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Determining the prevalence of use of over-the-counter (OTC) codeine-containing products in the central Johannesburg area: A mixed methods study.

Amirah Asmall



A dissertation submitted to the Faculty of Health Science, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Master of Pharmacy.

Supervisors:

Rubina Shaikh
Stephanie Leigh (de Rapper)
Zelna Booth
Nabeelah Bemath
David Bayever

Declaration

I, Amirah Asmall, declare that this dissertation is my own, unaided work and has not been submitted before for any degree or examination at any other University. All sources that I have used or quoted have been indicated and acknowledged by complete references. This dissertation is being submitted for the Degree of Masters in Pharmacy at the University of the Witwatersrand, Johannesburg.



Amirah Asmall	25/04/2023
	Date

Ethics declaration

I, Amirah Asmall, declare that I am registered with the University of the Witwatersrand for the degree in Master of Pharmacy and have read the University's current research ethics guidelines. I accept responsibility for the conduct of the procedures in accordance with the Human Research Ethics Committee (HREC). I have obtained ethical approval from HREC (Appendix 1, M190643) to conduct my research.



Amirah Asmall	25/04/2023
	Date

Research Outputs

Poster Presentation

Amirah Asmall, Rubina Shaikh, Stephanie Leigh (De Rapper), Zelna Booth, Nabeelah Bemath, David Bayever. Determining the prevalence of use of over-the-counter codeine-containing products in the Central Johannesburg area: Qualitative Phase**.** Poster Presentation for the Faculty of Health Sciences Research Day, 15 September 2022, Johannesburg.

Drafts of research submitted for publication

Review Article

Amirah Asmall, Rubina Shaikh, Stephanie Leigh (De Rapper), Zelna Booth, Nabeelah Bemath. Combatting the Codeine Abuse Epidemic: A narrative review of global drug intervention strategies. (aimed to be published in Journal of Social and Administrative Pharmacy).

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LIST OF ABBREVIATIONS

AIFA	Italian Medicine Agency
AIHW	Australian Institute of Health and Welfare
CACC	Combination Analgesic Containing Codeine
CARA	Comprehensive Addiction and Recovery Act
CCP	Codeine Care Project
CPD	Continued Professional Development
CPS	Community Pharmacy Sector
D.A.R.E.	Drug Abuse Resistance Education
DAWN	Drug Abuse Warning Network
DALY	Disability-adjusted Life Years
DMP	Drug Monitoring Programme
DORA	Drugs and Poisons Information System
ED	Emergency Department
HCP	Healthcare Professional
LIP	Lock-In Programme
MLIP	Medicaid Lock-In Programme
NDSHS	National Drug Strategy Household Survey
NMS	Narcotics Monitoring System
NSAA	Narcotics Safety and Awareness Act
NSWPIC	New South Wales Poisons Information Centre
OHA	Oregon Health Authority
OrCRM	Oregon Coalition for Responsible Use of Medication
OTC	Over the Counter
PDMP	Prescription Drug Monitoring Programme
PSSA	Pharmaceutical Society of South Africa
SA	South Africa
SAHPRA	South African Health Products Regulatory Authority
UK	United Kingdom
US	United States
UNODC	United Nations Office on Drugs and Crime
USFDA	United States Food and Drug Administration

ABSTRACT

The abuse and misuse of codeine medication is a growing concern, in South Africa (SA) codeine combination products and cough syrups are available without a prescription, thereby making it easy to access these products from various pharmacies (Foley et al., 2018). The South African National Council on Alcoholism and Drugs claimed that codeine is the most abused OTC codeine drug in South Africa (Hodes, 2019). There is little known about the prevalence of opioid and codeine use in African countries (Harker et al., 2020).

Aim: The aim of the study is to analyse patterns of over the counter (OTC) codeine-containing products in central Johannesburg pharmacy sector and to explore the pharmacist perceptions on the effectiveness of current regulations.

Method: A mixed method research design was done by quantitatively analyzing the sales/usage patterns of OTC codeine medications in retail pharmacies in central Johannesburg for the retrospective period of January 2019 to December 2020 and by qualitatively interviewing twelve practicing retail pharmacists on their views regarding OTC codeine abuse/misuse in SA.

Results: The results obtained from the retrospective analysis of codeine sales demonstrated that Adco-dol and Gen-payne were the most frequently sold OTC codeine products in central Johannesburg. When the sales were described between the different income areas the high income areas highest sold product was Benylin with codeine. Both the middle and low income areas most sold product was Adco-dol. In the qualitative phase, practicing pharmacists were interviewed where it was found that OTC codeine is believed to be abused/misused in SA. Participants expressed concerns over factors which contribute to the abuse thereof, the ineffectiveness of the schedule 2 register and the possibility of the installation of a national database to control/monitor codeine use.

Conclusion: In this study it became apparent that OTC codeine is being misused/abused in SA with current regulations not adequately controlling or preventing this issue. There is an urgent need to re-evaluate the current regulations. This study highlighted the views of the ineffectiveness of the current schedule 2 register in SA along with the suggestion of a more monitored intervention strategy to curb this issue of codeine abuse/misuse. Most participants

agreed that the best way to prevent OTC codeine abuse/misuse was to up-schedule it to a prescription only drug or to implement a national database that is automated and integrated into the current pharmacy software

Chapter 1: Introduction and Rationale for Study

1.1 Background

The abuse and misuse of codeine medication is a growing concern facing the pharmaceutical and medical industry, with many studies stating that codeine-containing medication is one of the most commonly abused medication class (Sansgiry et al., 2017; Akande-Sholabi et al., 2019). "*Misuse*" is defined as the use of a medicine outside of the medicine label directions/healthcare practitioner's advice or the use of a drug in higher doses or for a longer duration than is recommended (Smith et al., 2013). Misuse can be unintentional at times (Copper, 2013). "*Abuse*" is defined by the US Food and Drug Administration (USFDA) as the intentional non-medical use of a drug for its psychoactive effects in order to feed an addiction or to experience a high (Smith et al., 2013). Although opioid misuse and abuse does occur at a smaller scale than the use of other illicit drugs, its abuse is associated with much greater risks of harm than drugs such as cannabis , due to the risks of fatal and non-fatal overdoses associated with opioid misuse (Webster, 2017). These findings are supported globally (Figure 1.1) and have been detailed in the World Drug Report of 2021 by the United Nations Office on Drugs and Crime (UNODC), where it was found that the non-medical use of opioids accounted for 12.9 million DALYs (Disability-adjusted life years; Healthy years of life lost due to disability and premature death) and contributed to 70% of DALYs attributed to drug use disorders globally (UNODC, World Drug Report 2021).

There are many factors that could have contributed to this rise in opioid misuse over the years, namely practitioners needing to treat pain and suffering of patients; which goes hand in hand with overreliance and excessive dosages being prescribed. In addition, the perceived undertreatment of pain in the past has pushed doctors to find more aggressive and effective pain management plans, coupled by the easy availability and excessive marketing of opioid products by the pharmaceutical industry in many countries globally (Weiner et al., 2017; Volkow et al., 2019). The rise in opioid abuse/misuse has highlighted the need for the healthcare industry to better manage pain while improving upon the safety of opioid use (Johnson et al., 2018).

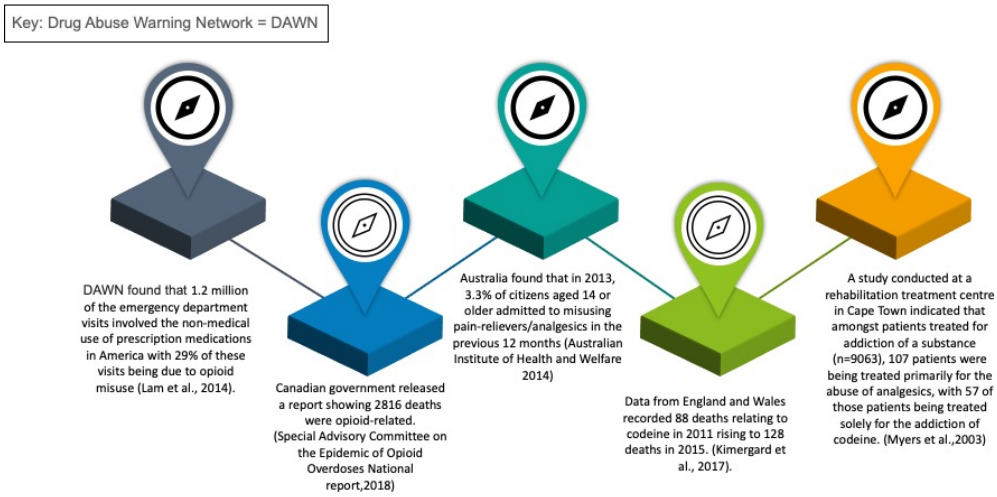


Figure 1.1: Opioid Abuse/Misuse Findings reported globally

1.2 Codeine

Codeine, a commonly abused opiate, is available in preparations that require a prescription, as well as over the counter (OTC) products (Parry et al., 2017). As depicted in Figure 1.2, the constant use of opiates can result in a neurological dependence on the drug, resulting in the patient experiencing withdrawal symptoms when the use of the drug is discontinued, further increasing the risk for abuse and misuse (Van Hout et al., 2016).

:

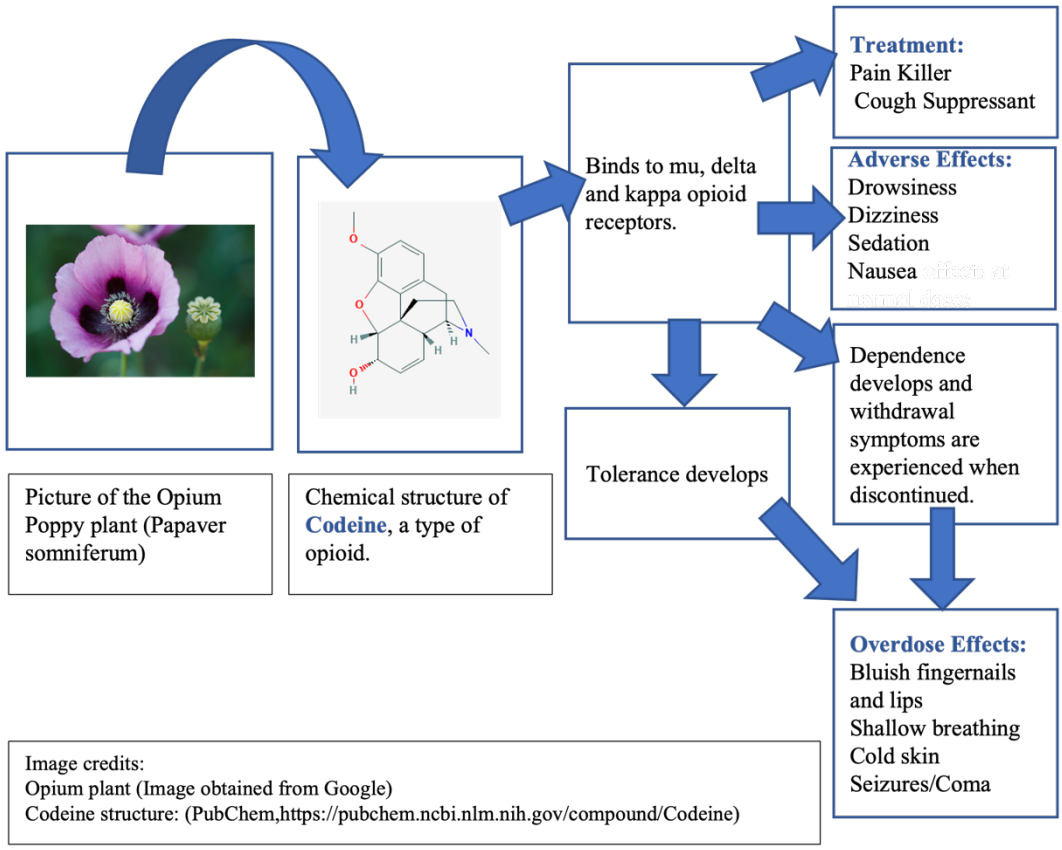


Figure 1.2: Depiction of codeine and its effects on the body when used excessively.

Chronic use of opioids eventually leads to a build-up of tolerance to the drug, resulting in users of the drug increasing the dose that is being taken in order to experience the same "high" (McCrorie et al., 2015; Militello et al., 2020). For users, this can be deadly as a patient is at risk of overdosing and experiencing toxic effects of the drug which include respiratory depression and death (Van Hout et al., 2016). Since codeine is available in OTC preparations, it is assumed to be relatively safe by the public as a prescription is not required. Due to patient lack of knowledge on the dependence and risk associated to problematic codeine use, many patients initially take the drug for a legitimate medical reason; and are unaware of the risk of addiction or withdrawal (Van Hout et al., 2016). Patients do not associate the withdrawal symptoms, such as a headache; with their previous use of a codeine containing medication as these symptoms are often reported to be flu-like symptoms such as fever and runny nose (West and Gossop, 1994; Lambert, 2020). As a result, patients often continue to seek OTC analgesics to "treat" the withdrawal symptoms. Ironically, the patient will find that only a codeine containing product can "treat" this type of headache, resulting in the patient seeking only codeine containing products, which feeds the dependence on codeine, and will likely lead to addiction (Militello et al., 2020).

1.3 Contributing factors associated with the abuse/misuse of codeine

There are various reasons for the intentional and unintentional misuse of codeine medication. To name a few examples, abuse/misuse is most prevalent in people with complex health issues suffering from chronic pain, stress, anxiety, insomnia and those who metabolize codeine to morphine ultra-rapidly (Heintze et al., 2018). A lack of alternative treatment, doctors prescribing patterns, patient expectations (i.e. patients expecting a quick fix) and the over promotion of pharmaceutical companies adds to the burden of over-the-counter (OTC) abuse/misuse (Johnston et al., 2004). Another major factor to consider is that of unpleasant withdrawal experiences (Nielsen and Van Hout., 2015). These factors are further discussed below.

1.3.1 Physiological dependence and abuse potential

Constant use of codeine and other opiates can result in drug dependence, causing the patient to experience withdrawal symptoms upon the discontinuation of use, further increasing the risk for abuse/misuse (Nielsen et al., 2010; Jones et al., 2012; Van Hout et al., 2016). A study by Bruneau et al. (2021) determined that patients who were chronically taking opioid medications

reported significantly increased opioid cravings as a result of withdrawal symptoms. Similarly, a study published by Pergolizzi et al. (2020) found that withdrawals symptoms are drivers behind continued opioid use as well as a key barrier to the discontinuation of opioids. The lack of awareness relating to the risk of addiction or withdrawal symptoms associated with codeine use increases the risk for abuse/misuse (Van Hout et al., 2016). This behavior further feeds the dependence on codeine, and will likely lead to addiction, albeit unknowingly.

1.3.2 Lack of patient awareness and education

The current availability of OTC medicines encourages self-care from patients, however, this accessibility contributes to the publics' perception with regards to safety and lack of awareness relating to risk of misuse and dependence (Van Hout and Norman, 2016). Due to the ease in availability of OTC codeine medications in multiple countries, it is assumed to be relatively safe by the public (Nielsen et al., 2013). This same sentiment was perceived by medical professionals, as is described in a study by Foley et al. (2018), where results indicated that 95% of medical professionals felt that patients did not understand the risk of dependence when taking OTC codeine-containing medicines. Studies conducted by Cooper and Neilsen et al., (2013) additionally found that participants in both studies expressed that there is a lack of public knowledge with regards to OTC medication misuse. This study further found that several participants were surprised that addiction could happen to them as they were unaware of the risks of addiction to certain medications. This contributes to patients abusing/misusing OTC medications, such as codeine, as these medications are not seen as addictive or dangerous. There is a need for better education to the general public on medication risks associated with misuse/abuse (Neilsen et al., 2013).

1.3.3 Student experimentation and peer influence

High school students and university students have been shown to be more likely to abuse/misuse opiates than adults (Johnston et al., 2004; McCabe et al., 2018). Lord et al. (2009) conducted a study amongst undergraduate pharmacy students in the United States, where it was found that the motives for misuse of prescription and OTC opioids were to "have fun" and to "de-stress or relax". This finding is further supported by a qualitative study conducted in Texas, where results indicated that college students used codeine for the euphoric effects; and because it was thought to be the "cool" thing to do at college (Peters et al., 2007). In South Africa (SA), the mixing of cough syrup containing codeine with a soft drink, such as Sprite (a lemon-lime

flavored soft drink); or with alcohol, is a common trend with locally posted videos being available on YouTube, providing steps as to how to prepare the concoction (Hodes, 2019). This concoction: known as "*Purple Drank*" or "*Lean*"; is very prevalent amongst young adults and teenagers and has detrimental adverse effects when ingested in high quantities (Agnich et al., 2013). The scale of this problem is supported by a finding of a South African study that codeine-containing suspensions came up as one of the most common medical waste products found in waste disposal sites (Hodes, 2019).

1.3.4 Lack of regulatory control

Abuse of OTC medication is most facilitated by their accessibility (Chiappini et al., 2020). Medication legislation introduced by each country has the potential to have a significant impact on how medication is perceived by the public, and advised by healthcare professionals (Ofori-Asenso and Agyeman, 2016). In some countries, codeine-containing products are freely available to the public without physician prescription, as OTC pharmaceutical products that is dispensed by the pharmacist. Often these products consist of codeine in combination with other drugs, such as paracetamol and ibuprofen, which also have potential for toxicity (Hamer et al., 2014).

1.3.5 Lack of pharmacist training

Community pharmacists are a trusted source of patient information or advice and have a prominent influence on the public's perception on safety and purchase behaviours in retail pharmacies; therefore the onus remains with the pharmacist to ensure the correct therapeutic need for the requested codeine-containing product and the suitability of the medication before dispensing (Hamer et al., 2014). Pharmacists are also responsible for monitoring and intervening when OTC medicines are being misused therefore, pharmacists need adequate training to identify and counsel potential abusers/misusers (MacFayden et al., 2001). A study conducted by Hamer et al. (2014) interviewed pharmacists in Australia and found that when it comes to addressing OTC codeine abusers/misusers, participants felt that having a clear guideline in place to follow would make it easier to counsel such patients. Many studies conducted have concluded that pharmacists felt that there is a gap in their training with regards to addressing and intervening against codeine misuse (Hamer et al., 2014; Carney et al., 2018). Due to this lack of training pharmacists would rather advise patients to seek their doctor's advice, yet this counselling falls within the scope of practice of a pharmacist. Adequate staff

training could reduce OTC medicine abuse/misuse however; the lack of pharmacist training discourages pharmacists from intervening with abusers/misusers, which further contributes to the increase in OTC misuse (McBride et al., 2003; Nielsen et al., 2010).

1.3.6 Patient-reported factors contributing to codeine abuse/misuse

A few studies focused on the perceptions of the public towards codeine abuse/misuse ((Nielsen et al., 2012; Cooper, 2013; Van Hout et al., 2015; Wells et al., 2018). The studies focused on the perceptions of people who are currently or were previous misusers, dependent on codeine medications. The main findings from these studies were that most participants initially used codeine medications for legitimate reasons, such as for pain, with the majority of participants in all studies stating how easily obtainable OTC codeine medication were from physicians and pharmacists. The finding of patients using OTC codeine for genuine medical issues supports the importance of proper education that needs to be provided to patients upon their first use of the medications. A participant from a study conducted in Australia expressed frustration over the lack of information given about the risks of codeine dependence upon first use as opposed to only receiving this advice after the problem had already escalated (Nielsen et al., 2012). The ease of obtaining OTC codeine medications stated above also gives many patients the false impression that these medications are safe to use regularly thus contributing to the abuse/misuse thereof (Van Hout and Norman, 2016).

1.4 Global Codeine use

Between 2010 and 2019 it was estimated that the number of opioid users doubled from just over 31 million to just under 62 million globally, with the main increase in these numbers being driven by new statistics made available from Asia and Africa (World Drug Report, 2021). In Australia it was determined that products containing codeine related to about one hundred deaths a year (Kirby, 2018). The global demand for codeine preparations increased by 27% in the decade of 2000-2010 (Van Hout et al., 2018). The same findings as determined in Australia were shown in the UK and Ireland, with a study determining that 1 in 10 patients exceeded the recommended codeine dose on the last occasion of use; and stated codeine dependence as an issue experienced in the countries with both prescription and OTC codeine products (Kimergard et al., 2017). A study conducted by Carney et al (2018) further supported this claim by indicating that pharmacy staff stated that the misuse of codeine is a significant public health issue in the UK and Ireland. Problems related to the misuse of OTC codeine was commonly

reported in Nigeria, Kenya, Chad and Zimbabwe (Degenhardt et al., 2019). A study conducted in Saudi Arabia on medical physicians found that 61.9% of the study participants agreed that the intentional misuse of codeine products by patients occurred commonly (Syed et al., 2021). In France it was determined in a study conducted on 53 purchasers of codeine at a retail pharmacy that 15% of purchasers were using codeine for non-medical reasons (Orriols et al., 2009). In Canada, between the period of 2011 and 2014 it was determined that 514 citizens of Ontario began methadone treatment for OTC codeine addiction (Yang and Zlomislic, 2015). In South Asia it was found that codeine containing cough mixtures was the most commonly misused medications (Chan et al., 2021).

1.5 Codeine use in South Africa

In South Africa (SA), codeine combination products and cough syrups are available without a prescription, thereby making it easy to access these products from various pharmacies (Foley et al., 2018). In SA, there has been a growing concern over use of codeine-containing products for non-medical use (Dada et al., 2015). The South African National Council on Alcoholism and Drugs claimed that codeine is the most abused OTC drug in South Africa (Hodes, 2019). A study analysing the sales of OTC codeine medications in 31 countries globally between the period of 2013 to 2019 found that South Africa was the leader in sales of codeine products (Richards et al., 2022). In South Africa, the abuse of codeine has become a major concern in recent times and is evident in an article published by Health-E News, South African television health news service, in 2018, which pointed out the widespread use of “codeine cocktails” by the youth (Harrisberg, 2018). The story showed how easily obtainable cough syrups such as Broncleer (contains 10mg codeine per 5ml) are in South African pharmacies despite existing regulations, and strategies aimed at controlling the use of codeine containing products. From this it can be seen that the pharmacist plays an important role in preventing the abuse and misuse of medications, as it is the pharmacist’s responsibility to use their discretion when dispensing medication. In recent years it can be seen that there is a need for the implementation of an effective initiative as codeine medications are still being heavily abused and misused and it is therefore not being effectively controlled with the existing regulations.

South Africa has attempted a few strategies to control the abuse and misuse of codeine medications. In SA, it is compulsory for all schedule 1 and 2 medications to be recorded in a register specific to that schedule (Carney et al., 2016). The pharmacist is expected to record the

amount, name and quantity of medication dispensed (Van Hout, 2016), however these registers are not linked so an individual may obtain medication from different pharmacies without any suspicion being raised by pharmacists in the community. The alarm with regards to codeine abuse was noted by the South African Community Pharmacist Sector who launched the Codeine Care initiative in 2013 with the aim to control codeine abuse however, due to there being no national database linking all retail pharmacies the initiative has not been impactful (Hodes, 2019). The idea of a national database either being effective or ineffective in managing codeine abuse/misuse is further explored.

1.6 Rationale for study

Over recent years, many countries have been researching methods that would be most effective in combatting the opioid crisis. In the United Kingdom (UK), a harm minimization model was developed to identify misuse of easily abused medications by keeping record of the purchase of these products (Fleming et al., 2004). A community in the UK also attempted to identify misusers by programming the cash registers to restrict sales of abusive products (Cooper, 2013). In Australia, there was an up-scheduling of analgesics containing codeine products, followed by a regulation passed which stated that all medicines containing codeine will require a prescription (Hamer et al., 2014). In Northern Ireland, Hughes et al. (1999) conducted a study where it was suggested that pharmacists should remove codeine and misused products from sight or refuse the sale if abuse is suspected. From the findings mentioned above it can be seen that a national database could be implemented in order to link all pharmacy systems to prevent misusers from obtaining products elsewhere. This database could be a starting point to prevent the abuse/misuse of all highly addictive OTC medications.

Many countries have resorted to the rescheduling of codeine containing medications to a higher schedule, which is to be accessible only upon the receipt of a prescription. This strategy, although effective in other countries, will not be feasible in SA due to the social and economic problems that exist in the country (Hodes, 2019). Up-scheduling of codeine medications would burden a healthcare system which is already overburdened (Van Hout, 2016) as there will not be enough doctors for every patient requiring medication for a common migraine or cough. The majority of the country is also under financial strain and cannot afford to visit a general practitioner for minor ailments (Hodes, 2019). The codeine debate has been debated by the Pharmaceutical Society of South Africa (PSSA) in 2019 where it was suggested by the society

that the South African Health Products Regulatory Authority (SAHPRA) implement stronger and more concerted action against individuals engaging in the mass supply and dispensing of codeine products for non-medical use (Manolis, 2019). Furthermore, SAHPRA released a statement recently stating that they are aware of the illicit sales of codeine and are currently reviewing the scheduling status of codeine-containing medicines (Msiza, 2022).

