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Opioids: What Role Can the Pharmacist Play?

A thesis submitted in total fulfilment of the requirements for the degree of Doctor of Philosophy

PENELOPE WOOD - B.PHARM (HONS)
DEPARTMENT OF PHARMACY AND BIOMEDICAL SCIENCE, COLLEGE OF SCIENCE, HEALTH & ENGINEERING, LA TROBE UNIVERSITY, VICTORIA, AUSTRALIA

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ABSTRACT

The non-medical use of pharmaceuticals is a priority issue identified in the Australian National Drug Strategy because of the associated harms not just to individuals but also to the broader community. Pharmacists are a key component in the supply of opioids but is merely supplying the medication enough? Given the increase in harm from the use of pharmaceutical opioids, it is important to ask what role can Australian pharmacists play in reducing risk and managing dependence and other opioid related harm? In Australia research has focused on the role of the hospital pharmacist in opioid supply. While the hospital pharmacist plays an important role especially in initiation, most opioids are supplied through the community pharmacy. Therefore, it is imperative that the community pharmacist role be explored further to determine the impact they can have in the safe supply of these medications. This not only includes the supply of opioids but also roles in harm reduction, early intervention, and prevention. Using a combination of quantitative and qualitive methodology this thesis i) explores the current role of pharmacists in the supply of opioids ii) investigates tools, referral pathways and competencies for pharmacists to undertake expanded roles in opioid management and risk reduction; and iii) identifies some of the barriers and enablers for treatment of opioid dependence in rural and regional Australia. There is potential for the expansion of the pharmacist's role in opioid management to include greater roles in opioid risk reduction, identification, and early intervention. But despite this opportunity, there are still many barriers to overcome relating to time, remuneration, pharmacist education and training, knowledge, and confidence. There is a need to further develop and test strategies and resources for enhancing pharmacists' willingness, skills, and confidence in communicating with patients regarding problematic opioid use, collaborating with physicians to improve pain management and prevent opioid misuse, conducting screening for problematic opioid use, and referring patients to and participating in substance use treatment.

STATEMENT OF AUTHORSHIP

Except where reference is made in the text of the thesis, this thesis contains no material published elsewhere or extracted in whole or in part from a thesis accepted for the award of any other degree or diploma. No other person's work has been used without due acknowledgment in the main text of the thesis. This thesis has not been submitted for the award of any degree or diploma in any other tertiary institution. All research procedures reported in the thesis were approved by the relevant Ethics Committees.

I hereby certify that this thesis is in the form of a series of papers. I have included as part of the thesis, verification from any co-authors attesting to my contribution to any jointly authored papers. (Appendix 2) The extent of my contribution to jointly authored work is listed below.

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Penelope Wood 6th March 2021

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KEY DEFINITIONS, ACRONYMS AND ABBREVIATIONS

Addiction - addiction is defined as a chronic, relapsing disorder characterized by compulsive drug seeking, continued use despite harmful consequences, and long-lasting changes in the brain. It is considered both a complex brain disorder and a mental illness (National Institute on Drug Abuse, 2021).

BMI-MTM - Brief Motivational Intervention-Medication Therapy Management

CACC – combination analgesics containing codeine

CDC – Centre for Disease Control and Prevention

CNCP – chronic non-cancer pain

Dependence – in 1964 a WHO Expert Committee introduced the term 'dependence' to replace the terms 'addiction' and 'habituation'. Dependence can refer to both physical and psychological elements. Psychological dependence refers to the experience of impaired control over drinking or drug use while physiological or physical dependence refers to tolerance and withdrawal symptoms (World Health Organisation, 2021).EMCDDA – The European Monitoring Centre for Drugs and Drug addiction

GP – general practitioner

MATOD – medication assisted treatment for opioid dependence (also known as ORT, OST and OAT)

Misuse - for the purpose of this thesis the European Monitoring Centre for Drugs and Drug Addiction's (EMCDDA) definition of misuse was used: 'the use of a psychoactive medicine for self-medication, recreational or enhancement purposes, with or without a medical prescription and outside accepted medical guidelines (European Monitoring Centre fo Drugs and Drug Addiction, 2021).

MME – milligram morphine equivalent

NDSHS – national drug strategy household survey

NSP – Needle Syringe Program

Opioid - a generic term that refers both to opiates and their synthetic analogues

OAT – opioid agonist therapy (also known as ORT, OST and MATOD)

OEP – opioid exit plan

ORT – opioid replacement therapy (also known as OAT, OST and MATOD)

OTC – over-the-counter. This refers to medication that can be purchased in the pharmacy without a prescription. In the Australian context depending on scheduling requirements this may or may not require the involvement of a pharmacist.

OUD – opioid use disorder

PBS – Pharmaceutical Benefits Scheme

PDMP – Prescription drug monitoring programs

Persistent pain - pain that goes on for longer than would be expected after an injury or illness

PO – prescription opioids

Problematic drug use - is defined by the EMCDDA as 'injecting drug use or long duration or regular use of opioids, cocaine and/or amphetamines' (European Monitoring Centre fo Drugs and Drug Addiction, 2012)

PSA – Pharmaceutical Society of Australia

PWID – people who inject drugs

RESPOND - Resources Encouraging Safe Prescription Opioid and Naloxone Dispensing

ROOM – Routine opioid outcome measure

SBIRT - Screening, Brief Intervention, and Referral to Treatment

SHPA – Society of Hospital Pharmacists

TGA – Therapeutic Goods Administration

THN – take home naloxone

LIST OF APPENDICES

CHAPTER 1: INTRODUCTION AND BACKGROUD

To start the journey, chapter one outlines the experience of the researcher as a pharmacist and why they developed such an interest in opioids, specifically, the role that pharmacists can play in managing and reducing harm from these complex medications. It then explores what opioids are and their role, highlighting codeine due to the specific role pharmacists had in its supply and the extensive changes in the last ten years to legislation governing its supply. The harms that can result from opioid use and the supply of opioids from within the hospital setting where often opioid use for pain is initiated are discussed. Finally, the reader is provided with the specific aims and objectives of this work and an overview of the remaining chapters.

1.1 SITUATING MYSELF AS THE RESEARCHER

I have worked in pharmacy practice for over 20 years in various roles including community pharmacy, academia, support roles for the quality use of high risk medicine (especially opioid medicines), and more recently as a General Practice pharmacist with a special interest in addiction and pain management. I started my pharmacy career working in community pharmacy as a student pharmacist. The first pharmacy I worked in had a large medication assisted treatment for opioid dependence (MATOD) program. I thought this was the norm, but it wasn't until later in my career that I discovered the great disparity in which pain, opioids, and opioid dependence, is managed in primary care including pharmacy. This first experience with opioid dependence and addiction spurred my curiosity. How did the people on the program get where they were? What led them there? What drugs were they using and why? This curiosity led me to think about how I as a pharmacist could better support these patients.

In my time as a pharmacist I have seen significant changes regarding the role of opioids in pain management - from a necessity to a limited role in persistent pain, and this has been associated with many changes in regulation, policy and access to these medications. In Australia, I have seen codeine upscheduled from a pharmacy only medicine to a pharmacist only medicine, and eventually to prescription only. I have been part of the introduction of the real time monitoring programs MedsAssist© and then SafeScript© in Victoria and have provided feedback about possible further regulations on pack sizes of medications, in particular, upon discharge from hospitals, and who can prescribe fentanyl. Alongside this I have also seen changes in the management of opioid dependence with the introduction of Suboxone© tablets and then Suboxone© films and the increased capacity of primary care to provide this to patients. More recently I have seen the introduction of long acting buprenorphine injections which could

dramatically change the accessibility and acceptability of MATOD for people who have problematic opioid use.

I believe that pharmacists have a significant role to play in the way opioids are supplied to patients and that with education and support this can be optimised to reduce risk and harm from these problematic medications. Therefore, with this research I wanted to explore how pharmacists can better support people with pain when they are prescribed opioids to ensure we reduce harm and risk and get the best outcomes for them. Additionally, if people have developed dependence or problematic use what is the pharmacist's role in supporting harm reduction and management? Of note is the lingering stigma still associated with opioid dependence which can act as a barrier to receiving and giving good quality care.

The readers of this thesis will be presented with an evaluation of the role of the pharmacist in the supply and management of opioids. I approach the research questions above with my knowledge and skills as a pharmacist and my interest and expertise in pain management and opioids. Through this prism I interpret and explain the research, and as such, I have chosen to discuss the research in the first person.

1.2 OPIOID ANALGESICS

Opioids are a class of analgesic drug indicated for the treatment of moderate-to-severe acute pain and chronic pain associated with malignancy (Rossi, 2020). Opioid drugs mimic endogenous opioids by activating opioid receptors in the central and peripheral nervous systems to produce analgesia, respiratory depression, sedation, and constipation. They reduce transmission of the pain impulse by acting pre- and post-synaptically in the spinal cord, and by modulating the descending inhibitory pathways from the brain (Brunton, Hilal-Dandan, & Knollmann, 2017). Physical dependence is common and withdrawal symptoms (e.g. nausea, vomiting, diarrhoea, sweating, and anxiety) occur if chronic treatment is stopped abruptly or an antagonist such as naloxone is given (Rossi, 2020). Commonly prescribed opioid medications in Australia include morphine, codeine, oxycodone, tramadol, and fentanyl (Mabbott & Storey, 2016). Before its upscheduling to prescription only in 2018, over-the-counter (OTC) combination analgesics containing codeine (CACC) were the most commonly sold opioid analgesic due to their accessibility in the community (Degenhardt et al., 2016).

Opioids work well in acute pain, but their role in chronic non-malignant pain is limited. Research has shown that opioids provide little, if any, benefit for chronic noncancer pain and can cause

significant harm (Busse et al., 2018; Krebs et al., 2018), at best they reduce pain intensity by 30% to 50% (Samir Patel & Laxmaiah Manchikanti, 2008). Chou et al (2015) concluded that the *"evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function".* They also found that there was a dose-dependent risk of life-threatening adverse effects including respiratory depression (Alam et al., 2012; Chou et al., 2015). In patients taking opioids for chronic non-malignant pain, about 80% experience at least one adverse effect and 44% remain on opioids long term (Kalso, Edwards, Moore, & McQuay, 2004; Samir Patel & Laxmaiah Manchikanti, 2008). Opioids are also known to cause hyperalgesia and allodynia via glial cell activation (Barratt, Klepstad, Dale, Kaasa, & Somogyi, 2015). Furthermore, while recent research has uncovered how opioid effects can vary significantly across ethnic groups (Barratt et al., 2015; Somogyi, Coller, & Barratt, 2015; Somogyi et al., 2016) such drug science principles do not get applied when prescribing these medicines. Opioid dosing requirements also decrease with age due to increased risk of adverse effects such as respiratory depression, sedation and falls (Chau, Walker, Pai, & Cho, 2008).

Despite limited evidence for their use, there has been an increased utilisation of strong opioids in the treatment of persistent pain. Opioid use in persistent pain has dramatically increased in the last ten years (Drug utilisation sub-committee (DUSC), 2014; Rogers, Kemp, McLachlan, & Blyth, 2013). In Australia in 2014, over 13 million prescriptions for opioids were written with oxycodone and codeine containing products accounting for more than 8 million of these (Mabbott & Storey, 2016). Degenhardt et al believe this is an underestimation and that there is a higher utilisation than what is estimated based on prescription data, as this fails to take into account OTC medications (Degenhardt et al., 2016). A number of explanations may account for the increase in opioid utilisation in Australia, including changes in PBS listings, prescriber/patient preference for specific treatments, the ageing population, expectations of pain relief by pain sufferers, reliance on passive pain treatments such as conventional medications, an increase in treatment availability, increasing survival rates and an increase in prevalence of pain and/or reduced availability of illicit drugs (Ballantyne, 2017; Blanch, Pearson, & Haber, 2014; Roxburgh et al., 2015).

There is geographical variation in the utilisation of opioids across Australia with areas outside major cities showing higher utilisation rates of all types of opioids (Australian Comission on Safety and Quality in Healthcare, 2016). Areas with indicators suggestive of greater disadvantage also have higher rates of utilisation. Complex social determinants of health and pain are likely to play a role in the higher opioid utilisation in more economically disadvantaged communities (Australian Comission on Safety and Quality in Healthcare, 2016).

1.3 CODEINE

Before its rescheduling to prescription only in 2018 codeine was the most commonly sold opioid in Australia due to its accessibility in the community (Degenhardt et al., 2016). Codeine was first isolated in the 1830s in France by chemist Jean-Pierre Robiquet, to replace raw opium for medical purposes. Its main use then was as an antitussive (Foundation for a Drug-Free World, 2020). More recently codeine has been utilised for its analgesic properties. It is often described as a weak opioid analgesic and used to treat mild-to-moderate pain such as pain associated with headaches, dental surgery/toothache, dysmenorrhoea, musculoskeletal pain, earache, neuralgia, cold and flu symptoms, sore throat, surgery, trauma/burns and fever (Rossi, 2020).

Codeine is a pro-drug that is metabolised via cytochrome P450 2D6 (CYP2D6) to morphine but there can be significant pharmacokinetic and pharmacodynamic variation between individuals (Meyer, 2000; Somogyi, Barratt, & Coller, 2007). Approximately 6% to 10% of Caucasians and 1% to 2% of Asians lack the CYP2D6 isoenzyme and derive no analgesic benefit from codeine. Conversely, some people (up to 10% of Caucasians and up to 30% of North Africans) are ultrarapid metabolisers and are at higher risk of morphine toxicity (Dean, 2017; Meyer, 2000; Yiannakopoulou, 2015). Drugs that interact with CYP2D6 also have the potential to alter an individual's response to codeine (Lam et al., 2014; Meyer, 2000). People with normal metabolic capacity are capable of converting 30mg of codeine to approximately 3mg of morphine (Wilcox & Owen, 2000). In these normal metabolisers the onset of action is 15-30 minutes with a duration of action of 4-6 hours (Rossi, 2020).

In most countries, OTC codeine sales are limited to pharmacies or medical practitioners, except in Denmark, where OTC codeine products are permitted to be sold from supermarkets, petrol stations, health and beauty shops and other retail outlets (Foley, Breindahl, Hindersson, Deluca, & Kimergård, 2016). Until 2018 in Australia, codeine was available OTC but had to be in combination with other pharmaceutical drugs such as paracetamol, ibuprofen, or aspirin. CACC are rarely recommended as first line therapies as there is some doubt as to whether the amount of codeine available in OTC CACC (8-15mg per tablet) is sufficient to provide any additional pain relief above that of the non-opioid analgesic it is combined with (Shaheed, Maher, & McLachlan, 2016). The recommended dose of codeine according to the Australian Medicines Handbook is 30-60mg every 4 hours (Rossi, 2020). Shaheed et al in their 2016 systematic review concluded that doses of codeine greater than 30mg are generally required to provide additional analgesic effect over and above the non-opioid analgesic alone and that 60mg of codeine is needed for

additional pain relief in combination with aspirin, paracetamol and ibuprofen, yet the lower opioid doses found in CACC may be sufficient to cause side effects such as nausea, constipation, dry mouth and sedation (Shaheed et al., 2016).

Despite the fact that OTC CACC can work well for some patients who use them appropriately for acute pain, and are considered to be safe when used in recommended amounts, they can cause tolerance, dependence, medication overuse or potentially serious medical issues if used inappropriately or over long periods (Reed et al., 2011). The potential for codeine to be misused or for dependency to develop has been documented in several case series (Frei, Nielsen, Dobbin, & Tobin, 2010; Sproule, 2011) and a randomised, double blind, placebo-controlled drug administration study (Babalonis, Lofwall, Nuzzo, Siegel, & Walsh, 2013). Sometimes codeine is used to attain euphoric effects, in others a psychological or physical dependency may have developed as a result of chronic pain or self-medication for mental health issues including trauma or anxiety (Kirschbaum, Barnett, & Cross, 2020).

Prior to rescheduling in 2018 there had been a growing number of Australians who had developed dependence on OTC CACC (Monheit, Pietrzak, & Hocking, 2016; Roxburgh et al., 2015). Many who developed dependence (both physical and psychological) were people who had regularly taken OTC CACC for a therapeutic condition (such as persistent pain). They frequently needed to take these medicines in greater quantities to achieve the same therapeutic effect. Often this progression to dependence was not immediately realised (Kirschbaum et al., 2020). Continued codeine use has also been attributed to the calming effects on mood (Kirschbaum, Barnett, & Cross, 2020) and users report feelings of 'euphoria' and such 'positive' sensations which make it difficult for them to stop taking the medicine. In a 2020 Tasmanian study many participants described their use of codeine as a mechanism for coping with life stressors, akin to alcohol (Kirschbaum et al., 2020).

In Australia the overall rate of codeine-associated deaths more than doubled from 3.5 per million in 2000, to 8.7 per million in 2009, although only 7.8% of the deaths were attributed to codeine toxicity alone (Roxburgh et al., 2015). Since 2009, the Coroners Court of Victoria has reported more than 50 deaths each year where codeine was a contributing factor (Monheit et al., 2016). When a patient becomes dependent on codeine in combination products there is often escalation of doses with some people ingesting up to 60 tablets per day (Cock, Edmonds, & Cock, 2015). The high doses of the non-opioid analgesics used in combination with codeine cause the biggest problems, with increasing morbidity and mortality. Prolonged high doses of ibuprofen and aspirin have been associated with hypokalaemia, gastrointestinal haemorrhage

and nephrotoxicity; paracetamol taken in higher than recommended doses can result in hepatic damage and fatality, with a great cost to the Australian health care system (Chetty et al., 2003; Frei et al., 2010; Lewis et al., 2005; Nielsen, MacDonald, & Johnson, 2018).

Pharmaceutical regulatory changes can have an impact on patterns of drug prescribing and hence use (Monheit et al., 2016). Regulatory controls are required to assist in minimising codeine related harm. Regulations dictating codeine accessibility differ around the world. Codeine containing analgesics are readily available OTC without a prescription in several countries including the UK, Denmark, South Africa and Ireland (Carney et al., 2016). In other countries such as Austria, France, Germany, the USA and Australia, codeine is only available on prescription (Therapeutic Goods Administration, 2018). Initially in Australia, OTC CACC was available in pharmacies as a Schedule 2 "Pharmacy Only Medicine". In Australia medicines are placed in schedules according to the appropriate level of control over access and availability needed to protect the health of the public (Therapeutic Goods Administration). OTC medicines are either in Schedule 2 (Pharmacy Only Medicine) or Schedule 3 (Pharmacist Only Medicine). Schedule 2 medicines can only be sold in pharmacies under the supervision of a pharmacist but are available for purchase via self-selection without interaction with a pharmacist; Schedule 3 medicines require the direct involvement of a pharmacist to establish a therapeutic need and to provide professional advice (Tan & Emmerton, 2009). CACC were available OTC because they were deemed safe for most people for short term use (3–5 days). Longer term use requires referral for further investigation and alternative treatment (Pharmaceutical Society of Australia, 2015). Despite this, pharmacist management of inappropriate use of OTC CACC had been reported as lacking, particularly with regard to identification of an overuse issue, communication with the patient, referral and treatment (Nielsen, Cameron, & Pahoki, 2010).

On the 1st of May 2010, due to safety concerns about the harm that can occur through misuse, OTC CACC were deleted from Schedule 2 and added to Schedule 3 in Australia (Scheduling & Committee Governance Section/ Regulatory Education and Planning Branch, 2016). This meant that direct pharmacist involvement was required in all sales and pharmacists had a legal and professional responsibility to determine the therapeutic need for the medication before it could be supplied (Scheduling & Committee Governance Section/ Regulatory Education and Planning Branch, 2016). At this time pack sizes for CACC were also restricted in an attempt to minimise harm (Scheduling & Committee Governance Section/ Regulatory Education and Planning Branch, 2016; Tobin, Dobbin, & McAvoy, 2013). It was expected that upscheduling would reduce misuse of these medications.

These regulatory measures were evaluated in several ways. A qualitative study confirmed upscheduling achieved one of its aims, that pharmacists became more aware of those who were misusing codeine, through monitoring frequency of supply (Hamer, Spark, Wood, & Roberts, 2014). However, pharmacists described difficulties, specifically, their capacity to have challenging conversations in busy pharmacy settings and establishing appropriate therapeutic need (Hamer et al., 2014). Identification of people misusing and/or dependent on OTC CACC can be difficult for pharmacists, partly due to people frequenting several pharmacies, and no mechanism to record OTC CACC sales across multiple pharmacies (Cooper, 2013a; Hamer et al., 2014). Furthermore, pharmacists experienced difficulty communicating product risks or addressing suspected dependence with people, possibly due to concerns about aggressive behaviour if misuse and/or dependence was raised (Nielsen et al., 2010). Additionally, it has been identified both in Australia and overseas that once a pharmacist has recognized that there is an issue, they are unsure of the best treatment strategies or the appropriate referral pathways (Cooper, 2013a; Cooper, 2013b; Hamer et al., 2014; Nielsen et al., 2010).

Despite the 2010 scheduling change, concerns surrounding harm associated with OTC codeine persisted. In 2016 the Australian National Drug Strategy Household Survey established that 75% of people who had misused pharmaceuticals had used CACCs (Australian Institute of Health and Welfare, 2017a), an increase from 33% reporting such use in 2013 (Australian Institute of Health and Welfare, 2014). Similarly, calls to an Australian poisons centre regarding codeine misuse increased from 2004-2015, with no decrease in call trends post 2010 (Cairns, Brown, & Buckley, 2016), and the proportion of people seeking opioid substitution therapy for codeine dependence continued to climb, increasing from 2.7% in 2014 to 4.6% in 2016 (Roberts & Nielsen, 2018). Subsequently, the Australian Therapeutic Goods Administration (TGA) determined the risk of potential harm outweighed the likely benefit gained from OTC access to low-dose CACC and in December 2016, announced the decision to up-schedule CACC to become Prescription Only Medicines from February 2018 (Roberts & Nielsen, 2018; Therapeutic Goods Administration, 2016). This meant that all codeine containing products would only be available via a doctor's prescription (Therapeutic Goods Administration, 2016).

1.4 WHY SCRUTINISE OPIOIDS?

Opioids are widely used medicines, with increasing morbidity and mortality from use and misuse in many countries across the world (Pezalla, Rosen, Erensen, Haddox, & Mayne, 2017; Special Advisory Committee on the Epidemic of Opioid Overdoses, 2019). In the last two decades there

has been a shift in the cause of opioid overdose deaths, from illicit drugs such as heroin, to pharmaceutical opioids driven by increased opioid analgesic prescribing (Roxburgh et al., 2017). Global estimates show a doubling worldwide in the use of opioid analgesics between 2001 and 2013, largely driven by increased prescribing in North America, Western and Central Europe and Australia (Berterame et al., 2016). Research confirms that there is considerable use of opioids in Australia (Degenhardt et al., 2016; Gisev et al., 2018) and that the increase in opioid use and harm is consistent with that which has been seen overseas (Blanch et al., 2014). More than three million Australians are prescribed an opioid annually, which represents approximately one in seven people aged over 14 years old (Lalic, Ilomaki, Bell, Korhonen, & Gisev, 2019). In Victoria, opioid dispensing per annum doubled from 1.64 million prescriptions in 2006 to 3.32 million prescriptions in 2013 (Berecki-Gisolf, Hassani-Mahmooei, Clapperton, & McClure, 2017). The increase in Australian opioid prescriptions has been linked to the increase in the range of opioid formulations available (Islam, McRae, Mazumdar, Taplin, & McKetin, 2016; Rintoul, Dobbin, Drummer, & Ozanne-Smith, 2011).

While several opioids have been classified as essential medications for acute pain or chronic cancer pain by the World Health Organization (WHO), their use in other conditions has increased in recent years (Leong, Murnion, & Haber, 2009; Mabbott & Storey, 2016; World Health Organization, 2016b). Opioids are used frequently to treat chronic or persistent non-cancer pain despite a lack of evidence supporting their long-term efficacy and safety for this indication (Ballantyne & Shin, 2008; Blanch et al., 2014; Chou et al., 2015). Trends also show an increase in use of pharmaceutical opioids within Australia for both medical and non-medical purposes, with non-medical use of prescription opioids within the community doubling between 2007 and 2010 (Roxburgh, Ritter, Slade, & Burns, 2013).

Increases in opioid-related harms and opioid-related mortality have been reported in Australia and many parts of the world (Bohnert, Valenstein, Bair, & et al., 2011; Fischer, Jones, & Rehm, 2013; Roxburgh, Bruno, Larance, & Burns, 2011). This has been associated with the surplus of prescription drugs accumulating in communities in Australia (Blanch et al., 2014; Paulozzi, Zhang, Jones, & Mack, 2014). In Australia, opioid overdose deaths increased by 64% in the decade to 2015, driven largely by deaths involving pharmaceutical opioids (Roxburgh & Burns, 2017). Data from the Coroners Court of Victoria revealed that pharmaceutical drugs contributed to 80% of Victorian overdose deaths in 2009-2016 (Hinchey, 2017). In 2015, accidental drug-related deaths in Australia (1,489) were more than twice the number of deaths resulting from car accidents (712) (Penington Institute, 2017). Of these accidental drug-related deaths, opioids were the second most implicated drug class behind benzodiazepines (Coroner's Prevention Unit, 2017). In 2013,

70% of the 668 accidental opioid deaths in Australia involved prescription opioids, a stark comparison to the 1990s when illicit opioids were responsible for the majority of opioid-related mortality (Roxburgh et al., 2017).

1.4.1 OPIOID DEPENDENCE AND PROBLEMATIC USE

Problematic opioid use can encompass non-medical use, use for a medical purpose but without a valid prescription or monitoring by a health professional, obtaining excessive quantities, dependence including iatrogenic dependence, self-medicating and diversion. Results from the 2016 National Drug Strategy Household Survey (NDSHS) showed that approximately 1 million Australians (4.8%) aged 14 or older misused (non-medical use) a pharmaceutical drug in the previous 12 months (Australian Institute of Health and Welfare, 2017b). This is likely to be an underestimate due to the design of the survey which required self-reporting. Sometimes the misuse was deliberate in order to get the euphoric effects from these medications, in others an inadvertent dependence may have occurred as a result of chronic pain or self-medication for mental health issues including trauma or anxiety. Chronic pain and mental illness have been shown to be higher among people who have used pharmaceuticals for non-medical purposes (American Psychiatric Association, 2013).

Opioid dependence is considered a serious public health issue. Opioid dependence refers to dependence on any form of opioid including prescription, non-prescription, illicit, oral, injection, rectal or dermal (World Health Organization, 2013). The WHO international classification of disease clarifies dependence syndrome as

> "*a cluster of behavioural, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state*."(World Health Organization, 2016a)

Indicators of dependence in patients taking prescription opioids could include: repeated requests for specific or stronger forms of opioid containing analgesics, complaints of ongoing unresolved pain, stress and anxiety, frequent prescription loss or requests for early refills, and pharmacy or doctor shopping (Claire Van Hout, 2014). An opioid use disorder can be diagnosed using The Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V) (American

Psychiatric Association, 2013). One in five people using long-term opioids (an estimated 150,000 Australians) meet the criteria for an opioid use disorder, and half of those meet diagnostic criteria for pharmaceutical opioid dependence (Degenhardt et al., 2015). This represents a population comparable in size to estimates for the population of heroin-dependent people at the peak of the 'heroin epidemic' in the 1990s (Law, Lynskey, Ross, & Hall, 2001).

Results from a recent five-year, community-based, prospective cohort of people prescribed opioids for chronic non-cancer pain (CNCP) investigated factors independently associated with problematic opioid use. They found the risk factors most consistently associated with problematic opioid use were younger age, substance dependence, mental health histories and higher opioid doses. This highlights the need for an individual assessment of risks and benefits for patients taking opioids for CNCP, and an avoidance of overreliance on opioid dose as a predictor of these problems (Campbell et al., 2020).

In Australia, some people are unaware or deny the risks of excessive use of opioids and despite these risks being explained, still want to obtain opioids. Contrastingly in South Africa there has been a shift in public awareness and patients are more accepting and even requesting opioid-free products (Carney et al., 2016). The majority of people begin taking opioids for genuine medical reasons but some people continue use or increase the dose due to the "*buzz*" it gives them or the *"calm*" associated with use (Cooper, 2013b). These people find that opioids can help them cope, particularly with significant life events such as bereavements, or problems with work or relationships (Cooper, 2013b). Recognition of tolerance, withdrawal and dependence often occurs later in the cycle of misuse and this can be complicated by untreated pain (Carney et al., 2016).

Overdose and dependence are not the only challenges to the safe use of prescribed opioids. Other morbidities are common in populations who are prescribed opioids. Half of the population of opioid users report moderate to severe depression, and one in three report a lifetime alcohol use disorder (Campbell et al., 2015; Larance et al., 2016). Benzodiazepine use, a common contributor to opioid overdose related morbidity and mortality, is reported by one in three people prescribed opioids for chronic pain (Nielsen et al., 2015; Sun et al., 2017).

Problematic opioid use and dependence can lead to many complications such as toxicity and overdose, medical and psychological complications, social and family disruption, child welfare issues, violence and drug-related crime, and the spread of blood borne diseases (World Health Organization, 2013). This can create a burden on the healthcare system, Medicare, the PBS and

ultimately the taxpayer. Due to the potential harms of these medications there is a strong case for active regulation and monitoring at every level of supply.

1.5 HOSPITAL SUPPLY OF OPIOIDS

A substantial number of opioid medications are commenced in hospital but there are significant risks associated with continued opioid use after discharge. These include ongoing chronic use, respiratory depression, dependence, overdose and even death (Society of Hospital Pharmacists Australia, 2018). Emerging evidence indicates that initial opioid prescribing patterns determine the risk for transition to prolonged opioid treatment for chronic non-cancer pain (Deyo et al., 2017). This increase in risk of prolonged treatment increases as the length of the prescription exceeds five day's supply (Shah, 2017). A study published by Allen et al in 2020 looking at opioid use in a number of Victorian metropolitan hospitals found that of 1450 surgical patients 59% (858) were dispensed opioids on discharge, with immediate-release oxycodone the most common medication, and 27% of these patients were still requiring opioids two weeks after discharge (Allen et al., 2020). They concluded that the quantities dispensed were excessive in most cases, and that over two-thirds of the patients receiving opioids at discharge had leftover opioid medication at the time of follow-up adding to the community reservoir of opioids (Allen et al., 2020).

The transition between different levels of care can increase risk of medical errors, especially during transition from hospital to primary care. Admission and discharge from hospital have been associated with a higher risk of an adverse drug reaction or error (Macintyre, Huxtable, Flint, & Dobbin, 2014; Roughead, Semple, & Rosenfeld, 2016). A study of medication errors in seven countries found that poor coordination of care was a key factor (Lu & Roughead, 2011). Lack of thorough review at discharge presents a risk that patients will continue on unnecessary medicines, including pain medications for prolonged periods of time (Halme, Beland, Preville, & Tannenbaum, 2013). One of the biggest risks when opioids are prescribed on discharge is that unused medication may get out into the community increasing the risks of harm and other unintentional consequences. A 2017 systematic review found a significant proportion of opioids supplied after surgery were not used, not stored securely and retained instead of appropriately disposed of. These left-over opioids may be an important contributing factor to the nonmedical use of these products leading to injury or even death (Bicket, Long, Pronovost, Alexander, & Wu, 2017).

1.6 AIMS & OBJECTIVES

Pharmacists are a key component in the supply of opioids but is merely supplying the medication enough? Given the increase in harm from the use of pharmaceutical opioids, it is important to ask what role Australian pharmacists can play in reducing this risk and managing dependence and other opioid related harm.

This research aimed to:

- Investigate current pharmacist practice and roles in supply of opioids nationally and internationally.
- Evaluate the use of a clinical tool for managing OTC CACC requests and codeine dependence.
- Explore what are considered core competencies for Australian pharmacists in opioid supply and how well these competencies are currently met by practicing pharmacists.
- Test the implementation of a routine opioid outcome monitoring tool in community pharmacy.
- Explore barriers and enablers to opioid replacement therapy (ORT) in rural areas of Australia.

1.6.1 THESIS OVERVIEW

Chapter two, Pharmacist's role – literature review, sets the scene of the role of the pharmacist from their broader role in medication supply to more specifically their current role in the supply of opioids including in hospital, non-community, and community settings. In Australia research has focused on the role of the hospital pharmacist in opioid supply. Whilst the hospital pharmacist plays an important role, as this is where opioids are often initiated, many opioids are supplied in Australia through the community pharmacy. Therefore, it is imperative that the community pharmacist role be explored further to determine the impact they can have in the safe supply of these medications. This not only includes the supply of opioids but also roles in risk and harm reduction, early intervention, and prevention.

Chapter three, Methodology, gives an overview of pharmacy practice research and the different approaches commonly used in pharmacy practice research design - empiricist (quantitative) or interpretative (qualitative). This then leads into the various methods and reasons behind the design chosen for each of the five published manuscripts included in this thesis. The methods

used for each study were varied and employed a combination of empirical and interpretative approaches.

Chapter four, Non-prescription supply of combination analgesics containing codeine in community pharmacy: A simulated patient study, (publication one) investigates the management of non-prescription combination analgesics containing codeine (NP-CACC) direct product requests in community pharmacies in Victoria, Australia. This study used a covert simulated patient method in which the pharmacy was scored on their performance. One hundred and forty-five pharmacy visits were completed. Adequate questioning to establish therapeutic need only occurred in 50% of pharmacy visits, safety established in 17% of visits, and adequate counselling provided in 17% of visits, illustrating the need for improved awareness of assessment and management of patients requesting NP-CACC.

Chapter five, Implementation of a clinical tool to assess and address pain management requests in the pharmacy, (publication two) evaluates the use of clinical tools for managing OTC CACC requests and codeine dependence. Evaluation of these tools was undertaken using responses to multiple choice questions and feedback from pharmacist surveys. Of the 904 pharmacists who responded to the evaluation survey, 66.7% had not used the tool in the preceding 12 months. The most common reason why pharmacists did not access the tools was that they had no knowledge of them. Further research needs to be conducted into how to best promote and increase awareness of online clinical tools to pharmacists and determine the best way to integrate these tools effectively and efficiently into current practice.

Chapter six, Core competencies for Australian pharmacists when supplying prescribed opioids: a modified Delphi study, (publication three) explores what are considered core competencies for Australian pharmacists in opioid supply and how well these competencies are currently being met by practicing pharmacists. Development of specific core competencies for pharmacists may facilitate consistent and safer opioid supply. Expert pharmacists in the area of opioid supply from across Australia were sent a series of questionnaires via a modified Delphi study, with the aim to reach consensus on which items should be considered competencies for opioid supply by Australian pharmacists. Participants were also asked to rate how well they perceived that practicing pharmacists met each of the competencies. All competency items presented to participants reached immediate agreement with a variable result as to how well practicing pharmacists are perceived to meet them. Further research may help determine priorities for training and education.

Chapter seven, Routine opioid outcome monitoring in community pharmacy: outcomes from an open-label single-arm implementation-effectiveness pilot study, (publication four) reports on the testing of the implementation of software-facilitated Routine Opioid Outcome Monitoring (ROOM) in community pharmacies in Victoria and New South Wales, Australia. Pharmacists completed baseline and follow up interviews to measure change in knowledge and confidence following training on, and implementation of ROOM. Paired t-tests compared pre-post scores. Patients that participated were invited to complete a brief evaluation survey. Measures of feasibility and acceptability were also collected. Pharmacists' confidence in identifying and responding to opioid-related problems significantly increased from baseline to follow up across several domains, however scores indicated that there was still significant scope to further increase confidence in responding to opioid-related problems. ROOM is feasible and acceptable, though more extensive pharmacist training with opportunity to practice skills may assist in developing confidence and skills in this challenging clinical area.

Chapter eight, "A lot of people call it liquid handcuffs" – barriers and enablers to opioid replacement therapy in a rural area, (publication five) explores the barriers and enablers to opioid replacement therapy (ORT) in rural areas of Victoria and New South Wales. A qualitative study design incorporating semi-structured interviews was used to explore views of people using ORT. Barriers to ORT were restrictiveness, stigma, the medication, and structure of the program. Enablers were structure of the program, access to takeaway doses, effect on drug use and the medication itself. To improve access and retention in ORT programs action is needed to facilitate programs meeting the needs of rural people, including reducing cost of medication and cost of access, addressing the restrictiveness of programs and effect on employment opportunities, and stigma associated with drug use and addiction in rural communities. Geographical distance, inability to gain and maintain social connections including employment, and lack of community education addressing stigma are significant barriers to ORT in these areas.

Chapter nine , Conclusion and future directions, brings together the five publications in the context of the current policies and strategies that exist, and identifies barriers and opportunities for the possible expansion of the pharmacist's role in the management of opioids, and areas where further research could be undertaken to address some of these barriers and opportunities that have been identified in these studies.

CHAPTER 2: PHARMACIST'S ROLE – LITERATURE REVIEW

Chapter two discusses the role of the pharmacist from their broader role in medication supply to more specifically their current role in the supply of opioids across the different settings within which pharmacists work including hospital, community/retail and within medical practices and other health services. I also explore what the expansion of the pharmacist's role in opioid management could look like and the potential barriers to this expansion encompassing training and education, and harm reduction strategies such as naloxone supply, opioid agonist treatment and prescription drug monitoring programs.

Pharmacists have an important role to play when it comes to patient safety and the quality use of medicines. There have been several narratives written about the evolving role of the pharmacist within health care both internationally and in Australia. Over the past four decades, we have seen the role of the pharmacist grow from that of being primarily responsible for safely and accurately manufacturing and distributing a medication to a patient, to a health practitioner working alongside doctors, nurses, and other healthcare professionals in diverse and specialised practice settings to assure appropriate medication therapy management (Blouin & Adams, 2017). As one of the most accessible health care professionals in the community, pharmacists have an opportunity to progress their role to meet the changing health care needs of individuals and society (Blouin & Adams, 2017). The unique skills of pharmacists provides an opportunity to deliver innovative patient care services including optimal medication utilisation to manage acute and chronic disease, wellness and prevention services and patient education as well as other roles that are beyond the previously perceived scope of pharmacy practice (Blouin & Adams, 2017; Goode, Owen, Page, & Gatewood, 2019).

In Australia the integration of community pharmacy into primary health care faces challenges, including the lack of incorporation into Primary Health Networks, and the current service and remuneration models (Dineen-Griffin, Benrimoj, & Garcia-Cardenas, 2020). With the evolution of some of the more complex services and clinical roles for pharmacists, there is potential for reduction in the significance of the role of community pharmacies. However, community pharmacists' roles have evolved to the point where they are starting to be recognized as the medication management experts of the health care team (Dineen-Griffin et al., 2020). This is supported by the visions and policies of the Australian professional bodies such as the Pharmaceutical Society of Australia (PSA) and The Pharmacy Guild (Dineen-Griffin et al., 2020). Further, there is scope for improvement and expansion of the pharmacist's role in supply of medications, in particular the supply of opioid medications, in primary care.

This narrative review compromised of a search of the literature relating to pharmacists and opioid management both in Australia and internationally. A search was conducted using individual and combined key terms such as pharmacist, role, opioid management, codeine, opioid supply, hospital, community pharmacy, naloxone, harm reduction, education, methadone, buprenorphine and naloxone in biomedical databases including Medline, Embase, Ovid, and PubMed as well as *Google Scholar* and was restricted to articles in peer reviewed journals published in the last 10 years. A snowballing approach was also used incorporating reference lists of relevant papers. Research such as systematic reviews and meta-analysis were prioritised due to their breadth of coverage of the current literature. Once collected the articles were then analysed and divided into themes and analysed based on relevance to the overarching question "the role of pharmacists specifically in opioid supply".

2.1 PHARMACIST'S ROLE IN SUPPLYING OPIOIDS

As healthcare systems change and evolve to address the opioid crisis, the potential exists for pharmacists to make a positive impact in this space. The American Society of Health System Pharmacists (ASHP) and the American Pharmacists Association (APhA) have released statements and policies advocating for pharmacist involvement in such areas as patient education and opioid overdose prevention (Chisholm-Burns, Spivey, Sherwin, Wheeler, & Hohmeier, 2019; Reynolds, Causey, McKee, Reinstein, & Muzyk, 2017). Similarly in Australia, the Society of Hospital Pharmacists and the PSA have been strong advocates for pharmacist involvement in the management of opioid use including development of pharmacist opioid stewardships programs in both hospitals and general practices (Pharmaceutical Society of Australia, 2020; Society of Hospital Pharmacists of Australia, 2019). This has been supported by the federal government in conjunction with the Pharmacy Guild of Australia with the Pain MedsCheck trial (Australian Government Department of Health, 2015).

