



**University of
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**Role of Community Pharmacists in Optimizing Opioid Therapy
for Chronic Non-malignant Pain Patients in Pakistan**

Thesis submitted to the University of Nottingham
for the degree of Doctor of Philosophy

Ayesha Iqbal
PhD Research Student
Student ID: 14342114
Ayesha.Iqbal@nottingham.ac.uk

Supervisors
Professor Claire Anderson
Dr Roger Knaggs
Dr Li Shean Toh

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Abstract

Background

Chronic Non-Malignant Pain (CNMP) is one of the most common conditions in both high-income countries (HICs) and low middle-income countries (LMICs). CNMP can have a substantial impact on people, communities and puts an economic burden on the society. Opioids are commonly used worldwide for CNMP management. However, their use might have contributed to opioid use-related harm and increased mortality. There have been substantial reports of opioid diversion and misuse in Pakistan. Community pharmacists (CPs) might be able to help optimise the use of opioids in CNMP management but there is no regularised CP-based patient-centred services in Pakistan.

Aim and objectives

The aim of the study was to explore the potential role of CPs in opioid optimisation in people with CNMP in Pakistan. Objectives of this study included systematically exploring the role of CPs in opioid optimisation in CNMP management, exploring the current use of opioids in Pakistan and identify the role CPs can play to optimise the use of opioids in people with CNMP and explore factors that might influence the development and delivery of role of CPs in an opioid optimisation service.

Methodology

Conceptual guiding framework

The UK Medical Research Council (MRC) guidelines for complex interventions was used as conceptual guiding framework for exploring the aim of this study. The data was collected in two phases:

Phase 1: Systematic review

The systematic review followed the 27-item PRISMA guidelines and studies between January 1990-June 2020 were included. All studies where pharmacists in ambulatory care settings helped in optimisation of opioids in the treatment of CNMP, as individuals or as part of a team were included and were descriptively synthesized.

Phase 2: In-depth qualitative methods (Interviews, focus groups and case studies)

Two studies were conducted to collect the data. The first study constituted of semi-structured interviews and focus groups from four stakeholder groups: pharmacy policy makers, people with CNMP, doctors and CPs. The second study included non-participant multiple case study observations in six community pharmacies. The data in phase two was collected from November 2019–December 2020.

Data analysis

Interviews and focus groups with all stakeholders in phase two were inductively analysed using reflexive thematic analysis using N-Vivo 12. For case studies, reflexive thematic analysis as well a cross case synthesis method using explanation building technique was used to analyse the data across six cases.

Data triangulation

Findings from both studies in phase two were triangulated using two steps; comparing, and categorising. Any code or subtheme about a particular phenomenon or a theme across both studies were brought together using one sheet one paper data visualisation technique.

Diagrammatic model development

Schematic diagrammatic models were developed in this thesis usual process mapping data visualisation technique. This was done selecting and representing events and situating data in time/process meaningfully.

Results

In this study 98 stakeholders participated (38 females). A total of 240 hours (40 hours/case) were observed during a six-week period of non-participant observational case studies in six community pharmacies.

Phase 1: Systematic review

In the systematic review 14 studies were included in the final data synthesis (total number of participants n=1175). Interventions by pharmacists decreased opioid dose in four studies and improved patient opioid safety in five studies. Qualitative studies showed positive perception of stakeholders for the development of CP role in optimisation of opioid therapy for people with CNMP. No actual interventions involving CPs or studies from LMICs were identified.

Phase 2: Focus groups, interviews and case studies

These studies were able to identify reasons contributing towards the non-availability of opioids, factors contributing towards the unsafe use of opioids and certain actions that can be taken by CPs to overcome existing barriers contributing to the unsafe use of opioids and help optimise their use. These studies also highlight advantages and benefits of developing the role of CPs in optimising opioid use in people with CNMP.

In addition, these studies identified multiple level barriers and facilitators for the development and delivery of CP opioid service. They also helped identify strategies to overcome the perceived barriers and to leverage the facilitators in order to develop and deliver an opioid service.

Data visualisation helped develop diagrammatic models after triangulation. Firstly, a logic model was developed that identifies the possible actions that can be undertaken by CPs to help overcome the barriers causing/contributing

towards unsafe use of opioids. Secondly a CP proposed opioid service model was developed, tailored to the health system of Pakistan, that is anticipated to help optimise the use of opioids in people with CNMP. Finally, a CP opioid service logic model was developed that shows strategies perceived to develop and improve the capability of CPs to deliver the opioid service and help optimise the use of opioids.

Conclusion

This thesis explored the process, the need and service delivery of CP role in opioid optimisation. This thesis identified factors contributing towards unsafe use of opioids (logic model), what can be done by CPs to help people use opioids in an optimised manner (CP proposed service model), what challenges might CPs face while delivering the service and what can be done to improve the development and delivery of a CP opioid service for people with CNMP using opioids (CP service logic model). The findings provide policy makers with possible steps and actions that may be followed to facilitate the development and delivery of a CP service for opioid optimisation in Pakistan.

List of full article publications

1. Ayesha Iqbal*, Roger David Knaggs, Claire Anderson, Li Shean Toh. Role of pharmacists in optimising opioid therapy for chronic non-malignant pain; A systematic review. *Research in Social and Administrative Pharmacy*. 2022 Mar;18(3):2352-2366. doi: 10.1016/j.sapharm.2020.11.014. Epub 2020 Nov 24. PMID: 33309322.
2. Ayesha Iqbal*, Roger David Knaggs, Claire Anderson, Li Shean Toh. Logic model for opioid safety in chronic non-malignant pain management, an in-depth qualitative study. *International Journal of Clinical Pharmacy* (2022). <https://doi.org/10.1007/s11096-022-01493-6>

List of conference publications

1. Ayesha Iqbal, Claire Anderson, Roger David Knaggs, and Li Shean Toh. Utilising community pharmacists for optimising opioid therapy in people with chronic pain; challenges and opportunities using the Social Ecological Model. 2021. *International Journal of Clinical Pharmacy*, vol. 43, no. 3, pp. 791-791.
2. Ayesha Iqbal, Li Shean Toh, Roger David Knaggs, Claire Anderson. 2021. Factors promoting self-medication and irrational use of opioids in chronic non-malignant pain management in Pakistan: A qualitative in-depth investigation. *International Journal of Pharmacy Practice*, 29(Supplement_1), pp. i32-i33.

Oral presentations

1. Oral short presentation titled "A community pharmacy implementation logic model for opioid optimisation service development and implementation in Pakistan" at Internal Social Pharmacy workshop (ISPW), at University of Sydney from 11-14 July 2022.
2. Oral presentation in Second Innovation in Pharmacy Conference, Pakistan, on "Emerging role of community pharmacists in Pakistan as pain management specialists," September 17-18, 2021. (virtually)
3. Short oral presentation titled "Factors promoting self-medication and irrational use of opioids in chronic non-malignant pain management in Pakistan: A qualitative in-depth investigation." at HSRPP conference, University of Reading, 2021.

Poster presentations

1. Presented a poster titled "To explore the development of role of community pharmacists for increased access to opioids for the management of chronic non-malignant pain in a LMIC, Pakistan" at IASP 2022 World Congress of Pain from 19-23 September 2022. (virtually)

2. Presented a poster titled “Role of community pharmacists in optimizing opioid therapy for chronic non-malignant pain management- a logic model” at 55th Annual Scientific Meeting of The British Pain Society (BPS ASM 2022) to be held in London, United Kingdom on 13-15 June 2022.
3. Presented a poster titled” The need to develop competency-based pharmacy education in Pakistan” at FIP PPR SIG 2022, Utrecht, the Netherlands, 4-5 July 2022. (virtually)
4. Presented a poster titled “A non-conventional realist informed approach for logic model development for intervention design and implementation” at FIP PPR SIG 2022, Utrecht, the Netherlands, 4-5 July 2022. (virtually).
5. Presented a poster presentation titled “Utilizing community pharmacists for optimizing opioid therapy in people with chronic pain: challenges and opportunities using the social ecological model” in the Pharmaceutical Care network (PCNE) conference Basel 2021 from 3-6 February 2021. (virtually)
6. Presented a poster presentation titled “Factors promoting self-medication and irrational use of opioids in chronic non-malignant pain management in Pakistan: A qualitative in-depth investigation” in Health Services Research and Pharmacy Practice Conference 2021, 8th April 2021–9th April 2021. (virtually)
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Indeed, with hardship [will be] ease.

94:6 QURAN

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List of Abbreviations

Adverse drug reactions	ADRs
Adverse drug events	ADEs
American Society of Health-System Pharmacists	ASHP
American Society of Interventional Pain Physicians	ASIPP
Anti-narcotic force of Pakistan	ANF
Anti-tuberculosis	TB
Basic health Units	BHUs
Basic pay scale	BPS
Blood pressure	BP
Center for Disease Control	CDC
Chronic non-malignant pain	CNMP
Cognitive behavioural therapy	CBT
Community pharmacists	CPs
Complementary and alternative medicine	CAM
Computer assisted qualitative data analysis software	CAQDAS
Consolidated criteria for reporting qualitative research	COREQ
Continuous professional development	CPD
Critical Appraisal Skills Programme	CASP
Cumulative Index to Nursing and Allied Health Literature	CINAHL
District Headquarters	DHQs
Drug regulatory Authority of Pakistan	DRAP
Drug-related problems	DRPs
Electronic health records	HER
Essential medicine list	EML
Expert Recommendations for Implementing Change	ERIC
General practitioner	GP
Good Manufacturing Practice	GMP
Grading of Recommendations Assessment, Development and Evaluation Working Group	GRADE
Gross domestic product	GDP
Grounded theory	GT
Health related Quality of life	HRQOL
High income countries	HICs
International Narcotics Control Board	INCB
International Pharmaceutical Abstract	IPA
Interpretive phenomenological analysis	IPA
Intervention Research Logic Model	IRLM
Intra venous	IV
Islamabad Capital Territory	ICT
Joanna Briggs Institute	JBI
Khyber Pakhtunkhwa	KPK
Low-middle income countries	LMICs
Masters in philosophy	M.Phil.

Ministry of National Health Services Regulation and Coordination	NHSRC
Morphine milligram equivalent	MME
Narcotics control board	NCB
National health policy	NHP
National Institute for Health and Clinical Excellence	NICE
Non-governmental organizations	NGOs
Non-randomised controlled study	NRS
Non-steroidal anti-inflammatory drugs	NSAIDs
Opioid use disorder	ODD
Outpatient departments	OPD
Over the counter	OTC
Pakistan Medical and Dental Council	PMDC
Pakistan Medical Association	PMA
Pharmacist led-medication review	Pharmacist-led MR
Pharmacovigilance	PV
Pharmacy Council of Pakistan	PCP
Doctorate in philosophy	PhD
Prescription data monitoring systems	PDMs
Prescription only medicines	POMs
Randomised controlled trials	RCTs
Reflexive thematic analysis	RTA
Rural health centres	RHCs
Short Form	SF-12 PCS/MS
Social Ecological Model	SEM
Specialised Medical teaching institutes	MTIs
Standards for Reporting Qualitative Research	SRQR
Sustainable Development Goal	SDG
Tehsil Headquarters	THQs
The Lancet Commission on Palliative Care and Pain Relief	LCPCPR
The Risk of Bias	RoB
Thematic analysis	TA
United Nations	UN
United Nations Office on Drugs and Crime report	UNODC
United States of America	USA
Universal health coverage	UHC
Upper middle-income countries	UMICs
World Health Organisation	WHO

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Introduction to thesis

Motivation for the study

Developing the role of community pharmacists (CPs) in Pakistan to be more patient-centred is hypothesized to improve the healthcare system and optimize medicine use in chronic conditions like chronic non-malignant pain (CNMP). Pakistan, due to expected increase in problems with CNMP, high opioid consumption and easy availability of opioids, might be experiencing unsafe use of opioids. CPs play an important role in delivering patient care services in high income countries. However, they are being underutilised with respect to their capacity to deliver health services in Pakistan. Hypothetically, developing the role of CPs should help people use opioids safely. However, their role in optimizing opioid therapy for CNMP management in Pakistan has not been explored before. Therefore, the literature review provides an overview of available literature regarding problematic use of opioids, the role of pharmacists in opioid safety and an overview of community pharmacy services in high income countries, low middle-income countries and Pakistan. The thesis then presents an appropriate methodology showcasing the methods undertaken to collect, analyse and present data. The next chapter shows the findings of this original research study and discusses it considering evidence from other research studies and available literature. The thesis concludes with the implications of these research findings on policy and practice and provides directions for future research.

Introduction to thesis

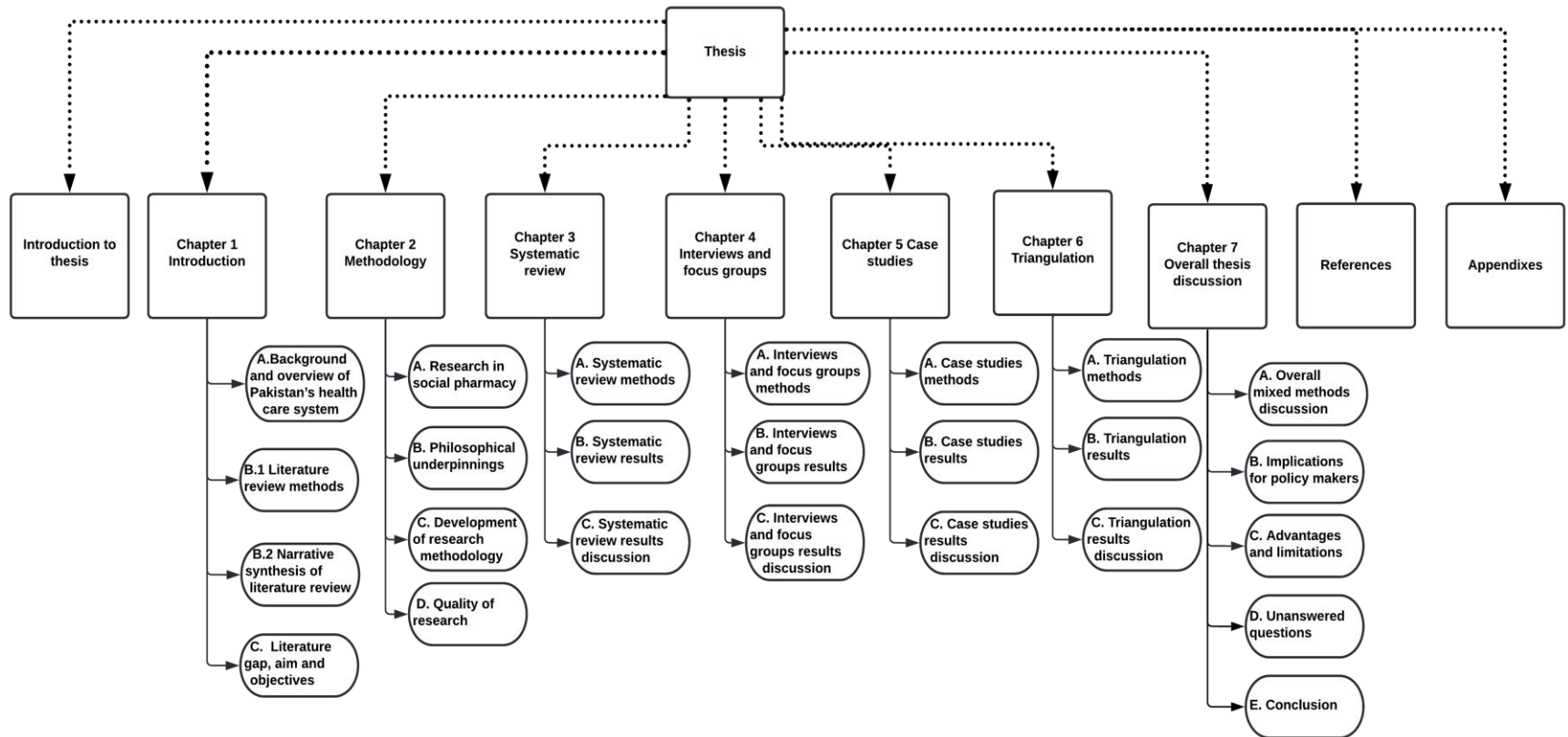


Figure 1.1: Overview of thesis

Figure 1.1 shows the overall structure of this thesis.

Chapter 1: Introduction

Chapter 1: Introduction, background and literature review

Chapter 1 (Figure 1.2) in this thesis is divided into three subchapters:

- A. Background and overview of Pakistan's healthcare system
- B. Literature review (methods, narrative synthesis)
- C. Literature gap, aim and objectives

Chapter 1: Introduction

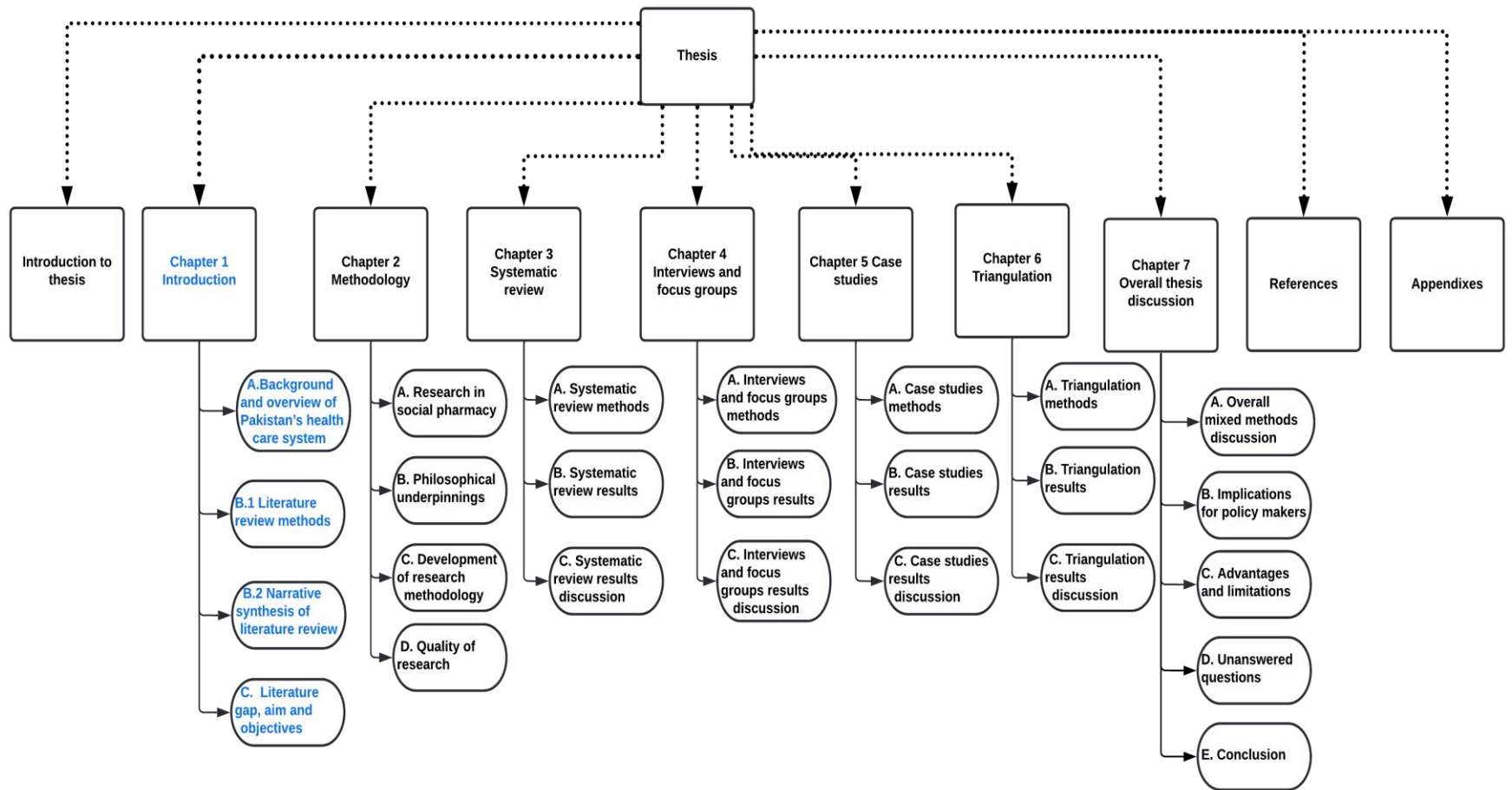


Figure 1.2: Overview of chapter 1 in this thesis

Chapter 1: Introduction

Figure 1.3 below represents the main sections covered in each of chapter 1's three subchapters and provides an overview of what to expect in each of them.

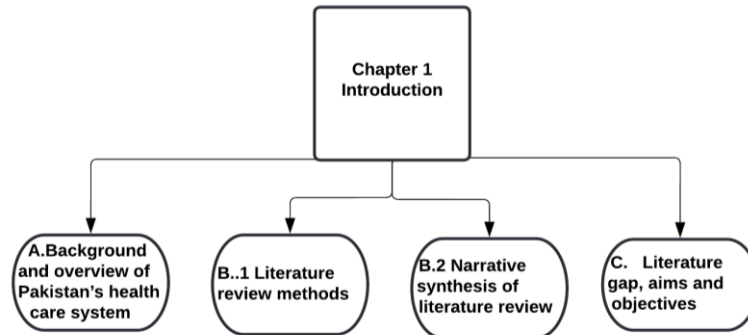


Figure 1.3: Overview of chapter 1

1.1 Subchapter A: Pakistan healthcare system and pharmacy overview

This subchapter provides context about the healthcare system, the use of medications and an overview of the pharmacy profession in the country to help understand the results of this research study (Figure 1.3).

This overview will facilitate the understanding of the results of this study and will cover the following main areas:

- Health and pharmacy laws
- Organization and ministries
- Public and private healthcare system
- Pharmacy profession (emphasis on community pharmacy)

1.1.1.A Pakistan healthcare laws and system

1.1.1.A.1 Overview of Pakistan

The World Bank designates the countries throughout the world into four groups: low-income countries (LICs), lower-middle income countries (LMICs), upper-middle income countries (UMICs) and high-income countries (HICs). These classifications are subjected to revision every year based on gross national income per capita in United States Dollar (USD) [1].

Pakistan (Islamic Republic of Pakistan) is an LMIC located in South Asia [2], with a population of over 220 million [3]. Pakistan has an area of 881,913 km² (340,509 square miles) and had a 59% literacy rate in 2018-2019 [4-6].

1.1.1.A.2 Federal and provincial geographical allocation

Pakistan has four provinces called Balochistan, Punjab, Sindh and Khyber Pakhtunkhwa (KPK); a separate federal area called Islamabad Capital Territory (ICT); and two self-governing areas of Gilgit Baltistan and Azad Jammu and Kashmir (AJK) Figure (1.4). There are two types of governing tiers: federal and provincial.

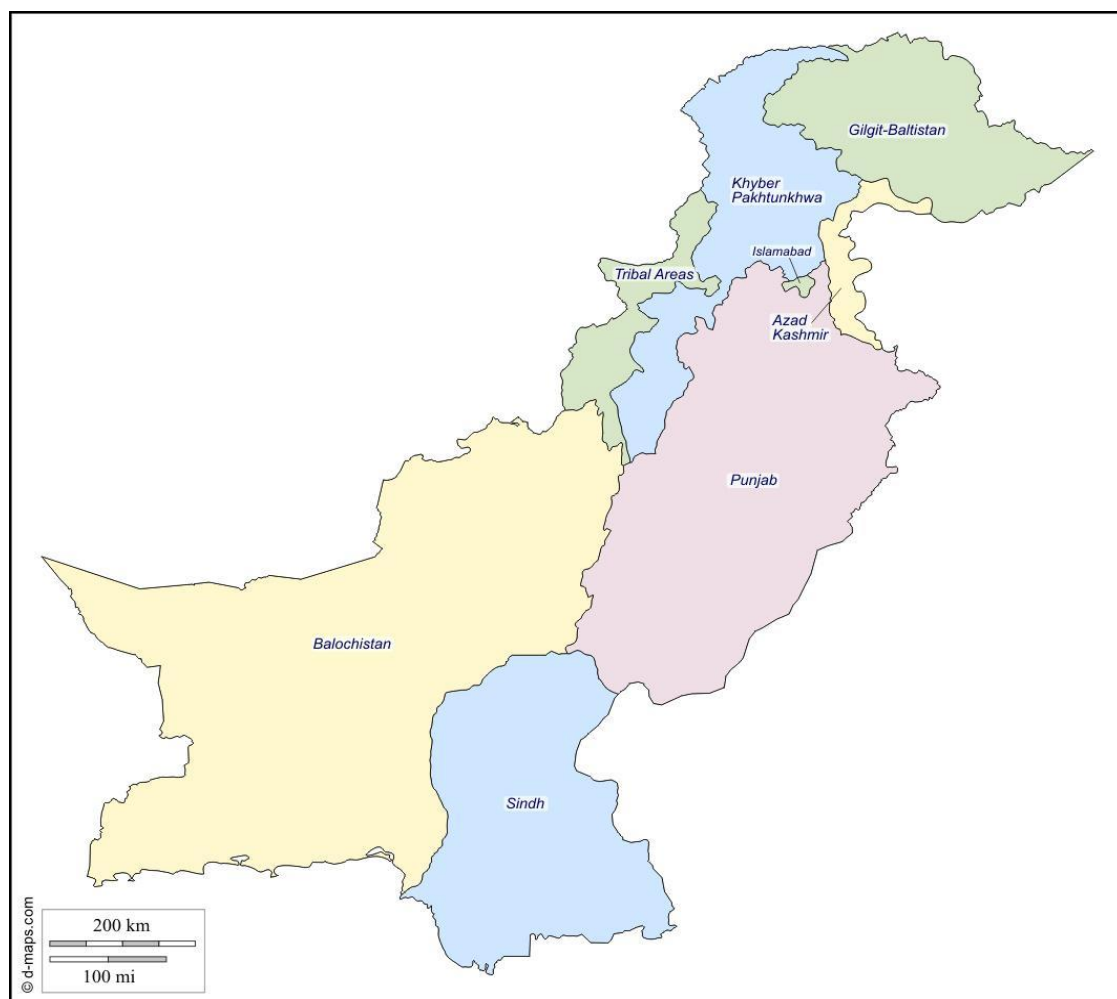


Figure 1.4: Map of Pakistan [7]

1.1.1.A.3 Ministry and departments

The Ministry of National Health Services Regulation and Coordination (NHSRC) is a cabinet-level ministry formed in 2013 by the Government of Pakistan. It is primarily liable for regulating the healthcare system and health-related policies in the country.

1.1.1.A.4 Pharmacy, drug laws and regulation

The regulation of the pharmacy profession and pharmaceutical industry in Pakistan involves implementation and enactment of three major acts: The Pharmacy Act 1967, Drug Act 1976 and the Drug Regulatory Authority Act 2012 (DRAP Act 2012). These acts are enacted by two major government bodies: Drug Regulatory Authority of Pakistan (DRAP) under the federal government and pharmacy services divisions under provincial ministries. In addition, the maintenance of educational standards as well as issuing of medicine sale licenses required by community pharmacies or medicine stores to operate are regulated by the Pakistan Pharmacy Council (PCP). DRAP and PCP both also come under the jurisdiction of NHSRC [8, 9]. The enforcement of Drug Act 1976 is the responsibility of both federal and provincial

governments as this act contains information about the manufacturing, quality maintenance and sale of quality drugs (medicines) in each province in the country. Thus, these three entities regulate the pharmacy profession in the country.

1.1.1.A.5 Federal and provincial drug law enforcement

In Pakistan, the planning of pharmacy and pharmaceutical laws, implementation responsibility and exercise of power are shared between federal and provincial governments. Under the Drug Act 1976, the regulation of sale of medicines is the responsibility of both federal as well as provincial governments. Drug rules therefore exist at both levels of the government to regulate the a) sale of medicines, b) practice of pharmacists and c) quality control in their respective domains/rules [10].

In Pakistan, amendments to existing drug laws and acts can be made by each province to address their specific health and medical needs. These amendments require approval from the respective provincial assembly. In 2017, Pakistan underwent Schedule-G amendments to classify medicines into different categories and restrict their sales without a prescription. Federal drug inspectors are responsible for enforcing drug laws in federal ICT according to the DRAP Act 2012, while provincial drug inspectors follow their respective province's laws under the Drug Act 1976 [10].

It is important to mention that in Pakistan narcotic medicines including strong pharmaceutical opioids like morphine, fentanyl and others are additionally regulated by the Pakistan Narcotics Control Board (PNCB). The PNCB regulates pharmaceutical opioid manufacturing, distribution and usage at the same level as illicit drugs and substances like diamorphine (heroin¹) and crystal methamphetamine (Ice) with the help of the Anti-Narcotic Force (ANF) of Pakistan.

1.1.1.A.6 Recent amendments and reforms

Over the last 15 years, amendments were made to the existing provincial and federal drug sales due to concerns about drug misuse and the absence of track and trace records of distributed and dispensed medicines and to discourage and control the expansion of unlicensed medical store premises [11, 12].

The latest 2017 amendments focus on three major points:

1. Only a pharmacist can establish or run a community pharmacy shop whereas pharmacy technicians can establish or manage a medical store after obtaining the respective drug sale licenses.
2. Schedule-G medicines include anti-leprosy medicines, vaccines, anti-sera, immunosuppressants, anaesthetics, specific antibiotics, inotropic

¹ Please note the word heroin is used alongside diamorphine in this thesis because of its context to be used as a street drug of misuse

medicines, prostaglandins, Alpha Blockers, narcotics (including all opioids such as morphine, buprenorphine, nalbuphine, fentanyl, pethidine, tramadol, codeine), psychotropics, Tricyclic Anti-depressants (TCA) and hormones along with others [9]. These have been strictly classified as prescription-only and can only be procured or dispensed under the direct supervision of a qualified pharmacist (additionally need a separate narcotic sale license issued to a pharmacist).

3. The pharmacist is legally responsible for rational use of Schedule-G medicines as well as patient counselling and must ensure that the dispensing of these medicines follows a valid legal prescription along with record keeping. The following information needs to be recorded in the pharmacy register at the time of purchase of medication stock and before dispensing:

- Serial number
- Date of purchase, sale
- Invoice number
- Name of drug
- Name of manufacturer
- Batch number
- Quantity purchased
- Name and age of the patient
- Name of prescriber
- Name of hospital/clinic of prescriber
- Quantity sold
- Quantity remaining
- Signature of the qualified person (pharmacist)

1.1.1.A.7 Laws regarding pharmacy establishment and medical stores

Pharmacies and medical stores in Pakistan are governed and regulated under the drug rules and their amendments (as shown above). To operate a commercial establishment selling/dispensing medicine, drug sale licenses must be obtained prior to any procurement, dispensing and/or sale of medicines. The licensing rules are also applicable to registered pharmacies doing online businesses, as per the rules of the respective province they have obtained a license in. Depending on the license obtained, an establishment selling medicine may be classified as a community pharmacy or a medical store.

There are three types of drug sale licenses in Pakistan, license A, B and C as shown in Table 1.1 below.

Table 1.1: Types of medicine sale licenses in Pakistan

Type of License	Issued to (qualification required)	Mandatory for opening
License A	Pharmacist (pharm-D)	Community pharmacy, wholesale
License B	Pharmacy technician (2-year diploma)	Medical store, wholesale
License C	Dispensers (provincial pharmacy exam pass)	Wholesale only, can be employed in pharmacy or a medical store in presence of higher license holders (A and B)

A total of four types of commercial sale licenses can be obtained by these three license holders as shown in Table 1.2 below:

Table 1.2: Drug sale license for opening a community pharmacy and a medical store, before and after drug amendments

Type of license	After 2017 amendments (license)
Medical store license 9	A, B (excluding Schedule-G medicines)
Distribution (wholesale) license 10	A
Narcotics license 11	A, B
Community pharmacy license 12	A (all medicines)

Earlier, License A pharmacies were allowed to sell all medications but after the drug rule amendments a separate narcotic sale license (form 11) must be obtained by a community pharmacy shop if the premises will sell narcotic medicines like opioids. However, it must be highlighted that if a shop has a category A sale license, category B and C license holders (even without displaying their license) can perform all activities inside the pharmacy under the supervision of a qualified pharmacist (including the dispensing of Schedule-G medicines).

As narcotic medicines can only be procured and dispensed with a pharmacist license, this makes the presence of license A holder (pharmacist) mandatory while dispensing of opioid medications.

1.1.1.A.8 Prescribing laws

In Pakistan, only doctors (MBBS-physicians/surgeons and BDS-dentists/surgeons) with valid Pakistan Medical and Dental Council (PMDC) registration have the legal authority to prescribe medicines. Drug Law 1976 [13] requires each prescription to have the signature and registration number of the prescriber.

1.1.1.A.9 Healthcare system (primary, secondary, tertiary)

A healthcare system is the backbone of any country to provide equal health facilities to the public [14]. The healthcare system of Pakistan is complex because it includes services and facilities from both the public sector and private sector as shown in Figure 1.5 below. It is important to highlight that the community pharmacy sector is completely privatised, including the pharmacies found inside public sector healthcare institutes [15, 16].

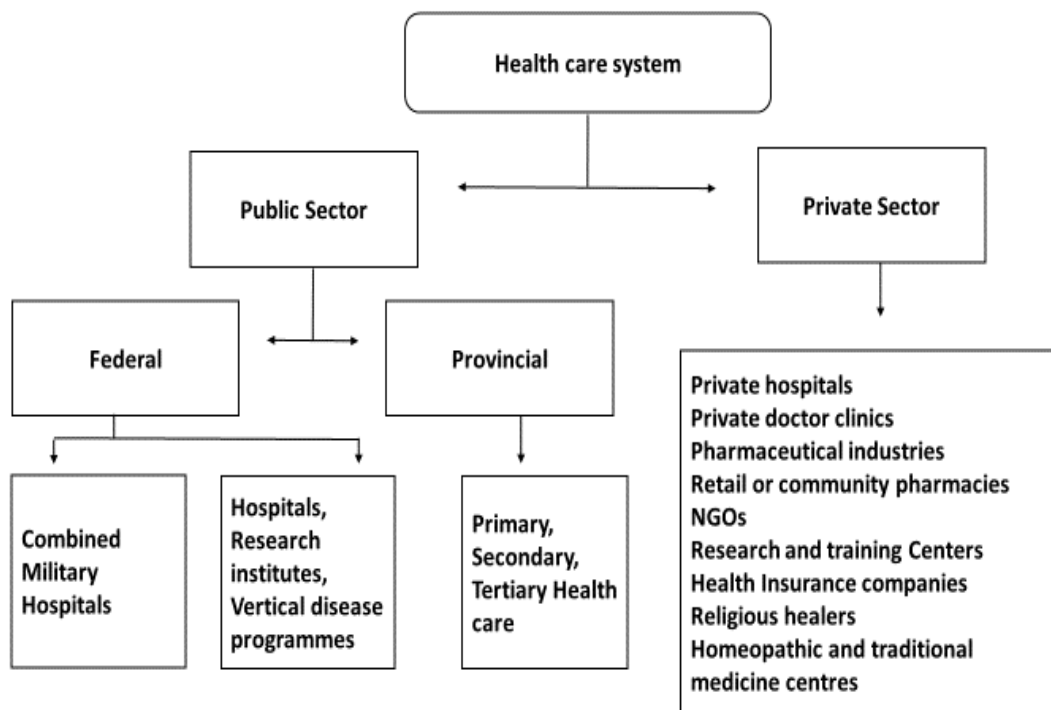


Figure 1.5: General overview of Pakistani healthcare system

1.1.1.A.10 National Health Vision 2025

After the devolution of powers (decentralisation) to provinces in 2012, every provincial health department aimed to develop policies and strategies using the World Health Organisation (WHO) health system framework. The WHO health system framework comprises of six building pillars: health funding, health service delivery systems, workforce for health, health information systems, leadership and authority, essential medicines and technology [17, 18].

However, due to the lack of a central health policy and common disputes amongst provinces in 2015, NHSRC developed “National Health Vision 2025” in order to meet the United Nation’s (UN) third Sustainable Development Goal (SDG) of public health promotion and Universal Health Coverage (UHC) to provide equitable access to affordable genuine medicines and medical services. The National Health Vision (2016-2025) is now a uniform strategic planning resource for federal and provincial governments. It currently helps

unidirectional efforts for achieving improved health for all Pakistanis by achieving SDG and UHC goals [19, 20].

1.1.1.A.11 Healthcare budget and costs

Healthcare is provided through either public or private sector in Pakistan (Figure 1.5). Although there is no official figure for out-of-pocket health expenditure, evidence from grey literature suggests more than 70% of health spending costs consists of out-of-pocket payments, private health insurances, money donations and aids provided by non-government organisations (NGOs) [10, 21-24].

1.1.1.B Pharmacy profession in Pakistan

A pharm-D graduate can either work in the government-regulated sector under the standard basic pay scale system budgeted by government or can get hired in the private sector [9]. After obtaining the respective licenses (Table 1.2), pharm-D graduates can also open their own private businesses including manufacturing, distribution and community pharmacy setups. Current literature reports about 55% of pharmacists in the country are involved in production sector, 15% work at public sector institutes, 15% work in sales and promotional marketing, 5% work in teaching and research, and 10% are engaged in community pharmacy setups [10, 25, 26].

1.1.1.B.1 Community pharmacy

Shops and establishments selling medicines are part of the private sector and are referred to as medical or drug stores, chemist shops, drug outlets or community pharmacies as per the display of a license of a qualified person as stated above in Table 1.1.

1.1.1.B.1.a Medical stores and shops

There were approximately 80,000 medicine-selling establishments in 2017 out of which 45,000–55,000 are believed to be wholesale and medical stores [18, 27]. These pharmacies and medical stores serve as the leading distribution channel for medicines and are responsible for more than 80% of all dispensing of medicines in the country [10]. These pharmacies and medical stores are in urban as well as rural areas and may be found in commercial and residential zones. They can either be a separate store or found as a section in commercial merchandise shops such as grocery stores and/or cosmetics stores. They are also found inside hospital premises and can be either independent pharmacies (mostly in rural areas and small cities) or chain pharmacies (big cities and federal area).

1.1.1.B.1.b Staff

The presence of a qualified pharmacist is not assured because in Pakistan non-pharmacist license holders can also open up a medicine selling establishment and dispense medicines. The staff running these establishments and dispensing medications might vary depending upon the

license and qualification of personnel in these medical stores and pharmacies. Staff members can include a qualified pharmacist (license A), pharmacy assistant (license B), dispensers (license C), salesman (people having no dispensing-related education or qualification), medical doctors (where medicine shop is present inside private doctor clinics²), nurses, nursing technicians and homeopathic doctors [28].

1.1.1.B.1.c Community pharmacy services

The dispensers (pharmacists, pharmacy technicians, salespersons) in pharmacies and medical stores perform varied functions including procuring drugs, stocking, dispensing, auditing, storekeeping as well as may act as an accountant or store manager. Depending upon the establishment the services offered may or may not include compounding, diagnosing, prescribing, dispensing, counselling and administering of drugs and vaccines [29]. Extended patient-oriented pharmacy services are almost non-existent in community pharmacies or medical stores [5].

1.1.1.B.2 Essential drug list

In Pakistan, an essential medicine list (EML) was first made available in 1994 and has been subject to revision in accordance with national and international standards in 1995, 2000, 2003, 2007, 2013 and 2018. However, it must be highlighted that the availability of medicines on the EML such as morphine for pain management is not guaranteed across medicine dispensing establishments across the country [9, 30, 31].

² Private clinics are similar to general practitioner (GP) surgeries in the United Kingdom (UK), but people have to pay

Narrative literature reviews can be problematic due to a lack of systematic methods and potential for subjective biases [32]. However, if authors take steps to minimize biases, they can be useful for presenting a summary of data. In this thesis, the literature review was undertaken to provide an overview of relevant literature and the following section now presents how the narrative literature review was undertaken in this thesis.

1.2.A Subchapter B, subsection A: Literature review methodology

This research study focused to explore the role of CPs in opioid optimisation in people with CNMP. Thus, the literature review focused on three main areas, CNMP prevalence, the use of opioids in CNMP management and to explore the role of CPs in medication management with an emphasis on opioid optimisation in CNMP as shown in Figure 1.6 below.

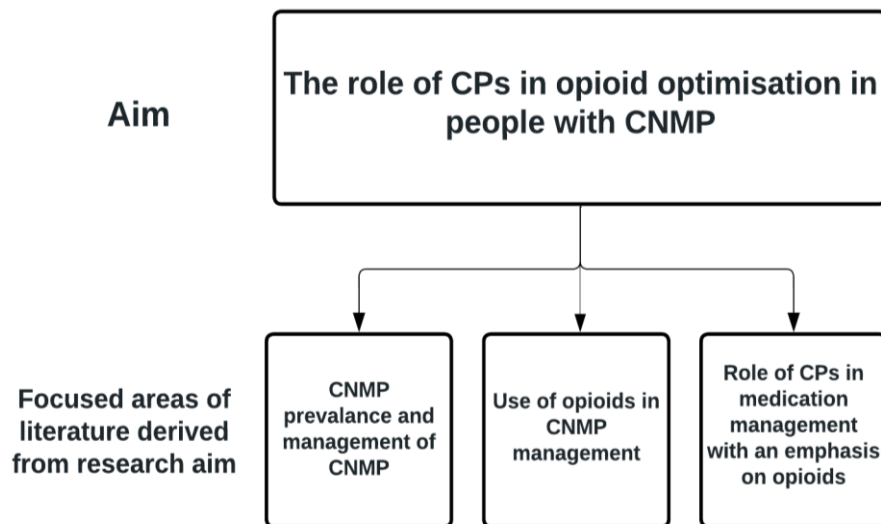


Figure 1.6: Focused areas for literature review

Three separate literature reviews were conducted relevant to each focused area. The synthesized evidence in each literature review is presented in the form of a narrative in the next subsection, bringing all three reviews together, to inform the research gaps and aim and objectives of this study. Each literature review was conducted in three focused tiers: HICs, LMICs and Pakistan. Published research articles, reviews, books, thesis and reports related to these topics were broadly searched for after 1990 (pharmaceutical care concept and the development of pharmacy practice).

- The first review aimed to search for prevalence of CNMP in HICs, LMICs and Pakistan. Inclusion criteria was inclusive of all study designs and contents provided in English language. Exclusion criteria included

all palliative care, cancer-related pain prevalence and pain prevalence in children as it was beyond the scope of this research study.

- The second literature review explored the use of opioids in the management of CNMP in HICs, LMICs and Pakistan. This included exploring the use of opioids in the management of CNMP as well as reporting and exploring opioid-related use, side effects and/or harm in outpatients only. The inclusion criteria included all studies stating the use of opioids in the management of CNMP. The exclusion criteria in this literature review were opioids being used in cancer pain as well as studies reporting the use of and/or side effects from opioids in hospitalised patients only. These were excluded because the overall study aimed to explore the role of CPs in CNMP, which is a chronic condition and patients are usually ambulatory or found in outpatient settings. As care for admitted patients is essentially different than ambulatory care patients, the literature review focused only on ambulatory settings.
- The third review aimed to identify and explore the role of CPs in medication management services in community pharmacies with an emphasis on opioids in CNMP management. The inclusion criteria included all community pharmacy activities and services that can optimise the use of medicines/opioids in the management of CNMP. Exclusion criteria included all opioid optimisation services for people within admitted/in-patient settings as well as services for opioid substitution therapies or services for people with misuse and addiction. This was purposely excluded because the aim was to understand the care provision by CPs for people with general chronic medication management needs, rather than focusing on a particular class of people with special needs (addiction, substance use disorder, withdrawal, substitution therapies and identifying abuse).

1.2.A.1 Search strategy for literature review

Three free text areas (prevalence of CNMP, use of opioids in the management of CNMP and role of CPs in medication management services in opioids) were created as shown in Figure 1.6 (above) and Table 1.3.

Table 1.3: Database free word random searches words

Database	MeSH headings with an explode functionality (where applicable), using Boolean operators and/or as necessary	Free term word(s) searches across different databases (using Boolean operators and/or as necessary)
Literature review one:	Pain Pain Management Chronic Pain Pain Perception	Prevalence of pain, chronic pain Incidence reported of pain, chronic pain Global Burden of Chronic Pain

Chapter 1 Subchapter B, subsection A: Literature Review-Methodology

Prevalence of CNMP in HICs, LMICs and Pakistan		Global burden of disease Pain management Managing Pain in low Resource Settings CNMP management Consequences of CNMP
Literature review two: Use of opioids in the management of CNMP in HICs, LMICs and Pakistan	Opioids Opiate Analgesics, Opioid Opioid-Related Disorders Opioid Epidemic Analgesics, Narcotic Opiate Overdose Opioid use disorder	Opioids over use/misuse Opioid related morbidity and mortality Global consumption of opioids Opioid utilisation in chronic pain Opioid related adversity, side effects and adverse effects Opioid related deaths Abuse/misuse/unsafe use of opioids The use of narcotic pain medicines The use of opioid medications
Literature review three: Role of CPs in medication management services in opioids in HICs, LMICs and Pakistan	Pharmacist Pharmacists Community pharmacist Pharmacy shop Health Services Administration Organization and Administration Medication Systems Medication Review Drug utilisation review Patient safety	Role of community pharmacists in medicines Role of community pharmacists in opioids Role of pharmacists in medicines Role of pharmacists in medications reviews Role of pharmacists in medicine safe use Role of community pharmacists in medication management in extended pharmacy services Pharmaceutical care practice services Barriers and facilitators of community pharmacists to opioid optimisation in chronic pain Barriers and facilitators of community pharmacists trying to optimise opioids

These searches were carried out using various databases and the keywords for the searches were reinforced with the use of MeSH terms as per each database. The databases used included MEDLINE (OVID) /PubMed, CINAHL, EMBASE, International Pharmaceutical Abstracts (IPA), Web of Science, ProQuest, Pakistan Research Repository by Higher Education, Google Scholar, policy documents, news reports and blogs. Vocabulary and alternate spellings (UK and American) were adjusted and were used interchangeably across databases. The set of terms/ free word terms used for each review has been shown in Table 1.3. After all the basic searches (having free terms and MeSH

headings) were combined into an individual search, they were intersected using AND/OR as applicable.

In each database, the titles found were screened based on the relevance of the study to the focused areas of literature review to gain likelihood of conducting a focused and meaningful search. If the study seemed relevant to one of the three selected areas (Figure 1.6), the next step was to read the abstract and if it seemed relevant, a full article reading followed. All the relevant data was narratively synthesised and is provided under different subheadings in the literature review. Further scoping for relevant studies was achieved using Google Scholar as well as the references of the included studies. All references were managed using Endnote X8 (San Francisco, Clarivate Analytics) [33]. This search strategy was assumed to have the most likelihood of finding relevant studies important for the literature review considered relevant for this research study.

1.2.B Subchapter B, subsection B: Narrative synthesis of literature review

A narrative synthesis of the three literature reviews is now presented in this subsection.

1.2.B.1 Chronic non-malignant pain prevalence and management using opioids

1.2.B.1.1 Pain

According to the latest definition by the International Association of Study of Pain (IASP) [34], pain can be defined as *“An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”*. Pain is one of the most common reasons people seek the advice of a healthcare professional [35].

1.2.B.1.2 Types of pain

Pain is usually categorised into two broad types: acute and chronic pain. Any pain that persists for more than three months or 12 weeks is commonly categorised as chronic pain [36]. Chronic pain is a complex and distressing problem that has an impact on individuals as well as whole societies. Chronic pain is usually a result of an injury or a disease(s), but it can be a separate condition in its own and not just a symptom of other diseases. Chronic pain therefore is a condition that has been given its own taxonomy and medical definition [37]. Chronic pain can have malignant (cancerous) or non-malignant origins. CNMP refers to persistent pain beyond 12 weeks which is due to a non-cancerous condition or disease. Chronic pain can be neuropathic pain (for instance pain originating in nerves) or nociceptive pain (musculoskeletal in origin and arises from structures such as muscles, bones, or ligaments) [38]. It can also be nociplastic pain, which is the *“pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain”* [39]. Chronic pain is reported to be more prevalent among women, older people and in people working in physically demanding occupations [40].

1.2.B.1.3 Chronic pain prevalence

The World Mental Health Survey [41] in 2008 surveyed 17 countries and reported that the prevalence of chronic pain (including both non-malignant and malignant conditions) in the last 12 months was found to be 37.3% in developed countries and 41.1% in developing countries (seven LMICs countries). The survey reported that although CNMP was found to affect people of all ages, women and older people were usually overrepresented in this cohort in all countries. This remains consistent with the statistics from a

survey [35] conducted in 2018 (n=17, 10 developed and seven developing countries) that also reported similar percentages and stated that approximately 35-38% people have chronic pain in developed countries whereas 40% individuals from developing countries had chronic pain as per IASP definition.

1.2.B.4 Literature review 1: CNMP prevalence

CNMP is one of the biggest challenges in healthcare [35]. CNMP includes neuropathic, musculoskeletal and visceral pain and accounts for around 70% of pain experienced by older patients [40]. Among all conditions, low back pain and neck pain are the most commonly reported, whereas according to one estimate surgery and trauma account for 25% of the CNMP burden [42].

1.2.B.4.a CNMP prevalence worldwide

Elzahaf et al. [43] conducted a systematic literature review in 2012 on the prevalence of CNMP (19 studies, 65 surveys, 34 countries, n=182019 respondents) and reported worldwide mean prevalence of pain lasting >three months at 30.3%. It is important to mention that 16/19 included articles reported low back pain or neck pain only showing high prevalence of these two CNMP conditions in HICs.

1.2.B.4.b CNMP prevalence in LMICs

A systematic review and meta-analysis of the global burden of chronic pain without clear aetiology [44] in 2016 reported a 34% prevalence of chronic pain in LMICs. Many conditions were reported such as back pain, headache, musculoskeletal pain and pelvic pain. The prevalence of chronic pain was found higher in older people and people working strenuous physical jobs. Another meta-analysis [45] of 12 studies with 29,902 individuals in 2019 reported that 7,263 individuals had chronic pain. The overall pooled prevalence of chronic pain after correction for publication bias was 18%, which is quite similar to the prevalence of CNMP in HICs. The studies included in this meta-analysis were from Latin American, Asian and African countries and the chronic pain prevalence ranged from 13% to 51%. The study highlighted that the prevalence range might not be because of people having less pain but was majorly attributed to the individual reporting systems of countries. The meta-analysis reports statistics from four Asian countries: India, Nepal, Iran and China [45]. It does not, however, report about the prevalence of chronic pain in Pakistan.

A 2021 review [46] also focused on the prevalence of chronic pain in LMICs and used the world health survey data (2002-2004) of 52 countries. This review focused on adults who were older than 25 years and the overall weighted age and gender standardized prevalence of pain across LMICs was estimated to be 27.5%, which is slightly higher than the previous studies conducted globally. The review also reported significant variation in chronic

pain prevalence across countries, ranging from 9.9% to 50.3%. This review also attempted to explore the country-level contextual factors to explain cross-country variations in the prevalence of chronic pain and found that women, older people and people from rural populations reported chronic pain more frequently [46].

It must be highlighted that in comparison to HICs, LMICs might have a similar or even higher prevalence of CNMP because of higher incidence of road traffic and industrial accidents, poverty, physically straining labour and a higher incidence of diabetes and human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) [47].

1.2.B.4.c CNMP prevalence in Pakistan

There were no systematic reviews or meta-analysis found that estimated the overall prevalence of CNMP in Pakistan. However, to understand the prevalence of CNMP, I looked at studies reporting common CNMP conditions and diseases from Pakistan that are now presented below.

A 2017 study [48] from South East Asian countries including Pakistan reported that 40.6% people in that study suffered from backpain, which as stated previously is one of the most common reasons of CNMP. A 2019 study [49] from Pakistan found that out of 306 participants in that study, 53.9% of patients were suffering from chronic neuropathic pain. A 2022 [50] study from Pakistan surveyed household females and reported that CNMP conditions were prevalent among a cohort of 1,100 participants. The study reported that out of the cohort, 34.5% had chronic knee pain, 31.4% had low back pain, 20.4% reported neck pain and 13.7% reported shoulder pain.

It is important to signify that Asian countries including Pakistan are expected to see a 60% rise in the population of older people between 2015 and 2030 [51]. This rise may predict an increase in CNMP conditions such as skeletal disorders, joint pains, neuralgias and other chronic conditions, which are also commonly reported in older people in Pakistan [52-54].

The global burden of disease (2016) [55] report states that the incidence of non-communicable diseases is increasing Pakistan. The report highlights that Pakistan might have a high incidence of chronic neuropathic pain, including diabetic neuropathy, post-amputation pain and a growing number of people with chronic postsurgical pain. In addition, known risk factors for chronic pain (for example psychological trauma, interpersonal violence and low socio-economic status) are presumed to be higher in Pakistan than in HICs [55]. According to the global burden of diseases report (2010) [56], years lost to disability (YLD) also have been significantly reported in Pakistan arising from low back pain, traffic and workplace accidents, diabetes and diseases like AIDS, which while unable to directly provide statistics for CNMP prevalence,

are able to indicate that CNMP prevalence might be high in Pakistan although not reported extensively and exclusively.

1.2.B.5 Literature review 2: CNMP management and current opioid practicing guidelines

Chronic pain is a complex condition that is influenced by biological, psychological, and social factors. Its management requires a multifactorial approach aimed at improving pain and patient outcomes, such as improved functionality and quality of life (QoL). Analgesic medications, including prescription, over-the-counter (OTC), and pharmacist-only drugs, are commonly used in the management of chronic pain. Paracetamol, NSAIDs, gabapentinoids, antidepressants, and opioids are among the most commonly used medications. It is important to contextualize pain management within local, national, and international guidelines and understand the psychosocial nature of CNMP.

WHO in 1986 [57] released a document addressing cancer pain relief that proposed a three-step analgesic ladder for the management of chronic pain in cancer patients as shown below in Figure 1.7.

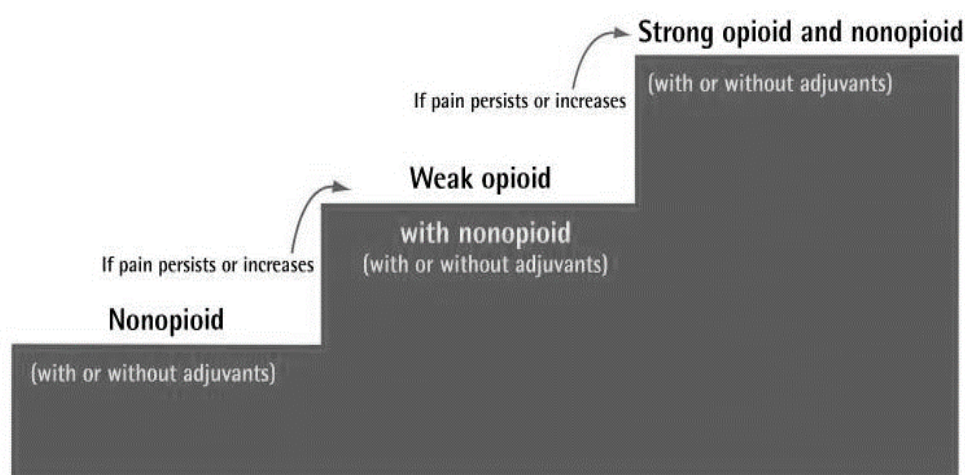


Figure 1.7: WHO analgesic ladder for pain relief in palliative care in cancer (adapted from WHO) [58]

According to the WHO analgesic ladder [58] the provider prescribes opioid analgesics to patients based on the patient's report of how serious the pain is. But as the ladder was first launched in 1986 and specifically for cancer pain management it debatably does not provide much guidance for CNMP management. Even so, it is still being extensively used as a guide to prescribe opioid analgesics for CNMP conditions in many countries [40]. During the last decade, the 'opioid crisis' has led many countries to realise the limitations of the WHO analgesic ladder. HICs are now creating pain management guidelines according to local needs and in light of new evidence. For example, the 2018 guidelines published by American Society of Interventional Pain

Physicians (ASIPP) [59] now recommend using non-opioid analgesics (NSAIDs, OTC analgesics) as well as non-pharmacological treatments. IASP also suggests developing a pain management plan that is reflective of the type of pain and then deciding medications that targets that pain. For example, in the case of chronic nociceptive pain (inflammatory) using steroids or NSAIDs might be beneficial; whereas antidepressants or anticonvulsants might be suitable for neuropathic pain conditions; and in conditions that do not have inflammatory pain, opioids might be used. Thus, the generic reliance on opioids without taking individuals' specific needs for different types of pain needs to be changed. Most countries from LMICs including Pakistan lack CNMP management guidelines and still use the WHO analgesic ladder for pain management [40]. This could mean that opioids might still be prescribed for managing moderate to severe CNMP without establishing individual needs. This may be producing opioid-related side effects and harm without significantly improving patient outcomes.

WHO in 2019 [60] announced to revise pain management guidelines because of concerns about the opioid overdose crisis in the USA and the increased risk of misuse and harm reported worldwide when it came to pain medicines including opioids. WHO also acknowledges the lack of access to essential pain medicines in LMICs. WHO thus aims to ensure that people in severe pain have access to effective pain control medication including opioids when needed as part of the UHC agenda. However, the medicines should be used safely as to avoid misuse and reduce opioid-related harm. WHO is currently undergoing developing pain management guidelines [60] and is working on "*Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines*" to help increase access while promoting the safe use of pain medicines including opioids.

1.2.B.5.a The use of opioids in CNMP management

Opioids refer to all natural, semisynthetic and synthetic opioids [61]. WHO recognises opioid medications including morphine as essential medicines for pain management [62]. Opioid medications can make an enormous and beneficial contribution towards pain management and well-being of people with acute and cancer pain [63]. Although there is a lack of substantial benefit of opioids for long-term use in CNMP management they are widely used [64-67]. A 2018 systematic review and meta-analysis by Busse et al. [68] assessed the opioid efficacy in CNMP by reviewing 96 randomized control trials (RCTs) and found that opioids provided no benefits when compared to either placebo, ibuprofen or acetaminophen in pain improvement. No positive effects or changes of opioids were reported even in physical, social functioning, emotional or role functioning. In addition, opioids were found to increase the incidence of side effects when compared to placebo.

Furthermore, the review found that persistent high dosage of opioids was linked with an increased risk of serious adverse effects such as overdose, addiction and even mortality.

As stated above, despite the lack of evidence regarding opioid medications beneficial use in CNMP management they are extensively used. Below I have attempted to provide a brief overview of the world global opioid consumption in two broad categories of HICs and LMICs.

1.2.B.5.b The Global consumption of opioids in CNMP in HICs

Many countries have experienced an increase in opioid prescription rates in the last two decades. In a 2019 study [69], the top three consumers of opioids were reported to be the United States of America (USA), Germany and Canada (40,240; 28,862 and 26,029 defined daily dosages of opioids per million inhabitants, respectively). There is also an increasing trend of the use of prescription opioids in countries such as France [70], Italy [71], Spain [72] and Australia [73].

A 2020 systematic review and meta-regression [74] of 42 studies reported almost one-third of patients with CNMP were prescribed an opioid (31%, n= 5059098). Most studies in this review were from the USA (n = 28), followed by the UK (n = 4 studies), Spain (n = 3 studies) and Canada (n = 3 studies) with single studies from Norway, Denmark, Australia and India. The use of opioids was reported to be even higher (42%) in patients with chronic low back pain despite high dose opioids not being recommended in guidelines. It must be highlighted that the review reported that for CNMP management in HICs, stronger opioids are more commonly prescribed than weaker opioids, which could give rise to increased opioid-related harm in these countries.

1.2.B.5.c Problematic use of opioids in HICs

The literature review identified many studies reporting opioid-related harm, side effects and opioid use disorder (OUD) for people using opioids for CNMP management. I have briefly provided an overview of the extent of the problem to show OUD is prevalent in people with CNMP using opioids and can result in an increased patient harm.

1.2.B.5.c.1 Opioid use disorder in HICs

A 2017 Cochrane review of existing reviews (systematic, meta-analysis) [75] showed several adverse events associated with the medium and long-term use of opioids for CNMP. The absolute event rate for any adverse event with opioids in trials as compared to a placebo was reported to be 78%. The review highlighted that there could be a 7.5% absolute rate for any serious adverse event in people using long-term opioids.

Opioids can also cause intentional or unintentional addiction, which might lead to OUD. OUD is defined by the Diagnostic and Statistical Manual of

Mental Disorders (fifth edition) or DSM-5 [76] as “*a problematic pattern of opioid use leading to clinically significant impairment or distress*”.

When an opioid is discontinued or prescribers reduce the dose some people do not find themselves craving for opioids, yet for many people the need to take opioids becomes more as they experience reduced analgesic effects and thus are in constant need for increased doses. Thus, physiologic dependence on opioids leading to increased dose, frequency, opioid misuse, abuse and dependence are common with these medications [77, 78]. The incidence of opioid prescription misuse leading to OUD has been rising and can have fatal consequences [79, 80].

Literature reports that various risk factors such as individual, personal, genetic, family, peer, social and environmental factors may directly or indirectly contribute to increased vulnerability to develop OUD with opioids. For example individual factors such as history of substance use, younger age, severe pain and mental disorders [81] or personal factors such as divorce or unemployment might also increase the risk of opioid misuse [76].

From 2002-2011, in USA 25 million people used opioids for non-medical reasons and more than 11 million misused the medications. In 2016 over 200 million opioid prescriptions were dispensed and in 2017 around 1.7 million people were diagnosed with OUD [82].

In Canada, approximately 37% of people diagnosed with OUD reported using prescribed opioids whereas 26% people reported obtaining opioids through both prescriptions and illicit ways [82]. This is further endorsed by a 2021 systematic review [83] that projected average rates of opioid misuse to be 21-29% and for developing addiction to be 8-12% while using opioids. Thus, it is important to realise that people with CNMP when prescribed opioids have a high risk of developing OUD, which can then lead to opioid-related morbidity and mortality. A brief overview of this is provided in the paragraphs below.

1.2.B.5.c.2 Mortality and opioid crisis

The opioid epidemic or ‘opioid crisis’ is a term usually used for the overuse, misuse, abuse and overdose related deaths related to the use of opioids [84]. Literature reports that in the USA, the mortality associated with opioids increased up to five times in 2017 as compared to 1999 [85], accounting for deaths of 218,000 people. This opioid crisis is endorsed by another report that stated that in the USA the opioid-related mortality increased by 292% between 2001 and 2016 [86]. In addition, another study [87] looked at the North American opioid crisis and reported that prescribed opioids were responsible for 28% of deaths in 2019.

In Canada, reportedly 17,602 people died from an opioid-related death between January 2016 and December 2020, constituting an opioid crisis [82, 88-90]. Another estimate shared that in Canada in 2019 [91], 10.3 deaths per

100,000 population were related to opioids. This remains similar to the 2018 opioid-related deaths in the USA [92], where 13.3 per 100,000 population died from opioids. I must emphasize that these death statistics include both prescription as well as illicitly obtained opioids, including fentanyl, hydromorphone and diamorphine. In Australia between 2011–2015 [93], the number of people dying from an overdose with diamorphine was half the number of people who died from a prescribed opioid.

In contrast with HICs, there is a lack of studies reporting opioid-related mortality and morbidity from LMICs including Pakistan. Similarly, there is a dearth of studies from LMICs including Pakistan reporting on the number of people using opioids, the conditions they use them for and the outcomes of opioids on people using them for CNMP management.

It is important to highlight that the deaths associated with opioids reported in HICs should not be considered because of misuse and overdose only. There could be many underlying reasons and factors that extenuate the risks of opioids for some people, societies and countries more than others and might cause OUD leading to opioid-related morbidity and mortality [94]. As previously shared, CNMP management is so complex and multimodal that no one therapy can be generalised for everyone due to its biopsychosocial nature. New guidelines, like for example IASP, recommend considering the origin of pain as well as patients' individual needs when selecting medicines for CNMP management. It is thus vital to understand individual, social and environmental factors affecting the pain as well as its management. Assessing individual risk factors might help in optimising the use of opioids and avoiding opioid-related harm. This, however, is currently not an approach undertaken in LMICs, including Pakistan. Healthcare team members who might help in medication counselling, risk assessment, medication reviews, identifying misuse, diversion and the adherence with opioids needs to be further explored in these countries.

1.2.B.5.d The global consumption of opioids in LMICs

Many studies and reports have substantially highlighted the lack of access to potent synthetic opioids for pain management in LMICs. For more than 50 years the UN convention emphasises [95] that certain medications are *“indispensable for the relief of pain and suffering”* and thus their availability must be ensured. However, the Lancet Commission on Palliative Care and Pain Relief (LCPCPR) published a report in 2017 [63] describing the global problem of low access to opioids and shared an *“access abyss”* of opioids for people living in LMICs. The authors estimated that in 2015 over 60 million people in the world were suffering from symptoms that needed pain relief. Lack of access to opioids has also been highlighted by WHO, which shares that 80% of the world's population (5.5 billion out of 7 billion people) have

insufficient access to opioids to treat moderate-to-severe pain. This is despite the fact that morphine, fentanyl and methadone are included in the WHO's Model of EML [95]. Lack of access to opioids for pain relief has also been reflected in research studies and a 2018 scoping review [96] analysing more than 100 full text documents, including articles, reports and grey literature also reported the same.

All countries are required to submit an annual opioid usage data to the International Narcotics Control Board (INCB). This data can then be used to evaluate the use of opioids in LMICs.

A study [97] looking at global consumption of prescription opioid analgesics between 2009-2019 reported tramadol, codeine, and oxycodone were the most consumed opioids in UMICs in 2019 and accounted for 70% of total opioid morphine milligram equivalent (MME) consumed. In LMICs, even fewer opioids were available when compared to UMICs and in 2019 tramadol, tapentadol and codeine accounted for 87.7% of total MME consumption in LMICs as shown in Table 1.4 below.

Table 1.4: Morphine Milligram Equivalent (MME)/1,000 inhabitants/day for the top four most consumed opioids from 2009-2019, adapted from Jayawardana et al. [97]

	2009			2019		
	Median	IQR	95% CI	Median	IQR	95% CI
HICs						
Oxycodone	26.7	5.8 – 95.9	11.4 - 71.3	42.9	6.2-130.0	17.1 - 87.0
Tramadol	69.1	19.2 – 139.0	33.6 - 94.8	82.8	33.2 – 131.0	48.6 – 114.9
Fentanyl	57.6	16.6 – 137.0	22.4 – 121.4	71.5	23.0 – 122.0	36.5 – 92.1
Morphine	13.5	7.0 – 75.0	8.3 – 30.9	12.2	6.1 – 51.3	9.0 – 26.9
UMICs						
Tramadol	3.9	3.0 – 9.1	2.8 – 7.8	16.6	6.6 – 22.8	9.7 – 22.4
Codeine	1.4	0.4 – 6.1	0.6 – 4.5	3.3	0.7 – 20.1	0.8 – 16.7
Oxycodone	0.1	0.0 – 0.4	0.0 – 0.4	1.1	0.3 – 4.8	0.3 – 4.6
Morphine	0.9	0.0 - 3.0	0.0 – 1.9	2.0	0.8 – 4.2	0.8 – 4.0
LMICs						
Tramadol	1.8	1.3 – 2.4	1.2 – 2.5	4.3	1.5 – 5.8	0.8 – 6.7
Tapentadol	NA	NA	NA	3.3	1.8 – 8.2	0.3 – 13.1
Codeine	1.1	0.9 – 3.0	0.1 – 4.2	4.1	1.1 – 5.5	0.7 – 7.5
Nalbuphine	0.1	0 – 0.7	0.0 – 0.8	0.3	0.0 – 1.7	0.0 – 2.7

IQR= Interquartile range, CI= Confidence interval

Although the overall consumption of opioids like tramadol has increased from 1.8 to 4.3 MME and codeine from 1.1 to 4.1 MME between 2009-2019 in LMICs, it is still well below the rates observed in HICs despite them having access to potent opioids. Table 1.3 shows that in LMICs, tramadol accounted for over 50% of MME opioid consumption from 2009 to 2019 [97].

With less availability of potent opioids, the pain management options significantly reduce and findings from the 2016 ACHEON study [98] of 10 Asian countries reported inadequate CNMP relief. Out of 1,305 patients in that study, 89.3% of patients reported experiencing moderate to severe pain (in the last 24 months). Despite being on pain therapies, 78.3% (n=1,022) of patients were experiencing pain that had lasted for more than six months. Out of the cohort, 80.8% patients reported CNMP to be affecting their daily living. This study also surveyed a total of 695 physicians, of whom 63.6% considered opioids necessary for treating CNMP. However only 4.4% of patients were prescribed opioids due to lack of access to potent opioids [98]. This thus indicates that people in LMICs with CNMP might be experiencing insufficient analgesic relief even while being on pain management therapies with non-opioid analgesics. Having less access to pain management options like potent opioids can further exacerbate existing health inequalities and remains in violation of the UN UHC criteria.

1.2.B.5.e Lack of potent opioids in Pakistan

Pakistan lacks access to potent opioid medications due to strict control and institutional barriers. As stated in subchapter 1, opioid medications like morphine are controlled by the ANF, which is under the Narcotics Control Board (NCB), with the same level of control as diamorphine (heroin) and other synthetic drugs of misuse. According to one estimate [99], it takes around 8-10 months for morphine to become available at hospitals once it has been ordered. Estimates suggest that out of the total opioids allowed by NCB, around 80% is sent to oncology wards in highly specialised hospitals and only a limited quota is allocated to public sector tertiary care and military hospitals. This does not even sufficiently cover the pain management of patients with acute post-operative pain. Almost negligible amounts of potent opioids are available to treat CNMP in Pakistan through private expensive hospitals [100], which in itself stands in contrast to the UHC agenda of equitable access to medicines. Available pharmacotherapies for pain management, even for palliative care, are mostly limited to tramadol oral (immediate and delayed release) and injectable, tapentadol oral (immediate release), nalbuphine injectable and adjuvant non-opioid analgesics (Table 1.5 below) [101].

Table 1.5: Availability of pharmaceutical opioids in South Asia, adapted from Larance et al. [101]

Country	Opioid medications listed as available for medical and scientific use
Afghanistan	Codeine, dextropropoxyphene, diphenoxylate, morphine, pethidine, pholcodine
Bangladesh	Fentanyl, morphine, pethidine, pholcodine
Bhutan	Codeine, dextropropoxyphene, fentanyl, morphine, pethidine

India	Buprenorphine, codeine, dextropropoxyphene, diphenoxylate, ethylmorphine, fentanyl, hydrocodone, methadone, morphine, pethidine, pholcodine, sufentanil, thebaine, trimeperidine
Maldives	Fentanyl, morphine, pethidine
Nepal	Codeine, dextropropoxyphene, ethylmorphine, etorphine, fentanyl, methadone, morphine, pethidine, pholcodine
Pakistan	Buprenorphine, codeine, tramadol, dextropropoxyphene, diphenoxylate, fentanyl, morphine, fentanyl, pethidine, pholcodine
Srilanka	Codeine, etorphine, fentanyl, methadone, morphine, pethidine

The literature review identified that there might be an overuse of available weaker opioids as well as the use of illicit opioids in LMICs including Pakistan. The following paragraphs report briefly the overuse and misuse of weak opioids, with tramadol presented as a case study of a medicine being misused extensively through LMICs.

1.2.B.5.f Problematic use of opioids in LMICs

The United Nations on Drug and Crime (UNODC) reports 2017 [102] and 2021 [103] both show that due to weak drug enforcement, both licit and illicit opioids can be found in LMICs. In addition, a 2011 review paper [101] provided an overview of the availability, diversion, misuse and injectable use of pharmaceutical opioids in eight countries from South Asia. Although the study shows high prevalence of misuse of available opioids, the mechanisms and factors for diversion and misuse remain majorly unexplored.

The UNODC review [103] reports that weak narcotic analgesics are widely available OTC throughout the South Asia region, particularly in Afghanistan, Pakistan and India [34,35]. The report also states that in the past 15 years, a decline in use of natural opiates in South Asia has been accompanied by an increase in pharmaceutical opioid misuse and an increasing use of injectable opioids, particularly in Bangladesh, India, Nepal and Pakistan. It has been suggested that the higher purity and lower cost of buprenorphine compared with diamorphine (heroin) contributed to this shift [35,42].

1.2.B.5.g Use of tramadol in LMICs

1.2.B.5.g.i *The prescription use of tramadol in LMICs*

A 2017 study [104] of pain specialists from seven countries in Southeast Asia including Pakistan reported that due to the non-availability of morphine and other strong opioids, prescribers in LMICs prescribe tramadol and it is widely used to treat moderate to severe pain (n=15). Other reasons for prescribing tramadol in the management of chronic pain included efficacy, safety and tolerability, ready availability, reasonable cost, multiple formulations, patient compliance and tramadol being a non-controlled prescription medicine. The respondents were against the controlled regulation of tramadol. They perceived it would reduce its medical availability and adversely affect the

quality of pain management, which is already inadequate due to lack of access to potent opioids [104].

WHO has assessed tramadol as a candidate to be put under international control several times but to not further aggravate the 'opioid access abyss', it has been kept off international regulation. Recent studies [19, 41] have been calling for reclassification of tramadol and caution in prescribing it because of fear of its misuse and diversion. The 2018 WHO critical review [105] of tramadol advised against the international scheduling of this drug; however, many HICs and UMICs have now placed national controls to stop its misuse and diversion [41]. This thus calls into question the idea that 'weak opioids' are safer. It is important to highlight that in most LMICs, tramadol is not restricted as a controlled medicine, which makes it susceptible to overuse/misuse and self-medication [104].

1.2.B.5.g.ii Tramadol misuse

Tramadol is prescribed as a pain medication but because of its stimulant effects it can allow people to feel high (elevated) while taking dangerously high doses. The literature review identified that there is a 'tramadol misuse crisis' that has significantly emerged in LMICs, which is now briefly presented below.

The UNODC reports 2017 [102] and 2021 [103] both state that in West, Central and North Africa, Asia and the Middle East tramadol has emerged as a major opioid of concern. The reports state that tramadol is in high demand among African countries especially Togo, Ghana, Nigeria, Mauritius, Libya and Egypt. In Nigeria, tramadol misuse was reported to have a prevalence of approximately 54.4% and over 91% of those who used it reported to have obtained it without a prescription [102, 103].

A 2021 study from Ghana [106] also explored the misuse of tramadol and a cross-sectional survey of 420 people showed that 77.6% of the respondents' used tramadol while 83.9% of the participants were taking at least one more substance or drug of abuse. The major reasons for opioids misuse stated in this study were the increased mental acuity as well as enhanced sexual experience people experienced while taking this medication. In most LMICs, tramadol is unregulated and remains readily available in pharmacies, medicine shops and the black market and can be easily acquired without a prescription [107].

1.2.B.5.h Problematic use of opioids in Pakistan

As stated previously for LMICs, there is a paucity of research studies from Pakistan providing statistics on consumption of prescription opioids for specific conditions and the misuse or the harm associated with them. The UNODC Report 2008 [108] stated that drug users from Pakistan were reported to be using illicit diamorphine (heroin) and opioids such as

morphine, codeine, pentazocine, buprenorphine, as well as benzodiazepines for non-medical purposes. A subsequent survey conducted by UNODC in 2013 [109] again showed an estimated 6.7 million people aged 15-64 years (the population was 181.7 million in 2013 [110]) to have used opioids (including all kinds of licit and illicit opioids) in the past year. Out of these, 4.25 million were considered to be suffering from OUD.

Furthermore, amongst them around 1.6 million people were reported to have misused a prescription opioid. The report mentioned because of absence of a centralized health prescription recording and management system, the classification of misuse was based only on the measurement and detection of people seeking opioid medicines from a pharmacy or a medicine retail outlet without a valid prescription [109]. Thus, this may not be a true reflection of the magnitude of the possible misuse problem.

A 2019 Pakistani study [111] reports the concerns of 350 doctors regarding the opioid use and misuse through a cross-sectional survey. Out of the total participants, 40.5% prescribed opioids for acute pain, 24.7% for CNMP and 34.8% reported they prescribed opioids for both acute pain and CNMP. Only a minority of these doctors (29%) reported screening their patients for opioid addiction. Majority (88%) of the respondents anticipated the misuse of their prescribed opioids by people. Around 74% doctors also held a belief that patients were self-medicating their pain and might be misusing opioids. Among the reasons for misuse, doctors considered addiction (54%) as the most common reason followed by the role of pharmaceutical companies (43%) and pharmacies (41%) as responsible for opioid diversion by “over-selling” these medications.

In Pakistan, after Schedule-G amendments, a prescription is needed to obtain opioids like tramadol from a community pharmacy. However a 2021 study [112] from Pakistan reported illicit sale practices of controlled Schedule-G medications in a major city of Pakistan and showed opioid medicines (including tramadol) were being dispensed without a prescription. Another study, Iqbal et al. (2020) [113] reports data from 740 people showing that tramadol is the most used opioid for CNMP conditions. This remains in congruence to the opioid global consumption data presented earlier, where tramadol was found to be the most used opioid in most LMICs.

Another phenomenon that was identified was self-medication with analgesics in Pakistan. Among the studies, self-medication with analgesics was common in general public (mostly geriatric population) [114-116] as well as students (young population) [117, 118]. As mentioned before, both groups might be vulnerable to opioid-related harm. There were no studies specifically reporting the statistics on tramadol being purchased OTC for pain management. However, in Pakistan tramadol is commonly

available/dispensed/purchased [112] as shown above and there is a possibility that people could be self-medicating with tramadol. Further studies need to investigate the precursors and impact of using tramadol without medical advice. This remains overall in congruence with the data even from HICs, where pain is one of most common conditions people buy OTC pain medicines for. However, the difference arises where people in LMICs including Pakistan can obtain prescription-only analgesics OTC and could be experiencing greater opioid-related harm as compared to HICs.

With Pakistan's health vision, policy makers are being sensitized to promote the availability and accessibility of opioids to provide effective pain relief for those who are in need. However, with the ongoing situation of diversion of pharmaceutical opioids for non-medical reasons, further research is needed to understand how and why people might be misusing opioids. The 2021 study [112] that reported the sale of opioids without prescription (above) suggests that the physical presence of pharmacists at community pharmacies/drug stores is necessary to overcome the illicit sale practices of Schedule-G medicine. But how CPs might overcome unauthorised dispensing/misuse of opioids remains unexplored in Pakistan.

The next subsection presents an overview of the role of pharmacists in medication safety.

1.2.B.6 Literature review 3: Role of pharmacists in medication safety

Every healthcare team member has an integral role in patient care. Within the context of opioid medication, the main aim is to promote the safe use of opioids and help avoid OUD as well as opioid-related harm in people with CNMP. CPs globally are among the most readily accessible healthcare providers and can be approached by the public. They offer the benefits of extended opening hours without prior appointments, availability on weekends and can be found in rural locations and small towns. Thus, CPs can provide education and counselling about opioid medicines.

This third literature review now presents an overview of the role and impact of pharmacists in patient care in HICs, LMICs and Pakistan.

As seen in the literature, optimising medication experience does not involve a linear set of principles. Any discrepancy in the pharmacy practice pathway can lead to inadequate patient care compromising optimisation of medications.

Moreover, in real life, many socio-ecological factors such as country laws and regulations, inappropriate prescribing and medication administration, inadequate patient care instructions, patient behaviour, patient related factors and inappropriate or insufficient outcome monitoring impacts and determines the pharmacy practice pathway delivered by pharmacists [94].

How much pharmacists can contribute towards improving public health remains highly dependent on the national policies, laws and regulations, and the public health agenda within that respective healthcare system. Hence, there is a need to explore the kind of services CPs are offering in HICs, LMICs and in Pakistan under the core principles of pharmaceutical care to understand their current roles in community pharmacy practice and identify (any) gaps in patient care for CNMP management with opioids.

1.2.B.6.a Role of pharmacists in HICs

In 1990, the concept of 'pharmaceutical care' was introduced by Hepler and Strand [119], which stated that "*Pharmaceutical care is aimed to identify, resolve and prevent the actual and potential drug-related problems*". The practice and role of pharmacists based on the concept of pharmaceutical care is commonly termed as pharmacy practice. Under pharmaceutical care, the most frequently used term is "pharmacist-led medication reviews" for pharmacists in HICs.

Pharmacist-led medication review (pharmacist-led MR) programmes have been commissioned in different countries under different names such as Medication Therapy Management (MTM) in the USA, MedsCheck in Canada, Enhanced Structured Medication Reviews (SMR)³ in UK, New Medicine

³ Both general practitioners and pharmacists can perform them in primary care networks (PCN's)

Service (NMS) in the England, Medicines Therapy Assessment (MTA) in New Zealand, Medication Management Review (MMR) in Jordan, NetCare in Swaziland and Clinical Medication Review (CMR) in Australia among others [120]. Table 1.6 below shows pharmacist-led MR under other names in different countries and emphasises that the concept of pharmaceutical care is versatile and is adapted by different countries according to their health systems. These services are also subjected to change: Medication Use Reviews (MURs) are no longer commissioned in the UK in community pharmacies and now Structured Medication Reviews (SMRs) are offered by pharmacists working in the general practitioner (GP) settings.

Table 1.6: Pharmacist led-MR services/ programmes adapted from Mubarak et al. [121]

Country	Nomenclature describing medication review
UK	Structured Medication Reviews (SMR), New Medicine Service (NMS), Medicine Reconciliation, Medicine Optimisation, Chronic Medication Review
USA	Medication Therapy Management, Comprehensive Medication Review, Drug Utilisation Review
Australia	Home Medication Review, Domiciliary Medication Management Reviews, Residential Medication Management Review, Medscheck
Canada	Medcheck
Switzerland	Poly Medication Check
Spain	Medication Review with Follow-Up
Netherlands	Medication Monitoring and Optimisation
New Zealand	Medicine Adherence Services, Medicine Use Review, Pharmacy Long term Conditions Services, Comprehensive Medicine Management, Medicine Therapy Assessment, Community Pharmacy Anticoagulation Management Services
Belgium	New Medicine Service
Brazil	Pharmacotherapy Follow-Ups

*UK= United Kingdom, USA= United States of America

These pharmacist-led MR programmes/services can be delivered in community pharmacies within primary care clinics, community pharmacies, hospital pharmacies or even specialised healthcare units depending upon the service. Literature review recognised the benefits of pharmacist-led MR services/ programmes within individual roles as well as within multi-disciplinary healthcare teams by identifying and resolving drug-related problems (DRPs) and improving patients' medicine use [120, 122, 123]. In the paragraphs below, I attempt to collate evidence regarding the pharmacist-led MR specific to CNMP management.

1.2.B.6.b The role of the pharmacist in CNMP management in HICs

The preliminary literature review identified many studies with different study designs such as observational cohorts, RCTs, non-randomised trials, qualitative studies and reviews reporting pharmacist-led MRs to be successful in reducing pain intensity, improved physical functioning and reported high patient satisfaction. However, due to the vast number of studies reported

from multiple countries, it is not possible to report each study's findings. In addition, I must emphasize that reporting each study findings separately might have limited clinical implications due to small effect size and nature of reported data within individual studies and clinical trials (randomised, non-randomised and observational). Therefore, in the paragraphs below I narratively present evidence only from systematic reviews and meta-analysis that focused on comprehensively synthesizing the impact of pharmacist interventions in chronic pain management in an attempt to present summated high-quality evidence.