There is little known about the prevalence of opioid and codeine use in African countries (Harker et al., 2020). As a result of this, this study aims to examine the existing literature on how best to tackle this dire issue in South Africa by reviewing all published articles evaluating different types of intervention strategies used in various countries. In addition, this study aims to assess OTC codeine sales data in the central Johannesburg region in order to determine the factors associated with or contributing to codeine abuse and misuse. The codeine analgesic usage from 2019 to 2020 will be analysed using dispensing data from retail pharmacies. This study, by making use of both quantitative and qualitative study methods, will give a well-rounded evaluation of codeine abuse and misuse; as well the professional opinions and comments surrounding this problem and the potential way forward at a more controlled and regulated codeine sector in South Africa.

1.7 Aim

The aim of the study is to analyse patterns of over the counter (OTC) codeine-containing products in central Johannesburg pharmacy sector and to explore the pharmacist perceptions on the effectiveness of current regulations.

1.8 Study Objectives

1.8.1. Determining the OTC codeine analgesic usage from 2019-2020 in retail pharmacies within the central Johannesburg region.

1.8.2. Exploring the perceptions of pharmacists to the existing regulations in the prevention of OTC codeine abuse and misuse.

1.8.3. Exploring the attitudes and perceptions of practicing pharmacists towards the control of codeine medication use.

An overview of how each objective was achieved is shown in Figure 1.3 below.

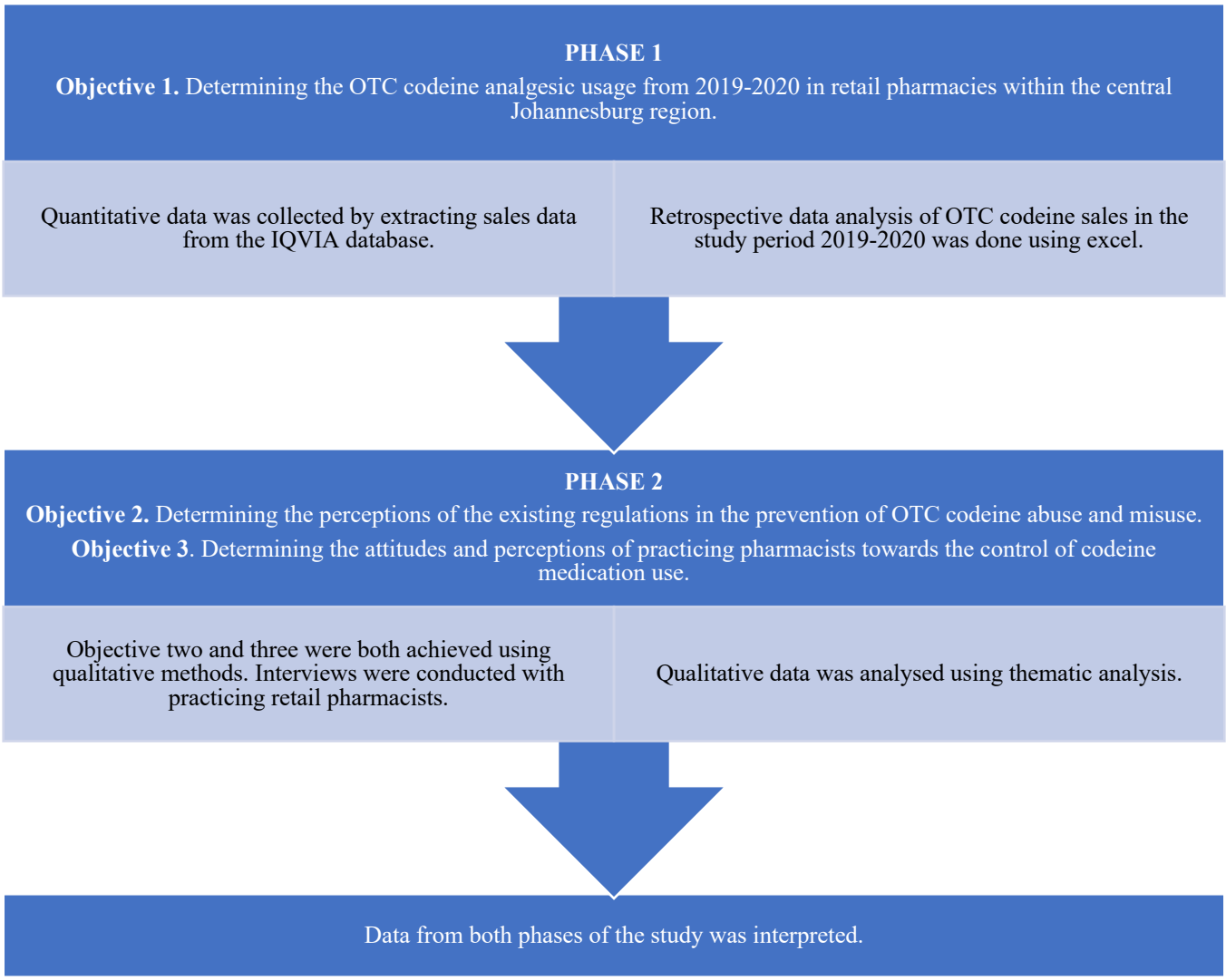


Figure 1.3: Overview of Study research design

1.9 Synopsis of Dissertation

Chapter One of this dissertation provides background information to the study. This chapter outlines the issue of codeine misuse globally and then focuses to the issue in South Africa. A summary of the aim and objectives is included at the end of the chapter.

Chapter Two of this dissertation provides a narrative literature review focusing on the intervention strategies implemented and attempted around the world. The review gives further information on the issue currently being experienced with regards to codeine misuse and gives insight into what intervention strategy could be the most effective in preventing this misuse.

Chapter Three of this dissertation provides an explanation of the methodology and study design. The study methods used for both the quantitative phase (phase 1) and qualitative phase (phase 2) are explained.

Chapter Four of this dissertation displays the results of the study. The quantitative data is presented in the form of graphs, figures and tables to show the sales/use of OTC codeine in retail pharmacies in central Johannesburg. The qualitative data is presented by displaying the experiences of practicing pharmacists extracted from the interviews conducted. This is done through the use of quotations.

Chapter Five of this dissertation provides the discussion which includes the analysis of the results chapter presented above. Both the quantitative and qualitative results are discussed independently at first followed by the integration of data from both phases.

Chapter Six of this dissertation outlines the future recommendations, strengths, limitations and conclusion of the study.

Chapter 2: Combatting the Codeine Abuse Epidemic: A narrative review of global drug intervention strategies.

2.1 Introduction

The abuse and misuse of medication is a growing global challenge facing the healthcare industry (Cooper 2013; Weisberg et al., 2014). It is also a public health concern, due to the detrimental adverse events associated with the abuse/misuse of many medications. Opioids have been identified by multiple countries as one of the most commonly abused and misused conventional medications (Morley et al.,2017; Carney et al.,2018). Although the abuse/misuse of opioids occurs at a smaller scale than other illicit drugs, such as cocaine, it is associated with greater risks of harm related to the consequences of overdosing (Degenhardt et al., 2014). The World Drug Report further reported that opioids contributed 70% in 2017, and 76% in 2018, toward the negative health impact cases reported for drug use disorders, globally (United Nations Office on Drugs and Crime World Drug Report, 2017; World Drug Report, 2018). Furthermore it was determined in the 2021 report that opioids contributes to majority of deaths caused by drug use disorders (United Nations Office on Drugs and Crime World Drug Report, 2021).

Opioids are commonly used for their beneficial therapeutic properties (Inturrisi, 2002; Geppetti and Benemei, 2009). Codeine, an opioid that is commonly indicated for its analgesic and antitussive properties, has been associated with increasing reports of abuse/misuse (Dada et al., 2015; Van Hout and Norman, 2016; Carney et al., 2018; Peechakara and Gupta, 2021). The constant use of codeine can lead to both drug dependence and withdrawal symptoms upon discontinuation of use thus increasing the risk for abuse/misuse (Nielsen et al., 2010; Jones et al., 2012). Literature has indicated that codeine and other opioids abused/misused are a notable challenge, as indicated in Figure 2.1 which shows a compilation of statistics extracted from prior research papers. It is important to note that the statistics depicted in Figure 2.1 are highly underrepresented, as the majority of abusers are not able to seek treatment due to financial strain, or are not willing to access treatment facilities due to the stigma associated with abuse, or are in denial of the abuse (Yang et al., 2017).

1

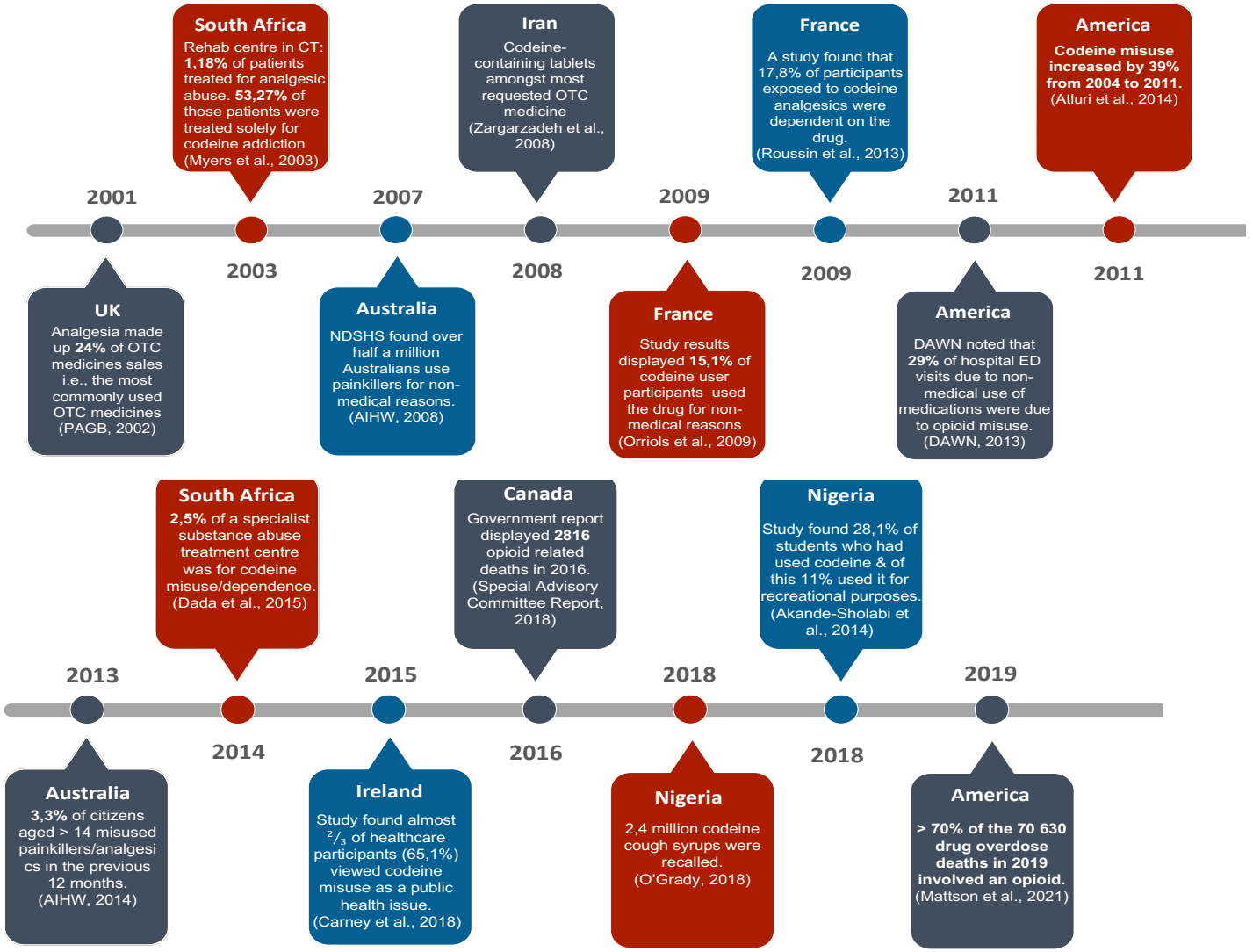


Figure 2.1: Opioid misuse statistical data from various countries

The data shown in Figure 2.1 indicates that opioid abuse/misuse is a problem that has been researched in multiple countries worldwide. Due to the recognised abuse/misuse of opioids, many countries have attempted to report or cite this problem and develop strategies to address this. However, no research appears to have reviewed and compared different types of strategies that have been implemented across different countries. This narrative review therefore, aims to synthesise and discuss existing literature on intervention strategies attempted and implemented worldwide to combat opioid medication abuse/misuse. This narrative review aims to determine and compare both the strengths and limitations of the various intervention strategies, thereby allowing for the identification of the most effective intervention strategies to combat codeine abuse/misuse and areas for future research.

2.2 Intervention strategies

Over recent years, many countries have been researching methods that would be most effective in combatting the problem of medication abuse/misuse. It is evident that various programs, strategies and methods have been developed globally in an effort to reduce codeine abuse/misuse, ranging from regulatory reform to prescription drug monitoring programmes.

A major challenge facing policy makers in the pharmaceutical field is how to ensure the availability of codeine-containing medications for those with legitimate therapeutic need whilst reducing the consumers' risk of misuse and dependence (Norman et al., 2016). Therefore, it is of utmost importance that intervention strategies and policies are implemented in order to ensure patients are provided with this equal balance of access to these medicines and protection. In reviewing the literature, six categories of interventions were identified, as depicted in Figure 2.2. In some instances, countries have implemented more than one type of strategy, however, the interventions were implemented independently. However, if the interventions were integrated in a particular country or region, this was classified as a multidimensional/integrated strategy. These six categories are detailed below.

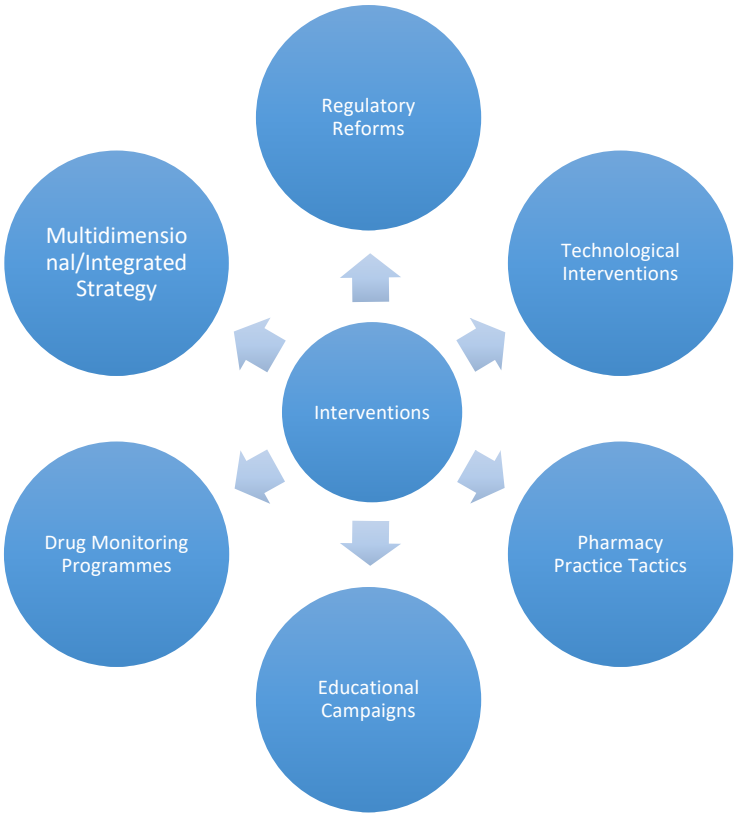


Figure 2.2: Diagram displaying various intervention strategies discussed in this review.

2.2.1 Regulatory reforms

Abuse of OTC medication is facilitated by their accessibility (Chiappini et al., 2020). Medication legislation introduced by each country can have a significant impact on how the medication is perceived by the public and advised by healthcare professionals (Ofori-Asenso and Agyeman, 2016). At present, the regulations and policies controlling the sale of codeine medications varies around the world, which have been briefly summarized in Figure 2.3. As can be seen in Figure 2.3 the accessibility and availability of codeine medications is widely and easily available to the public in most countries therefore this section of the review will look into the impact resulting from regulatory reforms. Regulatory reforms denote interventions related to regulation or legislation changes with the goal of deterring medication abuse. Research has indicated that legislation is vitally important to the pharmacist in medication abuse prevention, in order to empower them to engage with potential interventions and to further encourage a consistent approach across all pharmacists (Webster, 2012).

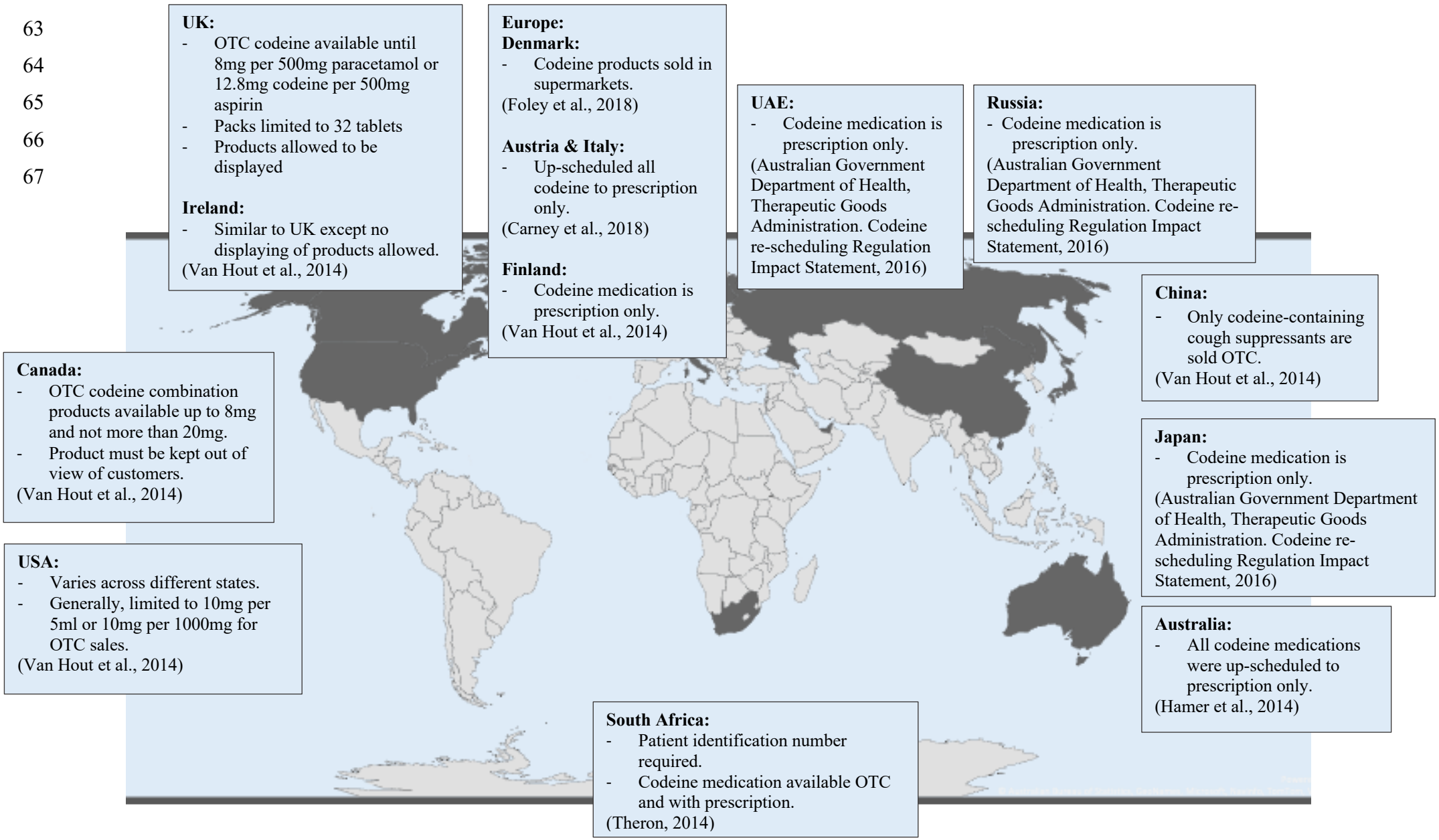


Figure 2.3: Diagram showing the differences in regulations around the world regarding codeine sales

2.2.1.1 Australia

Australia implemented an initial up-scheduling of low strength (less than 15mg) codeine-containing medications in May of 2010 from a schedule 2 to a schedule 3 medicine, thus preventing the sale of such medications without pharmacist consultation. However, cold and flu medication containing codeine remained available to patients without pharmacist consultation (Cairns et al., 2016; Cairns et al., 2019). The legislation was reviewed, as the up-scheduling of low-strength codeine-containing products did not prove to curb codeine misuse and reports still displayed a great deal of codeine-related deaths (Roxburgh et al., 2015; Cairns et al., 2016). This resulted in a further up-scheduling of all codeine-containing medications to a schedule 4 medicine (prescription only) that was implemented in February 2018 (Cairns et al., 2019). A study conducted by Hamer et al. (2014), determining the views of working pharmacists towards this up-scheduling of codeine-containing analgesics, found that the inclusion of pharmacists in the sale of codeine-containing medications greatly increased their awareness of its misuse. However, as records are confined to their respected pharmacy, due to the lack of a centralized dispensing systems, the monitoring of suspected misuse of OTC codeine-containing medications is restricted. A major concern amongst participants was the lack of time to have detailed consultations with patients regarding their use of OTC codeine-containing medications. The qualitative study was beneficial in understanding the views of Australian community pharmacists towards the regulation changes and its effectiveness; however, these opinions may not be transferable to other contexts within and outside Australia. Additional qualitative studies looking at this issue more recently would aid in determining current views of pharmacists.

Two studies were conducted by Cairns and colleagues in 2016 and 2019, to determine the effect of the re-scheduling as an intervention strategy. Both studies determined cases of codeine misuse by analyzing the calls made to the New South Wales Poisons Information Centre (NSWPIC). The initial study displayed no decrease in codeine misuse. The latter study, however, did have significant findings that indicated that the re-scheduling did have a positive effect on codeine misuse. The main findings from these studies suggest that the up-scheduling of codeine did result in a decrease in overall codeine harm. The findings are significant albeit the limitations present. Specifically, the study published in 2019 can only provide a proxy for codeine use as there was no control population (Cairns et al., 2019). Both studies are susceptible to reporting bias since poison information centre calls are voluntary, as a result of

this, the depiction of codeine misuse from these calls are not a true estimation (Cairns et al., 2019). A study conducted by McCoy et al. (2022) aimed to establish the impact of the regulation change in Australia. The study determined that the up-scheduling of codeine products significantly reduced codeine use and the prevalence of opioid use disorders.

2.2.1.2 The United Kingdom (UK)

In the UK, legislation relating to medicine packaging was amended in the Medicines and Healthcare products Regulatory Agency public assessment report, stating that all codeine-containing medications must contain an additional warning on the medication package/box which explicitly states the risk of addiction that is easily visible for patients (Fingleton et al., 2016). However, this type of intervention can be easily ignored/overlooked by customers. This followed the understanding established amongst the drug companies in the UK to reduce the pack size to 32 tablets (Tobin et al., 2013). Neither study was able to determine if these strategies were effective in curbing codeine misuse.

2.2.1.3 Italy

In 2014, the Italian Medicine Agency (AIFA) modified the summary of product characteristics of codeine-containing medicines limiting their use for a maximum of three days (Lombardi et al., 2019). Lombardi et al. (2019) analyzed the effect of the AIFA intervention on codeine/paracetamol combination products using a quasi-experimental interrupted time series analysis. Although the study did display a significant decrease in the prescription trends of codeine/paracetamol medications following the implementation of the AIFA legislation, there was a simultaneous increase in the use in long-acting opioids over the study period which could indicate that misusers shifted to using long-acting opioids as a result of the regulation change (Lombardi et al., 2019). The limitation to be noted when analyzing prescription records is that the statistics obtained does not show actual drug consumption by the patient, thereby not providing the true drug utilization value (Lombardi et al., 2019).

Lombardi et al. (2019) further reported that the implication of restricting codeine use directly resulted in the use of other opioids. This could imply that patients either have a misuse/dependence problem or patients who suffer from chronic pain rely on these OTC codeine medications to cope. In terms of the present review, it must be noted that although the AIFA intervention seemed to be effective when for the control prescription medications, it may

not be effective for OTC medication misuse. It is difficult to limit the use of OTC codeine medications to three days as that would include influenza and headache medications, this would disadvantage patients genuinely needing easy access for acute conditions. There are no further studies found from other countries that determine whether amending the medication packaging was effective.