Many studies have been conducted internationally, particularly in the US, where the opioid crisis highlights the role of pharmacists in helping to control the burgeoning epidemic. While there are similarities in policy and application of opioids for pain relief globally, there are also vast differences in demographics, access to health care and how healthcare systems operate. Much of the research and experience derives from the US, and as such, its application to other countries around the world including Australia should be done with caution. Outcomes of these studies have provided substantial evidence that pharmacists can make an impact through appropriate pain management, use of Prescription Drug Monitoring Programs (PDMP), opioid overdose prevention training, medication reviews and counseling, among other interventions

(Chisholm-Burns et al., 2019; Compton, Jones, Stein, & Wargo, 2019; Cox, Tak, Cochella, Leishman, & Gunning, 2018; Doong, Gaccione, & Brown, 2016; Duvivier et al., 2017; Goodin, Fallin-Bennett, Green, & Freeman, 2018; Matheson, Bond, & Tinelli, 2007; Norwood & Wright, 2016; Stewart, Zborovancik, & Stiely, 2017; Thakur, Frey, & Chewning, 2019; Uosukainen, Turunen, Ilomäki, & Bell, 2014; Watson & Hughes, 2012).

A scoping review by Samaha et al explored whether the opioid crisis had changed pharmacy practice regarding the treatment of non-cancer pain in the USA (Samaha, Vanier, & David, 2020). The studies they reviewed demonstrated pharmacists contribute in pain management and opioid use but overall, they found that that the opioid crisis has not modified the nature of pharmacy practice around pain and opioid management. This may have changed more recently as their search concluded in December 2018. The focus on opioid deaths and the number of studies reporting pharmacy practices relating to opioid and pain management has greatly increased since then. These practices include collaboration in interdisciplinary teams and intensive patient counseling to help achieve treatment goals by customizing treatment plans while reducing opioid use. Despite this, Samaha et al identified that the opioid crisis presented a unique opportunity to improve pharmaceutical care in real-life settings, but there were limits and barriers. Shortcomings in communication, knowledge gaps in pain management, and public health policies limiting stakeholders' responsibility may explain the lack of large-scale implementation of the pharmaceutical practices. A critical analysis of pharmacists' knowledge of pain treatment and opioid management and comparison with actual needs in practice and patients' expectations would therefore be beneficial (Samaha et al., 2020). This information could then feed into the development of extended roles for pharmacists in this area.

A mixed-methods study by Blue et al exploring US pharmacists' perceived role in combating the opioid crisis yielded some interesting perspectives. Mixed methods are a valuable tool to allow participants the opportunity to comment and qualify quantitative responses. Most participating pharmacists agreed there was need within their communities to address the opioid epidemic and that the profession should have a role in the community response, including provision of patient education and naloxone distribution. This agreement may be due to responder bias as those with an interest in playing a role in the opioid crisis may be more likely to respond. Despite this, a small number of participating pharmacists believed that either the epidemic was not pertinent to their practice or that pharmacy as a profession should not be involved (Blue et al., 2020). It would be interesting to explore further why these pharmacists felt this way. A study using focus groups conducted in Oregon USA examining the pharmacist's role in opioid safety found that both pharmacists and patients agreed that pharmacists were responsible for

medication safety. Pharmacists expressed discomfort filling potentially high-risk opioid prescriptions and noted barriers such as lack of clinical information and reluctance to police high-risk prescribing. Patients were concerned about pharmacists potentially overstepping their professional responsibilities by interfering with prescribers' clinical decisions (Hartung et al., 2018). Information obtained from focus groups and interviews is useful for the detail it can provide regarding specific issues and the opportunity to explore meaning behind specific comments. A limitation to this study and that of Blue et al above is they are only representative of one particular US state and depending on demographics, legislation, policy and support available in the different states both clinician and patient experience in other states and other countries could differ vastly.

There are several potential roles, strategies, and interventions for practicing pharmacists in addressing opioid misuse, and abuse. These could be implemented at an individual patient level, in collaboration with other health professionals, or at a community level and could include:

- collaboration with the healthcare team on opioid exit plans (OEP) and discharge planning;
- distribution of naloxone/opioid rescue kits, and education/training on their appropriate use for patients and support persons;
- management of pain clinics in primary care settings under collaborative practice agreements;
- provision of medication reviews and/or medication management;
- provision of counseling and education on appropriate pain management (including opioids);
- use of risk stratification and mitigation practices including PDMP and treatment agreements;
- adherence monitoring such as urine toxicology and pill counts;
- monitoring for inappropriate prescribing or hazardous drug combinations that prescribers may not be aware of, such as co-prescription of other central nervous system depressants including benzodiazepines and pregabalin;
- standardised screening tools for opioid misuse risk;
- abuse-deterrent opioid formulations;
- referral of high-risk patients to addiction treatment resources, specialists, or involving specialists in treatment planning;

- education of prescribers and other health professionals concerning appropriate pain and opioid management;
- provision of academic detailing;
- recommendations to prescribers prior to issuing prescriptions (or prior to dispensing), based on chart review and/or consultation;
- provision of community education, outreach and overdose prevention training;
- information and education on opioid risks, proper storage and disposal of medications, and the harms of sharing medications with others;
- implementation of drug take-back programs/return unused medicine (RUM) programs;
- information on treatment options and the supply of opioid agonist therapy (OAT) to manage substance use disorders;
- training programs and continuing education on pain and opioid management as well as overdose prevention. (Akers, Hansen, & Oftebro, 2017; American Pharmacists Association, 2014; Australian Government Department of Health, 2015; Bach & Hartung, 2019; Berland, Fox, Tofighi, & Hanley, 2017; Bratberg et al., 2020; Chaudhary & Compton, 2017; Chisholm-Burns et al., 2019; Cochran et al., 2016; Compton et al., 2019; Cox et al., 2018; Denisco et al., 2011; Duvivier et al., 2017; Genord, Frost, & Eid, 2017; Gregory & Gregory, 2020; Gugelmann, Shofer, Meisel, & Perrone, 2013; Larson et al., 2018; Liebschutz et al., 2017; McCauley, Back, & Brady, 2013; McCauley et al., 2016; Pharmaceutical Society of Australia, 2020; Reynolds et al., 2017; Riley & Alemagno, 2019; Rosenberg-Yunger, Ellen, & Mickleborough, 2018; Shaefer, Barreveld, Arnstein, & Kulich, 2016; Society of Hospital Pharmacists of Australia, 2019; Stevens et al., 2019; Stewart et al., 2017; Strand, Eukel, & Burck, 2019; Tewell, Edgerton, & Kyle, 2018; Tran et al., 2017; Waszak, Mitchell, Ren, & Fennimore, 2018).

These roles have been advanced in the UK where pharmacist prescribing has been legislated. There has been moderate success with pharmacist independent prescribing clinics to treat opioid dependence, where there has been a reduction of opioid prescribing, without patient satisfaction being compromised (Hill, Marr, & Smith, 2019).

Nielsen and Sproule in their editorial for the SHPA publication, Journal of Pharmacy Practice and Research, advocate for a specialised role for pharmacists in pain and addiction in Australia. Currently, addiction medicine is not recognised as a specialist area in pharmacy practice in Australia and it is not yet recognised as one of the 29 disciplines of the SHPA's Specialty Practice

program. They state that there is a need for pharmacists as clinical pharmacotherapy specialists in addiction medicine. They believe that pharmacists can contribute, particularly in settings involving complex opioid therapy management, such as where patients are not responding to first-line opioid agonist therapy, or are on high-risk opioid therapy for chronic pain (Nielsen & Sproule, 2019).

2.2 OPIOID SUPPLY SETTINGS

Practice by pharmacists can be quite different in hospital and general practice settings compared to community settings. The roles and interventions in these individual settings are explored further below regarding opioid management.

2.2.1 HOSPITAL & NON-COMMUNITY PHARMACY SETTINGS

As medicines experts working in an acute setting, hospital pharmacists have a key role in reducing the risk of inappropriate medicine prescription, supply and use. Pharmacists also have an obligation to optimise medicine management and safety for patients (Society of Hospital Pharmacists of Australia, 2019). A substantial number of opioid medications are commenced in hospital and there are significant risks associated with continued opioid use after discharge. Several strategies have been undertaken in Australia to address opioid risk on discharge. These strategies include limiting quantities supplied, the use of opioid risk screening tools, patient education, and communication with the patient's GP (Downie, Wood, Summers, McDonough, & Wong, 2019). South Australia's Department for Health and Ageing developed a 'Clinical Guideline for prescribing opioids on discharge' in late 2013. This had recommendations pertaining to the appropriateness to prescribe opioids on discharge, the quantity of opioids to be prescribed, patient education and communication with the primary care provider (Department of Health South Australia, 2015). The guidelines offered pragmatic recommendations to decrease opioid associated risks but adherence by prescribers and the effectiveness in reducing opioid associated risks remains unreported.

Currently, there are no government mandated Australian or Victorian guidelines regulating the prescribing of opioids upon discharge from hospital. An online survey sent to all Victorian hospitals identified that few appeared to have discharge supply guidelines to provide governance around medication safety (Downie et al., 2019). This study also highlighted four aspects of opioid management at discharge as identified by the literature. These were: (1)

reducing opioid quantity at discharge (2) providing the patient's GP with appropriate discharge information (3) providing the patient with appropriate written and verbal information and (4) the use of opioid risk screening tools (Downie et al., 2019). When patients are discharged from hospital with opioids, it is important that they understand the risks, to ensure they take their opioid medication safely and that expectations around the duration of use and ongoing treatment are managed appropriately (Macintyre et al., 2014). Patients should also be aware of adverse effects, including sedation, constipation and impairment to performing complex tasks such as driving, and the safe storage and disposal of opioid medication to prevent accidental overdose (Macintyre et al., 2014). In addition, information about the dangers of mixing opioid analgesics with other central nervous system depressants, such as alcohol or benzodiazepines, and the signs and symptoms of overdose, should be emphasised.

The adoption of antibiotic stewardship has attempted to address the problem of antibiotic over-prescribing (Buising et al., 2008), therefore it would be logical to suggest a role for a similar program involving pharmacists in opioid prescribing, particularly in the transition of opioid analgesic management from the hospital to the primary care setting (Genord et al., 2017). Opioid stewardship has been investigated as a possible role for pharmacists in hospitals and other primary care settings around the world and addresses inappropriate opioid prescribing and supply, among other quality and safety activities (Society of Hospital Pharmacists of Australia, 2019). There have been several studies that have looked at adding pharmacists to team-based care programs for pain and opioid management. These have demonstrated a reduction in opioid prescription and doses (Boren, Locke, Friedman, Blackmore, & Woolf, 2019; Genord et al., 2017; Tilli, Hunchuck, Dewhurst, & Kiran, 2020; Tran et al., 2017).

Genord et al investigated a pharmacist-led opioid exit plan (OEP) practice model and the potential role that pharmacists can have at the point of admission, during postoperative recovery, and on discharge in acute pain management patients in a hospital setting in the USA (Genord et al., 2017). The OEP tool model included a medication reconciliation review and PDMP search before admission, interdisciplinary rounds with the medical team to provide optimal inpatient postoperative pain management, clinical assessment of outpatient prescriptions with opioid discharge counselling, and medication evaluation of prescribed pain regimen and opioid discontinuation status at the post-discharge follow-up appointment. They concluded that a hospital pain management team operating a pharmacist-led OEP can be key to guiding appropriate prescribing practice of opioids and assisting with transitions of care on discharge (Genord et al., 2017). Another American study looking at feasibility of a pharmacy-delivered opioid intervention program in the emergency department found that patients were happy with

the information they received and that it improved their understanding of opioid side effects. The pharmacists' intervention included counselling on opioid safety, opioid adverse effects, proper disposal, naloxone and opioid overdose (Winstanley, Mashni, Schnee, Miller, & Mashni, 2017).

In Canada, Tilli et al developed and tested a role for pharmacists as opioid stewards, to reduce opioid and benzodiazepine doses in co-prescribed patients. Their intervention increased the number of patients on care plans and an opioid taper, and decreased the dose of opioids (Tilli et al., 2020). Another Canadian study, conducted in a non-dispensing pharmacist clinic, explored the impact of pharmacist-led medication assessments on opioid utilization and found that that medication assessments by pharmacists that followed the policies and procedures of the Saskatchewan Medication Assessment Program resulted in statistically significant reductions in mean daily morphine equivalent doses among patients with chronic noncancer pain (Bhimji, Landry, & Jorgenson, 2020). In Australia, Victorian research looked at the impact of pharmacists assisting with prescribing and undertaking medication review of oxycodone prescribing and supply for patients discharged from surgical wards in a metropolitan hospital. They found that having a hospital ward pharmacist review the doctor-prepared prescriptions reduced the proportion of patients who were supplied oxycodone at discharge but not the amount of oxycodone supplied per patient (Tran et al., 2017).

Allen et al studied post-surgical opioid stewardship across Australia and New Zealand and found that there was great variability in opioid stewardship practice which could be due, in part, to the current limited evidence base for the individual measures, in addition to challenges in research translation (Allen et al., 2019). Some of the measures employed at various organisations included in the study were: co prescribing of adjunct analgesia, education of junior medical staff, limits on prescribed quantity, a discharge prescribing guideline, routine pharmacist medication counselling, written patient information, pre-admission patient education, and routine GP communication and advice (Allen et al., 2019). The SHPA also found that there were sizeable gaps in the provision of medication reconciliation, clinical review of patients, risk factors and review of postsurgical analgesic use by Australian hospital pharmacists. The provision of pain services and stewardship also varies significantly within hospitals (Society of Hospital Pharmacists of Australia, 2019). Hospitals across Australia were surveyed, with the finding that less than 5% of respondents indicated that their hospitals had formal opioid stewardship programs, and 13% reported a limited program. This study showed that less than one-fifth of Australian hospitals had some form of hospital-wide opioid stewardship model (Society of Hospital Pharmacists of Australia, 2019).

2.2.2 COMMUNITY PHARMACY SETTING

Community pharmacists are a group of highly skilled health professionals involved in the supply of many drugs, including pharmaceutical opioids. They are accessible to people and therefore have opportunity to interact with patients more frequently than some other healthcare providers such as GPs. This puts them at the forefront of management of the opioid epidemic. Much work has focused on the role of GPs, but community pharmacists have been often overlooked as a potential point for identifying and managing problematic pharmaceutical opioid use.

Researchers show that pharmacists are interested in engaging in prevention and early intervention activities to reduce opioid misuse, toxicity and overdose and help patients with opioid use problems through the provision of medication education, addiction treatment information, counselling, or brief intervention (Cochran, Field, Lawson, & Erickson, 2013; Hagemeier, Alamian, Murawski, & Pack, 2015; Hagemeier, Murawski, Lopez, Alamian, & Pack, 2014; Wu, Ghitza, Burns, & Mannelli, 2017). The Centre for Disease Control and Prevention (CDC) recommends that discussion with patients about long-term use of opioids to manage pain should occur early in the opioid prescribing process (Shah, 2017). The National Institute for Health and Care Excellence (NICE) guidelines recommend that when prescribing strong opioids for pain, communication and provision of information are important especially around concerns such as dependence, tolerance and side effects. Education should be provided in both written and verbal format and should include the indications for strong opioids, effectiveness, speed of onset of pain relief, risks of taking medications inappropriately, opioid abuse, misuse, and diversion. It should also focus on common side effects such as constipation or drowsiness and include a conversation on serious side effects such as respiratory depression that can occur when large doses of opioid are administered. These effects should be discussed not only when filling new prescriptions but regularly addressed for existing opioid prescriptions. It is also important to counsel on safe storage and the proper disposal of unused medication to prevent diversion out into the community (Bennett et al., 2012; Gregory & Gregory, 2020).

In the US, community pharmacist interventions have included motivational interviewing (Cochran et al., 2019) and patient education (Irwin et al., 2020; Kadakia, Rogers, Reed, Dark, & Plake, 2020). Cochran et al advocated for the development of a behavioral health framework for opioid medication misuse in the community pharmacy setting based on a modified Screening, Brief Intervention, and Referral to Treatment (SBIRT) protocol (Cochran et al., 2016). After

consultation with stakeholders, they concluded that the framework should focus on screening efforts and adaptation of the SBIRT model for community pharmacy and concentrate on capitalising on the pharmacists' knowledge of medication management. They suggested, however, that patients who misused opioids often had problems that exceeded the core competencies of the pharmacist. Because of this they additionally speculated that interventions for acute needs should be team-based and encompass the range of disciplines that interface with medication misuse. They recommended a patient-centered intervention model, where the factors that uniquely contribute to individual onset and maintenance of opioid misuse are taken into account (Cochran et al., 2016).

Further work by Cochran et al included a pilot randomised clinical trial looking at community pharmacy intervention for opioid medication misuse. They implemented a Brief Motivational Intervention-Medication Therapy Management (BMI-MTM) model and examined its impact on medication misuse and concomitant health conditions (Cochran et al., 2019). They screened patients for prescription opioid misuse at point-of-service using the Prescription Opioid Misuse Index (a brief questionnaire developed to assess opioid misuse) (Knisely, Wunsch, Cropsey, & Campbell, 2008). The BMI-MTM comprised of 4 specific evidence-based practices which included: (1) medication therapy management, (2) brief motivational interviewing, (3) patient navigation, and (4) naloxone training and referral. These intervention components were delivered sequentially. They found that the BMI-MTM was a feasible misuse intervention tool, associated with superior satisfaction and outcomes than standard medication counselling for patients. Patients felt the pharmacist ensured medication safety, increased confidence to manage their medications, and listened to their concerns (Cochran et al., 2019). These findings suggest community pharmacy may represent an underutilised but potentially valuable resource for identifying and intervening with misuse of opioid medications

A systematic review looking at patient education interventions for prescription opioids identified that even though there were several well-documented interventions identifying methods to manage opioid-use disorder, there were less intervention studies providing education to patients before they received opioid prescriptions. The authors suggested that although it might be possible that pharmacists were already providing education to patients about their opioid prescriptions, literature in this area was lacking and there was a missed opportunity for pharmacists to participate in addressing the opioid epidemic (Kadakia et al., 2020). Another 2019 systematic review recognised that the most reported strategy by pharmacists to address drug misuse was referral back to the doctor. Eight of the studies also identified the benefits of real-

time prescription monitoring systems in addressing drug misuse (Hoppe, Ristevski, & Khalil, 2020).

Australian pharmacists, like many pharmacists around the world, face several challenges when supplying prescription opioids in the community. A study undertaken by Makdessi et al highlighted difficulties in detection of potential abuse/misuse; poor professional relationships with prescribers and limited engagement with patients. They found that despite pharmacists expressing concerns with the rising issue of prescription opioid misuse they did not report any change in their practice to mitigate the issue (Makdessi, Day, & Chaar, 2019). This could be related to confidence and comfort to intervene as reported in a recent study by Alvin et al exploring community pharmacists' preparedness to intervene with concerns around prescription opioids. They found that despite pharmacists commonly experiencing concerns when supplying prescription opioids there was still a cohort of pharmacists who are uncomfortable in intervening (Alvin, Picco, Wood, Mnatzaganian, & Nielsen, 2020). Female gender was associated with reduced comfort to intervene with patients when concerned about supplying prescription opioids, yet females were significantly more likely to discuss concerns with prescribers. Practicing within a large chain pharmacy was associated with greater comfort to intervene when concerned about prescription opioid supply, while post-graduate education about substance use disorders was associated with increased likelihood of discussing concerns with patients. Practicing in rural areas was associated with less likelihood to discuss concerns with patients, while years of practice reduced the odds of discussing concerns with prescribers. Pharmacists that indicated greater comfort in intervening when concerned about prescription opioids were more likely to discuss concerns with both patients and prescribers. These findings highlight the need for a system-wide effort to improve confidence and comfort in intervening and responding to concerns with prescription opioid use, which may serve to increase collaboration between pharmacists and prescribers. Targeted training needs to take into consideration specific factors such as gender and years of practice to help increase comfort in discussing concerns related to prescription opioids, which in turn may improve communication with prescribers and patients (Alvin et al., 2020).

2.3 EDUCATION, TRAINING AND RESOURCES

Even though community pharmacists are well positioned to reduce risks from opioid-prescribing they often lack resources and training to effectively support these activities. A recent systematic review (Hoppe et al., 2020) identified a link between attitudes and practice strategies of

pharmacists towards drug misuse management and years of practice. Pharmacists with more years of practice experience rated higher in the overall management of drug misuse, obtained higher knowledge scores regarding pain and pharmacotherapy, and experienced fewer barriers to opioid screening and the provision of interventions (Hoppe et al., 2020). This is in contrast to the recent Australian study by Nielsen et al which showed each additional decade practicing as a pharmacist was associated with reduced engagement with screening with the Routine Opioid Outcome monitoring (ROOM) tool (Nielsen, Sanfilippo, et al., 2020). They identified time and staff training as linked to the effective management of drug misuse.

The Resources Encouraging Safe Prescription Opioid and Naloxone Dispensing (RESPOND) Toolkit is an educational package developed to provide community pharmacists in the US with a comprehensive education program and practice resources on prescription drug misuse, prescription drug monitoring programs (PDMPs), and naloxone dispensing (Alley et al., 2020). This resource has been evaluated for its effectiveness to improve pharmacists' knowledge and assess changes in pharmacists' attitudes and beliefs toward opioid use disorder (OUD) and PDMPs. Researchers found that pharmacists' knowledge and attitudes toward OUD, perceived behavioral control to address OUD, resources to address OUD, and perceptions regarding PDMP-associated difficulties improved significantly as a result of use of the resource. They concluded that the RESPOND Toolkit was an effective and scalable training resource for community pharmacists, with the potential to promote behavioral shifts that supported opioid safety among patients (Irwin et al., 2020). Further research could determine whether such a tool could be adapted for the Australian environment.

2.4 HARM REDUCTION STRATEGIES

Harm reduction can be defined as a set of policies, programs and practices aimed at reducing negative consequences associated with drug use or other risky behavior (Hagemeier & Dowling, 2018). Harm reduction is an integral component of Australia's overall national drug and harm reduction policies and interventions can be applied to any legal or illegal drug to mitigate harm without necessarily reducing use (O'Keefe, Ritter, Stoove, Hughes, & Dietze, 2020). There are several harm reduction strategies that have been employed around the world in a bid to reduce morbidity and mortality from opioid use. These include PDMP, needle syringe programs (NSPs), MATOD and the take home naloxone program (Bach & Hartung, 2019; Hagemeier & Dowling, 2018; Hallinan, Osborn, Cohen, Dobbin, & Wodak, 2011; Hawk, Vaca, & D'Onofrio, 2015; O'Keefe et al., 2020; Saloner et al., 2018). There are opportunities where community pharmacy can play a role in most, if not all these strategies. Because pharmacists see patients more frequently than other health providers, they have additional opportunities to address problematic opioid use by

identifying aberrant behavior, alert prescribers to inadequate pain management, educate patients on the risks of opioid misuse, abuse, and diversion and provide harm reduction strategies such as recommending naloxone and referral for opioid use disorder treatment (Bach & Hartung, 2019; Bailey & Wermeling, 2014; Bratberg, 2017; Gregory & Gregory, 2020; Hammett et al., 2014; Vorobjov, Uusküla, Abel-Ollo, Talu, & Des Jarlais, 2009).

There are many examples where pharmacists already have impact in the area of opioid-related harm. Research has examined screening, brief intervention and referral to treatment (SBIRT) with opioids in ED settings, and established training requirements and frameworks for care within community pharmacy (Bach & Hartung, 2019; Cochran et al., 2016; Strand et al., 2019; Winstanley et al., 2017). Pharmacists generally have a positive attitude toward providing health promotion and harm reduction programs and express some interest in increasing their role in this area (Watson & Hughes, 2012). Despite this, negative attitudes towards community pharmacy services for drug misuse still exist, especially among pharmacists who do not dispense MATOD (Uosukainen et al., 2014). Common barriers to expanding harm reduction strategies in community pharmacists' practice include lack of time and training, insufficient remuneration, fear of attracting unruly clientele and inadequate communication between health providers (Thakur et al., 2019; Watson & Hughes, 2012). Strategies to mitigate some of these barriers to participation in harm reduction programs by pharmacists are warranted. As one of the most accessible health care providers, community pharmacists are in an ideal position to provide meaningful services, however, in order to do so, pharmacists require additional support in the form of better health team and system integration, as well as remuneration models (Watson & Hughes, 2012).

2.4.1 PRESCRIPTION DRUG MONITORING PROGRAMS

Prescription drug monitoring programs (PDMP) are important harm reduction tools to identify patterns of dangerous use of high-risk prescription drugs (Lindley, Cox, & Cochran, 2019). Though only recently introduced in Australia they have been used in some jurisdictions overseas for some time. PDMP analyses have primarily shown reduced opioid prescribing (Ali, Dowd, Classen, Mutter, & Novak, 2017; Bao et al., 2016; Dowell, Zhang, Noonan, & Hockenberry, 2016; Kreiner et al., 2017; Moyo et al., 2017; Young, Kreiner, & Panas, 2018) with unclear results for impact on opioid overdose (Nam, Shea, Shi, & Moran, 2017; Patrick, Fry, Jones, & Buntin, 2016; Paulozzi, Kilbourne, & Desai, 2011) or misuse (Ali et al., 2017; Haegerich, Paulozzi, Manns, & Jones, 2014). Integration of PDMPs in pharmacy practice may improve a pharmacist's ability to

make informed clinical decisions and exercise sound professional judgment giving pharmacists additional opportunity to address opioid-related risk (Norwood & Wright, 2016; Wixson, Blumenschein, Goodin, Talbert, & Freeman, 2015). Despite PDMP being seen as a vital tool for pharmacists to help identify patients at risk for opioid prescription drug misuse or overdose, in the US where it is not mandatory in all states, it is vastly underutilised (Wu et al., 2017). A 2013 report estimated that only approximately 36% of licensed US pharmacists had registered to use the PDMP (Kreiner, Nikitin, & Shields, 2014). More research is needed to better understand barriers and facilitators for more effective utilisation of PDMP (Wu et al., 2017).

One potential barrier could be the limited access to patient focused decision support for pharmacists if patients are identified as at risk (Lindley et al., 2019). This was identified by work in this thesis (publications one and two) when looking at codeine use and led to the development of a clinical tool to assist, (Wood, Tucci, Anderson, & Mnatzaganian, 2019) as discussed in chapter five. Without tools such as this to accompany PDMP the pharmacist's response to patient risk information is subjective (Lindley et al., 2019). It is thus critical for such decision support tools to be developed, tested and implemented to guide pharmacists' action once risk is identified (Lindley et al., 2019).

Merely identifying the patient and refusing to dispense the medication is insufficient. If a patient is identified as obtaining opioids from multiple providers or there are other issues that are revealed with a PDMP search, pharmacists should immediately contact all prescribers to alert them (Gregory & Gregory, 2020). If the pharmacist is not able to receive clarification in a timely manner, the pharmacist should use professional judgment to decide if they should dispense all or part of the prescription (Gregory & Gregory, 2020) bearing in mind the potential harms from abrupt cessation. Clear and thorough documentation should be kept in the patient's dispensing history with regard to all communication with prescribers and the dispensing outcomes with clear justification as to why the choice to dispense or not dispense was made (Gregory & Gregory, 2020). Other reported limitations for pharmacists using PDMP include administrative burden, technical issues, and prescriber concerns (Doong et al., 2016). A study in the US by Wixson et al highlighted that utilisation of PDMP varied according to different pharmacist and community pharmacy characteristics in particular the practice environment and location (Wixson et al., 2015).

An important factor highlighted by research internationally is that the impact of PDMP is limited without mandatory involvement from other healthcare providers (Doong et al., 2016). Given the recent implementation of a mandatory PDMP, SafeScript, for pharmacists and prescribers in

Victoria, Australia, future research could evaluate the implementation process, effectiveness and unintended outcomes of the program to allow more effective implementation in other Australian states. Of interest would be pharmacists' impressions of the program, ease of use, workload burden and interactions with patients.

There has been a reported disconnect between pharmacists and prescribers which in the past has forced pharmacists to make decisions about patient care while lacking important health information (Löffler et al., 2017; Rigby, 2010; Thornton, Anyanwu, Tata, Al Rawwad, & Fleming, 2020). Access to PDMP has somewhat reduced this issue, but in order to resolve it, there needs to be a better flow of information between the pharmacist and prescriber (Thornton et al., 2020). One possible solution is to enhance the Electronic Health Record (EHR) interoperability to include PDMP databases, so that pharmacists have access to the same clinical information that prescribers rely on. Having real-time access to patient EHRs along with the PDMP would provide the community pharmacist with important information to assist in clinical decision-making and may help identify patients at risk for opioid use problems or toxicity, thereby improving the provision of patient-centred services (Wu et al., 2017). More importantly, this integration could also lessen the gap between prescribers and pharmacists and unite them in their efforts to address problematic opioid use (Thornton et al., 2020).

Further opportunities for PDMP could lie in the recording and management of naloxone distribution. Because no other real-time system exists to report the extent of pharmacy-based naloxone supply, PDMP are a tool that pharmacists, researchers, and public health advocates could use to measure co-prescribing and to help increase naloxone distribution (Bratberg, 2017).

2.4.2 NALOXONE

Naloxone, an opioid antagonist, reverses opioid induced respiratory depression. Substantial evidence supports the provision of naloxone for opioid toxicity management (McDonald & Strang, 2016; Olsen, McDonald, Lenton, & Dietze, 2018). Take-home naloxone (THN) programs involve training peers, family or friends of people at risk of opioid toxicity in the use and provision of this drug (Lenton, Dietze, & Jauncey, 2016; O'Keefe et al., 2020). In 2010, Scotland became the first jurisdiction to implement a national THN program (McAuley, Best, Taylor, Hunter, & Robertson, 2012). THN programs commenced in Australia in 2012 in the Australian Capital Territory and there are currently THN pilot trials in certain states in Australia that make naloxone available without a prescription and free to people who may experience, or witness, an opioid overdose (Dwyer et al., 2018). The pilot will end in early 2021 and it will inform the supply

of THN to the Australian community (Australian Government Department of Health, 2019). There is also opportunity for THN programs to be successfully implemented into community pharmacies to increase access and awareness of opioid overdose recognition and response (Akers et al., 2017).

In 2016, naloxone was made available for purchase OTC in Australian pharmacies (Lenton et al., 2016; Pricolo & Nielsen, 2018). Making naloxone available OTC served to increase the number of locations where it can be accessed (Pricolo & Nielsen, 2018) but unfortunately uptake by people has been limited as cost is still a major barrier (Dwyer et al., 2018; Lenton et al., 2016; Pricolo & Nielsen, 2018). A study by Akers et al in the US found that many people may prefer to use a pharmacy for access to naloxone rather than go to a needle-exchange centre, because they may prefer getting the information and the kit from their trusted pharmacist. They also may not want to schedule GP appointments for THN information, or they may find it difficult to bring up their illicit opioid use with their GP. In either case, pharmacists can fill a public health need by providing opioid toxicity information and THN (Akers et al., 2017).

Research has established a capacity for, and interest in, pharmacist-led naloxone supply and involving pharmacists in assessing and responding to opioid-related risk (Green, Dauria, Bratberg, Davis, & Walley, 2015; Nielsen, Menon, Larney, Farrell, & Degenhardt, 2016; Rose, Lutnick, & Kral, 2014). Pharmacists can independently initiate naloxone supply in several jurisdictions, including Australia (Bailey & Wermeling, 2014; Green et al., 2015; Lenton et al., 2016). Pharmacy-based interventions are feasible, desirable, and accessible to people who are at risk for overdose and expands the reach of naloxone to individuals beyond those currently being served by community-based and harm reduction organisations (Green et al., 2015; Zaller, Yokell, Green, Gaggin, & Case, 2013).

In the US Thakur et al conducted a systematic review examining the roles for pharmacists dispensing naloxone, barriers to this, and pharmacist training (Thakur, Frey, & Chewning, 2020). They found that pharmacists are often underutilised without programs to support their roles. A key barrier identified was limited pharmacist training to identify and educate patients at risk of toxicity. This resulted in a lack of pharmacist confidence about dispensing naloxone and communicating with patients (Thakur et al., 2020). Similarly, in an Australian study, pharmacists reported being not confident in either identifying people to receive naloxone or training people to use naloxone, especially with OTC supply. A number of pharmacists were not able to answer correctly questions on naloxone administration (Nielsen et al., 2016). This was supported by a further Australian study looking at pharmacy practice after the down–scheduling of naloxone to

be available OTC. They identified core barriers to pharmacist provision of OTC naloxone which included limited understanding of opioid overdose, confusion about the role and responsibilities of pharmacists in providing OTC naloxone, concerns about business, stigma related to people who inject drugs and system-level challenges (Olsen et al., 2019). In other studies a lack of time, reimbursement, and lack of support from management were barriers to implementing naloxone services (Green et al., 2017; Nielsen et al., 2016; Nielsen & Van Hout, 2016; Thakur et al., 2019).

An Australian study also identified that although the majority of pharmacists supported naloxone use, pharmacists reported being somewhat less comfortable in supplying this to customers on MATOD and to customers purchasing syringes compared to supplying naloxone to chronic pain patients on a high opioid dose (Nielsen et al., 2016). Pharmacists have also identified being uncomfortable with naloxone provision for fear of decreased trust between the patient and pharmacist and misunderstanding as to why the pharmacist is offering naloxone (Lindley et al., 2019; Thornton, Lyvers, Scott, & Dwibedi, 2017).

These studies show that educational programs to prepare both practicing and student pharmacists are needed. Future research should focus on approaches to improve pharmacist confidence in naloxone dispensing and promotion of safe opioid use among patients and caregivers (Nielsen et al., 2016; Olsen et al., 2019; Thakur et al., 2020; Thornton et al., 2017). It is promising that most community pharmacists in Australia have identified that they are willing to attend training on providing naloxone and preventing opioid overdose (Chun et al., 2019). Greater willingness to attend training has been associated with younger age, being female, fewer years of practice, not having attended previous education on substance use disorder, and higher confidence in issues relating to substance use disorder (Chun et al., 2019).

2.4.3 MEDICATION ASSISTED TREATMENT OF OPIOID DEPENDENCE

Four OAT options are currently utilised in Australia for MATOD – Methadone liquid; Suboxone (buprenorphine/naloxone) film; Subutex (Buprenorphine) tablet and health professional administered buprenorphine long acting injection (Sublocade and Buvidal). OAT works by replacing the current opioid drug used with a legally obtained and monitored longer acting opioid. This reduces the harms associated with self-injecting and withdrawal symptoms and cravings or “hanging out”. Buprenorphine and methadone are now listed on the WHO’s Model Essential Drugs List (Carrieri et al., 2006). More than 30 randomised controlled trials report moderately strong evidence of efficacy of methadone and buprenorphine as treatment options as measured by reduction in non-prescribed opioid use, reduction in mortality, and retention in

treatment (Farrell, Wodak, & Gowing, 2012). Methadone is seen as the gold standard for treatment for MATOD around the world. It is the medication most widely used to treat opioid dependence. Its efficacy has been established in diverse settings and across multiple outcomes (Gourevitch, 2009). Methadone was introduced in Australia in 1969 (Gowing, Ali, Dunlop, Farrell, & Lintzeris, 2014) and is classed as a full opioid agonist, in that it binds to and activates the mu receptors in the brain, and when you increase the dose you get increased effects (Dolan & Alam-Mehrjerdi, 2015). Buprenorphine acts in a similar way to methadone but is longer lasting so therefore can be taken every second or third day (Dolan & Alam-Mehrjerdi, 2015) and is less likely to produce euphoric effects. Buprenorphine is classed as a partial agonist; it still binds to the mu receptors in the brain but only partially activates them. As such, buprenorphine has a ceiling effect, reaching a maximum level and even with increasing dose you don't get an increased effect (Dolan & Alam-Mehrjerdi, 2015). This makes buprenorphine less likely to cause overdose and thus a relatively safer option than methadone for OAT.

Community pharmacies are conveniently located within local communities and provide an ideal opportunity for MATOD delivery outside potentially more stigmatised specialist drug treatment clinics, whilst also relieving the burden of long waiting lists for treatment at these clinics (Chaar, Hanrahan, & Day, 2011). The Victorian MATOD system is described as a 'community-based' model chosen to de-stigmatise treatment of drug dependence while making MATOD readily available in the community. Pharmacy has a large role to play in this system but The Victorian Pharmacotherapy Review and other studies identified costs as well as stigma and discrimination as barriers (Digiusto & Treloar, 2007; King, Berends, & Ritter, 2013). This can be magnified in regional and rural areas where additionally there is limited service delivery (opening hours, location and varied dosing fees) and patient choice and can be compounded by negative attitudes of pharmacists and staff (Chaar et al., 2011; Ritter & Chalmers, 2009; Shepherd, Perrella, & Hattingh, 2014). In contrast, Le and Hotham found that an opportunity for a greater quality in care may exist in a rural community, given the pharmacist has an increased capacity to develop a personal relationship with the patient (Le & Hotham, 2008).

In a Finnish study, pharmacists who dispensed MATOD were seen to have a more positive attitude towards the management and treatment of opioid dependence than pharmacists who did not. Respondents from MATOD pharmacies were significantly more likely to perceive dispensing MATOD as part of a pharmacist's professional role, and that dispensing should take place in community pharmacies instead of substance misuse clinics. They were less likely to be worried about MATOD clients' impact on the pharmacy safety or public image and were less likely to be concerned about diversion or feel uncomfortable providing services to clients with

drug dependence (Uosukainen et al., 2014). Similar results have been reported in Scotland and New Zealand (Matheson et al., 2007; McCormick, Bryant, Sheridan, & Gonzalez, 2006).

The effective delivery of MATOD for people with opioid dependence in Australia is an on-going challenge. Consumers of MATOD services at pharmacies are generally well satisfied with the services provided, but indicate that more health needs could be addressed at the pharmacy (Chaar et al., 2011). Despite this, community pharmacies do not always embrace providing MATOD services and some choose not to provide drug treatment services at all (Chaar et al., 2011). Currently there appears to be a higher demand for MATOD service provision, especially in rural areas, than what is being provided through pharmacies. There are a number of barriers that are possibly contributing to the reduced uptake including lack of adequate remuneration, difficulties communicating with the prescriber, variability in patient stability and having to take on large numbers of patients (Winstock, Lea, & Sheridan, 2010). Obstacles to further expansion of MATOD services may be remedied with awareness, government support, more involvement in decision making and most importantly, dedication to the profession's core values - providing equitable healthcare to everyone (Chaar et al., 2011). Addressing stigma and improving remuneration and access will be important for future success.

2.5 SUMMARY

Pharmacists have an important role to ensure the safe supply of medications including high risk medications such as opioids. Even though pharmacists have a principal responsibility in the supply of these high-risk medications, governed by legislation and professional practice guidelines, this role has not been clearly defined. Pharmacists' practice can be quite variable and dependent upon factors such as training, setting of practice, motivations, ethics, interests and previous experience. The aims of this research are to define more clearly an expanded role for pharmacists in supply of opioid medication, for both pain and dependence, to reduce harm and risk from these medications and improve patient outcomes. A focus will also be on competencies required to perform such a role to a suitable standard and how pharmacists can be supported with tools in their role of opioid supply. In Australia the research has been focused on the role of the hospital pharmacist or GP in opioid supply with less information available about the role of the community pharmacist in primary care. The hospital pharmacist plays an important role as this is where a number of opioids are initiated but as the majority of opioids are supplied through the community pharmacy, it is imperative that the community pharmacist role be explored further to determine the impact they can have in safe supply. Opportunity exists for

pharmacists in many spheres of opioid supply and management including screening and early intervention, opioid stewardship, risk reduction and dependence management. Despite this research needs to focus on increasing pharmacist knowledge, experience and confidence in these areas.

CHAPTER 3: METHODOLOGY

In this chapter pharmacy practice research and the different approaches commonly used in pharmacy practice research design - empiricist (quantitative) or interpretative (qualitative) are explored. Using these overarching approaches the various methods used throughout this thesis and reasons behind the designs chosen and strengths and limitations for each of the five published manuscripts included are delved into further.

3.1 PHARMACY PRACTICE RESEARCH

The pharmacy profession worldwide has undergone a shift from traditional roles such as dispensing and compounding, to more cognitive roles consisting of patient counselling, patient-centred care and provision of clinical advice to other health care colleagues (Bond, 2006). Many conditions that were once primarily managed in a hospital setting are now managed in the primary care setting, and roles previously delivered by doctors, are now being delivered by other health-care professionals including pharmacists (Babar, 2015). The rise in chronic diseases, with a parallel rise in medication use and medication-related problems, the ageing of the population, and gaps in healthcare provision, especially in primary care, have established a rationale for more effective deployment of healthcare professionals such as community pharmacists to help address the unmet needs of patients (Krass, 2015). This places pharmacists in a position to utilise their expert drug knowledge and their accessibility in the community enables them to take on new roles and responsibilities (Bond, 2006).

