) can be used to explain potential benefits, adverse effects and therapeutic boundaries. These can include; no early prescriptions; no replacement of lost prescriptions or medications; single prescriber with deputy; regular pharmacy.

7. **Opioid therapy for dependency / addiction:** Opioid Substitution Therapy includes daily pickups, observed medication taking and urinary drug screening. This may be suggested where there are concerns about misuse of opioids. Opioid dose and duration are guided by a doctor with training in addiction medicine. Weaning and ceasing is an alternative strategy to maintenance therapy.
8. **Redirecting opioid therapy for chronic non-cancer pain:** Across the developed world it has been common practice to maintain patients with chronic non cancer pain on long term opioids despite lack of supporting evidence. In part this was a consequence of misinterpreting evidence from acute pain management. Chronic pain evidence has become clearer in recent years and a change in therapy is now required. The following steps are recommended to redirect the management of patients on long term opioids for chronic pain:
   i. Patient education regarding the potential harms and limited benefits of long term opioid therapy.
   ii. Screening for opioid induced endocrine problems.
   iii. The medical goal is opioid cessation while developing non-pharmacological supportive care.
   iv. A time frame to stopping medication is negotiated between the patient and prescribing doctor.
   v. A treatment agreement (verbal or written) can be helpful to explain adverse effects and routine therapeutic boundaries (no early prescriptions; no replacement of lost prescriptions or medications; single prescriber with deputy; regular pharmacy). Random urinary drug testing can be considered as an additional measure.
   vi. Shift the focus to evidence based active management strategies (see www.hnehealth.nsw.gov.au/pain /Community resources).
   vii. The involvement of a pain medicine specialist and multidisciplinary pain management team can be helpful.
9. **Opioid rotation:** Opioid rotation can be used to lower the total opioid dose to facilitate tapering and cessation.
10. **Driving:** Most studies of driving performance show minimal significant psychomotor or cognitive impairment in patients on stable long-term opioid therapy. However the combination of long term opioid use with benzodiazepines or other psychoactive medication can produce significant driving impairment. The following recommendations aim to reduce the risk of driving related harm:
   i. Patients starting opioids should not drive.
   ii. Patients on stable long term opioid regimes are unlikely to be significantly impaired in driving performance. However performance cannot be medically guaranteed and assessment in a driving simulator and/or via on-road driving tests is recommended to exclude driving impairment.
   iii. Patients on long term opioids combined with benzodiazepines should not drive. If either agent is ceased the person is safe to drive after one week.

iv. Patients on maintenance opioids who combine long and short acting agents should not drive for 6 hours after a short acting dose.
v. Patients on long term opioids should not drive for one week after a dose increase.
vi. Patients on long term opioids should not drive if they feel sedated for any reason eg. sleep deprivation or the use of additional drugs including alcohol or cannabis.

Appendix 8. Participant Information Statement

HUNTER INTEGRATED PAIN SERVICE (HIPS)

SURGICAL SERVICES/PAIN MANAGEMENT
JOHN HUNTER HOSPITAL
LOOKOUT ROAD, NEW LAMBTON HEIGHTS
(PO Box 664J, Newcastle NSW 2300)
Phone - 61 02 492 23435 Fax - 61 02 4922 3893
Email: HIPS@health.nsw.gov.au

Hunter Integrated Pain Service Study - Reference number2019/ETH11763

How can opioid reduction be better supported?

Reducing opioid medication is often one of the most difficult things people with chronic pain are asked to do. Options to make this easier involve getting information, getting support and learning to manage pain in different ways.

Hunter Integrated Pain Service (HIPS) offers a pathway to help with opioid and other medication reduction. HIPS is planning to study the process to make the pathway better and easier for people coming to the service.

If you are on opioid medication you will get a phone call a few weeks after this workshop. As well as checking how you are going you will be invited to join the study.

Joining the study is completely voluntary and your treatment or relationship with HIPS clinicians will not be effected if you chose not to. The study is being run by a student researcher.

What does being in the study mean for me if I chose to be included?

If you have chosen further appointments or phone support to help with opioid reduction the information we routinely collect from you can be used in the study. With your permission information HIPS has collected about you including general demographic information, opioid dose, importance, confidence and satisfaction ratings will be included in the study but when we publish and present the results of this study will not be identifiable.

In addition to what you would usually do with us we will ask you a few extra questions about your medication use and there will be an extra phone call at the end to wrap up.

If you have chosen discharge from HIPS we would also appreciate you being part of the study. You will be asked a few extra questions about your medication use and have a phone call in about 12 months to wrap the study up. With your permission information HIPS has collected about you including general demographic information and opioid dose will be included in the study but when we publish and present the results of this study will not be identifiable.

Being in the study will not cost you anything. You may experience feelings of distress about reducing or discussing medication reduction. If you experience these feelings please discuss this with a HIPS clinician.

