PRESCRIPTION OPIOID ANALGESIC DRUG MISUSE: WHAT CAN WE LEARN FROM DOCTOR-SHOPPING BEHAVIOUR

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Doctor shopping, drug seeking, drug abuse, opioid drugs, drug dependence, pharmaceutical drugs, pharmaceutical opioids, prescription drugs, prescription drug monitoring, prescription opioids, substance use disorder,

Table of Contents

Contents

List of Figures

List of Tables

List of Abbreviations

Abbreviations

Abbreviation	Full title
DDU	Drugs of Dependence Unit (see MRQ)
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition – Text Revision
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
GP	General Practitioner
HDPR	*Health (Drugs & Poisons) Regulation 1996* (Qld)
ICD-10	International Classification of Disease, 10th Edition
ICD-9-CM	International Classification of Disease, 9th Edition (Clinical Modification)
mcg	microgram (one millionth (1×10^{-6}) of a gram)
mg	milligram (one thousandth (1×10^{-3}) of a gram)
MODDS	Monitoring of Drugs of Dependence System
MRQ	Medicine Regulation and Quality (formerly DDU)
NDS	National Drug Strategy (Australia)
OME	Oral Morphine Equivalent
OST	Opioid substitution treatment
PBS	Pharmaceutical Benefits Scheme (Australia)
PDMP	Prescription Drug Monitoring Program
POA drugs	Pharmaceutical Opioid Analgesic drugs
SUD	Substance use disorder
SUSMP	Standard for the Uniform Scheduling of Medicines and Poisons (also known as the Poisons Standard)
TGA	Therapeutic Goods Administration (Australia)

Statement of Original Authorship

The work contained in this thesis has not been previously submitted to meet requirements for an award at this or any other higher education institution. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made.

Signature: QUT Verified Signature

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Abstract

Emerging evidence supports that prescription opioid analgesic (POA) drugs have become widely misused over the last 20 years in Australia. Prescription drug seeking or doctor shopping can allow potentially drug-dependent persons to obtain POA drugs for misuse and diversion. However, there is a lack of consensus in regards to definitions of doctor shopping.

A first study sought input from a range of experts in the fields of drug dependence and pain management to determine whether there was agreement on what levels of doctor shopping or POA drug misuse might relate to substance misuse disorders. A Delphi study was undertaken over two iterations to see if agreement could be reached. Results did not support consistent agreement between experts with only general consensus that dependence or abuse could be related to even minimal levels of doctor shopping.

In a second study, these elements of doctor shopping were then tested in the Queensland POA drug-monitoring database of all 248,389 persons who received POA drugs in 2013. The aim of the study was to determine what elements of doctor shopping could discriminate between non-problematic and potentially aberrant POA drug use.

A total of 15,545 persons who were potential doctor shoppers were assessed on prescription activity variables, volumes of drugs obtained, and known drug dependence status. Results found a sub-population of 2,842 persons not previously identified as drug dependent that appeared to be aberrant POA drug users based on volume of prescriptions obtained and drugs consumed.

A third study examined historical prescription records to determine the length of time persons had been exposed to prescription opioids and whether this exposure was related to aberrant POA drug use. Results found that the majority of aberrant POA

drug users had similar previous years' levels of consumption, and non-aberrant POA drug users had limited previous years POA drug consumption.

Outcomes suggest that doctor shopping is not consistently relate to aberrant POA drug use. Chronic long-term prescribing of multiple prescriptions for high doses and volumes of drugs with any level of doctor shopping could equally suggest a person at risk of having or developing drug misuse disorders on POA drugs. This suggests that policy and intervention focus on doctor shopping as a key issue of POA drug misuse might require further examination. Results, also suggest that long-term high dosage patients are perhaps a more appropriate target of interventions to reduce harms related to POA drugs use.

Chapter 1: Introduction

1.1 INTRODUCTION

In the last two decades there has been a significant increase in the prescription of opioid analgesic (POA) drugs across most Western countries, particularly in the United States of America (Campbell et al., 2010; Dowell, Haegerich, & Chou, 2016; Gilson & Dahl.J., 2004; Manchikanti, 2008; Sehgal, Manchikanti, & Smith, 2012; Vowles et al., 2015). Australia has experienced a similar rise in the rates of prescription of POA drugs over the same timeframe (Bell, 1997; Berecki-Gisolf, Hassani-Mahmooei, Clapperton, & McClure, 2016; Blanch, Buckley, Srasuebkul, Litchfield, & Pearson, 2015; Dobbin, 2010a; Karanges, Blanch, Buckley, & Pearson, 2016; Leong, Murnion, & Haber, 2009; Roxburgh, 2011).

Opioid analgesic drugs are an accepted and essential part of conventional pain management treatment. These drugs are similar in chemical structure to illicit heroin, and the cause of similar physiological effects. Opioids – licit or illicit – are prone to being abused and causing dependence and other harms when used inappropriately, however recent evidence suggest particular formulations are more likely to be misused than others.

Australia is signatory to the *United Nations Single Convention on Narcotic Drugs of 1961* (United Nations, 1988), under which heroin is considered an illicit drug and subject to various legal sanctions by signatory governments to prevent its production and supply, and reduce the harms caused by its misuse. The broader policy response to manage illicit drugs is captured in Australia's National Drug Strategy (Ministerial Council on Drug Strategy, 2004, 2011).

Pharmaceutical opioid analgesic (POA) drugs, on the other hand, are legal in most countries' jurisdictions and are subject to legislation and regulation in regards to their import, production, supply and use, as are other medications. In Australia this process is administered by the Therapeutic Goods Administration (TGA)

(Commonwealth of Australia, 1989). The use of many medications in Australia is subsidised by the Commonwealth Government under the Pharmaceutical Benefits Scheme (PBS) administered by Medicare Australia (Medicare Australia, 2011).

Reasons for this increase in the use of POA drugs include: an increasing prevalence of chronic pain conditions (Access Economics Pty Ltd, 2007; Blyth et al., 2001; Zacny et al., 2003); improved quality of care by use of these drugs in palliative care and pain management (American Academy of Pain Medicine & American Pain Society, 1996; Zacny, et al., 2003); safer and improved extended release versions of POA drugs (Passik, 2009); more confidence or less reticence by medical practitioners in the use of these drugs (Cicero, Inciardi, & Surratt, 2007; Elise Bailey, 2006); and successful marketing and promotion of certain POA drugs by pharmaceutical companies (Elise Bailey, 2006; Van Zee, 2009).

There is also evidence that the increased volume of prescribed POA drugs might not be accounted for by the increases in prevalence of chronic or palliative pain management in the community (Hollingsworth, 2013, Manchikanti, 2007; Manchikanti, 2008; Manchikanti et al., 2012). This issue remains untested at this point; however, it implies that a proportion of these POA drugs are being used for non-therapeutic purposes. It is now widely held that the increasing availability of these drugs has led to greater numbers of people being exposed to the potential risks of misuse (Fischer, Gittins, & Rehm, 2008; Joranson, Ryan, Gilson, & Dahl, 2000; McCabe, Teter, & Boyd, 2006).

There are a number of negative consequences associated with this increase in use of POA drugs. These drugs have been linked to significant increases in drug-related harms such as dependence and abuse, overdose, and death (Fischer & Rehm, 2009; Florida Medical Examiners Commission, 2010; Graham, Gold, & Goldberger, 2009; Hall, 2008; Layne, Pellegrino, & Lerfald, 2009; McLellan & Turner, 2008; Rintoul, Dobbin, Ozanne-Smith, & Drummer, 2010). Furthermore, epidemiological evidence shows that non-medical use and abuse of these drugs has similarly increased in the general population (Amari, Rehm, Goldner, & Fischer, 2011; Becker, Sullivan,

Tetrault, Desai, & Fiellin, 2008; Centers for Disease Control, 2010a; Fischer, Nakamura, Rush, Rehm, & Urbanoski, 2010; Manchikanti, 2008; Maxwell, 2005). A systematic review by Vowles and others of 38 studies of opioid use in chronic pain found rates of misuse between 21% and 28%, and rates of addiction between 8 and 12 per cent (Vowles, et al., 2015).

In Australia, use of POA drugs has increased almost 400% in the period from 1990 to 2014 (Karanges, et al., 2016). The main factors influencing this increase appears to be the 17-fold increase in the use of long-acting opioids, such as morphine and methadone between 1990 and 2000; and then marked increase in oxycodone, codeine and other POA drugs between 2000 and 2011 (Hollingworth, Gray, Hall, & Najman, 2015; Karanges, et al., 2016). Campbell and others (2015) found evidence of dependence in a sample of Australian chronic pain patients on long-term POA drugs at rates of 8.5% within their lifetime and 4.7% in the past year (Campbell et al., 2015). There is limited Australian evidence based on large-scale community surveys and key informant research that suggests POA drug are also being used for non-medical purposes, and being more frequently used by illicit drug users as substitutes for illicit drugs (Cogger & Kinner, 2009; Crime and Misconduct Commission, 2010; Degenhardt et al., 2006; Dobbin, 2009; Iversen, Topp, & Maher, 2010). However, there is limited information about the extent of the inappropriate use of these drugs in the Australian population and the harm caused (Berecki-Gisolf, et al., 2016; Rintoul, et al., 2010).

There is evidence that an increasing incidence of people are entering drug treatment services reporting POA drugs as their primary drug of dependence (AIHW (Australian Institute of Health and Welfare), 2009a, 2009b). It has been suggested that this phenomenon could be largely due the established illicit drug-misusing population that is using POA drugs as alternative sources to other illicit opioid drugs. Initial research in this area shows that these drugs users are not obtaining prescriptions for POA drugs themselves, but obtaining the drugs after they are possibly diverted from prescription recipients (Crime and Misconduct Commission, 2010; Fischer, Gittins, Kendall, & Rehm, 2009; Inciardi, Surratt, Kurtz, & Cicero, 2007; Inciardi et al., 2010).

It has been further hypothesised that another population of drug misusers are emerging who have only been exposed to POA drugs by being prescribed these by medical practitioners (Dart, 2006; Edlund et al., In Press; Fischer, Gittins, et al., 2008; Fredheim, Skurtveit, Breivik, & Borchgrevink, 2010). It is suggested that this population might be unrelated to known illicit drug-using populations (Nielsen & Thompson, 2008). These first-hand POA drug consumers might be at risk of developing drug dependence or abuse due to their therapeutic exposure to these drugs. Therefore, it is possible there is an emerging population of persons with drug-related harms that is different from the known illicit opioid users.

Drug-seeking behaviour is one key indicator that suggests possible drug misuse or dependence. The amount of time a person devotes to obtaining drugs of dependence is one criteria used in most accepted diagnoses of drug dependence or abuse, such as DSM-IV-R (American Psychiatric Association, 2000) or ICD9-CM (Medicode (Firm), 1996) or ICD-10 (World Health Organisation, 2007). Furthermore, the DSM 5 (American Psychiatric Association, 2014) released during the course of this study also retained a criteria for substance use disorders related to the amount of time a person devoted to obtaining their substance of dependence (See Appendix A). However, there are different understandings of problematic prescription drug use that are pertinent. The American Academy of Pain Medicine proposed the construct of 'addiction' (Campbell et al, 2016), that is different again from the construct of dependence derived from the DSM. This highlights some of the diverse opinion in expert fields in this area and the complexity of assessing substance use disorders with POA drug use.

'Doctor shopping' is the common term used to describe the behaviour of obtaining multiple prescriptions for POA drugs from multiple prescribing doctors for dosages in excess of accepted therapeutic limits (Brettingham-Moore, 2010; Mailloux, Cummings, & Mugdh, 2010; Martyres, Clode, & Burns, 2004; Medicare Australia, 2011; Pradel et al., 2009). It is suggested that 'doctor shopping' could be used as one diagnostic criterion in attempting to assess opioid drug dependence or abuse in POA drug-using populations.

Medicare Australia in 1996/97 identified more than 10,000 persons as 'doctor shoppers' for any class of drug (Medicare Australia, 1998). 'Doctor shopping' was defined as visiting 15 or more different general practitioners within 12 months and obtaining more prescription medication than is clinically necessary (Medicare Australia, 1998). It was estimated this cost the community over $31 million in possibly unwarranted consultations and subsidised prescriptions (Medicare Australia, 1998). The definition does not establish what is meant by 'more medication than necessary', nor does it provide clarity on how many prescriptions were obtained, how many prescribers consulted and only suggests these criteria have a possible relationship to substance use disorders.

Each Australian state has different state-based legislation to regulate POA drugs. Queensland is one of the few states that maintains a prescription drug-monitoring system of POA drugs that records all prescriptions dispensed at community pharmacies via its health department, Queensland Health. This information allows for the complete capture of the state's POA drug prescribing in the general community and the identification of people engaged in 'doctor-shopping' behaviour. This capture of an entire population dataset in an area of emerging public health concerns around POA drug misuse gives a unique opportunity to examine and analyse aspects of this issue.

The aim of this research is to identify and describe the population of persons engaged in 'doctor shopping' and to determine what characteristics of the POA drug-misusing population and their drug-seeking behaviour suggest substance misuse disorders and what factors might discriminate them against other persons receiving POA drug therapy. These results could determine whether central database records of dispensed POA drug prescriptions, and what particulars of those records, might help identify and monitor problematic POA drug use. To be able to appropriately identify and reduce misuse of POA drugs and their diversion into the community where they could cause harm when used outside of a therapeutic regime is important for healthcare providers and regulators. However, a critical consideration is that any actions to reduce

inappropriate use of POA drugs do not inadvertently lead to their use being limited in legitimate therapeutic circumstances. This is a particular conundrum in the management of POA drugs, because, as opposed to illicit drugs, the initial means of supply is within the control of healthcare providers and regulators.

This thesis is presented in five sections: the first section (Chapter Two) is a literature review and research overview of the area of POA drug use and the phenomenon of doctor shopping, and establishes the underlying concepts and ideas. The next sections are three studies to understand the concepts of doctor shopping and quantify and describe that behaviour. The first study (Chapter Three) involves seeking the views of various experts on their definition of problematic POA drug use and doctor-shopping behaviour. The second study (Chapter Four) takes the outcomes of the first study and seeks to apply a definition of doctor shopping using the information from a single year of dispensing of the prescription drug-monitoring program (PDMP). The final study (Chapter 5) then examines those persons identified in Study Two to investigate their historical prescription records to investigate patterns over time in the establishment of doctor-shopping behaviour. A final summary and conclusion of all studies in presented in the last section of this thesis (Chapter Six).

Chapter 2: Literature Review and Research Overview

A review of the literature has been conducted to provide background and context to the emerging concern of POA drug misuse. The review will also determine gaps in current knowledge, especially as it relates to determination of misuse and dependence on pharmaceutical opioid drugs and how this might be determined via prescription drug monitoring.

The preliminary literature review is in eight sections. The following nine areas set out the various dimensions around POA drug use:

1. Opioid analgesic drug defined
2. Policy context of opioid drugs
3. Clinical context of opioid drugs use
4. Evidence of increasing supply and availability
5. Costs and benefits of increased supply
6. Concepts and theories in opioid drugs use
7. Populations of opioid drug users
8. Relevance of 'doctor shoppers'

The final section examines the current practice of managing pharmaceutical opioid dependence in Queensland, Australia, and the opportunities available to address the gaps in knowledge in this area, particularly through the use of prescription drug-monitoring systems.

2.1 OPIOID ANALGESIC DRUGS DEFINED

'Opiates' refer to any drugs derived from the opium poppy, whereas the term 'opioid' refers to any synthetic narcotic that produces the same effects as opiates. However, opioid has become a general term to describe both opioids and opiates. Opioid drugs are also defined by their action, as any substance that binds to the

particular opioid receptors in the human brain (Gutstein & Akil, 2006). Opioid analgesic drugs refer to the class of pain-relieving drugs that act on the central nervous system (American Academy of Pain Medicine & American Pain Society, 1996; American Academy of Pain Medicine & American Society of Addiction Medicine, 2001).

'Analgesic' is the broad medical term that refers to any medication capable of reducing or eliminating pain, and can include non-opioids or opiates. For ease of reference the more general and widely-accepted term 'pharmaceutical opioid analgesic' (POA drugs) will be used throughout to describe pharmaceutical preparations of opiates and opioids.

POA drugs include preparations such as morphine, methadone, oxycodone, pethidine and others. Opioid analgesic drugs can be used to treat acute and chronic pain conditions and are also used as substitution agents to manage persons dependent on illicit opioids such as heroin. This is discussed in more detail in later sections.

Table 2.1 sets out the full range of POA drugs available in Australia, the opioid/opiate status of each drug, as well as brand names used by particular pharmaceutical companies. The list of drugs presented here are only those known as controlled or 'Schedule 8' drugs in Australia (Commonwealth of Australia, 2010). These Schedule 8 drugs are POA drugs that are only available on prescription and have extra controls on their use. The form or preparation of each POA drug that is the subject of this study is presented in Table 2.1. The table also includes the form of the drugs – such as whether it is a tablet, capsule or liquid – and the indicated means of administering or route of administration of each drug. Both features potentially have been associated with the inappropriate use of particular POA drugs. Figure 2.1 illustrates the two most commonly prescribed POA Schedule 8 drugs – morphine and oxycodone controlled-release tablets – in the various dosage sizes that are available in Australia.

Table 2.1.

POA drug preparations available in Australia as Schedule 8 drugs

Generic name	Opioid/ Opiate	Common brand name	Preparation	Route of administration
Buprenorphine	Opioid	Subutex**	Tablet	Sublingual
		Suboxone*	Strip	Sublingual
		*	Liquid	Oral
		Temgesic		
Codeine	Opiate		Tablet	Oral
Fentanyl	Opioid		Patch/Matrix	Topical
Hydromorphone	Opioid	Dilaudid	Tablet	Oral
Methadone	Opioid	Physeptone	Tablet	Oral
		Methadone **	Liquid	Oral
		Methadone **	Liquid	Oral
		Biodone	Syrup	Oral
Morphine	Opiate	MS Contin*	Tablet	Oral
		MS Mono*	Tablet	Oral
		Kapanol*	Capsule	Oral
		Morphine	Ampoule	Intravenous
Oxycodone	Opioid	Endone	Tablet	Oral
		OxyContin*	Tablet	Oral
Oxycodone + Naloxone		Targin	Tablet	Oral
Pethidine	Opioid		Ampoule	Intramuscular
Tapentadol	Opioid		Tablet	Oral

**controlled/slow release preparations*

***opioid substitution preparation treatments*

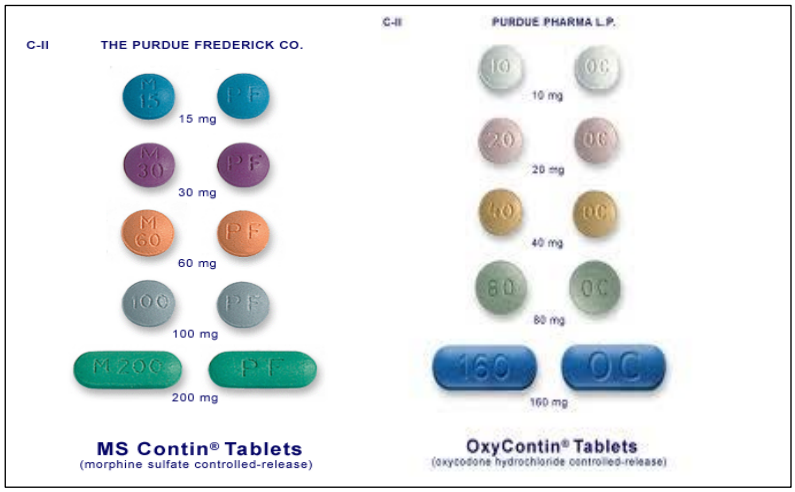

Figure 2.1. Pictures of morphine and oxycodone controlled-release tablets

(source Purdue Pharma)

Some POA drugs are in other drug schedules – such as tramadol, which is a Schedule 4 drug – and are not subject to the same levels of controls or monitoring via prescription drug-monitoring under Australian law. Some opioid drugs, such as lower strengths of codeine, are available as 'over-the-counter' medications that can be sold by pharmacists to patients without a doctor's prescription. These preparations are also not monitored. This study covers those POA drugs that are in set out in Table 2.1.

Opioid drugs are chemically similar in structure and action to illicitly-used heroin. All opioids have similar neurochemical actions and generally cause similar effects. Opioids are classed as 'depressant drugs' due to their actions on the central nervous system that cause sedation and respiratory depression (Gutstein & Akil, 2006). Opioids also act in various ways on certain opioid receptors in the human brain to limit the reception of pain responses from the body to the brain (Gutstein & Akil, 2006).

Opioids can also stimulate the release to the neurotransmitter dopamine that is associated with sensation of pleasure (Gutstein & Akil, 2006). The human brain produces its own opioids, known as endogenous opioids (Gutstein & Akil, 2006), by which it regulates pain responses. Non-endogenous opioid drugs possess particular

structures that allow them to bind to the same receptor sites as endogenous opioids to either mimic or increase the endogenous opioid effects.

Synthetic analogues of opiates, known as opioids, were first derived in the early 19th century and were patented as proprietary drugs by pharmaceutical corporations (Brownstein, 1993). Recent innovations over the last two decades have seen the release of some sustained release preparations of morphine, known as Kapanol™, MS Contin™, MS Mono™, and oxycodone, marketed as OxyContin™ (Elise Bailey, 2006; Manchikanti, 2007) (see Table 2.1). These preparations for oral administration include retardant agents to ensure the opioid is more slowly absorbed into the gastro-intestinal tract, so the dosage effect can be sustained for a six or twelve hour time period (Bruera et al., 1998; Watson, Moulin, Watt-Watson, Gordon, & Eisenhoffer, 2003).

Different opioid preparations are not all of equivalent, or equal, analgesic dosage or strength. To compare the dosages of different opioids equianalgesic tables are used that relate dosage to equivalent dosage of morphine, or the dose of a certain preparation required to equate to a therapeutic dosage of morphine. Table 2.2 below sets out examples of equianalgesic comparisons for the commonly prescribed POA drug preparations in Australia.

Table 2.2. *Total daily oral morphine equivalent table for Australian POA Schedule 8 drugs**7

Drug		Recommended research OME Conversion factor
ORAL PREPARATIONS		
Swallowed		
Morphine	mg/day	1
Oxycodone	mg/day	1.5
Hydromorphone	mg/day	5
Codeine	mg/day	0.13
Dextropropoxyphene	mg/day	0.1
Tapentadol	mg/day	0.4
Methadone	mg/day	4.7
Buccal/Sublingual	mg/day	
Buprenorphine	mg/day	37.5
Fentanyl	mcg/day	0.1
TRANSDERMAL PREPARATIONS		
Buprenorphine	mcg/hr	25
Fentanyl	mcg/hr	3
PARENTERAL PREPARATIONS		
Morphine	mg/day	3
Oxycondone	mg/day	3
Hydromorphone	mg/day	15
Pethidine	mg/day	0.4
Fentanyl	mcg/day	0.2
Methadone	mg/day	13.5
Buprenorphine		75
RECTAL PREPARATIONS		
Oxycodone	mg/day	15

Note: mg-milligrams, mcg-micrograms
*Excerpt from (Nielsen, 2014)

2.1.1 Evidence for increased opioid supply and availability

From an international perspective, many countries have limited access to pharmaceutical opioid analgesic preparations. The 'Montreal Declaration' (International Association for the Study of Pain, 2011) of the International Association for the Study of Pain representing 84 countries declared chronic pain was under-recognised and under-treated in most countries of the world. The United Nations has recognised access to pain treatment as a basic human right (Lohman, Schleifer, & Amon, 2010) and opioid analgesic drugs are recognised as essential medicines (World Health Organisation, 2013).

The United Nations under the provisions of the *Single Convention on the use of Narcotic Drugs* (United Nations Office on Drugs and Crime, 1961) collects data on worldwide opioid analgesic consumption by country. Since 1986, it found that a small number of developed countries consume most of the world's POA drugs, whilst the remaining countries consume only a small proportion, but contain over 80% of the world's population (International Narcotics Control Board, 2014).

Prescriptions for POA drugs have increased significantly in the last two decades, particularly in the United States of America. Medical use of morphine and oxycodone increased 59% and 22% respectively from 1991 to 1996 (Joranson, et al., 2000). The volumes of sales of opioids per person increased from 74 milligrams per person per year in 1977 to 329 milligrams in 2006 (Manchikanti, 2008), which represents a 347% increase.

In Australia the prescribing rates of opioid analgesic drugs has steadily increased over the past two decades (Bell, 1997; Berecki-Gisolf, et al., 2016; Degenhardt, et al., 2006; Dobbin, 2010a; Karanges, et al., 2016; Leong, et al., 2009). Data from the Commonwealth Government's Office of Chemical Safety's (Commonwealth of Australia, 2011) monitoring of wholesale supplies of all opioid drugs shows there has been an over 900% increase in POA drugs sales since 2001. Figure 2.2 below graphically shows this increase by POA drug type.

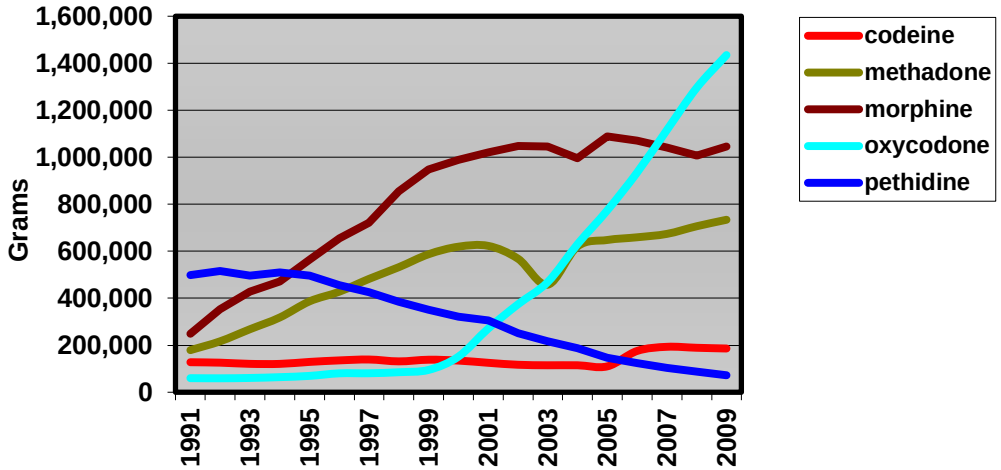

Figure 2-2. Australian wholesale sales of POA drugs by drug type (1991-2009) Source: (Commonwealth of Australia, 2011)

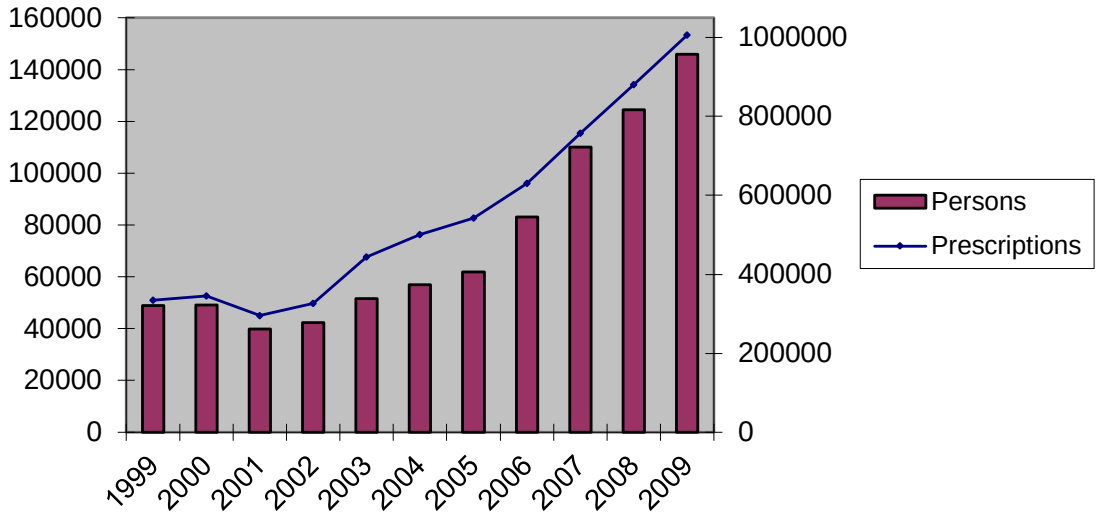

Figure 2-3. Opioid Analgesics person and prescription count, 1999-2009 for Queensland, Australia. Source: (Drugs of Dependence Unit, 2010)

Queensland Health's annual statistical reports show similar increases in the rates of POA drugs being dispensed on prescriptions in the general community, with a greater than 300% increase from 2001 to 2009 for total prescriptions issued for, and persons receiving, prescriptions of POA drugs (Drugs of Dependence Unit, 2006, 2010). Figure 2-3 above graphically shows this increase over 10 years.

Suggested reasons for the increased use of POA drugs include: an ageing population with increased chronic pain management requirements; increased use in

acute pain conditions and palliative care; doctors' comfort and confidence in using new formulations of POA drug preparations; and marketing campaigns by pharmaceutical companies (Gilson, 2004; Zacny, et al., 2003). The dramatic rise in use of POA drug prescribing has led to suggestions of overprescribing or inappropriate use of POA in pain management (Manchikanti, 2007). This over-use has been proposed as a cause of increased exposure to persons with these drugs and ease of access which has been associated with the rise in the drug-related harms where POA drugs are the principal drugs of use.

Controlled release preparations of the morphine (e.g. MS Contin ™, Kapanol ™) and oxycodone (e.g. OxyContin™) were launched in the Australian market in 1991 and 2001 respectively. These preparations all obtained subsidy status under the PBS at this time, and a rapid escalation in the prescription of both preparations can be shown after their release dates (See Figure 2-3 above).

The above factors and introduction of new drug preparations appear to have contributed in some combination to the current situation of high volume prescribing of POA drugs and associated harms.

2.2 COSTS AND BENEFITS OF INCREASED OPIOID SUPPLY AND AVAILABILITY

POA drugs have legitimate therapeutic applications and are prone to misuse and the cause of harm. It is important therefore to consider both the benefits and detriments of increased access to these drugs for the community.

2.2.1 Benefits of increased supply and availability

The legitimate use of pharmaceutical opioid drugs for certain indicated conditions provides effective and appropriate treatment for many individuals and helps relieve considerable suffering. In particular, greater access to and improved formulations of POA drugs has provided benefits to persons suffering pain conditions, in palliative or end of life treatment, and for the treatment of those people with opioid dependence.

Persons suffering from short-term or acute pain conditions due to injury or recovery from surgical procedures benefit significantly from the use of POA drugs in the short-term. POA drugs also have an established pain management treatment in palliative care and cancer pain treatments. A recent Australian review examining the clinical and research literature to date found there was reliable evidence for the efficacy of POA drugs in the management of acute pain conditions (Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine, 2010).

However, there is more contention about the use of POA drugs in the treatment of chronic non-malignant or persistent pain conditions. In an assessment of the prevalence of chronic pain in Australia, Access Economics suggested more than one-third of the population would experience such a condition at some point in their life (Access Economics Pty Ltd, 2007; AIHW Australian GP Statistics and Classification Centre, 2008). Rosenblum and et al (Rosenblum, Marsch, Joseph, & Portenoy, 2008) summarised these concerns. Firstly, there remain questions as to the safety and efficacy of POA drugs in treatment of chronic pain; and secondly there are concerns about their abuse liability. Shifts in attitudes to these concerns have led to different levels of restrictiveness or liberalness with the use of POA drugs for chronic pain conditions. Most recent reviews now question the efficacy of POA drugs for treatment of chronic pain conditions (Chou et al., 2015; Martell et al., 2007). However, with chronic un-resolving pain conditions that are not responding to other treatments, POA drugs are often front-line treatments. There is some consideration that for those patients who are not at risk of abuse or dependence, maintenance on POA drugs might be the optimal course of treatment (Noble et al., 2010).

POA drugs also form the basis of medically-based substitution treatments for people who are dependent on heroin and illicitly obtained opioids. Methadone and buprenorphine are prescribed in controlled doses to assist stabilising drug dependent individuals. This reduces the risk of harms such as injecting drug use, the acquisition of blood borne viruses, and engagement in criminal activity to support illicit drug use

(AIHW (Australian Institute of Health and Welfare), 2009b; Commonwealth of Australia, 2007)).

There is increasing evidence that much of the increased use in POA drugs is not supported by their use as an appropriate treatment for many persistent pain conditions (Dowell, et al., 2016). While the utility of the use of POA drug to treat long term pain conditions is not the topic of this study, this overuse is linked to other problems. There is also now increasing evidence of individuals developing abuse or dependence on POA drugs, and of the 'leakage' or diversion of these drugs outside of the doctor-to-patient supply chain, as well as other evidence of harms derived from inappropriate use of these drugs.

2.2.2 Costs of increased supply and availability

Recently there has been increasing concerns that POA drugs are becoming more frequently misused and making greater contributions to drug-related harms in the Australian community. Coronial investigations in the United States of America into the deaths of celebrities – actor Heath Ledger and entertainer Michael Jackson – found that POA drugs were associated with their fatalities.

International evidence

In the USA, reports from the last 15 to 20 years have shown that the increasing prescription volume of these drugs is related to greater drug-related harms (Compton & Volkow, 2006; Joranson, et al., 2000; Manchikanti, 2008). This includes growing numbers of persons being admitted for opioid dependence treatment and for overdose at emergency departments where POA are the principal drugs of concern. POA have also been more frequently found as significant contributors in cases of drug-related deaths (Centers for Disease Control, 2010a, 2010b; Coolen, Lima, Sabel, & Paulozzi, 2009; Fischer & Rehm, 2009; Graham, et al., 2009; Layne, et al., 2009; Okie, 2010).

General community surveys have also corroborated rises in inappropriate use of POA drugs. A US study detailed the prescription drug abuse of nine different POA

drugs using four different data sources (Schneider et al., 2009). Furthermore, a 2007 household survey data in the US estimated that 5.2 million people used POA non-medically in the last month (Substance Abuse and Mental Health Services Administration, 2009).

Australian evidence

POA drug misuse is now recognised as an emerging public health concern in Australia (Bruno, 2007; Degenhardt, et al., 2006; Dobbin, 2009, 2010a; Rintoul, et al., 2010; Royal Australasian College of Physicians, 2009). This issue presents significant challenges to treatment providers and regulators. The increasing prevalence of chronic pain suggests there will be a growing role for the use of POA drugs in management of these conditions (Access Economics Pty Ltd, 2007; AIHW Australian GP Statistics and Classification Centre, 2008). However, over-prescribing could inadvertently create risks of harm to some sections of the community (Dobbin, 2009, 2010a). Furthermore, the licit status of POA drugs means regulators can also play a role in influencing community use of these drugs. The challenge is to do so in a manner that does not restrict individuals' access to legitimate and appropriate treatment but, at the same time, reduce the harms associated with misuse.

Household survey data from Australia in 2007 estimates 0.2% of the population had used a pain-killer/analgesic drug for non-medical purposes in the last month, and 4.4% had ever used any pain killer/analgesic drug for non-medical purposes in their lifetime (AIHW (Australian Institute of Health and Welfare), 2007). However, data from both sources has some limitations as these questions are not related to POA drug-use alone.

There is evidence that the use of POA drugs has increased in illicit drug users over the last 10 years (Stafford et al., 2009). Injecting drug users are increasingly reporting injection of, and acquisition of, POA drugs (Cogger & Kinner, 2009). Furthermore, there is increasing reports of persons entering formal treatment programs

for opioid dependence reporting POA drugs as their primary drug of dependence (AIHW (Australian Institute of Health and Welfare), 2009b).

There is some converging evidence of the increased availability of, and misuse of, POA drugs in the general community. It is reasonable to conjecture that Australia might experience similar trends in harms to the USA given similar trajectories of POA drug prescribing. Dobbin has suggested that based on current volumes of prescribing of POA Australia is at the same point that the USA was in the early 1990s, when harms associated with controlled-release oxycodone misuse began rapidly escalating (Dobbin, 2010a). Recent studies show the increasing use of POA drugs in Australia (Karanges, et al., 2016; National Centre for Education and Training on Addiction, 2013)and a corresponding increase in associated harms (Berecki-Gisolf, et al., 2016; Nicholas, Lee, & Roche, 2011; Roxburgh, 2011)

There is little direct information available about the possible population not in formal treatment programs that might be experiencing health related problems associated with POA drug misuse.

2.3 THE POLICY CONTEXT OF OPIOID DRUGS

The policy context around the use of opioids is focussed on the medical application of these drugs in therapeutic circumstances, and the illicit use of these drugs as either illicit or licit preparations. This section will discuss the policy context in Australia around therapeutic use, illicit drugs, and the growing convergence of these areas. The application of these policies in regards to the monitoring and surveillance of POA drugs in Australia is also discussed.

2.3.1 Illicit opioid drugs policy

In the case of illicit drugs, Australia is signatory to a number of UN conventions (United Nations, 1988) that provide internationally agreed legal mechanisms to address illicit drug supply, and allows for international cooperation in the interdiction of the trafficking of illicit drugs across national boundaries. Heroin is one drug covered

in such conventions. Adherence to these treaties also imposes obligations on how signatory countries can regulate illicit drugs within their own borders. For the benefit of clarity, the illicit opioids referred to here are non-pharmaceutical opioids. POA drugs that are diverted or used for non-medical reasons are potentially considered illicit; however, this will be addressed in the next section.

All drugs and medicines, POA drugs, and illicit drugs are subject to scheduling under the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) or the 'Poisons Standard' (Commonwealth of Australia, 2010). Heroin is listed as a Schedule 9 – Prohibited Substance. As with licit drugs, each state and territory adopts particular legislative and regulatory frameworks in general agreement with the Commonwealth. In Queensland, heroin, cocaine and methamphetamine are considered illicit drugs under the *Drugs Misuse Act 1986* (Queensland Government, 1986) and certain criminal penalties apply to individuals possessing or selling these drugs. If not obtained via legitimate means – for example, by prescription – POA drugs are considered illicit drugs under provisions of the *Drugs Misuse Act 1986* (Queensland Government, 1986).

The national policy position on the management of illicit drugs, including heroin and the misuse of pharmaceutical drugs is the National Drug Strategy (NDS) (Ministerial Council on Drug Strategy, 2004). As with other aspects of policy and legislation in Australia, this policy is adopted in full or part by the constituent states and Territories. Queensland has its own Queensland Drug Strategy (Queensland Government, 2006) that is largely based on the NDS.

The harm minimisation approach set out in the National Drug Strategy (Ministerial Council on Drug Strategy, 2011) is based on the underpinning concepts, demand reduction, supply reduction and harm reduction. Demand reduction refers to strategies to reduce the uptake of drugs. Supply reduction refers sanctions and regulation of licit and illicit drugs, and harm reduction is about reduces harms caused by drug use.

This study is focussing on strategies of supply reduction, to reduce individuals' exposure to non-therapeutic use of POA drugs, either via directly prescribed drugs or by diverted drugs. Similarly, outcomes of this study are focussed on harm reduction strategies, that recognise there are legitimate uses of POA drugs and better informed treatment decisions should lead to better prescribing. Furthermore, in the National Pharmaceutical Drugs Misuse Framework for Action (Australian Government, 2012)identified that there needed to be improved education of prescribers, better monitoring and regulation of pharmaceutical drugs as well as implementation of real-time reporting of dispensing events in PDMPs. This study also aims to provide information for the prescribing clinicians and facilitate how prescribing information could be effectively used in any future PDMPs with real-time reporting capabilities. Regulatory actions can also act as supply reduction strategies and might be developed from outcomes of this investigation. A regulator or professional body might implement sanctions against errant prescribers or dispensers to limit their abilities to prescribe or dispense, based on information about their management of drug seeking patients. . Potentially improved prescribing of opioid and a reduction in iatrogenic opioid dependence might be considered a demand reduction strategy. This study is a health focussed approach to improve treatment outcomes of patients and improve clinical practice particularly focussed on the supply issue related to doctor shopping.

2.3.2 Pharmaceutical opioid drugs policy context

Pharmaceutical preparations are regulated according to various international treaties in regards to their manufacture, and supply is administered by the International Narcotics Board (United Nations, 1988). Australia is signatory to various United Nations Conventions in regards to the appropriate use of opioid analgesics and treaties about individuals' rights to receive appropriate medical treatments for their illnesses (United Nations, 1961).

Individual countries are signatories to these treaties and conventions and regulate the use of these drugs within their jurisdictions. In Australia, pharmaceutical drugs and medicines are regulated under the *Therapeutic Goods Act 1989* (Commonwealth of

Australia, 1989). This Act is administered by the TGA that lists all medicines and poisons under *The Schedule for the Uniform Scheduling of Medicines and Poisons* (SUSMP) (Commonwealth of Australia, 2010).

The SUSMP includes nine schedules that broadly equate with the degree of access of these substances. Lower scheduled drugs are available for direct purchase in supermarkets (Schedule 1 & 2), in pharmacies (Schedule 3) and higher scheduled drugs require prescriptions by medical practitioners or special permits for use via the TGA. POA drugs are listed as Schedule 8 drugs.

Each Australian state and territory jurisdiction sets its own legislation and regulations around these drugs. For the most part, these regulations seek to restrict the use of POA drugs to registered health practitioners. The use of POA drugs in therapeutic circumstances in Australia is limited to certain health practitioners who are registered according to national and state legislations. This is primarily medical practitioners, dentists, optometrists, veterinary surgeons, pharmacists and some other professions in different jurisdictions.

State and territory-based legislation also sets limits around POA drugs use in regard to the treatment of certain conditions, reporting of long-term treatment, and requirements for authorities for treatment in some instances. In Queensland, the *Health (Drugs and Poisons) Regulation 1996* (Queensland Government, 1996) set out these requirements for use. Examples of these requirements are provided in Appendix B.

Pharmaceutical preparations for human therapeutic use are also included under Australia's Pharmaceutical Benefits Scheme (PBS), and a certain proportion of their cost is subsidised up to and within certain dosage and supply limitations (Medicare Australia, 2011). This scheme seeks to offset costs of widely used beneficial drugs in the treatment of certain conditions to the general population.

In Australia, most POA drugs are liable for subsidy under the PBS. This means that most of these drugs are available at a low cost. Furthermore, medical practitioners can also choose to prescribe drugs as non-PBS, or 'private' prescriptions, where treatment might be outside of PBS approval, and where the patients meets the full unsubsidised cost of the drugs.

The policy context of the use of POA drugs in Australia is governed by three levels of control: one international, one national, and the other state and territory-based. There are minor differences in regulation between states and territories, mostly based on different legislative frameworks. However, the Australian policy context in relation to POA drugs is similar to other similar jurisdictions, such as the United Kingdom under its Medical and Healthcare Products Regulation Agency (U.K. Department of Health, 2011), and the USA under its Food and Drug Administration (U.S. Department of Health and Human Services, 2011).

Since 2009, a number of policy initiatives in Australia have been suggested to address this public health concern. The College of Physicians proposed a 'Prescription Opioid Policy' (Royal Australasian College of Physicians, 2009). The Pharmacy Guild of Australia proposed 'real-time' reporting of all dispensed POA drug prescriptions to allow for better monitoring (Pharmacy Guild of Australia, 2010). In response to these growing concerns the Australian Government commissioned the National Pharmaceutical Drug Misuse Framework for Action (Australian Government, 2012) that sets a range of strategic policy options to address this issues, that has been adopted in-principle by the state and territory jurisdictions.

For health professionals such as doctors and pharmacists there are legal, professional and ethical obligations in regards to their treatment of patients. For POA drugs, a treatment provider could be subject to legal action if they provide drugs outside of the legal framework. In a treatment setting, health professionals are liable to actions against them by patients or the Courts should their treatment cause harm to a patient, and where that treatment was outside of established practice or was the result of demonstrable negligence. Where patients misuse or divert POA drugs outside of

treatment recommendations, it is less clear as to the responsibility of the treating health practitioner. Furthermore, a health practitioner denying treatment to a person without reasonable justification for doing so could also be subject to similar actions against them by regulators, patients, or the courts. Hence, the calls for comprehensive and real-time prescription drug monitoring.

In recognition of the growing concerns around the misuse of POA and other pharmaceutical drugs, the Australian Commonwealth Government commissioned the Australian National Pharmaceutical Drug Misuse Framework (2012-2015) (National Centre for Education and Training on Addiction, 2013) to provide strategic recommendations on how to manage these concerns. As with the NDS, each state and territory jurisdiction has agreed in principle to this framework and can choose to adopt recommended measures.

2.3.3 Monitoring and Surveillance

Medicare Australia collects information on all medications that are subsidised under the PBS – POA drugs being one class of such drugs. Medicare also conducts a 'Prescription Shopping Program' (Medicare Australia, 2011) that can inform doctors of a patient obtaining drugs beyond a certain threshold or upper limit. Medicare's focus is primarily to reduce inappropriate expenditure on PBS medication, and as such they have not pursued a broader research agenda into this area, particularly around POA drugs. The last population data produced by Medicare in this area was over 10 years ago (Health Insurance Commission, 1998).

The overall monitoring of POA drugs across Australian jurisdictions is inconsistent, making it more difficult to ascertain accurate measures of use and related harms. While Medicare Australia monitors all prescription drugs subsidised under the PBS, 'private' prescriptions that do not attract a PBS subsidy are not monitored. Due to the reactive and inconsistent nature of monitoring prescriptions and limits to monitoring systems, there are few actual sanctions preventing individuals obtaining multiple prescriptions for large amounts of POA drugs from multiple doctors (Medicare Australia, 2011; Wilsey et al., 2010).

Each Australian state and territory has different legislation to regulate POA drugs as a class of 'controlled drugs'. Queensland, Northern Territory, Tasmania, and South Australia all maintain a prescription monitoring system in some form that collates POA drug dispensing. New South Wales, Victoria, and the Australian Capital Territory have no such system in place.

In Queensland, all POA drug prescription information – PBS and private – once dispensed at community pharmacies is transmitted to Queensland Health for input in to a central database. This information allows for the complete capture of the state's POA drug prescribing in the general community, excluding hospital inpatients, and thus the identification of people engaged in doctor-shopping behaviour.

The formation of the Medicines Regulation and Quality (MRQ) (formerly Drugs of Dependence Unit (DDU)) of Queensland Department of Health, in its present form, followed a recommendation for the creation of a discrete monitoring unit by the 1979 Australian Royal Commission of Inquiry into Drugs (Williams, 1980). All state and territory governments established monitoring units in their respective health departments; however, not all decided to directly monitor prescription activity via prescription databases.

To implement the Williams' recommendations, Queensland began a manual monitoring system of POA drug prescriptions. This process was enhanced in 1983 by the introduction of a computer system, known as the *Monitoring of Drugs of Dependence System* (MODDS) database. The current version of the system has been in operation since 1996. MODDS collects all the information of controlled (Schedule 8) drugs – of which most are POA drugs – dispensed by community pharmacies in Queensland. The MODD system also facilitates the provision of a state-wide confidential telephone enquiry service for medical practitioners and pharmacists.

The Australian National Pharmaceutical Drug Misuse Framework (2012-2015) (National Centre for Education and Training on Addiction, 2013) supported the establishment of real-time prescription drug monitoring programs within all jurisdictions as one of its recommendations. These jurisdictional systems were to be linked to each other and allow access to prescribing doctors and dispensing pharmacists.

2.3.4 Rise of Prescription Drug-Monitoring Programs

One of the key population level responses, especially in the USA and Canada, has been the implementation of prescription drug-monitoring programs (PDMPs) and 'real-time' reporting of dispensed prescriptions (Clark, Eadie, Kreiner, & Strickler, 2012; Finklea, Bagalman, & Sacco, 2013; Laura Morgan, 2013). The rationale behind this response is to provide appropriate and contemporary information to clinicians for managing patients, and regulators to monitor individual and population level patterns.

Some 48 out of 51 USA states (Blumenschein et al., 2011) and the majority of Canadian provinces now have some form of jurisdictional prescription drug-monitoring programs (PDMPs). Initial reviews of the effectiveness of these programs in the USA have returned mixed results (Blumenschein, et al., 2011; Paulozzi, Kilbourne, & Desai, 2011). It is suggested that these programs and the provision of information alone is not sufficient to address the broader issue of prescription drug misuse (Laura Morgan, 2013; Prescription Drug Monitoring Program Center of Excellence at Brandeis, 2013; Shand, Campbell, Hall, Lintzeris, & Degenhardt, 2013; Strassels, 2012).

An Australian policy review – the National Pharmaceutical Drug Misuse Framework for Action (National Centre for Education and Training on Addiction, 2013) – also supports real-time prescription monitoring along with range of other strategies, there needs to be appropriate workforce development, greater accessibility and availability to specialist treatment services, improved clarity of roles of programs as either regulatory or medicine management, appropriate regulation and policing

policies, and ongoing evaluation of the programs to evaluate their effects on misuse of POA drugs (Shand, et al., 2013).

Real time PDMPs have many potential benefits. They can allow prescribers, dispensers and regulators, contemporaneous information about prescription usage on which to make treatment decisions. As such they can prevent further prescribing or dispensing if a health professional has clear evidence of overuse or drug seeking. From a regulatory or oversight perspective they can allow for intervention to prevent further prescribing or dispensing, and potential actions against patients, and health practitioners if there are concerns about their prescribing. Overall, if they are effective in limiting misuse and dependence they should represent savings to a health budget.

Some issues around the implementation and use of PMDPs need clarification as it is not clear that they are established or used in consistent ways across jurisdictions and this can influence their use. Firstly, whoever the authorising agency is will set the use of the PDMP. An enforcement agency, such as the USA's Drug Enforcement Agency, will be potentially using a PDMP to detect criminal activity. Whereas a medical or pharmacy board might be seeking to regulate activities of registered health practitioners. Alternatively, a health agency might use a PDMP to integrate with, or supplement health treatment records to improve treatment. Secondly, the legislative environment can influence whether providing and accessing data is mandated or supported. The ease of use and ability to access, and level of access for certain users could also affect uptake and use by relevant practitioners. The timeliness, quality and extent of information in PDMPs can also affect usage and utility. Real-time or close 7to real-time information that was reliable and historically accurate would be ideally most useful. If PDMPs included other treatment information or regulatory advice or warnings these could potentially add to their value in clinical settings. Furthermore, changes in information systems and data exchange, such as electronic prescribing and dispensing and cloud based computing could also facilitate good systems.

However, real time PDMPs could have some limitations, especially when they ae not linked to broader records of a person's healthcare history. Most PDMPs are

focussed on monitoring POA drugs and misuse of other drugs that could interact with opioids would escape scrutiny. PDMPs are potentially expensive and complex to implement and could represent monies diverted from health treatment or preventive programs. Without appropriate guidance treatment providers might misinterpret legitimate prescription obtaining as drug seeking and cease treatment. There have been some reports of a 'chilling' effect in some state of the USA when PDMPs have been implemented (Reisman, Shenoy, Atherly, & Flowers, 2009) . That is prescribers or dispensers default to a do not prescribe/dispense position if there are any concerns and potentially deny patients appropriate treatment. Alternatively prescribers might not recognise problematic or aberrant usage of POA drugs

There is the risk of contention between prescribers and dispensers, as they might view the same information differently. A dispenser might choose to not dispense a prescription if they hold concerns about a person's POA drug obtaining even if the prescriber had not formed the same views. Furthermore, regulatory or legal peril, prescribers or dispensers might have greater liability in patient outcomes. There appear to be potential issues in implementing PDMPs effectively in jurisdictions if the policy intent is not clear (Gilson, 2010a; Gilson, 2010b; Gilson, Maurer, & Joranson, 2007).

However, regardless of the broader contextual concerns, PDMPs offer the opportunity to capture large volumes of objective information on a person's drug prescription history over time. For health practitioners to make informed decisions based on this information to guide their treatment choices there needs to be understanding of appropriate clinical use of POA drugs in pain conditions and recognition of evidence of drug dependence and misuse with this class of drugs. This emerging public health area represents a complex problem for treatment providers with potentially conflicting or co-occurring clinical conditions. Appropriate use of prescription information within PDMPs could add valuable information to assist decision-making.

2.4 THE CLINICAL CONTEXT OF OPIOID DRUGS

The greatest increases in POA drug prescribing is in the controlled-release preparations of oxycodone and morphine (Bell, 1997; Degenhardt, et al., 2006; Dobbin, 2009, 2010a; Leong, et al., 2009). These preparations are central to the public health concerns relating to POA drug misuse (Cicero, Inciardi, & Munoz, 2005; Cicero, et al., 2007).

POA drugs are indicated for use in the treatment of chronic and acute pain, and are widely supported as an appropriate pain management therapy (American Academy of Pain Medicine & American Pain Society, 1996; Passik, 2009; Zacny, et al., 2003). In the case of short-term and acute pain conditions, a limited course of POA drugs can be provided and then ceased on the resolution of the pain condition (Rosenblum, et al., 2008). Chronic pain conditions might last for many years, and long-term therapy over months or years might be required to provide an individual appropriate pain relief (American Academy of Pain Medicine & American Pain Society, 1996; Eriksen, Sjøgren, Bruera, Ekholm, & Rasmussen, 2006; Kahan, Srivastava, Wilson, Mailis-Gagnon, & Midmer, 2006; Rosenblum, et al., 2008).

Chronic non-malignant pain has multiple and complex causes, and can often involve extensive and expensive testing procedures such as X-rays, magnetic resonance imaging scans, and consultations with specialist medical practitioners such as physicians and neurologists (American Academy of Pain Medicine & American Pain Society, 1996; Zacny, et al., 2003). The other complexity for practitioners is the subjective nature of pain conditions. Although diagnoses and overt pathology can indicate possible causes of pain and verify actual injuries, an individual's response or ability to manage pain is often idiosyncratic (American Academy of Pain Medicine & American Pain Society, 1996; Passik, 2009; Passik & Kirsh, 2008; Zacny, et al., 2003). Therefore, many of the aspects of pain management rely on patient's self-reports to ascertain levels of pain, and success or otherwise of treatments (Zacny & Lichtor, 2008b).

In general, immediate release preparations of opioids are used to treat acute pain or breakthrough exacerbations of pain in chronic conditions (American Academy of Pain Medicine & American Pain Society, 1996; National Prescribing Service, 2010; NSW Therapeutic Assessment Group, 2002). Extended release medications are used to primarily treat chronic conditions. However, most clinical guidelines suggest that POA drug therapy should only be undertaken and maintained if the pain appears to be opioid responsive; that is, there is an analgesic effect produced by administration of the drugs (Kalso et al., 2003; Nicholson, 2003; Schug, Merry, & Acland, 1991). Titrating the POA drug type dose to an appropriate level to achieve analgesic effects can be a complex process. Most clinical guidelines advise particular caution using POA drugs, and nominate adverse consequences of prolonged use such as dependence and abuse.

As mentioned previously, the American Academy of Pain Medicine and the American Pain Society established clinical guidelines in 1996 in the USA. There are a variety of similar guidelines in Australia. Most state regulatory agencies publish some form of standard guideline (NSW Therapeutic Assessment Group, 2002), and these are mostly consistent with the USA guidelines. The National Prescribing Service (National Prescribing Service, 2011), a not-for-profit professional medicines group, provides standard guidelines on the use of POA drugs for medical practitioners in Australia (National Prescribing Service, 2006, 2010).

A Cochrane review recently published a review of use of opioids in chronic non-malignant pain (Noble, et al., 2010) and suggested that, “proper management of a type strong painkiller (opioids) in well-selected patients with no history of substance addiction or abuse, can lead to long-term pain relief (for) some patients with a small risk of developing addiction, abuse, or other serious side effects…” ((Noble, et al., 2010).

The major concerns with chronic use of POA drugs is that treatment could cause or lead to misuse. Patients who are inappropriately managed on these drugs could develop dependence (Bieber et al., 2007; Craig, Diana, & Maren, 2007; Fudin,

Levasseur, Passik, Kirsh, & Coleman, 2003; Kahan, 2006; Rosenblum, et al., 2008). Alternatively, patients who are drug dependent might seek to obtain prescriptions to maintain their dependence or divert to illicit drug markets (Inciardi, et al., 2010; Kraman, 2004; Martyres, et al., 2004). Furthermore, opioid dependent individuals might also suffer chronic pain conditions and require POA drug treatment (Fudin, et al., 2003; Markowitz et al., 2010; Moore & McQuay, 2005).

It remains a significant challenge for clinicians using POA drugs to differentiate between appropriate therapeutic use and dependence. The complexity of presenting conditions (American Academy of Pain Medicine & American Pain Society, 1996; Becker, Sjogren, Bech, Olsen, & Eriksen, 2000; Noble, et al., 2010; Potter & Jones, 1992), the lack of readily accessible specialist support (Becker, et al., 2000; Potter & Jones, 1992), and the nature of general models of therapeutic relationships rely on a bond of trust between practitioner and their patient (Bendtsen, Hensing, Ebeling, & Schedin, 1999; Bhamb, 2006). To further complicate matters, the underlying concepts of abuse and dependence are also contentious and problematic, particularly in relation to the chronic use of POA drugs. Illustrating this, in 2015 Degenhardt and others sought to classify a sample of long term POA drug using persons for problematic use disorders using version of current and past DSM and ICD classifications. The results found inconsistent levels of classification of problematic opioid use across different editions of the DSM and ICD (Degenhardt et al., 2015). This is a particular concern for treatment providers in this area of treatment, many who are non-expert in diagnosis of substance use disorders and who are seeking to treat what are primarily presenting pain conditions.