It is not enough to just suggest that pharmacists can perform these new roles. There needs to be evidence-based evaluation to demonstrate efficacy and benefit. Services must be proven to be cost effective and acceptable to patients and other health care colleagues (Bond, 2006). To enable an evidence-based approach to pharmacy, the field of pharmacy practice research has been developed. Its focus is to explore how and why people access pharmacy services, the costs of pharmacy services, the outcomes for patients, and comparison of these costs and outcomes to similar services delivered by other providers (Babar, 2015). In the UK pharmacy practice research has led to changes in health service delivery for pharmacy including supplementary prescribing, repeat dispensing, management of chronic conditions, support for self-care and increased roles in lifestyle advice, including smoking cessation (Bond, 2006).

Pharmacy practice-based research is essential to the advancement of practice; however, pharmacists are often reluctant to participate in such research (Awaisu & Alsalimy, 2015). In

Australia there is recognition of the value of research to the pharmacy profession and factors encouraging individual Australian pharmacists to participate in research include a desire to improve the profession, the opportunity to learn more about disease management, to provide enhanced services to patients, and personal interest (Peterson, Jackson, Fitzmaurice, & Gee, 2009). Despite this, it can be challenging to convince pharmacists to participate (Krass, 2015). Although there is a growing appreciation of the critical role of research in establishing new clinical pharmacy services, this has not translated into widespread engagement and normalisation of practice research into the professional culture of pharmacy. A range of strategies are needed to influence attitudes, enrich knowledge and skills, build communities of research practice and thereby empower practitioners to commit to and become collaborators in research to advance the societal value of community pharmacy (Krass, 2015).

The approaches taken in pharmacy research and hence this thesis can be summarised under the broad areas of understanding and describing the way care is accessed and delivered (publications one and five), identifying areas for improvement (publications one and three) and evaluating new service models (publications two and four) (Babar, 2015). Pharmacy practice research can provide the evidence required to inform policy change and implement new services and roles. Such evidence is needed to influence policymakers, other healthcare professionals and the public, that these non-dispensing clinical roles, including advanced roles in opioid management, are feasible and add value to patient care (Krass, 2015).

3.2 PHARMACY PRACTICE RESEARCH METHODOLOGY

As discussed by Parastou Donyai in Babar “Pharmacy practice research methods" (2015), (Donyai, 2015) researchers are often divided into two vastly different philosophies forming the underpinning of their pharmacy practice research - empiricist (quantitative) or interpretative (qualitative). Empiricists are seen to take the positivist truth-seeking approach to knowledge creation and, less so, work that takes a more open-ended, interpretative approach. Interpretative researchers are labelled as those who view ‘science’ more as an ideology than a singular truth, and that meaning is not necessarily to be derived from clear, testable outcomes of empirical research. Instead, for interpretative researchers, meaning can be just as validly derived from studying people and social structures in open systems to explore interactions and subjectivities (Donyai, 2015). A strength of the research included in this thesis is that it draws upon both empiricist and interpretative approaches to explore the pharmacist’s role in opioid management.

There is no inherently 'correct' or 'truthful' way of conducting pharmacy practice research, but what is deemed acceptable depends on the context in which the pharmacy practice research is being conducted (Donyai, 2015). Those who subscribe to the empiricist tradition believe that science can provide an objective, value-free picture of the world. This is based on the theory that people and social structures can be studied 'scientifically', akin to laboratory research, assuming a limited number of variables relating to people can be identified, their behaviour and interrelationship observed, while accounting for or avoiding interference from external or confounding variables, to generate causal theories (Donyai, 2015; Winit-Watjana, 2016). In this way, the scientific 'truth' can emerge through the empirical evidence. If the 'truth' determined in this way yields unexpected results, this may be defended by highlighting the superiority and robustness of the scientific method. Alternatively, results may be contested by identifying methodological deviations in the work that invalidated the resulting 'truth' (Donyai, 2015). However, interpretivists believe people and social structures are too complex to study in simple closed "empiricist" systems. This is because social objects are inherently complex, and this can interfere with assumptions made by empiricist researchers. As such, outcomes cannot ever be predicted and ascertained with any degree of certainty. Interpretivist researchers focus on the importance of language and communication in creating knowledge and thus explore and examine people's thoughts and experiences in detail for their qualitative meanings without the need for creating value-free, generalisable knowledge (Donyai, 2015; Winit-Watjana, 2016).

In this thesis the studies looking at pharmacist practice and behaviour (publications one, two, three and four) were quantitative as they involved the investigation of the implementation of a tool or process that could be easily quantified and outcomes tested or evaluated. Publication five, chapter eight, was more complex as it explored the experiences of people in a health program. It is learnt very quickly when first practicing as health professionals, that people are not black and white and there are many shades of grey when it comes to health-related behaviour. The influences and drivers of this behaviour are not always predictable. This was especially relevant for publication five, where the drug using cohort can be a particularly stigmatised group therefore, a quantitative method was potentially not going to yield truly representative responses and reach the target audience that was required. Qualitative studies are invaluable in accessing these 'hard-to-reach' populations (Neale, Allen, & Coombes, 2005) and because of the capacity of qualitative research to explore and explain human behaviour, it is valuable in destigmatising drug and alcohol addiction with more accurate information that reflects the daily reality of the lives of people who use drugs (Neale et al., 2005). Feelings of trust and rapport between the researcher and study participants facilitate discussions about intimate

information (Neale et al., 2005) and the qualitative researchers' sensitivity to the social and cultural specificity of their study population can foster an awareness and empathy that encourages those being researched to disclose their vulnerabilities (Allen, 2002).

3.2.1 QUANTITATIVE PHARMACY PRACTICE RESEARCH

Quantitative methods are extensively used in pharmacy practice research, and include collecting observational, behavioural or self-reported data or making use of existing datasets (Green & Norris, 2015). In quantitative research the primary aims are to establish general laws or statements that apply across different participants at different times. The study design, the nature of the data and the way they are collected should lend themselves to objectivity (Green & Norris, 2015; Winit-Watjana, 2016). Data should be collected in an impartial manner. A research hypothesis is established at the outset of the study and by using standardised instruments consistency is maintained in data collection (Green & Norris, 2015). The aim is to produce generalisable data in such a way that studies can be repeated with another sample at a different time to produce similar results (Green & Norris, 2015).

The quantitative methods used in this thesis included a covert simulated patient methodology, a quantitative questionnaire, an open labelled one-arm observational implementation-effectiveness methodology and a modified Delphi study. The method chosen was dependent on what was being investigated and more detailed information about each methodology used can be found in each individual chapter. Below is a summary of the benefits and limitations of each method and why each method was chosen for the individual study.

3.2.1.1 COVERT SIMULATED PATIENT

For publication one, Byrne et al, (chapter four) a covert simulated patient methodology was used (Byrne, Wood, & Spark, 2018). Prior to conducting this study there was much debate throughout the profession, regulators and the medical fraternity about how pharmacists were supplying OTC CACC and whether allowing pharmacists to supply OTC CACC was a safe and effective way the public was to gain access to these medications. In the past pharmacy practice research has tended to rely heavily on self-report data from the people involved when studying behaviours and attitudes (Babar, 2015). We wanted to gain a true account of the practice of pharmacists in supplying these medications to the public, therefore a direct observation strategy was used. A meta-analysis of health behaviours showed that asking people questions or measuring their behaviour can have a small change in their behaviour (Rodrigues, O'Brien, French, Glidewell, &

Sniehotta, 2015). This can be because people change their behaviour or answers to be more socially acceptable thus leading to social desirability bias. Covert observation is a method that can be used to reduce response biases. The covert observation method eliminates factors such as the Hawthorne effect and response bias such as social desirability bias and self-report bias of methods like surveys (Babar, 2015). Actors or researchers who present themselves as normal patients to healthcare providers and record details of their care are known by a variety of names, such as mystery shoppers, surrogate patients, undercover care seekers or simulated clients/patients (Madden, Quick, Ross-Degnan, & Kafle, 1997). In order to assess the usual standard of care in a pharmacy, a mystery shopper may be more likely to elicit a typical response than when the pharmacist is aware they are being observed (Norris, 2002). This is a useful way to assess quality and/or consistency of care. In community pharmacy mystery shoppers have been used to explore the questions pharmacy staff ask, advice given, and products recommended (Chalker, Chuc, Falkenberg, Do, & Tomson, 2000; Driesen & Vandenplas, 2009; Neoh, Hassali, Shafie, & Awaisu, 2011). When using covert observation, ethical issues need to be thoroughly addressed including: should informed consent be obtained from participants?; what is the public good being achieved?; should individual pharmacies or staff be identified in results?; how can potential good from the study be weighed against any risk to participants (Madden et al., 1997)? Further information about the methodology used can be found in publication one (chapter four).

3.2.1.2 QUESTIONNAIRES

Publication two, Wood et al (chapter five) utilised a quantitative approach via an anonymous questionnaire to gauge opinion from as broad a range of participants as possible to allow for statistical significance and greater generalisability of the results (Wood, Tucci, et al., 2019). Surveys or self-report data are a common methodology in pharmacy practice research and provide information about the opinions, knowledge and practices of pharmacists, pharmacy staff, customers, the general population and other health professionals (Babar, 2015). Self-reported data have several advantages. They are generally quicker to collect, as a single researcher can recruit a large number of participants in a short period of time (Babar, 2015). Despite this, there are a few disadvantages. It is inherently more subjective, there are limits on what people may be able to report and the data may be biased. Questions can range from open-ended, free-response questions through to psychometrically validated instruments (Babar, 2015). A specific limitation to self-reported data is the extent to which people are accurately able to report on their behaviour or thought processes (Nisbett & Wilson, 1977). Question order

can also change responses, with preceding questions influencing later questions, or even whether a participant completes a survey (Marsden & Wright, 2010). Non-response can also be a challenge facing pharmacy practice researchers using this method as to whether those that choose not to respond have a perspective that is being missed in the study. This creates a non-response bias and can threaten the validity of the research (Babar, 2015). Non-response may also be attributed to research fatigue from the ever increasing requests from retailers and market researchers to complete surveys (Babar, 2015; Dillman, 2002). Further information about the specific methodology used for publication two can be found in chapter five.

3.2.1.3 MODIFIED DELPHI TECHNIQUE

A modified Delphi technique was used for publication three (chapter six) to gain the consensus of experts on what should be considered competencies for best practice for pharmacists in Australia for supply of opioids (Maher, Nielsen, Summers, & Wood, 2020). The Delphi technique is a widely used and accepted method for gathering data from respondents within their domain of expertise (Hsu & Sandford, 2007). A Delphi technique was chosen as there is a lack of competency standards in Australia relating specifically to opioid supply. Competencies developed in Canada were used and Australian pharmacists with known expertise in opioids were asked to consider if they would be applicable for Australian practice. The Delphi technique is well suited as a method for consensus-building by using a series of questionnaires delivered using multiple iterations to collect data from a panel of selected subjects. Subject selection, time frames for conducting and completing a study, the possibility of low response rates, and unintentionally guiding feedback from the respondent group are areas which should be considered when designing and implementing a Delphi study (Hsu & Sandford, 2007). The Delphi technique is an important data collection methodology with a wide variety of applications and uses for people who want to gather information from those who are immersed and imbedded in the topic of interest and can provide real-time and real-world knowledge (Hsu & Sandford, 2007). See chapter six for more information on the specific modified Delphi technique used for publication three.

3.2.1.4 OBSERVATIONAL IMPLEMENATION-EFECTIVENESS METHODOOGY

For publication four (chapter seven) an open labelled one-arm observational implementation-effectiveness methodology was used (Nielsen, Kowalski, et al., 2019). The study tested a multifaceted approach to implement pharmacist-led screening and brief intervention (SBI) in a

community pharmacy setting through the use of the Routine Opioid Outcome Monitoring (ROOM) tool which had been developed previously by co-authors (Nielsen, Picco, et al., 2020). A multifaceted implementation approach was used incorporating strategies of participatory research, academic detailing, computerized decision-making support and multidisciplinary collaboration. This was chosen as such approaches have been demonstrated to be more effective than single interventions in previous work (Arnold & Straus, 2005; Chaillet et al., 2006; Grol & Grimshaw, 2003). The co-design process involved consultation with pharmacists and consumers in addition to input from the research team and advisory committees including pain and addiction medicine specialists. The intervention was planned to be inexpensive, brief and scalable so that it could be implemented in a wide range of settings, including geographically remote settings where opioid-related harm is high and interventions such as naloxone provision are crucial due to long wait times for ambulance attendance (Nielsen, Kowalski, et al., 2019). By delivering the ROOM SBI to all patients receiving repeat opioid prescriptions for noncancer pain it was hoped this would reduce stigma that can result from targeting patients with specific characteristics and inform a better understanding of prevalence of opioid-related risk among those prescribed opioids (Nielsen, Kowalski, et al., 2019).

The study design had several strengths. These included the use of a self-completed screening tool through a digital interface encouraging accurate responses and eliminating social desirability bias. To ensure time efficiency, purpose-built software that integrated within pharmacy dispensing software was employed so that delivery of the ROOM SBI was embedded in a pharmacy workflow. This included automated informed consent and data collection procedures, and technology-facilitated intervention with automated tailored patient and prescriber information. Other strengths included the testing of feasibility in a range of pharmacies and collection of a range of patient and pharmacist rated acceptability measures (Nielsen, Kowalski, et al., 2019).

Limitations of the study design included analyses based on pre/post measures, the use of a single condition with no comparison arm, and a lack of longer-term patient follow-up. Although recognized as a limitation, these features are consistent with a pilot implementation trial (Nielsen, Kowalski, et al., 2019). A detailed explanation of this method can be found in the protocol publication " Routine opioid outcome monitoring in community pharmacy: Pilot implementation study protocol" (Appendix three) (Nielsen, Kowalski, et al., 2019).

3.2.2 QUALITATIVE PHARMACY PRACTICE RESEARCH

Qualitative research answers the "why" questions by establishing close personal contact with the person(s) being studied (Kaae & Traulsen, 2020). Qualitative research within the health sciences has developed as a method to gather an in-depth understanding of human behaviour, as well as to find the underlying reasons, attitudes, and motivations that govern such behaviour (Auta, Strickland-Hodge, & Maz, 2017; Kaae & Traulsen, 2020; Rosenthal, 2016; Winit-Watjana, 2016). In pharmacy practice research, qualitative methods are most often used to identify, improve, and develop current practices (Kaae & Traulsen, 2020).

Qualitative research, like all scientific research, must follow rigid criteria in order to provide trustworthy results that contribute to further development of pharmacy practice. This includes validity, reliability, and transferability of the research process and results (Johnson, Adkins, & Chauvin, 2020; Kaae & Traulsen, 2020). There are four essential aspects of qualitative analysis. These are: 1) Participant selection, this must be well reasoned and the inclusion must be relevant to the research question 2) the methods must be appropriate for the research objectives and setting 3) the methods must be comprehensive enough to provide rich and robust descriptions of events studied and 4) the data must be appropriately analysed and findings adequately corroborated (Kaae & Traulsen, 2020; Rosenthal, 2016).

3.2.2.1 DESCRIPTIVE STUDY

The final publication (chapter eight) used a qualitative descriptive semi-structure interviewing method to gain in-depth knowledge about the lived experiences of people on the MATOD program in rural areas (Wood, Opie, Tucci, Franklin, & Anderson, 2019). A qualitative descriptive study is the method of choice when direct descriptions of phenomena are desired with the goal to provide a comprehensive summary of events in the everyday terms of those events (Sandelowski, 2000). For years there has been a focus in research on patient-centred care. For pharmacy practice research, this means being aware of and trying to understand where patients are "coming from" and what and who informs and influences the patient's views about medicine and treatment (Babar, 2015). It was important for publication five to allow participants to tell their personal story which would be difficult to do through a research tool such as a questionnaire that does not allow for the same richness in data. An important element of qualitative research is that it need not follow distinct, predetermined stages, but can allow researchers instead to move back and forth between research questions, collecting and analysing data in an iterative process. It was important to not only capture details of events but

thoughts, feelings and emotions connected to these experiences “in their own words”(Babar, 2015).

3.2.2.1.1 SEMI-STRUCTURED INTERVIEWS

Data collection in qualitative descriptive studies is directed toward discovering the who, what, and where of events or experiences (Sandelowski, 2000). Semi-structured interviews were used to collect the data for publication five. Interviews are a common and useful method for investigating the subjective understandings, feelings, values, attitudes, experiences, and/or ideas of persons affected by pharmacy practice. Interviews are a type of conversation between the researcher and interviewee/s for the purpose of exploring the perspective of the interviewee/s (Kaae & Traulsen, 2020; Rosenthal, 2016). Interviews vary according to the degree of structure, i.e., the extent to which the interviewee will influence the direction and content of the conversation (Kaae & Traulsen, 2020; Rosenthal, 2016) - fully structured, unstructured, and semi-structured. There is no strict delineation between these and, depending on the research question, they can be mixed. The most used interview form is the semi-structured interview, hence this was used in publication five (chapter 8), where the researcher focuses on relatively few, specific questions. However, the order and weight of questions depends on the answers of the interviewee, as the purpose is to explore their deeper perspectives. Often the researcher probes (asks the interviewee to elaborate further on an answer they have given) in order to get a better understanding of the issue at hand (Kaae & Traulsen, 2020; Rosenthal, 2016).

As patients’ accounts in semi-structured interviews are detailed and rich and often beyond the immediate comprehension of the researcher, noting down the interviewee’s answers during the interview is insufficient for capturing all the relevant information therefore, interviews should be audio-recorded. It is also important to create a trusting environment during the interview in order to allow the interviewee to feel safe to express their true opinions. Reflecting about where to conduct the interview to create this atmosphere is crucial. For publication five this was done by choosing a neutral meeting place and allowing the interviewee to tell their story to the researcher before delving more directly into the structured interview containing potentially more confronting questions. As lifeworld accounts are complex and not fully predictable, conducting interviews of an inductive nature, i.e., applying learning from one interview to the next is highly recommended (Kaae & Traulsen, 2020). This technique was also employed in publication five by ensuring previous interviews were transcribed and read before conducting the next.

The ethical concerns in doing interviews are particularly focused on informing the interviewee about the purpose of the research project. In addition, it is important to protect the anonymity of the interviewee throughout the research process and be aware of the asymmetry of power in the interview situation where the researcher often defines the process (Kaae & Traulsen, 2020; McGrath, Palmgren, & Liljedahl, 2019). This was of concern and importance in the cohort that was used in publication five and was addressed in detail in the relevant ethics applications as people who use drugs often already feel marginalised.

Additionally, qualitative research is extremely dependent on the skills of the researcher when conducting individual interviews. There is always the danger that the results can be easily influenced by the researcher's personal biases (Babar, 2015). To overcome this the initial interviews for publication five were done by two researchers together to minimise any unconscious bias and to provide feedback for improvement in subsequent interviews.

3.2.2.1.2 DATA ANALYSIS

Once interviews are conducted and audio recorded the next step is analysis. The first stage in the analysis process is to transcribe audio recordings into written data. Keeping the exact wording is essential, as well as including supplementary notes in the transcribed text if the interviewee showed a physical reaction at some point during the interview (body language) (Kaae & Traulsen, 2020; McGrath et al., 2019). There is no strictly defined way to analyse transcribed interviews. Qualitative content analysis is the analysis strategy of choice in qualitative descriptive studies (Sandelowski, 2000). In publication five a meaning condensation approach was used. Meaning condensation, according to Kvale (Kvale, 1996) "entails an abridgement of the meanings expressed by the interviewees into shorter formulations" and is often linked directly to the interview guide. Within each theme quotes pertaining to the theme are highlighted to obtain an overview of the process, whilst still being open to new and interesting statements made by the interviewee that are not directly linked to the existing themes. When the entire interview has been coded, the different quotes for one interviewee within one theme are condensed and the meaning expressed by the interviewee interpreted in the researcher's own words. When this process has been conducted for each participant, patterns of similarities or differences between participants can be identified (Kvale, 1996).

3.2.2.1.3 VALIDITY AND RELIABILTY

Validity and reliability are important concepts for qualitative research. Validity is a measure of whether the intention of the research has been presented adequately. An important quality element in qualitative research is obtaining richness of data which allow for interpretation that goes beyond a purely descriptive account. This includes being open to finding unexpected patterns in the collected data (FitzPatrick, 2019; Kaae & Traulsen, 2020). Reliability is whether two independent researchers using the same methods, would arrive at the same results whilst being mindful placing too much emphasis on reliability and reducing the creativeness of the researcher (Kvale, 1996). Even though the reliability of data analysis is often described as when the researchers involved reach consensus on the results, having a group of researchers who don't manage to obtain consensus on the results could likewise be argued to be an important contribution to research (Malterud, 2001) as different possible understandings of the studied practices can be presented which yield an even deeper insight into the phenomenon (Kaae & Traulsen, 2020).

The validity and reliability in publication five was assured as rich data was gained by audio recorded semi-structured interviews that were transcribed verbatim and showed complex social themes beyond those that were expected. The data was analysed independently by two researchers to ensure all the different possible understandings of the interviewees were captured.

3.2.2.1.4 STRENGHTS AND LIMITATIONS

The openness and flexibility of qualitative research has advantages. It creates openness since it is carried out in an informal, relaxed atmosphere that invites participants to be open and honest, encouraging them to expand on their responses. This in turn can open up new areas of interest not initially considered, with the added advantage of allowing respondents to answer questions in as much detail as they want (Kaae & Traulsen, 2020). Qualitative research collects data in naturalistic settings, making it possible to get more valid information about respondents' attitudes, values, and opinions since it opens the possibility for people to explain. As such, qualitative approaches are especially responsive to local situations, conditions, and stakeholders' needs (Kaae & Traulsen, 2020) such as those of people in the MATOD program in regional and rural Victoria and New South Wales as highlighted in publication five.

The major limitation of qualitative research in general, and this is also applicable to the descriptive study included in this thesis (publication five) is that fewer people are usually

studied. Therefore, the results are unlikely to be representative of the population, in this case people on the MATOD program, making it impossible to generalise to other patients on the MATOD program in other areas of Australia. Qualitative studies are time-consuming and labour intensive— in terms of both data collection and data analysis. Critics say that qualitative research has lower credibility with many administrators and policy makers, who often prefer percentages, statistics, and tables (Babar, 2015). Further information on the descriptive methodology employed in publication five can be found in chapter eight.

3.2 SUMMARY

Pharmacists play an important role in supply of opioid medications therefore this thesis focuses on them as the key participants. The methods used for each publication in this thesis were varied and employed a combination of empirical (quantitative) and interpretative (qualitative) approaches. The quantitative methods used included a covert simulated patient methodology (chapter four), a quantitative questionnaire (chapter five), an open labelled one-arm observational implementation-effectiveness methodology (chapter seven), and a modified Delphi study (chapter six). A qualitative descriptive design with semi-structured interviews was chosen for the final study (chapter eight). The method chosen was dependent on what was being investigated and previous work in the area and each method has its associated strengths and limitations. Further details on the specific methods used can be found in the relevant chapters.

CHAPTER 4: NON-PRESCRIPTION SUPPLY OF COMBINATION ANALGESICS CONTAINING CODEINE IN COMMUNITY PHARMACY: A SIMULATED PATIENT STUDY

Community pharmacists are skilled health professionals who are centrally involved in the supply of medications. When any request is made for a medication a pharmacist must decide whether it is appropriate to supply the medication or not (Hanna & Hughes, 2010). If a pharmacist thinks that a medicine is not suitable for the condition, is unsafe for the person, or is being misused, they may suggest another treatment, refuse the sale of a product and/or refer the patient to a doctor or other appropriate medical service. Community pharmacists have an important role to play in monitoring and intervening in medication use, particularly OTC medicine misuse (MacFadyen, Eadie, & McGowan, 2001). Pharmacists employ a variety of methods to identify people misusing medications such as frequents requests for a product, requesting large quantities or the observation of pharmacy assistants (MacFadyen et al., 2001).

Identifying people overusing OTC CACC may not be straightforward for pharmacists. Prior to the first upscheduling of codeine in 2010, some Australian pharmacists were found to use appearance as a means of identifying misuse of OTC CACC (Hamer et al., 2014), however codeine dependent people understood this and often "dressed up" to get easier access to medication (Nielsen et al., 2010). Frequency of supply was also used as a method of identification, but this may not be effective in identifying misuse either as pharmacists lacked a mandatory real-time monitoring system for OTC CACC sales and were only aware of sales occurring in their pharmacy (Nielsen et al., 2010; Nielsen, Tobin, & Dobbin, 2012). Internationally, pharmacists self-reported varying methods of identification of people suspected of misusing codeine. Some pharmacists recognise certain behaviours such as lack of eye contact or agitation, or some just have a "sense" of requesters or those requesting specific products (Carney et al., 2016) but there seems to be a lack of a consistent systematic method.

Numerous studies have identified that managing codeine dependent people is challenging for pharmacists (Albsoul-Younes, Wazaify, Yousef, & Tahaineh, 2010; MacFadyen et al., 2001; McBride, Pates, Ramadan, & McGowan, 2003). When a pharmacist suspects a person is overusing an OTC medication, they may employ strategies to reduce misuse. Most pharmacists will intervene by asking the person to seek their doctors' advice (MacFadyen et al., 2001). Other strategies used by pharmacists include telling people that they no longer sell the product, refusing the sale, recommending alternative pain management options, educating people about

the risks of high doses or confronting people about their overuse (Albsoul-Younes et al., 2010; Hamer et al., 2014; MacFadyen et al., 2001). These strategies are unlikely to assist people manage any possible dependence. Pharmacists and experts in addiction suggest keeping the product out of sight and staff training to be the most effective ways to decrease OTC medication misuse (McBride et al., 2003). People have been found to be reluctant to talk about their misuse of OTC medications and are unresponsive to any advice given by pharmacists (Nielsen, Cameron, & Pahoki, 2013; Wazaify, Hughes, & McElnay, 2006). Similarly, pharmacists have been identified as being uncomfortable discussing codeine dependence with codeine users (Nielsen et al., 2013).

Many of the aforementioned studies were based on pharmacist self-reporting, but this can be influenced by bias in particular social desirability bias. We wanted to know how these self-reported strategies aligned with what pharmacists were doing in practice. This first published manuscript addresses this by conducting a covert simulated patient study. As the pharmacists were unaware that they were being observed it gave a truer account of how requests for OTC CACC were being managed.

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Non-prescription supply of combination analgesics containing codeine in community pharmacy: A simulated patient study

Georgia A. Byrne, B.Pharm. (Hons.), Penelope J. Wood, B.Pharm. (Hons.), M. Joy Spark, PhD *

Department of Pharmacy and Applied Science, La Trobe Institute for Molecular Science, LaTrobe University Bendigo, Victoria 3550, Australia

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ABSTRACT

Background: The inappropriate use of non-prescription combination analgesics containing codeine (NP-CACC) has become a significant health issue in Australia.
Objective: To investigate the current management of NP-CACC direct product requests in community pharmacies located in Victoria, Australia.
Methods: A covert simulated patient (SP) method was used to observe the responses of pharmacy staff during an NP-CACC request. Four SPs were trained to complete 1 of 2 scenarios. Each scenario involved a direct product request for Nurofen Plus (200 mg ibuprofen, 12.8 mg codeine) with identical reason for use, symptoms, and medical history but varied previous product use. Scenario One (Sc1) involved a first time NP-CACC user and in Scenario Two (Sc2) the SP had used NP-CACC regularly for the past month. Each visit was documented by the SP immediately after they left the pharmacy. A NP-CACC supply score, created from 4 outcomes (pharmacist involvement, establishment of therapeutic need, establishment of safety and provision of counselling), was given to each pharmacy visit (maximum of 8) during data analysis.
Results: 145 pharmacy visits were completed. Both scenarios were performed in most of the 75 pharmacies visited (73 Sc1 and 72 Sc2). Treatment was provided in the majority of visits but refused in 37(24%) because the SP was unable to provide photo identification. A pharmacist was involved (directly or indirectly) in 77% of visits. Adequate questioning to establish therapeutic need occurred in 50% of pharmacy visits, safety was established in 17% of visits, and adequate counselling provided in 17% of visits. The SP scenario did not significantly affect the NP-CACC supply outcomes. NP-CACC supply scores ranged from 1 to 8, ($Md = 5$) with only 1 pharmacy visit achieving the maximum score of 8.
Conclusions: The majority of pharmacy visits did not achieve a full score relating to NP-CACC supply, illustrating the need for improved awareness of how to assess and manage patients requesting NP-CACC.

Introduction

Non-prescription combination analgesics containing codeine (NP-CACC) are indicated in the short term treatment of moderate to severe acute pain. Designed to provide greater analgesia compared to single-ingredient preparations, these products contain a non-opioid analgesic combined with codeine, a weak opioid. In Australia, NP-CACC containing 8–15 mg of codeine phosphate in fixed dose combinations with ibuprofen, paracetamol or aspirin are classified as Schedule 3: Pharmacist Only Medicines.[1] This classification allows these medicines to be available without a prescription from a pharmacist and requires professional advice upon supply. Professional guidelines for the provision of NP-CACC from pharmacies recommend: assessment of the patient's presenting condition, establishing if the request is safe and appropriate and provision of adequate product counselling.[2] Pharmacists are expected to apply professional judgement and adapt these guidelines to all practice situations. NP-CACC are considered safe in the short term with legislation restricting use to a maximum of five days.[1] A recent review commissioned by the Australian Therapeutics Goods

* Corresponding author. Department of Pharmacy and Applied Science, La Trobe Institute for Molecular Science, LaTrobe University, PO Box 199, Bendigo, Victoria 3552, Australia.
E-mail address: j.spark@latrobe.edu.au (M.J. Spark).

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Administration found that NP-CACC provide clinically significant pain relief for acute pain.[3] NP-CACC have a limited role in chronic or persistent pain with guidelines suggesting referral for further pain management.[2]

Use of NP-CACCs for extended periods can sometimes lead to harm. These products are internationally recognised in the top five NP products that are frequently used incorrectly.[4] In Australia, the inappropriate and poor quality use of NP-CACC has emerged as a health issue.[5] Exceeding the maximum daily doses or long term use can have adverse health effects including dependence. Codeine dependence is a serious health concern characterised by a number of features including exceeding therapeutic doses, continued use despite adverse health consequences as well as experiencing withdrawal symptoms upon cessation.[6] Harms with continued NP-CACC use are associated with high doses of accompanying simple analgesics (ibuprofen, paracetamol or aspirin) consumed along with the codeine.[7] Published cases have mainly investigated harms associated with ibuprofen, a non-steroidal anti-inflammatory drug[8–10]; with gastrointestinal complications due to ibuprofen toxicity recognised as the most common morbidity alongside codeine dependence.[10] Peptic ulceration, perforation and haemorrhage and pyloric stenosis have also been regularly documented.[7] Renal failure, anaemia secondary to severe blood loss from gastrointestinal complications and severe hypokalaemia producing neurological and cardiac adverse effects are other life-threatening injuries caused by ibuprofen toxicity. Persons dependent on NP-CACC have claimed to be generally uninformed of the harms associated with inappropriate NP-CACC use.[11] This suggests that warning purchasers about the potential risks for exceeding the maximum therapeutic dose and treatment duration may not be regular practice in community pharmacies.

Pharmacists face many challenges in the management of NP-CACC requests.[6,7,11,12] Issues can be categorised into the following key areas: identifying a therapeutic need and recognising, monitoring and intervening in inappropriate NP-CACC use. Pain is considered a subjective experience for individuals and NP-CACC dependent people can also be in genuine pain, complicating the issue of identifying a therapeutic need.[6] Finding an objective way to assess an NP-CACC request has been reported to be a challenge for community pharmacists.[11] Pharmacist responses to NP-CACC requests were perceived to be influenced by personal characteristics such as appearance and behaviour. In interviews with NP-CACC dependent people, participants alleged that appearance strongly influenced their ability to acquire codeine.[7] Community pharmacists have also reported that they often labelled requesters as either 'genuine' or 'misuser' based on these attributes.[12] Haphazard monitoring of NP-CACC sales has also been reported; with recording of NP-CACC sales found to vary, from recording every sale to recording only some sales based on assumptions formed by the frequency of NP-CACC request.[12] Furthermore, pharmacists have been perceived to be hesitant to intervene in potential inappropriate NP-CACC sales at the risk of causing offence to non-codeine dependent customers.[7] These qualitative studies reported that pharmacists may not have the necessary knowledge and skills to approach NP-CACC requests confidently and in an impartial manner.

The perceptions and opinions of pharmacists and NP-CACC dependent persons have been explored in a number of qualitative studies that examined NP-CACC supply through community pharmacies. Multiple challenges in pharmacy practice were identified through these studies. However, the results may not be a true representation of current practice. These studies were not based on direct observation of a clinical encounter but rather the opinions of study participants. Participant statements may be overestimated or underestimated thus introducing response bias.[13] To overcome this a direct observation method can be used.[13,14] The simulated patient (SP) method is one such observational method and has been shown to be an effective tool for evaluating current professional practice with trained SPs providing more reliable feedback than regular customers.[14,15]

The simulated patient method is an internationally recognised tool for measuring pharmacy research outcomes.[14] Topics have included management of lower back pain,[16] smoking cessation,[17] supply of asthma reliever medication,[18] provision of emergency contraception[19] evaluation of a pharmacist training program for non-prescription analgesics[20] and assessment of intern pharmacists as change agents.[21] To date, management of requests for NP-CACC has not been assessed. The aim of this study was to investigate the current management of NP-CACC requests in community pharmacies located in Victoria, Australia.

Methods

A covert simulated patient method was selected to examine the interaction of community pharmacists and pharmacy staff with individuals requesting NP-CACC. This method has been increasingly used as an effective approach for evaluating current pharmacy practice and identifying areas for improvement.[14] An SP is defined as someone trained to make a covert visit to a pharmacy to enact a scenario and report on the behaviour of pharmacy staff without the staff being aware that they are being evaluated.[14,22,23] A standard data collection tool was used for all visits to reduce the risk of bias.[14]A covert SP visit ensured that the phenomenon known as the Hawthorne or Observer Effect (participant changing their behaviour as result of knowing that they are being observed) was reduced.[18] The SP interaction with pharmacy staff consequently occurred under conditions that closely reflected current pharmacy practice. Audiotaping the visits can be used to validate the reliability of SP self-reported data.[14] However, in this study audiotaping was not used as permission from pharmacy staff would have been needed prior to recording SP visits. This study was approved by the La Trobe University Human Ethics Committee (Application No. 15–033). Ethics approval required that only indirect feedback be given to the participating pharmacies through the Pharmacy Guild of Australia.

Setting

All community pharmacies in an area of Victoria that included both rural and metropolitan localities were identified as eligible for inclusion in the study. A 'Register Search' of the Victorian Pharmacy Authority's website was employed to locate pharmacies within north central Victoria (297 of 1329 pharmacies in Victoria) (http://www.pharmacy.vic.gov.au/index.php?view=register). In previous SP studies the total number of pharmacy visits per SP (median = 112) varied greatly.[14] Due to the large variation, 100 pharmacies were selected as the sample size and SPs aimed to conduct up to 150 pharmacy visits between them, with most pharmacies visited by two SPs (both scenarios). To ensure the randomized sample encompassed both metropolitan and non-metropolitan areas the identified pharmacies were divided according to the Australian Standard Geographical Classification – Remoteness Areas (ASGC-RA), into metropolitan [RA1; Major Cities (n = 148)] and non-metropolitan pharmacies [RA2; Inner Regional and RA3; Outer Regional (n = 149)].[24] A sample of 50 pharmacies was then randomly selected from each category using a random number generator. Pharmacies in the sample were then visited by

two different SPs during data collection until a total of 75 pharmacies had been visited. If pharmacy staff were known to the SP the visit was abandoned. The six community pharmacies used for the pilot study were not included in the main study.

Scenarios

To investigate the response of pharmacy staff to both a first time user and a repeat request, two scenarios, were developed by the research team. These scenarios were designed to be easily reproducible, appropriate for the SPs and from the research teams experience were commonly seen in community pharmacy. Anticipated questions were derived from the professional guidelines for pharmacists in the provision of NP-CACC[2] and the researchers' experiences in community pharmacy. Formal scenarios along with adequate training to standardise the visits were used to reduce any inconsistency between different SPs.[14] The scenarios involved the direct product request (DPR) for Nurofen Plus (codeine phosphate 12.8 mg, ibuprofen 200 mg). Nurofen Plus was selected as it is a common brand requested by patients seeking ibuprofen-codeine NP-CACC products in Australia.[8] Direct product requests have commonly been used for covert SP studies conducted in Australia,[22] with additional scenario information only being provided by the SP when appropriately prompted by pharmacy staff. To ensure simplicity, each scenario involved identical information relating to the intended product use, symptoms, medical history and treatment history. However, the response given by the SP regarding previous NP-CACC use varied; specifically, in Scenario 1 (Sc1) (Appendix A) the requestor was a first time NP-CACC user and in Scenario 2 (Sc2) (Appendix B) the requestor had a frequent history of NP-CACC use for the past month. The main emphasis of Sc1 was to observe the extent of questioning from staff and counselling provided with any treatment offered and Sc2 was a referral to a health professional (e.g. doctor) for further pain management. The two different scenarios enabled data to be gathered on the variation in the management of two different NP-CACC use histories.

Staff at some community pharmacies request photo identification (ID) to monitor the sale of NP-CACC by recording personal details of purchasers in the pharmacy dispensing software or Project STOP, a national database used to monitor the supply of pseudoephedrine-containing products. The Project STOP database can be accessed by both registered pharmacies and the Australian police and is not authorised for monitoring of NP-CACC sales.[25] Despite this, some pharmacists are recording NP-CACC sales in the database.[26] For the protection of SPs they did not carry photo ID during a pharmacy visit; consequently they were unable to supply photo ID if requested and the associated outcome was documented. However, if requested, the SPs were prepared to supply a name and address for recording in the pharmacy's dispensing software.

Data collection

A standardised data collection form (Appendix C) was used for all pharmacy visits. Pharmacy demographics were completed prior to the visit. Immediately following each pharmacy visit, the interaction that occurred with pharmacy staff including who was involved in the interaction (pharmacist or other pharmacy staff), questioning and counselling provided, along with product information were documented by the SP onto a data collection form. The pharmacist was identified by their name tag or being referred to by another staff member. To reduce the potential for scenario and data collection fatigue, SPs were limited to a maximum of 10 pharmacy visits per day, on a maximum of five days a week.[27,28] There was no limitation on the distance that could be travelled in this time.

Simulated patients

To ensure continuity, four female volunteers of similar age (19–22 years) were recruited as SPs. Our SPs were chosen on the basis that they had reasonable intelligence, emotional maturity and also could be deemed trustworthy as recommended by previous studies.[14,28] More than two SPs were trained because data collected by one or two SPs has been reported to be more limited and less generalizable.[14] This was balanced against using too many SPs where difficulties can arise with standardising the approach. To minimize appearance effects[11] the SPs were asked to wear neat and tidy dress for each pharmacy visit. To ensure consistency in scenario replication, SPs only performed 1 of the 2 scenarios and comprehensive training was provided to ensure reliable data collection. SPs were trained by the research team via a series of workshops that involved role-playing to review and practice the assigned scenario and complete the data collection form with feedback continuously given. The scenarios were also practiced with current community pharmacists with knowledge of the study.

Pilot study

A pilot study ($n = 6$) was conducted to assess the SP data collection. Each SP visited two pharmacies from the pilot sample. The content and delivery of the scenario as well as the documentation of results in the data collection form was assessed by researchers. The data collection form was refined and modified to address issues identified during the pilot study.

Data analysis

Data from pharmacy visits were entered by the researchers into IMB SPSS vs23 and descriptive statistics calculated. A χ^2 test with Yates continuity correction for 2×2 tables, or Fisher's Exact Test when there were fewer than 5 responses in a cell,[29] was used to compare responses to individual questions with each scenario. Four outcomes for supply of NP-CACC were created based on legislation requirements and professional guidelines. According to Victorian legislation, pharmacists are required to be either directly involved or supervise the sale of all Schedule 3: Pharmacist Only Medicines to ensure there is a therapeutic need and provide appropriate directions for use.[30] In addition professional guidelines require assessment of safety and more comprehensive counselling.[2] Consequently the NP-CACC supply outcomes for this study were: (1) pharmacist involvement, (2) establishment of therapeutic need, (3) establishment of safety, and (4) provision of counselling (Table 1). Pharmacist involvement was scored, by the researchers, based on the level of pharmacist interaction as documented by the SPs. Professional guidelines[2] that suggest questions and actions to be completed by pharmacy staff were used to score each of the other outcomes. Adequate establishment of therapeutic need involved asking at least 1 question about the patient, 1 question about symptoms and 1 question about treatment history. For establishment of safety to be adequate pharmacy staff were required to ask the 3 following questions; any medical conditions, any medications or if the SP was currently pregnant or breast-feeding. Adequate counselling required provision of at least on piece of information about dosage, adverse effects and follow up advice. Referral to another health professional was a requirement for adequate counselling in Sc2 (repeated NP-CACC user) because of their ongoing use of a NP-CACC. A maximum score of 2 was given

Table 1
Scoring rubric for NP-CACC supply outcomes.