- If you want to withdraw from the study at any time, you are able to do so without giving a reason.
- You are welcome to get results of the study at the end by email.
- If you change phone numbers please ring and let us know

Should you have concerns about your rights as a participant in this research, or **you have a complaint about the manner in which the research is conducted**, it may be given to the researcher, or, if an independent person is preferred, to Dr Nicole Gerrand, Manager, Research Ethics and Governance Unit, Hunter New England Human Research Ethics Committee, Hunter New England Local Health District, Locked Bag 1, New Lambton NSW 2305, telephone (02) 49214950, email HNELHD-HREC@health.nsw.gov.au with the reference number.

Thank you for considering HIPS opioid reduction study

If you want more information you can ring HIPS on 49223435 The Hunter New England Human Research Ethics Committee of Hunter New England Local Health District, Reference [insert reference number when known? 2019/ETH11763], has approved this research.

Kathie Nickerson
Clinical Nurse Specialist, Student Researcher

Appendix 9. Study Participant Consent Form

Associate Professor Kerry Inder
RW1-38 Richardson Wing
School of Nursing & Midwifery
Faculty of Health & Medicine
University of Newcastle
University Dr, Callaghan NSW 2308
Phone: 02 4042 0522 | E: Kerry.Inder@newcastle.edu.au

Hunter Integrated Pain Service (HIPS)
Surgical Services/ Pain Management
John Hunter Hospital
Lookout Road, New Lambton Heights
(P O Box 664J, Newcastle, NSW 2300)
Phone: 02 49223435 Fax: 49225045
E: HIPS@health.nsw.gov.au

Hunter Integrated Pain Service Study - Reference number2019/ETH11763

PARTICIPANT CONSENT FORM

[Associate Professor Kerry Inder (Primary Supervisor), Kathie Nickerson (Student Researcher), Dr Hema Rajappa (Co-Investigator), Dr Gena Lieschke (Co-Investigator)]

I .....of

(name)

……

(address)

I have read and understand that the study will be conducted as described in the Information Statement, a copy of which I have retained.

I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort or potential side effect and of their implications as far as they are currently known by the researchers.

I understand that my participation in this study will allow the researchers and others, as described in the Information Statement, to have access to my medical record, and I agree to this.

I agree to participate in this study and understand that I can withdraw at any time without providing a reason.

I understand that my personal information will remain confidential to the researchers.

I have had the opportunity to have questions answered to my satisfaction.

I hereby agree to participate in this research study.

SIGNATURE: _____DATE: _____

Declaration by person conducting the consent process

I, the undersigned, have fully explained this research to the patient named above.

NAME: _____

SIGNATURE: _____DATE: _____

Appendix 10. Depression and Anxiety Stress Scale- 21 Questions

Interpretation: DASS severity ratings:

	Depression	Anxiety	Stress
Normal	0-9	0-7	0-14
Mild	10-13	8-9	15-18
Moderate	14-20	10-14	19-25
Severe	21-27	15-19	26-33
Extremely Severe	28+	20+	34+

Clinically significant change is indicated if there is a five or more point change on the full scale DASS, combined with a move to a different severity level*.

Validity: The developers of the DASS suggests that while there is no "fixed standard" the rule of thumb is that there should be no more than one missing item per 7-item scale

Reference: Lovibond, S.H. & Lovibond, P.F. (1995). *Manual for the Depression Anxiety Stress Scales*. (2nd. Ed.) Sydney: Psychology Foundation

http://www2.psy.unsw.edu.au/dass/DASSFAQ.htm

ePPOC Clinical Reference Manual

Australian Version 2 Dataset

Appendix 11. Pain Self-Efficacy Questionnaire

Interpretation:	The severity levels for the PSEQ are: <20 = severe 20-30 = moderate 31-40 = mild >40 = minimal Clinically significant change is indicated where there is a change of seven or more points coupled with a move to a different level of impairment#. The median scores for patients attending a pain clinic are around 24-25. This level is associated with moderate pain-related disability. Scores close to 40 are associated with working despite pain. Scores below about 18 are associated with stronger beliefs that pain relief must come before participation in PMP.
Validity:	At least 9 of the 10 items should be completed

ePOCC Clinical Reference Manual

Australian Version2 Dataset

Appendix 12. Importance and Confidence Rating Scale

Importance and Confidence Rating

Deciding to wean medication can mean be a big change in how you deal with pain.
You are more likely to have success weaning medication if it is important to you to stop and you feel confident about doing so.
This form may indicate to you if you are ready to make that change.

How important is it to you to wean medication: please circle the answer that feels the most correct.

Very Important	Important	Neither	Not Important	Not at all Important

How confident do you feel about weaning medication: please circle the answer that feels the most correct.