A 2021 review [124] studied the impact of different types of pharmacist interventions on pain management either alone or as part of interdisciplinary healthcare teams from 14 studies (n=2365) out of which six were RCTs. The review found that pharmacist-led interventions reduced pain intensity. The most common intervention was pharmacist-led MRs. The role of pharmacists in the review included reviewing prescriptions, medicines assessment for adverse medication-related effects, dose appropriateness and involved checking the effectiveness of the management plan or developing a management care plan and recommending it to the physicians (for example both primary care and/or specialists) to be implemented. The impact on pain management was found to be more effective if the pharmacist reviews occurred for at least three months. Opiate stewardship provided by pharmacists showed that the opioid dose was reduced; however, mixed results were noted on the impact of the pharmacist intervention on physical functioning, anxiety, depression and QOL of patients. Only one of the studies included in the review measured the economic costs. The study reported that the pharmacist intervention added an expense as compared to the ongoing treatment, therefore policy makers developing services should carefully investigate the economic benefits of these services to the health systems [124]. It must be highlighted that these pharmacist reviews were conducted in general practices, pharmacies, specialist clinics, rehabilitation centres and hospitals and the studies are unable to isolate the effectiveness of CPs roles. A 2019 Australian narrative review [125] presented information on the role of CPs in pain management. Despite the extent of CP roles in medication reviews for other diseases in Australia, the review found very limited role of CPs in chronic pain management. The review focused on understanding the role of pharmacists in international contexts and identifying the best practices undertaken by pharmacists that can help guide the development of the role of CPs in Australia. The review reported that studies from other countries showed that pharmacist-driven chronic pain interventions undertaken in community pharmacies are beneficial in alleviating and reducing pain symptoms. The review supports the notion that CPs can substantially improve

chronic pain management and recommended to policy makers to integrate pain management roles of CPs into community pharmacy practice.

A systematic review and meta-analysis [126] published in 2014 showed the efficacy of pharmacist educational interventions in pain management. Four RCTs were included, and participants diagnosed with chronic pain associated with knee pain, arthritis and cancer were included. Pharmacists delivered a wide range of educational interventions including medication reviews. The study showed that pharmacist interventions were helpful in reducing pain as well as helping reduce medicine related adverse events and harm in more than 50% of study participants (n= 335).

Another systematic review and meta-analysis [127] published in 2014 evaluated the effectiveness of pharmacist-led MRs in chronic pain management and showed the findings from five RCTs. In three of them, the only intervention was a pharmacist MUR but in the other two RCTs the pharmacist MUR delivered a multicomponent intervention along with other healthcare team members. These pharmacists delivered interventions in different settings such as community pharmacies, general practices and pain clinics. Patients in this review had only non-cancer pain conditions/diseases. All studies showed a significant reduction in pain scores, reduced medication-related adverse effects and improved physical functioning after pharmacist intervention.

These systematic reviews and meta-analyses show that although pharmacist' interventions might be effective in improving pain management, the specific role of CPs in CNMP management needs to be further explored. Another observation from these reviews is that there were no mechanisms studied through which patients benefitted from these pharmacist interventions. Most studies assessed the effect of pharmacist interventions through mostly quantitative measures, which shows an improvement in pain. However, they may fail to capture the context behind the success and failure of interventions. For example, patients may have felt more self-assured, confident, well taken care of or trusted the pharmacists more, which could have resulted in better adherence to the pharmacist's advice that could have improved the overall efficacy of interventions. In addition, there were different interventions with different interventional focuses and included multiple contact points with pharmacists. Thus, the exact interventional mechanism causing improved pain management has not been presented in these reviews. Further studies need to explore the underlying mechanisms that can either potentiate or limit the effectiveness of pharmacist intervention strategies.

Another limitation of these reviews is that the role of pharmacists in ambulatory care has been established to be effective but the role of CPs in

CNMP management remains unexplored. None of the reviews report any studies where pharmacists were involved in pain management from LMICs. This could mean that the methodology used in these studies for screening or the inclusion/exclusion criteria did not include studies from LMICs. Alternatively, there might be no role of pharmacists reported in pain management from LMICs. With the evidence presented in previous subsection about the need for pain management and opioid misuse and diversion in LMICs, the role of pharmacists needs to be further explored in pain management with respect to opioids.

1.2.B.6.c Role of pharmacists in opioid optimisation in HICs

The opioid crisis is an international public health concern as briefly shown in previous subsection. Pharmacists are in a strategic position to promote and implement effective opioid stewardship due to both their integral role within healthcare teams and frequent interactions with patients in community pharmacies. In addition, given the potential harms associated with opioids, pharmacists might help ensure and promote safe opioid use. Below I provide a brief overview of literature showing the outcomes of pharmacist interventions in people with chronic pain or CNMP using opioids.

A 2015 study from USA [128] reported the interventions of clinical pharmacists to help reduce the epidemic of prescription opioid misuse. The intervention included a telephone risk assessment by clinical pharmacists for people prescribed opioids. The clinical pharmacists also ensured safe opioid prescribing through a monthly assessment of patient opioid medication use, aberrant behaviours and side effects. Out of the 608 eligible patients using opioids in the study population, pharmacists recommended 66 changes to prescriptions for people using long-term opioids. In terms of outcomes achieved, the quantity of opioid(s) decreased by 33.3%, opioid therapy was discontinued by 22.7% and the refill was delayed in 19.7% of the study population. Prescribers showed a high acceptance of pharmacist recommendations and 61/66 (92.5%) were implemented.

A 2019 study [129] from USA reported the evaluation of an Opioid Misuse Risk Prevention Toolkit implementation in community pharmacy settings to screen all patients receiving opioid prescriptions for OUD. Out of the total, 26% of individuals (n = 107) receiving opioid prescriptions were identified as at some risk of misuse and 30% were at risk of an accidental overdose, which showed the utility and the feasibility of the screening tool at the community pharmacy level. It should be noted that while the study focused on demonstrating the feasibility of the tool for screening people at risk of opioid misuse, it advocates the beneficial role CPs can play in reducing the OUD in people using opioids.

A 2022 scoping review [82] presents evidence from 77 studies and reports that in 92% of the included studies, opioid stewardship interventions led by either a pharmacist alone or within an interdisciplinary team improved at least one outcome measure of optimising opioid therapy. The most prominent outcomes were patient education and medication therapy adjustments. This review provides a valuable insight that pharmacists (regardless of their specialty for example CP or clinical pharmacist) can contribute significantly to healthcare teams as they are able to offer medication expertise as well as have regular access to patients.

There is also vast literature showing the role CPs have in opioid substitution therapies for people with OUD [130, 131] and the role of pharmacists in opioid stewardship activities such as deprescribing, monitoring OUD, providing patient education and promoting harm-reduction strategies [132-136]. However, the literature review identified limited evidence reporting the role of CPs in opioids optimisation as part of existing or regulated services. Thus, there is a need to critically examine the vast number of studies available and identify the interventions and activities of CPs in opioid medication optimisation within a standard set of definition of “opioid optimisation” for people using opioids for CNMP management.

1.2.B.6.d The role of pharmacists in LMICs

It must be highlighted that the role of pharmacists in patient care has been substantially developed in and reported from HICs. However, studies reporting the role of pharmacists in pharmacy practice in LMICs vary substantially across countries and settings. In addition, many LMICs either lack regularised pharmacy practice services or have it at an infancy stage. As this thesis focuses on the exploration of CPs’ role, the literature review is limited to the role of CPs in disease management and optimisation in LMICs. The paragraphs below provide an overview of the current roles and/or services delivered by CPs reported from various LMICs.

1.2.B.6.d.i Role of community pharmacists in LMICs

A 2021 study [137] demonstrates the impact of CPs on chronic disease management. The study collates evidence from LMICs regarding CP roles in hypertension, diabetes, asthma/chronic obstructive pulmonary disease (COPD) and mental health conditions management. Some of the major findings of this review are presented below.

Within African countries, a study from Ghana reported that CPs' interventions significantly improved blood pressure (BP) and improved adherence of people to their hypertensive medications. Two studies from Nigeria also showed improvement in BP control and reduced risk of cardiovascular events by involving CPs in hypertension management. In Asia, a Pakistani study reported

that pharmacist interventions⁴ improved patients' levels of knowledge about hypertension, medication adherence, BP control and health related quality of life (HrQOL). Studies from Thailand and Nepal also reported a significant reduction in BP as well as an improved patient medication adherence resulting in better patient outcomes.

Improvement in diabetes management was reported from a significant number of studies including but not limited to countries like Brazil, Iran, India, Turkey, Malaysia and Pakistan. The interventions were mostly focused on patient education and adherence to the medication regimen. The review also collated evidence regarding mental conditions and reported that CP interventions were beneficial in managing mental health conditions. A meta-analysis of six RCTs of CP interventions in patients with depression showed that a group of 887 patients (using antidepressants for the first time or previously prescribed antidepressants) saw 64% of its patients demonstrating a significant improvement in medication adherence [137].

The most highlighted role of CPs from LMICs is their role in antimicrobial stewardship (AMS) programmes to avoid antimicrobial resistance. There are many studies of different designs advocating for the development of these pharmacist roles. These studies included narrative reviews [138, 139], scoping reviews [140], systematic reviews [141] and cohort studies [142], and signify the importance of CPs adherence in community pharmacy to regulatory requirements for antibiotic misuse and patient counselling can significantly improve the use of antibiotics in LMICs.

The studies above support that CPs in LMICs might be involved in patient care and their role in chronic disease management as well as medication optimisation should be further explored. It is important to highlight that although these studies were conducted in other LMICs, they might provide some insight into CP capabilities in patient care (none found in CNMP management, or opioid medications). Differences in the healthcare systems makes it hard to extrapolate their findings to Pakistan, therefore community pharmacy practice services need to be explored within literature relating to Pakistan.

1.2.B.6.d.ii Role of community pharmacists in Pakistan

Like many countries, community pharmacies are readily accessible to people in Pakistan [143] but the literature review identified that community pharmacy practice as regularised or mandatory services are almost non-existent in Pakistan [5]. Pakistan is currently shifting from a dispensing-oriented role to a more patient care-oriented role [144, 145], but the concept

⁴ Please note although the review focused on CPs, however this study when looked in detail showed the interventions given by clinical pharmacists in a hospital setting and not CPs.

of pharmaceutical care has not been taken up in the community pharmacy sector.

Many studies from Pakistan emphasized on shifting the role of CPs from medicine dispensing to patient-centred practicing [28, 144, 146-150]. But very few studies have actually assessed the practices of CPs in Pakistan and they found the quality of services/activities/interventions inadequate [146, 150]. With no mandated services, there is a paucity of literature regarding the role of CPs in medication management and medication optimisation and now I provide an overview of some of the studies that I found.

A 2011 study [151] evaluated the acceptability of a pharmaceutical care service with six components: medication management, keeping a customer medication card, providing discounts, community pharmacist consultancy, monitoring tests, and medicine home delivery. The study was conducted over two months in the largest Pakistani city of Karachi. A total of 285 patients using prescription medications participated in this study and none of them wanted to discontinue the services at the end of the study. This shows their high acceptance of CP services.

Another 2013 Pakistani study [152] reports the public perceptions about CPs and reported that 301/376 people wanted CPs to cater to their drug-related needs. To bring things into perspective, the community pharmacy practice is not even fully understood by pharmacists, and a 2017 study [27] from Pakistan reported that many CPs are not even aware of the scope and extent of extended pharmacy services.

With the recently changing landscape of pharmacy profession in Pakistan, a small number of pharmacies now have been reported to offer patient counselling services while dispensing medications and are located in the major metropolitan cities [28, 153].

With Pakistani government's agenda and vision to use pharmacists for public health improvement, preliminary patient-centred services have been launched in recent years as pilot projects in community pharmacies. These services include pharmacists as antimicrobial stewards and in anti-tuberculosis (TB) mass prevention programs [154]. It is essential to emphasize these pilot services are being tested out in urban densely populated residential and commercial areas [155-157]. A 2022 randomized, controlled, single-blind, pre-post-intervention study [158] evaluated the role of CPs in diabetes and hypertension and reported pharmacist counselling had a positive impact on blood glucose and BP management among patients suffering with both diabetes and hypertension after a six month intervention period.

The literature review found no studies from LMICs or Pakistan that have explored or presented the current or future role of CPs in optimization of

opioid therapy in people with CNMP. Therefore, the lack of these studies presents a literature gap.

1.2.B.6.e Designing need-based interventions

Many interventions and services may reach their intended outcomes during pilot studies or RCTs, however, when they are subjected to real world, they face many delivery, adoption and implementation challenges because of complexity in the real-life [159, 160]. Other studies [161, 162] also report that interventions can have several interactive and dynamic components that might require new behaviours by those delivering or receiving the intervention and may also require organisational or legislative changes. Interventions and/or services might also be impacted by socioeconomic and cultural environments and may impact the intervention reaching its intended outcomes. Thus, there is growing evidence that researchers should research the context and process of intervention delivery, and/or the implementation process along with the intervention's effectiveness. This might augment the knowledge and provide understanding to help improve the delivery of services in a way that will facilitate reaching the intended service or interventional outcomes [163, 164].

The UK Medical Research Council (MRC) framework for intervention design [157] also recommends that while designing a complex service or programme interventions, exploring the development of an intervention along with its delivery (the implementation process) should be focused to facilitate the uptake and diffusion of the intervention within real life systems. Inspired from this motivation, while exploring the role of CPs in opioid safety in Pakistan, it is important to explore and understand what kind of factors (barriers and facilitators) exist that could impact CP service delivery. Thus, knowledge of contextual determinants impacting CPs in Pakistan might help design and implement the service in a way that might create affordances to help reach the intended outcomes of the intervention.

1.3 Subchapter C: Rationale of the study/motivation of the study

This subchapter briefly summarises the major gap identified from the literature review and attempts to address them by developing specific aim and objectives.

1.3.1 Summary of the literature gap identified

My study's motivation is to explore how CPs in Pakistan might help optimise opioid therapy in people with CNMP. I conducted a focused literature review to identify how opioids are currently being used in the management of CNMP. This review helped me establish that opioids can cause serious opioid related adversity and even mortality. It is important to highlight that the literature review did not find statistics reporting on the opioid-related adversity, side effects, morbidity or mortality from LMICs or Pakistan. This could be attributed to the fact that most LMICs including Pakistan lack electronic health record systems and do not capture data electronically. So, although the literature represented a gap, the lack of electronic data did not allow designing quantitative objectives such as the incidence of opioid-related adversity in people with CNMP. But the literature review clearly help establish that people in LMICs and Pakistan might be misusing and/or using opioids unsafely. The literature review was unable to inform what factors might be contributing towards the unsafe use of opioids in Pakistan.

The second literature review identified that pharmacists in HICs have been helping with safe medication use and optimising medications for people with chronic conditions. However, specific studies related to CPs role in opioid optimisation in CNMP management were not widely reported even in HICs. Literature review also identified that CPs in HICs might be engaged in medication review services but there were no community pharmacy-based patient service in Pakistan.

These left a literature gap of what are the current factors contributing towards the unsafe use of opioids and exploring whether CPs can help overcome any of those factors and facilitate people with CNMP. If yes, what are the components of a CP opioid optimisation service tailored to Pakistan's current health system? As there are no CP services, there is also a need to explore how CP opioid service could be developed and best implemented in community pharmacies in Pakistan. These then led to an overall exploratory research question for this thesis "What can CPs do, within current context to help optimise opioids in the management of CNMP in Pakistan?"

1.3.2 Aim and objectives

Thus, to answer this question, my PhD research study aims to

“Explore the role of CPs in optimisation of opioids in people with CNMP in Pakistan”.

The research objectives (Figure 1.8) are as follows:

- Systematically explore the role of CPs in opioid optimisation in CNMP management
- Explore the current use of opioids in Pakistan and identify possible CP action(s) that may optimise the use of opioids in people with CNMP
- Explore factors that might influence the development and delivery of a CP opioid optimisation service

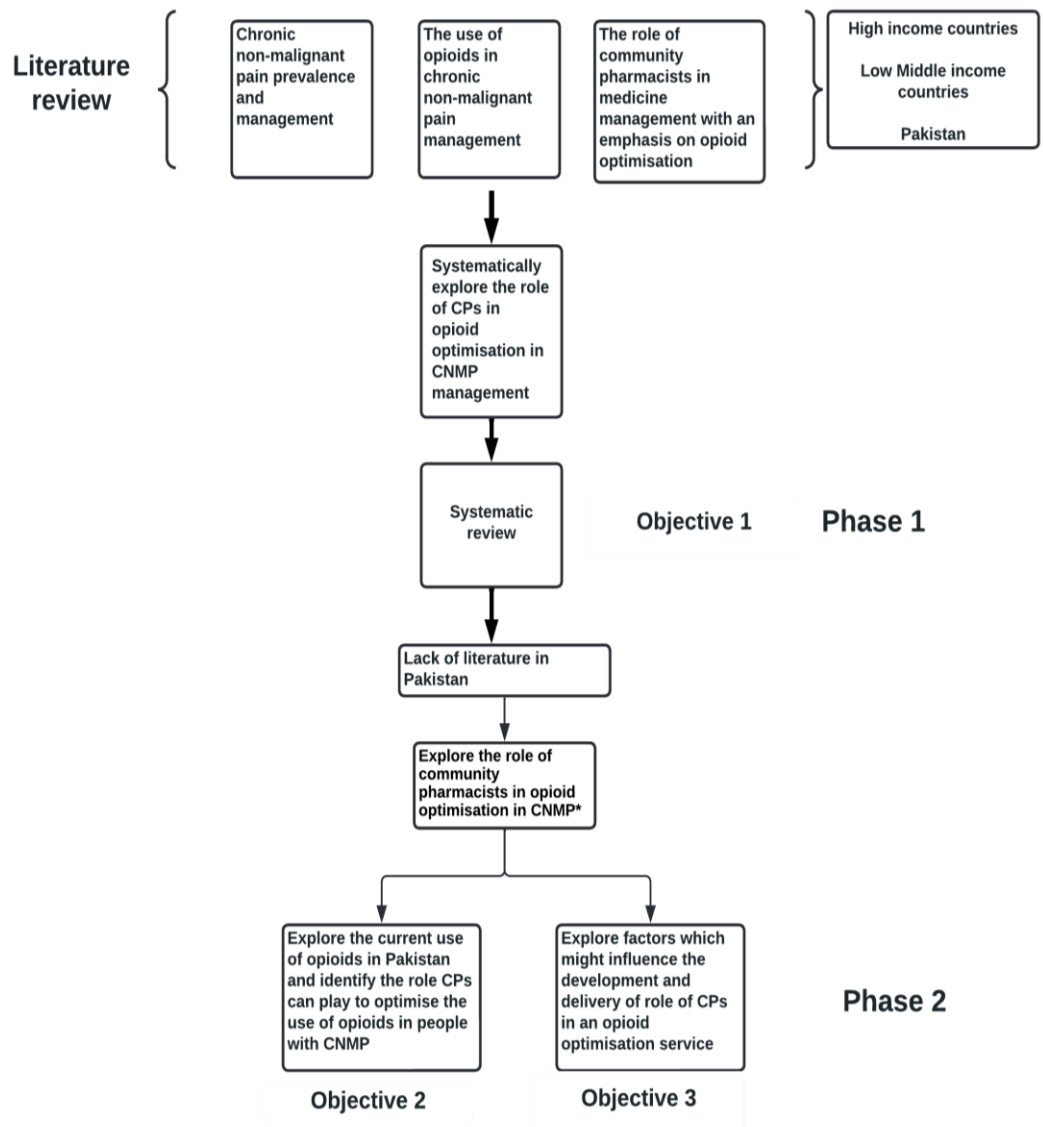


Figure 1.8: Summary of literature review, rationale of study and objectives of the study

*CNMP= chronic non-malignant pain, CPs= community pharmacists

Chapter 2: Methodology

This chapter is the second chapter of the thesis (Figure 2.1 below) and provides an overview to the methodological direction of my PhD research study.

Chapter 2 Methodology: Introduction

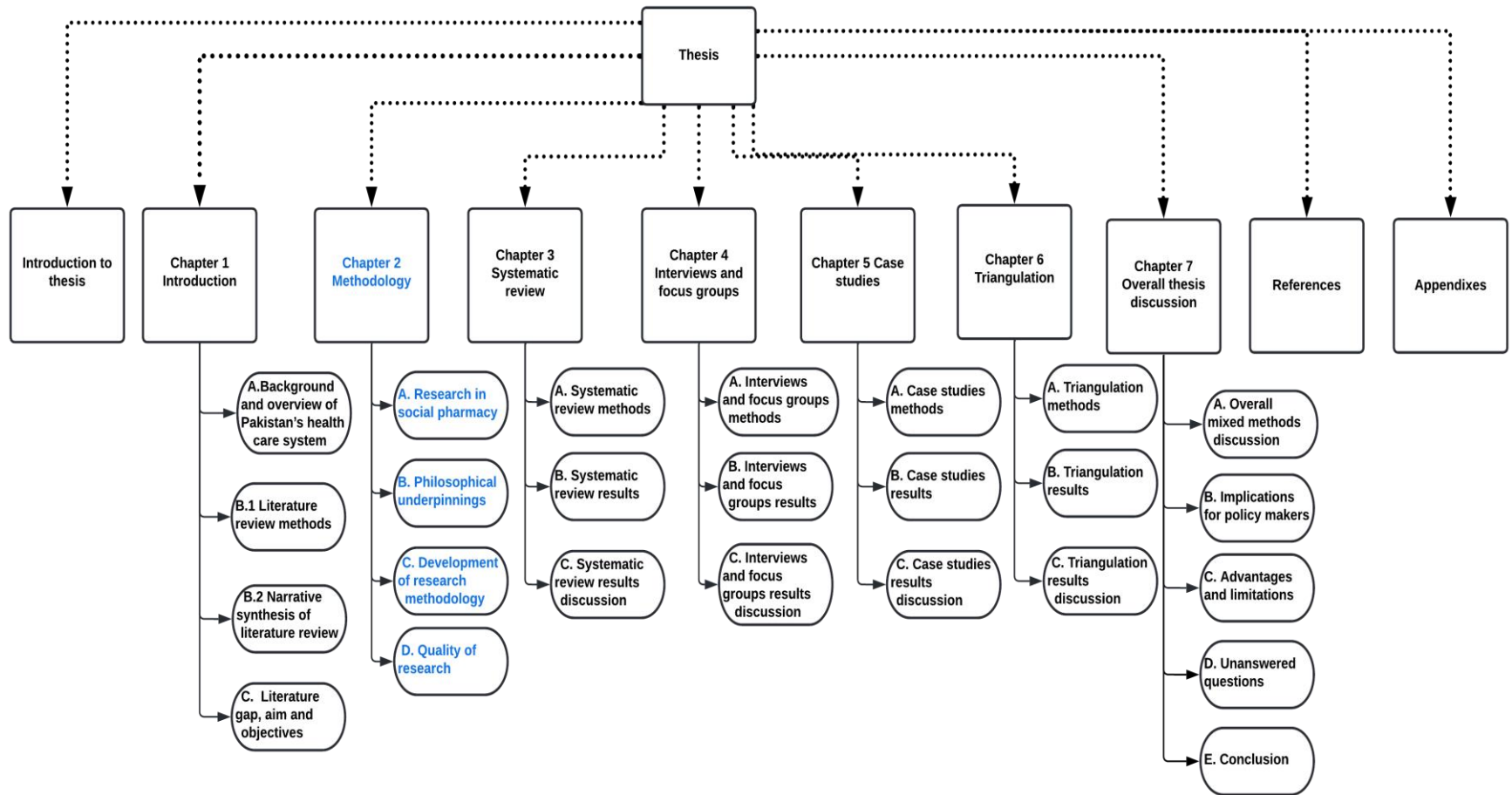


Figure 2.1: Overview of chapter 2 in thesis

Chapter 2 Methodology: Introduction

Figure 2.2 below presents an overview of the layout of this chapter.

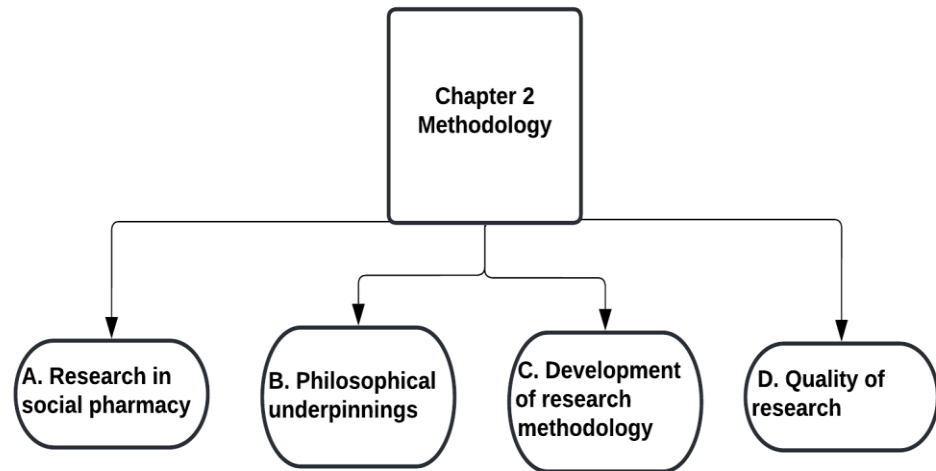


Figure 2.2: Methodology chapter overview

2.1 Subchapter A: Research in social pharmacy

2.1.1 Research

Scientific research involves “*the systematic and rigorous process of enquiry*” [165] that aims to explore, identify and explain different phenomenon, observations and theories contributing to new data generation [166]. In simple words research means the contribution to new knowledge or using existing information in an inventive way to generate new concepts and phenomena, which must be done using valid scientific and ethical principles following a logical and coherent systematic method.

2.1.2 Social pharmacy

My research project is in the area of social pharmacy, a branch of pharmacy that studies the elements and components of natural sciences within social sciences principles. Thus, research projects in social pharmacy usually have objectives that aim for a scientific element or outcome or action within the precursors and impact of intrinsic factors such as humanistic behaviours that may include medicine-related beliefs, knowledge, awareness and expectations. It may also include the influence of extrinsic factors like social settings such as the interrelationships with other people, healthcare providers as well as understanding and contextualising social realities within complex socio-political environments with varying regulations and policies [167]. With that perspective, the aim of my social pharmacy research project is to:

“Explore the role of CPs in opioid optimisation in the management of CNMP in Pakistan”

2.1.3 Conceptual framework for study

2.1.3.a Medical Research Council Framework

As my study sets out to explore a possible service development, the UK Medical Research Council (MRC) framework [168] for intervention design was used as a conceptual framework for this study as shown below in Figure 2.3. The MRC guidelines define that “intervention can be any activity, as a part of a service(s), or a new service, or a new health policy nationwide (for example,

smoking ban in public places)” [169].

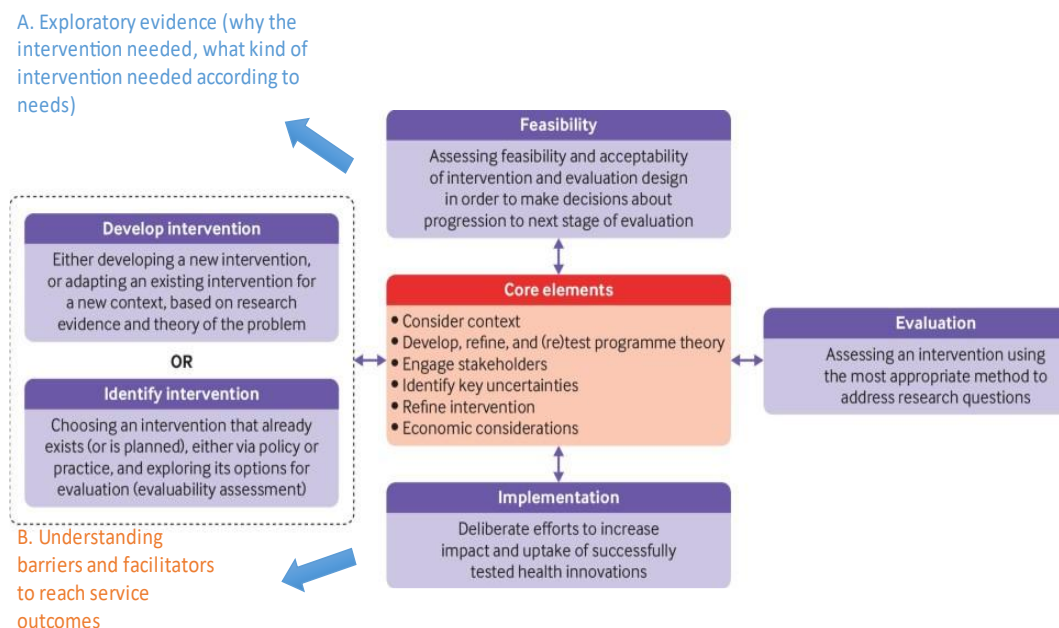


Figure 2.3: MRC framework the guiding conceptual framework of this project adapted from Skivington et al. [170]

The MRC framework highlights that research involving complex interventions has evolved and now should go beyond the usual approach of assuming that only developing an intervention and a subsequent successful pilot trial or RCT result will ensure that the intervention, when introduced in real life settings, will reach the desired outcome(s).

Several researchers [171-173] also argue that a social intervention is embedded in real systems and that existing factors and people may shape how the intervention may reach its outcomes. Thus, the complexity of an intervention should be regarded as when an intervention is delivered how it interacts with and within the system. This is supported by the MRC framework (Figure 2.3) that emphasises understanding and what will work and how should be explored along with the intervention design. This could include exploration or explanation of an intervention when applied within a specific system consisting of social entities, contextual determinants, multiple stakeholders, enacting within the influence of socio-political factors to be expected to reach its desired outcomes. This learning could help tailor the intervention to a real system in such a way that it is more likely to get its desired effects/outcomes.

2.1.3.b Theory of change

Silva et al. (2014) [174] provided a theory-driven approach to the design and evaluation of complex interventions by adapting and integrating a programmatic design and evaluation tool, Theory of Change (ToC) into the

MRC framework for complex interventions. ToC is able to provide an *'ongoing process of reflection to explore change and how it happens'* [175]. It is developed in collaboration with stakeholders and can be modified through the implementation evaluation process. It is visually represented in a graphic representation through which an intervention or strategy or service is expected to achieve its outcomes within specific contexts within the system in which implementation takes place. ToC is widely used in intervention design, implementation and evaluation. Moreover, the ToC provides explanation, modelling or sometimes helps articulate programme theories (realist research) of how an intervention or service might happen within the existing real life determinants leading to interventional outcomes [174].

2.1.3.c Approach undertaken in thesis

As shown in Figure 2.3, the MRC framework provided a conceptual framework for this study. Guided by the framework, a realist methodology was suited for this project to inform and develop initial programme theories of what will work and how. However, the preliminary literature search (conducted in the first year of PhD) revealed there was a lack of existing CP services in opioid optimisation in people with CNMP in Pakistan, other LMICs and HICs. Thus, a realist review was not possible in this case. Thus, a mixed-methods systematic review was then undertaken to explore evidence regarding the role of CPs, identifying what activities/interventions/services CPs were undertaking that could help optimise the use of opioids in the management of CNMP. The systematic review also aimed to explore the perception of stakeholders regarding the role of CPs in opioid optimisation as shown in Figure 1.8.

2.2 Subchapter B: Philosophical underpinnings informed the selection of appropriate methodology

Subchapter B gives an overview of research worldviews and justification of the chosen ontology and epistemology guiding the methodology for this project.

2.2.1 Paradigm

As mentioned previously the purpose or aim of research is to generate new knowledge [176]. However, what knowledge is and how one can achieve that knowledge remains unclear without selecting a paradigm. A paradigm *“is the perspective, or thinking or school of thought or set of shared beliefs, that informs the meaning or interpretation of research data”* [177]. In simple words, paradigm means how a researcher views the world. The principles, reflections, thoughts, beliefs of the person doing the research shapes their world view and guides them to approach, understands, interpret and analyse the world, which can guide how they will approach their research aims. A paradigm is informed by ontological and epistemological perspectives that helps suit the correct methodology.

2.2.2 Ontology and epistemology

Ontology is the philosophical study of *“the nature of being, existence, or reality (what we know)”* [178] whereas epistemology is the *“theory of knowledge (how we know)”* [178]. The philosophical paradigm and ontology influences what we can know and how we can know. There are four major philosophies of science commonly used in pharmacy and health services research: positivism, realism, interpretivism (constructivism) and pragmatism [179] that are now presented in the following paragraphs.

Simply put positivism is at one end of a spectrum that deals with objective realities and argues that only one absolute reality exists independent of *“human behaviours and mind and universal laws can be used to describe or predict it”* [180]. Opposite to this is interpretivism, which informs that there are only subjective realities, created within systems by those experiencing or those observing (as researchers) and continue to be true within their own realities [181, 182].

Realism offers a mid-approach between these two epistemological perspectives and offers that *“realists in the theory of knowledge are committed to the existence of a real world, which exists and acts independently of our knowledge or beliefs about it. However they hold that this external world is in principle knowable, and to some (discoverable) extent open to being changed on the basis of such knowledge as we are able to achieve”* [183]. Realism has many forms however for this thesis I am providing insights into critical realism.

Critical realism focuses on analysing the people, phenomenon and outcomes of interest within their societal realm [184]. This philosophical lens provides a perspective to explore how something which can be 'observed' happens and through which mechanisms. It also emphasises that there is another reality 'the real', which might be independent of human perceptions and remains different to the 'observable'. Critical realism offers that 'real' structures can cause observable events and exploring them might provide explanations to what can lead to generating the observable events. Astbury and Leeuw [177] advocate that "these 'real' events, processes or structures can be interpreted as mechanisms, which might not be directly observable however in the presence of certain contexts lead to the generation of predictable or observable events (outcomes of interest)".

The fourth paradigm of interest to this thesis is pragmatism [185] that offers the perspective that world can have outside realities (for instance single, multiple, objective, subjective), but the researcher should select the reality that can help provide sufficient knowledge regarding the research aims. Pragmatism encourages that "*truth (reality) is what is practical, meaningful and can provide answers*" [186]. In simple words pragmatism means to utilise any method that can solve the research problems or achieve the research answer regardless of being tied to a specific methodological way or lens. Thus, social pharmacy researchers' beliefs would inform what they are looking for and how they would gain that knowledge. Those in favour of positivist world view and beliefs would use objectivity as a central reality and usually use quantitative approaches to reach that objective knowledge. Positivists believe the truth can be replicated under similar circumstances, which infers generalisability and uses quantitative (numeric) methodology [187].

An interpretivist, on the other hand, chooses in-depth investigations using qualitative methods to discover deep meanings, social realities, meanings and the details of situations. Interpretivists believe that the truth or reality is subjective because humans are subjective, for example emotions are not apparently observable, yet their effect remains true and shape up the reality for those who experience it. Thus, events or phenomena involving humans require interpretation and going beyond objectivity.

Social constructivism is sometimes used interchangeably with interpretivism; however, it debatably offers a different philosophical lens that accentuates the importance of society and environment in the process of knowledge production [179]. It is usually argued that individuals (for instance 'social actors') construct social phenomenon (for instance reality) through social interactions and they are constantly subjected to revision [188]. The aim of constructivist research is to understand particular situations or phenomena,

influencing humans along with the contexts, societies and environments [180]. An interpretivist and social constructivist approach usually uses qualitative data collection methods such as interviews, focus groups and observations [179]. A realist would choose methods that might offer insights into what, how and why and maybe helpful to make causality claims. Pragmatists concentrate on logical reasoning and their focus is the research question, which becomes the most important determinant of their research philosophy to use any methodology that helps them reach meaning, truth and could help create new knowledge. Most pragmatic researchers use mixed methods to reach their research objectives [179].

2.2.3 Philosophical underpinning of my study

Being a pharmacist by background and the previous research experience I had in masters (quantitative research methodology) before starting this PhD, I was naturally more inclined to positivism. Nevertheless, quantitative methods never could sufficiently explain to me why people have different perspectives and routines about using medicines and what causes these perspectives to vary. Humans on the very core level oppose the idea of objectivity and may react differently at different times due to varying reasons that may be observable or hidden. With this view, for me any research involving human beings needs to have their humanity built (subjectivity) into the research process. I therefore reject the idea of positivism and refute the idea of closed realities when it comes to humans.

With this notion of subjectivity, my stance then moved to interpretivism to understand the subjective realities to understand the use of opioid medicines in people with CNMP and the role CPs can play to help them. A deep dive into people's experiences and their use of medicines can provide subjective experiences but fails to give an account of external influences precipitating or influencing a change in people's use of medicines, such as their social and political environments. Another possible drawback of this approach to me was that interpretivism solely focuses on people's experiences and provides a narration and explanation of a person's subjectivity. A researcher is also a person and as such I could only understand their subjectivities through my own lens and experiences. I acknowledge that I did have assumptions, especially after studying relevant literature and choosing the research areas to inform the research development. Interpretivism as a philosophical paradigm did not allow for enough flexibility to report a co-constructed experience of me (the researcher) and the people using opioids. The last reason for moving away from interpretivism was the MRC conceptual framework, which calls for understanding the development of interventions according to the real world they are delivered in. Merely reporting observed

phenomenon and subjective experiences of people using opioids in CNMP management fails to consider social complexities.

As the project intended to provide new knowledge to inform policy changes for intervention design and delivery in real world settings, I arrived at social constructivism to study the influence of contexts and cultures. Social constructivism emphasises the social impact on subjectivity of participants and could help me understand the multiple realities of people along with my own understanding and co-constructing meaning out of it. An advantage of this approach to me was that that it advocates for and was accommodating of both the stakeholders' views as well as my views to inform the research findings. However, with its ontological perspective it refutes the idea that an actual truth exists and follows a strict emphasis on subjectiveness of people and numerous realities, which inherently lacks generalisability. With the idea, to not only understand the current use of opioids by people but to provide policy makers with real world strategies for the development and delivery of CP services, I moved to critical realism as a philosophical point to stay between objective reality and subjectiveness of individuals and tried to arrive to a reality that can be taken forward to produce real life changes or policy impact and to explore the development of an intervention that could work in real settings. With critical realism it is possible to identify mechanisms that are activated or deactivated within certain contexts and can lead to realistic mechanisms able to produce a change. Using a realist evaluation, informed by critical realism, has been supported by the MRC framework (2021) [168]. However as previously stated, due to lack of relevant literature realist evaluation was not possible.

Therefore, at last I arrived at a pragmatic philosophical viewpoint.

Pragmatism led me to using an exploratory qualitative research design where the aim was to explore the current use of opioids and then design a suitable intervention and understand how it will be delivered to reach intended service outcomes without being restricted by an ontological and epistemological perspective. Thus in my research project, the choice of methods, data collection and analysis of findings remain influenced by pragmatism guiding each step in the research process, from data collection to data analysis to data presentation, identifying strategies, and building visual diagrams and models that helped me reach the research aim and objectives.

2.3 Subchapter C: Research methodology

2.3.1 Research design

Creswell (2017) [189] informs that the choice of research design is influenced by research questions or aim that helps guide the design of the research as well as the methodological considerations along the project. Popular research designs in social pharmacy research include qualitative, quantitative or a combination of both [188]. A major difference between quantitative and qualitative enquiries is that the results obtained through qualitative inquiries are rarely generalisable to the wider population [190] but may be transferable to other situations and circumstances and provides deep and rich understanding of the phenomenon under study [180]. In the healthcare sector, qualitative research has gained popularity in the past two decades. Many studies in social pharmacy use qualitative methods, to inform the development, implementation or evaluation of new interventions and/or services [191, 192].

2.3.2 Research design in this thesis (qualitative)

This study was designed using exploratory qualitative methodology to understand the role of CPs in opioid optimisation. The exploratory power of qualitative methodology to explore 'why, what and how' was leveraged in this study because I wanted to investigate why stakeholders (CPs and people with CNMP) behave in particular ways while dispensing/receiving opioid medications: their beliefs and concerns regarding the management of CNMP with opioids, the current use of opioid medications, their experiences of using and obtaining opioids, stakeholders' views of CPs and perception of stakeholders about CPs in optimising the use of opioids in people with CNMP. As anticipated, pragmatism offers no clear guidance on which methodological components to choose, and this allowed me the flexibility to use the perceived best tools or methods available to answer the research questions of this project.

2.3.3 Overview of study design

2.3.3.a Selection of research methods

There are several types of data collection methods available and researchers might use research methods, concurrently or sequentially to supplement other methods (triangulation) [193]. Combining different methods adds complexity to data collection and data analysis; however, it can provide a richer and stronger evidence base that cannot be achieved by a single method [193, 194].

Popular data collection methods in social pharmacy research include document studying as desk reviews, systematic reviews, narrative reviews, (non-) participant observations, case studies, semi-structured interviews and focus groups [194, 195]. Different researchers use different approaches and

there is no one fit to all approach. Pragmatism can thus work very well as a philosophical standpoint in qualitative research.

2.3.3.b. Methods used in this study

The data in this research project was collected in two phases (Figure 1.8) via different methods:

2.3.3.b.i Phase 1: Systematic review

The first phase constituted of a mixed methods systematic review to explore the role of CPs in opioid optimisation in CNMP management in HICs and LMICs and Pakistan.

The review [196] followed the 27-item Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [197] that evaluate healthcare interventions in conducting the systematic review. The systematic review was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO)-2019 (Registration number: CRD42019154805) [198]. Please find further detailed method of phase one listed under Chapter 3, subsection A.

2.3.3.b.ii Phase 2: Exploratory qualitative methods used in this study to collect data

In the second phase, I conducted two studies to reach exploratory research objectives: firstly, a combination of interviews and focus groups and secondly non-participant observational case studies to achieve the exploratory objectives of this research. Findings from both studies in phase two were triangulated to answer the overall research aim and objectives.

Please note, each study's methods overview, justification and detailed steps undertaken have been provided at the start of chapter 4, 5 and 6 respectively. Consolidated criteria for reporting qualitative research (COREQ) guidelines has been used in this thesis to provide trustworthiness in reporting steps undertaken in studies conducted in this research [199].

2.3.4 Sampling strategy

The sample size required for qualitative research is often difficult to estimate before a research project commences [180]. Qualitative methods usually focus on selection of participants or cases whom are thought to be 'information-rich' and relevant to the topic under investigation over a random selection [180, 200].

A purposive sampling technique was used in phase two to identify and invite stakeholders and community pharmacies who were perceived to provide meaningful data as per the inclusion criteria in this research study⁵. This technique was specifically suited for my project because this sampling

⁵ Please find inclusion criteria mentioned for each study; in each study chapter respectively

approach would help recruit participants and chose pharmacies whom were perceived to be “information rich” for this project [201].

2.3.5 Stakeholder and site selection (sampling framework)

2.3.5.a Sampling framework for interviews and focus groups

2.3.5.a.i Stakeholder selection

Based on the patient care pathway for people with CNMP in Pakistan, this study included four stakeholders: policymakers involved with pharmacy policy making such as members of pharmacy council, NHSRC and DRAP; people with CNMP; CPs; and doctors with expertise in CNMP management. For example, nurses (only found in hospitals in Pakistan) were excluded because of their irrelevance to patient care in ambulatory settings such as community pharmacies.

2.3.5.a.ii Sampling framework for case studies

To choose the type of pharmacies a scoping exercise was carried out in May 2019. Based on the scoping exercise, the community pharmacies and medical stores in Pakistan were found to be broadly divided into the following categories:

- A. In the capital (only), pharmacies who always have pharmacist available
- B. In the capital (only), pharmacies who have a pharmacist only till 5pm
- C. Pharmacies located in the outskirts of big cities, smaller towns and prominent rural areas, where pharmacists remain available for two to three hours a day
- D. Pharmacies located inside hospitals, which might have (single shift pharmacist, double or 24-hours pharmacists) or might not have pharmacists
- E. Pharmacies (urban, rural locations) where there is a pharmacy license displayed but no pharmacist available
- F. Rural area medical stores that sometimes have a displayed pharmacist license but no CP present

I decided to focus on pharmacies in cities where opioid controlled dispensing laws (Schedule-G amendments) were expected to be implemented, which excluded rural areas.

2.3.5.b Selection of city for participant recruitment and case studies

Islamabad, the federal capital, was chosen to recruit participants for interviews and focus groups and also to conduct case studies as this city was perceived to have applied the Schedule-G amendments as well as had ensured presence of CPs. This was an important criterion in this study as the exploration of development of a service could only be informed by observing

CPs working in existing systems (case study observations). In addition, Islamabad is multi-cultural and expected to have representative population from all provinces. Third, Islamabad complied with the university's international travel risk assessment policies and guidelines, which helped operationalise data collection.

In addition, to search for diversity of opinions in interviews and focus groups, I selected cities and rural areas within two adjacent provinces of Punjab and KPK. I travelled to potential participant recruitment locations within a three-hour (one side) drive distance. In cities where I had physical travel restrictions based on the university risk assessment procedures, the gatekeepers helped develop connections with participants using internet and telephone and helped me invite participants for the study who were then remotely interviewed/included in focus groups.

2.3.6 Data collection field trips

This phase involved me undertaking two field trips from the UK to Pakistan to facilitate ethical approvals, piloting, participant recruitment and data collection. The first trip was from October-December 2019 (pre COVID-19), while the second trip was from September-November 2020 (post initial COVID-19 restrictions). The process involved a pre-travel risk assessment by providing an anticipated travel itinerary to the university safety officer. The first field trip was mostly responsible for ethical approvals, site selection and recruiting and conducting interviews and focus groups (study 1). The second field trip mostly involved collecting data for case studies (study 2). Every field trip was planned and conducted in accordance with the field trip rules set out by the University of Nottingham.

2.3.7 Data saturation

Data saturation can be reached when there is enough information to replicate the study or when the ability to obtain additional new information has been attained or when further coding is no longer feasible [202-204]. Other studies and researchers have discussed thematic saturation as a way of arriving at data saturation; however, there are no concrete rules to determine when thematic saturation happens and thus the decision to cease data collection depends on the researcher [180]. In my project, data saturation was perceived to have been achieved when no new information was being obtained in subsequent interviews, focus groups and case studies.

2.3.8 Data analysis

According to Silverman (2014) [176], an inductive approach means the researcher explores themes within the data without any pre-conception whereas in deductive approach, a pre-defined/determined structure or framework anticipated either from a theoretical perspective, framework or

previous research provides a coding framework, which is then used to code data. As this was an exploratory study, inductive analysis was chosen. Commonly used analytical methods include Qualitative Content Analysis, Narrative Analysis, Discourse Analysis, Thematic Analysis (TA), Grounded Theory (GT) and Interpretive Phenomenological Analysis (IPA). Coding process can be done manually or electronically using computer assisted qualitative data analysis software (CAQDAS) [188].

One of the most common analytical methods used in social pharmacy and health research is TA. TA looks for patterns related to the study phenomenon and groups them into similar categories [205]. Braun and Clarke [206] suggest three ways to do TA: a coding reliability approach, a codebook approach, and a reflexive thematic analysis (RTA) approach. RTA is considered *“a reflection of the researcher’s interpretive analysis of the data conducted at the intersection of: (1) the dataset; (2) the theoretical assumptions of the analysis and (3) the analytical skills/resources of the researcher”* [207]. In RTA, the process of coding is flexible, fluid and changes as the data analysis continues and results in interpreting new patterns of meaning than the initially developed codes. This stands in contrast to the use of structured codebooks where pre-defined themes lead to data coding. RTA usually involve developing themes after multiple cycles of data analysis. Rigor in RTA is provided through a transparent reflection of the researcher’s interaction and interpretation of the data. Instead of multiple coders developing a consensus on data coding, other researchers or team members help reflexively sense check the data in terms of asserting context and meaning from data. It is important that the positionality and interpretation of the primary coder needs to be understood and discussed with other coders/team members to understand the reflexivity of the analytical process [207].

2.3.8.a Qualitative data analysis process in my study

As the study aim and objectives were exploratory in nature, an inductive RTA was the most suitable analysis method for the obtained data. I chose RTA because Braun and Clarke’s (2019) [207] posit RTA acknowledges and supports the researcher’s interpretation of meaning (constructivism), which helps in knowledge production. As opposed to other TA methods, RTA allowed me a theoretically flexible interpretative approach that helped me identify the phenomenon, patterns and themes from within the data without applying any priori perceptions from any framework or theoretical propositions, which was best suited to my exploratory study.

Please find the detailed RTA steps undertaken in each study listed under their respective chapters (4 and 5). Please note, I used an inductive approach in data analysis and no pre-existing theories, frameworks or published literature were taken into consideration [208].

2.3.9 Data triangulation

Data triangulation means to combine or compare data from different methods, sources, and/or analytical procedures to make meaningful conclusions [188]. Triangulation thus can provide validation of the data generated. There are five types of triangulations:

1. Data triangulation (multiple stakeholders arriving at same conclusions)
2. Investigator triangulation (different coders, investigators)
3. Theory triangulation (use of experts, people not directly related to data)
4. Methodological triangulation (multiple methods, may be from different research paradigms to answer same questions)
5. Environmental triangulation (environmental factors)

2.3.9 Data triangulation methods in my study

I used methodological triangulation that involved combining the phase two results of study 1 (interviews and focus groups) with study 2 (case studies). Methodological triangulation provides greater opportunities for accurate inferences by adding an overall understanding of key constructs and increased rigour and validity by enhancing the depth of findings, especially when comparing across two or more methods [209, 210].

2.3.10 Data visualisation techniques

Data visualisation is making its way into healthcare research [211] and has been defined as “*a graphical approach to the presentation of data*” that helps present data succinctly and efficiently [211]. Ravasi (2017) [212] also suggests that visualising data might aid researchers in the coding process and see themes and subthemes more clearly. They also propose that displaying data visually can help see the interpretative processes from raw data to analytical themes and subthemes. In this study two data visualisation techniques were used; one in data triangulation and the other to develop diagrammatic models.

2.3.10.a One sheet one paper technique

This technique was used to aid the data triangulation. One sheet one paper (OSOP) data visualisation method [213] was employed in this thesis to aid data analysis. This involves putting codes, subthemes, connections, interrelationships and/or themes as applicable to the project by the researcher on one sheet. This technique helps view large amount of contextual data all together on one sheet, making it more manageable and easier to visualise.

2.3.10.b Visual process mapping

The second data visualisation technique; visual process mapping was used to develop diagrammatic models in this thesis. Visual process mapping allows the researcher the opportunity to display “*tremendous detail in a small*

space” [214]. Visual process mapping demands reflexivity in its elaboration that helps the researcher make sense of data and organise or categorise data, events, relationships or phenomena — which otherwise might not be easy to follow from textual data — by analytical assumptions based on ‘seeing’ the data and then reflexively ‘articulating’ it. The semiotic sense implies that the translation changes the meaning and the visual map is not just a mere reflection of data but has an analytical lens added to it [215]. The process of visual mapping is not a method per se but rather a methodological tool that can enhance data analysis in at least two complementary and mutually supporting qualitative data analysis strategies: categorizing and connecting [216].

Please find the detailed methodology of data triangulation and visual process mapping steps undertaken for triangulation and model development in chapter 6, sub section A.

2.4 Subchapter D: Quality of research

2.4.a Rigor and trustworthiness

Rigor in qualitative research simply means “*the quality of being thorough and accurate*” [217]. In qualitative research where there are no objective methods or measurements as in quantitative studies (positivist), presenting a detailed account enables the readers to establish quality of data [217]. Researchers need to be careful of maintaining rigor in qualitative research because these studies deal with narratives of people rather than numbers (quantitative studies) and inherently are at a risk of subjectivity. Lincoln and Guba's [181] replaced validity and reliability with the concept of “trustworthiness” to assess the rigor of qualitative methodology. Trustworthiness simply means whether the findings of research project undertaken remain trustable. Lincoln and Guba defined trustworthiness of a qualitative study “*as the naturalist's equivalent for internal validation, external validation, reliability, and objectivity, which can be achieved by credibility, authenticity, transferability, dependability, and confirmability in qualitative research*” [181]. The following paragraphs inform the “trustworthiness” of this study using the criteria laid out by Lincoln and Guba.

2.4.a.1 Credibility

Credibility as a quality tool means whether the results in this research study are an accurate interpretation of the participants' meaning. Common strategies to ensure credibility employed in qualitative research suggests persistent observations, triangulation, member checking and prolonged engagement with the data. Credibility in my research is ensured through methodological triangulation, back translation methods and the constant discussion with the research team, which helped minimise distortions and bias.

2.4.a.2 Transferability

Transferability is often a questionable area where quantitative methods of generalisability do not apply to qualitative research because of the uniqueness and subjectivity of participants. Transferability could be considered as applicability in qualitative research. The researcher provides a ‘thick description’ of the participants and the research process to enable the reader to assess whether study findings are applicable to their own setting by making a transferability judgement. Lincoln & Guba (1985) [218] state “*it is in summary, not the naturalist's task to provide an index of transferability, it is his or her responsibility to provide the data base that makes transferability judgements possible on the part of potential appliers*”. Therefore, in my study transferability is provided by providing details of steps undertaken such as, collecting data from a meaningful purposive sampling, data saturation and providing an audit trail of steps undertaken from selection of methods to the

data analysis using thick descriptions throughout the methodology section using the COREQ criteria (Appendix 11).

2.4.a.3 Dependability

Dependability is seen as the qualitative equivalent to reliability in quantitative inquiry. Extensive audit trails, supervisor involvement during the whole project to ensure conformity checks as well as the provision of raw excerpts (quotes) have been provided throughout the results as well as in appendixes to allow the reader to decide whether the interpretation of the data is dependable or not.

2.4.a.4 Confirmability

Confirmability means the preferences and viewpoints are not based on the researcher interpretation and are instead grounded in the data. However, requesting the absence of a researcher's bias may not be even possible. It is thus important to be transparent about high level of reflexivity to address the bias the researcher will undoubtedly introduce. This was achieved by acknowledging my own positionality and carefully reflecting upon it (reflexivity⁶).

To summarize, I used the following methods in congruence where possible to ensure the four concepts of trustworthiness.

- Triangulation (methods triangulation)
- Use of a native pharmacy practice bilingual expert, pilot trials, hiring of a private translation company
- Regular meetings with supervisors (research team involvement in discussion and validation)
- An account of reflexivity

2.4.b Data management

Qualitative research usually generates massive amount of data and requires an organisational plan to collect, organise, protect, store and share data. Data collected in this project was of two types: non-electronic (paper-based) and electronic.

The data management and handling for both types has been mentioned below:

2.4.b.1 Paper-based data

Paper-based data included demographic forms, study forms, consent forms, case study forms, field notes and OSOP sheets obtained during analysis. Where these forms were collected virtually, they were printed. They were all stored in physical form in a secured cabinet.

⁶ Please see section 2.4.c: Reflexivity

2.4.b.2 Electronic data

The electronic data was secured in a university-provided password-protected laptop and Microsoft OneDrive was used to store the data online. Data was backed up every 24 hours to both local and remote media in encrypted format. Copies of all the data were also held on an external hard disk as a backup. All the study data will be archived in the University of Nottingham repository by my supervisor (CA).

NVivo 12® (QSR International, Melbourne, Australia) was used as software for the storage and management of the data, and assisted me by offering great flexibility for coding through multiple cycles of data analysis. Lucid Chart (Lucid Software Inc., United States), a web-based diagramming application, was used for the diagrammatic modelling in this thesis.

2.4.c Reflexivity

Reflexivity is an account of an ongoing and continuous critical reflection of activities undertaken within a researchers bias [219]. Therefore, throughout this research study I consciously considered to acknowledge my own positionality and bias in order to avoid an impact on this project. This required me to be reflexive from the start of data collection up until the end of the study.

2.4.c.1 Influence of UK student

In an LMIC such as Pakistan, people working in or linked to foreign countries are perceived as well-accomplished and usually treated with respect.

However, using my UK connection as a means to influence people to participate in my research was carefully thought about. I purposefully hid my foreign university and country connection until the time people voluntarily agreed to speak to me about the study.

I constantly reflected that the knowledge I had gained from literature review in my first year of PhD studies should not impact the quality of communication with people or my positionality of being somehow more knowledgeable than the CPs, especially in case studies. In addition, a neutrality was maintained throughout data collection so as not to assert any subconscious power over participants that could deviate them from their natural behaviour or their natural settings. All attempts were made to dress, talk and behave as normal within Pakistani society. As I am a native Pakistani, maintaining neutrality via an outer look as well as behaviour was not an issue.

2.4.c.2 My profession

I carefully considered the information I needed to provide to participants about myself. I concluded that introducing myself as a pharmacist could impact or influence the information being shared in interviews and focus groups. I therefore purposefully introduced myself as a researcher. The flip side was also considered: pharmacists might be able to relate better with a

pharmacist and be more willing and open to share their struggles and issues. However, them knowing my profession might have led them to omit information that they believed a pharmacist would already know and thus withhold rich information. I was, therefore, careful to steer the conversation away from my own positionality and profession throughout the data collection. This was intentionally done to avoid:

- People with CNMP discussing with me their pain medications.
- Allowing CPs to share their perceptions (focus groups) or dispense opioids in a neutral environment without the fear of being judged or criticised (case studies).
- Allow policymakers to share their perceptions without being influenced by the presence of a pharmacy professional.
- Allow a safe space for doctors to share their perceptions without having to check their opinions about pharmacists in the presence of a pharmacist.
- Not to steer the interviews or focus groups in any way by questioning or probing something specific that only a pharmacist in Pakistan would know or be aware of.

Being a pharmacist, I was able to identify many activities in case studies where the staff including pharmacists would not follow official rules and regulations while dispensing opioids. However, I asserted myself to be acknowledging of the fact that instead of fixating on identifying a non-professional or illicit dispensing procedure or behaviour, I must see and observe what underlay these events or behaviours. This required me to be rational about my own perceptions of supposed meaningful interaction and allowed me to maintain my neutrality without influencing the 'interaction' in anyway. The RTA method also allowed me to see beyond what stakeholders were saying and why, and not to predict their responses or meanings in a certain way that suited the research aim. In addition, pharmacist participants were invited to take part in this study through gatekeepers to neutralise my own professional impact on recruitment and to reduce conflict of interest as previously stated.

2.4.c.3 Gender

Being a female in Pakistan forced me to consider some methodological changes to my approach for data collection versus in the UK. I considered the implication of data collection in a relatively private space and whether I would be able to talk to potential participants while maintaining my safety in enclosed spaces with male participants. Certain steps were taken to ensure my safety, such as utilising lone worker policy, conducting data collection in official hours, using public places like restaurants, university conference rooms with CCTV cameras and accompaniment by a family member to

interviews in private offices with policymakers. Many females participated in this study and although it cannot be conclusively said, it can be presumed that me being a female resulted in a fairer representation of women in this study and informs a more inclusive exploration.

2.4.c.4 Lack of awareness of qualitative research methods

Before designing this project, I was aware that qualitative research studies in Pakistan are still in infancy. Many people are unaware of interviews, focus groups and case studies as data collection methods and this could lead to refusal to participate. Anticipating this, I spent time with possible participants explaining to them the purpose of the research as well as the research method. This helped overcome their unfamiliarity with qualitative research methods.

2.4.d Ethical approvals

Ethical approval for this study was obtained from the Research and Ethics Committee School of Pharmacy University of Nottingham, UK no. 018-2019 and Research Ethics Committee Hamdard University Islamabad, Pakistan no. HU-ERC-19-400, attached in Appendix 13.

It should be highlighted data collection via interviews and focus groups (face-to-face and online) were written into the initial ethics application and no changes were needed to be made to the ethics due to the COVID-19 pandemic, which forced all focus groups and interviews to be conducted virtually.

2.4.e Participant confidentiality and consent

I considered confidentiality and consent of participants as a crucial part of this study. A summary of steps undertaken to ensure confidentiality and consent is given below:

1. Participants interviewed privately in public places with their family members nearby (safety for females).
2. For focus groups, the participants completed a separate demographic form and were assigned numbers before the focus groups, for example p1, p2. In case studies, all the pharmacy staff members were already known to each other and there was no new member that could have caused data breach.
3. Participation in this study was completely voluntary and participants could withdraw at any time before interviews, focus groups and case studies.
4. Participants were offered reimbursement for their time and travel expenses.
5. Data handling as part of this project was designed to minimise risks of raw data being available outside the research team.

Chapter 2 Methodology: Subchapter D

2.4.f Training and personal development

As this project involved me doing qualitative research for the first time, I attended multiple courses and trainings relevant to qualitative methodology (Appendix 12).

2.4.g Summary

This chapter has described general methodology used in this thesis. Detailed methodology of each phase has been provided in respective chapters further along in this thesis.

Chapter 3: Systematic review

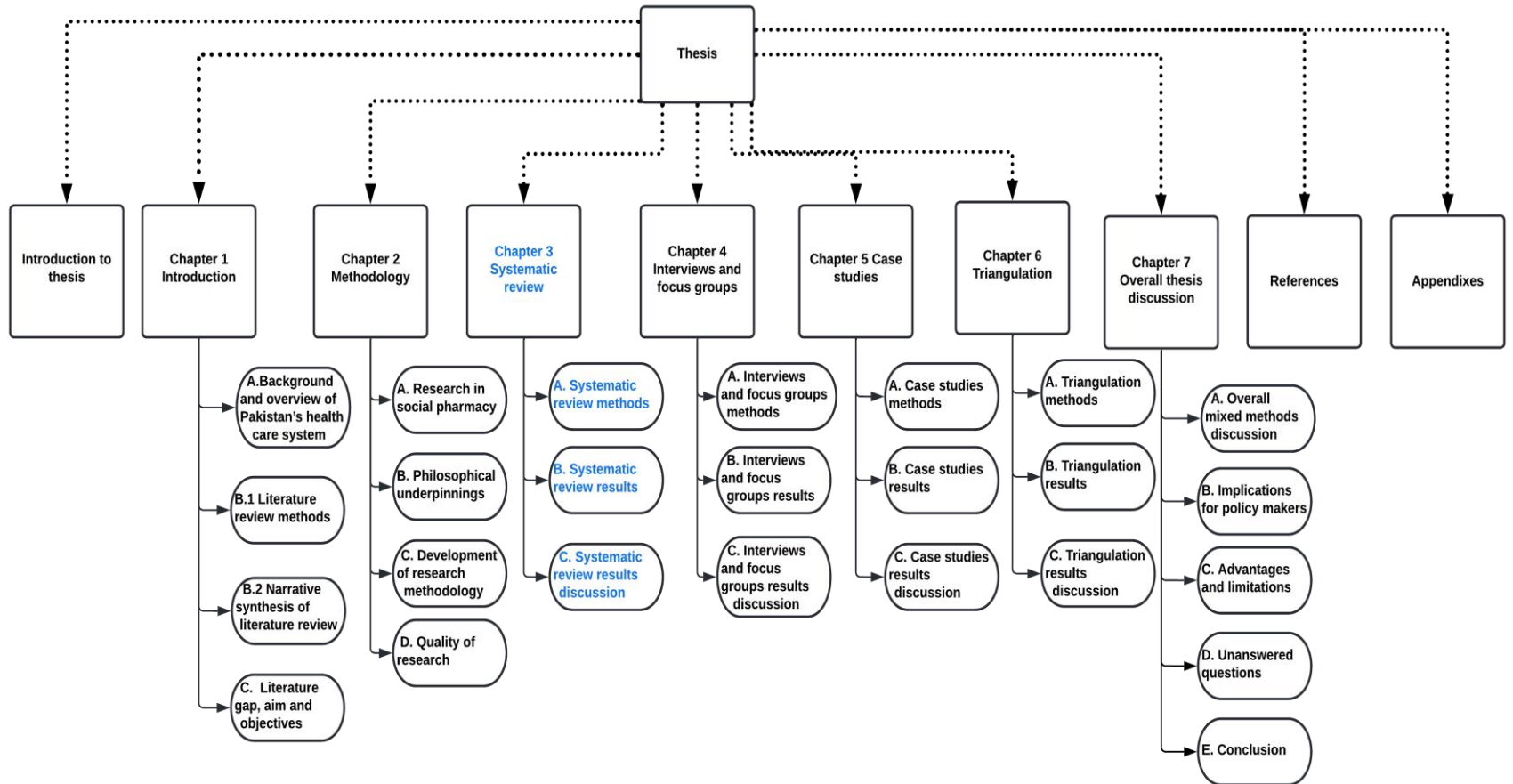


Figure 3.1: Overview of chapter 3 in thesis

Chapter 3: Systematic review

This chapter has three subsections as shown in Figure 3.1 above:

1. Methods
2. Results
3. Discussion

3.1 Subchapter A: Methods

3.1.a Eligibility criteria

This study aimed to assess all outpatient pharmaceutical care roles [119] of pharmacists in pain management of people using opioids. The review was a mixed-methods systematic review, so it included a range of study designs including both quantitative and qualitative studies and those using mixed methods. The review included a range of study designs, so no study-specific filters were applied. All the studies between January 1990 and June 2020 were included. The study selection in this review followed a Population, Intervention, Context, Outcomes (PICO) framework, which is shown below in Table 3.1.

Table 3.1: Framework for inclusion of studies in mixed-methods systematic review

PICO	Population, Intervention, Context, Outcomes
P: Population	People with pain originating from any origin except cancer pain and should be present for at least 3 months
I: Intervention	Any intervention by pharmacists, alone or in coordination with a healthcare team, which optimises opioid therapy in people with CNMP and improves patient medication experience in management of CNMP
C: Context	<p>CNMP</p> <p>Pain originating from any origin except cancer pain and should be present for at least 3 months</p> <p>Pharmacists</p> <p>May include either/or pharmacists in outpatient services, primary care services, secondary care services, community pharmacies, retail setup, clinical pharmacists, specialised pain clinics</p> <p>Settings</p> <p>All patient care settings such as outpatient clinical settings, community pharmacies and primary care services</p>
O: Outcomes:	<p>Outcome 1:</p> <p>Evaluation of pharmacist intervention that ensure people obtain the best possible outcomes while using opioid medicines in the management of CNMP</p> <p>Outcome 2:</p> <p>Perspectives and experiences of either people who received pharmacist intervention, pharmacists delivering the intervention or studies highlighting facilitators and barriers of intervention delivery by pharmacists to optimise opioid therapy in CNMP management</p>

All the studies where the people only had acute or chronic pain for less than three months or had pain conditions treated without opioids were excluded. Studies on cost reduction related to pain medicines or healthcare utilisation, inpatients, palliative care patients or cancer diagnosis, participants with issues of opioid addiction and abuse and illicit opioid use were also excluded, as were studies not written in English. Abstracts without a full-length article were excluded. Studies conducted with participants below the age of 18 years

were also excluded. Editorials, commentary, reviews, clinical practice guidelines, policy documents and professional society recommendations directing the role of pharmacists in optimising opioid therapy for people suffering from CNMP were excluded.

3.1.c Information sources (Search engines)

I did a comprehensive electronic database search in PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Psych Info, EMBASE, ISI Web of Science and Conference Proceedings and International Pharmaceutical Abstract (IPA). I also searched for similar reviews within the Cochrane Library, PROSPERO and the Joanna Briggs Institute (JBI).

3.1.d Search strategy

I first developed the preliminary search strategy using free text terms in four main domains (pharmacists, opioids, chronic pain and management/intervention) based on the systematic review’s aim. The initial search items are free text terms and medical subject headings (MeSH) headings for MEDLINE as shown in Table 3.2. Vocabulary and alternate spellings (UK and American) were adjusted and were used interchangeably across databases. Synonyms were identified by performing a basic search. An advanced search using truncation and wild card were also used to maximise the search results. Subject headings (if applicable) were used according to each respective database. Where applicable the explode option was also used. Truncation technique was also employed to broadens the search to include various word endings and spellings. After all the basic searches (having free terms and MeSH headings) were conducted, new searches were performed by intersecting using AND/OR operators as applicable.

Table 3.2 Free text terms and MeSH headings in Medline database

Pharmacist	Opioids	Chronic pain	Management/intervention
Pharmacists Community pharmacy services Patient care team Professional role Primary healthcare	Analgesics, opioid Analgesics, Opioid morphine meperidine methadone buprenorphine fentanyl hydrocodone oxycodone codeine narcotics Opiate	Chronic pain Pain measurement Pain management Chronic disease Pain Chronic non- cancer pain	Prescription drug misuse Pain management Patient compliance Counselling Community health services Patient care management Delivery of healthcare Healthcare costs Outcome and Process Assessment (Healthcare) Health services research Quality of life Health Knowledge, Attitudes, Practice Patient medication knowledge Patient Education handout Patient education Early intervention Pharmacy service hospital Education, pharmacy

			Drug monitoring Pharmaceutical services Prescription drug monitoring program Patient compliance Medication adherence Reduc* Taper Stop Terminat* Remove Substitu*
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*truncation

A Medline database search strategy has been presented in Appendix 1. The result was then filtered using language, adult age and year. The search strategy was also reviewed by the library staff at University of Nottingham. In addition, manual searches of bibliographies of all included studies were also performed and the search similar citation feature was used to enhance the search results by discovering additional relevant articles. I also did free word searches using Google Scholar and Science Watch to maximise the effort to include all published articles. At the initial outset, search results looking at the role of CPs in opioid optimisation for the management of CNMP showed no studies and only two ongoing trials were reported; therefore, the systematic review scope was further expanded and included the role of CPs in any ambulatory care settings.

3.1.e Data collection process

3.1.e.i Data screening

The searches were performed in all databases by me and reviewed independently by the research team (my supervisors CA, RK, LST). The research team's expertise is that they are academic or practicing pharmacists with expert knowledge in qualitative and quantitative methods as well pain and opioid management.

All eligible studies were exported to Endnote X8 software (San Francisco, Clarivate Analytics) [220]. Subgroups were then maintained for different databases in the Endnote software. Duplicates were removed using Endnote software. Full paper screening was done using a preliminary screening form designed for the review. The final inclusion of articles was based on mutual consensus of me and my supervisors. All included studies were given the format; "study number_ first author name_year of publication" as per PRISMA guidelines.

3.1.e.ii Data extraction

I independently extracted the data using two validated data extraction forms. The Cochrane Collaboration data extraction form [221] was used for studies including RCTs (with and without control groups), non-randomised controlled study (NRS) and observational cohort studies. The data extraction tool for qualitative studies for mixed-methods systematic review followed the National Institute for Health and Clinical Excellence (NICE) data extraction guidelines [222].

3.1.e.iii Risk of bias and applicability

For quality assessment, all articles were subjected to the risk of bias assessment using standardized tools and were discussed amongst the research team. For RCTs, I used the Risk of Bias (RoB) tool from The Cochrane Collaboration Handbook [223]. Other quantitative studies were observational cohort studies so I used the Newcastle Ottawa Cohort Scale (NOS) [224] for cross-sectional cohort studies. The risk of bias criteria was considered good, fair and poor respectively as per each scale [225, 226]. For risk of bias assessment in the qualitative studies, I used the Critical Appraisal Skills Programme (CASP) quality assessment tool [227] and the risk of bias was considered high, moderate and low [228]. As CASP lacks contextual details and has a positivist approach, I further used the Standards for Reporting Qualitative Research (SRQR) tool [229] to analyse more theoretically-rich perspectives when doing the qualitative assessment. The risk of bias across studies was assessed using the Grading of Recommendations Assessment, Development and Evaluation Working Group (GRADE) approach [196, 230].

3.1.f Synthesis of results

The data were synthesised by separately analysing qualitative and quantitative studies. The intervention was assumed to have a positive effect if there was a statistically significant decrease in any primary or secondary outcomes listed in the systematic review. Because of a lack of clinical trial studies as well as lack of overall studies, meta-analysis could not be conducted and the data were analysed descriptively. For qualitative studies, experiences and perspectives of people with CNMP, physicians, pharmacists, challenges and facilitators in the context of interventions delivered by a pharmacist were summarised from the findings or results sections of all studies [196].

3.2 Subchapter B: Results of systematic review

3.2.a Study selection (published [196])

Seven hundred and thirty papers were retrieved through database searches plus additional source searching via the search similar function. De-duplication via EndNote software resulted in 595 papers considered for preliminary screening. The titles and bibliography were screened in preliminary screening. Out of them, 300 were found to be eligible and were subjected to abstract screening. Out of 300, 47 papers were found to be eligible and were subjected to full paper secondary screening. From other sources, three papers were found eligible to be included. The final inclusion was 14 papers (12 quantitative study designs and two qualitative studies for data synthesis).

Out of the total 14 studies included in this review, one was an RCT [231], one had quasi-experimental study design [232], two were uncontrolled trials [233, 234], six were prospective cohort study designs [235-240], two were retrospective chart reviews [241, 242] and two were qualitative studies [243, 244]. The search process and screening are presented in a flowchart via PRISMA in Figure 3.2 below.

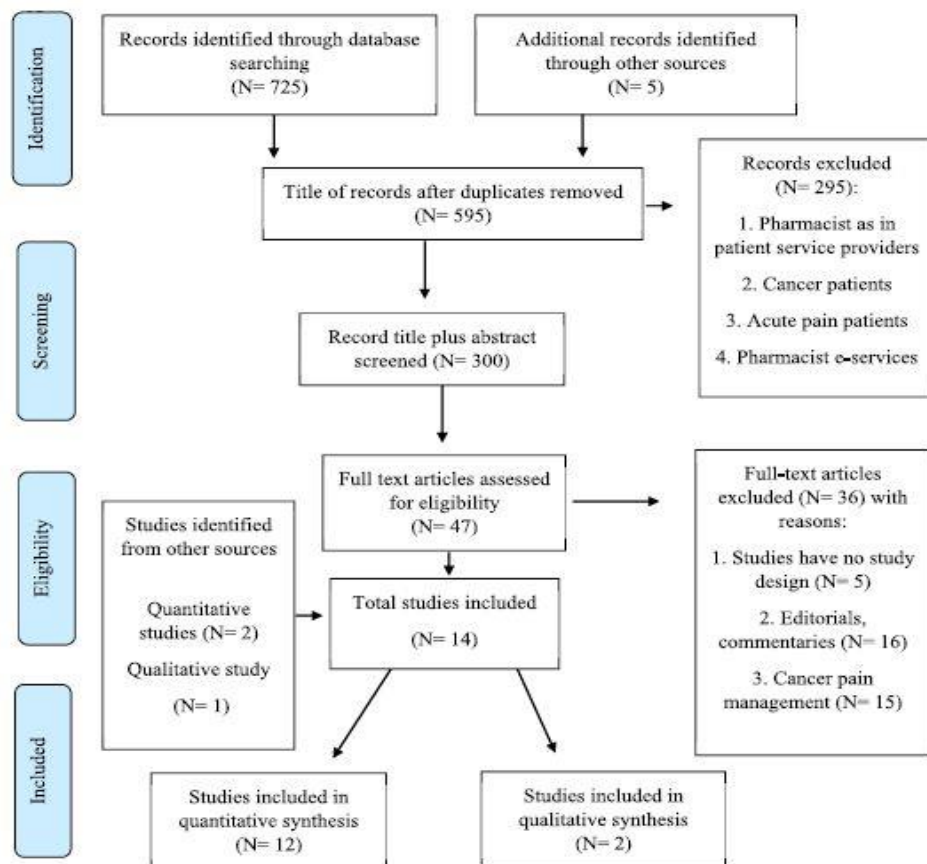


Figure 3.2: PRISMA flow diagram of systematic review

3.2.b Characteristic of studies and study participants

All of the study participants were receiving only opioid medicines except for two studies [237, 241], where some people were receiving opioids as well as NSAIDs and other pharmacological treatments for the management of chronic pain. One study [232] in this review did not mention whether the study participants with CNMP were using prescription opioids only or other analgesics as well. There were 1149 participants in total in all 12 quantitative studies. The majority of the participants in the studies were female [231, 232, 234, 236, 239-242] and mostly from white ethnic backgrounds [231-234, 238, 242]. Study characteristics such as location, invitation to participate in the studies, outcomes assessed in studies and comorbidities of participants (if any) to treat CNMP are shown in Table 3.3 below.

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Table 3.3: Study description and characteristics

Study (location)	Design	Mean Age (range in years)	Setting	Participant recruitment	Total no. of study participants Gender	Co-morbidities	Analgesics history (opioid plus if any)
1_Boren_2019 [242] (USA)	Retrospective chart review study	Age= 52.7 (40.2- 65.2)	People from Clinic outpatient clinic	Physician referral from primary care clinic to service	N= 383 (With pharmacist= 359) (Without pharmacist = 24) M= 196 F= 163	Anxiety N= 117 (32.6%) Depression N= 175 (48.7%) Insomnia N= 57 (15.9%)	None reported
2_Chelminski_2005 [233] (USA)	Uncontrolled trial	Age= 51 (27-76)	People attending an academic general medicine practice	Physician referral from primary care clinic	N= 85 M= 51 F= 34	Depression (51%)	None reported
3_Coffey_2019 [239] (USA)	Prospective cohort study	Age= 49.5 (None reported)	People attending unity Health Centre clinic	Physician referral from primary care clinic to service	N= 39 M= 18 F= 21	None reported	None reported
4_Cox_2018 [238] (USA)	Pilot study	Age= 57 (None reported)	People attending family medicine residency clinic	Self-selection from electronic medical records by pharmacists and recommendations provided	N= 45 M= 23 F= 22	Anxiety N= 27 (60%) Depression N= 25 (56%) Insomnia N= 20 (44%)	Oxycodone (49%) hydrocodone (27%) Extended-release morphine (20%) Tramadol (16%) acetaminophen (64%) Oral NSAIDS (42%),

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						Migraines N= 9 (20%) Bipolar N= 3 (7%) Other psychiatric condition N= 2 (4%)	gabapentin/pregabalin (38%), TCA (31%), Topical NSAIDS (27%)
5_Hadi_2015 [232] (UK)	Mixed-methods Quasi-experimental study	Age= 46.5 (22-86)	Nurse-pharmacist managed pain clinic (secondary care clinic)	Physician referral from primary care clinic to service Screening eligible patients at the pain clinic by the nurse or pharmacist	N= 79 M= 26 F= 53 Pain (post) score available for N= 36	Unclear	None reported
6_Tewell_2018 [235] (USA)	Prospective cohort study	None reported	Family medicine primary care clinic	Individual patient charts were reviewed by a pharmacist Eligible patients were contacted by telephone to meet a pharmacist for interview	N= 41 Gender not reported	None reported	None reported
7_Semerjian_2018 [241] (USA)	Retrospective chart review	Age= 52.2 (None reported)	Specialty pain clinic at an academic medical centre	Physician referral from secondary pain clinic to clinical pharmacist	N= 67 M= 23 F= 44	Depression, anxiety, and insomnia	Medication regimens of study participants including opioid and non-opioid analgesics

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8_Briggs_2008 [236] (UK)	Prospective cohort study	Age= 57 (27-86)	Secondary care clinic	A nurse and PCP referred patients to the NPLC	N= 65 Gender not reported	None reported	None reported
9_Bruhn_2013 [231] (UK)	Exploratory RCT	Age= 65 (None reported)	6 primary care clinics	Screened against eligibility by computerised search and then reviewed by PCP Eligible patients were sent an invitation pack (letter, information sheet, consent form) by practice staff	N= 193 M= 73 F= 120	Excluded patients with mental problems	None reported
10_McDermott_2005 [237] (UK)	Prospective cohort study	Two age groups: Age= 72 (29-64) Age= 68 (65-94)	Primary care clinic	Potential participants were sent: an information sheet describing the study; a form seeking signed consent to the three different parts of the study	N= 140 M= 53 F= 87	None reported	The most common prescription medicines used were paracetamol plus dextropropoxyphene, paracetamol plus dihydrocodeine, tramadol, paracetamol plus codeine, diclofenac, rofecoxib and topical NSAIDs
11_Lagisetty_2020 [234] (USA)	Pilot study	Age= 55.8 (None reported)	2 primary care clinics	All eligible candidates were mailed an introduction letter, an outline of the study and contact	N= 47 M= 21 F= 26	90% of patients had moderate to severe disability due to pain	Nondrug pain therapies N= 7 (15%) Opiates N= 42 (89%) Gabapentinoids N= 22 (47%)

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				<p>information</p> <p>Most eligible participants were recruited in person by the research team by identifying upcoming visits</p> <p>Referral by Primary care physicians were phoned to schedule an appointment</p>			<p>TCA and/or SNRI N= 15 (32%)</p> <p>Adjuvant therapies N= 27 (57%)</p> <p>Buprenorphine N= 9 (19%)</p> <p>Other N= 5 (11%)</p> <p>Naloxone prescribed or recommended N= 7 (15%)</p>
12_Tilli_2020 [240] (Canada)	Prospective cohort study	<p>Age (control)= 60 (None reported)</p> <p>Age (Intervention)= 57 (None reported)</p>	<p>Three primary care clinics</p> <p>(One was control)</p>	<p>All participants after EMR review and then screened manually by PI if fulfilled inclusion criteria</p>	<p>N= 35 (intervention) M= 11 F= 24</p> <p>N= 20 (control) M= 7 F= 13</p>	<p>Psychiatric comorbidity</p> <p>Depression</p> <p>Anxiety</p> <p>Substance use disorder</p> <p>Post-traumatic stress disorder or history of trauma</p> <p>Bipolar disorder or schizophrenia</p>	<p>None reported</p>

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13_Hartung_2017 [243] (USA)	Exploratory study	Age pharmacists = 39 (26-57) Age patients= 60.1 (30-77)	Urban and rural Pharmacists urban (47%) rural (26%) Patients urban (29%) rural (71%)	Purposive sampling via invitation using emails and flyers	Pharmacists N= 19 M= 8 F= 11 Patients N= 18 M= 6 F= 12	None reported	Patients using prescription opioids like oxycodone, hydrocodone, morphine
14_Tabeefar_2020 [244] (Canada)	Exploratory study	Age= 46 (27-63)	Urban	Purposive sampling via invitation using emails and flyers	N= 12 M= 4 F= 8	None reported	None reported

Non-Steroidal Anti-inflammatory Drugs=NSAIDS, Tricyclic Antidepressant =TCA and/or serotonin-norepinephrine reuptake inhibitor= SNRI, Electronic Medical Record = EMR, PI= Principal investigator, M= male, F= female

3.2.c Quantitative studies data result synthesis

The major results for pharmacist interventions in outpatient clinical settings and primary care services in quantitative studies were changes in dose of opioid medicines, effect on CNMP management, opioid medicine knowledge, QOL, adherence to standard treatment guidelines, alteration in the number of prescription medicines, type of analgesic medicine and doses, number of visits for inadequate pain management or referral, patient and physician acceptance and satisfaction and decreased frequency of medication related problems (MRPs). There was no evaluation of pharmacist interventions in community pharmacy settings for optimising opioid therapy in people with CNMP in these studies.

3.2.c.i Effect of pharmacist intervention on opioid dose(s)

Five studies [234, 238-240, 242] showed that the overall opioid dose was decreased after pharmacist intervention. One study [240] also showed that with pharmacist intervention, there was a fourfold increase in the number of people with an active opioid taper; however, in the control clinic, there were no active opioid tapers. Opioid dose increased in one study [233] where 48% participants had their opioid dose increased over three months and the overall mean opioid equivalent increased (Table 3.4 below).

3.2.c.ii Effect of pharmacist intervention on chronic pain

Five studies [231-233, 236, 239] showed that pharmacist intervention was statistically significant in pain reduction. In three studies [234, 237, 238], the pharmacist intervention was not significant in decreasing the pain scores (Table 3.4 below).