NP-CACC supply outcome	Score Allocation		
	0	1	2
1. Pharmacist Involvement	*No pharmacist involvement:* Pharmacist not involved in any aspect of the interaction.	*Indirect pharmacist involvement:* Pharmacist supervised interaction between SP and pharmacy staff member.	*Direct pharmacist involvement:* Pharmacist directly involved in interaction (either initial or after referral).
2. Establishment of Therapeutic Need	*No questioning:* No questions were asked to establish therapeutic need	*Partial Questioning:* At least 1 therapeutic need question[a] was asked.	*Adequate Questioning:* One question from each category[a] was asked.
3. Establishment of Safety	*No questioning:* No questions were asked to establish safety	*Partial Questioning:* At least 1 safety question[b] was asked.	*Adequate Questioning:* All questions[b] to establish safety were asked.
4. Provision of counselling	*No counselling:* No counselling points were provided.	*Partial Counselling:* At least 1 counselling point[c] was provided	*Adequate Counselling:* One counselling point from each category[c] was provided. SC2-and referral to a health professional

[a] Therapeutic need categories: identify patient: *"who is it for?"* Symptoms: *"what are you using it for?", "actual symptoms?"* or *"how long has symptoms been present?"* Previous treatment: *"have you had the product before?", "have you tried any other treatments?",* or *"were treatments effective?"*
[b] Safety questions: *"Are you on any other medications?" "Do you have any medical conditions? "Are you pregnant or breastfeeding?"*
[c] Counselling categories: Dosing: *"Take 1–2 tablets", "every 4–6* h", or *"maximum of 6 tablets in 24* h". Adverse effects: *"drowsiness", "constipation"* or *"upset stomach/take with food"* Follow up advice: *"not for long term use- 3 days only", "addiction warning",* and *"if pain persists seek medical advice"* or *"immediate referral to health professional".*

for each supply outcome documented as adequate (Table 1) with a maximum score of 8 possible for the NP-CACC supply score. A score of 7 or 8 indicated adequate provision of NP-CACC supply for the pharmacy visit. As outcomes were ordinal, measures of associations were used to describe the relationship between each variable.[31] Kendall's tau-*c* test was used to describe relationships between the scenarios and NP-CACC supply score. The Kruskal-Wallis test was used to compare NP-CACC supply score with pharmacy or visit characteristics. To ensure the alpha value for all tests was at a realistic level, a Bonferroni adjustment was applied to correct *p* values for multiple comparisons.[29] Results are presented as a percentage of pharmacy visits conducted.

Results

A total of 145 pharmacy visits were conducted in 75 randomized Victorian community pharmacies, 73 visits involved Sc1 and 72 visits involved Sc2. The community pharmacies visited were in both metropolitan (n = 38, ASGC-RA 1) and non-metropolitan areas (n = 37, ASGC-RA 2) and covered a range of pharmacy types and locations (Table 2). Each SP completed between 21 and 72 visits between July and August 2015.

The frequency of questions asked to establish therapeutic need or product safety and the counselling the SP received following their request for Nurofen Plus are shown in Table 3. In over 60% of pharmacy visits SPs were questioned about who the patient was (82.1%), the intended product use (64.1%), previous product use (66.9%), use of other medications (68.2%) or other medical conditions (66.7%). The only counselling provided in over 60% of SP visits was about taking the NP-CACC product with food (63.1%). There was no difference in the frequency of questioning between scenarios for all types of questions and most of the counselling. The SP using Sc2 was counselled less often about the number of tablets per dose or constipation as a side effect.

Table 2
Pharmacy characteristics.

Characteristic	Frequency (n = 75)	Percentage (%)
Pharmacy type		
Franchise/Banner group	16	21.3%
Friendly society	7	9.3%
Independent	33	44.0%
Discount	19	25.3%
Pharmacy location		
Street	50	66.7%
Shopping centre	19	25.3%
Medical centre	6	8.0%

A treatment was given in 74.5% of pharmacy visits (n = 108). This included 103 purchases of an NP-CACC containing ibuprofen and 5 purchases of a suitable alternative product; ibuprofen (Sc1 n = 1, Sc2 n = 2), ibuprofen and paracetamol combined product (Sc2 n = 1) and a recommendation to use paracetamol with diclofenac gel (Sc2 n = 1). Patients were more likely to receive treatment if the pharmacist was involved. Of interactions involving pharmacists 12.6% (14/111) resulted in no treatment, conversely, 67.6% (23/34) of interactions with no pharmacist involvement resulted in no treatment.

The only reason an SP did not obtain treatment was because they were not carrying photo ID. This occurred in 25.5% (n = 37, Sc1 *n* = 17, Sc2 *n* = 20) of pharmacy visits. In 9.0% (13) of pharmacy visits the first question asked was about photo ID, when photo ID was not available no further questions were asked. As no product was supplied these visits were not included in the results for establishing product safety or counselling. For the other 24 visits where no product was given further questioning occurred before the decision to refuse supply, therefore these visits were included in establishing supply but not counselling as there was no product to counsel about. Refusal to supply a NP-CACC without photo ID was not always consistent. In 5 pharmacies Sc1 was unable to purchase a NP-CACC without photo ID yet Sc2 was able to purchase it. Conversely, Sc2 was refused sale in 8 pharmacies in which Sc1 could purchase a NP-CACC without photo ID. A reason for requiring photo ID was provided by staff in 8 pharmacy visits where it was required for Project STOP recording. Staff requested a residential address to record the sale on the pharmacy's dispensing system in 17.2% of pharmacy visits (*n* = 25, Sc1 *n* = 13, Sc2 *n* = 12).

Strategies to reduce ongoing CACC use were used by pharmacy staff during some visits. These included advice about the recommended maximum duration of NP-CACC treatment, which occurred in 26.9% of interactions (*n* = 28) and a verbal addiction warning, which was provided in 3.9% of interactions (*n* = 4) (Table 3). A warning sticker about the risk of addiction *('for 3 days use only – may cause addiction')* was located on 9.7% of NP-CACC products purchased (*n* = 10) and a clear addiction warning was located on the front of the packaging on 11.7% of NP-CACC products purchased (*n* = 12).

The type of scenario presented at a pharmacy visit did not influence any of the 4 NP-CACC supply outcomes (Table 4).

Table 3
Questioning and counselling data (used for NP-CACC supply outcomes 2, 3 and 4). Responses where there was statistically significant difference between the two scenarios are in bold.

Results from data collection	Total Yes within scenarios	Yes Sc1[a] (n = 73)	Yes Sc2[b] (n = 72)	χ^{2}[c]	*p*	ϕ
2. Questions for establishment of therapeutic need (n = 145)						
Identify patient						
Who is it for?	119 (82.1%)	63 (86.3%)	56 (77.8%)	1.26	0.26	0.11
Symptoms						
What are you using it for?	93 (64.1%)	51 (78.5%)	42 (62.7%)	3.22	0.073	0.17
How long have you had symptoms?	13 (9.0%)	7 (10.8%)	6 (9.0%)	0.003	0.95	0.03
Actual symptoms?	7 (4.8%)	3 (4.6%)	4 (6.0%)	0.00	1.00	0.03
Asked 1 question about symptoms	*94 (64.8%)*	*51 (69.9%)*	*43 (59.7%)*	*1.22*	*0.27*	*0.11*
Previous treatment						
Have you had the product before?	97 (66.9%)	47 (72.3%)	50 (74.6%)	0.011	0.92	0.03
Have you tried any other treatments?	16 (11.0%)	12 (18.5%)	4 (6.0%)	3.73	0.053	0.19
Have you seen a health professional?	19 (13.1%)	11 (16.9%)	8 (11.9%)	0.32	0.57	0.07
Asked 1 question about previous treatment	*102 (70.3%)*	*50 (68.5%)*	*53 (73.6%)*	*0.25*	*0.62*	*0.06*
3. Questions for establishment of safety (n = 132)						
Do you have any medical conditions?	88 (66.7%)	45 (69.2%)	43 (64.2%)	0.19	0.67	0.05
Are you on any other medications?	90 (68.2%)	43 (66.2%)	47 (70.1%)	0.094	0.76	0.04
Are you pregnant or breastfeeding?	22 (16.7%)	10 (15.4%)	12 (17.9%)	0.024	0.88	0.03
4. Provision of counselling						
Dosing: (n = 103[d])						
Take 1–2 tablets	**52 (50.5%)**	**35 (63.6%)**	**17 (35.4%)**	**7.07**	**0.008**	**0.28**
Every 4–6 h	46 (44.7%)	29 (52.7%)	17 (35.4%)	2.45	0.12	0.17
Maximum of 6 tablets in 24 h	47 (45.6%)	24 (43.6%)	23 (47.9%)	0.056	0.81	0.04
Talked about at least 1 aspect of dosing	*62 (60.2%)*	*38 (69.1%)*	*24 (50.0%)*	*3.14*	*0.076*	*0.19*
Adverse effects: (n = 103[d])						
Drowsiness	27 (26.2%)	18 (32.7%)	9 (18.8%)	1.92	0.17	0.16
Constipation[e]	**13 (12.6%)**	**12 (21.8%)**	**1 (2.1%)**	**7.35**	**0.002**	**0.30**
Upset stomach/take with food	65 (63.1%)	38 (69.1%)	27 (56.3%)	1.31	0.25	0.13
Talked about at least 1 adverse effect	*75 (72.8%)*	*44 (80.0%)*	*31 (64.6%)*	*2.35*	*0.12*	*0.17*
Follow up advice						
Not for long term use (3 days only) (n = 108)	28 (26.9%)	16 (28.6%)	13 (25.0%)	0.04	0.84	0.04
If pain persists seek medical advice (n = 108)	23 (21.3%)	11 (19.6%)	12 (23.1%)	0.04	0.84	0.04
Immediate referral to health professional (n = 108)[e]	3 (2.8%)	1 (1.8%)	2 (3.8%)	0.42	0.61	0.06
Verbal addiction warning (n = 103[d])[e]	4 (3.9%)	4 (7.3%)	0 (0%)	1.95	0.12	0.19
Gave at least 1 piece of follow up advice (n = 108)	43 (39.8%)	22 (39.3%)	21 (40.4%)	0.00	1.00	0.01

[a] Scenario One (first-time NP-CACC user).
[b] Scenario Two (Using NP-CACC for 4 weeks).
[c] Yates continuity correction (2 × 2 tables).
[d] Documented responses specific NP-CACC products.
[e] Fisher's Exact Test (less 5 in a cell).

Table 4
Scenario versus NP-CACC supply outcomes.

NP-CACC supply outcome		% Sc1[a] (n = 73)	% Sc2[b] (n = 72)	df	Kendall's Tau-*c* (τ_c)	*p*-value[c]
1. Pharmacist involvement (n = 145)						
No involvement	34 (23.4%)	18 (24.7%)	16 (22.2%)	2	−0.025	0.77
Indirect (supervised) Involvement	31 (21.4%)	13 (17.8%)	18 (25%)			
Direct involvement	80 (55.2%)	42 (57.5%)	38 (52.8%)			
2. Establishment of therapeutic need (n = 145)						
No questioning	15 (10.3%)	8 (11.0%)	7 (9.7%)	2	−0.136	0.11
Partial questioning	58 (40.9%)	23 (31.5%)	35 (48.6%)			
Adequate questioning	72 (49.7%)	42 (57.5%)	30 (41.7%)			
3. Establishment of safety (n = 132)						
No questioning	39 (29.5%)	19 (29.2%)	20 (29.9%)	2	0.013	0.89
Partial questioning	71 (53.8%)	36 (55.4%)	35 (52.2%)			
Adequate questioning	22 (16.7%)	10 (15.4%)	12 (17.9%)			
4. Provision of counselling (n = 103)						
No counselling	12 (11.7%)	5 (9.1%)	7 (14.6%)	2	−0.180	0.036
Partial counselling	74 (71.8%)	38 (52.1%)	42 (58.3%)			
Adequate counselling	17 (16.5%)	12 (16.4%)	2 (2.8%)			

[a] Scenario One (first-time NP-CACC user).
[b] Scenario Two (repeated NP-CACC user).
[c] Bonferroni adjusted alpha level = 0.01.

Pharmacist involvement

A pharmacist was identified as being directly involved in SP interactions in 55.2% of visits ($n = 80$). A pharmacist supervised the SP interaction in 21.4% of visits ($n = 31$) and there was no pharmacist involvement in 23.4% of visits ($n = 34$).

Establishment of therapeutic need

Adequate questioning by pharmacy staff to determine therapeutic need occurred in 49.7% of pharmacy visits ($n = 72$). Partial questioning occurred in 40.9% of visits ($n = 58$) and there was no questioning to establish therapeutic need in 10.3% of visits ($n = 15$). Only

10.8% of Sc1 interactions ($n = 7$) and 9.0% of Sc2 interactions ($n = 6$) involved questioning to determine symptom duration (Table 3).

Establishment of safety

Adequate questioning by pharmacy staff to determine the safety of the NP-CACC product occurred in 16.7% of visits ($n = 22$). There was partial questioning in 53.8% of visits ($n = 71$) and no questioning by staff in 29.5% of visits ($n = 39$). Enquiring if the SP was pregnant or breastfeeding occurred in 15.4% of Sc1 interactions ($n = 10$) and 17.9% of Sc2 interactions ($n = 12$) (Table 3).

Provision of counselling

Provision of adequate counselling occurred in only 16.5% ($n = 17$) of pharmacy visits when a NP-CACC was supplied ($n = 103$). Partial counselling was received in 71.8% of pharmacy visits ($n = 74$) and no counselling occurred in 11.7% of visits ($n = 12$). Adequate counselling for Sc2 (repeated NP-CACC user) required immediate referral to a health professional this only occurred in 2.8% of all Sc2 visits ($n = 2$).

NP-CACC supply score

A NP-CACC was supplied in 103 of the 145 pharmacy visits. NP-CACC supply scores ranged from 1 to 8 ($Md = 5$, $IQR = 4–6$), with only 1 visit accomplishing all outcomes (Fig. 1). This pharmacy visit involved Sc1 (first time NP-CACC user). An adequate NP-CACC supply score (7 or 8) was achieved at 13 visits, 9 Sc1 visits and 4 Sc2 (repeat NP-CACC user) visits. A χ^2 test with Yates continuity correction revealed that the difference in adequate NP-CACC supply score between Sc1 and Sc2 visits was not statistically significant ($\chi^2 = 0.86$, $p = 0.35$, $\phi = 0.12$, small effect size[32]). Over 50% of pharmacy visits responded to the SP visit with at least partial completion of each of the 4 NP-CACC supply outcomes ($n = 67$, Sc1 $n = 34$, Sc2 $n = 33$). Of the pharmacy visits with a NP-CACC supply score of 5 or above, 14.5% ($n = 15$, Sc1 $n = 10$, Sc2 $n = 5$) scored 0 for 1 outcome within the score.

The impact of visit characteristics (scenario, SP) and pharmacy characteristics (ASGC-RA classification, pharmacy type or location) on NP-CACC supply scores was investigated using Kruskal-Wallis tests. No significant difference was found between NP-CACC supply score and any of the pharmacy or visit characteristics: Scenario $\chi^2(1, 103) = 0.54$, $p = 0.46$ [scenario 1 ($Md = 5$, $n = 55$) or scenario 2 ($Md = 5$, $n = 48$)]; SP χ^2 (3, 103) = 3.12, $p = 0.37$ [SP 1 ($Md = 5$, $n = 21$), SP 2 ($Md = 5$, $n = 22$), SP 3 ($Md = 6$, $n = 12$), SP 4 ($Md = 5$, $n = 48$)]; ASGC-RA classification χ^2 (1, 103) = 1.84, $p = 0.17$ [metropolitan ($Md = 5$, $n = 54$) or non-metropolitan pharmacy visits ($Md = 5$, $n = 49$)]; Type of pharmacy χ^2 (3, 103) = 5.98, $p = 0.11$ [Independent ($Md = 5$, $n = 49$), Discount ($Md = 5$, $n = 23$), Banner group/Franchise ($Md = 5$, $n = 20$) or Friendly society ($Md = 6$, $n = 11$)]; Pharmacy location χ^2 (2, 103) = 0.092, $p = 0.95$ [Street ($Md = 5$, $n = 71$), shopping centre ($Md = 5$, $n = 22$), or Medical centre ($Md = 5.5$ $n = 10$)].

The consistency of NP-CACC supply between visits was investigated using a Wilcoxon Signed Rank Test which revealed no significant difference between visits $z = -0.48$, $p = 0.63$, $r = 0.07$. The median NP-CACC supply score, for both visits, was 5. Seventy-five percent (n = 77) of pharmacy visits achieved this score or above.

Discussion

The management of NP-CACC requests reported in this study was suboptimal. Both scenarios involved a direct product request (DPR) which has previously been shown to be related to reduced patient assessment and counselling compared to symptom based requests.[33] DPRs have been reported to be more intimidating for pharmacy staff with fewer opportunities to engage with the patient[33] and therefore exchange of clinical information may be less likely.[22] There was no significant difference in NP-CACC supply outcomes for the two scenarios used in this study (Table 4). The variability in NP-CACC supply scores (1–8) illustrates that awareness of the management of NP-CACC requests is limited and potentially pharmacists and pharmacy staff may not be implementing current professional guidelines.

A variation in the degree of pharmacist involvement during pharmacy visits was observed. Due to legal requirements,[30] it was expected that there would be either direct or indirect (supervised) pharmacist involvement in all sales. Encouragingly, the majority of sales involved a pharmacist. The 23% of interactions that did not involve a pharmacist did not meet the Pharmacist Only Medicine provision requirements. These results coincide with findings from a previous study, conducted before pharmacist involvement was a legal requirement, where NP-CACC dependent people reported limited pharmacist interaction during NP-CACC requests until patterns of frequent use were established.[11] More frequent questioning from pharmacists when purchasing NP-CACC has been identified as an important factor for NP-CACC requesters seeking support.[11] Therefore, the early intervention from pharmacists may decrease the frequency of problematic use and increase the number of users seeking support.

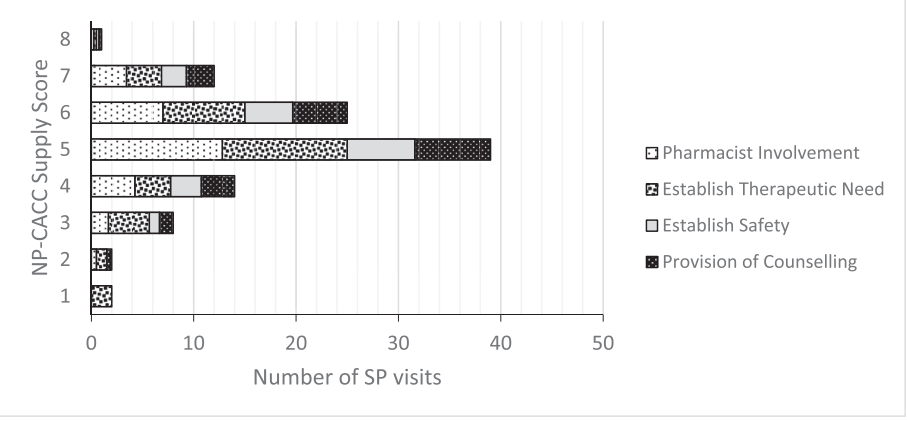

Fig. 1. Frequency of NP-CACC supply scores showing how each outcome contributed to the scores.

Therapeutic need is required, by legislation, to be established by pharmacists prior to supplying any NP-CACC.[30] Most SP interactions involved a question from at least 1 of the 3 categories that would enable the pharmacist to establish therapeutic need, while 10% involved no questions for this outcome. A previous study reported establishing therapeutic need for NP-CACC as difficult of pharmacists; identifying limited time with patients and the subjective nature of pain as major barriers.[12] Enquiring about the intended product use has been previously reported by NP-CACC users as the standard question asked by pharmacy staff during NP-CACC requests.[11] In this study, the intended product use was only asked during 64% of visits and the most frequent question related to identifying the intended patient (82%). When establishing therapeutic need and safety it is of equal importance to identify the intended patient and the intended use, consequently both of these questions should be asked for every sale. Furthermore, only 8% of pharmacy staff involved in Sc2 (repeat NP-CACC user) interactions asked questions about symptom duration and consequently were able to identify ongoing NP-CACC use. Ongoing pain requires referral for a further investigation and development of a pain management plan.[2,34]

The way pharmacy staff responded to the SP not carrying photo ID was unexpected. When treatment with an NP-CACC was refused due to a lack of photo ID, in very few interactions was an alternative solution for pain management offered. Pharmacists could potentially be compromising patient duty of care when refusing sale without an alternative pain solution. It is not specifically known why photo ID was required, as staff rarely provided a definite reason and this study was conducted prior to the implementation of any real-time monitoring programs for codeine in pharmacy. Recording sales in either the pharmacy's dispensing software or in the program Project STOP[25] were sometimes offered as reasons. The variability in the recording of sales highlights the subjective nature of recording and compounds the difficulty of identifying inappropriate users. To help identify patients who are at risk of codeine dependence the Pharmacy Guild of Australia has recently rolled out a real-time recording system across Australia – MedsASSIST.[26] The usefulness of MedsASSIST may be limited because its use is not mandatory. There is also a risk the system will be used as a policing tool rather than a clinical support tool and patients will be turned away without a product or advice. MedsASSIST will potentially reduce inappropriate sales of NP-CACC but if these patients are not offered support or help for their dependency or pain problem will they then turn to sourcing the opioids they need from alternative, possibly illegal sources?

Counselling was not provided in 12% of product purchases in this study. The most frequent counselling point utilised was that the SP should take the product with food to avoid an upset stomach (63.1%), in reference to the ibuprofen content of the product. The industry has moved away from this recommendation due to the variable effect food can have on the absorption of ibuprofen and thus affect its onset of pain relief action and patient's perception of effectiveness.[35] When NP-CACC dependent people were asked about advice they received, the maximum daily dose was the most common advice reported.[11] In comparison less than half of requests in this study were provided with advice about the maximum dose. Advice should also be given about the risks of taking above the maximum dose, in this case gastric ulceration and renal disease, as knowledge of risks could potentially prevent the misuse of these products and perhaps the development of dependence from the outset. Repeated use and DPRs have been reported to result in reduced counselling.[33] Pharmacy staff should not assume patients who request a product have used it before or if they have used it previously they have been provided with appropriate counselling and are aware of the correct dosing, adverse effects and maximum treatment duration. Notably, cautioning SPs on the risks of dependence and the maximum duration of NP-CACC treatment was limited. This reinforces results from a previous study which identified NP-CACC dependent people were unlikely to be warned about the harms of inappropriate NP-CACC use.[11] Providing adequate warnings may reduce potential harms associated with the NP-CACC use including dependence to the codeine content and complications such as gastrointestinal ulceration from ibuprofen or other accompanying non-opioid analgesics.[2]

Our findings illustrate the need for improvement in the management of NP-CACC sales. Change is needed to reduce the rates of inappropriate NP-CACC use leading to dependence and other adverse health complications. MedsASSIST will help this to some extent but a systematic approach should also be considered to assess NP-CACC requests and avoid subjective evaluations during pharmacist-patient interactions. Further research is needed to investigate reasons for the management of NP-CACC being identified as sub-optimal in this study when compared to current professional guidelines. Implementing a clinical tool for the provision of NP-CACC products that provides guidance on patient assessment, counselling and referral, as suggested by a recent Delphi study,[36] may assist in improving current practice. Such a tool could be used in combination with the Pharmacy Guild's MedsASSIST real-time monitoring database. These support tools would give community pharmacists access to information that will assist them to identify potential at risk patients and provide guidance about appropriate clinical decisions and referrals. The need for improvement is not confined to the management of NP-CACC. Other studies conducted in Australia looking at management of Pharmacist Only Medicines have shown similar results with regard to questioning and counselling provided.[15,18] This implies that perhaps further work can be done with regard to education and resources for pharmacists in managing all Pharmacist Only Medicine requests.

The strength of this study lies in the methodology chosen. Conducting a quantitative SP study in both metropolitan and non-metropolitan community pharmacies ensured that a wide demographic was covered in the sample. Additionally, the covert nature of the SP visits ensured the data collected represented current pharmacy practice without influence by the Hawthorne effect However, relying on the recall of SP for data may have affected the accuracy of the study results and could be seen as a limitation of the study. As this technique is reliant on the human cognitive process, especially memory and recall, this may affect the accuracy of the data collected leading to discrepancies between the actual behaviour compared to the reported behaviour. SPs are more likely to forget than fabricate information and are more likely to underestimate the performance of staff.[37] Comprehensive SP training, completion of a pilot study and recording results immediately post-pharmacy visit aimed to reduce the impact of SP recall. A further limitation is the ability of the SP to identify the pharmacist. Often pharmacists are identifiable from the other staff due to name badges and clothing/uniform but if this is not possible there may have been an underestimation of the pharmacist involvement in the documentation of interactions. It has been suggested that covert SPs have face validity when the target does not know or suspect that they are a SP.[38] This was not assessed in our study due to the covert nature of the study and therefore could have possibly influenced the result. Despite it not being assessed there was no reporting by SP that they thought they were detected.

Conclusion

The current management of NP-CACC requests in community pharmacies located in Victoria, Australia could be improved. Results indicate that a number of pharmacies are not asking adequate questions to establish therapeutic need, which is a legal requirement, and to ensure the product is safe to use. Whilst many are providing counselling with product supply often this is only partially adequate. Overall the study demonstrated that the majority of Victorian community pharmacies visited could improve the supply outcomes for requests for NP-CACC, illustrating the need for improved awareness of how to assess and manage patients requesting NP-CACC in community pharmacy practice.

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Appendix A. Scenario one (first time codeine user)

Direct Product Request: "Can I please have a packet of Nurofen Plus[1]".

The patient

Female.
Requesting Nurofen Plus[1] for herself.
Never had the product before.

Current condition

(Adaptive to suit each Simulated Patient):

Complaint	Back pain. I had a back spasm a couple of days ago while playing *netball/gym/calisthenics*. *Physio/Osteopath/Trainer* recommended trying Nurofen Plus.
Symptoms	Back feels stiff, constant dull ache, sudden movements and bending cause worsening pain.
Had this injury before?	Yes. Have seen *physio/osteopath* in the past but the injury still comes and goes. Have used Nurofen[a] in the past but would rather try something stronger this time. I have tried ice packs/heat packs and stretches with no relief. Have not seen a health professional for this current condition.
Prior medical history	No other medications. No medical conditions. No allergies. Not pregnant or breastfeeding.

[a] Common brand containing Ibuprofen 200 mg.

Appendix B. Scenario two (repeat codeine user)

Direct Product Request: "Can I please have a packet of Nurofen Plus".

The patient

Female.
Requesting Nurofen Plus[1] for herself.
Has had Nurofen Plus[1] before.

Current condition

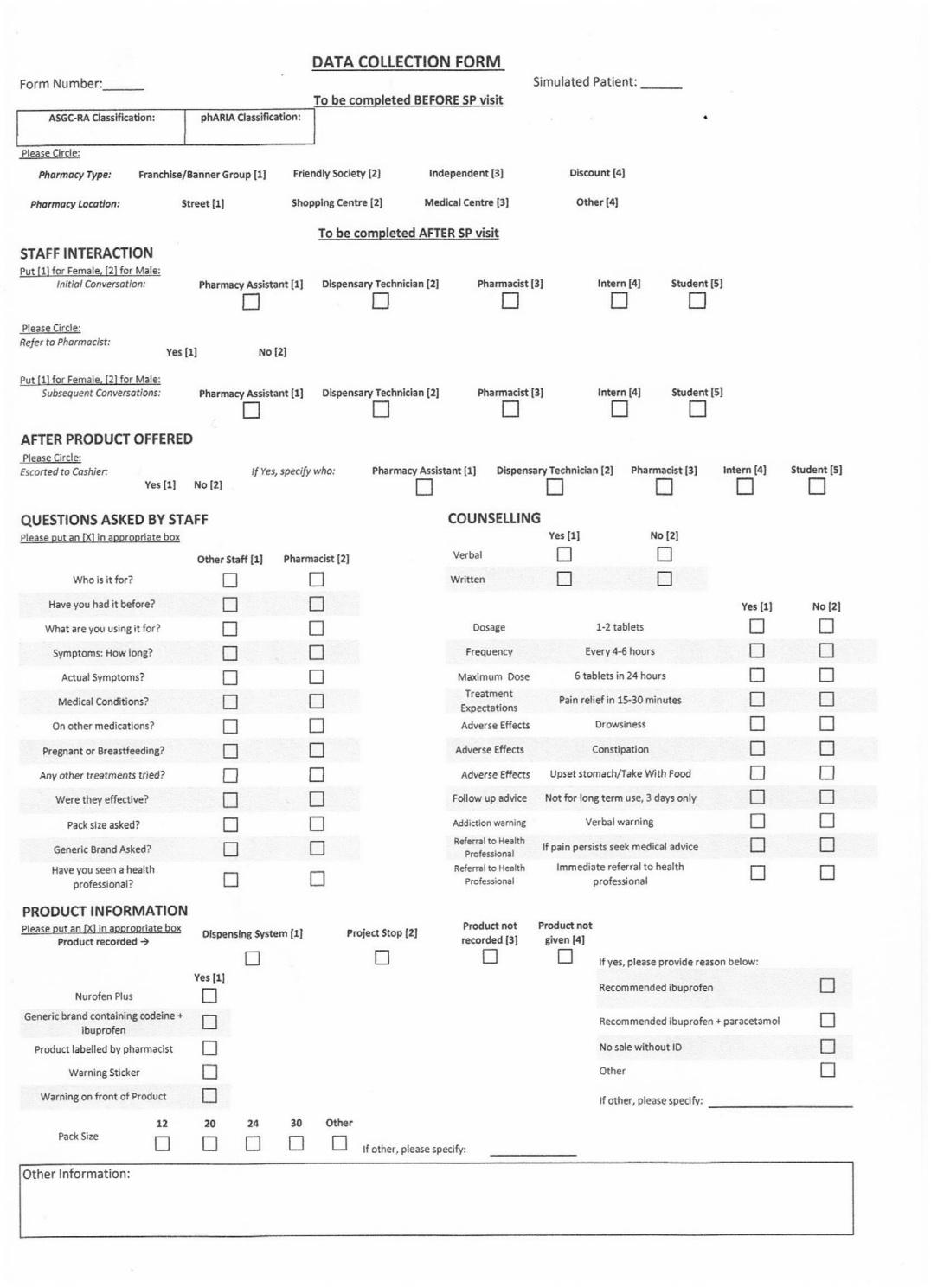
(Adaptive to suit each Simulated Patient):

Complaint	Back pain. I had a back spasm for a few weeks ago while playing *netball/gym/calisthenics*.
Symptoms	Back feels stiff, constant dull ache, sudden movements and bending cause worsening pain.
Had this injury before?	Yes. Have been taking Nurofen Plus[a] for nearly a month now. I take it regularly as the pain returns when I stop using it. I take 6 tablets each day. Have seen *physio/osteopath* in the past but the injury still comes and goes. Would like the largest pack available. I have tried ice packs/heat packs and stretches with no relief. Have not seen a health professional for this current condition.
Prior Medical History	No other medications. No medical conditions. No allergies. Not pregnant or breastfeeding.

[a] Common brand containing Ibuprofen 200 mg and Codeine 12.8 mg.

[1] Common brand containing ibuprofen 200 mg and codeine 12.8 mg.

Appendix C. Data collection form



DATA COLLECTION FORM

Form Number:_____ Simulated Patient: _____

To be completed BEFORE SP visit

ASGC-RA Classification:	phARIA Classification:

Please Circle:

Pharmacy Type: Franchise/Banner Group [1] Friendly Society [2] Independent [3] Discount [4]

Pharmacy Location: Street [1] Shopping Centre [2] Medical Centre [3] Other [4]

To be completed AFTER SP visit

STAFF INTERACTION

Put [1] for Female, [2] for Male:

Initial Conversation: Pharmacy Assistant [1] ☐ Dispensary Technician [2] ☐ Pharmacist [3] ☐ Intern [4] ☐ Student [5] ☐

Please Circle:

Refer to Pharmacist: Yes [1] No [2]

Put [1] for Female, [2] for Male:

Subsequent Conversations: Pharmacy Assistant [1] ☐ Dispensary Technician [2] ☐ Pharmacist [3] ☐ Intern [4] ☐ Student [5] ☐

AFTER PRODUCT OFFERED

Please Circle:

Escorted to Cashier: Yes [1] No [2] *If Yes, specify who:* Pharmacy Assistant [1] ☐ Dispensary Technician [2] ☐ Pharmacist [3] ☐ Intern [4] ☐ Student [5] ☐

QUESTIONS ASKED BY STAFF

Please put an [X] in appropriate box

	Other Staff [1]	Pharmacist [2]
Who is it for?	☐	☐
Have you had it before?	☐	☐
What are you using it for?	☐	☐
Symptoms: How long?	☐	☐
Actual Symptoms?	☐	☐
Medical Conditions?	☐	☐
On other medications?	☐	☐
Pregnant or Breastfeeding?	☐	☐
Any other treatments tried?	☐	☐
Were they effective?	☐	☐
Pack size asked?	☐	☐
Generic Brand Asked?	☐	☐
Have you seen a health professional?	☐	☐

COUNSELLING

	Yes [1]	No [2]
Verbal	☐	☐
Written	☐	☐

		Yes [1]	No [2]
Dosage	1-2 tablets	☐	☐
Frequency	Every 4-6 hours	☐	☐
Maximum Dose	6 tablets in 24 hours	☐	☐
Treatment Expectations	Pain relief in 15-30 minutes	☐	☐
Adverse Effects	Drowsiness	☐	☐
Adverse Effects	Constipation	☐	☐
Adverse Effects	Upset stomach/Take With Food	☐	☐
Follow up advice	Not for long term use, 3 days only	☐	☐
Addiction warning	Verbal warning	☐	☐
Referral to Health Professional	If pain persists seek medical advice	☐	☐
Referral to Health Professional	Immediate referral to health professional	☐	☐

PRODUCT INFORMATION

Please put an [X] in appropriate box

Product recorded → Dispensing System [1] ☐ Project Stop [2] ☐ Product not recorded [3] ☐ Product not given [4] ☐

	Yes [1]
Nurofen Plus	☐
Generic brand containing codeine + ibuprofen	☐
Product labelled by pharmacist	☐
Warning Sticker	☐
Warning on front of Product	☐

If yes, please provide reason below:

- Recommended ibuprofen ☐
- Recommended ibuprofen + paracetamol ☐
- No sale without ID ☐
- Other ☐

If other, please specify: _____

Pack Size	12	20	24	30	Other
	☐	☐	☐	☐	☐

If other, please specify: _____

Other Information:

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4.1 SUMMARY

The aim of this simulated patient study was to investigate the current management of NP-CACC direct product requests in community pharmacies located in Victoria, Australia. This study identified that patient requests were not being managed in a uniform manner and there was scope to support the pharmacies and pharmacists in their role. Results indicated that a number of pharmacies were not asking adequate questions to establish therapeutic need, which is a legal requirement for schedule three medicines in Australia, and to ensure a product is safe to use. Whilst many were providing counselling with product supply often this was only partially adequate. This shows a potential gap in practice and knowledge of pharmacists and an area that could be further supported.

CHAPTER 5: IMPLEMENTATION OF A CLINICAL TOOL TO ASSESS AND ADDRESS PAIN MANAGEMENT REQUESTS IN THE PHARMACY

The aforementioned study and the work by Hamer et al (Hamer et al., 2014) showed that intervention by pharmacists is not particularly easy when it comes to supply of opioid medication and pain management. There are several challenges faced by community pharmacists in the provision of opioid medications including an increase in workload, confrontational interactions, difficulties associated with establishing therapeutic need especially because of the subjective nature of pain, lack of time for detailed consultations, variation in procedures of different pharmacies when supplying these medications and a lack of monitoring of use between pharmacies. Managing people suspected of opioid dependence was identified by Hamer et al as problematic and many pharmacists found it difficult to initiate a conversation about opioid dependence with patients (Hamer et al., 2014).

Gibbins et al in their Delphi study looked at ways that pharmacists could be supported in managing inappropriate use of OTC CACC (Gibbins, Wood, & Spark, 2017). They found that strategies identified as effective and likely to have the most impact on OTC CACC misuse/dependence in a community pharmacy setting were: utilisation of a national real-time database to monitor product sales to aid identification of at-risk users; development of a referral pathway for management of people who pharmacists have identified as at-risk, and training to improve pharmacist communication with people.

MedsASSIST© was developed by The Pharmacy Guild of Australia and implemented in community pharmacies across Australian in March 2016 (The Pharmacy Guild of Australia, 2016). MedsAssist© is a real-time recording and monitoring system for OTC medicines containing codeine and was designed to help pharmacists identify patients who are at risk of codeine dependence. It was developed in response to concerns over patient safety and as an effective alternative to requiring patients to attend the doctor to get a prescription for these medications. By utilising the MedsASSIST© tool it was hoped that pharmacists would become better at identifying patients who might be at risk of, or who have already become dependent on, OTC CACC.

A system such as MedsAssist© is useful to identify potential misusers of OTC CACC but it does not address the issue of how to manage such a patient. Of concern is that pharmacists use real-time monitoring as a policing tool rather than a clinical management tool and patients are turned away without being offered treatment or alternative pain management options, as was

seen to some extent in the previous simulated study (Byrne et al., 2018). With this in mind, we developed a "HealthPathways" clinical tool centred on OTC codeine management. Pharmacists could utilise this tool in their everyday practice to manage requests for OTC CACC in a consistent manner and help identify and then manage inappropriate use of these medications. The question remained as to whether pharmacists would access and utilise the tool and if so, would they find it useful? Therefore, this next study evaluated the clinical tool that was developed.

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Implementation of a clinical tool to assess and address pain management requests in the pharmacy

Penelope Wood[a,*], Joseph Tucci[a], Karen Anderson[b], George Mnatzaganian[b]

[a] Department of Pharmacy and Applied Science, La Trobe Institute for Molecular Science, La Trobe University, Edwards Rd Bendigo, Victoria, 3550, Australia
[b] Department of Community and Allied Health, La Trobe Rural Health School, College of Science, Health and Engineering, La Trobe University, Edwards Rd Bendigo, Victoria, 3550, Australia

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ABSTRACT

Background: Morbidity and mortality associated with inappropriate use of over-the-counter combination analgesics containing codeine (OTC CACC) in Australia resulted in it being upscheduled in 2010 from "Pharmacy Only" (Schedule 2) to "Pharmacist Only" (Schedule 3), and further to "Prescription Only" (Schedule 4) in February 2018. There have been a number of concerns and challenges identified by community pharmacists in the provision of OTC CACC. In practice, sub-optimal management of patients accessing these medications has been demonstrated. To assist the management of patients using OTC CACC, the development of a management and referral pathway would be advantageous.

Objectives: To evaluate the use of an online interactive clinical tool and/or clinical information via an online PDF-based platform for managing OTC CACC requests and codeine dependence.

Method: Two interactive online clinical tools to aid management of patients who presented requesting OTC CACC were developed. Evaluation of these tools was undertaken using responses to multiple choice questions and feedback from pharmacist surveys.

Results: Of the 904 pharmacists who responded to the evaluation survey, 66.7% had not used the tool in the preceding 12 months. The most common reason why pharmacists did not access either the online interactive, or online PDF clinical tools was that they had no knowledge of them. Older age of the pharmacist (50 years or older compared to younger than 30) predicted tool access (adjusted proportional odds ratio = 3.16, 95% CI 1.72–5.80, $p < 0.001$). The access of the tool was positively associated with it being perceived as useful (adjusted odds ratio = 14.7, 95% CI 6.7–32.5, $p < 0.001$).

Conclusion: A number of pharmacists participating in the evaluation had never accessed either the online interactive or online PDF clinical tool, as they were not aware of them. Further research needs to be conducted into how to best promote and increase awareness of online clinical tools to pharmacists, especially younger pharmacists, and determine the best way to integrate online clinical tools effectively and efficiently into current practice.