2.2.1.4 United States of America

Between 2003 and 2010, the state of Florida experienced a rapid increase of what is known as '*pill mills*. This term was attributed to physicians, pain clinics and other healthcare providers who were responsible for dispensing large quantities of prescription medications, outside their scope of standard medical practice (Kennedy-Hendricks et al., 2016). This led to the implementation of a legislation in 2010/2011 which stated that pain clinics are to identify a licensed physician as responsible for clinic operations, limit dispensing of opioids to a 72-hour supply per patient, and prohibited advertising of controlled substances. A second law, which took effect in July 2011 prohibited physicians from dispensing most narcotic medications on-site and increased criminal penalties for doctors and clinics involved in drug diversion. The legislation changes resulted in the arrest of 47 pill mill owners, practitioners and other staff where 189 million dollars' worth in asset seizures and the suspension of 92 DEA registrations (Kennedy-Hendricks et al., 2016). Kennedy-Hendricks and coworkers further reported a decrease in the number of deaths attributable to overdose from codeine occurred as a result of these regulations.

The regulations passed in Florida aimed at reducing the mortality associated with opioid overdose. Two studies concluded that the policy changes were attributable to a decline in opioid prescription and mortality over the respective study periods (Johnson et al., 2014; Kennedy-Hendricks et al., 2016). These results could be related to other interventions (such as increased educational campaigns), as it is challenging to evaluate the contribution of each policy's effect on opioid related mortality (Johnson et al., 2014). Both studies fail to compare their findings to the numbers in other states who have not implemented the policy changes. At present it is not apparent if these legislative changes are still making a significant and positive impact. These studies display that regulation changes relating to stricter prescribing practices and increased criminal penalties for prescribers can be effective in preventing the access to misuse of opioids. When considering OTC medications, stricter regulations like those

mentioned above can provide a positive impact on the misuse; however, pharmacists play a big role in the monitoring of OTC medication use as opposed to the prescriber (Compton et al.,2019).

2.2.1.5 South Africa

South Africa (SA) has attempted a few strategies to control the abuse/misuse of codeine medications. Regulation changed to reduce maximum codeine concentration from 20mg to 10mg (Foley et al., 2018). In SA, codeine containing products comprising of 10 mg of codeine are considered schedule 1 or 2. In SA, it is compulsory for all schedule 1 and 2 medications to be recorded in a register specific to that schedule. The pharmacist is expected to record the amount, name and quantity of medication dispensed (Van Hout, 2016); however, these registers are not linked across pharmacies so an individual may obtain medication from different pharmacies without any suspicion being raised by pharmacists in the community.

There are currently no studies conducted in SA reporting on the direct effect of the use of schedule registers in SA. There was a survey, however, conducted by Carney et al (2018) to determine the views of pharmacists on codeine medication misuse. The survey results displayed that SA had a significantly larger number of codeine-containing cough syrup products dispensed (27.9%) compared to the UK (0.8%) and Ireland (18%). This could relay that the current regulations in SA are not effective in controlling codeine misuse. The study further reported that South African pharmacists believed that there is a need for the training and education of pharmacists in substance use disorders (Carney et al., 2018).

2.2.1.6 Nigeria

Over recent years Nigeria has been battling with the abuse of codeine medications especially codeine-containing cough syrups. In 2017, it was reported that 3 million bottles of codeine were being consumed daily in the Nigerian states of Kano and Jigawa (Mustapha et al.,2019). As a result of this steady rise in crime, abuse and deaths associated with codeine medication abuse, the Nigerian government decided to implement stricter control on the domestic production on 1 May 2018 (Ezenwa et al.,2019). This policy banned the import and production of codeine-containing cough syrups. This policy was put in place however currently there does not seem to be any evidence-based studies or articles to display and determine the effectiveness of this regulation change, and no literature published since the change in regulation has

determined why these commonly abused substances continue to still be in widespread use (Ezenwa et al.,2019). Even though it is believed that codeine medication is still being widely used despite the regulation change, some pharmacists did feel that that the regulation did result in a decrease in demand for the drug from the public in their respective pharmacies (Ezenwa et al., 2019).

Regulatory responses have largely focused on up-scheduling and improved guidelines for the restricted supply of non-prescription codeine medications, which is to be accessible only upon the receipt of a prescription (Hamer et al., 2014). The difficulty with this approach, is that up-scheduling applies not only to analgesics, but to cough and cold medications as well which are highly effective for symptomatic relief of self-limiting viral illnesses (Van Hout and Norman, 2014). This strategy, although effective in certain countries, will not be ideal or feasible for third world countries. Due to the social and economic problems that exist in those countries up-scheduling of codeine medications would burden healthcare systems which are already overburdened, as there will be insufficient doctors for every patient requiring medication for common self-limiting conditions such as a migraine or cough (Van Hout, 2016; Mishriky et al., 2019). When those medicines are not available OTC, it creates barriers for low-income patients to access primary care for minor ailments, and results in the overburdening of clinicians and patients along with additional costs to taxpayers (Le Roux, 2013).

2.2.2 Drug Monitoring Programmes

Upon searching the literature, it was found that many countries implemented a type of drug monitoring programme to decrease medication abuse. For example, a study looking at the use of a real time prescription drug monitoring programme (PDMP) in an emergency department in Ohio found that after physicians reviewed patients' history, they changed their opioid prescription in 41% of cases (Islam and McRae, 2014). Drug monitoring programmes (DMP) are nationwide or statewide electronic software databases designed to aid healthcare providers in the monitoring and reducing abuse/misuse of medications by collecting and distributing patient's medication data (Davis et al., 2015).

2.2.2.1 Australia

Australia has attempted multiple electronic database interventions, namely: Project STOP, DORA (Drugs and Poisons Information System Online Remote Access) and MedsASSIST.

Project STOP, an electronic tracking system, was launched in 2005 in Queensland (Mazerolle et al., 2016). This system aims to help community pharmacy healthcare providers make more informed medical decisions for pseudoephedrine products (Webster, 2013). Project STOP has three main objectives, namely: to improve pharmacist's ability to identify suspicious medication requests, to assist pharmacists in determining which patients have a legitimate therapeutic need for the medication, and to provide intelligence to the police along with health agencies regarding any data suggesting illicit activities (Ransley et al., 2012; Devaney et al., 2015). The availability of this system in the pharmacy has allowed pharmacists access to vital information as opposed to having to rely on limited records/data stored in pharmacies (Webster, 2013). The database runs a check on patients' photo-identification card numbers with the requested product name, once the number is checked there is a 'match screen' that appears which provides pharmacists with information to help them determine the legitimacy of the sale (Ferris et al., 2016). Upon this check, if the patient's identification number is linked with the purchase of at least one other pseudoephedrine containing medicine within the recommended therapeutic period then the pharmacist is allowed access to the individual's medication sale pattern for the previous 100 days (Ferris et al., 2016).

It was determined that by the end of 2015, 95% of pharmacies in Queensland (1021 pharmacies) were making use of Project STOP (Ferris et al., 2016). Webster (2013) conducted a study amongst 620 community pharmacists in both Queensland and Victoria on their use of Project STOP. It was determined that majority of respondents in both jurisdictions concurred that Project STOP was the most effective programme for aiding them in making therapeutic decisions (Queensland = 97,1%, Victoria = 88,2%); a just as large percentage of participants stated they had refused sales of pseudoephedrine medications (Queensland = 95,1%, Victoria = 83,2%) as a result of the identification of suspicious sales made through the use of Project STOP (Webster, 2013). However, Webster's (2013) study has possible respondent bias as participants with positive experiences towards the intervention are more likely to participate. This program also includes the police, who mobilize pharmacists in a guardianship position that is supported by a real-time database. This database supports the police in discovering illicit medication activities (Mazerolle and Ransley, 2005). The study by Webster (2013) displays that pharmacists are more positive and committed to performing their role in an intervention when support is received from policing partners on condition that they are made aware of how the police are utilizing the information. It should be noted that these studies found on Project STOP focus solely on the pharmacist's engagement with the software as opposed to the

effectiveness of the campaign itself. There was no study found examining data/statistics on the impact and effectiveness of the initiative.

In 2009, Tasmania implemented a PDMP referred to as DORA in 2011, the system enabled clinicians to view dispensing information/data about all schedule 4 and 8 medications (Boyles, 2019). DORA was able to provide confirmation on whether a patient had been confirmed as drug dependent or if a patient had been treated in the state for an opioid use disorder in the past or currently (Boyles, 2019). The implementation of this programme has aided healthcare professionals in maintaining up to date on information and data, therefore permitting more timely advice for patients.

It can be deduced that DORA has contributed to the reduction in opioid related harms in Tasmania; however, the extent of this reduction has not been determined or yet published (Boyles, 2019). The article published by Boyles briefly explained the software and the reason for its design/implementation, but the DORA software outcomes and efficacy testing results were not undertaken and reported. It is difficult to determine if DORA is effective due to this lack of published information of the initiative so one can only speculate and correlate. There is a need for a study examining the effects DORA had on the abuse of Tasmania's schedule 4 and 8 medications in order to determine its impact. In relation to this review, due to the lack of information on the success or downfall on the system, no conclusion can be made as to whether or not this type of software can be effective in controlling OTC codeine misuse.

The Pharmacy Guild of Australia (Pharmacists' Owner Representatives) had reservations about the management of OTC combination analgesics containing codeine (CACC). Due to these concerns MedsASSIST, a real-time monitoring system, was developed (Wood et al., 2019). Furthermore, HealthPathways was developed by the opioid management team in Australia with the purpose of the platform being to identify codeine misusers who required treatment referrals (Hamer et al., 2014). HealthPathways is an interactive clinical decision support system which provides information to a provider at the point of sale in order to effectively aid in better decision making and intervention (Bryan et al., 2008). This system works to provide consistent standardized care, as each 'pathway' provides a definitive plan of management as well as referral for patients based on evidence-based best practice (Robinson et al., 2015). The Pharmacy Guild intended to ensure that MedsASSIST was utilized as a clinical tool as opposed to a policy therefore, an online PDF version of the WVPHN

HealthPathways interactive tool was installed. The tool could be used as a reference, available for use by practicing pharmacists (Wood et al., 2019). This service was additionally offered as an educational module on the Continued Professional Development (CPD) platform to increase exposure to the information (Wood et al., 2019).

Wood et al. (2019) conducted a study where the statistics of HealthPathways was assessed during the period of March 2016 until March 2017. A noted challenge was that the most common reason (79,6%) as to why pharmacists had not made use of the clinical tool was the lack of awareness of what these tools were. This indicated that although an intervention tool can be successfully implemented into practice, there needs to be great awareness and education surrounding new innovations. From the pharmacists who had made use of the tool perceived it as useful in increasing their confidence in the management of CACC requests and dependence. Despite the change made in Australia to up-schedule codeine products to prescription only in 2018, clinical systems like these are still useful in pharmacies for better decision making and medication supply (Wood et al., 2019).

2.2.2.2 United States of America

The early 2000's marked a new wave of PDMP implementation in all states except Missouri (Bao et al., 2016). A study conducted in 2002 by the United States (US) General Accounting Office found that the programme's across America differed drastically in their design, application and objectives. With regards to objectives some states place an emphasis on educational measures whilst other states placed no focus on such (Wang and Christo, 2009). With regards to the design/functioning of the programme, different states differed in the types of medications covered and the government agencies regulating the data being collected (Wang and Christo, 2009).

In Florida, mandatory dispenser reporting to the newly established prescription drug monitoring programme (PDMP) began in September 2011, resulting in a 27% decline in opioid related overdose deaths from 2560 to 1892 (Johnson et al., 2014). Florida's PDMP makes use of an electronic database which collects information about prescription products dispensed within the state (Johnson et al., 2014). Florida-based physicians and dispensers have voluntary access to the information stored on the database where they able to review an individual's history to identify problematic practices such as physician shopping (Rutkow et al., 2015).

While the evidence is mixed and inconclusive, many states associate their PDMP's with a lower rate of prescription drug abuse and a change in the general prescribing practices of practitioners (Haegerich et al., 2014).

Bao et al. (2016) assessed the effect of PDMP's in America by collecting data, i.e. reason for physician visit, diagnosis determined and information on medications prescribed, from outpatient care visits in the 24 states with a PDMP implemented. The study considered all patient visits who stated pain as their primary reason for visit. The limited effect found on the overall prescribing of opioids and pain medications is partially related to the low uptake of prescribers registering on the programme (Bao et al., 2016). A concern with the implementation of these systems is that this can result in unintended consequences such as over-cautious prescribing or the prescribing of higher scheduled opioids (Norman et al., 2016). Results indicated that after the implementation of PDMP's, the prescribing of schedule 3 opioids did not change in a clinically or statistically significant way. This lessens concerns that prescribers will prescribe stronger opioids as a result of the increased medication monitoring (Bao et al., 2016). Findings indicated that although PDMP's were linked with a significant reduction in opioid analgesic prescribing in the first six months following implementation, no successive reductions were significant (Bao et al., 2016). However, it is not known whether the above finding was causal or associational. The investigators were also unable to determine if these patients' pain needs were adequately met since the implementation of the software.

The state PDMP's in America have struggled to succeed as they inefficiently utilize the collected data and suffer from inadequate data collection as there is a lack of communication between pharmacies from different retail chains and different states (Shepherd, 2014). The painkiller abuse epidemic is also not being effectively combated as most states PDMP's do not require dispensers to utilize the program for the dispensing of painkillers (Shepherd, 2014). Due to this voluntary approach, a self-selection bias is introduced as already conscientious prescribers are more likely to voluntarily use these programme (Haffajee et al., 2015). Additional efforts are required with PDMP's to promote/educate Healthcare Professionals (HCP) on how to access and benefit from utilizing these systems in practice in order to increase pharmacist awareness and compliance with these initiatives (Perrone and Nelson, 2012; Wood et al., 2019). An additional concern raised lies with the privacy of patient information, both the American Medical Association and the American Society of Addiction Medicine stress the need for all information stored in the PDMP database to be treated just as well, if not better

than, any other medical records (Islam and McRae, 2014). Kentucky law permits the felony prosecution of practitioners who misuse data from PDMP's (Wang and Christo, 2009).

Although the uptake of PDMP use has been slow among providers, it has been determined by researchers that there is an association between PDMP use and reduced fraudulent prescription seeking behaviour (Baehran et al., 2010; Reifler et al., 2012). A study conducted in Virginia by Barrett and Watson (2005) on the perspectives of physicians on a pilot PDMP found that of the 130 physicians interviewed, only 11% of participants reported having used the programme to request information about a patient's prescription history. However, despite the low utilization of the PDMP database, 68% of participants felt that the database was useful for the monitoring of patient's history and did decrease the incidence of doctor shopping (Barrett and Watson, 2005). Doctor shopping could be reduced or even prevented by the implementation of a monitoring programme without mitigating other patients' access to treatment (Casati et al., 2012). Barrett and Watson's study was conducted over 10 years ago therefore these views/findings outdated.

It is evident that PDMP's have demonstrated a positive impact on medication abuse when implemented. If designed well, these systems will be used by HCP's. Amongst places where PDMP's are available for use, the most cited reason for not using this programme was a lack of time/time restraints therefore it is essential to design a system where data is inputted instantly, resulting in the collection of real time interstate data (Haffajee et al., 2015). PDMP's can help identify any fraudulent or illegal activity related to the dispensing of controlled substances and directly inform professional licensing boards of the problematic healthcare physicians (Islam and McRae, 2014). A study to determine the consumers' perspective on codeine sale found that majority of their participants found that their appearance, such as wearing a business suit, had a strong influence on their ability to access OTC codeine therefore a national database can eliminate this stereotype by identifying misusers despite their appearances (Nielson et al., 2012). An updated study examining longer trends is required to assess the current views and outcomes of the PDMP's in America and whether these software's are having a sustained effect.

2.2.2.3 Canada

In Ontario, the Narcotics Monitoring System (NMS), a prescription monitoring programme, and the Narcotics Safety and Awareness Act (NSAA), which allowed for the collection of

information regarding patient's prescriptions and health information, was introduced in November 2011 (Gomes et al., 2014). The NMS aimed to promote appropriate prescribing and dispensing practices through the capturing of prescription information of controlled medications dispensed on the system (Martins et al., 2018). This intervention was therefore more physician focused with the Ontario Ministry of Health and Long-Term Care monitoring the NMS prescription data with a focus on prescribing practice improvement.

Gomes et al (2014) conducted a time series analysis on the impact of the implementation of both the NMS and NSAA on the prevalence of potentially inappropriate prescribing in Ontario. The study determined that the prevalence of inappropriate opioid prescribing decreased by 40.3% between October 2011 and the end of the study period. This study determined that the introduction of both a prescription monitoring programme and a legislative change developed specifically for opioids resulted in a significant reduction in the prevalence of potentially inappropriate prescribing of these monitored medications in Ontario (Gomes et al, 2014). However, the findings from this study failed to link these findings to drug overdose hospitalizations and deaths. Martins et al. (2018) conducted a study where the opioid prescribing practices were linked to the hospitalization and mortality data. The study publication was limited in displaying the findings as Martins et al (2018) did not describe the findings in detail however it should be noted that a large amount of the opioid overdoses after the implementation of NMS involved non-prescription opioids (Martins et al., 2018). These findings further suggest that OTC codeine medications may need to be regulated, as such medications are easily abused if only prescription medications are being monitored in interventions.

2.2.2.4 South Africa

In South Africa, the Community Pharmacy Sector (CPS) of South Africa and the Pharmacy Society of South Africa (PSSA) designed an initiative to potentially prevent and control codeine abuse/misuse around the country. This initiative is known as the Codeine Care Project (CCP); a software designed to monitor purchases of codeine-containing products and can further be utilised to aid in the identification of individuals who may be misusing/abusing/dependent on codeine medications (Foley et al., 2018). The toolkit developed aims to equip healthcare professionals with safe dispensing and monitoring of codeine purchases, thus monitoring and regulating the sale of codeine-containing products. The

project utilizes a two-dimensional barcode printed on the packs of all codeine-containing medications coupled with a secure centralized database that serves to monitor the national purchasing of these products, with the national restrictions of sale being set at 4g (Van Hout et al., 2014). In theory, the CCP should effectively monitor the sales of codeine medications if the software is installed amongst all South African pharmacies nationwide; however, the project has not been successfully implemented in SA as yet. No study has been conducted to analyse the impact and effectiveness of the software as this would be difficult considering the CCP is not currently active.

DMP's typically exclude OTC medicines, therefore, pharmacists lack a real time monitoring system for OTC codeine-containing product sales. As a result, they are only aware of the sales occurring in their pharmacy (Hamer et al., 2014). The use of a real time system for both OTC and prescription codeine-containing medicines should be developed, as these systems will be beneficial to monitor/track dispensing, reduce inappropriate prescribing and ensure patients with a genuine need for the medications receive them whilst still flagging/identifying customers who misuse and purchase large quantities (Carney et al., 2018). Software programmes need to be both easy to use and be used by all pharmacists in a country in order to have a significant impact (Islam and McRae, 2014; Poon et al.,2016). Majority of participants in a survey conducted in South Africa (77,2%, n=95/123), Ireland (71,9%, n=334/464) and the UK (83%, n=107/129) expressed that they were willing to participate in a centralized system that monitors the provision of codeine medications within pharmacies (Carney et al., 2018). The implementation of a real-time monitoring system has demonstrated some negative consequences along with the positives. Figure 2.4 below displays a short summary of some of these pros and cons.

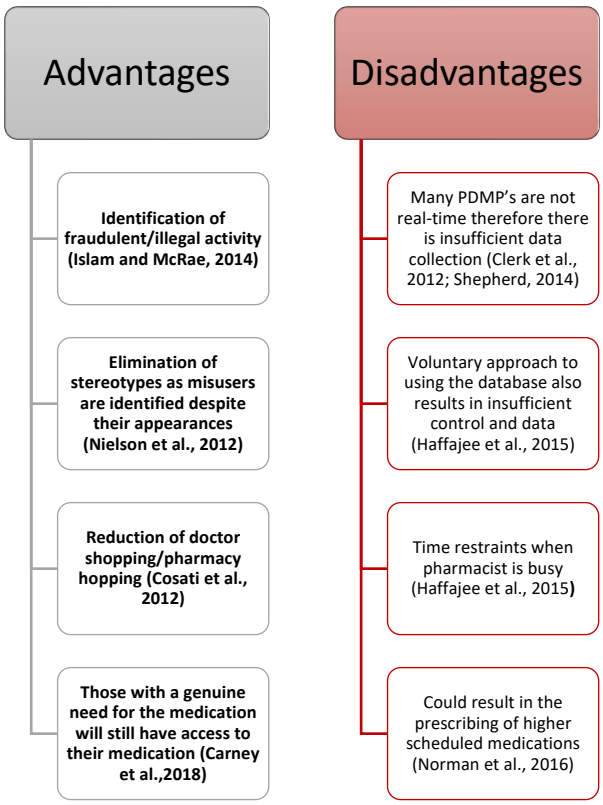


Figure 2.4: Real-time monitoring systems – advantages and disadvantage

2.2.3 Pharmacy Practice/Physician Tactics

Pharmacists are vital in the fight to combat medication abuse/misuse. Pharmacy practice tactics in this review pertain to efforts undertaken by pharmacy personnel in the pharmacy practice setting. This can range from minor changes in everyday pharmacy acts, such as removal of easily addictive medications from the sight of the customers to the attempt of a designed intervention conducted within the pharmacy setting to prevent medication abuse. Community pharmacies are excellent settings for public health posters encouraging people to approach their pharmacist if someone they know or themselves might have a problem with codeine-containing medicine use, these community pharmacies can introduce self-screening leaflet to be given with all patients purchasing codeine-containing medications to aid patients in identifying those with a codeine problem themselves (Norman et al., 2016). A noted downfall being the knowledge misusers possess to deceive pharmacists by knowing the best ways to present themselves (Nielson et al., 2010).

2.2.3.1 UK

Fleming et al. (2004) conducted a study in the UK where a harm-minimisation model was piloted. The model was outlined and discussed at an interdisciplinary exploratory conference before a study manual detailing the model was finalized. The model was created for the identification and possible treatment of OTC medication abusers/misusers, by recording OTC medication sales (Fleming et al., 2004). The model was partnered with an increase in educational information placed around the pharmacy in the form of posters and leaflets centered on the dangers of OTC medication abuse. The study did not yield any misusers who were willing to undergo treatment once being identified and approached by the pharmacists.

The idea of the harm-minimisation model does sound promising, but the practice of manually recording patients OTC medication sales might be unrealistic for busy pharmacies. This study was conducted over a decade ago so this initiative could produce differing results if implemented now using technology to record each sale as opposed to manually recording. Pharmacists piloting this model stated their lack of confidence when having to approach a potential abuser/misuser was a challenge (Fleming et al., 2014). The initiative was also only conducted in two pharmacies; therefore, a larger sample size of pharmacies would need to be included to further assess the effect of this idea.

A community in the UK also attempted to curb the misuse of OTC medication by programming the pharmacy tills to restrict the sales of abusive medications to one pack per customer and made use of customer loyalty cards in order to identify which customers were potentially misusing the medications (Cooper, 2013). This initiative proved to be somewhat ineffective as patients would just simply state that they would just purchase their medications elsewhere (Cooper, 2013). Such pharmacy practice tactics thus may require a larger scale implementation or the use of a universal drug monitoring programme in order to make a significant impact.

2.2.3.2 United States of America

Passik and Kirsh developed a way of opioid prescribing which they referred to as 'In and Out of the Box' prescribing (Kaye et al., 2017). This concept aimed at pointing out to physicians whether their prescribing of opioids deviated from other physicians in their community by comparing their patterns of prescribing with their fellow colleagues at regular intervals. This initiative would work by alerting physicians when their practice deviated or was 'out of the box' from majority of their colleagues and therefore influence the physician to either rethink their prescribing patterns or encourage him/her to seek extra training or education from pain specialists on opioids (Passik and Kirsh, 2008).

This initiative is a proposed concept that, to the authors' knowledge, has not been implemented or piloted. An explanation of how this method would function is all that is available, thus one cannot presume if this concept would prove to have a significant effect in changing prescribing practice and consequently decreasing opioid misuse/abuse. The 'In and Out of the Box' method would not have an impact on OTC codeine misuse/abuse as the concept focuses solely on the prescribing practices of physicians.

A 'universal precautions' approach has been suggested for the sale of OTC codeine in a study conducted by Nielson, Cameron and Pahoki (2013), where all patients are to be screened for risk and a minimal standard of precautions is applied to all patients. This approach aims to address the issue of timing of pharmacist intervention as codeine dependent patients are only identified upon the observation of a patient making frequent purchases therefore this approach is thought to help with early intervention and with that, prevention of dependence (Gourlay et al., 2005). Webster and Fine (2010) also supported the idea of universal precautions to be introduced whereby each patient would initially be evaluated by analyzing the patient's

behaviour, determining if the patient has any history of substance abuse, performing a physical exam and a urine toxicology test. This approach, however, has not been studied or implemented in order to confirm if it would be successful or impactful in reducing codeine dependence. It is merely suggested to control the OTC codeine epidemic and is an idea that could be considered to be tested and analysed for effectiveness.