2.4.1 What are the harms caused by POA drugs?

Conceptualising harms of prescription drugs has proven to be complicated. A generally popular dichotomy of hard drugs and soft drugs is often referred to in the media and colloquial accounts regarding drugs use. In illicit drugs, heroin might be referred to as hard drug and marijuana as soft drug. However, this dichotomy is limited when attempting to assess actual harms in a quantifiable method. For example, heroin is highly dependence-forming, can cause overdose deaths, can increase risks of

acquiring BBVs via unsafe injecting practices, but, a manageable dose has limited long-term deleterious physiological effects. In contrast, marijuana is less dependence-forming, but has known physiological effects due to prolonged use, and if ingested by smoking has a significant increased risk of throat and lung cancers. Therefore, harms might be better described on different dimensions.

Nutt et al, 2007 (Nutt, King, Saulsbury, & Blakemore, 2007) proposed that there are three main factors that together determine the harms associated with any drug of potential abuse (see Table 2.3). The three main factors are: physical harm of drugs, causing damage to organs or physical systems or having negative physiological effects, such as effects to respiratory or cardiac systems; dependence potential of a drug, related to the interaction between its pleasurable effects and its propensity to produce dependence behaviour or be abused; social harms, related to the various effects of intoxication, through damaging family and social life and associated costs with health care, social care and legal responses.

Table 2.3 Assessment of drug harms (Nutt et al, 2007)

Harm	Parameter	Description
Physical harm	1	Acute
	2	Chronic
	3	Intravenous harm
Dependence	4	Intensity of pleasure
	5	Psychological dependence
	6	Physical dependence
Social harms	7	Intoxication
	8	Other social harms
	9	Healthcare costs

2.4.2 What POA drugs cause harms and why?

The overarching harms associated with POA drugs are outlined in Chapter 2, and these broadly relate to the harms associated with opioid drugs and their risk of causing abuse or dependence. This is largely due to the active opioid ingredient of these drugs. However, different types of POA drugs have been more subject to misuse than others over time.

Considering whether a POA drug is more associated with harms is a complex consideration as the drugs themselves have been shown to have a legitimate therapeutic use, and have met appropriate clinical and regulatory safety standards for use in treatment settings. Evidence to date suggests there is a paucity of knowledge of the abuse liability of prescription opioids or the features of certain POA drugs that make them more sought after by persons who suffer substance misuse disorders (Centers for Disease Control and Prevention, 2012; Zacny, et al., 2003). Therefore, the types of drugs sought by drug-seeking or doctor-shopping patients could indicate particular concerns.

Dosage levels in particular preparations are a particular concern. For example, most POA drugs have varying dosage preparations to allow for moderation of treatment and dosages in response to a patient's pain levels and effects of the drug. However, higher dose preparations have more immediate value to drug dependent persons, as they represent the highest dosages available, and these are also more readily saleable and return higher value (Centers for Disease Control and Prevention, 2012; Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014; Compton & Volkow, 2006).

There is some evidence across jurisdictions that high-dose oxycodone, morphine and fentanyl preparations are most sought by drug-seeking patients and are more associated with non-medical use (Cepeda, et al., 2014; Dart et al., 2015; Dreifuss et al., 2013; Pilgrim, 2015; Zacny, et al., 2003). Therefore, for meeting dependence needs and diversion value, higher dose preparations represent most value for a person engaged in drug-seeking behaviour.

It appears that any opioid by virtue of its active ingredient can be potentially sought after by drug-dependent persons, and in certain circumstances persons with injecting drug use histories will seek to modify these drugs for injection (Black, Trudeau, Cassidy, Budman, & Butler, 2012; Degenhardt et al., 2013; Lankenau et al., 2011)). It is not clear if aspects of the preparations of certain POA drugs as ampoules,

tablets, capsules, or transdermal patches are more associated with abuse or dependence formation.

The other aspect of formulation that is of interest is the proliferation of the controlled-release preparations of morphine and oxycodone and, to a lesser extent, the matrix release patches of transdermal fentanyl. The controlled-release POA drugs offered a benefit in managing pain conditions by allowing doses to be released over longer time periods of 6 or 21 hours (Davis et al., 2003; Mucci-LoRusso et al., 1998).

A number of US, Canadian and Australian studies have now strongly suggested that controlled-release oxycodone (i.e. OxyContin™) is particularly associated with dramatic increase in POA drug misuse and related harms (Canadian Centre on Substance Abuse, 2010; Dunn, 2008; Rintoul, et al., 2010). The slow release nature of these classes of POA drugs has not proven to be a barrier to dependence formation even when taken orally. There is now ample evidence of their association with abuse and dependence (Butler, Black, Cassidy, Dailey, & Budman, 2012; Rafat & Sproule, 2015).

2.5 CONCEPTS AND THEORIES IN OPIOID ANALGESIC DRUG USE

Opioid drugs are most commonly used for pain management, in medical treatments, and as drugs of dependence or abuse in non-therapeutic situations. This section seeks to outline the conceptual frameworks and underlying definitions around these different facets of opioid use to explain some of the common issues of opioid use. Some matters of contention between these areas are also discussed.

There are concepts that underpin human reactions to opioid drugs that are pertinent to both pain management and drug dependence. These are discussed below as they are relevant to later discussions around conceptual frameworks in pain management and dependence in regard to opioid drugs.

2.5.1 Drug concepts

The chronic or long-term use of opioid drugs, as with other dependence-causing substances, leads to certain physiological responses of the body. Increased tolerance to a substance is experienced over time, and chemical receptors in the brain undergo neuro-adaptation in the presence of high levels of opioids with long-term use. The individual will experience withdrawal symptoms on the cessation of use, or possibly when dose effects have dissipated (Gutstein & Akil, 2006; Zacny, et al., 2003). Table 2.4 below sets out some established definitions of these concepts.

With POA drugs, chronic use and cessation of use can induce some or all of the above physiological responses. This physiological response can occur regardless of whether a person is dependent on these drugs according to full diagnostic assessment. This issue is discussed further in the following sections.

Table 2.4.

Concepts in drug dependence

Concept	Description
Tolerance[a]	Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.
Withdrawal[b]	Physiological and psychological symptoms associated with withdrawal from the use of a drug after prolonged administration or habituation. The concept includes withdrawal from smoking or drinking, as well as withdrawal from an administered drug.
Neuro-adaptation[b]	The complex biological changes that occur in the brain with repeated or chronic exposure to a drugs. With repeated exposure, the body and brain often adapt to the presence of the drug. Through homeostatic or 'self-corrective' mechanisms, the nervous system attempts to compensate for the effects of the drug.
Physical dependence[a]	Physical dependence is a state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.

Source: a - (American Academy of Pain Medicine & American Society of Addiction Medicine, 2001) & b- (Heather, 1998)

2.5.2 Pain management

The International Association for the Study of Pain defines pain as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage' (Merskey & Bogduk, 1994).

Pain is typically classified as either acute or chronic. Acute pain is most commonly characterized as the result of disease or injury, and the cause can often be diagnosed and treated. Acute pain is self-limiting and confined to a given time and severity (Gutstein & Akil, 2006; Wolfert, Gilson, Dahl, & Cleary). Chronic pain is pain that persists over a longer period of time, and generally resistant to most medical

treatments. Common chronic pain conditions can include: headache, back pain, cancer pain, arthritic pain, neurogenic and psychogenic pain (Merskey & Bogduk, 1994).

The sensation of acute pain is the response to tissue injury by peripheral pain receptors and their specific nerve fibres (nociceptors). Chronic pain is believed to be the result of persistent activation of these fibres. This type of pain is known as 'nociceptive pain'. Chronic pain can also be caused by damage or dysfunction to the peripheral nervous system, and is known as 'neuropathic pain' (Merskey & Bogduk, 1994).

Opioid drugs cause certain inhibitory or excitatory neurochemical actions at various sites that can reduce the sensation of pain. Opioids are believed to have mild anti-inflammatory effects at injury site, act to reduce activity in the spinal cord, and have inhibitory excitatory on certain opioid receptors in the brain (American Academy of Pain Medicine & American Pain Society, 1996; Kahan, et al., 2006; Merskey & Bogduk, 1994). Figure 2-4 graphically describes this.

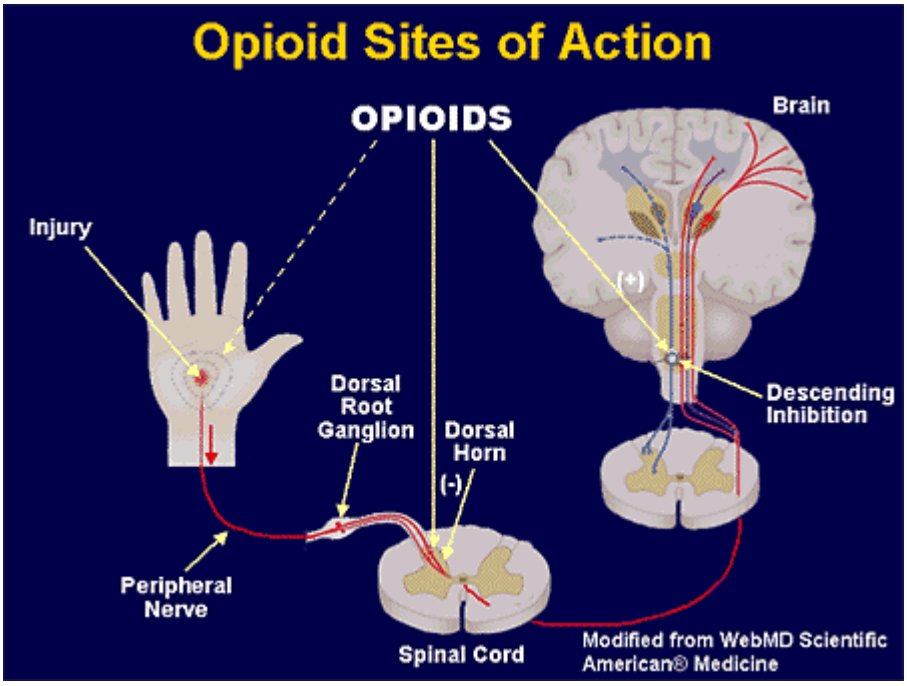

Figure 2-4. *Opioid sites of action in pain.* From: .

Acute pain conditions are generally considered better treated by those opioids that rapidly reach the pain receptors (Kahan, et al., 2006; Merskey & Bogduk, 1994). This usually means preparations of opioids that are injected into the muscle or the blood stream, or tablet forms that immediately release the full dose on oral ingestion into the gastro-intestinal system (Merskey & Bogduk, 1994). This means the effect of the opioid is achieved in a short time and the effects rapidly leave the system after the dose release. Thus for acute pain, a short course of rapid-acting opioids is considered optimal, as they would reduce the pain over the length of the episode.

For chronic pain conditions, the use of controlled-release opioids is the preferred method of treatment (Braden et al., 2008; Kahan, et al., 2006). This is because ongoing dosing can achieve a level of opioids maintained over a longer period of time, and provide improved pain control over the course of time to improve the functioning of an individual (American Academy of Pain Medicine & American Pain Society, 1996; Kahan, et al., 2006).

The known side effects of opioid use include sedation, constipation, the development of tolerance, and physical dependence (Gutstein & Akil, 2006). Hyperalgesia is also a possible outcome of long-term opioid therapy. This refers to an increased response to a stimulus which is normally painful, due to continued opioid use (Merskey & Bogduk, 1994).

It is not generally shown that exposure to opioids alone in pain management cases is sufficient to cause dependence (Noble, et al., 2010). However, it has been suggested that the risk factors commonly associated with development of dependence in individuals in general might be similarly related in people suffering pain conditions when exposed to opioids (Bieber, et al., 2007; Kahan, 2006; McCracken, Hoskins, & Eccleston, 2006; Rosenblum, et al., 2008). However, it is not well established as to what role pain conditions might play in mediating or moderating individuals' likelihood of developing dependence.

2.5.3 Dependence and abuse

The two most widely accepted diagnostic criteria for defining substance abuse and dependence are the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-IV) (American Psychiatric Association, 2000) and the World Health Organisation's International Classification of Diseases (ICD-10) (World Health Organisation, 2007).

Drug dependence is generally described as the set of maladaptive behaviour resulting from the inappropriate use of a substance, such that an individual demonstrates lack of control over their use of the substance, and that use assumes a significant priority in an individual's life to the detriment of their normal functioning. Dependence for both the DSM-IV and ICD-10 definitions requires the presence of behavioural, physiological and cognitive phenomena (American Psychiatric Association, 2000; World Health Organisation, 2007). The use of the term 'addiction' is not supported by either classification, but has been widely used in the field (American Psychiatric Association, 2010). For the benefit of this study the term 'dependence' will be used in keeping with accepted definitions.

Drug abuse or harmful use can be defined as inappropriate use for particular effects, but may or may not be associated with dependence. This is often characterized by patterns of use that are damaging to an individual's health and includes episodes of heavy consumption or binges (American Psychiatric Association, 2000).

The use of the diagnostic term 'dependence' – that includes physical and psychological aspects – has led to confusion across the domain, since the over-arching term 'dependence' has been adopted (American Psychiatric Association, 2010). This is particularly relevant in the area of POA drugs, given that chronic use can produce physiological symptoms such as tolerance and withdrawal, but not necessarily further psychological criteria for dependence (Banta-Green, Merrill, Doyle, Boudreau, & Calsyn, 2009a; Bieber, et al., 2007; Kahan, 2006; McCracken, et al., 2006; Rosenblum, et al., 2008). It has been suggested that the misuse of the term 'dependence" has led to the potential misdiagnosis of dependence, where only physical dependence was

evident in many cases of chronic POA drugs use (Kahan, 2006; Zacny, et al., 2003). The current revision of the DSM-5 – the fifth edition – has considered this matter of particular relevance and re-introduced the term 'addiction' into the nomenclature for these disorders (American Psychiatric Association, 2010). However, of particular note is that the DSM-5 has a definition of substance use disorders related to POA drugs sets out that tolerance and withdrawal are not indicators of use disorder if consistent with a treatment regime. However, these physiological indicators are to be considered counted in the context of 'aberrant' behaviour (Degenhardt, et al., 2015; Larance, Degenhardt, Lintzeris, Winstock, & Mattick, 2011)

Drug dependence can be conceptualized in terms of the use of a substance for initially pleasurable experiences where no therapeutic use supports it, and then continued use despite increasing negative consequences. At a neurochemical level initial use acts to stimulate the release of the neouro-transmitter dopamine thought to be associated with increasing pleasurable experiences (Brownstein, 1993). This behaviour is intrinsically reinforcing and encouraging of continued use. With chronic use, tolerance develops, neuro-adaptation occurs, and greater doses of the substance are required to achieve the same pleasurable effects (Heather, 1998), and reduce the experience of withdrawal effects(American Psychiatric Association, 2010; Gutstein & Akil, 2006).

The causes of dependence are best understood in the model of dependence that incorporates biological, psychological, and social and cultural influences, more commonly known as the 'biopsychosocial model'. This model arose largely out of opposition to medical or disease models of dependence and addiction (Marlatt, Baer, Donovan, & Kivlahan, 1988; Sarafino, Caltabiano, & Byrne, 1990). The biopsychosocial model describes the genesis of drug dependence as being based on particular proximal and distal contributing risk factors. These factors include biological factors (such as genetic predisposition), psychological factors (such as constructs of sensation-seeking or expectancies and mental illness), and social factors (such as substance use in families and peer networks) (Marlatt, et al., 1988; Newcomb & Earleywine, 1996). The model also describes the symptoms of dependence, in that a person will experience biological symptoms, such as neuro-adaptation, and

psychological and social symptoms of their condition (Marlatt, et al., 1988; Newcomb & Earleywine, 1996).

2.5.4 Drug dependence and pain management

Chronic use of POA drugs for either chronic pain management or dependence reasons can promote neuro-adaptation, increased tolerance, and withdrawal on cessation of use. The above conceptual understandings of drug dependence and pain management have been discussed as discrete phenomena. However, drug dependence and chronic pain conditions might co-occur in an individual, thus making the assessment and management of their condition more complex.

It is generally supported that where a chronic pain condition exists in an individual without drug dependence, or without particular risk factors for dependence, then appropriate treatment with POA drugs can be undertaken without risk of causing dependence (Noble, et al., 2010). However, there is considerable evidence suggesting that where drug dependence or particular risk factors for dependence co-exist with a chronic pain condition there is a greater risk of a person developing dependence on or misusing POA drugs (Bieber, et al., 2007; Fudin, et al., 2003; Rosenblum, et al., 2008). The particular complexity in these instances can be that an opioid-dependent person might exhibit hyperalgesia, and require higher levels of analgesia for pain management than an opioid-naïve individual (Catalano, White, Fleming, & Haggerty, 2011; Doverty et al., 2001).

Similarly, a person with drug dependence or at risk of developing dependence without a therapeutic need for analgesia and who is exposed to long-term POA drugs use also has a high risk of developing dependence on these drugs (Catalano, et al., 2011; Manchikanti, 2008). This situation could perhaps describe a misdiagnosed patient receiving POA drug therapy, or individuals exposed to POA drugs diverted to illicit markets.

The challenge for clinicians is in the assessment and management of persons thought suitable for POA drugs therapies to ensure appropriate pain management, and to reduce the possible risk of causing dependence and other harms.

2.6 DETERMINING SUBSTANCE DISORDERS WITH POA DRUGS

Diagnoses of abuse and dependence can only be authoritatively made by individual assessment of patients by clinicians using accepted diagnostic criteria. The two most widely accepted being DSM-IV-TR (American Psychiatric Association, 2000) and ICD-10 (World Health Organisation, 2007) definitions of opioid abuse and dependence. It should be noted that the current edition of the DSM-5 – was released in 2012 during the course of this study. However, the DSM-IV-TR criteria were used for purposes of the first study as this was the most currently used and widely known version.

A number of scales of opioid abuse and dependence are also used in clinical face-to-face assessment of a patient, or at least based on access to comprehensive clinical records. However, the majority of these scales are used in the context of illicit opioid use, not POA drugs use. Given the increasing understanding of the development of substance use disorder with prescription opioids in chronic pain management cases, a number of scales have been developed to detect the onset of, or susceptibility of patients to, substance use disorders on POA drugs (Banta-Green, et al., 2009a; Banta-Green, Merrill, Doyle, Boudreau, & Calsyn, 2009b; Banta-Green et al., 2011; Wilsey et al., 2008).

However, the vast majority of POA prescribing and treatment occurs in community settings (non-hospital/non-inpatient) and is provided by general practitioners (GP). The most common treatment scenario of concern would be that of a patient presenting with a pain condition and a GP deciding if POA drugs were an appropriate treatment option, and balancing the concerns of misuse or dependence. This study is to examine prescription database records that have been gathered for

regulatory purposes and this data cannot supplant a clinical measure, but can potentially serve a proxy for such.

Furthermore, opioid dependence or abuse in regards POAs is complicated by the fact that treatment might have been initiated due to legitimate medical conditions. It is often difficult for GPs to detect, assess and manage opioid dependence or abuse in their patient populations. This is not a shortcoming of GP abilities or their treatment, and could in part be due to aspects of increasing workloads, shorter patient consultation times, inability to obtain timely specialist reviews, and patients who for any number of reasons might not reliably report their condition or drug use history. Further, it might be a matter of routine in a general practice setting for a doctor to apply a measure of substance misuse disorders in assessing or reviewing chronic non-malignant pain patients. Therefore, dispensed prescription information might be the most utilitarian and accessible potential proxy measure to inform of potential cases of concern.

To compound this increasingly complex area, there are divergent views as to definitions of abuse and dependence (Minozzi, Amato, & Davoli, 2013; Rehm et al., 2013; Volkow & McLellan, 2016) and what is appropriate CNMP management in relation to the use of prescribed medications (American Pain Society in Conjunction with the Americian Academy of Pain Medicine, 2009; Chou, et al., 2015; Kissin, 2013).

In relation to substance misuse disorders with POA drugs, this is largely due to two underlying issues in chronic use of these drugs. Firstly, chronic use will induce physiological dependence over time, such that cessation of treatment will induce a withdrawal state. Secondly, general definitions of dependence include physiological and behavioural criteria to be met to satisfy a diagnosis of dependence. However, inappropriate pain by providing insufficient medication for pain management could also induce a withdrawal state, and/or behaviour that might be considered drug seeking. It should be noted that neither the DSM or ICD framework maintain that tolerance or withdrawal are necessary criteria for a diagnosis of a substance use disorder. This differentiation could be difficult for non-specialist clinicians.

Furthermore, the current DSM-5 now no longer retains a separate diagnoses of abuse and dependence but includes an overarching construct of 'substance use disorder'. Larance and others (2011) also suggested concepts such as 'non-adherence', 'extra-medical use', and 'aberrant behaviour' could also be useful concept of describing POA drug misuse (Larance, et al., 2011).

The term 'pseudo-addiction' has been coined in the US (Greene & Chambers, 2015) to describe this phenomenon. However, it is not a term widely used outside of the US, and has certain connotations that suggests this is either a less serious issue or that a patient might be deliberately misleading a doctor as to their condition or need for opioids.

A number of issues are of interest arise in this question. Firstly, whether there is any difference between expert groups in how they might assess POA drug use and dependence. Secondly, testing views of experts on the importance of the criteria of tolerance and withdrawal. And lastly, whether there could be a reasonable conceptual association to link drug seeking to doctor shopping as important criteria for establishing a diagnosis of dependence or abuse in regards to misuse of POA drugs.

Due to the significant public health concerns in this area, and the nature of the drugs involved, jurisdictional regulators have become involved in attempts to moderate prescribing practices and manage problematic drug procurement by patients. The monitoring of obtained and dispensed prescriptions can form crucial objective evidence as to the total drugs and drug-seeking behaviour of patients. The key response from many jurisdictions experiencing POA problems is to implement prescription drug-monitoring programs.

2.6.1 Definitions of Dependence and Abuse

Drug dependence and abuse in relation to prescription opioid misuse is a diagnosis that is subject to a range of opinions and some contention as to what level of use constitutes inappropriate use (Edlund et al., 2014; Garland & Black, 2014; Rehm,

et al., 2013). Increases in numbers of persons possibly seeking prescription opioids due to their substance abuse disorders or other non-medical reasons has become an increasing challenge for primary care providers and general practitioners.

The two most widely accepted diagnostic guidelines are DSM-IV-TR (American Psychiatric Association, 2000) – now superseded by the DSM-5 (American Psychiatric Association, 2013) – and ICD-10 (World Health Organisation, 2007) that both contain definitions of opioid abuse and dependence. Noting, however that the DSM-5 has dispensed with the constructs of dependence and abuse in favour of the overarching construct of substance use disorder (Hasin et al., 2013).

The ICD is a diagnostic system established by the World Health Organisation for the purposes of reducing disease burden across member countries. The DSM is produced and approved by the American Psychiatric Association and contains significant additional information around mental health disorders (APA, 2009).

The DSM-IV-TR diagnostic criteria for substance dependence and abuse and the ICD-10 criteria for dependence syndrome and harmful use are set out in Appendix A. There are a number of similar criteria in both, but the DSM-IV-TR contains extra behavioural criteria. Andrews (1999) found that the DSM was the preferred diagnostic criteria for mental health disorders and that there was some lower agreement in diagnoses of substance dependence across DSM and ICD compared to other mental health disorders. The DSM-IV-TR criteria are have more widely used than the ICD-10 criteria for clinical diagnosis purposes in Queensland via its advice to medical practitioners in guiding their assessment of drug dependence. The DSM-IV-TR diagnoses for substance abuse and dependence set out a total of four and seven criteria respectively.

The diagnostic decision requires the meeting of one or more criteria in a 12-month period for a diagnosis of abuse, and three or more criteria for a diagnosis of dependence. There is some contention about the use of the criteria of tolerance and

withdrawal in the case of prescription drug use. In the DSM-5, the constructs of dependence and abuse are now combined into an overarching diagnosis of substance use disorder (Hasin, et al., 2013) and the criteria of tolerance and withdrawal are not included as criteria that can be used to reach a diagnoses of a substance use disorder, but acknowledged as being relevant in the context of POA drugs (American Psychiatric Association, 2013).

For the purposes of this study the diagnostic criteria used in the DSM-IV-TR (American Psychiatric Association, 2000) for drug dependence and abuse were used. This is because they were the accepted criteria at the time of study, and would have been familiar to the widest range of experts in the field for purposes of eliciting responses.

2.7 POPULATIONS OF OPIOID DRUG USERS

Research and information about this emerging trend in a new class of drugs of abuse is incomplete and inconsistent. A recent US review highlighted the lack of comparable international evaluations to POA drug prescribing practices, volumes, and associated drug harms due to different survey measures used (Manchikanti, 2008; Zacny & Lichtor, 2008b). A significant Norwegian study in 2013 tracked a cohort of patients starting on POA drugs from their first exposure. This study found just over seven percent of patients were still on POA drugs after five years and over one third of these had doubled their original dose (Fredheim, Borchgrevink, Mahic, & Skurtveit, 2013). Recent Australian research and reviews have also suggested research is required into monitoring and trends of pharmaceutical drugs misuse, and the phenomenon of doctor shopping (Drugs and Crime Prevention Committee, 2007; Fry, Smith, Bruno, O'Keefe, & Miller, 2007; Karanges, et al., 2016; Roxburgh, 2011; Royal Australasian College of Physicians, 2009)

The dramatic increases in prescribing is exposing more of the population to POA drugs, and potentially to the risk of developing drug dependence (Manchikanti, 2007; Manchikanti, 2008). It is also suggested that given the issues of misuse following increased prescribing of POA drugs in the USA, Australia's increased prescribing

could be facing similar concerns (Dobbin, 2009, 2010a). However, at this time in Australia there is limited evidence as to the extent of these harms. There is possibly an increasing prevalence of POA drug dependence and abuse hidden from scrutiny by the usual drug monitoring and surveillance systems in Australia (Elise Bailey, 2008; Manchikanti, 2008).

There are potentially a number of sub-populations described by research to date that appear to be using POA drugs for legitimate and/or non-medical purposes. Broadly, there is the apparent dichotomy between those patients who are using drugs for therapeutic reasons, and those persons that are misusing them and suffer substance misuse disorders. Studies suggest these populations could be heterogeneous and dynamic, and not necessarily discrete. A brief analysis of the epidemiology of these hypothesised populations follows.

Minozzi and others (Minozzi, et al., 2013) conducted a systematic review of 17 studies involving a total of 88,235 participants and found the incidence of dependence developing following treatment with POA drugs ranged from 0 to 24% (median 0.5%); prevalence ranged from 0 to 31% (median 4.5%). They concluded that the available evidence suggests that opioid analgesics for chronic pain conditions are not associated with a major risk for developing dependence. However, in contrast, Edlund and colleagues (Edlund, et al., 2014) analysed the data of over half a million individuals with new chronic non-cancer pain episodes and found POA drug exposure was a strong risk factor for development of an opioid use disorder, with duration of treatment being more important than daily dose.

It is hypothesised that some individuals, through exposure to POA drugs alone and initiated on legitimate therapeutic grounds, could develop substance misuse disorders, such as dependence or abuse. This has led to the suggestion that this group represent an emerging ‘hidden population’ (Dobbin, 2014). The hidden population are persons who are not coming to the attention of traditional alcohol and drug treatment services, are not largely engaged in the illicit drug milieu, do not identify themselves as drug misusers, and might not be recognised as such by their treating practitioners.

There also appears to be an emergent population of persons using POA drugs for 'non-medical' purposes not derived from initial therapeutic exposure to POA drugs. Illicit opioid drug users might use POA drugs as substitutes, supplements or alternatives to heroin. Studies in the USA, Canada and Australia have found illicit POA drug has increased significantly over the last three decades. Investigations of these populations suggest there could be an emerging illicit POA drug-only sub-population; a dynamic group of users who use illicit opioids and POA drugs equally; and an older heroin-only using subgroup (Fischer et al., 2008). It is not clear for this population whether they are obtaining POA drugs directly from prescriptions themselves or via supplies diverted from other patients.

The reasons for this population using POA drugs has been suggested as influenced by shortages or disruptions in heroin supplies (Khosla, Juon, Kirk, Astemborski, & Mehta, 2011; Lankenau et al., 2012; Louisa Degenhardt, 2008; Zacny & Lichtor, 2008a), preferences for drugs of known quality and dosage, and the greater availability and access to POA drugs (Black, et al., 2012). It should also be noted that illicit drugs users might not be exclusively accessing prescription drugs, as many over-the counter medications containing codeine and paracetamol have been abused.

A further complexity in the illicit drug using population is that some of these individuals might require chronic pain management and treatment with POA drugs. Evidence is emerging that illicit opioid using persons maintain use of drugs throughout their life span and with the opioid substitution treatments are living longer than previously (Højsted, Nielsen, Guldstrand, Frich, & Sjøgren, 2010; Kahan, 2006). The complication here for patients is that appropriate disclosure of their histories might cause loss of access to treatment. The complication for treatment providers is managing a pain condition with POA drugs within the context of past or concurrent illicit drug use.

Within the context of persons receiving prescriptions, there exist the possibility of those who obtain POA drugs and do not have medical conditions or suffer from

substance use disorders. This population would be difficult to estimate, as it is assumed that most prescribers would prescribe for perceived legitimate needs of patients. The numbers of prescribers reprimanded or de-registered for negligent prescribing remains low (Gilson, 2010a; Joranson & Gilson, 1996; Stratton Hill Jr, 1996).

Figure 2.6 represents a proposed conceptual model of the populations of interest of POA drug users and how they might intersect or overlap. The proposed descriptions of these populations, their intersecting and discrete sub-populations, and those in which doctor-shopping behaviour might be expected to occur is described in the following sections. Populations and sections are not in proportion to any scale or size, and are only hypothetical at this stage.

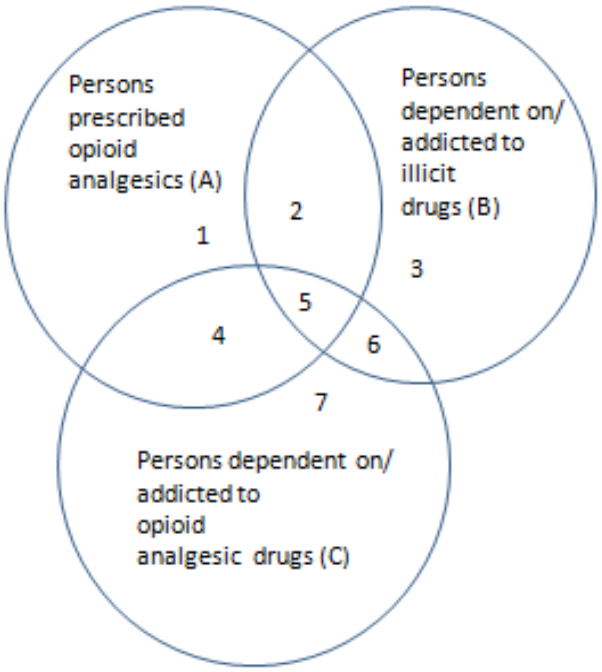

Figure 2-5. *Conceptual diagram of possible POA drug using populations*

The three intersecting populations in Figure 2.6 are made up of three overarching populations represented by the groups A, B and C, which are:

A: *Persons prescribed POA drugs* – this is the population of persons who at any time are being prescribed opioid analgesic pharmaceutical drugs for any reason. This group is captured by a prescription drug-monitoring program.

B: *Persons dependent on illicit drugs* – this is the population of persons who at any time are dependent on, or addicted to illicit drugs. For this study, it refers to persons primarily dependent on heroin, but is not necessarily limited to this illicit drug alone (see Note i).

Note i: Illicit street drugs refer to non-pharmaceutical preparations such as heroin, amphetamine, or cocaine, etc. Although diverted POA drugs are also considered 'illicit' in these circumstances they are considered a distinct other class of illicit drugs, as their primary source is via doctors' prescriptions, not larger-scale criminal operations.

C: *Persons dependent on POA drugs* – this is the population of persons who at any time are dependent on POA drugs. This population might be typified as those whose drug using careers began with POA drugs, as opposed to illicit street drugs (see Note i). Further, this use might have commenced during treatment for legitimate medical conditions.

It is proposed that there are four intersecting sections of these populations represented by the marked areas sub-populations 2, 4, 5 and 6, which are:

Sub-population 2 – This sub-population are those illicit drug-dependent persons who are prescribed POA drugs at any given time, but not dependent on them. For example, this could be an illicit drug user who is receiving post-operative pain relief. This population would not necessarily be expected to engage in doctor shopping. However, exposure to POA drugs might increase the risk of drug-seeking for POA drugs (see Note ii)..

Note ii: This population may require particular attention for their pain management needs as, if they are currently dependent on illicit drugs similar in action

to POA drugs, their tolerance for these drugs will be higher and they might require higher doses of POA drugs in comparison to an opioid naïve person (i.e. hyperalgesic).

Sub-population 4 – This sub-population represents persons addicted to, or dependent on POA drugs who are receiving prescriptions, but who are not addicted or dependent on illicit drugs. There would conceivably be a risk of doctor-shopping behaviour to be found in this sub-population.

Sub-population 5 – This sub-population represents persons dependent on POA and illicit drugs who are receiving prescriptions for POA drugs. This population might be most at risk of obtaining POA drug prescriptions for non-therapeutic reasons; that is, not having a medical condition apart from dependence that requires treatment with POA drugs. This sub-population could also potentially exhibit doctor-shopping behaviour. However, some persons might be treated for their dependence outside formal opioid substitution programs.

Sub-population 6 – This intersection between illicit drug-dependent and POA drug-dependent populations represents those persons who are not receiving POA prescriptions. Persons in this sub-population would be obtaining POA drugs from sources other than prescriptions, such as black market suppliers or diversion from legitimate recipients.

There are three discrete sections of the larger populations A, B and C that do not intersect with each other, and these are represented by the marked areas, 1, 3 and 7, which are:

Sub-population 1 – This sub-population represents those persons receiving POA drug prescriptions who are not dependent on illicit or licit drugs. It would be expected the risk of doctor shopping should be low in this sub-population. If doctor shopping for prescriptions occurred in this population, it could represent:

- a person receiving inadequate treatment by their treating doctors (see pseudo-addiction)
- a person not dependent on POA drugs but on-selling or diverting these medications, or engaged in some other criminal enterprise.

Sub-population 3 – This sub-population represents those persons dependent on illicit drugs who do not receive any prescriptions for POA drugs. This would not preclude these persons obtaining POA drugs for reasons of their drug dependence; however, supply would be from non-prescription or diversion. As distinct from sub-population C, these persons would be primarily dependent on illicit drugs.

Sub-population 7 – This sub-population represents those persons dependent on POA drugs who are not dependent on illicit drugs, nor are they obtaining POA drug prescriptions. These persons could be doctor-shopping but being refused prescriptions for POA drugs by doctors, or are obtaining other prescription drugs (e.g. benzodiazepines, tramadol) or obtaining over-the-counter medications. These persons might also obtain POA drugs from other illicit markets or persons diverting them for other purposes.

The more difficult behaviour to account for is where POA drugs could be diverted to other persons. Persons likely to divert prescribed POA drugs could be anyone, but more likely to be high dose, and/or doctor shopping persons. There is limited evidence of persons admitting to diversion of POA drugs. However, there is ample evidence from Australia (AIHW, 2012) and overseas (Alho et al., 2015; Dreifuss, et al., 2013; Nielsen et al., 2011) of persons' admissions to drug treatment programs from POA drug SUDs where they have reported access from non-medical sources. There is some evidence of police and crime reports (IDRS & Crime reports) of persons being prosecuted for offences of selling POA drugs and reports of pharmacy business thefts are also reported.

Persons like to divert POA drugs could fit in any particular category but assuming a person is obtaining POA drugs to meet a therapeutic or due to their SUD, then other POA drugs obtained above their personal needs could be diverted. Furthermore, a person with a history of illicit drug use might also be more likely to have associations with illicit drug use markets and greater opportunity to on-sell their POA drugs

Table 2.7, represents a further description of the populations and sub-populations in Figure 2-5 and indicates those sub-populations that might exhibit doctor-shopping behaviour.

Table 2.5 *Doctor-shopping in proposed illicit drug and opioid analgesic drug-using populations*

Population*	**Persons prescribed POA drugs**	**Person addicted/ dependent on illicit drugs**	**Persons addicted/ dependent on POA drugs**	**Doctor-shopping Risk**
Sub-population*	(A)	(B)	(C)	
1	+	-	-	Y
2	+	+	-	N
3	-	+	-	N
4	+	-	+	Y
5	+	+	+	Y
6	+	+	+	N
7	-	-	+	N

Note: Y- Yes; N-No;
+ member of sub-population; - not member of sub-population
* *See* Figure 2-5

The above model referred to in Figure 2-5 has the following assumptions and limitations. Firstly, the population boundaries might not be impermeable over time. A person's drug use and dependence status can change; that is, individuals could move between populations or exit the model entirely due to death, treatment completion, or other reasons. Secondly, drug use other than POA drugs might be involved, contributing to, or resulting from, an individual's dependence status, illicit drugs use, or doctor shopping.

Furthermore, the notion of primary drug of dependence might need clarification. During the course of a person's addiction/dependence they might change their primary drug of choice. This can happen for a number of reasons; for example, availability, price, or access. Primary dependence could refer to either initial drug use that leads to dependence, or drug of choice at a given time during an episode of dependence. This model does not suggest a temporal or causal relationship; that is, doctor shopping might result in dependence, or be due to a person's dependence.

Lastly, as previously discussed, other external or systemic factors might influence drug dependence or drug seeking; for example, heroin drought, lack of treatment places, policing or regulatory programs, prescription cost changes, new drug availability, GP/pharmacist training or programs, geographic location or other environmental variables. These proposed populations are hypothetical constructs at this time for potential testing in the study. It should be noted that members of these populations and their constituent sub-populations might change membership over time, or cease to be members of this group entirely.

2.7.1 Individual Risk Factors

Models of alcohol and drug dependence suggest that some individuals can possess risk factors that pre-dispose them to developing abuse or dependence. The biopsychosocial model of dependence states that there is a potential contributory and possible interaction between biological, psychological and social factors related to a

person's risk of developing alcohol or drug dependence or abuse. By extension the same model should be applicable in populations of persons misusing POA drugs.

The addictiveness of substances is a necessary a factor in formation of SUDs in persons. However, exposure alone to substances, does not necessarily lead to SUDs or problematic behaviour. The, biopsychosocial model has been applied to addiction as various biopsychosocial factors have been shown to be particularly relevant in predicting or accounting for susceptibility to developing SUDs when exposure occurs.

Shaffer et al (Shaffer et al., 2004)describe addiction as a syndrome that "Although distinct expressions of addiction have unique elements, these different manifestations also share many neurobiological and psychosocial antecedents and consequents (Page 371). These antecedents are often difficult to measure, in regard to genetic and neurobiological variables; of for psychosocial factors prone to interpretative or social biases when relying on subjective measures.

In persistent pain management with POA drugs a population is being exposed to dependence forming substances, albeit for assumed therapeutic reasons and within certain controlled circumstances. (Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008) reviewed 67 studies of persistent pain patients under long-term POA drug treatment. The authors found an overall rate of abuse or addiction of 3.27 per cent; and when those with a history of abuse/addiction were excluded the percentage of abuse/addiction was 0.19 per cent Of these studies over 11 per cent of persons were reported as showing aberrant drug related behaviour, however, when excluding those with a history of abuse/addiction only 0.59 per cent person showed such behaviour.

(Garland, Froeliger, Zeidan, Partin, & Howard, 2013) suggested that there is a "biobehavioral risk chain linking chronic pain, opioid analgesia, and addictive behaviours." They propose addiction in this context could be caused by chronic pain

linked to negative affect, neurochemical effects of POA drugs in conjunction with other psychological and cognitive factors.

However, studies to date have not conclusively identified biopsychosocial factors that are antecedents or consequents of POA drug related SUDs. This study seeks to explore the experts' views on these matters. The role of PDMPs might also allow for capture of relevant factors to assist in clinical assessment of risk for development of POA drug SUDs.

As PDMPs capture some demographic and other details of persons in receipt of POA drugs, some risk factors can be identified. The objective of this part of the study is to seek the views of experts as to what particular biological, psychological or social factors might be predictive of risk of POA drugs. These results could then be potentially tested in PDMP datasets based on relevant data items available.

2.8 DRUG-SEEKING AND DOCTOR-SHOPPING BEHAVIOUR

Medicare Australia in 1996/97 identified more than 10,000 persons as doctor shoppers for any class of drug and 9% of those drugs dispensed for doctor shoppers were for POA (Health Insurance Commission, 1998). Medicare defined 'doctor shoppers' as those people who saw 15 or more GPs in a year, had 30 or more Medicare consultations, and appeared to obtain more PBS medications than were clinically necessary. This equated to 1, 270 'doctor shoppers' for every 1,000 general practitioners (Drugs and Crime Prevention Committee, 2007). It was estimated this cost the community over $31 million per year in unwarranted consultations and subsidised prescriptions. The socio-economic costs of persons developing drug dependence from POA, or not being effectively treated for a condition with POA is unknown.

Drug dependence is a key indicator of inappropriate use of POA drugs. However, the defining of substance misuse disorders in a potentially heterogeneous population

is particularly complex. One proxy measure of drug dependence in this area could be that of drug-seeking behaviour or doctor shopping. This refers in a general sense to seeking multiple prescriptions for POA drugs from multiple prescribing doctors for drugs that might be in excess of expected therapeutic needs. Such behaviour could be suggestive of a person's loss of control of their POA drug use and serve as a proxy for an assessment of substance misuse disorder.

From a regulatory and clinical perspective, the challenge is to minimize public health and individual harms from the misuse of POA drugs in a manner that does not restrict individuals' access to legitimate and appropriate treatment. Prescription drug-monitoring programs offer an objective measure of some aspects of a person's individual drug use, but also can establish some normative parameters of use across the wider population.

PDMPs could offer valuable assistance to health practitioners to assist in their POA drug treatment decisions, as well as limiting the inappropriate flow of POA drugs that might be diverted for other purposes. This would then require some agreed upon definition of 'doctor shopping' and this is discussed as follows.

2.8.1 Defining doctor shopping

'Doctor shopping' refers to the behaviour of a person consulting multiple doctors for the purpose of attempting to obtain prescriptions for dependence-forming drugs. This is also known as 'prescription shopping', 'double doctoring' and other various terms (Sansone & Sansone, 2012).

Doctor shopping represents a behaviour that could be indicative of a person's misuse or dependence on prescription opioid medications. However, there are considerably varying definitions of what constitutes doctor shopping and even less evidence of an association between doctor shopping and prescription opioid drug problems.

There is a reasonably clear and established association between increased drugs use and development of abuse and dependence. For POA drugs, it could be reasonably assumed that a person obtaining increasing volumes of drugs is dependent on or abusing those drugs. What is less clear is what extent of drug seeking could indicate problematic misuse.

The phenomenon of doctor shopping refers to persons who consult multiple medical practitioners for multiple prescriptions of medications that are in excess of their therapeutic requirements. In terms of POA drugs, doctor shopping particularly refers to persons who are obtaining large volumes of POA drugs in excess of therapeutic requirements. Doctor shopping has been identified as a concern in terms of its costs to the Commonwealth Government's subsidised Medicare and Pharmaceutical Benefits Scheme (Medicare Australia, 2011); however, there is little known about the health implications of this phenomenon.

Doctor shopping for POA drugs is possibly an indication of opioid dependence or abuse according to established diagnostic criteria (American Psychiatric Association, 2000; World Health Organisation, 2007). It has also been suggested that doctor shopping could be suggestive of persons who are under-treated for their pain conditions in some cases, also known as 'pseudo-addiction (Zacny, et al., 2003). A recent Australian study of three state jurisdictions found there was little connection between POA drug obtaining and organised crime networks (Fry, et al., 2007). However, it is not entirely clear from the research to date as to whether persons doctor shopping might be obtaining drugs for pain management due to dependence, for abuse, for diversion to illicit markets, or for other purposes.

Drug-seeking behaviour can be considered one of the possible diagnostic criterion, within the DSM-IV definition of dependence (American Psychiatric Association, 2010). In particular, the DSM-IV describes a criterion of drug dependence as where "a great deal of time is spent in activities necessary to obtain the drug, use the drug or recover from its effects." (American Psychiatric Association, 2010).

Doctor-shopping behaviour is drug-seeking behaviour that is open to multiple interpretations, including possible drugs misuse. Therefore, doctor-shopping behaviour might serve as an indicator of possible POA drug dependence. However, any measure will need to have appropriate levels of sensitivity and specificity to capture the population in question, and not mislabel non-problematic behaviour.

Prescription drug-monitoring systems present one means by which largely objective prescription information can be routinely monitored to detect patterns of aberrant drug-seeking or doctor shopping. This could allow timely and cost-effective interventions and ongoing collection of trend data to assist public health interventions and clinical practice.

Converging evidence suggests that there is an increasing prevalence of misuse and dependence on POA drugs in Australia. However, a lack of consensus on many underlying issues has made it difficult to define the problem, understand the extent of misuse, and provide effective interventions.

POA drugs have the potential for problematic use, and these same drugs have a place in conventional medical treatments. Appropriate levels of sensitivity and specificity are required to identify problematic use of POA drugs, and to ensure appropriate use of these drugs is not compromised. Prescription records held in central monitoring databases could provide some objective evidence as to a person's drug-seeking activity and potential aberrant use of POA drugs that might help make some of these issues clearer.

Doctor shopping is widely held to be a behaviour of concern and associated with POA drug misuse and diversion. However, definitions of 'doctor shopping' are not well established nor is it understood what levels of drug obtaining might be problematic or indicative of substance use disorders. Regulators and clinicians are seeking to address the rising public health concerns around POA drug misuse. Strategic approaches to managing these concerns need to consider sound evidence

before making policy and treatment decisions. There is a considerable population of persons in the community with legitimate treatment needs and there could be significant implications in terms of unintended negative outcomes if regulatory or clinical policy decisions are made on a poor understanding of these issues. This study seeks to address this lack of knowledge.

The aim of this research is to determine the definition of doctor shopping that can identify aberrant POA drug use; identify and describe the population of persons engaged in doctor shopping to determine if there is an emerging and increasing POA drug-misusing population in Queensland; and determine whether central database records of POA drug prescriptions can effectively help identify and monitor this issue.

2.9 RESEARCH OBJECTIVES

The objectives of this research are to:

- Identify and describe the characteristics of the POA drug-misusing doctor-shopping population.
- Evaluate the extent and nature of POA drug-misusing or doctor-shopping behaviour over time.
- Consider the application of these findings to improve public health responses addressing current and possible emerging POA and other pharmaceutical drugs misuse problems.

These objectives give rise to three particular research questions that are to be addressed in three studies that will constitute this project.

The first study addresses the questions as to what level of drug-seeking behaviour would indicate inappropriate use of pharmaceutical opioids and when might that use constitute a clinical definition of abuse or dependence? That is, what definition, or definitions, of ‘doctor shopping’ behaviour in terms of prescriptions, dosage, drug type, frequency, and timeframe for POA drugs might indicate a person is

abusing, or dependent on, these drugs? This study will seek views of experts in the relevant fields to derive these definitions for testing in the subsequent studies.

The second study relates to the first. If certain definitions of doctor shopping behaviour can be derived from the first study, what are the characteristics of this potentially drug-misusing population? What parameters describe this population, in terms of demographics, drug use, and behaviour and what discriminates doctor shoppers from other prescribing behaviour of persons receiving POA drugs? This study will seek to apply a definition of 'doctor shopping' derived from the first study in a prescription drug monitoring program dataset with a complete year of POA drug dispensed records for the State of Queensland.

The final third study will examine historical aspects of doctor-shopping persons over previous years to investigate their prior prescribing patterns and to determine if historical drug use could be associated with current drug use patterns. Using the previously derived definition, the dispensing records of those persons identified as doctor shoppers will be examined over a 10 year period to examine antecedents to their POA drug use behaviour identified in Study 2.

The discussion aspect of this study will draw together the finding of the three studies to consider the utility of central prescription activity databases in improving public health interventions and monitoring and surveying trends in POA drugs use. The implications for these findings for clinical and regulatory practice and areas of further study will also be discussed.

Chapter 3: Study 1: Defining doctor shopping

3.1 INTRODUCTION

The aim of the first study is to examine aspects of various expert groups' understanding of prescription opioid analgesic (POA) drugs misuse and doctor-shopping behaviour to determine if agreement can be reached on criteria and definitions for these phenomena. These criteria and definitions are to be tested in prescription drug monitoring program (PDMP) in the second and third studies to test if they could be used to discriminate aberrant POA drug use.

The objective of this study is to define problematic drug-seeking or doctor-shopping behaviour and other possible factors that could be indicative of POA drug misuse by using drug dependence and pain management experts and specialists to derive criteria that can be tested in a PDMP. There are a number of issues identified in the literature review that are to be tested with the expert panel as these might add value to understanding prescription opioid misuse and drug seeking and could suggest testable criteria in a PDMP. These issues can be categorised as definitions of drug dependence and abuse, aspects of particular POA drugs, characteristics of persons who might misuse these drugs, and the defining of doctor-shopping behaviour and when it might be indicative of misuse of POA drugs.

The diagnosis of drug dependence and abuse is contentious in this area. Ideally, diagnosis should be undertaken as a clinical assessment in face-to-face consultation between a health practitioner and a patient. However, PDMP can offer objective information to assist in clinical assessment. Potentially some aspects of POA drug use could be more indicative of aberrant use than others. PDMPs can capture dispensed prescription drug details along with other limited demographic details. However, this data can still provide information types and preparations of drugs being used and the patterns of prescriptions sought over time.

This study will examine experts' views on assessing substance use disorders for POA drugs, what types and features of particular POA drugs might be more likely associated with aberrant use, and what factors might be associated with POA drug misuse. Lastly, the experts definitions of 'doctor shopping' will be examined across all experts to attempt to coalesce this into a single or unified definition. The following four sections discuss the above matters in more detail regarding the development of survey instruments to test understanding of these matters in a relevant expert group.

The aim of this study was to attempt to derive a consensus from the expert panel of their ranking of importance of particular DSM-IV-TR criteria for abuse and dependence on POA drugs. This study seeks to poll experts across the various fields of addiction, pain management, and general practice to examine their understanding of POA drug misuse to see if there can be a convergent working definition of POA dependence and abuse. From these definitions is intended to develop criteria based on drug-seeking or doctor-shopping behaviour.

3.2 METHODS

A modified Delphi Technique (Iqbal, 2009; Skulmoski, 2007) was used as the methodology to determine an understanding of definitions of drug dependence and quantify levels of different aspects of doctor-shopping behaviour for testing in the population database in later studies.

To examine these questions, experts were questioned on their views in a series of questionnaires using the methods of the Delphi Technique. This is where the views of a panel of experts are sought, and their collated views are fedbackto them , in order for them to review and revise their views. This is done iteratively over multiple rounds, with the intention to move towards a convergence of views where experts might start with divergent views.

3.2.1 Overview of Delphi Technique

The Delphi Technique is a research process that seeks to gain consensus across a range of experts by a series of questionnaires. Results of earlier rounds of questionnaires are fed back to the expert panel to see if they modify their responses based on the group's overall response. By a process of iteration each round seeks to move the expert panel to a consensus or agreed position on the question under examination.

Most applications of the Delphi Technique suggests an optimal number of between 30-50 panel members (de Meyrick, 2003; Iqbal, 2009; Linstone, 2002; Skulmoski, 2007) and that some level of participant attrition should be expected in follow-up rounds. Further, there is support for the use of a limited group of experts where the research topic is particularly specialised.

This methodology has since been modified by drawing on all (Wang et al., 2003) or some (Gupta and Clarke, 1996; Robertson and MacKinnon, 2002) of the definition set out by Linstone and Turoff (1975) who define the Delphi Technique as a method for structuring a group communication process so that the process is effective in allowing a group of individuals, as a whole, to deal with a complex problem.

This study is a variant of the classical Delphi Technique that is an iterative response-seeking expertise on a particular issue (van Zolingen and Klaassen, 2003). This study aims to arrive at a consensus across a panel of experts from different fields to achieve definitional criteria of a particular problem.

Use of Delphi Method in health research

The Delphi Technique has wide application, particularly in health-based research and has been used in over 1,000 published research papers since its development in the 1950s (de Meyrick, 2003). There has been less application to the use of this technique in the addiction and dependence field. This technique has been

used in similar and related studies in the development of assessment of clinical conditions where there is not necessarily an agreed position.

Delphi techniques have been used in the development of scales or assessment measures by (Nekolaichuk, Fainsinger, & Lawlor, 2005) of pain classification systems in cancer patients. (Green et al., 2009) used a similar technique in assessing illicit drug users' experience of drug-related effects, (Kingston et al., 2011) in developing strategies to help illicit drug users, and McBride et al to develop guidelines around access to controlled medications (McBride, Pates, Ramadan, & McGowan, 2003).

3.2.2 Development of Survey Questions

The broad objective of this study is to develop criteria to identify potentially drug-dependent or drug-abusing users of POA drugs from their profiles of POA drug obtainings in a prescription drug-monitoring program. Four topics areas were developed: what are the particular harms of POA drugs; what drugs and what aspects of POA drugs are most harmful; what is important in assessing substance use disorders in relation to POA drugs; and what might form an agreed definition of doctor shopping.

Initial questions were piloted by sending them to two experts known to the author – one in the addiction field and one in the pain management field – for review of the readability and suitability of the questions. Neither expert was invited to participate in the actual study. The following first-round questions represent the outcomes of that consultation. This pilot testing led to the modification of a number of first-round questions in regards to phrasing of the questions and types of responses requested.

Topics 1 and 2: What are the particular harms of POA drugs? What drugs and what aspects of POA drugs are most harmful?

The levels of harm articulated by Nutt et al (Nutt, et al., 2007) set out sub-categories of physical, dependence, and social harms (see *Table 2.3*). Initial pilot testing (see Section 3.2.2) found these parameters were not helpful in discriminating between different opioids and led to some lack of clarity in responses. However, the higher order concepts describing-levels of harm, in terms of physical, dependence, and social harms were understandable in pilot testing group and suggested as most likely

to encourage appropriate responses. Therefore, only three levels of harm, physical, dependence and social harms, were used in developing questions on opioid drugs harmfulness.

Two further questions on what features of POA contribute or reduce their potential for harm were included. This was to assess what, if any, features of a POA drug might be linked to its misuse or lack of misuse (e.g., injectability and controlled-release formulations). A further open-ended question was added to assess if there were any other reasons that the experts believed some POAs were more harmful than others.

Table 3.1

Question on harmfulness of pharmaceutical opioid drugs

No	Question
1	What pharmaceutical opioid drugs do you believe are most prone to cause physical harm?
2	What pharmaceutical opioid drugs do you believe are most prone to cause dependence?
3	What pharmaceutical opioid drugs do you believe are most prone to social harms?
4	What pharmaceutical opioid drugs do you believe are most prone to be abused?
5	What do you believe are the features of pharmaceutical opioid drugs that might contribute to the potential for harm?
6	What do you believe are the features of pharmaceutical opioid drugs that might reduce the potential for harm?
7	What other reasons do you believe some pharmaceutical opioid drugs might be more harmful than others?

In the first round experts were asked to suggest what opioid drugs, if any, were most harmful across the domains of physical harms, prone to cause dependence, most abused, caused social harms, and rate the features of POA drugs that might reduce or increase the potential for harms in free-text responses. The mentions of any listed POA drug was then counted from text analysis for the four domains of harm and resulted in

a total count for each drug under each domain of harm. For the benefit of this assessment only the active drug, not the type of formulation of drug, was counted. For example, controlled-release oxycodone (Oxycontin™) and immediate-release oxycodone preparation (Endone™) were both counted as oxycodone.

The second part of this questionnaire was to query experts on what aspects of POA drugs might make them more or less prone to misuse. The responses were given as free text and due to the range and variability of responses and lack of consistent terminology the results did not lend themselves to standard text count. For example, many experts rate the sustained-release preparations in either response; however, the terms used included: slow, controlled, length of half-life.

For the first round, respondents were able provide free-text responses to the questions in Table 3.1. The responses were then compiled to generate ranked lists of particular responses. For the second round, respondents were presented with the ranked list of responses from the first round and were then asked whether they agreed with the ranking or, if not, they could re-order the rankings. Furthermore, respondents could still add free-text to any items at this point.

Topic 3: What is important in assessing substance use disorders in relation to POA drugs?

Based on the biopsychosocial model of dependence the following questions (see Table 3.2) were developed to seek experts' views as to what particular biological, psychological and social factors were most associated with dependence or abuse of POA drugs. The first round of questions were free-text questions to garner the broadest responses.