Introduction

Codeine is a weak opioid analgesic used to treat mild-to-moderate pain. In Australia, codeine was available over-the-counter (OTC) until February 2018 in combination with analgesics including paracetamol, ibuprofen and aspirin. Although the exact prevalence of codeine dependence in Australia is unknown, the harms associated with overuse are well established, including serious morbidity (renal and hepatic failure, gastrointestinal issues) at a great cost to the Australian health care system.[1] The potential for codeine to be misused has been documented in several case series[2,3] and shown in a randomised, double blind, placebo-controlled drug administration study.[4]

There have been a number of concerns and challenges for community pharmacists in the provision of these OTC combined analgesics

Abbreviations: OTC, over-the-counter; CACC, combined analgesics containing codeine; CDSS, clinical decision support system; WVPH, Western Victoria Primary Health Network; CPD, continuing professional development

* Corresponding author. Department of Pharmacy and Applied Science, La Trobe Institute for Molecular Science, La Trobe University, PO Box 199, Bendigo, Victoria, 3552, Australia.

E-mail addresses: p.wood@latrobe.edu.au (P. Wood), j.tucci@latrobe.edu.au (J. Tucci), k.anderson@latrobe.edu.au (K. Anderson), g.mnatzaganian@latrobe.edu.au (G. Mnatzaganian).

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containing codeine (CACC) medications. These concerns included an increase in workload for pharmacists, challenges associated with establishing therapeutic need, inconsistent procedures of supply between different pharmacies and even different pharmacists, lack of monitoring of use between pharmacies and challenges in identifying and managing people suspected of opioid dependence.[5] A simulated patient study conducted in 2014 by Byrne et al. demonstrated this sub-optimal management of these patients in pharmacy.[6] To help with the management of patients using OTC CACC a Delphi study conducted by Gibbins et al. suggested that development of a referral pathway would be advantageous.[7]

In view of this, the Opioid Management Team at the Western Victoria Primary Health Network (WVPHN) developed a HealthPathways interactive clinical tool centred on OTC CACC management for pharmacists to utilise in everyday practice. The tool was aimed at improving the management of patients requesting OTC CACC products, as well as identification of individuals with dependence and problematic use, and facilitating/referring them to treatment, which has been identified in previous research as a challenge.[5] HealthPathways is a web based information portal for primary health care providers, including general practitioners, pharmacists and allied health professionals. It is designed to provide condition specific information on assessment, management, and local referral options for clinicians at the point of care.[8]

Despite the 2018 change in Australia whereby CACC are now only available via prescription, clinical tools such as this are still important and relevant in pharmacy to aid decision making around medication supply and condition management. This is particularly pertinent when high-risk medicines are being supplied. Despite CACC being upscheduled to prescription only, other opioids are still available OTC in Australia including in cough mixtures-pholcodine, dextromethorphan and dihydrocodeine, and in antidiarrhoeals – diphenoxylate and loperamide. After February 2018 the managing OTC CACC dependence clinical tool remained in use to assist pharmacists who identified dependency issues after the changes in their patients, especially in patients that had stockpiled OTC CACC prior to the change. The OTC CACC request tool was modified into a pharmacy pain management clinical tool to help pharmacists manage pain appropriately without OTC CACC.

Clinical decision support systems (CDSS) such as HealthPathways, have been used worldwide to assist with standardising the approach to healthcare. They have a primary function aimed at providing information to the provider at the point of care for decision-making and intervention. CDSS have been used for prevention and screening, medication dosing, medical management of acute diagnosis and chronic disease management. They can be utilised as a stand-alone system, like HealthPathways, or embedded in an existing electronic medical system with automated prompt functionality.[9] A systematic review conducted by Kawamoto et al. (2005) and Bryan and Boren (2008) found that while there was potential for significant improvement in practice and outcomes using such tools there was also marked variability surrounding the effectiveness of implementation and integration.[9,10]

The Pharmacy Guild of Australia was concerned about the management of OTC CACC by pharmacists, especially patient safety relating to these medicines. To combat this they developed a real-time recording and monitoring system for OTC CACC called MedsASSIST.[11] To ensure that MedsASSIST was employed as a clinical, rather than a policing tool, the Pharmacy Guild utilised an online PDF version of WVPHN HealthPathways interactive clinical tool as a reference for pharmacists. In an effort to increase exposure of this information, the Pharmacy Guild also offered the WVPHN HealthPathways interactive clinical tool as an education module on its myCPD online education platform.

As this was the first online clinical tool to aid recommendations and management of OTC CACC in Australia there was limited evidence about its uptake and usefulness. The aims of this study were to investigate the use of the clinical tool for managing OTC CACC requests and dependence as well as analyse pharmacists' understanding of the content and usefulness of the clinical tool in order to guide design of further tools to aid condition management in pharmacy settings.

Methods

The WVPHN Opioid Management Team, developed two clinical tools to aid pharmacists' management of patients who present requesting CACC:

1. Patient Requests for Combination Analgesics Containing Codeine – to guide pharmacists in the decision-making process regarding the appropriateness of CACC and counselling advice to provide with the product (Appendix A2).
2. Combination Analgesics Containing Codeine Dependence – to help pharmacists identify CACC dependence, initiate a patient discussion and provide advice/referrals (Appendix A1).

Development of the clinical tools

HealthPathways is an online health information portal and referral system developed by Streamliners and Canterbury District Health Board in New Zealand.[12] Each 'pathway' provides a definitive course of management and referral for patients based on evidence-based best practice with a focus on local resources and services.[12] The process of development is set by these organisations. The content of the web-based resources is developed in collaboration with regional hospital specialists, general practitioners and associated relevant primary care and allied health professionals. This approach supports and guides practitioners in providing consistent, standardised care for patients. Through communication and collaboration among health system representatives in the development of each clinical stream, each party takes on a vested interest in ensuring the currency and accuracy of each pathway.[12] The intended use of HealthPathways was originally for general practitioners but in recent times this has been expanded to pharmacists and other health professionals.

With reference to current literature and guidelines including the Therapeutic Guidelines,[13] The Pharmaceutical Society of Australia and The National Prescribing Service a draft HealthPathways for OTC CACC request management, as well as identification and management of dependence, were developed by the WVPHN Opioid Management Team. These drafts were further reviewed by content experts identified by The Pharmaceutical Society of Australia and updated accordingly. Updated pathways were circulated for review by additional experts in the field including from the Victorian Department of Health, The Pharmaceutical Society of Australia and academic specialists. Feedback was incorporated prior to the pathways being published online in March 2016.

In order to increase uptake and utilisation of the tool by pharmacists a continuing professional development (CPD) package was developed. To achieve this, a multiple-choice assessment (Appendix B) was added, and a template developed for implementation into practice such that, pharmacists could obtain different levels of CPD points depending on their engagement with and implementation of the material. As part of the accreditation process pharmacists were asked to provide feedback via an evaluation survey (Appendix C). This training package and associated CPD accreditation was facilitated by The Pharmaceutical Society of Australia/Australian Pharmacy Council.

The Pharmacy Guild of Australia utilised an online PDF version of the pathways in the MedsASSIST real time monitoring program and a version was available on their myCPD educational platform as an education module.

Survey design and data collection

Data were collected for the project from March 2016 until June

2017. This varied depending on the data collected. Access statistics, CPD results and CPD evaluations were collected from March 2016–March 2017. To give pharmacists time to become familiar with the tools, an Australian national cross sectional survey that investigated the utilisation of the tools was distributed in April 2017 and closed in June 2017. The cross sectional survey questions were adapted from a survey used to assess the use of HealthPathways by general practitioners (Appendix D). The questions investigated how often pharmacists used the clinical tools, as well as the perceived benefits and barriers to use. Pharmacists' demographic information was also collected.

Data collection via the cross sectional survey occurred from April to June 2017. A link to an electronic version of the survey was emailed to all pharmacists in the Barwon South West region (n = 198), all pharmacists who were members of the online Guild myCPD program, whether they were active or registered for the relevant CPD module or not (n = 22,000) and all pharmacists who completed the online quiz accessed through the online interactive HealthPathways platform (n = 229). There may have been some overlap with these participants but they could only complete the survey once using their individual email address. To encourage participation, respondents could elect to enter a prize-draw for one $100AU gift voucher. Reminders were emailed in May 2017 and again in June 2017 to pharmacists who had been sent the online link.

Data analysis

Descriptive and inferential statistics were used to describe and analyse the data. Number of times the tool was accessed (1 = never; 2 = rarely; 3 = sometimes; 4 = often) was modelled using ordered logistic regression that reported proportional odds ratios. Perceived usefulness of the tool (a dichotomous variable) was modelled using logistic regression. The models were adjusted for age, sex, working full time, pharmacy setting, being an intern pharmacist, number of pharmacists working in a pharmacy, and website used to access the tool. Years practicing as a pharmacist was not accounted for as it was highly correlated with age ($r = 0.72$). Statistical significance was set at a p value of < 0.05 (two sided). Stata statistical program (version 14, StataCorp) was used.

Ethics

Ethics approval was obtained from the La Trobe University Human Ethics Committee.

Results

Access statistics for the HealthPathways online interactive version of the clinical tool were collected from March 2016 until March 2017 and showed there were 135 unique page views of the "Patient requests for combination analgesics containing codeine" pathway and 119 unique views of the "Combination analgesics containing codeine dependence" pathway via the online interactive HealthPathways portal. Pharmacists spent on average 3.06 min on the pages. Additionally, by March 2017, 3098 pharmacists had accessed the online PDF version of the tool via The Pharmacy Guild of Australia myCPD education platform.[14]

CPD quiz

Pharmacists were only allowed to complete the quiz once and in total, there were 229 quizzes completed (n = 229) through the online interactive HealthPathways platform over the 12 month period from March 2016–March 2017. Of these 229 completions, 180 pharmacists (78.6%) met the 80% pass mark. Questions on GP referral, history documentation, signs of potential drug dependence, discussing opioid use, and action to take if suspect dependence were answered correctly by over 90% of pharmacists. Questions on signs of opioid withdrawal (61% answered correctly) and ibuprofen drug interactions (53.1% answered correctly) were the questions that pharmacists most frequently got incorrect. The number of participants who completed the quiz through The Pharmacy Guild's myCPD website was 3098. Of those, 2182 (70.5%) passed with a mark ≥ 80%. The Pharmacy Guild did not record data relating to which questions were answered incorrectly.

CPD evaluation

Of the 229 pharmacists that completed the CPD quiz through the online interactive HealthPathways platform, only 59 completed the associated evaluation (26%) (Appendix C).

All pharmacists who completed the evaluation found the activity relevant to their practice (91.5% entirely relevant, 8.5% partially relevant). Most pharmacists reported that the learning objectives were met (83.1% entirely met and 16.9% partially met). Satisfaction with the activity varied, with 76.3% of pharmacists entirely satisfied, 18.6% partially satisfied and 5.1% not satisfied. Additionally, the suitability of the delivery of the activity gained a mixed response with 84.7% of responding pharmacists finding it entirely suitable, 11.9% partially suitable and 3.4% finding it not suitable. The main dissatisfaction in both these categories related to the format of the quiz, in particular the fact that the mark and answers to the quiz were not available immediately. As CPD points and quizzes are not a usual component of the HealthPathways format the relevancy of these comments is limited. Comments were also made about an increase in confidence in selling codeine-containing products and that the activity was informative.

The Pharmacy Guild also conducted a CPD evaluation survey through their myCPD website[14] (n = 865) where pharmacists accessed an online PDF version of the clinical tool. The results were consistent with those gained from the interactive online HealthPathways platform CPD evaluation survey. The majority of pharmacists (83%) were satisfied with the online course and most (91%) found it relevant to their practice. The majority of free text responses commented on the benefit of the course, its ease of use and the quality of the information presented. Despite this, there were a number of participants who did not like the PDF format, and wanted to see more case studies used to consolidate the material which is not part of the current HealthPathways format.

Clinical tool evaluation via cross sectional survey

Of the 904 pharmacists who participated in the cross sectional survey, 50.1% answered most survey questions, of whom 66.7% had not used the clinical tool in the last 12 months. Over half of pharmacists who had accessed the clinical tool did so via The Pharmacy Guild myCPD website online PDF version.

Repeated access to the tool was more likely with older participants, or when access was via the HealthPathways interactive online platform (Table 2).

Table 3 shows that there were no statistically significant predictors of how useful a pharmacist found the tool apart from how often they used it.

The most common reason (79.6%) pharmacists did not access the clinical tools was because they were not aware of what these were. This was reinforced by the final free text question on the survey, where 52 participants took the opportunity to respond. The majority of the comments related to their lack of awareness and accessibility to the tools.

As described in Table 4 over half of the pharmacists that had used the clinical tools found them easy to access (54.3%) and navigate (53.7%). Over a third of pharmacists felt that they had improved their knowledge (39.7%) and confidence (39.1%) and the confidence of their patients (37.1%) and changed their clinical management (39.7%) including the way they made referrals (39.7%).

Table 1
Participant characteristics.

	N (%)
Sex	
Male	604 (66.8)
Female	300 (33.2)
Age categories in years	
Under 30	242 (26.8)
30–39	288 (31.9)
40–49	151 (16.7)
50 or over	223 (24.7)
Number of pharmacists working in the practice	
1	107 (11.8)
2–5	648 (71.7)
6 or more	149 (16.5)
Pharmacy in community setting	
Yes	849 (93.9)
No	55 (6.1)
Pharmacist employed full time	
Yes	551 (60.9)
No	226 (25.0)
Missing	127 (14.1)
Being an intern pharmacist	
Yes	33 (3.6)
No	744 (82.3)
Missing	127 (14.1)
Years practicing as a pharmacist	
1–4	187 (20.7)
5–9	176 (19.5)
10+	413 (45.7)
Missing	128 (14.2)
Website used to access tool	
MyCPD	570 (63.0)
HealthPathways	114 (12.6)
Other	92 (10.2)
Missing	128 (14.2)
Use of tools in practice in past 12 months	
Never	302 (33.4)
Rarely	42 (4.6)
Sometimes	39 (4.3)
Often	70 (7.7)
Missing	451 (49.9)

Table 2
Number of times tool was accessed: an ordered logistic regression of the outcome which had the following values: 1 = never, 2 = rarely, 3 = sometimes, 4 = often.

	Proportional odds ratio	95% Confidence Interval	P value
Age categories in years			
Younger than 30 (Reference)	1.00		
30–39	1.24	0.73–2.13	0.4
40–49	1.23	0.62–2.43	0.6
50 or older	3.16	1.72–5.80	< 0.001
Female sex	1.25	0.80–1.95	0.3
Working full time	1.18	0.74–1.89	0.5
Pharmacy in community setting	2.25	0.83–6.06	0.1
Being an intern pharmacist	0.73	0.26–2.06	0.6
Number of pharmacists working in the practice			
1 (reference)	1.00		
2–5	0.95	0.52–1.71	0.9
6 or more	1.88	0.88–4.00	0.1
Website used to access tool			
Other (reference)	1.00		
MyCPD	2.06	1.03–4.11	0.042
HealthPathways	5.89	2.60–13.35	< 0.001

Table 3
If participants used the tool how useful was it: a logistic regression.

	Proportional odds ratio	95% Confidence Interval	P value
Age categories in years			
Younger than 30 (Reference)	1.00		
30–39	0.72	0273–1.94	0.5
40–49	0.85	0.24–3.02	0.8
50 or older	0.56	0.18–1.75	0.3
Female sex	1.56	0.69–3.55	0.3
Working full time	0.55	0.20–1.46	0.2
Pharmacy in community setting	1.72	0.33–9.03	0.5
Being an intern pharmacist	2.89	0.42–19.95	0.3
Number of pharmacists working in the practice			
1 (reference)	1.00		
2–5	0.61	0.20–1.84	0.4
6 or more	0.97	0.24–3.97	0.9
Website used to access tool			
Other (reference)	1.00		
MyCPD	5.69	1.40–23.20	0.015
HealthPathways	3.22	0.68–15.35	0.1
Number of times tool was accessed			
Never/rarely (reference)	1.00		
Sometimes/often	14.73	6.67–32.53	< 0.001

Discussion

The results from this study have highlighted the difficulties of creating awareness and promoting clinical tools to pharmacists throughout Australia. Even when pharmacists were aware of the availability of the clinical tools, repeated access was limited especially in younger pharmacists. This presents a challenge when creating a tool that can be easily integrated and implemented in clinical practice. Despite this, pharmacists who accessed the clinical tools perceived them as useful. Some pharmacists reported that the tools had increased their confidence in managing requests for CACC and managing dependence on these medications. Further work is required to promote and increase pharmacist awareness of not only how to access the tools but also the benefit of using such tools and incorporating them in their clinical practice.

Repeated access to the tool was more likely if participants had accessed it via the HealthPathways interactive online platform. There could be a number of reasons for this including the engagement, support and promotion of the HealthPathways program in general by Primary Health Networks throughout Australia. This indicates that direct promotion of clinical tools may increase access and should be investigated further. Additionally, there appeared to be more dissatisfaction with the online PDF-based format presented on the MedsASSIST and myCPD platforms compared with the more interactive version available on the HealthPathways platform. Previous research has shown that integrated and interactive computer decision support tools were more effective than the more manual systems like the online PDF-based versions,[10], indicating that more integrative systems should be considered with future expansion of clinical tools into other conditions and medicines. A systematic review conducted by Kawamoto et al. (2005) discovered that 75% of clinical interventions succeeded when the decision support was provided to clinicians automatically as part of their workflow, whereas none succeeded when clinicians were required to seek the advice of the decision support system outside of their workflow. This indicates a need to embed these clinical tools to be part of the clinician workflow, preferably integrated within the clinical software.[10] Systems that provided clinical decision support at the time and location of decision-making and provided actionable recommendations were substantially more likely to succeed. Whilst being ideal this may prove to be difficult in Australian pharmacy settings

Table 4
Evaluation of the tool by those that had ever used it.

	Strongly agree N (%)	Somewhat agree N (%)	Neither agree nor disagree N (%)	Somewhat disagree N (%)	Strongly disagree N (%)
The HealthPathways/clinical tools were easy to access	30 (19.9)	52 (34.4)	50 (33.1)	12 (7.9)	7 (4.6)
The website is easy to navigate	27 (17.9)	54 (35.8)	49 (32.4)	14 (9.3)	7 (4.6)
HealthPathways/clinical tools is the first resource I consult for clinical information	21 (13.9)	30 (19.9)	63 (41.7)	25 (16.6)	12 (7.9)
HealthPathways/clinical tool has improved my knowledge	21 (13.9)	39 (25.8)	70 (46.4)	13 (8.6)	8 (5.3)
HealthPathways/clinical tool has changed my clinical management	21 (13.9)	39 (25.8)	72 (47.7)	11 (7.3)	8 (5.3)
HealthPathways/clinical tool has improved patients' confidence in my management	19 (12.6)	37 (24.5)	71 (47.0)	17 (11.3)	7 (4.6)
HealthPathways/clinical tool has changed my relationships with specialists	17 (11.3)	20 (13.2)	85 (56.3)	19 (12.6)	10 (6.6)
HealthPathways/clinical tool has changed the way I make referrals	19 (12.6)	41 (27.1)	68 (45.0)	16 (10.6)	7 (4.6)
HealthPathways/clinical tool has saved me time	14 (9.3)	29 (19.2)	75 (49.7)	20 (13.2)	13 (8.6)
HealthPathways/clinical tool has improved my confidence	17 (11.3)	42 (27.8)	75 (49.7)	9 (6.0)	8 (5.3)

given the variety of digital platforms that are already used and that the HealthPathways platform is not specifically designed with this capability. Effectiveness was also enhanced when clinicians had to document when they were not following recommendations, and feedback about performance was also seen to be useful.[10] Further work with regard to these factors could be undertaken to enhance the useability of the clinical tools studied and development of future clinical tools.

This study also highlights the need for pharmacists to be further informed and educated regarding the signs and management of opioid dependence and potential drugs interactions with anti-inflammatory medications.

Limitations

This study followed a cross-sectional design, and causal associations cannot be inferred. The study findings may have been affected by non-response bias with uncertainty as to whether the sample was representative of all pharmacists in the region. Distributing the survey to everyone within the Barwon South West region and all subscribers of the myCPd program rather than just users of the tool may have created bias by raising awareness of the tool, which may have affected the survey results. Our study's response rate appeared low and including all 22,000 subscribers of the myCPD program could have artificially lowered the overall response rate as we could not verify whether the pharmacists were active users or if they were registered to do the online modules. Whilst not atypical, there was a low response rate (26%) for the CPD evaluation survey, which may have introduced bias based on the motivation of those who chose to respond.

Further research

Opportunities for subsequent research include: evaluating the effects of clinical tools on patient care and outcomes; the number of referrals to outside services and the quality and appropriateness of these referrals; and a cost-benefit analysis of utilising such clinical tools into practice. Studies looking at pharmacist outcomes i.e. provision of advice, treatment given and patient outcomes could be a useful measure of effectiveness and usefulness of these tools in a clinical setting, as identified by Bryan and Boren (2008).[9]

Conclusions

A large number of pharmacists participating in the evaluation had never or rarely accessed the online clinical tool designed to help pharmacists manage OTC CACC requests and codeine dependence, as they were not aware of it. Despite this, some pharmacists who had accessed the clinical tools found them relevant to practice increasing their knowledge and confidence in supplying CACC medications. There is potential to use such tools in managing other medical conditions and the supply of other medications in the pharmacy setting. Further research needs to be conducted into how to best promote and increase awareness of these tools to pharmacists and to determine the best way to implement such clinical tools effectively and efficiently into current practice.

Conflicts of interest

There are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sapharm.2018.12.009.

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5.1 SUMMARY

The aim of this study was to evaluate the use of an online interactive clinical tool for managing OTC CACC requests and codeine dependence. Several pharmacists participating in the evaluation had never accessed the clinical tools, as they were not aware of them. Pharmacists need to have knowledge of the tools that are available to them if they are to be utilised to their full potential. Research needs to be conducted into how to best promote and increase awareness of online clinical tools to pharmacists and determine the best way to integrate them effectively and efficiently into current practice. A range of dedicated tools, if utilised, may assist in opioid supply and management. However, there are many factors that may contribute to a pharmacist's willingness to intervene. These include confidence, and knowledge, and are issues that need to be explored further.

CHAPTER 6: CORE COMPETENCIES FOR AUSTRALIAN PHARMACISTS WHEN SUPPLYING PRESCRIBED OPIOIDS – A MODIFIED DELPHI STUDY

Whilst it is reasonable to suggest that pharmacists need to play a role in opioid management and supply them with tools to do this, it is important to ask, whether Australian pharmacists have the required skills to enable them to supply opioids safely and be effective in managing opioid use and misuse. This was investigated in the Delphi study we conducted looking at what opioid experts believed should be core competencies that Australian pharmacists should meet when supplying opioids.

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RESEARCH ARTICLE

Core competencies for Australian pharmacists when supplying prescribed opioids: a modified Delphi study

Ella Maher[1] · Suzanne Nielsen[2] · Richard Summers[1] · Pene Wood[1]

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Abstract

Background In the past decade, there has been an increase in prescription opioid related harms. These include dependence, non-fatal and fatal overdose. Pharmacists play a an important role in safe opioid supply. As most opioids are supplied through pharmacies, pharmacists are in a prime position to reduce harms associated with opioid use. Development of specific core competencies for pharmacists may facilitate consistent and safer opioid supply. *Objective* To reach consensus on which competency items identified by the Association of Faculties of Pharmacy of Canada's Opioid Working Group are considered core competencies for Australian pharmacists in opioid supply and assess expert pharmacists' perceptions of how well these competencies are currently met by practicing pharmacists. *Setting* Expert pharmacists in the area of opioid supply from across Australia. *Method* A series of questionnaires were presented to Australian opioid expert pharmacists via a modified Delphi study, with the aim to reach consensus on which items should be considered competencies for opioid supply by Australian pharmacists. Items were rated on a 6-point Likert scale and analysed using Statistical Package for the Social Sciences® (SPSS). Participants were also asked to rate how well they perceived that currently practicing pharmacists met each of these competency items. *Main outcome measure* Consensus on competency items for pharmacists when supplying prescribed opioids. *Results* All competency items presented to participants reached immediate agreement. When rating whether participants perceived currently practicing pharmacists met these competencies, results were variable. The competencies that participants rated practicing pharmacist met to a higher degree reflected knowledge and skills items that can be applied to all medications and were not opioid specific. The lower rated competencies appeared to be related to newer or more complex or specialised areas of opioid supply. *Conclusion* There was strong agreement by participants on what should be considered core competencies for Australian pharmacists in opioid supply. Given the large number of items identified, further research may help determine priorities for training and education.

Keywords Australia · Competencies · Delphi · Knowledge · Opioid harm · Opioid misuse · Pharmacist · Prescription opioids

Impacts on practice

- Expert pharmacists who have content knowledge related to opioid supply above that of what is expected of a regular practicing pharmacist, perceive that there are gaps in competencies among practicing pharmacists in Australia.
- An important gap is whether practicing pharmacists are currently meeting all competencies necessary for responsible provision when supplying opioids.
- Further investigations should include priority areas for the training of pharmacists to optimise pharmacy practice in the context of opioid supply.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11096-020-01060-x) contains supplementary material, which is available to authorized users.

✉ Pene Wood
p.wood@latrobe.edu.au

[1] Department of Pharmacy and Biomedical Science, College of Science, Health and Engineering, La Trobe University, PO Box 199, Bendigo, VIC 3552, Australia

[2] Monash Addiction Research Centre, Monash University, Peninsula Campus, 47-49 Moorooduc Hwy, Frankston, VIC 3199, Australia

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Introduction

Opioids are widely used medicines, with an increasing number of lives lost from use and misuse of prescription opioids in many countries [1–3]. North America records the highest prevalence of non-medical use of opioids at nearly 4 per cent of the population aged 15–64 [3]. In Australia, more than three million people are prescribed an opioid annually, which represents approximately one in seven Australians aged over 14 years old [4]. Harm related to opioid use including dependence, non-fatal and fatal overdose is also on the rise in Australia. Opioid overdose fatalities almost doubled over a ten year period, from 3.8 per 100,000 people in 2007 to 6.6 per 100,000 people in 2016 [5]. Most (59%) opioid-related deaths involve prescribed opioids [6]. As one of the main suppliers of prescription medicines, including opioids, pharmacists play an important role in ensuring safe and appropriate use.

In Canada, in response to a 10-year plan launched by the Canadian Centre on Substance Use and Addiction in 2013 [7], the Association of Faculties of Pharmacy (AFPC) of Canada Opioid Working Group drafted a set of competency statements [8], after the completion of an environmental scan of the curriculum used in undergraduate pharmacy programs in Canada. These statements have been produced under three sub-groups proposed by an initial framework; 'pain', 'opioids', and 'opioid overdose and opioid use disorder'. 'Knowledge' (relating to the information that pharmacists know and understand) and 'Skills' (things that pharmacists must do in practice) items were identified to guide undergraduate pharmacy courses in meeting the teaching of these competencies.

Both Australia and Canada report opioid-use problems stemming from licit and illicit use, but the specific types of opioids involved are not necessarily the same. There are differences in the types of opioids prescribed, with hydromorphone being more commonly prescribed in Canada, whilst tramadol and buprenorphine are more common in Australia. Regarding illicit opioids, heroin remains a proportionally larger source of opioid harm in Australia but in Canada, illicit use of fentanyl is more common [9]. The impact of this is that opioid users may have different trajectories and contact with the hospital and medical system and their care could require different strategies. Additionally, there are some differences in the healthcare systems, pharmacist training programs and Canada implemented real time prescription monitoring in some regions almost two decades ago. These differences in timelines and responses to opioid related harm may result in different needs and requirements of pharmacists in the two countries. Therefore, the competencies for opioid supply by pharmacists could have different requirements between the two jurisdictions [9]. It is unknown how well these competencies relate to practice in Australia, nor how well currently practicing pharmacists in Australia meet these competencies.

The Pharmaceutical Society of Australia's (PSA) National Competency Standards Framework for Pharmacists in Australia [10] exists to guide pharmacists to practice safely and effectively. The standards contain a set of five domains, each with related standards required to be met by pharmacists. To assist this, the framework also provides a set of enabling competencies for pharmacists to achieve the standards. The domains are: (1) professionalism and ethics, (2) communication and collaboration, (3) leadership and management, (4) medicines management and patient care, and (5) education and research. This is the only specific set of competency standards for supplying medication by pharmacists that are published in Australia, though they do not relate specifically to the supply of opioids, and little research specifically relates to competencies surrounding opioid supply by pharmacists in Australia.

Aims

To establish consensus on which competency items identified by the Association of Faculties of Pharmacy of Canada's Opioid (AFPC) Working Group are considered core competencies for Australian pharmacists in opioid supply and assess expert pharmacists' perceptions of how well these competencies are currently met by practicing pharmacists.

Ethics approval

Ethics approval was obtained from the La Trobe University Human Research Ethics Committee (Reference Number: HEC19167).

Method

A modified Delphi technique, with up to three iterations, was adopted to reach consensus on a set of core competencies that should be met by pharmacists in Australia when supplying prescribed opioids.

The Delphi method typically adopts a series of questionnaires, dispersed to a panel of experts. Between each round (or questionnaire), responses are summarised, and data are analysed and incorporated into the next round, as a method of providing controlled feedback to participants. This aims to facilitate arrival at consensus amongst the participating group of experts, whilst eliminating confounding factors such as dominating personalities [11, 12].

For the purpose of our study, consensus was defined as either 75% agreement (somewhat agree, agree or strongly agree) or 75% disagreement (somewhat disagree, disagree or strongly disagree). This was chosen based on a recent systematic review, which found that 75% was the median value used as the definition of consensus [13].

Purposive sampling was used to construct a list of experts to invite to participate in the study. The inclusion criteria for experts were twofold, whereby participants must be (1) currently registered pharmacists, and (2) have content knowledge related to opioid supply above that of what is expected of a regular practicing pharmacist, such as, work in a specialist field, involved in research or policy development. The research team aimed to recruit a spread of pharmacists practising in multiple regions across Australia, including both clinical and regulatory settings. Experts were identified by the research team and invited via e-mail to participate in the study. A snowballing method was adopted in the initial stages of recruitment, where experts who had agreed to participate were asked to recommend others who satisfied the inclusion criteria. There is no consensus in the literature on the most appropriate number of participants to include in a Delphi study [14]; however 15-20 participants are commonly used [15]. Therefore, to allow for attrition, a target expert panel size of a minimum of 30 was decided upon.

The first questionnaire (Appendix 1) was developed based on the Association of Faculties of Pharmacy (AFPC) of Canada Opioid Working Group's opioid set of competency statements. Canada's competencies were selected as both Australia and Canada have a similar demographic profile (within a 10% variance of each other), including sex, life expectancy at birth, median age, population aged 25–54, population living in urban areas, health expenditure and privately funded health care [16].

Pilot testing of questionnaires is recommended to minimise the burden on participants, to reduce response error and to improve the quality of the data collected [17]. In recognition of this, a cognitive interview was conducted with two local participants, before the large-scale release of each questionnaire. A cognitive interview involves participants individually completing the questionnaire by responding out loud in the presence of a researcher to provide insight into how respondents' interpret questions and allow for identification of any issues [17].

All questionnaires were completed via an online survey platform (Qualtrics). Participants were given three weeks to complete each survey, and reminder e-mails were scheduled to be sent to unfinished respondents at both the one and two-week marks. Entry into a prize draw to win one $100 gift card, was offered as an incentive to partake in the study and was drawn at the conclusion of data collection. Participants received one entry for every questionnaire completed.

The first-round questionnaire (QR1, Appendix 1), required participants to rate how strongly they either agreed or disagreed that each skill or knowledge item for opioid supply described by the AFPC's Opioid Working Group should be a core competency for Australian pharmacists. This was done using a 6-point Likert scale (1 = strongly disagree (StD), 2 = disagree (D), 3 = somewhat disagree (SwD), 4 = somewhat agree (SwA), 5 = agree (A) and 6 = strongly agree (StA)), which was chosen to avoid a mid-point option. Participants were also given the opportunity to make any comments, or suggestions about further items to include in the subsequent round, to reduce the risk of limiting the results [18]. Participant demographic data (gender, age, years registered as a pharmacist, state/territory of practice, location of practice (metropolitan, regional or rural) and practice setting) was also collected.

Statistical Package for the Social Sciences® (SPSS) was used to analyse the data generated from QR1. The percentage agreeance, mean and standard deviation of responses were calculated for each item. The comments were reviewed to identify any new suggestions and assess for trends.

The second-round questionnaire (QR2, Appendix 2) was produced based on the results obtained from QR1. The expert participants were asked to rate how strongly they either agreed or disagreed that the newly identified skill and knowledge items from QR1 should be considered as additional core competencies for pharmacists when dispensing prescribed opioids. This questionnaire also asked the experts to rate, in their opinion, how well each competency from both QR1 and QR2 are currently met by practicing pharmacists in Australia. This data was again analysed using SPSS® to calculate the percentage agreeance, mean and standard deviation. Both questionnaires are provided as supplementary material (Appendix 1 and 2).

Results

Fifty-seven participants were identified through purposive sampling and were invited to participate in this study. Thirty-four agreed to be included on the expert panel. Thirty-one responses were received for QR1 and 27 were received for QR2. The demographic data collected from the 31 respondents in QR1 are summarised in Table 1. Participants included those of various ages, (26–70 years), level of experience (4–49 years), working in multiple settings across both metropolitan, regional and rural Australia. Half (n = 16, 51.6%) of the respondents were from Victoria.

Questionnaire round 1 (QR1)

Thirty-one out of 34 questionnaires (91%) were returned. Each knowledge and skills item put forth to the

Table 1 Participant demographic data

Variable	Frequency [n (%)]
Gender	
Male	17 (54.8%)
Female	14 (45.2%)
Age	
26–30	4 (12.9%)
31–40	11 (35.5%)
41–50	3 (9.7%)
51–60	5 (16.1%)
61–70	5 (16.1%)
> 70	3 (9.7%)
Years practicing	
4–9	7 (22.6%)
10–19	9 (29%)
20–29	3 (9.8%)
30–39	3 (9.8%)
40–49	9 (29%)
State/Territory of Practice	
New South Wales	6 (19.4%)
Northern Territory	1 (3.2%)
Queensland	2 (6.5%)
South Australia	1 (3.2%)
Tasmania	3 (9.7%)
Victoria	16 (51.6%)
Western Australia	1 (3.2%)
No answer	1 (3.2%)
Practice Setting*Participants were able to choose multiple options	
Community Pharmacy	8 (25.8%)
General Practitioner Clinic	2 (6.5%)
Hospital	10 (32.3%)
Primary Health Care Centre	4 (12.9%)
Regulatory	5 (16.1%)
University	8 (25.8%)
Other	6 (19.4%)
Multiple locations	10 (32.3%)
Location of Practice	
Metropolitan	20 (64.5%)
Regional or Rural	8 (25.8%)
Other	1 (3.2%)
No answer	2 (6.5%)

participants in QR1 reached consensus at the end of round 1. Participants were in consensus that every item put forth should be included as a core competency for pharmacists when supplying prescribed opioids in Australia. The percentage agreeance, mean, and standard deviation for each item are shown in Table 2. From respondent comments, twelve new items were identified to be included in QR2, which are shown in italics in Table 2.

The aim of the Delphi method is to facilitate development of consensus within a group, via a series of questionnaires where controlled feedback is given to participants [11, 12]. As consensus was reached after round 1, controlled feedback was not required in our study, other than to identify consensus on new items that had been identified in QR1. Consecutive rounds were not needed to reach consensus on the original items, or new items identified from QR1 and presented in QR2.

Questionnaire round 2 (QR2)

Questionnaires were sent out to participants who had completed QR1 (n = 31). Most (n = 27, 87%) completed QR2. Twelve new items were added from respondent comments in QR1. All reached consensus agreeance upon the conclusion of the QR2. The average rating of agreeance for all items put forward in QR1 and QR2 was calculated to be 5.49 out of a possible 6, with a range between 4.42 (± 0.92) and 5.94 (± 0.25).

In QR2, participants were also asked to rate, on a scale of 1-100, how well, in their opinion, practicing pharmacists in Australia currently meet each competency item. The average value for each item ranged from 31.89 (± 20.85)/100 (describe indications for an opioid rotation and perform/conduct an opioid rotation) to 80.44(± 18.59)/100 (understand the legal requirements around opioid supply, storage and destruction for relevant jurisdictions of practice) (Table 2). Figure 1 shows the correlation between the level of agreement for inclusion as a core competency and rating of how well current pharmacists practice each item ($r = 0.66$, $p < 0.0001$).

Discussion

Australian opioid expert pharmacists reached consensus on all core competency items relating to opioid supply. Perceptions on whether Australian pharmacists currently meet these competencies in practice were variable. Pharmacists tended to be considered more competent at skills and knowledge items that related to the supply of all medication in general rather than opioid-specific skills and knowledge items. Skills related to more complex and specialised areas of opioid supply generally received lower ratings. We discuss these findings in more detail below.