Very Confident	Confident	Neither	Not Confident	Not at all Confident

Name_____

Appendix 13. Reduction Influence Questionnaire

To allow us to understand your weaning experience a little more could you answer the following questions.

The length of time I have taken opioid medication is:

Under 1 year	1-2 years	2-5 years	5-10 years	Over 10 years

In that time the dose of opioid medication I am taking has:

Reduced	Not changed	Increased a little	Increased moderately	Increased a lot

The reason I am weaning or considering weaning medication is:

Personal	Health	Family	GP decision	Government regulations

I am involved in the decision to wean:

Not at all	A little	Moderate amount	A fair amount	Very much

How much support do you have in weaning?

None	A little	Moderate amount	A fair amount	Considerable amount

Appendix 14. Satisfactory Rating Scale

Please pick the answer you think most closely describes your experience.

Did you find that attending MES group/phone support (delete whichever is not needed for printing) was helpful with weaning medication?

Not at all	Not really	Undecided	Somewhat	Very much

Did you find the information provided helped with weaning medication?

Not at all	Not really	Undecided	Somewhat	Very much

Did you find the manner of the presenters helped with weaning medication?

Not at all	Not really	Undecided	Somewhat	Very much

Thank you for this valuable information.

Qualitative Satisfaction Rating Scale

Please describe how MES group and phone calls support have helped or not helped with weaning opioid medication.----------
---

What do you think would improve MES group and phone support?----------
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Appendix 15. Verbal Consent Information

Step 1	Ask "Would you like to continue active pain treatment with HIPS?"	**Yes**	Is it okay if we take a few minutes of your time to discuss a study about the usual phone contact pathway that is used at HIPS to support patients to wean from opioids? We know that weaning from opioids can be difficult. At HIPS we offer a pathway to support patients with chronic pain to wean their opioid medication. This pathway is run by an experienced specialist pain nurse and involves monthly phone calls to check how patients are going with weaning their opioid medication, and to offer support and guidance in circumstances where patients might experience difficulties with weaning their medication. The HIPS nurse involved in this work is currently undertaking a study as part of her Master's degree with the University of Newcastle. The study is looking at how good the pathway is in helping patients wean their opioids. Because you are on opioids, you qualify to be invited to join the study. Would you be interested in hearing more about the study so that you could consider participating in the project? *Go to Step 2.*
		No	*Go to step 3.*
Step 2	Ask: "Would be interested in being involved in this study if you are eligible?"	**Yes**	Thanks for considering taking part of in the study, let me tell you a bit more about the study so that you can make a decision if you'd like to participate if you are eligible. First, it is important that you know: • your participation in the study is voluntary, and if you decide not to participate, your care with HIPS or HNELHD will not be affected • your information will be confidential • you are free to withdraw from the study at any time without the need to provide any explanation • there are no costs associated with taking part in the study If you agree to participate in the study: • Information about your medication dose, how ready and confident you are during the weaning process and information such as your age and sex will be collected. • At the completion of the study you will receive a phone call from a research staff member who will ask about your satisfaction with the phone support pathway. • Information collected for the study will be used by the student to write a research report, to present at conferences and will be published in journal articles. None of these publications will have information that could identify you as an individual, or any patient involved in the study. Would you like to agree to participate in this study? Thank you. We will send a letter containing the information we have discussed and relevant contact numbers. If you need to clarify anything about the study, have complaints about the conduct of the study, or decide

			to withdraw from the study you will find the appropriate contact details in this information leaflet. Thank you again, your participation is very much appreciated. You should anticipate that the study nurse will make contact with you in the next couple of weeks.
		No	"Thank you for your time today. Your decision not to participate in the study will not affect your ongoing appointments or care from the HIPS team."
Step 3	Say: "Would you agree to being part of a study involving one phone call in 12 months?"	**Yes**	We respect your decision to not want to participate in the opioid reduction pathway. Would you be open to a research nurse calling you in 12 months to see if you have reduced your opioid medication and what dose you are on? We would like to do this is to see how patients who do the pathway compare to those who don't? If you agreed to this phone call the only information we would need from you is the dose of opioid you are taking at the time so we can combine this with information you have previously provided to HIPS about your age, sex and opioid dose. This information would be included in the study but will not include details that could identify you. Would you be happy to be involved in this way? Thank you we will have the research nurse call you in 12 months from today.
		No	Thank you for discussing this today.