3.2.c.iii Effect on opioid medicine knowledge

One study [235] reported the effect of pharmacist intervention on increasing opioid knowledge and awareness after the pharmacist education and counselling to detect opioid overdose, 83% (N= 41) participants' bought naloxone. Another study [239] also showed improved patient opioid medicine knowledge after pharmacist intervention. Lagisetty et al. [234] also showed that pharmacist intervention improved patients' knowledge about buprenorphine.

3.2.c.iv Effect on Quality of life

One study [231] used the Short Form (SF)-12 PCS/MS (Physical Component Summary and Mental Component Summary) and no significant difference was observed after pharmacist intervention. Another study [232] measuring the QOL using SF-36 also found no statistically significant differences in the mean

PCS or MCS scores but the difference within individual domains were found to be significant after pharmacist intervention (Table 3.4 below).

3.2.c.v Effect on adherence to standard treatment guidelines

Two studies [238, 242] showed overall adherence to treatment guidelines for patient safety increased after pharmacist intervention. Annual urine screening was found to increase in both studies after pharmacist intervention, as shown in Table 3.2 below. Adherence to prescription drug monitoring programs was also seen in Cox et al's study [238], where an increase was seen in performing detailed medication reviews, and in 45 people it increased from 12 people to 26 (P= .001).

3.2.c.vi Effect on prescribing medicines

Cox et al. [238] showed that the pharmacist intervention was not significant in reducing the mean number of opioid analgesics prescribed but the prescribing of non-opioid analgesics increased (P= .002). The pharmacist intervention also resulted in increased naloxone prescribing by primary care physicians to improve patient safety.

3.2.c.vii Effect on patient primary care visits

Boren et al. [242] showed that there was an increase in access to a physician due to the pharmacist's availability to review pain patients. The decrease in the number of visits by pain patients to primary care was also seen in Lagisetty et al's study [234], where the number of visits of people with CNMP decreased following the pharmacist intervention (Table 3.4 below).

3.2.c.viii Referral to secondary care

Cox et al. [238] indicated that pharmacist intervention resulted in increased referrals from primary care physicians to pain specialists and physical therapists. Briggs et al. [236] used the referral parameter in a different context as compared to Cox et al's study [238], where they showed that overall few referrals were needed and indicated ability of pharmacist–nurse clinic to manage chronic pain patients and a reduced need of further review by specialised care physicians.

3.2.c.ix Acceptance of pharmacist recommendation

Six studies [231, 232, 234, 237, 239, 240] showed high acceptance of pharmacist management plan and recommendations and reported high implementation rate by physicians for opioid medicines.

3.2.c.x Satisfaction of people with pharmacist intervention

Most of the people were satisfied with the pharmacist intervention in five studies [231, 234, 236, 239, 240]. In one study [239], majority of patients (70%, N= 39) remained overall satisfied with the pharmacist intervention,

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except they were dissatisfied with the pain relief although their pain score had improved ($P = < 0.0001$).

3.2.c.xi Medication related problems

Semerjian et al. [241] showed that more than one MRP was identified in the majority of participants visiting the pharmacists during the study duration. A total of 820 MRPs were identified by pharmacists and only 125 were referred to other primary care members showing that a clinical pharmacist was able to intervene and directly respond to the majority of MRPs arising in people using prescription opioids.

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Table 3.4: Nature of intervention, primary and secondary outcomes, follow-up, risk of bias

Study	Type of Intervention	Person measuring/ reporting outcome	Intervention delivered by	Follow-up	Primary outcomes results	Secondary outcome results	Risk of bias
1_Boren_2019 [242]	Medication reviews	Pharmacist (Part of intervention)	Multi-disciplinary team	0 to 24 months (1-20 visits)	After five visits with the pharmacist an average decrease of MED 270 mg/day was observed between initial and final visit	Annual urine toxicological screen increased from mean 54% to 84% Signed medication agreement increased from mean 27% to 67% Physician access was increased by 1197 additional visits	Fair quality ^a
2_Chelminski_2005 [233]	Medication reviews Modified or titrated a patient's pain medications Consultation with the primary care physician	Research assistant (Independent of intervention)	Multi-disciplinary team	0 and 3 months	Pain (BPI) scores improved on an average of 12 to 15% Baseline average pain (NRS-11) improved from 6.5 to 5.5 (P= 0.003)	Mean PDI score improved from 47 to 39.3 (P < 0.001) Average CESD score improved from 24.0 to 18.0 (P < 0.001) Proportion of depressed patients decreased from 79% to 54% (P= 0.003)	Poor quality ^a

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					<p>Mean daily opioid dose in MME increased from 72 mg per day to 91 mg per day</p> <p>48% of patients had their opioid dose increased over 3 months. People receiving opioid medicines increased from 93% (baseline) to 97% (follow-up)</p>		
3_Coffey_2019 [239]	<p>Educational video by student pharmacist</p> <p>Knowledge assessment</p> <p>Referral to secondary care</p> <p>1-hour direct MTM session (3-14 days later) with pharmacist</p>	Unclear	Multi-disciplinary team	0 and 12 months	<p>Average pain scores (NRS-11) decreased from 8.3 to 5.6 P= 0.0001</p> <p>Average MED decreased from 19.7 to 11.8 mg/day P= 0.001</p> <p>Overall total MEDD/ patient decreased from</p>	<p>Physician acceptance: 88% (29 of 33) of recommendations for narcotic medications were implemented</p> <p>High patient satisfaction (N= 33)</p> <p>Improved patient knowledge= Correct responses to questions were given on an average of 76% to 94%</p>	Poor quality ^a

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	plus opioid misuse risk assessment Management plan discussed with patients and sent to doctors electronically				20.5 to 18.1 mg/day P= 0.3		
4_Cox_2018 [238]	Dose calculation Retrospective medication review	unclear	Physician plus pharmacist	0 and 4 months	Average pain (1-10 scale) scores increased from 5.3 to 5.5 (P= .783) Mean MME/day decreased by 14% (P= .001) Average MMEs/day: Based on prescription directions decreased from 151 to 125 mg/day Based on number of pills	Urine drug screening increased from mean of 15 people to 27 (P= .001) Adherence to PDMP increased from 12 people to 26 (P= .001). Referrals by primary care physicians to: a. Pain specialists increased from 17 to 21 (P= .046) b. Physical therapist from 33 to 34 (P= .317) Prescribing of opioid analgesics mean= 1.6 to 1.5 (P= .219) Prescribing of non-opioid analgesics mean= 2.1 to 2.4 (P= .002) Prescribing of naloxone increased= 6 to 22 (P= .009).	Poor quality ^a

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					<p>prescribed per month: 135 to 116 mg/day</p>	<p>Total recommendations provided= 301 out of which 114 were implemented</p> <p>Most common recommendations Provided:</p> <ul style="list-style-type: none"> a. Initiate/change non-opioid analgesic therapy= 100% b. Opioid taper = 96% c. Refer the patient to a pain specialist= 93% d. Offer an outpatient naloxone prescription= 82% <p>PCP acceptance:</p> <ul style="list-style-type: none"> a. Offer an outpatient naloxone prescription= 54% b. Complete a urine drug screen= 52% c. Taper opioid therapy= 51% d. Initiate/change non-opioid analgesic therapy= 49% 	
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5_Hadi_2015 [232]	<p>Medication review by pharmacist</p> <p>Patient education by nurse</p> <p>Recommendation to primary care physicians</p> <p>Referrals to secondary care</p>	Pharmacist and nurse (part of the intervention)	Nurse and pharmacist	0 and 3 months	<p>Reduction in mean BPI pain interference= 7.1 to 6.1 (P= 0.02)</p> <p>BPI pain intensity:</p> <p>a. Worst pain= 8 to 7.5 (P= 0.02)</p> <p>b. Least pain= 5 to 4 (P= 0.12)</p> <p>c. Average pain= 7 to 6 (P = 0.02)</p> <p>CPG:</p> <p>a. Median pain intensity score= 76.66 to 73.33 (P= 0.02)</p> <p>b. Median disability score= 70 to 73.33 (P= 0.89)</p> <p>No improvement in CPG score was observed in majority of the patients= 21 (61.7%)</p>	<p>No statistically significant differences were found in the PCS overall mean scores= 28.8 to 30.8 (P= 0.15) or the MCS overall mean scores of 36.3 to 41.2 (P= 0.08)</p> <p>In individual domains scores, statistically significant improvements were found in physical role (P= 0.01), bodily pain (P= 0.01) and social functioning (SF) (P= 0.03)</p>	Poor quality ^a
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<p>6_Tewell_2018 [235]</p>	<p>Medication review by pharmacist</p> <p>Patient education</p> <p>To give Naloxone prescription</p>	<p>Unclear</p>	<p>Pharmacist</p>	<p>Follow up unclear</p>	<p>Pharmacist educated all 41 participants and 83% procured naloxone (69% of all candidates who received a prescription for the medication)</p>	<p>NA</p>	<p>Poor quality ^a</p>
<p>7_Semerjian_2018 [241]</p>	<p>Medication review</p> <p>Identification of Medication drug related problems</p> <p>Referral to secondary care</p> <p>Drug safety testing</p> <p>Patient counselling</p>	<p>Pharmacist (part of the intervention)</p>	<p>Pharmacist</p>	<p>No follow-up-chart review</p>	<p>The pharmacist was able to discontinue opioid therapy completely in 2 long-term opioid users</p> <p>Intervention:</p> <p>Dose adjustment= 84%</p> <p>Medication counselling= 47% of the time</p> <p>Non-pharmacologic counselling= 13% new</p>	<p>At least 1 MRP was identified in 98.7% of the 380 visits included in this study</p> <p>In 27.1% of visits, only one MRP was identified</p> <p>One MRP= 71.6% 2-3 MRPs= 60.5% More than 3 MRPs= 11.1%</p> <p>The mean number of MRPs per visit was 2</p> <p>Categories of MRPS:</p> <p>a. Medication refills needed= 43%</p> <p>b. Medication appropriateness/effectiveness = 18%</p> <p>c. Miscellaneous=</p>	<p>Poor quality ^a</p>

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					medication for countering side effect of ADR= 70%	17% d. Safety= 16% e. Non-adherence/patient variables= 6%	
8_Briggs_2008 [236]	Pharmacist medication review Nurse role unclear	Unclear	Nurse plus pharmacist	0 and 6 months	Average pain scores (NRS-11) improved from 8 to 6.3 (P= 0.0001)	92% of patients were either satisfied or very satisfied with their overall care Referrals by pharmacists to specialised care units= 13/120 patients	Poor quality a
9_Bruhn_2013 [231]	Prescribing arm: Pharmacist as independent prescriber and medication review Review arm: Patient medication review only and recommendation communicated to PCP Control arm- no pharmacist review only PCP	Research team by follow-up questionnaires	Physician plus pharmacist	0, 3, and 6 months	Within-arm improvement in pain (CPG) in the prescribing (P= 0.003) and review arm (P= 0.001), but not in the control arm	SF-12 PCS/MSD: PCS domain showed a statistically significant improvement in control arm (P= 0.02) and MCS domain showed statistically significant deterioration in the control arm (P= 0.002) however no significant effect was observed in the scores in both the trial arms The non-categorised HADS scores showed a statistically significant improvement within the prescribing arm for Depression (P= 0.022) and Anxiety	Poor quality b

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						(P= 0.007) only Patients who were satisfied: 39/46 (85%)	
10_McDermott_2005 [237]	Two methods: a. Pharmacist medication review (medical charts) and questionnaires, recommendations made to primary care providers b. Pharmacist medication review via medical charts and interview with the patients and recommendations made to primary care physicians	Unclear	Physician plus pharmacist	6 months	As compared to baseline, 18 people progressed to higher CPG, 29 maintained the same CPG, and 20 progressed to a lower CPG Incomplete responses to the CPG questionnaire= 14 In 81 recommendations the change in mean score for current general health was -0.06 and for current	a. Review plus questionnaires: 192 recommendations (N= 113, 85.6%) of all patients reviewed, out of which 107 (55.7%) were related directly to analgesic use Physician acceptance: Recommendations had fully been carried out in 77.0% of patients (87/113), partially completed in 8.8% (10/113), and not implemented at all in 14.2% (16/113) b. Review plus interview: 11 recommendations were made, for 9/23 individuals Physician acceptance: Recommendations had fully been carried out in 9/11 people	Good quality ^a

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					psychological health +0.04		
11_Lagisetty_2020 [245]	<p>60-minute meeting, where pharmacist reviewed pain history, medication history, response to prior medicine and risk factors</p> <p>Pharmacist discussed recommendation with the patient and if agreed by the patient the pharmacist then contacted the patient's PCP</p> <p>Pharmacist provided additional support to primary care</p>	Unclear	Physician plus pharmacist	4-month follow-up	<p>No significant improvement in reducing pain (PEG) 6.2 to 6.1 (P= 0.84)</p> <p>Mean opioid dose reduced from 36 to 29.1 mg/day (P= 0.23)</p> <p>Before intervention, the OME mean was 36.0. After intervention participants had an average opioid dose reduction of 7 OME (19%) without worsening pain (P= 0.23)</p>	<p>Improved patient knowledge about buprenorphine:</p> <p>a. Heard of buprenorphine= 22 to 30 (P= 0.021)</p> <p>b. Believe buprenorphine is used for detox and/or OUD treatment= 17 to 13 (P= 0.013)</p> <p>c. Believe buprenorphine is used to treat pain= 14 to 20 (P= 0.06)</p> <p>Pharmacist recommendation:</p> <p>a. Add or change non-opioid pain medication= 30 (64%)</p> <p>b. Switch to buprenorphine= 20 (43%)</p> <p>c. Add non-pharmacological measures= 8 (17%)</p> <p>d. Switch to other opioid formulation= 6 (13%)</p> <p>e. Pharmacist agreement with or support for current plan= 4(8%)</p>	Poor quality ^a

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	physicians with patient follow-up, education, and dose					<p>f. Opioid taper= 3 (6%) g. Refer to specialist for pain, mental health disorders, or substance use disorder= 2 (4%) Switch to buprenorphine at follow-up was 2/20</p> <p>Physicians' acceptance:</p> <p>a. Primary care physician acknowledged recommendations= 35/46 (76%) b. PCP accepted/followed at least 1 part of recommendations= 34/46 (74%)</p> <p>Decreased mean clinic visits= 10.4 to 8.9 (P= 0.06) Both stakeholders generally satisfied with intervention</p>	
12_Tilli_2020 [240]	<p>Patient identification through medical record queries</p> <p>Developing care plans</p>	Pharmacists	Physician plus pharmacist	6 months	<p>Change in pain unremarkable</p> <p>Intervention clinic= mean opioid MME decreased by</p>	<p>Physician acceptance 24/32 (75%)</p> <p>Patient acceptance rate 13/24(54%)</p>	Good quality ^a

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	<p>Discussing recommendations with physicians</p> <p>Discussing implementing recommendations</p>				<p>11%, from 50.5 to 44.7 mg/day</p> <p>Control clinic= mean opioid MME increased by 15% from 62.3 to 71.4 mg/day</p>	<p>Opioid taper increased from 14 to 66% in intervention clinic (increased four times)</p> <p>Control clinic, the active opioid tapers remained zero</p>	
13_Hartung_2017 [243]	<p>Two focus groups methods used. Face-to-face and online</p> <p>Crystallisation-immersion approach</p>	Unclear	Not applicable	Not applicable	<p>Community pharmacist role in opioid medication safety was perceived essential by stakeholders</p> <p>Both the stakeholders were unclear about the role and extent of pharmacist services in community pharmacy setup in opioid optimisation</p>	<p>Challenges and barriers:</p> <p>a. Faced by pharmacists included difficult communicating with primary care physicians, attitude of people who were prescribed high doses of opioid medicines, lack of access to patient records</p> <p>b. Faced by people included pharmacists overstepping their professional roles, time consuming, lack of awareness of pharmacist roles, uncomfortable</p>	Low quality c

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14_Tabeefar_2020 [244]	Interviews conducted via 2 methods. Face-to-face and telephone Thematic analysis approach influenced by grounded theory		Not applicable	Not applicable	Development of expanded role of pharmacists in opioid safety was perceived to be beneficial by pharmacists	Barriers included lack of training and confidence, high volume of workload, gaps in communications with Primary care physicians, inadequate monitoring, lack of patient medical information and unrealistic patient expectations about recovery from pain	Moderate quality ^c
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a= NOS scale criteria, b RoB tool of the Cochrane Collaboration Handbook, c= CASP criteria, Morphine equivalent dose = MED, Brief Pain Inventory= BPI, Medication therapy management= MTM, Morphine equivalent daily dose= MEDD, Morphine milligram equivalent = MME, Quality of Life = QOL, Hospital Anxiety and Depression Scale= HADS A and D, Medication related problems= MRPs, Chronic pain grade= CPG, milligrams diazepam equivalent= MDE, Numeric Rating Scale-11= NRS-11, Patient Satisfaction Questionnaire Short Form= PSQ-18, Pain, Enjoyment, General Activity= PEG, Chronic Pain Grade= CPG, Physical and Mental Health Composite= PCS/MCS, Randomised Controlled trial= RCT, Nurse-pharmacist led-clinic= NPLC, Quality of Life Short form= QOL SF, Prescription drug monitoring program= PDMP, Pain Disability Index= PDI, Morphine equivalent dose= MED, Oral Morphine Equivalents= OME, Pain, Enjoyment, General Activity= PEG, NA= Not applicable

3.2.d Qualitative data synthesis

Two qualitative studies were included in this systematic review. Hartung et al. [243] studied 18 people with CNMP and 19 CPs, whereas Tabeeifar et al. [244] studied nine CPs (Table 3.3) as shown above.

Hartung et al. [243] show that both the stakeholders perceived the role of pharmacists in opioid medication safety as integral. People widely accepted and were satisfied with the pharmacist role in delivering opioid medicine safety education and advice, which is consistent with the quantitative results of this systematic review [231, 236, 240]. However, the stakeholders perceived there is a lack of clarity about the role and extent to which a pharmacist can intervene to optimise prescription opioid use. People with CNMP considered that there might be ambiguity in the role of CPs because they were concerned that pharmacists sometimes overstep their job responsibilities by meddling with prescribers' clinical judgment in altering the dose or refusing opioid prescription medicines. People also considered that pharmacists discussing their medications with the primary care physicians is time consuming and felt uncomfortable and scared when they had to wait for the opioid medicines to be dispensed or refused. People also considered it unfair and unsatisfactory that the pharmacists and primary care physicians would decide on a therapeutic regimen remotely, without involving them, which resulted in confusion and mistrust in pharmacists.

CPs generally found it difficult dealing with people who were prescribed high opioid doses or were refilling their prescription before due time. Rejecting the prescription or communicating and discussing their concern with the primary care physicians was, in general, a difficult process for pharmacists.

Pharmacists also mentioned lack of access to patient records as a major barrier to optimising patients' opioid therapy according to peoples' individual needs in the community pharmacy setting. The authors provided three recommendations to utilise pharmacists to improve medication safety in people using opioids. Pharmacist access to patient medication records should be improved, new services in the community pharmacy setting should be introduced which utilises pharmacists in opioid medication safety, and education of pharmacists and prescribers on safe and effective opioid prescribing and dispensing in management of CNMP should be improved.

Tabeeifar et al. [244] also explored in depth perceptions of pharmacists about the role of community pharmacists in opioid safety in CNMP management. Similar to Hartung et al. [243] the role of pharmacists was perceived to be beneficial by the participants, by providing patient education and monitoring the appropriate use of opioids for medicine optimisation and CNMP management. However, pharmacists anticipated barriers in implementing the opioid safety roles, which included lack of training and confidence in opioid

medicine safety. According to participants opinions, other barriers that hinder the role of CPs in opioid safety is high workload, gaps in communications with primary care physicians, inadequate monitoring, lack of patient medical information, unrealistic patient expectations, inadequate access to alternative treatments for opioids and the lack of policies in utilizing all members of healthcare team.

Pharmacists in Tabeefer et al's study [244] suggested developing skills to perform opioid optimisation roles, by getting specialized training and education in opioid safety and CNMP management, which is consistent with Hartung et al. [243]. Additionally, educating people about their pain and defining the treatment outcomes as improved physical functions might also help in possible pain management and avoiding diversion and opioid overdose. The participants in the study also suggested that documenting and monitoring of opioid prescriptions should be remunerated as pharmacy services. The stakeholders expressed that clear policies and guidelines should be developed which can facilitate and motivate the pharmacists to practice their expanded roles in opioid safety and pain management. Neither study used theory to influence the study design or analysis. Both Hartung et al. [243] and Tabeefer et al.'s study [244] explored the perception of stakeholders within existing community pharmacy services delivered as part of routine service provision.

Three quantitative studies [231, 232, 234] included in this systematic review also explored stakeholders' opinion about the pharmacist intervention using qualitative methods and the extracted data is included in this section of this review. Lagisetty et al. [234] explored the primary care physicians' opinion about the intervention delivered by pharmacists via qualitative interviews. The primary care physicians expressed that the intervention delivered by the pharmacists was effective in primary care settings and easy to comprehend by both primary care physicians and people with CNMP. However, primary care physicians provided suggestions to improve the intervention, by increasing communication with patients and increased use of protocols and algorithms to simplify the intervention. The primary care physicians were also concerned that although the intervention by pharmacists was beneficial, there was shortage of specialised pharmacists in existing primary care service models. Hadi et al. [232] and Bruhn et al. [231] explored perceptions, experience and satisfaction of people with CNMP with the pharmacist intervention. The participants in both studies were mostly satisfied with the pharmacist intervention because of ample consultation time, specialised knowledge regarding opioid medicines and individual need-based assessments done by the pharmacists. Bruhn et al. [231] also assessed the stakeholders' satisfaction via interviews and primary care physicians and pharmacists were

in general satisfied with the intervention outcomes. However, some primary care physicians expressed that the interventions were of minor nature and shared some concerns about the cost effectiveness of including pharmacists in primary care.

Perception of stakeholders [231, 232, 243-245] shows that pharmacists can be beneficial in optimizing opioid use in CNMP management in outpatient care settings, primary care or community pharmacies, which resonates with the findings from the quantitative studies in this review; however, clear guidelines and trainings should be developed which can facilitate pharmacists in performing these roles.

3.2.e Risk of bias

Of the 14 studies included in this review, two studies were assessed to be good quality [237, 240], two studies were graded as fair [242, 244], whilst the remainder were categorised as poor [231-236, 238, 239, 241, 243] (Table 3.4). In most of the studies in this review, pharmacists assessed outcomes and were involved in the direct and indirect selection of participants. The assessment of outcomes was undertaken by the pharmacist as part of the intervention in four studies [232, 239, 241, 242] while in three studies [231, 233, 238] the outcome assessment was done by an independent research assistant. In the studies where the pharmacists assessed the outcomes, a risk of confirmation bias was introduced hence the actual effect of intervention might have been influenced. In the studies [234-237, 240], information about who did the outcome assessments was missing and was responsible for bias in those studies. There was no information on allocation concealment in any of the studies, neither from the team delivering the intervention nor the participants; however, Bruhn et al. [231] and McDermott et al. [237] described that participants were divided into different arms randomly. The method of allocation, however, remains unclear.

Tabeefer et al. [244] failed to provide any demographic information about participants and the criteria used to purposely sample among willing participants, which introduces bias. Overall, Tabeefer et al.'s study [244] was considered to have moderate credibility according to CASP criteria and indicates moderate quality in the SRQR assessment tool for reporting qualitative work because the authors' made efforts to neutralize their own influences and potential bias by including a non-technical neutral person, who had no background information about the study area. In Hartung et al.'s study [243], the authors failed to discuss their interpretation and presentation of their study findings. The study also lacks in author reflections and does not address any techniques to enhance the trustworthiness of data, for example no audit trail was provided and no triangulation of data with existing

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literature. Overall, the study lacks credibility using CASP criteria and indicates poor quality in the SRQR assessment tool for reporting qualitative work.

3.3 Subchapter C: Discussion of systematic review findings

3.3.a Opioid and pain outcomes

This mixed-methods systematic review integrates evidence from 14 studies where the main intervention delivered by pharmacists was medication review in people using opioid medicines for pain management. The impact of pharmacist intervention in reducing the dose of opioid medicines was considered in five studies, out of which the dose of opioids increased only in one study [233]. The increase in dose could be attributed to the fact that pharmacists were managing other comorbidities like depression, anxiety, and sleep disturbances in addition to pain, where dose of prescribed opioids can significantly increase [246]. The pharmacist intervention effect on pain was assessed in eight studies and pain improved in all except three studies [237, 238, 240]. In all the studies, the pain outcome results were self-reported by the participants; however, this is considered normal in pain studies as pain is a subjective experience [247, 248].

3.3.b Improved patient safety and patient satisfaction

This review shows that patient safety can be improved by identifying MRPs while using opioids for CNMP management by a pharmacist review [235, 243]. This is also in accordance with the findings of other studies, where the pharmacist role has been documented in improving medication safety in patients by identifying MRPs in other diseases [249-251]. Study participants in the studies in this review were overall satisfied with the education, counselling and services provided to them by the pharmacist for optimising opioid medicines in CNMP management, which is consistent with the findings of other studies in other diseases [250-256].

3.3.c Acceptance of pharmacist recommendations by other stakeholders

This systematic review provides evidence that the recommendations by pharmacists after medication review of people using prescription opioids were generally well accepted by the primary care physicians, which is also supported by the findings of other studies. Moreno et al.'s [256] study shows that primary care physicians highlighted that the contribution of clinical pharmacists are necessary, and their roles should be expanded in medication management in primary care. Karleen et al. [257] shows the primary care physicians perception about role of clinical pharmacists in opioid management, patient education, and promoting adherence to standard guidelines, which is similar to findings from this review. Study findings in this review show that pharmacists reviewing people with pain helped to reduce the number of their visits to primary care physicians. The pharmacists also successfully managed people with CNMP and the need for referral to specialised care or primary care physicians was less [249, 258].

This review highlights certain barriers perceived by stakeholders that hinder the role of pharmacists in community pharmacies in optimisation of opioids in CNMP management. These include gaps in communications with primary care physicians, inadequate monitoring due to lack of access to patient medical information, the lack of a comprehensive approach by utilizing skillset of all members of healthcare team and service remuneration, which have been found consistent with the results of a survey conducted in a UK study for developing community pharmacy services [259]. Other perceived barriers highlighted in this systematic review in different settings show that the pharmacists feel less confident due to lack of specialised education and training in CNMP management especially with opioids [260, 261]. Additionally, the primary care physicians in primary care settings perceive that while the current nature of interventions is feasible and contributes towards better patient outcomes, pharmacists should use specified protocols and algorithms to simplify the intervention. Primary care physicians also expressed their general concerns over the cost effectiveness of these interventions and sustainability due to lack of specialised pharmacists currently in primary care settings.

3.3.d Cost analysis

No study included in this review has performed a cost-benefit evaluation for the role of the pharmacist. However, Lacey et al., in this review shows that pharmacist reviewing pain patients helped in reducing the number of pain patient visits to primary care physicians, which increased their overall availability to patients with other diseases. So, the inclusion of pharmacists in primary care may be cost-effective, which is also demonstrated by other similar studies [249, 258].

3.3.e Patient involvement

It is noteworthy that the pharmacists and physicians' remote communication was a dissatisfying factor for patients, as the patients were not aware or part of the mutually agreed changes in the treatment plan. This review shows the perception of people with CNMP wanting to be involved in decisions on therapeutic regimes in order to facilitate better patient outcomes. This is similar to other studies where participants wanted to be part of the decision making for a treatment plan. So it is important that when discussing new models of care in opioid safety in CNMP management, people should be made aware and involved to improve individual health outcomes and satisfaction [256, 262-264].

3.3.f Challenges to pharmacist roles in opioid optimisation

The participants in the studies included in this review considered that providing opioid optimisation service in community pharmacies might increase workload, which is consistent with the findings of other studies in

literature [265, 266]. However, the impact of pharmacist workload on patient health outcomes and optimisation of opioids have not yet been explored. Despite the perceived barriers, the studies in this review demonstrate the possibilities, stakeholders' opinions, satisfaction, and the impact of a pharmacist review in improving patient outcomes and optimising opioid therapy in people with CNMP, which is consistent with the findings from other studies [251-253, 267, 268].

3.3.g Lack of community pharmacist mandated roles

It is interesting to note that there are many articles, editorials and commentaries [260, 264, 269-271] that suggest and recommend that pharmacists can have a promising role in reducing opioid-related harm when they encounter people with CNMP in outpatient settings and their role should be further developed. However, this review identified a lack of research studies, especially in community pharmacies. Two pilot trials are currently in progress [272, 273], that are evaluating the role of CPs in opioid safety.

3.3.h Lack of studies from LMICs and Pakistan

Overall, there is a lack of research studies and trials in the HICs and no studies in LMICs evaluating outcomes, impact and stakeholder opinions about the role of pharmacists in opioid optimisation in people with CNMP in outpatient, primary care and community pharmacy settings. The lack of studies from LMICs might be due to lack of potent opioids and patient-centred pharmacist roles in developing countries [47, 274-276]. Therefore, further research is needed to explore pharmacist roles in developing countries, which may help with the availability, controlled opioid sales and optimisation of opioid therapy in people with CNMP.

Chapter 4: Interviews and focus groups

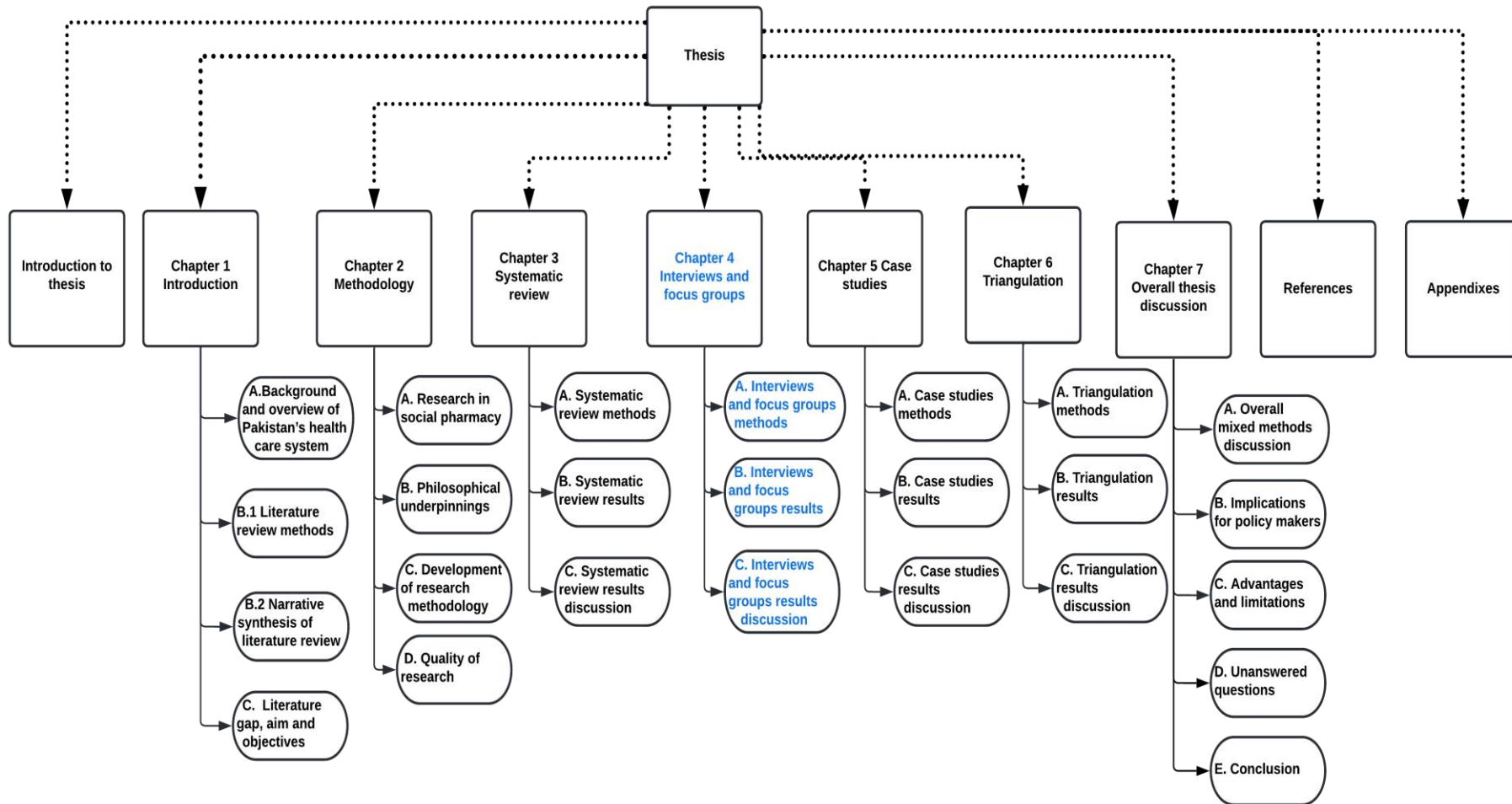


Figure 4.1: Overview of chapter 4 in thesis

The following section now provides overview of two data collection methods use in phase two, study 1:

1. Interviews

2. Focus groups

4.1.1 Interviews as data collection method

In the health field, interviews are an important data collection method and have been extensively used to collect data from stakeholders [277]. Properly conducted interviews have the potential to provide meaningful insights and in-depth perspectives that might not be achievable by any other method(s) [278]. Thus, interview was one method chosen for data collection to obtain participant in-depth responses.

Interviews are conducted using three approaches; structured, semi-structured and unstructured. Structured interviews are usually presented in open-ended questions in surveys. Unstructured interviews might have no pre-designed questions. Semi-structured interviews are also referred to as in-depth or open-ended interviews that may use an interview guide that can provide a framework or list for qualitative enquiry within a focused research area [188]. Bryman [278] states that semi-structured interviews typically have greater flexibility in terms of changing the sequence of questions or even adding new ones as the interview progresses.

So, in my PhD project, a semi-structured approach was used that allowed a certain degree of exploration and allowed for me to elicit natural responses by encouraging participants to speak at length about focused research area. This also offered a flexibility that allowed people to share their own in-depth views regarding the desired research area. In addition, as interviews are one-to-one with the researcher, this method offered participants privacy and allowed them to freely share their perspectives.

Despite the advantages of interviews, it must be highlighted that the interview method can have certain limitations. Interviews rely on and can assess or collect only what participants share they think they do, but it is quite possible that in reality their conversations reflect a socially accepted reality and they can pretend to appear more righteous, moral and upright, especially when it comes to medication use and adherence to the prescribed regime.

4.1.2 Focus groups as data collection method

Focus groups usually involve a small group of people ranging from four to 12 people discussing a focused research area, topic or a set of questions in the presence of a moderator. Focus groups emphasise on facilitating an interaction amongst the participants as compared to a one-to-one conversation with the researcher as in interviews [279]. Focus group methodology offers many strengths such as facilitating an in-depth discussion,

cohesion of participants regarding a particular study topic, bringing congruence as well as putting forward rival explanations, interpretations or experiences, helping people share different perspectives and enables knowledge exchange about the investigated topic resulting in a more meaningful and rich data [279]. This method was particularly useful in my study as it stimulated discussions, encouraged debates on the merits and demerits and helped obtain a wide range of perspectives and experiences regarding the current use of opioids and perception of people about the role of CPs in opioid optimisation.

A disadvantage of this method is dominant people in the focus group overpowering the discussion and influence them in certain ways or in a particular direction. This can make the results biased, unidirectional and not a true reflection of all members of the group [279]. By acknowledging this methodological limitation, I tried to allocate participants based on equal representation of gender, participants with varying years of experience, participants from private and public sector organisations and varying geographical regions. In addition, to avoid power asymmetries, where already known, I had taken precautions of purposively assigning participants into different focus groups to prevent junior professionals from being in the same group as their immediate bosses or seniors. Thus, with careful planning and moderation, the focus groups were smoothly carried out to avoid any dominance. Another disadvantage of focus group usually is that it requires all participants to be present at the same time and may result in people withdrawing or avoiding participating.

Focus groups were conducted with different stakeholders using a semi-structured topic guide (Appendix 2), which had open-ended questions to facilitate and prompt discussion. The size of the focus group was ideally kept between five to eight members on average and was based upon prior studies [279]. However, the actual number varied slightly in some groups because of the number of volunteers signing vs showing up on the day of the focus group.

4.1.3 Inclusion /exclusion criteria for participants

4.1.3.a Inclusion criteria

The inclusion criteria of selecting participants in phase two for study 1 (interviews and focus groups) were:

1. Ability to give informed consent.
2. Must be at least 18 years of age.
3. Volunteer to participate in focus group or interview (online or face-to-face) and/or case study.
4. Must belong to one of the following:
 - a. Pharmacist: Currently working in a community pharmacy

setting (full time or part-time), must be a licensed pharmacist in Pakistan and should be dispensing opioids at least once every week.

- b. People with CNMP: Suffering from CNMP since at least 12 months and/or using prescription opioids for at least 12 months.
- c. Doctor: Currently working in a clinical setting (full time or part-time), must be a licensed doctor in Pakistan and prescribing opioid analgesics for CNMP since at least 12 months.
- d. Policy maker: Member of professional bodies, like DRAP, Pharmacy Council of Pakistan or an employee at the pharmacy services department in the Ministry of NHSRC.

4.1.3.b Exclusion criteria

1. Below the age of 18 years.
2. People with CNMP having current diagnosis of substance use disorder/drug addiction/ getting rehabilitation for drug addiction or history of substance use disorder.

4.1.4 Data collection methods

4.1.4.a Choice of participation in different methods

All stakeholders except policy makers were given the option to join a focus group. Policy makers such as members of PCP or DRAP are geographically very widely spread to be invited to attend focus groups. It would have taken more than six hours to drive to and from the focus group site for them, which was perceived to massively impact their participation. Additionally, the lack of anonymity in face-to-face focus groups was perceived to impact the shared data to be only politically correct and could have resulted in withholding data. Hence policy makers were offered only interviews. For other stakeholders, both interviews and focus groups (face-to-face and virtual) were offered. Willingness of people to participate, better representation of people from different cultures/locations, be logistically compatible for data collection and COVID-19 related social distancing restrictions were taken in account where stakeholders opted for both methods.

For example, people with CNMP, might be reluctant or unable to travel to focus group sites due to pain and could have resulted in decreased participation if they were only offered focus groups [280]. In addition, being a native from Pakistan, I knew that people visiting from far off rural areas usually do a day's visit to the doctor office and inviting them only to focus groups could have led to decreased representation of people from diverse socio-cultural backgrounds. Again, being a native, knowledge of the socio-cultural factors led me to anticipate that females (especially from

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conservative, illiterate, rural areas) might not be allowed to attend focus groups in close proximity with other males [281]. Thus, interviews were offered and preferred in such instances to help ensure maximum chances of participation for people from diverse backgrounds and provide them with neutral and supportive environments for data sharing.

4.1.4.b Data collection tools

Semi-structured data collection tools were developed for the interviews and focus groups (Appendix 2). The data collection tools being 'semi-structured' provided the required independence for further topics to emerge freely based on participants' responses and observations [180].

The literature review conducted in the first year of PhD as well as the systematic review informed of the lack of literature around the role of CPs in opioid optimisation in Pakistan. Secondly, the development of 'quality health services' was targeted and therefore CP service was explored using the WHO quality health services definition [282] as a baseline. This definition includes six core constructs: safe, effective, patient centred, timely, efficient and equitable. Thirdly, the MRC framework guided the broad categories to be explored during a service design, for instance the need of CP opioid service and identifying and understanding the development, design and delivery of such a service. Additionally, as Pakistan lack CP services, the semi-structured data collection instruments reflected the lack of exposure to CPs and explored the perception of stakeholders regarding CPs as healthcare providers providing quality services. Four different topic guides were prepared for each stakeholder respectively and reviewed firstly internally within the research team (supervisors) (Appendix 2). As the topic guides were meant to collect data from people in Pakistan, they were translated into Urdu (national language of Pakistan) by me. The external validity of these topic guides for content validity and face validity was then done by a native speaker who is an expert of pharmacy practice field using the back translation method. In addition, the piloting of topic guides was carried out by showing the interview guides to one person from each stakeholder group (virtually). The topic guides (both versions, English and Urdu) were administered to each respective stakeholder who was asked to comment on the structure, clarity and coherence of words used in the translated guide. No changes were recommended in the Urdu or English version after translation in the topic guides, neither by the expert or respective stakeholders.

4.1.4.c Participant identification and recruitment for focus groups and interviews

I looked for potential participants from places where I had high chances of finding respective stakeholder groups as shown in Figure 4.2 below. I also contacted gatekeepers whom I identified based on my previous knowledge of being a native of Pakistan who could help me connect as well as gain access to

different stakeholders. To further increase participation and reach, the snowballing sampling technique was also applied to get to participants of interest (participants were encouraged to invite/pinpoint me to other individuals, which were from my desired population of interest) to generate meaningful data. People from each stakeholder group who showed an interest to participate in this study were screened using the eligibility criteria and then invited to participate in this study.

4.1.4.c.i Invitation

Participants were invited using flyers designed for this study via direct handover, display of flyers, snow balling and through gate keepers as shown in Figure 4.2.

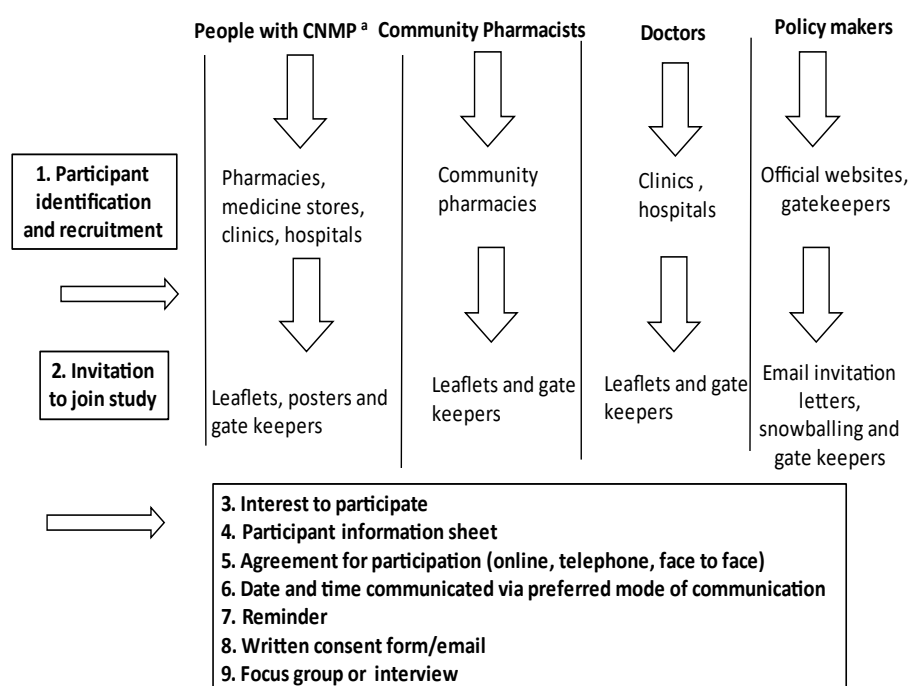


Figure 4.2: Participant identification, purposive sampling and recruitment

Policy makers were recruited via emails using a study invitation letter (Appendix 4). All content of the flyers and the invitation letters were reviewed by the research team (supervisors) and subjected to an ethics approval. A full process of recruitment is provided in Appendix 10 for each stakeholder.

4.1.4.d Data collection via interviews/focus groups

4.1.4.d.i Booking and reservations for data collection sites

University and hospital seminar rooms were pre-booked for the data collection as per the demographics of stakeholders. Where inconvenient for participants with CNMP, restaurants and cafes located closer to them were booked. For pharmacists and doctors, focus groups were conducted in doctor offices or hospital and university seminar rooms. For virtual focus groups,

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Microsoft Teams® was used. For policy makers, their offices, telephonic calls or internet calls through Zoom® were used to conduct interviews.

People, especially females, were usually accompanied by their family members when they arrived for the interview as this is considered a norm in Pakistan. This was true for me as well. However, all interviews were done making sure no third person was in hearing range. The timings of the interviews and venues were chosen carefully to ensure safety and provided cultural appropriateness to inspire participation of females. In case of focus groups, no such safety measures were taken because there were usually more than two females to ensure fair representation of participant views, but timings were still carefully chosen as a balance to facilitate working professionals, local transport times and not be considered unsafe for females (late PM times). Comfort and security of all participants was made a priority to ensure natural, confident and trusting environments to achieve a relaxed atmosphere to achieve a rich perspective of participants.

4.1.4.d.ii Equipment

The equipment used included two audio recorders, extra batteries, a notebook and pen for taking notes, printed materials including consent forms and a participant instruction sheet before the commencement of interviews and focus groups.

4.1.4.d.iii Steps undertaken during interviews and focus groups

Interviews and focus groups participants filled the consent form upon arrival. They were informed of the interview ground rules such as the option to pause or interrupt the interview at any time should the interviewee feel uncomfortable or distressed. In case of focus groups, the participants were informed that no disrespectful comments or gestures towards other participants would be tolerated. They were also informed that I might prompt participants to share their perspectives on a certain point of discussion when needed. I did not make any discreet notes during interviews and focus groups to avoid discomfort of participants or unintentionally promoting or discouraging the topic they were discussing/sharing. All focus groups were moderated by me.

4.1.4.e Steps undertaken post interviews/focus groups

The interviews/focus groups ended with participant(s) being informed that the recorders will be turned off. No further information was shared by participants after the recorders were turned off in any interview or focus group. After the interviews/focus groups finished, the participants were handed a form to collect basic demographic information. As the participants were unknown to me, a voice sample was taken after focus groups from each

participant to correlate their voice to their study number (for example, participant 1). After the participants left, I scribbled notes about the overall reflection and summary of each interview/focus group, which was used to examine if there were any new points discussed as compared to previously collected data to identify data saturation.

4.1.4.f Inconvenience allowance and transport allowance

Doctors, CPs, people with CNMP were offered an inconvenience allowance (because of researcher presence, time, discomfort, disruption in daily work). Travel expenses were reimbursed for travel to and from focus group and interview sites on the day of focus groups and interviews. The participants were offered money as well as given an option to donate the money to charity. Almost half participants either refused the inconvenience allowance or donated it.

4.1.4.g Researcher bias

My role as a researcher during data collection was substantially considered. This study involved handing participants an information sheet that allowed them to view my position as a pharmacy PhD student from a foreign university. This proved helpful in recruiting doctors, policy makers and pharmacists. However, being a foreign PhD student proved especially difficult in inspiring people with CNMP to participate in this study. The public usually view interviews as a method where (foreign) journalists collect data to defame Pakistan. All possible attempts were made and steps taken, such as showing ethical approvals as well as my student card, to satisfy the participants. Other than the methodological limitation of recruitment, it cannot be anticipated how much impact me being an international student had on the nature of data generated. It can, however, be assumed that once people understood I belonged to Pakistan and was collecting data towards the fulfilment of a PhD degree, they agreed and were more neutral, receptive and accepting of participating in this research study.

4.1.4.h Data transfer

The interview/focus groups audio files were transferred from both audio recorders to a personal password protected laptop from where the files were stored in a secure location online (One Drive) as well as manually stored on a password protected solid state drive (SSD). Every recorded audio file was deleted from the recorders each time after the data was moved.

As most people in Pakistan commonly speak a mixed language combining Urdu and English, the data needed to be translated from Urdu to English before data analysis could take place. Any statements and words spoken in

English were transcribed verbatim in the transcription, while maintaining the meaning of the sentence.

4.1.4.i Data translation and transcribing in my study

“Maintaining accuracy when representing people’s views and perspectives when using qualitative research approaches is important but challenging, particularly when the research project is conducted in one language and then analysed and synthesised in another” [282]. Each language has its own distinct form of expression of meaning. There are two main kinds of translation — form-based and meaning-based. Form-based translation attempts to follow the form of the source language whereas meaning-based translation makes every effort to communicate the meaning of the source language text in the natural form of the target language [283] while maintaining the integrity of the meaning. Meaning-based translation is commonly used when translating across languages in qualitative research.

A high quality of translation and meaning retention can be achieved by employing spot checks by bilingual experts [284], member checking (participants reading the back translated transcripts) or back translation method [285]. Many researchers, rely on back translation in cross cultural research using multiple languages as a reliable method to ensure transparency and quality of the research as shown below in Figure 4.3.

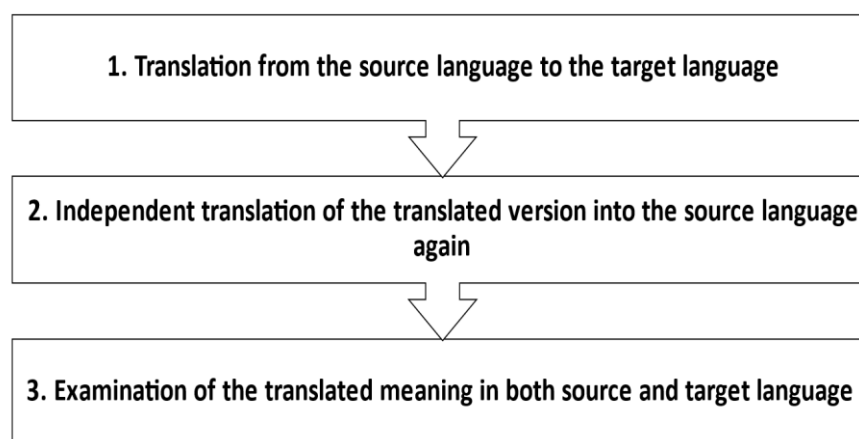


Figure 4.3: Back translation steps [283]

In my study, the purpose of translation was to replicate the message in the second language (English) while preserving its meaning. I manually translated each interview and focus group and prepared the transcripts using Microsoft Word as shown in Figure 4.4 below.

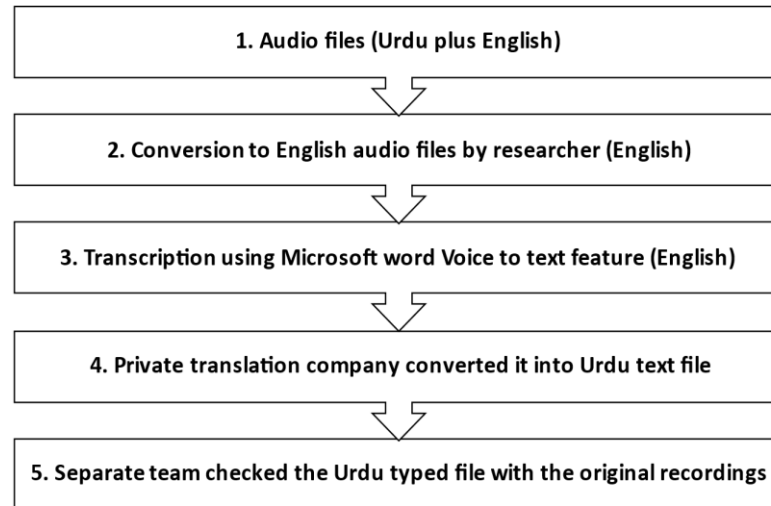


Figure 4.4: Translation and back translation overview

There is a lot of merit in researcher transcribing data themselves as it helps them connect and familiarise themselves with the data. Therefore, data transcribing coherently informed my understanding of the meaning of conversations and was the first step of my data analysis. It must be highlighted that no member checking was employed in this study. The participants were from different literacy levels and the translated transcripts were in English language and thus could not be sent to all participants. As the data was not purely in English and the supervisors do not speak Urdu thus to ensure the quality of translation, I used a private translation company Rabi translation (Nexgo services International Private Limited based in Islamabad) to back translate the transcripts to verify that the meaning remained the same across both languages. As the company is Pakistan-based, the cultural aspects, socio-political contexts, mnemonics and slangs were comprehensible to the translation company. Additionally, in Pakistan, Urdu and English (both British and American) are the two officially used languages and therefore me as well as the people in the translation company should be considered bilingual.

Out of the transcribed word document in English, around 40% were randomly selected in each stakeholder category and sent to the translation company for checking the quality of translation. Figure 4.4 shown above entails the steps undertaken during this process. No discrepancies were found or suggested during translation. The translations and transcribing were done halfway during data collection and provided an opportunity to reflect whether additional probing questions should be added in the topic guides. It also provided me with the opportunity to reflect on my data collection skills and allowed me to progressively improve my interview and focus group

moderation skills. A small excerpt of a transcribed interview has been provided in Appendix 14.

4.1.4.j Data analysis in interviews and focus groups

I followed the six-steps of RTA developed by Braun and Clarke and analysed the data for all four stakeholders obtained from interviews and focus groups together. The following paragraphs below highlights my experience of each step in RTA:

4.1.4.j.i Step 1: *Become familiar with the data*

This step was achieved in two ways. While translating and transcribing the interviews, I listened to the audio files again and again and that helped me understand the data better. Once transcribed, I made sure to go over the transcripts multiple times to familiarize myself with the data.

4.1.4.j.ii Step 2: *Generate initial codes*

This step began by sorting data systematically and organising it. This was achieved by reading the data carefully and then dividing it into significant units called codes. Codes in this study were labels, assigned to sentences or even whole paragraphs of an excerpt. I coded each portion, paragraph or even part of sentences that seemed relevant or meaningful or interesting regarding the use of opioids or role of pharmacists in all interviews and focus groups. Codes were developed, modified and revised using multiple coding cycles throughout the analytical research phase. This process persisted until all the meaningful data was assigned a code and it was organised into subthemes. All the coding was facilitated by N-Vivo 12, a CAQDAS software designed to assist with the data analysis. As part of RTA, I developed the initial codes and my supervisor (CA) checked initial coding for methodological and analytical consistency.

4.1.4.j.iii Step 3: *Search for themes*

A theme is a collection of similar or dissimilar or interconnected subthemes and codes, which offer an overarching outline about the data and/or research question. As Braun & Clarke (2006) explains, there are no hard and fast rules about what makes a theme. After the codes had been organised into subthemes emergent themes were identified. The data had many codes and subthemes but there was a conspicuous pattern of data falling into similar categories from all four stakeholder data groups and different themes were developed. This step went under multiple cycles of revisions and discussions with the entire research team (supervisors) and enabled a critical assessment of the emergent themes.

4.1.4.j.iv Step 4: Review themes (findings validation)

The process from coding to theme development followed an iterative process and was repeatedly revised. I presented my analysis to the research team (supervisors) to discuss the themes and resolve discrepancies if any. All members of the research team sense checked the themes and underlying contents and provided their feedback.

4.1.4.j.v Step 5: Define themes

After multiple cycles of revisions and discussion with the research team (supervisors) the final step was to align and group codes and subthemes into broader themes to create an in-depth coherent explanation as per research aim and objectives.

4.1.4.j.vi Step 6: Write-up

Please note all the four stakeholders' data were analysed together. Their results are presented in the next subchapter.

A diagrammatic summary of analytical processes and steps undertaken during the analysis of interviews and focus groups is shown in Figure 4.5 below.

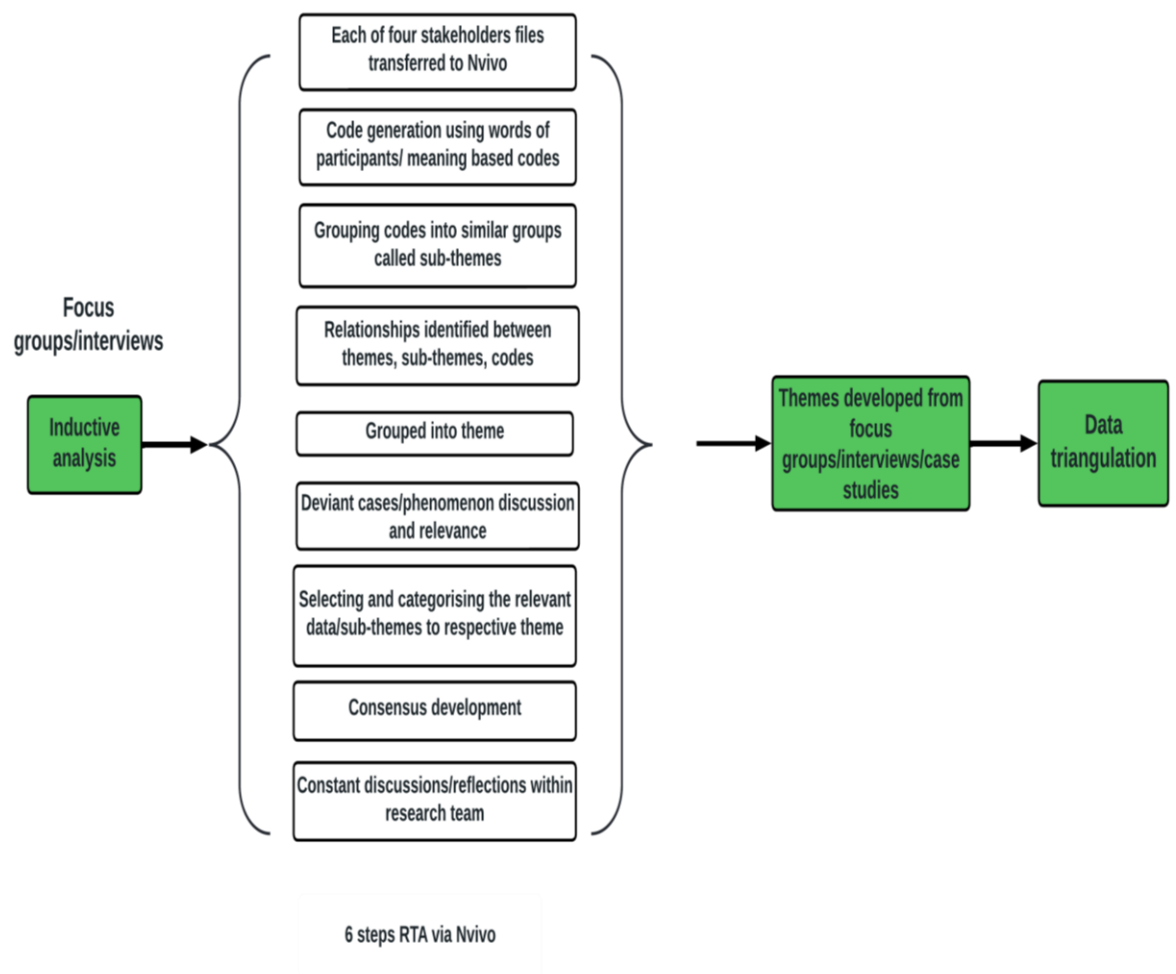


Figure 4.5: Data analysis of interviews and focus groups

Chapter 4: Interviews and focus groups Subchapter A methodology

4.1.4.k The impact of COVID-19 on data collection in interviews and focus groups

The data collection via interviews and focus groups continued during the COVID-19 pandemic virtually. For interviews, WhatsApp (internet) calls and mobile calls were used. The calls were recorded using digital recorders where each participant was informed in advance of turning the recorder on and off. Some of the interviews were conducted virtually from within the UK; however, all interviews and focus groups were scheduled at times that were convenient for the participants in Pakistan. Microsoft Teams® was used for virtual focus groups, and every participant was sent a link to join the Teams website.

Outlook email IDs and steps were drafted to help participants download, access and use Teams to join the focus group. It must be highlighted that one of the potential advantages of virtual focus groups was that it allowed participation from a much larger geographical area (including far-flung areas from different provinces), which is believed to have resulted in a richer data. The impact of digital data collection was not observed, and no stakeholder refused to participate during COVID-19 because of data being collected virtually.

4.2 Subchapter B: Results

4.2.1 Demographics of participants of interviews and focus groups

A total of 98 stakeholders participated in this study out of which 38 were female. The demographic information of stakeholders is given in Table 4.1 below.

Table 4.1: Stakeholder demographics

Stakeholder group	Policy makers (interviews)	People with CNMP (interviews)	Doctors (focus group discussion)	Community pharmacists (focus group discussion)
Gender (female %)	0% n= 11 (male) n= 0 (female)	50% n= 7 (male) n= 7 (female)	48% n= 16 (male) n= 15 (female)	33% n= 24 (male) n= 12 (female) Case studies 66 % n= 2 (male) n= 4 (female)
Virtual	04 interviews	08 interviews	02 focus groups	01 focus group
Age range in years (mean)	31-58 (47.90)	31-75 (58.92)	24-74 (31.12)	24- 38 (28.47)
Years of experience (mean)*	20-35 (14.9)	1.5-20 (6.7)	6-45 (5.83)	1-16 (2.87)
Response rate (approached vs declined)**	15 agreed but 4 refused due to time commitment	18 agreed but 4 did not respond after initial agreement, or failed to show-up for interview	38 agreed but 8 did not respond after initial agreement, or failed to show-up for FGs discussion	40 agreed but 6 did not respond after initial agreement, or failed to show-up for FGs discussion

*= For people years of continuous opioid use

**= response rate provided as per COREQ criteria for people agreed to participate but due to other time commitments could not make the interview or focus group discussion.

Interviews lasted from 50 minutes to 1 hour and 30 minutes (on average), whereas focus groups lasted between 1.15 hours to 2 hours. On average it took around 24-48 hours for transcribing a two-hour focus group. Interviews on average took less time (around 24 hours).

4.2.2 Data saturation

In interviews with policy makers, data saturation was achieved after the sixth interview and five more interviews were conducted. In interviews with people with CNMP, data saturation was achieved at ninth interview and a further five interviews were conducted. In focus groups with doctors, data saturation was achieved after the second focus group discussion and three more were conducted. For CPs, data saturation was achieved in the third focus group discussion and two more focus groups were conducted to find new information.

4.2.3 Themes developed in interviews and focus groups analysis

This subchapter now presents the findings from the inductive RTA of interviews and focus groups from four different stakeholders as shown in Figure 4.5. A total of six themes were developed, which are now presented as subsections 1-6.

1. Chronic non-malignant pain management
2. Opioids and chronic non-malignant pain management
3. Factors contributing towards unsafe use of opioids
4. Benefits of a CP opioid service
5. CP service components and activities
6. Challenges and barriers for CPs in delivering an opioid service

Please note where the data is presented using the phrase “all stakeholders”, it means that particular phenomenon was shared in all stakeholder groups. In other cases, stakeholder groups have been specified. Additional data (one quote each from each stakeholder group where possible) related to below respective subthemes has additionally been provided in Appendix 15.

4.2.4 Subsection 1: Chronic non-malignant pain management experience

Stakeholders shared their perception about CNMP and its management in Pakistan.

4.2.4.a Perception of pain

All stakeholders shared that CNMP is not considered a serious condition or disease rather a phase of life that every person has to bear as part of an aging process. Stakeholders suggested that lack of awareness about pain impacts a person's behaviour towards its treatment. A doctor and policy maker shared:

“In Pakistan pain is not considered a disease.... it is considered a symptom, because of old age, lack of sleep, irritability due to other diseases... and so on... It's a common understanding of people that as you get old.... as you age, you will get pain... because the bones are not working, the joints are not working. People don't take it seriously... otherwise if they have any other apparent reason that might be causing pain, they might not even bother to visit a doctor...” **Doctors Focus Group-1, P5**

“Pain is a part of life here... people have becomes used to it...” **Policy Maker 4-Interview**

People with CNMP and CPs also stated that pain is not considered a serious condition by the doctors to be managed effectively. A person with CNMP shared:

“Pain it is not taken seriously... When a person is feeling pain... and if you tell the doctors, they don't take it seriously... and eventually all

*of the time you have to suffer and tolerate the pain..." Patient 7-
Interview*

The doctors, however, shared that pain management is one of the primary focus of their treatment however due to health illiteracy people might not comply with the doctor's advice. A doctor shared:

"That is the first complain, the disease comes after... so we have to take care of the pain foremost..." Doctors Focus Group-2, P5

Doctors and people with CNMP also highlighted public perception of pain is also one of the primary reasons that people suffering from CNMP do not seek out continuous medical help and continue taking their pain medicines either as self-medication or prescribed medications.

"I think pain... pain is only considered seriously... when they cannot tolerate it anymore... normally people keep using paracetamol, Vorin (diclofenac), tonoflex (tramadol)... they try to control their pain themselves by taking these medicines... so they will take it one day, they will take it for a week, for six months... if the pain is still there... then they will go and seek a doctor's help... only in that situation they think that... now this constitutes an alarming situation... otherwise they don't visit doctors just for pain relief..." Patient 13-Interview

4.2.4.b Ineffective pain relief and suffering

Doctors and people with CNMP shared that Pakistan has an inadequate pain management system that leaves people experiencing insufficient analgesic relief. Pakistan lacks specialised pain management facilities/units, CNMP management specialists and lack of potent opioids, which contributes towards people's non-adherence to therapeutic regimes as well as gives rise to self-medication.

"From last 10 years or so, I think there are two centres, which I know that are specialised for pain management... there are no CNMP centres..." Doctors Focus Group-5, P6

"Currently... for long-term pain management... there are only two products left... Tramadol... or nalbuphine... we have to rely only on these two medicines..." Doctors Focus Group-4, P1

"Even there were some days that I would pick four tablets of paracetamol all at one time and then take it again after some time... and there was no relief... and a time came where I was taking almost 12 tablets almost every day of pain medicines... I

wanted pain relief somehow, but I was not getting any... I was suffering with so much pain ...” Patient 12-Interview

Doctors shared in people on whom non-opioid analgesics are not able to provide effective pain relief, people have to constantly use opioids despite possible side effects or risk of adversity. Policy makers and doctors suggested policy makers should look into developing the role of CPs who can help doctors monitor and manage the use of opioids for people on persistent opioid use, which might help optimise the use of opioids and avoid opioid related side-effects.

4.2.4.c In availability of potent opioids for pain management in community pharmacies

Doctors, policy makers and CPs shared that there is an overall lack of potent synthetic opioids for CNMP management. Morphine despite being on EML, is very well controlled and is only scarcely available in hospitals for cardiac and terminal cancer patients. Treatment with morphine thus requires hospitalisation, which can further overburden the already constrained healthcare system.

“Morphine is only available in hospital... we get limited quota. Sometimes even for cancer terminal patients we do not have morphine. And let me give you an example, morphine is available in injectable form. It has short duration of action, for effective analgesia we need to give at least twice a day, that means the patient has to be hospitalised, that means one extra bed is taken. We already have so much over-crowding in hospitals” Doctors Focus Group-5, P6

Doctors and CPs shared morphine tablets are not available in community pharmacies and this currently a hurdle in the management of CNMP conditions. Thus, the doctors manage CNMP with other available opioids and medicines, which sometimes are unable to provide effective analgesic relief in severe pain, even in combination with other analgesic medications.

“Morphine sulfate tablets... they are not available at community pharmacy level... there are specific hospitals in which morphine sulfate, (is) very rarely available in their in-patient pharmacies and even the tablets, along with injectable (morphine) are also controlled in those institutions...” Pharmacists Focus Group-5, P1

“For a patient who is needing morphine sulfate tablets... so then we had to take special permission and we had to get them imported from abroad... so narcotics... not available are an issue” Doctors Focus Group-5, P3

Stakeholders believed that continuous pain suffering may have negative impact on a person’s perception about medicines, trust on doctors and the healthcare system and may cause issues such as self-medication, non-

adherence with the prescribed regime and doctor shopping. Policy makers shared that the government is currently looking into improving the availability of morphine in community pharmacies by developing controlled and regulated channels and hoping to improve the availability and utilisation of opioids in the country.

“We still do not have potent opioids in pharmacies... Like in advanced countries... We have developed a system in the hospital sector where pharmacists control it... So, we need to develop something similar in community sector that will allow rational use of opioids like morphine in CNMP management...” **Policy maker 3-Interview**

4.2.5 Subsection 2: Opioids and chronic non-malignant pain management

4.2.5.a Perception of opioids

Doctors, CPs and policy makers shared that people in Pakistan perceive opioids as common OTC analgesic medicine because of its easy availability, which is why they use the medicines in an unsafe way or according to their own choice. This may contribute to self-medication, non-adherence to therapeutic regime and lack of subsequent doctor’ reviews.

“Tramadol... it is an opioid analgesic... it is very commonly prescribed, it is very commonly used by people themselves, it is one of the most common pain medicines currently being used...so the general concept of the patients, is that they consider this medicine like paracetamol... that this is a normal pain medicine... one of the major reasons for this perception is that the people, the dispensers and the technicians present in the community pharmacies, they actually provide tramadol as an OTC medicine without prescription...” **Pharmacists Focus Group-5, P1**

4.2.5.b Addiction to opioids

People with CNMP shared that some people might be worried about opioid medicines’ side effects and addiction.

“Is there anyone who can listen to me? Where I can discuss my medicines... their side effects... the way I feel, I don’t want to become an addict... not only my symptoms but also my worries.... my apprehensions.... if there was a prescription... which was according to my needs... you do not know... how desperate I feel...” **Patient 1-Interview**

“Because I knew... this could cause addiction... and the doctor has prescribed me tramadol. But that’s it, he does not care if I get addicted, so if I don't have that much pain on the fifth day, I stop

using it... I will not extend it to 15 consecutive days... so I break the cycle of continuous use (to avoid addiction) ...” Patient 11-Interview

However, other people shared that despite understanding the side effects related to opioid medicines, people might not stop using these medicines because of the analgesic relief they experience, which is not gained by other medicines.

“I don't want to get addicted... and it is so difficult to not use. What can I do? I don't have any other options...” Patient 7-Interview

4.2.5.c Experience of using opioids

People shared their experience of pain relief and a desire to continue using opioid medicines for the management of persistent chronic pain.

“So, when they administer that injection to me... I am like on cloud nine after... so peaceful...so relieved... I cannot explain that to you... feeling absolute relief after so much suffering was amazing... every day I want the injection and I would not have any kind of peace in that day if I did not get the injection ... if there is a medicine helping me... I am willing to go (take an injection) every day...” Patient 12-Interview

“If I don't take these medicines then I cannot function... the pain becomes so unbearable that it becomes intolerable for me... you can consider them that I cannot do anything without these medicines now... no matter whatever painkiller I take... they have no effect on me except this...” Patient 13-Interview

Doctors and people also highlighted that the analgesic relief people experience with opioids causes people to deter from the prescribed regimen. A patient shared:

“I am tempted... to overdose... or sometime take the medicine earlier than the scheduled time... just to avoid the pain getting worse...” Patient 10- Interview

People with CNMP, CPs and doctors shared that people are unable or unwilling to discontinue these medicines because of fear of extreme chronic pain's impact on their daily life.

“The side effects of medicine will come later... but pain limits my activity and I have to travel a lot for my business... meet people... how can I not use this medicine... even if it has side effects... which I assume every medicine has... so I continue using the medicine...” Patient 1-Interview

“In this country, people believe medicines (opioids) are needed... if we refer them for physiotherapy... and tell to use paracetamol... they will

not even leave our office... they actually demand... medicines (opioids)..." **Doctors Focus Group-3, P4**

Other stakeholders shared contrasting views: some CPs and people with CNMP highlighted that intentional prescription opioid misuse is not common in Pakistan. Doctors, policy makers and other CPs, however, shared that addiction with prescription opioid medicines such as nalbuphine and tramadol is common, especially in upper educated elite class, where people escape the stigma of using illegal substances of misuse (for example, diamorphine [heroin]), but obtain euphoria from opioids and may contribute to problematic use of opioids.

"Opioid misuse is a problem in Pakistan definitely. I have seen young patients who are addicted to opioid derivatives such as tramadol, nalbuphine and demand injection from healthcare professional without any indication..." **Doctors Focus Group-5, P5**

4.2.5.d Factors causing non-availability of potent opioids

Stakeholders shared that many potent opioids as well as morphine tablets, a medicine listed in the EML of Pakistan, are not available in community pharmacies. Several factors were identified that could be contributing to non-availability of potent opioids in the country as shown in paragraphs below.

4.2.5.d.i Potential of misuse

CPs, doctors and policy makers shared due to easy availability of medicines without prescription, the system's inability to track opioid control due to lack of centralised digital systems and the potential of misuse and fear of misuse of opioids, the government has restricted potent opioids like morphine in community pharmacies.

"One thing we could do to avoid misuse was to have less publicly available medicines... we had them in past... but as you know systems here are not developed... there is no secret that prescription medicines are sold in Pakistan in community pharmacies without prescriptions ..."

Policy Maker 3-Interview

4.2.5.d.ii Dispensing by non-specialised people

Policy makers, CPs and doctors shared that currently pharmacy technicians, dispensers and non-qualified persons illegally dispense, prescribe and administer medicines without a prescription, which is why the government has restricted potent opioids to be available only in specialised hospitals.

"These dispensers, 'Mr' dispensers are doing these kinds of activities... Tramadol (injection) if they have pain or maybe a steroid (injection)... they will administer and dispense anything..." **Doctors Focus Group-5, P3**

“The patient goes to a pharmacy/medical store... anyone in that store a technician... salesperson or whoever he or she is... That I'm having this problem which medicine should I take... So according to the judgment of that person whatever he thinks is best for the patient, he will dispense it to them...” **Pharmacists Focus Group-3, P1**

4.2.5.d.iii Lack of CPs ability for controlled dispensing

All stakeholders shared that conventionally CPs have had no role in controlling medicine dispensing without a prescription. Policy makers, people and pharmacists shared that the implementation of Schedule-G amendments, which utilises CPs to restrict unauthorised dispensing, has been variable, with CPs providing control over dispensing in some establishments.

“I needed the medicine... so when I asked for the medicine, he (CP) refused it... that do you have a prescription? If not, we cannot dispense it... so there was a role, in which pharmacists are controlling without prescription sale....” **Patient 11-Interview**

On the other hand, policy makers and CPs highlighted that in some establishments CPs might not have the autonomy to refuse opioid dispensing without prescriptions due to a conflict with an organisation or proprietors business interest and this results in opioid dispensing and administration without authorisation.

“In a country like Pakistan... lock and key system... the thing is there are other people beside the pharmacist in a shop...profit making is the goal, others will dispense...” **Pharmacists Focus Group-5, P3**

“If we talk about the sale, procurement in retail pharmacies and the government laws... They are present... there is sale restrictions as well... but in reality... still sale (opioid medicine) is going on...” **Policy Maker 2-Interview**

4.2.5.d.iv Lack of strict penalties

Policy makers and CPs highlighted that there is weakness in implementation of the Schedule-G law due to lack of proper regulation and lack of strict penalties, which allows illegal dispensing, prescribing and administration of opioids to continue despite new rules.

“Now misuse of prescription medicines especially opioids... no penalty. For CPs dispensing medicines without prescription let's talk about it first... The final case goes to a first-class Magistrate... the penalty is only Rs 500 (£2.50) ... an opioid medicine is more expensive than the penalty...” **Policy Maker 2-Interview**

4.2.5.d.v Opioids are quota medicines

Pharmacists and policy makers shared that there is an overall lack of potent

opioids because the government allocates a specific quota to specific industries for manufacturing every year to avoid the misuse of opioids.

“As far as the license is concerned because industries don't get licensed to manufacture morphine and other potent opioids... so, overall quantity is less” **Pharmacists Focus Group-3, P2**

Pharmacists also shared that there is a very selective process of allowing certain industries to manufacture opioids; therefore, there is an overall lack of specific dosage forms and quantity of opioid medicines in the country. Pharmacists stated that many manufacturers do not like to bid for or apply to DRAP for the manufacturing licenses of these medicines because of difficulty in controlling the raw material, the industrial stocks and assuring legal distribution to pharmacy vendors due to human (prone to corruption) and system deficiencies (lack of regulation).

“No matter how much that industry would be reputed... whatever case they present in front of the anti-narcotics force... the reason why they don't want to start... the manufacturing of these kinds of drugs is... there are a lot of checks... you have to follow them around you have to go and attend their meetings ... ask again and again... please allow to manufacture these drugs... but they're not allowed... they don't allow...” **Pharmacists Focus Group-5, P3**

CPs, policy makers and doctors highlighted that potent opioids like morphine are listed under EML, which is why they are provided to the public at a subsidised rate. Normally the industries can cope up with subsidized rates enforced by government, because of large orders and balancing the ratio of profit by selling more unit items. However, because of restriction on the quantity of opioids manufactured due to being quota medicines, the industries are not keen on obtaining licenses to manufacture these opioid medicines, which reduces the national capacity to produce opioids and translates down to a lack of availability of potent medicine for pain management.

“The pharmaceuticals got the price set at Rs 12... it was even less than their manufacturing cost. So, they thought, and they left it (stopped manufacturing), as a bad job and they said that we're not going to manufacture it...” **Doctors Focus Group-4, P4**

4.2.5.d.vi Import processes difficult

CPs, policy makers and doctors shared that the import of potent opioid medicines also remains a huge challenge for the pharmaceutical sector as the entire process of ordering these medicines, restriction on their quantity due to quotas, affordability, and justifying their use and border control rules makes the process of importing these items very cumbersome.

“The process to get these medicines imported from outside (foreign) is very lengthy and difficult... and there would have to be a limit on how much you are importing... there will be a specific quantity, also not everybody can import... these import these medicines from outside the country... It will become very expensive ...” **Pharmacists Focus Group-3, P2**

4.2.6 Subsection 3: Factors contributing towards unsafe use of opioids

4.2.6.a Regulation

Stakeholders highlighted; Pakistan has an inadequate regulatory workforce to control the unsafe use of opioids. Despite being under regulation, opioids remain freely available without prescription.

“Currently the regulators (drug inspectors) are so scarce that there are maybe one or two people in the whole district... How can they enforce the proper rules in all shops?” **Policy Maker 8-Interview**

Different policy makers highlighted that after drug rule amendments, opioid dispensing can only be done by qualified pharmacists. However, as there is no pharmacist in most retail outlets, medicines are dispensed by pharmacy assistants and salespeople. One policy maker shared:

“The major problem is availability of pharmacist... when the pharmacist is not present, how can they control...” **Policy Maker 4-Interview**

All stakeholders highlighted the impact of pharmaceutical marketing promotions and highlighted the over prescribing of opioids. A doctor stated:

“In this whole scenario... we are missing a very vital point... the pharmaceutical marketing... the market influences a lot of medicine prescribing... they control in a way with their incentives which drug should be more prescribed, this is unethical but unfortunately happening...” **Doctors Focus Group-1, P1**

Doctors, pharmacists and policy makers highlighted that most prescriptions do not conform to legal requirements due to lack of regulatory checks on physician prescribing practices, which may promote unsafe prescribing of opioids.

“Sometimes prescription comes which have normally eight to 10 medicines... The pharmacist actually holds his head (become exasperated) ... and all of them belong to the same classification of

drugs... Like three or four they did ... from the same class... Two of them would be multinational. Two will be from the business (promotional) products... So, this is an issue for opioid safety..."

Pharmacists Focus Group-3, P2

Stakeholders suggested that this phenomenon might also result in lack of rational prescribing, substandard prescriptions and overprescribing of opioids (Appendix 15). Policy makers emphasized that a possible strategy would be to ensure the regulatory system is sufficiently staffed to ensure that opioids are distributed and dispensed as per strict regulations, as prescription-only-medicines (POMs) in the presence of qualified pharmacists.

4.2.6.b Black market and weakness in regulating distribution channels

Medicine distribution channels inside Pakistan are poorly regulated and a pharmacist shared:

"Even if an item is banned, that can also be found there... imported black market items... everything is available... These markets supply these medicines all over the country... They are found in every city... No check is in place..."

Pharmacists Focus Group-3, P8

Doctors and pharmacists both shared that not only weak opioids like tramadol and nalbuphine remain easily available without prescription, but even morphine, which is highly regulated and controlled by the ANF, can be purchased in open markets (black market) and could be contributing to opioid-related side effects.

"Let me tell you a story.... we had a patient who was having severe pain... he wanted something strong to treat his pain.... so, he would ask us to prescribe morphine.... cause morphine is a controlled substance in Pakistan.... and availability is not... easy... so, we refused.... because it is not available in the community pharmacy sector...so he visited three or four different cities... And he arranged morphine for himself... I don't know how he did it... but even morphine which is a controlled substance... can be found... outside hospitals... Which shows the weakness of the system..."

Doctors Focus Group-2, P7

Pharmacists shared that regulators (drug inspectors) have very limited access to and control over black markets, thus allowing opioids to remain freely available in the system to be used by people without proper medical advice or prescriptions.

“The person in (these) markets... He is running 100-million-dollar business... he's not an ordinary person... he is not earning in lacs, he is earning in crores... he has a lot of power... money as well as influence... these drugs are available in communities through the black-market sale and causing excessive misuse in pain management...” **Pharmacists Focus Group-3, P7**

4.2.6.c Healthcare system deficiencies

4.2.6.c.i Access to pain management

Doctors stated that Pakistan lacks a proper pain management pathway and facilities. One of the doctors shared:

“From last 10 years or so, I think there are two centres, which I know that are specialised for pain management... there are no CNMP centres...” **Doctors Focus Group-5, P6**

“Currently... for long-term pain management... there are only two products left... Tramadol... or nalbuphine... we have to rely only on these two medicines...” **Doctors Focus Group-4, P1**

Stakeholders perceived the combination of these factors leads people to visit non-specialist physicians or overuse available opioids, which could substantially increase the risk of opioid-related side effects in the long-term pain management and affect the quality of care.

4.2.6.c.ii Digital health systems

Pharmacists highlighted that Pakistan lacks an integrated digital health system and one pharmacist shared:

“We do not even know how many people experience these undue effects and ADRs... the reporting systems are missing... the situation in patient safety is terrible right now...” **Pharmacists Focus Group-2, P5**

Doctors also shared that lack of patient records and medication history affects their ability to provide need-based patient care and may result in compromised patient care.

“We do not know who the patient is, what treatment they have had before, what drug allergies they have... what has been effective, chronic conditions especially, we currently rely on patients giving us this information, which can be complete or incomplete depending upon patient...” **Doctors Focus Group-5, P6**

Chapter 4: Interviews and focus groups Subchapter B results

In addition, pharmacists and doctors shared that lack of digital health systems allow prescription adulteration and also results in lack of prescribing records data (Appendix 15), which might be contributing towards unsafe use of opioids. Doctors also shared that lack of electronic prescription data systems puts the responsibility to collect all essential parameters regarding detailed medical and medication history on the doctors' and further constrains their limited time with the patients.

“In those five minutes... diagnose... acquire past medical history... past medication history... past surgical history... psychological history... and also do a differential diagnosis... make sure no drug is interacting... make sure it is the correct dose... without having a blood profile... without even knowing the proper age of the patient in many cases... without knowing any comorbidities... it is impossible... the doctor is not a machine, not a computer... even it will take more than five minutes to feed all that information in a computer... but the doctors are doing their best in that situation... (yes-nodding) it is a barrier... for opioids situation” **Doctors Focus Group-1, P5**

Stakeholders shared that a possible strategy is that the government needs to invest in developing digital health systems and supportive infrastructure to promote the safe use of medicines and facilitate patient data sharing across healthcare professionals, which might help optimise the use of opioids.

4.2.6.d Business-oriented medicine outlets

Pharmacists, policy makers and doctors highlighted the profit-making intentions of medicine outlet proprietors that results in increased dispensing and a lack of refusal on self-medication with opioids. A doctor shared:

“Even if the doctor writes the medicine for one month for example, if the patient asks for three months of dose, they will gladly give, because, if they made profit of Rs 100 from one box, now the profit is Rs 300... there are no consequences of dispensing it more, who will ask them?... See there is a huge flaw... in the system that is causing medicine misuse...” **Doctors Focus Group-2, P6**

4.2.6.e Doctors overburdened

Pharmacists and doctors also shared that doctors see a large number of patients in clinics and hospitals, which affects their ability to engage in safe medicine practices as well as compromises their ability to counsel patients for subsequent medications reviews, discouraging self-medication and perform risk assessment for opioids.