Community pharmacists are a trusted source of patient information or advice and have a prominent influence on the public's perception on safety and purchase behaviours in retail pharmacies therefore the onus remains with the pharmacist to ensure the correct therapeutic need for the requested codeine-containing product and the suitability of the medication before dispensing (Hamer et al., 2014). A participant from a study conducted in Australia expressed frustration over the lack of information given about the risks of codeine dependence upon first use as opposed to only receiving this advice after the problem had already escalated (Nielsen et al., 2012). Such pharmacists are also responsible for monitoring and intervening when OTC medicine is being potentially misused therefore, pharmacists need adequate training to identify/counsel potential abusers/misusers (MacFayden et al., 2001).There have not been many interventions of this kind being extensively analyzed as they are usually done in a particular pharmacy, with no evidence as to whether the strategy would be effective when implemented at a larger scale.

2.2.4 Educational Campaign

Educational awareness plays a vital role in decreasing medication abuse or misuse especially with OTC medications (Perrot et al.,2019). Many customers use OTC medicines less stringently as it is assumed to be safer (Berry et al.,2004). Upon searching the literature, it was found that America was found to have a large-scale educational drug abuse intervention which focuses solely on the youth. According to Johnson K et al. (2005), if the youth is empowered with cognitive behavioural skills than the prevalence of abuse will decrease. Additionally, Faggiano et al. (2008), found that programmes focussing on life skills decrease the use/misuse of substances in a school setting. There were no other published studies found examining various other medication abuse educational initiatives during the literature search.

2.2.4.1 United States of America

D.A.R.E. (Drug Abuse Resistance Education) is an educational initiative that is conducted in America (Dare, 2020). This initiative consists of talks offered to parents/the community to provide parents with vital facts and information regarding the reasons why teenagers are vulnerable to the misuse of OTC drugs as well as prevention strategies that parents could utilize at home. The programme is police officer led and includes a series of talks and activities that take place at various schools. The lessons are based around a decision-making model designed by D.A.R.E. which is to Define, Assess, Respond and Evaluate. This model is taught to students to provide them with the mindset to make safe and healthy decisions. D.A.R.E. have also launched a programme to their campaign titled 'Opioid and OTC Drug Abuse Prevention', which they have put into effect from the 1st July 2018 that has a bigger focus on OTC abuse/misuse. Each grade has different focuses and personalized lessons targeted for each age group. This initiative focuses on changing the mindset of students in school from a kindergarten level thereby creating a deeply embedded awareness of the dangers of OTC abuse/misuse from a young age which can delay the initiation of drug use by enhancing communication competence and refusal skills (Hecht et al., 2010). This campaign not only aids students against OTC abuse/misuse, but also against other high risk behaviours such as alcohol abuse. This is achieved by focusing on good decision making and the ways to avoid unsafe/unhealthy decisions. This initiative is not naive to the fact that children will be exposed to substance abuse and thus equips young children with the skills/mindset to make the best decision in bad situations.

The initiative is believed to be the most widely disseminated substance use prevention intervention with the programmes network spread throughout the US and 44 other countries (Hecht et al., 2010). By 2007 there was more than 36 million school children around the world participating in this drug prevention programme, D.A.R.E. reported that more than 75% of American school districts have incorporated their project (Pan and Bai, 2009). D.A.R.E.'s utilization of law enforcement officers as the instructors/teachers at these lessons contributes to the success of the campaign. The programme has shown to have short term effects on the outcome of drug use and psychosocial behaviour but has not proven to provide a long-term effect on drug use (Pan and Bai, 2009). However, further critical reviews and expert research/opinions is needed to assess the true success of the campaign. Whilst educating the youth could deter drug abuse, D.A.R.E. shows that such an intervention would not be the most

effective intervention to significantly decrease medication abuse/misuse amongst students both short and long term.

Hecht et al., (2010), investigating the effects of the D.A.R.E. programme indicated that there were significant effects or outcomes determined from the initiative. A meta-analysis of the effectiveness of the D.A.R.E. programme was conducted by Pan and Bai (2009). This study mainly determined that D.A.R.E. showed a less than small effect on both drug abuse and psychosocial behaviour impact. There is a need for a more updated review on the impact of this initiative as the current schedule would differ from the one examined in these studies. It is difficult to determine the long-term effects of D.A.R.E. as one would need to follow-up with school students who participated in the programme, to assess who still abused medication and if any made different choices due to the lessons taught. For OTC codeine it would be beneficial to inform people from a young age of the dangers of OTC abuse/misuse as most schools focus abuse curriculums on illicit drug use (Darnell and Emshoff et al., 2008). However, as this type of intervention cannot be accurately evaluated for significance, one cannot deduce if implementing codeine abuse/misuse education programmes at a school level would have a long-term impact.

2.2.5 Technological interventions

Technological interventions are relevant at present with younger people interacting mainly with technology. Technology allows for interventions to be tailored to specific sub-groups and can be delivered anytime with minimal workforce (Marsch and Borodovsky, 2016). The literature search for this review did not find many of these such interventions in relation to medication abuse as technological interventions are fairly recent.

2.2.5.1 United States of America

In July 2016, the Comprehensive Addiction and Recovery Act (CARA) passed in America, including initiatives addressing the countries opioid crisis. Within this act, a programme for at risk beneficiaries called Lock-In programmes (LIPs) was discussed (Roberts et al., 2016). Medicaid Lock-In Programmes (MLIP) were designed to identify Medicaid patients who are at risk of health-related issues caused by the potential over-utilization of controlled substances. Once these individuals are identified, their access is tightly regulated and as a result the patient is required to use a single pharmacy/prescriber to obtain certain controlled substances for a

specified period of time (Skinner et al., 2016). By restricting people to use a single provider, this allows the provider to best coordinate the medical care of the 'high risk' beneficiary as excessive use of healthcare services is regularly attained through doctor or pharmacy hopping (Roberts and Skinner, 2014). Until CARA was passed, LIPs did not catch much attention in communities in comparison to other opioid interventions; however, currently LIPs are used in most Medicaid programmes (Roberts et al., 2016). Another benefit of this programme is the requirement to deliver educational materials to all LIP enrollees regarding the purpose of the programme along with resources on substance use disorders (Roberts et al., 2016).

Most LIP studies do not assess the effectiveness of the programme besides a few peer reviewed papers and some grey literature (Roberts et al.,2016). These studies indicate three consensus LIP outcomes, namely, LIPs have been associated with a decrease in opioid prescription claims, medical service claims have decreased, and insurance benefit expenditure has decreased (Roberts et al., 2016). Skinner et al. (2016) conducted an interrupted time series analysis of the monthly opioid prescriptions per patient who were enrolled in the MLIP at any point during the study period. Results indicated that enrollment in the MLIP resulted in a reduction in the average of number of opioid prescriptions filled per month and the number of pharmacies visited to obtain these prescriptions (Skinner et al., 2016). However, data obtained from LIPs are narrowly focused as this programme fails to capture opioid use occurring through cash payments and other sources of insurance. Furthermore, there are differing definitions for "high risk" beneficiaries that are defined by the MLIPs (Roberts et al., 2016; Skinner et al., 2016). States have an economic incentive for implementing these programmes if LIPs prove to successfully reduce doctor/pharmacy hopping and non-medical use of opioids as these Medicaid programmes will reduce state expenditure for medically unnecessary health care services required to treat adverse health outcomes from non-medical use of these medications (Roberts and Skinner, 2014).

This type of intervention cannot cover all misusers as it functions with a specific medical aid which not be utilized by all citizens in a country. It is also difficult as an ongoing means of abuse prevention due to that fact that abusers would simply resort to paying cash once aware of this initiative. Moving forward it is recommended by Roberts et al. (2016) for these programmes to move towards a more distinctive approach to determining high risk opioid use such as evidence-based milligram morphine equivalent thresholds and accounting for comprehensive opioid use with PDMP data. Thereby supporting the view that more than one

strategy needs to be implemented. The abovementioned studies regarding MLIP also fail to display the experiences and opinions of HCPs to the MLIP programme.

2.2.5.2 UK

In 2015 a total of 49% of individuals who were surveyed in Great Britain reported searching online for health-related information in the previous three months as opposed to only 18% back in 2007 (Cooper, 2019). It seems promising for online forums to be utilized; however, there is a need for them to be monitored and for more active advice to be offered (Cooper, 2019). Online groups such as Overcount and Codeine free, both functions to provide support issues related to OTC and prescription abuse/misuse.

Cooper (2013) conducted a study which looked to explore what treatments and forums individuals in the UK who considered themselves addicted to OTC medications utilised. Participants recruited from Overcount and Codeine free were interviewed. The online forums were positively received by some participants who stated they continuously engaged with them whilst others stopped use after the first time (Cooper, 2013). Cooper later conducted a qualitative netnographic study on internet forum use for codeine addiction advice, he collected data from Mumsnet and used the phrase 'codeine addiction' to search the site. The responses to these requests for advice regarding codeine medication abuse/misuse included mostly of supportive responses along with warnings of adverse effects whilst other responses included recommended self-treatment advice such as tapering or the cold turkey method (Cooper, 2019). Cooper's (2019) study has provided further insight into the opportunities online sites serve in providing support to medication abusers, a major factor being that many people are ashamed/embarrassed and feel more comfortable posting anonymously online for help. The study, however, only obtained data from one online forum so it cannot claim that online support groups are effective in reducing codeine misuse and if the findings are transferable.

2.2.6 Multidimensional /Integrated Strategy

In this review the referral to a multidimensional/integrated strategy was developed to indicate when more than one type of intervention strategy was implemented in a country. Interventions were only included here if literature available analyzed the different strategies together to show if an impact was made collectively. Such a strategy was only found in America.

2.2.6.1 United States of America

The state of Utah conducted a statewide media campaign using the slogan 'Use Only as Directed' which ran for one year from May 2008 until May 2009 (Johnson et al., 2011). All awareness campaign initiatives directed the public to the 'Use Only as Directed' website which was generated to provide the public with information with regards to the safe use of prescription medications (Johnson et al., 2011). A survey was conducted which yielded the results regarding the effectiveness of this campaign, with 52% of participants stating that the social media messages seen made them less likely to share their prescription medicines with others and 51% of the opinion that the media messages resulted in them being less likely to take medicines that were not prescribed specifically for them (Johnson et al., 2011).

The campaign duration resulted in insufficient monitoring of the outcomes. Johnson et al. (2011) mentioned the important limitations of this intervention, there was no framework in place to evaluate the impact of the program on pain medication misuse therefore results stated are purely descriptive. Associations can only be made as one cannot formulate a definitive outcome/finding between the intervention and any improvement amongst pain medication users. Focusing on OTC codeine-containing medications, a statewide educational campaign can be helpful in most countries as many customers are unaware of the easy manner in which one can fall victim to codeine medication dependence/abuse. However, a media campaign of that level would be costly, and one would need investors to successfully create awareness on the issue.

2.2.6.2 Oregon

Opioid-related mortality tripled from 2.1 per 100 000 residents in 2000 to 6.5 per 100 000 residents in 2015, in Oregon (Hedberg et al., 2019). Oregon has since made multiple efforts to eliminate the opioid crisis in their state by implementing and planning multiple interventions. The state of Oregon developed an opioid strategy (Opioid Initiative) in collaboration with the governor's office which consisted of five action statements to serve as goals for the state to reach (McCarty et al., 2014).

The Opioid Initiative was structured to improve population health in four areas, namely to reduce the patient risks by improving access to non-opioid treatments; supporting medication assisted treatment and naloxone access to reduce the harms to those already taking opioids;

reducing the number of pills in circulation through opioid prescribing guidelines, safe storage and disposal; and lastly, using data to inform and evaluate policies (Hedberg et al., 2019). In March 2015, the Oregon Health Authority (OHA) initiated a learning collaborative focusing on the reduction of opioid overdose and prescribing which then went on to become a statewide performance improvement project in July 2015 (Hedberg et al., 2019). OHA assembled a taskforce team to develop statewide opioid prescribing guidelines to optimize care and safety. Subsequently the OHA created a web-based interactive dashboard run by the Public Health Divisions. The dashboard presents state level data on opioid prescribing, overdose hospitalization and deaths. This dashboard consists of data from multiple sources such as Oregon's PDMP, hospital discharge data, death certificates, medical examiner investigations and emergency medical services data systems (Hedberg et al., 2019). The taskforce presented two prescriber education chances with continuing medical education credits (Holton et al., 2019). Furthermore, the Oregon Coalition for Responsible Use of Medication (OrCRM) convened seven regional summits with over one thousand participants to promote regional action plans (Holton et al., 2019). OrCRM serves to help pharmacies implement these suggested action plans. The coalition has aided pharmacies to install medication collection boxes in accordance with their goal of providing a safe way to dispose of unwarranted opioids, which is important as leftover medication is one way that drives abuse/misuse (Holton et al., 2019).

It can be assumed that the state's efforts have made an impact with the rate of prescription opioid deaths in Oregon declining 17% from 4,7 per 100 000 population to 3.9 per 100 000 population from 2015 to 2016, the sharpest decline of any state (Hedberg et al., 2019). This decrease in prescribing and deaths related to opioid use in Oregon shows promise that the initiatives are having an impact (Hedberg et al., 2019) however, the decline could have been due to other factors as Hedberg et al. merely made an assumption based on the statistics.

It is apparent after reviewing the strategies implemented that each intervention comes with its own strengths and limitations, as can be seen in Table 2.1 below which provides an overview of what has been reviewed in this article. Some countries have tried individual strategies which have proven to not be the most effective however, various literature examining these strategies have put forward the idea that implementing more than one type of strategy might be effective (Roberts et al., 2016; Holton et al., 2019; Wood et al.,2019). This same sentiment is apparent

when looking at the information displayed in this review as each strategy had a limitation that another type of intervention strategy could solve.

When designing and implementing an intervention strategy, significant consideration needs to be taken towards ensuring the continued availability of codeine containing medications for legitimate use whilst preventing the misuse of those medications, thus a real time system/national database style intervention could provide this protection whilst still allowing patients with a need for analgesia access to the medicines (Norman et al., 2016). The development of a real time monitoring system with national surveillance for prescribed products warrant expansion to targeting sales of OTC medicines as many interventions reviewed in this article focused on monitoring prescription medication use.[14] Pharmacies could access information about recent codeine sales by their patients by using real-time sales monitoring of OTC codeine products (Nielsen et al., 2013). For example, table 2.1 shows multiple interventions where it is mentioned that there was a difficulty in assessing impact/utilization due to sales data being confined to the respective pharmacy, lack of communication between pharmacies and patient's pharmacy hopping. These issues potentially may be addressed by the countries having a centralized pharmacy software. However, the impact of such an intervention will require further research.

Table 2.1: Summary/Overview of findings on Intervention Strategies from article

	Intervention Type	Strengths	Limitations	Significant findings/points
1. Regulatory Reforms				
Australia	- Up-scheduling of codeine medication	- Increased pharmacist awareness of codeine misuse	- Sales records confined to respective pharmacy - Both studies examining regulation change had possible reporting bias	NO SIGNIFICANT FINDINGS FROM STUDIES EXAMINED
Europe	- Medicine packaging change - Limited duration of codeine use	_____	- Intervention easily ignored by patients - Restriction on codeine use resulted in use of other opioids - Statistics obtained did not show true drug consumption	NO SIGNIFICANT FINDINGS FROM STUDIES EXAMINED
United States of America	- Legislation regarding physician presence, limiting duration of use and prohibiting advertising - Increased criminal penalties for physicians	- Reported a decrease in the number of deaths attributable to overdose from codeine	- Studies did not compare findings to states where legislation was not implemented to assess impact - Findings could be related to another intervention	- Two studies concluded that the policy changes were attributable to a decline in opioid prescription and mortality over the study periods - Not apparent if these legislative changes are still making a significant and positive impact.
Africa	- Schedule register - Banning of codeine cough syrup imports and production	_____	- No literature published examining regulations	NO SIGNIFICANT FINDINGS FROM STUDIES EXAMINED
2. Drug Monitoring Programmes				
Australia	- MedsASSIST - Project STOP - DORA	- Gives access to vital patient dispensing information	- Possible respondent bias	- Large percentage of participants stated they refused sales of

		- DORA has contributed to the reduction in opioid related harms in Tasmania	- Studies found on Project STOP focus solely on the pharmacist's engagement with the software as opposed to the effectiveness of the campaign itself. - Difficult to determine if DORA is effective due to this lack of published information of the initiative	pseudoephedrine medications as a result of the identification of suspicious sales made through the use of Project STOP. - DORA has been linked to a significant reduction in prescription medicine related deaths in Tasmania
United States of America	- PDMP's	- Many states associate their PDMP's with a lower rate of prescription drug abuse and a change in the general prescribing practices -	- Lack of communication between pharmacies from different retail chains and different states	- After the implementation of PDMP's, prescribing of schedule 3 opioids did not change in a clinically or statistically significant way - PDMP's were linked with a significant reduction in opioid analgesic prescribing in the first six months following implementation, no successive reductions were significant
Canada	- Narcotics Monitoring System	- More emphasis on better prescribing practices	- No data looking on effect on hospitalization/across different pharmacies	- Prevalence of inappropriate opioid prescribing decreased by 40.3%
Africa	- Codeine Care Project	_____	- Software not active therefore no data on efficacy	NO SIGNIFICANT FINDINGS FROM STUDIES EXAMINED
3. Pharmacy Practice/Physician Tactics				

Europe	- Harm-minimisation model - Restricting sales per customer	_____	- Larger sample size needed to assess efficacy - Patients stated could purchase from another pharmacy	NO SIGNIFICANT FINDINGS FROM STUDIES EXAMINED
United States of America	- In and Out of the Box - Universal Precaution	_____	- Has not been implemented or piloted	NO SIGNIFICANT FINDINGS FROM STUDIES EXAMINED
4. Educational Campaigns				
United States of America	- D.A.R.E.	- Most widely disseminated substance use prevention intervention -	- Critical reviews and expert research is needed to assess the success of the campaign - Difficult to determine the long-term effects of D.A.R.E. as one would need to follow-up with school students	- Less than small effect on both drug abuse and psychosocial behaviour impact
5. Technological Interventions				
United States of America	- CARA	- Reduction in the average of number of opioid prescriptions filled per month	- Cannot cover all misusers as it functions with a specific medical aid - Abusers could resort to paying cash once aware of this initiative	- Associated with a decrease in opioid prescription claims, medical service claims have decreased, and insurance benefit expenditure has decreased - Reduces doctor/pharmacy hopping
Europe	- Online Support Groups	- Online forums were positively received by some participants	- Obtained data from one online forum so it cannot claim that online support groups are effective in reducing codeine misuse	NO SIGNIFICANT FINDINGS FROM STUDIES EXAMINED

6. Multidimensional/Integrated Strategy				
United States of America	- Utah media campaign - Oregon Opioid Iniative	- Oregon assembled a taskforce team to develop statewide opioid prescribing guidelines -	- No framework in place to evaluate the impact of Utah campaign - Oregon decline in opioid deaths could be related to other factors	- Rate of prescription opioid deaths in Oregon declining 17% - Both studies found on Oregon's multidimensional efforts are of the view that this strategy could be the most effective

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2.2.7 Summary

Opioid overdose/abuse is a complex problem requiring multifaceted solutions, it seems that more extensive research is required on the main factors leading to abuse/misuse of these drugs in order to design a multifaceted initiative that combines strategies mentioned in this review (Kennedy-Hendricks et al., 2016). Additionally, it is important that prevention efforts remain flexible and responsive to changing trends in OTC abuse/misuse. In order to be successful and have a significant impact, future and current clinical interventions and systems should be implemented to be integrated as part of the workflow of pharmacists and other healthcare professionals (Kawamoto et al., 2005).

From the literature reviewed, it also appears that a multidimensional strategy that gives thought to public health policies/initiatives appears to address the abuse/misuse of opioid medications (e.g., Holton et al., 2018; Hedberg et al., 2019). This will enable consideration and inclusion of a wide range of health policies, pharmacy practice and software initiatives in abuse/misuse strategies that may be required to lead a sustained change in the opioid epidemic (Holton et al.,2018). In considering the advantages and limitations of various intervention strategies, a multidimensional strategy, that incorporates the implementation of a national database which links all pharmacy systems to prevent misusers from obtaining products elsewhere, may help address the abuse/misuse of all the highly addictive OTC medications. Future research is required to explore such interventions.

Chapter 3: Methodology

This chapter outlines the research methodology that was used to conduct this research. It begins with a discussion on the chosen paradigm and method. An explanation on the appropriateness of the method is followed by a brief description on how the research was conducted, including the study design, procedure, sampling, data analysis process and ethical considerations.

3.1 Research Methodology

The convergent parallel mixed methods study design, developed by Creswell and Plano Clarks (2011), was used in this study to enable concurrent analysis of the quantitative and qualitative phases. This design enhances the validity of the data and minimizes the inaccurate interpretation of results (Guest and Fleming, 2014). A convergent parallel method is where the researcher conducts both phases independently of each other until the interpretation phase as can be seen by Figure 3.1 below. The quantitative phase (objective 1) and qualitative phase (objective 2 and 3) were conducted simultaneously to meet the objectives of the study. Upon completion of data collection, the data was integrated when interpreted. This study design was chosen as it allows for the data of both the quantitative and qualitative phases to be prioritized equally, the results are presented independently and findings are integrated in the discussion (Guest and Fleming, 2014). The study was split into two phases and the study design and study analysis for both phases are explained below.

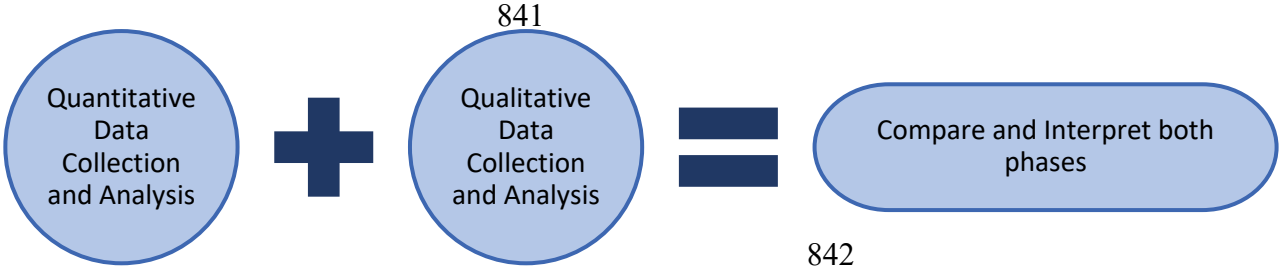


Figure 3.1: Research design process using a convergent parallel mixed method design

3.2 Phase 1: Quantitative study

3.2.1 Study Site

Phase 1 of the study was carried out in the City of Johannesburg. Retail pharmacies (66) located within central Johannesburg were selected. This area of Johannesburg was selected due to the large variation in population demographics, income statuses, and the distribution of both residential and business areas. It also contains a large number of shopping centres and pharmacies that are in close proximity to both public and private schools and universities. The pharmacies selected for this study included independently owned pharmacies and franchise pharmacies. Pharmacies that serve lower, middle, and higher income communities were also selected. By selecting pharmacies serving different income communities, the use of codeine amongst the different socio-demographic classes could be compared.

3.2.2. Sample and sampling method

The sample for this study was based on the pharmacy data provided by IQVIA. IQVIA is a company which aggregates pharmacy and health data in order to aid the healthcare industry clinical research. IQVIA is an information, services and health technology company which collects pharmacy data from multiple sources and suppliers around the world (Tran et al., 2020). The central Johannesburg region was selected as this gave an adequate amount of retail pharmacies in the city to be representative of the OTC codeine usage. The sample further provided enough variation to ensure all demographic factors could be determined and compared. The database provided by IQVIA gave information regarding the pharmacy OTC codeine sales from retail pharmacies in Johannesburg, each OTC codeine product sales number was provided per pharmacy for a 24 month time period.

3.2.3 Study design/data collection

This study involved the data retrieval of OTC codeine sales in central Johannesburg. The quantitative data was retrospective and was extracted from the IQVIA database. Codeine sales for the period of January 2019 to December 2020 were extracted and analyzed. IQVIA, an institute for human data science, provided a database which included the OTC codeine products sold in Johannesburg retail pharmacies. The number of each product sold was provided per month over the given time period for each pharmacy. The extracted OTC codeine sales were then organized into a Microsoft Office Excel spreadsheet. The excel document included the

pharmacy and codeine product sale number per month. The demographic factor compromised of the income status of the area which the pharmacy is located (i.e. high income, middle income or low income). The data was then transferred to STATA 17, a statistical software, in order to determine descriptive statistics. The excel arrangement/clean-up of the data was reviewed by a biostatistician to ensure data was correctly recorded. To ensure validity and strength of results, the biostatistician was further advised when determining the descriptive statistics needed and how best to determine this using the statistical software.