Firstly, there seems to be strong international agreement around important aspects of opioid supply. This was demonstrated by the strong agreement from Australian pharmacists with core competencies identified in Canada. Considerable thought and expert input had gone into the Canadian report therefore the strong agreement may reflect this. Further, Gregory and Gregory recently considered the role that pharmacists play in the prevention of opioid misuse in the US, and in providing safe opioid supply [19]. Here, understanding mandatory requirements, clinical side effects, risks associated with interactions, identifying when collaboration with the prescriber is necessary, determining when pain management is not adequate and evaluating

Table 2 Results QR1 and QR2[a]

	How much do you agree or disagree that each item should be included as a core competency? (6-point Likert scale)[b]			How well do you think practicing pharmacists currently meet this item? (1–100)	
	Mean	Standard Deviation	% agreement (4–6)[b]	Mean	Standard Deviation
Opioids and Society					
Describe the history of opioid use and societal consequences of uncontrolled use[c]	5.19	0.95	96.8		
Describe the contemporary history of opioid use and societal consequences of uncontrolled use	5.07	0.78	100	54.00	19.09
Understand the broader drivers of opioid use in the community, such as social determinants of health, commercial determinants (i.e. pharmaceutical companies) and inappropriate prescribing	5.48	0.70	100	48.59	17.52
Describe the history of abused substances other than opioids	4.93	0.88	96.3	41.07	16.42
Understand how language choices can contribute to stigma and the importance of person first language choices	5.27	1.04	88.5	39.00	20.23
Opioid Physiology					
Outline the families of classic opioid peptides: enkephalins, endorphins, and dynorphins and their respective physiologic roles	4.42	0.92	87.1	40.78	21.49
List the opioid receptors mu, delta, kappa and sigma and their role in the endogenous opioid system	4.94	1.06	90.3	46.52	23.98
Opioid Pharmacology					
Describe the pharmacologic mechanism of action of opioids at the opioid receptor sites and descending inhibitory pathway	5.23	0.99	93.5	51.52	17.89
Describe the action of opioid agonists, antagonists and mixed agonist-antagonists and identify agents that demonstrate these properties	5.74	0.51	100	63.52	20.48
State the difference between opioids and opiates	4.77	1.06	83.9	44.00	25.85
Understand illicit/non-medicinal use of a range of opioids, including both heroin and prescribed opioids	5.48	0.77	96.8	47.15	25.60
Describe opioid-induced respiratory depression and its reversal by opioid antagonists	5.94	0.25	100	67.48	26.17
Describe opioid-induced constipation and its management	5.81	0.48	100	80.30	15.17
Understand the mechanism of action of atypical opioids (opioids that have both opioid and non-opioid mechanisms of action) i.e. tapentadol, tramadol and buprenorphine	5.67	0.68	96.3	57.26	22.56
Opioid Pharmacokinetics and Drug Interactions					
Discuss the pharmacokinetic differences among available opioids and opioid antagonists	5.35	0.80	100	51.19	20.72
Be familiar with abuse-deterrent formulations	5.42	0.62	100	70.19	20.83
Outline pharmacogenetic differences that influence the effect of opioids	5.19	0.83	96.8	45.30	26.50
Discuss the rationale (advantages/disadvantages) for each route of administration and dosage formulation of available opioids	5.45	0.72	100	63.19	22.33
Outline the clinically important drug interactions with opioids and their management	5.81	0.48	100	64.93	21.08
Therapeutic Use of Opioids					
Discuss the pharmacodynamic differences among available opioids and opioid antagonists	5.29	0.82	96.8	57.19	22.56
Describe the clinical effects of opioids	5.77	0.56	100	76.59	17.81
Discuss the common and serious side effects of the opioids and their management	5.90	0.40	100	76.41	16.88
Describe the allergic reactions caused by various opioids and their management	5.26	0.73	100	56.07	24.37
Describe symptoms of opioid induced hyperalgesia and the proposed causative mechanism and management	5.45	0.72	96.8	36.70	21.72
Outline the place of opioids in the management of acute and chronic pain	5.87	0.34	100	61.81	21.21
Distinguish between the terms opioid tolerance, dependence, and substance use disorder/addiction as they relate to the use of these drugs for the management of pain	5.71	0.46	100	54.37	22.40
Discuss precautions for opioid use in special populations: pediatrics, geriatrics and pregnancy	5.61	0.56	100	48.70	23.85

Table 2 (continued)

	How much do you agree or disagree that each item should be included as a core competency? (6-point Likert scale)[b]			How well do you think practicing pharmacists currently meet this item? (1–100)	
	Mean	Standard Deviation	% agreement (4–6)[b]	Mean	Standard Deviation
Understand safe use of opioids in high risk populations such as those who are already experiencing opioid use disorder and those who have a mental health disorder	5.48	0.70	100	51.15	19.04
Outline when the use of opioid replacement therapy (i.e. methadone or buprenorphine), is appropriate	5.48	0.80	100	52.89	19.37
Opioid Education					
Outline safe prescribing practices, appropriate quantities, storage and destruction of unused opioid prescriptions	5.74	0.58	100	70.19	20.97
Provide essential patient education to ensure safe use	5.94	0.36	100	61.59	18.56
Opioid Dispensing					
Document opioid prescriptions and relevant patient/prescriber communication	5.65	0.66	96.8	66.81	27.26
Describe the situations in which contacting the prescriber is required	5.77	0.50	100	72.22	21.68
Understand the legal requirements around opioid supply, storage and destruction for relevant jurisdictions of practice	5.81	0.48	100	80.44	18.59
Be able to recognise signs of intoxication and withdrawal from a variety of substances before dispensing opioids	5.44	0.89	92.6	57.85	20.96
Opioids and Pain Management					
Identify and assess those patients/conditions that can benefit from the analgesic effects of opioids in acute and persistent pain.	5.39	0.80	96.8	61.07	23.32
Be familiar with alternate drug and non-drug treatments for pain.	5.81	0.54	100	65.70	22.09
Course of Opioid Therapy					
Identify an appropriate length of therapy for opioid use	5.45	0.81	96.8	50.07	16.56
Describe indications for an opioid rotation and perform/conduct an opioid rotation	4.84	1.32	87.1	31.89	20.85
Demonstrate how to use opioid equianalgesia tables	5.52	0.93	93.5	56.56	24.18
Describe the indications for an opioid taper and design an opioid taper	5.35	1.23	90.3	43.19	24.34
Discuss appropriate tapering regimens for cessation of long term opioid use	5.42	1.12	90.3	39.52	22.45
Opioid Monitoring					
Demonstrate how to monitor for efficacy and toxicity in a patient taking opioids	5.61	0.62	100	57.22	20.96
Outline appropriate monitoring for patients taking long-term opioids (e.g. 5 A's of monitoring chronic pain—activity, analgesia, adverse effects, aberrant behaviour, affect)	5.39	0.76	100	45.85	19.37
Identify appropriate opioid use treatment agreements to be used by the patient, physician and pharmacist	5.45	0.62	100	43.18	20.41
Opioid Overdose Training					
Provide education on overdose management, including signs and symptoms of opioid overdose, how to use naloxone to reverse an overdose, and emerging best practices	5.84	0.37	100	52.30	24.78
Understand the role of opioid antagonists/reversal agents, such as naloxone, to respond to acute opioid toxicity for 'overdose' with illicit opioids	5.81	0.40	100	58.15	25.23
Understand the role of opioid antagonists/reversal agents, such as naloxone, to respond to acute opioid toxicity for 'overdose' with opioids prescribed for pain	5.74	0.53	100	52.70	25.59
Identify and discuss risk factors that can contribute to overdose risk e.g. COPD, sleep disturbed breathing, dose increase, combination with other sedatives including alcohol etc	5.89	0.32	100	54.19	28.00

[a]Items presented in QR1 are displayed in regular font, items identified from comments in QR1 and presented in QR2 are displayed in italics

[b]1 = Strongly disagree, 2 = disagree, 3 = somewhat disagree, 4 = somewhat agree, 5 = agree, 6 = strongly agree

[c]Modified for QR2

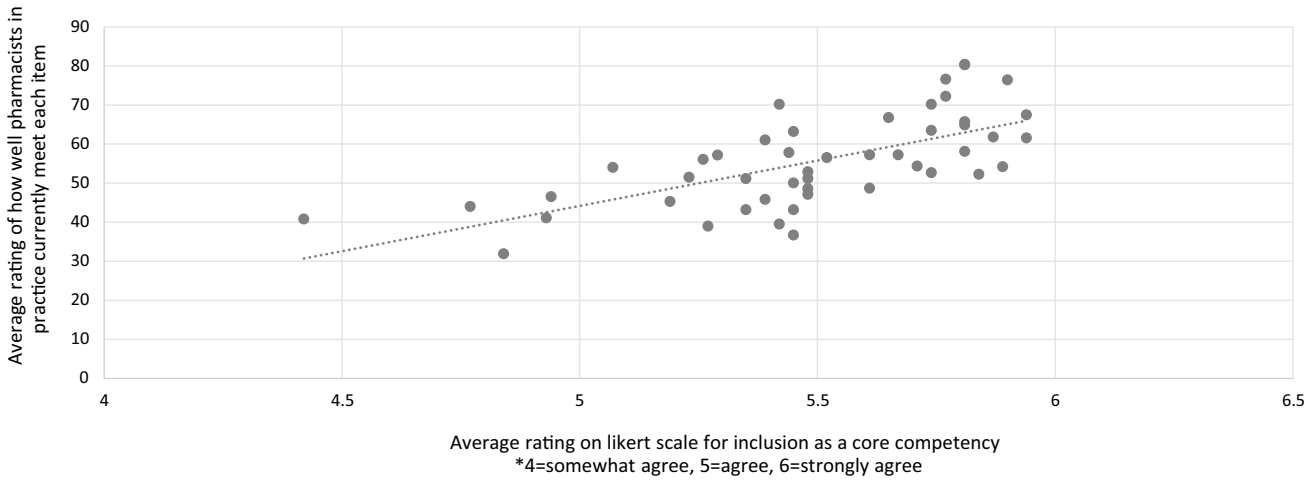

Fig. 1 Ratings for inclusion as competencies versus current practice by pharmacists ($r = 0.66$, $p < 0.001$)

and addressing overdose risk were identified. This aligns with the items that presented with the highest average rating on the Likert scale in our study. Consistent with the US study, all items under the section headings 'Opioid Education', 'Opioid Monitoring' and 'Opioid Overdose Training' received 100% agreement in this study (a rating of 4–6 on the Likert scale). This suggests competencies that Australian experts deemed important for pharmacists when supplying opioids have international relevance.

Additionally, there were themes for competencies that received the lowest average ratings for how well participants believe Australian pharmacists currently demonstrate proficiency. These competencies included newer, more complex and specialised concepts and areas of practice. For example, 'describe symptoms of opioid induced hyperalgesia and the proposed causative mechanism and management', 'outline the families of classic opioid peptides: enkephalins, endorphins, and dynorphins and their respective physiologic roles', and 'outline pharmacogenetic differences that influence the effect of opioids'. These notions may be considered more complex and specialised and not used in every day practice, and their lower ranking may be reflective of the fact that these may not have been included as part of the course structure when many of today's practicing pharmacists completed their training or if included not commonly used in practice and therefore forgotten. Other concepts such as opioid rotation and tapering regimens may have received lower ratings due to a general perception that the concept of opioid rotation and tapering regimens may be a more specialised area of pharmacy practice, and perhaps something that would require additional training on top of the minimum requirements to be competent in. Guidelines for pharmacists have been published in the area of opioid tapering in Canada [20] though given recent reports of increased mortality after opioid cessation [21], this appears to be an area of clinical practice where further research is needed to determine best clinical practice.

These findings raise some additional challenges. With limited time and space in already crowded pharmacy curricula, which competencies should be considered a priority? Although we can see clearly that some competencies had higher agreement than others, participants were not asked to compare or rank the competencies for importance therefore we do not know which competencies would be considered a higher priority. This leaves the question of where resources should be directed towards—training for pharmacists to reach a high standard of competence in the items that are deemed a priority, or should the focus be on items in which pharmacists were considered less competent? As the list of items presented in this study was extensive, further research could evaluate which of the items are considered more important. Also, additional research could explore the curricula of Australian pharmacy schools and the degree to which they do or do not cover these standards and identify which items should be covered in undergraduate studies and which may be related to further study for pharmacists specialising in areas involving pain or dependence. This will inform skill development for current and future pharmacists in Australia, to enable a consistent standard of practice to be met in the workforce.

Future research is also required to identify how new competencies can be more effectively implemented in Australia. A study was conducted in 2003 which aimed to describe an effective training program in competency-based clinical pharmacy in Australia [22]. The study suggests that practice-based teaching, implementing a one to one learning ratio between the mentor and the tutor is the most effective way to implement the training. It also defines various ways to assess competence, including through objective testing, simulations and direct

observations. It would be useful to further explore this and to apply it to training programs and assessment of newly developed competencies for pharmacists when supplying opioids. Current assessment of how well competencies are being met in the workforce, is undertaken by a self-assessment tool provided by the PSA, which, whilst useful for self-development, may produce biased results as a national assessment tool [23].

There are some caveats to consider with our research. Only opioid experts were invited to participate in this study; therefore, our results may not be the reflective opinion of all practicing pharmacists in Australia. The fact that over half of the experts included in the study were situated within Victoria may also bias the results to reflect Victorian perceptions which may be different given the early uptake of real-time prescription monitoring in that state. Future investigations are required to determine whether this can be considered the general opinion of all practicing pharmacists in Australia. The broad range of settings of pharmacy practice (e.g. community pharmacy, hospitals and primary care clinics), and the range of different settings our experts came from, may have contributed to variable responses in how pharmacists were perceived to meet the different competencies. Future studies could explore specific sets of competencies relating to the practice of pharmacists in differing roles.

Conclusion

Both the use of, and harms associated with prescription opioids is on the rise worldwide including in Australia. Pharmacists should be equipped to address this issue, through providing safe opioid supply, appropriate patient education, assessing and managing risk of opioid toxicity and completing interventions where necessary. The introduction of a set of competencies specifically related to the supply of prescribed opioids by practicing pharmacists may allow for these roles to be undertaken in a more consistent and effective manner. Opioid experts reached consensus on all items presented to them in this study, though current pharmacists' practice was thought to vary in relation to these competencies. Future research may identify which areas regarding opioid knowledge and skills should be the focus of workforce development activities.

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6.1 SUMMARY

This research aimed to reach consensus on competency items that could be considered core competencies for Australian pharmacists in opioid supply. There was strong agreement by participants on what should be considered core competencies for Australian pharmacists. Given the large number of items identified, further research may help determine priorities for training and education. If we do upskill pharmacists to ensure they are meeting what experts believe are core competencies for supplying opioids, is there a broader role for pharmacists in not only the supply of opioids but in early screening and brief intervention when there are signs of problematic opioid use?

CHAPTER 7: ROUTINE OPIOID OUTCOME MONITORING IN COMMUNITY PHARMACY: OUTCOMES FROM AN OPEN LABEL SINGLE-ARM IMPLEMENTATION-EFFECTIVENESS PILOT STUDY

Community pharmacists are central in the supply of pharmaceutical opioids. As such, community pharmacies are an ideal location for screening and early intervention to reduce opioid-related harm (Brummel et al., 2014; Green et al., 2015; Lindley et al., 2019; Wu et al., 2017). It has been demonstrated that education provided in pharmacies can improve patient knowledge of medications and reduce ongoing use (Northey, McGuren, & Stupans, 2015; Reeve et al., 2017; Tannenbaum, Martin, Tamblyn, Benedetti, & Ahmed, 2014). Screening and brief interventions (SBI) for substance use are effective in primary care (Bashir, King, & Ashworth, 1994; Kypri, Langley, Saunders, Cashell-Smith, & Herbison, 2008; Reid, Fiellin, & O'connor, 1999) and there is demonstrated feasibility and acceptability for pharmacist-led SBI for detecting risky alcohol use (Dhital, Whittlesea, Norman, & Milligan, 2010; Khan et al., 2013). Risk screening may play an important part in predicting individuals at risk of developing dependence to medications, including opioids. The more that an individual exhibits aberrant behaviours such as unsanctioned dose increases or using all their medications too early, the more likely it is that they are misusing or dependent on their medication (Webster & Webster, 2005). While improved patient awareness and education about risks of these medications, and monitoring for adverse events and expectations of treatment may improve outcomes, there has been limited research on the intervention of pharmacists in this space.

Best practice suggests that for all patients prescribed opioids, outcomes and opioid-related risk should be monitored using a 'universal precautions' approach (Gourlay, Heit, & Almahrezi, 2005). Monitoring should ideally assess a range of outcomes including analgesia, activity or functioning, dependence/addiction, adverse effects, and effect on mood (Gourlay et al., 2005). There are additional important aspects of opioid safety that warrant assessment with ongoing supply. Alcohol (Campbell et al., 2015; Larance et al., 2016) and benzodiazepine use (Nielsen et al., 2015; Sun et al., 2017) are common among patients prescribed opioids for chronic pain and can increase the risk of adverse events, toxicity or overdose. Depression is also a common co-morbidity shown to be independently associated with non-medical use of prescribed opioids (Gilam et al., 2019). Other common opioid-related adverse effects, such as constipation, can also adversely affect quality of life (Prichard, Norton, & Bharucha, 2016; Velazquez Rivera, Velazquez Clavarana, Garcia Velasco, & Melero Ramos, 2019). Hence, it is important to take a holistic approach to monitoring. To date most studies have focused on detecting risk of problematic

opioid use without assessing a broader range of opioid-related measures that are important for patient safety and quality of life, or screening for current opioid use disorder.

Research to establish models of regular outcome monitoring in pharmacy and how to implement such models, including an understanding of what approaches may best support behavior change are lacking (Wu et al., 2017). Hence the next studied looked at this in the context of opioid supply in community pharmacy.

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Routine opioid outcome monitoring in community pharmacy: Outcomes from an open-label single-arm implementation-effectiveness pilot study

Suzanne Nielsen[a,b,*], Louisa Picco[a], Michala Kowalski[b], Paul Sanfilippo[a], Pene Wood[c], Sarah Larney[b], Raimondo Bruno[b,d], Alison Ritter[e]

[a] Monash Addiction Research Centre, Monash University Peninsula Campus 47-49 Moorooduc Hwy, Frankston, 3199, Victoria, Australia
[b] National Drug and Alcohol Research Centre, University of New South Wales Sydney, NSW, 2052, Australia
[c] Department of Pharmacy and Biomedical Science, Latrobe University, PO box 199 Bendigo, Victoria, 3552, Australia
[d] School of Medicine, University of Tasmania, Churchill Ave, Sandy Bay, 7005, Hobart, Australia
[e] Drug Policy Modelling Program, Social Policy Research Centre, Kensington Campus, University of New South Wales, Sydney, Australia

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ABSTRACT

Background: In response to rising harms with prescription opioids, recent attention has focused on how to better utilise community pharmacists to monitor outcomes with opioid medicines.
Objective: This pilot aimed to test the implementation of software-facilitated Routine Opioid Outcome Monitoring (ROOM).
Methods: Community pharmacies in Victoria and New South Wales, Australia, were recruited to an open-label single-arm observational implementation-effectiveness pilot study. Pharmacists completed baseline and follow up interviews to measure change in knowledge and confidence following training on, and implementation of ROOM. Paired t-tests compared pre-post scores. Patients that participated were invited to complete a brief evaluation survey. Measures of feasibility and acceptability were collected.
Results: Sixty-four pharmacists from 23 pharmacies were recruited and trained to conduct ROOM. Twenty pharmacies (87%) were able to implement ROOM, with four pharmacies completing the target of 20 screens. Pharmacists completed ROOM with 152 patients in total. Forty-four pharmacists provided baseline and follow-up data which demonstrated significant improvements in confidence identifying and responding to unmanaged pain, depression and opioid dependence. Despite increases, low to moderate confidence for these domains was reported at follow-up. Responses from pharmacists and patients indicated that implementation of ROOM was feasible and acceptable.
Conclusions: Pharmacists' confidence in identifying and responding to opioid-related problems significantly increased from baseline to follow up across several domains, however scores indicated that there is still significant scope to further increase confidence in responding to opioid-related problems. ROOM is feasible and acceptable, though more extensive pharmacist training with opportunity to practice skills may assist in developing confidence and skills in this challenging clinical area.

Introduction

Reducing harm related to prescription opioid use remains a priority in many high income countries.[1–3] In Australia, opioid overdose deaths continue to increase, driven largely by deaths involving prescription opioids.[4] Australia has one of the highest rates of prescribed opioid use in the world, with three million Australians prescribed an opioid each year.[5] These high rates of use and escalating mortality call for new approaches to reduce opioid-related harm.

In addition to concerns around opioid overdose and opioid use disorder, there are several other important aspects of opioid safety and quality use of opioid medicines that warrant assessment with ongoing opioid supply. Alcohol use[6,7] and benzodiazepine use[8,9] are common among patients prescribed opioids for chronic pain and can increase the risk of adverse events and overdose. Depression is also a common co-morbidity which has been shown to be independently associated with non-medical use of prescribed opioids.[10] Other common opioid-related adverse effects, such as constipation, can also adversely affect quality of life.[11,12] Hence, it is important to take a holistic approach to monitoring. To date most studies have focused on detecting risk of

* Corresponding author. Monash Addiction Research Centre, Monash University Peninsula Campus, 47-49 Moorooduc Hwy, Frankston, 3199, Australia.
E-mail address: Suzanne.nielsen@monash.edu (S. Nielsen).

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problematic opioid use without assessing a broader range of opioid-related measures that are important for patient safety and quality of life, or screening for current opioid use disorder.

Best practice suggests that for all patients prescribed opioids, outcomes and opioid-related risk should be monitored using a 'universal precautions' approach.[13] Monitoring should ideally assess a range of outcomes including analgesia, activity or functioning, addiction, adverse effects and affect or mood.[13] Although there are lengthy tools for clinical assessment by opioid prescribers,[14] few have developed methods to facilitate time-efficient routine use in primary care or community pharmacy setting, for example, by allowing patient self-completion.

This gap represents an important clinical opportunity. Community pharmacists are highly trained accessible healthcare professionals who are central in the supply of prescription opioids. As such, community pharmacies are an ideal location for screening and intervention to reduce opioid-related harm. Research to establish models of regular outcome monitoring and how to implement such models, including an understanding of what approaches may best support behavior change are lacking.

The theory of planned behaviour, which focuses on understanding three essential conditions of behaviour change: C - capability, O - opportunity, M − motivation, resulting in new B – behavior (termed the COM-B)[15] was used to design the clinical intervention and choose implementation strategies, with different aspects designed to increase the pharmacists' capability, motivation and opportunity to identify and respond to prescription opioid-related problems. This included training and education to increase capability, automation of procedures which were embedded in dispensing software and prompts to increase opportunities to intervene, highlighting the opportunities for pharmacists to have an important role in responding to these harms, in addition to financial incentives, to increase motivation.

Our pilot implementation study aimed to test if a computer-facilitated screening and brief intervention can assist pharmacists to screen for opioid-related risk. The intervention, called Routine Opioid Outcome Monitoring (ROOM), was developed according to the existing frameworks for monitoring opioid supply model[16,17] and validated for self-completion in people taking opioids for chronic pain.[18] ROOM is embedded into dispensing software to support provision of assessment, education, and referral back to the opioid prescriber if appropriate.

Aims

The study aimed to pilot the implementation of ROOM in community pharmacy practice and test whether:

1. Training and support to deliver ROOM increases pharmacists' knowledge and confidence in clinical domains related to opioid-safety;
2. ROOM facilitates patient education, naloxone delivery and referral;
3. ROOM is feasible and acceptable to pharmacists and patients.

Methods

A protocol paper was published prior to completing recruitment and data collection.[16] Relevant details are also outlined below. The intervention design and implementation strategies were informed by the Consolidate Framework for (CFIR).[19] The FISpH adaptation of CFIR further informed factors specific to community pharmacy.[20] The theory of planned behavior informed the choice of implementation strategies,[15] and the RE-AIM framework informed the choice of implementation outcome measures.[21] An implementation-effectiveness design was chosen to have a dual focus on implementation and clinical effectiveness of ROOM.[22] We measured aspects of implementation at the pharmacy and pharmacist level, in addition to measures of effectiveness in terms of identifying opioid related problems, and the clinical outcomes for patients who participated in the study.

Study design and setting

Open-label single-arm observational pilot implementation-effectiveness study with community pharmacies in Victoria and New South Wales, Australia. Baseline interviews with pharmacists were completed between March 2018 and April 2019, and follow-up interviews with pharmacists were completed between August 2018 and August 2019.

Participants

Eligibility criteria

Pharmacies. Eligible pharmacies were located in one of three participating Primary Health Network regions (Central and Eastern Sydney, Western Sydney, and Western Victoria) in the two participating states of New South Wales and Victoria to gain experience in a range of metropolitan, regional and rural settings through the pilot. Additional eligibility criteria included: (i) dispensing at least five opioid prescriptions per day; (ii) willingness to perform all study related tasks; (iii) having a tablet, computer or other device to complete the ROOM screening tool; (iv) willingness for up to three pharmacists at the site to receive training and participate in the study; and (v) willing and able to recruit 20 patients to participate in the study.

Patients (pharmacy customers). Eligible patients were 1) attending an enrolled community pharmacy to receive a repeat supply of opioids for non-cancer pain; 2) aged 18 years or over; 3) able to provide voluntary informed consent; and 4) willing and able to self-complete the ROOM tool in the pharmacy.

Recruitment

Pharmacy recruitment

Pharmacies were recruited via professional pharmacy networks (e.g. The Pharmacy Guild of Australia) and recruitment through participating Primary Health Networks in participating regions.

Patient recruitment

The software developed for the study enabled pharmacist prompts to be delivered via the dispensing software to alert pharmacists when eligible opioid prescriptions were dispensed. The software prompted pharmacists to offer the ROOM tool to patients receiving a second or subsequent opioid prescription and who were aged 18 years or older. Pharmacists who had been trained on the study procedures were asked to confirm patient eligibility before inviting participants to be involved in the study. A brief scripted verbal explanation was given, and a computer tablet or other internet-enabled device was provided for completion of online informed consent and the questions that formed the ROOM tool.

Study procedures

Pharmacy procedures

Initially the owner or pharmacist-manager was invited to participate in the study and provided written informed consent. The owner or pharmacist-manager then invited additional pharmacists within their pharmacy to participate. Pharmacists were invited to complete a baseline survey (with online informed consent) to assess current knowledge, confidence, perceptions and practices relating to monitoring opioid outcomes in the pharmacy. Identifying information was not collected from pharmacists to reduce the risk of social acceptability bias. Following completion of the baseline survey, pharmacists participated in a 1 h training webinar covering all aspects of delivering the ROOM intervention including the provision of relevant counselling based on the participants' response.

Once pharmacists were trained, the pharmacy was provided with access to the ROOM software and was asked to recruit 20 consecutive patients to complete the ROOM tool, after which a follow-up online survey was sent to the individual pharmacists. Pharmacists continued to have access to the software after they had completed ROOM with 20 participants. Pharmacists were prompted to query any outcomes from the previous visit when the patient next attended the pharmacy.

Pharmacist training

The 1-h webinar (live or prerecorded) covered the content of the ROOM tool which includes a three-item pain scale assessing pain intensity and interference (Pain, Enjoyment, General Activity [PEG[23]]) to measure pain outcomes, screening for opioid use disorder, screening for depression, risky alcohol use and opioid-induced and constipation) and key clinical counselling points in response to positive screens. Assessment questions were embedded throughout the webinar to ensure pharmacists were able to respond correctly after the training and as a means to determining that pharmacists were engaging with the training materials. Additional professional development resources were identified on a review of the recently published education articles on each aspect of the ROOM (pain management, opioid dependence, depression, alcohol brief interventions, opioid-induced constipation and motivational interviewing). These were provided following the webinar for further self-directed continuing education on pharmacist request.

Patient procedures

After providing online informed consent, participants (patients) self-completed the 12-item ROOM tool. Concurrently, the pharmacist completed the dispensing checks (pre-determined check-boxes) based on their review of the patient's history. These identified risk factors associated with opioid dependence and overdose (e.g. dose >100 mg morphine equivalent, concurrent benzodiazepine use, escalating opioid use, multiple opioid formulations or multiple prescribers). Based on the responses, summary documents with tailored health information were generated (examples in supplementary material). Where indicated, pharmacists were instructed to provide patients with brief education on opioid overdose risk and offer naloxone. On completion of the ROOM screening questions, patients were invited to leave an email address to receive a brief evaluation survey to capture their satisfaction with the screening tool, counselling provided by the pharmacist, intentions to follow-up with their opioid prescriber/s, and naloxone supply. Evaluation surveys were anonymous and patients were assured all information was confidential to reduce likelihood of social desirability bias. Those who completed the evaluation survey could enter a draw to win an iPad.

Pharmacists were instructed to contact the patient's prescriber to discuss their concerns if serious safety issues were identified, in addition to forwarding a summary of the outcomes directly to the prescriber.

Pharmacist reimbursement

Pharmacists were reimbursed AUD$20 for completion of baseline and follow-up surveys, AUD$40 for participating in the training webinar and AUD$20 per ROOM intervention completed.

Measures

Data were collected on patient age category (10-year groups), gender, current medications (3-month history), ROOM tool responses which assessed current pain,[23] opioid use disorder,[17] mood,[24] alcohol use[25] and constipation,[16] and outcomes from delivery of the ROOM intervention (e.g. medication changes at next patient visit) (See Supplementary Table 1 for items in the ROOM tool).

Measures collected from pharmacists included demographic and pharmacy characteristics, frequency of current opioid and naloxone supply, attitudes towards harm reduction, and knowledge and confidence around identifying and responding to problems with prescribed opioids. These measures were based on those used in a previous nationally representative study of community pharmacists,[26] and are all described in detail in the published study protocol.[16]

Outcomes

The primary outcome was change in confidence in identifying and responding to opioid related risks, and knowledge on naloxone use. Secondary outcomes included: (i) the proportion of patients who reported they were offered naloxone, and of those offered naloxone, how many received it (either purchased it over the counter or supplied with a prescription); (ii) the proportion of patients who either self-reported that they attended/intended to attend an appointment with their opioid prescriber and documentation of medication changes by the prescriber following participation in ROOM.

Feasibility and implementation outcomes included acceptability of the ROOM tool to patients and pharmacists and the proportion of pharmacies that completed the ROOM with 20 patients.

Sample size and analyses

Sample size calculations using G*Power software determined the study was powered to detect changes in the primary outcome of changes pharmacists' knowledge and confidence pre- and post-study results using paired-t-tests. A previous study of Australian pharmacists determined that pharmacists were able to correctly answer 1.8 out of 5 (standard deviation, [SD] = 1.7) questions on naloxone use.[26] A meaningful change was defined as most questions correctly (a score of 3 out of 5). Assuming a pre-intervention mean of 1.8 (SD = 1.7) and a correlation of 0.7 between measures, 25 pharmacies with three pharmacists each (75 total) would provide 90% power to detect a post-intervention mean of 3.0 (SD = 1.7) as a statistically significant improvement at a two-sided significance level of 0.05. Similarly, previous data indicate that 34% of pharmacists were confident that they could identify appropriate patients with opioid-related risk and provide them with naloxone.[26] To be able to detect a meaningful increase from 34% to 60% (i.e. the majority) of pharmacists reporting such confidence, a sample size of 59 pharmacists achieves 95% power to detect such a change as a statistically significant difference at a significance level of 0.05.

The study design allowed for up to 500 patients to complete ROOM (up to 20 patients/pharmacy). This maximum sample size was not required to be recruited to meet the aims of the study, as screening rates were considered an outcome of the study.

Ethics

The study was approved by the Human Research Ethics Committee of the University of New South Wales (UNSW HREC reference: # HC17760) and ratified by La Trobe University and Monash University.

Results

Sixty-four pharmacists were recruited from 23 pharmacies in Victoria (n = 11) and New South Wales (n = 12), Australia (See Fig. 1a). Most pharmacists were female (n = 44, 69%) and were aged 25–34 (n = 25, 39%) (Table 1). A mix of pharmacy types were recruited representing independent, small and large chain pharmacies. Most pharmacists (n = 32, 50%) were practicing in metropolitan locations outside capital cities.

Mean confidence scores in identifying and responding to most opioid-related problems improved (Table 2). There was increased confidence identifying three of the five areas examined (unmanaged pain, depression and opioid dependence) and increased confidence responding to four of the five areas examined (unmanaged pain, opioid

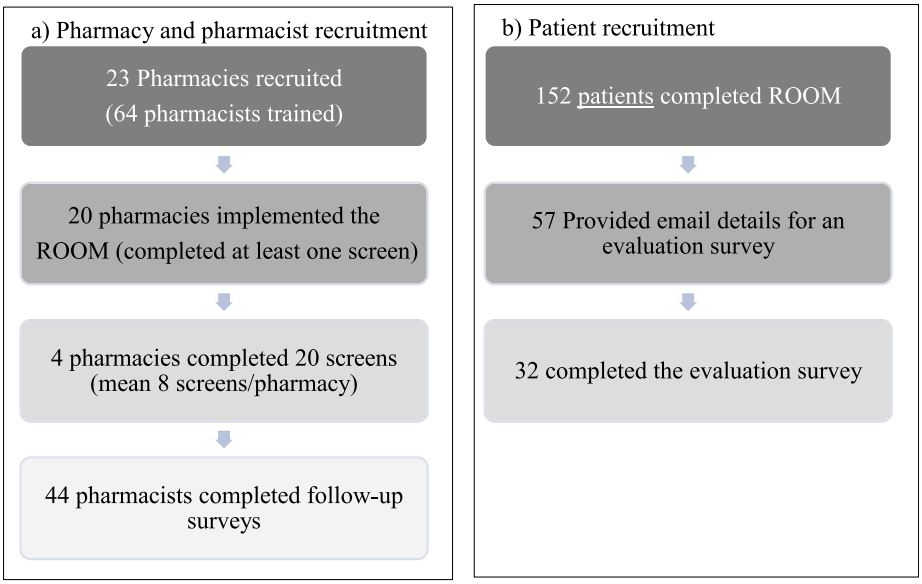

Fig. 1. a & b: Flowchart of pharmacist and patient recruitment.

dependence, depression and risky alcohol use). Most pharmacists reported moderate but not high confidence. A small reduction in overall comfort intervening when concerned about a prescription for opioids was identified. There were differences in baseline comfort [F(2, 41) = 7.52, p = 0.002] for pharmacists that increased (n = 11), decreased (n = 18) or did not change their comfort levels (n = 15), with those whose comfort increased reporting lower comfort at baseline (mean = 2.63/6, SD = 0.92) compared with those that did not change (mean = 3.33/6, SD = 0.72) or decreased in comfort (mean = 4.22, SD = 1.39). Tukey tests showing that the group that reported decreased comfort at follow up were significantly more comfortable than the other two groups at baseline. Knowledge relating to naloxone did not significantly increase.

Pharmacists completed ROOM with 152 patients. Most were male (n = 74, 63%) and the largest group was older than 64 years (n = 61, 42%) (Table 3). The most common opioid that was dispensed to prompt ROOM was oxycodone (n = 76, 50%) followed by codeine (n = 35, 23%). Thirty-six people (23.7%) were prescribed multiple opioid

Table 1
Study characteristics of pharmacists (n = 64[a]).

Characteristics			N (%)
Pharmacists	Age	25–34 years	25 (39.1)
		35–44 years	19 (29.7)
		45–65 years	20 (31.3)
	Gender	Male	20 (31.3)
		Female	44 (68.8)
	Years of practice, Mean (SD)		12.59 (10.88)
Place of practice	State/Region	NSW	37 (57.8)
		VIC	27 (42.2)
	Setting/Type	Independent	14 (21.9)
		Small multiple/chain (2–9 branches)	23 (35.9)
		Large chain (10 or more branches)	27 (42.2)
	Location	Capital city	20 (31.2)
		Other metropolitan urban centre (population equal to or greater than 100,000)	32 (50.0)
		Rural location (population between 5001 and 99,999)	10 (15.6)
		Remote (population less than or equal to 5000)	2 (3.1)
	Other services offered	Return of unwanted medicines	54 (84.4)
		Opioid agonist treatment	48 (75.0)
		Pain management services	22 (34.4)
		Mental health services	9 (14.1)
		Diabetes screening	38 (59.4)
		'Medscheck' (medication review)	61 (95.3)
		Home medication reviews	50 (78.1)
		Blood pressure screening	63 (98.4)
		Other	41 (64.1)
Prescriptions	Prescription opioid supply	More than ten times a day	15 (23.4)
		Several times a day	40 (62.5)
		Around once per day or less	9 (13.1)
	Currently stocks naloxone (n = 50)	Yes	16 (25.0)
		No	28 (43.8)
		Don't know	6 (9.4)

[a] Unless otherwise stated.

Table 2
Change in pharmacist knowledge and confidence, paired *t*-test (n = 44).

		Baseline	Follow-up	n	t	p	Cohen's d
Confidence identifying (mean out of 4#, SD)	Unmanaged pain in patients on opioids	2.1 (1.0)	2.4 (0.9)	44	2.01	0.051	0.30
	Patients who may be developing dependence on opioids	2.0 (0.8)	2.5 (0.9)	44	3.68	<.001	0.55
	Patients who may have depression and chronic pain	1.9 (0.9)	2.3 (0.9)	44	3.12	0.003	0.47
	Patients with risky alcohol use and chronic pain	1.5 (1.0)	1.8 (0.8)	42	1.61	0.115	0.25
	Patients with constipation taking opioids	2.8 (0.9)	2.9 (1.0)	44	0.75	0.460	0.11
Confidence responding to (mean out of 4#, SD)	Unmanaged pain in patients on opioids	2.1 (0.7)	2.5 (0.8)	43	3.18	0.003	0.49
	Patients who may be developing dependence on opioids	1.8 (0.9)	2.3 (0.8)	44	4.19	<.001	0.63
	Patients who may have depression and chronic pain	1.8 (0.9)	2.3 (0.7)	43	3.87	<.001	0.59
	Patients with risky alcohol use and chronic pain	1.5 (1.0)	2.1 (0.8)	44	4.37	<.001	0.66
	Patients with constipation taking opioids	3.1 (0.8)	3.2 (0.8)	44	0.60	0.555	0.09
Naloxone knowledge	Score out of 5 for selected items (relation to naloxone pharmacology and administration) from the OOKS~	2.6 (2.0)	3.1 (1.0)	44	−1.57	0.124	0.24
Comfort^	In general, how comfortable do you feel intervening when you are concerned about a prescription for opioids? (mean, SD)	3.5 (1.2)	3.1 (1.2)	44	−2.00	0.052	−0.30

Mean score out of 4 on a five point scale where 0 was 'not at all confident' and 4 was 'extremely confident'. ^Mean score on a 6 point scale where 1 was 'not at all comfortable' and 6 was 'extremely comfortable'; ~ pharmacists who indicated that they had never heard of naloxone were not asked naloxone knowledge questions and were given a default answer of 'don't know'. OOKS = Opioid Overdose Knowledge Scale.

Table 3
Study characteristics of patients (n = 152[a]).

Characteristics			N (%)[a]
Demographics	Age (n = 147)	18–54 years	58 (39.5)
		55–64 years	28 (19.1)
		>64 years	61(41.5)
	Gender (n = 119)	Male	74 (62.2)
		Female	45 (37.8)
Medications		Qualifying opioid oxycodone	76 (50.0)
		Qualifying opioid codeine	35 (23.0)
		Qualifying opioid other	41 (27.0)
	n = 146	Opioid dose > 100 mg OME	42 (28.8)
		Prescribed > 1 opioid or opioid formulation	36 (23.7)
		Concurrent sedative or hypnotic prescription	31 (20.4)
Pain		Mean (SD) pain score (/10 - past 7 days)	6.07 (2.5)
		Mean (SD) pain interference with enjoyment of life	6.33 (2.7)
		Mean (SD) pain interference with general activity	6.34 (2.8)
Opioid Use Disorder[b]	In the past three months in times of worse pain did you use more opioid medicines than prescribed?	Not at all	92 (60.5)
		A little	38 (25.0)
		Quite a lot	19 (12.5)
		A great deal	3 (2.0)
	In the past three months did opioid medicines cause you to feel slowed down, sluggish or sedated?	Not at all	58 (38.2)
		A little	67 (44.1)
		Quite a lot	21 (13.8)
		A great deal	6 (4.0)
	In the past three months did opioid medicines cause you to lose interest in your usual activities?	Not at all	86 (56.6)
		A little	44 (29.0)
		Quite a lot	17 (11.2)
		A great deal	5 (3.3)
	In the past three months did you worry about your use of opioid medicines?	Not at all	65 (42.8)
		A little	59 (38.8)
		Quite a lot	21 (13.8)
		A great deal	7 (4.6)
Possible Opioid use disorder		Endorsed 3 or more OWLS items	61 (40.1)
Possible Mood disorder		PHQ-2 (>3)	33 (21.7)
Risky Alcohol use		Screen positive for current risky drinking in past 12 months	58 (38.2)
Constipation		Are you experiencing constipation?	46 (30.3)
		Medication if yes	38 (82.6)

[a] Unless otherwise stated.
[b] OWLS = Opioid use disorder screening tool that measures Overuse, Worry about opioid use, Losing interest in other activities and feeling Slowed down or sedated.

Table 4
Effects of ROOM on interactions with patients on opioid-related topics.

Topic	Increased	No change	One-way[a] X,[2] p
Pain management	21 (61.8)	13 (38.2)	1.44, p = 0.230
Opioid-safety	18 (52.9)	16 (47.1)	0.02, p = 0.888
Mental health	14 (41.2)	20 (58.8)	0.74, p = 0.390
Risky alcohol use	10 (29.4)	24 (70.6)	4.98, p = 0.026
Constipation	24 (70.6)	10 (29.4)	4.98, p = 0.026

[a] Testing the null hypothesis that for each topic scores for 50% of individuals have improved.

formulations. Mean scores for pain severity and the interference of pain on functioning suggested moderate pain. Four out of ten patients screened positive for opioid use disorders, four out of ten reporting risky alcohol use, two out of ten screened positive for depression, and three out of ten reported constipation. The majority (92%) of these were already taking a medicine for their constipation.

Outcomes after implementation

Pharmacists reported a mean score of 6.8 (SD = 2.2)/10 for ease of using the ROOM tool, 7.4 (SD = 1.9)/10 for the relevance of the information provided and 6.9 (SD = 1.9)/10 for the usefulness of the printed information. Most reported use of the ROOM tool increased interactions with patients in relation to pain management (62%), opioid safety (53%) and constipation (71%) (Table 4). For the mental health and risky alcohol use, most pharmacists (59% and 71% respectively) reported no change in their interactions with customers (Table 4). No pharmacists reported that ROOM reduced their interactions with customers on any topic.

Four out of 23 pharmacies completed 20 ROOM screens; one pharmacy achieved this within the intended two-month timeframe and continued to screen after reaching this target. Sixteen pharmacies commenced screening yet did not reach 20 screens. Six pharmacies completed 1–3 screens, seven pharmacies completed 3–7 screens and three pharmacies completed 9–13 screens. Three pharmacies did not begin screening, despite undertaking all the necessary training (Fig. 1a).

Thirty-two of the 44 pharmacists that completed the follow-up survey had completed ROOM with patients and provided information on time-spent delivering the intervention. These pharmacists (n = 32) spent an average of 10.1 min (SD 6.2, range 2–30) discussing results with patients, and considered AUD$27.4 (SD 4.6) to be reasonable remuneration for time spent providing the intervention. Pharmacists were asked on a five point scale from 'not likely at all' to 'very likely' about continuing to conduct ROOM under a variety of scenarios (Table S1). Of the 32 pharmacists who delivered ROOM (44%, n = 14) reported that they were 'very likely' to continue to provide ROOM if they continued to receive a professional service fee and had access to the software at no cost. This reduced to one pharmacist saying they were 'very likely' to do this if there was no service fee. With no service fee and a fee to access the software, most (59%, n = 19) said they were 'not at all likely' to continue ROOM.

Patient acceptability and outcomes

Of the 152 patients that completed the ROOM tool in a pharmacy, 57 (21%) provided an email to receive an evaluation survey (Table 5, Fig. 1b). Just over half (56%, n = 32) completed the survey and five respondents initiating the survey but didn't complete it. Of those that completed the survey, half (n = 16, 50%) were male and were an average age 61 years (SD = 14) old. They rated the ease of completing the tool as 8.6 (SD = 1.9)/10, the relevance of information provided as 8.8 (SD = 1.4)/10, and the usefulness of information and resources as 8.4 (SD = 2.1)/10.

Table 5
Patient reported outcomes using ROOM tool (n = 32).