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“There will be four doctors sitting in one room... they will be seeing their patients, there is so much (incoming) information... I am speaking about the OPD (outpatient departments) clinics in the government hospitals... where majority of the people in this nation are going to seek healthcare...” **Doctors Focus Group-1, P5**

Doctors highlighted that providing opioid information to the patient is an essential parameter to ensure medicine adherence and CPs should be more involved in patient care. One doctor shared:

“We need pharmacist in medicine stores to educate people for rational use and make sure they use it as intended, before giving them more (potent) medicines...” **Doctors Focus Group-5, P6**

4.2.6.f Lack of awareness of opioid medicines

Stakeholders shared poverty, lack of proper health facilities in rural areas and lack of health literacy contribute towards unsafe opioid use.

“The general concept of the patients is that they consider this medicine (opioid) like paracetamol that this is a normal pain medicine... Tramadol is still treated the same... just like an OTC analgesic...”
Pharmacists Focus Group-5, P1

People also engage in self-medication or demonstrate non-adherence to prescribed opioid regimens as well as avoid subsequent medical reviews due to lack of awareness. Stakeholders identified a possible strategy and shared that CPs might be able to provide counselling and medicine information to people using opioids, which may help optimise their use.

4.2.6.g Doctor shopping

All stakeholders shared that ‘doctor shopping’ is common in people with CNMP due to uncontrolled pain, insufficient analgesic relief or after they develop tolerance.

“I am taking these medicines for years now, medicines are not effective anymore... that is why I visit different doctors, maybe they can help”

Patient 6-Interview

All stakeholders shared that it is also a social norm for people to visit more than one doctor to acquire a confirmed diagnosis and get satisfaction that they are being treated correctly by the doctor. Another viewpoint shared by people explaining ‘doctor shopping’ was that if their pain was not controlled, people may visit another physician. Pharmacists shared that in the latter case people usually would continue using both doctors’ prescribed medicines in hope of getting satisfactory pain relief, which was insufficiently relieved by using one doctor’s medicines. Policy makers and pharmacists highlighted that

when people visit doctors, they provide a list of symptoms of diseases or conditions they have, regardless of the specialisation of the doctor and could possibly get prescribed duplicate opioid medicines⁷.

“Actually, I saw his prescription... the patient had joint pains... so one of the medications was I think tramadol in combination... and the other prescription had tramadol only... I asked the patient if you're taking one, why do you need the other? So, the patient told me... that see, I went to the doctor, and he wrote me this medicine... which was giving me pain relief... But then I had flu and (an) infection, so I went to another doctor... so he asked me about my diseases... and wrote that prescription ... So now I am taking both the doctor medicines... so then I tried to intervene and tried to tell the patient... but the patient refused and said no... no... the doctor has told me to take these medicines and I will take it... this is the problem in our setup...”

Pharmacists Focus Group-3, P4

Doctors and pharmacists shared that most people do not understand the risks associated with taking more opioids (increased dose or frequency) or duplicating them (therapeutic duplication), which could increase the risk of adverse events and CPs providing more medicine information to people might help overcome such risks.

4.2.6.h Unauthorised dispensers

Pharmacists and doctors shared that dispenser (pharmacist and non-pharmacist), actively participate in providing recommendations or prescribing medicines according to symptoms of the people and dispensing it to them, which might contribute towards unsafe use of opioids.

“The patient goes to a pharmacy/medical store... Anyone in that store a technician... salesperson or whoever he or she is... That I'm having this problem which medicine should I take... so... whatever he thinks is best for the patient, he will dispense it to them...”

Pharmacists Focus Group-3, P1

4.2.6.i Demand for opioid injections

Pharmacists and doctors shared that a common social practice in Pakistan is that people prefer getting injections for quick relief.

“I am talking about villages over here... the people leave their houses... with a set mind, that we have to go to that “doctor” (quack, dispenser) ... and they will administer an injection...”

Doctors Focus Group-4, P1

⁷ Due to lack of medication records, the doctor might not be even aware of unintentional duplication

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Doctors and policy makers stated that this social perception translates into increased opioid injection usage by both those who demand an injection and those who unlawfully administer them and substantially increase the risk and harm associated with opioids.

Policy makers suggested improving social awareness about diseases and medications might motivate people to use their medicines more cautiously and the government should target public awareness about opioids, regulate dispensing and strictly monitor the unsupervised and unlawful administration of opioids and promote safe use of medicines.

4.2.6.j People's lack of trust and perception of doctors

All stakeholders highlighted that majority people try to obtain the medications from medicine shops and pharmacies for persistent pain as self-medication because of lack of trust on doctors due to pharmaceutical promotions, the economic costs and the overall convenience it offers.

“Nobody cares... if you go there is one doctor sitting.... if you go after a month there is another doctor ... then that second doctor will give his own treatment... sometimes even starts the same medicine again... how can I ask the doctor? Even if the medicine has no effect, we also go to another doctor... and we tell him that this medicine is not working... so he writes another medicine... you should try this one... which is the same when I buy from shop...so why not skip the doctor and keep buying?” **Patient 1-Interview**

People with CNMP contributed that that doctors exhibit empathy based on social class of the people.

“Nobody tells us the benefit or the side effects of the medicine.... not doctor even... if I ask, they will get angry... so I do not ask... when they look at me, they think I am illiterate... so they do not think of me as worthy to answer...” **Patient 1-Interview**

However, one doctor shared:

“In this country, people believe medicines (opioids) are needed... if we refer them for physiotherapy... and tell to use paracetamol... they will not even leave our office... they actually demand... medicines (opioids)...” **Doctors Focus Group-3, P4**

Doctors emphasized that a lack of transparency in communications with patients, and the refusal to comply with unnecessary and unjustified opioid demands, usually impacts the physician-patient relationship. This may precipitate uncertainty in physicians' professional advice and potentiate non-adherence as well as self-medication. Stakeholders shared improving public

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awareness about opioid medications might help with adherence to the prescriber's guidance.

4.2.6.k Perception and awareness of pharmacists

People with CNMP and pharmacists shared that even in locations where CPs are present, most people purchasing opioids do not ask for opioid information because of lack of awareness about the pharmacist's role in medicines information, counselling and review.

"Also, our people... they're not even aware to ask this medicine information before buying the medicine..." **Patient 3-Interview**

Stakeholders collectively agreed the role of pharmacists is integral in promoting the safe use of opioids and developing specialised roles in opioid safety and improving public awareness about such roles can be beneficial for people with CNMP.

4.2.6.l Uncontrolled chronic pain

Stakeholders shared that people with CNMP tend to increase the dose or frequency of medicines by themselves according to pain intensity. People also shared they might intentionally overdose on opioids:

"I think pain is a thing which does not let you forget... I am tempted... to overdose... or sometime take the medicine earlier than the scheduled time... just to avoid the pain getting worse..." **Patient 10-Interview**

Doctors and pharmacists also shared that recently there have been reports of people using (illegal) heroin (diamorphine) or morphine from the black market to help achieve relief in unresolved persistent pain. People who have insufficient relief with analgesics might also try complementary and alternative medicines (CAM), herbs, faith healing or techniques from licensed or unlicensed professionals, increasing the overall risk of harm.

"If I share something with you... I read a news or was it a report? They actually linked the heroin addicts in the country... and they interpreted that because the legal medicines (morphine) are so difficult to obtain... and people are suffering from pain conditions and it is so difficult to obtain morphine, few places (specialised hospitals) or only in black markets... that people might be tempted and may potentially go towards the use of illegal drugs... this will be very problematic" **Pharmacists Focus Group-5, P2**

4.2.6.m Health literacy

Doctors and pharmacists highlighted that people, due to health illiteracy take a combination of medicines without understanding the potential of harm.

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They advise each other on medications, share medications without understanding any synergistic effects or drug interactions, and remain at high risk of opioid-related adverse effects.

“Mostly they are uneducated... they do not agree to us... so they constantly keep on using the medicines... especially these addictive medicines” **Pharmacists Focus Group-1, P1**

4.2.6.n Mental health conditions, addiction and tolerance

Policy makers, and doctors emphasized that people with CNMP with sleep disorders or mental health issues might be at a higher risk of overusing opioids because of possibly developing addiction or longing for the euphoric or sedative effects of opioids.

“So, when she (aunt) takes the medicine, she is happy... she is good... but when she leaves it... she gets very moody and cannot sleep... and has too much pain...” **Patient 2-Interview**

Some stakeholders shared that people might be misusing opioids to get the euphoric effects whereas others disagreed and said there might be other drugs of misuse and substances of abuse available that are preferred over medicines.

“Opioid misuse is a problem in Pakistan definitely. I have seen young patient who are addicted to opioid derivatives such as tramadol, nalbuphine and demand injection from healthcare professional without any indication...” **Doctors Focus Group-5, P5**

Pharmacists highlighted that despite people developing tolerance to opioids, they keep using and increasing the dose in hope of getting analgesic relief.

“There is a dependence element... even genuine patients... are using the medicine but it is not giving them any effect anymore because they are already tolerant to it... and they cannot leave it because they are dependent on it... and they keep paying and using a medicine that does everything to them except pain management” **Pharmacists Focus Group-4, P6**

4.2.6.o Self-medication

One doctor shared:

“People are treating their pain themselves... and the worst part is even under proper supervision it can be tricky, so a person treating it

themselves or by asking people around them... it's dangerous..."

Doctors Focus Group-2, P8

All stakeholders shared that most people practice self-medication, directly by observing or asking other people who have visited doctors.

"If the doctors are writing combinations, they are actually supervising and monitoring... but people learn this, they combine all medicines... and then they stop visiting doctors, and they continue using (the medicines) themselves and keep justifying they are using doctor-advised medicines..." **Pharmacists Focus Group-5, P1**

Doctors also shared that people also advise and recommend other people about using opioid medications, which might contribute to self-medication and using opioids without a doctor's supervision.

"Also, there is one more problem. Everyone is a doctor! Everyone recommends to each other..." **Doctors Focus Group-5, P6**

4.2.6.p Lack of review

People shared that most people are reluctant or unable to go for a subsequent review because of economic reasons (poverty) or difficult access to doctors or because of lack of trust in doctors.

"Normally the people do it (self-medication) like this because access to the doctor... In government hospitals and private appointments are difficult to get..." **Patient 7-Interview**

Doctors shared that if the awareness of people can be improved about opioids and the importance of frequent medication reviews as well as review with doctors, it might help with patient compliance and help optimise their use of opioids.

4.2.7 Subsection 4: Perceived benefits of developing the role of CPs (opioid service)

4.2.7.a Financial benefits for pharmacists

Doctors shared that launching an opioid service would provide direct financial benefits to pharmacists by legally obligating retail outlets to hire CPs. This will increase CP hiring, ensure a competitive salary package and help improve CP motivation and their desire to efficiently provide opioid services in pharmacies. This will help in the overall fidelity as well as sustainability of this service.

"If these services could be developed... it will essentially make the role of a pharmacist mandatory... those pharmacists will then be hired for their services... they will improve (professionally)... they will have

experience... and they will contribute to the healthcare system..."

Doctors Focus Group-1, P4

4.2.7.b CP societal value awareness and community acceptance (non-financial)

Pharmacists suggested delivering an opioid optimisation service will help develop a positive pharmacist-public relationship and improve CP awareness in the society. Increasing public awareness might improve: CPs professional image, their societal value and increase public demand for services, which might improve CPs motivation to work in community pharmacies and deliver such services in the future.

"I think this would be a very good way to increase the public awareness... everyday daily patients would come to the pharmacy to buy their medicines... and such practices are started at every pharmacy shop... and the public would start accepting the role of pharmacists... And I think it will also improve the public health concept in Pakistan of pharmacists and their role in it... and they can help the patients. It would improve and even the pharmacists... who are currently... they are feeling this depressed kind of state... this will improve a lot..."

Pharmacists Focus Group-5, P1

Policy makers, pharmacists and doctors shared that improved public awareness can motivate proprietors to hire CPs and help ensure their presence in pharmacies that could improve delivery of future service.

4.2.7.c Organisational benefits (financial and non-financial)

All stakeholders shared that if CPs can deliver patient-oriented services in pharmacies, this will create a positive image of that establishment in the public domain and people will actively seek medicine outlets where CPs deliver such a service. Influx of people might result in increased sales and customer satisfaction, which might motivate the current organisation as well as other pharmacies to hire and support CPs. Stakeholders shared proprietors supporting the adaption of the opioid service for organisational benefits will help CPs deliver the service efficiently and help reach desired service outcomes.

"Even new pharmacy shops opening in the future... they might use the pharmacist card... and their consultations as a marketing tactic to improve their sales and customers... And satisfy their customers..."

Doctors Focus Group-5, P1

4.2.7.d Patient financial benefits

Doctors stated that developing opioid optimisation service will help improve the use of opioids and help patients use opioids more safely without suffering

the adverse effects of opioids, which might help reduce the overall costs for them.

“The misuse of... abusive drug... will lessen, the adverse drug reactions (ADRs) and at the same (time, it) will decrease burden on health system and will save their (public) money and will keep them away from irrelevant people like quacks, unnecessary doctor visits...”

Doctors Focus Group-5, P1

In addition, a CP highlighted:

“CPs can help substitute expensive medicines with cheaper alternatives, that too is a role of pharmacist...”

Pharmacists Focus Group-4, P3

4.2.7.e Patient clinical benefits

Different stakeholders suggested different aspects of developing the role of CPs and its benefits for the people. Stakeholders shared that CPs might be able to rationalise the use of medicines, provide education and counselling, help identify high risk people, identify potential therapeutic duplication, discourage self-medication, perform comprehensive medication reviews and may be able to guide patients to adhere to their therapeutic regime.⁸

“The pharmacists in community pharmacies... they should provide...advice, counselling about opioid medicines... signs of overdose... interaction checks... Specially with other CNS depressants... these are very basic things, which needs to be done...”

Policy Maker-3 Interview

4.2.7.f Health system benefits

Policy makers shared that developing the role of CPs in opioid safety may help improve the availability of potent opioids because CPs can help control and prevent the misuse and diversion of these medicines. CPs might also help reduce self-medication, which can give regulators confidence to allow dispensing of potent opioids in pharmacies and can help provide increased public access to potent opioids and help reach better patient and health system outcomes.

“So, they (CPs) can counsel, review, adjustments... so much... even controlling (misuse, self-medication) ... adherence... once we know, medicines are safely being used, only after a valid prescription, an

⁸ Please find different quotes spread through subsection 5 of this chapter: Possible action of CPs

authentic prescription, essential potent pain medicines (like morphine) can then be dispensed in pharmacies” **Policy Maker 9-Interview**

Policy makers and doctors also highlighted that currently Pakistan’s health system is highly overburdened but launching a CP opioid optimisation service will help reduce the overall patient burden by reducing the overutilisation of public health facilities for unmanaged chronic pain conditions, medication reviews and dose adjustments.

“If the pharmacist is involved in kind of keeping a check and review that how the medicine is behaving in particular patients and whether the patients are at high risk or not this could help save a lot of precious time of the doctors... in order to help doctors provide medical and diagnostic services to public... we need to get the load off them... right now the responsibility is on their shoulders... first to diagnose and then to make patient understand every medicine, every side effect... every nook and corner... and obviously they don’t do it... because to be honest they can’t... if they do tell each and every thing about medicine they will be spending 20 minutes on every patient... in 20 minutes they see three people in private clinics and five people in hospitals...” **Policy Maker 8-Interview**

4.2.8 Subsection 5: Possible CP actions that can help optimise the use of opioids

The fifth theme was the actions/activities that can be undertaken by a CP, which might help optimise the use of opioids. The following actions/components were identified altogether in all four-stakeholder group interviews/focus groups and the quotes (from all stakeholders) have been additionally presented in Appendix 15.

4.2.8.a Opioids dispensing and record keeping as per legislation

Policy makers stated that currently it is clearly defined in the legislation that CPs are required to ensure that opioids should be dispensed on a valid prescription and the patient, prescriber and opioid information needs to be recorded.

“Currently, there is legal obligation to maintain a special register by the pharmacist in that pharmacy... it is still not widely implemented... but... they have to follow it... some are following it religiously... while some are transitioning...” **Policy Maker 5-Interview**

People, CPs and policy makers shared that as a minimum in the opioid service, CPs need to maintain opioid dispensing records and ensure regulatory

requirements have been met as per the current Schedule-G amendments, which becomes a facilitator for implementing future service.

“No medicine should be dispensed without a pharmacist signature...a legal system... he should sign it and he should properly check it...”

Patient 1-Interview

4.2.8.b Patient education and counselling

All stakeholders agreed patient counselling and education needs to be a component of opioid service and will help improve the use of opioids by people. One of the doctors highlighted:

“Only the pharmacist has the knowledge... They have got a proper degree; they know the conditions for the medicine... They know the side effects... They know the dosage... They are able to guide the patients properly...” **Patient 3-Interview**

“The consumer is the patient... the doctor already has prescribed; he has done his job... The power then comes on to the patient how to use the medicine... and who can tell that information besides a pharmacist? How to get better use and avoid harmful effects... The most important thing is patient counselling...” **Pharmacists Focus Group-4, P5**

All stakeholders suggested that patient education and counselling should be according to the need of the people and CPs should be trained to communicate opioid medicine information to people according to their respective needs.

“There should be pharmacists involved to educate them and counsel them... with pictorial references... (patient needs) varies patient to patient” **Doctors Focus Group-5, P5**

“Many of these people are less educated, so the pharmacists can help point them visually, how to use which medicine... maybe differentiate with the help of colour of medicines... shapes... it is essential” **Doctors Focus Group-1, P5**

“If they can help me understand these medicines... see I am educated but I do not understand...the medical terms...” **Patient 4-Interview**

Stakeholders also said CPs should counsel people and help in maintaining realistic expectations with opioids, which might help avoid overuse, misuse and avoid non-adherence with the advised regime (Appendix 15).

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4.2.8.c Medication review

Doctors, policy makers and CPs shared that there is a need to perform comprehensive medication reviews. Policy makers also shared that CPs could engage the patients and discuss their medications as well as use prescriber information on prescriptions to avoid any therapeutic duplication, self-medication and adherence issues.

“One thing important is review; pharmacists should be doing review and guide for adherence” **Doctors Focus Group-5, P6**

“The pharmacists in community pharmacies... they should provide...advice, counselling about opioid medicines... signs of overdose... interaction checks... Specially with other CNS depressants... these are very basic things, which needs to be done...” **Policy Maker-3 Interview**

Different stakeholders also shared different components in a medication review and suggested that CPs could help in reducing polypharmacy, identifying and stopping drug-drug interaction, stopping self-medication, provide cheaper therapeutic substitutions, eliminate medication errors and rationalisation of opioid medicines according to a patient’s individual needs (Appendix 15). Such actions might be able to help overcome factors contributing towards the unsafe use of opioids and help reach the service outcomes.

4.2.8.d Referrals to doctors

Patient and doctors shared that guidance should be provided to the patient to visit the doctor in case of self-medication with opioids or if people are using opioids continuously without review or experiencing any adverse effects.

“Especially the pharmacist should be able to tell if the patient needs to go back to the doctor... I think to make him understand and convince him to go to the doctor is also the role of a pharmacist... Especially in those cases where we are buying the medicines for the fourth or fifth time... without a doctor's review...” **Patient 7-Interview**

4.2.8.e Identify high risk people

All stakeholders stated that even if people have prescriptions for opioids, CPs need to be trained to be able to identify people at high risk (of opioid-related adversity, polypharmacy, drug interactions), as well as must be able to identify any red flags in patient behaviour such as over-or under-use, addiction, tolerance and side effects.

“Detecting or making sure there is no misuse and opioid abuse... Either the dose is high... Maybe the patient is compromised hepatically or

renally... Maybe they are using another medicine... that can induce an interaction..." **Doctors Focus Group-1, P7**

4.2.8.f Communication with the doctors

Doctors suggested that CPs can help identify problematic use or people experiencing adverse effects. However, as CPs are not legally allowed to change medicines, therefore there should be communication between prescribers and CPs where CPs can highlight the need to alter the medicine or dose. This might ensure optimum opioid use by people with CNMP.

"The one who wrote the medicine is the person who needs to change it, pharmacists should not do it, it is against the law. If there is an ongoing problem which they identify they should refer them back or communicate to doctors" **Doctors Focus Group-1, P4**

However, this was perceived by stakeholders to be the most difficult component of the opioid service. Stakeholders shared that currently, the development of the technology required for this step requires massive infrastructural changes and needs support from government authorities. A doctor shared:

"Well having digital systems would be awesome... however, we have to be realistic. Instead of waiting years for these systems (digital systems) to develop, we should be smart. Implement their (CP) role first in the current scenario, with whatever we have in hand. Make it so that it doesn't require too many resources, or the policy makers will not approve... Patient care always upgrades, it's not a new thing, but the current need is to have them (CPs) involved first" **Doctors Focus Group-5, P1**

Policy makers suggested that the government has started looking into digitalisation of health systems and integrating all healthcare data and hopefully this will allow interdisciplinary collaboration and might facilitate a future opioid service.

4.2.9 Subsection 6: Factors (Barriers and facilitators) for CPs to deliver an opioid service

4.2.9.a CP individual challenges and barriers

The following paragraphs presents an overview of the individual level enablers and barriers to CPs to deliver an opioid service (Table 3 Appendix 15).

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4.2.9.a.i CP knowledge

4.2.9.a.i.a General knowledge (undergraduate degree knowledge)

All stakeholders shared mixed perceptions about the general knowledge of CPs.

“Currently they (CP) are not being utilized for that (opioid service) although they have the competency, and they have the capacity to do these kinds of things...” **Policy maker 11-Interview**

“The entire curriculum is designed in a way that it does not accommodate practice-related things... they're missing... the only focus on what is a drug how it is manufactured... but in regards to clinical pharmacy and pharmacy process practice aspect... the core area, the entire topic is missing...” **Pharmacists Focus Group-3, P2**

It was shared that academics from pharmaceutical sciences and pharmacology are usually involved in teaching these subjects and there is a lack of involvement of experts (preceptors) from the pharmacy practice field, which may create a deficiency in the knowledge of pharmacists. In addition, a lack of competency-based pharmacy education results in deficiencies in CP skills and remains a current barrier for delivering quality opioid service in future.

“Where the teacher is not competent himself or herself... they are unable to give the required competency to the students...” **Policy Maker 2-Interview**

Pharmacy policy makers remained optimistic for pharmacists delivering opioid service and one of them shared a possible facilitator:

“We are doing revised curriculum every few years, where all these new needs are identified, deficiencies are recognized and then we change and upgrade curriculum of pharm- D to reflect that...” **Policy Maker 11-Interview**

Policy makers, doctors and CPs suggested upgrading the curriculum with more clinical content, involving field experts to teach pharmacy students and launching community pharmacy mandatory clerkships might help them develop their competencies for community pharmacy medication review services.

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“We had some industry hours and hospital hours mandatory training as a degree requisite... but till now no community pharmacy training, requirements... we need to start these clerkships... there are amendments needed and there are certain changes required in the current curriculum...” **Policy Maker 5-Interview**

4.2.9.a.i.b Specialised knowledge and advanced training

Different stakeholders had different views about advanced opioid-specific knowledge and competency of pharmacists to deliver an opioid service. One doctor shared:

“I think the CPs have good knowledge regarding opioids sources and other pain medicines and can fairly review the opioids therapy and adjust according to patients’ individual profile” **Doctors Focus Group-1, P1**

Other policy makers, doctors and pharmacists suggested that although CPs might have good theoretical knowledge of opioids and chronic pain conditions, they might be lacking advanced clinical skills required for opioid optimisation service. Doctors, policy makers and pharmacists suggested upgrading the pharmacy curriculum and providing training to include more practice-based clinical scenarios will help improve CPs’ pharmacy practice knowledge and help develop their competencies.

“Pharmacists are well-educated but not that well educated... to currently give specialized services... we are in a need to arrange training sessions for pharmacists... the role of the community pharmacists in monitoring opioid therapy... all the things related with the management... it needs to be in that training” **Policy Maker 11-Interview**

4.2.9.a.ii CP skills and competencies to deliver an opioid service

4.2.9.a.ii.a CP competency

Stakeholders shared deficiencies in the skills and competencies of CPs to deliver an opioid service. Policy makers and CPs also highlighted the deficiencies in the pharmacist’s basic skills and competencies that are required to deliver an opioid service.

“We pharmacists have never been in community setting. Ever! it is our first exposure... and we are overwhelmed... we don’t know how to manage everything...” **Pharmacists Focus Group-2, P1**

“Competency... I think why they are shy... in facing the public or giving answers to the public... You need competency... we have to answer to the public...we do not get any extra money or respect for that... We will have to face the physician as well... it is not easy to face the doctors...” **Policy Maker 2-Interview**

Policy makers shared that although currently there are no continuous professional development (CPD) opportunities for pharmacists, pharmacy professional bodies’ support in developing CPD could be a way to deliver professional training course. This could help develop as well as periodically update CPs competencies and help them deliver the opioid service.

“If I start the first thing and the last thing... it would be the training of the pharmacists that is needed... they need some kind of training... especially when we talk about specialized community pharmacy services or specialized clinical pharmacy services...” **Policy Maker 11-Interview**

“CPE (Continuous Professional Education) is not a theoretical phase... this has already been conducted and is working.... and the main focus of CPE is to build the role of community pharmacist and develop pharmacy services...” **Policy Maker 5-Interview**

Policy makers, doctors and CPs stated that such capacity and competency building training might also improve acceptance of CP’s professional advice by doctors and help in the overall sustainability of a future opioid service.

“From my opinion if you talk with logic, with evidence-based facts... I do not think that a doctor will consider it interference in his domain...” **Doctors Focus Group-5, P1**

They also believed organisation providing in-job training (orientation sessions) for CPs as well as external training (CPD) might help prepare CPs for an opioid service delivery by giving them specialised skills and knowledge. This will help boost their confidence to engage with the public as well as improve the service outcomes.

4.2.9.a.ii.b Interpersonal skills

All stakeholders believed that a lack of community pharmacy skills required for specialised services would make CPs less confident in proactively approaching people for medication counselling and engaging them with reviews. This might become a barrier for future service.

“When the pharmacist arrives in the field, (their) communication skills are not even developed... how can they convince people?” **Pharmacists Focus Group-1, P1**

Improved CP motivation, knowledge and developing good interpersonal skills can become a facilitator to reach service outcomes. A patient shared:

“So, I think the key to the people is that if anyone is explaining to them in a nice manner about medicines... even if they don't get too much information but they get happy on that... and they will accept it... and I think they will also follow the advice...” **Patient 13-Interview**

Policy makers and CPs shared that interpersonal skills might be improved by introducing community pharmacy clerkships as well as clearly defining roles and responsibilities of CPs in an organisation to help facilitate good inter-staff relationships and the successful provision of an opioid service.

4.2.9.a.iii.b CP clinical skills

Policy makers, CPs and doctors shared that CPs currently might not have adequate clinical skills that might be needed for delivering an opioid service. A policy maker shared:

“In our curriculum... the major focus... is towards industrial pharmacy... with that training and education... that pharmacist when goes into a community pharmacy cannot survive in that system... because he has not been trained...” **Policy Maker 5-Interview**

All stakeholders suggested introducing community pharmacy clerkships, including preceptors, including pharmacy practice and clinical contents and training pharmacists for opioid-specific knowledge will help with the proper implementation of future opioid service.

4.2.9.a.iii CP interest and motivation

Policy makers, CPs and doctors shared that CPs are motivated to provide patient services; however, they easily become demotivated in non-supportive pharmacies. A doctor shared:

“I have seen some pharmacists, who are very motivated... but as soon as they come in this field, like in a medicine shop they become demotivated... I don't know why... maybe they come with high hopes, but the general behaviour is disappointing...” **Doctors Focus Group-1, P6**

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Policy makers anticipated that most CPs lose their motivation because their perceptions and expectations of working in a community pharmacy is usually to participate in patient care or work in a managerial role, which is different to their current roles (dispensing, stocking).

“Our pharmacists... they have their own problems... their own tantrums, their own thoughts... they do not want to work in community setups. They think this job is not suited to their professional competency...” **Policy Maker 4-Interview**

Policy makers and CPs believed lack of career progression opportunities, societal perception of being incompetent and an unattractive salary package also contribute towards CPs; lack of motivation and might result in CP switching jobs or pharmacists moving out of the country. Lack of sufficient number of CPs may impact the nationwide implementation and scalability of an opioid optimisation service in future.

“I think other people will also agree with me if I say that pharmacists do not choose a community pharmacy as a career... It is only joined for a temporary stay... for maybe two, three or four years...” **Pharmacists Focus Group-5, P3**

“There is a stigma attached to working in community pharmacies... people think after university education you are working like a common shop keeper...” **Pharmacists Focus Group-4, P5**

“The pharmacist actually thinks that if the level for my compensation is this, why should I go to the next level and perform services... so until the government steps up, creates law, compensations, and a minimum fixed pay scale, CPs would be not happy” **Pharmacists Focus Group-5, P3**

“Many benefits abroad, so most of the pharmacists...ummm... they are flooding out of the country...” **Policy Maker 7-Interview**

Pharmacists also highlighted that this social perception, besides directly demotivating CPs, also becomes a huge barrier when they try to engage with people. Unless people are aware of the pharmacy profession, the acceptance of their advice remains low, which might impact the service in reaching its intended outcomes. Some pharmacists remained hopeful that the landscape of community pharmacy-based career is changing and one of them shared:

“In our organization... the pharmacist normally starts from branch manager, area manager, area head and then they go to the

corporate office. This is the complete hierarchy...” **Pharmacists Focus Group-1, P3**

Stakeholders suggested improving the motivation of CPs by offering them good remuneration, developing inter-disciplinary care models and improved public recognition as a healthcare professional. These steps may help them become a potential facilitator to deliver an opioid service in future.

4.2.9.a.iv CP security

Pharmacists and doctors shared that CPs do not have any local communication or complaint channels with their professional bodies, which could become a potential barrier for pharmacists who want to lodge complaints or bring attention to a particular problem, specially against their employer (current barrier) deterring them from properly delivering the opioid service in future.

“If you are getting a problem... In the community pharmacy and you want to report it somewhere... there is no procedure at all... who to approach... Who to tell...?” **Pharmacist Focus Group-3, P7**

“They (pharmacists) cannot challenge the entire system, they have to just exist and go with the flow of that shop, otherwise the owner will fire him...” **Doctors Focus Group-5, P1**

Both doctors and CPs suggested establishing networks and communication with their professional bodies as well as having government audit and feedback systems to help CPs with problems or issues they might encounter while delivering the service.

4.2.9.a.v Lack of job description

Policy makers and CPs highlighted that CPs might be assigned different roles in different organisations depending upon their organisational aims and vision as well as pharmacy management. Lack of defined job responsibilities of CPs in pharmacies, externally as well as internally might become a potential barrier to help deliver a standardised service.

“And their contract, nothing has been assigned... there is nothing that can specify... what the role of a pharmacist is...” **Pharmacist Focus Group-1, P2**

CPs shared developing clear guidelines and job descriptions might help define the role of CPs within organisations and help them deliver services properly.

4.2.9.b Organisational challenges and barriers for CPs

4.2.9.b.i Location

CPs and policy makers shared that the location of a pharmacy directly translates to the number of customers it gets and this can either become a facilitator or a barrier for CPs in delivering the opioid service, depending upon the CP workload workforce and the organisation/pharmacy's support for its CPs.

“The location... this also matters a lot... (people) exiting (hospitals) they will only go to that front row of pharmacies... So, if there is a hospital... and they have their OPD (outpatient department... in one building... so all the people... and (all) the OPDs they also run at the same time... (this) translates into a lot of burden on those pharmacies...” **Pharmacists Focus Group-2, P1**

All stakeholders shared that location might also impact the implementation of laws.

“Only the big medicine stores (reputed pharmacies) in prominent locations ... they have actually hired a pharmacist... you can find pharmacist over there... because they have a lot of customers, and it is very good for the business image...” **Patient 5-Interview**

Stakeholders shared strategies like strict implementation of laws and policies via enhanced regulatory systems might help overcome management reluctance to hire CPs, who can then deliver the opioid management service. Improved capabilities of CPs might improve the service outcomes and help with the sustainability of the service.

4.2.9.b.ii Organisational capacity for communications

Policy makers highlighted the lack of systems to connect pharmacists to doctors and one of them shared:

“The pharmacists cannot directly contact the physicians themselves because there is no communication channel, no electronic health record systems either, and so the CP has to say to the patient e.g. that the third medicine is not correct... please go and get this medicine changed...” **Policy maker 2-Interview**

For a successful opioid service, CP-doctor communication should be facilitated. Stakeholders therefore suggested strategies like new interdisciplinary models of healthcare, developing and switching to digital

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health systems and improving CP knowledge and skills to inspire confidence in CPs to talk to doctors.

4.2.9.b.iii Organisation culture and vision

All stakeholders highlighted that the aim and vision of an organisation or individuals who own or manage the pharmacies might become a facilitator or a barrier for CPs to deliver an opioid service.

“Where the community pharmacy setups or owners or even the pharmacists themselves have developed a specialised role...if you ever visit those pharmacies, over their CP provide wholesome services... medication related information.... and they are counselling patients for their medicines... they are also doing counselling for the disease management... about the limitations of the medicine as well...” **Policy maker 5- Interview**

Pharmacists and policy makers stated that old pharmacy businesses (owned by pharmacy technicians) and organisations that do not have qualified pharmacist managers could be unaware of the professional competencies of CPs, which could cause under-utilisation or reluctance of managers or establishments towards CP opioid service and may become a service provision barrier.

“If you go to a meeting, your in-charge is a non-technical person... if you talk to them about medication safety... concerned about medication misuse... they don't even know what antibiotics programs are, what is resistance...what opioids can do” **Pharmacists Focus Group-2, P3**

All stakeholders shared that the culture and vision of most pharmacies is to earn money, which might be a barrier for CPs trying to deliver the service.

“The role of a pharmacist is rationalizing the use of medicines... how can a pharmacist rationalize the use of medicine when the owner gets a profit from every box he sells? This is why we don't have pharmacies allowing pharmacists to do any clinical based roles in the community pharmacies...” **Pharmacists Focus group 4, P5**

However, CPs and policy makers highlighted that for independently owned pharmacies (pharmacist proprietor) and reputed chain pharmacies, brand recognition and establishing a reputation in the market to attract customers might also be a prime focus.

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Stakeholders suggested that supportive pharmacy management could be a facilitator for CPs to deliver an opioid service because they can help provide resources such as dedicated space, dividing daily pharmacy tasks, CP signposting and hiring of additional staff, all of which can support and improve the capability of CPs in delivering a future opioid service. Policy makers and CPs also suggested that compliance of CP management might be ensured by developing and enforcing CP-favourable strict.

4.2.9.b.iv Service compatibility with organisation

Stakeholders shared that if the opioid optimisation service generally remain compatible with the pharmacy's internal capacity and workflow it will have a better chance of adaption within the pharmacy and result in improved capability of CPs to deliver the service. One pharmacist shared:

“So, now if we talk about the initiatives... with some of the initiatives... later we realized that in some cases the patient does not want it... And our dispensing time actually increases because... of which the patient is not compliant on those activities... or maybe the pharmacy did not have that much manpower and eventually we had to forgo those activities...” **Pharmacists Focus Group-3, P1**

4.2.9.b.v CP autonomy

All stakeholders shared that optimising the use of opioids would require ensuring opioids are dispensed after a valid prescription, stopping polypharmacy and stopping self-medication of opioids. However, CPs and doctors shared as this lies against the business interest of most pharmacies, the lack of CP autonomy to refuse opioid dispensing within an organisation could become a barrier for delivering the future opioid service.

“We were actively told not to interrupt them... there were two opioids... with different brand names in a prescription... High doses. But we cannot say anything (stop dispensing) ... because we were specifically told not to say anything...” **Pharmacists Focus Group-4, P1**

“The pharmacist does not have any power... the managers in the community pharmacies they actively discourage pharmacists to perform these kinds of roles...” **Pharmacists Focus Group-5, P1**

Stakeholders suggested having strict laws and policies and their strict implementation might help overcome the organisational resistance and support CPs into delivering these services in the future.

4.2.9.b.vi Adequate staff

Stakeholders shared that most pharmacies are understaffed, which pressurises CPs to participate in dispensing medications and this would become a barrier for CPs trying to engage people as part of an opioid service. Huge patient load could also impact the time CPs get to spend with people as well as impact the nature and quality of advice given to people filling opioid prescriptions during future service implementation. A pharmacist shared:

“When I work on a Saturday.... because most of the clinics in the hospital in front of my pharmacy they are not working that day so the patient load which I receive is very less... so, I also laugh on myself... that day I become a true pharmacist... I really deal with the patients in a very good way... I communicate them in such a good manner... I'm doing such good counselling... but in the normal weekdays... Because there are so many people... even we are angry... the patients are angry... because they are waiting and, in such instances, we do not give time to the patient... not even counselling, just 1+1 or 2+2 and that too by writing on box (medicine)... not verbally...” **Pharmacists Focus Group-2, P1**

“The whole focus (becomes)... that in one hour instead of dealing three patients with quality... we (pharmacists) should handle 10 patients in that time...” **Pharmacists Focus Group-3, P1**

Adequate staffing might help CPs to engage with people; however, adequate staffing was identified to be linked to the organisational aim and vision and could become a barrier or facilitator for future service.

4.2.9.b.vii Organisation layout and workflow

Stakeholders highlighted that a CP's visibility and access by the public will impact the CP's capability to deliver the service. One of the pharmacists shared:

“Counselling counters are non-existent... missing...” **Pharmacists Focus Group-1, P2**

Some pharmacists highlighted that the presence of a CP might be deliberately hidden by proprietors because of fear of reduced potential sale of medicines. Whereas other CPs shared that the Schedule-G implementation requires CPs to be stationed near narcotic cabinets, usually found at discreet locations in pharmacies. While this offers CPs a strategic advantage to control the unauthorised sale of opioid medications, this could also compromise their

visibility and ability to interact with the public and might become a barrier for future service. Improving the visibility of the CP in pharmacies need to be focused on and pharmacy management and allied staff should actively participate in signposting people acquiring opioid medication towards CPs. This might help achieve a meaningful CP-public interaction and help achieve service outcomes.

“There should be a sticker or notice displayed in every medicine shop... that this is the pharmacist...how else will we know?” **Patient 1-**

Interview

4.2.9.b.viii Customer satisfaction

People and CPs shared that if a service or activity increases the satisfaction of customers, then people will focus on visiting only those pharmacies and this might result in increased business for that establishment.

“In the federal (capital), most of the pharmacies have a pharmacist just to increase their reputation and their sale, it shows they are a proper pharmacy, that’s why I prefer to go there...” **Patient 5-**

Interview

If people find the opioid service useful and with more people becoming aware and demanding to speak to CPs for opioid optimisation service, other pharmacy organisations might be inclined to adopt the opioid service and facilitate CPs, which might help and support the delivery of future service.

4.2.9.c Community and societal factors

4.2.9.c.i Community perception and awareness of CP roles

All stakeholders perceived that the public perception of CPs and their roles would affect the utilisation and acceptance of future service and may either become a barrier or a facilitator for service sustainability. CPs, people and policy makers shared that people, in general, lack awareness of CPs’ roles in managing medications and chronic diseases. A pharmacist shared:

“First of all, a layman has no... they don't even know what the difference between a pharmacist and a doctor is... before telling him anything you have to explain the role of a pharmacist... if you try to talk to him, they will consider you a doctor... this is... they will again and again ask for other medicines.... ask you to prescribe them...”

Pharmacists Focus Group-3, P5

Other stakeholders stated that people’s individual characteristics like health literacy, social norms, past medication experience, motivation to self-care, doctor’s guidance to consult CPs, CP awareness as well as dependence on medications like opioids are all determinants that may become facilitators or

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barriers towards acceptance of an opioid service in future. The quotes below give a brief overview, of different scenarios shared by CPs, which could affect a person's acceptance of CPs roles and their services.

"Most of the people who agree with the pharmacist... are those people who are familiar with the healthcare systems or setups or affiliated somehow with the hospitals... they know what a pharmacist is..." **Pharmacists Focus Group-4, P1**

"If we try to ask the patient... what is your problem... sometimes they will tell us, sometimes they don't... they are already stressed... emotionally, mentally, financially... they think we are trying to talk to them because we are going to add more medicines... so that we can sell more medicines... so as such people... pose a resistance... without any fault of theirs... let's be honest... because people don't know... how much a pharmacist can help them that is why they rarely seek a pharmacist..." **Pharmacists Focus Group-4, P2**

"Right now, people do not trust a pharmacist advice if it contradicts prescriber information... if you are a good pharmacist and you have convinced the patient... what happens is after that the patient feedbacks to prescriber... the prescriber gets angry... and starts questioning our authority and devalues our contributions ... next time the patient avoids talking to us when buying medicine..." **Pharmacists Focus Group-2, P1**

Strategies such as improving public awareness might help with public acceptance of future service and help reach service outcomes.

4.2.9.c.ii Public demand

People and policy makers shared a culture is now emerging where, people visiting pharmacies approach CPs for medicine information. They believed that the utilisation of future opioid service will be high because of an overall public interest in getting medicine information, convenience and potential benefits it might offer.

"Obviously... if we know everything about the medicine.... my treatment my condition will improve... Even if I don't get any benefit... then I can go to the doctor.... I can tell him his medicine is not working... maybe he changes it.... At least I will know that the medicine was supposed to do this... a pharmacist also knows about the medicine..." **Patient 1-Interview**

In addition, all stakeholders highlighted that in a democratic government, the political will to initiate policy changes is derived from public demand for such services and can intrinsically drive the politicians towards supporting the development of future public health services.

“If the government doesn't want any reforms... it is because they (the governments) are not pressured by the public, so no reforms happen...” **Doctors Focus Group-3, P5**

Stakeholders shared improving public awareness might help them realise the benefits of this service, which might help create a demand of this service as well as increase its utilisation and help with service development, delivery and sustainability.

4.2.9.c.iii Resistance of pharmacy technicians (chemists)

Pharmacists highlighted that pharmacy technicians might not be supportive of CPs future opioid service. CPs and policy makers shared that their reservations might be derived from their perception that new amendments supporting CPs will make them redundant as both are currently only involved in medicine dispensing.

“All of you must know... in 2016, 2017 in the last government... A law was made by the previous Punjab government... it is called Schedule-G... Proper notifications were made on the government level...and proper notifications, just to suspend that law... a law that was already made by a previous government... why... because all the owners (pharmacy technicians commonly known as chemist) they actually went on a strike...” **Pharmacists Focus Group-3, P8**

Policy makers and CPs highlighted that the role of allied staff is vital to help facilitate CPs in delivering an opioid service and developing specialised CP roles in patient care and clearly defined job responsibilities might help segregate CP roles from pharmacy technicians and help overcome their resistance and ensure their support towards opioid service delivery.

4.2.9.c.iv Perception of doctors

Mixed perceptions were presented, where pharmacists and patients highlighted that doctors might not accept opioid optimisation service because of professional rivalries, a lack of an interdisciplinary healthcare approach in the country and pharmaceutical marketing influencing prescribing practices.

“No, they (CPs) have the knowledge... but the doctors think of them as nothing... they think of them as rivals... they want to suppress them... if they have written a prescription, so (they believe) the pharmacist has no right to have any objection on that...even if they (CPs) are right” **Patient 11-Interview**

Doctors, on the other hand, remained very optimistic for development of an opioid service. Doctors shared that any reservation to CP opioid service would be derived from their lack of trust in pharmacist competency and not due to any non-professional or unethical reasons. One policy maker shared:

“I have seen both types of prescribers... those who would like a pharmacist’s intervention and those who don’t even like the pharmacist’s face... There are doctors... who actually ask the pharmacists for dose related queries... then there are also those kinds of doctors who will get very upset and offended... (even) if you try to correct them even with references...” **Policy Maker 5-Interview**

All stakeholders stated that it is important that doctors should support CPs in delivering the service, which will help it reach its intended service outcomes.

4.2.9.d System

4.2.9.d.i Laws and policies

Policy makers and CPs shared that there are currently no laws that support community pharmacy services, and this is currently a barrier for CPs to deliver an opioid service.

“A pharmacist can do nothing if the law does not give them the power to do... to practice according to law... and implement that...” **Doctors Focus Group-3, P1**

“See it should be mandatory by law otherwise people will find a way not to follow it” **Doctors Focus Group-5, P5**

Policy makers also highlighted that inadequate regulatory workforce and lack of strict penalties might also allow for overlooking of the laws in community pharmacies and could result in poor delivery of future service.

“It again comes back to the implementation of laws and lack of strict penalties... now when it comes to the implementation of law... see there should be accountability... until there is accountability nothing can be stopped...” **Policy Maker 2-Interview**

All stakeholders shared that CP-favourable laws should be established to support the development, implementation and sustainability of an opioid service.

4.2.9.d.ii Community pharmacy sector privatised

Community pharmacies in Pakistan are currently not considered a part of the healthcare system. A CP shared:

“Has the government decided a pay scale or a minimum basic pay for pharmacists in community pharmacy shops? The government has not even given an approval for a specific pay scale for the pharmacists in community pharmacy setups. These are privately owned businesses, private deals, nothing to do with government... So, the owners they, according to their choice or according to the revenue they generate... they pay the pharmacist...” **Pharmacists Focus Group-5, P1**

CPs shared that the lack of a properly governed remuneration system as well as less salaries paid by the owner of pharmacies can cause them demotivation to change careers, which may aggravate the problem of lack of a CPs, thus becoming a barrier for future opioid service.

All stakeholders suggested that developing government sponsored proper remuneration of services, will help facilitate the service delivery, its sustainability, as well as help overcome many barriers like resistance to adopting services by pharmacies or CPs’ lack of motivation.

“We need financial support for CPs in pharmacies... this should be looked at by the government...” **Policy Maker 2-Interview**

Policy makers’ support was identified as necessary for the advocacy required for the allocation of health budget to develop a service remuneration model for CPs and help facilitate service delivery in future.

4.2.9.d.iii Pharmacist policy makers

Pharmacists and doctors shared that health policy makers majorly constitute of doctors, who generally lack the motivation to advocate for CPs’ service development, which becomes a barrier for future service development.

“I think sadly what I can say... that the most senior in these positions is normally a doctor... and he does not understand the need of a pharmacist...” **Pharmacists Focus Group-1, P2**

“The thing is there is no pharmacist representation on policy level...”

Pharmacists Focus Group-4, P4

A CP also added:

“So basically, right now formerly the DG (district general) health, a doctor... was the acting head of the Pharmacy Council of Pakistan... so this is all confused... that is why no one knows who is responsible, and how to develop” **Pharmacists Focus Group-3, P1**

Stakeholders stated that in addition, the lack of pharmacy practice policy makers (Pharm-D) has been a substantial barrier for developing CP-based patient centred services.

“The people (pharm-B) in higher influential positions, in these regulatory bodies... Their concepts for the pharmacy profession are very old... they do not know the extent of what a CP or a clinical pharmacist can do nowadays... They are old school...” **Pharmacists Focus Group-5, P1**

However, policy makers shared that this barrier has been already identified at government level and one of them shared:

“In Pakistan, the current new government has created pharmacist position in the special health task force... previously in the special task force... there never was a pharmacist... but right now...there is a very senior pharmacist included... this is a very big change right now... the committee responsible to make the health policy... there are two pharmacists in that committee... they're both from pharmacy practice...” **Policy Maker 2-Interview**

Policy makers highlighted that recently an independent pharmacy service department within the ministry of NHSRC has been launched to facilitate the development of CP sector. This might become a huge facilitator for future opioid service development and sustainability.

“There are different sections now developed... there have been individual department's now in the health ministry for community pharmacy services... so this is the start... and I think we will see new services legally announced soon...” **Policy Maker 8-Interview**

Policy makers mostly remained hopeful that these new initiatives will give

pharmacists stronger legislative positions in policy making, and this will help provide advocacy, which will become a facilitator for developing, launching and supporting an opioid service in the future.

4.2.9.d.iv Pharmacy professional body role

Policy makers and CPs stated that the pharmacy council is understaffed and there is a deficiency of pharmacy council members in every province, which could act as a barrier towards prospective CP roles and competency development.

“Unfortunately, I think the pharmacy council needs to revamp itself... the whole staff constitutes of... one officer ...and one clerical position... There is no one else.... all the rest are honorary.... so, there is a process going on right now which is currently concerned with the revamping of the pharmacy council... we want to revamp the structure... till now it's a very conventional role... under which the pharmacy council is currently working...” **Policy Maker 6-Interview**

Other policy makers remained optimistic and shared that the pharmacy council has starting the development of CPD channels, which could facilitate the provision of training required for an opioid service and help in delivering it more effectively. One policy maker shared:

“CPE is not a theoretical phase... this has already been conducted and is working.... and the main focus of CPE is to build the role of community pharmacist and develop pharmacy services...” **Policy Maker 5-Interview**

Doctors and CPs shared that the lack of professional advocacy could be because members of the pharmacist representative bodies are themselves unaware of the specialised roles of CPs due to lack of exposure and expertise (B-pharm). They may lack motivation and the “will” to promote and advocate for the utilisation of pharmacists for patient-centered services and interventions.

“Councils and associations do; support, develop and progress... So, for pharmacists, this is the fault of the council... These oldies (senior, B-Pharm), when they don't own their pharmacists... they don't speak for them... then nothing can change...” **Doctors, Focus Group-4, P3**

“Currently at all the top positions right now are B-pharmacists... I might be wrong... but he might not know the proper role of a pharmacist... like how much a pharmacist can practice in the community setup...” **Pharmacists Focus Group-4, P1**

Stakeholders shared the lack of the professional pharmacist bodies' advocacy to the government could be a potential barrier for an opioid service

development and delivery. Another policy maker shared:

“Obviously the role of the pharmacy associations is very big and...if they don't outright speak for the pharmacist, then obviously this is a problem... definitely that will translate down an impact to the community or new services in hospitals or community pharmacies...”

Policy Maker 11-Interview

All stakeholders highlighted the value and importance of support and advocacy of pharmacy policy makers for a future opioid service development.

4.2.9.d.v Foreign funding

Policy makers and pharmacists shared that foreign funding is a strong stimulus for strategic policy alignment and focus of the government in Pakistan.

“Nowadays if government wants to work on something... they make it top priority... and why ... because they are getting a funding or donation for it...” **Pharmacists Focus Group-3, P1**

However, current lack of foreign funding to develop and promote CP roles in opioid optimisation was identified as a barrier.

“As far as pain is concerned... opioids are concerned...CPs... no funding has been promoted... I do not think...” **Policy Maker 4-Interview**

4.2.9.d.vi Pharmacy workforce

Pharmacists and policy makers highlighted that implementing an opioid optimisation service nationwide would require a massive number of pharmacists to be involved. They shared:

“See there are more than 70,000 medical stores in Pakistan... and qualified personnel are I think 25 to 30,000... there's still a huge gap...”

Policy Maker 3-Interview

“Even now, you can't find a pharmacist in more than 5000 pharmacies across the entire country” **Pharmacists Focus Group-5, P3**

Policy makers also highlighted that CPs are distributed non-uniformly, with more pharmacists in urban locations. Prominent reasons reported by stakeholders included lack of motivation, social stigma of being perceived as a shopkeeper, lack of jobs (rural), exploitation by proprietors and lack of growth

opportunities in the community pharmacy sector. It was also highlighted that pharmacists who want to pursue community pharmacy as a career are migrating abroad because of better remuneration, service conditions and social acceptance. Thus, policy makers shared even with an increased national capacity to produce pharmacists because of more pharmacy schools (facilitator), due to CP organisational challenges reduced CP workforce might be available to deliver future service and could become a service barrier.

“I mean pharmacists, they will not go and sit in rural areas and practice... no motivation... no incentives... no payment... so why?”

Policy Maker 4-Interview

“See initially we had CPs in hundreds ... but now we have in thousands...” **Policy Maker 11-Interview**

Other stakeholders remained optimistic about the adoption of future opioid service and stated that community pharmacy sector has now changed, especially because of new drug law amendments requiring CPs to be hired for narcotic dispensing. Stakeholders shared CPs can now be found in all major pharmacies in big cities to facilitate the implementation of Schedule-G amendments, and overcomes the barrier of lack of CPs.

“I'm sure there is not too many resources, or you know kind of things (changes), required from the state, for these services... it could be adapted right away...many CPs, everywhere...” **Policy Maker 9-**

Interview

Pharmacists also shared that an opioid service might be quickly adapted and help reach service benefits.

“I think the (current) role the pharmacists are doing to some extent is checking (reviewing) the prescriptions...so not an unheard role...”

Pharmacists Focus Group-2, P1

Policy makers, pharmacists and doctors shared that developing remuneration system, enhanced regulation, and enabling the support of pharmacy managements might help in increasing the CP motivation, which could help with the adaptation, scalability and sustainability of an opioid service in future.

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4.2.9.d.vii Quality assurance system

Policy makers and CPs highlighted that the current number of drug regulators is inadequate to support the regulation and strict implementation of the future opioid service.

“They (regulatory authority) have very less staff... even in a big district there are one or two drug inspectors... and they keep check on all these vast number of pharmacies... so, in reality, it is impossible for two people to keep a check on all these pharmacies in the district... until and unless... there is a team of at least eight or nine members in a district... service, making sure it is being delivered... it needs people (regulators)...” **Policy Maker 8-Interview**

Pharmacists and doctors highlighted that a possible strategy is for the government to focus on reforming the pharmacy regulatory bodies and increase the number of regulators, which will help provide uniform and standardised regular checks and ensure fear of accountability for CPs and pharmacies and thus facilitate the implementation of a future opioid service.

“When an auditing system is proper... there is no way people will not follow it... when the implementation of the law through the regulating bodies is enforced...” **Pharmacists Focus Group-1, P2**

4.2.9.d.viii Lack of communication systems

All stakeholders shared that currently there are no digital health systems that can facilitate CP-prescriber communication and this remains a barrier for an optimum opioid service.

“No, absolutely not... no communication. The doctor and pharmacist are separate. They are not linked as far as I am aware... there is no computer system connecting them... and they're not working together...” **Patient 3-Interview**

Others added that a lack of digital health systems implies there are no databases or records of number and type of medicine prescribed or dispensed to a person for CNMP management, which could become an additional barrier for pharmacists trying to optimise opioids for the management of CNMP. Policy makers and doctors shared that developing a digital health system is a current priority of the government and might help improve the service fidelity and help reach service outcomes.

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4.2.9.d.ix Strategic policy alignment

Stakeholders shared that revising health policies and upgrading health systems requires political will, which is derived from many extrinsic (UHC directives, foreign pressure, SDG) and intrinsic factors (national socio-political context), which can either become barriers or facilitators in the overall development and implementation of a future opioid service.

“The thing I feel could influence the implementation and development of these kinds of initiatives is sustainability and the desire to achieve and develop Pakistan as an advanced state... so WHO, UHC... so these kinds of external influences are important... if there is a political will these things can happen...” **Policy Maker 8-Interview**

Policy makers shared the government has identified a deficiency in the pharmacy sector; therefore, the government is hiring consultants from different pharmacy sectors such as community, hospital and industry to understand and promote the current needs of the public and harness the potential role of the pharmacy workforce, which becomes a big facilitator for developing and implementing specialised services like CP opioid service.

“National Medicine Policy... after so many years it has been revived... there is an emphasis on developing the community pharmacy...” **Policy Maker 7-Interview**

Others added that an opioid service aligns with the government’s interest to optimise the use of medications as part of UHC agenda and will help decrease the load on the government health facilities, which might be another strong facilitator to developing these services.

“The thing is that the government is taking it very seriously... they are strictly monitoring all these kinds of things especially with medicine safety issues... there are reforms in the healthcare sector...” **Policy Maker 11-Interview**

4.2.9.e Service characteristics

4.2.9.e.i Nature of innovation

All stakeholders shared that currently there are no mandated community pharmacy-based medicine review services. CPs might be providing volunteer services, which are unregulated and non-uniform in nature. Thus, an opioid optimisation service would be a first step towards CPs providing legalised patient-related service and is expected to face a lot of innovation challenges.

“The community pharmacy setup is still not built and there are no pharmacy services... would be challenging” **Policy Maker 9-Interview**

Current facilitators, according to stakeholders, include the government's current agenda to improve public health, Schedule-G enforcement and increasing public awareness.

4.2.9.e.ii Duration of intervention

CPs shared due to lack of patient medical records in pharmacies, lack of prescriptions (majority of times), absence of past medicine information as well as public health illiteracy, they might require substantial time analysing, rationalising and individualising opioid medications in the review stage in opioid optimisation service. This could potentially lead to long queues, increased patient wait time and may result in patient disengagement, which might become a barrier for service delivery. However, people with CNMP remained optimistic and one person shared:

"If I think the pharmacist has enough knowledge.... he understands my situation... he understands my other diseases... I will of course be very willing to speak to him... I will wait for him to review my prescription..." **Patient 5-Interview**

All stakeholders suggested that a possible strategy to overcome public disengagement would be to improve the awareness of people about the benefits of this service despite the long waiting times. In addition, improving CP skills and improving their capabilities might help towards service fidelity and might help in reaching service outcomes.

4.2.9.e.iii Cost of intervention

Policy makers highlighted that currently there are no government-sponsored payment models for CPs as they work in privately-owned businesses. Doctors, pharmacists and policy makers discussed that maybe patients should pay for this service as they pay for other health-related consultations as the Pakistani healthcare system already relies on out-of-pocket payments by the public. However, other policy makers remained opposed to it. One policy maker shared:

"Patient is bearing the cost of the entire health system... so it is very difficult (to pay for more services) ... in our country... the economy! the per capital income... is not sufficient that he can pay the doctor... and pay the pharmacist for community pharmacy services... this is not a possibility right now... the patient is managing the doctor fees, with much difficulty..." **Policy Maker 2-Interview**

People with CNMP and policy makers also highlighted that because patients bear the cost of private consultation services with doctors, this has already

given rise to an increase in self-medication and relying on the public to pay for opioid optimisation service would become a potential barrier for utilising this service.

“This (payment) would really become difficult... but health should be free... doctor should also be free... pharmacist should also be free... the government should sponsor this... it will not be difficult then...” **Patient**

2-Interview

Doctors and policy makers suggested that this service should be mandatory without any additional payment. But all stakeholders agreed without a suitable remuneration model, CPs might not be motivated to deliver the service properly and the quality of service could become questionable. Doctors, CPs and policy makers stated that a possible strategy to improve service delivery would be to remunerate the CP opioid service as a healthcare service. A policy maker also shared a possible facilitator:

“Right now, the health minister is really focused to develop health reforms... for improving public health, these services will be well supported...” **Policy Maker 9-Interview**

Policy makers shared although there is no pharmacy services payment model. With the government currently focused on involving CPs in public health initiatives, payment models can be developed provided there is sufficient advocacy by policy makers and substantial benefit of these services to the system.

4.3 Subchapter C: Discussion of findings from interviews and focus groups

The following section now provides a discussion about the major findings identified in this chapter.

4.3.1 Unavailability of potent opioids and uncontrolled pain

Chronic pain management often presents as a challenge to both patients and their healthcare providers [284]. My study identifies further challenges such as lack of pain management centres [40, 285-287], potent opioid medications, lack of potent analgesic medicines [288, 289], and specialist doctors in Pakistan that might be contributing to people suffering from unmanaged CNMP.

Morphine, despite being listed on EML of Pakistan, is non-existent in primary care and remains available in tertiary setting hospitals only and is restricted to specialised oncology and cardiology units [289]. This situation is similar to other LMICs where opioids for the management of CNMP remains partially available or entirely inaccessible [288, 290]. Therefore, similar to my study, many studies from LMICs report that people might be suffering from inadequate analgesic relief and continue suffering from CNMP [40, 291]. My study findings show that lack of availability of opioids is due to the government's fear of misuse. This is also reported by other studies from LMICs [274, 292] where governments due to "opioid phobia" have limited access to opioids as a strategy to reduce misuse and diversion. However, national policies in LMICs including Pakistan need to be careful regarding banning opioid analgesics due to fear of misuse, because studies from the US highlight that revised opioid safety health policies, aimed at controlling prescription opioid misuse, decreased prescription opioid misuse and diversion but resulted in an unintended consequence of providing motivation to people with opioid use disorders to shift to illegal opioid substances, failing overall to decrease opioid-related mortality [293-297]. It is well established that people using opioids might make a switch towards illegal substances such as heroin (diamorphine) [298-307]. Interestingly, my results also report there could be a possibility that people might be switching to alternative illegal substances (diamorphine [heroin]) because of absence of effective opioid analgesics to manage severe debilitating pain. Studies from other LMICs also report natural opiate use has declined with an increase in prescription opioid (pharmaceutical) misuse such as tramadol, nalbuphine, codeine, fentanyl and buprenorphine, particularly in Bangladesh, India, Nepal and Pakistan [101]. Pakistan already has a very high number of heroin (diamorphine) addicts

amongst the southeast Asian countries [308-311]; therefore, further research is warranted to understand any possible connections of people with CNMP with resolved or unresolved pain, past opioid medication history or concurrent history with future illicit drug seeking behaviours.

4.3.2 Factors contributing towards unsafe use of opioids

4.3.2.a Inadequate regulatory system and workforce

My study findings highlight that currently there are many health system level challenges and weaknesses such as inadequate regulatory systems, lack of access and unequal healthcare resources, poor quality of digital health systems, corruption in the health system, weak implementation of drug sale laws, easy availability of medicines, practising quacks and black-market distribution and sales of controlled items throughout the country, which might be contributing towards the non-availability of opioid medicines as well as unsafe use of opioids. Similar to my study, Bashir et al. (2021) [112] reports that despite Schedule-G amendments, opioids remain freely available for dispensing and purchasing by the public without a prescription or even a CP present. Other studies [312-314] from Pakistan also highlight lack of an adequate regulatory workforce for medicines regulation that leads to nationwide inability and competence to regulate medicines and medicine services by regulatory authorities.

The ability to purchase POMs without a prescription is an ongoing problem reported in LMICs and raises serious concerns for patient safety [315-317]. Other studies [318, 319] from LMICs also report easy availability of medicines, lack of regulatory checks and untrained or unlicensed staff in medicine outlets involved in dispensing and prescribing, majorly resulting in self-medication and contributing to the unsafe use of medications.

4.3.2.b Digital healthcare systems

My study highlights that Pakistan lacks patient electronic health records as well as drug utilisation data due to inadequate digital health systems. Digital health systems can help track the prescribing and dispensing of opioids and can be valuable tools for prevention and identification of opioid drug misuse, diversion and inappropriate prescribing [320]. In advanced countries like US the [321] and the UK [322], prescription data monitoring systems (PDMS) have been utilised to identify high opioid prescribing from certain locations. Although, Pakistan currently may lack the ability to gather reliable healthcare data, developing digital systems might help identify opioid-related adversity and may help improve patient safety in people with CNMP conditions.

4.3.2.c Inappropriate or inadequate prescribing

My study findings indicate that most doctors in the government healthcare facilities are overburdened and might not have time, enough patient

information or necessary facilities such as independent consultation rooms, which could negatively impact the overall quality of care provided by them and can increase the risk of unsafe use of opioids. Similar facts have been reported by another study from Pakistan [323], where overburdened doctors were found to be a significant risk factor for increased prevalence of medication errors. This is also evidenced by the findings from a 2016 study from Pakistan, which reports that among 300 randomly selected patients in 10 primary healthcare centres an average consultation time of 2.2 min (standard deviation (SD) = 0.8) with doctors was recorded.

People also shared that the doctors lacked empathy towards their condition and would not entertain their concerns regarding the lack of effect of pain medicines. These findings are not unique to Pakistan and a study conducted in the UK by Hadi et al. (2017) [324] also reported that people with CNMP shared that doctors spent less time in consultation and lacked empathy towards their pain. The study recommended that patient inclusivity, understanding and acceptance might be necessary for the success of pain management treatment. Policy makers should look into involving CPs who could provide opioid medication reviews and patient counselling that might help promote the safe use of opioids.

4.3.2.d Pharmaceutical industry

Another finding highlighted by this study was that doctors might participate in irrational prescribing of opioids including polypharmacy as well as engage in therapeutic duplications because of pharmaceutical company incentives to prescribe more medicines. Other studies from Pakistan also report that more than half of pharmaceutical companies in Pakistan engage in unethical marketing and promotional activities [325-327] and were identified as a factor in irrational prescribing of medicines. Pharmaceutical marketing influenced doctor practices is not unique to LMICs and has also been reported in developed countries such as New Zealand [328] and the US [329, 330]. In the US, pharmaceutical companies pushed opioid prescriptions by inappropriate pharmaceutical promotions, which became a major contributing factor towards the opioid crisis and resulted in enormous opioid-related mortality and morbidity [329, 331, 332].

A recent 2021 global opioid consumption report [97] suggests that the pharmaceutical industry has shifted its marketing strategy to new economies in Latin America, Asia, Middle East and Africa and might be using aggressive marketing practices similar to those that precipitated the opioid epidemic in the US. As evident from studies from Pakistan [325-327], irrational prescribing might be prevalent and thus national policy makers as well as international organisations like WHO, UNODC and IASP need to carefully plan strategies along with Pakistani government in order to overcome opioid-related

adversity.

4.3.2.e Lack of CPs and non-pharmacy dispensers and salespersons

This study indicates that medicine stores and pharmacies might be run by pharmacy technicians or salespersons who might engage in excessive opioid dispensing and prescribing (advice) without any authorisation and contribute to the unsafe use of opioids. This was attributed to the fact that most establishments do not hire CPs despite drug rule amendments due to lack of regulators and regulatory visits. It should be highlighted that despite Schedule-G amendments, even in pharmacies with a CP, medicine outlets in Pakistan still operate without the involvement of pharmacists and this could enable many problems to continue in the society such as self-medication, adverse drug reactions, medication errors, inappropriate use of opioid medicines, OTC availability of POMs and lack of medication reviews. This remains congruent to findings from other South Asian LMICs [333]; although there are often statutory requirements that the owners or managers of medicine selling establishments should have a degree in pharmacy or hire a pharmacist, the operational activities including dispensing of opioids are often run by non-certified assistants or salespersons who have little knowledge of the medicines they are dispensing. These findings have also been reported in other studies [334, 335] from Pakistan that report that the lack of CPs involvement results in unsafe use of various medicines.

4.3.2.f Self-medication

Chronic pain is one of the most documented reasons for self-medication as a first response towards CNMP [336]. My study highlights that due to easy availability of POMs, people might be self-medicating with opioids for obtaining relief from CNMP. Problems identified in this study due to self-medication were lack of medication reviews, drug-drug interactions, side effects, tolerance, and drug dependence and misuse, which can substantially increase the risk as well as overall patient costs [337]. Similar findings are reported in other studies from Pakistan reporting self-medication precursors such as easy availability of medicines, lack of public awareness, influence of pharmaceutical marketing, lack of regulatory checks, poverty, social norms, lack of access to health facilities and untrained or un-licensed staff administering and dispensing medicines [318, 319, 338].

4.3.2.g Unauthorised opioid administration and quacks

My study findings report that to obtain effective analgesic relief from persistent uncontrolled CNMP, people might visit quacks who prescribe, dispense and administer opioids, and thus could be contributing towards the unsafe use of opioids. Although not looking specifically at opioids, a 2019 report [339] from the Punjab province in Pakistan stated that 70,000 to 80,000 unqualified quacks were involved in illicit medical practices as well as

prescription of all kinds of medicines, including veterinary medicines. My study reports that people from far-flung and remote areas might prefer to get medications, especially injectable opioids, from quacks because the health facilities are difficult to access. Other reasons highlighted were the convenience of getting medicines as well as lack of health literacy, which might be contributing towards people approaching quacks. Lack of public awareness, poverty and non-availability of health services is also reported in other studies [340-342] from Pakistan, which were found to be prompting people's visits to quacks.

4.3.2.h Opioid dependence

My study results show that developing tolerance or dependence on opioids could prompt people to use more opioids (frequency) or in a higher dose than before in order to achieve satisfactory analgesic relief. Other studies [343, 344] also report people using more opioids than the recommended advice and could probably exhibit 'opioid seeking behaviour'. The effect of opioid-seeking behaviour have been detrimental in terms of opioid-related morbidity and mortality [79, 80]. Thus, monitoring, counselling as well as giving people with CNMP opioid-related medicine information is essential to promote the safe use of opioids [345]. As doctors were identified to be overburdened in my study findings, developing the role of CPs in patient education and opioid optimisation might help optimise the use of opioids.

4.3.2.i Health literacy and lack of information sources

Studies [346, 347] report that people's knowledge and attitudes are important contributing factors towards self-medication, misuse and diversion of opioids. My study highlights that people with CNMP in Pakistan might have less health literacy, awareness and knowledge regarding medicines and pain management, which could be majorly contributing towards their unsafe use of opioids. Low health literacy has also been reported in another study from Pakistan to have a negative impact on the use of medicines [348]. A 2020 US study [349] also highlights the relationship of health literacy with the use of opioids and reports it may contribute to opioid misuse as well as results in an overall unmanaged pain experience in people with chronic pain. My study identifies that improving health literacy regarding pain management and opioid optimisation can be improved by involving CPs as well as through public educational programmes and this remains congruent to other studies [350-352] from Pakistan advocating for the role of CPs in patient counselling.

4.3.2.j Doctor shopping

People in Pakistan can visit as many doctors as they want (doctor shopping), which might be resulting in polypharmacy, therapeutic duplications as well as significant interactions and may exacerbate unsafe use of opioids in people with CNMP. Significant factors precipitating doctor shopping reported in my

study are social beliefs, insufficient pain relief and mistrust in doctors. Rasool et al. [353] also highlights that doctor shopping in Pakistan was found to be linked with an increased risk of polypharmacy, drug interactions and an increased overall healthcare cost [353]. It is important to highlight that doctor shopping was one of the biggest contributors in opioid crisis in the US [354] in people with OUD. Although the precursors for doctor shopping in Pakistan currently differ from US [355], the consequences in terms of opioid safety for people remain real. In addition, in LMICs like Pakistan, people are not just doctor shopping [355, 356], my findings report that they might engage in “pill shopping or pharmacy shopping” due to easy availability of medicines without prescriptions as well as lack of electronic prescription or dispensing records. Both these phenomena can contribute significantly towards the unsafe use of opioids. My study highlights that developing the role of CPs could help reduce self-medication and help control unauthorised pill shopping and ensure controlled dispensing that may help promote safe use of opioids.

4.3.3 Determinants and possible strategies for delivering a future opioid service model

The following paragraphs discuss the factors identified in my study that can either facilitate or become barriers for future opioid service provision by CPs. Please note that a recent study by Aziza et al. (2022) [357], takes a similar approach to my study and explores the role of CPs in opioid optimisation in the UK. The authors used a similar methodological approach to my study by using qualitative exploratory methods to understand the current barriers and facilitators to providing an opioid optimisation service in community pharmacies in the UK. Even though the UK and Pakistan are widely different, surprisingly many factors in their study are congruent to my study findings. Nevertheless, the context of the factors substantially varies in both countries and thus instead of presenting them altogether here, I have presented them across various subheadings in the discussion chapter to provide a more coherent discussion.

4.3.3.a Availability of community pharmacists

In terms of facilitators identified towards the opioid service provision, my findings show there might be an increased trend of CP hiring in pharmacies in urban locations due to recent drug rule amendments. Increase in the number of CPs have been reported in other studies from Pakistan too and could help deliver CP services in future [149, 358-362].

Similarly, barriers identified in my study such as lack of uniform availability of CPs across the country also remains congruent to the findings of other studies from Pakistan [149, 358-361]. The lack of pharmacists in Pakistan is also highlighted in WHO’s Implementation Strategy Report (2011) [363], which stated that Pakistan had 0.61 pharmacists per 10,000 population and clearly

indicates the shortage of pharmacists as per the need of the population [364]. In the USA, there were nine and in France 11 pharmacists were present for a population of 10,000. It is important to acknowledge that this workforce density of pharmacists in Pakistan is representative of only the registered pharmacists at the time of graduation and is not a true reflection of how many pharmacists are currently working across different sectors of the pharmacy profession. The workforce situation might be more dire than anticipated with more pharmacists' leaving the country to take up jobs to improve their livelihoods in better positions in other countries [365]. A 2018 Matloob, et al's study [366] from Pakistan shows that there might be an approximately 50% percent shortage of pharmacists due to excessive turnover.

In addition to an overall pharmacy workforce shortage, the major barrier for a future opioid service is the shortage of CPs in Pakistan. Two studies, Ali and Khan (2016) [367] and Haq et al. (2017) [368], reported that Pakistan had around 8,100 registered pharmacists and around 31,000 pharmacy technicians and diploma holders in 2015, but there were more than 50,000–63,000 wholesale and retail drug outlets in the country at that time. According to the latest available WHO global health workforce observatory data [369], in 2019 there were 33,455 registered pharmacists (1.55 pharmacists per 10,000 population) in Pakistan. Shortage of CPs is also highlighted by the PCP [370], who reported that around 70% of graduating pharmacists work in the industrial sector, while only 10% are currently working at community pharmacies.

Similar to the reasons identified in my study, other studies from Pakistan also state that the lack and non-uniform distribution of CPs — despite increased number of pharmacy schools — might be attributed to the lack of opportunities in rural areas, minimal salaries, resistance of medicine store employers to hire CPs and weak regulation [149, 358-361]. A 2013 study by Azhar et al. [371] remains in congruence to my findings and reports that the lack of proper remuneration and opportunities in community pharmacies are the reason for low percentage of pharmacists working in the community pharmacy sector.

My study added other reasons beyond those already known in literature about the lack of pharmacists in the community pharmacy sector. The findings showed that there might be an overall lack of motivation and enthusiasm of CPs working in pharmacies due to the social stigmas associated with a CP's duties, like medication dispensing, which are perceived to be similar to the role of non-pharmacist staff (pharmacy technician or a non-graduate salesperson). In addition, the lack of professional autonomy due to non-supportive and exploitative pharmacy managements and the insecurity

of CPs due to lack of complaint channels with pharmacy professional bodies might result in less pharmacists choosing community pharmacy as a career. Other reasons observed in this study also showed there could be a possible lack of social desirability and disrespect of the public towards their patient engagement roles, which might also be contributing to CP demotivation and reluctance to work in pharmacies. All these factors as well as those listed in other studies [149, 358-361, 371] can impact pharmacists' motivation and result in an overall less inclination to choose community pharmacy as a career and progress in it, which aggravates the problem of lack of CPs and becomes an opioid service barrier. Lack of CPs is not only limited to Pakistan but is also common in other developing countries [372], and neighbouring countries like India [373] and Bangladesh [374] have also reported similar socio-ecological barriers contributing towards absence of CPs in their respective countries. My findings support that supportive policy initiatives as well as developing standard guidelines, improving the work conditions, developing CP remuneration models and career growth opportunities might be substantive strategies to improve the CP motivation and increase their inclination to join pharmacies. This in turn can promote their presence and help deliver an opioid service with proper motivation that might help reach service outcomes. Other identified strategies to improve the motivation of CPs recognised in the study were an increased regulatory workforce and developing quality assurance systems that might be able to overcome non-supportive pharmacy management and facilitate hiring of CPs and facilitate the adaption of an opioid service in the future [375].

4.3.3.b Lack of regulatory bodies and quality assurance systems

My findings highlight that there is currently an inadequate regulatory system, that becomes a barrier for a future opioid service. This is consistent with other studies from Pakistan exploring the development of community pharmacy services [312, 313]. Interestingly, the impact of 'lack of regulatory visit' was also observed to be linked to Schedule-G's weak implementation and in majority establishments pharmacy technicians and salesmen were observed to be dispensing opioid medicines without a prescription or even the involvement of CPs. This remains consistent with findings from other studies from Pakistan who also report that pharmacy technicians and salesmen commonly engage in providing medicine-related information and prescribing medicines including all kinds of POMs as well as OTC medicines [376-378], even as they might have less knowledge about diseases, medication, storage and procurement of medicines as compared to pharmacists [112, 313, 376, 379, 380]. My study also found that in the absence of CPs or in busy hours, the non-pharmacist staff was found to be dispensing opioids despite the legal requirements as well as providing

information to people. For a successful CP service provision, it is imperative that there is a 'meaningful' interaction of CPs with the public, thus non-pharmacist staff dispensing opioids represents a missed opportunity for medicine information exchange and interaction and can impact the delivery of the service and could result in compromised patient care in future.

My findings suggest strategies like regulatory reforms, increased number of regulators, developing quality assurance systems and developing clear laws, policies and guidelines will help ensure CPs are present in pharmacies and are involved in patient interactions while dispensing opioid medications, which might help achieve service outcomes.

4.3.3.c Lack of pharmacist representation in policy making

My study highlighted that Pakistani health policy makers have been predominantly doctors and there is a lack of pharmacist representation at the policy level, which was identified as a development as well as a service delivery barrier [381]. This has also been reflected in other studies from Pakistan where the lack of advocacy by policy makers has been highlighted as a reason for lack of community pharmacy practice services so far [360, 382]. However, a facilitator identified in my study was that under the UHC agenda the government is promoting and developing CP roles in healthcare to improve the use of medicines and increased access to essential medicines and thus have involved pharmacists in the policy making mandate. The National Health Vision Pakistan 2016–2025 [383] also highlights inclusion of pharmacy policy makers in centralised health policy making to develop and improve the pharmacy profession and becomes a facilitator for CP opioid service development [384]. Support and advocacy of policy makers for the development and successful delivery of pharmacy services has also been reported as a strategy in another study from Pakistan [385], as well as is one of the ASHP Opioid Task Force report (2019) [386] strategies.

However, it is essential to highlight that policy making can be influenced by many extrinsic factors such as political gains of politicians, health policy strategic focus and directives, international funding, public demand as well as intrinsic factors like belief, motivation and personal values of the policy makers.

4.3.3.d Privatized healthcare, remuneration models and payment of services

Community pharmacies in Pakistan are privatised and thus the government lacks a service structure for payment to CPs. In my study, three models were proposed: out-of-pocket public payment systems, inclusion of CP-based services as a mandatory practice within pharmacies with no extra payment and extra payment of services to CPs by the government for service provision. As Pakistan is a LMIC, out-of-pocket systems might further increase the social class difference and health inequality and may further destabilise the UHC

agenda that aims to improve access to medicines and services without incurring additional costs to people. Poverty has been highlighted to be linked with health inequity in other LMICs as well [387].

Another proposal was to make the opioid service mandatory as part of existing job requirements. This was perceived to work initially in the trial phase but a lack of incentives for service provision could impact CP motivation. My findings report that appropriate payment of a service can motivate CPs to deliver the service properly and help reach service outcomes. This is similar to the study by Aziza et al. 2022 [388], which states that opioid optimisation by CPs need to be remunerated as a service otherwise the lack of CP motivation can hinder the quality of service provision. Similarly, a recent community pharmacy exploratory study by Hashmi et al. (2022) [389] in Pakistan also advocates that regulating and remunerating the community pharmacy sector as health services might help with the success of future CP patient-centred services.

It is important to highlight that while a lack of compensation for CP patient care services is a commonly cited barrier to service provision, a 2019 systematic review [390] showed mixed evidence of the effect of remuneration on CPs behaviour change in regards to achieving intervention outcomes. Therefore, whether remuneration of an opioid service in Pakistan might help reaching future service outcomes needs to be further explored. Nevertheless, developing a remuneration model for CPs in Pakistan might not be easy and allocation of sufficient health budget could either facilitate or become a barrier for future services. This is implied from the fact that historically governments in different political tenures have allocated different health budgets [360, 391]. Pakistan usually allocates a low budget to its health sector. To put things into perspective, according to World Bank estimate (2017-18) [392], Pakistan spent \$45, Iran spent \$484, and Qatar spent \$1,716 per person on health per anum. The World Bank estimated that to implement and achieve the UHC agenda, Pakistan needs to spend \$86 per person per anum in the next 5 years. A 2017 Lancet study [393] also predicted that improved health disparity in Pakistan requires increased allocation of government funds for improved health. Proper advocacy of policy makers with evidence-based benefits of opioid service could motivate governments to assign health budget and develop remuneration systems.

4.3.3.e Communication with doctors

My findings report that CPs communicating with the doctors might result in an optimised use of opioids. Similarly a 2018 survey from Canada [394] also reports that most CPs (89.6%) (n= 542) need to contact physicians in one to three out of 10 opioid prescriptions, but many pharmacists (71.8%, often or very often) reported difficulties communicating with physicians. Although my

study findings show that developing digital systems might be useful to connect CPs with doctors, Aziza et al.'s (2022) study [388] shows that it might be difficult to get doctors to use these communication systems and was reported to be impacting CP motivation for service provision.

My findings report both positive and negative perceptions of doctors about developing the role of CPs in opioid optimisation and could either facilitate or become a barrier for an optimum service provision. The following paragraph presents the three major reasons identified in my study as to why doctors might have apprehensions and may not collaborate with CPs.

Firstly, participants in my study shared that those doctors who might be unethically prescribing opioids due to pharmaceutical company marketing might not be supportive of CP roles, as the opioid optimisation service includes rationalisation of opioids and decrease unnecessary usage and sales of opioids. Another reason was that CPs advising people to go back to doctors for dose or medicine alteration was perceived negatively by doctors as CPs creating public mistrust in their advice. The third reason for doctors' resistance towards CPs' roles was the lack of confidence in CPs knowledge and skills. This remains in congruence to another study findings from Pakistan [395] and doctors in their study remained apprehensive towards pharmacists providing patient care without receiving any training.

A contradiction to the above perception was also found in my study, where majority study participants including doctors were keen on the development of CP roles in opioid optimisation and viewed CPs as necessary healthcare professionals helping manage patients with chronic pain conditions, opioid dose adjustments, patient counselling, medication review and ADR monitoring relevant to opioids. This remains consistent with other studies from Pakistan [396, 397]. However, it must be acknowledged that none of the studies from Pakistan so far have specifically explored doctors' perceptions about developing CP roles specific to pain management or opioid optimisation.

Thus, a coordinated and upskilled multidisciplinary health workforce is required, using the full skill set of all health professionals. Legislative support and guidelines might help enable and support interdisciplinary trust and collaborative team approach and help lead to better service outcomes.

4.3.3.f Public awareness of CP roles

My study identified mixed views about the perceptions of the public towards the acceptance of CP roles, which again can impact CP capability to deliver the proposed opioid service as well as having their advice accepted. Findings indicated that the majority of the public lack awareness about CPs role in medication management, consistent with the findings of other studies from Pakistan [398-401]. Aziza et al. (2022) [388] also reported that public attitude

and acceptance might be a challenge for UK CPs while delivering an opioid service and may impact reaching service outcomes.

My study as well as other studies [402, 403] highlight that improving public awareness of CP roles might lead to improved utilisation of CP services as well as help ensure that people accept and follow the advice given by CPs and help reach service outcomes.