Table 3.2

Questions based on individual risk factors under biological, social and cultural domains.

No	Question
1	What biological factors do you believe are most relevant in the development of a substance misuse disorder related to pharmaceutical opioid drugs?
2	What psychological factors do you believe are most relevant in the development of a substance misuse disorder related to pharmaceutical opioid drugs?
3	What social or cultural factors do you believe are most relevant in the development of a substance misuse disorder related to pharmaceutical opioid drugs?
4	What other factors do you believe are most relevant in the development of a substance misuse disorder related to pharmaceutical opioid drugs?

For the first round, the experts provided free-text responses. For the second round, the most common responses for each question were compiled. Respondents were presented with the un-ranked list of responses under each category above and were asked to rank their level of importance. The respondents could still add free-text to add any items at this point.

Topic 4: Definition of substance use disorders on POA drugs

These questions were developed using DSM-IV-TR criteria for substance abuse and dependence as set out below in Table 3.3. For each criterion a question was developed to solicit a rating on the importance of each criterion in reaching diagnosis. This led to 11 questions of phrased variants of DSM-IV criteria of abuse and dependence.

Table 3.3

DSM-IV-TR criteria and derived survey questions

	DSM-IV TR criteria for substance use disorders.	Question
	Substance dependence – three or more occurring in a 12 month period.	
1	Tolerance as defined by either of the following: - A need for markedly increased amounts of the substance to achieve intoxication or desired effect; Markedly diminished effect with continued use of the same amount of the substance.	How important is evidence of tolerance in assessing person for substance use disorders on pharmaceutical opioid drugs?
2	Withdrawal, as manifested by either of the following: The characteristic withdrawal syndrome for the substance; Taking the same (or a closely related) substance to relieve or avoid withdrawal symptoms	How important is evidence of withdrawal symptoms in assessing a person for substance use disorders on pharmaceutical opioid drugs?
3	Use of a substance often in larger amounts or over a longer period than was intended.	How important is the amount of the drug being taken, in assessing a person for substance use disorders on pharmaceutical opioid drugs?
4	Persistent desire or unsuccessful efforts to cut down or control substance use	How important are attempts to reduce or control drug use, in assessing a person for substance use disorders on pharmaceutical opioid drugs?
5	Spending a great deal of time spent in obtaining, using, or recovering from the effects.	How important is time spent in obtaining drugs, in assessing a person for substance use disorders on pharmaceutical opioid drugs?
6	Social, occupational, recreational activities given up or reduced because of use	How important are the effect of drug use on social, occupational, or recreational activities, in assessing a person for substance use disorders on pharmaceutical opioid drugs?
7	Continued use despite social, legal, medical, psychological, and other problems	How important are social or interpersonal problems, in assessing a person for substance use disorders on pharmaceutical opioid drugs?
	Substance abuse – a maladaptive pattern of substance use indicated by at least one of the following occurring in a 12 month period	
1	Recurrent use resulting in a failure to fulfil major role obligations at work, school, or home	How important are the drug use effects on work, school or home obligations, in assessing a person for substance use disorders on pharmaceutical opioid drugs?
2	Recurrent use in situations in which use is physically hazardous (e.g., driving while intoxicated)	How important is drug use in hazardous situations, in assessing a person for substance use disorders on pharmaceutical opioid drugs?
3	Recurrent substance-related legal problems	How important are drug-related legal problems, in assessing a person for substance use disorders on pharmaceutical opioid drugs?
4	Continued use despite a persistent or recurrent social, occupational, psychological, or physical problem that is caused or exacerbated by the substance use	How important is continued drug use despite health or psychological effects, in assessing a person for substance use disorders on pharmaceutical opioid drugs?

For the first round, respondents were requested to rate each response on a 5-point Likert-type scale from 'Very important' to 'Unimportant'. A free-text section was provided to allow for the inclusion of any other criteria participants believed were relevant.

For the second round, respondents were presented with the ranked list of criteria that resulted from the first round and were then asked whether they agreed with the ranking or, if not, they could re-order the rankings.

Doctor-shopping behaviour

The main aim of this study was to determine an appropriate definition of the term 'doctor shopping' and determine threshold levels of POA drugs use or drug-seeking behaviour for objective dispensing criteria. This was to allow for identification and possible prediction of persons of interest from monitoring and regulatory standpoints and provide assistance in clinical decision-making to assist in treatment and prescribing decisions.

Table 3.4 below sets out the questions used in this part of the survey. As described above the term 'doctor shopping' has a wide and varied application and multiple meanings so all experts were asked their opinions of this definition. This was to ascertain if there was actual disparity amongst the expert community and to see if a unified definition could be derived.

The second questionnaire asked the experts what criteria suggested a person might be suffering a substance use disorder. This included criteria derived from literature searches, such as frequency of consultation, number of prescriptions obtained, and timeframe of behaviour. Again, this was designed to garner views across the expert panel to work towards a possible range of objective criteria that could be tested in the database. The final question was a further free-text question to assess if any other criteria could be considered relevant in assessing doctor shopping.

Table 3.4

Questions on drug-seeking behaviour

No	Question
1	What do you understand by the term ‘doctor shopping’ or ‘prescription shopping’ in the context of potential misuse of pharmaceutical prescription medications?
2	What extent (frequency of consultations, prescriptions obtained, volume of drug obtained, over what time period) of doctor/prescription shopping do you believe would suggest a person is suffering from a substance use disorder?
3	Are there any other features of doctor/prescription shopping that you believe are relevant in considering whether a person is suffering from a substance use disorder?

For the first round, experts were asked their general understanding of the term ‘doctor shopping’, measureable variables that might describe doctor shopping, and for any other relevant factors. The initial responses from the first round sought to force respondents to suggest particular levels of prescriptions obtained, doctors consulted, pharmacies dispensing, and average daily dose in morphine equivalent milligrams that might suggest a substance misuse disorder. This led to a number of respondents suggesting that in a clinical assessment any element of drug seeking could be indicative of problems.

In the second round the question was amended further to have respondents indicate what levels of drug seeking might indicate either no cause for concern (green light), some heightened levels of concern (amber light), or definite concerns (red light).

3.2.3 Participants

A panel of experts were drawn from the fields of chronic pain management, addiction and dependence, the general practitioner community, and across both Australian and international domains (see Table 3.5). This was to obtain the various stakeholders in both definitional issues and actual clinical management of these conditions.

Table 3.5

Proposed class of experts by speciality and nationality to be recruited for Delphi study

Specialty	***Australia***	***International***	***Total***
Pain management	15	15	30
Addiction/Dependence	15	15	30
General practice	30	-	30
Total	60	30	90

International experts were mainly drawn from the USA and Canada due to the similar prescription opioid issues in these jurisdictions to Australia and each country's adoption of prescription drug-monitoring programs. However, other experts from the published literature were not excluded if they were from other jurisdictions.

Searches were conducted via the internet for professional pain management and addiction associations and bodies where members were involved in clinical treatment of patients or where a clinical qualification was a prerequisite of membership. A full list of organisations is attached in Appendix C. Emails were sent to organisations to seek their involvement and distribution via membership pathways. Where requested, details of ethical approval and study protocol was provided if the organisation required prior review before distributing to their members.

Literature searches were also conducted of PubMed, Ebsco Scholar, Google Scholar and other internet search engines on authors published on prescription opioids and pain management topics. Searches were conducted using the search terms:

- prescription, pharmaceutical, opioid, drug, abuse, dependence, misuse, addiction
- chronic, persistent pain management, drug seeking, doctor shopping, prescription shopping, double doctoring,

Authors were then reviewed based on their published curriculum vitaes, if available, to determine those who indicated clinical qualifications. Experts were chosen by their known contribution to their respective fields as published authors in

the area of POA drug misuse. Australian general practitioner participants were recruited via approaches to the alcohol and drug or chronic pain interest groups that accepted membership from non-specialists, such as the Australian Pain Society and the Australian Professional Society on Alcohol and Drugs (see Appendix C).

Initial introductory emails were then sent to a number of organisations to request distribution of information about the study to members. This included email address details for interested participants to respond to. Similarly, initial email invitations were issued to individuals of interest identified via literature and web-based searches.

3.2.4 Survey media and distribution

To provide ready access to the expert panel the survey questions above were constructed in the online survey poll, Survey Monkey™ (Survey Monkey Inc., 2011). Survey Monkey allows construction of online questionnaires, access to users over the internet, and compilation of responses into various formats of files for export and later statistical analysis.

Survey Monkey (Survey Monkey Inc., 2011) also allows for tracking of survey respondents as individual participants can be given unique links to access the survey. This means appropriate follow-up can be done to encourage non-responders. Furthermore, for this application of the Delphi Technique, the responses to the second iteration of the study could be linked to the initial responses in the first round of the study.

Two rounds of the questionnaires were conducted and the reasons for this are discussed later in the Results section. The questionnaire rounds were uploaded to the Survey Monkey (Survey Monkey Inc., 2011) website and password protected. The full versions of Version 1 and Version 2 of this survey are provided in Appendix D as they appeared online in Survey Monkey and includes the full versions of the first and second round surveys.

Survey Monkey (Survey Monkey Inc., 2011) is widely used as a survey or data collection tool across social science and academic research. There are some limitations and concerns around the use of online surveys. Buchanan and Hvizdak (2009) identified concerns around security and storage of data, design of questions, anonymity of responses, and ability to verify appropriate respondents completing surveys (Buchanan & Hvizdak, 2009).

In regards to security of data, this study largely used responses linked to a set of named respondents with email addresses in the actual Survey Monkey program. A full paid subscription was procured for the purposes of the study to allow for use of the full range of program features, thus limiting unauthorized access from other parties.

The Survey Monkey program does limit the format of questions and responses to a set repertoire of variations. Once initial questions were conceived and constructed they were appropriately modified. Initial modifications were minor and the actual initial questions and form of response (Likert type scales, free text or ranked lists) did not substantially alter the nature of the questions. Survey questions in the Survey Monkey form were also piloted with a test group of two experts and, based on their responses, further minor amendments were made to some of the wording of questions for improved ease of comprehension.

The respondents were advised that their responses would be anonymous for the purposes of reporting the outcomes of the study. However, they were also informed that their email addresses were linked to individual web links to Survey Monkey for purposes of follow-up and later rounds of the study. Respondents were informed of this in the preliminary background information on the study and offered further details of the research protocol if required. Once information gathering was completed data was removed from the site. All analysis and reporting did not use any identifying information. Verification of respondents was achieved by preliminary contacts by email in the first instance.

On receipt of the results from Round 1 each of the questionnaire categories were assessed and collated to develop a second-round questionnaire to feedback to the expert panel the compiled results. The responses from Round 1 are described in the following sections. The results from Round 1 were fully compiled before the second round of questions were re-issued to all of the original respondents who agreed to further participation.

3.3 RESULTS

3.3.1 Participants

Sixty-one recipients responded to the first round of the survey. Of the first-round participants, 29 reported as male, nine as female, and 23 didn't report gender. Eighty per cent of respondents were from Australia and New Zealand, and 20% were from Canada and the United States of America.

Of the self-nominated area of speciality, where reported, 32 (52%) self-nominated as primarily working in drug dependence, 21 (34%) as primarily working in pain management, with 4 respondents reporting working in both fields. The remaining four participants reported as being primarily researchers and did not report a primary field of work.

Almost half of the respondents (n=30) were medical practitioners and 9 reported as being nursing or allied health professionals. Twenty-one persons reported as having research roles in universities with 6 participants reporting having PhDs. Over a quarter (n=17) reported working in hospitals.

Just under half the respondents (n=27) responded to the second round of the survey. A summary of the differences between Round 1 and 2 respondents is shown in Table 3.6 with the classification of respondents by gender, country and primary speciality area reported to show the level of attrition in participation across the two rounds.

Table 3.6

Details of responding participants for Round 1 (n=61) and Round 2 (n=27) of Delphi Study

	Round 1		**Round 2**	
	n	%	N	%
Gender				
Male	29	48%	20	74%
Female	9	15%	7	26%
Missing	23	38%	0	0%
Primary field				
Drug dependence	32	52%	16	59%
Pain management	21	34%	7	26%
Both	4	7%	2	7%
Neither	3	5%	2	7%
County of origin				
Australia	39	64%	21	78%
New Zealand	10	16%	1	4%
USA	9	15%	2	7%
Canada	3	5%	3	11%

The Round 2 had a higher proportion of female respondents and more Australian respondents engaged in this round. However, the proportion of participants by primary field of work appeared to remain similar across both rounds of the study. It should be noted that for Rounds 1 and 2 not all participants responded to all questions, and the numbers of actual item responses are reported in the results.

3.3.2 Response to Delphi Study

The results are reported for Round 1 and 2 for each section of the survey in the following results.

What are the harms of POA drugs and what drugs cause harm and why?

Table 3.7 and Table3.8 show the results of experts' views over two rounds of the Delphi Study for particular POA drugs they agree as being the most harmful.

Table 3.7

Round 1 - Harmfulness of POA drugs combined ranking by experts by category of harm for each POA drug type (n=61)

POA Drug	Physical Harm	Dependence causing	Abuse prone	Social harms
Oxycodone	17	22	22	12
Morphine	14	15	12	7
Fentanyl	8	8	5	1
Hydromorphone	3	3	1	1
Methadone	2	2	1	0
Pethidine	4	5	4	0
Codeine	2	4	4	2
Buprenorphine	3	0	3	0
Any Opioid	9	7	3	1

Table 3.7 shows the experts' rankings from Round 1 of the survey where they ranked drug type for each of the dimensions of harm. For each type of harm, the two most commonly available POA drugs – oxycodone and morphine – are listed as the two most harmful for each dimension.

After the first round of surveying, the question was modified to combine all dimensions of harm into a question on the overall ranking of what was the most harmful of all POA drugs. Using the results of Round 1, a proposed ranking of POA drugs in the order set out in Table 3.7 was presented and respondents able to alter the rankings.

Table 3.8 shows the list of the most harmful of the POA drugs reduced to those most commonly used and accessible – oxycodone and morphine – being ranked first and second respectively.

Table 3.8

Round 2 - Harmfulness of POA drugs overall combined ranking by experts for each POA drug type (n=27)

Drug	Minimum	Maximum	Mean	SD	Mode
Oxycodone	1	4	2	0.84	1
Morphine	2	5	3	0.82	2
Fentanyl	1	5	3	1.08	3
Hydromorphone	2	5	4	0.81	4
Any opioid	1	5	4	1.76	5

Experts were also asked about particular aspects of POA drugs that could potentially increase or reduce harms. In Round 1 this was asked as an open question with a free-text response. The resulting responses classified under commonly reported themes are shown in Table 3.9. Interestingly, similar themes of extended release, high potency, rapid onset and injectability were reported as aspects that could increase and decrease harms.

Table 3.9

Round 1 – Harmfulness of POA drugs – Aspects of POA drugs that might increase or decrease harms combined responses of all experts (n=61)

Aspects of POA drug	Description
Increasing harm	
Extended release	- extended release preparations being linked to misuse - ease of adulteration of preparations for other routes of administration - increased access and availability
High potency	- high dose preparations and high volumes of drugs being prescribed
Injectable preparations	- injectable preparations such as pethidine
Injectability	- ease of transformation of table/capsule preparations to injectable forms, lack of "limiter" antagonist medications such as naloxone in newer POA preparations
Rapid onset	- immediate onset formulations can induce dependence, encourage abuse due to increased euphoric effects, full agonist action
Reducing harm	
Extended release	- sustained release also mentioned as reducing harms, improved pharmacokinetics and transdermal patch preparations
High potency	- improved pain management, limiting access with fewer prescriptions, lower volumes of drugs prescribed
Injectable/injectability	- tamper resistance, harder to convert to usable injectable preparations, inclusion of antagonist medications activated on adulteration of drug
Rapid onset	- appropriate short-term use or immediate release preparations

In Round 2 the results of Table 3.9 were reduced to unranked options for increasing and decreasing harms and the expert respondents were requested to rank them accordingly. Table 3.10 shows the resultant rankings based on the Round 2 responses. The results show experts ranked injectable and high-dose preparations as aspects most likely to cause harms, and extended release and high-dose preparations as most likely to reduce harms in POA drugs.

Table 3.10

Round 2 - Harmfulness and protective features of POA drugs combined responses of all experts (n=27)

POA drug feature	Minimum	Maximum	Mean	SD	Mode
Increase harmfulness					
Injectable preparations (ampoules, vials)	1	5	2.30	1.35	1
High potency/dose formulations	1	5	2.74	1.10	2
Rapid onset/immediate release preparations	1	5	3.30	1.30	3
Injectability of preparations	1	5	2.93	1.21	4
Extended/controlled/slow release preparations	1	5	3.52	1.81	5
Decrease harmfulness					
Extended/controlled/slow release preparations	1	4	1.52	1.12	1
High potency/dose formulations	1	4	2.07	0.47	2
Injectable preparations/injectability of preparations	1	4	2.67	0.92	3
Rapid onset/immediate release preparations	2	4	3.56	0.70	4

Individual risk factors

In Round 1 respondents were requested to nominate in a free-text response any particular biological, psychological or cultural factors that might predispose a person to risk of developing a POA drug SUD. The respondents provided the list of free-text responses to the classes of individual risk factors and the most commonly reported responses were grouped in like classes under each category. These are reported in Table 3.11 and examples of indicative responses are provided.

Table 3.11

Round 1 – Individual risk factors under biological, psychological and cultural classes that might predispose persons to SUDs with POA drugs as reported by experts (n=45)

Class of Individual risk factor	Indicative responses
Biological	
- Genetics	- Genetic predisposition, vulnerability
- Age	- Young persons
- Biology	- Metabolism
- Chronic pain	- Comorbid pain and dependence
- Family history	- Family history of substance dependence,
Psychological	
- Mental health issues	- Mood, anxiety disorders, PTSD, impulse control issues, personality disorders, psychoses
- Low self-efficacy	- Poor self-efficacy related to pain
- Expectancies/beliefs	- Beliefs about harms effects
- History of dependence	- Links to street drug culture, exposure to illicit drugs
Cultural	
- Peer use	- Acceptance amongst subgroup, social availability
- Lack of social support	- Dislocation from family or significant others, normative influences, social isolation, poor social networks
- Low socio-economic status	- Poverty, unemployment, disability
- Availability of POA drugs	- Poor prescribing practices, lack of guidelines, pharmaceutical promotion
- Poor parenting/upbringing	- Poor normative influences, learnt behaviour from family

The responses from Round 1 in Table 3.11 report a broad range of factors under each category. These summarised sub-factors for each class of individual risk were then presented to the experts in Round 2 in un-ranked list and the respondents were requested to rank the list from highest to lowest level of risk within in each factor of biological, psychological and social.

Table 3.12 below shows the expert respondents from the Round 2 of the study. The rankings of the compiled risk factor reported in Round 1 for each of the classes of risk factors that are considered most related to a POA substance misuse disorder were ranked as number 1 through to higher-numbered lower-ranked risk factors.

Genetic predisposition, concurrent mental health issues and peer use were ranked as the highest risk factors, under biological, psychological, and cultural categories of risk respectively for the risk of developing a SUD with POA drugs. Interestingly, chronic pain and a previous drug dependence history were not highly ranked in the biological and psychological factors respectively.

Table 3.12

Round 2 – Ranks of individual risk factors for development of SUDs with POA drugs under biological, psychological and social classes as ranked by experts (n=27).

Risk Factor	Minimum	Maximum	Mean	SD	Mode
Biological					
Genetics	1	5	1.67	1.24	1
Age	0	5	2.67	1.30	2
Individual biology (absorption/metabolism)	1	5	3.11	1.01	3
Chronic pain conditions	1	5	3.63	1.18	4
Family history	1	5	3.74	1.40	5
Psychological					
Mental health issues	1	4	1.63	0.88	1
Low self-efficacy	0	3	2.26	0.76	2
Expectancies/beliefs	3	4	3.48	0.51	3
Previous history of dependence	1	4	2.48	1.37	4
Social/cultural					
Peer use	1	5	1.93	1.21	1
Lack of social support	1	4	2.48	0.70	2
Low socio-economic status	1	5	3.37	1.01	3
Availability of prescription drugs	1	5	2.74	1.51	1 & 4
Poor parenting/upbringing	0	5	4.30	1.38	5

Definitions of substance use disorders on POA drugs

In Round 1 experts were presented with the list of criteria for drug dependence and abuse from the DSM-IV-TR (American Psychiatric Association, 2000) and were requested to rank them according to their potential importance in determining SUDs with POA drugs. Table 3.13 and Table 3.14 show the results of the responses after Rounds 1 and 2 of the Delphi Technique for ranking the importance of particular criteria for drug dependence and abuse.

The results from Round 1 are shown in Table 3.13 with the initial ranking of each criteria, from 1 – highest-ranked or most important – to 11 – lowest ranked or least important.

Table 3.13

Round 1 - Ranked DSM-IV-TR substance abuse and dependence criteria ranked by experts in order of importance in determining SUDs with POA drugs (n=48)

DSM-IV-TR Criteria	Min	Max	Mean	SD	Rank
How important are the drug-use effects on work, school or home obligations, in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	4	1.73	0.84	1
How important are the effects of drug use on social, occupational, or recreational activities, in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	4	1.77	0.88	2
How important are social or interpersonal problems, in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	4	1.92	0.92	3
How important is the amount of drug being taken in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	4	2.25	0.93	4
How important is time spent in obtaining drugs in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	5	2.17	0.95	5
How important are attempts to reduce or control drug use in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	5	2.02	1.00	6
How important is continued drug use despite health or psychological effects in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	5	1.77	1.02	7
How important is evidence of tolerance in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	4	2.15	1.03	8
How important is drug use in hazardous situations in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	4	1.98	1.04	9
How important is evidence of withdrawal symptoms in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	4	2.27	1.07	10
How important are drug-related legal problems, in assessing a person for substance use disorders on pharmaceutical opioid drugs?	1	5	2.19	1.14	11

These results were then presented in Round 2 to the experts in the ranked order from Table 3.13 and respondents were able to adjust the ranks accordingly based on their particular views. Table 3.14 shows the results of the second ranking.

Table 3.14

Round 2 - Ranked DSM-IV-TR criteria for substance abuse and dependence (n=27)

DSM-IV-TR Criteria	Min	Max	Mean	SD	Mode	Rank
Effects on social, occupational, or recreational activities	1	7	2.2	2.04	1	1
Effects on work, school or home obligations	1	8	3.1	2.07	2	2
Continued use despite health or psychological effects	1	8	3.1	1.54	3	3
In hazardous situations	3	10	4.6	1.67	4	4
Social or interpersonal problems	4	11	5.8	1.62	5	5
Attempts to reduce or control use	2	7	5.1	1.55	6	6
Drug-related legal problems	0	11	7.3	2.25	7	7
Time spent in obtaining drugs	1	11	7.3	2.16	8	8
Evidence of tolerance	0	11	7.8	2.91	9	9
Evidence withdrawal symptoms	0	11	8.1	3.13	10	10
Amount of drug taken	1	11	9.3	2.46	10	11

It appears that the experts ranked behavioural and social problems as most important in considering substance use disorders related to POA drugs (see Table 3.14). They also agreed the evidence of tolerance and withdrawal symptoms was least important along with amount of the drug taken. The time spent in obtaining drugs was overall ranked eighth of all the criteria.

Doctor shopping behaviour

First, experts in Round 1 were asked a general question to elicit their broad definition of doctor shopping. The general consensus amongst experts in Round 1 in response to the first question was agreement for most (n=40) that doctor shopping was behaviour of persons seeking multiple prescriptions from multiple doctors. A number of experts (n=6) qualified this definition to include an element of deceptiveness on the part of the patient such that prescribers would be unaware of other prescriber's activities. Two experts suggested that doctor-shopping behaviour suggested a person might be dependent or have lost control of their drug use. A further four experts noted that doctor-shopping behaviour could be linked to on-selling or illicit sales of drugs.

Second, the experts were asked to describe a level of doctor shopping by nominating a particular number of prescriptions obtained, prescribers consulted, dispensing pharmacists seen, and an estimated average daily dose in oral morphine milligrams equivalent in a given time period that would indicate a person is suffering a SUD with POA drugs. This included a free-text field for further explanation.

In Round 2 in the second question the experts gave responses suggesting that obtaining a prescription within the prescription period of a previous prescription from another doctor could be cause for concern. There was a considerable range of responses for the number of doctors (ranging from 2 or more to multiple); numbers of prescriptions (any extra prescription from another doctor to up to four per year from multiple doctors); and the obtaining of maximum doses or any unsanctioned doses. Experts varied in their views that the behaviour could be taking place in time periods ranging from a week to a year.

Given the range and variability of the responses it was decided to change the second questions in Round 2 in an attempt to facilitate responses. The Round 2 questions requested the numbers of prescriptions obtained, prescribers consulted, dispensers involved and milligram dosage obtained over a two-month period; two months emulating the reporting requirements for long-term treatment in Queensland under the relevant legislation(Queensland Government, 1996).

Furthermore, the question was varied to request the respondents to nominate the lowest levels of doctor shopping by these criteria in three different categories. These categories were explained using a traffic light system: a green light meant there was no concern to continue prescribing; an amber light meant a prescriber exercise caution before further prescribing; and red light was where a prescriber might choose not to prescribe.

Table 3.15

Round 2 – Traffic light criteria for categories of doctor shopping based on prescriptions, prescribers, dispensers and average daily dose (OME-mg) consumed over any two-month period (n=27)

Doctor shopping criteria	Min	Max	Mean	SD	Mode
Green light					
Prescriptions obtained	1	12	2.9	2.42	2
Doctors consulted	1	5	1.6	0.96	1
Pharmacies dispensing	1	5	1.6	1.05	2
Average daily dose*	5	400	124.3	120.46	60
Amber light					
Prescriptions obtained	1	13	4	2.88	2
Doctors consulted	1	8	2.6	1.4	2
Pharmacies dispensing	1	8	2.5	1.48	2
Average daily dose*	10	700	161.6	159.72	60 & 100*
Red light					
Prescriptions obtained	1	24	6.2	5.22	3
Doctors consulted	1	10	3.7	1.7	3 & 4*
Pharmacies dispensing	1	10	3.5	1.77	3
Average daily dose**	20	800	222.8	233.22	60 & 120*

** *multiple modes*

Table 3.15 above sets out the responses in Round 2 to the amended questions on what criteria for doctor shopping they would consider to continue to prescribe (green light), prescribe with caution (amber light), and not prescribe (red light). Experts appeared to support that some level of drug-seeking – consulting more than one prescriber and dispenser, and obtaining approximately three prescriptions with a dose of up to 120 mg per day oral morphine equivalent (OME) – would not necessarily be a barrier to further prescription of POA drugs. However, up to five prescriptions and more than two prescribers and pharmacists, and consumption of up to 220 milligrams (OME) would raise concerns, and levels beyond that further prescribing should not proceed.

3.4 DISCUSSION

The results of the Delphi Technique study over two rounds with the expert panel presented mixed outcomes. The experts agreed that oxycodone and morphine POA drugs are most associated with harms. However, it is less clear what aspects of these POA drugs might make them more or less harmful. The experts agreed that injecting use and high-potency preparations were the most harmful features. However, they suggested that controlled-release and high-potency preparations could be protective features. Overall, this suggests that the participants are knowledgeable in this area and are aware of the association between the increased accessibility of oxycodone and POA drug-related harms in Australia and the USA. There is some inconsistency in this response, given that most oxycodone use is in the controlled-release preparations; a feature that experts agreed was protective.

There was an apparent contradiction in the results in the experts' assessment of sustained release preparations being viewed as both increasing and reducing harms. This is potentially reflective of two contradictions. Firstly, there is real potential for sustained release preparations to improve pain management and reduce inadvertent dependence in compliant persons adhering to their dosage. On their introduction in the late 1990s and early 2000s, sustained release preparations were superior to other immediate release preparations that then were most available on the market(Butler, et al., 2012; Hallinan, Osborn, Cohen, Dobbin, & Wodak, 2011). However, with increasing use there was widespread diversion of the sustained release preparations. Drug dependent and abusive users then discovered means to subvert the sustained release mechanism in the preparations to obtain effects similar to immediate release preparations (Fischer, Nakamura, Ialomiteanu, Boak, & Rehm, 2010; Okie, 2010; Shram et al., 2010).

In determining individual risk factors across biological, psychological and cultural domains the experts agreed that genetics was the most important biological factor; mental health issues, exclusive of SUDs, the most important psychological factor; and peer use the most important cultural factor. It is noted that experts did not highly rate a chronic pain condition as a risk factor for developing a SUD with POA

drugs. Overall, the listed factors do not appear markedly different from generally reported risk factors across the drug dependence literature for the development of any SUDs. Potentially the questions in these parts of questionnaire were too broad. Perhaps the questions were open to alternative interpretations did not allow experts to readily discriminate between those persons on POA drugs long term for pain management purposes in comparison to those persons who might be obtaining POA drugs from non-medical sources.

The experts' ranking of the DSM-IV-TR SUD criteria in order of importance over the two rounds found agreement in social and behavioural criteria as most important. The criteria for tolerance and withdrawal were ranked lowest, with the exception of one. This supports the changes in the newly-released DSM-5 in regards to sub-classification of opioid use disorders, where tolerance and dependence are now not supported as the most salient diagnostic criteria. This again supports the fact that the experts in the study are knowledgeable of the field.

The experts also set criteria for doctor shopping that might indicate whether a person is suffering a SUD with POA drugs. A traffic light system was used to effectively force the experts to nominate a level of doctor shopping in which they had no concern about further prescribing (green light); some concerns (amber light) and the level at which they would not recommend further prescribing of POA drugs (red light). This suggested a range of prescribing above four prescriptions from more than two different prescribers, and two different dispensers for a mean daily dose of over 160 milligrams (OME) would cause initial concerns. The experts also agreed that at a level of prescribing above six prescriptions from more than three different prescribers, and three different dispensers for a mean daily dose of over 220 milligrams (OME) they would consider not further prescribing.

These results appear to be consistent some of the review results in the recent Centers for Disease Control Safe Opioid Prescribing Guidelines (Dowell, et al., 2016). The review found that patients on daily doses of greater than 100 milligrams OME were almost at twice the risk of a fatal overdose and over three times the risk of any

overdose of those patients prescribed between 50-100 milligram OME. Similarly the review found overdose mortality rates rose rapidly up to doses of 200 milligram OME per day. These results seem to suggest some validity to the experts' categorisation of different levels of concern.

Overall, this use of a modified Delphi technique was helpful in drawing on a range of experts in different domains across different countries. This also allowed for the testing of a number of complex questions over an iterative process to allow experts to moderate their views based on the larger group's response. Where the responses accessed areas with established or related research they were consistent with knowledge in the field, supporting that the expert selection was sound and that the Delphi Technique was effective in extracting this consensus information.

There are some limitations to acknowledge. The first is the expert panel recruitment did not achieve anticipated numbers, and many participants that did respond did not quite fit the exclusive classification of either drug dependence or pain expert. Therefore, the study could not analyse differences in understandings between these fields.

There was also an almost 2:1 ratio of self-nominated drug dependence experts to pain experts, so any results might reflect a bias towards the views of drug dependence experts. Furthermore, there was significant atrophy of participants across the two rounds, with an over 50% loss of participants from Round 1 (n=61) to Round 2 (n=27). Also, the non-participating respondents completed all parts of the survey in either of the rounds they contributed to. This leads to some caution interpreting the results of a reasonable representation of pain and drug dependence experts, and the full respondents to only Round 1. It should also be noted some questions developed in Round 1 were used to derive materials for the next round's rankings. For these questions, only one round of expert ranking was effectively undertaken in Round 2. Further iterative rounds were not undertaken given the significant loss of participants between the two rounds.

The DSM-IV-TR criteria for the use of a substance in larger amounts over longer periods is related to the construct of impaired control. This is perhaps related to a substance use disorder with POA drugs. However, this could also conceivably be associated with aspects of poor pain management or tolerance over different time periods. As such this criterion as set out in the questionnaire might have been open to multiple interpretations by the experts.

It should also be noted that DSM-IV-TR diagnostic criteria for abuse and dependence state in overarching statements that they require consideration of "a maladaptive pattern of substance use leading to clinically significant impairment or distress …" (American Psychiatric Association, 2000). This statement was not included in the survey nor directly operationalised in questions in Delphi study, as the design was to examine the importance or contribution of each criterion. However, the criterion 'how important are the drug use effects on work, school, or home obligations in assessing a person for substance use disorders on pharmaceutical opioid drugs" is arguably more conceptually closer to describing 'clinically significant impairment or distress' than the other criteria. This similarity might have influenced this choice by the experts.

3.4.1 Conclusion

The results of this study suggest that defining substance use disorders with POA drugs, understanding the aspects of harms and the harmful characteristics, understanding what characteristics predispose persons to develop SUDs, and what levels of doctor-shopping or drug-seeking suggest problematic use are complex questions. In regards to the different POA drugs, it appears oxycodone and morphine are the two most likely to be associated with problematic use. However, it is less clear based on the formulations and routes of administration of POA drugs which would be ranked more highly. The experts rated injectability as the feature most likely to be associated with harms, and extended release the feature most likely to be a protection against misuse. This suggests a contradiction as the most common forms of oxycodone and morphine are controlled-release preparations, and are the drugs driving most of the increased consumption in Australia (Vowles, et al., 2015). In relation to the

question of the type of POA drug and characteristics associated with misuse, it should be noted the increased use and access to oxycodone, especially in a controlled-release formulation, could confound any ability to isolate a particular POA drug or its characteristics as more likely to be misused, as the prescribing and treatment environment does not allow equal access to all the different drug types and formulations. Furthermore, it is largely now known that controlled release oxycodone is readily able to be re-purposed and used in injectable forms.

The experts' ranking of individual characteristics that predispose a person to develop a SUD with POA drugs suggest, in most cases, characteristics that predispose someone to develop a SUD with any dependence-forming drug. From the point of view of the larger study, there are limited factors that might be accessible from the information in a PDMP. Of particular interest is the rating of younger persons, persons with a chronic pain condition, and persons with previous SUDs as likely risk factors for developing SUDs with POA drugs. Potentially these characteristics can be captured in dispensed prescription data held in a PDMP.

There is also some difficulty in potentially using higher order concepts in PDMPs as they currently stand. At present most PDMPs are limited to, at best, including age and gender information. PDMPs are not clinical management tools per se, given the reasons for their development. However, potentially future iterations might consider information as important supporting information to assist in clinical and medical decision making. However, it is suggested that evidence and research should drive data collection, as expansion of system is costly, might not add value and could compromise use by clinicians. Perhaps consideration of linkage to other systems is more relevant, however the use of these concepts given current results are not readily able to be used in the following studies.

Doctor shopping is not an unlawful activity under most State and Territory legislation in Australia. At its most basic form it could represent a person exercising freedom of choice in order to choose another health practitioner. At worst, it might represent overt criminal activity to obtain drugs for illicit markets. The issue for the implementation

of real-time monitoring is to provide information to prescribers and dispensers about a person's POA drugs use history when they are making treatment decision and before a prescribing or dispensing decision is made.

Doctor shopping in its pejorative sense is broadly defined as a person seeking prescription drugs from multiple doctors for purposes other than therapeutic needs. This implies the person seeking the drugs is either obtaining them for their use due to a SUD or that they are diverting them for other purposes. However, other explanations could account for a person's apparent POA drug-seeking. For instance, a person whose pain was undertreated could seek further drugs from other prescribers . This is the phenomenon of 'pseudo-addiction' used in USA literature (Fellers, 2016; Robinson & Reiter, 2016). Alternatively, in palliative care situations or aged care scenarios, a person might be receiving prescriptions from multiple prescribers for high doses of drugs for legitimate treatment needs.

Defining set criteria for doctor shopping by the experts, given this diversity for use in Study 2 to test in a PDMP therefore could not produce clear guidance or definitive definitions for person's POA drug use that might be indicative of a person suffering a SUD. This does raise some issues for consideration in the progress towards developing real-time PDMPs at significant cost to the health budget. If there is a lack of general agreement across experts in defining doctor shopping from objective prescription information, then this might be also a challenge for the broader community prescribing community.

Chapter 4: Study 2: The doctor-shopping population

4.1 DEFINING DOCTOR SHOPPING

This study examines whether doctor-shopping behaviour could potentially identify POA drug abuse or dependence within a regulatory prescription drug monitoring program (PDMP) database. In Study 1 there was a lack of agreed definitions for what described doctor shopping or aberrant drug-seeking of prescription opioids. The only agreed position was, at a minimum, that any amount of extra drug-seeking beyond a person's primary prescriber could be considered an indicator of concern. Overall, experts also did not rate drug-seeking behaviour highly as an important diagnostic criterion in assessing what criteria might be important in assessing person for SUDs on POA drugs.

This finding of varied definitions of doctor shopping is consistent with previous research in the field (Cepeda, Fife, Berlin, Mastrogiovanni & Yuan, 2012; Han, Kass, Wilsey & Li, 2014; McDonald & Carlson, 2013; Nordmann et al., 2013; Peirce, Smith, Abate & Halverson, 2012; Wilsey et al., 2011; Worley, 2012; Worley & Hall, 2012)) that suggests there are multiple definitions of what might constitute doctor shopping. The general definition discussed in Chapter Two (see Section 2.8.1) is that doctor shopping is seeking prescriptions from multiple doctors and obtaining dosages in excess of what might be needed for therapeutic reasons. The results from Study One suggest that any drug-seeking behaviour meeting that criteria could be indicative of a SUD, depending on the individual circumstances.

The common data elements that appear to define 'doctor shopping' are the number of doctors (or prescribers) consulted, the number of prescriptions obtained and/or number of dispensers used, and the time period during which the activity has taken place (see Section 2.8). Furthermore, there is an actual and implied element in

these definitions that the actual drug dose being obtained is in excess of therapeutic need.

Study 2 aims to determine if levels of doctor shopping – as determined by the numbers of prescribers consulted, numbers of prescriptions obtained, numbers of dispensers seen, and volume of drug consumed – indicate different patterns of POA drugs usage that might discriminate aberrant or problematic drug seeking from non-problematic drug seeking. The study also aims to determine if aberrant patterns of drug seeking could provide evidence supporting a substance misuse disorder, such as dependence or abuse.

Potentially, the diagnostic criteria of the DSM-IV-TR for dependence could be tested within prescriptions records. The criterion of 'substance taken in larger amount and for longer period than intended' and 'much time/activity to obtain, use, recover' (American Psychiatric Association, 2000) suggest elements of dosage that is greater than therapeutic doses and extended periods of time engaged in drug seeking. Potentially, doctor-shopping activity that involves seeing greater numbers of prescribers, obtaining large volumes of prescriptions, and attending high number of dispensers over longer time periods could be more indicative of dependence than activity that was of lesser duration.

Furthermore, the DSM-IV-TR criteria of 'substance taken in larger amount and for longer period than intended' and 'tolerance (marked increase in amount; marked decrease in effect)' (American Psychiatric Association, 2000) suggest that increasing or high dosage is also associated with drug dependence, especially in association with drug-seeking behaviour. Possibly, high or increasing dosage of POA drugs obtained by doctor shoppers could be a proxy for diagnostic criteria associated with dependence. Potentially, POA drug dosages that are greater than accepted therapeutic levels in association with doctor-shopping activity suggest converging evidence of drug dependence.

There is generally accepted evidence suggesting that there is limited efficacy of dosages of POA drugs at over 100-120 mg per day of Oral Morphine Equivalent (American Pain Society in Conjunction with the Americian Academy of Pain Medicine, 2009). Further, doses above 120 mg per day have also shown to be correlated with an increased risk of death (Gomes, Mamdani, Dhalla, Paterson & Juurlink, 2011). Dosages greater than 200mg per day are considered high dosages by the American Academy of Pain Medicine Opioid Guidelines (Chou, Fanciullo, Fine, Adler, Ballantyne, Davies, Donovan, Fishbain, Foley & Fudin, 2009).

It has been reported that the risk of death increases for person on doses between 200-400mg per day OME (Gomes, Juurlink, et al., 2011). Guidelines in determining high-risk dosages across the population consider levels of low, medium and high dosage to inform clinicians. The American Pain Socity suggests a low dose is 100mg OME per day, a medium dose between 100-200 mg OME per day, and a high dose greater than 200mg OME per day ((Chou et al., 2015)). A person engaging in doctor shopping might be at greater risk of harm at higher levels of consumption than a non-doctor shopping person, as the consumed dose would not be that sanctioned by their treating doctor.

Shorter-term aberrant POA drug doctor-shopping could indicate drug abuse under DSM-IV criteria. Doctor shopping in only one or two quarters of a year might not necessarily indicate a person has developed tolerance. This pattern might suggest a person is prepared to continue drug seeking despite there being possible legal consequences of this behaviour. This is not a definitive definition, nor does it meet any more than one criteria of the DSM-IV TR definition of abuse. However, for the purpose of this study, this concept of short-term aberrant POA drug doctor-shopping is proposed to serve as an approximation of a definition of drug abuse.

For both definitions of doctor shopping, it should also be noted that a high dosage of POA drugs over a certain time period does not necessarily correlate with dependence or abuse. Within the population of persons being prescribed POA drugs, many will be on high dosages over lengthy periods of time for ostensibly legitimate

persistent or acute pain management conditions. This study is not examining whether pain management treatment provided in the non-doctor shopping context is appropriate or not.

A further complexity in investigating this population is that a person might also drug seek or doctor shop infrequently, for short time periods across a year, and have periods of either no POA drug seeking (but still obtain POA drug prescriptions below a defined doctor shopping threshold) or obtain no POA drugs. These patterns are open to multiple interpretations. Short-term use POA drugs with low levels of drug seeking could represent successful acute pain management. Longer-term or persistent use of POA drugs with limited evidence of doctor shopping could suggest inadequate chronic pain management where a person might be supplementing drugs from other prescribers.

Therefore, this study considers describing doctor shopping in terms of its constituent elements – prescriptions, prescribers, dispensers and volumes of drugs obtained – as well as the frequency and persistence of this behaviour. Furthermore, describing levels of POA drugs dosage and the frequency or persistency of POA drug prescribing over time might assist in discriminating aberrant use from legitimate use, and potential dependence from abuse, with the prescription database records.

It is suggested that amongst a larger population of potential doctor-shopping patients there might be distinct sub-population of persons suffering drug dependence or abuse, poorly-managed pain management patients, or persons involved in diverting POA drugs for other purposes. These potential sub-populations are described in Chapter Two (Section 2.7). It is hypothesised an examination of doctor-shopping sub-populations should allow discrimination between potentially different categories of POA drugs users (Queensland Government, 1996)based on their levels of doctor shopping as described by the numbers of prescribers consulted, prescriptions obtained, dispensers seen, dosages obtained, and the frequency of that behaviour over time.

4.2 METHODS

This section sets out the description of the MODDS database and the operationalisation of the data elements of interest. The methods of extracting the study datasets and the methods of describing and analysing these are also discussed.

4.2.1 Description of the MODDS database

Data is collected by the Department of Health (DoH) of the Queensland Government for the purposes of state legislation (Queensland Government, 1996), and Medicare data is collected by the Commonwealth Government for the purposes of administering payments under the Pharmaceutical Benefits Scheme (PBS). Medicare collects all prescribed and dispensed drug data, of which POA drugs are, in part, liable for PBS subsidies. The DoH collects all POA drugs data that are Schedule 8 drugs under the SUSMP, and includes all PBS and private prescriptions dispensed community pharmacies. This does not capture treatment for patients in hospital or when POA drugs are provided to patients on discharge from hospital.

Under Queensland legislation (Queensland Government, 1996) community pharmacies are required to submit records of dispensed controlled (Schedule 8) drug (i.e. POA drugs) prescriptions to the DoH on a monthly basis. Since 1996 the DoH has maintained a PDMP known as the MODDS database to collate and store this information and undertake its regulatory compliance functions. Appendix F shows details of a sample prescription and the information elements represented. This is also set out in The highlighted elements of the prescription are those entered into the MODDS database as data elements that describe a dispensed prescription event.

Table 4.1

MODDS database summary data elements

Category	Variable name	Example
Drug details	Drug name	Oxycodone controlled-release
	Formulation	Tablets
	Drug formulation dose	80mg
	Total quantity prescribed	20
Patient details	Name	Mr John Citizen
	Date of birth	20 August 1985
	Gender	Male
	Address	20 Brown Street, Corinda QLD 4006
Prescriber details	Name	Dr Jenny Brown
	Address	Corinda 7 Day Medical Centre, 34 Corinda Rd Corinda 4011
Pharmacy details	Name	Mr Han Solo
	Address	Corinda Amcal Pharmacy, 22 Sherwood Rd, Corinda QLD 4006

The system is regularly screened for data quality issues and has a regular process at data input to detect possible patient aliases. A range of business processes are employed to maintain data quality and ensure accurate matching of new data against the correct patient and doctor records.

The MODDS database is on an Oracle Database platform (Oracle Corporation, 2011) and is comprised of a number of interrelated data tables. The system has an over-arching interrogation application, 'Oracle Discover' (Oracle Corporation, 2011), that allows for the production of 'flat' data files that can be extracted for the purposes of statistical analysis.

The DoH has currently developed a 'doctor shopper' query for monitoring purposes. However, the DoH has not developed a single definition for 'doctor shopping'. It is proposed to further develop this query tool to assist in producing appropriate datasets for the following studies. This query is designed to identify doctor

shopping by the user input variables as to the number of prescriptions and the number of different doctors consulted over a certain time period. For example, a user could interrogate the system to examine those patients who had seen 10 doctors or more and obtained 50 prescriptions or more over a set six-month period, where start date and end date parameters are entered.

The MODDS database also records details of patients' admission and discharge to formal opioid substitution treatment programs, and other administrative data related to legislative functions of the DoH. A person is then classified within the system based on whether certain regulatory or administrative actions have occurred.

Details of the operation of the DoH and the MODDS database is subject to intellectual property limitations for Queensland Health and the claim of 'public interest immunity' as an exception to Queensland's *Right to Information Act 2009* (Queensland Government, 2009). This means that some aspects of the system cannot be revealed, as DoH functions involve regulatory activity and public availability of that knowledge could compromise the DoH's activities. Therefore, only those elements relevant to this study are discussed.

Queensland Health data is also subject to provisions of confidentiality under the *Public Health Act 1991* and the *Health Services Act 1991*. The MODDS database and its data code and structure are a Queensland Health asset and intellectual property and are subject to restriction from full public disclosure. Therefore, full operational structure of the database cannot be revealed. The relevant data elements that are used to extract the study population and derive data items for the study are discussed in the following section.

4.2.2 Prescription opioid drugs in the MODDS database

Data from MODDS includes all POA drugs that are Schedule 8 drugs or controlled drugs (Queensland Government, 1996; Schedule 8 (Commonwealth of Australia, 2010) dispensed at community pharmacies. This excludes some POA drugs,

such as tramadol that are Schedule 4 drugs, and some forms of codeine that in some doses are Schedule 3 and 4 drugs. This study examines opioid drugs only, so all non-opioid controlled drugs were excluded in data extraction. This excluded all controlled psychostimulant drugs (dexamphetamine and methylphenidate) and benzodiazepines (flunitrazepam and alprazolam) that are captured by the MODDS database. The opioid substitution treatment drugs of methadone syrup and liquid and buprenorphine and buprenorphine-naloxone tablets and sub-lingual film were retained as they are opioids. However, they are discussed further in the course of the study as patients in receipt of these drugs have been formally admitted to opioid treatment programs.

The opioid drugs are classified in the MODDS database under 'Drug IDs' and 'Drug Group IDs'. All drugs with a particular dosage formulation are allocated individual 'Drug IDs'. For example, different dosage forms of morphine slow-release tables, capsules and sachets each have individual 'Drug IDs' However, all would have the same 'Drug Group ID' as they are all forms of the same drug class. Appendix G shows the full list of drugs in the MODDS databases.

4.2.3 Prescribers (doctors)

The number of prescribers consulted is intrinsic to a definition of doctor shopping. If all prescriptions are undertaken by the same doctor, then such an episode of supply is outside the parameters of interest for this study as this does not involve multiple prescribers; hence, does not quality as an example of doctor shopping. There can still be questions as to the appropriateness of supply of POA drugs in these circumstances which could be related to the professional practice of the prescriber.

If it is assumed that a standard prescription is issued for a month or 28-day supply, then a single doctor issuing one prescription in a month might be considered legitimate supply. Two or more doctors prescribing to a person could be explained by in a number of ways that might also constitute legitimate supply of drugs. For example, two doctors at the same practice might see the same patient; possibly there might another specialist doctor also involved in treating the patients with the general practitioner, and prescriptions can overlap over month period. Furthermore, different

combinations of drugs might be required at different times for patient. For example, short acting POA drugs are often prescribed for 'breakthrough' pain in concert with controlled release POA drugs. Patients can also lose drugs and might also be travelling or moving across a jurisdiction and consult multiple doctors in their travels.

At the lowest threshold of possible doctor shopping, more than one prescribed event with different prescribers within the same 28-day period of another prescribed event – especially where doctors were at different practices – could be indicative of doctor shopping over a set time period, dependent on the number of prescriptions and amount of drugs obtained.

It should be noted that in this definition only consultations with prescribers that result in a dispensed prescription can be captured by the database; that is, if a person consults multiple doctors to obtain prescriptions that are not issued, they could be doctor shopping but not obtaining prescriptions.

4.2.4 Prescriptions

If a person consults at least two doctors in a set period, they could have obtained at least two prescriptions. From the information in the MODDS database, a prescription event will equate to a doctor consultation. However, some prescriptions from the same doctor might be 'repeat' prescriptions. These are prescriptions written for multiple dispensing at some future time period, usually 28-day intervals, without the need to return to consult the prescribing doctor.

Some USA studies examine prescription supply that has occurred within the intended period of supply of a prescription (Johnson, McFarland, Corelle & Woodson, 1994; Tanskanen et al., 2014)); that is, if a prescription is written for a 28- day supply, then a second dispensing event of another prescription after the initial dispensing event could constitute an incident of aberrant obtaining. However, the MODDS database does not capture this information and it is anticipated actual obtained dosage of drugs is a better measure and more likely to be correlated to problematic use. For defining

doctor shopping the baseline threshold will be that a person must have at least four dispensed prescriptions within a three-month period. This is one more prescription than might be expected in a one prescription per month (28-day period) in a non-aberrant treatment regimen. The MODDS data only contains details of dispensed prescriptions; that is, those events where the prescribed medicines are actually supplied to a patient by a pharmacist in a community pharmacy. This includes all POA drug dispensed prescriptions, including those subsidised under the PBS, as well as those non-subsidised or private prescriptions.

The MODDS dispensing information does not include:

- POA drugs provided to persons as part of hospital inpatient care or those POA drugs that might be provided on discharge from hospital
- Attempts at obtaining prescriptions that were refused by prescribers; and
- Non-filling of obtained prescriptions by persons who had obtained prescriptions.

It is possible that details of consultations captured by Medicare Australia under funding arrangements could give some indication of unsuccessful attempts to obtain prescriptions. Further, the MODDS database includes doctor enquiries and this information might allow for an estimate of drug seeking that did not result in a prescription being issued.

4.2.5 Dispensers (pharmacists)

The number of pharmacists a person consults to have prescriptions dispensed is a potential indicator of problematic drug obtaining. For instance, if a person obtains multiple prescriptions from multiple prescribers and has them filled at different pharmacies, there is concern this could suggest a method to conceal their obtainings from a single pharmacist who might question such activity. At the least the behaviour suggests poor health management as a single dispensing pharmacist would not be in a position to give any medication management advice as they would not have a complete medication history within their pharmacy records.

A number of US studies have used different pharmacies dispensings as an indicator of doctor shopping (Peirce, Smith, Abate, & Halverson, 2012; Yang et al., 2015). However, in the Queensland context there is no regulatory or other mechanism to limit a person to a single pharmacy business. Even repeat prescriptions can be dispensed at different pharmacies. There is limited evidence in the Australian context to suggest that patients routinely confine their medication dispensing to single pharmacy as they might to a single medical practitioner or practice ((Nielsen, 2015)).

Therefore, while multiple pharmacy dispensing could be a factor it might be more appropriately used as a secondary or latent factor to better discriminate within a proposed doctor shopping population.

4.2.6 Time period

Doctor-shopping definitions are based on some measure of multiple consultations of doctors and obtaining of prescriptions that imply the drugs obtained are in excess of therapeutic needs. This raises the question as to over what period of time in which prescriptions are obtained and dispensed is of interest to reliably capture the behaviour.

Such a time period needs to be short enough to adequately capture a supply of drugs that could indicate possible misuse. However, the period of time over which drugs are being obtained should be long enough to capture use that might reflect a pattern of chronic behaviour, rather than aberrant single events. Furthermore, the time period should be of sufficient length to allow for calculation of average daily dose that might reflect actual consumption – assuming that the drugs obtained are consumed by the person prescribed.

The longest dispensing period for a opioid analgesic drugs is 28 days, due to both pack sizes of medications (MIMS), funding or approval requirements for PBS subsidised items, and the general principles of appropriate clinical governance of these

medications by prescribers in not allowing patients too many drugs at any one time and general recommendations suggesting a monthly review of a patient's treatment (National Prescribing Service, 2006, 2010; Royal Australasian College of Physicians, 2009).

Shorter time periods, less than a month, could potentially not capture prescription obtainings of concern. For example, in a single month, prescriptions dispensed on the last days of the previous month would not be counted even though the medication dispensed might be consumed in the month of interest and in conjunction with prescriptions obtained in this month. Similarly, prescriptions dispensed at the end of a calendar month could represent medications to be consumed fully or partly in the next month. Therefore, a single month is considered too short a period to examine for this behaviour.

The American Pain Society (2009) in its comprehensive guidelines for treatment of chronic pain with POA drugs suggested that short-term treatment was treatment lasting less than three months, and, where conditions were long-term, the preiod is greater than three months (American Pain Society in Conjunction with the Americian Academy of Pain Medicine, 2009; Chou et al., 2015).

In the regulatory context, most Australian jurisdictions have set reporting or permit requirements for treatment of a patient that is to extend beyond 8 weeks (Queensland Government, 1996). Continuous treatment for more than three months with a POA drug would seem to indicate a person suffering from a persistent or chronic pain condition. There is less evidence to suggest what time period would suggest a person was dependent or abusing POA drugs.

In assessing abuse and dependence, the DSM-IV-TR and DSM-5 defintions set out that a number of criteria need to be met over a 12-month period (American Psychiatric Association, 2000, 2013). In terms of prescription and illicit opioid use this does not necessarily give guidance as to how long a period of time someone might

need to be exposed to opioids to develop dependence. Dependence suggests that the definition can be met in any timeframe within a year.

There is some support in the pain management literature that pain that is not resolving after more than two months of treatment with opioids might not be appropriate for continued opioid treatment (Chou, Fanciullo, Fine, Adler, Ballantyne, Davies, Donovan, Fishbain, Foley, Fudin, et al., 2009). Furthermore, treatment beyond two months might suggest at least some level of tolerance or neuroadaptation in response to opioid consumption.

However, a two-month period might not adequately capture opioid consumption that continues beyond a two-month threshold. An optimal time period would capture any standard prescribing practice of supply greater than two months of prescriptions at the most sensitive level of prescribing. Therefore, a prescribing interval of interest would necessarily need at least to be over a three-month period to capture the minimum level of prescribing that went beyond a two-month period.

In Australia, most jurisdictions recognise long-term prescribing as prescribing for greater than two months or eight weeks (Hua, Shen, & Ge, 2015). This is usually the threshold at which a treatment provider is required to notify or seek authority from the relevant jurisdictional health department. Furthermore, there is some evidence that acute pain conditions or post-procedural pain management usually resolve in the six weeks after injury or procedure (Burke, 2016; Huxtable, Roberts, Somogyi, & Macintyre, 2011). Chronic pain conditions are often described as those conditions lasting beyond a six week period (Access Economics Pty Ltd, 2007; American Academy of Pain Medicine & American Society of Addiction Medicine, 2001; Ospina & Harstall, 2002; Rosenblum, et al., 2008). There is no consistent evidence in the literature that exposure to opioids for periods of two months or longer are associated with development of SUDs with POA drugs. However, consistent and long-term use of POA drugs is a necessary criterion for considering a diagnosis of dependence.

In Australia many drug preparations are prescribed and dispensed in 28 days periods and packaged as packets of 28 tablets. This means in many cases prescriptions are usually for 28 day or close to one calendar month. Two prescriptions could arguably represent two months of treatment for most of the main forms of POA drugs – morphine and oxycodone – that come in 28-tablet packages.

This study aims to detect doctor shopping or drug seeking that could be related to aberrant POA drugs use and a substance use disorder. A greater than two-month period suggests a timeframe that is of interest to regulators and possibly indicative of chronic treatment. However, to adequately capture treatment extending beyond a two-month period, a minimal timeframe of interest was set at three months to better capture POA drug use. In using a three-month time period the study can better capture apparent aberrant drug obtainings. For a three-month period, long-term prescribing could be represented by at least three prescriptions in that time period: one prescription for each month, assuming most prescriptions are written for a 28-day supply. Obtaining two or less prescriptions in a three-month period suggests possibly short-term treatment and less likelihood of aberrant POA drug use.