3.2.4 Statistical Analysis

This study was a retrospective study in which the data was summarized to show codeine prevalence/use using both percentages and frequencies. Descriptive statistics were used to show results of the OTC codeine products sold. This was done as descriptive statistics summarize quantitative data by describing the relationship between variables in the chosen sample (Kaur et al., 2018). This statistical method of displaying data therefore was chosen to best organize and display the different comparisons found on the codeine medication sales data. The aim being to summarize the findings. The results were displayed in the forms of graphs and tables.

3.2.5 Ethical Clearance

Ethical clearance was approved for the study by the Medical Human Research Ethics Committee of the University of Witwatersrand. The ethical clearance number is M190643 and the certificate is attached in the appendices (Appendix 1). Ethics clearances were further issued for any amendments made to study and are attached. First amendment approved was a change of study title (Appendix 3) and the second one was the change in the study period (Appendix 2) due to the data received from IQVIA. All identifying pharmacy names and information was kept completely confidential, all IQVIA data was kept on a password locked computer only accessible by the researcher.

3.3 Phase 2: Qualitative study

3.3.1 Study Site

Phase 2 of the study was also carried out in the City of Johannesburg. Retail practicing pharmacists working in pharmacies located within central Johannesburg were selected. The selected pharmacies were located in areas of Johannesburg which had a large variation in

population demographics, income statuses, and the distribution of both residential and business areas as was done in Phase 1. The pharmacies included independently owned pharmacies and franchise pharmacies. Pharmacists working in pharmacies that serve lower, middle, and higher income communities were also selected.

3.3.2. Sample and sampling method

A non-probability, purposive sampling method was utilized in this study. Participants (12) were chosen based on inclusion criteria for the study. Purposive sampling means the choice of participants are made due to qualities participants possess (Etikan, Musa and Alkassim, 2016). The researcher recruited participants based on their proficiency with the phenomenon of interest i.e., being a practicing retail pharmacist. Participants were chosen if they were a practicing pharmacist in Johannesburg at a retail pharmacy. Participants who participated gave consent prior to commencement of the interview procedure. Participants who were not practicing in Johannesburg were excluded from this study.

3.3.3 Study design

Phase 2 of the study consisted of semi-structured pharmacist interviews which were conducted amongst practicing retail pharmacists. Due to the COVID-19 pandemic the interviews were conducted virtually, over Zoom or Microsoft Office Teams. The interviews aimed at exploring the perceptions of practicing pharmacists towards OTC codeine abuse/misuse in South Africa, their opinions on existing regulations in place and views on a possible future intervention strategy. A qualitative descriptive approach will be utilized as this approach looks to describe and explore participants experiences related to certain interventions (Kim, Sefcik and Bradway, 2016). This study sought to determine the experiences and insights of participants in order to motivate for future interventions. The experiences of the participants were explored in relation to codeine medication abuse/misuse, the effectiveness of existing regulations and the views of the pharmacists relating to the implementation of a national database. The interview guide was designed based on research made for the quantitative phase as well as the literature reviewed. The questions in the interview were opinionated and open-ended to allow participants to speak openly on their perceptions/views of the topic. Probing questions were added during the interviews where relevant. A total of 12 interviews were conducted until data saturation was reached. Data saturation is reached if new data has become redundant of data already collected (Sandelowski, 2008) or the amount of data that is needed until nothing new is being found

(Fusch and Ness, 2015). During the interview process the researcher continued until no new data was obtained and the prominent responses in the interviews became redundant of data across all participants interviewed. The length of the interviews varied from twenty minutes to an hour depending on participants responses.

3.3.4 Data Collection Tool

A semi-structured interview schedule (Appendix 4) was used in order to determine the opinions of practicing pharmacists towards codeine misuse/abuse and the potential implementation of a national database. A semi-structured interview was chosen as this method allowed for more flexibility during the interview process. The questions included in the interview guide were chosen after reviewing existing literature on medication abuse studies (see Table 3.1 for a reference table showing the literature that inspired the chosen questions).

Table 3.1: Reasons for choice of questions included in the interview guide

Questions	**Reference***
Demographic Questionnaire	These questions were developed through consultation of the article titled: *Surveillance and uncertainty: community pharmacy responses to over the counter medicine abuse. Health & Social Care in the Community by Richard Cooper, 2013.*
Question 4: **In your years of practice, have you ever had any experiences of OTC codeine misuse/abuse by patients? Can you please tell me a little about these experiences?** **Question 5:** **What do you do at your pharmacy if you suspect misuse or abuse?** **Question 7:** **What do you feel is the pharmacist's role in the misuse/abuse of these medications?**	These questions were developed through consultation of the article titled: *The up scheduling of combination analgesics containing codeine: The impact on the practice of pharmacists. Research in Social and Administrative Pharmacy by Hamer et al., 2014.*
Question 8: **What do you think of the existing strategies in place to manage misuse/abuse of these medications, such as the schedule 2 registers?**	This question was developed through consultation of the article titled: *"Codeine Is My Helper". Qualitative Health Research by Van Hout et al., 2016.*
Question 12:	These questions were developed through consultation of the article titled:

What do you think would work to ensure pharmacists make use of the database in practice? **Question 13:** **Would you be happy to utilize a software in practice? If so, then why and if not, then why.**	*Development of a community pharmacy-based model to identify and treat OTC drug abuse/misuse: a pilot study by Fleming, McElnay and Hughes, 2004.*

*Questions were developed based on previous literature articles on this topic

3.3.5 Data Collection Tool Validity

Upon completion of the interview guide the data collection tool was piloted on two practicing retail pharmacists to ensure questions were understandable and provided insight into the information required to achieve the objectives. The pilot interviews allowed for the interview guide to be amended based on the feedback received as well as gave the researcher guidelines to improve/avoid when conducting the interviews. Both pilot interviews confirmed that the questions asked from the interview guide were clear and easy to understand therefore no questions were amended or removed from the tool.

3.3.6 Ethical Clearance

Ethical clearance for data collection of the study was approved by the Medical Human Research ethics committee of the University of Witwatersrand. All the information acquired from participants remained anonymous with no identifying information noted during data collection. Pseudonyms were used for participants. Participation was voluntary where participants could withdraw at any moment. There was no harm in participating in this study and no remuneration was offered. Consent forms for the interview and for recording of interview session (Appendix 5) were sent to participants to be completed prior to commencement of interview. The ethical clearance number is M190643 (Appendix 1).

3.3.7 Study procedure

Following ethical approval, the recruitment of participants and subsequent interviews commenced. Participants were contacted telephonically and via email to participate due to limitations in contact posed by the COVID-19 pandemic. Once a research consent form was signed, an appointment was made with the relevant participant to conduct the interview. The participants were given a short demographic questionnaire to fill out before the interview

(Appendix 6). The interview was recorded, and the recording was kept on the researcher's password locked computer. Interview recordings were then transcribed by the researcher.

3.3.8 Data Analysis

All interviews were voice recorded and transcribed in order to be analyzed. All interviews were transcribed by the researcher. The transcribing process aided the researcher in becoming familiar with the interviews. Braun and Clarke's (2006) method of thematic analysis was utilized to analyze the interview data. Thematic analysis is a method used to report patterns or themes within data. Figure 3.2 below shows the steps that was taken when analyzing the prescribed interviews. The transcribed interviews were read over a few times by the researcher to gain proper understanding of interview content, codes were then determined first across each interview individually before common codings were noticed. A combination of deductive and inductive codes was utilized. Deductive codes are developed before analysis and inductive codes are developed based on the data i.e., the interview answers, a combination of the two was utilized by the researcher to use deductive codes based on research/existing literature whilst allowing for codes/themes to emerge direct from the data with the inductive codes (Fereday and Muir-Cochrane, 2006). A codebook was created initially consisting of the deductive codes with a definition/explanation of what each code is. Upon data analysis the codes were redefined/added then the identified codes were clustered under main headings/themes thus identifying themes in the data. These themes were identified by collating the codes for each interview into a table format, similar codes from across all interviews along with the reference quotations were grouped together in the table. Once these codes were arranged to group all similar codes together it was easier for the researcher to identify themes. The interview code table was then read over again to ensure themes were most accurate and all key findings were included. Supervisors then reviewed the themes to make sure the analysis was rigorous. Once themes were determined the results could be displayed and discussed.

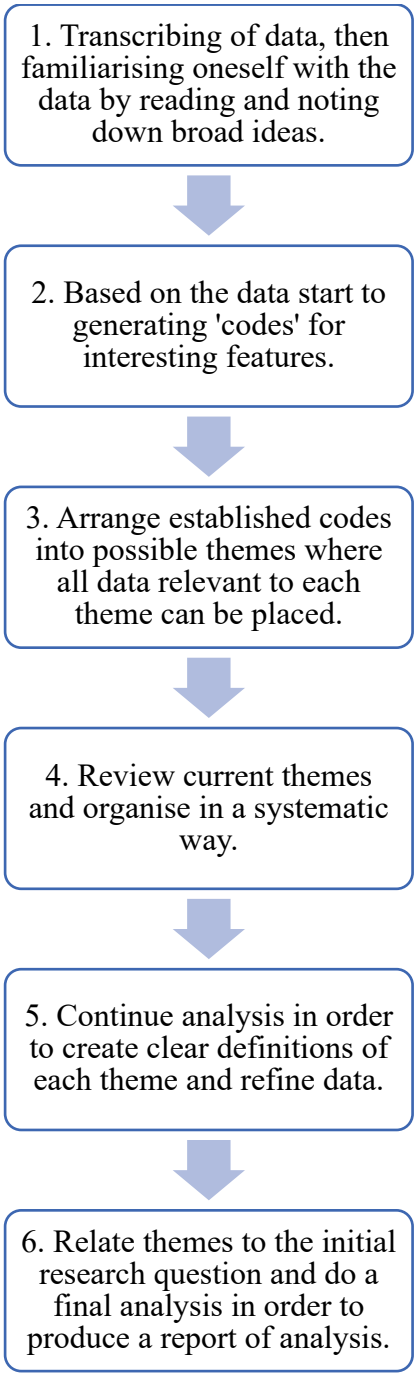


Figure 3.2: Steps of thematic analysis based on Braun and Clarke (2006)

Chapter 4: Results

This study employed a convergent parallel mixed methods study design for data collection and analysis. Therefore, this study allowed for both phases to be analysed independently and then interpreted together in the discussion of this thesis. The results chapter is presented in two sections. The first section being the quantitative results where the over the counter (OTC) sales data has been analysed and displayed using descriptive statistical methods. The quantitative data findings are displayed in the form of graphs and interpretation. The second section of this chapter includes the qualitative results and major themes found from the semi-structured interviews. Specific quotations were included as examples of the responses given.

4.1 Phase 1: Quantitative Phase (Determining the OTC codeine analgesic usage from 2019-2020 in retail pharmacies within the central Johannesburg region.)

4.1.1 General characteristics of pharmacies analysed

The OTC codeine sales data was provided for retail pharmacies in the central Johannesburg region for a two-year time period (January 2019 to December 2020). A total of 66 pharmacies were analysed in this study. The majority of the retail pharmacies provided were franchise pharmacies (n=43) which represented 65.15% of the sample population. The remaining pharmacies were independent pharmacies (n=23) which represented 34.85% of the sample. A franchised pharmacy is a corporation with two hundred or more pharmacies all operating under one nationwide name, whereas independent pharmacies are individually owned pharmacies (Nind et al., 2022). According to the statistics provided by Medpages, a complete and up to date healthcare database, there are 533 registered franchise/chain pharmacies as opposed to 237 registered independent pharmacies in Gauteng (Medpages, 2022). Franchise or chain pharmacies therefore make up the majority of the registered retail pharmacies on the South African Pharmacy's Council (SAPC) register. These findings are therefore congruent with these statistics and are in accordance with the pharmacy demographic relationship in terms of the registration of pharmacies in South Africa (Medpages, 2022).

4.1.2 Total OTC codeine usage and sales

Across the 66 pharmacies investigated, 2 156 845 OTC codeine products had been sold over the study period. These sales consisted of 20 different OTC codeine-containing products, with

the name of each product listed in Table 4.1. Of these products, 16 were formulated as tablets and 4 were syrups.

Table 4.1: OTC Codeine Medication Products analysed

Medication Product Name	**Codeine composition (mg)**	**Medication Type**
ACURATE®	10	Tablet
ADCO-DOL®	10	Tablet
ADCO-NAPACOD®	8	Tablet
BENYLIN & CODEINE®	10	Syrup
BETAPYN®	10	Tablet
GEN-PAYNE®	10	Tablet
IBUCOD®	10	Tablet
LENADOL®	10	Tablet
LENAPAIN®	10	Tablet
MYPRODOL®	10	Tablet
NUROFEN PLUS®	10	Tablet
PROPAIN®	10	Tablet
PYNSTOP®	10	Tablet
SINUTAB SINUS PAIN ES®	10	Tablet
STILPANE®	10	Syrup
STOPAYNE®	10	Syrup
SYNDOL®	10	Tablet
TENSODOL®	10	Tablet
TENSOPYN®	10	Tablet
TENSOPYN PAED®	8	Syrup

Based on these findings, tablets were identified as the major formulation that is being sold. This is expected due to the larger variety of codeine containing tablet products available as compared to the syrups. The range of codeine composition for the products ranges from 8 mg to 10 mg, with most formulations consisting of 10 mg of codeine. The total sales between each year for franchise and independent pharmacies analysed in this study can be seen in Figure 4.1

which gives a month by month comparison of the total sales of codeine products for 2019 and 2020, respectively.

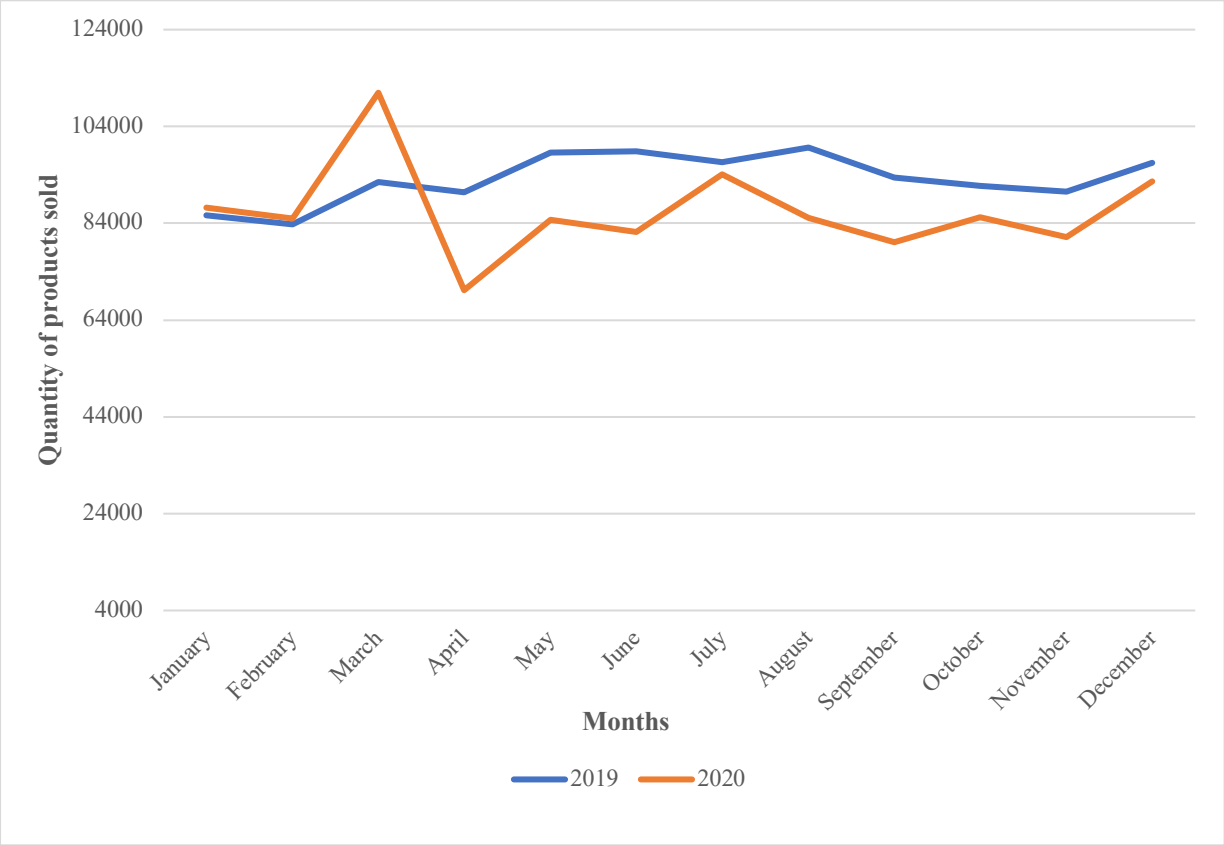


Figure 4 1: Monthly comparison of OTC codeine sales per year

From the graph it can be seen that OTC codeine sales significantly increased in March 2020; which may be attributed to the COVID-19 pandemic. The reason for the spike specifically in March of 2020 could be due to the fact that the countrywide lockdown commenced during that month, this factor is discussed in the discussion chapter below. The total sales volume decreased by 3.7% from 1 118 253 units in 2019 to 1 038 592 units in 2020. As can be seen in Figure 4.1, that sales of codeine containing products drop after March and then started to slowly pick up again as the lockdown regulations fluctuated and eased at various points in 2020 (Jassat et al., 2022). From the line graph it can be deduced that there were slight increases in the codeine sales trends in 2020 around the same time of the COVID-19 infection waves.

The codeine sales were then interpreted further to determine the most frequently sold medication as is displayed in Figure 4.2.

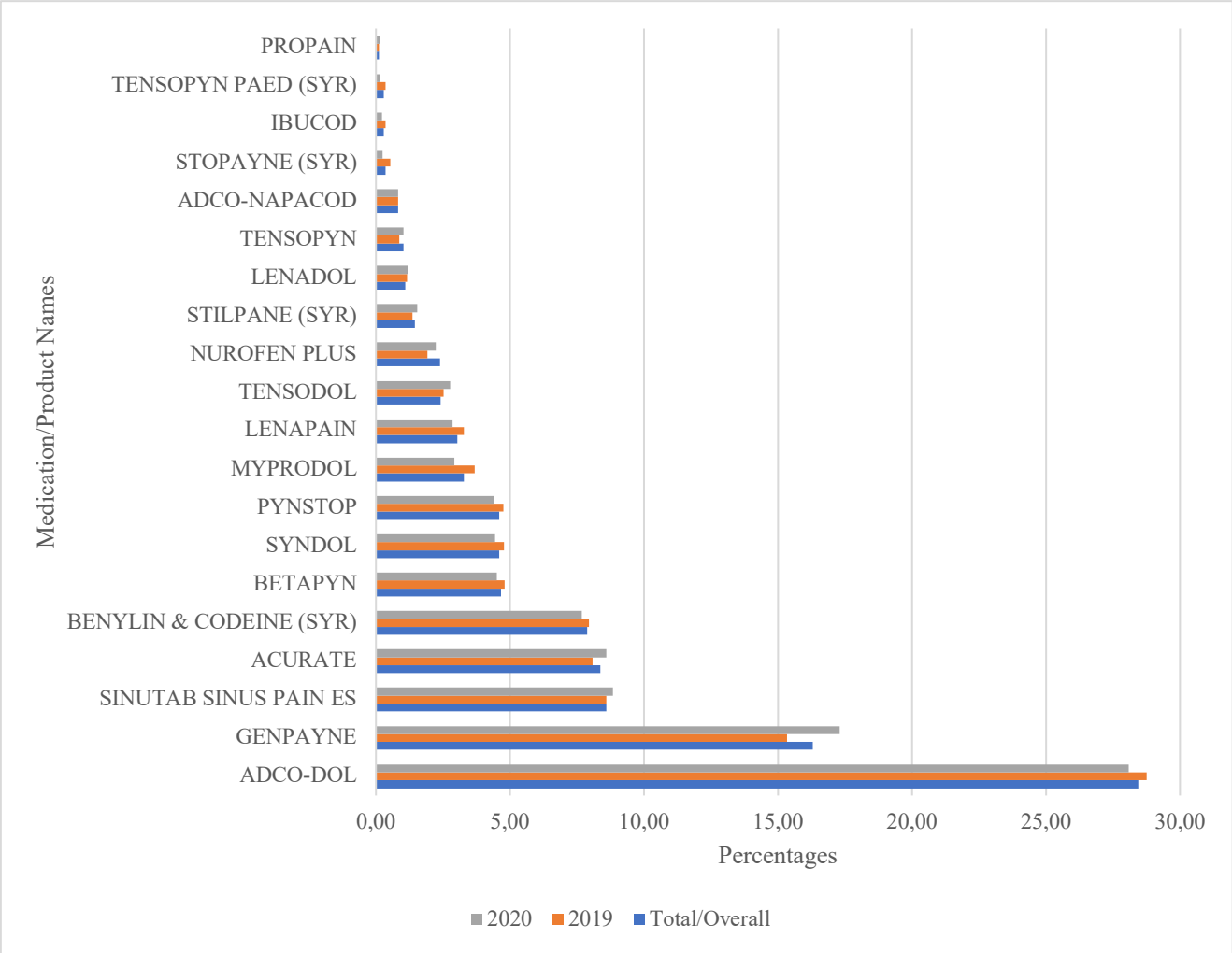


Figure 4.2: Percentage of OTC codeine products sold between 2019-2020

Adco-dol was the most frequently sold medication overall (28.42%) followed by Gen-payne (16.28%). The three highest sold products in 2019 were Adco-dol (28.73%), Gen-payne (15.33%) and Sinutab (8.58%) compared to 2020, where the three highest sold products were determined as Adco-dol (28.08%) followed by Gen-payne (17.29%) and then Acurate (8.85%). Both years proved Adco-dol and Gen-payne to be the two most frequently sold OTC codeine containing products. When comparing the sales of Adco-dol to Gen-payne, 321 316 units of Adco-dol were sold in 2019 and 291 597 units sold in 2020, a total volume sales decrease of 4.24% between the 2019 and 2020. However, when looking at Gen-payne there were 171 470 units sold in 2019 and 179 560 units sold in 2020, therefore a total volume sales increase of 2.30% between 2019 and 2020. The most frequently sold codeine-containing product amongst independent pharmacies was Benylin with codeine, while Adco-dol was most prominent amongst the franchise pharmacies investigated. All medications contain 10mg codeine besides Tensopyn paediatric and Adco-Napocod which each contain 8mg. Sales of these containing 8mg of codeine have much less sales compared to others.

4.1.3 OTC codeine sales based on income areas

The pharmacies studied were classified according to high-, middle- and low income areas based on which area they were located in. This was determined using the city of Johannesburg website (www.joburg.org.za) which detailed such information per region in Johannesburg. The Figure 4.3 shows that of the 66 pharmacies, 24.24% (n=16) were classified as being located in high income areas, 53.03% (n=35) were located in middle income areas and 22.73% (n=15) were located in low income areas.

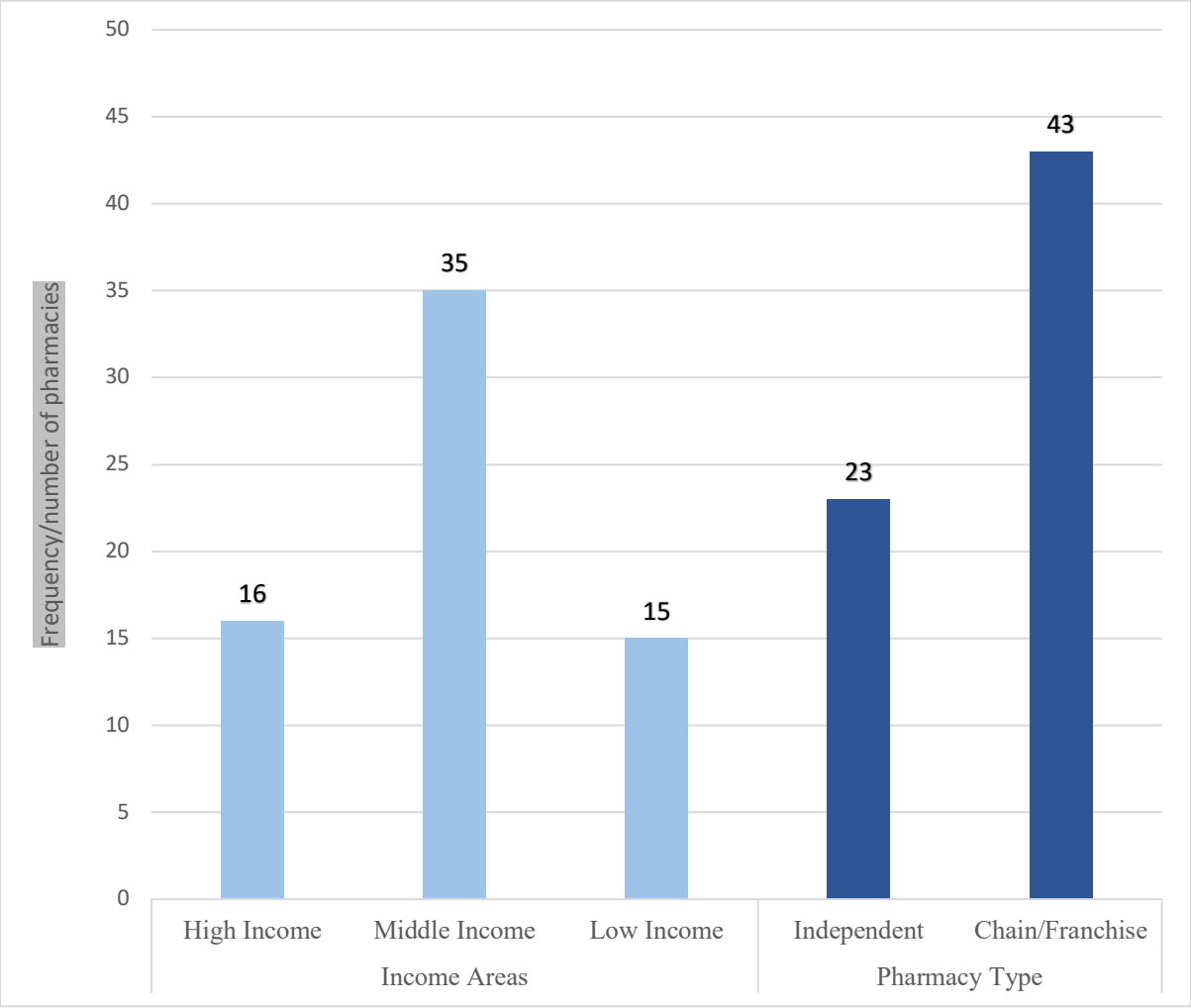


Figure 4 3: General characteristics of the 66 pharmacies analysed

The OTC codeine product sales were determined for each income status area to determine if different income areas were purchasing similar products and which products had the highest sales per area. The results of this are summarised in Figure 4.4.