What (if any) follow-up with a health professional did you have following the screen (pick one)	n (%)
Discussion with pharmacist only	16 (50.00)
Discussion with pharmacist and referral for GP	5 (15.60)
Referral for GP only	0
No follow-up	8 (25.00)
Other	3 (9.40)[a]
What has happened following the referral to your GP	
I attended a referral appointment with a GP	3 (60.00)
I have made an appointment with my GP	2 (40.00)
I have not yet followed up following the GP referral but I plan to	0
I do not plan to follow up with the GP	0
What information did you receive as a result of the screen (mark all that apply)?	
Received information about pain management	20 (62.50)
Received information about managing problems and side effects with opioids	14 (43.80)
Received information about mood	9 (28.10)
Received information about alcohol use	10 (31.20)
Received information about naloxone	6 (18.80)
Received information about constipation	13 (40.60)
Did not receive any information	8 (25.00)
Received naloxone#	1 (16.67)

[a] Other responses included referring to pain specialists and/or ongoing involvement with the opioid prescriber; #Participant indicated naloxone was via prescription rather than purchased over-the-counter.

Most (n = 32) reported that ROOM led to discussions with either the pharmacist (50%, n = 16) or the pharmacist and their GP (16%, n = 5) (Table 5). Of those referred to their GP, all had either attended an appointment or made an appointment following completion of ROOM. The most common topics that patients reported receiving information on were pain management (63%, n = 20) and problems with opioids (44%, n = 14). Six patients indicated that they received information about naloxone, with one patient receiving naloxone on a prescription as a result of ROOM.

Some outcomes were not able be assessed due to incomplete data collection through the software program, including failure for the data to be collected or software not performing as expected (See Table S2).

Discussion

Given rising opioid-related harm, there is a need to improve identification of opioid-related risk and provide evidence-based responses. We implemented a pharmacist-led intervention to monitor opioid-related outcomes and provide brief education/information for the pharmacy customer and their prescriber. Training and implementation of ROOM increased pharmacists' confidence in responding to a range of opioid-related problems, though mean scores indicated moderate but not high confidence at follow-up. Pharmacists were least confident in the areas of mental health and substance use, though these areas were where the greatest gains in confidence were observed.

Pharmacists' mean ratings of acceptability of the study software and tools (7 out of 10) were lower than patients (mean of 8 or 9/10). Pharmacists' ratings may reflect that some aspects of the software could be more intuitive or easy to use. Despite this, ROOM appeared acceptable to pharmacists and patients. One pharmacy continued ROOM after meeting their target of 20 interventions, suggesting that the intervention was not sustained in the absence of financial incentives and support from the study team. There was also an association with the reported likelihood of maintaining the intervention with the availability of a service fee, where pharmacists' reported low likelihood of screening without receiving a professional service fee.

Previous research has identified time as a barrier in engaging in overdose prevention,[26] and preferences for training around naloxone

have demonstrated that most pharmacists prefer training that is up to 1 h.[27] For this reason, our training was limited to a 1-h webinar. We found, on average, confidence at follow-up was at moderate levels (e.g. mean score of 2.5/4) indicating that brief training may be insufficient. Pharmacists' scores did not increase naloxone knowledge though it was notably higher than that in an earlier Australian study,[26] suggesting either that recent educational activities have increased pharmacists' knowledge, or that those that took part already had knowledge on this topic. Either way, the training did not further enhance this knowledge, nor did it result in meaningful levels of naloxone supply. Overall comfort to intervene when concerned about prescription opioids decreased slightly. This decrease was driven by reductions in comfort by those that reported the highest levels of comfort as baseline, suggesting that some may have overestimated their comfort prior to undertaking ROOM.

The design of ROOM[16] was informed by a behavior change theory that suggests that three domains of Capability, Opportunity and Motivation are required for behavior change to occur (the COM-B model).[15] Behaviour change in community pharmacy practice has been found challenging in other areas such as mental health. A pilot study implementing a mental health management intervention found that 45 out of 100 pharmacies recruited were unable to implement the intervention,[28] suggesting that achieving implementation in 20 out of 23 pharmacies could be perceived to be a successful outcome, despite some pharmacies not reaching the target of 20 screens. Similar to Hattingh, Kelly, Fowler, Wheeler,[28] we considered a range of evidence based strategies to facilitate implementation including prompts, training, incentives, pharmacy support, workflow and management support. Further work may explore other strategies to further facilitate implementation.

We found, using ROOM, that pharmacists were able to identify a broad range of opioid-related risk factors including possible opioid use disorder, risky drinking, high opioids doses - all established risk factors for overdose.[29] This highlights how key the provision of naloxone is among this population.[30–32] Despite this, only one quarter of pharmacists reported that their pharmacy stocked naloxone, few patients reported discussing naloxone with their pharmacist and just one patient received prescribed naloxone through the intervention. This indicates considerable scope to increase pharmacists' role in opioid overdose prevention. Low rates of naloxone stocking are not unique to Australia[33,34] and indicate the need for broad efforts and international leadership in this area.

This pilot study design has a number of strengths. These include the use of software embedded in pharmacy dispensing programs and recruiting a broad range of pharmacies to increase the generalizability of the findings. Limitations include analyses based on pre-post measures, the lack of a comparison arm, the low rate of patient survey completion, and some pharmacists' loss to follow-up, primarily due to staff changes over the course of the study, which were common. Finally, there were limitations with the software that resulted in some data fields not being captured and able to be analysed. Despite this, this pilot work provides a foundation for future implementation work to enhance the role of pharmacists in this area. Other studies have demonstrated extended pharmacists roles in related clinical areas such as pharmacist-led naloxone co-prescribing,[35] identifying potential opioid misuse,[36] and pharmacist-led chronic pain clinics.[37] Taken together there is an emerging evidence base in terms of how to extend the reach of community pharmacy to reduce opioid related harm and improve pain management outcomes.

Conclusion

We demonstrated that ROOM is acceptable to community pharmacists and patients, and is able to identify patients with meaningful opioid-related risk. Further work is needed to enhance the implementation and sustainability of this intervention as part of routine care to address opioid-related problems with prescribed opioid for pain.

Data statement - research data for this article

Due to the sensitive nature of the questions asked in this study, participants were assured raw data would remain confidential and would not be shared.

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CRediT authorship contribution statement

Suzanne Nielsen: Conceptualization, Methodology, Writing - original draft, Funding acquisition. **Louisa Picco:** Data curation, Writing - original draft. **Michala Kowalski:** Conceptualization, Methodology, Writing - original draft. **Paul Sanfilippo:** Formal analysis, Writing - original draft. **Pene Wood:** Conceptualization, Methodology, Writing - original draft. **Sarah Larney:** Conceptualization, Methodology, Writing - original draft. **Raimondo Bruno:** Formal analysis, Writing - original draft. **Alison Ritter:** Conceptualization, Methodology, Writing - original draft.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sapharm.2020.02.009.

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7.1 SUMMARY

This pilot study aimed to test the implementation of a computer facilitated SBI. Findings demonstrated that while most pharmacies were able to implement the SBI (ROOM), there was considerable variability in screening rates (Nielsen, Picco, et al., 2019). As such, we explored further why some pharmacists were comfortable in implementing ROOM, while others were not (Nielsen, Sanfilippo, et al., 2020). Our findings indicated that there were both demographic and practice characteristics of pharmacists that were independently associated with a greater likelihood of conducting screening and brief intervention for opioid related problems. Multivariable analyses showed that each additional decade practicing as a pharmacist, lower knowledge of naloxone and lower confidence in identifying unmanaged pain were all independently associated with reduced engagement in screening after controlling for other variables (Nielsen, Sanfilippo, et al., 2020). This demonstrates that a range of factors are important for successful implementation of opioid screening tools in pharmacy. This has been shown in other work (Moullin, Sabater-Hernández, & Benrimoj, 2016) and is consistent with literature that demonstrates that knowledge alone does not equate to behavior change in clinical practice (Abbasi, 2011).

CHAPTER 8: "A LOT OF PEOPLE CALL IT LIQUID HANDCUFFS" – BARRIERS AND ENABLERS TO OPIOID REPLACEMENT THERAPY IN A RURAL AREA

The gold standard of management of opioid dependence in Australia is MATOD (Gowing et al., 2014). MATOD allows safe administration of a prescribed opioid, while minimising the harm of unsanctioned drug use and allowing abstinence from concomitant drug use (Gowing et al., 2014). MATOD should be person centered, with a range of treatment options along the continuum of recovery, addressing each physical, social or psychological need identified (Gowing et al., 2014). MATOD is an important component of community-based approaches, allowing treatment provision on an out-patient basis. It is associated with high rates of retention and opioid abstinence and enables individuals to tackle major health, psychological, social and legal issues and facilitates the treatment of co-morbid medical and psychiatric conditions (Tetrault & Fiellin, 2012; World Health Organization, 2004).

On a snapshot day in 2018, just over 50,000 clients received MATOD treatment for their opioid dependence at 2,852 dosing points across Australia. Eighty-nine percent of these MATOD dosing points were pharmacies (Australian Institute of Health and Welfare, 2019). Supervised dispensing and administration of MATOD in community pharmacies plays a crucial role in enhancing compliance, treatment monitoring and minimising diversion, particularly in rural and regional areas where access to treatment can be an issue (Chaar et al., 2011).

Despite similarities in the profile of drug users in urban and rural areas, access to services is significantly limited in the latter (Day, Conroy, Lowe, Page, & Dolan, 2006). A 2009 report on the Australian MATOD system identified that most associated problems were compounded in rural or remote locations, including access to prescribers and dosing, travel costs, stigma, discrimination, and poor workforce support (Ritter & Chalmers, 2009).

While there is a plethora of research on MATOD programs, there is limited research on MATOD delivery in rural Australia where geographic and social features of the environment complicate service delivery. Very few studies describe the delivery of MATOD from a client perspective but rather focus on the views of prescribers, pharmacists and others involved in service delivery. Ensuring effective and equitable ORT access in regional and rural areas is essential and a qualitative approach provided a critical means to do this. Our research investigated the perceived barriers and enablers from a client perspective to accessing and remaining in ORT treatment in rural communities in Victoria and New South Wales (NSW).

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"A lot of people call it liquid handcuffs" – barriers and enablers to opioid replacement therapy in a rural area

Penelope Wood [a], Cynthia Opie[b], Joseph Tucci[a], Richard Franklin[c], and Karen Anderson[d]

[a]Department of Pharmacy and Applied Science, La Trobe Institute of Molecular Sciences, La Trobe University, Bendigo, Australia; [b]Department of Rural Health, University of Melbourne, Shepparton, Australia; [c]College of Public Health, Medical and Veterinary Sciences, James Cook University, Townsville, Australia; [d]Rural Health School, College of Science Health and Engineering, La Trobe University, Bendigo, Australia

ABSTRACT

Introduction: Opioid dependence is a complex health condition often requiring long-term treatment. The main objectives of treatment are to reduce dependence and the associated morbidity and mortality. Opioid replacement therapy (ORT) is an effective pharmacological therapy for opioid dependence. The aims of this research were to explore barriers and enablers to ORT in rural areas of Australia.

Design and Methods: A qualitative study design incorporating semi-structured interviews was used to explore views of people in ORT. Interviews were analysed for emergent themes and issues.

Results: Barriers to ORT were restrictiveness, stigma, the medication and structure of the program. Enablers were structure of the program, access to takeaway doses, effect on drug use and the medication.

Discussion: To improve access and retention in ORT programs action is needed to facilitate programs meeting the needs of rural people, including reducing cost of medication, addressing the restrictiveness of programs and effect on employment opportunities, and stigma associated with drug use and addiction in communities.

Conclusions: Barriers and enablers to ORT programs exist in the rural areas studied. Geographical distance, inability to gain and maintain social connections including employment, and lack of community education addressing stigma are significant barriers to ORT in these areas.

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Introduction

Opioid dependence is a complex health condition requiring lengthy treatment. (World Health Organization, 2009) Opioid replacement therapy (ORT) is the most effective pharmacological therapy for opioid dependence. (Amato et al., 2005) In Australia, ORT is provided for heroin dependence (Ritter & Chalmers, 2009) and increasingly for management of pharmaceutical opioid dependence. ORT is associated with significant reductions in illicit opioid use, criminal activity, overdose deaths and behaviours, which increase the risk of HIV transmission, while improving physical and mental health, and social functioning. (World Health Organization, 2004) ORT is an important component of community-based approaches, allowing treatment provision on an out-patient basis. It's associated with high rates of retention and enables individuals to tackle major health, psychological, social and legal issues. (World Health Organization, 2004)

The health of people in rural Australia is poorer than their urban counterparts with reduced access to medical treatment at a greater cost. (Strong & Strong, 1998) This includes drug and alcohol treatment and harm minimisation programs. Despite similarities in profile of drug users in urban and rural areas, access to services is significantly limited in the latter. (Day, Conroy, Lowe, Page, & Dolan, 2006) A 2009 report on the Australian ORT system identified that most associated problems were compounded in rural or remote locations, including access to prescribers and dosing, travel costs, few service providers, stigma, discrimination and poor workforce support. (Ritter & Chalmers, 2009) The Victorian Pharmacotherapy Review and other studies identified costs as well as stigma and discrimination as barriers. (Digiusto & Treloar, 2007; King, Berends, & Ritter, 2013) A study conducted with health professionals in rural and remote Australia identified that despite ORT being "highly valuable to the community" it was not without problems. These health professionals suggested that travel time and costs, employment issues, opening hours of the GP clinic and pharmacy, GPs' time constraints and privacy were key barriers to accessing harm minimisation programs. (Peterson, Northeast, Jackson, & Fitzmaurice, 2007)

Whilst there is a plethora of research on ORT programmes, there is limited research on ORT delivery in rural Australia where geographic and social features of the environment complicate service delivery. Very few studies describe the delivery of ORT from a client perspective but rather focus on the views of prescribers, pharmacists and others involved in service delivery. Ensuring effective and equitable ORT access in regional and rural areas is essential and a qualitative approach provides a critical means to do this. This research investigates the perceived barriers and enablers from a client perspective to accessing and remaining in ORT treatment in rural communities in Victoria and New South Wales (NSW).

CONTACT Penelope Wood P.Wood@latrobe.edu.au PO Box 199 Bendigo, Victoria, 3552 Australia.

Methods

A qualitative narrative design with semi-structured interviews was employed. Two rural Australian communities (in Victoria & NSW), were selected. These farming communities are more than 100 km from a regional centre. In Victoria, the emphasis is on a community model of ORT. (Drugs and Poisons Regulation Branch, 2016) Provision of services is primarily through general practitioners (GPs) and community pharmacies with specialist services to treat more complex dependence problems. (King et al., 2013). In NSW, ORT is funded and managed through both public and private sectors. (New South Wales Department of Health, 2011) The NSW model has primary sites co-located within hospitals or community health. These sites generally provide assessment, prescribing, dispensing and limited case management. Most staff are trained nurses, while prescribers are visiting specialists or sessional GPs. There are minimal ORT provisions by community prescribers and dispensers. (Berends, Larner, & Lubman, 2015)

Adults over the age of 18, currently engaged in ORT in the studied rural communities, were recruited voluntarily. Service providers were supplied with information and asked to promote the research with ORT patients. Participants were asked to contact the chief investigator to arrange an interview if interested. Participants already enrolled were encouraged to disseminate information about the research to recruit further participants.

Twelve semi-structured interviews (6 in each community, 1 hour in length) were conducted with researchers (CO and PW), audio recorded and transcribed verbatim. For accuracy of data each transcript was sent to participants for authentication. Written informed consent was obtained before interviews. The interview (Appendix 1) was used to gain narratives from participants including their childhood experiences, impact that dependence had on their lives, and experiences with treatment, especially ORT. Recruitment continued until consistency in concepts and insights into lived experiences of opioid dependence and ORT emerged, without the presentation of new themes. (Fusch & Ness, 2015) Data were de-identified, coded and analysed for common emergent themes using NVivo data analysis software (11 for Windows). (Qrs International Pty Ltd, 2015) Data were analysed separately by researchers and compared for consistency.

Approval for this research was obtained from Human Research Ethics Committees (HREC), in each presiding jurisdiction: Goulburn Valley Health HREC 23/GVH/16 (Victoria), Murrumbidgee Local Health District (NSW) HREC 16/GWAHS/84 and La Trobe University.

Results

Demographics

Twelve participants in total, with equal representation from the two areas (Table 1).

Themes emerging from interviews were organised into barriers and enablers. Barriers to ORT were restrictiveness, stigma, medication and program structure. Enablers were organised into sub-themes including social, physical and mental enablers, program structure, including access to takeaway doses, the effect on drug use and medication. No barriers or enablers were unique to any particular location.

Table 1. Patient demographics.

GENDER	Male	Female		
	8	4		
AGE	**18–25**	**26–35**	**36–45**	**46–60**
	1	2	3	6
EMPLOYMENT STATUS	**Employed**	**Unemployed**		
	0	12		
REGION	**Victoria**	**NSW**		
	6	6		
DEPENDNECY	**Heroin**	**Prescription/ pharmaceutical opioids**	**Both**	**Other**
	3	4	4	1
TREATMENT	**Methadone**	**Suboxone**		
	9	3		

Barriers

Restrictiveness

A common barrier for the ORT program for participants was lack of freedom. If they had more freedom, engagement and satisfaction with programs would be greater, highlighted by one participant: *"I would stay on the methadone if I had my freedom."* (Participant 12). The main issues restricting freedom included having to collect doses daily and not be given "takeaway" dose (doses that can be taken from the pharmacy and taken at a later time), and travel to a designated pharmacy or hospital. For those living out of town this was time consuming and expensive. Regular dose collection (daily or several times weekly) meant restrictions in seeing family or for recreation"*…when you're stuck in the one town, you start to get a bit edgy and that. It would be nice to go away for a couple of days or something."* (Participant 10).

These restrictions meant patients wanted to leave the program *"I want off it, only for the simple fact is it's - draining, you can't live a normal life. I can't wake up and be normal like everybody else."* (Participant 4). They likened the program to being incarcerated *"they took my takeaways away – the Methadone doctor here - which has made my life now, back to liquid handcuffs, it's worse than um, my corrections order."* (Participant 4).

Restrictiveness of having to be near a dosing pharmacy made it difficult to find employment in a rural area *"…the painter that painted our house after we had the walls fixed - he gave me a job and I started painting - but I couldn't keep it through the stupid chemist hours…it was a seven o'clock start to leave to come to XXXXX from all the way like half an hour - backwards, forwards. Yeah, he didn't like it, so I just stopped working for him."* (Participant 9). Living in a rural area had limitations in range of work available to people who had used drugs or had histories of incarceration *"…a lot of the people around my area know that I've been in gaol. Dairy farms all closed down. That's the only thing I really know - in this area. I've got no training."* (Participant 5).

Stigma

Participants felt stigmatised by family, community, the pharmacist, pharmacy staff and prescriber. *"I break out into a sweat just walking into town. I do. I get anxious. I'm still trying to pick up on being part of the community."* (Participant 5). A

number of participants felt classed as a "junkie" even if their dependence was prescription painkillers or they were using ORT to manage chronic pain as well as dependence. They felt this stigma caused them to lose friends and affected their capacity for employment. *"I hate the whole stigma that comes with it, the Chemist, the doctor's appointments, the whole [crying] I feel like I haven't got my life really back, but I have…"* (Participant 4). Anonymity was compromised in rural areas *"I don't want to do it down the chemist because I'll bump into people I know and I have a lot of respect for myself. I don't want to have anyone know that I'm on it. I try to keep it a big secret."* (Participant 7).

The medication

The medication presented as a barrier to some. Problems included issues with dose, interference with other medications and diet, developing tolerance to the medication, side effects (sleepiness and cardiac issues), being unable to consume alcohol and dependence on methadone in particular, with one participant resigned to lifelong treatment. *"Probably stay on it for the rest of my life because it's hard to come off."* (Participant 6).

The program

Structure of the program was also a barrier. Lack of social and mental health support and a focus on drug and alcohol counselling was raised *"… they sort of were only focused on drug and alcohol counselling. They didn't really want anything to do with all the mental health and stuff like that."* (Participant 3).

Cost of the program was a major issue particularly for participants from Victoria where the system is community based. The additional costs of travel added to the financial burden *"if you're like me and you're 50 kilometres out and you've got to do 70, 80 or 90 kilometres every day to pick it up and pay for it every day it becomes challenging, the money - financial side of it."* (Participant 5). Some participants felt attending the pharmacy to collect doses was a barrier, as they did not like mixing with other dependant people and were sometimes harassed outside to sell their takeaway doses.

Other barriers included waiting to access the program, which can be longer in rural areas *"…they made an appointment for me … at the clinic to get on methadone or Bupe, right, which is Suboxone, but there was a waiting list of a month."* (Participant 11).

Enablers

Social

The majority of the enablers related to social factors. These included getting finances organised: "*Since I've been on the methadone, I went to a financial advisor, he helped me out and stabilised me. Now I'm virtually out of debt."* (Participant 1), providing security, allowing them to attempt to mend broken relationships and regain a social life. *"Now I'm on the methadone I think a lot straighter. I go fishing, I can go camping. When I was on the other gear I didn't want to do any of that sort of stuff."* (Participant 1). Having a team and seeing someone regularly for assessment, particularly a drug and alcohol counsellor, seemed to be important: *"You sort of do a lot better when you've got someone that you see regularly."* (Participant 3). One participant felt they got more help in an ORT program than when they were taking painkillers. The program allowed people to get parole and prevent further incarceration as illustrated by participant 8, *"Ever since I've been on Suboxone I have not had one problem with the law and I am - I guess I'm more secure…."* The ORT program was seen as an alternative to residential rehabilitation programs, as it was cheaper and didn't come with risk of losing housing, sometimes even supporting retention of housing. The birth of a child was a motivational factor for one participant to start ORT. *"I do have to stay on the methadone to just keep it all equal, going and I can do the best - be the best version of me that I possibly can be for the children…"* (Participant 7).

Physical

Motivation for starting and remaining on ORT was that it stopped people from dying. *"…it was either go on methadone or overdose and die."* (Participant 10). Some found they received significant pain relief from methadone. *"I wish they gave me methadone when the accident happened because it's so good for the pain"* (Participant 1).

Mental

There were perceived mental benefits of ORT. *"Yeah. I found once I went onto the methadone, total mood swing changed, thoughts changed, whole life changed because it was so easy to operate with."* (Participant 1). Participants found using ORT made them feel normal again. They felt it kept them grounded and helped with coping skills and keeping clear thoughts and emotions under control. *"At first it was just a way of, I guess dealing with not being able to deal with the world straight."* (Participant 8). Some participants felt the program was more successful if you were in the right mindset and if health professionals were gentle.

The program

Enabling structural features of the program included access to a pharmacy (especially one within walking distance), "*It's a lot easier when I can walk, saves asking people for rides and that*." (Participant 6); being confined to one dose a day and only having access to one medication (reducing temptation of using more). Awareness of available programs enabled people to get access to treatment and the ORT program was cited as being "*… a lot easier to go to the chemist than to go to a dealer…*" (Participant 8).

Most perceived access to takeaway doses as an enabler to remaining on the program. Despite this, a couple of participants found having to pick up doses every day as more beneficial for them *"I'm on daily pick-ups now. I quite like that anyway, because it keeps me up and having to go down the street every day."* (Participant 3). Others felt that having takeaways was easier for them to travel and stay connected with families. Takeaways … *"brings people closer to their family because they can go and visit."* (Participant 2). Not having to go into the pharmacy daily saved participants from having to mix with others with dependency issues.

Drug use

Participants found the ORT program stopped them taking other drugs and blocked the effects of heroin. ORT stopped withdrawal effects and cravings for heroin. Heroin "*…. it just wouldn't do it for me. I don't know what it's done, whether it's fried the receptors or what, I just don't have any interest in it whatsoever. I could sit here and watch you do it, I could help you do it. I could help six other people do it and leave the room without breaking a sweat.*" (Participant 9).

The medication

The medications themselves were enablers. Participants on buprenorphine/naloxone appreciated it was difficult to overdose on. Seeing ORT as a medication used for pain or maintenance made the program more acceptable and being able to dose daily was perceived as a benefit "*…with my counsellor helping me find the right medications and stuff like that, it's been a really big help.*" (Participant 3).

Discussion

ORT programs are effective in reducing inappropriate opioid use (Mattick, Breen, Kimber, & Davoli, 2009). However, treatment delivery strategies that improve patient outcomes such as frequent patient contact, observed dosing and limited takeaway doses, may decrease treatment availability, practicality, acceptability, enrolment, and retention for some in rural areas. The treatment paradigms most convenient for patients and prescribers (e.g. infrequent clinic visits, reduced oversight, providing longer-duration supplies of medication) may increase risk of medication diversion, misuse and undermine treatment outcomes. (Sigmon, 2014) This paradox poses significant barriers to widespread therapeutic delivery of effective medications to opioid-dependent patients, particularly in rural areas with fewer services and unmet need for treatment thus potentially needing a more individualised approach. (Sigmon, 2014)

This study identified barriers and enablers to both accessing and remaining in ORT programs in the rural communities of Victoria and NSW, where our study was located. No enablers appeared to be unique to rural areas and while many of the barriers were similar to those identified in other studies (Berends et al., 2015; Day et al., 2006; Digiusto & Treloar, 2007; Fraser, Valentine, Treloar, & Macmillan, 2007; King et al., 2013; Peterson et al., 2007; Ritter & Chalmers, 2009), they may be more pronounced in rural areas due to geographical distance and the lack of both anonymity and employment opportunities.

In rural areas considerable travel is required to access services, when they are available. (Berends et al., 2015) The main issues identified in this study included having to collect doses daily, involving travel to the pharmacy or hospital. For those living out of town this was time consuming and expensive. Costs of travel added to significant financial burden on patients receiving ORT in the private sector. Day et al. (2006) reported that for rural patients treatment was often accessible only by private car and some participants hitchhiked into town daily to receive ORT if they could not afford private travel. (Day et al., 2006) In rural America, the situation is similar to rural Australia. Major barriers to ORT treatment included travel times of approximately 60 minutes per clinic visit with reported cost of $48.84 USD per week for transportation. Many reported missing at least one clinic visit and medication dose due to transportation. Additionally, participants reported that travel time for their opioid treatment had interfered with their ability to maintain employment. (Sigmon, 2014)

Having to be near a dosing pharmacy was restrictive, and makes it hard to find employment for anybody on ORT programs, and in rural areas this is compounded by limitations on range of work available, especially for people with histories of drug use and/or incarceration. Not being able to travel for employment, to see family, friends or recreational purposes, impedes social recovery and is seen as a barrier for remaining in ORT. In rural areas, distances are often greater, public transport more limited therefore more time and resources are needed for travel thus the problem can appear magnified. A report from the National Centre in HIV Social Research identified that having takeaway doses contributed to finding and retaining employment, fulfilling family responsibilities, capacity to travel for work and leisure, self-esteem and a sense of progress in treatment, control over contact with other clients, confidentiality in treatment and cessation of illicit drug use. (Fraser et al., 2007) This needs to be balanced with safety. Recent changes to the ORT policy in Victoria were a result of coroners' findings that methadone takeaway doses had significantly contributed to deaths involving methadone overdose. The latest policy has reduced the number of recommended methadone takeaway doses. (Drugs and Poisons Regulation Branch, 2016) Due to its better safety profile in overdose, buprenorphine/naloxone has less stringent rules surrounding availability of takeaway doses. (Drugs and Poisons Regulation Branch, 2016) In view of these issues, there could be a trend toward buprenorphine/naloxone to overcome the barriers of lack of methadone takeaway doses but it is important to acknowledge that due to its different pharmacology buprenorphine/naloxone is not suitable for everyone. (Tanner, Bordon, Conroy, & Best, 2011)

Privacy was also a concern for people prescribed ORT. Participants in the Day et al study felt that drug use was particularly stigmatised in rural areas. Participants raised concerns about attitudes of employees of pharmacies where methadone was dispensed and of drug services including prescribers and GPs. [6] This was also a finding in this study. Participants identified stigma from the community, healthcare professionals and family as a significant barrier that was enhanced by living in a small town where anonymity was limited. Cooper and Nielsen (2017) identified that strategies to address generalised opioid-related stigma needed to be employed including education of the community and healthcare sector around opioid dependence being a medical condition. (Cooper and Nielsen, 2017)

Contemporary approaches to ORT might expand program reach and reduce demand for face-to-face visits. Approaches could include programs utilising sustained-release formulations of opioid agonist medications such as buprenorphine implants. (Sigmon, 2014) Other alternatives include the use of mobile health platforms providing customized content and

support via telephone offering benefits in cost, consistent delivery, access, privacy and convenience. Web-based platforms also hold potential for extending access to clinical support, education and monitoring to patients living far from clinics. (Sigmon, 2014) Roving dispensing buses between regional towns could be another option. (Ritter & Chalmers, 2009) Reductions in the number of visits would reduce the burdens of time and travel for patients, thereby making it easier for patients to participate in prosocial activities (e.g. employment, educational opportunities and family responsibilities). These novel approaches need to be balanced against degree of patient oversight to maximize treatment access and outcomes while minimizing risk of non-adherence and diversion. (Sigmon, 2014)

Limitations of this research include generalisability to all Australian rural areas. Each region is unique in attitudes and employment opportunities and may present its own challenges depending on attitudes and skills of health professionals and the models implemented. Depending on location and availability of services, people may need to travel further to access ORT. Not all participants in this study were initiated on ORT in a rural area and this may influence experiences of the program. Methadone was the predominant treatment for participants; therefore, barriers and enablers represent issues faced with methadone more than buprenorphine/naloxone.

The effective delivery of ORT for people with opioid dependence in rural Australia is an on-going challenge. There barriers to the ORT program, which are amplified in rural areas due to the size of the community, distance from services and family and social characteristics. Geographical distance, lack of anonymity, access to takeaway doses and the effect these factors have on employment opportunities are significant factors impeding participants staying in treatment in rural Victoria and NSW, highlighting deficits in a one size fits all model. There needs to be flexibility of options to increase retention and improve social and emotional health. Addressing stigma and improving access will be important for future success.

ORCID

Penelope Wood http://orcid.org/0000-0002-0374-3366

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APPENDIX

In-Depth Semi-Structured Interview Procedure

Introduce Interviewer.
Introduce Project.
Discuss PLS and consent.
Discuss confidentiality, voluntary participation, Pharmacotherapy Program clinicians not knowing who participates.

1. Tell me about yourself.

   i. Where did you grow up
   ii. Your family
   iii. Your friends

iv. When you began using opioids

2. Describe how your life began to change once using opioids.

i. When did you realise you were addicted
ii. Did your general health change
iii. Were you employed – did this change
iv. Were you in a relationship – did this change
v. Did you have your own home – did this change
vi. Were you close to your family – did this change
vii. Did your friend group change
viii. Sport and leisure activities – any change

3. Describe the moment that you decided you wanted to enrol into a pharmacotherapy program, what happened at that time?

i. Where did you go for help
ii. Who provided help
iii. Did you believe the program would help
iv. Did you set goals that you believed you could achieve
v. Have these goals changed
vi. Has the program been easy
vii. Have you dropped out and started again
viii. What caused you to drop out
ix. What led to starting again

4. Has pharmacotherapy changed your life in any way?

i. Family
ii. Friends
iii. Relationships
iv. Employment
v. Drug craving
vi. Drug seeking behaviour
vii. What aspects of the program have made a difference

5. Where do you see yourself in five years time?

i. Is pharmacotherapy a part of your long term future
ii. Is the program supporting you to achieve your goals

Is there anything else you would like to add?
Thank you for taking the time to be interviewed and for sharing your experiences with me.

8.1 SUMMARY

The aims of this research were to explore barriers and enablers to ORT in rural areas of Australia. The results highlight that among other issues, an accessible and equitable service by community pharmacy is an important factor in reducing barriers and improving access to MATOD in rural areas. Reduction of the stigma associated with enrolment in, and greater societal acceptance of, these crucial health programs is also needed.

CHAPTER 9: CONCLUSION & FUTURE DIRECTIONS

In 2013, Dowell et al. wrote about "risky drugs, not risky patients," to emphasize that opioids possess significant risk regardless of who uses them (Dowell, Kunins, & Farley, 2013). This thesis highlights the important role pharmacists can play in reducing this risk, but more tools, training and education need to be developed to support this expanded role. Through a simulated patient study, it was identified where support and training could be improved for managing requests for opioids for pain. The work also identified that despite the availability of tools to support pharmacists in opioid supply and management there needs to be awareness and access to these tools to have an impact on practice. Routine opioid screening is seen as feasible and acceptable by community pharmacy, but opioid specific skills and expertise may be lacking, and education and curriculum development could be a means to address this. As well as knowledge, confidence in addressing opioid issues also needs to be considered when developing training if pharmacists are going to have a role in screening and early intervention for problematic opioid use. Unfortunately, stigma still appears to be an issue that needs to be addressed for some pharmacists and pharmacy staff providing harm reduction services, in particular MATOD. This contrasts with the approach taken in managing nicotine dependence with nicotine replacement therapy, where the health benefits are more widely understood and condoned.

The opioid epidemic has been labelled as a crisis that should not be underestimated. The experience from the US provides insight into what we can expect in Australia if more work is not done to prevent and intervene early in problematic opioid use. The non-medical use of pharmaceuticals is a priority issue identified in the Australian National Drug Strategy because of the associated harms not just to individuals but also to the broader community (Australian Institute of Health and Welfare, 2017b). Problematic prescription drug use is a complex problem that needs to be addressed by society and health professionals together; both health professional and community awareness programs are needed. In finding a solution, careful thought and consideration needs to go into developing meaningful interventions to improve both pain management and substance misuse prevention without compromising treatment for patients who have a genuine need, such as palliative patients, whether they have a dependence history or not (Glod, 2017).

Access to safe, high quality, and effective care for people suffering from persistent pain is a high priority that requires a team-based, person-centred strategy to minimise inappropriate opioid supply (Wu et al., 2017). Higher use of opioids in rural and remote areas (Australian Comission on Safety and Quality in Healthcare, 2016) may reflect a lack of pain related services and

alternative treatments. Suitable funding, and models need to be investigated. Projects like Pain Revolution's – Local Pain Educator program, Project ECHO (Extension for Community Healthcare Outcomes) for chronic pain, telehealth, and local pain champions could all be part of the solution. Pharmacists can contribute to these solutions as they are increasingly becoming involved in new pain management innovations such as the recent Community Pharmacy Pain MedsCheck trial (Australian Government Department of Health, 2015).

Several strategies have already been implemented across Australia to try and reduce the risk and harms from the use of opioid medications. These include restriction of access to codeine medicines, changes to the PBS requirements for the prescribing of opioids, including requirements for a multidisciplinary approach and regular review of prescribing by another GP or pain specialist, and the introduction of real-time prescription monitoring across Victoria (SafeScript). The full impact of these measures on the use, risks and harms of opioids is yet to be realised. SafeScript only became mandatory in early 2020 therefore, there is lack of information about utilisation, usefulness and actions from alerts generated by the system. It has hopefully provided the opportunity to improve collaboration between patients, prescribers and pharmacists in the provision of opioid medications in a safe and monitored manner and achieve better outcomes whilst reducing risk.

Collaboration between doctors and pharmacists is an important factor in the holistic management of patients using and dependent on opioids. However, a number of interprofessional barriers between doctors and pharmacists have been reported, including pharmacists having difficulty contacting doctors, often due to the receptionist 'gatekeeper' role, and doctors not being aware of the training and practices of pharmacists (Löffler et al., 2017; Rigby, 2010; Thornton et al., 2020). Despite this, pharmacist– physician collaboration has been shown to improve health outcomes for people in a number of conditions such as hypertension, diabetes and asthma (Benavides, Rodriguez, & Maniscalco-Feichtl, 2009; Carter et al., 2008; Ramser et al., 2008; Rigby, 2010). Pharmacists and physicians working together could assist to manage opioid dependent people in a more effective manner. One such opportunity to work together and increase access to MATOD could be shared care prescribing of MATOD by pharmacists and prescribers. This could be especially beneficial for increasing access to MATOD in rural areas. In addition to this, pharmacists may also have a potential role in administering the new long acting buprenorphine injections.

There is much potential for the expansion of the pharmacist's role in opioid management to include specialised opioid stewardship, greater roles in opioid risk reduction, roles in

identification and early intervention to prevent opioid related harm, treatment of opioid dependence and a role in improved effective pain management. Hospitals in Australia are advocating for improved opioid management by pharmacists with the SHPA releasing their paper "Reducing Opioid Related Harm: A hospital pharmacy landscape paper" in November 2018 (Society of Hospital Pharmacists Australia, 2018). They presented a number of key recommendations which included the development of evidence based guidelines for the prescribing and dispensing of analgesics post-surgery and supporting the implementation of opioid stewardship programs in public and private hospitals nationally (Society of Hospital Pharmacists Australia, 2018). The Australian Pharmaceutical Society are also advocating for pharmacists in opioid stewardship roles. In their 2020/21 federal budget submission they called for the government to *"Allocate $4 million for an 18-month pilot program of opioid stewardship pharmacists in general practices to reduce the harm caused by opioid medicines."* (Pharmaceutical Society of Australia, 2020).

Despite opportunity there are still many barriers to overcome to expand the role of pharmacists in opioid management. The majority of these relate to time, remuneration, training, resources and collaboration opportunities. In the community pharmacy setting, the pharmacist's time is often limited by normal workflow activities, such as verifying filled prescriptions, receiving phone calls, educating patients on their prescriptions, and monitoring technician work (Lindley et al., 2019; Wu et al., 2017). It could also be argued that the evolution of modern pharmacy practice has resulted in impersonal service with the utilisation of mail order, online, mobile apps and delivery pharmacy services or family members picking up prescriptions on behalf of patients. This does not allow for in-person screenings or assessment. In such settings, pharmacists can often only evaluate the patient solely on their prescription profiles or through PDMPs without direct communication. Additionally, tools cannot replace clinical judgement. Whilst useful, they cannot consider every single scenario, situation or patient factor. Pharmacists utilising opioid screening tools need to allow for multiple factors when making decisions to intervene with a patient, and whether to dispense. Thought must be put into the approach when administering screening questions and considering an intervention to ensure it is non-confrontational, non-judgemental and reduces the stigma associated with opioid use problems (Lindley et al., 2019). Training is an important factor here to ensure pharmacists are equipped with the skills to undertake this.

Future research needs to focus on how pharmacists could be used in the supply and management of opioids and opioid dependence in a cost-effective way that meets the needs of people using opioids. There is a need to further develop and test strategies and resources for

enhancing pharmacists' willingness, skills, and confidence in communicating with patients regarding problematic opioid use, collaborating with prescribers to improve pain management and prevent opioid misuse, conducting screening for problematic opioid use, and referring patients to and participating in substance use treatment. Opportunities also exist in the development of new and innovative approaches for harm reduction led by pharmacists, and in the examination and evaluation of the pharmacists' role in referral services, interventions and screening.

Utilising and building on the expertise that pharmacists have could potentially help carve out a specialised role for advanced practice pharmacists in the field of pain and addiction management. In this era where there is much debate and consideration regarding development of the roles of these highly trained health professionals, the area of pain and addiction management presents as an entirely suitable and necessary focus.

APPENDICES

APPENDIX 1: Other related authored publications

- Hamer, A. M., Spark, M. J., Wood, P. J., & Roberts, E. (2014). The upscheduling of combination analgesics containing codeine: the impact on the practice of pharmacists. *Research in Social and Administrative Pharmacy*, *10*(4), 669-678.

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- Downie, S. P., Wood, P. J., Summers, R. J., McDonough, M., & Wong, G. O. (2019). Hospital discharge opioid guidelines and policies: a Victorian survey. *Journal of Pharmacy Practice and Research*, *49*(1), 18-26.

- Nielsen, S., Kowalski, M., Wood, P., Larney, S., Bruno, R., Shanahan, M., Lenton, S., Dietze, P., Green, T., Murnion, B. & Ritter, A., (2019). Routine opioid outcome monitoring in community pharmacy: pilot implementation study protocol. *Research in Social and Administrative Pharmacy*, *15*(8), 1047-1055.

- Nielsen, S., Sanfilippo, P., Picco, L., Bruno, R., Kowalski, M., Wood, P., & Larney, S. (2020). What predicts pharmacists' engagement with opioid-outcome screening? Secondary analysis from an implementation study in community pharmacy. *International Journal of Clinical Pharmacy*, 1-10.

- Mckenzie, M., Johnson, J. L., Anderson, K., Summers, R., & Wood, P. (2020). Exploring Australian pharmacists' perceptions and attitudes toward codeine up-scheduling from over-the-counter to prescription only. *Pharmacy Practice (Granada)*, *18*(2).

- Alvin, M., Picco, L., Wood, P., Mnatzaganian, G., & Nielsen, S. (2020). Community pharmacists' preparedness to intervene with concerns around prescription opioids: findings from a nationally representative survey. *International Journal of Clinical Pharmacy*, 1-9.

- Opie, C., Wood, P., Haines, H., & Franklin, R. (2021), 'Here comes the junkies', the lived experience of opioid dependence by rural Australians. *Journal of Addiction Nursing, 32*(1) E1-E10.