4.3.3.g Community pharmacy management

Successful delivery of community pharmacy-based services requires community pharmacy management support [403]. However, my study indicates that pharmacy management decisions to support an opioid service delivery remains contextualised and may become a barrier or a facilitator towards enabling CP capability to deliver the service and achieving outcomes. Findings reported that when the pharmacy management perceives the service to be in contradiction to their business motives, they might not facilitate or support CPs to deliver the opioid service. Two studies [389, 400] from Pakistan also report that in Pakistan the prime focus of most pharmacies is profit making rather than patient care. Both studies indicated that non-supportive organisations might be responsible for CPs resigning from working in non-supportive establishments and this can become barrier for future services, which is also reported in my findings. This is also reported in a 2019 US study [404], where CPs shared that the management would pressurise them to abandon activities that might reduce the sale of opioids. The US study presents similar findings to my study, that the compliance of pharmacy management to services can be ensured if they value and believe that adapting and delivering such services will be beneficial for their organisation's reputation in the market, ensuring loyalty of customers and improved business [404].

Another consequence of non-supportive management identified in this study was the lack of time and resources available to CPs to engage with patients. Similar to my findings, Aziza et al.'s [388] study also reported that CPs need time to review each opioid prescription and having a detailed conversation with every patient would not be feasible without additional staff present to help with dispensing of other medicines.

The opioid task force report (2019) [386] suggests that policy makers should provide service delivery roadmaps to support organisational change to achieve effective delivery of opioid stewardship programmes and services. Such initiatives supported by policy makers might help guide the regulators to ensure that CPs are provided the best environment and receive adequate support within organisations to help with the service delivery leading to service outcomes.

4.3.3.h Knowledge and training

My study findings suggest that although CPs might have good theoretical knowledge about opioids, they might lack advanced knowledge and skills required for opioid service provision in community pharmacy settings. This remains consistent with findings from many studies from Pakistan [149, 400, 405-411]. My study identified a lack of community pharmacy residency programmes and the absence of a clinically-focused curriculum might be contributing to the deficiencies in the skills of Pakistani pharmacists. Similar to my study findings, other studies from Pakistan [149, 410, 411] also report that the lack of clinical preceptors as well as shortage of clinical and pharmacy practice academics teaching undergraduate degree programmes might be responsible for the deficiency in practical skills required for community pharmacy patient-centred services. My findings highlight that due to deficiency in knowledge and skills, CPs might feel less confident to engage patients and that could become a barrier for future services. This is in congruence to the study by Aziza et al. (2022) [388], which also identified hesitancy to engage patients due to deficiencies in the knowledge and training of CPs specific to opioids management and shared that UK CPs do not receive any formal courses or training on how to review opioid prescriptions and identify misuse [388]. Similarly, only around 16% CPs in a 2014 study [412] from the USA (n=640) reported that they had received training regarding opioid management in their undergraduate degree programmes and very few reported to be confident to communicate with patients about opioid prescription misuse.

My study suggests that improving the knowledge as well as providing training opportunities for CPs in Pakistan could improve CP skills, which might in turn help improve the fidelity of the opioid optimisation service. Other studies from Pakistan [405, 408, 413-415] also state that CPs need to learn practical skills that are required to deliver CP-based services in disease management and medication reconciliation. Similar strategies have been reported by an exploratory study from Canada [244], which suggests curriculum revision to improve pharmacy education as well as offer post graduate trainings to help build pharmacist capacity in opioid optimisation in people with CNMP.

A 2021 Australian study [416], exploring a CP opioid optimisation intervention in community pharmacies, also states that improving CP knowledge and skills can improve the confidence of CPs to engage and deliver services and improve fidelity. However, similar to my study, the authors emphasise that only focusing on improving knowledge, skills and confidence might not be adequate to improve service delivery and other determinants like CP and public beliefs about the intervention, characteristics of the pharmacist and the pharmacy, complexity of the intervention and incentives are all factors

that can impact the CP motivation and capability for service delivery and subsequently facilitate or hinder reaching service outcomes [416].

4.3.3.i Opioid optimisation service novelty

Community pharmacies are an integral part of healthcare systems and are utilised in many countries across the world to improve access to essential medicines and deliver patient-centred services [417]. My study indicates that there are currently no community pharmacy patient-oriented services in Pakistan, which is why the development of opioid optimisation service will face an innovation challenge.

Chapter 5: Case studies

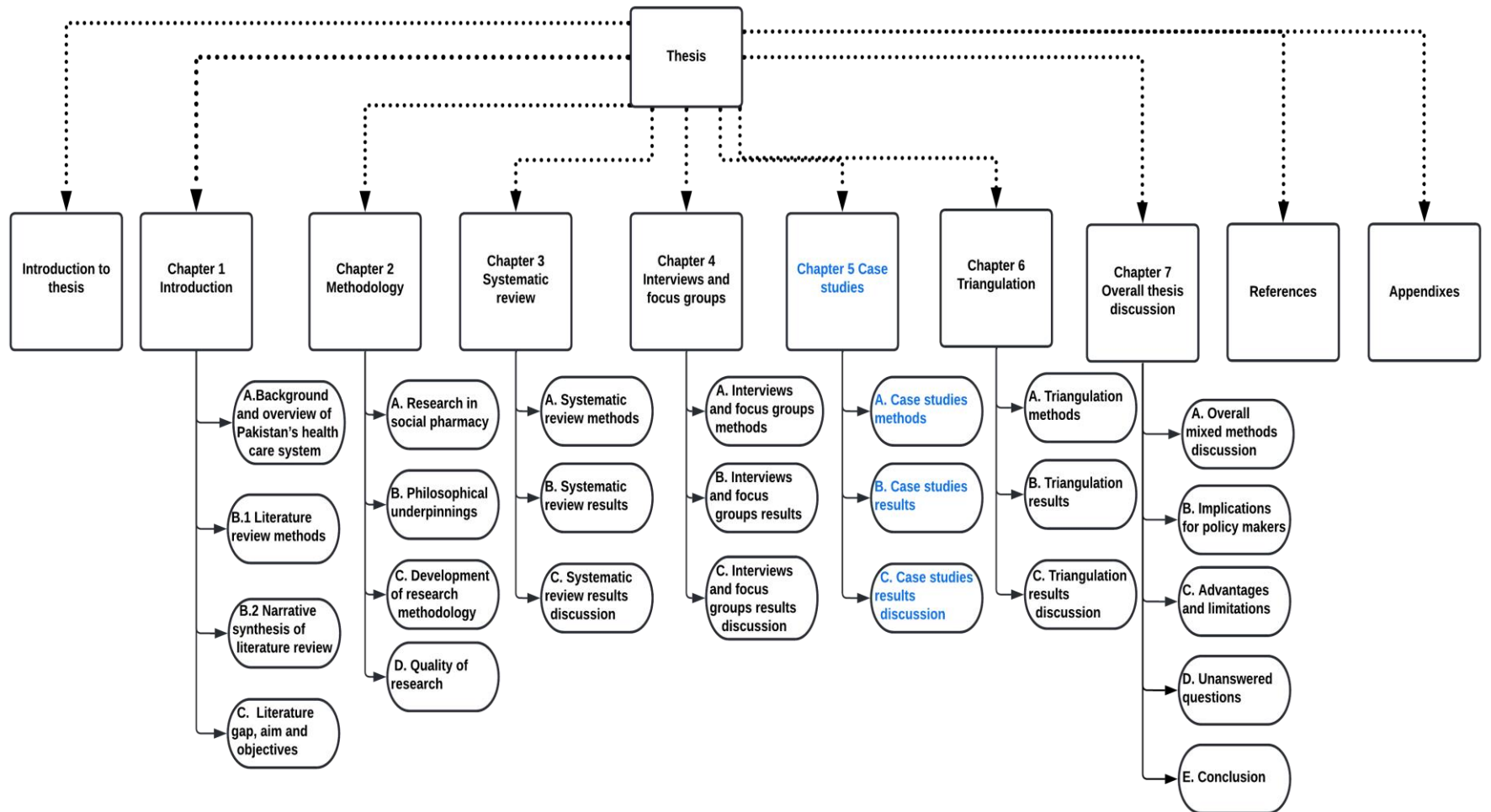


Figure 5.1: Overview of chapter 5 in thesis

5.1 Subchapter A: Case study methodology

Case studies have been extensively conducted in community pharmacy settings to investigate community pharmacy services provision, consumer behaviours and implementation of services [418]. Yin [209] describes that case studies *“are investigations to a particular phenomenon (the case) in depth and within its real-world contexts”*.

In addition, observational studies can provide perspective and understanding of behaviours of groups of people within certain environmental contexts, which can help provide detailed information regarding the phenomenon [419] and can be useful for designing new interventions.

As I aimed to understand the use of opioids by people with CNMP as well as explore their interactions with CPs to help understand the kind of service that is needed, is possible and how such a CP service can be delivered, the nature of questions required a more in-depth analysis of the processes and behaviours of those involved in these processes. Therefore, I used multi-site observational case studies to explore the same phenomenon in different settings, with different participants bringing different meanings to this phenomenon. Multi-site observations are beneficial because a) they offer exploring factors across sites, b) can provide more rigour to the findings because multiple case studies *“represents a strong start towards theoretical replication”* [209] as shown in Figure 5.2 below.

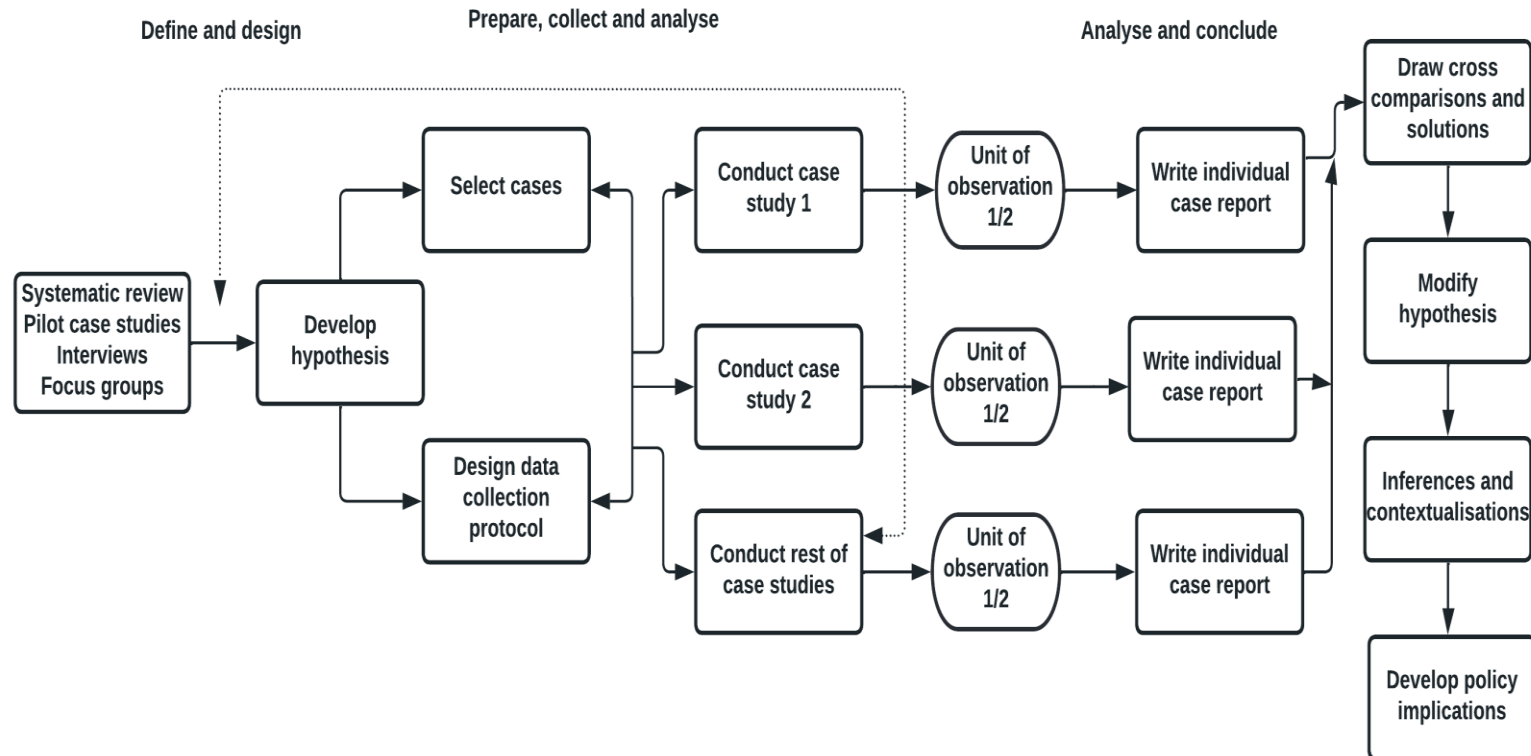


Figure 5.2: Multiple case study design (adapted from Yin 6e) [213]

An observational case study can be either participant or non-participant. A non-participant case study has the researcher simply observe and record details of specific events of interest without influencing or interfering with them [420]. This is particularly important because people might exhibit a Hawthorne effect when observed. The Hawthorne Effect *“is the tendency, particularly in social experiments, for people to modify their behaviour because they know they are being studied, and so to distort (usually unwittingly) the research findings”* [421].

An advantage of observation by a non-participant researcher was that instead of relying on people’s account of their actions — such as those obtained by interviews, focus groups — they can be directly observed [188]. Another advantage is that they allow to capture data that might seem too trivial or insignificant to participants for sharing [422]. Major disadvantages of this method is that they are time consuming, difficult to carry out well and heavily reliant on the researcher to observe and interpret phenomenon [423]. Therefore, I used a non-participant observational multiple case studies approach where I recorded observations as field notes, separately for every case guided by a data collection form (Appendix 3). The form was developed specifically for this study to ensure a certain level of consistency in data collection across all sites.

5.1.1 Data collection tool

The six WHO quality of care core constructs mentioned previously were also used to draft a semi-structured data collection instrument for non- participant observational case studies (Appendix 3). The purpose of developing a semi-structured data collection instrument in case studies was to identify CP-delivered activities, facilitators, challenges and strategies that could impact CP service provision and impact providing optimal patient care in people using opioids for the management of CNMP. The instrument was validated by discussions within the research team and a pharmacy practice expert from Pakistan.

5.1.2 Piloting of case study sites

Piloting of case studies was carried out in December 2019 and included one day (eight hours each) of observations in the selected types of pharmacies⁹. Piloting added more components under the six WHO broad constructs and informed the development and refinement of case study data collection instrument to become broader.

The refined instrument was then again discussed with the research team (supervisors) and the pharmacy practice expert from Pakistan. No changes were recommended. Please note that although the instrument remained

⁹ Please see 2.3.4.b Sampling framework for case studies for details

semi-structured, it allowed recording of every action. It was only developed as a systematic guide to ensure uniform data collection across sites as well as to facilitate the minimal data collection in each setting.

5.1.3 Selection and invitation of pharmacies (sampling strategy)

Based on the scoping exercise¹⁰, I decided to focus on pharmacies where opioid controlled dispensing laws (Schedule-G amendments) were expected to be implemented, which excluded rural areas. Before invitation, a list of eligible pharmacies was made in Islamabad based on the inclusion criteria. A direct approach to pharmacies was considered best to invite them in this study. Within eligible pharmacies that volunteered in each category, pharmacies were randomly chosen based on a draw and invited to participate in the study. The consent form was signed in-person before the case studies started by all pharmacy staff including managers (if different from CPs). All staff was assured that all findings would remain anonymous and would not be able to be tracked back to participants or the pharmacies. During the conduction of case studies, a flyer was displayed on the door and prominent locations in these pharmacies showing that a research study was being conducted and people with any reservations or further questions were directed to seek more information from the counter. This was all designed to ensure an overall semi-covert approach so as not to disturb the routine workflow.

5.1.4 Inclusion/exclusion criteria and invitation to participate

Each pharmacy falling in the first four categories (A to D) as shown in sampling framework (2.3.5.a.ii Sampling framework for case studies), were eligible to be invited to this study. Out of the eligible pharmacies, the pharmacies chosen for case studies were selected based on the following parameters.

1. Manager or management (pharmacist vs non-pharmacist)
2. CPs presence (full-time or partial)
3. Residential/commercial
4. Presence of a nearby hospital/clinic
5. CP gender (male/female)

5.1.5 Data collection in case studies

The case studies' observations were conducted after the first wave of COVID-19 (October-November 2020) in Pakistan, after easing of social distancing rules. After obtaining consent from staff, I conducted observations in six different cases. Observations were carried out for one week (6 days), Monday to Saturday, for each of the six pharmacies. The observations were carried out

¹⁰ Please find scoping information listed under section 2.3.4.b Sampling framework for case studies

from 9am to 5pm or 3pm to 10pm, depending upon the pharmacy operational times.

I would usually stay close to the pharmacist's location in these pharmacies to facilitate observation of the CP and people's interaction with them. However, in case of no people acquiring medicines/filling prescriptions, I would move around in the pharmacy observing different situations and making notes.

All staff/pharmacist interactions with the public on opioid medications were recorded on the data collection form (Appendix 3).

Any interaction or activity involving opioid medications was recorded. This included requests for opioids with and without prescriptions, dispensing, record keeping, conversations, requests for specific brands, staff changing brands and/or offering other therapeutic options, changing or altering the dose, referrals to doctors, questions regarding the use of medicines from either party, counselling or/and any informational activity as well as any advice about visiting faith healers or CAM use. I did not include encounters related specifically to the dispensing of non-opioid analgesics medicines. Information recorded about the people included their gender, number of people present at the pharmacy, number of medicines, prescription (private or hospital), the way they approached the pharmacist, the time they arrived, the average amount of time spent, the number of prescriptions and items on each prescription, as well as any activity or comment regarding the CPs (when the prescription was shared with me to point out anomalies or examples).

Other information recorded in the case studies included physical parameters of pharmacies such as the number of counters, staff on counters, medicine procurement, stocking, shelving, ordering, number of staff members, placement of medicines, narcotic cabinets, IT equipment and software, attributes of the manager, assigned tasks, warehouse, record keeping, billing and dispensing. The presence and sale of other cosmetic, health, beauty and grocery products in the pharmacy by the same staff members was also considered and recorded, where applicable. Outside the pharmacy, the locality, accessibility to pharmacy, signboards (pharmacy, medicine shop), the opening and closing hours, parking, locality, presence of clinics or hospitals as well as its location in rich or poor residential community was also recorded and used in the analysis to make inferences.

All notes were taken in shorthand using memo writing technique. A full account of the observations was completed at the end of each day. There were no formal interviews with case studies participants and my perceptions of ongoing CPs activities and people's behaviours and actions regarding opioid medicine related events were recorded as "impressions" so they could be differentiated from the rest of the empirically-observed field notes. No audio or video recordings were made during observations.

All non-formal conversations between myself and community pharmacy staff members were drafted as communications. Thus, direct observations, field notes, informal communications and my impressions were drafted as case report findings and have been presented in the next subchapter.

5.1.6 Researcher bias and Hawthorne effect

My role as a researcher during data collection was substantially considered. As mentioned previously, in case studies I wanted to observe the interaction between the pharmacists and people purchasing opioids for CNMP, which led me to adopting a non-participant observer role. This was aimed at minimising any influence on the possible action or activity in the pharmacy. My identity as a pharmacist could make staff uncomfortable, thinking they might be judged for their professional abilities while interacting with people. To minimise this influence, the staff members only knew that a PhD student was collecting data for research and the participant information sheet had sufficient data on the nature of study. To understand how my background as a pharmacist as well as a female was influencing the data collection by observations, I reflected on my positionality every day after data collection as personal short records. They were taken into consideration during data analysis.

It must be highlighted that any note taking or data recording in field work might draw the attention of participants and alert them [424]. Therefore. Even though data was recorded through note taking in case studies, every attempt was made to keep it as inconspicuous as possible. This was achieved in two ways. The field notes were drafted using pen and paper using the data collection form (Appendix 3), when the observed participants (pharmacists and staff) were not paying any visual attention to me. Secondly, my personal mobile phone was used to record data as short notes, giving the impression that I was using mobile phone for personal texting/messaging while the interactions were taking place. This was done to lessen the anxieties of the staff members and to allow for a more natural flow of interactions. That said, not having actively advertised my pharmacist training does not mean that I might not have influenced the staff in community pharmacies. I did notice specific behaviours (Hawthorne effect), which I suspected were because of my presence. However, the staff did not know how many days I would be staying and observing, thus the Hawthorne effect was neutralised on the 2nd or 3rd day of observations and thus this limitation has been accounted for.

5.1.7 The impact of COVID-19 on data collection in case studies

As the observational case studies took place from September-November 2020, the lockdown and social restrictions had eased down and this facilitated my presence in an acceptable proximity to hear the conversations. An important change observed during the COVID-19 pandemic versus the pilot

case studies was the installation of protective glass shields in one pharmacy, which could have possibly impacted my ability to hear the conversations. However, the CP counter had no glass shield as the pharmacist was stationed at a discreet counter in the back of the pharmacy and thus there was no impact from this on the data collected. Moreover, most patients and staff members opted not to wear face masks, so their voices were not muffled. In cases where people did wear masks, they would pull the masks down to speak so the quality of conversation was not affected.

5.1.8 Data preparation

Field notes, observations and communications were used to fill in the case study forms and were then converted to meaning-based narrative descriptions for each case study. A case study field form having raw data has been provided in Appendix 14.

5.1.9 Transcribing and translation in case studies

For case studies, all the data was collected using the English language and only direct verbatim quotes said in Urdu were translated and written by me as communications. As there was no audio recording, the translations could not be verified but from back translation report of transcripts it can be confidently assumed that it should have similar accuracy and quality. Another important consideration is that even though my translation of conversations cannot be validated, the case studies' observations inherently allow a researcher to carefully construct meaning and inference and the case study findings are the presentation of the phenomenon of interest through the researcher's lens that can help overcome the translation checking deficiency.

5.1.10 Data analysis

5.1.10.a Unit of analysis and units of observations

"The unit of analysis (in a case study) is the entity that you wish to say something about at the end of your study and it is considered the focus of your study. A unit of observation is the item (or items) that you observe, measure, or collect while trying to learn something about your unit of analysis" [425].

The unit of case study analysis in my study was the "interaction" of people with CPs while buying/acquiring opioid medications. However, interactions remain fallible and can happen differently with different people in different settings and times [209]. Thus, the generalisability of individual actions to be predicted remains a complex challenge in analysing case studies. The final aim of the case studies was to arrive at a high level of logical reasoning and understanding what kind of CP service might help optimise the use of opioids.

5.1.10.b Analysis of case studies

As per Yin [213], there are five techniques commonly used in case study analysis:

1. Pattern matching (theoretically predicted vs empirically observed or predicted in one case and matched with another)
2. Explanation building (explains and develops new hypothesis, what will work and how)
3. Time-series analysis (follows how and why change happened over time)
4. Logic models (tracing activities and their strategies to their intermediate outcomes, leading to desired outcomes and provides context)
5. Cross-case synthesis (only applicable to multiple case studies, pattern matching and comparisons across cases and help develop logic model) [209]

Case studies were analysed using cross-case synthesis as shown below:

- In the first step, the codes in case studies across all six cases were developed independently using the RTA method ¹¹, to develop codes, subthemes and themes in each case. The findings were validated by the research team in RTA step 4 as previously stated.
- In the second step, the codes, subthemes and themes were explored across all six cases to identify whether any similar or dissimilar “*patterns, insights or concepts*” emerged across different cases using pattern matching technique [209]. This was done descriptively.
- In the third step, the six cases underwent in-depth exploratory analysis to understand what, why and how the CP-patient interaction could lead to an optimised use of opioids in people with CNMP by studying convergence and deviance of codes/subthemes across cases. The pattern matching technique in this step involved, tracing events or activities able to cause or produce an intermediate action or outcome, which in turn could produce or was predicted to produce another immediate or a desirable action or outcome, leading to actions that could be perceived to optimise the use of opioids.
- In the fourth step, although viewing the codes helped find similarities across different cases, analysing and understanding these codes within each case study parameters helped inform the analytic interpretations of aspects/events/experiences not as a separate “unit of meaning” but as part of the outline formed by the convergence of meanings with respect to individual cases using explanation building [209] and helped develop rich narratives about each theme/subtheme. These analytical techniques also facilitated the process in identifying and describing many strategies. Some observed patterns across cases can be

¹¹ Please see Chapter 4, subheading Data analysis in interviews and focus groups

described and interpreted with a high level of accuracy but others might only be interpreted with a certain level of probability [426]. All the findings were subjected to constant reflections and discussions and a consensus was developed on the subthemes and themes. A summary of analytical processes and steps undertaken during the analysis of case studies is shown in Figure 5.3 below.

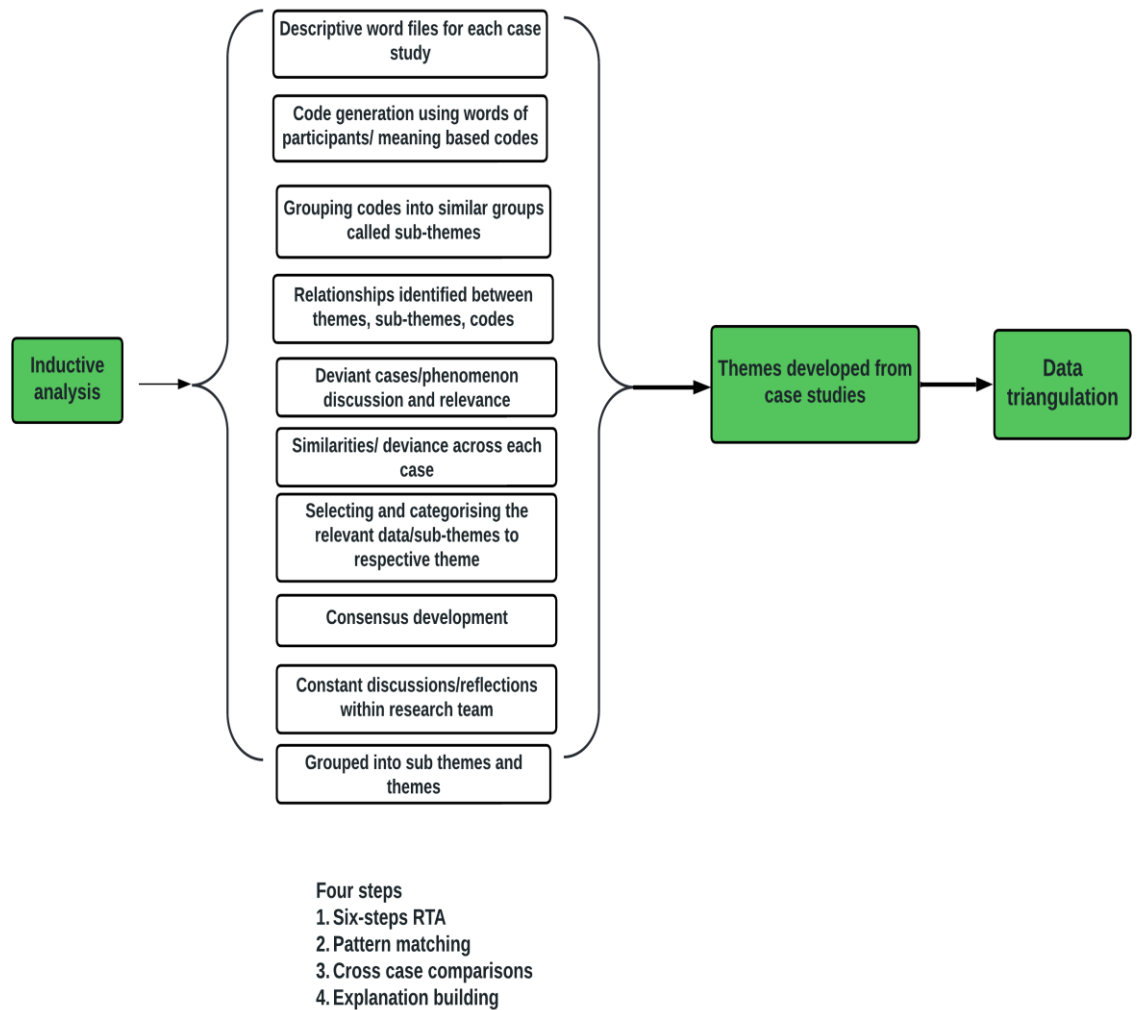


Figure 5.3: Data analysis steps for case studies

5.1.11 Case study findings validation

The research team helped validate the findings in two stages while analysing case studies:

1. Firstly, the analytical findings in all case studies were validated against the raw field notes data being collected and crosschecked for whether the subthemes and themes were representative of the data respectively. This was employed at step 4 within the RTA analysis.

2. Subthemes and themes were constantly subjected to reflection and discussion within the research team, to validate the findings.

5.1.12 Inconvenience allowance

Pharmacies where case studies took place were offered an inconvenience allowance (to cover disruption in daily work due to presence of the researcher). All case study sites opted to receive an inconvenience allowance.

5.2 Subchapter B: Results of case studies

5.2.1 Demographics of case studies

A total of 240 hours (40 hours/case) were observed during a six-week period of non-participant observational case studies in six community pharmacies. The demographics have been shown in Table 5.1 below.

Table 5.1: The demographics of chosen cases

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Pharmacist gender	Female	Female	Female	Male/female both pharmacist*	Male	Male
Chain/individual community pharmacy	Big, reputed chain	Independent	Small chain	Big reputed chain	Independent	Independent
Locality	Residential (city outskirts)	Residential/commercial	Commercial	Commercial	Residential and commercial both	Big city residential sector but city outskirts
Footfall	Footfall medium	Footfall low	Footfall very high	Footfall very high	Footfall medium, small city	Footfall very low
Pharmacy management (owner/manager)	Manager non-pharmacist Owner non-pharmacist	Owner is also pharmacist Pharmacist is also manager	Owner non-pharmacist Manager non-pharmacist	Owner non-pharmacist Manager pharmacist	Owner pharmacist (himself) Manager pharmacist (himself)	Owner non-pharmacist the dispenser himself Owner is also manager (non-pharmacist)
Hospital (s)/ doctor clinic(s)	Hospital/clinic not near	Near private hospital	Hospital not near /doctor clinic not near	Government hospital near	Private clinics near	Private clinics near
Pharmacy technician / dispenser s	1 technician , 3 dispensers	1 technician , 1 dispenser	No technician but dispensers	No technician but 8 dispensers	No technicians but two dispensers	1 technician , (the owner), no dispensers
Pharmacist timings	10 to 4 pm	10 to 4 pm	9 to 5 pm	Pharmacist from 9	Average time	Pharmacists present

				to 5pm, 6 pm to 2 am	spent by pharmacis t 6-7 hours in shop	2 to 4 hours, twice during the entire duration
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* only female was observed due to chosen time

5.2.2 Data saturation

In most case studies, data saturation was achieved on the third day except case study two and three, where data saturation was achieved on second and fourth day, respectively. The case studies continued for a total of six days in each case to minimise the Hawthorne effect.

5.2.3 Case studies findings

The RTA in case studies helped develop the following three themes:

1. Factors/reasons contributing towards the unsafe use of opioids
2. Possible actions/activities by CPs that can help optimise the use of opioids
3. Challenges and barriers for CPs to deliver an opioid optimisation service

The case study subthemes of all cases have been provided in Appendix 15 (brief form).

5.2.3.a Factors/reasons contributing towards unsafe use of opioids

5.2.3.a.i Regulation

5.2.3.a.i.a Unauthorised opioid dispensing and easy availability of medicines

It was observed that dispensers attending to the people had access to opioids in almost all cases (either opioid cabinet or store) and were involved in dispensing opioids. CPs at the outset were apparently trying to follow Schedule-G laws and refused opioid medicines without a prescription. However, in majority cases dispensing happened with or without CP's consent. It was observed that people might have prescriptions; however, even if they didn't, opioid medications were still being dispensed, mostly by dispensers following their manager's orders, going against the Schedule-G amendments. The reasons observed for unauthorised dispensing included the organisational overall aim of business and profit generation and targeting customer happiness and satisfaction to ensure loyal customers. Pharmacies, where there was a high chance of inspection by drug regulators, followed the laws more strictly. This effect translated down from the management, which directly or indirectly dictated the behaviour of the pharmacy staff. In almost all pharmacies, the Schedule-G implementation for opioids-controlled dispensing remained overall poor due to weak regulation.

5.2.3.a.i.b Regulatory visits

Communication with the staff revealed that the inspection by regulators (drug inspectors) was inferred to be location dependent, and inspectors might visit community pharmacies in easy, prominent and high traffic locations.

However, remote areas within a city are easily bypassed. The interpersonal relationships of regulators with the community pharmacy management were also found to impact the inspection visit as well as nature of the enquiries and inspection quality.

5.2.3.a.i.c Effect of regulation on pharmacy management

Another impact of “drug inspector absence” was found to be linked to hiring of pharmacy staff. Depending upon the chance of regulatory arriving visits, the pharmacy staff could consist of either pharmacists, dispensers and/or salesmen. These staff members were primarily observed to be involved in stocking, auditing and dispensing of medicines. However, they also frequently ‘prescribed’¹² opioid medicines, if the public would discuss and ask. Lack of “regulation fear” was also observed to assist in active dismissal of law-abiding activities of CPs by pharmacy managements, which created friction between CPs (trying to follow laws) and their managements and impacted the motivation of the CPs, resulting in either broken CP-employer relationship, CPs faking narcotic dispensing records or disengaging entirely from the implementation of opioid safe laws, thus contributing to unaccounted for and unregulated dispensing of opioid medications.

5.2.3.a.ii Business and customer focused

All pharmacies were focused on keeping customers happy by providing the medicines they asked for, with or without prescriptions. The overall aim of these shops was to “sell more medicines”, even in the pharmacies where “narcotic dispensing by prescription-only” was advertised and tried to be implemented (by pharmacists). The pharmacies were found to either dispense as per prescription, change medicine according to the customer’s preferences, dispense when the patient asked for a particular medicine (without a prescription), advise/prescribe medicines (where pain was discussed without taking any particular name) and refer to doctors. All activity focussed on not compromising the potential sale as well as improving public experience, to ensure repeat customers.

5.2.3.a.iii Impact of social perception on acceptance of opioid laws

In one case, the CP was observed to be stamping prescriptions to indicate dispensing, so that the same prescription cannot be used again. This was perceived negatively by the customers and frowned upon. Despite the

¹² Prescribing of opioids in pharmacies constitute of orally recommending a medicine

pharmacists and staff members trying to explain the legality and patient safety concern, people pointed out that *“other neighbouring pharmacies were not making their life more difficult”* and shared they would have to go back to doctors and pay them fees to get their prescriptions again because they *“ruined it”*, as they could have used it many times. Some people considered the CP’s law-abiding behaviour a marketing, *“pretending”* to be upright and moral or trying to portray good (standards) of the shop and thus being *“show-offs”*. Others appreciated and liked the initiatives. However, they shared that getting prescriptions every time to fill in medication is difficult as the *“doctor will write the same medicine again, so why pay the fee again, they are just doing business”*. Getting asked for a prescription while purchasing opioids was not liked by the public, especially by people who arrived without a prescription. Most of the people threatened they would not come back to the shop. This caused a dilemma for the CPs, as their job description asked them to facilitate the dispensing, help customers and improve *“customer”* satisfaction, and help improve the business’ outlook and profit. In addition, peoples’ negative attitudes and complaints caused them distress. Implementing Schedule-G amendments for patient safety against the organisational aim(s) was found to be overwhelming for the pharmacists as well as emotionally taxing as they struggled to find a balance.

5.2.3.a.iv Public perception of opioid medication

It was also observed that people might lack the knowledge about opioids being different to other OTC analgesics. This can be inferred from the fact that a refusal to dispense opioids without a prescription was met with different reactions, where some people seemed not to be aware of the new laws and sharing *“why do I now need a prescription as I never needed one before?”* Some people were observed to remain confused about why laws exist for only opioids and not for other medicines.

5.2.3.a.v Impact of patient load on CP/staff

Lack of adequate staffing in pharmacies for dispensing was observed to be impacting CP capability to maintain opioid records. During rush hours, CPs were found to be focused on dispensing (all medicines) and dealing with customers to avoid patient rush. In some pharmacies, CPs collected the scans of prescriptions (probably to commit the dispensed records later to the narcotic register). However, no opioid medication review checks were made on the prescription. The prescriptions were not even stamped to indicate dispensed items. In other pharmacies, CPs and allied staff, who had full access to narcotic medicine cabinets, dispensed opioids without maintaining any dispensing records. Later, in some cases, CP were observed entering fake records in the narcotic register to make up for unaccounted dispensing.

5.2.3.a.vi Digital systems capacity

It was observed that a standard community pharmacy might have the organisational capacity (software, computers and Wi-Fi) to maintain the narcotic dispensing records electronically, but these systems are being utilised only for billing and stocking, perhaps due to a lack of centralised policy for maintaining digital dispensing records. In addition, three of these community pharmacies were observed to have advanced software, which could help keep track of patient identification, dispensing records, date of next refill and also had data sharing options to help communicate with other pharmacies or even with private clinics and hospitals.

5.2.3.a.vii Lack of public engagement and people's reluctance to go back to doctors

Most people were observed to proceed towards the salespersons in the pharmacies. They would make a purchase and go away without enquiring about any medicine information. However, a few people (mostly educated people with private doctor prescriptions arriving in the afternoon), who knew or were perceived to have had a past conversation with the pharmacist, were inclined to speak to pharmacists and specifically asked the salespersons about the CP. Depending upon the organisation's internal workflow, either the pharmacists would come and speak to them or they were brought to the pharmacists in their assigned locations. People without a prescription (self-medicating, self-managing) were observed to be more difficult to convince to go back to doctors for review (especially when they experienced lack of analgesic effect of medicines). However, they were fairly receptive to pharmacist suggestions and advice and even asked the CP to recommend them medicines. Such actions can lead to self-medication and illegal prescribing and dispensing, and can contribute to the unsafe use of opioids.

5.2.3.a.viii Opioid information

CPs were observed to be providing general knowledge about opioid medicines such as dosage and frequency only when they assumed the researcher is observing. People also were observed to be not asking any technical or opioid-specific questions. CPs were observed to be using their mobile devices to look up information about side effects and dose adjustment queries. From the data observed, it cannot be inferred whether the CPs lacked advanced skills and knowledge specific to opioid medication —or because the people did not ask for additional information or perhaps due to there being no legal obligation to counsel patients. Majority people acquiring opioids did not receive any specific opioid medication-related instructions/information and were not made to understand the risks associated with using these medicines.

Chapter 5 Case studies: Subchapter B results

5.2.3.a.ix Telephonic delivery (by staff) bypassing CPs

Medication home deliveries were observed in one of the pharmacies. There was no restriction on what medications were home delivered but the staff was heard to ask for opioid prescriptions to be sent via WhatsApp (whether the prescriptions were subsequently sent or not could not be established). Even though the opioid items were dispensed, the dispensing record of these items was not entered in the narcotic register by the staff, or by the CP. From this observation it can be inferred that there might be missed entries or discrepancies in the opioid record maintained within pharmacies. It can also be inferred that opioid medicines may be dispensed without checks or reviews, even after the new amendments.

5.2.3.a.x Prescription adulteration

In pharmacies where there was an attempt to strictly implement the laws, opioids were attempted to be dispensed only after a valid prescription. In these pharmacies, the CP shared prescriptions with the researcher, where opioids, barbiturates and benzodiazepines had been added in a different ink at the end of the prescription. There were also changes made to the dose and duration. When asked by the CP, the person replied that *“the doctor had forgotten to add, and when I went back it was another doctor who wrote this medicine”*. CP shared that this was common especially in their area because of a nearby government hospital and usually many people arrive late in the evening. The CP said *“these people are aggressive”* and instead of refusing them outright, the staff would normally tell the patients that *“these medicines are short these days (out of stock)”*. However, the CP shared, *“other neighbouring pharmacies will dispense the medicines, because they are not compliant with the laws as they do not have proper CPs”*. This highlights prescription adulteration as well the disadvantage and limitations of manual prescription systems.

5.2.3.a.xi Possible misuse of opioids

From the data available, it cannot be reliably inferred whether people acquiring opioids without prescription or in higher quantities were misusing opioids for euphoric reasons (non-medical reasons) or just self-medicating. However, it was reported by a CP (case 4) that people with misuse intention of opioids usually come late in the night. It must be highlighted that in all pharmacies except one, usually only dispensers were available at late hours, and they were observed to be more relaxed in their compliance with Schedule-G laws, dispensing opioids to anyone that asked for them. A lack of sufficient regulatory checks was perceived to be linked to such actions, as the pharmacies in question had no fear of repercussions or penalties.

Chapter 5 Case studies: Subchapter B results

5.2.3.a.xii Sub-standard prescriptions/Schedule-G required information missing

Apart from the private hospitals' prescriptions (both digital and handwritten), almost all arriving prescriptions were observed to be improper and every doctor had recorded different information on the prescription. The private hospital prescriptions were observed to have a standardised format and doctors had filled all the required information. The lack of standardised information such as prescriber's name, diagnosis, quantity dispensed, patient name, dosage form, duration and review/stop date could not be found in most prescriptions, and CPs usually left those columns blank in the narcotic register. This reflects the inability of the CPs to maintain proper records as per laws.

Some prescriptions had patient diagnosis, unusual lab reports, past medical history and past medication but CPs were observed not to pay any attention to these or talk to patients about them. This resulted in a random pattern of available medicine information and in the absence of comprehensive patient records, it can be inferred that it will be very difficult for CPs to make an informed decision on the rationality of the prescriptions for the patients. Most of the un-digitised prescriptions arriving at pharmacies were found to be incomprehensible as well as having incomplete disease and medicine related information and most people seemed oblivious to what they were prescribed. This was further confirmed by people actively asking the pharmacy staff: *"which medicine is this, I can't understand the writing"*, *"what will this medicine do"*.

5.2.3.a.xiii Polypharmacy

Polypharmacy was also very commonly observed. Prescriptions were often observed to have two or three same opioids (generic) having different brand names. Other non-opioid analgesics like NSAIDs were also commonly prescribed along with opioids. Other medications such as steroids, vitamins, supplements, gastric and allergy medicines were common without any diagnosis or indication in the prescription. Doctors were observed to be over prescribing analgesics (high dose and frequency), as well as mixing and matching different analgesics. It was not clear from prescriptions why there was more than one opioid medicine prescribed. However, the reasons for such prescribing behaviours cannot be inferred from the data observed. From the prescription itself, it was not clear if a prescription had been dispensed previously and thus this could allow unregulated use of opioids by people.

5.2.3.a.xiv Doctor shopping

People arriving at pharmacies sometimes filled more than two opioid prescriptions, from different doctors for similar opioid medications. In addition, there were many cases where people filling a different prescription

would verbally ask for opioids (demanded medicine by taking a brand name without a prescription) and get them dispensed. It was suspected that people without a prescription could be either self-medicating or receiving opioids without any clear evidence of potential medical history, patient notes, past medication records or even diagnosis.

5.2.3.a.xv Brand name prescribing

In all cases, prescriptions had brand names of the opioid medications, and many of the prescriptions were found to have therapeutic duplication as well as other analgesics. CPs commonly engaged with changing brand names of medications on peoples' request for *"either a better medicine or a cheaper medicine"*.

3.3.3.a.xvi People awareness about opioids and self-medication

Many patients or their family members were unable to understand the prescribed medications and frequently asked the pharmacy staff to show them the medicine box before purchasing the medicine. Literate people, after getting medicines, spent time trying to read the medicine boxes or taking out the literature and reading it. Upon finding out if it was a medicine they had previously used and which *"does not work"* or they *"had it at home"*, they would then either proceed to ask the dispenser for *"something else"* or a *"better medicine, which is stronger than this"* or leave without purchasing the medicine (observation of non-adherence to therapeutic advice, potential of doctor shopping). In cases where the customer asked for a different or stronger medication, the staff would usually oblige them, thus earning their loyalty in the form of future visits and leaving both parties satisfied. Such exchanges indirectly provided a positive reinforcement to illegal prescribing, dispensing and self-medicating and may contribute to unsafe use of opioids.

5.2.3.a.xvii Lack of awareness of new medicine sale laws

In all observed pharmacies, people tried to acquire opioid medicines without a prescription. In some instances, when dispensing was refused, people seemed to be confused as to why they needed a prescription as they never needed one before. It was also observed that only one pharmacy had the new rules printed and displayed as a public notice and that too in a remote corner near the CP station. Upon explanation from the CP or staff, some people appreciated the initiative. Most people, however, verbally protested about this new rule. CPs shared that *"these people instead of going to a doctor to get a prescription would look for shops where this law's implementation is weak"*. They shared that refusing to dispense medicine is not good for their organisation's business, but their manager is compliant because they are a *"proper pharmacy"* and hence they follow laws (reputable chain pharmacy, pharmacist manager). In other instances, people arriving with repeat

prescriptions — where the dispensing of opioids (presumably) was followed in the presence of CP after a valid prescription — seemed to be aware of the rules and were observed to be compliant with the changes to the rules. It can be inferred that public awareness is key to compliance with the new policies and laws, and helps facilitate the implementation of new rules and changes in pharmacies. Strict regulation on non-compliant pharmacies also needs to be enforced to avoid creating confusion for the public.

5.2.3.a.xviii Uncontrolled pain/demand more medicine (non-adherent/non-compliant)

Most people were observed to try to purchase enough medicines to last them for three to six months. The reasons shared with CPs for this behaviour were that they “*lived far away*”, or “*they have a lot of pain and take medicines as required*” and “*other family members also need this medicine*”. This implies that people use more than the medicines prescribed as well as might be sharing medicines with their family members and could be using opioids unsafely without a doctor’s review.

5.2.3.a.xix Using more than 6 months old prescription (lack of review by doctor)

Some prescriptions shared by the CPs were more than six months old (some as old as three years). This was especially observed in case 1, where after being initially refused because they did not have a prescription, people would return with an old prescription (residential area pharmacy). This could indicate a patient’s lack of frequent review with the doctors and the continuous use of opioids. In all such cases, even with an old prescription, opioids were dispensed as resistance of CP to dispense on an old prescription was not welcomed by people and they were observed to become very aggressive and complained to the pharmacy manager. Upon the manager’s instruction, the CP would dispense medication, which suggests CPs might not be at full liberty to refuse opioid medications and have to follow organisational rules and instructions.

5.2.3.a.xx Educated people asking for/reading leaflet

Some people were observed to read medicine leaflets (present inside the box) before purchasing, which indicated that they want to understand/find out more about the medication. It could not be inferred what information they wanted but upon asking a question from the staff (usually about side effects, dosage, food interaction), they were guided towards the CP for answers. The CP would either directly answer the question or look up the desired information on the internet using their mobile phones. Only two instances were recorded where people asked about drug-drug interactions of opioid with another medicine or opioid use with another barbiturate, which

indicates they might be aware of the medicine they were using, as well as understand the role of CPs.

5.2.3.b Possible actions/activities undertaken by CPs that can help optimise the use of opioids

5.2.3.b.i Opioid medicine information given to people

In most cases where people asked, CPs were able to give opioid medicine related information either directly or by looking it up on their mobile phones. It must be highlighted that most people did not ask specific questions related to opioids and most of them seemed generic questions relating to side effects, dose and food interactions. It must be highlighted that pharmacies might not have local resources (for example hard copies of: British National Formulary (BNF), pharmapedia, drug manual) or Internet access to help CPs view medicine information online (IT software, Wi-Fi-enabled computers and phone lines can facilitate CPs).

5.2.3.b.ii Identification of therapeutic duplication

In cases where people had prescription(s), CPs recognised therapeutic duplication with the same opioid medicine within/across prescriptions. However, it was observed that some CPs lacked information about different brands. Staff bringing them medicine boxes (physically) to enter details of the batch was especially helpful in CPs identifying the duplication. CPs usually informed the patient that both were the same medicine and guided them to use one. They only dispensed one medicine (the price was shared with people and their choice was considered while dispensing one of the two medications). This CP activity was observed in both supportive and non-supportive managements.

5.2.3.b.iii Therapeutic substitution

CPs were observed to provide alternative medicines on people's demand usually either due to high price or "*the medicine did not work on me*". Alternatives of medicines were offered not just as brand substitutions but also as generic substitutions. It must be highlighted that although CP and allied staff were observed changing medications (it is considered normal), it is not legally allowed to amend the prescription to the generic version of a medicine without a doctor's approval. Dispensing opioid medicines without a prescription on customer's demand by CP/allied staff was also observed in almost all pharmacies, which is against the current Schedule-G laws. However, CPs were not seen actively recommending opioid medications and prescribed only OTC analgesic medications and herbal supplements.

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5.2.3.b.iv CP advice offered

CPs were found guiding and providing medicine information to the people, but the conversations were mostly initiated by the customers. Advice offered included possible side effects (drowsiness mostly), suggesting OTC medicine for pain relief, information about dosage, frequency, adherence, missed dose and referral to doctors or physiotherapists or CBT. Thus, it can be inferred CPs can possibly provide counselling and advice to patients about medicine, their disease or simply what could be the next step for them.

5.2.3.b.v Record keeping

CPs were found to be following laws (Schedule-G implementation) and maintaining opioid dispensing records but not properly. The CP's capability to keep a record of narcotic dispensing was observed to be influenced by people's demand, pharmacy management, allied staff support and the CP's own perception of and discipline to follow laws.

5.2.3.b.vi Narcotic dispensing stamp

The CP in one case was observed to be stamping prescriptions after medication had been dispensed. This action can help stop the prolonged use of a prescription as well as counter over-purchasing of opioids using the same prescription (pill shopping) from other pharmacies. This might be able to motivate people to go for subsequent medication reviews as well as educate them to not continue the medication for more than the prescribed period without a doctor's review.

5.2.3.c Challenges and barriers for CPs to deliver an opioid service

5.2.3.c.i Regulation impact on CP ability to follow laws

Community pharmacies where there was a high chance of inspection via drug inspectors were found to be more strictly following the laws. This effect translated down from the management, which directly or indirectly dictated the behaviour of the pharmacy staff. CPs trying to follow the laws and refusing dispensing of opioids without prescriptions to customers even under valid safety concerns, was an action perceived as "undesirable" and usually complicated their organisational as well as interpersonal relationships.

Communication with the staff informed that the interpersonal relationships of regulators with the community pharmacy management were also found to impact the inspection visit and its quality.

Another impact of "drug inspector absence" was found to be linked to hiring of pharmacy staff members. Depending upon the chance of regulatory visits, the pharmacy staff could consist of a combination of pharmacists, dispensers and/or salesmen.

It could be inferred that only pharmacies where either the management was more supportive of the CP role as a marketing tactic or facing higher regulatory oversight were following protocols slightly better and had created CP roles to maintain dispensing records. In several instances, CPs seemed to be trying to follow Schedule-G laws; however, people in general were able to obtain opioid medications and the CPs had to maintain fake dispensing records to account for the unauthorised dispensing.

5.2.3.c.ii Autonomy to refuse medicines

CPs might not have the authority to refuse the illegal dispensing of opioid medicines due to non-supportive managements. The implementation of Schedule-G remained variable. Reputed pharmacies on the outset seemed to be fairly compliant with the laws. However, closer observation revealed that even these pharmacies had several flaws in the manual systems they employed for keeping opioid records, thus allowing for the possibilities of altered or faked records. It was observed that the pharmacy operations were subject to business considerations, and staff members were instructed to avoid upsetting customers. The lack of support from the pharmacy's management can be perceived as a barrier for CPs trying to follow Schedule-G implementation.

5.2.3.c.iii Positioning of pharmacists

CPs were usually found in remote corners of the pharmacies. In some organisations it seemed to have been deliberate to facilitate narcotic dispensing or as a respect for female pharmacists by the management, as per social norms.

However, even in pharmacies, where there was no restriction of gender or the narcotic cabinet was in a centralised place, CPs were observed to be positioned away from dispensing counters. It was observed their location inside the pharmacy was sometimes derived from their own refusal to be in the same capacity and perform the same role as dispensers. CPs mostly seemed to get offended if stationed at the pharmacy counters, where they had to fill the prescriptions and dispense medications like other salespersons or pharmacy technicians. This behaviour was observed to be influenced from pharmacy management support as well as interdisciplinary relationships. Such interpersonal differences and negative perceptions can cause an impact to "teamwork and team spirit" and impact the provision of a future opioid service.

5.2.3.c.iv Visibility of CP and organisation's internal workflow

A pharmacist's location and job responsibilities in pharmacies are context dependent on the management and may vary even in the same pharmacy

(due to gender or morning/evening shifts). The managements of community pharmacies were inclined to use the presence of a pharmacist as a marketing tactic. They considered the 'CP' as a specialised and valued health professional inside the pharmacy and treated them as 'professionals or officers' and ensured the allied staff understood their role, authority and position clearly. Most pharmacists had been assigned the roles of controlling and facilitating narcotic dispensing and managerial tasks. Despite the narcotic cabinets being at a discreet location to control dispensing and CPs mostly stationed near them in supportive pharmacies, the presence of CPs was clearly highlighted and pronounced. However, this position of CP also might be a potential barrier in pharmacies where allied staff are non-cooperative and might not facilitate in signposting people or bringing them to talk to the CPs, thus resulting in less CP-public interactions.

5.2.3.c.v Public awareness about role of CPs

Majority of people arriving at pharmacies were found to not ask any medicine-related questions. But some of the people asked to speak to a CP and were taken to the CP by the dispensers. These people had specific questions about the medicines they were getting. For example, "*Does medicine A interact with B?*" Another person showed the CP two medications and asked, "*Both of them can cause sleep, is it okay if I take them together, would it cause any major side effects?*" People were observed to carefully listen to the CP and thanked them. It was inferred that these people probably have had a "past meaningful conversation" with the CP in the same or another pharmacy, and were expecting to meet the pharmacist and get information.

Instances where pharmacists tried to engage people themselves and tried to discuss their medications were met with mixed reactions. Some would agree to listen and discuss their medication, while others were reluctant and refused to listen to the information offered. People without a prescription (self-medicating, self-managing) were more difficult to convince to go back to doctors for review. However, they were receptive to pharmacist suggestions and advice about signs and symptoms of opioid-related harm.

Thus, people's acceptance or refusal of a CP's advice depends on their knowledge and perception of CPs, their past interactions, their own personal desire and motivation to seek medical information, and the behaviour and support of the pharmacy staff. Moreover, public awareness is key to compliance with new policies, laws and services and could help facilitate the implementation of new rules and changes in pharmacies.

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5.2.3.c.vi Perception/awareness of public about new laws

CPs asking for opioid prescriptions were negatively perceived by the people buying opioid medications and this even involved vocal complaints. This was observed to be causing CPs demotivation, resulting in their reluctance to comply with the law. The practice of pharmacists stamping prescriptions to mark them as dispensed was negatively perceived by people, who were observed to complain outright that other *“neighbouring pharmacies were not making their life more difficult”*, and that they would have to go back again to doctors and pay them fees to get a fresh prescription because the pharmacy *“ruined it”* and that they could have used it many times. In addition, managements’ lack of support in refusing medications was observed to cause CPs to struggle. Non-compliant people and non-supportive management/allied staff members would be a barrier to CPs in implementing a future opioid service.

5.2.3.c.vii Organization focus

All pharmacies were found to be operating with business interest. All activities, the conduct and job responsibilities of the staff were aligned to meet the organisational goals. In chain pharmacies, along with profitmaking, brand distinction of being a *“proper pharmacy”* was also observed to be a motivation in the structure of the pharmacy. Customer satisfaction to ensure loyalty was also observed as an organisational goal. CPs’ jobs and responsibilities varied according to the organisational aims and the managements were observed to be supportive towards CP implementation of laws in more reputed pharmacies. In addition, the respect, value and visibility offered to a CP in supportive organisations was observed to motivate CPs and they were generally more confident, showed more patient engagement, good relationship with staff and an overall propensity to follow laws and help people understand their medicines more.

5.2.3.c.viii Public behaviour and social perception

Noncompliance of people due to lack of awareness may become challenging for CPs refusing or reducing opioid medication dispensing. Moreover, any activity that might decrease the potential sales or reduce customer satisfaction was not welcomed by the pharmacies’ managements. The CPs in some organisations shared that *“they felt insecure due to lack of support from the pharmacy management to refuse opioids”* and had resigned to follow a neutral way to deal with customers rather than confronting problematic people. In addition, most CPs were observed to have struggled to keep customers happy when following the law to dispense opioid with a valid prescription. However, in pharmacies where the regulator’s chance of arrival was higher, the pharmacy was following the Schedule-G amendments better,

despite compromised potential sales and public complaints. The behaviour of CPs was observed to be very professional in guiding the public about why they were being refused dispensing. This explanation was met with mixed reactions from people. A few people remained verbally aggressive and stormed away or returned with a prescription.

5.2.3.c.ix Pharmacist counter

Only in one pharmacy did the CP have a dedicated counter at the back, which facilitated communications with people without compromising/affecting the daily dispensing¹³. In other pharmacies, CPs either avoided going to main counters or were distracted by fresh customer arrivals and could not give dedicated time and attention to the people asking for opioid information. Lack of a dedicated CP counter was observed to impact CPs' capabilities to scan, record and dispense opioids according to Schedule-G amendments.

5.2.3.c.x CP attitude

CPs were usually stationed near narcotic cabinets, which helped them to dispense opioids when asked by staff. However, as allied staff usually had access to these cabinets as well, the insistence of CP to remain only in a specific portion of the pharmacy (which is usually at a far corner) seems to stem from a desire to stay unnoticed and undisturbed by the public. In some cases, it was observed that pharmacists remained seated at the end of pharmacies as they considered themselves above other staff members in the hierarchical structure. CPs, unless asked by the manager, were observed to be reluctant to dispense medicines like other salesmen and therefore avoided front counters and remained stationed in their narcotic corner.

5.2.3.c.xi Pharmacist relationship with allied staff

CPs' skills, motivation, experience, background, and attitude were found to affect interprofessional relationships in pharmacies as well as dealing with the public. In locations where there was a clear distinction between a pharmacist and pharmacy staff roles, the overall daily activities such as dispensing, narcotic record keeping, billing, patient handling and stocking were found to be smooth. It was also observed that defined roles had helped assign tasks and helped reduce friction between the staff members. The entire pharmacy staff was found to be working towards one unified goal, dispensing medicines in the most optimum way.

Pharmacy technicians were observed to have more reservation towards CPs as compared to other salesmen (non-pharmacy). Their reservation was observed to be linked to the lack of CP role in the pharmacy, as they were

¹³ Please also see subheadings; visibility of CP and attitude of CP

handling dispensing, shelving, stocking and even procurement. In addition, all CPs were found to have a dedicated/separate area in the pharmacy, whether assigned by the pharmacy management or chosen by the pharmacists themselves. The reason for this particular segregation, especially when chosen by the CP, seems to stem from a desire to ensure a power of authority over other allied staff. This powerplay of presenting and alienating themselves due to being 'proper pharmacists' and perceiving themselves to be the 'managing officers' was found to cause friction between CPs, managers and allied staff. In the worst cases, the relationship broke down completely and they were openly found vocally complaining about each other. Defining segregated roles will help facilitate the implementation of service and overcome interprofessional resistance.

5.2.3.c.xii Management impact on CP support

From observations and communications, it can be assumed that the establishment manager's knowledge, awareness as well as the organisation's vision and aims influence their intention to hire CPs (for brand highlighting or to avoid trouble with regulators) and these factors play a major role in their behaviour towards CPs and staff. CPs were found to be involved in patient counselling and providing medicine information in supportive organisations as they were viewed by the pharmacy management as a promotional marketing tactic to increase the number of customers as well as improve sales. In cases where the pharmacy manager was a non-pharmacist or the pharmacy was independently owned by a pharmacy technician, the managements were overall found to be non-supportive towards CPs trying to follow laws or improve patient safety — because their activities were perceived to be against the business interest of these establishments. Thus, the implementation of Schedule-G laws was found to be variable. CPs in these organisations were also not provided with sufficient resources (support staff, dispensing station, equipment such as printer/scanner or autonomy to refuse opioids dispensing) to maintain the narcotic dispensing according to the law. It was observed that CPs working in non-supportive pharmacy environments were suffering more from an identity crisis than their counterparts working under supportive managements. Support from management was found crucial in the implementation of new laws, services and keeping CPs motivated.

5.2.3.c.xiii Digital and IT capacity

Pharmacies were found to be equipped with basic IT equipment, which could help maintain stock and batch entries, record and trace dispensing, share data with other pharmacies/doctors and manage comprehensive patient independent profiles for medication review. CP shared *"the software has the*

capacity to record and flag up a particular dispensing record; however, drug inspector checks only whether we have prescription scans and narcotic register [and so] that is all what we do". Furthermore, despite having the capability to do it digitally, pharmacies were implementing Schedule-G record maintenance manually. The manual process, it was observed, would make it easier for pharmacies to alter/update records as needed. Even the expiry dates of medications were observed to be manually checked, which could potentially result in a mistake (medicines arriving, distributor name, items in inventory were entered on the digital system but not the dates of stock expiry). A CP shared, "Now at this time (9:57pm) how do I talk to a doctor? And even if I called in the daytime, how will the doctor remember who this patient was; there is no prescription record or patient file except in private hospitals". It can be presumed that having basic or advanced IT systems might help overcome some CP challenges like reviewing prescriptions and maintaining an electronic dispensing record, which could help improve the time taken to deliver a service as well as minimise errors.

5.2.3.c.xiv Communication with doctors

In instances where CPs found therapeutic duplicates, or very high doses, or very expensive medications, or in instances where people mentioned they were not getting any pain relief, they would guide the customer to speak to their doctors about their condition or change doctors (potential of doctor shopping) because of lack of communication channels with doctors. Majority of people seemed unwilling to go back to doctors and insisted that CPs provide them with other alternatives. CPs were observed to provide alternatives but clearly referred them to doctors to discuss these problems in detail. Lack of communication channels with prescribers was observed to be a challenge for CPs and they were found to be interacting/changing prescriptions without legal authority. However, it has to be acknowledged, such medicine shop "staff" activities such as changing the brand name (if unavailable), therapeutic duplication, and pharmacoeconomically adjusting it according to patient demand, are considered normal in the society and are fairly common. In general, CPs were mostly not found to be altering the dose or suggesting a different frequency of medications except when the dose was missing or there was an unmistakable error or generic duplication.

5.2.3.c.xv Skills of pharmacists

5.2.3.c.xv.a Advanced opioid knowledge

CPs were found to be providing a generic set of instructions about dose and frequency and nothing specific to opioids. In case of a specific query related to opioids in the initial days of observation period, almost all CPs (except case 6, who did not engage at all with people) were found to be motivated and

were observed looking up the query using their mobile phones (this points to a lack of internal resources to help CPs). At other instances during the latter part of the observations, CP motivation to help people was found to have diminished and they were observed as distant, cold, unapproachable and dealing with them as quickly as possible (possible Hawthorn effect). From the data observed it could not be confirmed whether CPs had or lacked advanced opioid knowledge.

5.2.3.c.xv.b General knowledge and skills

Most of the CPs were observed to be ill-prepared for a community pharmacy setting (no knowledge of brand names) and were found negatively impacting the overall dispensing time and quality. It was observed that CP with less years of experience lacked “people/social” skills and were found to be struggling inside pharmacies with day-to-day activities. Managers were heavily reliant on other staff to help with the daily tasks.

5.2.3.c.xvi Insecure and vigilant

CPs shared that they did not have any communication channels to raise concerns or share their complaints about the lack of management support in following laws to their professional bodies and drug regulators. They also shared that there was no unity amongst CPs and shared, *“And then what happens? I will lose the job. No one will do strike for me that I was fired. It is their (owner) business, tomorrow here will be another pharmacist in my place. No one will do strike, everyone will say I was stupid. I can’t challenge this system. Anyhow I can’t quit this job, it pays well as compared to others. It is just one thing. Now I don’t get involved in patient dealing. I stay here in my area and deal [with] narcotics as per law”*.

It was also observed that CPs were trying to avoid legal complications on their license (as by law they are the responsible person) by staying within the “legally allowed actions” as well as maintaining an observant eye on the pharmacy to detect any fraudulent or illegal activity. Such “inspective” instances were usually met with resistance by the staff and management and resulted in increased tension between CPs and allied staff. CPs were observed to feel isolated in their struggle and were found to have developed safety mechanisms to safeguard their job and professional license by faking records of illegally dispensed items.

5.2.3.c.xvii Gender

Female CPs were observed to have been treated differently, varying from assigned duties to the hours they were required to keep. Female CPs were not tasked with storage and procurement, physical checks in warehouses, shelving of medicines or even dispensing, as opposed to their male

counterparts. This difference may be attributed to culture. A CP shared, “*My manager is really very nice; he does not ask me to stand like a salesman on the counter because I am female and therefore I am able to fully maintain narcotics dispensing (case 4)*”. Another female CP shared, “*I stay in my corner because if I move, I will be in the way of others (salesmen); this space (space behind counters) is very small for me to navigate without asking them to free up space (case 1)*”. However, in any case there was no restriction on CP to arrive at dispensing counters and one female CP (case 3) was observed to be fully involved in dispensing and patient engagement.

The desire of female CPs to interact with and participate in daily tasks of pharmacies was observed to be linked with the management’s support, their relationship with allied staff or their own personal reasons (self-perception and motivation). Overall, if there was support from the management and accepting staff, females were found to move around pharmacies as well as dispense at counters, which infers that female gender and social obligations might not hinder opioid service provision. In addition, the staff members were observed to be mostly pinpointing the public towards the pharmacist assigned location and helped facilitate a CP-public interaction.

5.2.3.c.viii Infrastructure, location of the pharmacy on patient engagement

Many community pharmacies were observed to have limited parking spaces, causing people to block other vehicles. As a consequence, people arriving at pharmacies were observed to be almost always in a hurry. With the dispensing capacity ranging from 2-8 people at pharmacies, depending upon the available staff, CPs were observed to find it challenging to get a customer’s attention to speak about their dispensed medications or experiences of using opioid medications, especially when people were in a rush or already had spent time in a pharmacy. Another consequence of high patient load was the impact on the non-pharmacist staff’s capability and willingness to volunteer to engage or support in guiding the public towards CPs. Many dispensers were observed to mislead people when asked if the pharmacist was in *by telling them that that pharmacist was out*. This was observed to be motivated by a desire to dispense medicines faster and avoid long queues. With fewer people and no queues, the interactions between pharmacy staff (CPs, dispensers) and people were more meaningful and proper. Floor space, adequate workforce, public willingness and support of allied staff might be crucial factors that could either facilitate or become barriers for CP-public interaction.

5.2.3.c.ix Locality

Community pharmacies near hospitals face patient loads at specific times, leaving staff shorthanded and pressured to fill prescriptions quickly, which

resulted in most pharmacy staff not following narcotic Schedule-G protocol and dispensing opioids like normal medicines.

Even in pharmacies that were fairly compliant with Schedule-G protocol, high patient load would see the allied pharmacy access opioid cabinets directly and work as a team to deal with patient load. People arriving at pharmacies near hospitals and clinics during OPD hours usually carried a prescription (hospital admission slip/prescription) and were comparatively more receptive to listen to the pharmacist's advice than people without a prescription. Hiring of CP (full-time, part-time) and their nature of engagement inside pharmacies was also found to be location dependent and subject to regulatory visits.

5.2.3.c.xx Lack of pharmacist availability

It was observed that the presence of a pharmacist ranged from 6 hours/day in the smaller pharmacies (only to cover the time where regulator could officially arrive) to 14 hours/day in the bigger pharmacies (they had two CP shifts, to cover opioid record maintenance and answer any patient queries).

These pharmacies utilised pharmacists to maintain narcotic records, which shows that the hiring of pharmacists could have been due to the new legislation. However, within the same city, an independent pharmacy with a non-pharmacist owner, had a pharmacist license on display but it was observed that the pharmacist arrived for a total of six hours (two hours on day three, four hours on day five) during the observations. The owner shared, *"What will the pharmacist do here? I only need the license and we have a proper agreement; we call him only if we need his help (possibly when drug inspector comes), otherwise he doesn't come"*. The pharmacist was also found to be only auditing the stock and did not attend to any person arriving at the pharmacy. The non-participation of the pharmacist in this case shows that the establishment was primarily interested in the pharmacist license to meet regulatory requirements instead of the CP services that the pharmacist might offer. It has to be highlighted that this is common in Pakistan and has always been the case; however, recent amendments have now brought about changes to CP roles and presence. It was further observed there was a complete lack of narcotic dispensing record keeping in this particular establishment, which was found to be linked to the lack of the awareness of the owner to the new legislation. There was also a hint of general annoyance and dismissal of the owner to the new laws. He shared, *"They make new laws and the next day the law is changed. They keep issuing notices"*.

5.3 Discussion of case study findings

5.3.1 Easy availability of medicines and non-pharmacy dispensers dispensing medications

It was observed that despite Schedule-G amendments in Pakistan, opioids are still dispensed without prescriptions, with CPs having little or no control over the unauthorised dispensing in majority establishments, even in the federal capital. It was also observed that CPs' availability could not be ensured around the clock to facilitate Schedule-G dispensing. The study also found that dispensers (not pharmacists) were majorly involved in dispensing opioids without maintaining a proper dispensing record as per law. These findings remain similar to the study by Bashir et al. (2021) [429], who conducted their study in 200 pharmacies and reported that a CP was found only in 11 pharmacies and opioids and other Schedule-G medicines were freely dispensed without prescriptions by dispensers and salespersons. This allows people to acquire opioid medications without authorisation, and allows aberrant self-medication practices to continue, and thus could contribute to the unsafe use of opioids.

Another interesting similarity between Bashir et al's study [427] and my study was that both report people demanding opioids for non-medical use and indicate a possible misuse problem. Bashir et al [427] reported that out of 200 pharmacies, 56 pharmacies reported that more than 200 suspected addicts come to them every week and try to obtain opioids. One male and one female simulated patient made a total of 400 visits to acquire a prescription opioid, and 318 times they were able to purchase a medication. The study reported that four pharmacists provided opioids without prescriptions only to females. However, this low number of dispensed opioids by CPs could simply be due to relation to lack of CPs in majority establishments. Nevertheless, my findings also report where CPs were supported, especially in reputed chain pharmacies in central locations, they were observed to refuse dispensing of opioids without prescription. This was attributed to the desire of pharmacy establishments to highlight their standards in following laws as well as the higher chances of regulatory visits in prime locations. This remains consistent with Bashir et al's study [112], which reports that the lack of implementation of Schedule-G amendments was due to the weak regulatory system. Both mine and their studies recognises improving regulatory systems might help with strict enforcement of laws and may support CPs presence as well as their capabilities to refuse unauthorised dispensing and reduce self-medication and help achieve safe use of opioids.

Another recent study (2022) from Pakistan also reports lack of Schedule-G amendments enforcement and reports the sale of antibiotics without a CP or a prescription [428]. As previously reported ¹⁴, sale of medicines without a prescription, lack of CPs and unauthorised dispensing is a common problem in LMICs. This indicates that developing laws might not be sufficient and policymakers should look into strengthening regulatory systems and enforcement.

5.3.2 Business and profit-making motives of community pharmacies

This study's findings show that managers and owners in most medicine shops and pharmacies are focused on generation of profit or brand reputation, which is congruent with the findings of other studies from Pakistan [389, 400]. Hence any activity decreasing the sale of medicines or decreasing customer satisfaction was not supported by the management and the CPs were observed to be struggling between enforcement of laws or focusing on profits and customer satisfaction. Lack of CPs' ability to stop self-medication and refuse medications was found to be impacting CP motivation and resulting in their disengagement from helping patients. Not having pharmacists in medicine shops or CPs disengagement might represent a missed opportunity for a CP to help avoid self-medication, adverse drug reactions, medication errors, misuse of controlled substances like opioids, inappropriate use of medicines, OTC availability of prescription medicines and lack of medication reviews [334, 335].

Medicine profit making is not unique to Pakistan and is reported in many studies. The systematic review by Miller (2016) [429] also states that profit making strategies by pharmacy owners in LMICs is common and is a challenge for CPs trying to ensure patient-centred services or practices. Similarly, CPs in a 2019 US study [404] also reported that the pharmacy management would pressurise them to abandon such activities that might reduce the sale of opioids. Compliance of pharmacy management to services can be ensured if they believe that utilising CPs as a promotional tactic to survive within a competitive market will be beneficial for their organisation's reputation in the market, ensure loyalty of customers and improve profit [404].

5.3.3 Self-medication and health literacy

It was observed that people who seemed to have better literacy were more predisposed to asking out for a CP to discuss their medication, perhaps because they were more familiar with the role that a CP plays in medication counselling and safety. Another study from Pakistan [430] mentions that better qualification or education of a person might improve disease management after receiving counselling from a CP, as it may improve

¹⁴ Discussion of Chapter 4

patients' knowledge and help clarify any questions related to medicine use. It should be highlighted that having adequate literacy does not ensure safe medicine use and numerous studies from Pakistan report that even medical and pharmacy students might engage in self-medication practices [431, 432]. As reported in my study findings, the refusal of medicines to people who are self-medicating might result in unsatisfied customers who might stop visiting that pharmacy, thus leading to loss of business that could complicate the CPs' relationships with their management and may even result in CPs withdrawing from following laws or faking false opioid dispensing records to protect their professional license.

5.3.4 Counselling time and patient satisfaction

My study findings report that people arriving at certain times were observed to be in a hurry due to lack of adequate parking facilities outside the pharmacy. The number of people waiting and the time people had already spent in the pharmacy waiting for their turn were all observed to impact the nature and duration of the conversations the people and the pharmacy staff had during dispensation of opioids. This is also reported in a recent Pakistani study by Abdullah et al. (2022) [433], which reports that majority participants were generally not satisfied with pharmacies and complained about lack of opportunity to talk to CPs, overcrowding, lack of adequate staff, lack of sufficient floor plan and the inability of CP to provide equal services to everyone. Lack of CP-public interaction is also reported in another Pakistani study that states that out of a total sample of 371 people, about 84% people were mainly handled by salesman (83.8%, n= 311), 12.7% by pharmacy assistants (n=47) and 3.5% (n=13) by a pharmacist. The study reported a mean dispensing time of about 1.11 minutes (SD=5.61) with a range of 0.5-6 minutes, depending upon the availability of staff and the placement of medicines [434]. Lack of opportunity and less time available to the CP to interact with people was observed in my study too, where CPs did not have sufficient time for proper patient engagement in rush hours, especially when the pharmacies are located near public sector hospitals. This was attributed to the fact that CPs needed to maintain the Schedule-G requirements as well as handle dispensing to support the allied staff to deal with customer load. In pharmacies where the number of dispensers was sufficient, the dispensers helped attend people and dispense medication whereas CPs were able to focus on people who needed prescription medication and were able to offer them counselling services as well as maintain the records. Sufficient time is also needed to help motivate people to discuss their medication as well as allow CPs to review their medications. The quality of this interaction might lead people to adhere to CP advice and use their medications in an optimised manner. A Pakistani study by Abdullah et al.'s (2022) [433] also reported that

CP time was a factor that was found related to people's satisfaction and their intention to adhere to the CP's advice. Only 30% (n= 900) people in their study reported that a CP was available for patient counselling and majority people, especially with high literacy, wanted to spend more time with CPs and discuss their medications. It should be highlighted that although people in their study were unsatisfied with the overall time spent with CPs, they reported satisfaction with and trust on the CP's advice and knowledge.

Another study from Pakistan [435] also reports approximately half of the patients were dissatisfied with the waiting time, the knowledge of the counselling person and complained that the pharmacy staff lacks interest in patient recovery. Optimal counselling can improve patient compliance with their medication.

5.3.5 Telemedicine services

My study indicates that people could be acquiring opioids by ordering them for home delivery and bypassing the Schedule-G amendments (without providing a prescription). During COVID-19 telemedicine services [436] and medication deliveries [437] proved really useful and were accepted worldwide due to the lockdown of cities, transportation, and markets. Individuals engaged in seeking healthcare advice via telephone calls with trained pharmacists, who provided counselling, education and pharmaceutical care and fulfilled public medication-related needs. However, my study finds that as Pakistan has no centralised digital health systems and people have manual prescriptions, they can order their medicines via telephone services and bypass having to present prescriptions, as required by Schedule-G drug amendments. The practice offers convenience to people with mobility issues or excessive pain, but also opens the door to self-medication or unsafe use of opioids. Additionally, as is common with in-person dispensing, these telephone services are also handled by non-pharmacist dispensers and salespersons and presents a missed opportunity for CP-patient interaction, where CPs can provide them medication counselling and reviews.

Online and telephonic pharmacies have been known to provide convenience to the public [438], but it should be highlighted that unregulated e-markets in the US aided in the overall opioid medicine diversion and opioid crisis [439-442]. Legitimate online pharmacies are rising in LMICs, including Pakistan [443, 444], but with limited regulatory checks, this could potentially become a safety challenge for medicines like opioids that have a high risk of causing harm when used without proper supervision [439-442] and policy makers need to look into developing standardised protocols and laws for telephonic or e-dispensing of medications.

5.3.6 Female gender

My study provides insights into what female CPs might be experiencing in the community pharmacies. My study found female CPs to be in a slightly different role and physical space in pharmacies than their male counterparts. Some CPs had stationed themselves into pharmacy corners either due to personal choice or were forced there ('out of the way' locations) as a respectful culturally-derived gesture, depending on the organisation and management. The reasons behind pharmacy managements' selective exclusion included facilitating female pharmacists in avoiding facing the public (mostly men) and being sensitive to the social and cultural limitations of women. This also involved making the workplace 'easier' for women by assigning them less strenuous physical tasks, which may otherwise include stocking of medicines, bringing medicines from storage warehouses and dealing with long public queues. Whether the people coming to a pharmacy could reach the CPs in their assigned location was observed to be management and staff dependent.

When it comes to an opioid optimisation service, this study recognises the need of the public to be able to approach a CP regardless of their gender. Having inclusive policies and supportive managements can facilitate CP-public interaction and help with the fidelity and sustainability of future services. Although this study featured an even distribution of both genders in the CP role¹⁵, other studies from pharmacy [445, 446] as well as medical science fields [447, 448] in Pakistan have highlighted an overall deficiency of female workers in professional healthcare roles, despite high admittance into higher education institutes such as pharmacy schools and medical colleges. These studies [445, 446] report unsafe and non-inclusive workplace policies as well as societal and family pressures as the major reasons listed for lack of female health workforce. Although my study was not focussed on exploring female CP's in-depth experiences of working in pharmacies, future studies should explore how pharmacies can be made more inclusive for women. Studies [446, 449] from Pakistan suggest making workplaces more inclusive and policy makers developing policies and guidelines supporting women professionals might help overcome current gender barriers.

Please note that polypharmacy, lack of electronic prescriptions and prescription adulteration, obtaining opioids for suspected euphoric reasons, self-medication and doctor shopping were also observed in case studies. The discussion of these factors contributing towards the unsafe use of opioids as

¹⁵ Due to selective purposive sampling to include a diverse range of both men and women

Chapter 5 Case studies: Subchapter C discussion

well as their impact on CPs in delivering an opioid service have been previously discussed in chapter 4 subchapter C.

Chapter 6: Combined findings from interview, focus groups and case studies (triangulation)

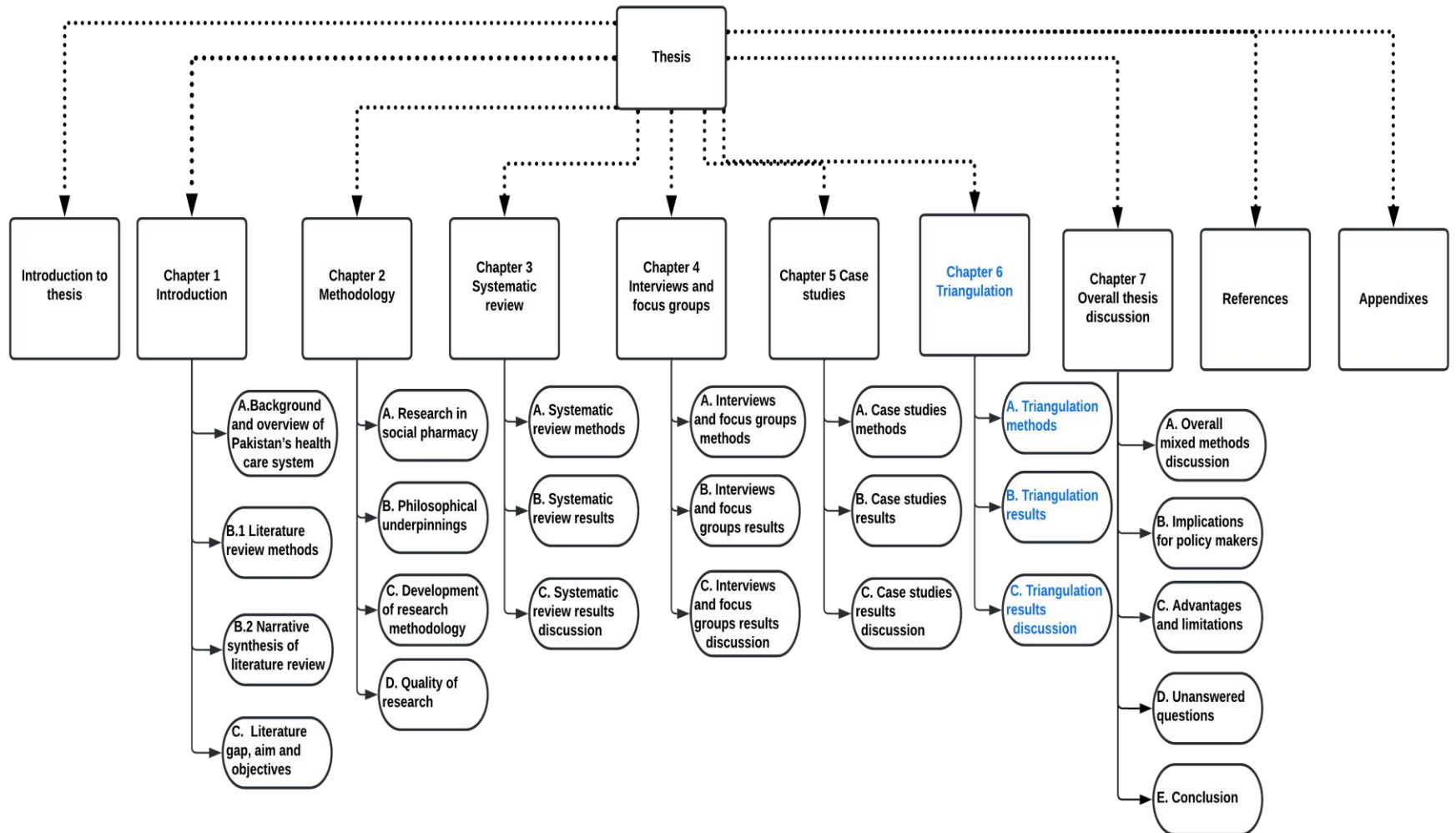


Figure 6.1: Overview of chapter 6 in thesis

6.1 Subchapter A: Methodology used for triangulation

This chapter shows the triangulated findings of interviews and focus groups with case studies.

6.1.1 Methodological triangulation justification

As this was an exploratory multi-methods study, the findings were triangulated by bringing together information or context about specific phenomena, actions and strategies reflected under subthemes and/or themes in both studies (interviews/focus groups and case studies). Please note all related data to a theme or subtheme was converged from both studies, rather than picking only similar findings across methods. This was done because the aim of using two methods in this research study was to supplement data collection and provide wider perspectives and data about the phenomena of interest, which would not have been possible to achieve by one method alone.