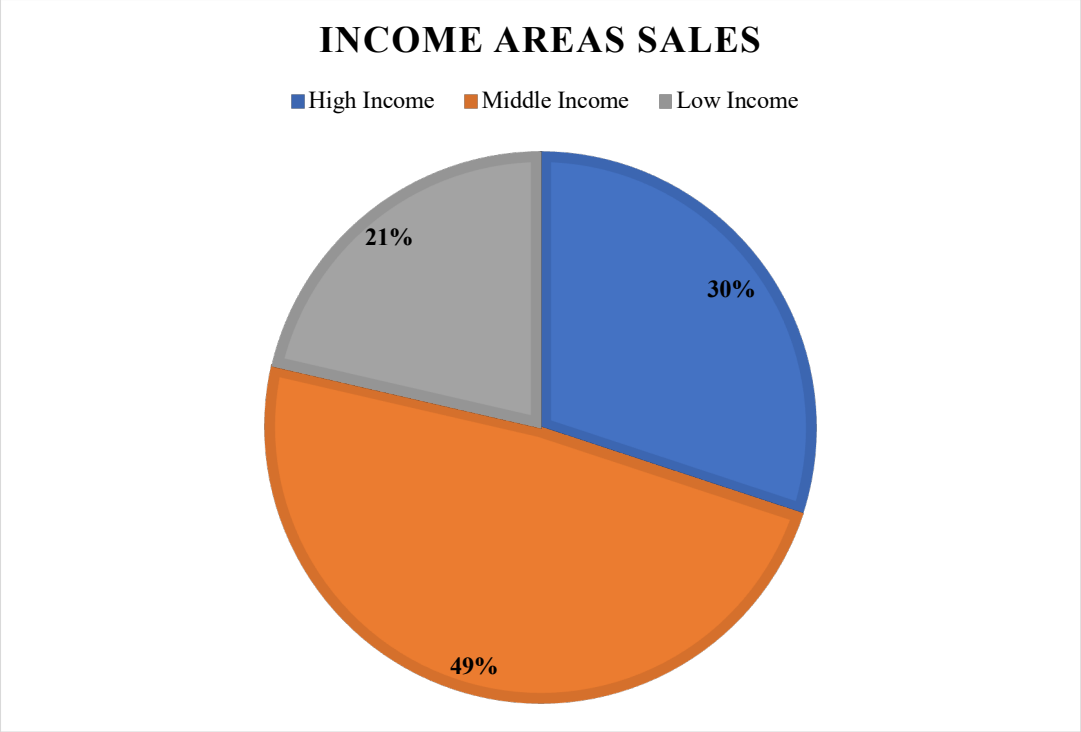


Figure 4.4: Total codeine sales per income area status

Pharmacies located in middle income areas had the highest number of codeine medication sales followed by the pharmacies located in high income areas, however, this could be due to the fact that pharmacies located in the middle income areas represented the majority of the sample population assessed (n= 35; 53%). There was a similar number of pharmacies located in high income (n=16; 24%) and low income areas (n=15; 23%), however, the total codeine sales was higher in the pharmacies located in high income areas. The frequency of products sold in each income status area was assessed and provided for in Figure 4.5.

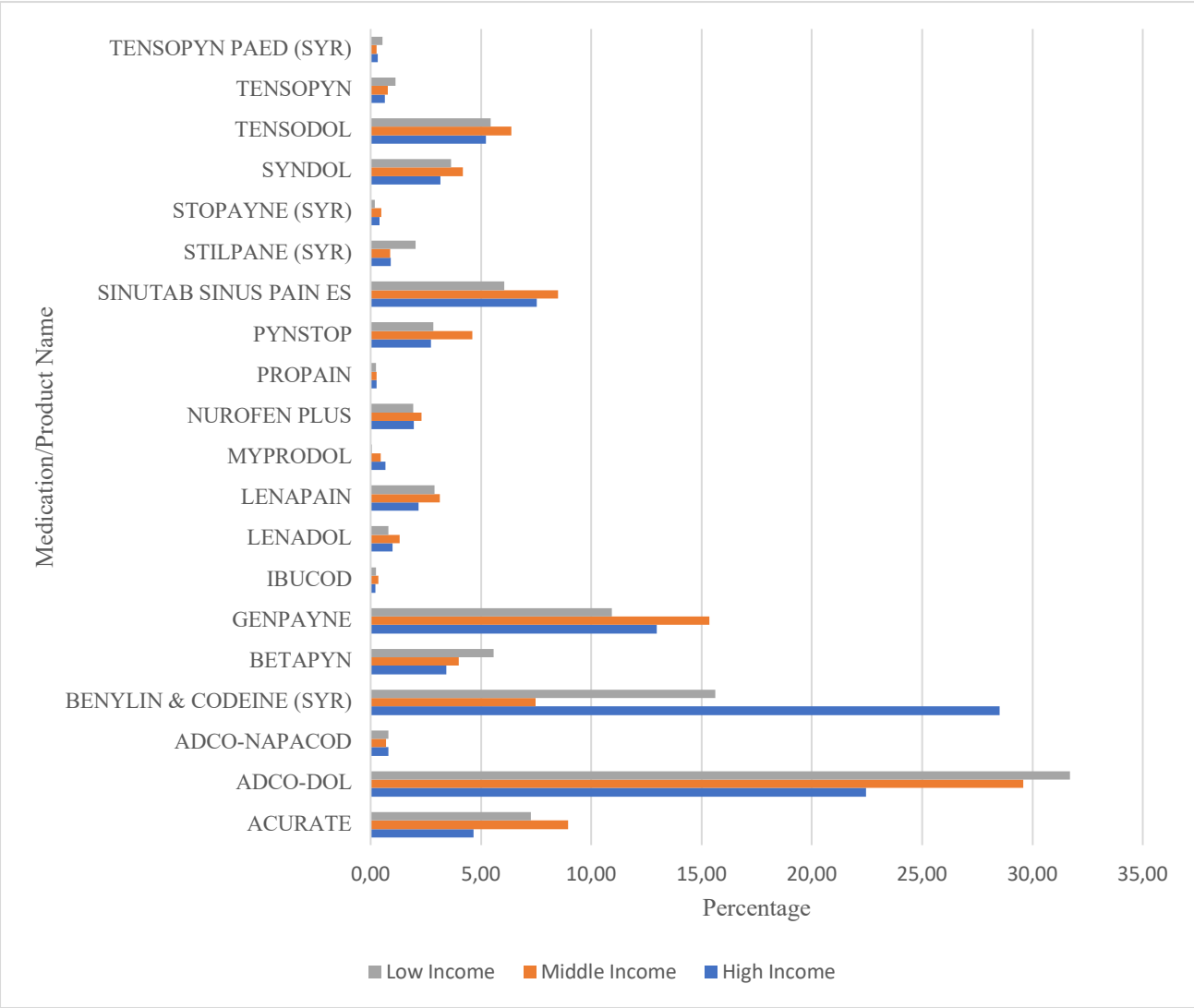


Figure 4.5: OTC codeine product percentage sales in each income area

When looking at the pharmacies located in high income areas, Benylin with codeine (28.49%) was the most frequently sold OTC codeine product followed by Adco-dol (22.44%) and then Gen-payne (12.97%). Pharmacies located in middle income areas had Adco-dol (29.57%) as the most frequently sold OTC codeine product followed by Gen-payne (15.34%) and Acurate (8.94%). Lastly, when looking at the pharmacies that are located in low income areas Adco-dol (31.67%) was also the most frequently sold OTC codeine medication followed by Benylin with codeine (15.61%) and then Gen-payne (10.92%).

4.1.4 Summary of codeine product usage

The top five most frequently sold codeine containing products sold, across Gauteng pharmacies in Johannesburg was determined (Figure 4.6).

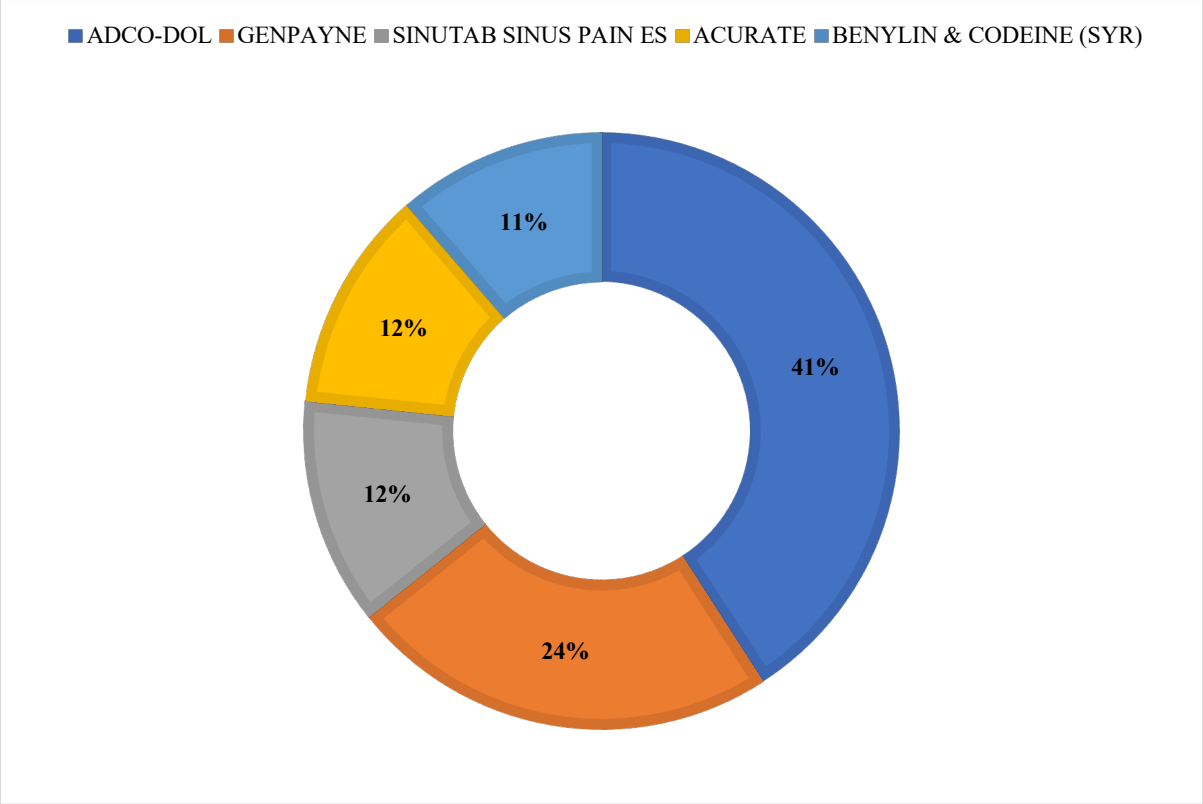


Figure 4.6: Five most sold OTC codeine products overall

The five codeine-containing products most commonly sold were identified as Adco-dol (41%), Gen-payne (24%), Sinutab (12%), Acurate (12%) and Benylin with codeine syrup (11%).

4.2 Phase 2: Qualitative Phase (Determining the attitudes and perceptions of the existing regulations in the prevention of OTC codeine abuse and misuse and the control of codeine medication use)

This section consists of the results obtained from the thematic analysis of the 12 semi-structured qualitative interviews which were conducted amongst practicing retail pharmacists in Johannesburg. Upon analysis of the interviews, four main themes were identified and are displayed in this chapter. Participants are expressed P1 to P12 (P1 = Participant 1 etc.).

4.2.1 Participant Demographics:

As was mentioned in the methodology there were 12 practicing pharmacists who participated in the qualitative phase of this study. The demographic questionnaire was filled out by participants prior to the commencement of the interview. The demographics portion of the survey aimed to identify the gender, ethnicity, highest qualification, age, years of work

experience, pharmacy field, and current retail position. Figure 4.7 below displays a summary of the participant demographics.

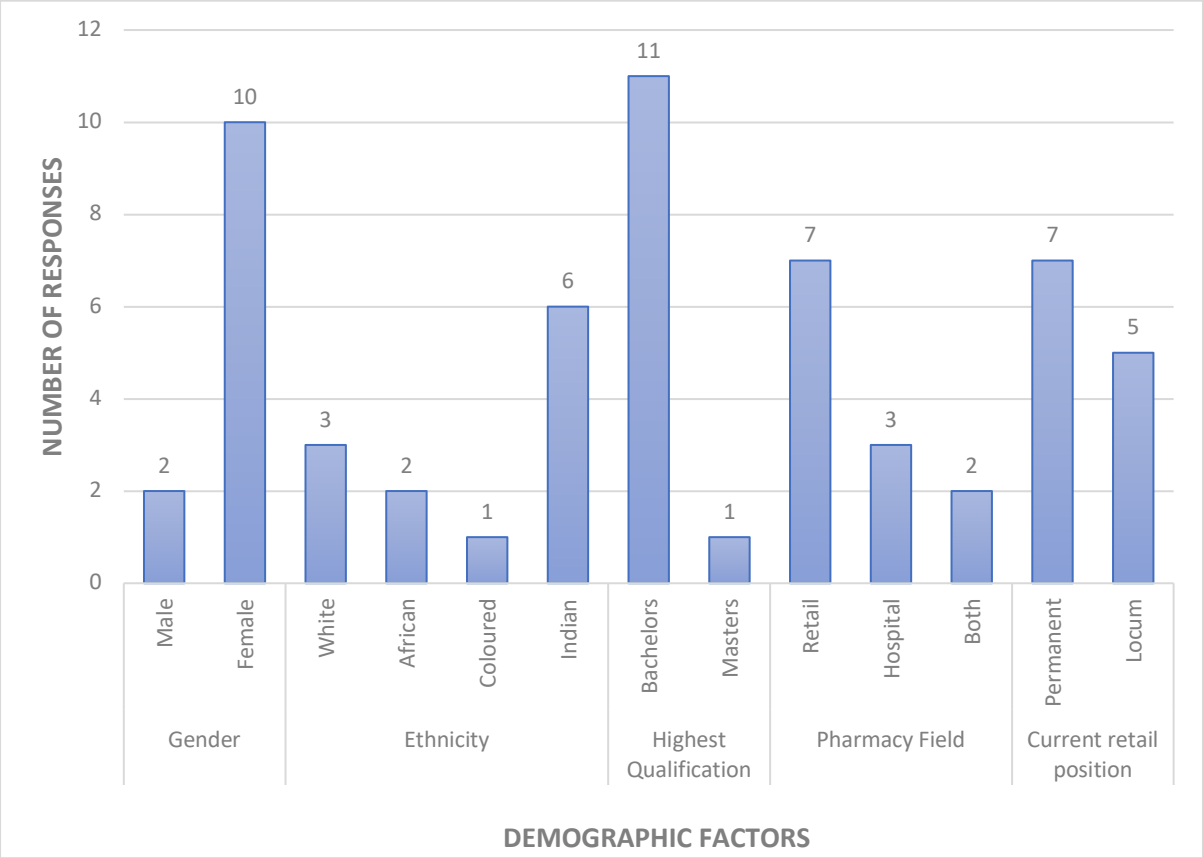


Figure 4.7: Participant demographic information

The last two demographic questions collected were numerical data, namely, the age of the participants and the years of work experience. With regards to age, the mean age was 36.08 (SD = 11.55), with the maximum age being 56 and the minimum age being 24. Regarding the years of work experience, the mean years of work experience was 10.17 (SD = 10.83), with the maximum years of experience being 33 years and the minimum years of experience being 1 year.

4.3 Qualitative Analysis Results

Upon thematic analysis, the themes and subthemes are presented in Table 1 below. This section displays the results by presenting each theme below.

Table 4.2:Themes and Subthemes determined upon analysis

Themes	Subthemes
4.3.1 Over-the-counter (OTC) codeine abuse/misuse being a problem in the South African context	4.3.1.1 Perceptions of pharmacists on OTC codeine use in South Africa 4.3.1.2 The perceived influence of OTC codeine abuse/misuse by age group
4.3.2 Contributing factors to the abuse/misuse of OTC codeine	4.3.2.1 Healthcare Professional's role in contributing to the abuse/misuse of codeine 4.3.2.2 Pharmacy hopping by patients enabling abuse/misuse of codeine 4.3.2.3 Business aspect of retail pharmacies contributes to abuse/misuse
4.3.3 Ineffectiveness of the Schedule 2 register in the management of abuse/misuse of codeine	----
4.3.4 Up-scheduling of codeine as a suggested strategy to control codeine abuse/misuse	----
4.3.5 Implementation of a national database to control codeine abuse/misuse	4.3.5.1 Attitudes towards the database 4.3.5.2 System requirements for a national database: the need for automation and integration into the existing pharmacy system 4.3.5.3 Educating the public on reason for database installation due to the codeine use issue

4.3.1 Over-the-counter (OTC) codeine abuse/misuse being a problem in the South African context

One of the core themes identified in the analysis was that OTC codeine abuse/misuse does exist within the South African context. Specifically, the following two subthemes were identified:

the perceptions of pharmacists on OTC codeine use in South Africa and the age groups perceived to be most commonly abusing or misusing codeine in South Africa.

4.3.1.1 Perceptions of pharmacists on OTC codeine use in South Africa

All participants (N=12) expressed concern that codeine is being misused in South Africa (SA), as can be seen from the quote below:

> P11: "There was always people coming in for codeine syrups and they wouldn't have any symptoms. But they would know all the brand names, they would know where they were on the shelf at over the counter and still wanted to use the codeine even with no symptoms. And if we ever told them that there was no stock because we knew that they were addicted then they wouldn't want any other syrup, they would only want codeine."

According to P11's comment, there is suspicion of misuse due to the patients requesting the product with no symptoms present. Misuse was similarly mentioned by P3 who stated, "A lot of people coming for codeine substances, for various reasons, and a lot of the reasons are not really what codeine is therapeutically for". As can be seen from this quote, P3 believes that codeine is being misused because patients are requesting the medication for reasons that codeine is not intended to be used for. From the above quotations it can further be seen that there is not just one codeine product being mentioned by participants but rather it is mentioned that various codeine substances are being misused since patients are requesting the medications for reasons not therapeutically meant for. A quote from P5 supports this sentiment; "Some people complain that they are buying Adco-dol for people who are addicted to Adco-dol. Then I see a lot of Benylin with codeine cough syrup and Stilpain, Sinutab with codeine is another one that is misused a lot".

4.3.1.2 The perceived influence of OTC codeine abuse/misuse by age group

From the interviews conducted, participants perceived that the abuse/misuse of codeine in South Africa is more prevalent in particular age groups. The issue of abuse/misuse of OTC codeine products was mentioned by all participants (N=12) and seems to lie between two age groups namely those who are younger and those who are older. Although all participants flagged that age is linked to abuse/misuse, there were discrepant views surrounding which age groups were the most prominent in the abuse and misuse of OTC codeine medications. The

majority of participants (n=8) felt abuse/misuse is prevalent among both the older and younger age group. This is illustrated by the quote from P3 below:

> P3: "It was sort of between the younger group that sort of looked like they just started varsity, that sort of age, and then the older group was largely more sort of people in their mid-fifties to sixties, of that point where some of them had retired and it seemed like a way to numb them because they felt like they had nothing more to do with their lives. But why I particularly made reference to the youngsters was because it was, how can I say it, I never would have thought that so many youngsters could be addicted to something like Stilpane syrup, it was just alarming to me to experience that. So it's not that it was just the young people coming in there were both youngsters and older people, majority in the age groups that I mentioned in my experience but for me I was just taken aback by how youngsters would really fight for it."

Similarly, P8 stated, "I feel like it is actually an equal trend between two groups like I can tell you that there are young people, so if I am saying young, I am talking maybe a 16-year-old ranging to about a 25-year-old and then definitely old people misusing as well".

A few participants (n=3) felt it was just the younger age group as can be seen from quote P2; "Yeah like the young guys like maybe 19,20 or 21 are the main culprits using codeine for the wrong reasons", along the same lines P4 also supported the idea of the younger age group misusing codeine; P4: "I would say it is probably guys that are about 17 to 25, that is my guessing/estimating, they are the problem group." and only 1 participant felt it was only the older age group as can be seen from the quote from P7; "You see mainly the elderlies that were gone for maybe a surgery and been giving it for pain relief and then become addicted to it."

4.3.2 Contributing Factors to the abuse/misuse of OTC codeine

Participants identified that there were several factors that contribute to the abuse/misuse of codeine medication. The participants identified various factors; some participants mentioned the same contributing factors, but others spoke to different factors. These factors were then split into the respective sub-themes and displayed below. The subthemes included the role which healthcare professionals play in contributing to the abuse/misuse of codeine

medications, pharmacy hopping by patients enabling abuse/misuse of codeine, and the business aspect of retail pharmacies contributing to abuse/misuse.

4.3.2.1 Healthcare Professional's role in contributing to the abuse/misuse of codeine

Many participants (n=10) mentioned the role they feel pharmacists play in contributing to the abuse/misuse of codeine medications. The participants discussed how pharmacists facilitate or indirectly contribute to drug abuse/misuse, as certain participants (n=5) supported the idea that they have experienced pharmacists in the retail setting falling guilty of handing out codeine medications without questioning or suggesting a codeine medication to a patient without proper counselling on the addictive qualities of the medication. This sentiment was mentioned by participant 2 shown in the extract below.

> P2: "I avoid codeine by all means but a lot of us pharmacists, a lot of pharmacists just say oh Adco-dol will help, or Lenapain and I feel like we can contribute in that regard. Yes, pharmacists we already know the effects of codeine, the risks that are involved but if you go around there suggesting Adco-Dol to a patient I feel like it is a bit irresponsible"

As can be seen from the quote above the ease in dispensing the codeine product can be viewed as a contributing factor to the abuse/misuse of codeine. A similar sentiment was also mentioned by participant 7 below.

> P7: "I also think that pharmacy, in particular, enables people to continue their addictions because they always just give the product and they give more than what they are supposed to. Like the legislation says only one box of Adco-dol forties are allowed and they will give five boxes. I think they (pharmacists) do contribute to it intentionally and unintentionally"

According to the quotes above, pharmacists in the participant's experience are guilty of contributing to abuse/misuse by easily giving out and recommending codeine medications to patients.

Some participants (n= 5) further indicated that doctors play a key role in contributing to the abuse of codeine through their prescribing practices specifically it was felt that doctors over-prescribe medication and write up prescriptions without the proper monitoring in place. For example, P1 mentioned that doctors were prescribing codeine products constantly; "Patients

get prescribed codeine quite a lot you know from doctors. I think the doctors that prescribe it constantly over and over again is also part of the problem." Similarly, P8 mentioned that doctors over-prescribe codeine medications without proper monitoring and consultation; "You had doctors there who had been seeing their patients for years on codeine products without consulting any specialist and their doctor is just prescribing this over and over again". These quotations demonstrate the over-prescription of codeine by healthcare professionals without further investigation or follow-up regarding the reasons why, suggesting that doctors failing to monitor patient condition progress and the ease by which pharmacists dispense/recommend these codeine products are possible contributing factors to codeine abuse/misuse.