Doctor shopping is broadly defined as a person seeing multiple doctors for more POA drugs that would appear required. In a three-month period this could be three or more doctors for four or more prescriptions. This sets a minimal and sensitive lower threshold of possible doctor shoppers. Two doctors in this period could reasonably represent a GP and a specialist or two GPs at the same practice, or another locum doctor, so is too sensitive a criterion. Three doctors in three months was set as the lower threshold for the number of prescribers. Four prescriptions over three months could represent one more prescription than would be expected in most routine treatment settings. Therefore, the criterion for dispensed prescriptions was set at four prescriptions over any three-month period.

Longer time periods, six or twelve months, were considered as possible study intervals. However, using these longer time periods was more difficult to reliably detect possible doctor shopping. For these longer periods the numbers of prescriptions were more stretched and less able to be shown as greater than the expected therapeutic

need. Potentially the longer timeframes might have not been sensitive to short-term doctor-shopping activities. For the purposes of the study annual figures were also calculated to allow for comparisons with the three month time periods.

4.2.7 Drug consumption levels – approximation of daily dosage

There is considerable inconsisitency across the literature in recommending what dosages of POA drugs might be hamful or problematic for individuals. This variability in tems of patient needs and complexity of pain management has led to many clinical guidelines around POA drug use not setting dose thresholds. Guidelines tend to focus on appropriate assessment and titration of dosage levels and patient monitoring to determine effects in initiating POA drugs treatments.

There is generally accepted evidence that there is limited efficacy of dosages of POA drugs at over 100-120 mg per day of Oral Morphine Equivalent (Holliday, Hayes & Dunlop, 2013). Guidelines to determine risky dosages consider levels of low, medium and high dosages to inform clinicians. The American Pain Society suggests a low dose was 100mg OME per day, a medium dose was between 100-200 mg OME per day, and a high dose was greater than 200mg OME per day.

Calculation of consumption at daily dosage level for most mediciations in the course of treatment assume a single practitoiner, coordinated treatment management, and that patients are consuming drugs as prescribed. However, for the population of of interest for this study – that is, potentially drug-seeking, drug-dependent, or abusing patients seeking drugs from multiple doctors – that can not be assumed. For example, a doctor-shopping patient can receive mulitple prescriptions from multiple prescirbers for different POA drugs with overlapping or discrete dispensing dates. Further, the instructions of a prescriber on any given prescrption could vary from ‘take as needed’ to a daily consumption regime.

There is also concerns that high-volume obtaining patients might be onselling or diverting some or part of the medications. Alternatively, there could be parties involved in organised criminal enterprise obtaining POA drugs under false IDs for direct diversion to illicit markets. Another potential issue is that patients could be prescribed short term courses of extra POA drugs for 'breakthrough' pain, that is short of acute exacerbations of pain within the context of persistent pain management. This could create apparently higher doses in some periods of dispensing. However, short course breakthrough prescribing is generally limited to less than a few weeks at a time in most longer time periods.

An approximation of daily dosage consumption levels could be useful in classifying persons as potentially drug-dependent, drug-seeking, or otherwise consuming POA drugs at beyond accepted therapetic levels. A proxy measure of daily drug consumption was developed to allow classification within the sub-population of potential doctor-shoppers that correlates with actual consumption levels. For each three-month quarter the total drug dosage by oral morphine equivalent milligrams (OME) was obtained for all POA drugs dispensed in that quarter. The total OME per quarter was then divided by the number of days in that quarter to give an approximation of a daily dose of OME milligrams. This gives an approximate daily dosage figure, and from this a person could be classifed as either Low, Medium or High dose levels as shown in Table 4.2 below.

Table 4.2

Estimation of approximate daily dose from actual quarter POA drugs dispensed (Oral Morphine Equivalent – mg)

Dose level	Actual volume POA drug dispensed/quarter	Approximate daily dose
Low	<9000mg	<100mg/day
Medium	9000-18000mg	100-200mg/day
High	>18000mg	>200mg/day

This measure is an approximation to allow for comparison across each of the different drug types and to allow for each person in each quarter but does have certain

limitations. This measure assumes consistent consumption across the dosing period, which might be applicable for long-acting medications. This assumption can not universally be held for immediate-release preparations, such as oxycodone (Endone™) tablets. These preparations are often take on an 'as needed' basis.

The measure cannnot account for drugs obtained before the commencent of that quarter. This could lead to an underestimate of daily dosage. Secondly, drugs obtained towards the end of a quarter that might be consumed in the following quarter are included, potentially inflating a daily dosage estimate. However, for persons obtaining drugs across all four quarters of the study period this variability will be reflected in all quarters of the study period, potentially evening out these estimates. Given these limitations, and that other established measures of daily dosage might not be applicable in high-volume drug-seeking patients, this measure is used as the best approximation across all persons to allow for classification.

4.2.8 History of drug dependence

The MODDS database has a number of classifications based on DoH regulatory actions and confirmed diagnoses of drug dependence or notifications of long-term treatment with POA drugs. These classifications are set out in Table 4.3.

Table 4.3

MODDS Classifications

Classification	Description
Regular	A person has been in receipt of at least one POA drug prescription, but not subject to any regulatory action*
Report	A person has had a long-term treatment report submitted to the Department of Health by a treating medical practitioner to meet legislative obligations
Approval	A person has had an approval issued to a medical practitioner to treat them with controlled drugs as they have been diagnosed as drug dependent**
Program	A person has been admitted to the Queensland Opioid Treatment Program for management of their drug dependence by a medical practitioner.

** Note – Classification of a person in the MODDS system starts as 'Regular' once a prescription event generates a person within the system. The classification status is then changed to either report, approval or program based on the above described events.*

***Note – Drug dependence here refers to a legislative definition; however, the Department does refer to DSM or ICD diagnostic criteria in providing advice to medical practitioners.*

A 'Program' classification includes those persons who have had or are currently registered in a formal opioid treatment program (OTP) for their opioid dependence and are receiving opioid substitution drugs, such as methadone or buprenorphine (Subutex and Suboxone). As such, the extracted records capture a range of persons who have been diagnosed by medical practitioners as drug dependent.

Once a person is admitted to the OTP, their classification remains 'Program' regardless of subsequent discharge or other reports or approval events. The Report, Approval, and Program status represent an increasing order of classification, such that a person once classed at one level cannot have their classification regress to the lower level classification, but they can be classed at the next level higher in the event of actions described in the table.

Furthermore, those persons classified as 'Approval' status have had a formal legal instrument granted to a doctor to treat them with POA drugs because that doctor

'reasonably believed they were drug dependent' as required under the relevant legislation (Queensland Government, 1996). Drug dependence in these situations usually refers only to the use of POA drugs and not illicit or injecting drug use. This is different from persons determined as candidates for OTP treatments whose use of opioids usually involves illicit drugs, either heroin or illicitly obtained POA drugs, and whose use of these drugs might involve injection.

For the benefit of this study, in considering issues of drug dependence on POA drugs, the above classifications give three initial categories of interest; those persons with admissions or potential admissions to OTP treatment; those persons who are considered dependent on POA drugs, but not suitable for OTP treatment; and those persons who have not been considered dependent on opioids at present. The 'Report' status refers to legal requirements of doctors to report patients who have received two or more months of treatment with POA drugs to the DoH. All other persons who were other 'nil-reports' status were categorised as having no current or previously known drug dependence, nor any prescribing doctor notifying the Department they were undertaking long-term treatment of that person. These two classifications – 'nil reports' and 'report' – were combined into a single category of 'unclassified' as they represent that sub-population with no formal assessment of drug dependence.

4.2.9 Extract of possible doctor-shopping population

The definition of 'doctor shopping as seeing multiple prescribers and obtaining multiple prescriptions was used to extract the population of interest.

Table 4.4

Criteria for defining minimal definition of doctor shopping

	Extraction variable	Criterion
1	Number of prescribers	>2 in any one quarter
2	Number of prescriptions dispensed	>3 in any one quarter
3	Time period of activity	Each 3-month calendar quarter

The following discussion sets out the reasons for the numbers of doctors, prescriptions, and time periods used to extract the study population. The Oracle Discover queries were developed to extract potential doctor-shopping persons and their relevant details from the MODDS database for the 2013 calendar year. These queries sought to extract any persons who had been dispensed three or more prescriptions from three or more different prescribers in any one calendar quarter (three-month period) of the year (see Table 4-2).

Table 4.5

Calendar year quarters for extraction of doctor shoppers

Quarter 1	Quarter 2	Quarter 3	Quarter 4
1 January – 30 March	1 April – 30 June	1 July – 30 September	1 October - 31 December
Q1	Q2	Q3	Q4

An Oracle Discoverer query was run for each quarter of 2013 based on the above criteria, and four separate files were created. Each file contained the person's demographic and classification details and summary of details of numbers of prescribers, prescriptions, and dispensers. The four files were then unified into a single file by linking them with the unique person PPID. This produced records of the person's POA drug prescriptions across all quarters of 2013. This file included one case per person per line of data.

Data was extracted in four individual files for each quarter and then combined in a single, longer file for each quarter via the Merge File add Cases SPSS function. This file was now restructured using the SPSS Restructure function to create a file for each individual person and the four quarters of their prescribing history was included in each case record.

Based on the persons identified in the above database queries another set of queries was developed to extract details of the prescriptions dispensed for each person in each quarter. This data allowed for full details of each prescription, including type and class of drug and total milligrams dispensed for that drug. This file included multiple lines per persons to account for all prescriptions dispensed to the person in that quarter.

These prescriptions were not unified due to the complexity of the data, where a person's ID had multiple prescription details listed against them for each quarter. However, this data was summarised to create a total dosage dispensed by Oral Morphine Equivalent (OME) milligrams. This summary figure for each quarter was then added to the original prescription summary files to give a total OME dosage dispensed per quarter for each person.

The use of set three-month quarter periods (e.g. January to March, April to June) across the study captured all persons who met the study's doctor-shopping criteria in those time periods (see Table 4.5). However, it is possible that some persons meet the doctor-shopping criteria for three-month periods within 2013 that are not captured within the quarter set for the study. For example, a person could meet the doctor-shopping criteria in the three months from March to May. That person's prescription activity might not have met the doctor-shopping criteria in either of the quarters January to March or April to July. Therefore, the study would not capture potential doctor-shopping persons and thus underestimate the number of persons engaged in doctor-shopping activity in the study year.

To verify if there were any non-identified doctor-shopping persons, all three-month periods within 2013 were investigated to determine if further persons were not captured in the quarters set out in Study 2. Table 4.6 below shows other possible three-month periods that occur in the year, in the column 'Other Quarters'.

Table 4.6

All possible three-month periods in 2013 for doctor shopping analysis via MODDS database.

Month	Study Quarter	Other Quarters
January	Quarter 1	
February		Quarter 1a Feb-Apr
March		Quarter 1b Mar-May
April	Quarter 2	
May		Quarter 2a May-Jul
June		Quarter 2b Jun-Aug
July	Quarter 3	
August		Quarter 3a Aug-Oct
September		Quarter 3b
October	Quarter 4	
November		
December		

To generate this data Oracle Discoverer queries were executed for all the periods set out in Table 4.6. All the relevant data elements were extracted in the same manner as the procedure set out above for the previous data extraction described in this section.

4.2.10 Frequency of doctor shopping

The extent or frequency of doctor shopping and drug obtaining, in the absence of the criteria for doctor shopping, could potentially discriminate between drug-seeking behaviour, indicative of a substance use disorder (SUD) and legitimate therapeutic treatment regimens.

It could be considered that low-level of POA doctor shopping might resemble abuse, and longer-term doctor shopping resemble dependence. Also, short-term exposure to POA drugs, in the absence of doctor shopping, suggests acute pain management treatment, and longer-term treatment with POA drugs, in the absence of doctor shopping, suggests treatment of a chronic or persistent pain condition. A

proposed model of how level of doctor shopping and frequency of POA drug obtainings might relate of pain management or SUDs and consumed dosage levels is show in Table 4.7 and Table 4.8, respectively.

Table 4.7

Proposed model combining levels of doctor shopping and drug obtaining – possible diagnoses

	Frequency of POA drug obtaining	
Doctor Shopping	Low	High
Low	Acute pain management	Chronic pain management
High	Abuse	Dependence

Table 4.8

Proposed model combining levels of doctor shopping and drug obtaining – dose levels

	Frequency of POA drug obtaining	
Doctor Shopping	Low	High
Low	Low-Medium dose	Low-Medium dose
High	High dose	High dose

As set out in Table 4.7 above the following relationship between the levels of doctor shopping and frequency of doctor shopping behaviour are hypothesised. A high level of doctor shopping could be characterised as behaviour of a person obtaining large numbers of prescriptions, from a large number of different prescribers, and being dispensed at multiple different dispensers. A low level of doctor shopping could be characterised as behaviour of a person obtaining lesser numbers of prescriptions, from a lesser number of different prescribers, and being dispensed at multiple different dispensers. In considering the frequency of doctor shopping over time, a low frequency low level doctor shopper might represent a person seeking extra pain relief for an acute pain condition; and a low level doctor shopper with a high frequency of activity over time, could represent a person seeking ongoing extra pain relief for a chronic pain condition. In contrast, a high level doctor shopping patient, displaying low frequency of this behaviour over time, might represent a response with the SUD of abuse;

whereas a high level doctor shopper exhibiting high frequency behaviour might represent a person with a dependence type of SUD.

The extracted data is described and analysed to investigate if the abovementioned variables can be used to discriminate or identify doctor-shopping persons that are more likely to have potential SUDs from those persons who might be in receipt of long-term POA drug treatment.

4.3 ANALYSIS

All analyses were performed using SPSS (IBM Corporation, 2011) to identify potentially distinct groups within the sub-population of unclassified persons that met the criteria of a potential doctor shopper in any one quarter of 2013. A two-step cluster analysis was performed as this technique can classify large datasets and is robust to violations of assumptions of normality, independence between variables, and can manage outlying variables effectively (Norusis, 2008).

The analysis of similarity between the clusters was determined using the log-likelihood method, as this method is supported as being able to account for both continuous and categorical variables – which are intended to be used in the analysis of doctor shopping. Determination of the optimal number of clusters was performed automatically in the procedure selecting the Bayesian Information Criterion (Norusis, 2008).

Table 4.9

Variables for entry in two-step cluster analysis for unclassified population for unclassified persons

	Variable
1	Mean unique prescribers consulted each quarter*
2	Mean prescriptions dispensed per quarter*
3	Mean unique dispensers dispensing per quarter*
4	Mean volume of OME (mg) dispensed per quarter*
5	Total quarters doctor shopped
6	Total quarters POA prescriptions dispensed
7	Mean dose level quarter dispensed

**for each quarter where POA drugs only were dispensed*

Measures included in the analyses are described previously and include those listed in Section 4.2 above. All measures were those potentially related to prescribing activity, such as unique prescriber, unique dispensers, and prescription volumes. Other drug consumption variables include volumes of drugs obtained, dose level, and other time-related variables of quarters where minimal doctor shopping was met, as well as total quarters in which POA drugs were dispensed.

Differences in the proportions across clusters were assessed with Chi-square tests. The clusters were then compared using one-way analysis of variance with Scheffe's post-hoc tests and Chi-square tests. The level of significance was set at $p<.05$.

4.4 RESULTS

4.4.1 Persons who received a POA drug prescription

The records of total population of adults (18-80 years) who received any POA drugs in 2013 was extracted from the MODDS database by Oracle Discover Query and then exported into SPSS for further analysis.

The data extracted was for each quarter and reported details of each person who had prescriptions dispensed in that quarter of their demographic details (date of birth and sex) and a summary form of dispensing records (number of prescribers, number of prescriptions, number of dispensers, date of first and last dispensing, days between first and last dispensing dates, and the MODDS classification at the time of extract). Records were extracted from the MODDS database using Oracle Discoverer Queries to extract all records of any individuals receiving opioid prescriptions for each quarter (three-month period) for 2013.

A total of 248,389 persons, almost 5.3% of the Queensland population (Australian Bureau of Statistics, 2006) received at least one prescription and in total received 1,589,933 POA drug prescriptions in 2013.

All persons under 18 years of age (n=3,579) and over 80 years (n=26,049) of age were excluded from this study. Non-adults under 17 years were excluded as they are unlikely to be independently seeking POA drugs and there is limited evidence to date that this demographic is the subject of drug-seeking behaviour for this class of drugs by doctor shopping. Furthermore, much of the epidemiological evidence discussed in Chapter 2 refers to the adult population. Also in Australia, Medicare and subsidy arrangements often have children included under parents Medicare cards and health insurance policies, where they are co-habiting. Persons under 18 years who are drug seeking or on longer term POA drugs, might be more likely to be distinct from the adult population. The study is primarily examining adults who are not in aged care situations. As such persons over 80 years of age were also excluded as these persons are more likely to be receiving POA drugs for terminal illnesses, unlikely to be ambulatory and drug-seeking by doctor-shopping behaviour. Furthermore, multiple prescribers in this older age group might be indicative of a mix of care providers in aged care facilities or other situations and could be misclassified as doctor shopping patients.

There were 218,761 persons aged between 18-80 years of age (Mean age=51.98$\pm$16.52 years), and this represents 6.7% of the Queensland population for this age group. Where gender was known, 37.2% (n=81,352) were female, and 26.2% were male (n=57,236). Persons between 18-80 years of age were prescribed a total of 1,313,897 POA drug prescriptions for this year. Any person who has seen three or more doctors and obtained four or more prescriptions in any one quarter in 2013 was selected under the most conservative definition of potential doctor shopping. The following section examines the prescription activity of the potentially doctor-shopping population within each quarter, or three-month period, of 2013.

A secondary data query was performed to extract all persons who might have been potential doctor shoppers for any other three month periods as described in Table 4.6. This was to test for any potential doctor shopping persons not captured in the initial extraction above. The Principal Personal Identification numbers (PPIDs) for all cases from this extracted data set were compared against the PPIDs extracted for the four calendar-month quarters from described earlier. The results of the matching process found there were no new cases identified in the secondary extractions for the other three-month periods that were not in the originally extracted cases. This means that the cases originally extracted include all persons in 2013 that meet a potential doctor-shopping criteria at any time in the year.

4.4.2 Potential doctor-shopping population

Based on MODDS-extracted data of summaries of prescription records, 15,545 persons met the criteria for possible doctor shopping (consulted three or more doctors and obtained four or more prescriptions) in at least one of any of the four quarters of 2013. As shown in Table 4.10, this included 15,545 persons and this represents 7.1% of the adult Queensland population, 18-80 years of age who received a POA drug prescription in 2013 (0.005% of the entire Queensland adult population of the same age range) and accounted for over 27% of all POA drugs prescriptions in this year.

Table 4.10

Total persons and POA prescriptions x potential doctor shopping status

Doctor shopping	Persons	(%)	Prescriptions	(%)
Non doctor-shopping	203179	92.9	953621	72.6
Possible doctor-shopping	15545	7.1	360515	27.4
Total	218761	100	1313897	100

Of the potential doctor-shopping population, where gender was known, 7905 (50.85%) persons were female, and 7054 persons (45.38%) were male and the mean age for the entire population was 54.23±15.1 years. In comparison, the Queensland population projection for 2013 for persons aged 18 to 80 years reports 50.22% females

and 49.78% males (Australian Bureau of Statistics, 2014). Table 4.11 sets out the age categories for the potential doctor shoppers, and shows almost 60% of these persons were aged between 40 and 60 years of age.

Table 4.11

Persons by age category for all potential Queensland doctor shoppers in 2013 (n=15,545)

Age range	Frequency	%
18-20 years	64	.4
21-30 years	906	5.8
31-40 years	2084	13.4
41-50 years	2795	18.0
51-60 years	3011	19.4
61-70 years	2966	19.1
71-80 years	2538	16.3
Missing	1181	7.6
Total	15545	100.0

4.4.3 Doctor shoppers by drug-dependence status

Table 4.12 sets out the MODDS classification of this population and shows almost three-quarters of the population (72.3%) were 'Nil report' patients, meaning those persons had not been subject to any regulatory action by Queensland Health nor had they been reported to the Department for their long-term POA drug treatment. Less than 4% had ever been or were currently on formal opioid treatment programs for dependence. Approximately 20% (3132 persons) had been reported in receipt of lengthy treatment, almost 4% (587 persons) were under drug treatment approvals, and another 4% (583 persons) had OTP histories. For the benefit of later analysis, all 'Nil report' and 'Report' persons are grouped as a broader 'Unclassified' category (n=14,378) representing all persons who have not previously been classified as drug dependent. This unclassified category represents over 92% of all potential doctor shopping persons.

Table 4.12
MODDS classification of potential Queensland doctor shoppers in 2013 (n=15,545)

Classification	Frequency	Per cent
Nil report	11,246	72.3
Report	3132	20.1
Approval	585	3.8
Program	582	3.7
Total	15,545	100.0

4.4.4 POA drugs prescribed for potential doctor shoppers

The second extracted file linked drug types and dosage dispensed for each of the individual prescriptions for each of the doctor-shopping persons prescribing summaries so that this drug type and dosage information could be amalgamated to show each person's more detailed prescription records. A total of 360,515 POA drug prescriptions were dispensed in 2013 for this population and this was 387,001,476 milligrams based on Oral Morphine Equivalent (OME) conversions for all the drug types (Nielsen, Degenhardt, Hoban, & Gisev, 2014). Table 4.13 sets out all the POA drug dispensed and the volumes and proportions of prescriptions and OME (milligrams) accounted for by each drug type.

Oxycodone prescriptions account for almost two-thirds of prescriptions issued and almost 60% of drugs by volume dispensed. The next most commonly used POA drug was morphine slow-release preparations that accounted for almost 8% of prescriptions, almost 15% of volume of drugs dispensed. This is in keeping with known data from Australian prescribing trends (Degenhardt, et al., 2006; Dev, Loveday, Ballantyne, & Kemp, 2010; Dobbin, 2010a; Leong, et al., 2009).

Table 4.13
POA drugs dispensed by prescriptions and OME milligrams in 2013 (n=15,545)

Drug name	Rxs	%	OME(mg)	%
Alfentanil Injections	1	0.000	140	0.000
Buprenorphine + Naloxone Sub-Lingual	2530	0.007	17082862.5	0.044
Buprenorphine Patches	27351	0.076	398445.6	0.001
Buprenorphine Sub-Lingual	646	0.002	2655447.75	0.007
Codeine Oral	3020	0.008	695371.3	0.002
Fentanyl Injections	113	0.000	85.26	0.000
Fentanyl Patches	32914	0.091	2281833.08	0.006
Fentanyl Sub-Lingual	388	0.001	1963.6	0.000
Hydromorphone Extended Release Oral	9269	0.026	22768960	0.059
Hydromorphone Injections	485	0.001	3307710	0.009
Hydromorphone Oral	1282	0.004	2654910	0.007
Methadone Injections	13	0.000	60075	0.000
Methadone Liquid	2948	0.008	17612208.95	0.046
Methadone Oral	6099	0.017	16769788	0.043
Morphine Injections	3556	0.010	3751305	0.010
Morphine Oral	4913	0.014	7174630	0.019
Morphine Slow Release Oral	28369	0.079	56606695	0.146
Oxycodone Hcl Controlled Release Oral	94762	0.263	165603195	0.428
Oxycodone Hcl; Naloxone Hcl Dihydrate	30131	0.084	29125417.5	0.075
Oxycodone Injections	9	0.000	2400	0.000
Oxycodone Oral	107785	0.299	36619522.5	0.095
Oxycodone Suppositories	731	0.002	724320	0.002
Pethidine Injections	3133	0.009	992540	0.003
Pethidine Oral	1	0.000	200	0.000
Remifentanil Injections	1	0.000	10	0.000
Tapentadol	65	0.000	111440	0.000
Total	360515	1.000	387001476	1.000

Note: Rxs-prescriptions, OME – oral morphine equivalent.

4.4.5 Prescribing and doctor-shopping activity across the year

A person of interest for this study could have met the study criteria for doctor shopping in any one of the four quarters of 2013. Many persons who might have met these criteria for less than four quarters may have also obtained prescriptions in the other quarters, and/or had no POA drugs dispensed in the other quarters. The measure of how many quarters a person met the doctor shopping criteria, and how many other

quarters they received POA drugs, are of interest in potentially separating drug-seeking behaviour from ongoing legitimate long-term therapy.

The frequency and chronicity of doctor-shopping activity and POA drug-prescribing allows for assessment of how prolific a person's drug-seeking activity is, in regards to possible doctor shopping, and also how extensively they are exposed to POA drugs in terms of their continuity of prescribing across the year. For this population, persons could have met the criteria for doctor shopping in one, two, three or four quarters of 2013. Table 4-10 below sets out how many persons meet the doctor-shopping criteria in how many quarters. Also included are the volumes of prescriptions and total milligrams dispensed for those persons, and the proportions they account for of total prescriptions and volumes of POA drugs dispensed. For example, 74% of persons in the study only met the doctor-shopping criteria in any one quarter of 2013, and this group accounted for almost 60% of all prescriptions and volume of POA drugs dispensed in 2013.

Table 4.14

Total doctor shopping quarters POA drugs dispensed by persons by prescriptions and by volume of drugs for possible Queensland doctor shoppers in 2013 (n=15,545)

Quarters	**Persons**		**Rxs**		**OME(mg)**	
	n	%	n	%	n	%
1	11,504	74.0	211,913	58.8	223,719,506.2	57.81
2	2784	17.9	89,236	24.76	98,080,209.52	25.34
3	925	6.0	39,761	11.03	43,393,141.82	11.21
4	332	2.1	19,490	5.41	21,808,618.46	5.64
Total	15,545	100.0	360,400	100.0	387,001,476	100.0

Table 4.15 below shows the total numbers of quarters the study population received any POA drugs and included the percentage of prescriptions and volumes of drugs dispensed for each group. From this perspective, over half of the study population received prescriptions for all four quarters of the year, and this group accounted for over three-quarters of all prescriptions and over 80% of total volume of drugs dispensed.

Table 4.15

Total quarters POA drugs dispensed by persons by prescriptions x volume of drugs for possible Queensland doctor shoppers in 2013 (n=15,545)

Quarters	Persons	%	Rxs	%	OME(mg)	%
	n	%	n	%	n	%
1	2392	15.4	15,987	4.44	8,841,157.66	2.28
2	2667	17.2	31,235	8.67	22,485,750.53	5.81
3	2348	15.1	42,733	11.86	34,020,908.2	8.79
4	8138	52.4	270,445	75.04	321,653,659.6	83.11
Total	15545	100.0	360,400	100.0	38,700,1476	100.0

Combining the number of quarters a person doctor shopped by the study criteria by total quarters in which they had been dispensed POA drugs can describe in greater detail different levels of drug seeking in the context of long-term treatment not characterised by drug-seeking behaviour. That is a person's doctor shopping and non-doctor shopping access to POA drugs can be examined over the study year. This allows examination of how frequently a person might have doctor shopped and also the oterh quarters in which they might have obtained POA drugs.

The following three tables (Table 4.16, Table 4.17, and Table 4.18) show a matrix of persons classified by number of drug-seeking quarters and number of quarters prescribed for 2013, and the volumes of prescriptions and OME (milligrams) dispensed for each sub-group. The tables also include the proportion by percentage that that cell accounts for of the entire number or volume of that table.

For example, 2,392 (15.4%) of persons in the study population appeared to doctor shop in one quarter and did not obtain POA drugs in any other quarter (Table 4.16) and accounted for almost 4.5% of all the prescriptions dispensed by number (Table 4.17) and over 2% of OME milligrams volume of total POA drugs dispensed. Further, almost one-third of all persons in the study group seemed to doctor shop in one quarter and received POA drugs in the other three-quarters of the year (

Table 4.18). This group accounted for over 40% of all prescriptions and volumes of drugs dispensed.

Table 4.16

Total quarters doctor shopped for all quarters dispensed POA drugs – number of persons and proportion of total persons per category for all possible Queensland doctor shoppers in 2013 (n=15,545)

		Quarters dispensed				
		1	2	3	4	Total
Quarters Doctor Shopped	1	2,392	2,317	1,695	5,100	11,504
		15.4%	14.9%	10.9%	32.8%	
	2	-	350	528	1906	2784
		-	2.3%	3.4%	12.3%	
	3	-	-	125	800	925
		-	-	0.8%	5.1%	
	4	-	-	-	332	332
		-	-	-	2.1%	
	Total	2,392	2,667	2,348	8,138	15,545

Table 4.17

Total quarters doctor shopped x all quarters dispensed – POA drug prescriptions dispensed and percentage of total prescriptions for all possible Queensland doctor shoppers in 2013 (n=15,545)

		Quarters dispensed				
		1	2	3	4	Total
Quarters Doctor Shopped	1	15,987	24,646	26,819	144,461	211,913
		4.44%	6.84%	7.44%	40.08%	
	2	-	6,589	11,846	70,801	89,236
		-	1.83%	3.29%	19.65%	
	3	-	-	4,068	3,5693	39,761
		-	-	1.13%	9.90%	
	4	-	-	-	19,490	19,490
		-	-	-	5.41%	
	Total	15,987	31,235	42,733	270,445	360,400

Table 4.18

Total quarters doctor shopped x all quarters dispensed – OME(MG) of POA drugs dispensed and proportion of total volume of drugs dispensed for all possible Queensland doctor shoppers in 2013 (n=15,545)

			Quarters dispensed			
		1	2	3	4	Total
Quarters	1	8,841,157.66	16,952,353.55	20,673,766.26	177,252,228.8	223,719,506.2
Doctor		2.28%	4.38%	5.34%	45.80%	
Shopped	2	-	5,533,396.98	9,536,928.332	8,3009,884.2	98,080,209.52
		-	1.43%	2.46%	21.45%	
	3	-	-	3,810,213.6	39,582,928.22	43,393,141.82
		-	-	0.98%	10.23%	
	4	-	-	-	21,808,618.46	21,808,618.46
		-	-	-	5.64%	
	Total	8,841,157.66	22,485,750.53	34,020,908.19	321,653,659.6	387,001,476

4.4.6 Approximate levels of POA drugs consumption

An approximate measure of daily dosage of POA drugs by OME milligrams can allow classification of persons into low, medium and high dosage to describe consumption level. Based on the method set out in Section 4.4.6 an approximate level was calculated for each persons and averaged across the number of quarters in which they received POA drugs in the year.

Table 4.19 shows how many persons in the study were in each dosage category and the volume of prescriptions and total OME milligrams of drugs dispensed for each group. Over three-quarters (77.6%) of all potential doctor-shopping persons had an average drug consumption of less than 100 milligrams per day (OME) per quarter prescribed in 2013. Further, this group accounted for just over 60% of all prescriptions dispensed; however, this was less than one-quarter (23.4%) of the total volume of drugs by milligrams OME. In contrast, the high-dose persons, consuming on average more than 200 milligrams OME in any quarter, were only 11.1% of all persons receiving almost one-quarter of all prescriptions (22.4%) but accounting for over a half (56.5%) of the drug consumed by volume of milligrams OME.

Table 4.19

Mean approximate daily dosage levels per quarter dispensed for all possible Queensland doctor shoppers in 2013 (n=15,545)

Daily dose estimate	Persons		Prescriptions		Volume of drugs	
	N	%	n	%	Sum	%
Low dose (<100mg/day)	12,065	77.6%	21,9008	60.8%	90,325,153.11	23.4%
Medium dose (100-200mg/day)	1,755	11.3%	60,740	16.9%	77,864,201.10	20.2%
High dose (> 200mg/day)	1,725	11.1%	80,652	22.4%	218,812,121.81	56.5%
Total	15,545	100.0%	360,400	100.0%	387,001,476	100.0%

Note: mg=oral morphine equivalent dosage

4.4.7 Drug dependence status of potential doctor shoppers

The particular sub-population of interest for this study are those persons who have not been already identified as drug dependent, either as being on a formal opioid treatment program (e.g., OTP status) or under a legally-approval issued by the Department to a treating doctor (e.g., Approval status). As set out in Table 4.20 these persons will be referred to as 'Unclassified' persons and subject of further analysis for this study. The reason for this is that these persons are of most interest to monitoring and surveillance methods as they are being prescribed POA drugs by doctors frequently, or at least to meet the minimal doctor-shopping criteria; however, they have not been assessed as drug dependent at this time. The 'Unclassified' persons also are being dispensed over 90% of all prescriptions and accounting for 88% of the volume of OME (mg) being dispensed for 2013 for this sub-population (see Table 4-16).

Table 4.20

Numbers of POA drug prescriptions and OME (mg) dispensed for potential doctor-shopping patients by drug-dependence classification (n=15,545)

	Persons	**%**	**Prescriptions**	**%**	**Total OME(mg)**	**%**
Classification						
Unclassified	14,378	92.5%	317,166	88.0%	301,625,878.4	77.9%
Approval	585	3.8%	25,449	7.1%	41,013,279.55	10.6%
OTP	582	3.7%	17,785	4.9%	44,362,318.11	11.5%
Total	15,545	100%	360,400	100%	387,001,476	100%

Table 4.21 below sets out the differences in the variables of interest for each of the classifications of drug dependence. A one-way ANOVA was performed comparing the means for each of the variables of interest and all were found to be significantly different from each other at levels $p<.001$. The levels for the 'Unclassified' persons across all variables are lower than either of the 'Approval' or 'OTP' persons. The Unclassified category also accounted for over 92% of all potential doctor shoppers. This suggests that this population includes a wide range of prescribing behaviour, much of which might not be aberrant or representative of any substance misuse disorders. Therefore, the following analyses focus on the 'Unclassified' population to further examine this issue: these persons' dependence status was indeterminate, and it would be expected this sub-population would include both legitimate therapeutic use and aberrant use.

Table 4.21

POA drug prescription use and demographic variable x drug dependence status for all potential doctor shoppers for all possible Queensland doctor shoppers in 2013 (n=15,545)

	Unclassified (n=14,378)			**Approval** (n=585)			**OTP** (n=582)			**Test statistic**	
POA drug prescription use										F	
Prescriptions per quarter											
Mean & SD	7.05	±	4.83	11.78	±	8.86	8.84	±	6.59	267.57	**
Range	1.75	-	124.00	1.75	-	76.33	2.25	-	81.25		
Prescribers per quarter											
Mean & SD	2.56	±	0.94	2.87	±	1.42	2.72	±	2.33	28.98	**
Range	1.50	-	29.50	1.50	-	12.50	1.50	-	49.75		
Dispensers per quarter											
Mean & SD	1.81	±	1.03	2.72	±	1.66	2.84	±	2.32	395.34	**
Range	1	-	29.75	1	-	14	1	-	44.75		
OME (mg) per quarter											
Mean & SD	6186.45	±	11117.39	18467.35	±	19173.83	20765.66	±	20125.44	684.44	**
Range	12.60	-	262732.50	34.65	-	168637.50	42.00	-	122250.00		
Quarters doctor shopped											
Mean & SD	1.34	±	0.67	1.71	±	0.93	1.46	±	0.75	87.11	**
Range	1	-	4	1	-	4	1	-	4		
Quarters obtained prescriptions											
Mean & SD	3.01	±	1.16	3.60	±	0.82	3.38	±	0.92	103.94	**
Range	1	-	4	1	-	4	1	-	4		

Demographic characteristics									
Gender									
Females	7445.00		(54%)	241.00		(41.3%)	219.00		(52.8%)
Males	6349.00		(46%)	343.00		(58.7%)	362.00		(47.2%)
Mean age	55	±	15	45	±	11	39	±	10
Range	18	-	80	19	-	75	19	-	80

***p* <.001

4.4.8 Descriptive analyses of variables of interest

The variables of interest for further analysis were examined using IBM SPSS for Windows (IBM Corporation, 2011) to investigate for assumptions of normality, identification of outliers, and independence. It is expected that this sub-population will include a large majority of cases that are unremarkable and representative of normal treatment regimes or slight variations from these. However, it is also expected there will be a small proportion of persons at the extreme ranges of variables due to high-levels of drug-seeking. This means there is expected to be violations to the assumptions of normality in the variables of interest.

It is noted that all variables of interest relate to a dispensing event, such that a prescriber, prescription, dispenser and dose amount are all elements of a dispensing event, so it is expected there is a violation of assumption of independence. Table 4.22 below shows means and standard deviations for all prescription level variables of interest and Table 4-19 shows the skewness and kurtosis description of each variable.

Table 4.22

Means of variables of interest – Unclassified population of all possible Queensland doctor shoppers in 2013 (n=14,378)

Variable	Mean	SD
Mean Prescriptions x Quarter	7.05	4.83
Mean Prescribers x Quarter	2.56	.94
Mean Dispensers x Quarter	1.81	1.03
Mean drug volume (OME-mg) x Quarter	6,186.45	11,117.38

Table 4.23

Skewness and kurtosis –variables of interest – Unclassified population (n=14,378)

	Skewness	SE	Kurtosis	SE
Mean Prescriptions x Quarter	4.45	0.02	51.59	0.04
Mean Prescribers x Quarter	4.64	0.02	75.42	0.04
Mean Dispensers x Quarter	4.23	0.02	60.59	0.04
Mean drug volume (OME-mg) x Quarter	5.68	0.02	62.17	0.04
Total quarters prescribed	-0.65	0.02	-1.14	0.04
Total quarters doctor shopped	2.08	0.02	3.92	0.04

The following four histograms (see *Figure* 4-1, *Figure* 4-2, *Figure*4-3, *Figure* 4-4) show the distribution for each of the prescription level variables with the overlay of a normal distribution.

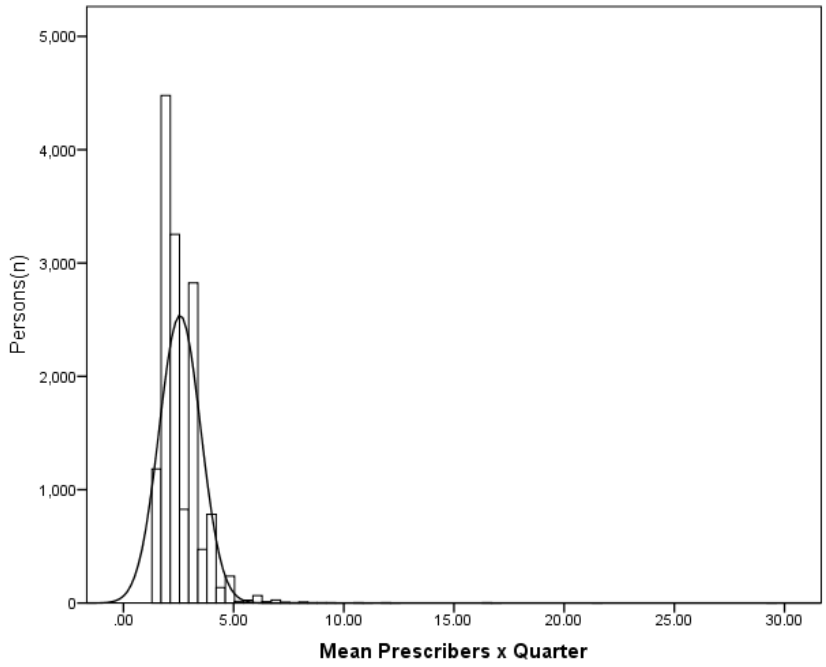

Figure 4-1. Histogram of mean prescribers by quarter for Unclassified population – normal distribution overlaid (n=14,378)

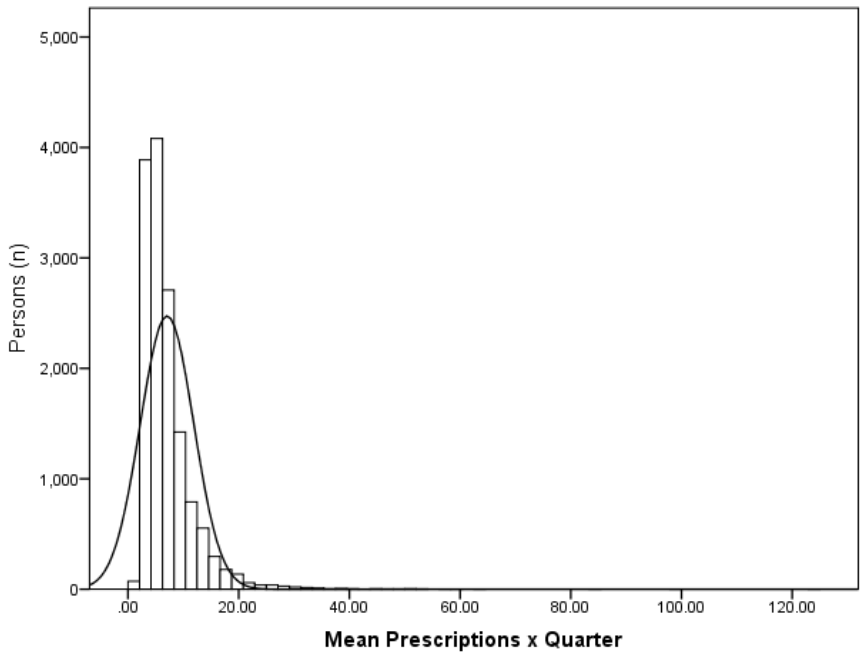

Figure 4-2. Histogram of mean prescriptions by quarter for Unclassified population – normal distribution overlaid (n=14,378)

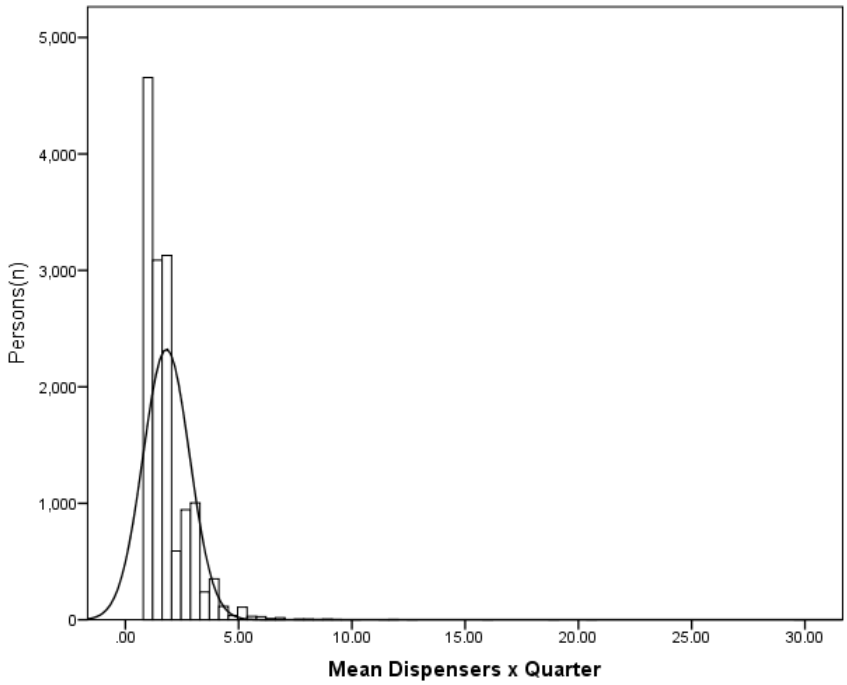

Figure 4-3. Histogram of mean dispensers by quarter for Unclassified population – normal distribution overlaid (n=14,378)

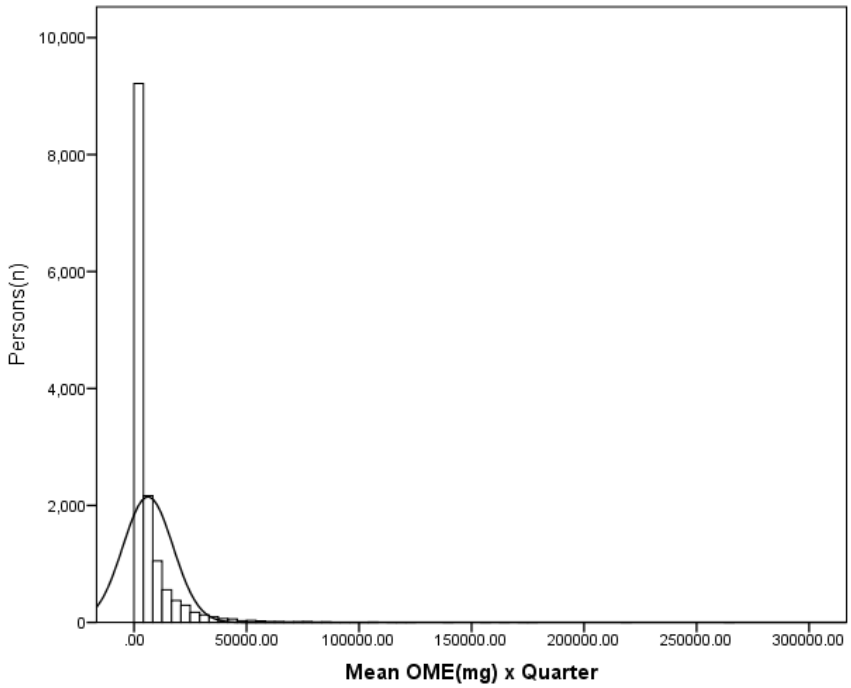

Figure 4-4. Histogram of mean (OME) mg obtained by quarter for Unclassified population – normal distribution overlaid (n=14,378)

Initial univariate descriptive analyses of individual continuous variables of prescriptions obtained, prescribers consulted and OME milligrams reported above obtained suggested small numbers of outliers or extreme values in each variable. To further analyse outliers in these variables scatter plots distributions were generated of combinations o undertaken using SPSS of Windows to investigate these cases. Scatterplots were constructed using Chart Builder function with selection of Scatterplots.

To examine for outliers in regard to the volume of POA drugs obtained, scatterplots were constructed for each of the variables, mean prescribers, prescriptions, and dispensers per quarter as the Y – Axis, and mean OME milligrams per quarter as the X – Axis (Figures 4.5 to 4.7). A further scatterplot was also constructed with total prescriptions for the year (Y-Axis) and total OME milligrams obtained for the year (X Axis) as shown in Figure 4.8. Results were further investigated using SPSS descriptive statistics to describe the volume and extent of potential outliers based on visual inspections of the scatterplots to determine the limits of each variable that appeared to contain the majority of cases.

The first scatter plot distribution examined the mean prescriptions per quarter and mean oral morphine equivalent in milligrams (OME) obtained in each quarter of 2013 for the unclassified doctor shopping patients (See *Figure* 4-5). In this distribution over 99 per cent of persons obtained 20 or fewer prescriptions on average each quarter and obtained a mean of less than 50,000 milligrams OME in each quarter they were prescribed. These persons accounted for 98.3 per cent of all prescriptions dispensed and 90 per cent of the volume of OME milligrams dispensed for the year. Of this distribution there were 122 cases or less than one per cent of total cases, that obtained more than 20 prescriptions and more than 50,000 milligrams OME on average for each quarter. Of note in this analysis, this group of outliers representing just over one percent of potential doctor shoppers obtained ten per cent of the total volume of OME milligrams dispensed to this population for the entire year.

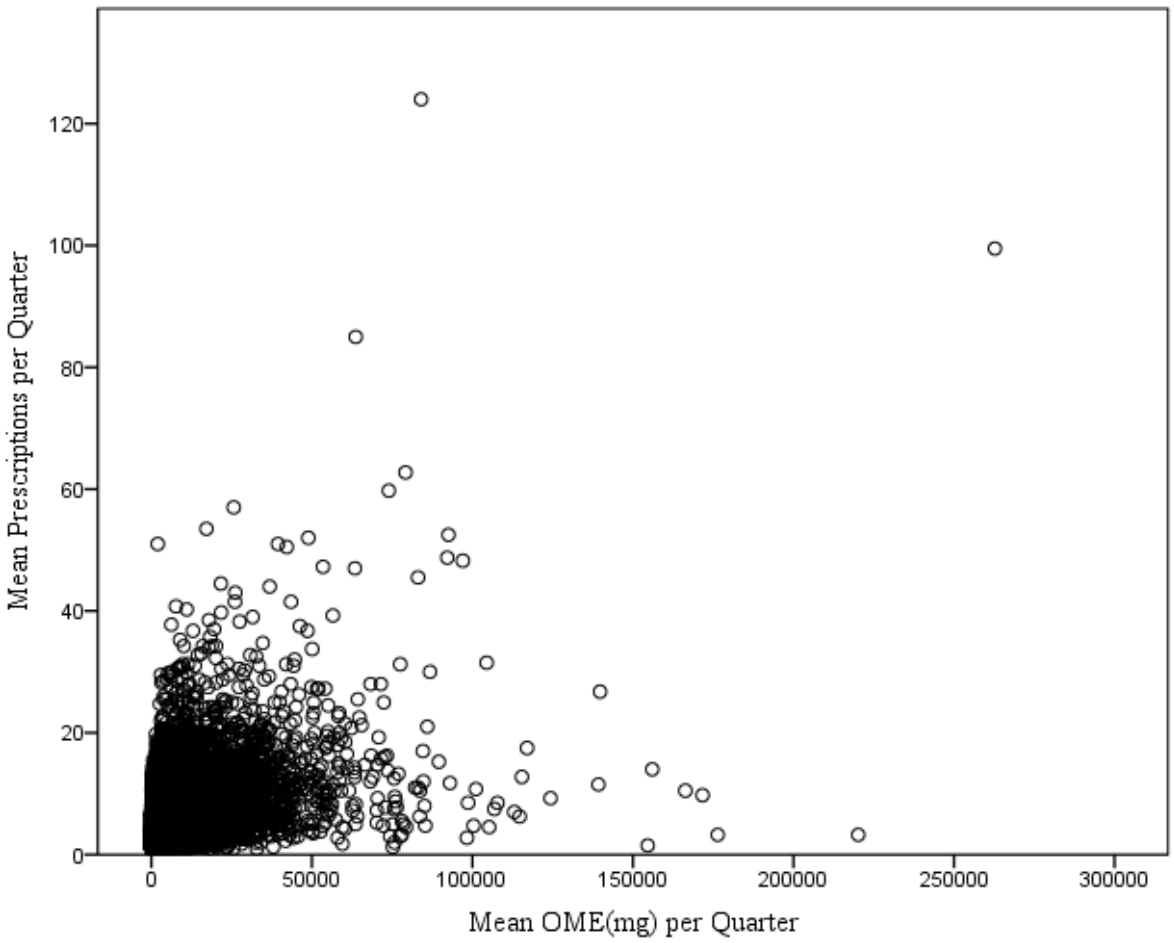

Figure 4-5. *Distribution of total oral morphine equivalent in milligrams by mean prescriptions per quarter of 2013 for all potential doctor shopping persons (n=14,378)*

The second scatterplot in *Figure* 4-6 describes the mean prescribers per quarters and mean prescriptions per quarters for all unclassified doctor shopping persons. The distribution of cases indicates 99 per cent of persons obtained 20 or fewer 20 prescriptions per average each quarter and saw five or less different doctors per quarter. These persons accounted for 98.7 per cent of the total prescriptions dispensed and 98.9 per cent of the total Oral Morphine Equivalent (OME) in milligrams dispensed for these potential doctor shopping patients. A total of 155 persons (one per cent) of this sub-population obtained more than 20 prescriptions per quarter and were prescribed by more than 5 different doctors per quarter but obtained less than two percent of the volume of prescriptions dispensed in number and OME milligram volume.

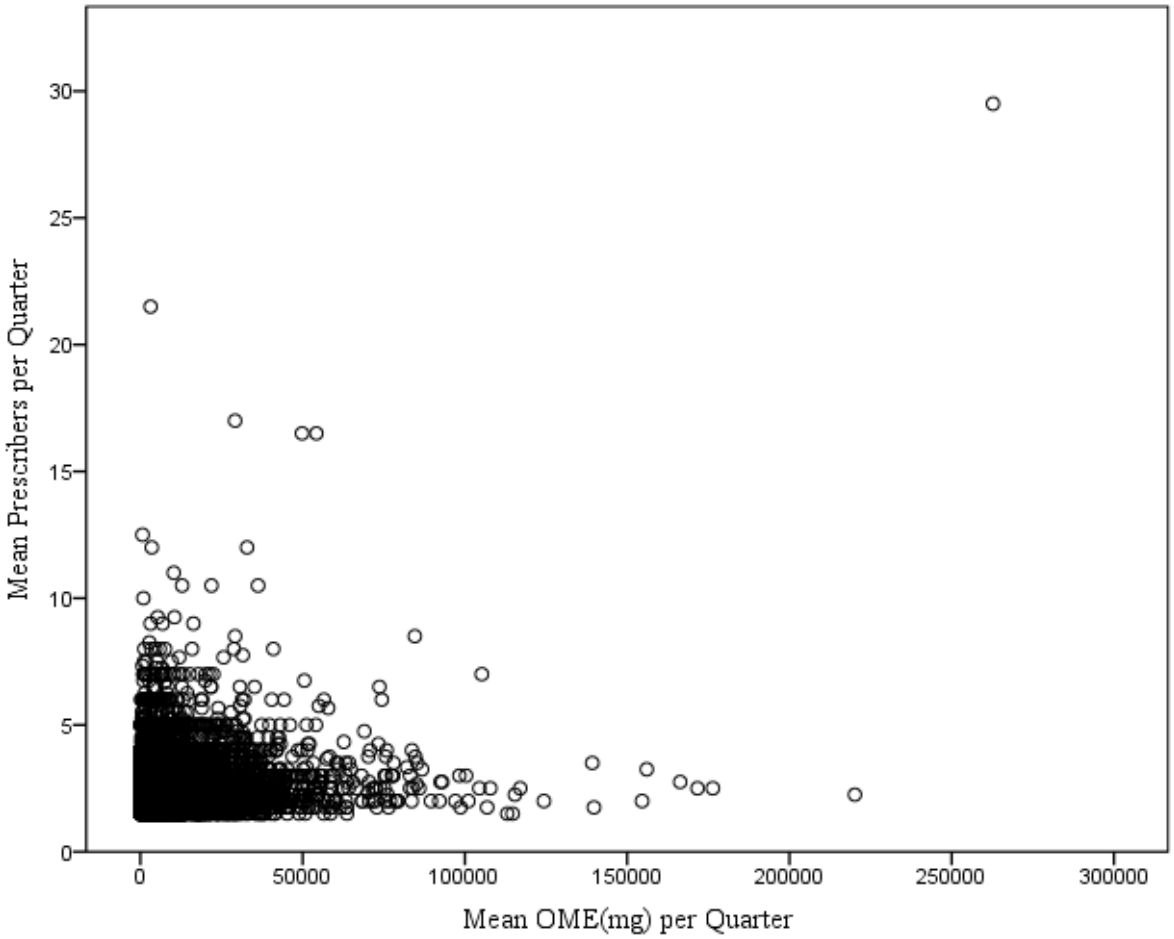

Figure 4-6. *Distribution of total oral morphine equivalent in milligrams by mean prescribers per quarter of 2013 for all potential doctor shopping persons (n=14,378)*

A further scatter plot distribution, as shown in *Figure* 4-8, was performed to describe mean OME in milligrams per quarter associated with the mean number of dispensers seen each quarter for all doctor shopping persons in 2013. Similar to the previous two figures, 98 per cent of potential doctor shopping persons saw 5 or less unique dispensers on and obtained 50,000 OME milligrams on average each quarter in 2013. The outlying or extreme just over one per cent of cases (n=148) consulting more than five different dispensers on average per quarter and obtaining more than 50,000 OME milligrams accounted for less three per cent of prescriptions dispensed and just over 14 per cent of the volume of OME milligrams dispensed in 2013.