6.1.1.a Methodological triangulation steps

Data triangulation process in my study was done in two steps as follows (Figure 6.2):

1. Comparing

As shown in Figure 6.2, the first step included comparing, contrasting, confirming and complementing the exploration of the different themes and subthemes in both studies. A detailed overview was taken of codes, subthemes and themes in both methods.

2. Categorising

Both similar and supplementing codes and subthemes about a particular context, phenomenon or themes from both studies were placed on one sheet of paper (OSOP). The repetition was deduplicated and resulted in comprehensive information gathered about a specific phenomenon, subtheme or even theme on one sheet.

The OSOP master sheet for triangulation has been provided in Appendix 9.

6.1.1.b Triangulated findings validation

The triangulation findings from both methods were validated by taking an extensive review of the triangulated themes using constant reflection and discussion with the research team.

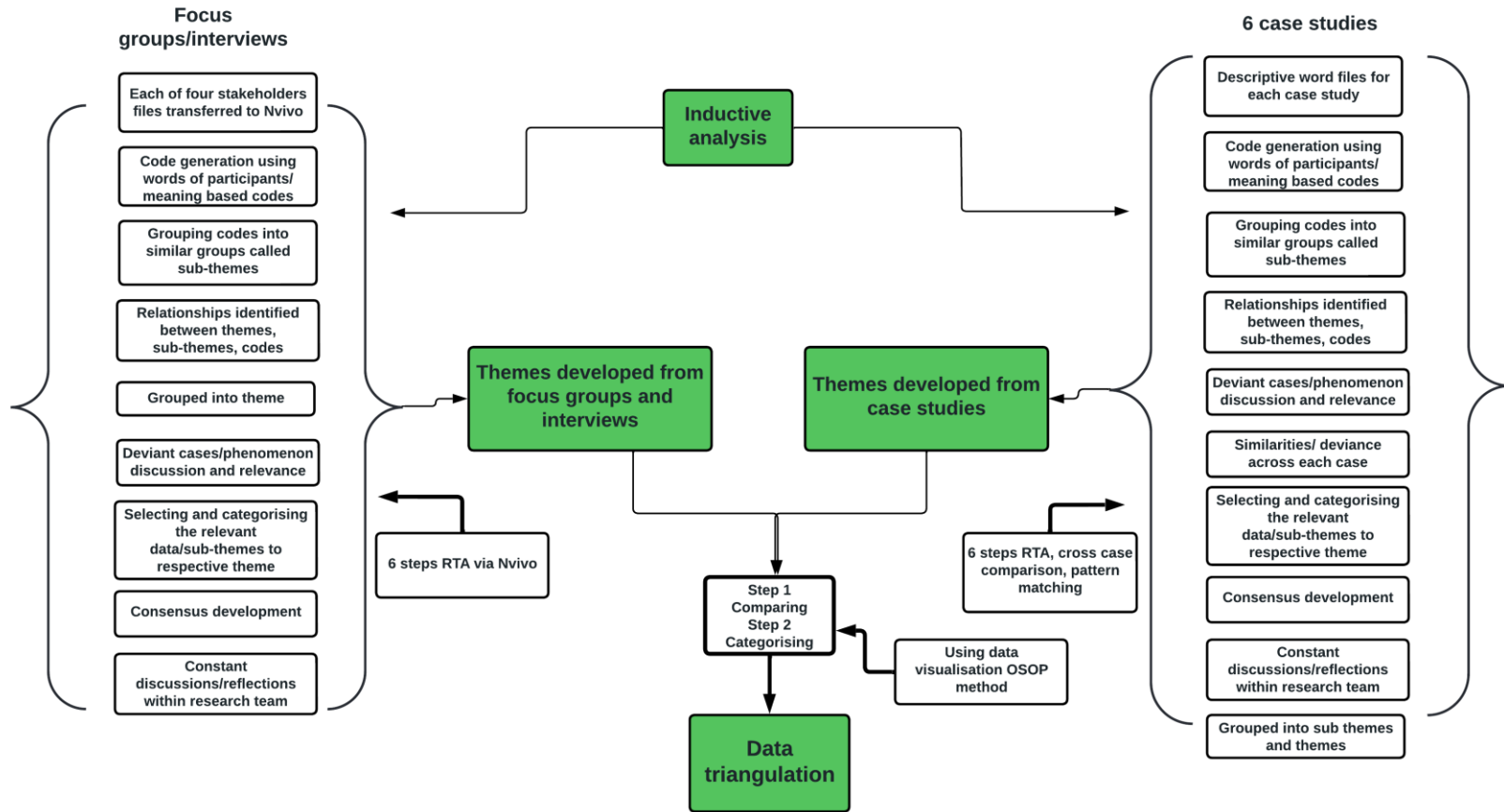


Figure 6.2: Overview of methodological data triangulation from interviews/focus groups and case studies

Chapter 6 Triangulation: Subchapter A methodology

6.1.2 Diagrammatic model development

After triangulation of data, the diagrammatic models (logic models and proposed intervention diagram) were developed using the data visualisation process mapping technique [450] as shown in Figure 6.3 below.

In this phase, all the data from both studies brought together on OSOP under each theme underwent process mapping by employing the following four steps:

1. Selecting and representing events

The relevant actions, factors, determinants identified within both studies as applicable to a specific theme were discussed within the research team to determine whether they were appropriate to the theme. They were then put on one sheet (OSOP) as per the objectives of this study.

2. Situating data in time/process

The relevant actions, factors, determinants related to a specific theme or a phenomenon were situated within each thematic diagram either by identifying their relationships with other subthemes as presented in data or by logically determining their placement on the map. For example, all factors contributing in their contextual capacities (system, community individual etc) identified in both studies towards unsafe use of opioids were logically arranged according to a patient's journey of acquiring medications, and then developed into a logic model of factors contributing to the unsafe use of opioids.

All diagrammatic models in this thesis were developed using the process described above.

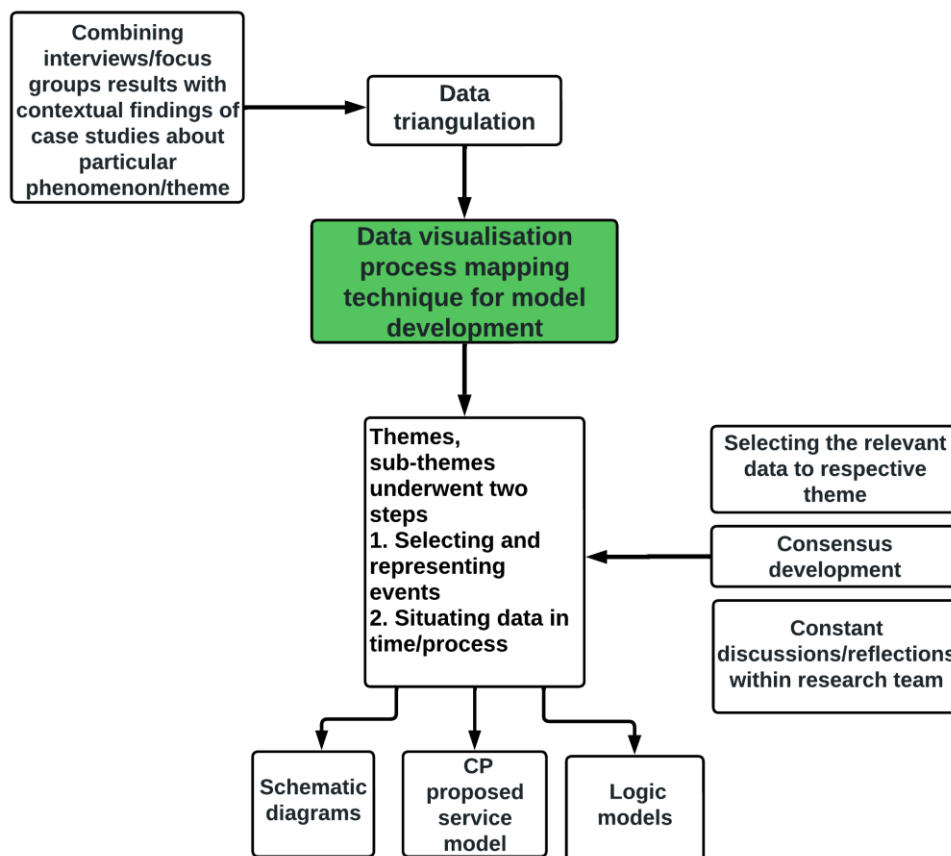


Figure 6.3: Diagrams and model development using data visualisation technique

6.1.2.a Model validation

All models presented in this chapter underwent extensive engagement and discussions within the research team (supervisors), which helped the enquiry move from individual subthemes or themes in individual studies to analytical interpretations and model development.

6.1.3 A step by step exemplar of how the CP proposed opioid service diagrammatic model was developed

6.1.3.a Methods used to develop proposed CP intervention/service

Below I present one example of how the CP opioid service's (proposed intervention) schematic diagram was developed.

6.1.3.a.i Data collection

Step 1

In study 1, the semi structured topic guide helped explore 'how CPs can help optimise the use of opioids and help overcome any existing challenges contributing towards unsafe use of opioids' using interviews and focus groups.

Chapter 6 Triangulation: Subchapter A methodology

Step 2

In study 2- case study observations, all CP actions that could help optimise the use of opioids in people with CNMP in community pharmacies were observed and recorded.

6.1.3.a.ii Data analysis

Step 3

Data analysis in phase 2, study 1 (please see chapter 4: Data analysis in interviews and focus groups for detailed methodological steps) resulted in the development of the theme: possible CP actions that can help achieve the optimised use of opioids.

Step 4

Data analysis in phase 2, study 2 (please see chapter 5: Analysis method of case studies) resulted in the theme: CP action perceived to promote optimised use of opioids.

6.1.3.a.iii Data triangulation

Step 5

Data from both themes from study 1 and study 2 about possible CP actions that can be undertaken to help optimise the use of opioids were brought together by putting all codes and subthemes on OSOP. Further steps listed under the heading Data Triangulation Method in my study, 6.1.1.a, resulted in proposing a set of perceived actions that CPs can take within existing contextual determinants that could help optimise the use of opioids.

6.1.3.a.iv Diagrammatic mapping

Step 6

The triangulated codes and subthemes then underwent a process mapping technique (as explained in 6.1.2) that helped create a schematic diagram of CP opioid service/intervention.

Figure 6.4 shows the full process of the development of the proposed intervention (service) model below.

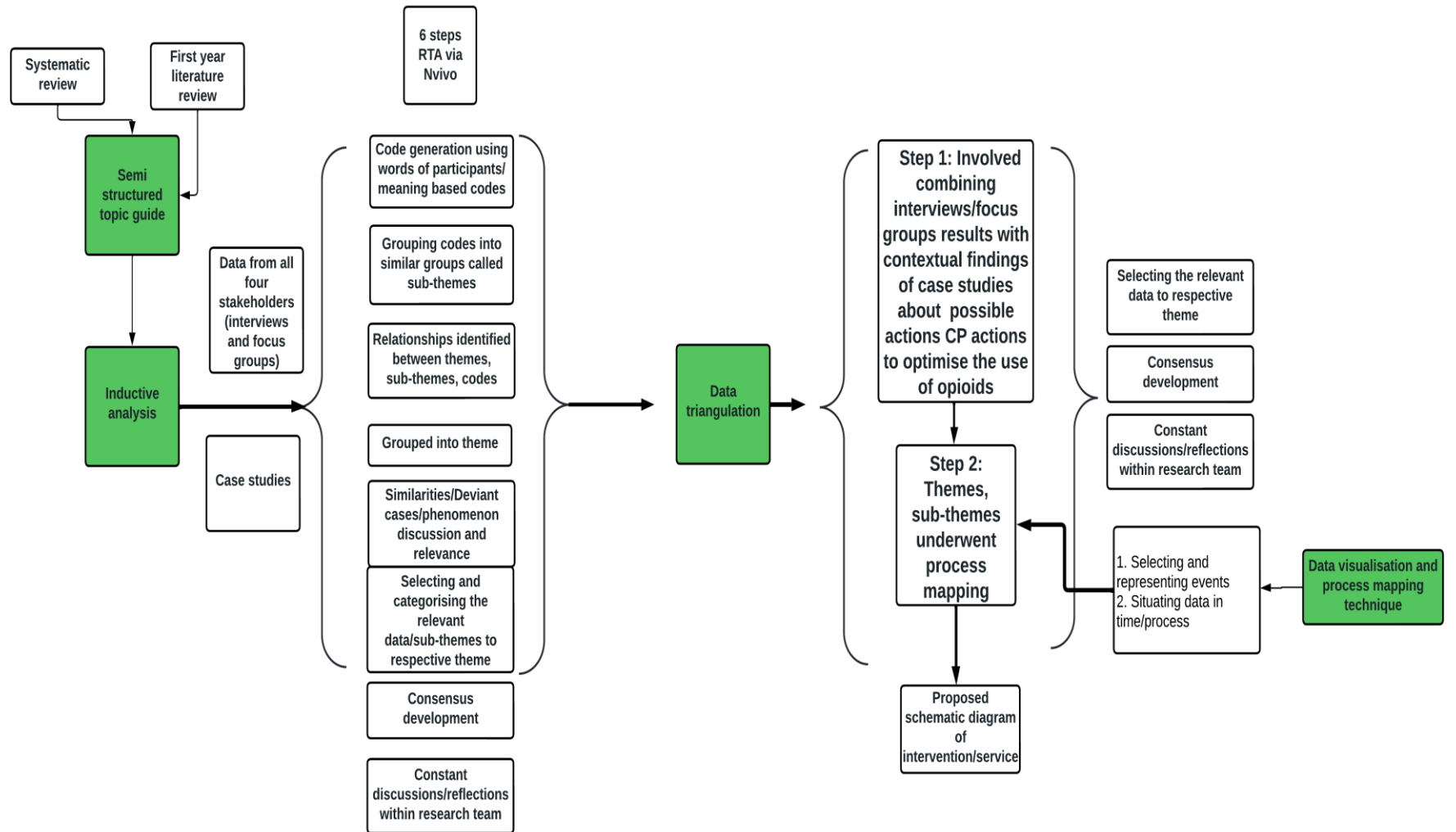


Figure 6.4: Overview of the process to develop CP opioid service proposed diagrammatic model

6.2 Subchapter B: Results of triangulation

6.2.1 Overview of triangulated findings

Triangulating findings from both studies that were similar and/or supplemented each other about a specific theme, subtheme, or even a phenomenon helped develop three overarching themes:

1. Factors contributing towards the unsafe use of opioids
2. Proposed CP actions that might help optimise the use of opioids
3. Strategies needed to overcome existing CP barriers to service delivery

After the triangulation, four models were developed in this thesis. The first two models are schematic diagrams, whereas the other two are logic models as shown below:

6.2.1.a First model

The first model is a schematic diagram of the journey of a person with CNMP to acquire opioids and shows factors that might be currently causing/contributing towards the unsafe use of opioids. The schematic diagram also shows perceived strategies as identified in both studies, which are needed at various time points to help overcome these challenges.

6.2.1.b Second model

The actions perceived/observed in both studies that can be taken by CPs to help overcome current challenges contributing to the unsafe use of opioids were developed into a schematic diagram of a proposed CP opioid service model that could help optimise the use of opioids¹⁶.

6.2.1.c Third model

The third model is a logic model that was developed by incorporating the actions perceived/observed to be taken by CPs (model 2) that might overcome current challenges contributing to the unsafe use of opioids into the first model. This model shows CP actions and their anticipated benefits to the system.

6.2.1.d Fourth model

The fourth model is a logic model that presents the strategies that might be needed to help develop and deliver a CP opioid optimisation service based on the existing barriers and facilitators identified/perceived within the triangulated findings.

The following subsections now shows details of how the data was triangulated and the development of each of these four models.

¹⁶ For step by step details, please find steps of triangulation listed under subsection 6.1.3

Chapter 6 Triangulation: Subchapter B results

6.2.2 Unsafe use of opioids

The subthemes from chapter 4 and 5 about the possible factors currently contributing towards the unsafe use of opioids as shown in both study findings have been collated and brought together as a supplement to each other and are shown below in Table 6.1.

Chapter 6 Triangulation: Subchapter B results

Table 6.1: Factors shared by stakeholders or observed contributing/contextualising the unsafe use of opioid

Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation)	Strategies shared by stakeholders	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/identified strategy which might overcome existing challenge
Chronic non-malignant pain experience	Ineffective pain relief and suffering	a. Due to inadequate pain management people might be experiencing inadequate analgesic relief b. People might be overusing, combining and might be non-adherent to prescribed dosage regimens	Developing the role of CPs can help doctors monitor and manage the use of opioids in uncontrolled pain	Uncontrolled pain and demand more medicines	Most people seem unsatisfied with their pain medications and were observed to complain about unmanaged pain and asked medicines (self-medication) from pharmacy staff/CP. It could not be inferred from the conversations if people had used opioids in past	CPs might be able to guide people and refer them to doctors and discourage self-medication
	Perception of opioids	People do not perceive opioids different than OTC medicines		Public perception of opioid medication	People were observed to demand opioid medicine without a prescription. Upon refusal of dispensing opioids, they asked why this medicine cannot be dispensed and needed a prescription	CP might be able to guide, counsel and educate people with CNMP about opioids as to how they differ from other OTC analgesics
Factors causing non-availability of potent opioids	Lack of CPs ability for controlled dispensing	a. Lack of CPs b. CPs despite the recent law amendments might not be able to stop dispensing of opioids without prescription	Improved implementation of laws requiring CPs to be present for opioid dispensing	Regulation impact on CP ability to follow laws Lack of pharmacist availability	CPs were not able to ensure opioids are dispensed after valid prescription(s) Weak Schedule-G implementation was observed	Improve implementation of laws

Chapter 6 Triangulation: Subchapter B results

					CP presence was found variable and was related to the management that seemed to be influenced by the regulatory visits and brand recognition and reputation of their pharmacy	
	Dispensing by non-specialised people	Non-pharmacist dispensers might be dispensing without prescription, advising (prescribing) and administering opioids without authority		Unauthorised opioid dispensing and easy availability of medicines	<p>Dispensers were observed to be dispensing opioids without a prescription</p> <p>Presence of CP might help control the dispensing as per laws however CPs might not have autonomy to refuse dispensing due to non-supportive management</p>	<p>Supportive laws supporting CP presence</p> <p>Supportive laws supporting CP followings laws</p> <p>Improved regulatory system</p> <p>Improve implementation of laws</p>
Unsafe use of opioids	Regulation	<p>a. Opioids remain freely available to purchase without prescriptions due to weak regulation</p> <p>b. Lack of CPs for enforcing new laws and maintaining records</p> <p>c. Unregulated pharmaceutical promotional activities causing over prescribing of opioids</p>	<p>Improve the regulatory system</p> <p>Increase the number of regulatory workforces</p> <p>Developing CP roles and proper implementation of laws might help</p>	<p>Regulation</p> <p>Unauthorised opioid dispensing</p> <p>Poly pharmacy</p>	<p>CPs were observed to be causing some level of restriction/control over opioid dispensing without prescriptions. However, whether CP can refuse opioid unauthorised dispensing depends on management/manager which seemed to be influenced by organisational aims and the chances of regulator arriving</p>	<p>Implementation of Schedule-G laws and strict regulation</p> <p>Management support to CPs to refuse opioid dispensing without prescriptions</p>

Chapter 6 Triangulation: Subchapter B results

		d. Improper prescriptions (lacking details, number of refills, indications etc)	control the unregulated dispensing		Poly pharmacy with same generic of opioid with multiple brands was observed. However, it cannot be inferred why there was more than one opioid prescribed from the data available (maybe unmanaged pain, maybe pharmaceutical marketing influenced practice)	
	Black market availability and sales	a. Unregulated distribution channels b. Strong opioids like morphine also available	Improving regulatory system	Not observed		
	Access to pain management	People lacks access to pain management facilities, pain specialists and potent morphine causing unsafe use/overuse of available medicines		Not observed		
	Digital health systems	a. Lack of patient records and medication history affects doctors' ability to provide need-based patient care b. Prescription adulteration	Developing and investing in digital health systems	Digital systems capacity Prescription adulteration	Software used for managing pharmacy had an inbuilt function of flagging up possible drug interactions/warning/special checks, maintain patient dispensing records, reminders for repeat prescription. Software was only being used to process billing	Implementation of laws to have minimum standards of pharmacy Clear guidelines and SOPs might help standardise pharmacies

Chapter 6 Triangulation: Subchapter B results

		c. Past prescribing/medication records missing			and stocking/dispensing audits	
	Business oriented medicine outlets	a. Medicine selling establishments focus on selling more medicines and making profit b. Weak implementation of Schedule-G as it requires dispensing only after prescription and decreases potential sales	Laws and strict regulation	Business and customer focused Autonomy of CP	Pharmacies were observed to be operating under business focused or brand recognition or customer happiness and loyalty focused CP seemed to lack autonomy to refuse opioids without prescriptions due to management	Implementation of Schedule-G laws and strict regulation
	Doctors overburdened	a. Doctors have too many patients and are unable to spend time patient counselling about opioids b. Lack of medication records, patient literacy and time pressure affect their ability to rationalise medications and identify high risk patients to opioid usage	Developing role of CPs to guide, educate and counsel people for opioids and help take burden off doctors	Not observed		
	Doctor shopping	a. Due to inadequate pain relief b. Social norm to go to more than one	Improving patient awareness,	Doctor shopping	On many instances it was observed that people were acquiring opioids on two prescriptions for the	CPs can help identify a possible interaction/duplication (while review) and

Chapter 6 Triangulation: Subchapter B results

		doctor for confirmed diagnosis and then use both doctor medicines	counselling and education		same patient's name, having similar opioid medicines simultaneously. With the conversations it could be inferred that people might even be using the two doctor medications at the same time	counsel patients how to use their medications
	People lack trust/perception of doctors	People prefer self-medication or avoiding doctors due to: a. Lack of trust on doctors due to pharmaceutical promotions, the economic benefits and the overall convenience b. Lack of empathy from doctors		People reluctant to go to doctors	People mostly remained reluctant to go back to doctors and asked the CP to advise them medication. The reason shared was lack of trust on doctors due to pharmaceutical marketing influenced practices and making profit	CP education and counselling might help educate people about the benefits to medication reviews and convince them to go to doctors
	Perception of pharmacists	People lack awareness about CP roles in medicines information, counselling and review	Improving public awareness about CPs	Educated people asking/reading leaflet	People might be aware of role of CPs and approach them to ask about medicine information, however majority people seemed unaware of CP role	Improving public awareness about CPs Better signposting and visibility CP proactive role in patient engagement
	Uncontrolled chronic pain	a. May try to use opioids more than the recommended dose b. May use morphine or illegal	Developing the role of CPs can help guide people about pain management	Uncontrolled pain and demand more medicines	Most people seem unsatisfied with their pain medications. It could not be inferred from the conversations if people had used opioids in past	CPs might be able to guide people and refer them to doctors, instead of self-medicating with analgesics

Chapter 6 Triangulation: Subchapter B results

		substances (diamorphine { heroin }) for pain relief c. May use CAM, faith therapy and get exposed to quacks	possible expectations and refer them to doctors			
	Health literacy	Due to health illiteracy take a combination of medicines without understanding the potential of harm, non-adherent, may not follow-up	Improved patient awareness	Doctor shopping Poly pharmacy	People either due to lack of awareness or intentionally might be doctor shopping and using medicines more than the prescribed dosage and frequency	Public education, counselling and improve awareness
	Addiction and tolerance	a. People with mental health issues might be at a higher risk of overusing opioids b. People might develop tolerance and may keep increasing dose/frequency c. Possibility of intentional misuse		Possible misuse of opioids	It was reported by CPs that people with misuse intention of opioids arrived at late times	CPs might be able to identify people using for recreational/misuse purposes and can help control unauthorised dispensing (done by dispensers) by properly following laws. They can also provide medicine information about possible side effects and guide people
	Self-medication	a. People might be self-medicating b. People might be recommending other people opioids c. People might be sharing opioid medicines with others	CPs might be able to educate and provide awareness to people	People awareness about opioids and self-medication People demand medicines	It was evident majority people arriving without prescriptions were self-medicating with opioids People might purchase more opioids as well as	CP making sure opioid dispensing is followed after a valid prescription and help implement laws and control unauthorised dispensing. CP referring/guiding/convinc

Chapter 6 Triangulation: Subchapter B results

					share opioids with family or friends	ing people for a visit to a doctor CP education and counselling people
	Lack of review	People reluctant or unable to go for a subsequent review because of economic reasons (poverty) or difficult access (location, prescriber unavailability) or lack of trust on doctors	CPs might be able to provide patient awareness and education (Doctors might help with that too but are already overburdened)		People might be using an old prescription for repeatedly obtaining medicines which indicates a lack of doctor review and a potential self-medication, medication/self-management	Patient counselling might help improve their review visits and adherence to doctors' advice

* OTC= Over the counter, CP= Community pharmacists

Chapter 6 Triangulation: Subchapter B results

The collated themes from both studies (Table 6.1) present the evidence around the current use of opioids in the management of CNMP and identify the gaps and deficiencies in the overall patient journey to acquire medicines that might be contributing towards the unsafe use of opioids in the management of CNMP in Pakistan. The collated themes in Table 6.1 also presents strategies identified in both studies that might help optimise the use of opioids. These strategies include mandating and strictly enforcing regulated supply of opioids only on prescriptions, increased public health awareness and literacy, improved access to potent opioids for adequate pain management, specialised doctors and pain facilities. Additional strategies include control and regulation of, unlawful dispensing, prescribing and administration of opioids as well as ensuring standardised prescribing. Other strategies targeting multilevel factors include patient counselling and monitoring adherence to therapeutic regimes, medication reviews and discouraging self-medication, self-dose adjustments and developing the role of CPs.

Factors and proposed strategies in both studies have been logically summated using data visualisation techniques (Figure 6.2, 6.3) and helped develop a visual schematic diagram as shown in Figure 6.5 below.

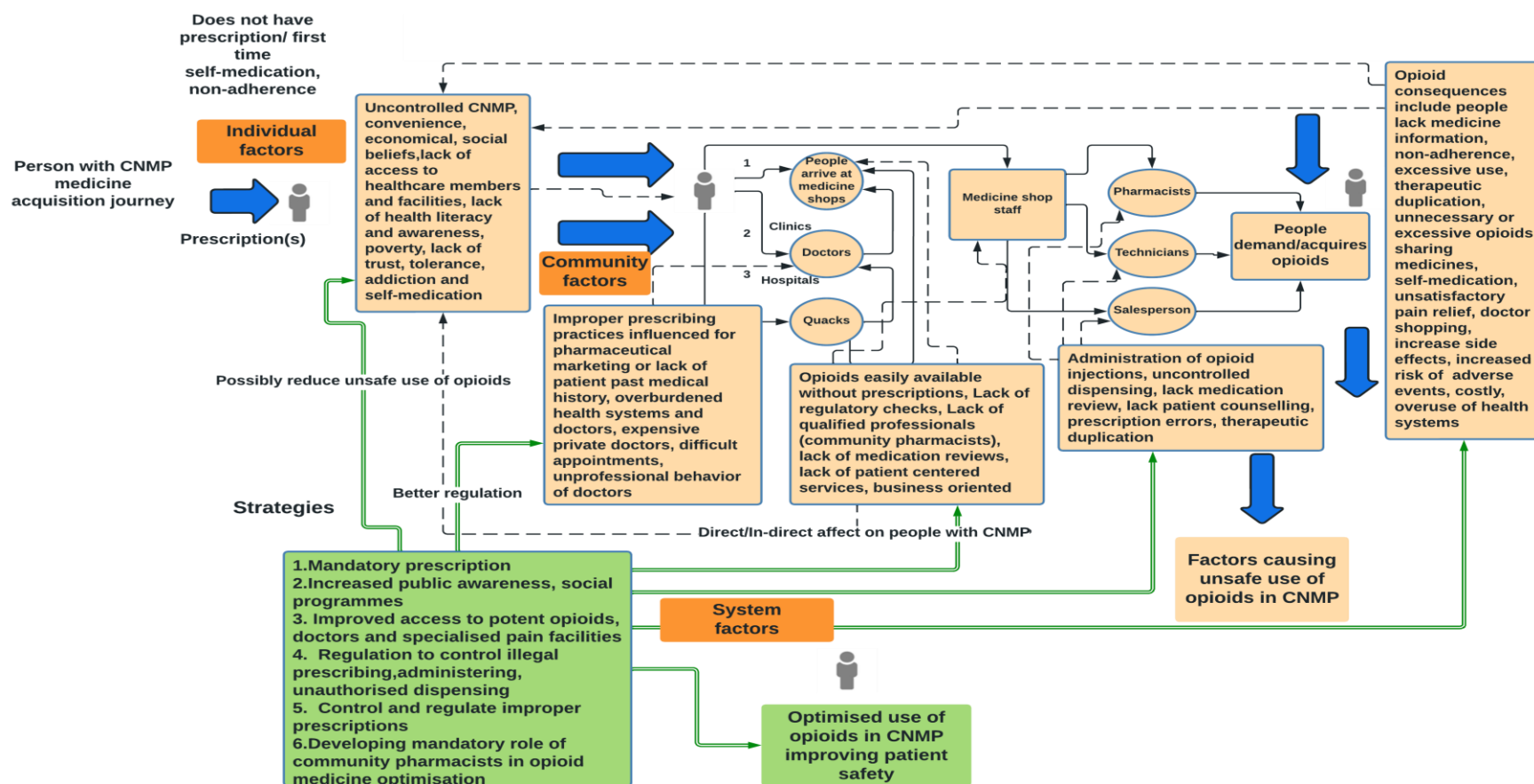


Figure 6.5: Schematic diagram of factors contributing towards the unsafe use of opioids in the management of CNMP in Pakistan¹⁷

¹⁷ Key for figure: The peach-coloured boxes provide location and target sites as well as current factors contributing towards unsafe use of opioids, the green box presents identified strategies, which are perceived to overcome current opioid unsafe use barriers, the green lines present possible strategies sites of various strategies identified

Chapter 6 Triangulation: Subchapter B results

6.2.3 Possible CP actions that can help optimise the use of opioids

The subthemes from chapter 4 and 5 about possible CP actions that might promote the safe use of opioids have been collated and brought together as shown below in Table 6.2 below.

Chapter 6 Triangulation: Subchapter B results

Table 6.2: Possible community pharmacist actions that can be undertaken to help optimise the use of opioids

Theme/sub theme Focus group/interviews chapter 4	Focus group/interviews (key interpretation)	Themes/subthemes Case studies chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might support CPs to deliver opioid service
<p>Opioids dispensing and record keeping as per legislation</p> <p>Health system benefits</p>	<p>Maintain opioid dispensing records and ensure regulatory requirements have been met as per the laws</p> <p>CPs can help control and prevent the misuse and diversion of these medicines</p>	<p>Record keeping</p> <p>CP advice offered</p> <p>Possible misuse of opioids</p>	<p>Although CPs might be able to keep the records of opioids dispensed however it was found variable depending on the people demand/acceptance, support of pharmacy management, allied staff support and CP own perception and discipline to follow laws</p> <p>CP may help identify high risk people, self-medication, misuse and diversion</p>	<p>a. Developing CP favourable laws and policies will support CPs</p> <p>b. Implementation of laws</p> <p>c. Enhanced regulatory system</p> <p>d. CP knowledge and skills</p>
<p>Patient counselling and education</p>	<p>Patient counselling and education as per the need, language or literacy of the people</p>	<p>CP advice offered</p>	<p>CPs can possibly provide advice to patients about medicine, their disease or simple what could be the next step in their course of action. Advice offered included possible side effects (drowsiness mostly), suggesting OTC medicine for pain relief, information about dose, frequency, adherence, missed dose and referral to doctors or physiotherapists or CBT</p>	<p>a. Developing the role of CPs and providing them legislative support as well as organisational support</p> <p>b. Improve CP knowledge and skills</p> <p>c. Improve CP motivation</p>

Chapter 6 Triangulation: Subchapter B results

<p>Medication review</p> <p>Patient clinical benefits</p>	<p>a. CPs need to perform comprehensive medication reviews</p> <p>b. Could identify high risk of opioid people, reducing polypharmacy, identifying and stopping drug-drug interaction, stopping medication, cheaper therapeutic substitutions, errors and rationalisation of opioid medicines according to patient individual needs (also perceived clinical benefits)</p>	<p>a. Reduction in therapeutic duplication</p> <p>b. Therapeutic substitution</p>	<p>a. CPs were observed to recognise poly pharmacy within/across prescriptions</p> <p>b. Alternates of medicines were offered, both brand substitutions and therapeutic substitutions. It should be noted CP and allied staff are not legally authorised to prescribe/amend therapeutic substitutions</p>	<p>a. Improve CP knowledge and skills</p> <p>b. Improve CP motivation</p> <p>c. Improved public awareness</p>
<p>Referrals to doctors</p>	<p>People should be guided/convincing to visit the doctor in case of self-medication with opioids or if people are using opioids continuously without review or experiencing any adverse effects</p>	<p>Referral to doctors</p> <p>Advice for CBT/physio/dentist/migraine specialist</p>	<p>CPs were able to guide people according to their specific needs and give them information about possible treatment places/services that might help with their condition</p>	<p>a. Improve CP knowledge and skills</p> <p>b. Improve CP motivation</p> <p>c. Develop digital health systems</p> <p>d. Provide organisational support such as CP counters, hardware/IT, adequate staff</p>
<p>Identify high risk people</p>	<p>Addiction and tolerance. People might develop tolerance and may keep increasing dose/frequency</p>	<p>Suspected opioid misuse by CP</p>	<p>CPs might be able to identify people with aberrant use of opioids. CPs can ensure opioids are dispensed only after a valid prescription and help educate people to be aware of potential side effects</p>	<p>a. Improve CP knowledge and skills</p> <p>b. Improve CP motivation</p> <p>c. CP autonomy required to refuse opioid dispensing without prescription</p>

6.2.4 Proposed CP opioid service model

Table 6.2 shows actions/activities from all stakeholder results and observed case studies that could either be delivered as isolated interventions or as a part of a series of service components to provide optimal patient care in people using opioids. These triangulated steps/actions were collated logically and strategically mapped in a schematic diagram as shown in Figure 6.6 as a multi-step opioid service using OSOP visual data display technique, enhanced with process mapping technique (Figure 6.4) depending upon patient needs.

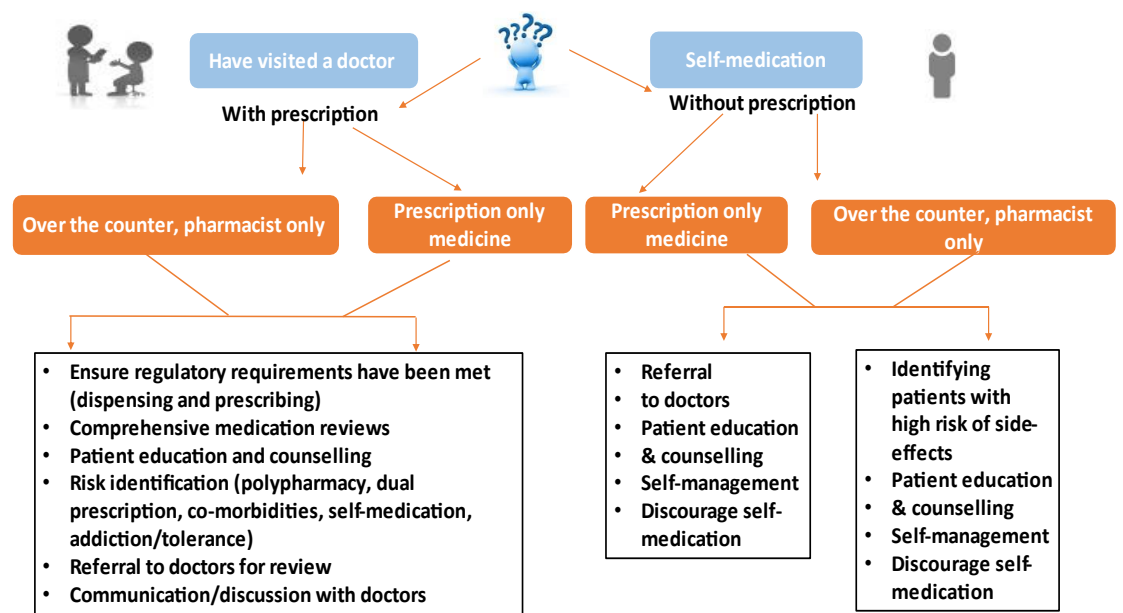


Figure 6.6: A schematic diagram of proposed steps/actions that can be undertaken by CPs in an opioid service to optimise the use of opioids in people with CNMP

OTC= Over the counter medication

It must be highlighted that although the steps are enlisted in this diagram there was no indication or implication identified within the studies that these proposed interventional actions need to be executed in the same order. In addition, different actions might be connected or even be harder to differentiate as different steps. However, all the actions presented were perceived to help overcome existing factors contributing to the unsafe use of opioids and help people with CNMP use opioids more safely.

6.2.5 CP opioid service logic model for safe use of opioids

As previously mentioned, the collated themes from both studies (Table 6.1) helped develop a schematic diagram that shows a holistic overview of certain gaps and deficiencies in the entire system that might be contributing towards

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the unsafe use of opioids (Figure 6.5). Table 6.2 then showed the possible actions/steps that can be undertaken by CPs and their perceived benefits for people. These CP actions were logically collated and displayed in appropriate places in the schematic diagram (Figure 6.5) and are perceived to overcome some of the existing barriers. This helped develop a logic model (Figure 6.6) that shows that CPs might be able to overcome certain challenges in a patient's journey currently contributing to the unsafe use of opioids.

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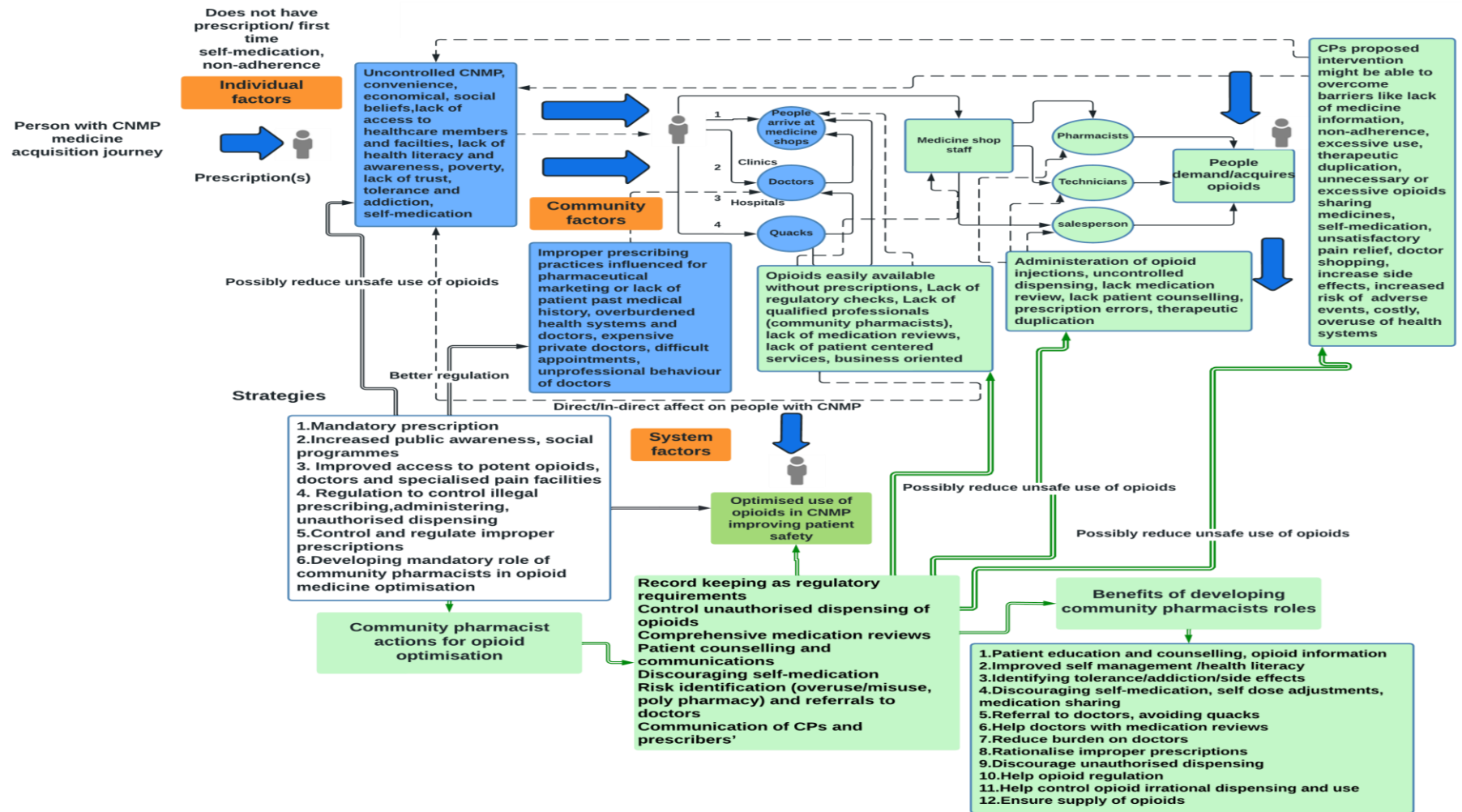


Figure 6.7: Logic model of factors contributing to unsafe use of opioids and corresponding CP actions perceived to optimise the use of opioids

Key: the green box presents identified CP roles perceived to overcome factors contributing towards unsafe use of opioids

6.2.6 Possible barriers, facilitators and identified strategies for developing and delivering the CP opioid service

The subthemes about barriers and facilitators, and strategies to facilitate CPs to deliver the future opioid service from chapter 4 and 5 have been collated and brought together as shown in Table 6.3.

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Table 6.3: Barriers, facilitators and identified strategies for developing and facilitating CPs to deliver an opioid service

Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter 5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/identified strategy which might overcome existing challenge chapter 5
Individual CP challenges and facilitators	Specialised opioid knowledge Pharmacy professional body role	a. Lack competency-based education (-) b. Lack of clinical preceptors (-) c. Lack of pharmacy practice academics (-) d. Curriculum revision every few years and have included clinical content (+)	<ul style="list-style-type: none"> • Improve advanced knowledge by curriculum redesign • Include clinical pharmacy and pharmacy practice experts • Maintain educational standards by identifying core competencies 	Skills of pharmacists Advanced and basic opioid knowledge	It cannot be inferred that CPs currently lack skills required for opioid related counselling (clinical skills, brand name knowledge skills, opioid medication information). However, CP were found searching the answers to such queries using their mobile phone, which could possibly indicate a deficiency	Appropriate CP skills required in-line of job and service, updated knowledge and training needed Local training resources needed
	General knowledge (undergraduate degree knowledge)	a. CP knowledge (+/-) b. CP training (+/-) c. Lack of community pharmacy clerkships (-)	<ul style="list-style-type: none"> • Improve advanced knowledge by curriculum redesign 	Skills of pharmacists Advanced and basic opioid knowledge	CPs currently were observed to lack skills required for opioid related counselling (clinical skills, brand name knowledge skills, opioid medication information)	Appropriate CP skills required in-line of job and service, updated knowledge and information)

¹⁸ The + indicates a factor which was a current facilitator for CP services whereas the – indicates a barrier, both signs indicate that it was indicated by some stakeholders as a barrier/facilitator or both

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
	Pharmacy professional body role	d. Lack of advanced clinical knowledge and skills (-) e. CPD has been launched for training CPs (+)	<ul style="list-style-type: none"> • Launch professional trainings (CPD) • Develop community pharmacy clerkships • Include clinical preceptors and field experts for content development 		CP searched drug interactions too (advanced)	<p>training needed</p> <p>Local training resources needed</p>
	CP skills and competencies to deliver an opioid service	a. Lack of knowledge, skills and competencies (-) b. Lack of confidence (-) c. Stakeholders perceived their role is important in opioid safety (+)	Introducing community pharmacy clerkships in undergraduate and training for pharmacists	<p>Advanced and basic opioid knowledge</p> <p>Competency and skills</p> <p>Therapeutic substitution</p> <p>Identify misuse</p>	<p>Most of the CPs were ill-prepared for community pharmacy settings (no knowledge of brand names) and were found negatively impacting the overall dispensing time and quality as well Schedule-G record maintenance.</p> <p>CPs currently were observed to lack skills</p>	<p>Appropriate CP skills required in-line of job and service, updated knowledge and training needed</p> <p>Local training resources needed</p>

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
					<p>required for opioid related counselling (clinical skills, brand name knowledge skills, opioid medication information)</p> <p>CP searched drug interactions too (advanced)</p> <p>However, CPs were observed to identify opioid misuse, therapeutic duplications and maintain some control over unauthorised dispensing</p>	
				CP interpersonal skills	CPs were observed to have mixed relationship with allied staff depending upon internal organisational support (clearly defined roles, CP respect) as well as communication and motivation skills of CP	CP management support for defining clear jobs and responsibilities of each staff member to avoid conflicting situations

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter 5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/identified strategy which might overcome existing challenge chapter 5
	CP technical skills	a. Lack of technical expertise (-) b. Lack of training opportunities (-) c. Pharmacy council support and CPD development launched in pilot phase (+)	Launch professional trainings (CPD) On-job training		CPs currently were observed to lack skills required for opioid related counselling (clinical skills, brand name knowledge skills, opioid medication information)	
	CP interest to join pharmacies	a. Unwilling due to social stigma (-) b. Lack of career growth options (-) c. Lack of motivation due to management (-) d. Less salary/remuneration (-) e. CP landscape changing and some organisations respect and value their contributions (+)	a. Interdisciplinary care models b. Service remuneration c. Supportive CP laws and policies	CP motivation Insecure and vigilant	CP motivation to deliver service might be dependent upon the respect and treatment given to them inside pharmacies by the management and staff	Supportive management might help with CP motivation to deliver proper service
	CPs values and motivation	a. Motivation (+/-) b. Lack of CPs workforce (-)	a. Improving CP communication with their professional	CP motivation	CP motivation to deliver service might be dependent upon the respect and treatment	Supportive management might help develop

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
		<p>c. Allied staff support (+/-)</p> <p>d. Lack of payment of service (-)</p> <p>e. Lack of complaint channels (-)</p> <p>f.</p>	<p>bodies and regulatory authorities</p> <p>b. Remuneration models</p> <p>c. Pharmacy policy makers support in helping CP career development pathways</p>	<p>Insecure and vigilant</p> <p>Social behaviour of people</p> <p>Allied staff behaviour</p>	<p>given to them inside pharmacies by the management and staff</p> <p>CPs motivation might be derived from public acceptance of their engagement, advice uptake and respect of CP</p> <p>CP might be supportive and may help guide/bring to interact with CPs (located discreetly)</p> <p>In rush hours CPs relies on allied staff for dispensing</p>	<p>internal guidelines, support CPs like visibility, allied staff, workload, time, training resources with CP motivation to deliver proper service</p> <p>Public awareness</p> <p>Implementation of Schedule-G laws and strict regulation</p> <p>Efficient regulatory systems with adequate regulatory workforce</p>

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
	Lack job description	Lack of defined CP responsibilities might impact CP service provision	Clearly defined job responsibilities / job description	Pharmacist relationship with allied staff	CPs need to rely on allied staff to get their support for CP-patient interaction by bringing/guiding/motivating people to talk to CPs, handling dispensing while CP are busy with people/stationed near narcotic corner remotely. Clearly defined job responsibilities were observed to support each other's roles and complement them	Clearly defined internal job descriptions Favourable laws and policies Pharmacist policy makers support and advocacy
Organisational facilitators and barriers for CPs	Location	a. Location of an organisation directly translates it the number of people arriving within a pharmacy (+/-) b. Location might also impact the implementation of laws and the support of managers towards hiring and facilitating	a. Developing and implementing CP strict laws and policies b. Supportive pharmacy management c. Improve CP capability by pharmacy	Locality impact on manager Locality impact on patient time/impact on patient engagement	The arrival of regulator influences how management/manager follows laws in the pharmacy (both sale of opioids, facilitating CPs to follow laws) Infrastructure like adequate parking, ample floor space, number of staff available to receive	Enhanced regulation Strict laws and implementation

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter 5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/identified strategy which might overcome existing challenge chapter 5
	Organisational capacity for communications	<p>CPs for delivering the service (+/-)</p> <p>a. Lack of communication (-) b. Existing computers, IT systems, software (+)</p>	<p>management support</p> <p>a. New interdisciplinary models of healthcare b. Developing and switching to digital health systems c. Improving CP knowledge and skills to inspire CP confidence to talk to doctors and gain their acceptance</p>	<p>Digital and IT capacity</p> <p>Communication with doctors</p>	<p>people might impact a CP-patient interaction</p> <p>Sometimes prescriptions require clarification from doctors, however there are no existing systems or even culture of CP contacting the doctors</p>	<p>Having digital health systems can help CPs talk to doctors</p> <p>Supportive laws and policies</p>
	Organisation culture and vision	<p>a. Aim and vision of organisation or individuals owning the pharmacies define the reason for hiring CPs (+/-) b. Profit making (+/-)</p>	<p>Enable support of pharmacy managers/proprietors through law enforcement, awareness of CP benefits to businesses</p>	<p>Organization focus</p>	<p>CP organisations were found to be operating within business interest. In chain pharmacies, along with profit making, brand distinction of being a "proper pharmacy" was also observed to be the motive. Other</p>	<p>CP management vital to enable/provide CPs support to deliver service/patient engagement</p>

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
	Benefits of service for organisation	c. Business reputation, loyalty of customers (+/-) d. Substantial benefits of hiring CPs, short term or long term (+/-)			organisational aims observed were customer satisfaction to ensure customer loyalty	
	CP autonomy	a. Lack of CP autonomy (-) b. Lack of legislative support (-)	Laws and policies providing legislative support and regulation to CPs	Autonomy to refuse medicines (laws implementation)	CPs might not have the authority to refuse opioid medicine illegal dispensing due to non-supportive managements/manager because of business interest	Improving legislation/ strict drug inspector visits (enhanced regulation) Pharmacy management support
	Organisational layout and workflow Duration of intervention	a. CPs visibility to public will impact the CP capability to deliver the service (+/-) b. Lack of electronic medical records (-), non-standard prescriptions, health illiteracy (-), lack of	Improving the visibility of the CP in pharmacies need to be focused and pharmacy management and allied staff should actively	Visibility of CP Positioning of pharmacist	Visibility of CP is pronounced where CPs are motivated, or in pharmacies where management want to highlight the role of CPs especially for improved customer satisfaction, brand recognition	Pharmacy management support to highlight and signpost people towards CPs

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter 5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/identified strategy which might overcome existing challenge chapter 5
Community level challenges and facilitators for CPs		<p>public awareness (+/-), physical space to accommodate people (-)</p> <p>c. Existing IT resources (+), Schedule-G amendment (+), increased public awareness (+)</p>	<p>participate in signposting people acquiring opioid medication towards CPs</p> <p>Improve public awareness</p>		<p>Lack of CP separate counter might impact visibility of CP</p> <p>Because of narcotic controlled dispensing, opioids are found in narcotic cabinets, which are at a side of a pharmacy and CPs are usually stationed near them to help facilitate dispensing/record keeping</p>	<p>Clearly defined internal rules and regulations guiding allied staff to support CP-public interaction</p> <p>Developing digital health systems</p> <p>Laws and policies (ensure standardised pharmacy)</p>
	Community perception and awareness of CP roles	<p>a. Public perception and awareness of CPs and their roles would affect the utilisation and acceptance of future service (+/-)</p> <p>b. People's individual characteristics like; health literacy, social</p>	Improving public awareness about role of CPs	<p>Public awareness about role of CPs</p> <p>Perception of public about new laws</p>	Public awareness is key to compliance of new policies, laws and service and helps facilitate the implementation of new rules and changes in pharmacies	<p>Improved public awareness</p> <p>Management support to make CPs visible and</p>

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
		norms, past medication experience, motivation to self-care, doctor's guidance to consult CPs, CP awareness as well as dependence on medications like opioids (+/-)		Educated people asking/reading leaflet	<p>Public awareness might be related to visibility of CP in the pharmacy</p> <p>Health literacy and past meaningful experience/knowledge of people about CPs may motivate people to engage with CPs</p> <p>People might be aware of role of CPs and approach them to ask about medicine information, however majority people seemed unaware of CP role</p>	<p>highlight their roles</p> <p>CP motivation, improved knowledge and skills</p>
	Public demand	Public demand to speak to CP increasing public interest in getting medicine information, convenience and potential benefits it might offer (+)		Public awareness about role of CPs	<p>Public awareness might be variable where people who know CPs roles were observed to be approaching for medicine information</p> <p>May depend on how CPs treat/behave with them</p>	<p>Public awareness about role of CPs</p> <p>Management support to highlight CP presence</p>

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
	Uncontrolled chronic pain	a. May try to use opioids more than the recommended dose and won't comply to CPs	<p>Developing the role of CPs can help guide people about pain management, possible expectations</p> <p>Patient counselling</p> <p>Improved public awareness</p>	Uncontrolled pain and demand more medicines	Most people seem unsatisfied with their pain medications. It could not be inferred from the conversations if people had used opioids in past.	<p>CPs might be able to guide people and refer them to doctors, instead of self-medicating with analgesics</p> <p>Improve public awareness of CPs</p>
	Resistance of pharmacy technicians	Resistant to CPs presence in pharmacies due to unclear roles (-)	Clearly defined job responsibilities / job description	Pharmacist relationship with allied staff	CPs need to rely on allied staff to get their support for CP-patient interaction by bringing/guiding/motivating people to talk to CPs, handling dispensing while CP are busy with people/stationed near narcotic corner remotely. Clearly defined job responsibilities were	<p>Clearly defined internal job descriptions by developing CP favourable laws and policies</p> <p>Pharmacist policy makers support and advocacy</p>

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
					observed to support each other's roles and complement them	
System	Laws and policies Pharmacist policy makers Strategic policy alignment	a. Lack of laws regarding supporting and utilising CPs (-), roles and definition of CP missing (-), lack of pharmacy policy makers (-) b. Weak implementation of existing laws (-), lack of strict penalties (-), lack of adequate number of regulatory workforce (-) c. Government strategic focus to improve health and inclusion of pharmacy policy makers, amended rules (+), increased regulators (+)	CP favourable laws should be established	Implementation of laws	Lack of regulatory checks, less chances of regulators arriving allowed pharmacies to operationalise within business/customer loyalty perspectives (result unauthorised sale of opioids) Arrival of regulator influences how management/manager provides CP autonomy to follow laws in the pharmacy (both sale of opioids, facilitating CPs to follow laws)	Better implementation of laws and policies Increased regulatory workforce

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
	<p>Community pharmacy sector privatised</p> <p>Cost of intervention</p> <p>Pharmacist policy makers</p>	<p>a. Lack of government remuneration system (-) leads to CP motivation (-), privatised pharmacies, non-supportive pharmacy managements (-)</p> <p>b. Supportive government strategic focus to develop pharmacy services (+), inclusion of pharmacist policy makers (+)</p>	<p>a. Enable support and advocacy of policy makers</p> <p>b. Developing remuneration systems</p> <p>c. Pharmacy policy makers advocacy for assortment of health budget</p>	CP motivation	CP might be motivated or non-motivated depending upon the salary, the way proprietors treat them (exploitation for license only) and autonomy they get inside pharmacy	<p>CP favourable laws and policies</p> <p>Supportive CP management</p> <p>Service remuneration</p>
	Pharmacy workforce	<p>a. Lack of CPs in medicine shops (-), CP missing in rural areas (-), lack of CP motivation (-), brain drain (-), lack of community pharmacy career progression or service structure (-), privatised sector and job insecurity (-), CP social stigma of being</p>	<p>Developing remuneration system, enhanced regulation, and enabling the support of pharmacy managements might help increasing the CP motivation</p>	Lack of pharmacist availability	The hiring of CPs was observed because of their license and the new law that opioids can be dispensed only in the presence of CP	<p>Strict laws and implementation</p> <p>Efficient and adequate regulatory system</p>

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
		less competent/shopkeeper (-) b. Increased number of pharmacists due to increased number of pharmacy schools (+), increasing trend to join pharmacies, Schedule-G amendments facilitating CP hiring	and capability to deliver opioid service			
	Quality assurance system	a. Lack of pharmacy regulator (-) b. Lack of check on regulators (-)	a. Improved regulatory system b. Advocacy and support of policy makers	Regulation	Whether CP can refuse opioid unauthorised dispensing is dependent on management/manager which seemed to be influenced by organisational aims and the chances of regulator arriving	Implementation of Schedule-G laws Enhanced regulatory system and strict regulation Management support

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Theme Focus group/interviews	Sub themes chapter 4	Focus group/interviews (key interpretation) ¹⁸	Strategies shared by stakeholders' chapter5	Themes/subthemes chapter 5	Case studies (key inferences)	Perceived strategy/ identified strategy which might overcome existing challenge chapter 5
	Lack of communication systems	a. Lack of communication doctor and CP (-), lack of medical and medication history (-), b. Government interest in developing digital health (+)	Develop Digital health systems	Communication with doctors Digital and IT capacity	Lack of communication channels due to lack of digital health systems with prescribers was observed to be a challenge for CPs and they were found to be interacting/changing prescriptions without legal authority	Develop digital systems Laws and policies (ensuring standardised pharmacies) Management support

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Table 6.3 above shows the collation of challenges and facilitators for CPs and presents multiple strategies identified in chapter 4 and 5 that can help with overcoming many existing barriers and leverage the current facilitators and influence the development and delivery of an opioid service. These are now elaborated below:

6.2.6.a Developing service remuneration model

Service remuneration was a strategy identified by stakeholders that could improve CP motivation to deliver the service and might improve future service sustainability. However, developing remuneration of this service was identified to be complex because payment for this service requires funds allocation from the health budget, which requires support and advocacy from policy makers. Public demand, foreign influence, policy initiatives such as achieving SDGs and/or UHC and pharmacy policy makers internal advocacy could help gain support from influential policy makers and help assign an allocated budget for the service.

6.2.6.b Enable support of policy makers

Supportive policy makers and their advocacy was a strategy identified by stakeholders as well as in case studies that could help overcome many current barriers. The findings reported that there is currently a lack of pharmacist policy makers (barrier) and having pharmacists in influential policy making positions might facilitate the development of supportive laws and policies, enforce strict regulation, clearly define job responsibilities and help develop remuneration models (as provided above) needed for CP service.

6.2.6.c Supportive laws and policies

Supportive laws and policies were perceived as crucial for a successful opioid service development and its fidelity. They could also impact CP motivation by providing them legislative support to help overcome current barriers like non-supportive pharmacy management, doctors' resistance and public resistance.

6.2.6.d Enhanced regulation

Lack of strict regulation was identified to be interlinked with many current barriers such as CPs' capability to stop dispensing without prescription, lack of CP hiring in pharmacies, lack of management support for CPs and lack of autonomy for CPs in following Schedule-G laws. Thus, enhanced regulation was identified as a strategy to help overcome these barriers.

6.2.6.e Developing digital health systems

Findings reported that developing digital systems might help deliver an opioid service. Existing IT resources in pharmacies might be able to facilitate the integration and adaptation of digital systems and might improve CPs' capability to deliver an opioid service in future.

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6.2.6.f Enable support of pharmacy management

Findings reported that the presence of CPs, organisational infrastructure, time and support of allied staff are all organisational determinants related to the vision and aim of the pharmacy management/establishment, which can impact CPs' capability and motivation to deliver a future opioid service. Supportive management was perceived as a strategy for improved delivery of the service. Favourable laws, policies and strict law enforcement by regulators can make the management to become supportive towards facilitating CPs in delivering any future CP-dependent service, such as opioid management in patients with CNMP. Other factors such as public demand, social acceptance, customer happiness, customer loyalty and satisfaction with CPs can also influence pharmacy management to support CPs.

6.2.6.g Increase public awareness

Improving public awareness is a strategy that can lead to increased public demand of the opioid service, findings show. Increased public awareness about the benefits of such a service might also lead to better engagement with CPs and may also help patients accept and adhere to their CP's advice about opioids.

6.2.6.h Improving CP knowledge and training

Improving CP knowledge and skills was another perceived strategy that might improve the competency, capability as well as motivation of CPs to deliver an opioid service in future. Findings report that pharmacy bodies would need to upgrade and revise the curriculum, introduce community pharmacy training in the undergraduate degree programme and develop advanced training and CPD that might help improve CP skills and competencies, which could then help reach better service outcomes. Findings also reported that improved CP competency might aid them in having a meaningful interaction with people and doctors and help overcome any reluctance or reservations (current barriers) about CPs delivering an opioid service.

6.2.7 CP opioid service delivery logic model

The strategies listed above were perceived to help overcome the current CP service delivery barriers and leverage facilitators (Table 6.3). In addition, these findings have been collated with the perceived benefits of an opioid management service (theme in chapter 4) and helped develop a logic model as shown in Figure 6.8 below.

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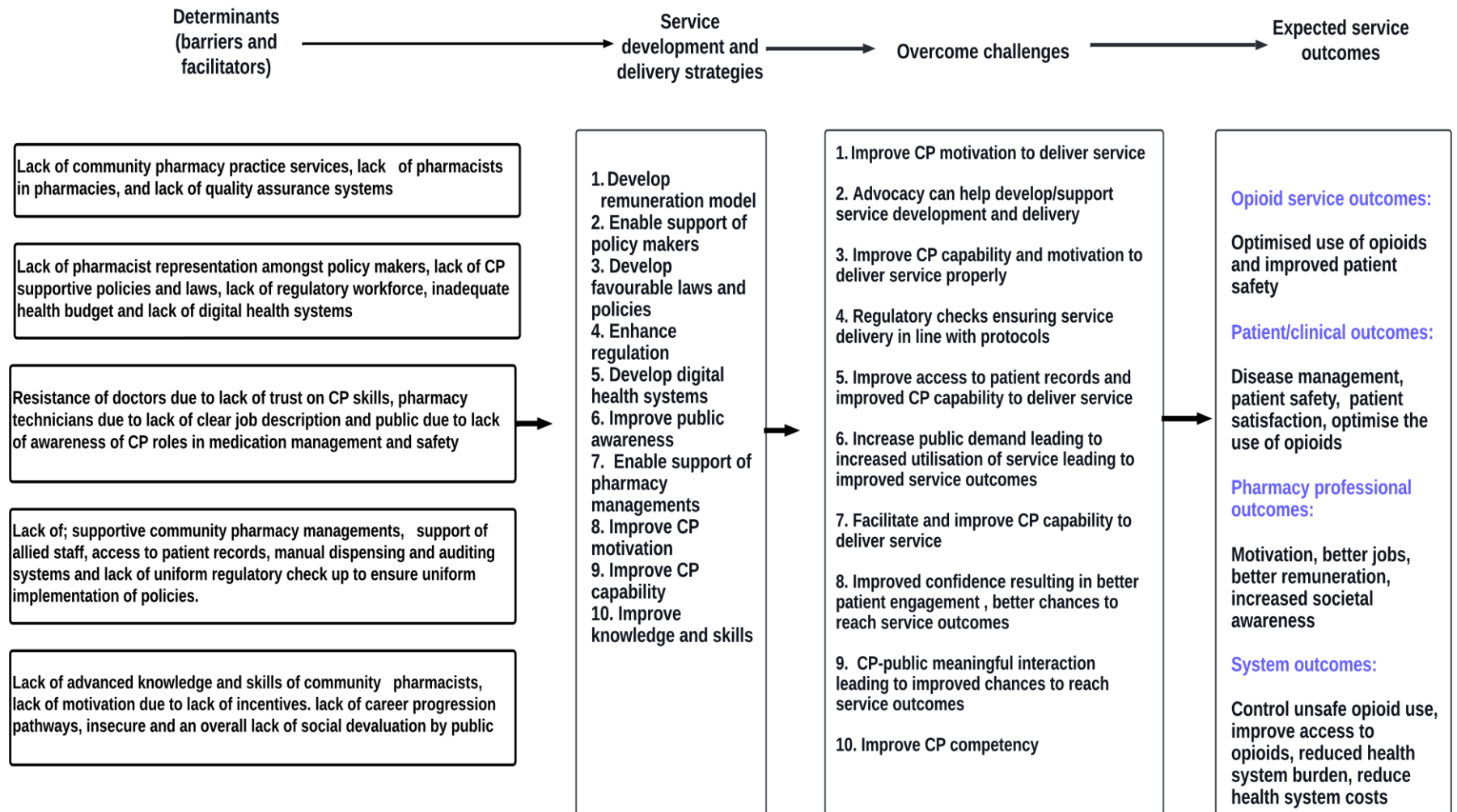


Figure 6.8: Logic model for community pharmacy opioid service delivery

6.3 Overall triangulated thesis findings discussion

This section discusses the overall triangulated findings of this thesis from interviews/focus groups and case studies. Please note that where applicable the findings from the systematic review also have been added to the discussion to make it richer. To facilitate reading, this subchapter has been divided into three subsections.

6.3.1 Factors contributing towards the unsafe use of opioids and CP opioid service logic model

Studies [161, 162] report that interventions can have several interactive and dynamic components that might require new behaviours by those delivering or receiving the intervention and may also require organisational or legislative changes. In addition, interventions and/or services might be impacted by socioeconomic and cultural environments and may prevent the intervention from reaching its intended outcomes. Thus, understanding the whole process and designing and delivering services according to context makes it likelier to reach intended outcomes.

The incorporation of logic models as a theoretical framework can be employed to justify how a desired intervention and formulated program can generate the intended results and beneficial outcomes. In the context of process evaluations, logic models are utilized to depict the fundamental concepts of interventions in a simplified, graphical format. Moreover, logic models can facilitate discussions among stakeholders to achieve a consensus on the necessity for change and how to proceed with it [451, 452]. Logic models have been extensively used in studies [451, 452] as tools capable of providing answers and helping picture the whole process, which helps understand where and in which context interventions can be delivered, help programme evaluations and refine the intervention design process.

My study provides a logic model after combining findings from case studies and focus group/interviews, showing that developing the role of CPs might target various factors that are currently contributing towards the unsafe use of opioids in Pakistan. The logic model also suggests that a CP opioid service could offer huge health system benefits in terms of controlling opioid misuse and diversion as well as well as promoting public safety.

As evident from the systematic review findings [196], the role of CPs in opioid optimisation is still scarcely reported in literature; however, as CPs have been beneficial in other diseases [120, 122, 123], it can be anticipated that there might be benefits to developing this service. The systematic review as well as findings from interviews/focus groups in my study anticipates that involving pharmacists in patient care for people with CNMP might help optimise the use of opioids and decrease opioid-related harm.

Although there is a lack of studies from other LMICs on factors contributing towards the unsafe use of opioids, a 2020 US study by Jalali et al. [94] presents risk factors of opioid misuse crisis due to individual, interpersonal, communal and societal factors. Even though most of the factors contributing towards opioids crisis in US contextually differ from those in Pakistan, the overlapping factors have been presented below.

Similar to the findings of interviews/focus groups in my study, they also report that people with mental health issues, persistent pain and people developing tolerance and addiction could be at higher risk of opioid-related harm. People with mental disorders might not significantly improve on the pain scales or reduce their opioid dose [246]. The US study [94] reported that the social relationships and societal impact were found to significantly shape the beliefs, attitudes and behaviours of people using opioids, congruent to my findings. Friends and family sharing medications was also a factor contributing towards the unsafe use of opioids in their study. My findings report that people were sharing medicine information as well as recommending opioids to each other, which then led to the purchase of these medicines and self-medication.

In the US study [94], factors such as pain management facility accessibility, over-prescription of opioids or under-treatment of pain, types of prescription opioid formulations available, community norms and access to legal and illegally obtained opioids were contributing towards the unsafe use of opioids. These factors were also reported in my findings from interviews/focus groups. However, the context, precursors and mechanisms of these factors significantly differ across both studies.

Regulation, pharmaceutical industry promotional influences and weak law enforcement [94] was also similar to my findings and were identified to be contributing towards the unsafe use of opioids.

This comparison between my study and the study by Jalali et al. [94] shows that both on the outset found similar factors contributing towards the unsafe use of opioids. However, the capacity of CPs, health systems, laws and economies widely differ between the US and Pakistan and emphasises that each country needs to independently explore, understand and contextualise effective strategies and develop interventions for its respective health system's needs and capacities to help overcome existing challenges.

Similar to my case studies and interviews/focus group findings, a 2016 systematic review by Miller and Goodman [429] identifies factors, challenges and determinants of poor practice of medicine selling establishments across LMICs contributing towards unsafe use of medications. The key inadequacies the study identified, similar to my study, are the illegal sale of a wide range of prescription only medications (POMs) without a prescription; the sale of

medicines that are either clinically inappropriate and/or in doses that are outside of the therapeutic range or not according to the need of the patient; the sale of medicines by dispensers and unqualified staff; limited provision of information and counselling on medicines; and changes to doctor's prescribed medications as per the demand of patients. The key precursors for poor practices reported in these establishments were profitmaking motivations, compliance with customer demands, illegal prescribing (recommending and dispensing) and administration of medications to ensure profit generation. These factors were observed in case studies and the interview/focus group findings helped ground them in understanding. Interview/focus group findings reported that profit making intentions, brand recognition and customer satisfaction were the top priorities of pharmacies and were contributing to poor medication dispensing practices. Another factor which was highlighted by [429] and remains similar to my findings is that lack of regulation or strict law enforcement was related to many of these aberrant practices taking place in medicine stores and pharmacies.

Strategies highlighted in my study such as regulating the supply chain of opioids [429], increased public health awareness and literacy [350-352], improved access to potent opioids for adequate pain management, specialised doctors and pain facilities [94], and developing the role of CPs to help in patient counselling, monitoring, medication reviews and discouraging self-medication with opioids [386] might reduce opioid-related harm and improve patient safety.

6.3.2 Community pharmacists opioid optimisation service model

Findings from the case studies and interviews/focus groups informed the development of a CP-delivered opioid service diagram (model) tailored to the current needs of people with CNMP. The components of the model can either be isolated interventions or be combined as an opioid service. It must be highlighted that although the findings from systematic review (chapter 3, subchapter 2) [196] showed no CP-based actual service in existence for CPs, they provided positive evidence of pharmacist services in other settings in opioid optimisation and patient outcomes.

Interviews/focus group findings reported that CP opioid optimisation service might help people avoid self-medication, decrease under or overuse of opioids, educate for self-management and improve patient adherence. Moreover, the role of CPs in medication reviews, disease managements and contributing to patient care as part of interdisciplinary teams in other diseases and medications is well known [453]. Optimising these factors was anticipated to help optimise the use of opioids, reduce overall patient cost as well as reduce the overuse of existing health systems [453, 454].

This is similar to the ASHP opioid taskforce report (2019) [386], which suggests that involving pharmacists might help conduct comprehensive medication management, safety and cost-effectiveness analyses, patient education, opioid risk assessment and monitoring in people using opioids and help improve opioid safety.

A 2022 systematic review and meta-analysis [455] of randomised controlled trials showed that CP-led medication reviews (a proposed component of the model) promoted significantly better management of chronic conditions and diseases and led to better clinical outcomes. Patient education, listed as a component in CP opioid service model, can also enable people to be more responsible towards the conscious use of medications and may lead to adherence with recommended treatment doses and help avoid unsafe use of opioids [386].

A 2021 commentary article [454] also advocates for and presents the benefits of CP-led interventions such as medication management reviews, monitoring and patient education to prevent, identify, and manage opioid crisis in community pharmacies. They also suggest that developing CP roles can offer substantial reductions in costs by potentially reducing excessive use of health services as well as individual costs bore by people with CNMP and help achieve better patient outcomes [454], which remains congruent with my study findings. The study by Aziza et al. (2022) [388] also suggested that patient education by CPs as part of an opioid optimisation service can help patients understand the limitations of opioids in CNMP management, maintain real expectations of medicines, the correct use of opioids, and associated potential risks, resulting in improved acceptance of deprescribing of opioids and a more optimised use of opioids.

The proposed model also suggests CPs following laws and stopping unauthorised dispensing and helping control self-medication and identifying potential misuse. CPs are acknowledged members of the healthcare team in developed countries who can help with the dispensing of controlled substances [456]. Both case study and interview/focus group findings highlighted that CPs might have the opportunity to control and limit unauthorised dispensing. This can in turn help overcome the government's fear of misuse and improve the availability of potent opioids in Pakistan and achieve UHC goals. CPs successfully discouraging misuse of a range of prescription and OTC medicines has already been reported in literature [268, 457] and remains supportive to my findings. In addition, opioid non-availability for pain management is an ongoing problem in LMICs [40, 291] and thus leveraging the potential role of CPs in control and avoiding misuse and diversion might offer substantial patient and health systems benefits in many LMICs.

Although there are no formalised CP services in Pakistan, CPs have been known to voluntarily provide patient engagement activities, such as medication counselling, switching to economical therapeutic alternatives, screening for therapeutic duplication, advising on dosage and food related queries, and answering patient queries on medicines [5, 400] — congruent with my case study findings. The quality evaluation of their advice as well as impact or benefit in patient care of these voluntary actions has not yet been reported and further research is needed to evaluate these metrics and determine CPs' benefit to the health system.

A 2022 RCT [430] in Pakistan evaluated the role of CPs in hypertension and diabetes management and reported that CPs counselling and review every 15 days of the interventional group (n=4) resulted in better blood glucose and blood pressure management. In addition, the study reported a statistically significant improvement in mean knowledge scores of patients with diabetes and hypertension in the intervention group. It must be noted the sample size in the RCT is very small and the results might be a false positive. Further research should look at trials evaluating the effectiveness of CP involvement in patient outcomes as well as study the impact of socio-ecological factors that might impact a CP's capability to deliver such interventions.

While this discussion brings strength to the components of the proposed opioid optimisation service model developed in my thesis, further research will be needed to validate the proposed model.

6.3.3 CP opioid service logic model

Triangulating the findings from case studies and interviews/focus groups many enablers and barriers along with strategies were identified towards the development and delivery of community pharmacy-based opioid optimisation service in Pakistan. These are discussed below.

A 2021 US study [458] explored challenges for CPs in opioid stewardship roles and reported stakeholder perceptions about CP roles in opioid safety. The study used a survey method and 215 CPs reported that the perceived major challenges were pharmacy organisational structure and operationalisation, lack of patient and prescriber clarity about pharmacist's scope of practice in opioid medication management, lack of public recognition of CPs as healthcare team members and time to support additional services [458]. All of these determinants were also identified in findings from case studies and interviews/focus groups as perceived barriers, which Pakistani CPs might encounter while delivering an opioid optimisation service.

Another 2021 study by Okoro and Nduaguba [459], although not specific to opioids and CNMP management, presents five key barriers that could impede chronic disease management medication review services by CPs in LMICs, all of which have been identified in my study as well. The study by Okoro and

Nduaguba [459] reports lack of supporting laws, recognition of CPs in patient care within health systems and the shortage of CPs due to their efflux out of the country in hopes of better careers and remuneration. Another barrier identified in their study was the lack of advanced clinical and therapeutic knowledge and skills of CPs in chronic disease management. Similar to my interview/focus group findings, these deficiencies were linked to the lack of advanced training or postgraduate degrees in clinical and social pharmacy or the lack of CP career opportunities. Similar challenges to those identified in my study were reported by them. In most LMICs, there is a lack of collaborative patient care practices of doctors and pharmacists — physicians prefer to work without pharmacist involvement and remain reluctant to modify patient prescriptions following pharmacists' recommendations. The last challenge reported in their study was the lack of reimbursement for community pharmacy services, which could result in lack of CP motivation to provide patient-centred services and could become a barrier for service provision, which is congruent with my findings. Interestingly, the strategies identified to overcome these challenges were also similar to my study findings. Their study suggested that healthcare policy reforms for multidisciplinary healthcare team approaches are needed to provide support to CPs to participate in patient care in medication reviews for chronic disease management. Another strategy identified in their study was to improve CPs' knowledge and provide clinical training to help develop their competencies to deliver such services and remains congruent with the strategies reported in my study. Their study also reports that government-sponsored remuneration systems should be developed for extended CP roles, which can provide CPs financial compensation for medication management and patient care [459], which again remains congruent with my findings.

A 2021 study by Lamba et al. [460] evaluates the role of pharmacies and medicine stores in six LMICs using case studies with an aim to explore how pharmacies could help create stronger health systems to improve patient outcomes. The study presents multiple facilitators and barriers spread across socio-ecological levels (micro, meso and macro) for the role of pharmacies in supporting health systems. It is important to highlight that although the study does not report about medicine services or CPs, it identifies similar determinants to my study that might impact the delivery of patient-centred services in pharmacies.

Similar to my study, they report that staff training in these establishments could increase knowledge, skills and compliance with guidelines and an increased social credibility in the community. These factors were reported to improve community trust leading to success of patient care initiatives and may contribute towards stronger health systems. In addition, they reported

that the aims and visions of these establishments may facilitate the staff towards patient care initiatives. Interestingly, they also reported that the support of management gets influenced by customer demand and profitability of their businesses. The study also reported that an increased customer burden could compromise or demotivate the staff to engage with customers/patients, which was observed/perceived in the findings of case studies and interviews/focus groups in my thesis as well. Their study reported that policy makers support and adequate quality assurance systems might lead to the success of patient care service [460].

A study by Atif et al. (2020) also explored CP-based patient centred services from Pakistan and indicated that CPs might face many challenges in delivering community pharmacy services. Similar to my case studies and interviews/focus groups findings, they reported that the success of CPs patient counselling or medicine management services will depend on the location, number of staff members in the pharmacy, support of pharmacy management as well as enforcement of laws and policies by regulators [5]. Many of the strategies to develop and help CP deliver opioid service identified in my study are similar to the strategies reported by the ASHP Opioid Task Force report published in 2019 in the USA [386]. ASHP Opioid Task Force report examined how CPs as medication experts can improve health of people using opioids. Similar to my study, the report [386] states that pharmacists should be involved in policy making to advocate and provide insights into developing policies and guidelines for opioid stewardship roles in community pharmacies. Other strategies reported were supportive interdisciplinary collaboration of doctors and pharmacists to promote the safe use of opioids, support by government, and developing remuneration systems to help implement CP services. As the taskforce was focused on a holistic approach for pain management and optimised use of opioids, they also highlighted the utilisation of CPs to target and counter bio-psychosocial determinants of health such as lack of patient health literacy, economic status, societal influence and individual level determinants contributing towards the unsafe use of opioids. All of these factors were identified in my study (chapter 4, subchapter 2) to be currently contributing to the unsafe use of opioids in Pakistan and supports the notion that a CP involvement might help overcome these challenges and improve patient safety.

The studies mentioned in the preceding paragraphs show that many of the development and service delivery challenges for CPs opioid optimisation service identified in my study might not be specific only to opioids and some of them might be barriers to extended community pharmacy services in Pakistan. Many strategies identified in my study such as favourable laws and policies, training and education of CPs and remuneration of services have

been proposed by other authors suggesting the development of role of CPs in Pakistan [385, 389] and other LMICs [461-463] to develop patient care roles for CPs.

It is important to highlight that although these strategies can provide understanding and knowledge to help with CP opioid service development and delivery in Pakistan, the determinants and their corresponding strategies presented in in my study might differ from other countries depending upon the unique health system of each country. Other studies would need to tailor strategies to their unique local context and health system architectures, consider capacity and resources available in each sector, workforce diversity and skill mix.

Chapter 7: Overall thesis discussion

This is the last chapter of the thesis and provides a summative discussion and conclusion to this thesis. This chapter has five sections as shown in Figure 7.1:

1. Thesis aims and the use of mixed methods
2. Implications of findings
3. Advantages and limitations
4. Unanswered questions
5. Conclusion

Chapter 7: Overall thesis discussion

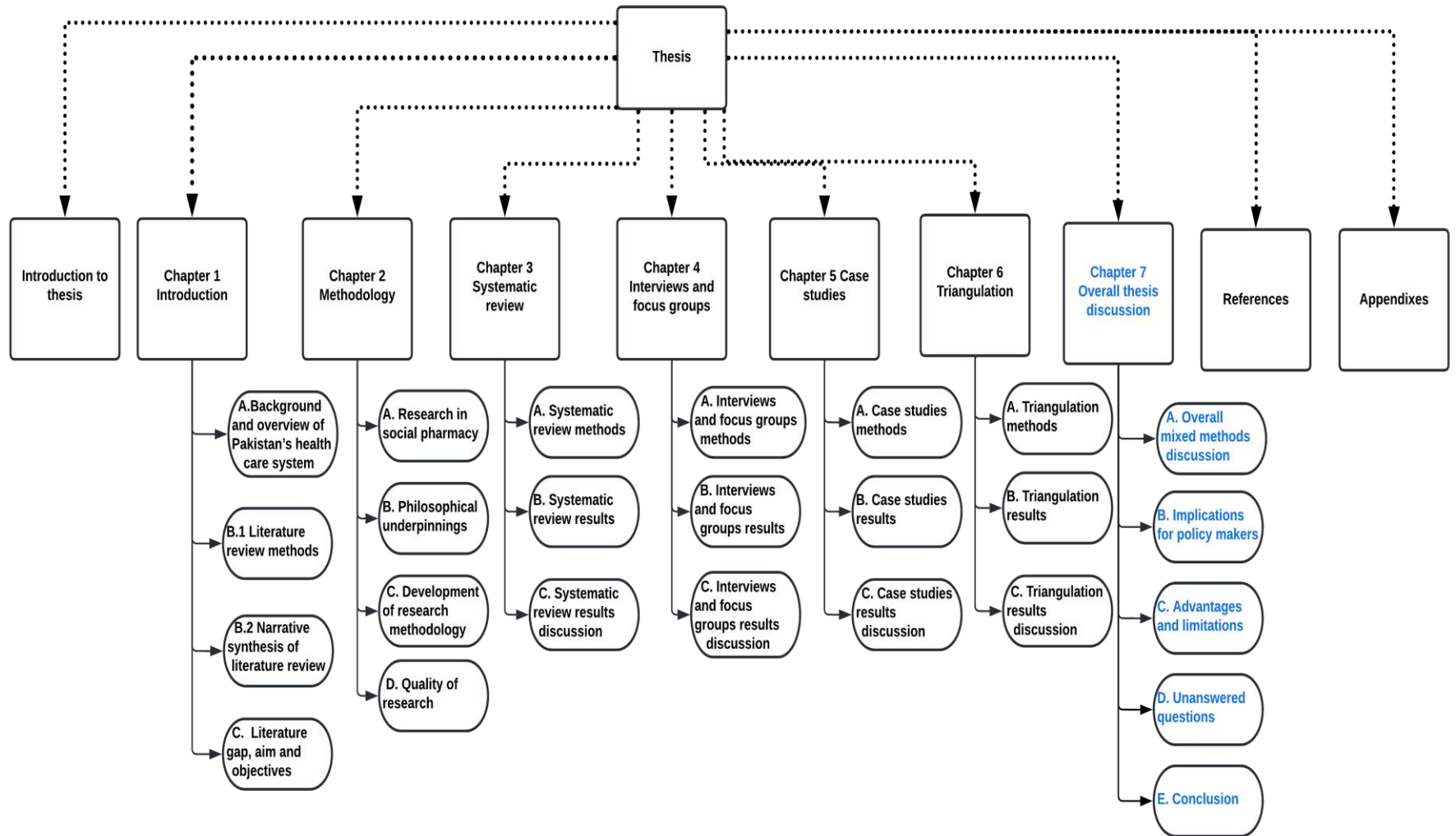


Figure 7.1: Overview of chapter 7 in thesis

Chapter 7: Overall thesis discussion

Please note the detailed discussion of thesis findings in light of other studies have been provided in chapter 6.3. In this chapter I provide:

1. Mixed methods discussion
2. The overall implications of thesis findings
3. Advantages and limitations
4. Unanswered questions
5. Conclusion

7.1 Overall mixed methods discussion

7.1.a Factors contributing towards the unsafe use of opioids and CP opioid service logic model

As the literature review informed there might be a misuse or overuse of opioids in Pakistan. However, there was no substantial information on why people were using opioids unsafely. The literature review could also not find relevant information regarding the role of CPs in opioid optimisation. Thus, the first aim of this study was to:

- Systematically explore the role of CPs in opioid optimisation in CNMP management

This was first explored through a systematic review. Chapter 3.2 provided an overview of how no formal CP services exist but individual studies reported certain actions taken by pharmacists in ambulatory outpatient settings were found to optimise the use of opioids. No studies were found from LMICs or from Pakistan. As the phase one (systematic review) was unable to provide any information about how CP roles relate to opioid usage in Pakistan, the second objective of the thesis became:

- Explore the current use of opioids in Pakistan and identify CP action(s) that may optimise the use of opioids in people with CNMP
- CNMP

Chapter 4.2 reported that the interviews and focus groups conducted as part of this study were able to inform:

1. Factors contributing towards the unsafe use of opioids
2. CP actions that might be able to overcome existing challenges contributing towards the unsafe use of opioids
3. The perceived benefits of developing CP roles in opioid optimisation

In Chapter 5.2, the findings of case studies undertaken as part of this study also revealed many gaps and factors contributing towards the unsafe use of opioids and identified opportunities where CPs might be able to intervene to help people use opioids in an optimised manner. The findings of chapter 4.2 and 5.2 were brought together to supplement each other and helped develop

a schematic diagram, showing factors contributing towards the unsafe use of opioids and the possible role that CPs might be able to play to alleviate this crisis and the overall benefits of such a role.