4.3.2.2 Pharmacy hopping by patients enabling abuse/misuse of codeine

Majority of participants (n=8) mentioned the issue of patients being able to get codeine medications from multiple pharmacies due to the pharmacy systems not being linked as can be seen from the quote from P6; "I have my own system and the next pharmacy will have their own system. There is no link so you could take it from me today but there are so many pharmacies in our area so you could get the medication from anywhere." Based on this, participants mentioned the issue of pharmacy hopping as a contributing factor to codeine abuse/misuse, with patients stating that if they were refused codeine medication from a pharmacy, they could easily obtain the medication from another pharmacy. This can further be seen in the quote below from P9.

> P9: "What happens with patients is that they just move from pharmacy to pharmacy. I mean if you don't get it from one place then you get it from somewhere else. You going to take a drive and go to another pharmacy. Schedule one is nothing, schedule one just gives my driver's license and says I stay in a random place, and I can then go to Dis chem then go to a Clicks then a ShopRite and I can get three boxes of Adco-Dols."

A similar sentiment was said by P7 with regards to the issue of patient's pharmacy hopping adding to the ease of being able to abuse/misuse codeine; P7: "…if I have noticed that the person is obviously abusing it but then at the same time I can't really do much because even though I refuse to give the medication they just going to go to the other pharmacists, they are pharmacy hoppers they can go to one pharmacy and get it and then go to another pharmacy and get it."; P7 explained how the lack of a linked pharmacy software system allows for pharmacy hopping, which is perceived as a problem that contributes to codeine abuse/misuse,

as it makes it difficult to stop abuse when it is discovered by the participants as patients are aware that they are able to purchase medication from another pharmacy.

4.3.2.3 Business aspect of retail pharmacies contributes to abuse/misuse

A popular concern expressed by most participants (n=9) was the business aspect of retail pharmacies playing a role in enabling abusers/misusers. This can be seen by comments made by P4, who said; "…there are pharmacies who have reputations for allowing it (codeine) and encouraging it because it's money and at the end of the day you are either pharmacists because you want to help people or you are a pharmacist as a businessman", and P11, who said; "…in private pharmacies it is about making the money so they give it to them so it is down to like the personal choice". As can be seen from the two quotes above both participants expressed the negative impact retail pharmacies have on the abuse/misuse of codeine. By retail pharmacies allowing the business side to drive the sales and therefore encourage the sales of medications in order to gain maximum profits.

4.3.3 Ineffectiveness of the Schedule 2 register in the management of abuse/misuse of codeine

Participants spoke about the current regulations in place in retail pharmacies, specifically the schedule 2 register and its role in the abuse/misuse of codeine. All participants except one (n=11) mentioned that the schedule 2 register is ineffective, the reasoning as to why it is deemed to be ineffective varied across participants. From the above mentioned participants, the majority of participants (n=10) viewed the register as being ineffective in managing the abuse/misuse of OTC codeine. With one participant offering a differing view; P4: "I don't think the register is effective in terms of deterring these people because they are still going to buy it. They don't care and they might even give a fake name to get it at different pharmacies."; from this quote it can be seen that P4 alluded to the register not being effective in discouraging patients from purchasing codeine, as opposed to other participants who stated the register's ineffectiveness in managing/controlling codeine abuse/misuse.

Regarding the 10 participants who mentioned the ineffectiveness of the register, there were two different reasons mentioned for this. A larger group of those participants (n=6) indicated that the schedule 2 register is simply not being used as can be seen from the quote; P2: "No, we never even used it (schedule 2 register) at my previous pharmacy, it is something that I

never knew about until later on in my career". This claim is supported by a quote from P9; "In my twenty years I don't think anyone has kept or used a schedule 2 register because the patients walks in for codeine then they just give it. The register has never been used." The remaining participants (n=4) flagged that it is not effective as there is not enough time for retail pharmacists to complete the register daily, as can be seen from the quote; P11: "…it is not effective because when you get so busy you don't have the time to make sure that you go and write down in a register". P1 supported this as can be seen from the quote; P1: "…the schedule 2 register is more admin, and a lot of people can't do it in a very busy pharmacy, so it doesn't get written down".

4.3.4 Up-scheduling of codeine as a suggested strategy to control codeine abuse/misuse

It was found that some participants (n=5) suggested that OTC codeine medication needs to be up-scheduled to be available by prescription only to control the abuse/misuse of the medication.

> P2: "At the end of the day a person can come and request for it like it is within their rights so let's not give them that power to say you can come and request it, let's just make it a schedule 4 so they need a script for it. If you put that barrier of getting a script that is more cost going to the doctor and all those barriers by up scheduling it, it would deter a lot of people because a lot of these people are cheap druggies. They actually you know can just afford this cheap stuff like Broncleer etc. so I believe that up-scheduling will make a huge difference."

As can be seen in the quote above the idea of up-scheduling codeine medication is felt by the participant as a means to prevent and deter the abuse/misuse of it. The same sentiment was also expressed by P7; "I do think because of the abuse they should look at the scheduling again. I think it would obviously make a difference because people won't just walk in and say they want it"; P7 shared the same belief on the idea of up-scheduling as a means to prevent the abuse of codeine medications. These participants stated that the change would be beneficial since it would limit the patient's ability to request codeine and restore the healthcare professional's control over the sale of medications.

4.3.5 Implementation of a national database to control codeine abuse/misuse

Participants mentioned their opinions and views on the strategy of the implementation of a national database in order to manage the apparent codeine abuse/misuse. A few subthemes

were identified within this theme and are presented below, the subthemes respectively consist of participant's general attitude towards the national database concept; the need for an integrated and automated system and lastly the need for public education surrounding a database installation and codeine abuse/misuse.

4.3.5.1 Attitudes towards the database

Nearly all participants (n=11) supported the idea of the possible installation of a national database as a potential strategy to control OTC codeine abuse/misuse as can be seen from the comment made by P10; “I think the main strategy would be a centralized system that monitors the use of codeine products because then you can track and see if someone went to another pharmacy. If you have a centralized system, then you can keep track of them properly”. Similarly, P7 expressed the same view; “I think that would make our job a lot easier, I think it would be good to centralize the system so that you can have an accurate history and record of codeine sales”; as can be seen from the quotes above participants felt the implementation of a centralized database would ensure proper tracking of codeine sales which would prevent the excessive purchase of codeine products. Further from this these participants displayed a positive attitude towards utilizing the database in their daily practice; P2: “I would love to do that and utilize such a software because then it would help, I actually feel this codeine use is a problem, it would make me happy to say you know I can’t give you because of this system”. As can be seen from the quote P2 expressed support for the system being implemented as it would give the participant control when refusing an abuser/misuser codeine medication due to the system controlling the amount dispensed per patient. Similarly, P8 mentioned the same thing; P8: “I would definitely use it. Why should I not do it if it is benefitting everyone. So, yes definitely I would be someone who would drive it and really try to make it work.” it is apparent from the above quote that the participants also expressed a positive response to the system.

Although 11 participants mentioned that the national database would be effective one participant mentioned otherwise; P9: “The database idea can’t work. It is very difficult to work because you know trying to implement a first world idea in a third world.”; as can be seen P9 believed the database cannot work in a third world country. The participant further mentioned that the implementation of such a system would push the sales of codeine medications onto the black market.

4.3.5.2 System requirements for a national database: the need for automation and integration into the existing pharmacy system

All participants expressed what they believed the database needed in order to be installed successfully and be utilized by pharmacists. Participants' responses and comments appeared to be concentrated on the potential system's automation and integration into the current pharmacy software.

Along with the assertions that they would use the system if it were developed, participants also stated a number of requirements that they would need to be included in the database design should it be implemented. All participants (N=12) stated that they would require the system to be completely automated; P1: "…if it is automatic then for sure pharmacists will be complying, and it would be really good"; as can be seen P1 expressed that the system being automated would ensure pharmacists would comply and use the system in practice as was also stated by P11; "I definitely think if it is integrated but more so if it is automatic, like I don't want to have to open another software and then do a list."; who further expressed the need for the system to be automated if implemented.

Many participants (n=10) mentioned that the database should be integrated into the existing pharmacy software as P12 said; "Integration is the most important part because we don't want to find ourselves doing extra work with regards to this"; therefore, P12 expressed the need for integration so that the pharmacist would not have extra work added onto their daily practice. This sentiment can also be seen in the quote below where P6 stated the system must be integrated because of the time saving factor.

> P6: "…it should not be a separate system to our current dispensing software because then it is going to be too cumbersome and time consuming. Must be sort of incorporated in your dispensing software. It can't be a separate software; it has to be integrated into the software we are currently using"

4.3.5.3 Educating the public on reason for database installation due to the codeine use issue

Many of the participants (n=8) upon discussing the national database concept mentioned the importance of educating the public on the reason for its installation, specifically some

participants (n=5) mentioned that there is a need to educate the public on the database installation itself as can be seen from the quote below.

> P5: "…the public needs to be addressed on the database installation. I think that it needs to be news and headlines, things like that because that's the only time they would actually know about it and then if they are more aware then they are less likely to fight with the pharmacist"

Similarly, to the quote above P11 expressed the same sentiment on educating the public on the database being installed; P11: "I definitely think education is needed on how the database will be installed so the public knows what to expect so educating the public on why would definitely help". Other participants (n=3) felt that there first needs to be public education on the general abuse and effects of the use of codeine followed by the education on the database itself as can be seen from the quote below.

> P8: "You have to gradually create the process and the beginning it should be education, well that is what I feel because you start with educating people so this is the story about codeine, this is why it is wrong and this what the side effects are, this what you need in order to purchase codeine and this is why the database is being installed. If people know it and you starting to implement it then they will be more willing towards the change."

As can be seen from the above-mentioned quotes, the participants expressed that in order to ensure the database's efficacy and the public's favorable reception of the system, patients must first be educated about codeine's addictive nature and the dangers of repeated use. As a result of this, the new database is being implemented with patients' safety and best interests in mind. The same sentiment was mentioned by P1 who also expressed that in order for the public to be more understanding/willing to accept the change in the pharmacy system there needs to first be education as seen below.

> P1: "I think maybe first educating them (patients) on saying that codeine use is not safe and a problem so then educate that we are upgrading our systems so that it is better and safer for you. They just need to know that we are doing it for the betterment of them."

From the quotes above it can be seen that overall, there needs to be education on the national database, some participants expressed the need for initial education on the risks of codeine use generally followed by education on the installation of the database in order to make for a more effective implementation of the system. Other participants expressed the need to merely educate the public on the implementation of the database itself.

4.3.6 Summary/Conclusion:

The thematic analysis was conducted, and the themes mentioned above in this section were identified during the analysis. The results of the analysis showed that OTC codeine abuse/misuse was identified by participants as being a problem in South Africa. The factors suggested as contributing factors to the abuse/misuse of codeine were the healthcare professional's role, the issue of pharmacy hopping and the business influence on codeine abuse/misuse. Current existing regulations namely the schedule 2 register was deemed ineffective. Linking to this the up-scheduling of codeine to prescription only suggested as a possible strategy in the control/management of codeine abuse/misuse. Lastly, the implementation of a national database was explored regarding participants attitudes towards the system being mostly positive, the need for an integrated/automatic software and the suggestion of educating the public on the issue of codeine use along with the installation of the database.

Chapter 5: Discussion

This chapter is divided into five sections. Section 5.1 provides a brief explanation of the purpose of this study. Section 5.2 discusses the results of the quantitative phase of the study and section 5.3 discusses the results of the qualitative phase of the study. Following from this, section 5.4 integrates the discussion of the quantitative and qualitative components in order to effectively answer the research question.

5.1 Purpose of the study

This study was conducted in order to determine the codeine usage and perceptions surrounding codeine abuse and misuse. The study aimed to analyse the OTC codeine product sales in central Johannesburg along with the perceptions on codeine use to determine whether it was felt that OTC codeine is being abused/misused. The objectives were identified in order to achieve this by means of describing the OTC codeine sales/usage for the time period of 2019-2020; and through qualitatively determining the views of retail pharmacists in Johannesburg towards codeine use and the existing regulations in place.

The quantitative methods provided the information on the OTC codeine sales in central Johannesburg by investigating the OTC codeine products most frequently sold. The qualitative methods provided information regarding the pharmacists' perceptions towards the issue of OTC codeine misuse and abuse in South Africa (SA). As one phase will balance out the weaknesses of the other, the integration of both these outcomes will give a comprehensive grasp of the findings and enable a greater analysis of them.

5.2 Discussion: Phase 1

The characteristics of the 66 pharmacies analysed were described in the results section. The sales data of OTC codeine products were analysed over the study period for each pharmacy. Codeine was stated as being the most abused OTC drug in SA based on the pharmaceutical trash analysed (Hodes, 2019). It was determined that a total of 2 156 845 OTC codeine products were sold over the two year period. The sales between each year was analysed, it should be noted that there was a slight difference in the sales/usage data between the two years as the total sales decreased slightly in 2020 compared to 2019. This could be attributed to the change in medication purchasing behaviour due the corona virus pandemic (Ayati et al., 2020).
When looking at the frequency of sales between March 2019 and March 2020 it can be seen that the frequency of sales in March 2020 is higher than that of the previous year. This finding,

however, was not statistically tested for. Nevertheless, the higher frequency of OTC codeine sales in March of 2020 suggests that this could have been associated with the commencement of the COVID-19 pandemic in SA wherein the lockdown regulation was implemented at the end of March 2020 (Perofsky et al., 2021). This is supported by a finding that there was a global increase in demand for medications in March of 2020 (Coman et al., 2022). The spike in sales in March 2020 is consistent with findings in the literature where multiple countries reported an increase in medication sales specifically in March 2020. In Germany it was determined that there was a surge of medication purchases a week prior to the implementation of the lockdown (Kostev and Lauterbach, 2020). The same sentiment was found in both Australia and America where it was determined that medication sales increased in March 2020 (Clement et al., 2021; Engstrom et al., 2021). Furthermore, a study conducted by Gomes et al. (2022) across 66 countries found that there was a short term increase in opioid purchases in March 2020 followed by a reduction between April and May 2020. This is consistent with the findings in this study.

Due to the implementation of lockdown the public might have stocked up on medications in their households as it was uncertain how long the strict lockdown would be in place for. This is because wave one of the COVID pandemic (between June and August 2020; Jassat et al., 2022) coincides with the increase in total codeine sales found between June and July. Following from this there was a second wave of COVID infections (between November 2020 and February 2021; Jassat et al., 2022) which also coincides with the increase in sales of codeine products seen between November and December of 2020. This idea of panic buying has also been reported in literature as a coping mechanism/response to the uncertainty of the pandemic (Arafat et al., 2020). Another study supported this by determining that adults were found to be panic buying medications during the COVID pandemic (Coman et al., 2022).

Adco-dol and Gen-payne were the two most sold and thereby most used OTC codeine products in central Johannesburg. This could be because both medications are used for pain/analgesia and the most common reasons documented for the purchasing of OTC medications is for pain relief specifically for headaches, muscle pain and fever (Selvaraj and Ramalingam, 2014). Another research study found that the most frequently reported abused/misused OTC codeine medications are analgesic products (Algarni et al., 2021). Other studies supported this finding as it was stated that Adco-dol was the most requested/most frequently reported as being misused and the most likely codeine medication to cause dependence (Van Hout et al., 2016;

Carney et al., 2018; Wells et al., 2018; Hodes, 2019). Codeine has a known abuse potential with studies finding that the increase and non-medical use of codeine causes increases the likelihood of physiological neuro-adaptation and the development of dependence (Nielsen and Van Hout, 2015). Regarding codeine concentration the two codeine products available OTC which contain 8mg had a small amount sold this could be due to lack of options for sale as well as these products being indicated more for paediatric use therefore chance of abuse/misuse is decreased.

When looking at the different income areas, the pharmacy locations were distributed between high, middle and low income areas. The sample included a much higher number of pharmacies located in middle income areas which possibly explains why middle income pharmacies had the highest frequency of OTC codeine sales. High income areas were found to have higher sales of codeine products compared to low income areas. This could be due to the higher income areas having easier access to retail pharmacies as previous research in SA found that there is an urban clustering of pharmacies and a lack of retail pharmacies in rural areas, with the areas of highest deprivation/poverty having fewer pharmacies per 100 000 population (Moodley and Suleman, 2020). Another possibility for this finding in the numbers could be due to the stressful and busy lives of businessmen which could lead to an increased use of codeine medications, as stress could be viewed as both contributing to, and a consequence of, codeine use and misuse (Van Hout et al., 2016). This finding regarding the total sales in each income status area was both supported by and contradicted in the literature. The literature was divided according to which socioeconomic group was found to use/misuse codeine most frequently. Some studies supported the findings that codeine use is higher in the high income areas (Harker, 2020; Maia et al., 2021). Other studies have suggested that increased barriers to accessing codeine medications in rural/low income areas play a role in their lower use when compared to higher income areas (Erthal et al., 2019; Richards et al., 2022). However, there was literature which contradicts this finding and rather were of the opinion that codeine use is higher in low income areas with one study in Canada determining that codeine use was three times higher in low income areas compared to high income areas (Smolina et al., 2016).

When examining the most sold product in each income area, Benylin with codeine was found to be the most sold product in the high income areas. The middle- and low income areas most sold product was Adco-dol. This could possibly be due to the cost of the syrup being higher than that of the Adco-dol tablet (Hodes, 2019). Adco-dol is more affordable and can be used

as pain analgesia for many acute conditions (Wells et al., 2018) therefore this may explain the high sales volume in middle and low income areas.

It can be seen from the findings that multiple OTC codeine medications are being used in SA. The findings in the quantitative phase found a slight decrease in total OTC codeine sales which was assumed to be attributed to the influence of the COVID-19 pandemic. Since the study was only a two year period between 2019 and 2020 it was not possible to determine if sales after 2020 matched that of 2019. The most frequently sold OTC codeine medications were found to be Adco-dol and Gen-payne suggesting that pain analgesia codeine medications are the most commonly used in SA. The income areas were extracted to determine the difference in products sold amongst different income areas. Further studies would need to be done to run inferential statistical tests on these factors to determine if there are any significant predictors of codeine sales in the SA context.

5.3 Discussion: Phase 2

The participants of the semi-structured interviews consisted of practicing retail pharmacists with varying years of experience in the retail pharmacy sector. The main themes were derived from the qualitative interview transcripts. Thereafter sub-themes were determined to best display the findings. Each theme and their respective sub-themes were determined based on the commonalities expressed across the quotes conveyed by all participants. This section of the discussion will briefly discuss each theme presented in the results section.

5.3.1 Theme 1: Over-the-counter (OTC) codeine abuse/misuse being a problem in the South African context

All participants felt that OTC codeine medications are being misused in South Africa (SA) attributing this to the fact that medications are being used by patients for the incorrect reasons and for reasons codeine is not intended to be used for. From the literature, it is evident that codeine abuse/misuse is an issue that has been researched by many countries (Roussin et al., 2013; Foley et al., 2018; Mattson et al., 2021). Similarly, research in the South African context has indicated that there is a growing concern around the non-medical use of codeine-containing products (Dada et al., 2015). This finding backs up the findings of another study that sent out surveys to pharmacy staff and discovered that the highest proportion of participants in South Africa reported codeine misuse as a problem in the country (Carney et al.,2018). Furthermore,

the research of codeine misuse in SA has been expressed in various studies as an issue in the country (Carney et al., 2018; Wells et al., 2018; Essack et al., 2020; Richards, 2022). In this theme it was also evident that the abuse/misuse of OTC codeine was not constrained to a singular product, but it was felt that multiple codeine medications are being abused/misused in SA. The literature referenced above regarding the codeine issue in SA supported this claim by similarly stating that the abuse/misuse of OTC codeine medications is not limited to a single product.

The second subtheme that was identified was that the issue of abuse/misuse is perceived to be subject to particular age groups. The participants suggested that the younger age group and the much older age group were most prominent in abusing/misusing codeine products. This supports other literature which reported on the growing concern regarding recreational misuse of codeine cough syrups by the youth of SA, where easy access to codeine was attributed contributing further to the increase in popularity of abuse by the young people (Essack et al., 2020). The abuse/misuse of codeine by the youth has also been stated by other studies (Gasa, 2018; Carney et al., 2018; Kimani et al., 2021). No studies were found which report on the elderly abusing/misusing codeine in SA; however, it can it is possible that the elderly are susceptible to misuse/at risk of developing codeine dependence due to the initial use for chronic pain/diseases (Norman et al., 2016). Though there has not been a lot of research conducted on the elderly codeine use in the South African context, research conducted internationally supports this view (Algarni et al., 2021; Chiappini et al., 2021). These studies found that the elderly were a concern in the misuse of OTC codeine analgesic medications, with the most cited reasoning being to deal with pain and to aid the elderly in sleeping (Algarni et al., 2021; Chiappini et al., 2021).

5.3.2 Theme 2: Contributing factors to the abuse/misuse of OTC codeine

The over-prescription/recommendation of codeine products by healthcare professionals without further investigation regarding the reasoning for why the patient needs this medication was suggested by participants in the current study as a possibly contributor to abuse/misuse. There was a further suggestion that doctors fail to monitor patient's conditions appropriately; and that pharmacists easily dispense and recommend codeine products. Based on this it was felt by participants that these factors/behaviours by healthcare professionals contribute to codeine abuse/misuse. Existing literature shows that healthcare professionals play a role in the

abuse in this way as is reflected in a study by Norman et al. (2016) which noted that repeated prescriptions by doctors can perpetuate codeine misuse. This is especially seen as a contributing factor to patients unintentionally becoming dependent on codeine medication and therefore unknowingly abusing the medication (Wolfert et al., 2010). As doctors are a trusted source of medication information, patients will repeatedly use a medication if it is being recommended/prescribed to them (Wolfert et al., 2010). Literature also acknowledges the influence of pharmacists in contributing to abuse/misuse of OTC addictive medications, with research indicating that pharmacists rarely question patients on OTC medications and easily dispense requested products (Kinnaird et al., 2019). Participants did not specify why pharmacists might do this, but it has been suggested in the literature that pharmacists are overworked and under pressure from patients to give out medications on time in a busy pharmacy, which reduces the pharmacist's opportunity to be vigilant and counsel patients (Sansgiry et al., 2017).

It was found in this study that participants felt the business nature of retail pharmacies would encourage the sales of codeine medications thereby contributing to the abuse/misuse of the medication. Similarly, another study found that retail business pressures in SA contributed to pharmacist decisions to supply OTC codeine products (Carney et al., 2016). Many participants also mentioned the lack of a linked system between pharmacy software's enabling patients to pharmacy hop. Pharmacy hopping is when patients visit multiple pharmacies concurrently to obtain the same medication (Yang et al., 2015). Participants in this study described pharmacy hopping as a means for patients misusing/abusing codeine to access codeine whilst avoiding suspicion. This is supported by another study conducted which determined that patients would access multiple pharmacies in different locations for codeine medications to successfully avoid any suspicion from pharmacists (Van Hout et al., 2016). Participants also expressed concern that the lack of a linked system between retail pharmacies enables patients to retrieve codeine medications from multiple pharmacies. This is in accordance with a study conducted by Sansgiry et al. (2017) which found that because there is no record/monitoring of OTC medication sales, pharmacists face a barrier in preventing abuse, as individuals seeking to abuse the product can easily visit different pharmacies for the same item.

5.3.3 Theme 3: Ineffectiveness of the Schedule 2 register in the management of abuse/misuse of codeine

The current regulations in place that are intended to monitor and control the abuse/misuse is the schedule 2 register. The register is intended to be filled out by pharmacists and should include the name and quantity of the medication sold (Carney et al., 2016). Participants felt that the schedule 2 register is being ineffectively used in the management of OTC codeine abuse/misuse, specifically they felt that the register was not having an impact as it is not being utilised in retail pharmacies or not being completed consistently due to a lack of sufficient time during busy workdays. The sentiment of pharmacists being overworked and busy was stated in literature thereby supporting the difficulties pharmacists would face in needing to manually complete a medicines register (Hassell et al., 2011; Sansgiry et el., 2017).

This study finding adds valuable research on the ineffectiveness of the register based on pharmacist's opinions as there is currently no studies found that examine the effectiveness of this register in SA. There was no literature found in SA that speaks to the impact and effectiveness of this register. Internationally there was also no research done on the use of a manual medicines register or record keeping in pharmacies to manage medication use similar to this register in SA. However, literature has suggested the possible impact of a linked electronic medicine register in pharmacies to monitor sales and therefore identify abuse (Wright and Twigg, 2016; Kebodeaux, 2019). Both studies found suggested the possibility of linking the patient medical records in community pharmacies in order to identify inappropriate OTC medicinal use, however both studies identified some concerns. One study felt that the extra time it would take retail pharmacists to constantly complete the register might not justify the limited benefits of it (Wright and Twig, 2016). Whilst the other study felt that OTC medications are not typically captured in detail therefore there will be an initial workload on capturing information and there will be difficulties in convincing all pharmacy retailers to agree to the concept (Kebodeaux, 2019).