APPENDIX 2: Statements of co-authorship

The following people and institutions contributed to the publication of work undertaken as part of this thesis:

Paper 1: Byrne, C.A., Wood, P.J., and Spark, M.J., Non-prescription supply of combination analgesics containing codeine in community pharmacy: A simulated patient study. Research in Social and Administrative Pharmacy; 2018. 14(1): p. 96-105.

Located in Chapter 4

Candidate contribution: The Candidate was a secondary author and research co-supervisor. With the first author and author three {primary supervisor and corresponding author), they contributed to the design and ethics approval of the research project. They provided advice and supervision for data collection and data analysis and the first draft of the manuscript. Along with author three they edited the first draft to ensure suitability for publication and made required changes post journal review.

Overall, the Candidate contributed approximately 20% to the planning, execution and preparation of the work for the paper.

We the undersigned agree with the above stated "proportion of work undertaken" for the above published (or submitted) peer-reviewed manuscript.

Signed Candidate Author 2:

Author 1:

Author 3:

Paper 2: Wood, P., et al., *Implementation of a clinical tool to assess and address pain management requests in the pharmacy.* Research in Social and Administrative Pharmacy, 2019. 15(7): p. 852-857**.**

Located in Chapter 5

Candidate contribution: The Candidate was the primary author and came up with the conception and design of the research project. They collected the data, were primarily responsible for the data analysis with guidance and contribution from author 4 and prepared the first draft of the manuscript. Overall, the Candidate contributed approximately 90% to the planning, execution and preparation of the work for the paper.

We the undersigned agree with the above stated "proportion of work undertaken" for the above published (or submitted) peer-reviewed manuscript.

Signed Candidate Author 1:

Author 2: Joe Tucci

Author 3: Karen Anderson

Author 4: George Mnatzaganian

Paper 3: Maher, E., Nielsen, S., Summers, R., and Wood, P. *Core competencies for Australian pharmacists when supplying prescribed opioids – a modified Delphi study*. International Journal of Clinical Pharmacy, 2020.

Located in Chapter 6

Candidate contribution: The Candidate was a secondary author and research supervisor. With the primary author and authors 2 and 3, they contributed to the conception, design and ethics approval of the research project. They provided advice and supervision for data collection and data analysis and the first draft of the manuscript. They edited the first draft to ensure suitability for publication with input from author 2 and made required changes post journal review.

Overall, the Candidate contributed approximately 30% to the planning, execution and preparation of the work for the paper.

We the undersigned agree with the above stated "proportion of work undertaken" for the above published (or submitted) peer-reviewed manuscript.

Signed Candidate Author 4:

Author 1: (Ella Maher)

Author 2: (Suzanne Nielsen)

Author 3: (Richard Summers)

Paper 4: Nielsen, S., et al., *Routine opioid outcome monitoring in community pharmacy: Outcomes from an open-label single-arm implementation-effectiveness pilot study.* Research in Social and Administrative Pharmacy, 2020.

Located in Chapter 7

Candidate contribution: The Candidate was a secondary author. With the primary author and other secondary authors, they contributed to the conception, design and ethics approval of the research project. They assisted with participant recruitment and the first draft and subsequent drafts of the manuscript including changes post journal review.

Overall, the Candidate contributed approximately 15% to the planning, execution and preparation of the work for the paper.

We the undersigned agree with the above stated "proportion of work undertaken" for the above published (or submitted) peer-reviewed manuscript.

Signed Candidate Author 5:

Author 1: (Suzanne Nielsen)

Author 2: (Louisa Picco)

Author 3: (Michala Kowalski)

Author 4: (Paul Sanfilippo)

Author 6: (Sarah Larney)

Author 7: (Raimondo Bruno)

Author 8: (Alison Ritter)

Paper 5: Wood, P., et al., *"A lot of people call it liquid handcuffs"–barriers and enablers to opioid replacement therapy in a rural area.* Journal of Substance Use, 2019. 24(2): p. 150-155.

Located in Chapter 8

Candidate contribution: The Candidate was the primary author and along with author 2 came up with the conception and design of the research project. With author 2 they collected the data and were responsible for data analysis with guidance and contribution from authors 2, 4 and 5. They prepared the first and subsequent drafts of the manuscript. Overall, the Candidate contributed approximately 75% to the planning, execution and preparation of the work for the paper.

We the undersigned agree with the above stated "proportion of work undertaken" for the above published (or submitted) peer-reviewed manuscript.

Signed Candidate Author 1:

Author 2:	Cynthia Opie
Author 3:	Joe Tucci
Author 4:	Richard Franklin
Author 5:	Karen Anderson

Appendix 3: Copyright statement

I warrant that I have obtained, where necessary, permission from the copyright owners to use any of my own published work in which the copyright is held by another party.

APPENDIX 4: Methodology paper

Routine opioid outcome monitoring in community pharmacy: Pilot implementation study protocol

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Routine opioid outcome monitoring in community pharmacy: Pilot implementation study protocol

Suzanne Nielsen[a,b,*], Michala Kowalski[a], Pene Wood[c,d], Sarah Larney[a], Raimondo Bruno[a,e], Marian Shanahan[a], Simon Lenton[f], Paul Dietze[g,h], Traci Green[i,j], Bridin Murnion[k], Alison Ritter[a,l]

[a] National Drug and Alcohol Centre, University of New South Wales, Sydney, Australia
[b] Monash Addiction Research Centre, Monash University, Melbourne, Australia
[c] Latrobe University, Bendigo, Victoria, Australia
[d] Western Victoria Primary Health Network, Geelong, Victoria, Australia
[e] School of Medicine, University of Tasmania, Hobart, Australia
[f] National Drug Research Institute, Curtin University, Perth, Australia
[g] The Centre for Population Health, Burnet Institute, Melbourne, Victoria, Australia
[h] The School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia
[i] Department of Epidemiology, Brown University School of Public Health, Rhode Island, USA
[j] Boston Medical Center, Injury Prevention Center, Boston University School of Medicine, Boston, USA
[k] Department of Addiction Medicine, University of Sydney, Sydney, Australia
[l] Drug Policy Modelling Program, University of New South Wales, Sydney, Australia

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ABSTRACT

Background: Increases in opioid use and related harms such as mortality are occurring in many high income countries. Community pharmacists are often in contact with patients at risk of opioid-related harm and represent an ideal point for intervention. Best practice in monitoring opioid-related outcomes involves assessing analgesia, pain functioning, mood, risks and harms associated with opioid use. Community pharmacists are well-placed to undertake these tasks.

Objectives: Our pilot study will test the implementation of a computer-facilitated screening and brief intervention (SBI). The SBI will support pharmacist identification of opioid-related problems and provide capacity for brief intervention including verbal reinforcement of tailored information sheets, supply of naloxone and referral back to the opioid prescriber. The SBI utilises software that embeds study procedures into dispensing workflow and assesses opioid outcomes with domains aligned with a widely accepted clinical framework.

Methods: We will recruit and train 75 pharmacists from 25 pharmacies to deliver the Routine Opioid Outcome Monitoring (ROOM) SBI. Pharmacists will complete the SBI with up to 500 patients in total (20 per pharmacy). Data will be collected on pharmacists' knowledge and confidence through pre- and post-intervention online surveys. Data on feasibility, acceptability and implementation outcomes, including naloxone supply, will also be collected.

Project impact: Our study will examine changes in pharmacists' knowledge and confidence to deliver the SBI. Through the implementation pilot, we will establish the feasibility and acceptability of a pharmacist SBI that aims to improve monitoring and clinical management of patients who are prescribed opioids.

Introduction

Increases in opioid use, opioid-related harms and opioid-related mortality have been reported in Australia and many parts of the world.[1–3] In Australia, opioid prescribing increased 15-fold between 1992 and 2012,[4] and opioid overdose deaths increased by 64% in the decade to 2015, driven largely by deaths involving pharmaceutical opioids.[5] Australia has one of the highest rates of prescribed opioid use in the world, with 13% of the population estimated to use a prescription opioid in a given year.[6] These high rates of use and escalating mortality call for new approaches to reduce opioid-related harm.

Australia is not alone in this challenge. The use of opioids for pain treatment has increased disproportionately in North America, Europe and Oceania.[7] Increases in opioid prescribing are strongly correlated

* Corresponding author. Monash Addiction Research Centre, Monash University, Peninsula Campus, Frankston, VIC 3199, Australia.
E-mail address: suzanne.nielsen@monash.edu (S. Nielsen).

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with increases in morbidity, such as opioid dependence, and mortality.[2] The gravity of this situation is highlighted by the recent *reduction* in US life expectancy, attributed to opioid overdose death,[8] described as an 'opioid crisis'.[9]

Overdose and dependence are not the only challenges to the safe use of prescribed opioids. Other morbidities are also common in populations who are prescribed opioids; half report moderate to severe depression, and one in three report a lifetime alcohol use disorder.[10,11] Benzodiazepine use, a common contributor to opioid overdose related morbidity and mortality, is reported by one in three in samples of people prescribed opioids for chronic pain.[12,13] Given the high-prevalence of opioid-related risk among those prescribed opioids, universal measures to identify and address this risk are warranted.

Community pharmacists are highly skilled health professionals who are centrally involved in the supply of pharmaceutical opioids. Research has established a capacity for, and interest in, pharmacist-led naloxone supply and involving pharmacists in assessing and responding to opioid-related risk.[14–16] Screening and brief interventions (SBI) for substance use are effective in primary care[17–19] and there is demonstrated feasibility and acceptability for pharmacist-led SBI for detecting risky alcohol use.[20,21] Algorithms have been proposed to support community pharmacists to identify potential opioid misuse,[22] and pharmacist-led chronic pain clinics have been shown to be feasible and acceptable.[23] Together this work suggests that community pharmacy may be a suitable setting for administering SBI for those who are prescribed opioids for pain.

There are many examples where pharmacists already have impact in the area of opioid-related harm. Research has examined screening, brief intervention and referral to treatment (SBIRT) with opioids in ED settings, and established training requirements and frameworks for care within community pharmacy.[24–26] Substantial evidence also supports the provision of naloxone for overdose prevention.[27,28] Pharmacists can independently initiate naloxone supply in a number of jurisdictions, including Australia, where naloxone is available as an over-the-counter medicine.[29–31] Prescription drug monitoring programs (PDMP) also give pharmacists additional opportunity to address opioid-related risk.[32] Despite this opportunity, and a strong foundation of research, few models for structured SBIRT exist to identify problems with opioids earlier in the course of risky opioid use, or to identify patients suitable for naloxone supply. Our pilot implementation study aims to address that gap by testing if a computer-facilitated brief intervention can assist pharmacists screen for opioid-related risk and facilitate provision of further assessment, education, and referral back to the opioid prescriber if appropriate.

Aims

Our pilot study will test the implementation of a Routine Opioid Outcome Monitoring (ROOM) SBI in community pharmacy practice. Specifically, we aim to:

1. explore whether training to deliver the ROOM SBI increases pharmacists' knowledge and confidence in delivering the SBI;
2. explore whether the ROOM SBI facilitates patient education, naloxone delivery and referral;
3. test whether pharmacist-delivered brief routine opioid outcome monitoring is feasible; and
4. test whether our intervention package is acceptable to pharmacists and consumers.

Methods

Study design and setting

An advisory committee was established prior to developing the intervention, to enable input of multiple stakeholders from pharmacy, primary care and specialist addiction and pain medicine health professionals, policymakers, and consumer organizations. We took a multifaceted implementation approach, including strategies of participatory research, academic detailing, computerized decision-making support and multidisciplinary collaboration, as such approaches have been demonstrated to be more effective than single interventions in previous work.[33–36] The co-design process involved consultation with pharmacists (n = 10) and consumers (n = 5), in addition to input from the research team and advisory committee. Pharmacists, consumer representatives, pain and addiction medicine specialists assisted developing the intervention, refining the patient and healthcare professional feedback messages, informing where screening would fit best in dispensing workflow, and how to present ROOM to patients; reflecting the demonstrated value of multidisciplinary approaches in this area.[37,38]

We are conducting the study in community pharmacies in three geographic regions within two states of Australia (Victoria and New South Wales), with the pharmacy locations selected to cover metropolitan, regional and rural settings. Based on the initial consultation as to what works in a busy pharmacy setting, our study leverages technology to embed the ROOM screening tool into pharmacy dispensing software to ensure the intervention is minimally disruptive to usual pharmacy workflow and is as automated as possible. First, the dispensing software prompts pharmacists to offer the screen (only once to each patient) when an eligible opioid is dispensed (i.e. a second or subsequent opioid prescription for non-cancer pain). The software determines eligibility automatically using the patient's medication history at the individual pharmacy. Second, the brief screening questions are self-completed by the patient using a computer tablet or non-dispensing computer while the patients' prescription is being dispensed, with these parallel processes designed to be time efficient for both the pharmacist and the patient. Finally, data entered by both the pharmacist and patient are used to inform the automated creation of tailored information sheets for the patient and their opioid prescriber. The pharmacist then delivers the brief intervention, providing education based on the key points on the patients' information sheet, with the pharmacist education acting as a verbal reinforcement for the tailored written material. Results are saved in the software to enable later review (e.g. to examine pain outcomes over time).

It is anticipated that the screening component (taking less than 5 min) would occur while the prescription is being dispensed, and the brief intervention component may take an additional 5–15 min of the pharmacist time (depending on the results of the screen) with the pharmacist verbally reinforcing the information and recommending follow-up with the prescriber where warranted. We are piloting the single administration of the ROOM tool (i.e. once per participant), but in routine practice it is envisaged that the tool would be administered repeatedly to monitor outcomes with opioids over time. The software platform itself is one that integrates with all 17 dispensing platforms in Australia, maximizing opportunities to sustain the intervention after the study.

Ethics

The study was approved by the Human Research Ethics Committee of the University of New South Wales (UNSW HREC reference: # HC17760) and ratified by Latrobe and Monash University.

Brief screening tool development

The ROOM screening tool was developed for use in community pharmacy settings, with the aim of addressing known barriers that may prevent pharmacists from identifying concerns with opioids in the absence of a structured intervention. The ROOM screening tool was designed for patient self-complete as: 1) not all pharmacists feel comfortable initiating discussions on mental health or substance use with patients[39,40]; 2) self-completion represents a fast and efficient way to

Table 1
Summary of items in the Routine Opioid Outcome Monitoring Tool.

Domain	Tool used	Relevant items
Analgesia	Three items assessing Pain, Enjoyment of life and General Activity (PEG)[57] (First item)	What number (out of 10) best describes your pain on average over the past 7 days?
Activity	PEG (3-item tool)[57] (Second two items) (Cronbach alpha 0.73–0.89)	What number (out of ten) best describes how, during the past week, pain has interfered with your enjoyment of life? What number (out of ten) best describes how, during the past week, pain has interfered with your general activity?
Adverse Effects	Two-part question on constipation Single item from Prescribed Opioid Screening Tool[58]	Are you experiencing constipation? (if yes, are you currently taking anything for constipation?) In the past three months did opioid medicines cause you to feel slowed down, sluggish or sedated?* (also below)
Aberrant Drug-Related Behaviors	4-item Prescribed Opioids Screening Tool to identify opioid dependence (validated against the CIDI, 77% sensitivity and 77% specificity against ICD-10 dependence)[58]	In the past three months in times of worse pain did you use more opioid medicines than prescribed? In the past three months did opioid medicines cause you to feel slowed down, sluggish or sedated? In the past three months did opioid medicines cause you to lose interest in your usual activities? In the past three months did you worry about your use of opioid medicines? (Options: not at all, a little, quite a lot, a great deal)
Affect	Patient Health Questionnaire-2 (PHQ-2)[56]	How often have you been bothered by the following problems: (not at all, several days, more than half the days, nearly every day) -Little interest in doing things -Feeling down, depressed or hopeless
Alcohol	Single question alcohol screening test.[55]	How many times in the past year have you had 4 (for women) or (5 for men) or more drinks in a day? ____

collect patient information; 3) allowing patients to self-complete questions on a secure computer or tablet device provides confidentiality, and removes the need for patients to disclose sensitive information verbally, addressing consumers expressed preferences for privacy and confidentiality[41]; and 4) patients are more likely to disclose problematic substance use when self-reporting via a computer, demonstrated by research in wide ranging populations from drug treatment samples[42] to oncology patients[43] which find increased reporting of sensitive information when a computer or tablet is used, rather than face-to-face interactions.

Best practice in monitoring opioid-related outcomes involves assessing analgesia, functioning, mood, dependence, and side effects including sedation and constipation.[44] Table 1 shows the content of the 12-item ROOM screening tool, which was developed based on the '4As' model of monitoring outcomes with opioids, focusing on four key domains of Analgesia, Activity, Adverse effects and Aberrant drug-related behaviors (or addiction-related outcomes).[45] These four domains are the same as those that initially informed the development of a 41-item clinician-completed assessment.[45] We did not use this tool as it is clinician completed, and the length (41 items) was inappropriate for brief screening. Instead, we developed a brief tool that covered the same domains of the original instrument using a range of validated brief screening tools. Tools that form the ROOM screening tool were selected based on the briefest validated measures available to cover these key domains. We also included an item measuring the fifth 'A' of affect (or mood) which has been commonly included as a recommended domain for routine monitoring.[46] An item to assess risky alcohol use was added due to the high prevalence of alcohol use disorder among people with chronic pain,[47] and the frequent involvement of alcohol in opioid overdose.[48] Consultation with community pharmacists and the advisory panel revealed that a holistic approach to the monitoring of patient outcomes with opioids using this framework was more relevant to a community pharmacy patient population, and more acceptable to pharmacists, than questions focusing solely on overdose risk and opioid-dependence.

Five overdose risk indicators, which the pharmacist completes as part of the dispensing checks, supplement the assessment via the ROOM screening tool. These five items were based on medication history and reflect characteristics associated with increased overdose risk including high opioid dose (defined as a daily dose of greater than 100 mg oral morphine equivalents), concurrent sedative medications (e.g. benzodiazepines), recent opioid dose increase, use of multiple opioid formulations, or receiving opioids from multiple prescribers and/or pharmacies.[1,12,49–51] If any identified overdose risk measure is endorsed, pharmacists are prompted via the software to offer naloxone to patients alongside the prescribed opioid.

Implementation frameworks

We used the Consolidated Framework For Implementation Research (CFIR) to consider factors that would promote implementation[52] and used the FISpH adaptation of CFIR[53] to identify additional factors specific to community pharmacy CIFR.[53] The theory of planned behavior informed the development of the intervention,[54] with different aspects of the intervention designed to increase the pharmacists' capability, motivation and opportunity to identify and respond to prescription opioid-related problems. These were enacted through training, automation of procedures, education about harms associated with opioids, and highlighting the opportunities for pharmacists to have an important role in responding to these harms.

Participants

Eligibility criteria

Pharmacies. Eligible pharmacies will:

a) Be located in one of three participating health regions (Central and Eastern Sydney, Western Sydney, and Western Victoria) in the two participating states of New South Wales and Victoria.
b) Dispense at least five opioid prescriptions per day;
c) Be willing to perform all study related tasks;
d) Have a tablet computer or other device that participants can complete the screening tool on;
e) Be willing for up to three pharmacists at the site to receive training and participate in the study; and
f) Be willing to recruit 20 participants to participate in the study.

Patients. Eligible patients will be:

a) receiving a repeat supply of opioids for non-cancer pain from an

enrolled pharmacy;
b) 18 years of age or over;
c) able to provide voluntary informed consent; and
d) willing and able to self-complete the Routine Opioid Outcome Monitoring tool in the pharmacy.

Criteria c) and d) require the patient to be collecting their medication in person.

Participating pharmacies (n = 25 pharmacies) will each invite 20 patient-participants who are being prescribed opioids to be involved in the study (n = up to 500 participants in total).

Recruitment

Pharmacy recruitment

Pharmacies will be recruited via professional pharmacy networks (e.g. The Pharmacy Guild of Australia), in addition to targeted pharmacist advertising through participating Primary Health Networks and word of mouth.

Patient recruitment

The purpose-built ROOM software integrates with the 17 different pharmacy dispensing software programs used in Australia. The software will identify potentially eligible participants (i.e. receiving a second or subsequent opioid prescription and aged 18 or older) at the point of dispensing opioid prescriptions. When prompted, pharmacists who have been trained on the study procedures will confirm eligibility and invite participants to be involved in the study, giving a brief verbal explanation and providing a computer tablet or other internet-enabled device for completion of online informed consent and screening. Participants will read the online participant information statement and indicate consent by ticking boxes to indicate that they agree to each of the study procedures. Following this, the patient will self-complete the 12-items in the ROOM tool. Where patients decline to participate this will be captured in the software (with brief reasons from a dropdown list) to inform feasibility.

Study procedures

Pharmacy procedures

The study will recruit 25 community pharmacies (Fig. 1). The owner or pharmacist-manager will be invited to participate and provide written informed consent. The owner or pharmacist-manager will invite additional pharmacists (up to 3 pharmacists per pharmacy) to participate. Pharmacists at participating pharmacies will initially be invited to complete a baseline survey (with online informed consent) to assess current knowledge, confidence, perceptions and practices relating to providing SBI in the pharmacy. Following completion of the baseline survey, pharmacists will participate in a training webinar covering all aspects of delivering the ROOM intervention including the provision of relevant counseling based on the participants' response (see Fig. 2).

Once all pharmacists at a given pharmacy who are involved in the study have been trained, the pharmacy will be provided with access to the ROOM software to commence the SBI with patients in the pharmacy. Each enrolled pharmacy will be asked to recruit 20 consecutive patients to complete ROOM. Once 20 patients at a pharmacy complete the SBI, a follow-up online survey will be sent to the individual pharmacists from that pharmacy. Pharmacists will continue to have access to the software after they have completed the SBI with 20 participants. Data will be collected on the ongoing delivery of the ROOM SBI after the initial 20 participants, and this will be assessed as a measure of sustainability of the program.

Outcome data will be collected by the pharmacist the next time a participant attends the pharmacy with an opioid prescription after completing the ROOM tool. At this visit the pharmacist will record any outcomes from the ROOM SBI.

Pharmacist training

Webinars will be used as the primary medium for training delivery as this offers the greatest flexibility for pharmacists outside metropolitan locations and those operating in extended-hours pharmacies.

The training webinar will cover the content of the ROOM tool, key counseling points when participants screen positive on any of the screening items, counseling points on the use of naloxone and opioid overdose symptoms, and referral processes where participants with clinically significant and immediate risk are identified as part of the study. Pharmacists will have the option to attend an interactive webinar with live assessment or watch a pre-recorded webinar and submit an assessment. The assessment questions will be embedded throughout the webinar for the pharmacists to complete during training. The assessment questions will serve a dual purpose of exploring whether the pharmacists were able to respond correctly after the training and as a means to determine whether participating pharmacists are engaging with the training materials. Qualified pharmacists are available to address pharmacist queries that arise during the training and to provide support at any time during the study.

Additional professional development resources on each aspects of the ROOM intervention (pain management, opioid dependence, depression, alcohol brief interventions, opioid-induced constipation and motivational interviewing) are provided following the webinar for further self-directed continuing education. These materials are provided in response to the pharmacist indicating areas that they would like to improve knowledge or confidence (submitted with the assessment quiz), and recognizes that different pharmacists will have different levels of expertise in each of the areas covered.

Patient procedures

After providing online informed consent, the participant will self-complete the 12-item ROOM screening tool, which includes the validated measures for pain, opioid dependence, depression and risky alcohol use[55–58] (See Table 1). Concurrently, the pharmacist will complete the dispensing checks to document identified risk factors demonstrated to be associated with both opioid dependence and overdose (e.g. dose > 100 mg of morphine equivalents, concurrent benzodiazepine use, escalating opioid use and presence of multiple opioid formulations or prescribers).[1,49] Based on the pharmacist- and patient-completed information, summary documents with tailored health information (based on the patients' responses) will be generated. It is intended that the pharmacist will then provide counseling to verbally reinforce the points raised through the screening, address any concerns raised, and provide information relating to medication safety. For example, where risky alcohol use is identified, the patient will receive information about current level of alcohol use and potential interactions with pain medication, and a brief intervention following the '5As' framework when reinforcing the printed information[59]; a patient that reports severe pain despite a high dose of opioids will be provided with information about pain management; and a patient with overdose risk will receive information on overdose risk and naloxone. Patients will only receive information relevant to their screening responses.

As part of the ROOM SBI the patient will receive:

- A printed patient summary, including tailored information based on the patients' responses to the screening tool, and information on opioid safety, safe storage, and safe disposal of opioids.
- Verbal reinforcement of printed information by the dispensing pharmacist;
- A summary letter for the patients' opioid prescriber; and
- When any opioid overdose risk factor is reported, information on naloxone and the offer of naloxone supply (see below).

Patients with any identified opioid overdose risk factors will receive brief education on opioid overdose risk and will be offered naloxone. Pharmacists will invite the patient to involve a family member or carer

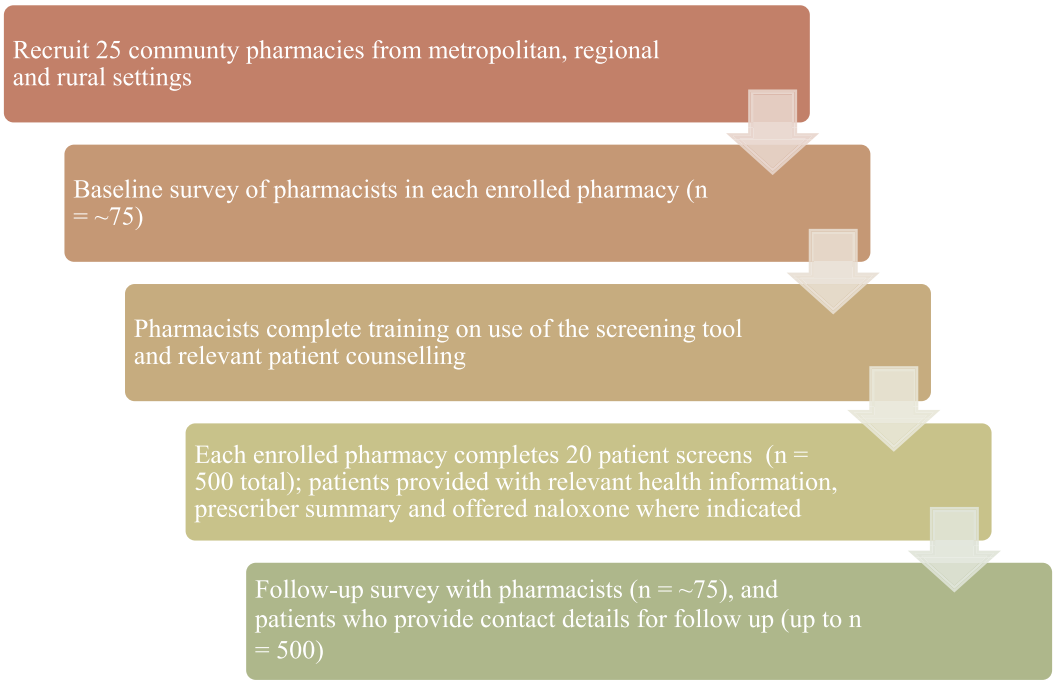

Fig. 1. Study flow of pharmacist and patient activities.

to receive information on naloxone if they are present, or alternatively will be provided with information for the carer or family member with an invitation for them to ask questions or receive additional information about naloxone at a later time if the patient is attending alone.

On completion of the ROOM screening questions, participants will be invited to leave an email address to receive a brief evaluation questionnaire. This will capture the patients' satisfaction with the ROOM tool, counseling provided by the pharmacist, intentions to follow-up with their opioids prescriber, and naloxone supply. Those who complete the evaluation survey can enter a draw to win an iPad.

Finally, pharmacists will be instructed to assess if, in their clinical opinion, there is any immediate issue of patient safety. This assessment is based on patient responses and pharmacists dispensing checks described above. In these cases, forwarding the printed patient information alone may not satisfy the pharmacist's duty of care, and pharmacists are instructed to directly contact the patient's prescriber to discuss their concerns. This is in addition to forwarding a summary of the outcomes directly to the prescriber via the standard procedures that pharmacy has in place for secure transfer of patient information (e.g. by post or secure file transfer).

Pharmacist reimbursement

Pharmacists are reimbursed $20 for completion of the baseline and follow-up surveys, $40 for participating in the training webinar and $10 per SBI completed.

Measures

Measures collected as part of the study are detailed in Table 2. Data will be collected from the patient or pharmacist directly and/or extracted from dispensing records or ROOM software. The ROOM software automatically collects data on patient age category (10-year groups), gender, current medications (3-month history), ROOM tool responses and outcomes from delivery of the ROOM intervention (e.g. medication changes or prescriber follow up collected at next patient visit). Outcomes measures will be collected at the subsequent patient visit at that pharmacy after the initial completion of the ROOM tool. Four pharmacist-completed questions will document patient follow-up with their GP, any medication changes and any other outcomes of the ROOM SBI.

Measures collected from pharmacists include demographic and pharmacy characteristics, frequency of current opioid and naloxone supply, attitudes towards harm reduction, knowledge and confidence around responding to problems with prescribed opioids. These measures are based on those used in a previous nationally representative study of community pharmacists which will allow an assessment of the representativeness of the study sample.[60] Additionally, pharmacists attitudes toward evidence-based practice are assessed using an adapted Evidence-Based Practice Attitude Scale (EBPAS),[61] at the baseline interviews and at the follow up interviews; as well as exploring satisfaction (from 0 to 10) on the ease of use of the monitoring tool,

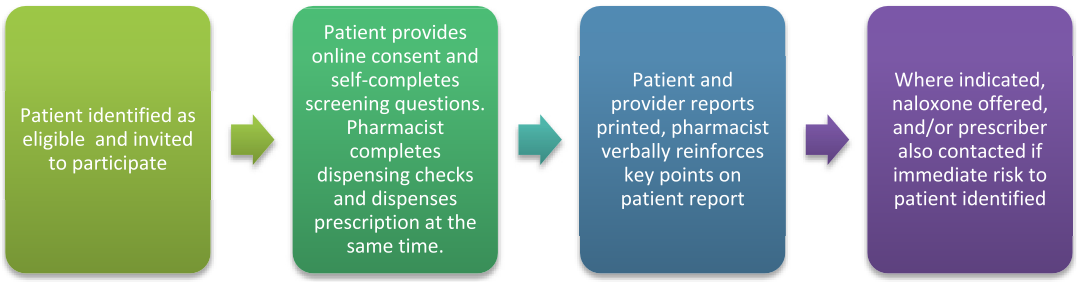

Fig. 2. Process of care with screening and brief intervention.

Table 2
Measures, data sources and timepoints for data collection.

	Measures	Baseline[a]	Follow-up (patient)	Follow-up (pharmacist)	ROOM software
Patient measures					
Demographics	Age (10 year groups), gender	✓			
Medication use	Current prescribed medication use (up to the past 3 months) (extracted from software with patients' consent)	✓			✓
ROOM questions	Current pain, opioid dependence risk, depression, alcohol use and opioid-induced constipation (see Table 1)	✓			
Acceptability of ROOM	Ease of use, relevance of information, time for completion (Score 0–10)		✓		
Outcome of intervention	Outcome of the Routine Opioid Outcome Monitoring (Topics on which counseling from drop down list, referral made and intentions to follow up from drop down list & details naloxone supply)		✓		
Pharmacist measures					
Demographics	Age (10 year groups), gender, years of practice[60]	✓			
Pharmacy setting	Pharmacy type (independent, small or large chain), location and other pharmacy services delivered (return of unwanted medicines, pain management services, mental health services, diabetes screening, Medschecks, home medication reviews, blood pressure screening and 'other'[60]	✓			
Prescription opioid supply	Frequency of opioid dispensing (< 1/day around once per day, several times a day or > 10/day), current strategies for problematic opioid use (4 point scale from never to almost always for making clinical notes, monitoring, discussing with customer, counseling on overdose risk, discussing side effects, calling opioid prescriber, referring back to prescriber, referring to drug treatment, telling customer drug is out of 'stock', refusing supply and notifying police), confidence in identifying and responding to problematic opioid use (5 point scale from not at all to extremely)[60]	✓		✓	
Implementation	Evidence-based Practice Attitude Scale[61] [adapted for pharmacy relevance] (reliability coefficient = .74)[63]	✓		✓	
Pharmacist training	Post-graduation training on pain, opioid dependence, mental health (Yes or no)	✓			
Harm reduction	Perceptions of harm reduction (Cronbach's alpha = 0.797)[60]	✓		✓	
Overdose risk and naloxone knowledge	Opioid Overdose Knowledge Scale 10 items with sum score range (0−45) (Cronbach's alpha = 0.83)[64]	✓		✓	
Naloxone supply	Is naloxone stocked and ever dispensed[60]	✓		✓	
ROOM outcomes	Pharmacist contact with prescriber, prescriber follow-up with patient, any medication changes, any other changes as a result of the SBI, and any other clinical outcomes (prompted to enter via dispensing software at next patient visit for opioid supply after completing SBI)				✓
Acceptability of intervention	Time taken to deliver the intervention (average in minutes), perceived remuneration value (in $AUD), satisfaction with ease, printout content and relevance of using ROOM tool (Scale 0–10)	✓		✓	
Implementation measures					
Reach	Proportion of eligible patients offered the screen, representativeness of the participants (compared with those eligible but not screened on age group, gender and type of opioids dispensed)				✓
Effectiveness	Proportion of patients with opioid-related risk where prescriber contacted & proportion of patients that received naloxone				✓
Adoption	1) Representativeness of pharmacies that volunteered for the study; 2) proportion of pharmacies that meet the target of 20 patients screened.	✓			✓
Implementation	Proportion of cases where intervention was delivered as per the study protocol (i.e. all steps completed and proportion of cases where medication risk factors are correctly identified)				✓
Maintenance	Number of pharmacies that continue using the ROOM tool after the initial 20 patients				✓

[a] Pharmacists complete baseline surveys before receiving training and access to the ROOM software.

relevance and usefulness of the printed information.

Data to assess implementation are collected according to the RE-AIM framework.[62] Measures of Reach, Efficacy, Adoption, Implementation and Maintenance are outlined in Table 2. These data are largely drawn automatically from the ROOM software, including information on rates of participation in the intervention and a comparison of patient characteristics of those that are screened versus those that decline to participate. These data will determine whether the intervention is reaching the target population, if those who complete the intervention are representative of the broader population of patients receiving opioids, and whether delivery of the intervention continues after the pharmacies complete the minimum of 20 patient screens. Fidelity of the intervention can be determined, in part by assessment of concordance between risk factors in the medication history and pharmacist documented risk-factors.

Outcomes

Outcomes to explore efficacy are:

E − 1. Change in pharmacist knowledge and confidence.
E − 2. The proportion of patients who report they were offered naloxone, and of those offered naloxone, how many received it (either purchased it over the counter or supplied with a prescription).
E − 3. Where risk factors were identified, the proportion of patients who either self-report that they have attended/intend to attend an appointment with their opioid prescriber one week following completing the ROOM SBI, or report to the pharmacist that they have attended a follow-up appointment with their GP at their next pharmacy visit.
E − 4. Medication changes by the prescriber following participation in the ROOM SBI.

Feasibility and implementation outcomes are:

FI-1. Acceptability of the ROOM tool to patients and pharmacists.
FI-2. Proportion of pharmacies that meet target numbers (n = 20) with ROOM tool within 2 months of completing the first screen.
FI-3. The proportion of eligible patients that are invited and consent to complete the ROOM tool.
FI-4. Representativeness of patients that complete the ROOM tool versus decline (based on comparison of characteristics from dispensing software).

Data collection methods

Pharmacists: Pre-intervention and post-intervention online surveys (Outcomes E − 1, FI-1).

Patients: 12-item screening tool completed on a tablet in the pharmacy, brief outcome-evaluation survey online: emailed 1 week after completing the monitoring tool (Outcomes E − 2, E − 3, FI-1).

Pharmacy dispensing software: Through the online program, data will be extracted to explore efficacy, feasibility and implementation outcomes (Outcomes E − 3, E − 4, FI− 2, 3, and 4).

For patients who participate in the project, data on age (in 10- year age groups), gender, pharmacist-identified risk factors relating to opioid supply, results of the screening tool, and a three-month snapshot of medications dispensed will be extracted for use in analyses to describe the sample and their level of medication-related risk. For patients who receive an eligible opioid prescription but decline to participate, data on age (in 10- year groups), gender and the opioid prescribed will be collected and compared to those that participate to assess sample representativeness across these variables. Data are provided in a de-identified format via a secure file transfer system to protect patients' privacy.

Sample size and analyses

Sample size calculations were conducted with G*Power software to ensure that the study was appropriately powered to determine changes in the primary outcome of pharmacists' knowledge and confidence in opioid-risk before and after training, comparing the pharmacist pre- and post-study results using paired-t-tests. A previous study of Australian pharmacists determined that pharmacists were able to correctly answer 1.8 out of 5 (standard deviation, [SD] = 1.7) questions on naloxone use.[60] A meaningful increase in knowledge would have pharmacists answering most questions correctly (a score of 3 out of 5). Assuming a pre-intervention mean of 1.8 (SD = 1.7) and a correlation of 0.7 between measures, 25 pharmacies with three pharmacists each (75 total) would provide 90% power to detect a post-intervention mean of 3.0 (SD = 1.7) at a two-sided significance level of 0.05. Similarly, previous data indicate that 34% of pharmacists were confident that they could identify appropriate patients with opioid-related risk and provide them with naloxone.[60] To be able to detect a meaningful increase from 34% to 60% (i.e. the majority) of pharmacists reporting such confidence, a sample size of 59 pharmacists achieves 95% power to detect a statistically significant difference with a significance level of 0.05. Both calculations demonstrate that with up to 75 pharmacists we are powered to detect these differences from training.

The sample size of 500 patients is a pragmatic choice to enable each pharmacy to screen at least 20 patients. To enable testing the procedures in a range of pharmacies we plan to recruit 25 pharmacies across three regions, with up to 20 screens per pharmacy, representing up to 500 patients.

In addition to demonstrating effective change in knowledge and confidence, data from the remaining outcomes measures will be used to determine recruitment rates and assess the prevalence of opioid-related risk among a broad number of people receiving prescribed opioids (n = up to 500), which will all inform power calculations for a later planned cluster randomized implementation-efficacy study. Descriptive statistics will be used to summarize the participant populations, medication histories, opioid-risk profiles and intervention outcomes.

Implications and discussion

There is an urgent need to identify opioid-related risk and reduce opioid-related harm. Our study will test a multifaceted approach to implement pharmacist-led SBI in a community pharmacy setting through use of our ROOM SBI. The intervention is planned to be low-cost, brief and scalable so that it could be implemented in a wide range of settings; including geographically remote settings where opioid-related harm is high and interventions such as naloxone provision are crucial due to long wait times for ambulance attendance. Delivering ROOM to all patients receiving repeat opioid prescriptions for non-cancer pain aims to reduce stigma that can result from targeting patients with specific characteristics and will inform a better understanding of prevalence of opioid-related risk among those prescribed opioids. The use of a self-completed screening tool encourages accurate responses through a computer interface and is time-efficient. We will determine if implementing the ROOM tool in community pharmacy settings is feasible and acceptable to patients and pharmacists, and if it leads to improved knowledge and clinical outcomes. Results will be used to inform future work that aims to leverage pharmacists' unique potential in identifying and responding to opioid-related risk.

Our study design has a number of strengths. These include the use of purpose-built software that integrates with pharmacy dispensing software so that delivery of ROOM is embedded in pharmacy workflow, including automated informed consent and data collection procedures, technology-facilitated intervention with automated and tailored patient and prescriber information, all of which assist pharmacists to deliver information in a time-efficient way. Other strengths include the testing of feasibility in a range of pharmacies and collection of a range of

patient and pharmacist rated acceptability measures. This detailed protocol, and the findings of this pilot may help pharmacies and pharmacists elsewhere implement similar interventions in a rigorous manner. Limitations of the study design include analyses based on pre-post measures, the use of a single condition with no comparison arm, and lack of longer-term patient follow-up. Although recognized as a limitation, these features are consistent with a pilot implementation trial.

Future research

Findings from our feasibility study will be used to inform a larger cluster randomized controlled implementation-efficacy study to compare the ROOM intervention with standard care. The cluster randomized trial will test the primary outcome of whether a brief pharmacy intervention can reduce opioid-related risk, improve patient knowledge and outcomes, and increase naloxone supply compared with standard care. The larger cluster randomized trial will target those with high risk identified through screening. The planned trial will include a detailed health economics assessment to determine if a pharmacy SBI is cost-effective compared to a low intensity intervention, such as passive information via a pamphlet, in identifying opioid-related risk and reducing opioid-related harms.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sapharm.2018.10.024.

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