7.1.b Proposed CP opioid service model

It must be highlighted that although the findings from the systematic review (chapter 3, subchapter 2) [196] showed no actual CP-based service in existence, they provided positive evidence for pharmacist services in other settings in opioid optimisation and patient outcomes.

As no CP service/model was found in the systematic review, the case study and interview/focus group findings helped define the steps/actions that CPs in Pakistan can take to optimise opioid usage, in line with the second aim of this study:

- Explore the current use of opioids in Pakistan and identify CP action(s) that may optimise the use of opioids in people with CNMP

All the perceived CP actions — identified in interviews/focus groups and case studies — were triangulated and helped develop a proposed CP opioid optimisation service model detailing a list of actions that can be undertaken by CPs to help optimise the use of opioids. Except one, all components in the proposed model — such as medication reviews, opioid risk assessment, patient education and counselling and a multidisciplinary approach towards medication management by pharmacists — were found in different studies in the systematic review and showed improvement in optimising opioid therapy in people with CNMP. Ensuring that regulatory requirements have been met was a distinct feature of this model identified within Pakistan's context, owing to the fact that people are able to acquire prescription medications without a prescription. The new Schedule-G amendments in Pakistan mandate an opioid to be dispensed against a prescription in the presence of a CP, to reduce the risk of self-medication and improve patient care. This was thus added to the proposed model as a step that can help overcome current factors contributing towards the unsafe use of opioids (self-medication, lack of review visits to doctors) in Pakistan.

7.1.c Factors that might influence the development and delivery of CP opioid service

Another gap identified in the literature was that there were no existing CP services in Pakistan. Thus, the third aim in this thesis was to:

- Explore factors that might influence the development and delivery of a CP opioid optimisation service

Findings in subchapters 4.2 and 5.2 were able to explore many factors impacting the development of CP roles in patient care as well as CPs' capability to engage with patients and deliver a service.

Chapter 7: Overall thesis discussion

The findings listed in Chapter 4.2 were able to provide a holistic overview of factors impacting CP service delivery dispersed across many socio-ecological levels (system, community, organisational, individual).

The findings provided in chapter 5.2 were able to provide a rich contextualisation of the factors reported in interviews/focus groups impacting CPs' capabilities. In addition, some new findings (telephonic deliveries, allied staff dispensing opioids without CP knowledge) were also reported to be impacting CPs' ability to regulate the dispensing of opioids in line with Schedule-G amendments.

The qualitative studies in the systematic review (chapter 3.2), Hartung et al. [243] and Tabeefer et al. [244] also reported similar barriers as identified in the findings of case studies and interviews/focus groups. Highly burdened CPs, gaps in communications with primary care physicians, lack of patient medical information, lack of interdisciplinary care models and lack of CPs' training and confidence were reported by both review studies to impact CPs' ability to deliver optimum services. The strategies reported in both systematic review studies to help CPs optimise opioids were also congruent with my findings. They included developing CP skills by providing specialized training and education in opioid safety and CNMP management. Another strategy in the systematic review articles was remunerating CPs for service provision to improve their motivation to deliver services. Stakeholders in both studies, similar to my study, also expressed that clear policies and guidelines should be developed, which can facilitate and motivate the pharmacists to practice their expanded roles in opioid safety and pain management.

7.2 Implications of overall thesis findings

The section below now presents the implications of my thesis findings.

7.2.a Implications for policy makers, national and international

7.2.a.i Policy makers at national level

As the role of pharmacists continues to expand, the added value and need for pharmaceutical-based care in relation to medication management in Pakistan is being extensively highlighted [28, 144, 146-150]. My thesis findings add to the literature that developing the role of CPs in opioid optimisation might improve patient care for people with CNMP in Pakistan.

In addition, in the national context, these findings can help policy makers understand the context and the specific determinants causing/contributing towards the unsafe use of opioids and target specific activities and interventions to overcome them. The findings also provide them with the perspective that CPs might be able to help overcome many current limitations and challenges causing unsafe use of opioids and this should be further explored. The study also proposes components of an opioid service

developed from stakeholder perspectives, in accordance with the health system's current needs and challenges. Please note the proposed intervention model has been designed on the basis of qualitative findings from my study and cannot be expected to be generalised across all pharmacies in Pakistan. It is recommended that before the model is used to run a trial or pilot, it should be externally validated to determine whether the steps proposed in the service model might be feasible in other community pharmacies in Pakistan. The study findings further present a CP opioid service logic model that provides information on what strategies can be targeted if CP opioid service are to be developed and then delivered in a successful manner. It must be highlighted that although this study focused specifically on exploring facilitators and barriers for a prospective CP opioid service, it also provides a baseline for future researchers looking to explore the role of CPs in other diseases or medications. The findings thus provide context and valuable knowledge for community pharmacy service development in Pakistan.

7.2.a.ii Policy makers at international organisations

The findings of this thesis can also help provide understanding and context to international organisations like UNODC, IASP and WHO, who have their regional chapters/offices in Pakistan and are trying to improve the use of opioid/pain medications as well as manage and reduce the burden of non-communicable conditions like chronic pain.

UNODC in Pakistan tries to control the diversion of pharmaceutical opioids, reduce the number of people using illicit opioids as well as improve the use of opioid medications. Their mission involves reducing the incidence of pharmaceutical drug misuse and diversion as well as prevent people suffering from OUD [102, 103, 464]. Thus, this study provides novel findings and provides an in-depth view of factors contributing towards diversion of pharmaceutical opioids, undertaken with a holistic health systems perspective. This study's findings can help guide their future initiatives and projects targeted at reducing pharmaceutical opioid diversion and disease management.

For an organisation like IASP, the findings of this project inform that people from Pakistan might have inadequate access to pain management facilities and potent opioid medicines. This study also informs the reasons for unavailability of potent opioids, overuse, misuse of and self-medication with opioids (for example, government's fear of opioid misuse, weak regulatory systems, lack of healthcare professionals' competencies in opioid management, inadequate training, inadequate CNMP centres and lack of access to potent opioids). This might help revise IASP's existing efforts [465, 466] to improve chronic pain management by helping improve overall

Chapter 7: Overall thesis discussion

competencies relevant to pain management and opioid safety for health professionals in Pakistan.

For WHO, this project presents stakeholders' opinions about self-medication with opioids and gaps in the health system leading to irrational use of opioids. The WHO mission and vision remains very clearly aligned to the improved health and wellbeing of all people in the world by promoting rational medication use as well as avoiding medication-related side effects [62, 95]. The UHC goals are one of the primary efforts of the WHO to help improve healthcare for people across the world by providing better access to medicines and medicine services [467, 468]. Thus, for WHO, this study provides knowledge around the unsafe use of opioids, unavailability of opioids and highlights that CPs can help improve the safety of opioids with strategically developed roles. The study findings also highlight the lack of access to pain medicines due to fear of misuse and diversion and propose a solution; to develop the role of CPs to help improve the regulation of opioids. This in turn might facilitate increased access to opioids across the country and help fulfil the UHC agenda of equitable access to essential medicines and medicine services.

7.2.b Implications for pharmacy profession

7.2.b.i Implications for pharmacy profession nationally

CPs are trusted members in HICs and have been widely reported to help with medication reviews in chronic disease managements, which can improve patient care [120, 122, 123]. However, as Pakistan has no CP services, this study's findings highlight the need and advantages of CP services in patient care, which opens up an avenue of new career possibilities for pharmacists and improves their job prospects in the country.

In addition, CPs may provide services in diverse locations to target a much wider population as compared to clinical pharmacists in the hospitals. During the COVID-19 pandemic, CPs served as an essential health workforce and their patient care efforts have been majorly acknowledged and extensively highlighted throughout the literature [459, 469, 470]. CPs' unique position and their patient-centred roles have also led many LMICs to explore the development and implementation of CP specialised roles [459, 471, 472]. Along with other studies from Pakistan [473, 474] suggesting the development of CP roles in extended patient services, this study adds that the development of specialised patient care roles for CPs may contribute to improving patient safety in people using opioids. The findings imply that CPs' involvement in delivering patient care services might improve the social as well as professional value of pharmacists and may in future give rise to multidisciplinary patient care models in Pakistan, which might provide benefit to the overall health system.

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7.2.b.ii Implications for pharmacy profession internationally

The systematic review in this thesis provides an extensive overview and provides promising evidence of the pharmaceutical care services provided by pharmacists in outpatient, primary care and community pharmacy settings and the positive perception of stakeholders about developing the role of pharmacists in optimising opioids in the management of CNMP. The findings of the review thus could be useful to any country looking into developing the role of pharmacists in opioid safety in ambulatory settings and might have global implications.

7.2.c Implications for health systems

7.2.c.i Improved public health agenda

Promoting safe opioid medication use by improving medication and disease management is largely beneficial for the people as well as for the overall health system. The overall findings of this thesis report that CPs' engagement with people with CNMP for using opioid medication might help reduce opioid-related harm and improve pain management. This might help reduce repeated visits to doctors and decrease the overutilisation of health systems for CNMP management visits. It might also help reduce the burden of patients on OPDs of public sector hospitals, thus improving availability of doctors to new patients. In addition, reduced repeated visits to private doctors and government health facilities might help lower the overall healthcare costs for people (for example travelling costs, fees, medication payment, self-medication costs) and is perceived to have improved economic benefits. Such impacts of CPs on patient care have been reported in literature from LMICs [459, 475, 476] and supports the implications of this study findings to develop CP roles to strengthen health systems. However, with no studies reporting the role of CPs in opioid optimisation from LMICs, further research is required to evaluate the economic benefits of CPs' inclusion in patient care for people with CNMP using opioids. CPs might also be able to improve public awareness and improve their use of opioids, thus contributing towards public health benefit.

7.2.c.ii Implementation of Schedule-G amendments

Study findings show that weak regulatory system and fear of diversion of opioid medications is the prime reason for potent opioid analgesics like morphine to be excluded from community pharmacies in Pakistan. This results in a lack of access to pain medications and might be impacting pain management in the country. This has also been extensively reported from other LMICs [40, 477], where lack of access to potent opioids is a major consequence of the lack of the health system's ability to regulate controlled opioid medications. My findings highlight that CPs helping implement strict regulations like the Schedule-G amendments might ensure controlled

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regulation. This may help with improved access to essential medicines (for example morphine) across numerous locations as well as discourage the overuse of weaker opioids, use of illicit substances, reduce black market purchases and overall reduce opioid-related harm in the country.

7.2.d Implications for future research from this project

The study provides a rich perspective and informs the factors currently perceived to be contributing towards unsafe use of opioids and they can be used as a knowledge base to understand, correlate, and develop new targeted interventions to overcome specific barriers to improved patient safety.

Externally validating the models generated in this thesis was beyond the objectives of this research study due to time and funding restrictions and is the next proposed step.

Future research should also focus on using different research methods to explore the relationships and/or strategies identified in my study to improve development, delivery and implementation of a CP opioid service.

Future research can also focus on using the data generated in this thesis in different and innovative ways. The data generated in this thesis might also in the future lend itself to secondary data analysis.

7.3 Advantages and limitations

7.3.a Advantages

This study has provided invaluable knowledge and insight into the exploration of a novel CP opioid optimisation service developed and tailored to the current health system needs. The use of data triangulation using case studies and interviews/focus groups allowed for an in-depth exploration and highlighted the diverse and intricate complexities in the conceptualisation and delivery of future opioid service within the real-life context. The inclusion of multiple stakeholders enabled the topic of exploration to be holistically captured and included diverse opinions. Additionally, using multi-methods further reinforced the overall trustworthiness of the findings.

In addition, while this study is qualitative and the exploratory findings from case studies and interviews/focus groups might not be applicable to other countries, the systematic review provides an overview of the role of pharmacists in ambulatory care settings internationally. The review was also mixed methods and combines studies from qualitative and quantitative mixed study paradigms, which helped search the available literature in dimensions and depth that would not have been possible to achieve by including studies of a single research design.

7.3.b Limitations

One of the major limitations of this study is that it focuses on the use of opioids currently available through community pharmacies in Pakistan. This

implies that the study findings are not indicative of the use of morphine, which is currently only available for cancer pain or cardiac pain in specialised hospitals. Further research would thus be needed to understand the precursors of use and misuse of morphine in people with CNMP in Pakistan. Another limitation is that this study only focuses on CNMP management and might not be able to provide information on needs of people with cancer pain, their use and experience of currently available opioids through pharmacies as well as their perspective about role of CPs.

In terms of limitations in the characteristics of participants, despite efforts, no female pharmacy policymaker could be involved in this study, which might have resulted in certain perspectives being missed. This was because no females held influential policy making positions in their respective organisations. However, the impact on the overall research findings is perceived not to be too significant in terms of service development and implementation, as there were female stakeholders in the other three stakeholder groups.

Another limitation was that this study only included doctors from government hospitals due to the sampling methodology used. However, this limitation has been accounted for by purposively selecting doctors who had both government jobs in the hospital setting and had private clinical practice, and hence are perceived to have provided their views from both perspectives. Due to the COVID-19 pandemic restrictions, the use of two different data collection modes (in person and virtually) could have influenced the results, but during analysis no such effect was observed, and the research team helped validate this. Also, literature reports that being reflexive about using different methods depends on the nature of research and the impact of using different data collection methods might not be substantial and pronounced in every research study [478].

The nature of the data is qualitative and inherently lacks generalisability, but rigorous steps have been taken to present a transparent account of the research and provides data that can be anticipated and contextualised in future projects. It also must be highlighted that the research aim was not to arrive at a generalisable set of findings but rather to explore delicate intricacies and differences that can bring subjective contextual details to this study that are otherwise not accessible. Thus, this study provides evidence as baseline research about exploring the development of possible CP roles in opioid safety, which can guide future research.

While internally validated by the research team, this thesis findings are still open to subjectivity as well as uncertainty. Although the research team members have expertise in opioids, pain management and qualitative research, none of them, except me, are from Pakistan. Thus, it is

recommended that before design and implementation of a pilot trial, the models/findings would need to be reviewed/subjected to external expert committees.

One of the limitations of the systematic review was the inclusion of studies published only in the English language and as full text publications; however, the extent of the effect of this on the findings of the systematic reviews is debatable [479]. In addition, as true with the whole study, the systematic review focused only on people with CNMP pain and hence the results might not apply to pharmacist interventions in cancer pain management. Another limitation of the review is the lack of substantial evidence for the isolated contribution of a pharmacist in opioid safety because the pharmacist in many studies was part of ambulatory care teams delivering the intervention. Also, it must be highlighted that in the review, all the studies had fairly small sample sizes and so, the statistically significant intervention effect might be a false positive result [480].

7.4 Unanswered questions

This research study is unable to answer or provide substantial information on the following:

1. The incidence or statistics on the occurrence of misuse, polypharmacy, intentional or unintentional misuse cannot be quantified through the available data.
2. The study used a qualitative approach that makes it inherently opposed to being generalisable. Thus, other researchers might not necessarily find all these factors and strategies if repeating the research and the findings of this study remain subject to change. However, the aim was to contribute to knowledge creation and provide in-depth exploratory findings regarding the role of CPs in opioids in Pakistan.
3. The study findings only present knowledge about some risk factors that might be precursors to misuse or overuse of opioids. The definitive correlation of these factors with the use of opioids in an unsafe manner cannot be answered through the data presented in this thesis and needs further testing via quantitative methods, which can be taken up by further research.
4. Although the study findings report that there might be decreased economic costs to the patients and health systems associated with developing role of CPs, the percentages or exact economic implications cannot be anticipated or generated through this study findings.
5. This study cannot provide specific information or pathways about the next steps, such as a trial phase to develop a CP service to optimise

opioid usage in people with CNMP. This study only informs a set of strategies that are perceived to help develop and improve the capability of CPs to deliver a future opioid service.

6. The study briefly sheds light on the need to develop digital health systems to improve patient care in opioid optimisation. But this study had a different aim and focus and the benefit of developing digital health systems for patient care or opioid optimisation in Pakistan needs to be separately explored.
7. This study was specifically targeted to explore the role of CPs in prescription-only opioids (Schedule-G) in CNMP management. Thus, the study findings do not reflect on role of CPs in any other pain management medications, such as OTC analgesics like acetaminophen or NSAIDS, and they remain unexplored and open to further research.

7.5 Conclusion

This thesis provides an overview of factors and challenges contributing towards the unsafe use of opioid medications and proposes a multi-component opioid optimisation CP service diagram along with its perceived development and delivery in Pakistan. The study informs strategies that could help overcome many current socioecological health system challenges and provide national and international policy makers and researchers with detailed knowledge of what possible steps can be undertaken to facilitate the development and implementation of a CP opioid optimisation service in people with CNMP in Pakistan.

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Appendix 1: Search Strategy for systematic review one data base example

Supplementary data

The following is the supplementary data to this article:

Appendix 1: Search strategy

The authors first created a preliminary search strategy using free text terms in 4 main domains (pharmacists, opioids, chronic pain and management/intervention). The initial search items as free text terms and medical subject headings (MeSH) headings for MEDLINE are attached as Table 4. Vocabulary and alternate spellings (UK and American) were adjusted and were used interchangeably across databases. Synonyms were identified by performing a basic search. An advanced search using truncation and wild card were also used to maximise the search. Subject headings (if applicable) were used according to each respective database. Where applicable the explode option was also used. After all the basic searches (having free terms and MeSH headings) were combined into an individual search, they were intersected using AND/OR as applicable.

Table 4

Free text terms and MeSH headings; example of Medline database

Pharmacist	Opioids	Chronic pain	Management/intervention
Pharmacists	Analgesics,	Chronic pain	Prescription drug misuse
Community pharmacy services	opioid	Pain measurement	Pain management
	Analgesics,	Pain management	Patient compliance
Patient care team	Opioid	Chronic disease	Counselling
	morphine	Pain	Community health services
Professional role	meperidine	Chronic non-cancer pain	Patient care management
Primary health care	methadone		Delivery of health care
	buprenorphine		Health care costs
	fentanyl		Outcome and Process Assessment (Health Care)
	hydrocodone		Health services research
	oxycodone		Quality of life
	codeine		Health Knowledge, Attitudes, Practice
	opiate		Patient medication knowledge
			Patient Education handout
			Patient education
			Early intervention
			Pharmacy service hospital
			Education, pharmacy
			Drug monitoring
			Pharmaceutical services
			Prescription drug monitoring program
			Patient compliance
			Medication adherence
			Reduc*

Raper
 Stop
 Terminat*
 Remove
 Substitu*

*truncation

Database: Ovid MEDLINE(R) ALL <1946 to November 01, 2019>

Search Strategy:

-
- 1 pharmacist.mp. (14861)
 - 2 pharmacists.mp. (30168)
 - 3 Pharmacists/ (15938)
 - 4 clinical pharmacist.mp. (1543)
 - 5 clinical pharmacists.mp. (1505)
 - 6 hospital pharmacist.mp. (413)
 - 7 hospital pharmacists.mp. (1115)
 - 8 community pharmacist.mp. (754)
 - 9 community pharmacists.mp. (2503)
 - 10 ambulatory care pharmacist.mp. (17)
 - 11 ambulatory care pharmacists.mp. (30)
 - 12 druggist.mp. (56)
 - 13 druggists.mp. (99)
 - 14 retail pharmacist.mp. (20)
 - 15 retail pharmacists.mp. (53)
 - 16 patient care team.mp. (63895)
 - 17 patient care teams.mp. (91)
 - 18 Patient Care Team/ (63650)
 - 19 health professional.mp. (8673)
 - 20 health professionals.mp. (44976)
 - 21 health personnel.mp. (168330)
 - 22 health personnels.mp. (49)
 - 23 Health Personnel/ (39090)
 - 24 professional role.mp. (14344)
 - 25 professional roles.mp. (975)
 - 26 Professional Role/ (13022)
 - 27 pharmacy.mp. (61045)
 - 28 exp Pharmacy/ (8267)
 - 29 pharmacies.mp. (15711)
 - 30 Pharmacies/ (7691)
 - 31 community pharmacy.mp. (5967)
 - 32 community pharmacies.mp. (3073)
 - 33 clinical pharmacy.mp. (3401)
 - 34 clinical pharmacies.mp. (2)
 - 35 retail pharmacy.mp. (236)
 - 36 retail pharmacies.mp. (341)
 - 37 commercial pharmacy.mp. (17)
 - 38 commercial pharmacies.mp. (17)
 - 39 out patient pharmacy.mp. (12)

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- 40 out patient pharmacies.mp. (2)
- 41 ambulatory care pharmacy.mp. (87)
- 42 ambulatory care pharmacies.mp. (8)
- 43 pharmacy service.mp. (11909)
- 44 pharmacy services.mp. (6227)
- 45 pharmaceutical service.mp. (177)
- 46 pharmaceutical services.mp. (12704)
- 47 exp Pharmaceutical Services/ (67235)
- 48 community pharmacy service.mp. (49)
- 49 community pharmacy services.mp. (4541)
- 50 Community Pharmacy Services/ (4372)
- 51 primary health care.mp. (87847)
- 52 Primary Health Care/ (74241)
- 53 primary health care service.mp. (224)
- 54 primary health care services.mp. (1116)
- 55 ambulatory health care.mp. (361)
- 56 ambulatory health care service.mp. (2)
- 57 ambulatory health care services.mp. (33)
- 58 ambulatory care.mp. (65281)
- 59 Ambulatory Care/ (42014)
- 60 pharmacy health care.mp. (11)
- 61 community health service.mp. (388)
- 62 community health services.mp. (31667)
- 63 Community Health Services/ (30983)
- 64 community health care service.mp. (17)
- 65 community health care services.mp. (52)
- 66 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 (547047)
- 67 opioid analgesic.mp. (1884)
- 68 opioid analgesics.mp. (3453)
- 69 Analgesics, Opioid/ (41624)
- 70 opiate analgesic.mp. (146)
- 71 opiate analgesics.mp. (269)
- 72 narcotic analgesic.mp. (615)
- 73 narcotic analgesics.mp. (1395)
- 74 narcotic.mp. (44288)
- 75 narcotics.mp. (20616)
- 76 Narcotics/ (16241)
- 77 opioid pain killer.mp. (0)
- 78 opioid painkiller.mp. (9)
- 79 opioid pain killers.mp. (4)
- 80 opioid painkillers.mp. (16)
- 81 opiate pain killers.mp. (2)
- 82 opiate painkillers.mp. (2)
- 83 narcotic pain killer.mp. (2)
- 84 narcotic painkiller.mp. (0)
- 85 narcotic pain killers.mp. (3)

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- 86 narcotic painkillers.mp. (5)
- 87 morphine.mp. (57397)
- 88 exp Morphine/ (37700)
- 89 fentanyl.mp. (21984)
- 90 exp Fentanyl/ (15453)
- 91 methadone.mp. (16417)
- 92 exp Methadone/ (12144)
- 93 buprenorphine.mp. or Buprenorphine/ (7271)
- 94 exp Buprenorphine/ (5052)
- 95 codeine.mp. (6809)
- 96 exp Codeine/ (6819)
- 97 opioid disorder.mp. (10)
- 98 opioid disorders.mp. (13)
- 99 opioid related disorder.mp. (5)
- 100 opioid related disorders.mp. (13677)
- 101 exp Opioid-Related Disorders/ (25157)
- 102 OUD.mp. (660)
- 103 prescription opioid misuse.mp. (258)
- 104 prescription drug misuse.mp. (1810)
- 105 exp Prescription Drug Misuse/ (12457)
- 106 opioid misuse.mp. (891)
- 107 opioid overdose.mp. (1317)
- 108 drug overdose.mp. (11924)
- 109 Drug Overdose/ (10771)
- 110 Opioid medication safety.mp. (2)
- 111 opia*.mp. (27257)
- 112 opiate.mp. (21543)
- 113 exp Opiate Alkaloids/ (84739)
- 114 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 (208412)
- 115 pain.mp. (686125)
- 116 exp Pain/ (383255)
- 117 chronic pain.mp. (41227)
- 118 exp Chronic Pain/ (12995)
- 119 chronic non-cancer pain.mp. (564)
- 120 chronic non-malignant pain.mp. (280)
- 121 non-cancer pain.mp. (771)
- 122 non-malignant pain.mp. (379)
- 123 chronic pain condition.mp. (384)
- 124 chronic pain conditions.mp. (1560)
- 125 chronic pain disease.mp. (28)
- 126 chronic pain diseases.mp. (26)
- 127 persistent pain.mp. (4955)
- 128 recurring pain.mp. (78)
- 129 repetitive pain.mp. (35)
- 130 untreatable pain.mp. (21)
- 131 idiosyncratic pain.mp. (2)
- 132 incurable pain.mp. (13)

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- 133 pain scale.mp. (5540)
- 134 pain scales.mp. (1048)
- 135 pain measurement.mp. (83579)
- 136 Pain Measurement/ (83159)
- 137 measuring pain.mp. (429)
- 138 pain service.mp. (555)
- 139 pain services.mp. (247)
- 140 pain clinic.mp. (1757)
- 141 pain clinics.mp. (1885)
- 142 exp Pain Clinics/ (1448)
- 143 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 132 or 133 or 134 or 135 or 136 or 137 or 138 or 139 or 140 or 141 or 142 (764300)
- 144 managing pain.mp. (906)
- 145 pain management.mp. (48698)
- 146 Pain Management/ (31862)
- 147 pain education.mp. (457)
- 148 counseling.mp. (97067)
- 149 Counseling/ (34767)
- 150 counselling.mp. (25848)
- 151 patient counseling.mp. (2403)
- 152 patient counselling.mp. (663)
- 153 pain counseling.mp. (10)
- 154 pain counselling.mp. (3)
- 155 patient compliance.mp. (63145)
- 156 exp Patient Compliance/ (73503)
- 157 medicine adherence.mp. (52)
- 158 medication adherence.mp. (22903)
- 159 Medication Adherence/ (17535)
- 160 Patient care management.mp. (4169)
- 161 exp Patient Care Management/ (751351)
- 162 delivery of health care.mp. (105332)
- 163 exp "Delivery of Health Care"/ (1039383)
- 164 Risk assessment.mp. (282979)
- 165 exp Risk Assessment/ (253905)
- 166 Health care cost.mp. (2075)
- 167 health care costs.mp. (47412)
- 168 Health Care Costs/ (37935)
- 169 Pharmaco-economics.mp. (72)
- 170 patient Safety.mp. (40485)
- 171 Patient Safety/ (18195)
- 172 Prescription drug diversion.mp. (256)
- 173 Prescription Drug Diversion/ (210)
- 174 quality of life.mp. (323711)
- 175 "Quality of Life"/ (183790)
- 176 Quality of health care.mp. (139731)
- 177 exp "Quality of Health Care"/ (6676872)
- 178 Acceptance of illness.mp. (170)
- 179 Patient medication knowledge.mp. (198)
- 180 Patient Medication Knowledge/ (160)

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- 181 patient education.mp. (97894)
- 182 Patient Education as Topic/ (83289)
- 183 Patient Education handout.mp. (5076)
- 184 Patient Education Handout/ (5035)
- 185 pharmacist education.mp. (79)
- 186 Education, Pharmacy, Continuing/ (891)
- 187 intervention.mp. (579918)
- 188 pharmacist intervention.mp. (577)
- 189 interventions.mp. (426043)
- 190 pharmacist interventions.mp. (514)
- 191 pharmacy intervention.mp. (119)
- 192 pharmacy interventions.mp. (136)
- 193 Early Medical Intervention/ (2736)
- 194 pharmacist consultation.mp. (82)
- 195 pharmacist consultations.mp. (34)
- 196 pharmacy consultation.mp. (31)
- 197 pharmacy consultations.mp. (25)
- 198 exp "Referral and Consultation"/ (72393)
- 199 Drug monitoring.mp. (25927)
- 200 Drug Monitoring/ (20125)
- 201 monitoring prescription.mp. (28)
- 202 monitoring prescriptions.mp. (15)
- 203 Prescription Drug Monitoring Programs/ (139)
- 204 drug information service.mp. (213)
- 205 drug information services.mp. (3886)
- 206 exp Drug Information Services/ (12195)
- 207 drug screening.mp. (35244)
- 208 Drug utilization review.mp. (3884)
- 209 Drug utilisation review.mp. (20)
- 210 "Drug Utilization Review"/ (3681)
- 211 Prescription screening.mp. (16)
- 212 medicine review.mp. (206)
- 213 medication review.mp. (1165)
- 214 MUR.mp. (486)
- 215 Medication therapy management.mp. (2323)
- 216 Medication Therapy Management/ (1901)
- 217 Medication therapy management service.mp. (14)
- 218 Medication therapy management services.mp. (141)
- 219 clinical pharmacy service.mp. (141)
- 220 clinical pharmacy services.mp. (645)
- 221 prescription drug monitoring program.mp. (240)
- 222 prescription drug monitoring programs.mp. (319)
- 223 Prescription Drug Monitoring Programs/ (139)
- 224 medication error.mp. (1579)
- 225 medication errors.mp. (14681)
- 226 exp Medication Errors/ (16433)
- 227 patient advice.mp. (82)
- 228 patient satisfaction.mp. (95989)
- 229 exp Patient Satisfaction/ (86017)

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230 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156 or 157 or 158 or 159 or 160 or 161 or 162 or 163 or 164 or 165 or 166 or 167 or 168 or 169 or 170 or 171 or 172 or 173 or 174 or 175 or 176 or 177 or 178 or 179 or 180 or 181 or 182 or 183 or 184 or 185 or 186 or 187 or 188 or 189 or 190 or 191 or 192 or 193 or 194 or 195 or 196 or 197 or 198 or 199 or 200 or 201 or 202 or 203 or 204 or 205 or 206 or 207 or 208 or 209 or 210 or 211 or 212 or 213 or 214 or 215 or 216 or 217 or 218 or 219 or 220 or 221 or 222 or 223 or 224 or 225 or 226 or 227 or 228 or 229 (7954067)

231 66 and 114 and 143 and 230 (2807)

232 66 and 114 and 143 (3153)

233 limit 232 to (english language and yr="1990 - 2020" and "all adult (19 plus years)")

Appendix 2: Semi-structured topic guides

Appendixes

Appendix 2

1. Interview guide for people having CNMP

The semi-structured approach shall be used and emphasis will be given to the below subtopics in the context of understanding the norms and expectations of people with CNMP when they visit and interact with prescribers and community pharmacists, buy opioid medicines, and use opioid medicines.

Pain management and health care related:

- Can you share your experience/ How do you feel about the current pain management options available to people in Pakistan?
- Can you share your pain management experience and journey?

Opioid medicine related:

- Can you share in your words experience of using opioids in the management of CNMP?
- Can you please share, your current journey of using opioids, and any factors that helps you, use your medications more effectively or feel as barriers towards using medicines safely?
- Where do you normally get your medicine information/medication review, and would you like to share your experience receiving opioid medication information?
- What do you think is needed in the future so that people can get the best benefits of opioid medicines, without experiencing any, avoidable side effects and harms, while using opioids (optimization)?
- What do you think about the attitudes of the community pharmacist and prescribers towards your pain management?

Interdisciplinary health teams:

- How do you feel if a pharmacist has a concern/suggestion about your opioid therapy and usage and engages you in counselling session or if communicates the new plan with your prescriber?
- How do you feel prescribers and community pharmacists can work together (as a team) to help manage pain by opioids? Any thoughts?

“If they highlight positive views about community pharmacy based pain management and opioid optimisation services, otherwise ask how services will be developed and implemented, opinions, views, suggestions or strategies to optimise the use of prescriptions opioids (general)”

Community pharmacist related (major priority)

- What in your perception is the role of community pharmacists in helping you manage opioid medications for chronic pain?
- What do you think about the current community pharmacist services for pain management?
- Where do you see the community pharmacist’s future role to help people using prescription opioids in managing chronic pain to maximise the benefits and reduce harm?
- What should be the key attributes of a satisfactory review service in community pharmacy to avoid prescription misuse and optimise opioid therapy in CNMP?
- (if positive role suggested) How can community pharmacist’s role be developed and implemented to help people use opioids?

“Ask if there anything they would like to add and highlight which wasn’t addressed during interview”

2. Interview guide for community pharmacists

The data will focus on obtaining community pharmacist perception on current use of opioids in the management of CNMP and possible services and strategies for optimization of opioid therapy.

Appendixes

Health system and pain management:

- Can you please share your views on current use of opioids in the management of chronic non-malignant pain?
- Can you share your views on chronic pain management in Pakistan?

Policies and legislation:

- What are your views regarding current opioid regulation (schedule-G) and access to opioids for the management of CNMP?
- What guidelines and information do you follow while reviewing patient opioid medicine regimens?
- What do you think is needed in the future in the optimization of prescription opioids?

“If they highlight positive views about community pharmacy-based pain management and opioid optimisation services), otherwise ask, opinions, views, suggestions or strategies to optimise the use of prescriptions opioids (general)”

Perception of the role of community pharmacist in optimization of opioid therapy:

- Do you think of any services pharmacist could provide for opioid therapy optimization?
- Are community pharmacists playing any role in patient education, counselling, review and monitoring (for misuse and addiction) in prescription opioids in CNMP?
- What do you think the key attributes of care in a service provided by community pharmacist to optimise opioid therapy should be? Any barriers?
- (if positive role suggested) How can community pharmacist’s role be developed and implemented to help people use opioids?

Any barriers?

- What is your experience when you review patient’s opioid medicine in CNMP? (prescription related)
- What is your experience when you counsel, educate, and provide medicine information to people suffering from CNMP to optimize their opioid use? (patient oriented)
- What is your experience when you discuss opioid medications (dose, repeats etc) with doctors? (doctors-oriented)

“Ask if there anything they would like to add and highlight which wasn’t addressed during focus group discussions”

3. Interview guide for doctors

The data will focus on obtaining doctors perception on current use of opioids and possible services for optimization of opioid therapy.

Health system and pain management:

- Can you please share your views on current use of opioids in the management of chronic non-malignant pain?
- Can you share your views on chronic pain management in Pakistan?
- What are your views regarding current opioid regulation (schedule-G) and access to opioids for the management of CNMP?
- What guidelines and information do you follow while reviewing patient opioid medicine regimens?
- What do you think is needed in the future in the optimization of prescription opioids?

Opioid medicine related:

- What is your experience when you review patient’s opioid medicine in CNMP? (prescription related)
- What is your experience when you counsel, educate, and provide medicine information to people suffering from CNMP to optimize their opioid use? (patient oriented)

Interdisciplinary approaches, health care team related:

Appendixes

- Do you feel prescribers and community pharmacists can work together as a team to manage chronic pain by opioids?
- How do you feel if a pharmacist has a concern/suggestion about an opioid therapy and usage or suggests a new plan with you?

“If they highlight positive views about community pharmacy-based pain management and opioid optimisation services), otherwise ask, opinions, views, suggestions or strategies to optimise the use of prescriptions opioids (general)”

Perception of the role of community pharmacist in optimization of opioid therapy:

- Do you think of any services pharmacist could provide for opioid therapy optimization?
- Are community pharmacists playing any role in patient education, counselling, review and monitoring (for misuse and addiction) in prescription opioids in CNMP?
- What do you think the key attributes of care in a service provided by community pharmacist to optimise opioid therapy should be? Any barriers?
- What do you want/expect from a community pharmacist when a CNMP patient goes to fill an opioid prescription?
- What are your current experiences?
- (if positive role suggested) How can community pharmacist’s role be developed and implemented to help people use opioids?

“Ask if there anything they would like to add and highlight which wasn’t addressed during focus group/interview”

4. Interview guide with policy makers

Health system and pain management:

- Can you please share your views on current use of opioids in the management of chronic non-malignant pain?
- Can you share your views on chronic pain management in Pakistan?
- What is the reason Pakistan lacks potent opioids, and how can the situation be improved to improve access to medicines? (only ask if they mention lack of opioids, or opioids for cancer pain managements)

Health care team related:

- Do you feel prescribers and community pharmacists can work together as a team to manage chronic pain by opioids?

“If they highlight positive views about community pharmacy-based pain management and opioid optimisation services), otherwise ask, opinions, views, suggestions or strategies to optimise the use of prescriptions opioids (general)”

Community pharmacist related:

- What is your opinion on utilising community pharmacists to avoid opioid prescription misuse and optimise opioid therapy in CNMP to maximise the benefits and reduce harm?
- What is your opinion of current community pharmacist services for CNMP management?
- Where do you see the community pharmacist’s role to help people using prescription opioids in managing CNMP (future role of the community pharmacist)
- (if positive role suggested) How can community pharmacist’s role be developed and implemented to help people use opioids?

Opioid medicine related:

- What should be the key attributes of a satisfactory review service in community pharmacy to avoid prescription misuse and optimise opioid therapy in CNMP?

“Ask if there anything they would like to add and highlight which wasn’t addressed during interview”

Appendixes

An example of semi-structured questions added based on preliminary interviews/FGS on 14-07-2020

The semi-structured approach shall be used and emphasis will be given to the below subtopics in the context of understanding the norms and expectations of people with CNMP when they visit and interact with community pharmacists. What stakeholders think what community pharmacist can do for optimising opioids for people with chronic non-cancer pain?

Community pharmacist related (major priority)

- Do you know what a community pharmacist is, where they are found, what is their role ? (If yes: proceed)
- What is the role of community pharmacists in medicine safety especially in opioids in Pakistan?
- Where do you see the community pharmacists' future role to help people using prescription opioids in managing chronic pain to maximise the benefits and reduce harm?
- Is Pakistan ready for community pharmacist-based patient care services like opioid service which can help people use medicines more effectively and help reduce harm/adverse effects?

(If say yes, or positive views then ask) What should be the key attributes of a satisfactory review service in community pharmacy to avoid prescription opioid misuse and optimise opioid therapy in CNMP?

- What are your views on: community pharmacists are competent? Motivated? and can/able to deliver such a service?

(if they mention there are no services then ask) What steps need to be taken in order to get community pharmacists to perform/ help people with opioid medicines?

(If they mention challenges and don't provide a perspective what can be done to overcome that challenge, ask them). So. what can be done that can help overcome this (XYZ) challenge?

- What do you perceive the benefits of such a service for people, pharmacists, health system?

Opioid medicine related:

- If any person wants information on opioid medicines, in your opinion whom shall they ask?
- How can opioid medicine knowledge be increased? Sources?
- Would you trust community pharmacist for opioid information if they provide as part of service?
- What steps can be undertaken to promote safe use of opioids? In your perception what are current problems causing unsafe use of opioids and what can be done to overcome them?

Health care related:

- How do you feel prescribers and community pharmacists can work together (as a team) to help the safe use of opioids? Any thoughts? How can this communication happen?
- How do you feel if a pharmacist has a concern/suggestion about opioid therapy and usage and engages people in counselling session or if communicates the new plan with your GP/prescriber?

“Ask if there anything they would like to add and highlight which wasn't addressed during focus group/interview”

Appendix 3: Case study form

Appendixes

Appendix 3:

Checklist for case study observation:

Pharmacy related:

- Was the person received by a pharmacy assistant- pharmacist- called a pharmacist—all dealing with pharmacy staff
- Infrastructure
- Rush hours vs free
- Overall pharmacy opening and closing times- holiday
- Dispensing process
- Number of staff
- Locality or geographical area possible effect
- Timings effect
- Review
- Layout-human factors- to reduce medication errors
- Medicine inventory
- Drug inspector visits
- Medicine entry
- medicine record keeping
- Medicine cabinet
- Ongoing services where staff is engaged
- Anything else

Personnel related:

- Pharmacist or pharmacy technician
- Who is receiving orders
- Who is filling prescriptions
- Who reviews
- Who stocks
- Time to dispense
- How many deliveries
- Any telephone contact with the prescriber
- Any telephone contact with the patient
- Anything else

Questions asked by the pharmacist (all-anything):

- Any assessment to detect is this prescription for the same patient
- Body language
- Attitude
- Engagement with the patient
- Conversation of the pharmacist
- Duration of time spent with a person filling prescription
- Differences between a new and refill
- Any difference in review or dispensing during consequent refills
- Any difference while giving information to male/female or old/young
- Questions asked if any by the staff or pharmacist
- Questions asked by the patients
- Anything else

Medicine related- product information- therapeutic goal (people):

- Feeling after starting a medicine
- Any medicine side effects, problems, concerns
- Do they want any information
- How do they take or use these medicines
- Do they know how to take the medicine
- Do they know signs of overdose and possible course of action
- Lifestyle advice
- Referral
- Information leaflet provided
- Social prescribing
- Any prescription medicine, OTC added
- Any risk establishment- alcohol- sedatives-mental health issue assessment
- Anything else

Any challenges/barriers/ feelings/concerns expressed by pharmacist or observed: (informal)

Appendixes

- What is their current experience and Influencers of interaction with CNMP patients taking opioids
- Are they satisfied with the current interaction provided by them in pain management
- Perception about benefit of interaction
- Was the patient approachable
- Any factors/barriers affecting the communication
- Internal: CNMP patient related, personal, knowledge, attitude, time
- External: Policy, guidelines, job description, timings, staffing, remuneration, Doctors, work load
- Medicine review-telephone
- **Anything else they added**

Appendix 4-7: Participant recruitment materials, demographic forms

Appendix 4: Recruitment materials/invitation letters

Invitation letter or email sample to members of Professional bodies

Invitation letter

Subject: Invitation to participate in a PhD research project” Role of community pharmacists in optimizing opioid therapy for chronic non-malignant pain patients”

Dear Sir or Madam,

My name is Ayesha Iqbal and I am a Doctoral student in the Pharmacy Practice and Policy Division in the School of Pharmacy at University of Nottingham. I am working on a research project under the supervision of Prof. Claire Anderson and Dr Roger Knaggs.

I am writing to you today to invite you to participate in a study entitled “Role of community pharmacists in optimizing opioid therapy for chronic non-malignant pain patients”. This study aims to gain in depth insight into the role of community pharmacists in chronic pain management using prescription opioids in non-cancer pain.

With your consent, interviews will be audio-recorded. Once the recording has been transcribed, the audio recording will be destroyed.

This project does not involve any professional and emotional risks and care will be taken to protect your identity. This will be done by keeping all responses anonymous and allowing you to request that certain responses not be included in the final project.

You will have the right to end your participation in the study at any time, for any reason, up until interview. In case you choose to withdraw after the interview all the collected information till that point will be used in the final analysis, but we will try using as little as possible personal identifiers.

All research data, including audio-recordings and any notes will be encrypted. Any hard copies of data (including any handwritten notes or USB keys) will be kept in a locked cabinet at University of Nottingham. Research data will only be accessible by the researcher and the research supervisors.

The ethics protocol for this project was reviewed by the Research Ethics Board School of Pharmacy, which provided clearance to carry out the research.

If you would like to participate in this research project, or have any questions, please contact me at (ayesha.iqbal@nottingham.ac.uk).

Sincerely,

Ayesha Iqbal

Flyer for Pakistan

Are you a community pharmacist?

“If you are working in a community pharmacy, you have a chance to have your voice heard”

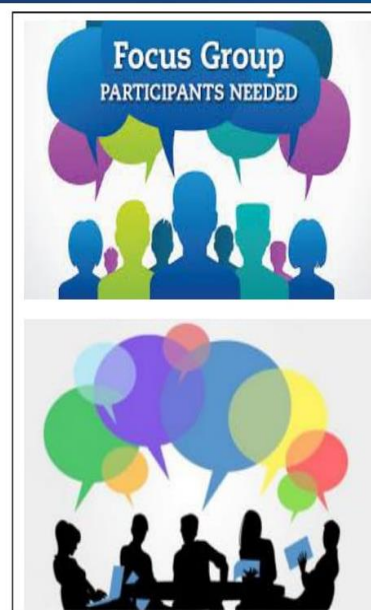
“Opportunity for community pharmacists to participate in a research study”

We are looking for community pharmacists who are dispensing opioid prescriptions for chronic pain management to participate. This study will help explore the role, perception and satisfaction with current services provided by community pharmacist to help improve opioid usage by people suffering from chronic pain.

Participants will be asked to join either in-person group discussions or an online discussion board as per their choice.

Participants will receive:

- Snacks or refreshments on site.
- Personal satisfaction to contribute towards acknowledgment of community pharmacist role and services in health care system.
- Inconvenience allowance for compensation of time
- Travel allowance (will cover to and from travelling only for in-person group discussions).



Location

In-person group discussions will be carried in a convenient location during a duration of two months depending upon the feasibility of participants.

Are you eligible?

- Currently working in a community pharmacy setting (full time or part-time) but should include dispensing opioids every week.
- Must be a licensed pharmacist.

If you're unsure if you meet the requirements, call or email a member of the study team:

Ayesha Iqbal
(Masters in Pharmacy Practice)
PhD student
Ayesha.Iqbal@nottingham.ac.uk



Do you suffer from Chronic Pain?

“If you are 18 or older, suffer from chronic pain, and are currently using opioid pain medicines you have a chance to have your voice heard.”

“Opportunity for adults suffering from chronic pain to participate in a research study”

We are looking for adults (18 years and above) who are using opioids for pain management to participate in a research study to explore role, perception and satisfaction with community pharmacist services in improving opioid usage by people suffering from pain.

Participants will be asked to join either in-person group discussions or an online discussion board as per their choice.

Participants will receive:

- Travel allowance (will cover to and from travelling only for in-person group discussions).
- Snacks or refreshments on site.
- Opportunity to meet and socialize with other people suffering from chronic pain.
- Inconvenience allowance for compensation of time

Location

In-person focus group discussions will be carried in a convenient place during a duration of two months depending upon the feasibility of participants.

Are you eligible?

- No diagnosed dependency on opioids.
- Having diagnosed chronic pain.
- Receiving prescription opioids for managing chronic pain since at least 12 months.



If you are unsure if you meet the requirements, email a member of the study team:

Ayesha Iqbal
(Masters in Pharmacy Practice)
PhD student
Ayesha.Iqbal@nottingham.ac.uk



University of
Nottingham
UK | CHINA | MALAYSIA

Are you a Doctor?

“If you see patients suffering from chronic pain and prescribe opioid painkillers, have your say and share your thoughts.”

“Opportunity for Doctors prescribing opioid analgesics for management of chronic non-malignant pain to participate in a research study”

We are looking for GPs who prescribe opioid analgesics for pain management in chronic non-malignant pain (CNMP) to participate in a research study to explore their perception about role of community pharmacist in optimizing opioid usage in people suffering from pain.

Participants will be asked to join interview, in-person focus group discussions or an online discussion board as per their choice.

Participants will receive:

- Travel allowance (will cover to and from travelling only for in-person group discussions).
- Opportunity to socialize
- Personal satisfaction of lending their voice towards patient care
- Inconvenience allowance for compensation of time

Location

In-person focus group discussions or interviews will be carried in a convenient location during a duration of two months depending upon the feasibility of participants.

OR

Online discussion board login will be communicated soon.

Are you eligible?

- Do you prescribe opioid analgesics for chronic pain?
- Prescribing opioids/managing chronic pain since at least 12 months.



FOCUS GROUP PARTICIPANTS WANTED!



YOUR OPINION MATTERS!

If you're unsure if you meet the requirements, call or email a member of the study team:

Ayesha Iqbal
(Masters in Pharmacy Practice)
PhD student
Ayesha.Iqbal@nottingham.ac.uk



University of Nottingham
UK | CHINA | MALAYSIA

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Appendix 5: Study Form

Name		Age	
Unique identifier number (assigned by the research team)		Gender	

Preferred mode of communication with the research team:

Preferred mode of communication	Telephone/mobile number	Email address	Postal address
Please provide details (at least one of them?)			

Volunteering to participate in one or all of the study phases:

Choice to enrol in	Focus group	Case study	Interviews

Choose whichever is applicable:

Choice to enrol in Focus group	Online focus group	Face to face focus group

Would you like to receive the results of the study when it is published online?	Yes	No
If yes please provide your preferred mode of communication and details		

Appendix 6: Demographic forms

Demographics for people having CNMP

Appendixes

1	Name: Code:_____	Gender: 1: Male 2: Female
2	Age of respondent In years-----	1: 18–28 years 2: 29–39 years 3: 40–50 years 4: 51–60 years 5: 61- above
3	Area of living	1: Urban 2: Rural
4	Duration of chronic pain	_____
5	Origin or cause of chronic	_____
6	Years of opioid use:	1-2 years 2-3 years 4-5 years 5-10 years 10-15 years 15-20 years 20 years and beyond
7	What is the highest Level of school you attend?	_____
8	What is your current occupation?	Employed full-time Employed part-time Retired Unemployed Still studying Self-employed Disabled or too ill to work Prefer not to say
9	Ethnicity	_____

Demographic for pharmacists

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1	Name: Code: _____	Gender: 1: Male 2: Female 3: Prefer not to say
2	Age of respondent In years-----	1: 18–28 years 2: 29–39 years 3: 40–50 years 4: 51–60 years 5: 61- above
3	Area of community pharmacy	1: Urban 2: Rural
4	Type of community pharmacy	Multiple chain pharmacy Small chain pharmacy Single store pharmacy
4	Years of experience:	1: less than 5 years 2: 5-10 years 3. 11-15 years 4. 16-20 years 5. 21-25 years 6. 26 years and above
5	What is the highest Level of school you attend?	1: Graduate 2: Postgraduate
6	What is your current occupation?	Employed full-time Employed part-time Retired Unemployed Self-employed
7	Average time spent in community pharmacy (per week)	_____
8	Average opioid prescriptions filled per week	1- 20 2- 20-40 3- 40-60 4- 60-80 5- 80-100 6- 100-500 7- 500-1000

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Demographics for Doctors

1	Name: Code: _____	Gender: 1: Male 2: Female
2	Age of respondent In years-----	1: 20–30 years 2: 31–40 years 3: 41–50 years 4: 51–60 years 5: 61- above
3	Area of practice	1: Urban 2: Rural
4	Years of prescribing opioids:	1-2 years 2-3 years 4-5 years 5-10 years 10-15 years 15-20 years 20 years and beyond
5	Specialized pain training?	Yes No
6	Guideline followed for CNMP management	_____
7	Hospital or Clinic (Government or Private)	_____

Demographics form for representatives of professional bodies

1	Name: Code: _____	Gender: 1: Male 2: Female
2	Age of respondent In years-----	1: 20–30 years 2: 31–40 years 3: 41–50 years 4: 51–60 years 5: 61- above
3	Area of practice	1: Urban 2: Rural
4	Member of:	DRAP PMDC Pharmacy Council Health Department
5	Position:	_____

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Appendix 7 : Consent forms

Consent form policy makers:

CONSENT FORM (Draft Version 01 / Final version 1.0: 22/10/2019)

Title of Study: Role of Community Pharmacists in Optimizing Opioid Therapy for Chronic Non-malignant Pain Patients

Name of Researcher: Ayesha Iqbal

Name of Participant: _____

Please initial box

1. I confirm that I have read and understand the information sheet version number 1.0 dated 22/10/2019 for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.
3. I understand that relevant sections of data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential.
4. I understand that the interview will be recorded and that anonymous direct quotes from the interview may be used in the study reports.
5. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.
7. I agree to take part in the above study.

Name of Participant Date Signature

Ayesha Iqbal
Name of Person taking consent Date Signature

02 copies: 01 for participant, 01 for the project notes

Consent form physicians:

CONSENT FORM

Appendixes

(Draft Version 01 / Final version 1.0: 22/10/2019)

Title of Study: Role of Community Pharmacists in Optimizing Opioid Therapy for Chronic Non-malignant Pain Patients

Name of Researcher: Ayesha Iqbal

Name of Participant: _____

Please initial box

1. I confirm that I have read and understand the information sheet version number 1.0 dated 22/10/2019 for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.
3. I understand that relevant sections of data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential.
4. I understand that the focus groups/interviews will be recorded and that anonymous direct quotes from them may be used in the study reports.
5. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.
7. I agree to take part in the above study.

_____	_____	_____
Name of Participant	Date	Signature
<u>Ayesha Iqbal</u>	_____	_____
Name of Person taking consent	Date	Signature

02 copies: 01 for participant, 01 for the project notes

[Consent form People having chronic pain:](#)

CONSENT FORM
(Draft Version 01 / Final version 1.0: 22/10/2019)

Title of Study: Role of Community Pharmacists in Optimizing Opioid Therapy for Chronic Non-malignant Pain Patients

IRAS Project ID:

Name of Researcher: Ayesha Iqbal

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Name of Participant: _____

Please initial box

1. I confirm that I have read and understand the information sheet version number 1.0 dated 22/10/2019 for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. I understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.
3. I understand that relevant sections of my medical notes and data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential.
4. I understand that the focus groups will be recorded and that anonymous direct quotes from the focus group may be used in the study reports.
5. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.
7. I agree to take part in the above study.

_____ Name of Participant	_____ Date	_____ Signature
<u>Ayesha Iqbal</u> Name of Person taking consent	_____ Date	_____ Signature

02 copies: 01 for participant, 01 for the project notes

Consent form Pharmacist

CONSENT FORM (Draft Version 01 / Final version 1.0: 22/10/2019)

Title of Study: Role of Community Pharmacists in Optimizing Opioid Therapy for Chronic Non-malignant Pain Patients

IRAS Project ID:

Name of Researcher: Ayesha Iqbal

Name of Participant: _____

Please initial box

1. I confirm that I have read and understand the information sheet version number 1.0 dated 22/10/2019 for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. I

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understand that should I withdraw then the information collected so far cannot be erased and that this information may still be used in the project analysis.

3. I understand that relevant sections of data collected in the study may be looked at by authorised individuals from the University of Nottingham, the research group and regulatory authorities where it is relevant to my taking part in this study. I give permission for these individuals to have access to these records and to collect, store, analyse and publish information obtained from my participation in this study. I understand that my personal details will be kept confidential.
4. I understand that the case study's/focus groups/interviews' will be recorded and that anonymous direct quotes from them may be used in the study reports.
5. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.
7. I agree to take part in the above study.

_____ Name of Participant	_____ Date	_____ Signature
<u>Ayesha Iqbal</u> Name of Person taking consent	_____ Date	_____ Signature

02 copies: 01 for participant, 01 for the project notes

Appendix 8: Participant information sheet

Only one example given here for one stakeholder, however this information was modified for different stakeholders and approved by ethics committee.

Appendix 8: Participant information sheets

Participant information sheet for policymakers



Participant Information Sheet
(Draft Version 01 / Final version 1.0: 22/10/2019)

Title of Study: Role of Community Pharmacists in Optimizing Opioid Therapy for Chronic Non-malignant Pain Patients

Name of Chief Investigator: Claire Anderson, Roger Knaggs, Li Shean Toh
Local Researcher(s): Ayesha Iqbal

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Ask us if there is anything that is not clear.

What is the purpose of the study?

The purpose of this study is to explore views and perceptions of current and future service provision by community pharmacists to optimise prescription opioid usage in people suffering from chronic pain. The study is exploratory which will help understand the perceptions of policy makers for community pharmacist role in optimising opioid

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therapy in people suffering with chronic pain in order to promote optimum service provision in community pharmacies.

Why have I been invited?

You are being invited to take part because you are a member of professional organization and are currently working in a setting related to reforms and revisions in health policies regarding prescription opioids. We are inviting other participants like you to take part in our interviews till a study saturation point is achieved.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. This would not affect your legal rights.

What will happen to me if I take part?

After providing consent to participate in this research study, you will be asked to give a face to face (FTF) interview (using a semi structured interview guide) with the researcher in your office.

You will be contacted by the research team in your favourable mode of communication (post, phone or email) to communicate date, time and venue.

All of the participants will be given a reminder 24 hours prior to interview.

The interview will take about 1 hour and the entire activity will take around 1 hours and 20 minutes.

All the participants will be asked to complete basic demographics form as well.

Expenses and payments

Participants will not be paid (an inconvenience allowance) to participate in the study.

What are the possible disadvantages and risks of taking part?

Participants agreeing to take part in this study will have to dedicate some time out of their schedules, which may be inconvenient at certain times because of the nature and timings of occupation.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get from this study may help in understanding the factors in consideration/revision of current service provision by community pharmacists to help optimise opioid therapy and avoid prescription opioid misuse.

What happens when the research study stops?

After the research study stops, the data will be stored and analysed by the research team. If the participants would like to be informed of study results and want a copy, they will be contacted after the publications are available online via email with the link for publication.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. The researchers' contact details are given at the end of this information sheet. If you remain unhappy and wish to complain formally, you can do this by contacting the local authorities.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against the University of Nottingham but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in the study be kept confidential?

We will follow ethical and legal practice and all information about you will be handled in confidence.

If you join the study, we will use information collected from you during the course of the research. This information will be kept **strictly confidential**, stored in a secure and locked office, and on a password protected database at the University of Nottingham. Under UK Data Protection laws the University is the Data Controller (legally responsible for the data security) and the Chief Investigator of this study (named above) is the Data Custodian (manages access to the data). This means we are responsible for looking after your information and using it properly. Your rights to access, change or move your information are limited as we need to manage your information in specific ways to comply with certain laws and for the research to be reliable and accurate. To safeguard your rights we will use the minimum personally – identifiable information possible.

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You can find out more about how we use your information and to read our privacy notice at:

<https://www.nottingham.ac.uk/utilities/privacy.aspx>.

The data collected for the study will be looked at and stored by authorised persons from the University of Nottingham who are organising the research. They may also be looked at by authorised people from regulatory organisations to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty.

Where possible information about you which leaves the [site] will have your name and address removed and a unique code will be used so that you cannot be recognised from it, however sometimes we need to ensure that we can recognise you to link the research data with your medical records so in these instances we will need to know your name and date of birth. We will also need this information if we need to follow up your medical records as part of the research, where we may need to ask the Government services that hold medical information about you (such as NHS Digital, the Office for National Statistics, among others) to provide this information to us. By signing the consent form you agree to the above.

Your contact information will be kept by the University of Nottingham for 3 years after the end of the study so that we are able to contact you about the findings of the study and possible follow-up studies (unless you advise us that you do not wish to be contacted). This information will be kept separately from the research data collected and only those who need to will have access to it. All other data (research data) will be kept securely for 7 years. After this time your data will be disposed of securely. During this time all precautions will be taken by all those involved to maintain your confidentiality, only members of the research team given permission by the data custodian will have access to your personal data.

In accordance with the University of Nottingham's, the Government's and our funders' policies we may share our research data with researchers in other Universities and organisations, including those in other countries, for research in health and social care. Sharing research data is important to allow peer scrutiny, re-use (and therefore avoiding duplication of research) and to understand the bigger picture in particular areas of research. Data sharing in this way is usually anonymised (so that you could not be identified) but if we need to share identifiable information we will seek your consent for this and ensure it is secure. You will be made aware then if the data is to be shared with countries whose data protection laws differ to those of the UK and how we will protect your confidentiality.

Although what you say to us is confidential, should you disclose anything to us which we feel puts you or anyone else at any risk, we may feel it necessary to report this to the appropriate persons.

What will happen if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw at any time, without giving any reason, and without your legal rights being affected. If you withdraw we will no longer collect any information about you or from you but we will keep the information about you that we have already obtained as we are not allowed to tamper with study records and this information may have already been used in some analyses and may still be used in the final study analyses. To safeguard your rights, we will use the minimum personally-identifiable information possible.

Involvement of the General Practitioner/Family doctor (GP)

This is not applicable to participants in this study.

What will happen to any samples I give?

Not applicable.

Will any genetic tests be done?

Not applicable.

What will happen to the results of the research study?

The results of the data collected from the study will be disseminated in thesis for the fulfilment of PhD degree. The results will be presented in scientific communities as well as conferences and published in peer reviewed journals. The data results will be produced and published within 2-4 years and if the participants have consented (above),

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they will be emailed a copy of the publication (if open access policy allows). The results will be completely anonymized in all above cases.

Who is organising and funding the research?

This research is being organised by the University of Nottingham and is being funded by University of Nottingham and Schlumberger foundation towards fulfilment of a PhD degree.

Who has reviewed the study?

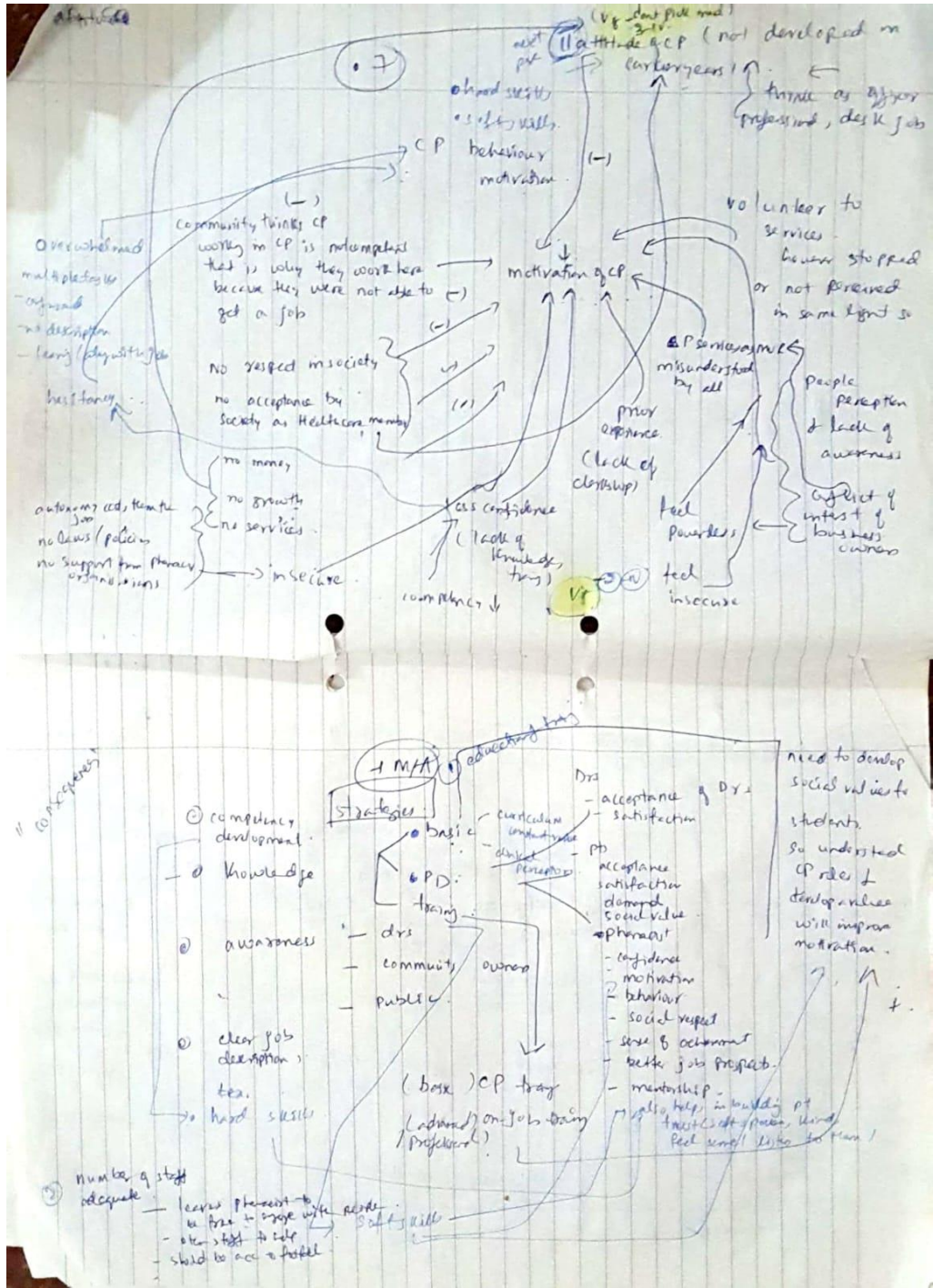
All research in healthcare is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by **School of Pharmacy**, Research Ethics Committee.

Further information and contact details

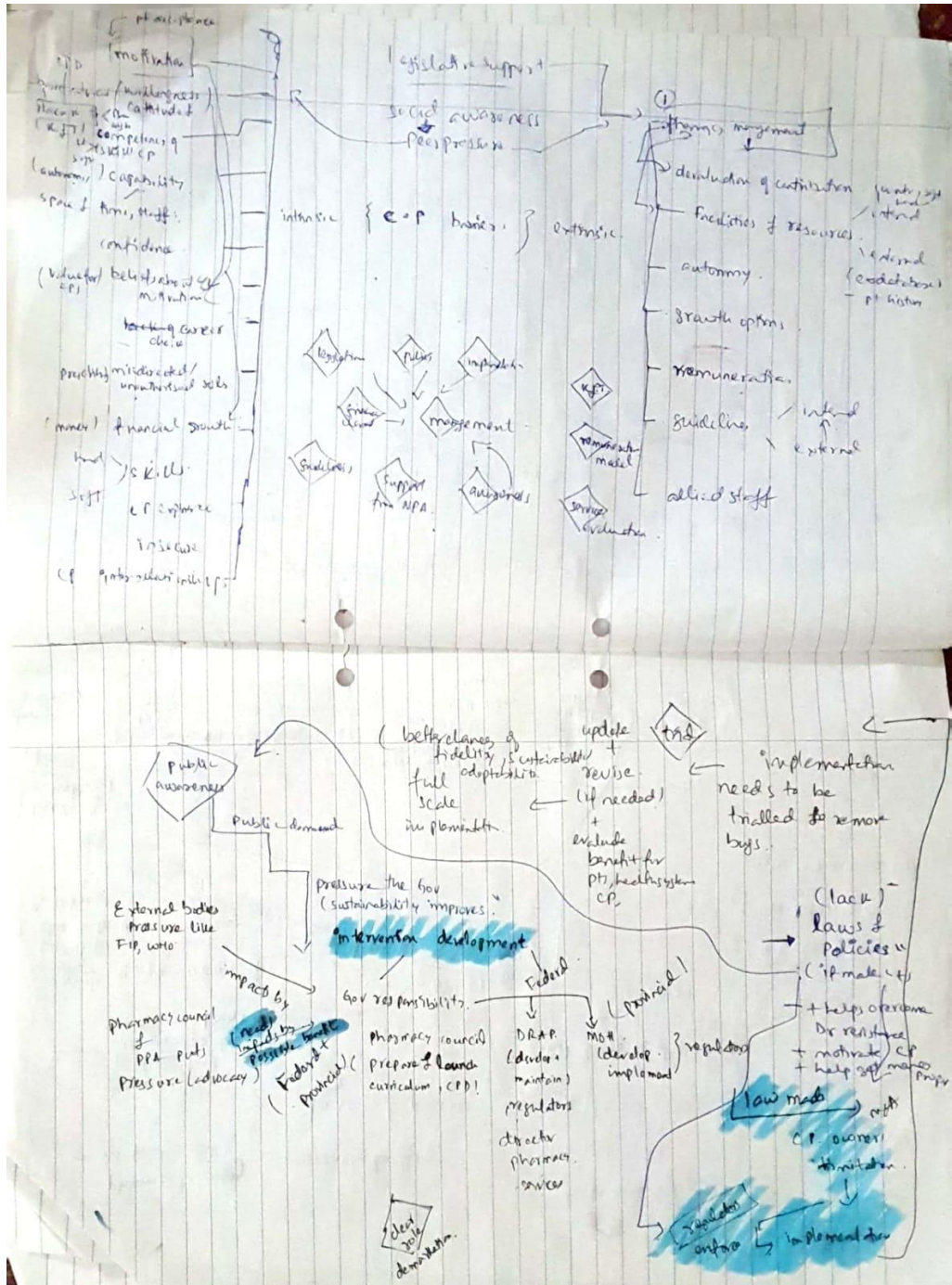
1. Ayesha Iqbal
PhD Research Student
Division of Pharmacy Practice and Policy
School of Pharmacy
University of Nottingham
Nottingham
NG7 2RD
United Kingdom
Telephone number: +44 (0) 115 951 5100
E-mail: Ayesha.Iqbal@nottingham.ac.uk
2. Claire Anderson
Professor of Social Pharmacy
Division of Pharmacy Practice and Policy
School of Pharmacy
University of Nottingham | Nottingham | NG7 2RD
Chair of Royal Pharmaceutical Society English Pharmacy Board
E-mail: Claire.Anderson@nottingham.ac.uk
T: 01159515389
3. Roger Knaggs
Associate Professor in Clinical Pharmacy Practice
School of Pharmacy | University of Nottingham | Nottingham | NG7 2RD | United Kingdom
Tel: +44 (0)115 846 6382 (Internal 66382) | Fax: +44 (0)115 846 6249
E-mail : roger.knaggs@nottingham.ac.uk
4. Li Shean Toh
Assistant Professor
School of Pharmacy/ Pharmacy Practice and Policy
Telephone: 0115 9515168
Email : lishean.toh@nottingham.ac.uk

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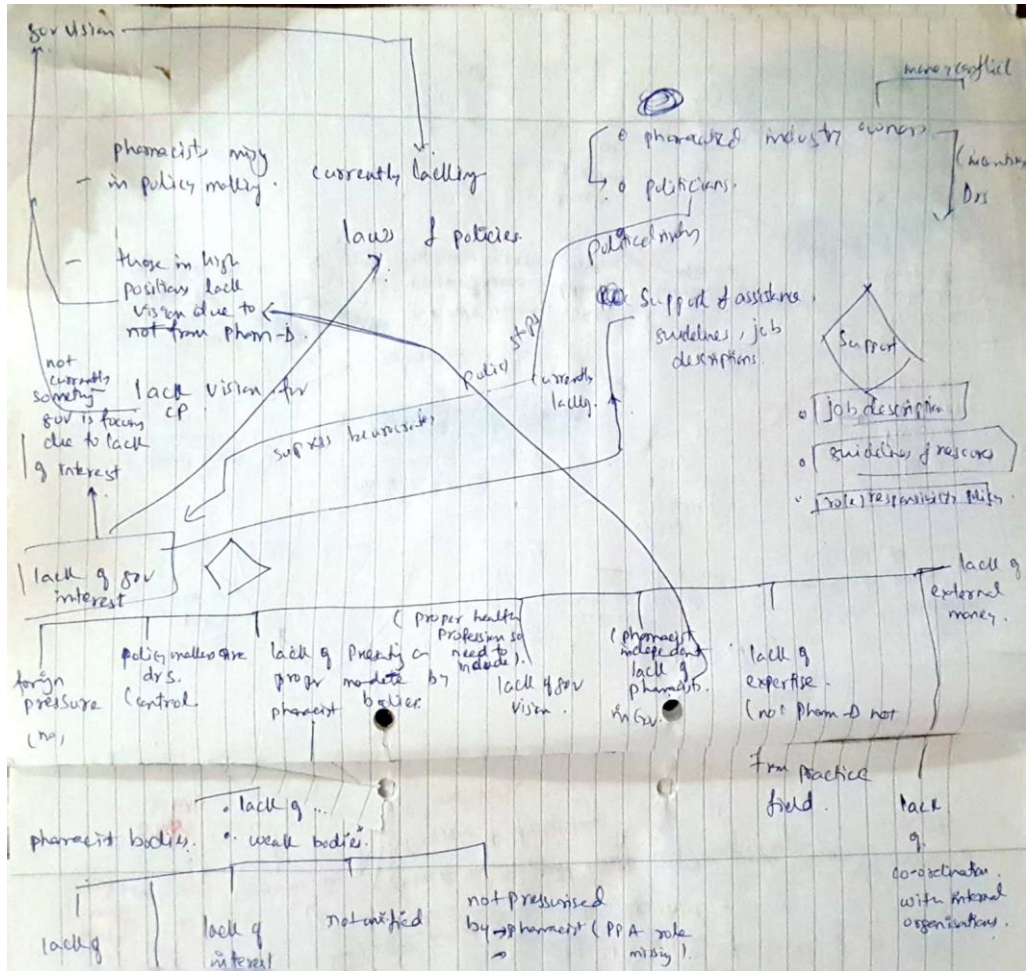
Appendix 9: OSOP initial paper themes and subthemes examples



Appendix



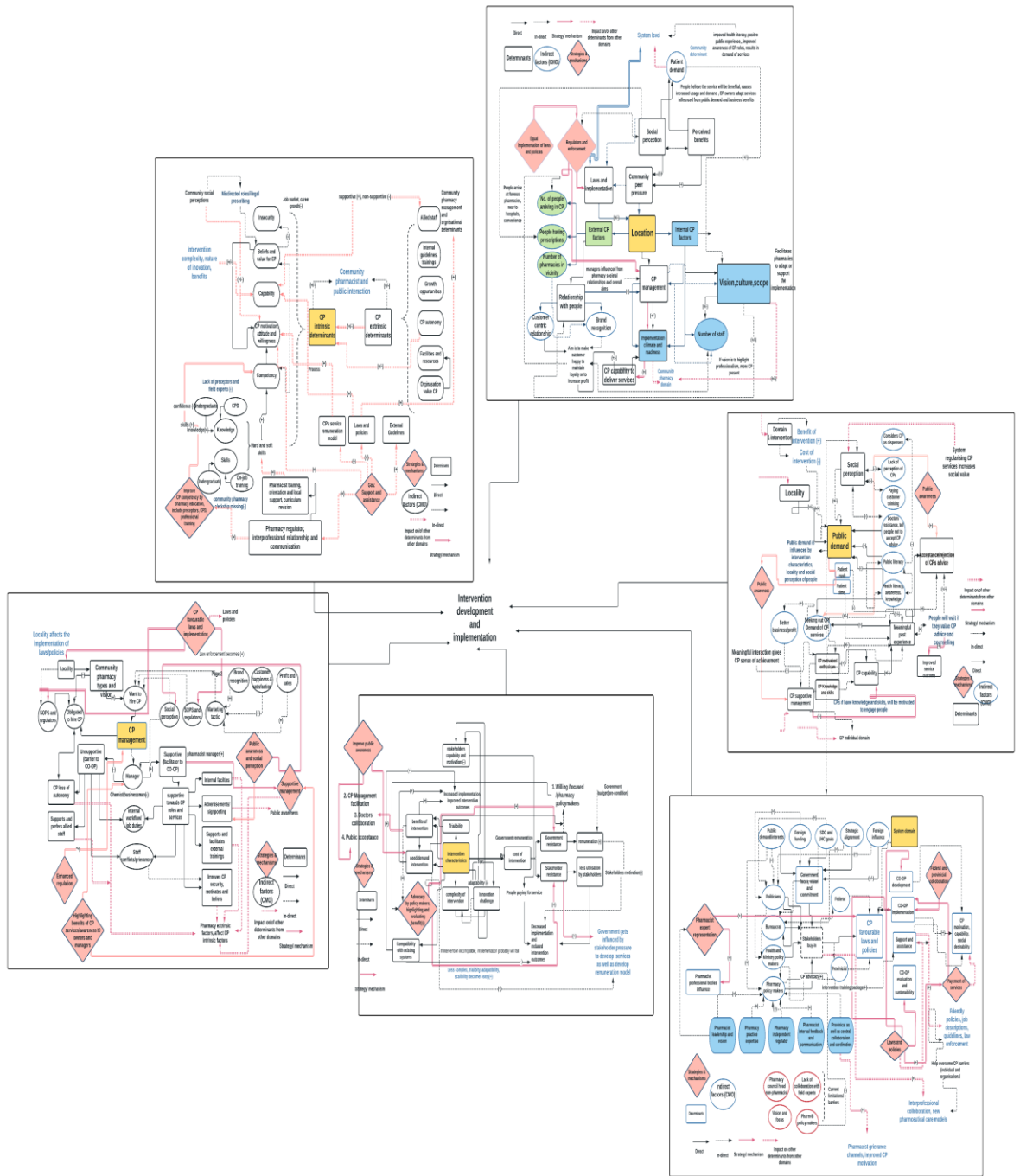
Appendixes



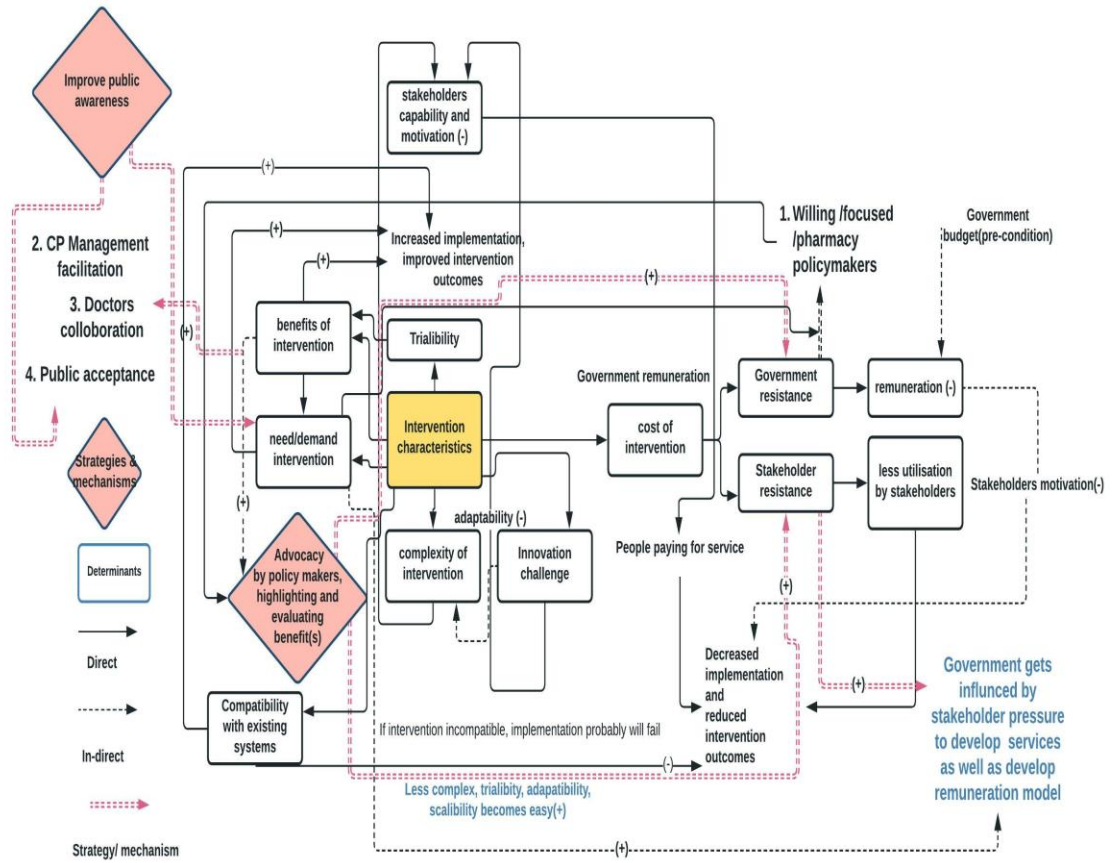
OSOP sheets mind maps drawn digitally

Full triangulation images provided just for reference

Appendix

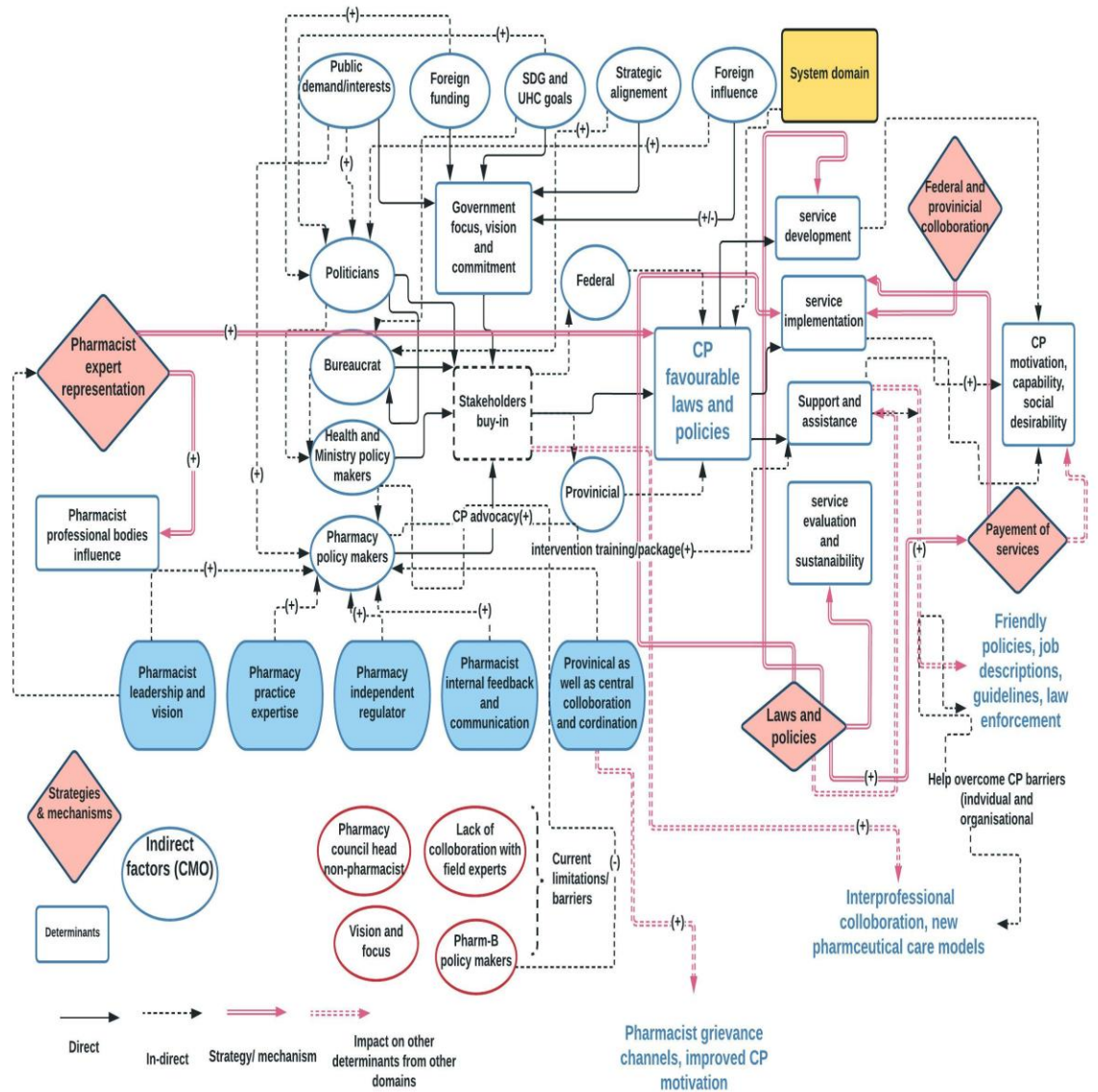


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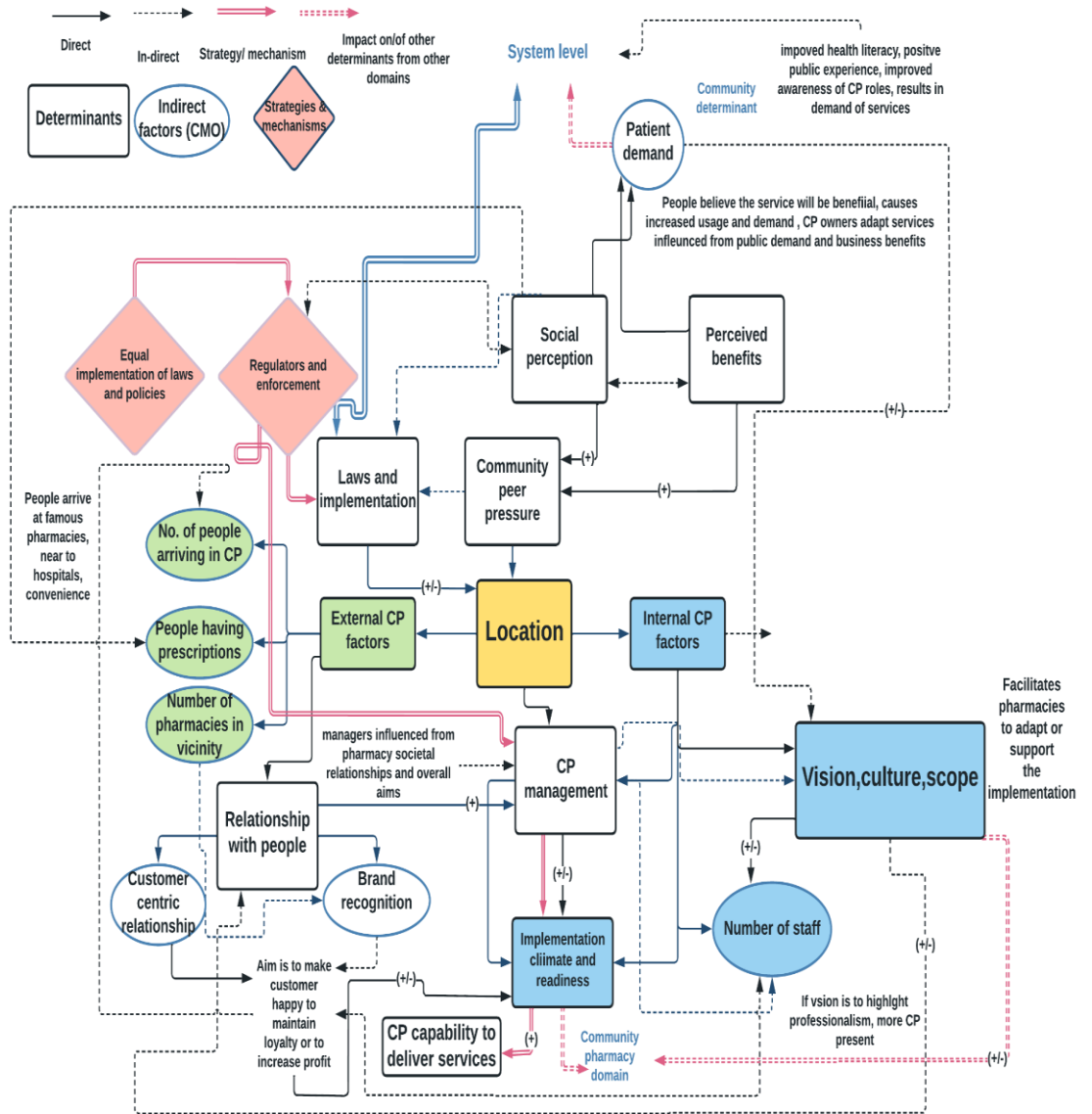
OSOP: Overview of interplay of determinants and identified strategies to overcome them in the intervention domain