5.3.4 Theme 4: Up-scheduling of codeine as a suggested strategy to control codeine abuse/misuse

Due to the ineffectiveness of the current existing regulations in place it was mentioned by some participants that SA should consider up-scheduling codeine to be available by prescription only. It was suggested that removing codeine medication from the OTC side would prevent

patients from being able to make a request for the product and thus deter the abuse thereof. The notion of up-scheduling codeine has been shown to have a positive impact in Australia where codeine was up-scheduled to be available by prescription only (McCoy et al., 2022). This change was evaluated, and it was found that the up-scheduling significantly reduced codeine use which suggests that this could be an effective strategy in reducing the abuse/misuse of codeine (McCoy et al., 2022).

Furthermore, it was suggested by participants in this study that by up-scheduling codeine products it would deter people in SA from abusing/misusing the medication due to the cost barrier of a doctor visitation. The issue of poverty in healthcare in SA is supported by a study conducted by Burger and Christian (2020) which determined that there is a significant disparity in the availability and affordability of healthcare between the poor in SA and the upper class. Additionally, a study conducted by Wells et al. (2018) found that 43% of the participants in SA disagreed on the notion of up-scheduling as it was felt that this would add an unacceptable expense to codeine. Up-scheduling could disadvantage those who need the medication for legitimate reasons by adding the additional cost of obtaining a prescription.

5.3.5 Theme 5: Implementation of a national database to control codeine abuse/misuse

The installation of a national centralized database was suggested by participants as a possible future intervention strategy that could effectively control the abuse/misuse of codeine whilst keeping codeine available OTC. It has been suggested that codeine misuse is sometimes unnoticed in SA due to the lack of a national database (Hodes, 2019). All except one participant in the sample supported the idea of the database and felt the system would be significant. A study by Carney et al. (2018) had also analysed the perceptions of pharmacy staff where they determined that 77.2% of participants would be willing to use a centralised database. The use of a system to monitor/control opiates exists in other countries such as Australia (Webster, 2013) and America (Bao et al., 2016). Both countries have found that the databases have had a positive impact in terms of decreasing opioid prescribing and opioid related harms (Webster, 2013; Bao et al., 2016; Boyles, 2019). The need for the system to be automated and integrated into the existing pharmacy software was expressed by all participants to ensure that they would be happy to utilise/support the database which is consistent with findings from literature that it is essential for such systems to have the data be inputted instantly in real time (Haffajee et al., 2015).

It was seen as an important factor by participants in this study that educating the public should be considered upon implementation of the database in order to ensure compliance from the public. Education on the risks of the medication abuse by pharmacists upon implementation of new national policies such as drug monitoring programmes was mentioned as important in research (Lynas, 2013; Finklea et al., 2014). This supported and added to studies which also felt educating the public on the addictive nature of codeine/codeine use was an important factor upon installing a database or introducing a new intervention strategy (Norman et al., 2016; Carney et al., 2018).

Qualitatively it was found that OTC codeine is felt to be abused/misused in SA and this not constrained to a single codeine product. Healthcare professionals were suggested as contributors to the abuse of OTC codeine and therefore could do more in preventing it. The qualitative findings of this study provided valuable insight into the opinions surrounding the schedule 2 register. Currently the schedule 2 register is the existing strategy in place to monitor and control OTC codeine dispensed/used. Due to the nature of the register, practicing pharmacists are the most relevant source to identify the effectiveness of this current regulation/strategy. This study added information that the current existing regulations are not being utilised and therefore indicates that the existing regulations are not effectively preventing or deterring OTC codeine abuse/misuse at present. Emphasis was placed on the possible installation of a national database and the consideration towards the up-scheduling of codeine to be available by prescription only.

5.4 Integration of the Quantitative and Qualitative Data

The quantitative and qualitative findings discussed can be examined together to determine the patterns of OTC codeine-containing medications. The quantitative gave an idea of the usage of OTC codeine products by displaying the most frequently sold medications whereas the qualitative adds value to this data by further providing current practicing pharmacists awareness of codeine sales and thereby the effectiveness of current regulations. This information then feeds into the pharmacist's views on a possible intervention strategy.

The quantitative findings found high frequency of use of certain OTC codeine medications. The qualitative findings explain this finding by indicating that there is an issue of abuse/misuse of codeine in SA. The qualitative findings further supported the quantitative findings of

different products being frequently sold by indicating that the abuse/misuse of codeine is not constrained to one product and can be seen across OTC codeine medications. The qualitative findings does not specifically highlight the prevalence around a specific codeine medication but rather that multiple codeine medications are generally abused/misused in SA. This finding is in accordance with current research and literature which all found that there are multiple codeine products being abused/misused (Wright et al., 2016; Carney et al., 2018; Algarni et al., 2021).

The qualitative discussion identified that age is perceived to play a role in the abuse/misuse, younger age group and the older age group were most commonly requesting/misusing OTC codeine medications. With findings stating that younger age group varies between 12 and 25, and the older age group being over 60 years old. This suggests that more research into demographic factors and their impact on codeine abuse/misuse is needed. Literature has suggested that codeine misuse could be influenced by demograhic factors such as age and gender (Scholz et al., 2019; Essack et al., 2020; Ino and Nakazawa, 2022). Further research is therefore needed to explore this in more detail.

When analysing further the product sold it was determined that independent pharmacies most sold codeine product was Benylin with codeine and chain/franchise pharmacies was Adco-dol. This finding could suggest the abuse of codeine by the youth as literature indicates that the youth commonly ingests OTC codeine cough syrups recreationally (Essack et al., 2020). However, the purchase of codeine syrups was not analysed or determined in this study therefore this is merely an assumption being made based on descriptive sales statistics and the current literature available. The sales were also not examined by patient information and age group therefore this was not determined in the study but is assumed. From the findings from both quantitative and qualitative it can be suggested that Benylin with codeine cough syrups were purchased more from the independent pharmacy branches as it can be perceived that independent pharmacies are not as busy and strict as a franchise pharmacy group which has multiple branches. This is suggested by a study that found that community/independent pharmacies typically dispense medication more easily while franchise pharmacies appear to follow current regulations and are more vigilant (Mokwele et al., 2022). Another study also supported this by suggesting that heavy codeine users purchase codeine products from small independent pharmacies as excessive purchasing will go unnoticed as opposed to a franchise pharmacy where the systems create a account profile for patients (Hode, 2019).

Regarding the time period analysed, there were specific time frames where medication sales/usage was higher than other months, for example the spike in codeine sales in March 2020. This was suggested to be the influence/reaction to the COVID-19 pandemic. The qualitative findings suggest that the healthcare workers could also have an effect on medications sold during such a time. With the qualitative suggesting that there usually is an issue of over-prescription and the lack of proper monitoring therefore under COVID-19 the extra burdens on healthcare workers suggests that they could have played a role in easily giving out medications. Literature determined that in some countries the pandemic saw a decline in medical consultations however there was a brief increase in codeine consumption/sales in March 2020 (Reinstadler et al., 2021). This, however, was not directly tested so it would need to be directly tested or researched. The quantitative and qualitative findings suggest that there are descriptive factors that might contribute to OTC codeine abuse/misuse. The qualitative didn't directly suggest this finding however, the quantitative findings found a difference in the frequency of codeine product sales within specific demographic areas. With regards to demographics the quantitative flagged the difference amongst various income areas and the qualitative suggested the role of age in the abuse/misuse of codeine. Together these findings suggest that the role/influence of demographic factors in codeine abuse/misuse needs to be researched and examined in depth in SA.

When integrating the qualitative and quantitative data it becomes apparent that OTC codeine is being misused/abused in SA with current regulations not adequately controlling or preventing this issue. The qualitative aids the limitations of the quantitative in providing personal pharmacist experiences with codeine in SA. Where the quantitative provides valuable insight into the OTC codeine products which are being most frequently consumed by the public, the qualitative adds contextualization to this information. Pharmacists need to be aware of the products most sold/used by patients in order to be more vigilant when dispensing those medications.

Chapter 6: Strengths, Limitations, Recommendations and Conclusion

6.1 Strengths and Limitations

6.1.1 Strengths

To the researcher's knowledge this study is the first study in South Africa to qualitatively explore the attitudes and perceptions towards the current strategy (Schedule 2 register). There is minimal research on the prevalence of use of OTC codeine in SA, this study provides current data on codeine usage/sales patterns. Conclusions/suggestions in the study were made from the results found and was supported by corresponding literature. Peer examination ensured scrutiny of the methods by those experienced in qualitative and quantitative research.

6.1.2 Limitations

This study is limited to the OTC codeine sales patterns of retail pharmacies in central Johannesburg. This does not include the sales patterns of the whole of Gauteng and therefore the codeine sales data is not representative of trends everywhere in Gauteng. A larger sample of the whole province would give a better indication of Gauteng codeine usage. These sales patterns are also not indicative of the whole of SA. In phase one of the study, OTC codeine sales patterns were evaluated retrospectively, sales were analysed from 2019 to 2020. The COVID-19 pandemic entered SA in 2020 therefore the codeine sales patterns could differ from the usual sales numbers however this does allow for a comparison in sales from 2019 to the changes in 2020 during the pandemic. Additionally, the IQVIA database which provide the sales of OTC codeine included a few pharmacies classified under undisclosed pharmacies which consisted of pharmacies who did not consent to have their information linked to the sales. The undisclosed pharmacies did not include pharmacy type and locations therefore these pharmacies could not be included so a small representation of retail pharmacies in central Johannesburg could not be analysed. Quantitative findings were purely descriptive in nature. The study thus did not conduct inferential statistical analysis to explore the difference in codeine sales/usage based on different socio-demographic factors. Phase two of the study used purposive sampling and participants had to consent, it may be possible that participants who experienced codeine issues in practice were more likely to participate. Participants were all located in Johannesburg therefore the findings/perceptions expressed might not be transferable to other contexts/provinces in SA.

6.2 Future recommendations and conclusion

6.2.1 Future recommendations

Based on this study there needs to be a re-evaluation of the Schedule 2 register to either implement a new strategy, such as the suggested up-scheduling or national database; or the implementation of more stringent monitoring of the schedule 2 register to ensure pharmacists start to use the register as it was intended. The public needs educating of the risks of OTC codeine addiction and dependence. A public educational initiative could be beneficial to inform the public on codeine and therefore deter unintentional misuse/dependence. The pharmacy systems need to be linked in order to prevent pharmacy hopping.

Further research could analyse the codeine sales patterns for the whole of the Gauteng province. This could be expanded further to compare the codeine sales between all provinces in SA. Future studies can research further opinions on the installation of a national database and how to design an effective database. Further research could be done to determine why certain codeine medications are being more frequently used than others along with the differences in sales of codeine products with regards to different sociodemographic factors. Future research could explore additional demographic factors linked to codeine misuse/abuse and use statistical tests to determine the role of these factors in codeine misuse/abuse. Further research could also explore the impact of the schedule 2 register in the pharmacy setting.

6.2.2 Conclusion

This study aimed to analyse patterns of OTC codeine-containing products in central Johannesburg retail pharmacy sector and to explore the effectiveness of current regulations/strategies. The study achieved this through the analysis of OTC codeine sales patterns and by determining the views and opinions of practicing pharmacists through semi-structured interviews.

The results of the study supported existing studies but also provided some new information. The study found that OTC codeine abuse/misuse is a recognised concern amongst practicing pharmacists as well as the factors contributing to the abuse/misuse thereof which is in line with current literature. Healthcare professionals play a vital role in the education and control/monitoring of patient medication use. At the same time healthcare professionals can also contribute to and enable the abuse and addiction to codeine medications. Findings were

successful in determining the views towards current regulations effectiveness as it was indicated that the schedule 2 register is felt to be ineffective with participants stating that the register has no effect in controlling OTC codeine use. This suggests that this strategy needs to be reconsidered or be implemented more stringently to possibly deter/identify codeine abuse/misuse.

The opinions of pharmacists were examined in order to determine a more controlled and regulated codeine sector due to the study findings of practicing pharmacists' opinions expressing the ineffectiveness of the current regulations in place. The large availability of OTC codeine means that there needs to be further regulations in place to control the abuse/misuse of codeine products. Most participants agreed that the best way to prevent OTC codeine abuse/misuse was to up-schedule it to a prescription only drug or to implement a national database that is automated and integrated into the current pharmacy software. Overall it was found in this study that Adco-dol and Gen-Payne were the most frequently sold OTC codeine products in central Johannesburg, and it was generally concluded from this study that OTC codeine is still suspected of being abused or misused. As a result, it is critical that current regulations be re-evaluated and that OTC codeine sales be more closely regulated in the future.

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Appendices:

Appendix 1: Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Ms A Asmall

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M190643

NAME: (Principal Investigator)	Ms A Asmall
DEPARTMENT:	School of Therapeutic Sciences Department of Pharmacy and Pharmacology Medical School University
PROJECT TITLE:	Determining the prevalence of use of over-the-counter (OTC) codeine-containing products in the Johannesburg area (Region B): a mixed methods study Study title change noted on 17/12/2019
DATE CONSIDERED:	2019/06/28
DECISION:	Approved unconditionally
CONDITIONS:	Approval applies to those Pharmacies which have formally consented to participate in the study
SUPERVISOR:	R Shaikh, S.De Rapper, Z Booth & D Bayever
APPROVED BY:	CB Penny Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2019/10/03

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. I **agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **June** and will therefore reports and re-certification will be due early in the month of **June** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

18.12.2019
Date

PLEASE QUOTE THE CLEARANCE CERTIFICATE NUMBER IN ALL ENQUIRIES

Appendix 2: Change of study period

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

2021/02/04

Ms A Asmall
School of Therapeutic Sciences
Department of Pharmacy and Pharmacology
Medical School
University

Sent by e-mail to: asmall.amirah540@gmail.com

Dear Ms Asmall

Re: **Protocol Ref No:** M190643
Protocol Title: *Determining the prevalence of use of over-the-counter (OTC) codeine-containing products in the Central Johannesburg area: a mixed methods study*
Principal Investigator: Ms A Asmall

Thank you for your e-mail of 2021/01/25.

I confirm that we have noted and approve of your proposal to change your data collection period to 2020/01/01 - 2020/12/31, so long as this meets with the approval of your supervisors.

Thank you for keeping us informed.

Yours Sincerely

I. Burns

.....
Mr I Burns
For the Human Research Ethics Committee (Medical)

CB Penny

.....
Dr CB Penny, Chairperson, Human Research Ethics Committee (Medical)

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Appendix 3: Change of study title

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

26 November 2020

Ms A Asmall
School of Therapeutic Sciences
Department of Pharmacy and Pharmacology
Medical School
University

Sent by e-mail to: asmall.amirah540@gmail.com

Dear Ms Asmall

Re: **Protocol Ref No: M190643**
Protocol Title: *Determining the prevalence of use of over-the-counter (OTC) codeine-containing products in the Central Johannesburg area: a mixed methods study Changes to study title noted on 2019/12/17 and*
Principal Investigator: Ms A Asmall

Thank you for your letter of 13 November 2020.

I confirm that your proposal to conduct the interviews with the participants remotely, rather than face-to-face, has been noted and approved.

Thank you for keeping us informed.

Yours Sincerely

G. Burns

.....

Mr I Burns
For the Human Research Ethics Committee (Medical)

CB Penny

.....

Dr CB Penny, Chairperson, Human Research Ethics Committee (Medical)

Works2000/Iain0007/Acknowledge.docx

Appendix 4: Semi-structured interview guide



Introduction:
Good Morning/Afternoon my name is Amirah, it is a pleasure to meet you. How are you doing today?
Thank you for taking the time to sit down with me today. My study is focused on the current abuse/misuse of over the counter codeine medications in order to motivate for a more regulated intervention strategy. So, the purpose of today's interview is to obtain your views as a practicing pharmacist towards the misuse and abuse of codeine medication as well as the strategies that could be effective in combatting this issue of medication abuse/misuse. Participation in this interview would require you to answer a few questions, your participation in this interview is entirely voluntary and you may withdraw participation at any time during the interview. Your answers will be audio recorded; however, they will remain completely confidential as only myself and my supervisor will have access to your information. In my study write up I will make use of pseudonyms to ensure anonymity and I will remove any identifying information. The interview should last approximately an hour. I have a copy of the consent forms and study information sheet that has my contact details on them if you would like to contact me. If you are happy to proceed, please may you read through and sign this consent form and then we can begin. If you have any questions at any point, please let me know.

Thank you, let us begin.

Question 1:
What do you enjoy most about being a pharmacist?

Question 2:
In your years of practice, have you ever had any experiences of OTC codeine misuse/abuse by patients? Can you please tell me a little about these experiences? (Prompt: Can you tell me about what happened?)

Question 3:
What do you do at your pharmacy if you suspect misuse or abuse?

Question 4:
What do you think about OTC codeine misuse/abuse in South Africa generally? (Prompt: Do you feel that it is a problem in the country? Why or why not?)

Question 5:
What do you feel is the pharmacist's role in the misuse/abuse of these medications? (Follow up: How do you feel pharmacists contribute to/facilitate the misuse of these medications?)

Question 6:

What do you think of the existing strategies in place to manage misuse/abuse of these medications, such as the schedule 2 registers?
(Follow up: Do you feel these strategies are effective and why?)

Question 7:
What strategies do you think should be put in place to address OTC codeine misuse/abuse?

Question 8:
What do you think about the installation of a national database that would link all pharmacy software's to manage OTC codeine misuse/abuse?
(Explain briefly on the idea of the national database if not aware)

Question 9:
What do you feel would make the implementation of such a database easier?
(For example, an educational campaign for the public)

Question 10:
What do you think would work to ensure pharmacists make use of the database in practice?

Question 11:
Would you be happy to utilize a software in practice? If so, then why and if not, then why.

Conclusion:
That is the last question I have. Thank you very much for your time, do you have any further questions for me?

It was a pleasure chatting with you, I really appreciate your contribution to my study. As I mentioned me and my supervisors contact details are on the information sheet, please do not hesitate to contact us if you have any questions. If you would like to find out more a summary of the study findings can be sent to you upon request in 6 months' time.

Thanks again, Enjoy the rest of your day.

Appendix 5: Consent Forms for interview and recording of interview



Participant Consent Form: Interview

Re: Determining the prevalence of use of over-the-counter (OTC) codeine-containing products in the Central Johannesburg area: A Mixed Methods Study

I hereby confirm that I have accurately read and understood the information sheet provided by the researcher, and I understand that the following will be done:

- I understand that participation is voluntary.
- I shall participate in this study towards the researcher's postgraduate master's project.
- I understand that I may withdraw from the study at any time.
- I give the researcher permission to use the interview data
- I understand that I have the right to not answer any questions I do not feel comfortable answering.

I hereby agree that I have understood the requirements of this project and I am willing to participate in the study.

Yours faithfully,

Pharmacist Signature: _____

Date: _____

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

WITS PHARMACY

Pharmacist Consent Form: Audio-Recording

Re: Determining the prevalence of use of over-the-counter (OTC) codeine-containing products in the Central Johannesburg area: A Mixed Methods Study

I, _____ hereby confirm that I have read and understood the information sheet provided and I understand the following:

- ☐ I give consent to be voice recorded during the interview.
- ☐ I confirm that I have given consent willingly and may withdraw from this study at any time without any negative consequences.
- ☐ I understand that I may mention if there are any answers I would not like to be recorded or used in the study.
- ☐ I understand that my answers will be kept confidential i.e. only the researcher and her supervisor's will have access to my answers.
- ☐ I understand that anonymity will be maintained in the study write up/results by the use of pseudonyms
- ☐ I give the researcher permission to use the recordings for her research project
- ☐ I give the researcher permission to use direct quotes from the recording

I hereby agree that I have understood the requirements of this project and I am willing to participate.

Yours faithfully,

Pharmacist's signature: _____

Date: _____

Appendix 6: Demographic Questionnaire



Demographic Questionnaire

Participant Number: __

Question 1:
What is your age? (Please fill in below)

_____

Question 2:
What gender do you identify with?

- ☐ Male
- ☐ Female
- ☐ Other (Please specify)

_____

Question 3:
What ethnicity do you identify with?

- ☐ African
- ☐ Indian
- ☐ White
- ☐ Coloured
- ☐ Other (Please specify)

_____

Question 4:
What is your highest degree that you have completed?

- ☐ Pharmacy Diploma
- ☐ Bachelor's in Pharmacy
- ☐ Master's in Pharmacy
- ☐ Doctorate in Philosophy

Question 5:

Which fields in pharmacy do you have experience in? Please indicate how many years' experience you have next to the selected fields.

- ☐ Retail Years: _____
- ☐ Hospital Years: _____
- ☐ Manufacturing Years: _____
- ☐ Other (Please specify) Years: _____

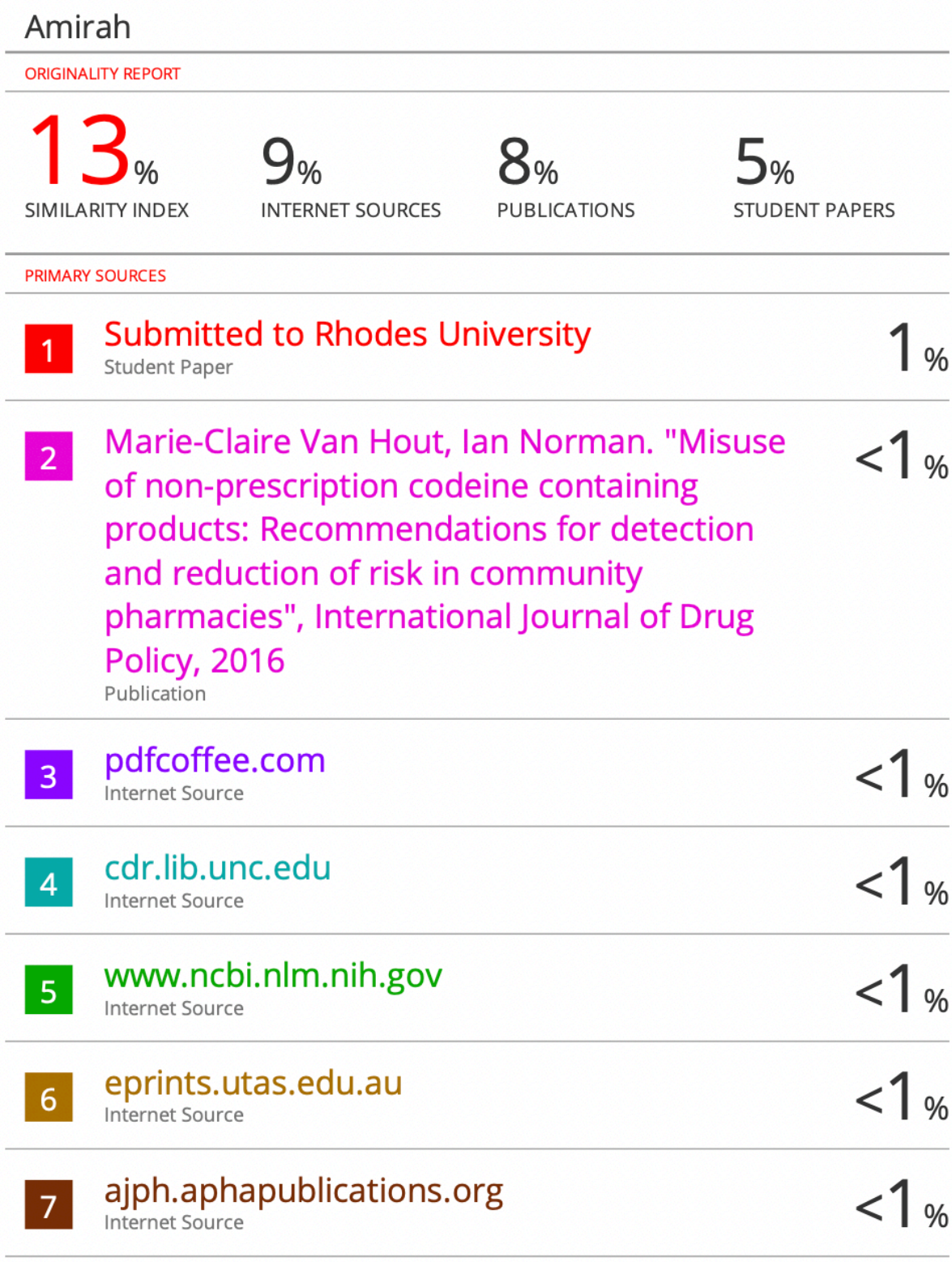
_____

Question 6:

At your current job in retail pharmacy, are you:

- ☐ Locum Pharmacist
- ☐ Permanent position

Appendix 7: Plagiarism Report- Turnitin



Amirah

ORIGINALITY REPORT

13%	9%	8%	5%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Submitted to Rhodes University Student Paper	1%
2	Marie-Claire Van Hout, Ian Norman. "Misuse of non-prescription codeine containing products: Recommendations for detection and reduction of risk in community pharmacies", International Journal of Drug Policy, 2016 Publication	<1%
3	pdfcoffee.com Internet Source	<1%
4	cdr.lib.unc.edu Internet Source	<1%
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