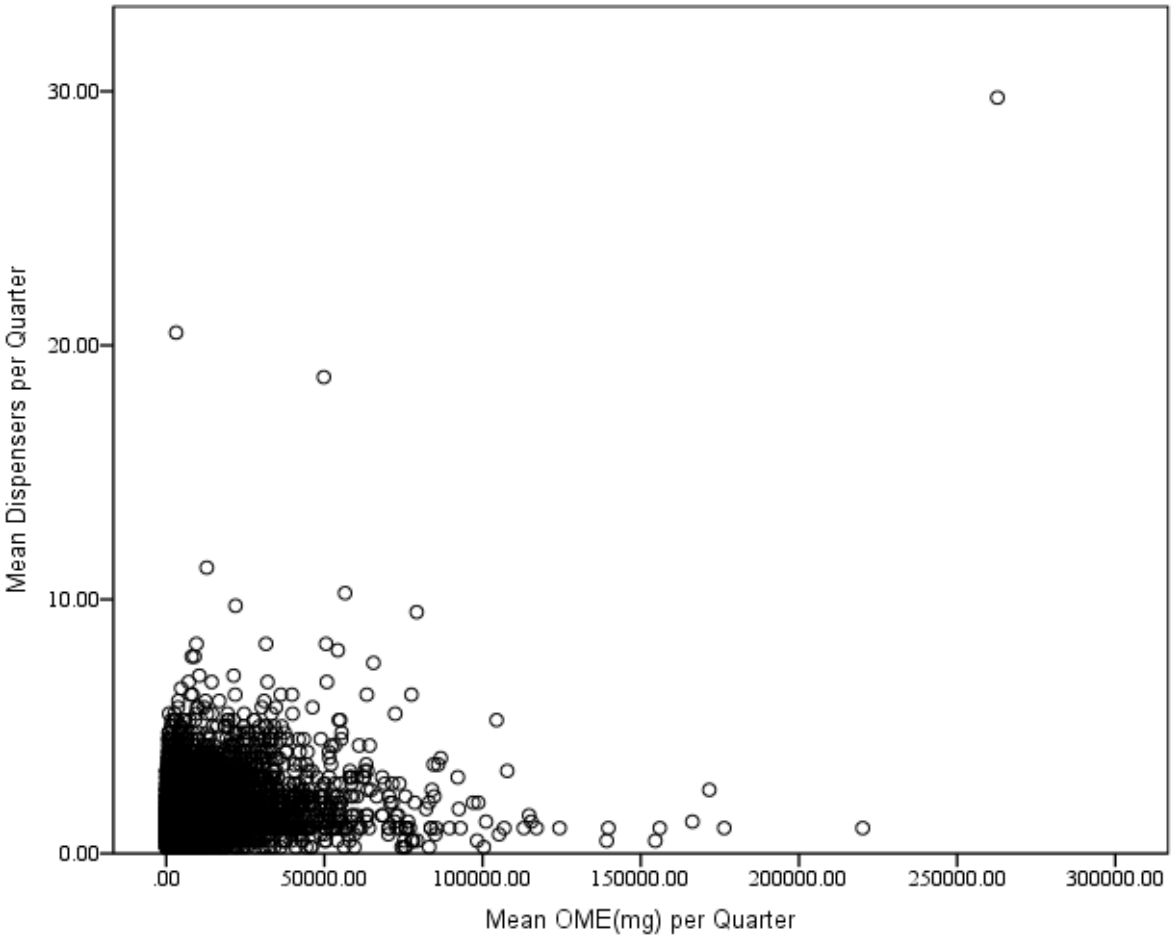

Figure 4-7. *Distribution of total oral morphine equivalent in milligrams by mean dispenser per quarter of 2013 for all potential doctor shopping persons (n=14,378)*

A final scatterplot distribution was produced for total OME milligrams by total prescriptions dispensed for all potential doctor shopping patients in 2013 (see *Figure* 4-8). More than 99 per cent of persons obtained 100 prescriptions or less and received

200,000 milligrams of OME milligrams over the calendar year of prescribing activity. However, in total volumes obtained the less than one percent of outlying cases accounted for 1.7 per cent of prescriptions dispensed in number and over ten percent of total volume of OME milligrams supplied.

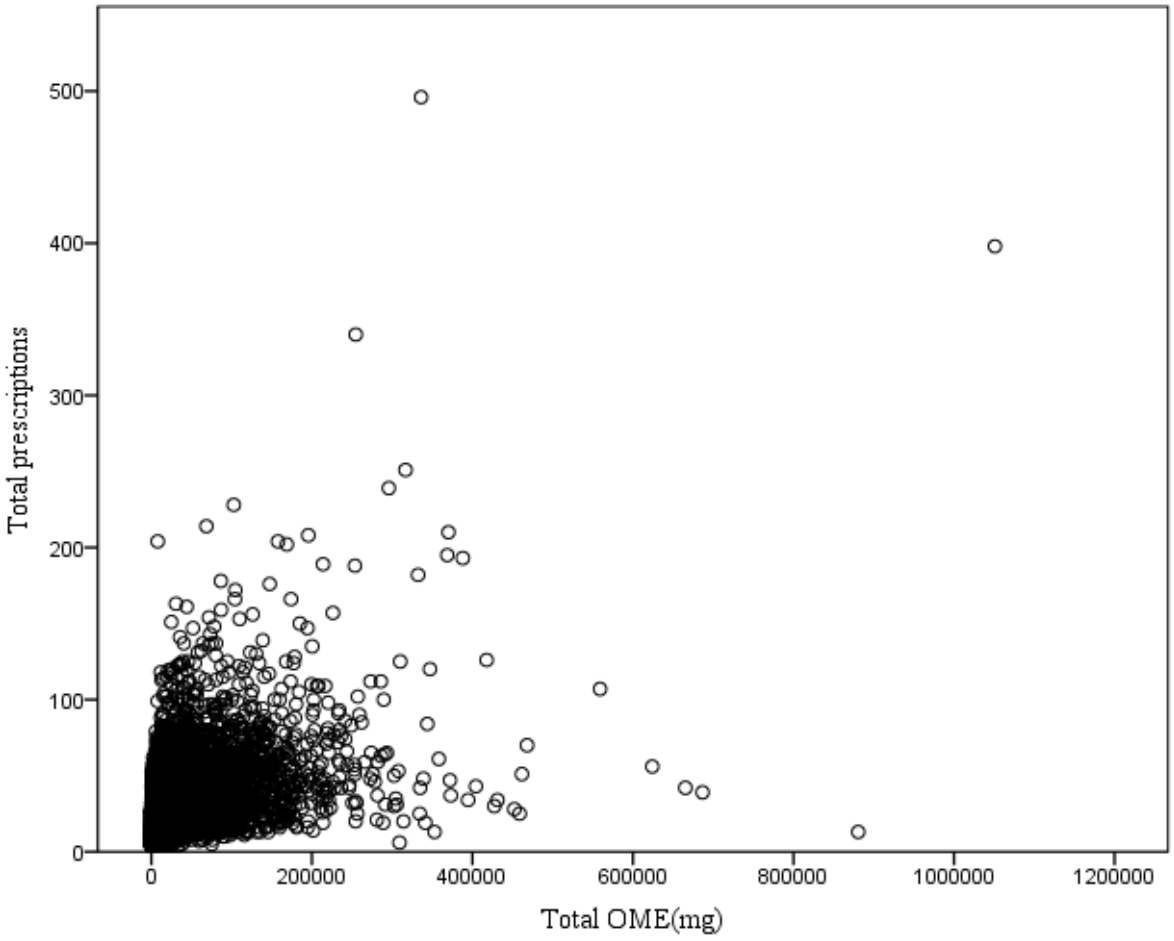

Figure 4-8. *Distribution of total oral morphine equivalent in milligrams by total prescriptions per for full year of 2013 for all potential doctor shopping persons (n=14,378)*

Figure 4-9 below shows the numbers of persons for each mean approximate dose levels for all 'Unclassified' persons for all quarters where POA drugs dispensed in 2013. 80.7% of 'Unclassified' persons received low-level doses (less than 100mg OME) of POA drugs for all quarters they were dispensed prescriptions in 2013. 80.7% of Unclassified persons received on average 100 milligram or less per day of POA drugs, this accounted for almost two-thirds of all prescriptions dispensed (65.2%) but less than one-third of volume of OME milligrams (28.1%). For those 8.6% of Unclassified persons consuming on average over 200 milligrams OME per day, this

accounted for almost one-fifth of all prescriptions (18.2%) and almost one-half of the volume of OME milligrams (49.5%) dispensed.

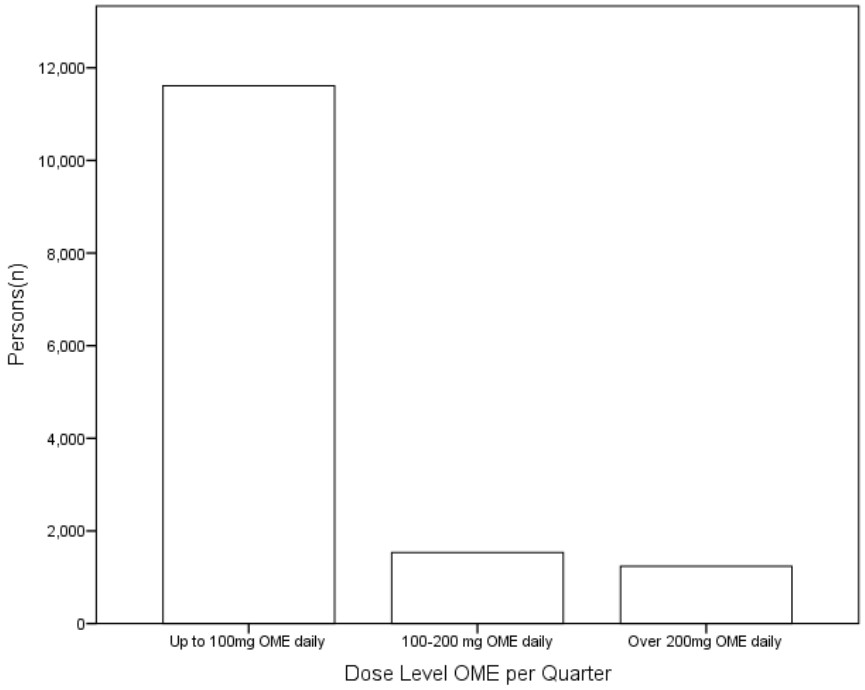

Figure 4-9. Histogram of frequency of persons mean dose level OME(mg) for all quarters dispensed for Unclassified population (n=14,378)

Table 4.24 below shows means and standard deviations for all prescription level variables of interest and Table 4.25 shows the skewness and kurtosis description of each variable. For this sub-population, each person seems to be being prescribed for three-quarters of the year but only doctor shopping for 1.3 quarters of the year.

Table 4.24

Means of variables of interest – Unclassified population (n=14,378)

Variable	Mean	SD
Total quarters prescribed	3.01	1.16
Total quarters doctor shopped	1.34	0.67

Table 4.25

Skewness and kurtosis –variables of interest – Unclassified population (n=14,378)

Variable	Skewness	SE Skew	Kurtosis	SE Kurt
Total quarters prescribed	-0.65	0.02	-1.14	0.04
Total quarters doctor shopped	2.08	0.20	3.92	0.04

The distribution of frequencies of quarters in which persons doctor shopped was negatively skewed. *Figure* 4-6 shows the numbers of persons by frequency of quarters doctor shopped in 2013. Most unclassified persons appeared to have only met a doctor shopping criteria in any one quarter of 2013 and fewer persons doctor shopped in two quarters, and less in three and four quarters.

The distribution of frequencies of quarters a person is prescribed POA drugs are positively skewed, such that most persons appear to be receiving prescriptions across all four quarters, with similar numbers of persons receiving prescriptions in one, two or three quarters (see *Figure* 4-7).

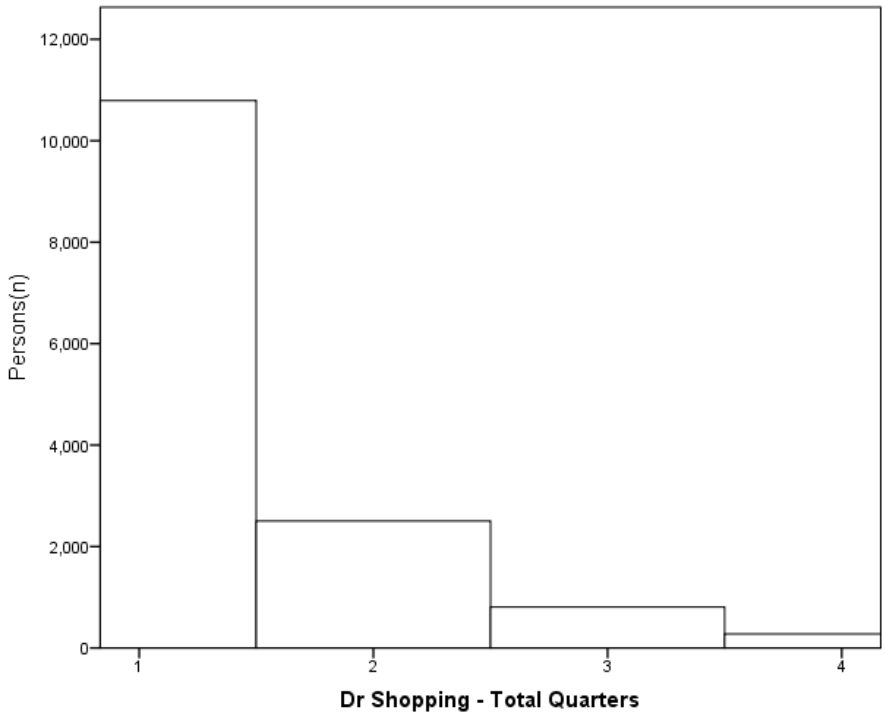

Figure 4-10. Histogram quarters doctor shopped for Unclassified population (n=14,378)

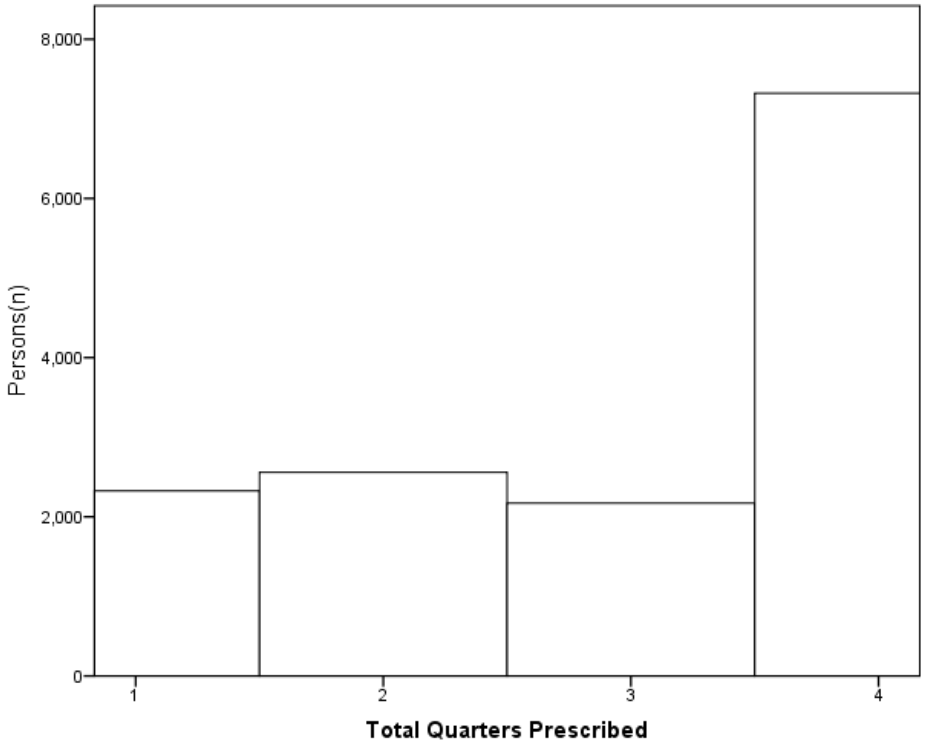

Figure 4-11. Histogram quarters dispensed for Unclassified population (n=14,378)

Table 4.26 reports the correlations between all variables of interest and shows that all variables are significantly correlated with each other. The highest correlation (.790) is between Mean OME (mg) per quarter and Mean prescriptions per quarter, which is an expected relationship. However, there are two negative correlations between mean quarters prescribed and mean prescribers per quarter (-.423) and mean dispensers per quarter (-.093). This suggests as prescribing becomes more frequent, numbers of unique prescribers and dispensers reduces.

Table 4.26

Bivariate correlations for all variables of interest – Unclassified population for all possible Queensland doctor shoppers in 2013 (n=14,378)

	Variable	1	2	3	4	5	6
1	Mean prescribers per quarter						
2	Mean prescriptions per quarter	0.284					
3	Mean dispensers per quarter	0.503	0.341				
4	Mean OME (mg) per quarter	0.113	0.790	0.180			
5	Mean quarters prescribed	-0.423	0.151	-0.093	0.185		
6	Mean quarter doctor shopped	0.368	0.320	0.216	0.193	0.318	

Note: All correlations are significant p<0.01 (2-tailed)

The description of the above variables of interest suggests some violations of the assumptions of normality for all continuous variables and lack of independence between variables. The variables of prescriptions, prescribers, dispensers, mean OME (mg) consumed appear to be highly-kurtosed and negatively skewed. This shows that the majority of cases in this population have low values, suggesting most cases might not represent aberrant patterns of use. There are a small number of extreme outliers particularly in mean prescriptions and mean OME (mg) consumed.

4.4.9 Doctor-shopping cluster analysis

The reporting of the Cluster Analysis following is based the recommendations of (Clatworthy, Buick, Hankins, Weinman, & Horne, 2005) for use of the technique in health psychology studies. Clatworthy et al (2005) suggested reporting on the computer program, the similarity measure, the cluster method, the procedure use to determine the number of clusters and the evidence for the validity of clusters. The full output of the SPSS for Windows two- step cluster analysis is reported in Appendix H.

The similarity measure chosen the 'log-likelihood' which is named 'distance measure' in IBM SPSS for Windows (IBM Corporation, 2011). Two similarity measures are available 'log likelihood' and 'Euclidean'. Clatworthy et al (2005) recommend squared Euclidean distance as the optimal distance measure to use in cluster analysis where groupings might be based on elevation of scores. However, Norusis et al (2008) state that if analysis included continuous and categorical variables then only 'log-likelihood' distance measure can be used. This analysis then used 'log likelihood' distance measure for the operation of the cluster analysis.

The cluster method chosen was the 2 Step Cluster Analysis in SPSS For Windows (REF) option under Classification methods. Two other cluster analysis methods, Hierarchical and K-Means are also available as options in SPSS for Windows (IBM Corporation, 2011). The 2 Step Cluster Analysis is the only method that can form

clusters where the variables are a mix of continuous and categorical (Norusis, 2008) as is the case with this study. As such the 2 Step Cluster Analysis method was chosen as the most appropriate means of analysis.

The 2 Step Cluster Analysis method in SPSS allows for user to set a maximum upper limit of the number of clusters, or specify a fixed number of clusters. SPSS also includes two options for clustering criteria for assessing the cluster model's fit to the data, Bayesian and Akaike Information Criterion. The 2 Step Cluster Analysis was run using both Information Criterion and there were no differences in models generated, so the default settings of Bayesian Information Criterion was retained and reported on in the following results.

The 2 Step Cluster Analysis also allows for continuous variables to be standardised if they have different scales and means. The analysis was run with standardised and non-standardised continuous variables, and the same cluster models was produced. Standardisation of the continuous variables is the default setting, and as such was retained and the following reported results are based on this setting.

Treatment of outliers can also be undertaken in the 2 Step Cluster Analysis and it is anticipated outliers will exist in the study population and could have an undue influence on cluster models formed. In IBM SPSS for Windows outliers can be nominated at as certain percentage level and this can lead to creation of a particular cluster for those outliers. The analysis was undertaken with outliers, with percentages set at the top five, ten and 20 per cent levels. This is lead to solutions with a large number of clusters between six and ten, and all reported as 'poor' solutions on cluster quality measure of cohesions and separation. Furthermore, no clusters in these solutions were found to be good representations of outliers in any of the contributing variables. As such no treatment for outliers was undertaken as per the default settings of the analysis and the reporting on the results following reflects this.

The validity of the cluster structure was tested by randomly diving the data set in two halves and repeating the cluster analysis as suggested by Clatworthy and others (2005). This testing was undertaken and reported the same outcomes in terms of cluster models for example population half sample.

The cluster analysis produced two distinct groups based on the seven prescription activities on the salient characteristic of each group: non-aberrant and aberrant POA drug use groups. Table 4.27 below sets out the difference between both clusters on variables of interest. The largest cluster, the normal POA drug-use group, consisted of 11,536 persons (80.2% of the unclassified persons) and has more females than males. As the group name suggests, this group has lower levels of POA drug activity and consumption across all variables, particularly in mean volume of prescriptions dispensed and POA drugs consumed per quarter which equated to low-level POA drug consumption of less than 100 milligrams OME per day. This group was named the 'Non-aberrant' group for further descriptive purposes and discussion.

The total population (n=11,536) of the non-aberrant use cluster all were in the low mean dose level per quarter dispensed; whereas the aberrant use clusters were predominantly spread in the medium-level, 1,533 (53.9%), and high-level doses, 12,355 (43.5%), with only 74 persons (2.6%) within the low dose group

Table 4.27

Differences in POA drug prescription use and demographic variable for all potential 'Unclassified' doctor shoppers by two-step cluster solutions (n=14,378)

	Normal use (n=11,536)			**Aberrant use** (n=2,842)			**Test statistic**	
POA drug prescription use							F	
Prescriptions per quarter								
Mean & SD	5.95	±	2.96	11.52	±	7.59	3,834.04	**
Range	1.75	-	29.00	2.5	-	124		
Prescribers per quarter								
Mean & SD	2.52	±	.78	2.74	±	1.42	119.67	**
Range	1.57	-	7.0	1.5	-	29.5		
Dispensers per quarter								
Mean & SD	1.72	±	.82	2.17	±	1.56	441.29	**
Range	1.0	-	7.0	1.0	-	29.75		
OME (mg) per quarter								
Mean & SD	2,365.43	±	2260.93	21,696.37	±	17,457.99	13,245.06	**
Range	12.60	-	9,020	636.48	-	262,735.50		
Quarters doctor shopped								
Mean & SD	1.27	±	.59	1.63	±	.88	674.23	**
Range	1	-	4	1	-	4		
Quarters obtained prescriptions								
Mean & SD	2.88	±	1.17	3.52	±	.92	725.905	**
Range	1	-	4	1	-	4		

Demographic characteristics						
Gender						
Females	6157		(55.9%)	1288		(46.3%)
Males	4854		(44.1%)	1495		(53.7%)
Mean age	56	±	15	52	±	14
Range	18	-	80	19	-	80

**p <.001

The smaller group comprises 2,832 persons (approximately 20% of the unclassified persons, 1.3% of the Queensland population that received POA drugs, and 0.09% of the Queensland population aged 18-80 years). This group has higher levels of POA drug activity and consumption across all variables, particularly in mean volume of prescriptions dispensed and POA drugs consumed per quarter, which equated to a high level POA drug consumption of greater than 200 milligrams OME per day. This group was named the 'Aberrant' group for further descriptive purposes and discussion.

For all of the variables of the study there were significant differences between the Aberrant and Non-aberrant clusters. However, there appeared small differences between both groups on variables of prescribers and dispensers, with less than a single prescriber or dispenser difference between either group on average. However, there is a far higher maximum range for dispensers and prescribers in the Aberrant group, suggesting there might be statistical outliers in this cluster. There were more distinct differences between both groups in the numbers of prescriptions dispensed and milligrams OME consumed per quarter. The Aberrant group appeared to obtain almost twice as many prescriptions and consume more than nine times the volume of POA drugs than those persons in the Non-aberrant cluster.

Overall, the Aberrant group, although only 20% of potential unclassified doctor shoppers, accounted for over one-third of all prescriptions dispensed and almost three-quarters of the POA drugs by milligrams OME consumed (see Table 4.28).

Table 4.28

POA drug prescriptions by volume and OME (mg) dispensed for *Unclassified population by two-step Cluster solutions (n=14,378)*

	Non-aberrant (n=11,536)		Aberrant (n=2,842)		Total
Total prescriptions	201,386.00	63.5%	115,780.00	36.5%	317,166.00
Total OME (mg)	83,461,962.61	27.7%	218,163,915.75	72.3%	301,625,878.36

Further examination of the approximate classification of the average daily dosage of POA drugs across all quarters dispensed in 2013 for both clusters is shown in *Figure* 4-12 below. This demonstrates that all persons in the Non-aberrant cluster were categorised as persons consuming less than 100 milligrams OME per day. For the Aberrant cluster almost all persons were classed as either medium (100-200mg/day) or high (>200mg/day) dosage consumers of POA drugs.

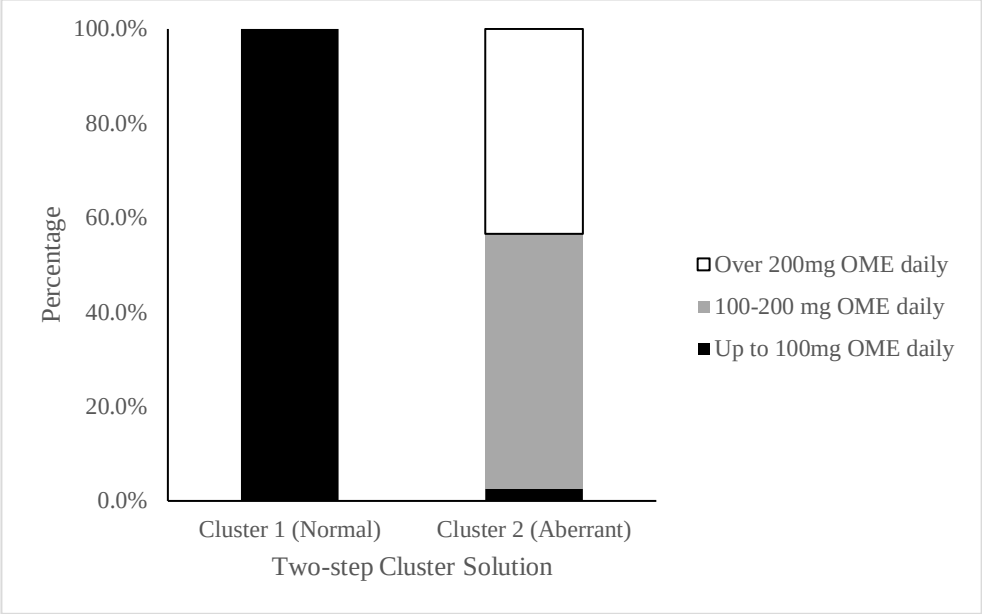

Figure 4-12. Percentage of persons for each cluster identified in the Cluster Solution classified by their approximate daily dose levels of POA drugs for Unclassified population (n=14,378)

Table 4.29

Total quarters doctor shopped x all quarters dispensed for all persons in Cluster 2 (Aberrant users) for *Unclassified population by Two-step Cluster solutions (n=2,842)*

		Quarters dispensed				
		1	2	3	4	Total
Quarters doctor shopped	1	203	170	146	1137	1656
		7.1%	6.0%	5.1%	40.0%	
	2	-	79	75	578	732
		-	2.8%	2.6%	20.3%	
	3	-	-	42	258	300
		-	-	1.5%	9.1%	
	4	-	-	-	154	154
		-	-	-	5.4%	
	Total	203	249	263	2127	2842

Table 4.30

Total prescriptions dispensed for all persons in Cluster 2 (Aberrant users) for Unclassified population by Two-step Cluster Solutions for all quarters doctor shopped x all quarters dispensed (n=2,842)

		Quarters dispensed				
		1	2	3	4	Total
Quarters doctor shopped	1	2376	3354	3899	46124	55753
		2.1%	2.9%	3.4%	39.8%	
	2	-	2000	2332	28949	33281
		-	1.7%	2.0%	25.0%	
	3	-	-	1832	14614	16446
		-	-	1.6%	12.6%	
	4	-	-	-	10300	10300
		-	-	-	8.9%	
	Total	2376	5354	8063	99987	115780

Table 4.31

Total volume of OME (mg) dispensed for all prescriptions in Cluster 2 (Aberrant users) for *Unclassified population by Two-step Cluster Solutions*

for all quarters doctor shopped x all quarters dispensed (n=2,842)

		Quarters dispensed				
		1	2	3	4	Total
Quarters doctor shopped	1	4117088.07	7607803.10	8273722.66	96858852.31	116857466
		1.9%	3.5%	3.8%	44.4%	
	2	-	3388768.80	4609677.94	52102898.57	60101345.31
		-	1.6%	2.1%	23.9%	
	3	-	-	2514445.32	24112615.94	26627061
		-	-	1.2%	11.1%	
	4	-	-	-	14578043.04	14578043
		-	-	-	6.7%	
	Total	4117088	10996572	15397846	187652410	218163916

4.4.10 Total year figures

The comparisons of the Aberrant and Non-aberrant groups from the Cluster Analysis compared the two groups on details of the prescriptions, prescribers and dispensers averaged over each of the quarters in which they obtained prescriptions. What is not captured is the total numbers of unique prescribers, unique dispensers and total prescriptions for each person over the entire year.

Potentially, a person's average number of unique prescribers consulted per quarter might not reflect the full extent of their consulting of different prescribers or dispensers. For example, a person could be consulting on average five unique prescribers over two quarters. This might represent, at minimum, the same five unique prescribers in both quarters or, at most, 10 different prescribers over the two quarters. This could represent another factor to discriminate Aberrant from Non-aberrant POA drug-obtaining behaviour. This question was further investigated in the dataset of the identified potential doctor shoppers used in the Cluster Analysis.

The PPIDs of Aberrant and Non-aberrant groups were used to extract data from the MODDS database of the total number of unique prescribers and unique dispensers over the entire 2013 calendar year. The total number of prescriptions was already available, based on the sum of prescriptions dispensed in each quarter for each case. Table 4.30 above sets out the details for each group below.

Table 4.32
Total unique prescribers, unique dispensers and prescriptions for three-month periods for Aberrant and Non-aberrant potential doctor shoppers in 2013 (n=14,378).

	Non-aberrant use (n=11,536)			**Aberrant use** (n=2,842)			**Test statistic**	
							F(1,4376)	
Total unique prescribers								
Mean & SD	4.52	±	1.76	5.57	±	3.94	452.318	**
Range	3	-	20	3	-	107		
Total unique dispensers								
Mean & SD	3	±	1.75	3.74	±	3.76	441.29	**
Range	1	-	17	1	-	86		
Total prescriptions								
Mean & SD	17.50	±	12.61	41.76	±	30.99	598.689	**
Range	4	-	106	4	-	496		

Table 4.32 above shows that for each variable of interest, the Aberrant group consulted more unique prescribers, unique dispensers and obtained more prescriptions than the Non-aberrant group across the entire year. The difference between the groups in the number of unique prescribers was just over one prescriber, and in numbers of unique dispensers less than one dispenser. In both cases the range was much greater for the Aberrant groups in both variables.

The most pronounced differences were in the total numbers of prescriptions obtained over the year. The Aberrant group obtained almost 2.5 times the number of prescriptions of the Non-aberrant group. Similarly, with the other variables, the range was much greater in the Aberrant group when compared to the Non-aberrant group.

This result is consistent with the results of the previous study where the two groups were compared on the averages of these variables within each quarter that a person was dispensed a prescription. There were significant but small differences between the Aberrant and Non-Aberrant groups for the numbers of prescribers and dispensers. Further, there was similarity in the significant difference between both groups and the numbers of prescriptions obtained.

4.5 DISCUSSION

This study examined persons in the Queensland population who were prescribed POA drugs in 2013 and met the minimal criteria of doctor shopping in any quarter of that year. Of those persons only those unclassified persons – those without any known history of drug dependence – were further examined to see if their doctor-shopping behaviour – as described in the variables of doctors consulted, prescriptions obtained, dispensers seen and dosages consumed – could allow discrimination of certain sub-populations of use. Of the total persons prescribed opioids in Queensland in 2013, 15,545 persons (71%) met these doctor-shopping criteria in any one quarter.

In terms of prescriptions, these persons were predominantly prescribed oxycodone preparations (65%), morphine preparations (10.3%), fentanyl patches (9.1%) and buprenorphine patches (7.6%). In terms of actual volumes of drugs consumed by OME milligrams, the drug consumption by volume was oxycodone products (60%), morphine products (16.5%), hydromorphone (6%), and methadone (4.6%) with all other POA accounting for the remaining consumption. This matched general population consumption and the overwhelming use of oxycodone products in all groups suggested the type of drug being consumed would not allow for any discrimination amongst users. It is not clear necessarily whether the pre-dominance of the use of oxycodone, morphine and controlled preparations, and their particular characteristics in and off themselves, compare to other POA drugs, have contributed to increasing misuse of POA drugs. There is some evidence of assertive promotion of these preparations, there access under the PBS subsidy being associated with increased use and then increased links to harms (Pilgrim, 2015; Rintoul, Dobbin, & Ozanne-Smith). However, other issues such as disruptions to illicit heroin supplies and there and increased accessibility and availability of controlled release POA drugs over other POA drugs, also appear to be related. Further studies examining patterns of misuse and preference for certain preparation by licit and illicit users using these preparations might be helpful understanding further whether particular qualities of certain POA drugs are more associated with harms., as this does not appear to be assessed at a population level by only examining dispensing data.

The study also examined the frequency of persons prescribing and frequency of doctor shopping over the year to investigate consistency and chronicity of POA drug-use behaviour. In this population, over half the persons received drugs in all quarters of the year, and almost two-thirds were prescribed POA drugs in three or more quarters. In contrast, almost three-quarters of persons demonstrated doctor shopping in only one quarter of the year, with just over 2% of persons' doctor shopping in all four quarters.

When the data was combined to examine the quarters in which persons obtained POA drugs and quarters in which they also doctor shopped it was found that almost 60% of persons had doctor shopped in any two quarters of the year, but were prescribed POA drugs in three or more quarters. This group accounted for over 70% of the prescriptions obtained and over three-quarters of the drugs prescribed by volume of milligrams (OME). A small proportion of persons (2.1%) doctor shopped for all four quarters of the year, accounting for over 5% of prescriptions and almost 6% of volume of OME milligrams dispensed.

Of the total potential doctor-shopping population, 14,378 persons had no recorded history of dependence on the MODDS database either as an OTP patient or under a drug treatment approval with POA drugs. This sub-population was further analysed with the known drug-dependent persons excluded.

A two-step cluster analysis was performed to see what grouping might form out of this sub-population, and the independent variables used were mean numbers of unique prescribers consulted, numbers of prescriptions obtained, numbers of unique dispensers involved in dispensing, and mean volume of milligrams (OME) consumed per quarter dispensed. The results provided two distinct clusters: one cluster of 11,536 persons (80% of the sample) obtained on average approximately 6 prescriptions, saw 2.5 different prescribers, 1.7 different dispensers and consumed a total of almost 2400 mg OME for each quarter. This level of consumption could be approximated to an

average daily dose of less than 100mg OME, which is considered low by clinical standards. This group was named the Non-aberrant group for further reference.

The second cluster of 2,842 persons (20% of the sample) obtained on average approximately 12 prescriptions, saw over 2.5 unique prescribers, were dispensed at 2 unique dispensers, and consumed over 20,000 mg OME for each quarter. This level of consumption suggests an approximate daily dose of over 200mg OME, which is considered high by clinical standards. This group was named the Aberrant group for further reference.

The differences between both groups on all variables were statistically significantly. However, the real differences of note appear to be in prescriptions obtained (in the order of almost 2:1 between the Aberrant and Non-aberrant group) and in volume of drugs in milligrams OME (in the order of 9:1 between the Aberrant and Non-aberrant group). While there were significant differences between persons in the Aberrant and Non-aberrant groups in regard to the numbers of prescribers and dispensers, these were less than whole number differences, making their utility in a PDMP-monitoring context less useful. Furthermore, in both groups, persons appeared to doctor shop at similar frequencies of approximately 1.5 quarters each year, but the Aberrant group appeared be have greater overall long-term prescribing frequency at closer to four quarters in the year, as opposed to the Non-aberrant group of closer to three quarters per year.

When total prescription records are examined, the variable of numbers of different doctors seen in a certain time period does not discriminate different populations of Aberrant and Non-aberrant POA drug recipients. Furthermore, the numbers of different dispensers involved in a person's drug supply does not discriminate Aberrant from Non-aberrant consumers of POA drugs. The results suggest that high-volume prescription and milligrams OME are the most powerful factors in determining Aberrant use. Based on the previous descriptive analysis this suggests that while there are large numbers of potential doctor shoppers for POA drugs

at any time this behaviour is infrequent and often in the context of other unremarkable long-term POA drug obtainings characterised by non-doctor shopping behaviour.

The descriptive results suggest that there is a small percentage, less than one per cent of person that might either on very high doses, obtaining high volumes of prescriptions, or consulting large numbers of different prescribers and dispensers. However, this sub-population was not identified as a distinct group in the cluster analysis. It appears that the outliers are either persons obtaining very high doses or consulting large number of doctors, or dispensers, or obtaining large number of prescriptions. These outliers are outliers on each of the variable of interest and not necessarily extreme cases of persons undertaking high volume doctor shopping. Further examination of these cases would be warranted in future investigations.

These results suggest that in the wider population of persons receiving any POA drugs in a year there are potential doctor shoppers in a small percentage (less than 10%). Of these possible doctor shoppers, approximately 7.5% are recognised as drug dependent via current regulatory processes undertaken by the Department of Health. However, over 90% of the possible doctor shoppers are not recognised as drug dependent. However, it cannot necessarily be assumed these 'unclassified' persons are suffering a SUD related to their POA drug use. Of these unclassified persons, most are consuming POA drugs at low dosages of less than 100mg OME per day and these persons could be considered at low risk of harm and potentially unlikely to be suffering a SUD related to their POA drug use. Almost one-fifth of the unclassified persons, the aberrant group, are consuming POA drugs at high-dose levels, greater than 200mg OME and are potentially at more at risk of harm or a classification of a substance use disorder.

Of the consumers of POA drugs, subsequent investigation of these persons does not suggest they are a homogenous population with high-frequency potential doctor-shopping or drug-seeking behaviour. Approximately three-quarters of this group will only meet the doctor-shopping criteria in any one quarter of the year and most will be routine consumers of POA drugs throughout the rest of the year in manner that would

not meet any criteria for doctor shopping. A small percentage of persons (just over 5%) of this Aberrant group demonstrates some form of potential doctor shopping across all quarters of the year. However, this number represents less than 1% of the total Queensland population receiving POA drugs, and less than 0.5% of the age-matched Queensland population.

The study has certain strengths and weaknesses needing elaboration, and that might support or limit implications drawn from the results. The major strength of this study is that it is a complete population capture of the persons of interest across the entire Queensland community. The information contains details of prescription drug types and volumes and known notifications for persons reported as drug dependent.

The limits to the data set are that it only includes dispensed prescriptions, so unsuccessful attempts to obtain prescriptions are not recorded. There are also no records of persons treatment with POA drugs within hospitals, or outside of Queensland, or in other circumstances such as imprisonment. There is also no mechanism to capture diversion of drugs by persons, however, there appears to be widespread collateral evidence of this (Cicero et al., 2011; Dobbin, 2010b; Hall & Degenhardt, 2007; Hall & Farrell, 2011; Miller & Degenhardt, 2009; National Drug and Alcohol Research Centre, 2012) . The data does not include any clinical or medical diagnoses, so there is no means to confirming person's medical conditions. Also the data does not include other lower scheduled drug use such, as benzodiazepines, or a person's use of over-the-counter drugs, which do appear to be related to greater risk of harms (Dormuth, Miller, Huang, Mamdani, & Juurlink, 2012; Pradel et al., 2010).

The results do not necessarily support the hypothesised subpopulations groupings of long term high volume doctor shopping persons, suggesting drug dependence, nor a short term high volume doctor shopping group suggesting persons who might be abusing POA drugs. The results are perhaps surprising given the assumed existence of a population of doctor shopping persons, and evidence of increased dependence on and diversion of POA drugs. However, the aberrant group identified as high prescription obtaining and high dose consuming persons, seem to

resemble the prescription and consumption patterns of known drug dependent persons within the POA drug using population.

It is possible that those persons who are drug dependent on POA drugs can meet their drug requirements within an established therapeutic relationship with a prescriber, without have to seek alternative sources of drugs. As such this population might be indistinguishable from, or overlap with persistent pain patients on chronic POA drug treatment. A possible interpretation is that these persons are in stable treatment and could be maintained on POA drugs in maintenance regimes not dissimilar to persons maintained in opioid substitution treatments.

It appears that the using doctor shopping behaviour as a proxy for drug seeking behaviour that could be a potential association with a SUD on POA drugs is not supported by this analysis. Perhaps given the complexity of the nature of SUDs and the previous lack of consensus by the experts this is a not unexpected outcome of this study. Furthermore, as PDMPs will most likely only contain dispensing and prescribing event as part of administration of regulatory matters, it is perhaps unlikely they will genuine health information or clinical management tools. The concept of aberrant POA drugs use discussed previously in the Chapter Two (Section 2.6) is perhaps a more relevant consideration for the use of PDMP data. Certainly, potential for individual harms from high dosages and the other potential that within this population is the source of diverted POA drugs is worth considering bringing to the attention of treatment providers and potential enforcement agencies. From a health perspective PDMP data would appear to be best to supplement clinical decision making and could also assist in better assessing risk of harm in individual cases.

Furthermore, it appears that the small proportion of this population on high dose POA drugs over long time periods also account for significant volumes of total drugs being prescribed. There is good evidence of persons reporting illicit use of POA drugs that were not obtained by prescription. Given, the economic incentives to on-sell or divert medications, it is possible there is significant opportunity for diversion of drugs in this population.

4.6 CONCLUSIONS

The results for this study suggest that the analysis of the entire potential doctor-shopping sub-population of Queensland POA drug consumers does not seem to show sub-categories of persons that are high-level doctor shoppers suffering substance use disorders. What the results do suggest is that there is a population of persons who routinely obtain prescriptions from multiple dispensers infrequently and those high POA drug consuming persons are involved in long-term therapeutic relationships with individual prescribers at least across the year of study. That is some persons who appear most of risk of harm are those that obtain more prescriptions and by virtue of that obtaining are consuming higher doses of POA drugs. Most of these persons obtain POA drugs across the year and for most of that time they are in relationships with individual prescribers and not apparently drug seeking. When these persons doctor shop it is for short periods of time and usually for not more than a three-month period.

Within this population there is a low-volume consuming group and high-volume consuming group. The high-volume consuming group is not distinct from the low-volume consuming group in terms of doctor-shopping activity. They are distinct in obtaining greater numbers of prescriptions and consuming larger volumes of POA drugs. The persons consuming drug at these higher volumes, while not apparently doctor shopping more than the low drug consuming persons, do appear to have consumption patterns resembling known drug dependent persons. The overall context suggests both populations are in long-term receipt of POA drugs within 2013. Further investigations on the study of historical prescribing records are undertaken in Study 3 to further describe and examine this phenomenon.

Chapter 5: Study 3 – Prescribing history of doctor shoppers

5.1 INTRODUCTION

The results of Study 2 suggest that aberrant POA drug use is most associated with higher-average daily dosages greater than 100mg per day. Within this sub-population of drug seekers, it is not clear that drug seeking – as defined by seeing multiple doctors and obtaining multiple prescriptions over certain time periods – establishes that a doctor shopping sub-population exists or that drug-seeking behaviour, such as doctor shopping, is a particular feature of this population of aberrant POA drug use.

In Study 2, an initial population of 14,378 possible doctor shoppers had no prior drug dependence records in the MODDS database. Of these, only 2,842 (18.3%) were categorised as aberrant POA drug consumers due to their higher consumption of POA drugs. Furthermore, the results of Study 2 show that long-term prescribing over multiple quarters is more typical for aberrant POA drug users than meeting even a conservative or higher threshold for doctor shopping in more than one quarter of the study year.

The results of Study 2 suggest that aberrant POA drug use is described by high-volume prescription obtaining over longer periods of time. Study 3 seeks to investigate POA drug dispensing in the 10 years prior to 2013 of the 14,378 persons from Study 2 with no notified drug dependence that were identified as potential doctor shoppers (consulted three or more doctors and obtained four or more prescriptions in any three month period of 2013) (see Section 4.2.2 – Page 178). This is to determine what aspects of prior exposure to opioids provide further evidence to discriminate other patterns of POA drug use.

Study 2 examined one year of prescribing records, and it is not apparent if the persons in that study year had long histories of exposure to POA drugs and what, if any, histories they had of potential doctor-shopping behaviour. Further examination of the historical antecedents of these persons' POA drug prescribing might provide further illustrative information.

The long-term POA drug use in persistent pain management is a contentious treatment option. There is limited benefit over certain dose thresholds and limited evidence of effectiveness of long-term treatment (Chou, et al., 2015; Martell, et al., 2007). There is also evidence suggesting there is a greater potential for development of dependence with high doses over the long term (Campbell, et al., 2015; Keller et al., 2012; Martell, et al., 2007). The results of Study 2 demonstrate it is not clear whether persons in 2013 are long-term users of POA drugs or have only recently commenced use. It is also of interest to understand this whether longer use in terms of how persons in Study 2 were classified as aberrant or non-aberrant POA drug users.

It could be hypothesised from current evidence that persons with long-term high-dosage usage of POA drugs over time are likely to have had ongoing use of these drugs at high levels; that is, aberrant group persons are more likely than non-aberrant group persons to have lengthy histories of high-dosage POA drug use. Furthermore, it might be expected that non-aberrant group persons should have shorter histories of POA drug use at lower volumes of consumption.

What is less clear is if doctor shopping is a behaviour might be related to longer term POA drug use for the aberrant and non-aberrant group persons. Potentially persons with long-term histories of high volume POA drugs use might show different patterns of doctor shopping than persons with lower volume POA drug use. These differences might not have been captured in the one year time frame of Study 2. Therefore, it is proposed to examine these relationships and to describe and investigate the POA drug obtainings in the 10 years prior to 2013 for the aberrant and non-aberrant group persons described in Study 2.

5.2 METHODS

Data for Study 3 was extracted from the MODDS database as previously described in Study 2. All 14,378 unclassified persons identified as potential doctor shoppers in Study 2 were used in this study. Summary prescription data for all persons were extracted for the proceeding 10 years: 2003 to 2012. This data extract included numbers of prescriptions obtained, unique prescribing doctors, and unique dispensing pharmacies for each person for each quarter of each of the 10 years to 2013. Noting that over this time only POA dispensed for persons within Queensland would be captured as a previous prescription.

A second extract of all the particular prescription details for the above summary data was then extracted using another Discoverer query. This extract included all the details of drug type and total milligrams dispensed for each prescription identified in the first extract. This included details of the drug type and volume in milligrams for each dispensed prescription. This extract allowed for the calculation of total oral morphine equivalent milligrams (OME (mg)) for each drug type based on the conversion factors used in Study 2 (Nielsen, et al., 2014). This data was then aggregated for each individual case for each person's record and from this a total OME (mg) was calculated for each year where prescriptions were dispensed for those cases.

The above two data files were extracted via Oracle Discoverer queries and then imported as 'comma separated variable' files that were managed in Microsoft Excel for initial data-checking and cleansing. The two Excel files, containing the summary data and the prescription detail data, were then imported to SPSS Version 20.0 (IBM Corporation, 2011). The two SPSS data files containing the summary prescription data and the aggregated OME milligrams data were then merged into a single file and details of each person's cluster assignment from Study 2 was also included.

5.3 RESULTS

5.3.1 Participants

A total of 14,378 persons who were identified as Unclassified persons in Study 2 were included in this study. This included 11,536 persons classified in Cluster 1 (Non-aberrant group) and 2,842 persons classified as Cluster 2 (Aberrant group) in the cluster analysis performed in Study 2. The demographics of this group are reported in Chapter 4. A total of 10,384 persons, just under three-quarters of the total persons, received at least a prior year prescription in the years 2003 to 2012 (7,853 persons: 68.1% of the Non-aberrant group; 2531 persons, 89.1% of the Aberrant group). This left 3,994 persons who received no prior year prescriptions in any of the preceding 10 years. It is noted that for these previous year records that persons in each were selected based on them being identified as possible doctor shoppers in Study 2. Therefore, in the preceding ten years, 2003-2012, they may not have demonstrated any doctor shopping behaviour.

5.3.2 Prescribing by years

The alternative view of the prescribing history of these persons is described by the number of years in which they had been dispensed any POA drugs. A single prescribing event in any quarter of any year would class a person as having been prescribed in that year.

Table 5.1

Persons in Non-aberrant and Aberrant groups classified by number of previous years in POA drugs prescriptions were dispensed (n=14,378)

Year dispensed	Two-Step Cluster Group membership: Non-aberrant		Aberrant		Total	
0	3683	32%	311	11%	3994	28%
1	2588	22%	428	15%	3016	21%
2	1562	14%	322	11%	1884	13%
3	1043	9%	267	9%	1310	9%
4	763	7%	252	9%	1015	7%
5	547	5%	196	7%	743	5%
6	408	4%	176	6%	584	4%
7	254	2%	150	5%	404	3%
8	186	2%	136	5%	322	2%
9	143	1%	146	5%	289	2%
10	359	3%	458	16%	817	6%
Total	11536	100%	2842	100%	14378	100%

Table 5.1 shows the proportions of persons of the Aberrant and Non-aberrant groups who were dispensed POA drug prescriptions by the number of years in which they were dispensed at least one prescription; however, this does not represent immediate sequential years, but only indicates the number of years in which a dispensing event occurred. For example, a person who has received a prescription in one other year (Years prescribed = 1) could have been dispensed a POA drug in any of the last 10 years. There were 3,994 persons who were shown as never having received a prescription in any of the previous 10 years to 2013 (Non-aberrant, n=3,683; Aberrant, n=311).

Of the Non-aberrant group persons, approximately one-quarter (22%) received a prescription in one year of the 10 years prior to the study, and over half (57%) in up to five other years. With the Aberrant group persons, over one-third (35%) received prescriptions in one to three years across 2003 to 2012. However, 16% (n=458) had been dispensed prescriptions for all of the 10 years prior to 2013.

Figure 5-1 represents this information graphically. Trends based on the number of other years where persons had been dispensed prescriptions from 2003 to 2012 show different distributions for the Non-aberrant and Aberrant groups. The Non-aberrant group appears to showing a diminishing trend of prescribing from greatest proportion of persons obtaining prescriptions in few other years. For the Aberrant group the distribution appears almost bi-modal with similar proportions of persons obtaining prescriptions in either one or ten other years.

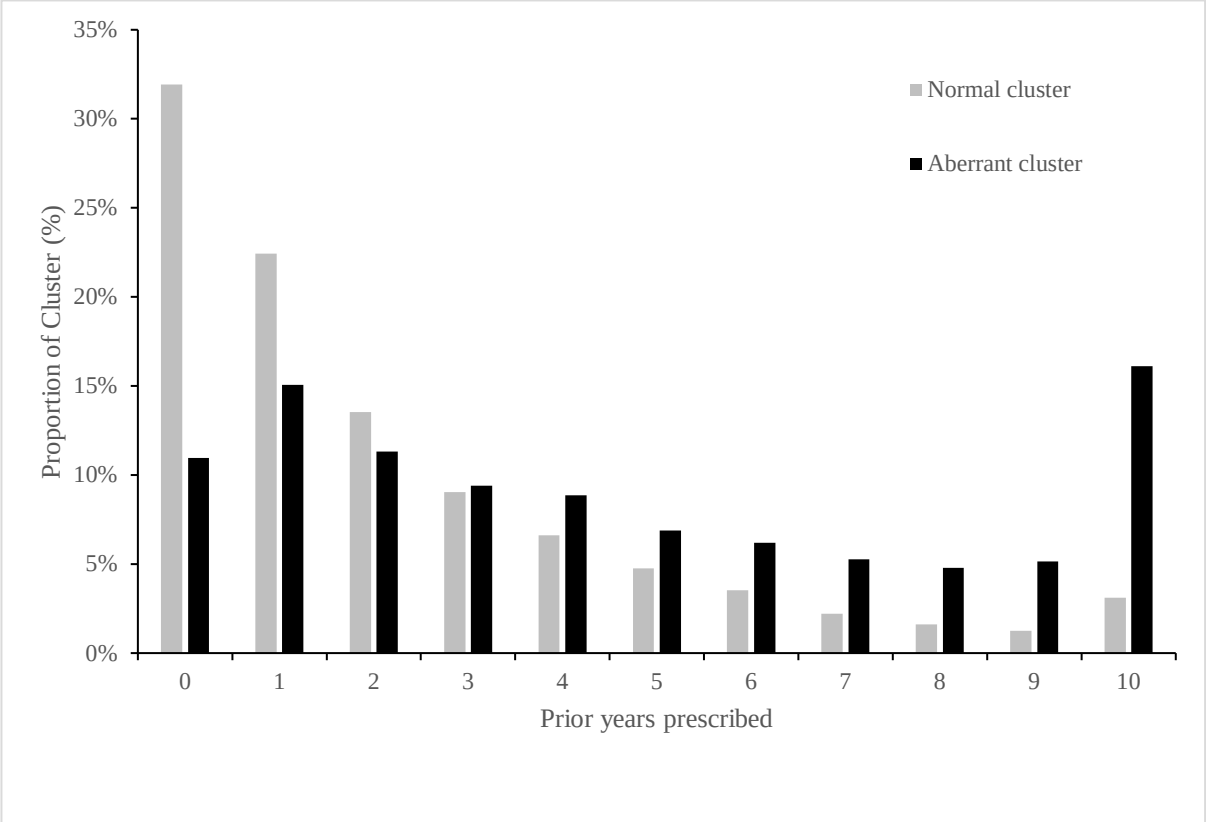

Figure 5-1. Proportion of persons in Non-aberrant and Aberrant groups by number of prior year in which they were dispensed POA drug prescriptions for years 2003-2012. (n=14.378)

Table 5.2 shows the gender for each category of years dispensed for each cluster. For the Non-aberrant group persons there appears similar proportions of males and females over number of prior years prescribed reflecting the increasing trend from 10 years to nil years of prior prescribing.

Table 5.2

Persons in Non-aberrant and Aberrant groups classified by number of previous years of POA drug prescribing and gender, with proportion of each gender shown for each group (n=13,794)

	Group membership							
Years	Non-aberrant				Aberrant			
prescribed	Female	(%)	Male	(%)	Female	(%)	Male	(%)
0	1728	(28.1%)	1575	(32.4%)	122	(9.5%)	152	(10.2%)
1	1371	(22.3%)	1114	(23.0%)	201	(15.6%)	213	(14.2%)
2	849	(13.8%)	679	(14.0%)	132	(10.2%)	185	(12.4%)
3	608	(9.9%)	431	(8.9%)	131	(10.2%)	133	(8.9%)
4	464	(7.5%)	297	(6.1%)	93	(7.2%)	159	(10.6%)
5	318	(5.2%)	229	(4.7%)	87	(6.8%)	109	(7.3%)
6	252	(4.1%)	154	(3.2%)	89	(6.9%)	87	(5.8%)
7	160	(2.6%)	94	(1.9%)	78	(6.1%)	72	(4.8%)
8	117	(1.9%)	69	(1.4%)	71	(5.5%)	65	(4.3%)
9	85	(1.4%)	58	(1.2%)	76	(5.9%)	70	(4.7%)
10	205	(3.3%)	154	(3.2%)	208	(16.1%)	250	(16.7%)
Total	6157		4854		1288		1495	

Note: 584 cases missing gender details

Table 5.3

Age of persons in Non-aberrant and Aberrant groups classified by number of previous years of POA drug prescribing (n=13,197)

Years prescribed	Two-step Cluster - Group membership					
	Non-aberrant			Aberrant		
	Age (years)	(SD)	n	Age (years)	(SD)	n
0	54.3	(16.0)	3059	51.6	(15.1)	285
1	55.7	(15.5)	2296	52.3	(14.6)	396
2	56.3	(15.6)	1452	49.8	(14.9)	310
3	57.3	(15.3)	997	49.3	(14.2)	262
4	57.3	(14.3)	742	49.9	(12.4)	250
5	58.1	(14.0)	540	50.5	(13.3)	194
6	59.4	(13.6)	408	52.4	(12.7)	176
7	59.3	(12.5)	254	52.8	(13.6)	150
8	58.0	(12.8)	185	53.6	(13.2)	136
9	57.6	(13.0)	143	54.8	(11.4)	146
10	59.0	(11.4)	359	56.1	(10.6)	457
Total	57.0	(14.8)	10435	52.2	(13.3)	2762

Note: 1,181 cases missing age details

5.3.3 Prescribing trends from 2003 to 2012

Table 5.4 and Figure 5-2 below shows the proportion of persons in each cluster that had any or no POA drug prescription dispensed in any of the quarters of the ten years preceding 2013: 2003 to 2012. Note that the percentage totals represent the proportion of persons in that class who were dispensed prescriptions in that calendar year. The totals do not add to 100% as a person can be counted in multiple years if they received prescriptions in different years.

Table 5.4 shows that almost 90% of the Aberrant group (86%) and over half of the Non-aberrant group (59%) received at least one prescription in 2012, the year immediately prior to the study period. In 2003, almost a quarter (22%) of the Aberrant group had been prescribed at least one POA drug prescription but only 6% of the Non-aberrant group had received a prescription.

Table 5.4

Number of persons in Non-aberrant and Aberrant groups classified by year in which they were dispensed any POA drug (2003-2012), (n=14,378)

Year dispensed	Group membership: Non-aberrant (n=11,536)		Aberrant (n=2,842)		Total (n=14,378)	
Nil years	3683	32%	311	11%	3994	27.8%
2003	734	6%	630	22%	1364	9.5%
2004	856	7%	709	25%	1565	10.9%
2005	980	8%	797	28%	1777	12.4%
2006	1278	11%	946	33%	2224	15.5%
2007	1689	15%	1072	38%	2761	19.2%
2008	2159	19%	1234	43%	3393	23.6%
2009	2738	24%	1447	51%	4185	29.1%
2010	3465	30%	1679	59%	5144	35.8%
2011	4565	40%	1991	70%	6556	45.6%
2012	6758	59%	2444	86%	9202	64.0%

Figure 5-2 shows the increasing proportion of persons in both 2103 prescribing groups receiving prescriptions in the previous 10 years. This figure excludes the 3,994 persons who had no record of previous POA prescriptions. For each year there was a greater proportion of Aberrant persons being prescribed POA drugs than Non-aberrant persons. This proportional difference was greatest in 2003, with almost four-fold proportional difference (Non-aberrant 6%: Aberrant 22%), and decreased over each year until 2012.