Appendix 16. Qualitative Data Synthesis Table

Concept	Study ID	Gender	Age category	Distance	Starting opioid Dose in oMEDD	Active or passive responces
Helpful						
Support	6 T1	M	>50	2	42	P
	9	F	<50	1	48	
	10 T1	F	<50	1	67	
	11	F	>50	3	88	
	13	F	>50	1	101	
	16	M	>50	2	147	
	21	F	>50	3	195	
	28	F	>50	1	360	
	30	F	>50	3	120	
	33	M	>50	3	50	
	34	M	>50	2	111	
	37	M	>50	1	75	
	39	F	>50	2	110	
	42	F F9 M5	>50 >12 <2	2 23- 9 1- 5	60 >5 <8	
Individualised	24	M	>50	1	58	A
Information	6 T1	M	>50	2	42	A
	9	F	<50	1	48	
	10 T1	F	<50	1	67	
	12 T1	M	>50	1	50	
	20	M	<50	1	50	
	30	F	>50	3	120	
	33	M	>50	3	50	
	34	M	>50	2	111	

Concept	Study ID	Gender	Age category	Distance	Starting opioid Dose in oMEDD	Active or passive responces
	36 T1	M	>50	3	75	
	39	F M6 F3	>50 >7<3	2 1-5, 23 -5	110 >1 <9	A
Education/strategies	6 T1	M	>50	2	42	
	8	M	>50	3	210	
	9	F	<50	1	48	
	10 T1	F	<50	1	67	
	21	F	>50	3	195	
	28	F	>50	1	360	
	33	M	>50	3	50	
	36 T1	M M4 F4	>50 >6<2	3 23 -5, 1-3	75 >3 <5	
Accountability	42	F	>50	2	60	A
Tries all suggested	33	M	>50	3	50	A
	36 T1	M M2	>50 >2	3 3-2	75	
Facilitator	8	M	>50	3	210	P
	11	F	>50	3	88	
	16	M	>50	2	147	
	21	F	>50	3	195	
	28	F	>50	1	360	
	30	F	>50	3	120	
	34	M	>50	2	111	
	39	F	>50	2	110	
	42	F M-3, F -6	>50 >9	2 23-8, 1-1	60 >6, <2	
Understands other issues	11	F	>50	3	88	P
	24	M	>50	1	58	
GP involvement	8	M	>50	3	210	A
	9	F	<50	1	48	
	10 T1	F	<50	1	67	

Concept	Study ID	Gender	Age category	Distance	Starting opioid Dose in oMEDD	Active or passive responces
	12 T1	M	>50	1	50	
	30	F	>50	3	120	
	33	M M-3 F-3	>50 >4, <2	3 3-3, 1-3	50 >2, <4	
Wants alternate med	27	M	>50	2	60	P
Wanted meds	34	M	>50	2	111	P
	37	M M-3	>50 >3	1	75 >1	
Unable to distinguish						
Doing it by self	2	F	>50	1	105	A
	15 T1	M	<50	1	150	
Still needs meds	1	M	>50	2	105	P
	2	F	>50	1	105	
	3 T1	M	>50	1	300	
Alternative meds	7 T1	M	>50	1	107	P
	14	F M-3, F-2	>50 >5	2	160	
Other issues	19	F	<50	2	50 >2	P
Unhelpful						
Doing it by self	4	F	<50	2	45	A
GP assistance	17	F	>50	1	159	A
Still needs meds	4	F F-3	<50	2	45	P
Change						
To consideration /listening	4	F	<50	2	45	P
To open mind (cannabis)	10 T1	F	<50	1	67	P
Face-to-Face	12 T1	M	>50	1	50	A
	28	F F-3	>50	1 1 -3	360	
Unable to distinguish						
	2	F	>50	1	105	

Concept	Study ID	Gender	Age category	Distance	Starting opioid Dose in oMEDD	Active or passive responces
No change						
No change but	1	M	>50	2	105	P
	3 T1	M	>50	1	300	
	16	M	>50	2	147	
Prefers face to face GP help	17	F	>50	1	159	
	27	M M-4, F -2	>50	2	60	
Other issues	19	F	<50	2	50	
More GP feedback	33	M	>50>6 <1	31-3, 23-5	50>3	A
No change good						A
	11	F	>50	3	88	
	13	F	>50	1	101	
	20	M	<50	1	60	
	21	F	>50	3	195	
	34	M	>50	2	111	
	36 T1	M	>50	3	75	
	39	F	>50	2	110	
	42	F	>50	2	60	
Phone based	30	F	>50	3	120	
	37	M	>50	1	75	
Praise	6 T1	M	>50	2	42	
	7 T1	M	>50	1	107	
	8	M	>50	3	210	
	15 T1	M	<50	1	150	
	24	M	>50	1	58	
Actually knew it	8	M F-6, M-10	>50 >14 <2	3 23 – 10 1-6	210 >6, <10	
Problems with other health professionals						

Concept	Study ID	Gender	Age category	Distance	Starting opioid Dose in oMEDD	Active or passive responces
	21	F	>50	3	195	
	19	F	>50	2	50	
	9	F	<50	1	48	
	14	F F-4	>50 >3, <1	2 23 -3	160 <2	

F = female; GP = General Practitioner; M = male;
Distance 1= <30 minutes from pain service location
2=30-90 minutes
3->90 minutes