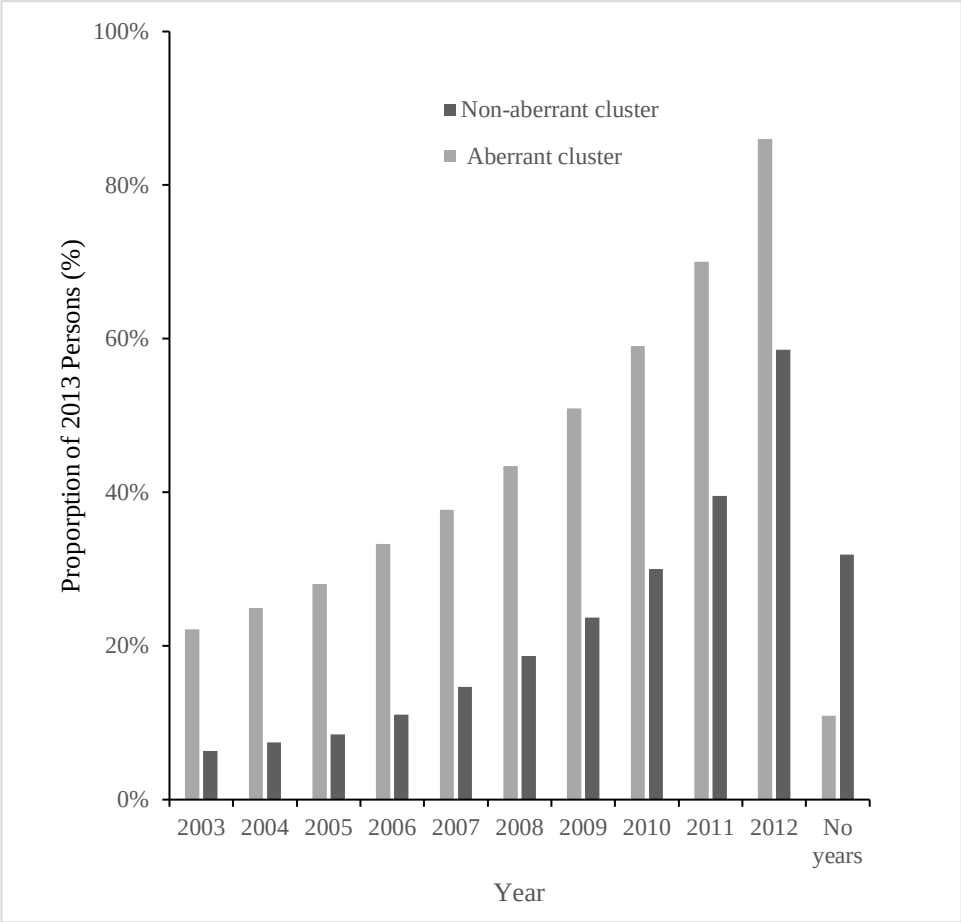

Figure 5-2. Percentage of persons in Non-aberrant and Aberrant groups who were dispensed POA drug prescriptions in 2003-2012 (n=10,384).

Figure 5-2 shows the proportion of persons prescribed in any quarter of the ten years (2003 to 2012) and includes the proportion of persons in each cluster who met the criteria for doctor shopping (consulting three or more doctors and obtaining four or more prescriptions in any three month period) in any of these quarters. With the Aberrant group just over one quarter of persons (27%) met the criteria for doctor shopping in the last quarter of 2012, whereas in the Non-aberrant group 11% of persons met the criteria in the same quarter. In first quarter of 2003, the proportion of persons in ether groups had decreased (Aberrant 3%; Non-aberrant < 1%).

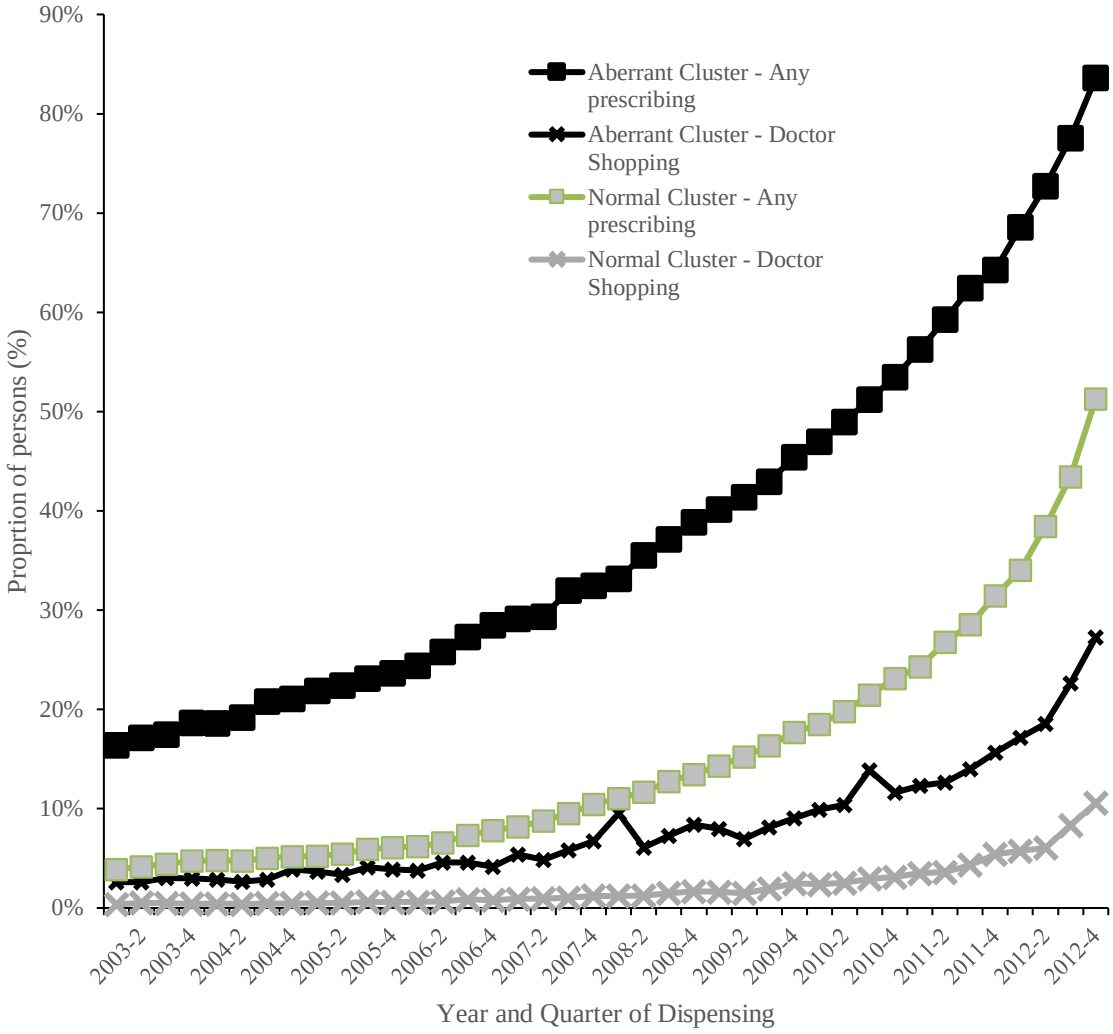

Figure 5-3. Percentage of persons in Non-aberrant and Aberrant groups who were dispensed POA drug prescriptions and persons who met the doctor-shopping criteria in any quarter in years 2003 to 2012 (n=10,384).

These descriptive results show increasing trends in prescriptions dispensed and potential doctor shopping over time, with greater proportions of Aberrant group persons obtaining prescriptions and doctor shopping over the last 10 years. To further compare the Aberrant and Non-Aberrant groups a number of variables used in Study 2 were used to compare prescribing in each of the preceding 10 years to 2013. The variables of mean prescriptions per quarter, mean prescribers per quarter, mean dispensers per quarter and mean Oral Morphine Equivalent milligrams (OME-mg) were calculated for any persons who had POA drugs dispensed in any calendar year from 2003 to 2012.

The full list of means and descriptive data for each of these variables for each group in each year are reported in the Appendix I. Furthermore, one-way ANOVA were performed for each variable set to compare means within each year and these are also reported in Appendix I.

Figure 5-4 shows the mean prescriptions dispensed per quarter for persons in either group who were prescribed POA drugs in a respective year. One-way ANOVAs found significant differences between Aberrant and Non-aberrant persons ($p<.0001$). For the Non-Aberrant persons there appears little change over the last 10 years in prescriptions dispensed per quarter, with a mean of 4.27±4.48 in 2003 and rising to a mean of 4.80±3.57. However, the Aberrant group showed a steady increase from a mean of 7.06±7.84 prescriptions per quarter dispensed in 2003 to 9.68±7.72 prescriptions dispensed per quarter in 2012.

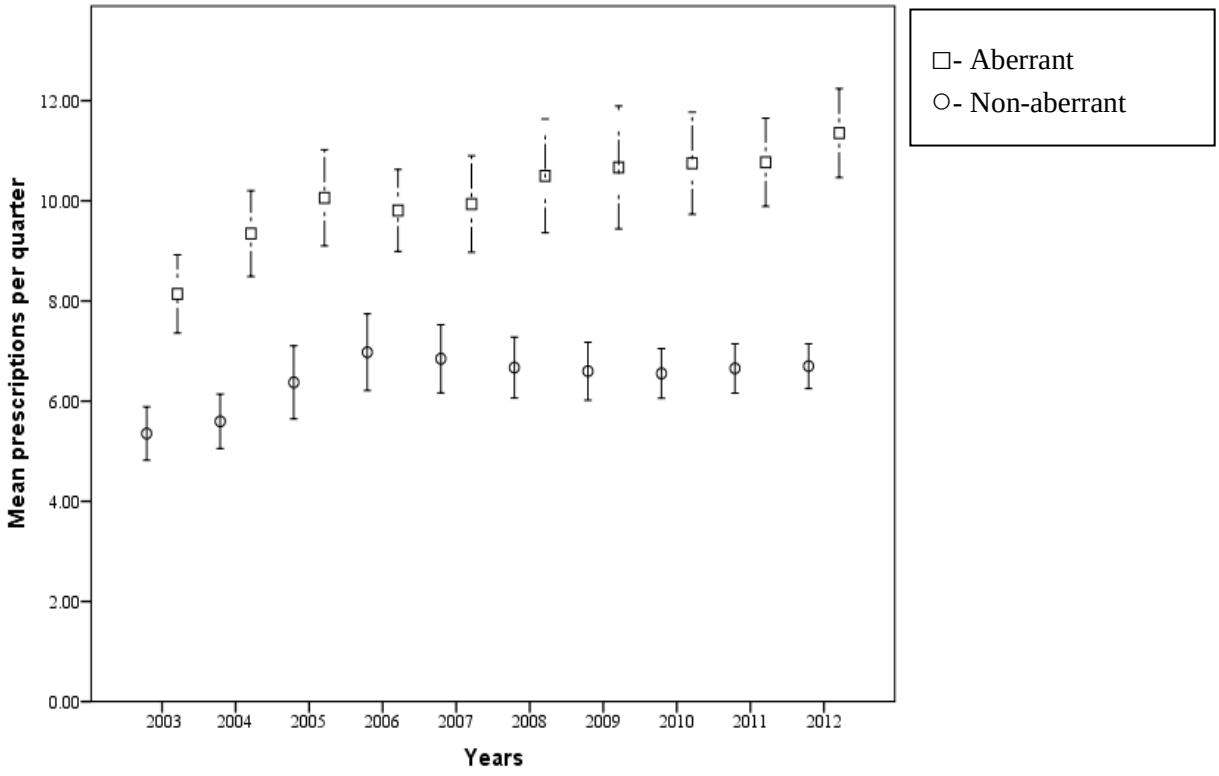

Figure 5-4. Mean prescriptions prescribed per quarter for persons in each group who were dispensed POA drug prescriptions in years 2003-2012 – including 95% Confidence Interval error bars (n=10,384)

Figure 5-5 shows the mean unique precribers involved in prescribing POA drugs per person each year. On average there appears small changes or gradual increases over time for persons in both groups in the mean numbers of unique prescribers seen. However, in 2012 mean numbers of prescribers exceeded two prescibers for the Aberrant group (Mean=2.18±1.42 prescribers). One-way ANOVA did find significant differences between mean prescribers for Aberrant and Non-aberrant persons, at $p<.0001$.

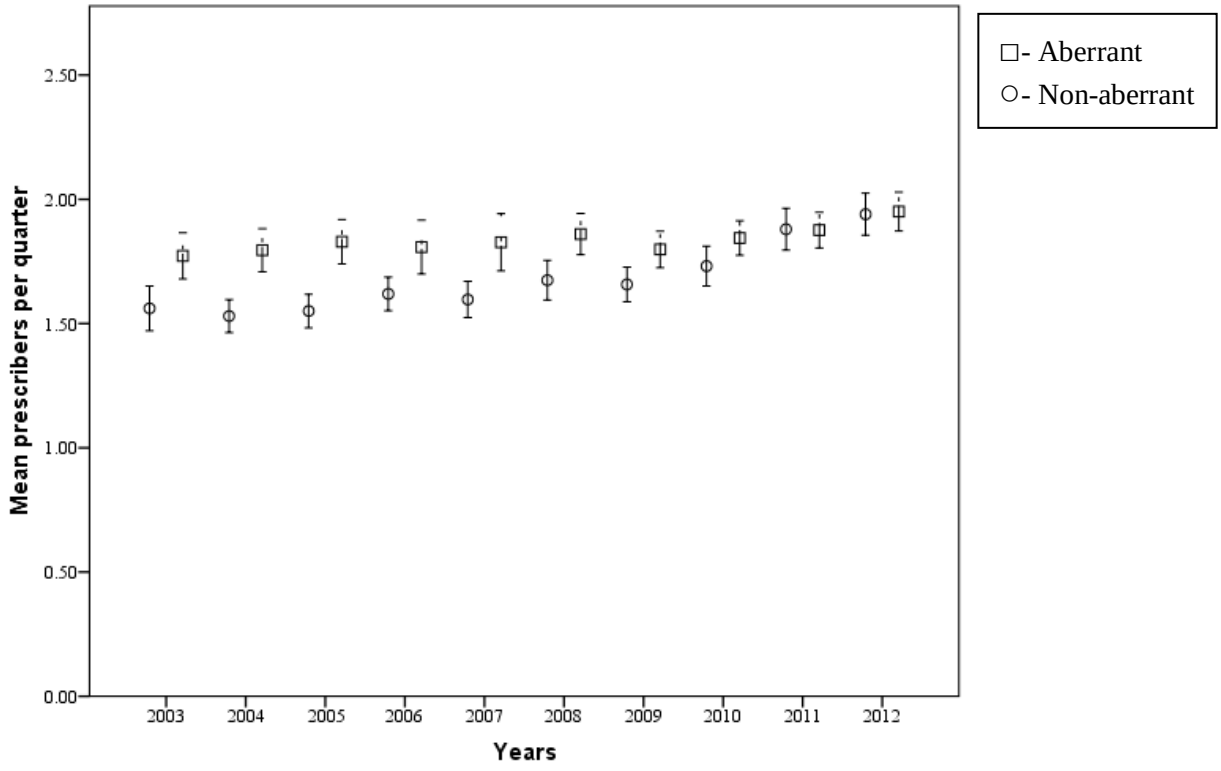

Figure 5-5. Mean unique prescribers who prescribed each quarter for persons in each group who were dispensed POA drug prescriptions in years 2003-2012 – including 95% Confidence Interval error bars (n=10,384)

Figure 5-6 compares the mean unique dispensers per quarter over each year between the Aberrant and Non-aberrant groups. This trends over 10 years show less evidence of increasing over time, and neither group in any one year showed a mean of greater than 2 unique dispensers seen. However, one-way ANOVAs did find that in each year the mean unique dispensers of Aberrant persons was greater than Non-aberrant persons.

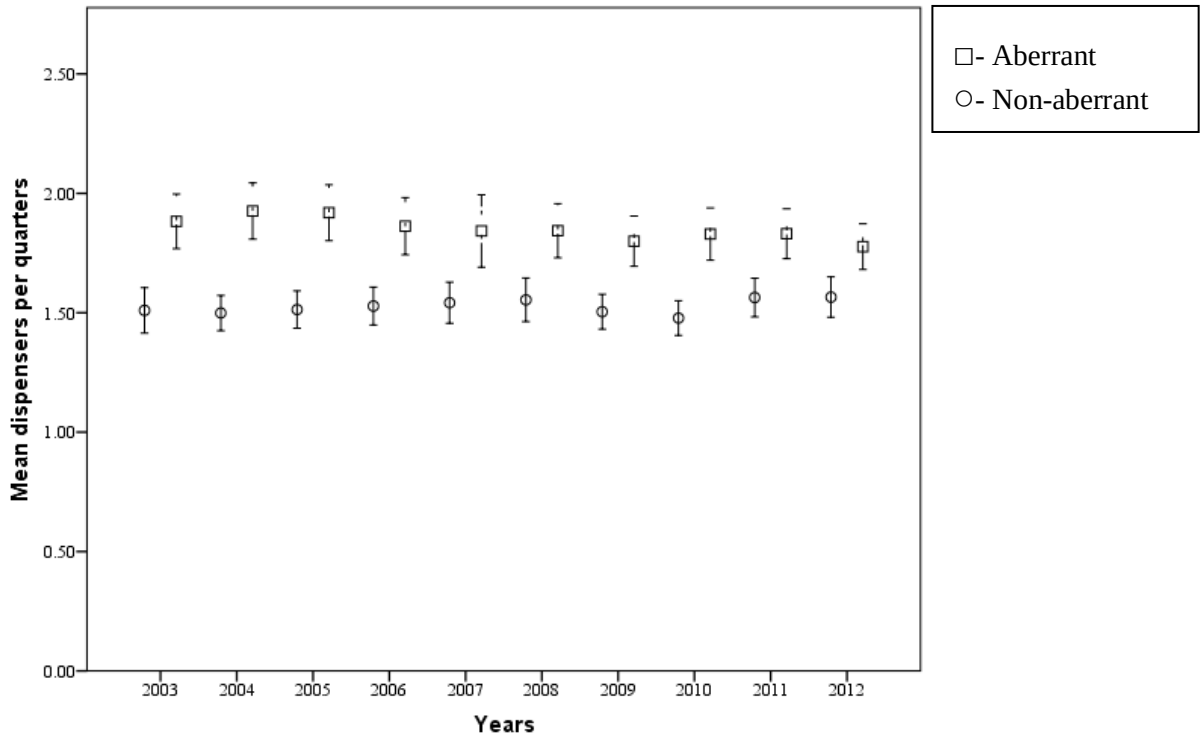

Figure 5-6. Mean unique dispensers who prescribed each quarter for persons in each group who were dispensed POA drug prescriptions in years 2003-2012 – including 95% Confidence Interval error bars (n=10,384)

Figure 5-7 shows the mean OME-mg dispensed per quarter for Aberrant and Non-aberrant persons in each year where persons were dispensed POA drugs. As with the previous variables, one-way ANOVAs revealed significant differences between both groups in each year, at $p<.0001$. The mean OME-mg per quarter in each year dispensed for Non-aberrant persons reduces for these persons over time: starting at 3376.29±6630.53 milligrams in 2003 and reducing to 1998.74±3175.51 milligrams in 2012. In contrast, the Aberrant persons OME-mg dispensed increased steadily over time from over 9000 milligrams in 2003 to over 16,000 milligrams in 2012.

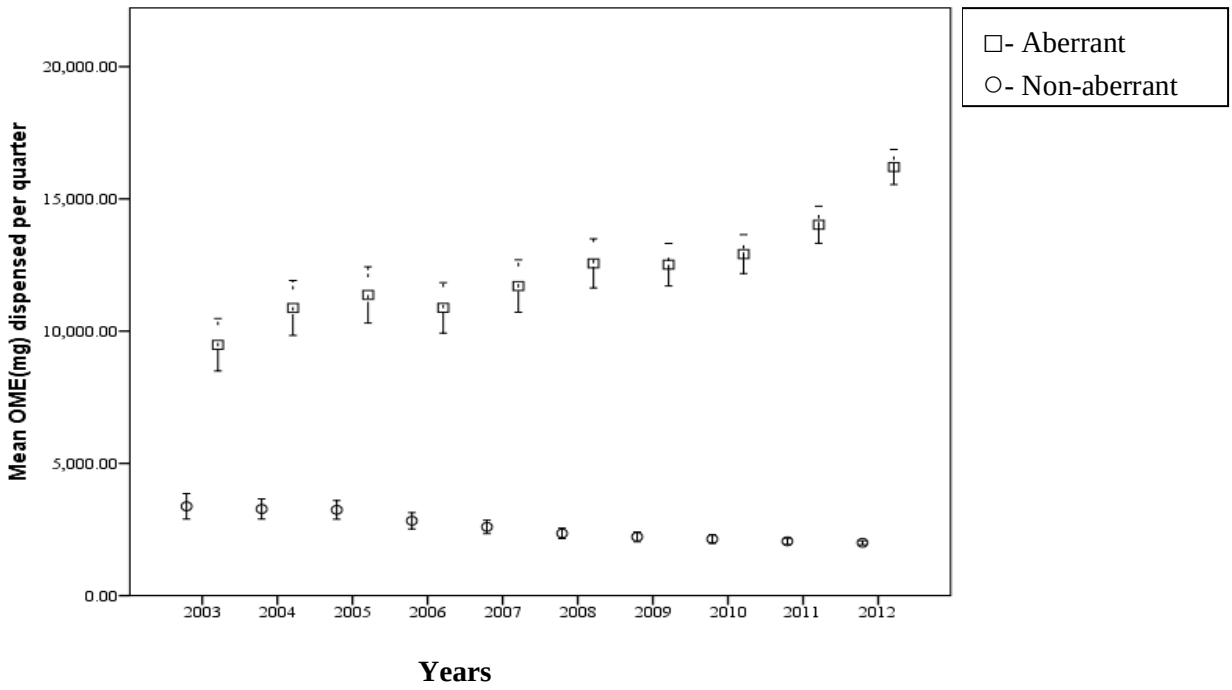

Figure 5-7. Mean Oral Morphine Equivalent milligrams (OME-mg) dispensed each quarter for persons in each cluster who were dispensed POA drug prescriptions in years 2003-2012 – including 95% Confidence Interval error bars (n=10,384).

The mean OME in milligrams per quarter for each year was obtained as per the procedure outlined in Study 2. From this the approximate daily dosage level for all persons' POA drug use could be obtained using the same method from Study 2 to classify a person's estimated drug consumption as either low (less than 100 milligrams per day); medium (between 100 – 200 milligrams per day); or high (greater than 200 milligrams per day).

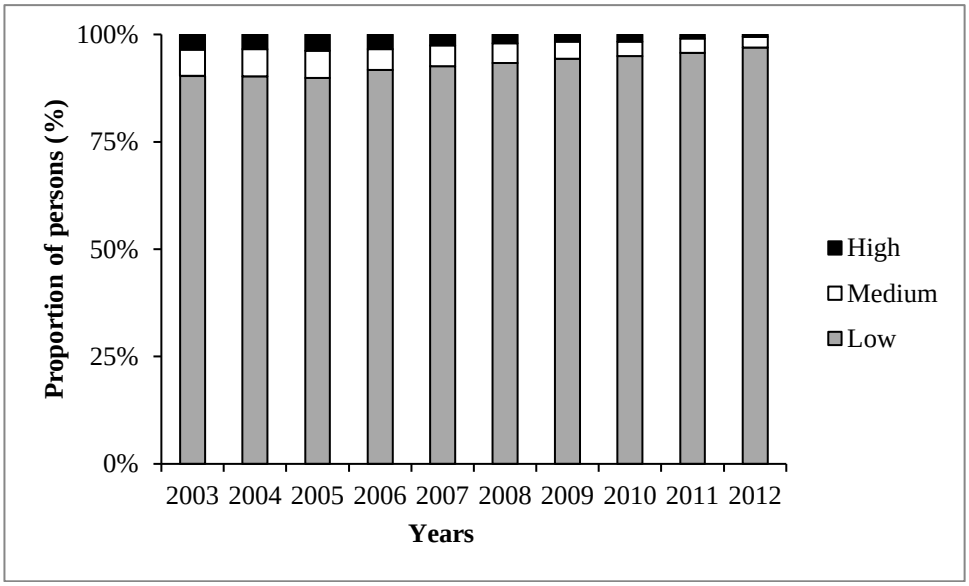

Figure 5-8. Non-aberrant group: Proportion of persons in each dose level of all persons in the Non-aberrant group who were dispensed POA drug prescriptions in years 2003-2012 (n=10,384).

For the Non-aberrant persons shown in *Figure* 5-8 over 90% of all persons were classified in the low dose category. In 2012, this was at the highest proportion of all years at 97%.

For the Aberrant persons shown in *Figure* 5-9 the proportion of persons receiving low doses over the preceding 10 years dropped from 65.8% in 2003 to 37.8% in 2012. The proportions of medium-dose persons and high-dose persons both increased over time and in the same direction such that the proportion of medium-dose persons increased over the same period from 16.5 to 29.8% and proportion of high-dose persons from 17.6 to 32.4%. This means that at 2003 almost two-thirds of Aberrant persons were low-dose consumers of POA drugs, and by 2012 almost two-thirds were medium or high-dose consumers.

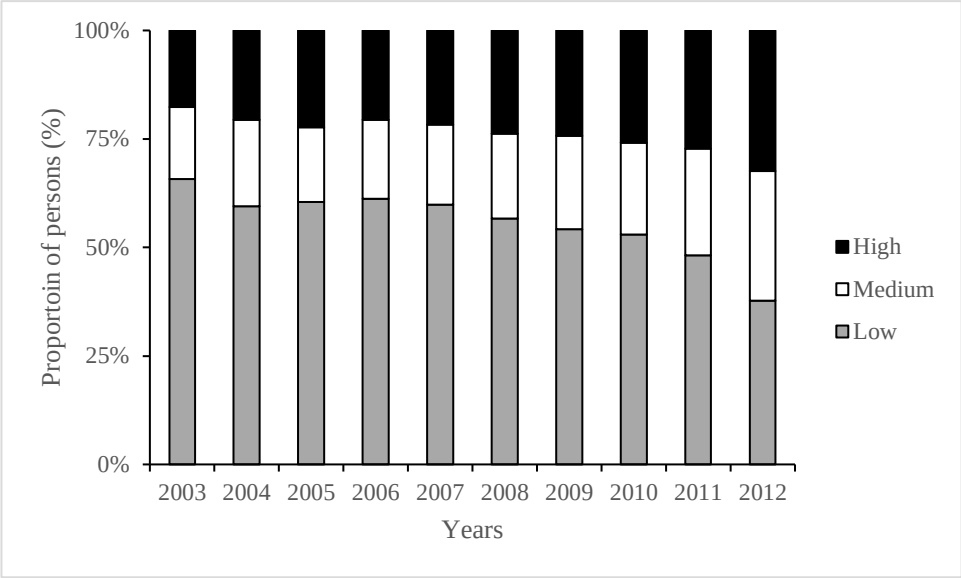

Figure 5-9. Aberrant group: Proportion of persons in each dose level of all persons in the Aberrant group who were dispensed POA drug prescriptions in years 2003-2012 (n=10,384)

5.4 DISCUSSION

This study sought to examine the historical POA drugs-prescribing patterns of the Aberrant and Non-aberrant persons identified in Study 2, which included all potential doctor-shopping persons with no histories of drug dependence. Historical records were extracted for these persons' records for the previous ten years to 2013: 2003 to 2012.

The strength of this study is the access to 10 years of data from the MODDS database to allow extraction of a history of POA drug prescribing for the Unclassified potential doctor shoppers from Study 2. However, further to the limitations from Study 2, another potential limitation is that the records will also not capture out of jurisdiction treatment, hospital inpatient or imprisoned persons and some persons' POA drug information might be incomplete. Also, by only using the sample of persons from Study 2, there is no other context of doctor shopping or POA drug trends for the full POA drug using population in these preceding years. The data extracted for each year was only for those Study 2 identified persons who were dispensed POA drugs any of the 10 previous years. As such analysis of trends and differences between and within Aberrant and Non-Aberrant persons over each year was not attempted as each year's sample potentially represented different subsets of the 2013 study population.

A potential limitation of this study is that there is no comparison within each previous year of prescribing of persons with similar POA drug use obtainings with the identified cohort of 2013 doctor shoppers, or actual doctor shoppers in those years. That is cases selected are already known later doctor shoppers, classed as aberrant or non -aberrant based on previous analyses. Therefore, it is not apparent what the historical course of other POA drug using persons might have taken and how similar or different they might be to the 2013 cohort of this study.

Furthermore, the previous Study 2 identified small numbers of outliers on variables of interest that were not doctor shoppers (see Section 4.4.8, Page153). The potential influence of outliers is unlikely given these results however it has not been able to tested for given the methods of data extraction.

In examining the numbers of previous years dispensings of POA drugs, it should be noted that almost one-third of all persons had no prior prescribings, and most of these persons were from the Non-aberrant group. For those persons with one and two years of previous prescribings, greater portions of the Non-aberrant persons than Aberrant persons were represented in these years. However, for three or more years of previous prescribings, at each year there were more Aberrant persons and there was a larger proportion of Aberrant persons (16%) prescribed for 10 years compared to only 3% of Non-aberrant persons. This suggests that for most of the Non-aberrant persons they only had a prior prescription history of up to three years, whereas the Aberrant persons had a far more varied and extensive history spread over the prior 10 years.

Examining the actual calendar years in which prescribing occurred showed that proportionally over a quarter of persons received prescriptions in the years 2009 to 2012, with fewer persons obtaining prescriptions in the earlier years of the prior decade. In contrast, the Aberrant persons showed great proportions of persons receiving prescriptions in all years, with almost a quarter of all persons having been prescribed in 2003, 10 years prior to the study period.

An assessment of potential doctor shopping also found there was limited evidence of historical doctor shopping for the Non-aberrant persons. However, for the Aberrant persons there was increasing evidence of doctor shopping. These results suggest a longer history of POA drug use for the Aberrant persons that extends over 10 years for a significant proportion of those persons. The Non-aberrant persons in comparison seem to have most persons experiencing limited prior year prescribing of POA drugs and most of that has occurred in the past three years.

The Aberrant and Non-aberrant persons were compared on the variables of unique doctors consulted, prescriptions obtained, unique dispensers seen, and volume of drugs consumed by milligrams OME on average per quarter prescribed within each calendar year. For each year there is limited separation in dispensers and prescriptions between the two groups. However, in terms of prescriptions obtained there were clearer differences. The Non-aberrant persons saw similar numbers of prescribers to the Aberrant persons, with no differences shown over the previous ten years, 2003 to 2012. In contrast, the Aberrant persons obtained increasing prescriptions over time in comparison to the non-Aberrant persons.

A similar pattern was evident with milligrams OME consumed in each quarter of the year prescribed from 2003 to 2012. The consumption of the Non-aberrant persons who received any POA drugs in the preceding 10 years on average remained at very low levels and appears to decrease leading up to 2103. In comparison, the Aberrant group persons' consumption increased steadily in the years approaching 2013. Furthermore, across the 10 years most of Aberrant group persons who received POA drugs were in the low category (less than 100mg per day OME). However, there appeared to be increasing proportions of Aberrant group persons in medium (100-200mg per day OME) and high dose (greater than 200 mg per day OME) over the 10 years until 2013.

These results suggest further confirmation of the results of Study 2: that the variable of prescribers and dispensers that indicate doctor shopping do not appear to discriminate between Aberrant and Non-aberrant use over time. However, also in

support of the Study 2 results, prescriptions obtained and volume of drugs consumed appear to be strong discriminatory factors between the two groups. In terms of non-aberrant there is a suggestion here that some persons can be maintained on low doses over long periods of time without evidence of developing problematic use. Alternatively, some persons appear to escalate dosage consistently over time however, they may or may not demonstrate doctor shopping behaviour, but will continue to obtain POA drugs at high dose and be subject to greater risk of harm.

This further suggests that, as was found in the study of persons in 2013, that doctor-shopping behaviour, in terms of ongoing consulting of multiple different doctors, is not a strong indicator of aberrant POA drug use even when historical prescribing trends are considered. Furthermore, as found in Study 2, high volume of prescriptions and high volumes of drug consumed are strong factors indicating aberrant use of POA drugs over time. This has particular implications for regulators and clinicians in moderating prescribing behaviour and managing persons who are in receipt of long-term opioid therapies and these are discussed in the following chapter.

Chapter 6: Discussion

6.1 INTRODUCTION

It is generally accepted that misuse of POA drugs is a significant public health concern in Australia, as well as the USA and Canada. The increasing prescribing of these drugs has led to increased access for many Australians. Increased use of these POA drugs is predominantly for genuine therapeutic pain management needs. However, there remain concerns in regards to over-prescribing, efficacy of long-term treatment for chronic pain, and misuse and diversion of these drugs, as well as the increasing evidence of harms from POA drugs use such as death, overdose, and the development of substance use disorders (SUDs). A particular focus of concern is the issue of 'doctor shopping', where persons obtain multiple prescriptions from multiple prescribers, unbeknownst to each prescriber, for doses in excess of therapeutic needs. POA drugs obtained via doctor shopping are believed to be promoting dependence and abuse in consumers and being diverted into illicit markets for non-therapeutic use.

The aim of this thesis was to identify and investigate doctor-shopping behaviour and examine its potential relationship to the misuse of and development of SUDs, in relation to POA drugs. The objectives of this thesis (see Section 2.9) were seek to develop a definition of doctor shopping through expert consensus, test that definition in a population of persons who had been prescribed POA drugs, investigate if doctor-shopping behaviour could discriminate between aberrant and non-aberrant POA drug use, and examine if there were any means to determine a relationship between doctor shopping and SUDs with POA drugs.

These objectives were articulated in three studies and the outcomes of these are set out in the following three sections. The implications for public health, monitoring and regulation, and individual person's health care are discussed in the final section.

6.2 STUDY 1: DEFINING DOCTOR SHOPPING

Study 1 examined a number of aspects of POA drug misuse and the relationship to SUDs and attempted to establish if some criteria for doctor-shopping behaviour could be agreed on that suggests a person could be suffering from a SUD due to their use of POA drugs. This was done using a Delphi Technique study with a number of experts across the domains of pain management and drug dependence. Experts were given a number of open-ended questions and over two rounds asked to moderate their responses based on the feedback of the collective responses of all expert participants. The intent of this was to use these criteria to test what patterns of POA drug prescribing this describes and whether it discriminates aberrant from non-aberrant POA drug use.

Doctor shopping is a term that is poorly defined in the literature and open to broad range of interpretations and as such has limited utility as a clinical assessment measure. It is not clear what the relationship is between doctor shopping and aberrant POA drug use or a person suffering a SUD. What is also problematic in teasing apart these issues is that many persons receiving POA drugs are doing so for treatment of genuine pain conditions. Leaving aside the question about the efficacy of long-term treatment, it might not always be clear to prescribers when a person on long-term POA drug treatment might have developed or is suffering a SUD. It can reasonably be assumed any persons on long-term treatment POA drug therapy will develop tolerance and suffer withdrawal on cessation or reduction of treatment given the known effects of POA drugs. As such the recognition of SUDs with POA drugs remains a complex matter for treatment providers in primary care settings.

The results of this study suggested there was limited support among experts for highly rating the DSM-IV criteria of tolerance and withdrawal in determining if someone has a SUD on POA drugs. However, much of the importance of the other criteria is problematic when used to determine SUDs on POA drugs as most relate to the use of illicit drugs. This is also an awkward definition, as POA drug use might be approved by a treating doctor in an ongoing manner and there might also be underlying

illness or disease that could equally explain a person's behaviour. Doctor-shopping behaviour might most closely relate to the DSM-IV criteria of 'time spent in obtaining drugs'. However, this was not highly ranked as a criterion for determining POA drugs SUDs by the experts. Furthermore, the amount of drug taken, which could arguably relate to drug seeking, was ranked the lowest of all DSM-IV criteria for determining a SUD. This might also be explained by the low ranking for criteria of tolerance and withdrawal, give than chronic pain patients could be maintained on high doses without meeting a definition of suffering a SUD.

The experts were then asked to set definitional criteria to outline what levels of doctor shopping, in terms of prescriptions, prescribers, dispensers and dose might indicate problematic POA drug use. The first round of responses was mixed, with many experts qualifying their responses by stating any level of use or doctor shopping could be potentially problematic for a particular individual. The second round was modified to ask experts to give green (unproblematic), amber (suspicions of misuse) and red (problematic use) traffic light assessments of the doctor-shopping criteria. The outcomes demonstrated differences between each of the traffic light categories in the expected directions: each variable of doctor-shopping increased from green to amber to red. Also, despite the dosage level of drug being ranked as the lowest of DSM-IV criteria, there were clear differences from the experts in what dosage level is relevant to determine problematic doctor shopping.

A particular conceptual issue in Study 1 was that questions were being asked to clinical experts to reduce their concerns to a set number of particular criteria for use in a database study. A clinical expert might use information about doctor shopping as part of building an assessment of a person's possible SUD. However, it would be unlikely they would rely on that information alone, and an assessment or review would most likely involve considerably more corroborative information before determining a diagnosis of a SUD.

Given the reservations expressed by many of the experts that any amount of doctor shopping would be indicative of problematic behaviour it was decided to use a

definition of doctor shopping that was the most conservative or minimal that might potentially capture potential misuse for investigation in Study 2. Therefore, a definition was established for all potential doctor shoppers (more than three prescriptions and three or more different prescribers within a three-month period) that could potentially detect any level of POA drug use that might constitute doctor shopping. This criterion was established to capture the range of experts' views that suggested any level of doctor shopping could be indicative of POA drug misuse. By setting this conservative level the Study 2 could capture the full population of potentially problematic POA drug use to examine the full extent of possible doctor-shopping definitions.

6.3 STUDY 2: THE DOCTOR SHOPPING POPULATION

Study 2 aimed to apply a doctor-shopping definition to a population of POA drug prescribed persons to identify potential aberrant use that might relate to a person with a SUD. However, Study 1 did not deliver a definitive doctor-shopping definition so the conservative and broad definition of doctor shopping was used to extract any persons who might have met that criteria within any quarter of the study year, 2013. This was to capture any person who at any time in 2013 might have been classified as a doctor shopper.

15,545 persons met these criteria in any one quarter of 2013 and were extracted from MODDS for all possible doctor shoppers in that year. This included all POA drug prescriptions dispensed at any community pharmacy across Queensland. Descriptive analyses of the patterns of POA drug use found that doctor shopping was an infrequent activity, occurring most frequently for only in one quarter of the year for most persons, and this was in the context of long-term prescribing across three or four quarters of the year.

A cluster analysis found there were two distinct sub-groups of persons within this population. There was a group defined as 'Non-aberrant' who were mostly typified by low-volume consumption of POA drugs of less than 100mg (OME) for any quarter. The second or "Aberrant" group was typified by persons consuming POA drugs at

medium levels (100-200mg (OME) per day) or high levels (>200mg (OME) per day) for any quarter.

Between the aberrant and non-aberrant groups there were significant differences in the variables of numbers of prescriptions, unique prescriber and dispenser seen and the approximate dosage of POA drugs obtained. The numbers of prescriptions and volume of POA drugs by OME (mg) seemed to best separate the two clusters statistically and descriptively.

The results of Study 2 suggest that doctor shopping as described in terms of consulting multiple prescribers for multiple prescriptions is evident but is not a defining feature of the aberrant POA drug-using sub-population, aberrant use is better discriminated from non-aberrant use by volumes of POA drugs consumed. However, the aberrant population does appear to be consuming POA drugs at similar levels to known drug dependent persons who are possible doctor shoppers

6.4 STUDY 3: PRESCIBING HISTORY OF DOCTOR SHOPPERS

Study 3 involved the sub-population of 15,545 unclassified persons that were categorised into the aberrant and non-aberrant clusters to describe their previous POA drug prescribing over the 10 years prior to 2013.

The results of Study 3 showed that Aberrant persons obtained POA drugs for longer periods of time and at greater volumes than Non-aberrant persons. Non-aberrant persons, regardless of the length of time over which they might have received POA drugs prior to 2013, rarely consumed these drugs at a high level of greater than approximately 200 milligrams (OME) per day over any quarter of a year in which they were prescribed. In contrast, Aberrant persons who obtained POA drugs were more likely to consume POA drugs at medium (100-200 mg (OME)/day) or high levels in any quarter of a year in which they were prescribed. This proportion of high and medium levels of consumption was also higher in the years closer to 2013.

Across all the years, Aberrant persons received more prescriptions on average per quarter than Non-aberrant persons. This suggests a considerable positive correlation with levels of consumption as might be expected. There appeared statistically significant differences between Aberrant and Non-aberrant persons in each of the 10 years, 2003 to 2012, in terms of numbers of prescribers and dispensers. However, these differences were only in the order of less than one prescriber or dispenser and, considering standard deviations, all showed considerable overlap. Therefore, to use these in PDMPs as variables to potentially discriminate or predict problematic drug-seeking might not have particular utility.

These results suggest the aberrant POA drug use over time is most related to high volume of prescribing and high levels of consumption but not necessarily related to drug-seeking behaviour by seeing multiple different prescribers or dispensers. There were greater levels of doctor shopping over time in Aberrant persons compared to Non-aberrant persons. However, it does not appear that this behaviour is consistent or continued over time for Aberrant persons, and does not appear to allow further discrimination with this group. This suggests that this Aberrant population is characterised by longer-term high-volume POA drug use over time. This population is more likely to show evidence of doctor shopping, but doctor shopping per se was not a particular defining characteristic of this group.

6.5 STRENGTHS AND LIMITATIONS

The thesis and its constituent studies have some strengths and weakness to consider in terms of drawing implications from the results presented. These strengths and weaknesses are discussed as follows.

This thesis is the first study to attempt to develop an expert consensus decision of doctor shopping behaviour for POA drugs and to operationalise a definition of doctor shopping or drug seeking behaviour in a prescription drug monitoring program. Real-time reporting PDMPs are being promoted as front-line regulatory mechanism to seek to moderate prescribing practices of health practitioners. It is important for that the information provided to practitioners is structured in a manner to promote sound

treatment decisions based on population level trends, to ensure POA drug are prescribed or not-prescribed to ensure the best treatment outcomes for patients. This study seeks to begin to help synthesis that information, so that real-time PDMP can add value and not complicate POA drug prescribing decisions.

A major strength of this study is that it is a complete population capture of the persons who are using POA drugs in the Queensland community. The information captured in the MODDS data contains details of prescription drug types and volumes and known notifications for persons reported as drug dependent. Furthermore that information has been recorded in a consistent and reliable manner over the last two decades to allow for maintenance of reliable historical and contemporary records. This data set is used for regulatory purposes so it is subject to quality assurance measures to improve the accuracy of the information, so there is high standard in terms of error checking and matching persons processes to ensure correct information is maintained. The MODDS dataset is also actively in use to provide prescriber information and support regulatory compliance activities of the Department of Health. As such this represents accurately the actual information prescribers are using to make treatment decisions.

Some limitations of these studies need to be considered. In terms of the population of persons of interest, these studies only capture prescriptions of POA drugs that are dispensed in Queensland community pharmacies. There is considerable evidence from multiple studies that persons suffering SUDs will also seek out and use other lesser-controlled opioid drugs, such as over-the-counter codeine and other drug types such as benzodiazepines. Information about a person's obtainings of these other drugs might aid in identifying doctor shoppers who suffer abuse or dependence. Furthermore, a person who is not resident in Queensland, who is incarcerated or has had periods of in-patient hospital care might have obtained treatment with POA drugs not apparent to this study over the course of 2013 in the case of Study 2 (Chapter 4) or over the course of the previous ten year in relation to Study 3 (Chapter 5). However, there is no prima facie reason to suggest that this would be systematically different between the Aberrant and Non-aberrant groups.

While there seems limited evidence of a population of high level doctor shoppers or outliers, this might still warrant further investigation. Other techniques of analysis might also be of assistance here. A facet of aberrant use that this might uncover is the possible differentiation between impaired person seeking POA drugs from multiple doctors from criminal enterprise or persons seek to consciously evade scrutiny by drug seeking in a manner to maximise obtainings without arousing suspicions of treatment providers or regulators. Furthermore, this study can not identify areas of diversion, where POA drugs might be being onsold to other parties. Potentially, this is just as possible in a non-doctor shopping or non-aberrant population, if a person was receiving a greater than therapeutic dose and was sufficiently motivated to divert their dispensed POA drugs.

Another issue is that a person might seek POA drugs from multiple prescribers and might be refused or denied a prescription. It should be noted that dispensed prescriptions only serve as an approximation of drug-seeking behaviour and might underestimate such behaviour as attempts to obtain drugs are not fully captured or are thwarted by diligent prescribers or regulatory mechanisms. For example, in Queensland a prescriber can call a 24-hour enquiry service and obtain a POA drug prescription history. Furthermore, the Department of Health routinely contacts prescribers when its surveillance techniques identify persons who are potential doctor shoppers.

The study population excluded those persons already diagnosed with drug dependence by not including opioid treatment patients and those notified to the Department of Health as drug dependent and thus under regulatory approval. The reason for this was to examine the unclassified population where there had been no controls or influences attempted on a person's drug-seeking behaviour. However, the known drug dependent OTP and approval patients do doctor shop for POA drugs. Further examination of how those persons sought drugs before their diagnoses could be of value.

Furthermore, there is no linkage with death data or treatment outcome data. Therefore, it is not clear for what reasons a patient might cease treatment. It could be

the resolution of a pain condition, hospital admission, a move out of the jurisdiction, death, or other reasons. Lastly, the studies also did not obtain any information about the patient or consumer experience in regard to the reasons they might be consulting multiple prescribers. This is a potential limitation in understanding the reasons why a person might seek alternative or supplementary POA drug treatment. The views and beliefs of patients might also provide further insights into this phenomenon.

6.6 SUMMARY AND RECOMMENDATIONS

The overall conclusion is that it appears that there is not a particular homogenous population of POA drug users characterised by a high level or frequency of doctor shopping behaviour. However, there is a POA drug using population of potentially at risk persons who are receiving high doses of POA drugs and large volumes of prescriptions over long periods of time, and persons in this population might be suffering SUDs. A particular profile or population of doctor shopping persons does not appear to be emergent feature of the POA drug using population in terms of persons consulting multiple doctors or dispensers. These persons have not been considered drug dependent, or reported to authorities as such, by their treating medical practitioner under current regulatory requirements nor have they had prior histories of known treatments for illicit drug use. While doctor shopping exists within this sub-population, it is not a behaviour that appears to be consistent or necessarily associated with aberrant POA drug use.

This overall finding seems at odds with some of the research and clinical literature and popular media that have given particular emphasis to the issue of doctor shopping. As mentioned previously the research literature is still not settled on the extent and implications of doctor shopping and drug seeking behaviour in large populations. The clinical literature is perhaps more focussed on known cases of harm such as POA drug-related deaths and SUDs related to POA drug use in drug treatment settings. Even the association is primarily about exposure to POA drugs, and linking doctor shopping to harms or SUDs is still limited with many findings still reporting substantial associations with diverted POA drugs in drug treatment settings and findings of coronial matters. Furthermore, popular and non-scientific accounts of rampant POA drug use and doctor

shopping, perhaps create an impression of a phenomenon that is more complex and nuanced than is portrayed.

There could be a variety of explanations for this finding. Potentially, aberrant drug-using persons appear to be being prescribed adequate levels of POA drugs to either manage their pain management needs or their dependence or a combination of both. Occasional or infrequent drug seeking across multiple prescribers occurs from time-to-time in the context of longer-term high volume POA drug consumption. Alternatively, these persons are being managed explicitly or implicitly for their drug dependence by being maintained of long-term dosages, well after their other medical requirements for POA drugs has been resolved. Effectively, managing persons on a regime similar to an opioid substitution program.

There could be a small proportion, of as yet undefined persons, who seek high volumes of drugs over short or extended periods of times. However, these persons would appear to be a small heterogeneous grouping, as their drug seeking or doctor shopping would seem sporadic and infrequent. Potentially, short-term POA drug seeking, in the context of a short POA drug-using history might represent behaviour to supplement an illicit opioid drug dependence disorder. However, the studies taken had no means to confirm or refute this. Conceivably persons with no established relationship with a prescriber, with possible symptoms of withdrawal, or intoxication, or other objective evidence of illicit drugs would be more heavily scrutinised by a first time prescriber and less likely to be prescribed POA drugs.

Limited episodes of doctor shopping in the context of a history of long-term POA drug prescribing could represent some change in treatment, treatment provider, pain condition or other factors that might lead to the initiation of doctor shopping to meet a pain management or dependence need until that person is re-established with a medical practitioner that manages their POA drug requirements effectively.

The overall picture of aberrant POA drug use suggests that long-term high dosage of POA drugs is the greater issue of concern in terms of being a public health risk. The results of this study suggest that a significant proportion of this aberrant population is consuming these drugs at either medium or high levels. Further evidence from this study suggests that as length of exposure increases there is a corresponding rise in the proportion of persons consuming POA drugs at high levels. This appears to be an issue for consideration of treatment provider particularly given the increasing evidence that there is a lack of support for the effectiveness of long-term use of POA drugs for chronic pain conditions (Chou, et al., 2015; Martell, et al., 2007).

This study's results suggest that higher-level long-term POA drug consumption appears to be a greater immediate concern than doctor-shopping behaviour. There is a small sub-population of persons on long-term opioid use over many years and at various times in their POA drug-using histories they might seek prescriptions from other prescribers. However, this behaviour is not regularly occurring over time and appears to be over short timeframes and these persons POA drug supply then returns to single prescriber suppliers over the longer term. These persons might also be unrecognised as suffering SUDs by their treatment providers. This population would also appear to represent the most likely source of diverted POA drugs that are being found in illicit markets and reported as being used for non-medical purposes.

It is of note that this study did not particularly identify any distinct sub-populations of persons who were either infrequent and high-level doctor shoppers, or any frequent and high-level doctor shoppers, that might be consistent with persons suffering SUDs of abuse or dependence. Similarly, no category of persons that might be potentially obtaining POA drugs for on-selling or diversion could be identified, noting that the studies did not seek to identify such a group of persons. It is of interest that a discrete no doctor-shopping population is found using the largely descriptive techniques of these studies, despite there being widespread acknowledgement of this phenomenon related to POA drug misuse. Potentially, however, other analyses including other variables of interest might detect such a population; however, this study

is using those variables that are those actually actively used in a PDMP for monitoring POA drug use by health-based regulators across a population.

Two major recommendations are suggested by the outcomes of this thesis's studies. The first is that a major focus on doctor shopping as a behaviour of concern is potentially unwarranted – certainly if that is to the exclusion of other concerns. The second, and related recommendation is that there appears to be a need for particular focus on persons maintained on long-term high dose POA drug therapies. The implications of the findings and recommendations are discussed below.

6.7 IMPLICATIONS

A particular implication of this study is an emphasis on managing POA drug misuse and diversion by focussing on doctor shopping alone is not supported as optimal approach. The greatest volume of POA drugs is being consumed by persons on long-term high dose treatment. There is a risk of those persons developing SUDs on POA drugs, and a risk these persons are the source of diverted POA drugs finding their way into illicit markets.

The results of the three studies of this thesis has implications in relation to management of the use and possible misuse of POA drugs in the Australian community. There are particular implications for the development and implementation of real-time PDMPs, the capacity and capability of health system to meet treatment needs, the overall strategic approaches to managing POA drug concerns, and the role of regulators of health professionals and POA drugs, and the impact on patients. These matters are discussed in more detail following.

A major implication of this study is that an emphasis on managing POA drug misuse and diversion by focussing on doctor shopping alone, or to the exclusion of other approaches, is not supported by this study's results as the optimal approach to managing POA drug misuse. The greatest volume of POA drugs is being consumed by persons on long-term high dose treatment. There is a significant risk of these persons

developing SUDs on POA drugs, and a reasonable assumption that these persons are the source of diverted POA drugs finding their way into illicit markets.

Real-time prescription drug-monitoring appears to have good face value utility in allowing treatment providers to improve monitoring of their patients POA drug use and there would appear to be considerable value in implementing these systems. However, this study's findings support that there is a lack of agreement on what constitutes drug dependence in context of doctor shopping for POA drugs and there are many patients maintained on long-term high dose POA drug treatment. Given these issues there is some concern that the provision of information without appropriate structure and supporting interpretative information could potentially create more confusion or uncertainty for treatment providers.

An unintended consequence to responding to aberrant POA drug use with ceasing of prescribing might cause more imminent harm to a patient on long-term treatment who most likely would exhibit significant withdrawal. Rapid cessation could also cause problematic drug-seeking use and this would have potentially greater costs to the medical and regulatory systems, as that person sought to re-establish their treatment regime. Some USA state jurisdictions have discussed a 'chilling' effect on POA prescriptions; that is, a significant reduction when PDMPs were introduced (Reisman, et al., 2009).

Some pain specialists have argued there should be compelling and justified reasons for attempting to change a person's POA drug regime, especially if they have been established on a certain dose for considerable time (Chou et al., 2009; Hallinan, et al., 2011). Alternatively, drug-dependent persons maintained on oral POA drug might be at less risk of harm than persons engaging in illicit injecting drug use. These options are perhaps sub-optimal care arrangements and persons with SUDs and persistent pain conditions should be offered best practice treatment options. However, management of POA drug misuse must be considered in the broader context of a harm minimisation framework and in the broader capacity of the healthcare system consider the limits of that system and how to provide the best outcomes for their patients.

It is recommended any such implementation of real-time PDMPs with access to treatment providers should consider providing treatment providers with support and training to be able to recognise problematic drug seeking behaviour, and also substance use disorders and inappropriate pain management treatment in long term POA drug using and apparently stable patients. Furthermore, development of information systems can represent significant investments, and often result in loss of expenditure in other areas such as treatment or prevention. Possibly appropriate health economic or return on investment analyses should consider the merits of particular approaches to determine the best allocation of limited health expenditure.

Persons who are on long-term POA drug treatment in primary care settings might require particular interventions to better manage their needs. PDMP real-time monitoring might also increase detection of persons that are not suitable for treatment in primary care or general practice settings or require more specialist review or treatment. Appropriate capacity within the health system to meet possibly increased pain management and drug treatment needs would also have to be considered. This could be managed by improving capacity of primary care providers or improving the capacity and access to specialist pain management or drug treatment services, or some combination of both. It is recommended that any approach to intervene in population wide POA drug use should consider and anticipate the potential flow on treatment needs this might create.

For treatment providers there are potentially a significant considerations in regards to managing persons with POA drugs. The first is that it is particularly complex in assessing SUDs in this area, and perhaps understanding aberrant behaviour as a signal for concerns is important. Secondly, that use of high doses or doses over 100 millligrams OME daily appears to be risky and more likely to lead to increasing dosages over time. The new CDC Guidelines (Dowell, et al., 2016) and other emerging guidelines suggesting maximum dosages of no more than 100 milligrams (OME) daily are particularly relevant.

In regard to the application and utility of PDMPs the implications are more complex. The first is cautionary in that doctor shopping per se might not be indicative of aberrant POA drug use. Treatment providers and regulators will need to be mindful of cases of false positives and ensure legitimate patients with non-problematic use are not denied access to treatment. Secondly, and also cautionary, is that no evidence of doctor shopping might not be the same as no evidence of problematic POA drug use. Treatment providers should be potentially alert to issue of dose escalation and PDMPs might be one of the appropriate tools to review and manage patients POA drug use over time. The third issue is that aberrant use appears more linked to prescriptions and high dosages over time, and less so to patients moving between prescribers who might be unaware of their actual use. Therefore, with new guidelines suggesting upper limits on prescribing, PDMPs can become professional practice improvement tools at best, or regulatory mechanisms to control errant prescribers at worst. In a worst case scenario prescribing limits could be imposed on prescribers by regulatory or enforcement agencies and this could erode the independent decision making of treatment providers.

Regulatory agencies and professional bodies might need to provide further guidance to practitioners about their obligations and requirements, and also to patients as to their rights to treatment and obligations in regard to the use of POA drugs. Prescribers will perhaps require increased training in pain management and SUD issues around POA drug use to improve patient care. Regulators and professional standards bodies will have to ensure health practitioners are appropriately informed about their obligations and professional requirements before they could legitimately enforce compliance with health practitioners' treatment and prescribing practices.

Patients will also need some information and support to understand any changes in their treatment regimes and their rights to treatment and requirements to use POA drugs lawfully. There is a risk that treatment providers using doctor shopping as reason to choose to refuse continue treatment, might cause their patients considerable harms and actual create apparent doctor shopping behaviour as they seek to find alternative treatment providers. The engagement of consumers is perhaps an issue with many implications. If patients are having long term treatment approaches modified without

their support or consent, there are now options for complaints and review of health practitioner practice across most Australia jurisdictions. If patients have been inappropriately managed over lengthy periods and they have developed SUDs as a result of this treatment, this is the potential of litigation or complaint action by that person against their treating health practitioner.

In Australia the national strategic approach established in the Pharmaceutical Drug Misuse – Framework for Action (Ministerial Council on Drug Strategy, 2011) is a comprehensive approach that appears to address the interventions required in a balance manner. As such consistent uniform adoption of the strategy across Australian jurisdictions would appear the best informed approach. Real-time prescription drug-monitoring with the capability of direct access by prescribers and dispensers, at present is a key strategic focus across Australian jurisdiction at present, derived from the above framework. As such it is recommended that the strategy framework recommendations should implemented would be most effective if implemented in comprehensive fashion rather than in part.

These results also suggest that the overall subsidisation of POA drugs under the PBS in Australia might need further examination. If there are large numbers of patients on long-term high dose POA drug treatment and in most cases these ongoing prescriptions meet requirements for PBS subsidies for prolonged treatment. The PBS seeks to ensure accessible and cost effective medicines for the community. If treatment with POA for a proportion of this population is not appropriate or effective, and given there are concerns about drug diversion, then continuing low cost access to POA drugs, potentially acts as a perverse incentive for practitioners and patients to maintain these treatment regimes. However, any changes to subsidised treatment and medicines would need careful consideration to ensure there is no disadvantage to patients with legitimate needs.

6.8 FUTURE STUDY SUGGESTIONS

The results also suggest further areas for investigation based on the available MODDS dataset and other matters requiring information from other sources. Areas of potential future study could focus on further aspects of patients, healthcare providers, role of regulators and the real-time PDMPs. These are discussed in the following section.

In current MODDs dataset, drug dependent patients, and non-doctor shopping patients were excluded from part or all of the study. For the known drug dependent persons, it might be worthwhile to investigate aspects of their reported SUDs and the relationship to their POA drugs use. For the non-doctor shopping patients, it would be assumed a significant proportion of these are also on long term high dose POA treatments. Further investigation of overall POA drug trends over time could also include the entire population receiving POA drugs and potentially identify time points when persons POA drug treatment changed.

Further qualitative information from patients as health care consumers is a largely untapped area of research and could shed further light on the reasons for some persons' drug seeking behaviour. Further quantitative or clinical information about patients' diagnosis and assessment of their conditions, could also add value and perhaps help discriminate or identify SUDs better. Information on patients who have experienced episodes of overdose on POA drug, or died and the causes of death would also be relevant in assessing POA drug related harms.

These studies in this thesis did not focus on aspects of the quality of prescribers. Potentially, poor prescribing practices or treatment outside of accepted professional standards by health practitioner could contribute to some of poor POA drug treatment outcomes. Further investigation into the role of prescribers and means of identifying poor practice could also have value and suggest targets for interventions.

Finally, if real-time PDMPs are to be implemented and this is done so with appropriate support and structure, then there is a unique opportunity to change in POA drug use due to a naturally occurring experiment. Ideally, any PDMP implementation would be undertaken with an evaluation component. There is the potential to examine the effect of such an intervention by contrasting the pre and post stages of the implementation of a real-time PDMP to assess its effect on prescribing practices and POA drug consumption.

6.9 CONCLUSION

This thesis set out to investigate the phenomenon of doctor shopping in order to ascertain the purported relationship to POA drug misuse. The aim of the studies was to provide doctor shopping definitions that could be operationalised in PDMPs to inform prescribers, identify aberrant POA drug use, and improve prescribing decisions and treatment outcomes. While it is not disputed that doctor shopping behaviour exists, the results of these studies did not identify a discrete doctor shopping population nor find an association with aberrant POA drug use. However, the studies did show concerning evidence of a sub-population of persons on high dose long term POA drugs, that could be at risk of, or suffering SUDs. The outcomes suggest that alarmist depictions of doctor shopping are not supported. It is recommended that Australian jurisdictions seeking to make considerable health investments in real-time reporting PDMPs might consider how such systems can also address long term high dose POA drug use to improve patient treatment outcomes and reduce drug diversion.

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Appendices

Appendix A: DSM-IV-TR & ICD-Diagnostic Criteria

Diagnostic and Statistical Manual of Mental Disorders- Fourth Edition -Text Revision (DSM-IV-TR): Criteria for Substance Dependence and Substance Abuse

DSM-IV_TR Criteria for Substance Dependence

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring at any time in the same 12-month period:
(1) tolerance, as defined by either of the following:
(a) a need for markedly increased amounts of the substance to achieve intoxication or desired effect
(b) markedly diminished effect with continued use of the same amount of the substance
(2) withdrawal, as manifested by either of the following:
(a) the characteristic withdrawal syndrome for the substance (refer to Criteria A and B of the criteria sets for Withdrawal from the specific substances)
(b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms
(3) the substance is often taken in larger amounts or over a longer period than was intended
(4) there is a persistent desire or unsuccessful efforts to cut down or control substance use
(5) a great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances), use the substance (e.g., chain-smoking), or recover from its effects
(6) important social, occupational, or recreational activities are given up or reduced because of substance use
(7) the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)
Specify if:
With Physiological Dependence: evidence of tolerance or withdrawal (i .e .• either Item 1 or 2 is present)
Without Physiological Dependence: no evidence of tolerance or withdrawal (i.e., neither Item 1 nor 2 is present)
Course specifiers (see text f or definitions):
Early Full Remission
Early Partial Remission
Sustained Full Remission
Sustained Partial Remission
On Agonist Therapy

In a Controlled Environment
(pp197-198. (American Psychiatric Association, 2000))

DSM-IV-TR - Criteria for Substance Abuse

A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:
(1) recurrent substance use resulting in a failure to fulfil major role obligations at work, school, or home (e.g., repeated absences or poor work performance related to substance use; substance-related absences. suspensions, or expulsions from school; neglect of children or household)
(2) recurrent substance use in situations in which it is physically hazardous (e.g. .driving an automobile or operating a machine when impaired *by* substance use)
(3) recurrent substance-related legal problems (e.g., arrests for substance-related disorderly conduct)
(4) continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights)
B. The symptoms have never met the criteria for Substance Dependence for this class of substance.
(pp199. (American Psychiatric Association, 2000)

Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5)

Opioid Use Disorder Criteria:

A minimum of 2-3 criteria is required for a mild substance use disorder diagnosis, while 4-5 is moderate, and 6-7 is severe. Opioid Use Disorder is specified instead of Substance Use Disorder, if opioids are the drug of abuse.

1. Taking the opioid in larger amounts and for longer than intended
2. Wanting to cut down or quit but not being able to do it
3. Spending a lot of time obtaining the opioid
4. Craving or a strong desire to use opioids
5. Repeatedly unable to carry out major obligations at work, school, or home due to opioid use
6. Continued use despite persistent or recurring social or interpersonal problems caused or made worse by opioid use
7. Stopping or reducing important social, occupational, or recreational activities due to opioid use
8. Recurrent use of opioids in physically hazardous situations
9. Consistent use of opioids despite acknowledgment of persistent or recurrent physical or psychological difficulties from using opioids
10. *Tolerance as defined by either a need for markedly increased amounts to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount. (Does not apply for diminished effect when used appropriately under medical supervision)
11. *Withdrawal manifesting as either characteristic syndrome or the substance is used to avoid withdrawal (Does not apply when used appropriately under medical supervision)

(American Psychiatric Association, 2014)

International Classification of Disease Ninth Edition, Clinical Modification (ICD-9-CM) classifications of drug dependence and drug abuse related to opioids

Drug dependence 304

- Drug dependence - replaced the term "drug addiction" and is defined as a state, psychic and sometimes also physical, resulting from the interaction between a living organism and a drug, characterized by behavioural and other responses that always include a compulsion to take the drug on a continuous or periodic basis in order to experience its psychic effects, and sometimes to avoid the discomfort of its absence. Tolerance may or may not be present. A person may be dependent on more than one drug.
- Physical and emotional dependence on a chemical substance. Compare drug dependency.
- Psychological craving for or habituation to the use of a chemical substance which may or may not be accompanied by physical dependency. Used for animal or human populations. Compare drug addiction.
- State of heavy dependence on any drug, including alcohol; sometimes defined as physical dependence but usually also including emotional dependence, i.e., compulsive or pathological drug use.

- 304 Drug dependence
- 304.0 Opioid type dependence
- 304.00 Opioid type dependence, unspecified convert 304.00 to ICD-10-CM
- 304.01 Opioid type dependence, continuous convert 304.01 to ICD-10-CM
- 304.02 Opioid type dependence, episodic convert 304.02 to ICD-10-CM
- 304.03 Opioid type dependence, in remission convert 304.03 to ICD-10-CM

See: http://www.icd9data.com/2013/Volume1/290-319/300-316/304/

(Medicode (Firm), 1996)

Nondependent abuse of drugs 305

- Drug abuse is a serious public health problem that affects almost every community and family in some way. Each year drug abuse results in around 40 million serious illnesses or injuries among people in the United States. Abused drugs include
    - amphetamines
    - anabolic steroids
    - club drugs
    - cocaine
    - heroin
    - inhalants
    - marijuana
    - prescription drugs

  drug abuse also plays a role in many major social problems, such as drugged driving, violence, stress and child abuse. Drug abuse can lead to homelessness, crime and missed work or problems with keeping a job. It harms unborn babies and destroys families. There are different types of treatment for drug abuse. But the best is to prevent drug abuse in the first place. nih: national institute on drug abuse

- Excessive use of distilled liquors
- Excessive use of drugs or chemicals with associated psychological symptoms and impairment in social or occupational functioning.
- Excessive use of habit forming medications
- Excessive use of habit forming medications.
- The use of a drug for a reason other than which it was intended or in a manner or in quantities other than directed.
- The use of alcoholic beverages to excess, either on individual occasions ("binge drinking") or as a regular practice.
- The use of illegal drugs or the use of prescription or over-the-counter drugs for purposes other than those for which they are meant to be used, or in large amounts. Drug abuse may lead to social, physical, emotional, and job-related problems.

- 305.5 Nondependent opioid abuse
- 305.50 Opioid abuse, unspecified convert 305.50 to ICD-10-CM
- 305.51 Opioid abuse, continuous convert 305.51 to ICD-10-CM
- 305.52 Opioid abuse, episodic convert 305.52 to ICD-10-CM
- 305.53 Opioid abuse, in remission convert 305.53 to ICD-10-CM

See: http://www.icd9data.com/2013/Volume1/290-319/300-316/305/default.htm

(Medicode (Firm), 1996)

Appendix B:
Summary of regulatory requirements for controlled (Schedule 8) drugs under the Health (Drugs & Poisons) Regulation, 1996 in Queensland, Australia.

Queensland Government

Queensland Health

Home > Clinical practice > Clinical guidelines and procedures > Medicines > Drugs of dependence > Regulatory requirements and resources

Regulatory requirements and resources

There are various regulatory requirements under the *Health (Drugs and Poisons) Regulation 1996*[1] regarding the prescribing of scheduled drugs of dependence (S8), including script requirements, and approvals/reports to the Chief Executive for the treatment of patients with known drug dependency.

- Treatment involving drugs of dependence[2]
- Scripts[3]

Treatment involving drugs of dependence

You need to complete a treatment report if you wish to treat a:

- known drug dependent person[4] (PDF, 432KB), with a drug of dependence (controlled drug, S8) or restricted drug (s4) of dependency
- person with a S8, for more than 8 weeks
- person with any "specified condition drug" other than for attention deficit disorder in a child or for treatment of narcolepsy.

This report is known as a Report to the Chief Executive:

- PDF version (PDF, 234KB)[5]
- Word version (DOC, 110KB)[6]

Scripts

Requirements for a valid schedule 8 script:

- Schedule 8 (S8) prescriptions are valid for 6 months
- S8 prescriptions are valid if the following is provided:
  - full name, professional qualifications and address of the prescriber
  - full name, address and date of birth of the patient
  - *the description and quantity (in words and figures) of the medicines to be dispensed*
  - *adequate directions for use*
  - *number of repeats (if any) and intervals at which they may be dispensed*
  - *words "specified condition" if the S8 drug prescribed is amphetamine, dexamphetamine, methylamphetamine, methylphenidate or lisdexamphetamine*
  - *signature of the prescriber.*
- For computer generated S8 paper prescriptions the information italicised must also be written in the doctor's own handwriting
- Only one S8 medication can be written on a prescription, except where multiple items are different forms of the same drug
- No other prescription medication can be written on an S8 prescription
- S8 prescriptions must not be written by a prescriber for self-administration.

Appendix C: Research Approvals

C-1 – Queensland University of Technology Ethical Approval

From: Research Ethics <ethicscontact@qut.edu.au>
To: Dr Kirsten McKenzie <k.mckenzie@qut.edu.au>, Mr William Allen Lefroy <w.
CC: Ms Janette Lamb <jd.lamb@qut.edu.au>
Date: 2/05/2011 4:30 pm
Subject: Ethics Application Approval -- 1100000526

Dear Mr Bill Loveday

Project Title:
Prescription opioid drugs misuse: what can we learn from 'doctor shopping' behaviour?

Approval Number: 1100000526
Clearance Until: 31/12/2015
Ethics Category: Human

This email is to advise that your application has been reviewed by the Chair, University Human Research Ethics Committee and confirmed as meeting the requirements of the National Statement on Ethical Conduct in Human Research. We note ethics clearance has already been obtained from another institution.

Whilst the data collection of your project has received ethical clearance, the decision to commence and authority to commence may be dependent on factors beyond the remit of the ethics review process. For example, your research may need ethics clearance from other organisations or permissions from other organisations to access staff. Therefore the proposed data collection should not commence until you have satisfied these requirements.

If you require a formal approval certificate, please respond via reply email and one will be issued.

This project has been awarded ethical clearance until 31/12/2015 and a progress report must be submitted for an active ethical clearance at least once every twelve months. Researchers who fail to submit an appropriate progress report may have their ethical clearance revoked and/or the ethical clearances of other projects suspended. When your project has been completed please advise us by email at your earliest convenience.

For variations, please ensure that approval has been sought from the lead university before completing and submitting the QUT online variation form.
http://www.research.qut.edu.au/ethics/forms/humVariation.jsp

Please do not hesitate to contact the unit if you have any queries.

Regards

Janette Lamb on behalf of the Chair, UHREC
Research Ethics Unit | Office of Research
Level 4 88 Musk Avenue | Kelvin Grove
p. +61 7 3138 5123
e. ethicscontact@qut.edu.au
w. http://www.research.qut.edu.au/ethics/

C-2 Queensland Health Ethical Approval

Queensland Government
Queensland Health

Enquiries to: Sue Jenkins-Marsh, Manager
Research Ethics & Governance Unit
Telephone: (07) 3234 0034
Facsimile: (07) 3234 0107
Ref: RD003410

Mr William Loveday
Locked Bag 21
Fortitude Valley QLD 4006

Dear Mr Loveday

Research Title: Prescription Opoid Drug Misuse - What can we learn from doctor shopping behaviour?

It is with pleasure that I am writing to inform you that your request for access to confidential health information for the above project has received approval under delegation by the Director-General, Queensland Health. In accordance with section 281, of the *Public Health Act 2005* the applicants listed in your application can access and use the specified confidential information, providing they act within the limits detailed in your application.

Please display this letter and a copy of your application when requesting the confidential information from the relevant data custodian and provide a copy of this approval to the Human Research Ethics Committee (HREC) that reviewed your protocol.

This approval commences on the date of this letter and is valid to 31 December 2014.
The specific data requested is for the period from 1 January 2000 to 31 December 2009.

This approval means that you must undertake the responsibilities and obligations of confidentiality of the information under the provisions of the *Public Health Act 2005*. You must take all reasonable steps necessary to ensure that the confidential information is kept confidential, including storing or disposing of all data, information, documents and associated correspondence in a secure manner. Unauthorised use or disclosure of confidential information may incur a penalty under the laws of the Queensland Government. These obligations includes, providing notification of any change in the names of persons who will be given the information for the research.

You are required to provide an annual progress report and a final report at the completion of your project, to the Research Ethics & Governance Unit . Templates can be found on the web page http://www.health.qld.gov.au/ohmr/html/regu/accs_conf_hth_info.asp

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C-3 Approval under the Health Act, 1937 to use public health information.

Melinda Butterfield - re letter from DDU

From: Susan BallanLyne
To: Melinda Butterfield
Date: 19/03/2010 1:57 PM
Subject: re letter from DDU
Attachments: Letter to Dr Young re research.doc; memo to kevin re research -approved

Good morning Jeannette,

Please find attached a letter requesting permission for Mr Bill Loveday and I to underteke research based in the DDU. Dr Kevin Lambkin as executive Director has approved the research and I have included his approval.

Please let me know if you require any further information.

Sue

Dr Sue BallanLyne
Director Drugs of Dependence Unit & Queensland Needle and Syringe Program
Phone 33289805
Mobile 0414301958

Dear Sir and All
I support. Best wishes Re the research
Please pass through on Ethics Committee as
outlined.

Appendix D: Expert bodies

Table C-1

Pain management and drug dependence organisations, that were approached for participants in the Delphi Technique for Study One – classified by country in which based, pain or addiction focus and associated journals (n=34)

Organisation name	*Internet webpage*	*Country*	*Pain*	*Addiction*	*Journal*
Addiction Treatment Forum	http://www.atforum.com/	USA		X	
Alcohol and Drug Council of Australia	www.adca.org.au	Aust		X	
American Academy of Pain Management	http://www.aapainmanage.org/	USA	X		
American Academy of Pain Medicine	http://www.painmed.org/	USA	X		Pain Medicine
American Association for the Treatment of Opioid Dependence	http://www.aatod.org/sitemap.html	USA		X	
American Association of Addiction Medicine	www.asam.org	USA		X	
American Board of Pain Medicine	http://www.abpm.org/	USA	X		
American Chronic Pain Association	http://www.theacpa.org/	USA	X		
American Chronic Pain Association	http://www.theacpa.org/default.aspx	USA	X		
American Pain Society	http://www.ampainsoc.org/	USA	X		Journal of Pain
American Society for Pain Management Nursing	http://www.aspmn.org/	USA	X		
Australian Pain Management Association	http://www.painmanagement.org.au/	Aust	X		
Australian Pain Society	http://www.apsoc.org.au/	Aust	X		
Australian Professional Society on Alcohol and Drugs	http://www.apsad.org.au/	Aust		X	Drug and Alcohol Review
Canadian Academy of Pain Management	http://www.canadianapm.com/	Can	X		
Canadian Centre on Substance Abuse	http://www.ccsa.ca/Eng/	Can		X	
Canadian Drug Policy Coalition	http://drugpolicy.ca/	Can		X	

Canadian Pain Society	http://www.canadianpainsociety.ca/en/	Can	X		
Canadian Society of Addiction Medicine	www.csam.org	Can		X	Canadian Journal of Addiction Medicine
Centre for Addiction and Mental Health	http://www.camh.net/	Can		X	
Centre for Applied Research in Mental Health & Addiction	http://www.carmha.ca/	Can		X	
Chapter of Addiction Medicine (Royal Australian College of Physicians)	http://www.racp.edu.au/page/australasian-chapter-of-addiction-medicine/	Aust		X	
Chronic Pain Australia	http://www.chronicpainaustralia.org.au/	Aust	X		
College of Physicians and Surgeons of Ontario	http://www.cpso.on.ca/	Can	X	X	
College on Problems of Drug Dependence	http://www.cpdd.vcu.edu/	USA		X	Drug and Alcohol Dependence
Drug and Alcohol Nurses - Australia	http://www.danaonline.org/	Aust		X	
Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists	http://www.anzca.edu.au/fpm	Aust	X		Pain Medicine
International Association for Pain & Chemical Dependency	http://www.iapcd.org/	Int	X	X	
International Association for Study of Pain	http://www.iasp-pain.org/	Int	X		Pain
Network of Alcohol and Drug Agencies	www.nada.org.au	Aust		X	
New Zealand Pain Society	http://www.nzps.org.nz/	NZ	X		Pain Research & Treatment
Pain Medicine Research Institute	http://sydney.edu.au/medicine/pmri/	Aust	X		
Queensland Self-Management Alliance	http://www.qsma.org.au/	Aust	X		
The American Society for Interventional Pain Physicians	http://www.asipp.org/index.html	USA	X		Pain Physician

Note: Aust – Australia, Can – Canada, NZ – New Zealand, USA – United States of America, Int – International (membership available to all nationalities).

Appendix E: Study 1 Questionnaires

Appendix E-1: Study 1 – Round One Questionnaire

Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping Behaviour

1. Introduction

The electronic monitoring of, and 'real-time reporting' of prescriptions of pharmaceutical opioid drugs is widely recognised as one means of reducing misuse and increasing appropriate use of this class of drugs. This information can be used to inform health practitioners to guide their decisions where possible aberrant drugs use is detected.

Substance use disorders (abuse & dependence) in relation to pharmaceutical opioids are poorly understood. There is diversity of opinion about what use constitutes problematic use and what is appropriate treatment in chronic opioid therapy.

Clinical diagnoses of substance use disorders are undertaken by health practitioners in their face to face assessment of patients, based on a range of criteria.

The use of prescription information, in the absence of clinical information, might not on its own be sufficient to allow clinicians to arrive at conclusions about a person's potential drug misuse.

However, database information derived from patterns of prescription events across populations, could be used to assist health practitioners in making better informed decisions on an individual's potentially problematic medication use.

This study seeks to obtain information from clinical experts,such as yourself, in regards to their experience with treatment of persons with pharmaceutical opioids where problematic use has occurred. The purpose is to derive methods to potentially assess, detect and predict, aberrant prescription opioid drug use behaviour that might be indicative of substance use disorders using a prescription monitoring program.

Participation will involve completing three rounds of a questionnaire based on the Delphi Technique. That is, the survey will be conducted in three iterations, where the results of the previous rounds will be reported back to you for further feedback. This is to obtain a convergence of opinion in defining this behaviour of concern. The questions will involve matters relating to opinions about dependence on and management with opioid analgesic drugs.

It is anticipated that the first survey should take at the maximum 30 minutes to complete, and further iterations will take less time. Second and third round questionnaires will be circulated within 3 weeks of the completion of each questionnaire.

This first study involves four separate but related surveys, on the following topics:

1. Utility of DSM-IV criteria in assessing substance use disorders involving pharmaceutical opioids;
2. Ratings of the harmfulness of pharmaceutical opioid drugs;
3. Assessment of risk factors for persons with substance use disorders related to prescription opioids; and,
4. Questions on prescription or doctor shopping definitions.

1. This study has obtained Ethics Approval of Queensland Health & Queensland University of Technology,

Do you wish to read the full copy of Participant Information of this Research Project?

- ○ Yes, I wish to read the Participant Information
- ○ No, I am happy to proceed with the survey

2. Participant Information for QUT Research Project

Misuse of Pharmaceutical Opioid Analgesic Drugs: Doctor shopping behaviour.
Queensland Health Ethics Approval Number HREC/11/QHC/1
QUT Ethics Approval Number 1100000526

Appendix E-2: Study 1 – Round Two Questionnaire

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

1. Introduction

You previously participated in Round 1 of this survey regarding issues of misuse of pharmaceutical opioids.

In completing Round 1 you also agreed to further participate in the following 2 rounds of the survey.

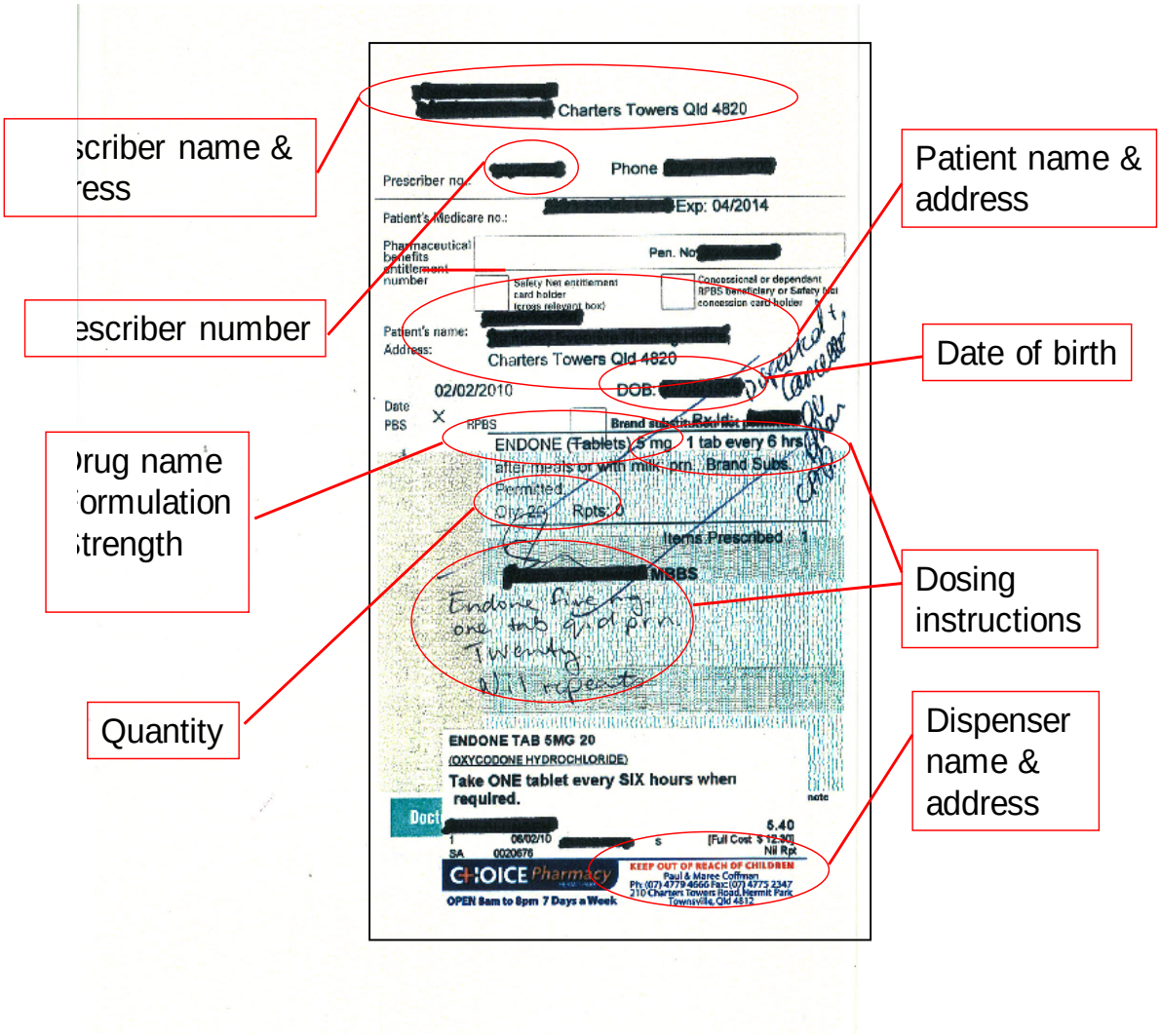
This study is using the Delphi Technique to collate and consider a range of expert opinions in this area. This technique involves feedback you participants of the total group results from the first survey and your own results to determine to ascertain if you would reconsider your answer on this based on the group's average response.

Once you have responded I will then feedback the results for a final time to see if you wish to reconsider any of your response for the second time based on the groups amended second round responses.

Page 1

Appendix F: Prescription details

A sample de-identified controlled (Schedule 8) drug prescription with data elements highlighted



Appendix G: Controlled (Schedule 8) drugs

List of all controlled (Schedule 8) drugs capture by the MODDS database as at 2013.

Drug Id	Drug Group Id	Drug Group	Generic Name	Strength	Unit Type	Trade Names	Drug Type
422	NULL	NULL	J	.000	AMPOULES	NULL	NULL
421	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCONTIN NEW-FORMULATION CR-T	80.000	TABLETS	OXYCONTIN	OXYCODONE
420	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCONTIN NEW FORMULATION CR-T	40.000	TABLETS	OXYCONTIN	OXYCODONE
419	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCONTIN NEW FORMULATION CR-T	30.000	TABLETS	OXYCONTIN	OXYCODONE
418	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCONTIN NEW-FORMULATION CR-T	20.000	TABLETS	OXYCONTIN	OXYCODONE
417	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCONTIN NEW-FORMULATION CR-T	15.000	TABLETS	OXYCONTIN	OXYCODONE
416	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCONTIN NEW-FORMULATION CR-T	10.000	TABLETS	OXYCONTIN	OXYCODONE
415	95	ALPRAZOLAM	ALPRAZOLAM 500MCG	.500	TABLETS	XANAX / KALMA	BENZODIAZEPINE
414	95	ALPRAZOLAM	ALPRAZOLAM 250MCG	.250	TABLETS	XANAX / KALMA	BENZODIAZEPINE

413	95	ALPRAZOLAM	ALPRAZOLAM 2MG	2.000	TABLETS	XANAX / KALMA	BENZODIAZEPINE
412	95	ALPRAZOLAM	ALPRAZOLAM 1MG	1.000	TABLETS	XANAX / KALMA	BENZODIAZEPINE
411	93	LISDEXAMFETAMINE DISMESILATE	LISDEXAMFETAMINE DISMESILATE 70MG	70.000	CAPSULES	VYVANSE	AMPHETAMINE
410	93	LISDEXAMFETAMINE DISMESILATE	LISDEXAMFETAMINE DISMESILATE 50MG	50.000	CAPSULES	VYVANSE	AMPHETAMINE
409	93	LISDEXAMFETAMINE DISMESILATE	LISDEXAMFETAMINE DISMESILATE 30MG	30.000	CAPSULES	VYVANSE	AMPHETAMINE
408	94	TAPENTADOL	TAPENTADOL (SR) 250MG	250.000	TABLETS	PALEXIA	OTHER
407	94	TAPENTADOL	TAPENTADOL (SR) 200MG	200.000	TABLETS	PALEXIA	OTHER
406	94	TAPENTADOL	TAPENTADOL (SR) 150MG	150.000	TABLETS	PALEXIA	OTHER
405	94	TAPENTADOL	TAPENTADOL (SR) 100MG	100.000	TABLETS	PALEXIA	OTHER
404	94	TAPENTADOL	TAPENTADOL (SR) 50MG	50.000	TABLETS	PALEXIA	OTHER
403	86	BUPRENORPHINE + NALOXONE SUB-LINGUAL	SUBOXONE SUB-LINGUAL FILM 1MG (PROGRAM)	1.000	MILLIGRAMS	SUBOXONE FILM	BUPRENORPHINE
402	73	FENTANYL PATCHES	FENTANYL PATCHES 100 MCG/HR 16.5MG	7.200	PATCHES	DUROGESIC	FENTANYL
401	73	FENTANYL PATCHES	FENTANYL PATCHES 75 MCG/HR 12.375MG	5.400	PATCHES	DUROGESIC	FENTANYL
400	73	FENTANYL PATCHES	FENTANYL PATCHES 50 MCG/HR 8.25MG	3.600	PATCHES	DUROGESIC	FENTANYL
399	73	FENTANYL PATCHES	FENTANYL PATCHES 25 MCG/HR 4.125MG	1.800	PATCHES	DUROGESIC	FENTANYL

398	73	FENTANYL PATCHES	FENTANYL PATCHES 12 MCG/HR 2.063MG	.864	PATCHES	DUROGESIC	FENTANYL
397	73	FENTANYL PATCHES	FENTANYL PATCHES 12MCG/HR 1.28MG	.864	PATCHES	DENPAX	FENTANYL
396	73	FENTANYL PATCHES	FENTANYL PATCHES 25MCG/HR 2.55MG	1.800	PATCHES	DENPAX	FENTANYL
395	73	FENTANYL PATCHES	FENTANYL PATCHES 50MCG/HR 5.1MG	3.600	PATCHES	DENPAX	FENTANYL
394	73	FENTANYL PATCHES	FENTANYL PATCHES 75MCG/HR 7.65MG	5.400	PATCHES	DENPAX	FENTANYL
393	73	FENTANYL PATCHES	FENTANYL PATCHES 100MCG/HR 10.2MG	7.200	PATCHES	DENPAX	FENTANYL
392	91	OXYCODONE HCL; NALOXONE HCL DIHYDRATE	OXYCODONE HCI 40MG, NALOXONE HCI (DIHYDRATE) 20MG	40.000	TABLETS	TARGIN	OXYCODONE
391	91	OXYCODONE HCL; NALOXONE HCL DIHYDRATE	OXYCODONE HCI 20MG, NALOXONE HCI (DIHYDRATE) 10MG	20.000	TABLETS	TARGIN	OXYCODONE
390	91	OXYCODONE HCL; NALOXONE HCL DIHYDRATE	OXYCODONE HCI 10MG, NALOXONE HCI (DIHYDRATE) 5MG	10.000	TABLETS	TARGIN	OXYCODONE
389	91	OXYCODONE HCL; NALOXONE HCL DIHYDRATE	OXYCODONE HCI 5MG, NALOXONE HCI (DIHYDRATE) 2.5MG	5.000	TABLETS	TARGIN	OXYCODONE

388	76	METHYLPHENIDATE LONG ACTING	METHYLPHENIDATE (SR) 10MG	10.000	CAPSULES	RITALIN LA (LONG ACTING)	AMPHETAMINE
387	90	KETAMINE SUB-LINGUAL	KETAMINE LOZENGE 50MG	50.000	LOZENGE	KETAMINE LOZENGE TUGUN COMPOUNDING	KETAMINE
386	83	HYDROMORPHONE EXTENDED RELEASE ORAL	HYDROMORPHONE (SR) 4MG	4.000	TABLETS	JURNISTA MR-TAB 4MG	HYDROMORPHONE
385	83	HYDROMORPHONE EXTENDED RELEASE ORAL	HYDROMORPHONE (SR) 64MG	64.000	TABLETS	JURNISTA MR-TAB 64MG	HYDROMORPHONE
384	83	HYDROMORPHONE EXTENDED RELEASE ORAL	HYDROMORPHONE (SR) 32MG	32.000	TABLETS	JURNISTA MR-TAB 32MG	HYDROMORPHONE
383	83	HYDROMORPHONE EXTENDED RELEASE ORAL	HYDROMORPHONE (SR) 16MG	16.000	TABLETS	JURNISTA MR-TAB 16MG	HYDROMORPHONE
382	83	HYDROMORPHONE EXTENDED RELEASE ORAL	HYDROMORPHONE (SR) 8MG	8.000	TABLETS	JURNISTA MR-TAB 8MG	HYDROMORPHONE
381	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCODONE HCL (SR) 15MG	15.000	TABLETS	OXYCONTIN	OXYCODONE
380	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCODONE HCL (SR) 30MG	30.000	TABLETS	OXYCONTIN	OXYCODONE
378	85	DEXAMPHETAMINE LONG ACTING ORAL	DEXAMPHETAMINE (SR) 7.5MG	7.500	CAPSULES	DEXAMPHETAMINE 7.5MG SR CAPSULES CUSTOM COMPOUNDING	AMPHETAMINE
377	88	KETAMINE SOLUTION/GEL	KETAMINE HCL 10% GEL	.100	GRAMS	KETAMINE 10%/KETOPROFEN10%/AMITIPTYLENE5%	KETAMINE
376	86	BUPRENORPHINE + NALOXONE SUB-LINGUAL	BUPRENORPHINE 8MG + NALOXONE 2MG SUB-LINGUAL	8.000	TABLETS	SUBOXONE	BUPRENORPHINE

375	86	BUPRENORPHINE + NALOXONE SUB-LINGUAL	BUPRENORPHINE 2MG + NALOXONE 0.5MG SUB-LINGUAL	2.000	TABLETS	SUBOXONE	BUPRENORPHINE
374	86	BUPRENORPHINE + NALOXONE SUB-LINGUAL	SUBOXONE SUB-LINGUALTABS 1MG (PROGRAM)	1.000	MILLIGRAMS	SUBOXONE	BUPRENORPHINE
371	62	COCAINE SOLUTION/GEL	COCAINE HCL SOLUTION/GEL 15%	.150	MILLILITRES	COCAINE HCL SOLUTION/GEL 15%	COCAINE
370	76	METHYLPHENIDATE LONG ACTING	METHYLPHENIDATE (SR) 27MG	27.000	TABLETS	CONCERTA	AMPHETAMINE
369	13	OXYCODONE INJECTIONS	OXYCODONE HCL 20MG/2ML	20.000	AMPOULES	OXYNORM	OXYCODONE
368	89	SUFENTANIL INJECTIONS	SUFENTANIL 250MCG/5ML	.250	AMPOULES	SUFENTA FORTE, SUFENTIL	SUFENTANIL
366	73	FENTANYL PATCHES	FENTANYL PATCHES 12 MCG/HR 2.1MG	.864	PATCHES	DUROGESIC	FENTANYL
365	84	BUPRENORPHINE PATCHES	BUPRENORPHINE PATCHES 20MCG/HR 20MG	3.360	PATCHES	NORSPAN	BUPRENORPHINE
364	84	BUPRENORPHINE PATCHES	BUPRENORPHINE PATCHES 10MCG/HR 10MG	1.680	PATCHES	NORSPAN	BUPRENORPHINE
363	84	BUPRENORPHINE PATCHES	BUPRENORPHINE PATCHES 5MCG/HR 5MG	.840	PATCHES	NORSPAN	BUPRENORPHINE
359	83	HYDROMORPHONE EXTENDED RELEASE ORAL	HYDROMORPHONE EXTENDED RELEASE 32MG	32.000	CAPSULES	PALLADONE	HYDROMORPHONE
357	82	KETAMINE INJECTIONS	KETAMINE HCL 200MG/2ML	200.000	AMPOULES	KETALAR	KETAMINE
356	30	FENTANYL INJECTIONS	FENTANYL CITRATE 1000MCG/20ML	1.000	VIALS	SUBLIMAZE	FENTANYL
355	77	FENTANYL SUB-LINGUAL	FENTANYL LOZENGE 1600MCG	1.600	LOZENGE	ACTIQ	FENTANYL

354	77	FENTANYL SUB-LINGUAL	FENTANYL LOZENGE 1200MCG	1.200	LOZENGE	ACTIQ	FENTANYL
353	77	FENTANYL SUB-LINGUAL	FENTANYL LOZENGE 800MCG	.800	LOZENGE	ACTIQ	FENTANYL
352	77	FENTANYL SUB-LINGUAL	FENTANYL LOZENGE 600MCG	.600	LOZENGE	ACTIQ	FENTANYL
350	76	METHYLPHENIDATE LONG ACTING	METHYLPHENIDATE (SR) 54MG	54.000	TABLETS	CONCERTA	AMPHETAMINE
349	77	FENTANYL SUB-LINGUAL	FENTANYL LOZENGE 200MCG	.200	LOZENGE	ACTIQ	FENTANYL
348	8	METHADONE ORAL	METHADONE LIQUID 5MG/ML (200ML) (NON-PROGRAM)	1000.000	BOTTLE	BIODONE FORTE SYR 5MG/ML (ML)	METHADONE
347	12	OXYCODONE SUPPOSITORIES	OXYCODONE 15MG	15.000	SUPPOSITORIES	PINDARA OWN BRAND	OXYCODONE
346	77	FENTANYL SUB-LINGUAL	FENTANYL LOZENGE 400MCG	.400	LOZENGE	ACTIQ	FENTANYL
345	6	MORPHINE INJECTIONS	MORPHINE TARTRATE 400MG/5ML	400.000	AMPOULES	NULL	MORPHINE
344	5	MORPHINE ORAL	MORPHINE SULPHATE 10MG	10.000	TABLETS	SEVREDOL	MORPHINE
343	5	MORPHINE ORAL	MORPHINE SULPHATE 20MG	20.000	TABLETS	SEVREDOL	MORPHINE
342	11	OXYCODONE ORAL	OXYCODONE HCL 10MG/ML (120ML)	1200.000	BOTTLE	OXYNORM CONCENTRATE (120ML)	OXYCODONE
341	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCODONE HCL (SR) 5MG	5.000	TABLETS	OXYCONTIN	OXYCODONE
340	11	OXYCODONE ORAL	OXYCODONE HCL LIQUID 5MG/5ML (250ML)	250.000	BOTTLE	OXYNORM LIQ	OXYCODONE
337	76	METHYLPHENIDATE LONG ACTING	METHYLPHENIDATE (SR) 36MG	36.000	TABLETS	CONCERTA	AMPHETAMINE

336	62	COCAINE SOLUTION/GEL	COCAINE HCL SOLUTION/GEL 25%	.250	MILLILITRES	COCAINE HCL SOLUTION/GEL 25%	COCAINE
335	64	COCAINE POWDER	COCAINE HCL POWDER 100MG	100.000	MILLIGRAMS	COCAINE HCL POWDER 100MG	COCAINE
334	30	FENTANYL INJECTIONS	FENTANYL CITRATE 100MCG/2ML	.100	AMPOULES	NULL	FENTANYL
333	76	METHYLPHENIDATE LONG ACTING	METHYLPHENIDATE (SR) 40MG	40.000	CAPSULES	RITALIN LA (LONG ACTING)	AMPHETAMINE
332	76	METHYLPHENIDATE LONG ACTING	METHYLPHENIDATE (SR) 30MG	30.000	CAPSULES	RITALIN LA (LONG ACTING)	AMPHETAMINE
331	76	METHYLPHENIDATE LONG ACTING	METHYLPHENIDATE (SR) 18MG	18.000	TABLETS	CONCERTA	AMPHETAMINE
330	76	METHYLPHENIDATE LONG ACTING	METHYLPHENIDATE (SR) 20MG	20.000	CAPSULES	METADATE, RITALIN LA (LONG ACTING)	AMPHETAMINE
329	21	CODEINE ORAL	CODEINE PHOSPHATE LINCTUS 5MG/ML (100ML)	500.000	BOTTLE	ACTACODE	CODEINE
327	81	REMIFENTANIL INJECTIONS	REMIFENTANIL HCL 2MG/5ML	2.000	AMPOULES	ULTIVA	REMIFENTANIL
326	81	REMIFENTANIL INJECTIONS	REMIFENTANIL HCL 1MG/3ML	1.000	AMPOULES	ULTIVA	REMIFENTANIL
325	33	HYDROMORPHONE ORAL	HYDROMORPHONE HCL 1MG/1ML (473ML)	473.000	BOTTLE	DILAUDID O-LIQ	HYDROMORPHONE
324	5	MORPHINE ORAL	MORPHINE HCL MIXTURE 1MG/ML (200ML)	200.000	BOTTLE	ORDINE	MORPHINE
323	80	OPIUM ORAL	OPIUM TINCTURE (100ML)	.500	BOTTLE	FOXLEE LINCTUS	OPIUM
322	5	MORPHINE ORAL	MORPHINE HCL MIXTURE 5MG/ML (200ML)	1000.000	BOTTLE	ORDINE	MORPHINE

321	74	ALFENTANIL INJECTIONS	ALFENTANIL 5MG/10ML	5.000	AMPOULES	RAPIFEN	ALFENTANIL
320	74	ALFENTANIL INJECTIONS	ALFENTANIL 1MG/2ML	1.000	AMPOULES	RAPIFEN	ALFENTANIL
319	11	OXYCODONE ORAL	OXYCODONE HCL 20MG	20.000	CAPSULES	OXYNORM	OXYCODONE
318	11	OXYCODONE ORAL	OXYCODONE HCL 10MG	10.000	CAPSULES	OXYNORM	OXYCODONE
317	38	BUPRENORPHINE SUB-LINGUAL	BUPRENORPHINE SUB-LINGUAL 1MG (PROGRAM)	1.000	MILLIGRAMS	SUBUTEX	BUPRENORPHINE
316	11	OXYCODONE ORAL	OXYCODONE HCL 5MG	5.000	CAPSULES	OXYNORM	OXYCODONE
315	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 120MG	120.000	CAPSULES	MS MONO	MORPHINE
314	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 90MG	90.000	CAPSULES	MS MONO	MORPHINE
313	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 60MG	60.000	CAPSULES	MS MONO	MORPHINE
312	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 30MG	30.000	CAPSULES	MS MONO	MORPHINE
311	38	BUPRENORPHINE SUB-LINGUAL	BUPRENORPHINE SUB-LINGUAL 8MG	8.000	TABLETS	SUBUTEX	BUPRENORPHINE
310	38	BUPRENORPHINE SUB-LINGUAL	BUPRENORPHINE SUB-LINGUAL 2MG	2.000	TABLETS	SUBUTEX	BUPRENORPHINE
309	38	BUPRENORPHINE SUB-LINGUAL	BUPRENORPHINE SUB-LINGUAL 0.4MG	.400	TABLETS	SUBUTEX	BUPRENORPHINE
308	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 15MG	15.000	TABLETS	MS CONTIN	MORPHINE

307	34	HYDROMORPHONE INJECTIONS	HYDROMORPHONE HCL 500MG/50ML	500.000	VIALS	DILAUDID	HYDROMORPHONE
306	34	HYDROMORPHONE INJECTIONS	HYDROMORPHONE HCL 50MG/5ML	50.000	AMPOULES	DILAUDID	HYDROMORPHONE
305	34	HYDROMORPHONE INJECTIONS	HYDROMORPHONE HCL 10MG/ML	10.000	AMPOULES	DILAUDID	HYDROMORPHONE
304	33	HYDROMORPHONE ORAL	HYDROMORPHONE HCL 8MG	8.000	TABLETS	DILAUDID	HYDROMORPHONE
303	33	HYDROMORPHONE ORAL	HYDROMORPHONE HCL 4MG	4.000	TABLETS	DILAUDID	HYDROMORPHONE
302	33	HYDROMORPHONE ORAL	HYDROMORPHONE HCL 2MG	2.000	TABLETS	DILAUDID	HYDROMORPHONE
301	31	FLUNITRAZEPAM ORAL	FLUNITRAZEPAM 1MG	1.000	TABLETS	ROHYPNOL, HYPNODORM	BENZODIAZEPINE
300	73	FENTANYL PATCHES	FENTANYL PATCHES 100 MCG/HR 16.8MG	7.200	PATCHES	DUROGESIC	FENTANYL
299	73	FENTANYL PATCHES	FENTANYL PATCHES 75 MCG/HR 12.6MG	5.400	PATCHES	DUROGESIC	FENTANYL
298	73	FENTANYL PATCHES	FENTANYL PATCHES 50 MCG/HR 8.4MG	3.600	PATCHES	DUROGESIC	FENTANYL
297	73	FENTANYL PATCHES	FENTANYL PATCHES 25 MCG/HR 4.2MG	1.800	PATCHES	DUROGESIC	FENTANYL
295	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 200MG	200.000	SACHETS	MS CONTIN	MORPHINE
294	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 100MG	100.000	SACHETS	MS CONTIN	MORPHINE
293	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 60MG	60.000	SACHETS	MS CONTIN	MORPHINE

290	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCODONE HCL (SR) 80MG	80.000	TABLETS	OXYCONTIN	OXYCODONE
289	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCODONE HCL (SR) 40MG	40.000	TABLETS	OXYCONTIN	OXYCODONE
288	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCODONE HCL (SR) 20MG	20.000	TABLETS	OXYCONTIN	OXYCODONE
287	69	OXYCODONE HCL CONTROLLED RELEASE ORAL	OXYCODONE HCL (SR) 10MG	10.000	TABLETS	OXYCONTIN	OXYCODONE
286	4	MORPHINE SLOW RELEASE ORAL	MORPH SULPHATE (SR) 10MG	10.000	CAPSULES	KAPANOL	MORPHINE
279	61	QUINALBARBITONE ORAL	QUINALBARBITONE 50MG	50.000	CAPSULES	SECONAL SODIUM	BARBITURATE
274	16	PETHIDINE INJECTIONS	PETHIDINE HCL 2500MG/50ML	2500.000	VIALS	NULL	PETHIDINE
272	16	PETHIDINE INJECTIONS	PETHIDINE HCL 75MG/1.5ML	75.000	AMPOULES	NULL	PETHIDINE
270	16	PETHIDINE INJECTIONS	PETHIDINE HCL 50MG/ML	50.000	AMPOULES	NULL	PETHIDINE
268	16	PETHIDINE INJECTIONS	PETHIDINE HCL 50MG/10ML	50.000	AMPOULES	NULL	PETHIDINE
267	16	PETHIDINE INJECTIONS	PETHIDINE HCL 50MG ATR SULPH 0.6MG 1ML	50.000	AMPOULES	NULL	PETHIDINE
266	15	PETHIDINE ORAL	PETHIDINE HCL 50MG	50.000	TABLETS	NULL	PETHIDINE
265	16	PETHIDINE INJECTIONS	PETHIDINE HCL 25MG/1ML	25.000	AMPOULES	NULL	PETHIDINE
262	16	PETHIDINE INJECTIONS	PETHIDINE HCL 100MG/2ML	100.000	AMPOULES	NULL	PETHIDINE
260	16	PETHIDINE INJECTIONS	PETH HCL 50MG PROMETH HCL	50.000	AMPOULES	NULL	PETHIDINE

			50MG HYOSC HBR .43MG 2ML				
259	16	PETHIDINE INJECTIONS	PETH HCL 100MG PROMETH HCL 50MG HYOSC HBR .43MG 2M	100.000	AMPOULES	NULL	PETHIDINE
258	16	PETHIDINE INJECTIONS	PETH HCL 100MG PROMETH HCL 25MG ATR SULPH .6MG 1ML	100.000	AMPOULES	NULL	PETHIDINE
257	NULL	NULL	PENTOBARBITONE SODIUM 50MG	50.000	CAPSULES	NEMBUTAL	BARBITURATE
256	NULL	NULL	PENTOBARB SODIUM 100MG	100.000	CAPSULES	CARBRITAL, NEMBUTAL, PENTONE	BARBITURATE
254	NULL	NULL	PENTOBARBITONE 50MG	50.000	TABLETS	NULL	BARBITURATE
252	NULL	NULL	PENTOBARBITONE 100MG	100.000	TABLETS	NULL	BARBITURATE
248	NULL	NULL	PENTAZOCINE BASE 60MG/2ML	60.000	AMPOULES	FORTRAL	PENTAZOCINE
247	NULL	NULL	PENTAZOCINE BASE 50MG	50.000	TABLETS	FORTRAL	PENTAZOCINE
245	NULL	NULL	PENTAZOCINE BASE 30MG/ML	30.000	AMPOULES	FORTRAL	PENTAZOCINE
244	NULL	NULL	PENTAZOCINE BASE 25MG	25.000	TABLETS	FORTRAL	PENTAZOCINE
243	NULL	NULL	PAPAVERETUM 5MG/ML	5.000	AMPOULES	NULL	PAPAVERETUM
241	NULL	NULL	PAPAVERETUM 20MG/ML	20.000	AMPOULES	NULL	PAPAVERETUM
240	42	PAPAVERETUM ORAL	PAPAVERETUM 20MG/ML	20.000	MILLILITRES	NULL	PAPAVERETUM
239	NULL	NULL	PAPAVERETUM 20MG HYOSCINE	20.000	AMPOULES	NULL	PAPAVERETUM

			HYDROBROMIDE 0.4MG 1ML				
238	NULL	NULL	PAPAVERETUM 15MG/ML	15.000	AMPOULES	NULL	PAPAVERETUM
237	NULL	NULL	PAPAVERETUM 10MG/ML	10.000	AMPOULES	NULL	PAPAVERETUM
235	42	PAPAVERETUM ORAL	PAPAVERETUM 10MG ORAL	10.000	TABLETS	OMNOPON	PAPAVERETUM
234	11	OXYCODONE ORAL	OXYCODONE HCL 5MG	5.000	TABLETS	ENDONE	OXYCODONE
233	11	OXYCODONE ORAL	OXYCODONE HCL 4.4MG TEREPHTH .38MG	4.400	TABLETS	PERCODAN	OXYCODONE
231	12	OXYCODONE SUPPOSITORIES	OXYCODONE BASE 30MG	30.000	SUPPOSITORIES	PROLADONE	OXYCODONE
230	13	OXYCODONE INJECTIONS	OXYCODONE HCL 10MG/ML	10.000	AMPOULES	OXYNORM	OXYCODONE
228	80	OPIUM ORAL	OPIUM TINCTURE	1.000	MILLILITRES	NULL	OPIUM
225	75	NORMETHADONE ORAL	NORMETHADONE HCL 1% (TICARDA DROPS)	.010	MILLILITRES	NULL	NORMETHADONE
223	NULL	NULL	PENTOBARBITONE SODIUM 30MG	30.000	TABLETS	NEMBUDEINE, PENTALGIN	BARBITURATE
222	6	MORPHINE INJECTIONS	MORPHINE TARTRATE 120MG/1.5ML	120.000	AMPOULES	NULL	MORPHINE
220	5	MORPHINE ORAL	MORPHINE SULPHATE SOLUTION 10MG/ML	10.000	MILLILITRES	NULL	MORPHINE
218	6	MORPHINE INJECTIONS	MORPHINE SULPHATE 5MG/ML	5.000	AMPOULES	NULL	MORPHINE
217	6	MORPHINE INJECTIONS	MORPHINE SULPHATE 30MG/ML	30.000	AMPOULES	NULL	MORPHINE
216	5	MORPHINE ORAL	MORPHINE SULPHATE 30MG	30.000	TABLETS	ANAMORPH	MORPHINE

215	6	MORPHINE INJECTIONS	MORPHINE SULPHATE 15MG/ML	15.000	AMPOULES	NULL	MORPHINE
214	6	MORPHINE INJECTIONS	MORPHINE SULPHATE 15MG ATROPINE SULPHATE 0.6MG 1ML	15.000	AMPOULES	NULL	MORPHINE
213	6	MORPHINE INJECTIONS	MORPHINE SULPHATE 10MG/ML	10.000	AMPOULES	NULL	MORPHINE
212	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 60MG	60.000	TABLETS	MS CONTIN, MOMEX	MORPHINE
211	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 30MG	30.000	TABLETS	MS CONTIN, MOMEX	MORPHINE
210	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 5MG	5.000	TABLETS	MS CONTIN	MORPHINE
209	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 10MG	10.000	TABLETS	MS CONTIN, MOMEX	MORPHINE
208	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 100MG	100.000	TABLETS	MS CONTIN, MOMEX	MORPHINE
207	6	MORPHINE INJECTIONS	MORPHINE SULPHATE 10MG & ATROPINE SULPHATE 0.6MG	10.000	AMPOULES	NULL	MORPHINE
206	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 50MG	50.000	CAPSULES	KAPANOL	MORPHINE
205	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 20MG	20.000	CAPSULES	KAPANOL	MORPHINE

204	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 100MG	100.000	CAPSULES	KAPANOL	MORPHINE
203	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 20MG	20.000	SACHETS	MS CONTIN	MORPHINE
202	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 30MG	30.000	SACHETS	MS CONTIN	MORPHINE
201	4	MORPHINE SLOW RELEASE ORAL	MORPHINE SULPHATE (SR) 200MG	200.000	TABLETS	MS CONTIN	MORPHINE
200	5	MORPHINE ORAL	MORPHINE LINCTUS	.000	BOTTLE	MORPHINE LINCTUS	MORPHINE
198	5	MORPHINE ORAL	MORPHINE HCL MIXTURE 4MG/ML	4.000	MILLILITRES	NULL	MORPHINE
197	5	MORPHINE ORAL	MORPHINE HCL MIXTURE 2MG/ML (200ML)	400.000	BOTTLE	ORDINE	MORPHINE
196	5	MORPHINE ORAL	MORPHINE HCL MIXTURE 10MG/ML (200ML)	2000.000	BOTTLE	ORDINE	MORPHINE
195	5	MORPHINE ORAL	MORPHINE HCL 5MG ASPIRIN 250MG (SOLUBLE)	5.000	TABLETS	NULL	MORPHINE
192	5	MORPHINE ORAL	MORPHINE 30MG TACRINE 15MG	30.000	TABLETS	MORTHA	MORPHINE
189	5	MORPHINE ORAL	MORPHINE 15MG TACRINE 30MG 1.5ML	30.000	AMPOULES	MORTHA NO 3	MORPHINE
186	25	METHYLPHENIDATE INJECTIONS	METHYLPHENIDATE HCL 20MG	20.000	AMPOULES	RITALIN	AMPHETAMINE
185	24	METHYLPHENIDATE ORAL	METHYLPHENIDATE HCL 10MG	10.000	TABLETS	RITALIN, ATTENTA, LORENTIN	AMPHETAMINE

183	1	METHADONE LIQUID	METHADONE HCL SYRUP 5MG/ML (PROGRAM)	5.000	MILLILITRES	NULL	METHADONE
182	8	METHADONE ORAL	METHADONE HCL 5MG	5.000	TABLETS	PHYSEPTONE	METHADONE
181	8	METHADONE ORAL	METHADONE HCL 2MG/5ML (500ML)	200.000	BOTTLE	PHYSEPTONE LINCTUS	METHADONE
180	9	METHADONE INJECTIONS	METHADONE HCL 10MG/ML	10.000	AMPOULES	PHYSEPTONE	METHADONE
179	8	METHADONE ORAL	METHADONE HCL 10MG	10.000	TABLETS	PHYSEPTONE	METHADONE
177	80	OPIUM ORAL	KAOLIN & OPIUM MIXTURE (200ML)	.000	BOTTLE	NULL	OPIUM
176	34	HYDROMORPHONE INJECTIONS	HYDROMORPHONE HCL 2MG/ML	2.000	AMPOULES	DILAUDID	HYDROMORPHONE
175	33	HYDROMORPHONE ORAL	HYDROMORPHONE HCL 2.5MG	2.500	TABLETS	DILAUDID	HYDROMORPHONE
169	31	FLUNITRAZEPAM ORAL	FLUNITRAZEPAM 2MG	2.000	TABLETS	ROHYPNOL, HYPNODORM	BENZODIAZEPINE
168	30	FENTANYL INJECTIONS	FENTANYL CITRATE 100MCG/20ML	.100	VIALS	SUBLIMAZE	FENTANYL
166	30	FENTANYL INJECTIONS	FENTANYL CITRATE 500MCG/10ML	.500	AMPOULES	SUBLIMAZE 500MCG/10ML OR 0.5MG/10ML	FENTANYL
164	30	FENTANYL INJECTIONS	FENTANYL CITRATE .157MG/2ML DROPERIDOL 5MG/2ML 2ML	.157	AMPOULES	NULL	FENTANYL
163	30	FENTANYL INJECTIONS	FENTANYL CITRATE 100MCG/2ML	.100	AMPOULES	SUBLIMAZE 100MCG/2ML OR 0.1MG/2ML	FENTANYL
151	NULL	NULL	DIAMORPHINE HCL 10MG/ML	10.000	AMPOULES	HEROIN	OTHER
149	28	DEXTROMORAMIDE INJECTIONS	DEXTROMORAMIDE BASE 5MG/ML	5.000	AMPOULES	PALFIUM	DEXTROMORAMIDE
148	26	DEXTROMORAMIDE ORAL	DEXTROMORAMIDE BASE 5MG	5.000	TABLETS	PALFIUM	DEXTROMORAMIDE

147	27	DEXTROMORAMIDE SUPPOSITORIES	DEXTROMORAMIDE BASE 10MG	10.000	SUPPOSITORIES	PALFIUM	DEXTROMORAMIDE
145	18	DEXAMPHETAMINE ORAL	DEXAMPHETAMINE SULPHATE 5MG	5.000	TABLETS	NULL	AMPHETAMINE
144	18	DEXAMPHETAMINE ORAL	DEXAMPHETAMINE SULPHATE 15MG	15.000	CAPSULES	NULL	AMPHETAMINE
142	18	DEXAMPHETAMINE ORAL	DEXAMPHETAMINE SULPHATE 10MG	10.000	CAPSULES	CUSTOM COMPOUNDING	AMPHETAMINE
140	22	CODEINE INJECTIONS	CODEINE PHOSPHATE 50MG/1ML	50.000	AMPOULES	NULL	CODEINE
139	21	CODEINE ORAL	CODEINE PHOSPHATE 30MG	30.000	TABLETS	NULL	CODEINE
138	23	CODEINE POWDER	CODEINE PHOSPHATE	1000.000	GRAMS	NULL	CODEINE
137	NULL	NULL	COCAINE NASAL GEL 5%	.050	GRAMS	COCAINE NASAL GEL 5%	COCAINE
136	62	COCAINE SOLUTION/GEL	COCAINE HCL SOLUTION/GEL 10%	.100	MILLILITRES	COCAINE HCL SOLUTION/GEL 10%	COCAINE
135	62	COCAINE SOLUTION/GEL	COCAINE HCL SOLUTION/GEL 0.5%	.005	MILLILITRES	COCAINE HCL SOLUTION/GEL 0.5%	COCAINE
134	62	COCAINE SOLUTION/GEL	COCAINE HCL SOLUTION/GEL 3% & ADRENALINE	.030	MILLILITRES	COCAINE HCL SOLUTION/GEL 3% & ADRENALINE	COCAINE
133	62	COCAINE SOLUTION/GEL	COCAINE HCL SOLUTION/GEL 5%	.050	MILLILITRES	COCAINE HCL SOLUTION/GEL 5%	COCAINE
132	62	COCAINE SOLUTION/GEL	COCAINE HCL SOLUTION/GEL 4%	.040	MILLILITRES	COCAINE HCL SOLUTION/GEL 4%	COCAINE
131	62	COCAINE SOLUTION/GEL	COCAINE HCL SOLUTION/GEL 2%	.020	MILLILITRES	COCAINE HCL SOLUTION/GEL 2%	COCAINE
130	62	COCAINE SOLUTION/GEL	COCAINE HCL SOLUTION/GEL 1%	.010	MILLILITRES	COCAINE HCL SOLUTION/GEL 1%	COCAINE
128	65	COCAINE INJECTIONS	COCAINE HCL 5MG/0.3ML	5.000	AMPOULES	COCAINE HCL 5MG/0.3ML	COCAINE

126	65	COCAINE INJECTIONS	COCAINE HCL 4% 1ML	4.000	AMPOULES	COCAINE HCL 4% 1ML	COCAINE
122	62	COCAINE SOLUTION/GEL	COCAINE HCL 15MG & MORPHINE HCL 15MG/10ML	15.000	MILLILITRES	COCAINE HCL 15MG & MORPHINE HCL 15MG/10ML	COCAINE
119	64	COCAINE POWDER	COCAINE HCL POWDER 1000MG	1000.000	GRAMS	COCAINE HCL POWDER 1000MG	COCAINE
116	57	BUTOBARBITONE ORAL	BUTOBARBITONE 100MG	100.000	TABLETS	SONABARB	BARBITURATE
115	NULL	NULL	BUTOBARBITONE 1000G	1000.000	GRAMS	NULL	BARBITURATE
114	38	BUPRENORPHINE SUB-LINGUAL	BUPRENORPHINE SUB-LINGUAL 0.2MG	.200	TABLETS	TEMGESIC	BUPRENORPHINE
113	39	BUPRENORPHINE INJECTIONS	BUPRENORPHINE HCL 0.6MG/2ML	.600	AMPOULES	TEMGESIC	BUPRENORPHINE
112	39	BUPRENORPHINE INJECTIONS	BUPRENORPHINE HCL 0.3MG/ML 1ML	.300	AMPOULES	TEMGESIC	BUPRENORPHINE
111	NULL	NULL	BROMPTONS MIXTURE	.000	MILLILITRES	BROMPTONS MIXTURE	OTHER
110	54	AMYLOBARBITONE ORAL	AMYLOBARBITONE 50MG	50.000	CAPSULES	NEUR-AMYL/AMYTAL SODIUM 50MG	BARBITURATE
108	54	AMYLOBARBITONE ORAL	AMYLOBARBITONE 50MG	50.000	TABLETS	AMYTAL, NEUR-AMYL	BARBITURATE
107	54	AMYLOBARBITONE ORAL	AMYLOBARBITONE 30MG	30.000	TABLETS	AMYTAL, NEUR-AMYL	BARBITURATE
105	54	AMYLOBARBITONE ORAL	AMYLOBARBITONE 100MG	100.000	TABLETS	AMYTAL	BARBITURATE
101	20	DEXAMPHETAMINE POWDER	AMPHETAMINE SULPHATE	1000.000	GRAMS	AMPHETAMINE SULPHATE	AMPHETAMINE
100	54	AMYLOBARBITONE ORAL	AMESEC 25MG	25.000	CAPSULES	NULL	BARBITURATE

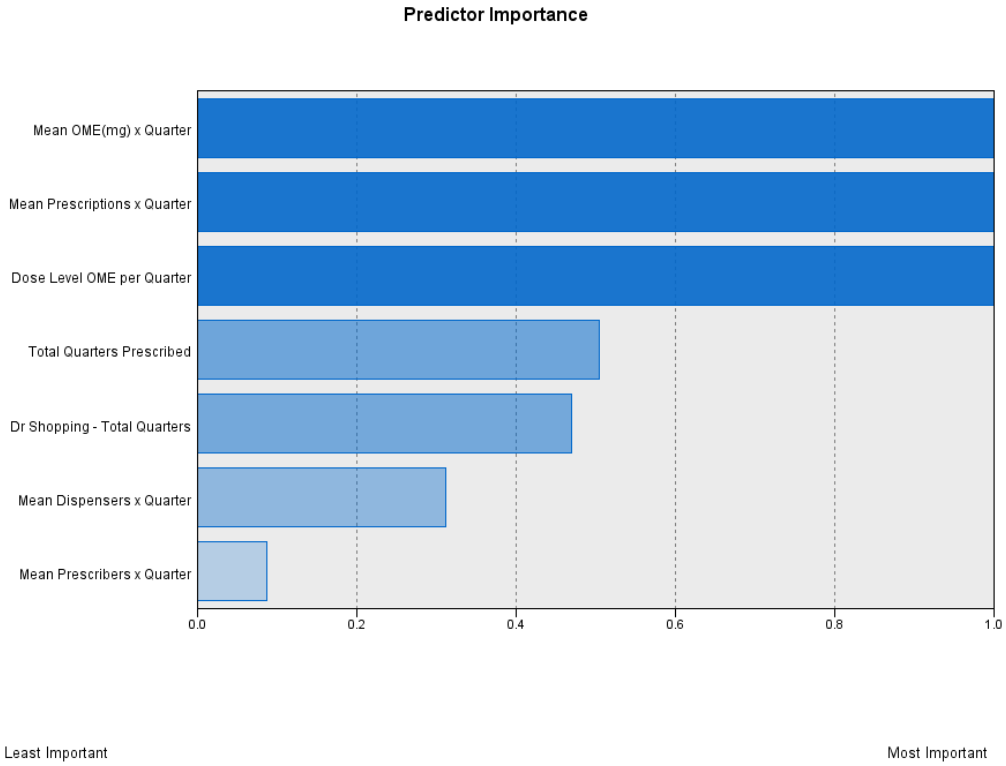
Appendix H: Two-Step Cluster Analysis results

SPSS for Windows results output from Two-Step Cluster Analysis

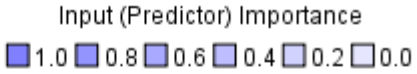
Model Summary

Algorithm	TwoStep
Inputs	7
Clusters	2

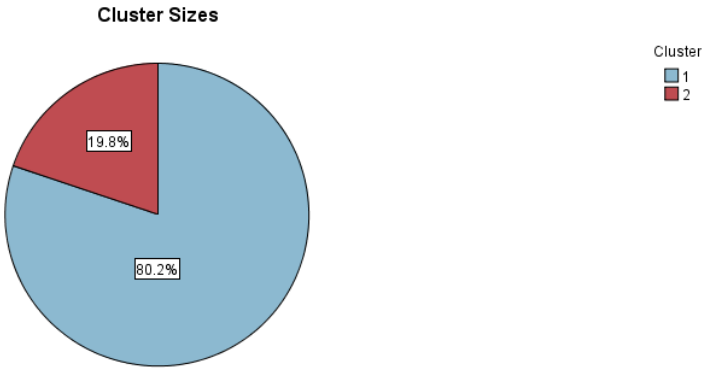
Cluster Quality


Predictor Importance
Mean OME(mg) x Quarter
Mean Prescriptions x Quarter
Dose Level OME per Quarter
Total Quarters Prescribed
Dr Shopping - Total Quarters
Mean Dispensers x Quarter
Mean Prescribers x Quarter
0.0
0.2
0.4
0.6
0.8
1.0
Least Important
Most Important

Clusters



Cluster	1	2
Label		
Description		
Size	80.2% (11536)	19.8% (2842)
Inputs	Dose Level OME per Quarter Up to 100mg OME daily (100.0%)	Dose Level OME per Quarter 100-200 mg OME daily (53.9%)
	Mean OME(mg) x Quarter 2,365.43	Mean OME(mg) x Quarter 21,696.37
	Mean Prescriptions x Quarter 5.95	Mean Prescriptions x Quarter 11.52
	Total Quarters Prescribed 2.88	Total Quarters Prescribed 3.52
	Dr Shopping - Total Quarters 1.27	Dr Shopping - Total Quarters 1.63
	Mean Dispensers x Quarter 1.72	Mean Dispensers x Quarter 2.17
	Mean Prescribers x Quarter 2.52	Mean Prescribers x Quarter 2.74

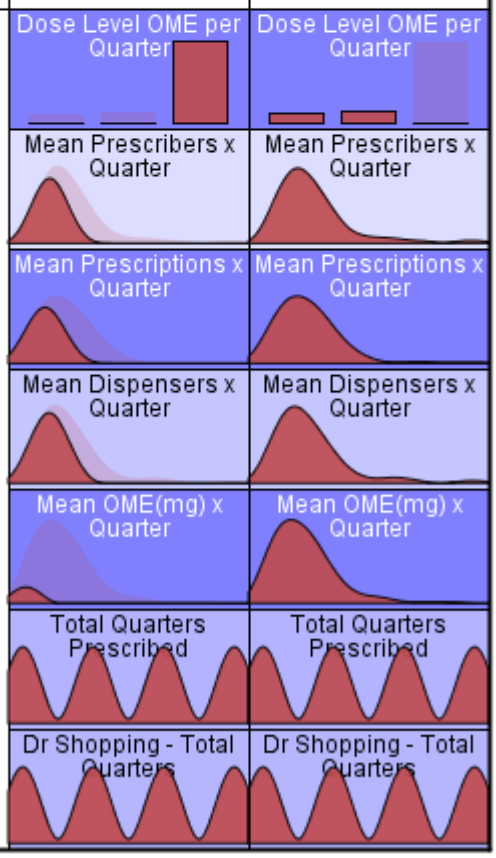


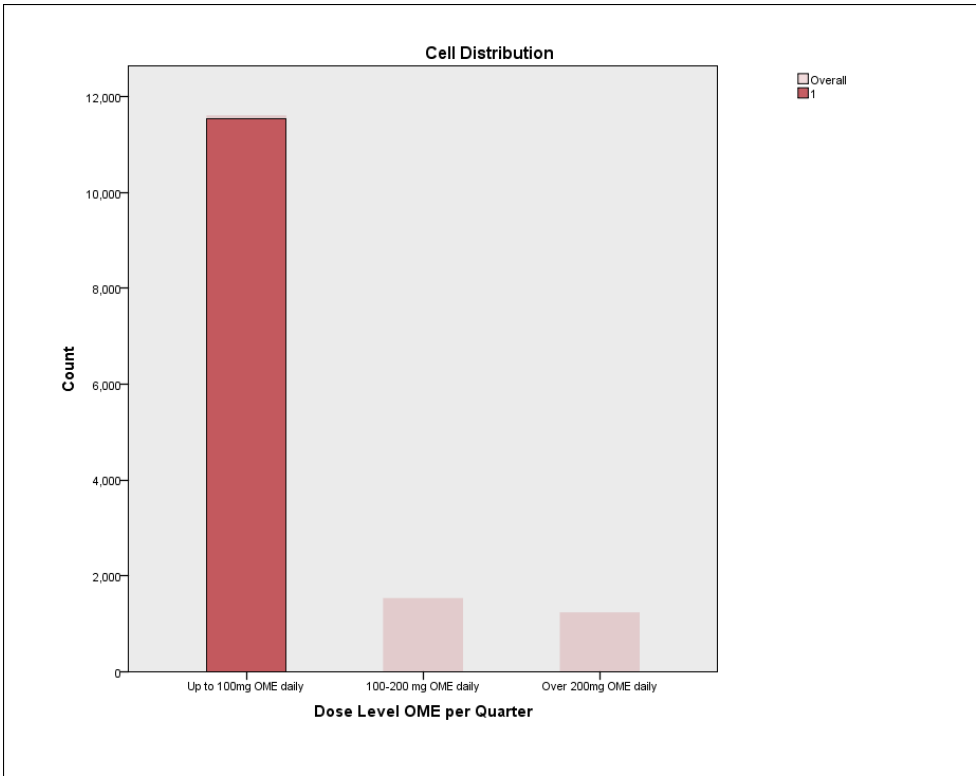
Size of Smallest Cluster	2842 (19.8%)
Size of Largest Cluster	11536 (80.2%)
Ratio of Sizes: Largest Cluster to Smallest Cluster	4.06

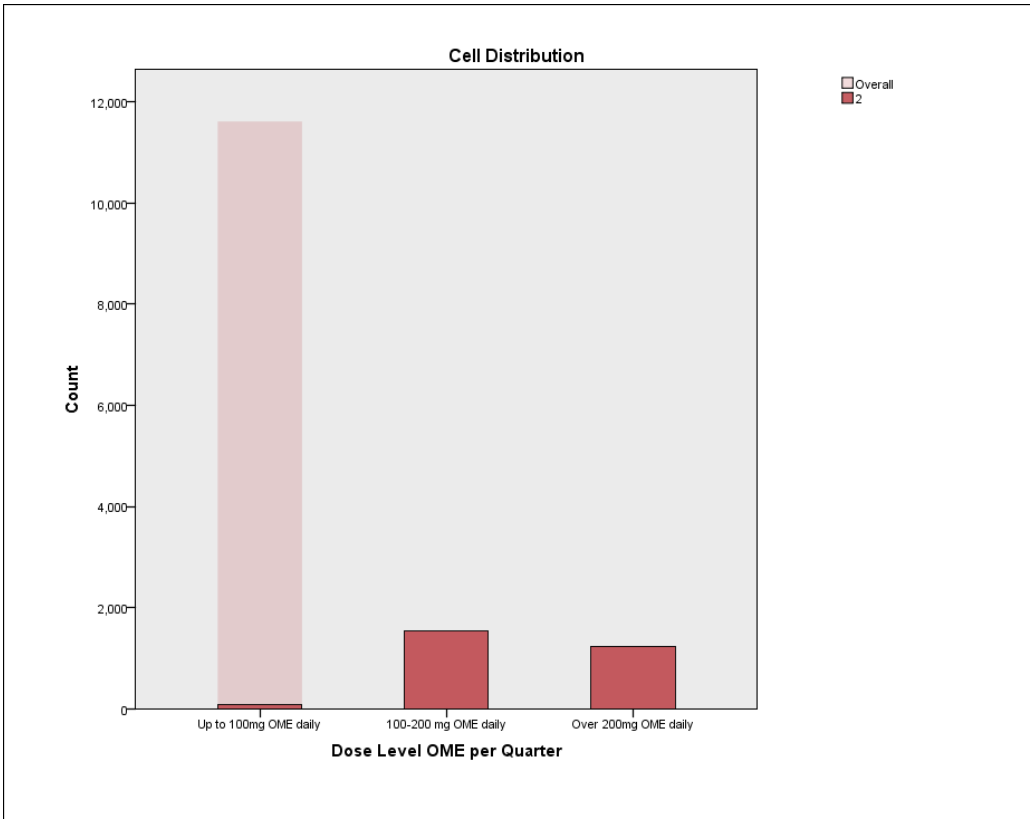
Clusters

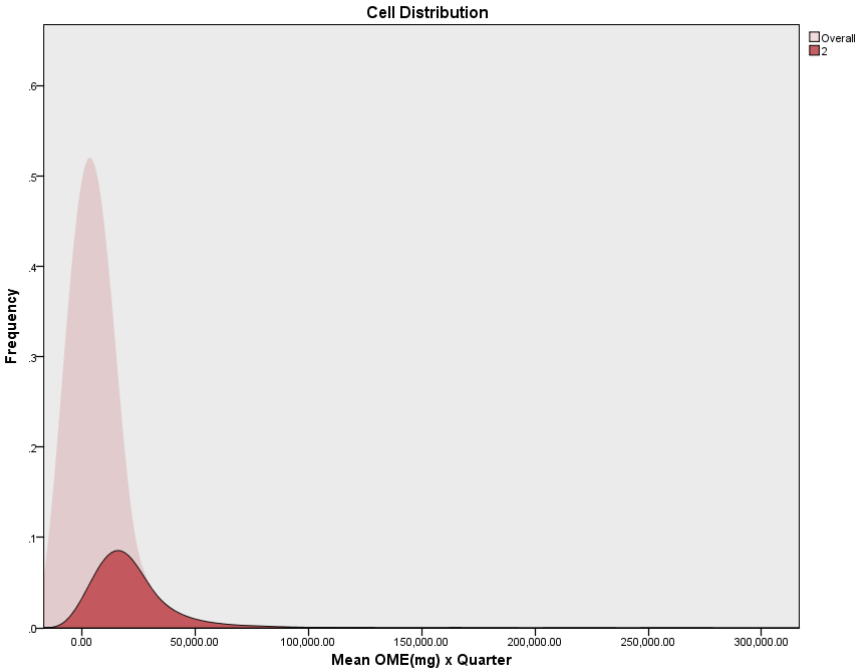
Input (Predictor) Importance

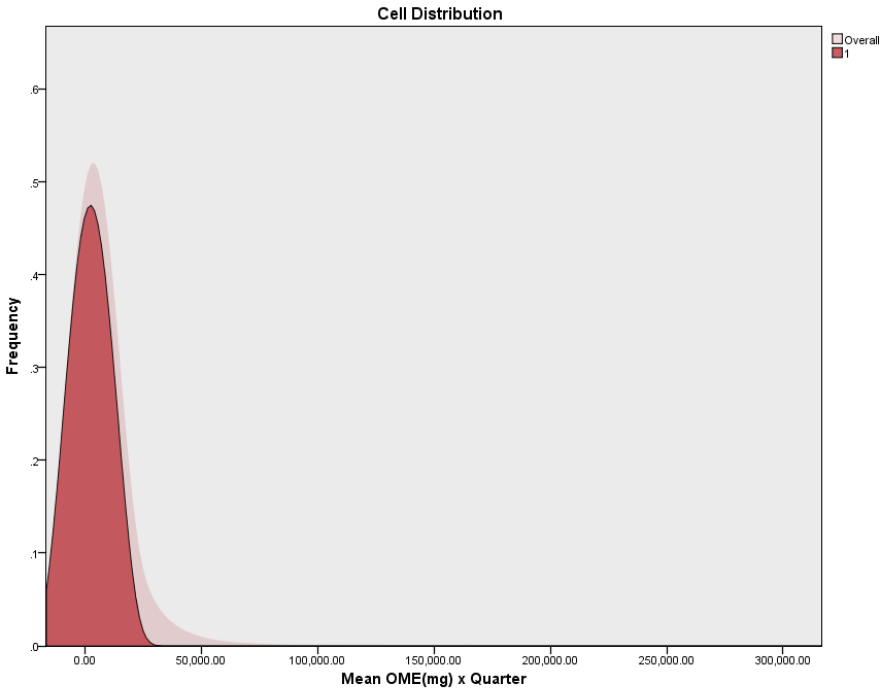
1.0 0.8 0.6 0.4 0.2 0.0

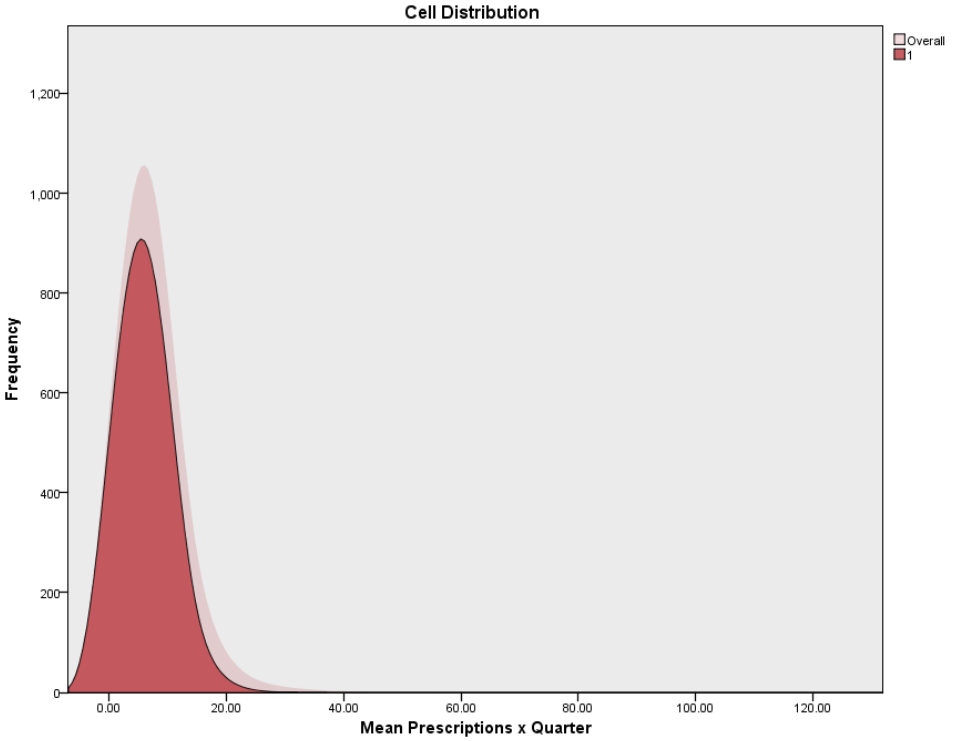
Cluster	1	2
Label		
Description		
Size	80.2% (11536)	19.8% (2842)
Inputs		

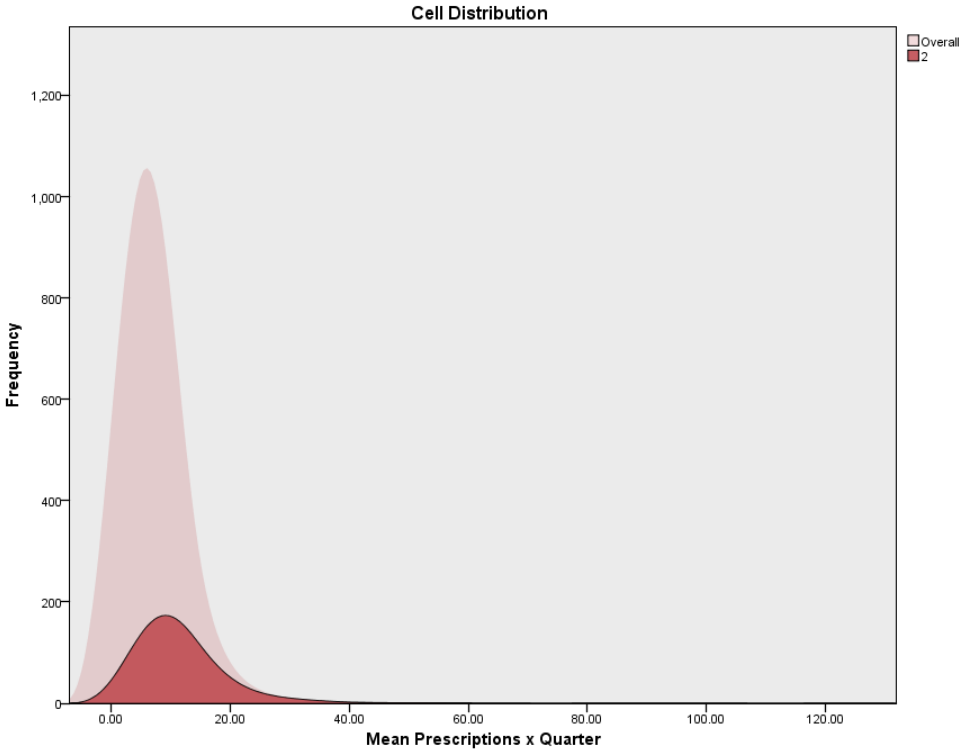

Cell Distribution
Overall
1
12,000
10,000
8,000
6,000
4,000
2,000
0
Count
Up to 100mg OME daily
100-200 mg OME daily
Over 200mg OME daily
Dose Level OME per Quarter


Cell Distribution
Overall
2
12,000
10,000
8,000
6,000
4,000
2,000
0
Count
Up to 100mg OME daily
100-200 mg OME daily
Over 200mg OME daily
Dose Level OME per Quarter


Cell Distribution
Overall
2
Frequency
.0
.1
.2
.3
.4
.5
.6
0.00
50,000.00
100,000.00
150,000.00
200,000.00
250,000.00
300,000.00
Mean OME(mg) x Quarter


Cell Distribution
Overall
1
Frequency
.0
.1
.2
.3
.4
.5
.6
0.00
50,000.00
100,000.00
150,000.00
200,000.00
250,000.00
300,000.00
Mean OME(mg) x Quarter


Cell Distribution
Overall
1
Frequency
1,200
1,000
800
600
400
200
0
0.00
20.00
40.00
60.00
80.00
100.00
120.00
Mean Prescriptions x Quarter


Cell Distribution
Overall
2
Frequency
1,200
1,000
800
600
400
200
0
0.00
20.00
40.00
60.00
80.00
100.00
120.00
Mean Prescriptions x Quarter

Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping Behaviour

1. Introduction

The electronic monitoring of, and 'real-time reporting' of prescriptions of pharmaceutical opioid drugs is widely recognised as one means of reducing misuse and increasing appropriate use of this class of drugs. This information can be used to inform health practitioners to guide their decisions where possible aberrant drugs use is detected.

Substance use disorders (abuse & dependence) in relation to pharmaceutical opioids are poorly understood. There is diversity of opinion about what use constitutes problematic use and what is appropriate treatment in chronic opioid therapy.

Clinical diagnoses of substance use disorders are undertaken by health practitioners in their face to face assessment of patients, based on a range of criteria.

The use of prescription information, in the absence of clinical information, might not on its own be sufficient to allow clinicians to arrive at conclusions about a person's potential drug misuse.

However, database information derived from patterns of prescription events across populations, could be used to assist health practitioners in making better informed decisions on an individual's potentially problematic medication use.

This study seeks to obtain information from clinical experts,such as yourself, in regards to their experience with treatment of persons with pharmaceutical opioids where problematic use has occurred. The purpose is to derive methods to potentially assess, detect and predict, aberrant prescription opioid drug use behaviour that might be indicative of substance use disorders using a prescription monitoring program.

Participation will involve completing three rounds of a questionnaire based on the Delphi Technique. That is, the survey will be conducted in three iterations, where the results of the previous rounds will be reported back to you for further feedback. This is to obtain a convergence of opinion in defining this behaviour of concern. The questions will involve matters relating to opinions about dependence on and management with opioid analgesic drugs.

It is anticipated that the first survey should take at the maximum 30 minutes to complete, and further iterations will take less time. Second and third round questionnaires will be circulated within 3 weeks of the completion of each questionnaire.

This first study involves four separate but related surveys, on the following topics:

1. Utility of DSM-IV criteria in assessing substance use disorders involving pharmaceutical opioids;
2. Ratings of the harmfulness of pharmaceutical opioid drugs;
3. Assessment of risk factors for persons with substance use disorders related to prescription opioids; and,
4. Questions on prescription or doctor shopping definitions.

1. This study has obtained Ethics Approval of Queensland Health & Queensland University of Technology,

Do you wish to read the full copy of Participant Information of this Research Project?

◯ Yes, I wish to read the Participant Information

◯ No, I am happy to proceed with the survey

2. Participant Information for QUT Research Project

Misuse of Pharmaceutical Opioid Analgesic Drugs: Doctor shopping behaviour.
Queensland Health Ethics Approval Number HREC/11/QHC/1
QUT Ethics Approval Number 1100000526

Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping Behaviour

RESEARCH TEAM

Principal Researcher: Bill Loveday, Doctor of Health Science student, QUT

Associate Researcher: Dr Kirsten McKenzie, Deputy Director & Senior Research Fellow
National Health Information Research & Training
Queensland University of Technology.

DESCRIPTION

This project is being undertaken as part of a research project as part of a Doctor of Health Science degree for the Principal Researcher with the Queensland University of Technology.

This study is being done to learn more about dependence on, and misuse of, pharmaceutical opioid analgesic drugs and the phenomenon of drug seeking known as 'doctor shopping'. There is a diversity of opinion across various stakeholders as to what constitutes misuse or inappropriate management with this class of drugs. The purpose of this project is to obtain a range of specialist opinions in regards to the determining definitions of drug dependence or abuse on pharmaceutical opioid analgesic drugs via measures of an individual's drug seeking and other behaviour.

The research team requests your assistance because of your interest in the field of drug dependence or chronic pain management.

PARTICIPATION

Your participation in this project is entirely voluntary. If you do agree to participate, you can withdraw from the project at any time without comment or penalty. Any identifiable information already obtained from you will be destroyed. Your decision to participate, or not participate, will in no way impact upon your current or future relationship with QUT or with Queensland Health.

Participation will involve completing multiple rounds of a questionnaire based on the Delphi Technique. That is, the survey will be conducted in three iterations, where the results of the previous rounds will be reported back to you for further feedback. This is to obtain a convergence of opinion in defining this behaviour of concern. The questions will involve matters relating to opinions about dependence on and management with opioid analgesic drugs.

It is anticipated that the first survey should take at the maximum 30 minutes to complete, and further iterations will take less time. Second and third round questionnaires will be circulated within 3 weeks of the completion of each questionnaire.

If you agree to participate you do not have to complete any questions that you are uncomfortable answering.

EXPECTED BENEFITS

It is not expected that this project will directly benefit you. However, it will assist improving knowledge in the field of this growing public health concern in Australia.

You will not be recompensed for your participation however the results will be made available to you on completion of the project.

Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping Behaviour

RISKS

There are no risks beyond normal day-to-day living associated with your participation in this project.

PRIVACY AND CONFIDENTIALITY

All comments and responses will be treated confidentially and will be made anonymous for analysis and feedback. The names of individual persons are not required in any of the responses.Please note that non-identifiable data collected in this project may be used as comparative data in future projects.

CONSENT TO PARTICIPATE

Submitting the completed online questionnaire is accepted as an indication of your consent to participate in this project.

QUESTIONS / FURTHER INFORMATION ABOUT THE PROJECT

If have any questions or require any further information please contact one of the research team members below.

Bill Loveday - DHS Student
School of Public Health
Phone : 61+ 7 0419 782 846
Email : bill.loveday@student.qut.edu.au

Dr Kirsten McKenzie - Principal Supervisor
Faculty of Health - QUT Deputy Director & Senior Research Fellow
National Health Information Research & Training
School of Public Health - QUT
Phone : 61+ 7 3138 9753
Email : k.mckenzie@qut.edu.au

*Please note that Mr Loveday is also a Queensland Health employee and works for the Drugs of Dependence Unit. This Unit has legislative responsibilities in monitoring activity and compliance with legislation in regards to the use of opioid analgesic drugs in the state of Queensland.

CONCERNS / COMPLAINTS REGARDING THE CONDUCT OF THE PROJECT

Both Queensland Health and QUT are committed to research integrity and the ethical conduct of research projects. If you do have any concerns or complaints about the ethical conduct of the project you may contact either Queensland Health Research & Ethics Governance Unit on +61 7 3234 0654 or email regu@health.qld.gov.au quoting approval number: HREC/11/QHC/1. However, you may also contact you may contact the QUT Research Ethics Unit on +61 7 3138 5123 or email ethicscontact@qut.edu.au quoting approval 1100000526.

Both the Queensland Health Research & Ethics Governance Unit and the QUT Research Ethics Unit are not connected with the research project and can facilitate a resolution to your concern in an impartial manner.

1. Thank you for helping with this research project. A copy of this Participant Information can be sent you if required. Please indicate below if you wish a copy sent to your email address.

◯ Yes, please send me a copy of the Participant Information.

◯ No thank you, I do not require a copy.

3. Diagnostic Criteria for Pharmaceutical Opioid Substance Use Disorders

The DSM-IV (TR) defines substance dependence as a maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by three or more, of seven, criteria occurring any time in the same 12-month period.

Substance abuse is defined as a maladaptive pattern of substance use leading to clinically significant impairment or distress as manifested by one (or more), of four, criteria occurring within a 12-month period.

There are concerns that the DSM-IV(TR) definitions of substance use disorders using these criteria, might be less applicable in diagnosing cases of dependence on, or abuse of, pharmaceutical opioids.

In general there appears to be a lack of consistency in the clinical assessment of problematic use of pharmaceutical opioids, due to the long-term therapeutic application of opioids in the treatment of chronic pain conditions.

Each of the following criteria are based on DSM-IV criteria for substance dependence and abuse. The following questions seek your views, as an expert, on the importance of each criteria in defining pharmaceutical opioid dependence and abuse.

Please indicate for each of the following criteria how importance you believe it is in determining that an individual suffers from a substance use disorder due to their use of pharmaceutical opioid drugs.

It would be appreciated if you could also give your reasons as to why you rated each criteria as you did.

*1. How important is evidence of tolerance in assessing a person for substance use disorders on pharmaceutical opioid drugs?

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

*2. How important is evidence of withdrawal symptoms in assessing a person for substance use disorders on pharmaceutical opioid drugs?

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

***3. How important is the amount of drug being taken, in assessing a person for substance use disorders on pharmaceutical opioid drugs?**

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

***4. How important are attempts to reduce or control drug use, in assessing a person for substance use disorders on pharmaceutical opioid drugs?**

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

***5. How important is time spent in obtaining drugs, in assessing a person for substance use disorders on pharmaceutical opioid drugs?**

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

***6. How important are the effects of drugs use on social, occupational, or recreational activities, in assessing a person for substance use disorders on pharmaceutical opioid drugs?**

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

***7. How important is continued drug use despite health or psychological effects, in assessing a person for substance use disorders on pharmaceutical opioid drugs?**

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

***8. How important are the drug use effects on work, school or home obligations, in assessing a person for substance use disorders on pharmaceutical opioid drugs?**

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

***9. How important is drug use use in hazardous situations, in assessing a person for substance use disorders on pharmaceutical opioid drugs?**

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

***10. How important are drug-related legal problems, in assessing a person for substance use disorders on pharmaceutical opioid drugs?**

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

***11. How important are social or interpersonal problems, in assessing a person for substance use disorders on pharmaceutical opioid drugs?**

- ◯ Very important
- ◯ Important
- ◯ Moderately important
- ◯ Of little importance
- ◯ Unimportant

Can you please explain your reasons for the above response.

12. Are there any other criteria or behaviour you believe might also be important in determining inappropriate use of pharmaceutical opioid drugs?

4. Harmfulness of pharmaceutical opioid drugs

The assessment of the harms of certain drugs, can take into account the physical harms caused by continued use, the potential for a drug to cause dependence, and the social harms caused by use.

Physical harms refer to the propensity of drugs to cause damage to organs or systems or have negative effects on physiological functions, eg, respiratory or cardiac.

Dependence potential of a drug is related to the interaction between its pleasurable effects and propensity to produce dependent behaviour or be abused.

Social harms related to drugs relate to various effects of intoxication, through damaging family and social life and associated costs with health care, social care and legal responses.

Pharmaceutical opioid drugs are produced in different forms, preparations and are designed for various particular routes of administration.

Please consider which pharmaceutical opioid drugs you believe are more harmful than others, and what reasons you think this might be so.

***1. What pharmaceutical opioid drugs do you believe are the most prone to cause physical harm?**

***2. What pharmaceutical opioid drugs do you believe are the most prone to cause dependence?**

***3. What pharmaceutical opioid drugs do you believe are the most prone to be abused?**

***4. What pharmaceutical opioid drugs do you believe are the most prone to cause social harms?**

***5. What do you believe are some of the features of pharmaceutical opioid drugs that might contribute to their potential for harm?**

6. What do you believe are some of the features of pharmaceutical opioid drugs that might reduce their potential for harm?

7. What other reasons do you believe some pharmaceutical opioid drugs might be more harmful than others?

5. Individual Risk Factors

The biopsychosocial model suggests that complex interactions between various biological, psychological and social factors contribute to the development of substance use disorders.

Biological factors can refer to genetic vulnerability to risk factors for drug use, vulnerability to pharmacological effects

of drugs, and the actual pharmacological effects of drugs.

Psychological factors often relate to learning and conditioning, self-concept, cultural and spiritual beliefs, stress and coping style, and mental health.

Social factors refer to social, cultural, economic and environmental, risk and protective factors (including normative influences, social networks and social identity).

Within these categories, what factors do you believe are most relevant in the development of a substance use disorder related to pharmaceutical opioid drugs?

***1. What biological factors do you believe are most relevant in the development of a substance use disorder related to pharmaceutical opioid drugs?**

***2. What psychological factors do you believe are most relevant in the development of a substance use disorder related to pharmaceutical opioid drugs?**

***3. What social or cultural factors do you believe are most relevant in the development of a substance use disorder related to pharmaceutical opioid drugs?**

***4. What other factors do you believe are most relevant in the development of a substance use disorder related to pharmaceutical opioid drugs?**

6. Drug seeking behaviour

'Doctor shopping' or 'prescription shopping' is broadly defined as a person who is attending multiple doctors and obtaining multiple prescriptions over a certain time for certain drugs.

Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping Behaviour

1. What do you understand by the term 'doctor shopping' or 'prescription shopping' in the context of potential misuse of pharmaceutical medications?

***2. What extent (frequency of consultations, prescriptions obtained, volume of drug obtained, over what time period) of doctor/prescription shopping do you believe would suggest a person is suffering from a substance use disorder?**

***3. Are there any other features of doctor/prescription shopping that you believe that are relevant in considering whether a person suffering from a substance use disorder?**

7. Demographic & Background Information

1. Please provide the following information about your professional practice.

	Yes	No
Do you primarily work in field of drug dependence?	◯	◯
Do you primarily work in the field of pain management?	◯	◯
Are you a registered medical practitioner?	◯	◯
Are you a registered nurse or allied health practitioner?	◯	◯
Do you work in a hosptial?	◯	◯
Do you work in private practice?	◯	◯
Do you work in a university or research facilitiy?	◯	◯
Do you undertake research in this field?	◯	◯

***2. Can you please provide details of your professional qualifications and affiliations.**

Degrees	
Professional associations	
Current position	
Years in practice	
Location (urban, rural, remote)	

3. Are you male or female?

- ◯ Male
- ◯ Female

4. Which category below includes your age?

- ◯ 17 or younger
- ◯ 18-20
- ◯ 21-29
- ◯ 30-39
- ◯ 40-49
- ◯ 50-59
- ◯ 60 or older

***5. Please provide the following information for the purposes of our response tracking.**

Name:	
Institution/Agency	
City/Town:	
State/Province:	
ZIP/Postal Code:	
Country:	
Email Address:	
Phone Number:	

8. The next round

Thank you for participation in the first round of this survey. All participants responses will be collated and merged and returned to you for further feedback.

Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping Behaviour

1. Do you agree to participate in the second round of this study?

◯ YES ◯ NO

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

1. Introduction

You previously participated in Round 1 of this survey regarding issues of misuse of pharmaceutical opioids.

In completing Round 1 you also agreed to further participate in the following 2 rounds of the survey.

This study is using the Delphi Technique to collate and consider a range of expert opinions in this area. This technique involves feedback you participants of the total group results from the first survey and your own results to determine to ascertain if you would reconsider your answer on this based on the group's average response.

Once you have responded I will then feedback the results for a final time to see if you wish to reconsider any of your response for the second time based on the groups amended second round responses.

2. Participant Information for QUT Research Project

Misuse of Pharmaceutical Opioid Analgesic Drugs: Doctor shopping behaviour.
Queensland Health Ethics Approval Number HREC/11/QHC/1
QUT Ethics Approval Number 1100000526

RESEARCH TEAM

Principal Researcher: Bill Loveday, Doctor of Health Science student, QUT

Associate Researcher: Dr Kirsten McKenzie, Deputy Director & Senior Research Fellow
National Health Information Research & Training
Queensland University of Technology.

DESCRIPTION

This project is being undertaken as part of a research project as part of a Doctor of Health Science degree for the Principal Researcher with the Queensland University of Technology.

This study is being done to learn more about dependence on, and misuse of, pharmaceutical opioid analgesic drugs and the phenomenon of drug seeking known as 'doctor shopping'. There is a diversity of opinion across various stakeholders as to what constitutes misuse or inappropriate management with this class of drugs. The purpose of this project is to obtain a range of specialist opinions in regards to the determining definitions of drug dependence or abuse on pharmaceutical opioid analgesic drugs via measures of an individual's drug seeking and other behaviour.

The research team requests your assistance because of your interest in the field of drug dependence or chronic pain management.

PARTICIPATION

Your participation in this project is entirely voluntary. If you do agree to participate, you can withdraw from the project at any time without comment or penalty. Any identifiable information already obtained from you will be destroyed. Your decision to participate, or not participate, will in no way impact upon your current or future relationship with QUT or with Queensland Health.

Participation will involve completing multiple rounds of a questionnaire based on the Delphi Technique. That is, the survey will be conducted in three iterations, where the results of the previous rounds will be reported back to you for further feedback. This is to obtain a convergence of opinion in defining this behaviour of concern. The questions will involve matters relating to opinions about dependence on and management with opioid analgesic drugs.

It is anticipated that the first survey should take at the maximum 30 minutes to complete, and further iterations will take less time. Second and third round questionnaires will be circulated within 3 weeks of the completion of each questionnaire.

If you agree to participate you do not have to complete any questions that you are uncomfortable answering.

EXPECTED BENEFITS

It is not expected that this project will directly benefit you. However, it will assist improving knowledge in the field of this growing public health concern in Australia.

You will not be recompensed for your participation however the results will be made available to you on completion of the project.

RISKS

There are no risks beyond normal day-to-day living associated with your participation in this project.

PRIVACY AND CONFIDENTIALITY

All comments and responses will be treated confidentially and will be made anonymous for analysis and feedback. The names of individual persons are not required in any of the responses.Please note that non-identifiable data collected in this project may be used as comparative data in future projects.

CONSENT TO PARTICIPATE

Submitting the completed online questionnaire is accepted as an indication of your consent to participate in this project.

QUESTIONS / FURTHER INFORMATION ABOUT THE PROJECT

If have any questions or require any further information please contact one of the research team members below.

Bill Loveday - DHS Student
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Dr Kirsten McKenzie - Principal Supervisor
Faculty of Health - QUT Deputy Director & Senior Research Fellow
National Health Information Research & Training
School of Public Health - QUT
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*Please note that Mr Loveday is also a Queensland Health employee and works for the Drugs of Dependence Unit. This Unit has legislative responsibilities in monitoring activity and compliance with legislation in regards to the use of opioid analgesic drugs in the state of Queensland.

CONCERNS / COMPLAINTS REGARDING THE CONDUCT OF THE PROJECT

Both Queensland Health and QUT are committed to research integrity and the ethical conduct of research projects. If you do have any concerns or complaints about the ethical conduct of the project you may contact either Queensland Health Research & Ethics Governance Unit on +61 7 3234 0654 or email regu@health.qld.gov.au quoting approval number: HREC/11/QHC/1. However, you may also contact you may contact the QUT Research Ethics Unit on +61 7 3138 5123 or email ethicscontact@qut.edu.au quoting approval 1100000526.

Both the Queensland Health Research & Ethics Governance Unit and the QUT Research Ethics Unit are not connected with the research project and can facilitate a resolution to your concern in an impartial manner.

1. Thank you for helping with this research project. A copy of this Participant Information can be sent you if required. Please indicate below if you wish a copy sent to your email address.

◯ Yes, please send me a copy of the Participant Information.

◯ No thank you, I do not require a copy.

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

3. Diagnostic Criteria for Pharmaceutical Opioid Substance Use Disorders

In Round 1 of the survey all participants rated the various DSM-IV(TR) criteria on how important they might be in assessing substance use disorders related to pharmaceutical opioid use. The results are shown below list from most important (1) to least important (11), based on all responses.

You might be aware of some issues with the proposed revisions of DSM-IV in the DSM-V,in regards to the criteria for substance use disorders.

In the context of long-term treatment with opioid medications, it is proposed that symptoms of tolerance & withdrawal be disregarded in diagnosing a substance use disorder .

Secondly, the criterion relating to 'drug related legal problems' is proposed to be omitted in the DSM-V, for most diagnoses of substance use disorder as it was found to add no extra diagnostic value in field trials.

Bearing the above in mind, and the questions ranked below, please consider if you would change the order of the rankings as set out here.

1. Please make any changes in the following ranked order by dragging and dropping the items. Alternatively you can mark any items as non-applicable (N/A).

	1. Effects on social, occupational, or recreational activities	N/A
	2. Effects on work, school or home obligations	N/A
	3. Continued use despite health or psychological effects	N/A
	4. In hazardous situations	N/A
	5. Social or interpersonal problems	N/A
	6. Attempts to reduce or control use	N/A
	7. Drug-related legal problems	N/A
	8. Time spent in obtaining drugs	N/A
	10. Evidence of tolerance	N/A
	10. Evidence withdrawal symptoms	N/A
	10. Amount of drug taken	N/A

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

***2. If you do not wish to change the rankings you can indicate below & move to the next question. You are welcome to provide any further comments if you wish.**

- ◯ I am satisfied with the ranked order
- ◯ I have made some changes

My comments

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

4. Harmfulness of pharmaceutical opioid drugs

You previously rated all opioid drugs based on their harmfulness across certain categories of harm,
1) the physical harms caused by continued use,
2) the potential for a drug to cause dependence, and
3) the social harms caused by use.

Overall for each category the same five drugs were nominated across the majority of respondents in different orders (oxycodone, morphine, any opioids, fentanyl & hydromorphone).

Considering these drugs how would you rate their overall harmfulness across all types of harm they might cause?

1. Please make any changes in the following ranked order by dragging and dropping the items. Alternatively you can mark any items as non-applicable (N/A).

☐	Oxycodone	☐ N/A
☐	Morphine	☐ N/A
☐	Fentanyl	☐ N/A
☐	Hydromorphone	☐ N/A
☐	Any opioid	☐ N/A

2. Do you believe there are any other pharmaceutical opioids that should be included the above list, or any of the above listed drugs that should be removed?

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

3. You previously rated all opioid drugs based on certain aspects that might increase their harmfulness.

Listed beneath are the five most frequently reported aspects from all respondents where (1) most frequent response, (2) the second most frequent response, and so forth.

Please make any changes to the rankings you believe appropriate by dragging and dropping the items in the order you best believe rates harmfulness of these factors. Alternatively you can mark any items as non-applicable (N/A).

	Extended/controlled/slow release preparations	N/A
	High potency/dose formulations	N/A
	Injectable preparations (ampoules, vials)	N/A
	Injectability of preparations	N/A
	Rapid onset/immediate release preparations	N/A

4. Do you believe there are any other aspects of prescription opioids that should be included the above list, or any of the above listed aspects that should be removed? If so, please add details below.

5. You previously rated all opioid drugs based on certain aspects that might reduce their harmfulness.

Listed beneath are the five most frequently reported aspects from all respondents where (1) most frequent response, (2) the second most frequent response, and so forth.

Please make any changes to the rankings you believe appropriate by dragging and dropping the items in the order you best believe rates harmfulness of these factors. Alternatively you can mark any items as non-applicable (N/A).

	Extended/controlled/slow release preparations	N/A
	High potency/dose formulations	N/A
	Injectable preparations/injectability of preparations	N/A
	Rapid onset/immediate release preparations	N/A

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

6. Do you believe there are any other aspects of prescription opioids that should be included the above list, or any of the above listed aspects that should be removed? If so, please add details below.

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

5. Individual Risk Factors

The biopsychosocial model suggests that complex interactions between various biological, psychological and social factors contribute to the development of substance use disorders.

Biological factors can refer to genetic vulnerability to risk factors for drug use, vulnerability to pharmacological effects of drugs, and the actual pharmacological effects of drugs.

Psychological factors often relate to learning and conditioning, self-concept, cultural and spiritual beliefs, stress and coping style, and mental health.

Social factors refer to social, cultural, economic and environmental, risk and protective factors (including normative influences, social networks and social identity).

The following ranked list show the most frequent responses for each set of factors. The first item is the most frequent response, and the second item, the second most frequent response and so forth.

Please consider the following lists. If you believe any items should be ranked higher or lower make any changes you consider appropriate.

1. Biological factors - Please make any changes in the following ranked order by dragging and dropping the items. Alternatively you can mark any items as non-applicable (N/A).

☐	Genetics	☐ N/A
☐	Age	☐ N/A
☐	Individual biology (absorption/metabolism)	☐ N/A
☐	Chronic pain conditions	☐ N/A
☐	Family history	☐ N/A

2. Do you believe there are any other biological factors that should be included the above list, or any of the above items that should be removed? If so, please add details below.

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

3. Psychological factors - Please make any changes in the following ranked order by dragging and dropping the items. Alternatively you can mark any items as non-applicable (N/A).

	Mental health issues	N/A
	Low self-efficacy	N/A
	Expectancies/beliefs	N/A
	Previous history of dependence	N/A

4. Do you believe there are any other psychological factors that should be included the above list, or any of the above items that should be removed? If so, please add details below.

5. Social or cultural factors - Please make any changes in the following ranked order by dragging and dropping the items.

	Peer use	N/A
	Lack of social suppport	N/A
	Low socio-economic status	N/A
	Availability of prescription drugs	N/A
	Poor parenting/upbringing	N/A

6. Do you believe there are any other social or cultural factors that should be included the above list, or any of the above items that should be removed? If so, please add details below.

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

7. Considering the categories of risk factors related to the development of a substance use disorder related to pharmaceutical opioid drugs, can you rank them them in order of importance from most important to least important? Alternatively you can mark any items as non-applicable (N/A).

☐	Biological	☐ N/A
☐	Psychological	☐ N/A
☐	Social	☐ N/A
☐	Cultural	☐ N/A

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

6. Drug seeking behaviour & prescription monitoring

Doctor shopping' or 'prescription shopping' is broadly defined as a person who is attending multiple doctors and obtaining multiple prescriptions over a certain time for certain drugs. Most respondents in the first round suggested a obtaining multiple prescriptions from multiple doctors could be a cause for concern as to a possible substance use disorder.

However, some respondents suggested alternative explanations that might account for drug seeking behaviour. A person with poorly managed persistent pain condition could possibly seek alternative sources of opioids. Furthermore, a person engaged in primarily criminal enterprise could be seeking to flout the system to obtain opioids for illicit markets for financial gain.

Prescription monitoring programs now employed in many USA, Canadian and Australian jurisdictions generally only contain information about prescription records. This can include details of numbers of prescriptions obtained, medical practitioners consulted, pharmacies involved in dispensing, and details of the type of drugs and dosages over certain time periods.

There are now large volumes of pharmaceutical opioids prescribed and the increasing numbers of patients in receipt of long-term therapy with these drugs. Therefore identifying or predicting aberrant patterns of drug seeking behaviour can be complicated, when examining limited information at population levels.

The potential of monitoring systems is allow for alerting of health practitioners when unusual patterns of prescription obtaining occur. However, this could be fraught with problems.

Too sensitive a level of possible aberrant behaviour would capture too many persons of interest. This would set unmanageable volumes of work for health regulators and potentially lead to the cause of unwarranted suspicion of patients by medical practitioners.

Setting a too specific a level might exclude many persons of interest who are potentially developing substance use disorders, or deliberately manipulating the system to obtain opioids for non-medical purposes,

Some PMPs employ assessment system that can classify persons of interest in terms of green, amber or red ‘traffic lights’ rating, where:

- Green signifies, no concerns,

- Amber, cause of further investigation, and

- Red, a direction not to prescribe with out particular authority or action.

Please consider, if you were asked to set limits as to what criteria you would rate as meeting the above criteria for green, amber or red lights in terms of a person’s obtaining of pharmaceutical opioid prescriptions WITHOUT any other direct knowledge of their clinical presentation.

***1. GREEN LIGHT - What is the 'HIGHEST LEVEL' of opioid prescription obtainings over the last 2 month period would you consider non-problematic? (Please provide answers in numbers)**

Prescriptions obtained	
Doctors consulted	
Pharmacies dispensing	
Average daily dose* (mg morphine equivalent)	

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

2. Are there any other issues in a person's prescription history that you believe would be relevant to the assessment of non-problematic opioid use?

***3. AMBER LIGHT - What is the 'LOWEST level' of prescription obtainings over the last 2 month period that you believe could indicate potential issues of inappropriate pain management or a substance use disorder? (Please provide answers in numbers)**

Prescriptions obtained	
Doctors consulted	
Pharmacies dispensing	
Average daily dose* (mg morphine equivalent)	

4. Are there any other issues in a person's prescription history that you believe would be relevant to the assessment of possible problematic opioid use?

***5. RED LIGHT - What is the 'LOWEST level' of prescription obtainings over the last 2 month period that you believe could indicate definite substance use disorder or drug diversion? (Please provide answers in numbers)**

Prescriptions obtained	
Doctors consulted	
Pharmacies dispensing	
Average daily dose* (mg morphine equivalent)	

6. Are there any other issues in a person's prescription history that you believe would be relevant to the definitive assessment of problematic opioid use?

ROUND 2 - Misuse of Pharmaceutical Opioid Drugs: Doctor Shopping

7. The next round

Thank you for participation in the first round of this survey. All participants responses will be collated and merged and returned to you for further feedback, if required.

1. Do you agree to participate in the final round of this study?

◯ YES ◯ NO