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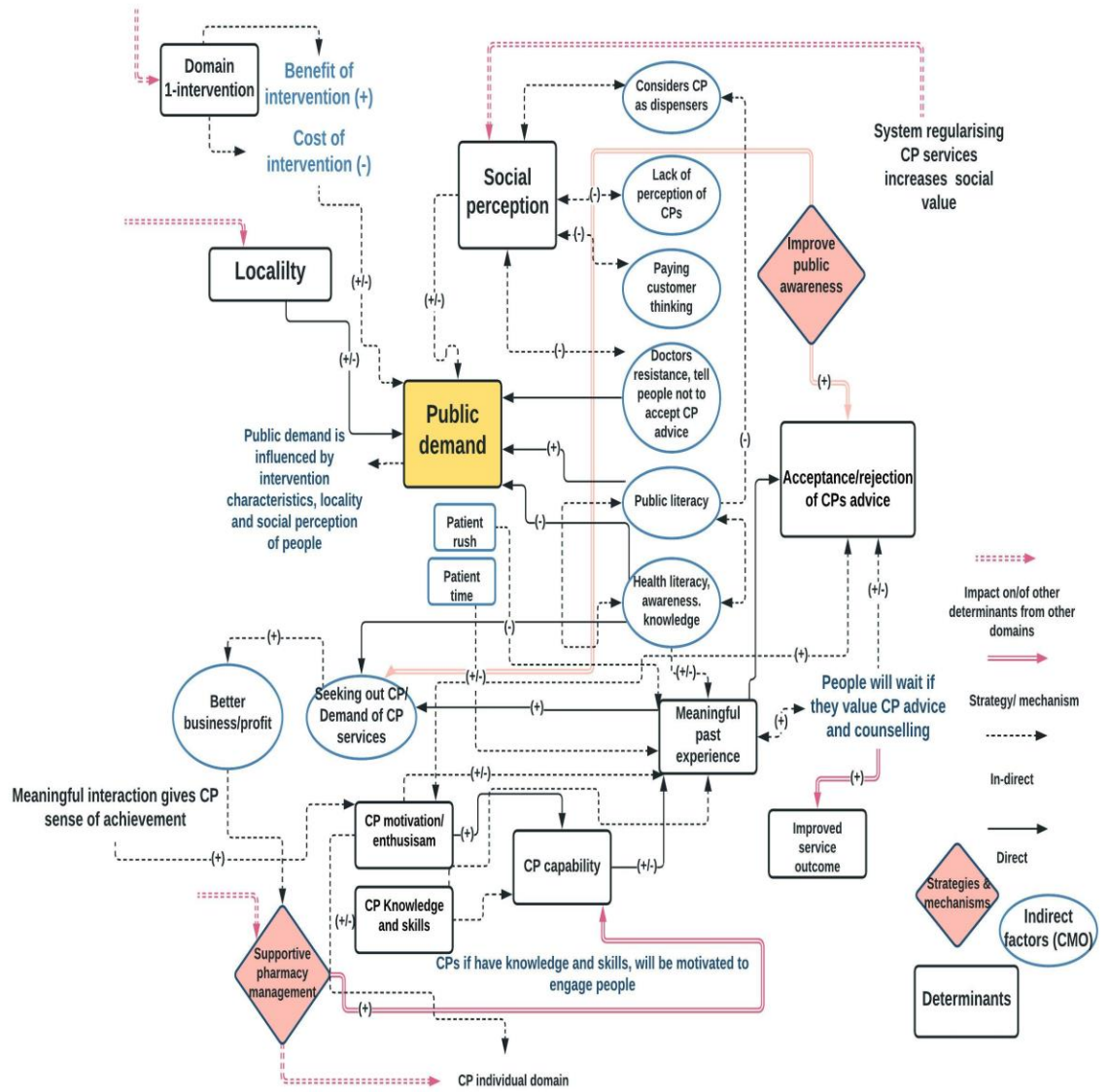
OSOP: Overview of interplay of determinants and identified strategies to overcome them in the system domain

Appendixes



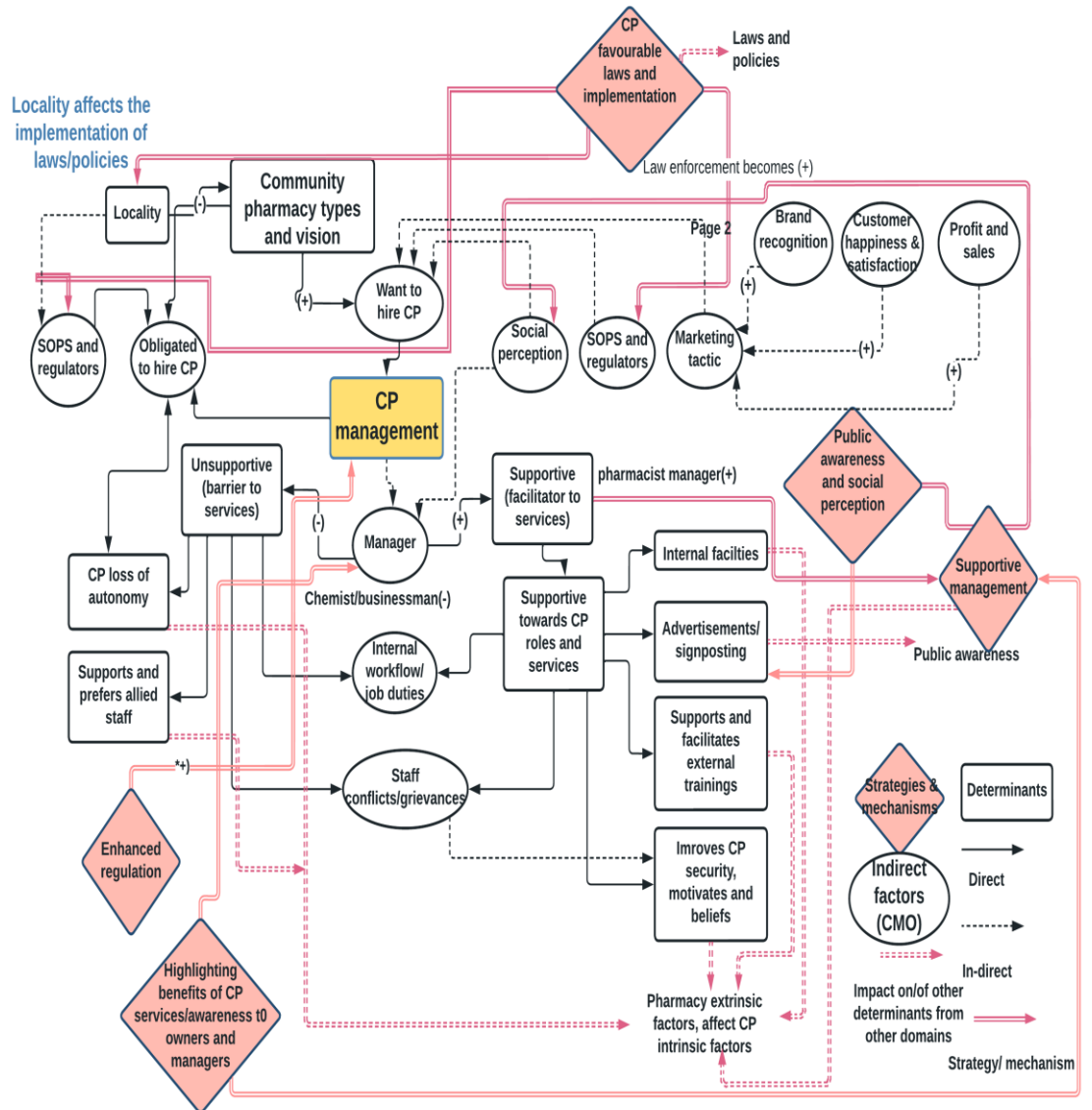
OSOP: Overview of interplay of the construct location and its impact on pharmacy management and identified strategies to overcome them in the community domain

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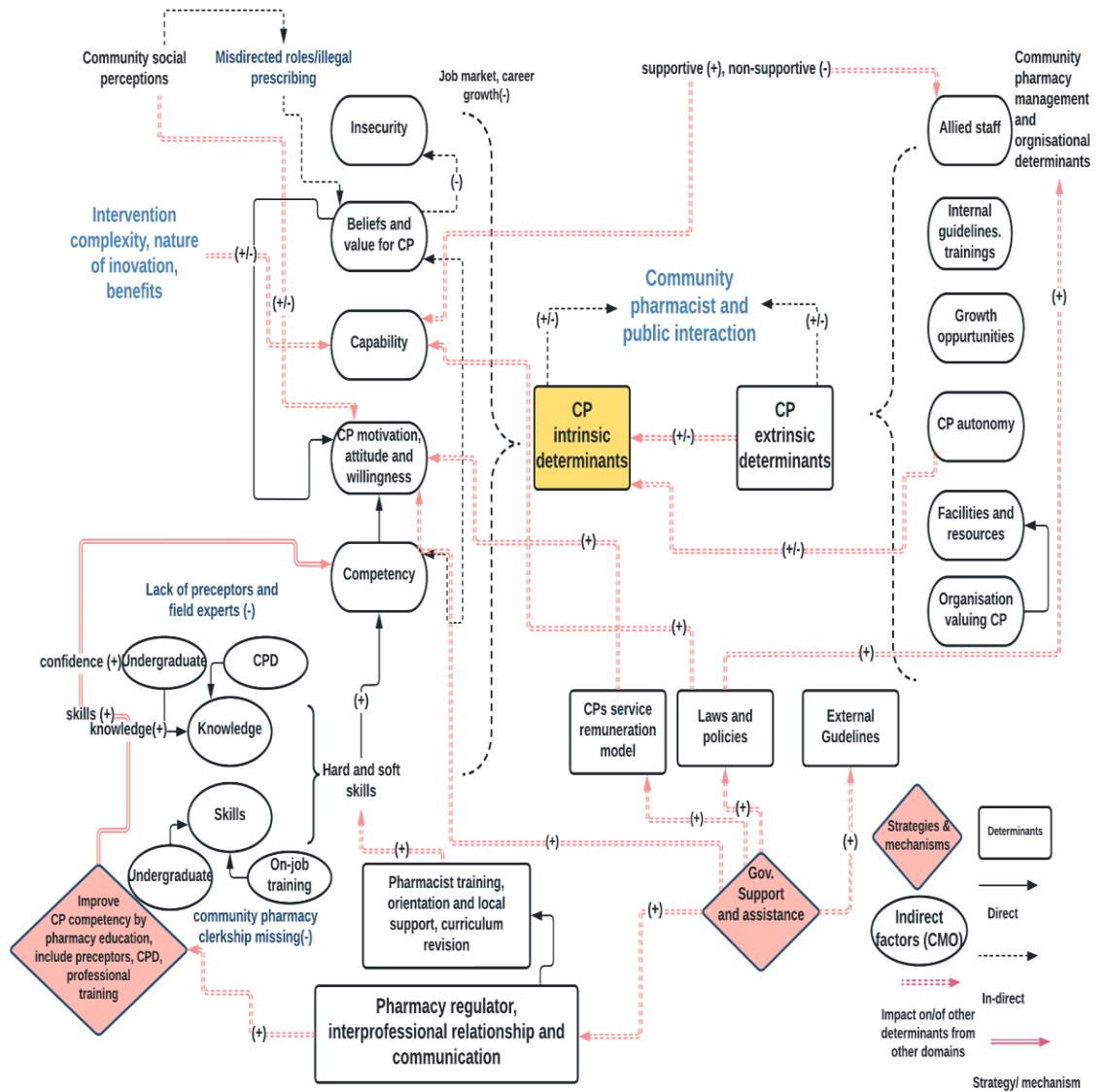
OSOP: Overview of interplay of the construct location and its impact on social perception and public demand and identified strategies to overcome them in the community domain

Appendix



OSOP: Overview of interplay of the construct pharmacy management and its impact on CP capability and identified strategies to overcome them in the community domain

Appendix 10



OSOP: Overview of interplay of the construct CP individual factors and its impact on CP capability and identified strategies to overcome them in the individual domain

Appendix 10: Full recruitment of each stakeholder

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Appendix 10

Different stakeholders were recruited as follows:

Policy makers

Policy makers were identified using professional websites and by using gatekeepers. Where the email address or contact numbers of policy makers could not be obtained from publicly available information (online), the information was obtained using gatekeepers or policy makers' snowballing. This led to preliminary informal meetings or a phone call with policy makers. Potential policy makers were given a brief overview about the study and were provided an invitation letter, participant information sheet and consent form via email or face-to-face, respectively. On agreeing to participate in this study a suitable time for interviews was set up which was followed by two reminders: one week and 24 hours before the interview. Policy makers were interviewed in their respective offices. The consent form was signed in-person for face-to-face interviews and pre-received via email for virtual or remote interviews.

People with CNMP

People with CNMP were anticipated to be found in clinics, hospitals, medicine shops and pharmacies as shown in Figure 2.7. Participants were recruited from both; private clinics (target population was rich and middle class) and day clinics or outpatient departments (OPDs) (target population was poor and middle class) in government hospitals in orthopaedic, neuropathic and neurology disciplines, based on CNMP conditions commonly prevalent in Pakistan. To include a diverse variety of diseases and economic statuses, people were also approached in community pharmacies directly by me or/and by the pharmacy staff who helped hand over flyers to potential participants filling opioid prescriptions. Snowballing was also applied to improve the reach to help recruit people from diverse backgrounds.

People were given choice to either attend interviews or focus groups, face-to-face or virtually. The people who volunteered to participate in this study were asked to share their details such as mobile/telephone number or email address and their choice of preferred method of communication at initial point of volunteering to participate in this study using the study form ([Appendix 5](#)). However, as stated previously people were found unwilling to make specific travels to attend focus groups and most participants insisted on conducting interviews using both face-to-face and virtual platforms. The consent form was signed in-person for face-to-face interviews and pre-received via email for online or remote interviews.

Doctors

I directly approached many doctors in their private clinics as well as in their offices and clinics in government hospitals (target population was experts and seniors in the field). I also visited doctor offices in wards in these hospitals to potentially invite junior doctors or trainees with less years of clinical experience. Participants also helped snowball to other doctors, which helped in getting a disparate mix of participants varying across diverse demographics. These doctors were handed flyers (where possible) as well as briefly given

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verbal information about the study by me. In case of interest potential participants were handed participant information sheet either in person or virtually to facilitate future contact. Doctors were also given choice to either attend interviews or focus groups, face-to-face or virtually using telephone, mobile phones or internet calls. A majority of doctors remained inclined to a face-to-face focus group (pre-COVID-19) in places conveniently located near them or virtual focus groups over individual interviews. The consent form was signed in-person by all participants before focus groups started and pre-received via email for virtual focus groups.

Pharmacists

As previously stated, I am a pharmacist by background and being from Pakistan I know many pharmacists closely. Many past connections were utilised as gatekeepers who helped identify and invite participants. I did not invite any pharmacists personally known to me to avoid the conflict of interest to participate in this study as a personal favour to me. I also visited random pharmacies in different cities and directly invited CPs to participate in this study **as shown in Figure 2.7**. Pharmacists working in pharmacies, inside hospitals (both public and private sector) as well as managing pharmacies inside doctor clinics, were also invited to participate in this study to include a diversity of opinions. These pharmacists also helped connect with other pharmacists (snowball sampling).

Pharmacists were also given the choice to either attend interviews or focus groups: face-to-face or virtually using telephone, mobile phones or internet calls. They did not show preference for one over the other. After discussion with supervisors, only focus groups were conducted to ensure a diverse range of opinions and facilitate group discussions as per research aims. Focus groups also facilitated data collection from a relatively large sample size when compared to interviews. The consent form was signed in-person before the start of focus groups by all participants. For remote focus group discussions, the consent form was pre-received via email (post COVID-19).

Appendix 11: COREQ checklist

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COREQ (Consolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
<i>Personal characteristics</i>			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	86-90
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	66
Occupation	3	What was their occupation at the time of the study?	66
Gender	4	Was the researcher male or female?	female
Experience and training	5	What experience or training did the researcher have?	117
<i>Relationship with participants</i>			
Relationship established	6	Was a relationship established prior to study commencement?	79, 147
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	81
Interviewer characteristics	8	What characteristics were reported about the interviewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	147
Domain 2: Study design			
<i>Theoretical framework</i>			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	63
<i>Participant selection</i>			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	78
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	78
Sample size	12	How many participants were in the study?	83
Non-participation	13	How many people refused to participate or dropped out? Reasons?	83
<i>Setting</i>			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	86
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	87
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	83
<i>Data collection</i>			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	76
Repeat interviews	18	Were repeat interviews carried out? If yes, how many?	no
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	87
Field notes	20	Were field notes made during and/or after the interview or focus group?	87
Duration	21	What was the duration of the interviews or focus group?	92
Data saturation	22	Was data saturation discussed?	83
Transcripts returned	23	Were transcripts returned to participants for comment and/or	no

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Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
<i>Data analysis</i>			
Number of data coders	24	How many data coders coded the data?	94
Description of the coding tree	25	Did authors provide a description of the coding tree?	no
Derivation of themes	26	Were themes identified in advance or derived from the data?	96
Software	27	What software, if applicable, was used to manage the data?	114
Participant checking	28	Did participants provide feedback on the findings?	no
<i>Reporting</i>			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	yes
Data and findings consistent	30	Was there consistency between the data presented and the findings?	yes
Clarity of major themes	31	Were major themes clearly presented in the findings?	yes
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	yes

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

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Appendix 12: Training undertaken during PhD

1. Introduction to Qualitative Interviewing, 18 November 2019. Nuffield Department of Primary Care Health Sciences, University of Oxford, UK.
2. Introduction to Analyzing Qualitative Interviews, 19-20 November 2019. Nuffield Department of Primary Care Health Sciences, University of Oxford, UK.
3. Introduction to NVivo 12, 21 November 2019. Nuffield Department of Primary Care Health Sciences, University of Oxford, UK.
4. Philosophy of Research- Social Science, October 2018 - January 2019. University of Nottingham.
5. Research Design- Practice and Ethics, October 2018 - January 2019. University of Nottingham.
6. Foundations in Qualitative Methods, February - June 2019. University of Nottingham.
7. Mixed Methods in Health Research, July 2019. University of Nottingham.
8. Individual and Group Interviews, July 2019. University of Nottingham.
9. Advanced Presentation Skills for Researchers (moderated online learning course).
10. Quantitative Evidence Synthesis (online).
11. Introduction to Qualitative Research Pilot (Online).
12. Research Interview Skills.
13. Getting Started with Mixed Methods Research.
14. ISPOR webinar: Qualitative Research in DCE.
15. Implementation Science Masterclass, a 3-day professional course and workshop conducted in July 2021 by King's College London (Virtually attended).
16. Qualitative Methods in Practice Seminar Series - Conducting Ethnographic Research.
17. Qualitative Methods in Practice Seminar Series - Using Datasets from Popular Culture.
18. Realist research sessions (Nottingham Realism group)

Other courses, which helped over the course of this research, are listed below:

1. Microsoft Word: Working Smarter
2. Microsoft PowerPoint: Research Poster Creation
3. Microsoft Word: Managing Long Documents
4. Structuring Your Thesis (Moderated online course)
5. Preparing for the viva (webinar)
6. Introduction to Endnote for Researchers
7. Nature of the doctorate and the supervision process
8. Lone Working

Appendix 13: Ethical approval letters



HAMDARD UNIVERSITY

Islamabad Campus

www.hamdard-isb.edu.pk

04-Park Link Road, Chak Shahzad, Islamabad. Phone: 051-8840000

No. HU-ERC-19-400

December 05th, 2019

Ms. Ayesha Iqbal
PhD Student
Pharmacy Practice and Policy Division
School of Pharmacy at University of Nottingham

SUBJECT: ROLE OF COMMUNITY PHARMACISTS IN OPTIMIZING OPIOIDS THERAPY FOR CHRONIC NON-MALIGNANT PAIN PATIENTS

Dear Ms. Ayesha Iqbal;

I am pleased to inform you that the above mentioned project has been approved by the "Research Ethics Committee" of Hamdard University for a period of one year.

2. For the continuation of project, if required in the next year, you have to send a progress report and a formal request asking for continuation of project. However, you do not need to submit REC application or pay any processing fee again.

3. Kindly keep the "Research Ethics committee" Secretariat posted about the progress of the project and submit the formal final report on completion.

Yours Sincerely

(Prof. Dr. Azhar Hussain)
Chairman

Research Ethics Committee

Appendix

Ethics form application



Clive Roberts

To AYESHA IQBAL



12/12/2019

You replied to this message on 16/12/2019 09:08.

Dear Ayesha Iqbal

Your application to the Ethics Committee is approved subject to dealing with some minor points:

- it is not clear why medical records would need to be kept from healthcare professionals (this is mentioned in the participation sheet)
- will the researcher ensure that both patient and the healthcare professional that are observed have agreed to be observed and take part in the study?
- are there any local regulations / is there any local approval that would need to be sought before undertaking the study in Pakistan?

The approval reference is 018-2019. For my records could you please let me have a copy of the final version after you have had a look at the comments above.

Best regards,

Clive

Appendix 14: Policy maker interview

A short excerpt of transcribed and translated interview of a policy maker

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Interview 6 PM:

I: Question I would like to ask is what in your opinion is the role of community pharmacist in chronic pain management with respect to opioids?

A: umm... Currently there is no role.... it does not exist right now..... but there definitely should be....

I: can you please tell me if the role of the pharmacist develops.. What should be the attributes of care in that service provision by community pharmacist to help optimise opioids therapy in chronic pain to stop reduce misuse as well as maximize the benefit?

A: ummm..... I think to make the pharmacist capable of performing this role first of all training is needed.... proper training.... the training can be achieved during there education... As well as after the education... it is a specialized role... it's not a generic role... every pharmacist cannot do this... not pharmacy can do this.... because even the sale of opioids in Pakistan is not from the community pharmacies... it is only being sold... in the hospital through a quota system... Their records are maintained.... look to develop these pain management services... in a community pharmacy setting.... I cannot see them developing in the near future... but again.... as the health care system in Pakistan is improving.... along with the role of pharmacist is also going to evolve.... any pharmacist performing any role is according to the capacity of the health care system... if the health care system empowers a pharmacist... as an individual as well as a professional.... only then ..the role of a pharmacist can evolve... 2 types of roles can be developed... the first time is need based..... if there is a need a pharmacist goes in and fulfills that need... and the 2nd.....ummm.... by pushing the pharmacist that they have to perform this role... as far as I know.... are you talking about opioids right... and their sale and trying to stop the misuse..... I don't see any role in the community pharmacies... but if you develop it.... at a pharmacy... hospital pharmacy level....where the opioid analgesics are dispensed... there is record keeping... if you want that pharmacist performe this role.... and you have to train them.... give them education.... and you have to train them which is called the in-service training...

I: What about the opioids that are available in the community pharmacies such as tramadol...Codeine etc.... In addition, these medicines are being sold at the

community pharmacies so in your opinion... so if to help with these sorts of prescriptions which are coming in the community pharmacy... what do you think a pharmacist can perform the role?

A:... See there.. a common person who does not know what kind of effects these medicines can cause.... The doctors say that they don't have time to educate the patient about the harmful effects...so in those cases definitely the role can be developed and is also needed...

..... all the ingredients that are required for any medicine dispensing service... all of them... will be included.... In addition..... specific instructions and education which are attached with these narcotic medicines.... so this will be the 2 focus areas in that role... one is the general.... like any medicines that is being dispensed by a community pharmacist all of that information should be part of that review.... Additionally.... the issues related with these medicines..... the problems associated when a patient uses these medicines.... or the overuse issues... or the underused issues.... so...the pharmacist should tell at this sort of information to the patient...

I: Speaking about giving in-service training to pharmacists... Do you think the current curriculum being taught in Pakistan... is it sufficient to produce capable competent pharmacists which can fulfill these patient safety roles?

A: ... see... This is a very interesting discussion.... As far as curriculum is concerned... and how far our education system is preparing the pharmacists.... How trained, is the pharmacist... when he or she comes out of the academic institution.... now see....

When our pharmacist goes out of the country... Within 6 months to one year... he or she performs at par... Equally... with pharmacists from all over the world.... Am I correct? But in Pakistan this does not happen... because... when he graduates and comes into the health care system... the mechanism is not available... where the pharmacist can be further taken upon and can be groomed... Pharm-D program in Pakistan is a 5 year degree... it requires years of study... 198 credit hours.... multiple dimensions..... So many more different dimensions have been added... let me give you my example when I did my Masters in clinical pharmacy.... I asked my teacher.... after graduation when I was sitting with him... I don't feel... that I am capable to go out and handle the patients on my own.... so he told me.... my dear we have provided you with the

methodology..... Now it's your own responsibility.... wherever you want to develop your skills.....

Is it in paediatrics... is it in oncology... is it in cardiology...

Wherever you want to develop yourself..... you have to spend 3 to 5 years.... then you will be able to specialize and you will be confident that you can handle a patient in that specific area.... now I am a specialized pharmacist for example in cardiology..... if I'm an infectious disease I will have enough knowledge for that.... if I am from drug information... similarly....

See the current curriculum which is being taught in the Pharm- D program in the Bachelor of pharmacy is already very overloaded.. There is a debate going on that the number of years should be increased from 5 to 6.... I don't think so.... there was a debate going on and credit hours should be further increased....

I don't think so.... in my perception... the credit hours need to be reduced.... and pharm -D is a generic degree... people need to understand this.... it is not a Masters degree.... it is not equivalent to the pharm-D in American system.... it's just not like that.... so you cannot expect a student.... do you have all those things that are unrealistic.... he has the basic methodology... his basic concepts are correct... he has learned the basic things..... he has the capacity to apply those concepts... It takes a couple of years in my opinion for someone to be able to handle things in a particular specialty....

This is a generic degree.. we need to understand this.... in my opinion it is a very good curriculum.... the issue with this is.... from one University to another the difference is between the training of the teachers.... the way... there is issue with the teaching methodology... I think these are the issues with the curriculum...

I: In your opinion as you said that it is a basic degree...what should be the future?

A:... having some residency programs after the 5 year degree would be helpful ..it will be..... but there is still need to create a mechanism for this....

I: in your opinion who is going to take that initiative to create this mechanism?

A:... In my opinion I think those people.... who are sitting in those positions they can create an opportunity... and they do not understand the role of a

pharmacist.... they do not have the capacity.... they're not trained themselves..... So this whole lot... first of all this whole lot needs to be taught and trained.... What is this all about..... Number 2.... In the second step.... You have to embed pharmacist in the system... train pharmacists... pharmacists those have been trained for these sort of activities..... the problem over here is... even in the hospitals...the pharmacy services are not developed... so when we sent our graduated pharmacist out there in the system... for example in the hospital they don't know where to go... what do... where to go... and the seniors over there who are already working as pharmacists, they do not have that orientation....

The current students who are studying the curriculum in a specific way.... so when they go ask them ..aha...immediately.. So you want to become a doctor.... but this is not your work.... your job is just this... and they tell them that role that scope which is being followed from the last 40 years , this is a huge barrier..... However, the orientation of such people is very important... Who are sitting in those positions where they can actually bring about a change... they have authority to do this....

I: What in your opinion is the status of advocacy for the role and rights of the pharmacist to promote patient safety in the health care system of Pakistan?

A: I think the first thing is to build the capacity of the pharmacists.... so that they are able to get that authority position.... where they can speak for themselves.... that's the first thing.... nobody gives you the position... served in a plate... that here please have this..... If you are unable to perform that function.. for that job then nobody gives you a position of authority.... so the first thing pharmacist need is to build up their level and skills to come to these sorts of position...

Having said that.... conventionally, up till now, those positions... have been under medical doctors in Pakistan... that is why we need even more effort.... to be capable enough to have that position from them.... even the purchase of medicines in hospitals is still being supervised by the doctors in a hospital....

So if you want to take the purchasing from the doctor and give it to the pharmacist.... as a rational step towards promoting their role in patient safety and medicine rationalization... I am just talking about this... As a very basic step.... this is not even concerned with pharmacist clinical services ..services.... even the purchase of medicines.... even this role is not.... even they're not willing to give this role to the pharmacists....this is the barrier..

In a hospital until the Medical Superintendent (MS) is a pharmacist...no changes can be implemented.. In this healthcare system, the dominance is doctors... They have taken over everything... In addition, they do not allow others to come forward, why because of lack of skills in pharmacists... Lack of advocacy... Lack of voice... Lack of platform..

The purchase is going on without a pharmacist.... and nobody is stopping it.... and this practice.... this is uncommon in the foreign countries..... Let us leave this.. let's talk about.... Deputy (DP) MS... We are not even talking about MS... a deputy MS role only... these are specialized areas.... at least have a pharmacist over there..... Until now, there is ... no role..., which was established... No services can be developed... neither any function....

But, still I would say we are slowly moving towards evolving the role of pharmacists.... the current scenario which we are facing right now.... the current role.... it was not 5 years ago.... it was not 10 years ago... but it is right now.... I think in this profession currently there is a lot of scope for opportunities... and.... things are evolving very quickly towards.... betterment of the profession.... and with the betterment of the profession..... This directly translate towards patient care.... in all domains... I will come to their role in CNMP management. .. After sometime.. That why it is so important.. to develop..

If there is a good pharmacist... a capable pharmacist.... he/she can perform at all levels... for example if he is standing in a community pharmacy and is performing his role while dispensing an opioid prescription.... all the checks... relevant to medicine dispensing as well as opioid dispensing... these should be there.. at least..

Currently, even with the basic medicines... people are not following any kind of steps or their a currently any role of a pharmacist in community pharmacies..... and the problem is that the pharmacists have given this role.... this opportunity in hands of.... what can I call them... illiterate people... business people... pharmacist are very happy with this.... they don't even bother.... that we want this role back... see if they were feeling some sort of discomfort... offense.... And I want my role back... But they are very happy with it... until they care deeply about their own position- their own role—their own position in society... this is my whole impression about this whole thing.... most of them ..they are not motivated at all.. its like.. they have given up.. even before trying to acquire their role in healthcare system..

I: In your opinion how should the visibility of the pharmacists be increased.... how to promotethe role how to project the role....?

A: ...see.... We're talking about medical care.... patient care..... Where is the doctor...? For example.. if you go to a hospital where can you find a doctor? Either he will be in a clinic or in a ward... they will be taking rounds (medical rounds)... or be in OT (operation theatres)... he is right beside his patient... if we talk about nursing care.... where is the nurse present?... they are right beside the patient..... Now we come to pharmaceutical care... where is the pharmacist...? Until and unless a pharmacist is present besides the patient... how can they have visibility....??

Nobody is talking about creating any role for the pharmacist when they're not there...until they are present in the community pharmacies.. until that time they do not even have the opportunity to interact with the patient..

Because people know you.. by the value you add... a common person do not understand, that when I get sick And I take Medicine... what can a pharmacist do for me....

A common person do not know what a pharmacist is.... they do not know what a pharmacist can provide to them ...when they are sick and taking their medicine... so until and unless if the pharmacist can provide a value addition.... And the only thing required in this is talk to the patient.... Meet your patient... if.....

I had two of my colleagues working in the Gulf area... and they told me that a very illiterate person from the desert came to them... and said... that pharmacy.. ABC (name of the pharmacy)... you know there is a doctor standing right over there.... the other doctor... one who is in the clinic and hospital is just... A writer/author ... he just writes the medicine... Until and unless this person in the pharmacy gives me the medicine... he is the only one who provides with the medicine... the other one is just a writer he only writes it... so this is the real doctor...

Chuckles

That was the impression of a pharmacist... In those countries, it is mandatory to have a pharmacist dispensing these medicines... We do not even have that... What to talk about patient safety... and specific roles... yes, I do not mean that... the role should not be developed... What I am saying is... That we have to

transition to pharmacists available in the community pharmacies through urban and rural areas.. We need to equip them in Universities... We need to create opportunities that can specialize them...like e.g. in CNMP management.. Opioid safety.. All other countries have these roles.. We need to create awareness of pharmacists... the health care system in any country is not complete without pharmacists... we are yet realizing the potential... The culture has begun but there are many barriers...so many.. However, exploring this role... Is essential...

... so those countries where the pharmacist adds a value to the system.... and without a pharmacist there is no medicine dispensing.... there is no medicine procurement.... so in our country the pharmacist... you are talking about community pharmacists in Pakistan? the owners of community pharmacies in Pakistan say that we have these barriers.... that we have to hire a pharmacist as well as a pharmacy technician.... a purchaser as well.... record keeper... and to serve the pharmacist for his tea and lunch.... to serve him... we have to hire a runner (clerk) as well....

Therefore, it does not happen... it cannot happen like this... All the community pharmacy owners... my friends my colleagues... my students... all of them say this one thing... we are ready to pay them.... Are they ready to take the responsibility of the community pharmacy? Are they ready to provide us services... are they ready to own the pharmacy...?

They are not ready to take the responsibility of the pharmacy.... when the pharmacist would not want to take the responsibility of the pharmacy.... so who will hire a pharmacist?

I: Can you elaborate a bit more.. Why do you think they are not prepared to take this responsibility?

A: ... our pharmacist think.. this is a white collar job.... this is not a white collar job.... It is a blue-collar job... OK... Even our pharmacist are.. suffering in the industry... the technician machine..... he completes the batch with one push of a button... and the pharmacist keep thinking all day... why the compression of the machine is not working properly...

So, the pharmacist needs to understand... that he is not an officer.... before becoming an officer... he has to go through all the steps in all that process.... in

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which he understands each and everything, about everything.. Should have a clear understanding of all the mechanisms involved...

So in my opinion... During the professional education... while the pharmacist is studying... Proper understanding... and proper motivation... should be provided during that initial education... it is a problem of attitude.... I think this is a problem of attitude... nothing else.... the pharmacist needs to understand that this is not a white collar job it's a blue collar job... he has to start and he has to do it with his own hands.... from taking the prescription from the patient... dispensing.... restocking.... reviewing... take an engineer's example.... until and unless the pharmacist could fulfill his role, his responsibility.... he cannot make others do it..... to make someone follow... you have to set an example first.. that's one thing...

Example of a case study raw data typing using shorthand

Community pharmacy- Private Chain pharmacy-
Observation week: December 2019- 15-20 December.
Timings: 9- 5 pm 4 days, 5-10 pm 1 day
Location: Federal capital, residential sector- footfall more than- 1000 -1500 persons per day (24 hour pharmacy): Other branches receive- more than 2000 per day in commercial areas
Pharmacist: Lady Pharmacist, 4 associate staff, 1 cleaner

Persons coming to pharmacy:

- Educated
- Rich- Posh
- Male and females
- Mostly old age people in day times
- Middle age people- buying opioid analgesics for themselves or family
- Middle age and people in early old age engage with conversation with pharmacist
- Women talking more, as female pharmacist
- No one approached for medication information about opioids
- Complain have to give prescription- although they are using for years
- Only 5 home delivery calls in the entire week
- Most rush hours between 11am to 2pm then 3pm to 8 pm
- People buy medicines as well as groceries
- Directly approach the counter
- Wait time is less than 1 minute
- Most people do not ask any information-
- Most asked information is expiry and price
- Ask discounts on price
- Normally patients come without prescription- repeat prescription
- Normally ask for medicines by asking name
- Prescription very few people

❖ Pharmacy related:

- **Was the person received by a pharmacy assistant- pharmacist- called a pharmacist—all dealing with pharmacy staff:**
 - Prescription filling is the duty of pharmacy staff- only 1 pharmacy technician
 - Patients if have a new symptom or persistent pain in a new area or is not getting better by usual tramadol tablets or capsules, and have increased dose and frequency themselves then approach pharmacist for something stronger
 - Minor ailments deal by pharmacist.
 - Pharmacist times- 9 to 4 pm Monday to Saturday
 - The pharmacy technician was available at 3 to 10 pm.
- **Infrastructure:**
 - Pharmacy has a fridge- has ac, is located in a sun faced location, single storey, and will get very warm in summers, but that is why have ac.
 - Pharmacy cleaned once every day- in morning- by a sweeper.
 - Pharmacy staff also responsible for stocking up groceries- but has two dedicated people for that role as well.
 - Medicine paid mostly by cash- but has option of card- Discount not given on card so people prefer using cash.
 - Two cash registers-
 - Software used- Abuzar software-

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- Inside pharmacy- the medicine counter is located right in front of the shop (the first thing you will see when you enter the shop), on the right side, shelves are stocked with groceries (non-perishable items, no fruit and vegetables)
- Medicine are placed in glass shelves and are installed in the background wall for keeping medicines, medicine storage is below the shop in basement, only keep most running items , otherwise stocking takes place every week and they are labelled with price and kept on shelves on display.
- No expiries mentioned newer stock at back in shelf- old in front.
- Items arranged according to type of medicine class- but no class displayed.
- Expiries are checked manually- does not feed into Abuzar software-
- Software updated only for medicine prices-rest no update.
- All pharmacy staff can assess the software.
- Money is counted after 10 pm.
- One pharmacy manager, which visits twice a week. (not a pharmacist)
- Narcotics and opioids are in a wooden cabinet, with wooden doors, and a simple hook that had a lock hanging on the loop, but did not see it locked, the cabinet was assessable by all pharmacy staff
- The medicine prescription would come directly through a staff member, no person directly approached the pharmacist
- Position of pharmacist was remote- the pharmacist was very shy, and kept very to herself, did not had much interaction with pharmacy staff
- All pharmacy staff members were males.
- The first 2 days the pharmacist would when received the order to dispense from pharmacy staff, take out the medicine herself, scan prescription (not in this order necessarily), do entry in register and then dispense- go talk to customer, ask a few questions, why using, since when using, any drowsiness- after 2 days, pharmacist used to be sitting in a corner and only resumed scanning and recording in the register (interestingly the pharmacist was doing entries for last month from scanned prescriptions, auditing of number of stock items available, batch number, stock left, while the researcher seemed to be taking notes
- The pharmacist showed no signs- dress- badge- white overall, uniform to be distinctive than others and to sign post she was a pharmacist
- The pharmacy itself- had no recognition or any counter, any label. Any signposting about the pharmacist presence or inviting to consult with a pharmacist, the entire pharmacy lacked with any information or advertising they had a pharmacist
- Separate cupboards for schedule G drugs... Under pharmacist supervision, which is accessed by pharmacy staff, the pharmacist only does entry in a narcotic register, and scans prescription normally, the staff does no entries in the register and dispenses 1 or maximum 2 boxes if they judge the patient is in pain- without prescription
- the same without prescription dispensing of opioids was done by pharmacist as well in three instances during the week
- The notice of DRAP has been advertised about no opioid medicine or schedule G drugs being sold without a prescription on the narcotic cupboard, which is not visible to customers
- Only 7 customers came which argued with the pharmacist- on not having a prescription, the pharmacist however supplied them tramadol (4) and Nalbin Injection (3) after they showed (possibly a prescription picture in their mobile- limitation).
- The scan and record were missing but the pharmacist took picture of the thing they were showing in her mobile phone.
- The pharmacy, medicine stocking, medicine ordering is managed by the staff- pharmacist seemed to not engage in these elements.

Medicine home deliveries:

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- Pharmacy staff also do them, no check by pharmacist- pharmacist not even aware, unless it has a narcotic. Prescription comes through mobile, as a picture and they save it and use it to fill their narcotic register.
- Only 5 home delivery calls in the entire week (not used much-people like to go and buy- most people have family members- which buy- middle age population buying for elders, cultural norms- (children live with parents and take care of them in old age- Norm)

❖ Narcotic register:

Name of Dr dispensing, patient name. In-stock, medicine stock number, date prescriber, quantity dispensed

Q asked by researcher about pharmacist non-involvement:

Pharmacy staff did not feel burdened when the pharmacist did not engage at all in the daily dispensing- they were used to it and said even in other shops the pharmacist act same, and think they are above the dispensing, one said, they don't know much dispensing as we, and pointed out they don't even remember the brands available, they have to ask us, so they don't engage in routine dispensing.

The staff also said that pharmacists do not stock and fill shelves as they think it is not their duty.

The staff said they had minimal interaction with the pharmacist besides the narcotic medicines

They think pharmacist is just spending their time and has been hired by the owner because of new legislation, that for schedule g drugs , they can only be dispensed after a pharmacist- they think most of the pharmacies are still overlooking and have part time pharmacists (in evening) or skip at all- as no customer will ask about a pharmacist in shop and the drug inspectors do not come in evening – even if they come most people will say our pharmacist has just stepped out for an errand or is on leave today. The proprietor normally have an informal contract with the pharmacist whose license is displayed in shop- if and when the drug inspector or law enforcing agency comes and asks for you, you will have to come that day or next day-

They think even when the drug inspector comes in even the narcotic register is not shown, which they ask to see records maintained, because they say it is under lock and key of pharmacist.

This is a normal situation- accepted and very conventional- in pharmacies across the country- however, since 3 years- in federal only or in very big cities- now the presence of pharmacists due to the narcotic law is there- but not around the clock, they are normally present in one shift. In their shop- the pharmacist is present from 9 to 4 Mon to Saturday. However, they feel. If she is not there, they can easily manage this activity without her as they are doing everything.

When asked why does the pharmacist does this kind of behaviour- the staff answered, she has an odd personality. She does not like to talk even to us so why will she talk to customers. This role needs people who can be proactive, deal the customers. Even if she talks with customers-, the customers feel a dullness, no passion or care. They though this is a public facing role and the pharmacist should have people skills. Even the manager says not to station her in front, as she is female, as well as non-social. They say she is all day immersed in her mobile phone.

They say when patients approach them for information and they ask the pharmacist, she has to check on her mobile on google.

They suspect the pharmacist has very few years of experience and lacks knowledge even about the available brands of medicines and of which companies. That is why- stays in a corner. They say we do not ask much about medicines and their details as very few patients ask. They think there are some people, who want to know but mostly they do not care what and why they are using. Just ask how many times a day and how many days, which they normally tell and write on a box if there is a prescription- if not, they don't tell.

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- **Dispensing process:**

No specific dispensing area, medicine on prescription dispense to patients with the same packaging transported to pharmacy by manufacturer, stocking by staff, ordering by staff (no role of pharmacist except schedule g medicine stocking and ordering)

- **Number of staff:**

Location: Federal capital, residential sector- footfall more than- 1000 -1500 persons per day (24 hour pharmacy): Other branches receive- more than 2000 per day in commercial areas

Pharmacist: 1 Lady Pharmacist, 4 associate pharmacy staff, 1 pharmacy technician.

Manager visits twice a week.

- **Locality or geographical area possible effect:**

The pharmacy is located along a main road , in a densely populated residential area with proper parking area, suitable sign boards are placed on both front and back ends of community pharmacy premises for people to identify, has a landing of 4 steps and no access for disabled people, has well lit signboard and says the word pharmacy on signboard.

- **Timings effect: patients visit effect if pharmacy is closed during rush hours**

- **Rush hours vs free:**

- Rush hour starts from 11- 2 pm then 3 PM till 8PM with very little changes on day, no doctor clinics near- so patient load usual- mostly chronic pain patients- using medicines for years as per the conversation of pharmacist with them- in the first 2 days- **Limitation- could not know if there was a new opioid pain killer user amongst us, because the pharmacist did not engage at all in the 3 days people asked an opioid for analgesic relief.**

- Overall pharmacy opening and closing times- holiday?

- Pharmacy 24 hours, shift hours- morning, evening, not seen myself, after 10 pm but when asked by researcher from staff, they said two pharmacy staff are present. No technician or pharmacist- just normal salesman, very few community pharmacies in capital that offer this feature of 24 hours-

- **Medication Review:**

No such activity recorded, the only thing observed was in first 2 days, the pharmacist when would dispense an opioid prescription would ask a few questions.

- **Other medicine interaction:** The presence of the pharmacist inside the pharmacy was just besides the narcotic cabinet, and that was the only medicine where the pharmacy staff would consult her or talk to her regarding. Only 4 instances were recorded, in the first day only, that pharmacist, went and dispensed medicines other than opioids, that too because she was standing behind the counter (where normal pharmacy staff is present, the front counters) and was directly approached by the customers, however the **four** days after that, pharmacist was in her corner- not engaging with patients at all. **Limitation-Suspected the pharmacist was doing this just because of researcher presence-**

- **Opioid medicine interaction:** First 2 days the pharmacist (. **Limitation-Suspected the pharmacist was doing this just because of researcher presence-**) dispensed the medicines and tried talking to people about their opioid medicine use- try to ask other benzodiazepine and barbiturate use, on the third day- no active initiation by the pharmacist- the pharmacist did not know how many days the researcher will be there

- One male said " I am not getting effective pain relief- or sometimes the effect wears off very quickly- I than take double the dose or take it before the time.." pharmacist cuts off and replies-

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“Can you consult the doctor ...as they will know your disease better and know why this medicine- which is actually very strong pain medicine... is not working for you.. ” Patient was dispensed Tramadol- 100mg BD.

- Another patient (female) asked “How long will I take this medicine.. as I am using this medicine since 2 years- and the doctor just keeps prescribing me- others people don’t take painkillers the way I am- every time doctor increases the dose and frequency and add more medicines.. ” Pharmacist reply:
“Females can tolerate pain a lot- why don’t you try tolerating it? If you do not want to continue using it... What exactly is your problem by the way, why are you taking this medicine...”
Reply:
“I had problems in my lower back while delivering my son- actually I had a C section earlier... so now I get this pain very often in my lower back... People say its common and this pain will not go... ”
Pharmacist replies:
“Oh yes... my sister have this pain too... and she is visiting ---- (doctor name)... maybe you should go there too... Change your doctor... this one is really good, gives good medicines...”
Patient asks the address, buys the medicines and leaves...
- **Actual Interaction: (first 2 days)**
Ask for prescription, if no prescription- refuse and when argued by customers, a possible prescription picture was shown after which dispensing took place.
Told about laxative use- only-
Told to avoid – medicines that makes drowsy
Asked not to drive when sleepy
- **Enquiries by pharmacist:**
Information asked, how long using for, how many days, what for, what other benzodiazepines or barbiturates (actual words used were **sleep medicines**) taken by the patients. In case of patient not being present himself or herself and a family member was buying medicine, the pharmacist asked why they are taking.
- **Information provided:**
 - The information provided was this medicine can cause addiction and to talk to Dr to **prescribe NSAIDS** to them (actual words used- which most people did not understand).
 - Other information provided was, pointing out not to use this medicine with this medicine more than the prescribed dose. (diazepam and tramadol)
 - Dose and frequency was either mentioned on the box, by pharmacist or given to pharmacy technician to write it on the box acc. to Drs Prescription.
 - People used to ask any food interactions- the pharmacist said, “**No interactions just eat it on full stomach- medicines cause less side effects, when eaten with food and milk**” (actual quote).
 - - in narcotics- prescription was asked- when had no prescription at all or could not even provide via mobile- were refused medicines- even though customers argues- 2 complete refusals-
 - In most instances people would have in mobile or physical-
 - No further thing recorded- as pharmacist did not share the prescriptions with researcher and did not even ask details from people- **so assuming- they were fresh prescriptions (not older than 3 months)-Interesting point over here, although the pharmacy had a narcotic stamp- the pharmacist did not use it once- on the prescription that opioid medicines have already been prescribed on this prescription-**

❖ Layout-human factors- to reduce medication errors:

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- Labelling of medicines was not done according to class wise medication
- No effective strategy- on lookalike or sound alike drugs
- Software did not support- any medication interaction checking
- Pharmacist did not engage and see medications
- No patient safety even in high doses were performed-
- No review or checks, all medicines were dispensed (stock was always there), 2 people bought medicines in bulk (suspected at least 6 month- no questions asked, instead were given 10 percent discount by the pharmacy staff- **encouraging behaviour**)

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Interesting point over here, although the pharmacy had a narcotic stamp- the pharmacist did not use it once- on the prescription that opioid medicines have already been prescribed on this prescription-

Medication error possibility due to human factors existed- no check or cross check by pharmacist before dispensing-

- **Medicine inventory**

Abuzar Software is installed to maintain medicine sale. Although software can be used to maintain inventory-but manual inventory was being maintained by pharmacy staff- (one designated person-amongst the staff- the pharmacy manager would also the manual inventory- and clear bills with the distributor- the manager would come in twice a week and all distributors would come on those days-)

- **Drug inspector visits**

From last 24 months- since the shop opened, only 1 visit was made, since then no visit of drug inspector as per pharmacy staff- pharmacist said she does not remember seeing a drug inspector however, she maintains the narcotic register records as per law.

The visit included

- Medicine entries- inventory: - did not know.
- medicine record keeping: Not checked-
- Medicine cabinet: Not checked
- Fridge: temp checked- temp is logged in by pharmacy staff as well-

No ongoing service except selling medicines.

- **Who is receiving orders?**

Most of the time its pharmacy tech receiving customers.

- **Who is filling prescriptions?**

Pharmacy tech

- **Who reviews?**

No review-

- **Who stocks:**

Pharmacy tech- even orders and checks the balance

- **Time to dispense:**

Immediate- maximum waiting time after medicine has been asked by name or given a prescription is 2 minutes- in rush hours; people have to wait around 2 minutes for invoice-

- **Any telephone contact with the doctors:**

No-

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Landline telephone available but used for home delivery orders or grocery related information- not used at all in 5 days by pharmacist or technician

- Any telephone contact with the patient:

Yes- for home delivery people. But they contact as per needed- no system in place for repeat orders-

- Anything else:

Internet access not available inside pharmacy- no books, reference materials present- no counselling station- no visibility of pharmacist-

❖ **Questions asked by the pharmacist (all-anything):**

- Any assessment to detect is this prescription for the same patient: in case of schedule G drug, yes pharmacists are legally bound to maintain record of patient's demographic, drug, prescriber, quantity etc.

- Body language:

Pharmacy staff says at night they are a bit more attentive- to make sure person with prescription is not drug abuser.. And are careful of dispensing at that time-

- Attitude of pharmacist:

Lacking in social skills, training, education, according to pharmacy staff. Does not like to help pharmacy staff, and refuses any activity- besides schedule G medicines

- Engagement with the patient:

Very little

- Conversation of the pharmacist:

In case of self-medication patient value, the opinion of pharmacist... however in this case, the person gets most information about dose, choice of selection of medicine, cheaper medicine from the pharmacy staff

- Duration of time spent with a person filling prescription: 2 to 5 minutes

- Differences between a new and refill:

No difference observed, (limitation- was not able to assess whether there was a new prescription or all were repeat)

- Any difference in review or dispensing during consequent refills: not applicable in this pharmacy

- Any difference while giving information to male/female or old/young.

No difference in case of Male, old or young, in case of female there are certain social and cultural barriers due to which female are hesitant to take info from any male attendant of pharmacy and same is the case of pharmacy staff... especially when talking about pain- location and cause- no private place is available for consultation- no counters, no place to sit-

- Questions asked if any by the staff or pharmacist:

Question asked only if patient is demanding medicine without prescription... that too in schedule G drugs- otherwise no questions asked-

If in case patient has no idea about which medicine would be best in their condition, the staff would advise medicines-

- Questions asked by the patients:

FAQ is whether to take medicine with or without food, dose, how many days...

- Anything else:

patients don't know about pharmacist- 99 percent people don't ask for a pharmacist- **only 3 people** in the whole week asked about pharmacist and that too when they were refused opioid analgesic without prescription.. Then directed to talk to pharmacist- (possibly hawthorn)

Medicine related- product information- therapeutic goal:

- ADR reporting system : no awareness of pharmacy staff
- Unable to identify side effects
- Unable to identify poly pharmacy
- Don't refuse bulk orders

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- Don't make sure patient understand how to use the medicine
 - Patient feeling after starting a medicine: no questions asked by dispensers.
 - Any medicine side effects, problems, concerns?
Nothing noted... that pharmacist- except two days- asked about any side effects- pharmacy staff also did not ask.
 - Do they want any information?
From pharmacy, staff very rare...
 - Information on how take or use these medicines? Dose is written on box- frequency is scribbled with a marker (permanent)- no verbal consultation observed in this pharmacy- food interactions frequently asked- told no interaction(see pharmacist section must)
 - Do they know signs of overdose and possible course of action?
Cannot comment- as no such conversation or activity or information was provided by either the dispensers or pharmacist-
 - Life style advice, rehab, physio?
Cannot comment- as no such conversation or activity or information was provided by either the dispensers or pharmacist-
 - Referral?
None except once- where pharmacist referred a female to a Dr Known to her personally.
 - Information leaflet provided:
leaflet present inside the packaging by manufacturer, however is not pointed by the dispensers or pharmacist that they can access medicine information- according to laws- local manufacturers have to include information leaflet in national language, however, most opioids brands although national did not have the Urdu leaflet-
Leaflet about home delivery for medicines and groceries- was provided to females especially-
 - Social prescribing?
Cannot comment in detail- People would ask about what to use mostly from dispensers, not from pharmacist- pharmacist- but self- medication was very common- for NSAIDS analgesics- pain relief- people coming without prescription(for opioids)
 - Any OTC added:
Mostly paracetamol- or NSAID- without giving PPIs
 - Any risk establishment- alcohol- sedatives-mental health issue assessment:
NO- asking about alcohol would be no- conventional and considered offensive, however, smoking was not even asked, as well as commonly used stimulants or depressants- no assessment of mental health issues, however – first 2 days pharmacist would ask- while dispensing opioids- if taking any other medicine for sleeping..
 - Anything else:
- ❖ **Any challenges/barriers/ feelings/concerns expressed by pharmacist or observed: (informal)**
- What is their current experience and Influencers of interaction with CNMP patients taking opioids?
When asked by the researcher- the stance and role of a pharmacist-
Random-Statements by pharmacists: (not exact words- remembered from memory)
 - Pharmacist engaging with people is difficult because of: less time with patient, asks no information, the entire responsibility falls on pharmacist to engage with people , convince to talk to them, make them trust u, make them listen to you, accept your advice (pharmacist said it is difficult to do that for every patient)
 - Pharmacist said- people don't like to be enquired for medicine- they don't appreciate, feels like being interrogated so pharmacists avoid
 - Pharmacist said they really have to struggle when refusing prescriptions- because people become aggressive- if the scene escalates- the manager is also non- supportive and has

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asked for such patients it is better to dispense the minimal quantity- but not refuse entirely...

- Pharmacist feels tramadol is being prescribed without establishing patient pain condition- or trying alternatives just to get patient satisfaction-
- Pharmacist feels people don't get the required analgesic relief from tramadol tablets- and then seek injections- of tramadol and then nalbuphine
- Pharmacist feels that patient have no idea- about the risk of opioids and addiction. Moreover, keep sharing medicines and advising others.
- Pharmacist feels necessary checks while dispensing schedule g medicines should be made mandatory
- Pharmacist feels the environment is not feasible for pharmacist to perform any patient centered roles and the management is more concerned with doing a good business and when they refuse medicines- the manager gets angry
- The pharmacist thinks they could be utilised in a more patient oriented activity instead of using them as salesperson- and feels unmotivated
- The pharmacists says the salary is not up to the mark- and says that pharmacists should be used as medication counsellors- and for consultations- but:
 - Does not have infrastructure to support
 - Manager not willing- although she has asked- many times for a counselling station-
 - Tried to celebrate and create awareness on specific disease days- and was not allowed or appreciated
 - Does not get extra payment- or incentives
 - Any activity by pharmacist in relation to patient safety- is not appreciated by the management- and feels they are only hired for the license and the new narcotic drug sales rules- otherwise they will not be there
 - Has tried to ask for attending training and awareness sessions arranged by Abbott pharma- however the manager does not allow and says to take non-paid leave if she wants to attend such activities
 - Pharmacist says- the software is unhelpful in relation to identifying interactions
 - Pharmacist says – what she was taught, the role and image of a pharmacist- she never experienced that social perception from people, and even if she tried to engage with patients- in terms of medication substitution or tapering the medicines off—people were non- complaint and would say the doctor knows more.
 - Pharmacist says- she is the only pharmacist- and if she were to perform additional duties, and specified roles like consultation- more pharmacists would be needed- that is why no such activities are being currently promoted-
 - Pharmacist says- they don't hire a pharmacist in second time- because pharmacist pay is more- than a dispenser- and they cant take more clerical work from pharmacist- and by law they need one licensed pharmacist-
 - Pharmacist feels, the payment she gets is although inadequate for a professional degree holder but is relatively better because she is working with a reputed chain pharmacy – however there should be some minimum criteria
 - Pharmacist says there is no ADR reporting system- or any grievances system- where they can complaint about pharmacy owners-
 - Pharmacist mentions no medication records, so have to trust the patient word- mostly people don't remember how long they have used medicine- becomes problem especially in opioid medicines-
 - Pharmacist feels- a lot of self-medication and opioid misuse is happening- due to the addiction properties of elements in educated people-

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- Pharmacist feels the misuse is more in adults- middle ages and above- old age people where they misuse it to stay calm during the day- and get sleep- and don't mind paying for these medicines
- Pharmacist says community pharmacies are private businesses- and the only focus is making profit- any activity- which increases their sale is welcome however rationalising prescriptions is highly un-welcomes- which has left her unmotivated-
- Pharmacist said- she wants to start an information group- via WhatsApp- but people are not willing-
- Pharmacist says- gets medicine information from Facebook pages, google, or soft books which she downloaded in her student ship

• Are they satisfied with the current interaction provided by them to patients?
Pharmacist feels they are doing their best as in their capacities and limited resources.

• Perception about benefit of interaction?

• Was the patient approachable?

Mostly no- sometimes yes- depends on the patient-

• Any factors/barriers affecting the communication:

Many- see above- informal barriers- for communication related-

Infrastructure does not allow- peaceful conversations-

❖ Internal:

CNMP patient related-

People with acute as well chronic pain kept coming to buy medicines- in case of chronic pain, most people had visited a Dr, had a prescription having an opioid- however for acute They seeked the dispenser or pharmacist opinion

- The scans of prescriptions were seen- in the record- and almost half of prescriptions in the file- had no stopping or duration dates of using opioids-
- Most of the prescriptions had previous history of taking opioid pain killers for pain-noted and despite that they were continued
- Last 6 months scanned prescriptions records were seen and most prescriptions were not that old and were below 3 months of issuance and had no stamp or dispensing record that could show whether they had been dispensed an opioid medicine on that or not-
- Mostly chronic long term users-
- The scanned prescription records had all prescriptions- controlled items including opioids, barbiturates, benzodiazepines (schedule G medicines) alone or in combination
- The record was maintained manually- and were checked by pharmacist-
- The prescriptions were from private prescriptions, government hospital outpatient paper, small pieces of paper with a doctor stamp and sign and sometimes just the doctors PMDC registration record
- **The quantity dispensed was not quantified and correlated with the records as active observations were going on-limitation**

❖ Personal:

Old , young, male female, medicine for self- medicine for someone, with prescription, without prescription, digital photo of prescription- all types of people came- mostly educated, rich people, mostly chronic patients on long term user, from the conversation with the dispensers the it was difficult to understand that the prescription was for their own use or buying for someone

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❖ Knowledge:

Because the people did not ask much information in regards to medicine, side effects, interactions, therapeutic alternatives, - from the data in hand- it might not be conclusive that whether they had any information about the opioid medicines or not-

❖ Attitude:

The people attitude varied according to them having prescriptions or not-

If they had prescriptions- the people- if they have- they will accept pharmacist counselling or appreciate pharmacist talking to them, but if they don't have prescription and pharmacist kind of talks to them enquiring about medicines, so people become aggressive and irritated

Some young age people, used a very polite tone while getting opioid medicine from pharmacist- and tried to explain – they had not brought the medicine, and they were buying for their mother or father and they were in extreme pain(pharmacist dispensed 1 box- to those people), the pharmacist told researcher, we see if there is a genuine person.. In addition, we can see that from their body language then we dispense it, we do not want people suffering and we give them **benefit of doubt (actual words)**, pharmacist feels that **being pharmacists we are here to stop diverted and irrational misuse- not make life difficult for patient, being a pharmacist we want to be facilitator.**

❖ Time

- External: Policy, guidelines, job description, timings, staffing, remuneration, Doctors, work load

No job description, no job contracts written just the deal of license with proprietor, salary is given vi account, no other benefits, policy lack of security influenced the pharmacist confidence, lack of manager support demotivated pharmacist, lack of job description was found to be a leading problem btw dispensers and pharmacy technicians

- Medicine review-telephone?

Not noted. Not once a call was about medicines.

- Anything else they added:

❖ Overall reflections:

Pharmacist seems overall demotivated, it seems has tried to do pharmacist based roles, but was not appreciated and was stopped by pharmacy manager- not to decrease sales by rationalising medicine- so pharmacist seems to have given up- and does only what the manager expects of her-

Pharmacist lacked in knowledge and social skills

Pharmacist has not a very friendly relation with technicians- and there seems a barrier amongst them- that could possibly be related to ill-defined job responsibilities- and non-social relationship-trust issues- both think this is responsibility of other- money also seems to be a factor to dispensers, that we do all work but pharmacist gets paid more- although she does nothing except maintain a register- which she does periodically- they feel, when pharmacist does nothing, they should only have their license displayed- they also seemed not to approach pharmacist if patients ask, because they feel pharmacist lacks in knowledge, expertise.. Manager seemed to not take this seriously- and has done nothing to mitigate this mistrust-

People- seemed to both accept and reject the pharmacist advice in instances, but it depends f they have a prescription or not- in case of no prescription- don't like the presence of pharmacist or advice and refuse to talk to her , instead seek technician- the technicians while dealing with such customers kept looking over to the researcher- and would say something- which could not be overheard- however patients used to go after that- The following day- the nalbuphine inj had been dispensed- against a hospital prescription- when the pharmacist had gone home- this kind of behaviour has been caught by the pharmacist- and says that she has specifically asked not to do them without verifying the prescription- and says she will take this matter with the manager-

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People like to ask about painkillers a lot- not able to understand from over the counter conversations- whether its acute pain or chronic- a lot of dispensing of NSAIDS was observed- opioid analgesics seemed to be somewhat controlled due to demanding prescriptions- and most people seemed aware of this rule-

The rules seemed to be controlling dispensing of controlled items- help reduce self-medication, and is supporting the presence of pharmacist- however except being a security guard for controlled items, the pharmacist is doing no role in patient safety, any review – any patient engagement- seems lacking-

Pharmacy manager is not a pharmacist- that might have led to disorganised pharmacy system, medicine management, seems to be concerned about running a business- also does not support the pharmacist in any pharmacist based initiative- the manager seems not to utilise the pharmacist in day to day activities- reasons might include, she is female- pharmacy technicians seems more experience and reliable-

Buying and other medicines seems a very linear process- in case of non- controlled item, people when walk into shop- approach a technician, who is usually standing with face towards public and is free, welcoming, people ask for medicine by name (mostly) or give prescription (v few instances) - technician goes, fetched the medicine off a shelf, brings, they pay, some ask discount some don't- and then go- nothing more-

opioid medicines- most would bring prescription- enter pharmacy, reach a welcoming technician- in day takes it to pharmacist, without a word, pharmacist takes prescription, scans it, and opens the unlocked cupboard, where she is sitting, gives the item and prescription back(no stamping), technician takes it, person pays and goes..

in case of non-prescription- person asks by name- technician will either say the person to talk to pharmacist- she is sitting in the corner- or if person tells them why they don't have prescription and refuses to talk to someone else- will go and tell pharmacist- they are asking medicine- the pharmacist may or may not- dispense- depending upon person, attitude of person, story of patient and by having a look- those people who became aggressive- did not get opioid dispensed- most people who get aggressive wanted tramadol and nalbin injections- the rest process stays same- imp point: pharmacist does not take too much trouble trying to explain- that this is in accordance to new ICT drug laws- and has been followed since more than 1 year- just mentions in a dry tone- we cannot give this medicine without prescription, and we cannot give even the notice is not visible to people-

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Appendixes

Appendix 15: Quotes for themes and sub themes in subchapter 3.2 from all four stakeholders and 4.2 for all case studies

Themes	Subtheme	Quote (stakeholder)	Inference/interpretation of main points	Case studies inferences
Unsafe use of opioids				
System	Lack of integrated and unified digital health systems	<p><i>"Let me share with you this picture... I received this prescription today... If you check this... All this prescription has been written in one colour...but nalbin and tramadol... It has been mentioned in a different colour... This was added later by somebody else..." Pharmacists fg2 p2</i></p> <p><i>"this is extremely important, because of lack of electronic system, we do not know who the patient is, what treatment they have had before, what drug allergies they have. Agree with P1, what has been effective, chronic conditions especially, we currently rely on patients giving us this information, which can be complete or incomplete depending upon patient. There is a concept of getting more than 2 diagnosis, they will go to one dr and then go to another just to see, did both of them diagnose same problem, I am not saying that is bad, I am saying things should be visible (to doctors)" Drs Fg5 P6</i></p> <p><i>"you cannot even control... How many times... A person takes that same prescription to many shops and get how many medicines... There is no record keeping... This is the problem... When the patient drugs are prescription we cannot refuse dispensing.... Even putting opioid medicines under prescription only sale will not work.. Their should be either keep the prescription, stamp it as dispensed or feed in record.. Some electronic software.. That is connected to all pharmacies.. So they know..." Pharmacists FG2 P2</i></p>	<p>Patient opioid prescribing/dispensing are manual</p> <p>Lack of drug utilisation data</p> <p>Lack of prescribing data</p> <p>Lack of disease burden</p> <p>Due to lack of records Drs in limited time have to assess patient needs (with less time, patient illiteracy it becomes more challenging)</p> <p>Unintentional medicine duplication happens due to lack of prescribing records</p>	<p>Fake ink added</p> <p>Narcotic stamping can help keep record of dispensing</p>
	Lack of National guidelines for opioid safety and CNMP management	<i>"Mind it, there are no .. Guidelines, guiding them towards specialised roles.." Pm5</i>	No guidelines for prescribing opioids,	

	Lack of regulatory body roles in control and check on opioid medicines	<p><i>"I have been working three years now.. No regulatory body has ever come to check the narcotics sale.. Nor I have seen a drug inspector particularly strictly asking this... Never.. He came.. Even in disguise and to get narcotic medications in bulk from me..." Pharmacists fg1 p1</i></p> <p><i>"There are certain deficiencies in the regulatory systems as well for example.. The drug regulatory authority and other regulatory authorities.. Have also ordered the physicians... Reducing or stop prescribing any natural or alternative medicine... It is not allowed but they are still prescribing.. They're still practicing...there is no control on opioids (in) their prescriptions.." Pharmacists fg5 5</i></p> <p><i>"There should be law enforcing agencies, which should make visits to these shops.. They should check there are no counterfeit medicines..." Patient 6</i></p>	<p>Lack of regulators</p> <p>Regulators distribution improper</p> <p>Counterfeit medicines allowed</p> <p>Sale of unauthorised herbal/Cam products continue</p>	<p>CAM dispensed</p> <p>Effect of regulation on opioids sale</p> <p>Effect of regulation on managers</p>
	Lack of pharmacists	<i>"With respect to pharmacy and community pharmacies specifically.... As far as sale of drugs.... And specifically opioid drugs in... the capital is concerned.... It is safe they are only available after the prescription of a doctor.... But as far as other cities are concerned... If you go to other provinces...like in Punjab...I think the drug sale rules are followed.... The rules say that only pharmacies having pharmacists... Can sell opioids... But in other provinces... The community pharmacies are currently run by the B-pharmacists (pharmacy technicians)... They are allowed to sell the opioid medicines... So category B pharmacists(pharmacy technicians)... Are also allowed to sell opioids in other provinces.. This is one component, which is causing issues.... PM7</i>	<p>Most areas cps are not present</p> <p>Proprietors hire CP license only, CP presence which is mandatory for opioid dispensing is lacking</p>	Lack of pharmacist
	Reasons related to Drs			

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	Patient load	<i>"These things even are not reviewed by the physician sometimes... because there is so much rush. There are so many patients.... sometimes there are 2 or 3 or 4 patients sitting in front of doctors at the same time.... all of them are speaking... I am speaking about the OPD clinics in the government hospitals... where majority of the people in this nation are going to seek health care..." Drs Fg1 P5</i>	Drs are unable to give proper time to patients because of too many patients. Drs focus on diagnosis and quickly prescribe and attend another patient. This results in lack of review, obtaining past opioid medication history and can contribute to unsafe use	
	Marketing and brand medicine prescribing	<i>"There should be generic prescribing.... This culture of promoting specific brand... Should be finished..." Drs fg3 p1</i>	Drs say brand prescribing is done due to higher quality and avoid counterfeit/substandard medicines Other stakeholders say reason is pharmaceutical promotional activities and results in excess prescribing and polypharmacy	Brands dispensing present always Poly pharmacy evident in prescriptions
	Poly pharmacy	<i>"Even if you go and then the doctor that you are having severe pain... they will write you 2 or 3 painkillers and tell you use it and you will be okay... And use this medicine.. So many pain killers" Patient 3</i> <i>"One thing over here is new opioids. Like fentanyl buprenorphine they are not available. So we are again and again prescribing amongst the limited (option available). So mostly our practice includes giving nsaid, Cox inhibitors in combo (with opioids) and seeing their effect.. But(we) monitor them" Doctors FG5 P6</i> <i>"So even if (the doctor) advise them to use other painkillers... besides opioids.. Never .. They never agree.. They say no, I have to go to job tomorrow... doctor normally prescribe them the opioid medication because it is important for them to have patient acceptance..." Pharmacists fg3 p2</i>	Might happen due to lack of potent opioids available To improve patient satisfaction Pharmaceutical promotions	Poly pharmacy

	Improper prescribing and prescription errors	<i>"Sometimes prescription comes which have normally 8 to 10 medicines.. The pharmacist actually holds his head (become exasperated).. And all of them belong to the same classification of drugs... Like 3 or 4 they did .from the same class... Two of them would be multinational.. Two will be from the business (promotional) products... So this is an issue for opioid safety.." Pharmacists Fg3 p2</i> <i>"I don't think there is even this concept.... On narcotic opioid prescription... The most important thing is number of refills.... Even in prescription there is no column or segment for refills... In the prescription there should be a specified please how many times do we refill.. And every time a pharmacist refills they should put a mark... Or a number.." Pharmacists fg2 p7</i>	Lack of rational prescribing Substandard prescription Overprescribing	Narcotic dispensing/stamping according to refills
	Attitude of doctors	<i>Nobody tells us the benefit or the side effects of the medicine.... Not doctor even.. If I ask they will get angry.. So I do not ask.. When they look at me they think I am illiterate.. So they do not think me as worthy to answer.. I do not know if someone like you who is educated will go and ask.. What their reaction will be.." Patient 1</i>	Stereotyping patients on social class and gives information/proper treatment to rich people(mostly in clinics)	
	Lack of communication systems	<i>"Any notes or alarming behaviour can also be scribbled into that system for drs to read.. Now the doctor is not aware now.... Because the patient never came in.... The doctor might not even know, how many times their prescription has been used to buy the medicine. And even how many people have used.. There is no record keeping.." Doctorsfg2- p6</i>	Cps-Drs need communication for patient care Lack of distal system is causing lack of communication	
	Medicine store and pharmacies			

	1. Un authorised dispensers (quacks)	<i>"Let us say if a new condition develops... The patient goes to a pharmacy/medical store... Anyone in that store a technician.. Salesperson or whoever he or she is.. That I'm having this problem which medicine should I take.. So according to the judgment of that person whatever he thinks is best for the patient, he will dispense it to them..." FG3 p1 Pharmacists</i> <i>"These dispensers.. Mr dispensers are doing these kinds of activities... Tramadol(injection) if they have pain or maybe a steroid (injection).. And the patient also gets happy.. That I have got treatment today.. The dispenser also happy, he charged him- so happy people don't even seek pharmacists or doctors or medical attention, their faith lies in that one man.." Focus group 5 DR1</i> <i>"Over here a dispenser, a salesperson... they will give you any medicine in any amount... any quantity... no questions asked..." Doctors Focus group-3, P4</i>	People due to convenience visit medicine shops and get opioid injections Traditional norm/belief-people have been asking dispensers to prescribe. administer Mostly females are subjected to these people where unauthorised person pays home visits and give injections Economical for people as don't have to pay Dr fee/travel to far off places	Dispensers prescribing
	2. Lack of pharmacist availability and specialised patient centered roles	<i>"Even if the pharmacists are present in community pharmacies... These medicines are dispensed without any patient interaction... No questions asked...because there are no roles" Pm2</i>	No CP mandated roles in patient care or medicine reviews	Cps helping implement schedule-G laws and stop opioid dispensing without prescription
	3. Medicine sale business	<i>"They try to sell more number of medicines... Expensive medicines... Without actually establishing the need of the patient..." Drs FG2 P2</i>	Don't refuse opioids even without prescription, make more sales Illegal prescribing of medicines	Business focussed activities
	People			

Appendixes

	Doctor shopping	"All this happens on daily basis, this is routine, people go from one dr to another and don't tell if they have visited another dr. They want relief, they sometimes tell, we went to another dr using this medicine, sometimes not. Even in covid people with positive result came n saw drs, and when the dr ordered test and confirmed covid they said oh we thought other dr was scaring us, u also found means maybe its true. With this level of people you cant ensure what or how they will use.." Drs fg5 p6	Doctor shopping is prevalent because people think if two doctors recommend same medicines , it means they have been prescribed proper medicine People Dr shop in search of better pain management	People bringing two or more prescriptions
	Perception of fake or substandard medicines	"I'm saying if the medicine was pure... So the pain should have finished by now, right? But it is still like that... So it proves.. That the medicine does not have any pureness in them... So we(people) normally ..increase the quantity of the medicine... But the thing is, it's not effective in pain.. As before.. No matter how much you consume... The number of medicine is also increasing, the dose is also increasing.. But still there is no effect.. So we have to use it.. We use more and more so it can have at least some effect" Patient 8	Due to lack of awareness about tolerance people think medicine is fake that is why it has no effect People shared if it's a substandard medicine it has less amount of potent drug so, they use more medicine so that they will get some relief	

	Review appointments difficult	"Nobody cares... If you go there is one doctor sitting.... If you go after a month there is another doctor.... Then that second doctor will give his own treatment... Sometimes even starts the same medicine again... How can I ask the doctor... Even if the medicine has no effect we also go to another doctor... And we tell him that this medicine is not working... So he writes another medicine... You should try this one... Which is same when I buy from shop.." Pt1 "Normally the people do it (self-medication) like this because the access to the doctor ... In government hospitals and private appointments are difficult to get... And over here sometimes." Patient 7	People are unable to book appointments with the same Dr and the new Dr gives his/her own medicine without listening to what patient has used People skip reviews because of distance, poverty (can't afford to pay the fee)	
	Misperception of opioid like OTC	"so the general concept of the patients, is that they consider this medicine like paracetamol that this is a normal pain medicine... One of the major reasons for this perception is that the people the dispensers and the technicians present in the community pharmacies, they actually provide tramadol as an over the counter medicine without prescription... Tramadol is still treated the same.. Just like an OTC analgesic.." Pharmacists fg5 p1	Due to lack of awareness people think opioids are same like OTC pain medicines Opioids available easily similar to OTC medicines	
	Perception of injectables	"I think in one way our rural population has a belief and faith... That every disease cure is an injection... The dispenser.. This start their day.. From their home... I have to give injection... And they leave their shop after carrying injections and IV infusions... I am talking about villages over here... The people leave their houses.. With a set mind that we have to go to that "doctor"... and he will administer an injection..." Drs 1	Both people and dispensers think injections are the treatment	
	Demand medicines	"They will insist that they want these opitoid medicines... They call themselves customers that we are paying customers, you have to give us this medicine..." Pharmacists fg1 p1 "Normally patients arrive at the community pharmacies... And regardless of the medicine, they demand it like an OTC medicine.." Pharmacists fg5 p1	People demand medicines as they believe no other medicine will work in their pain People demand medicines to get quick/better analgesic relief	People get aggressive without prescription People ask opioids without prescription
	Poverty	"In the rural settings to pay a fee of 500 or Rs 1000 for a patient.. So first of all the patient thinks that I have to pay this and then I have to pay for the medicines as well... So instead I will keep using a medicine last time the doctor prescribed.." Pharmacists fg3 p1	People are unable to afford the Dr fee, so self-medicate, or ask dispensers which medicines to use	People observed to ask dispensers which medicines to use

	Review appointments difficult	"Nobody cares... If you go there is one doctor sitting.... If you go after a month there is another doctor.... Then that second doctor will give his own treatment... Sometimes even starts the same medicine again... How can I ask the doctor... Even if the medicine has no effect we also go to another doctor... And we tell him that this medicine is not working... So he writes another medicine... You should try this one... Which is same when I buy from shop.." Pt1 "Normally the people do it (self-medication) like this because the access to the doctor ... In government hospitals and private appointments are difficult to get... And over here sometimes." Patient 7	People are unable to book appointments with the same Dr and the new Dr gives his/her own medicine without listening to what patient has used People skip reviews because of distance, poverty (can't afford to pay the fee)	
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	Misperception of opioid like OTC	<p>"so the general concept of the patients, is that they consider this medicine like paracetamol that this is a normal pain medicine... One of the major reasons for this perception is that the people the dispensers and the technicians present in the community pharmacies, they actually provide tramadol as an over the counter medicine without prescription... Tramadol is still treated the same.. Just like an OTC analgesic.." Pharmacists fg5 p1</p>	<p>Due to lack of awareness people think opioids are same like OTC pain medicines</p> <p>Opioids available easily similar to OTC medicines</p>	
	Perception of injectables	<p>"I think in one way our rural population has a belief and faith... That every disease cure is an injection... The dispenser.. This start their day.. From their home... I have to give injection... And they leave their shop after carrying injections and IV infusions... I am talking about villages over here... The people leave their houses.. With a set mind-that we have to go to that "doctor"... and he will administer an injection..." Drs 1</p>	<p>Both people and dispensers think injections are the treatment</p>	
	Demand medicines	<p>"They will insist that they want these opioid medicines.. They call themselves customers that we are paying customers, you have to give us this medicine..." Pharmacists fg1 p1</p> <p>"Normally patients arrive at the community pharmacies... And regardless of the medicine, they demand it like an OTC medicine..." Pharmacists fg5 p1</p>	<p>People demand medicines as they believe no other medicine will work in their pain</p> <p>People demand medicines to get quick/better analgesic relief</p>	<p>People get aggressive</p> <p>People ask opioids without prescription</p>
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	are able to guide the patients properly...	Counsel the patients about medication dose, side effects, adverse effects. Fg1 drs p1	most important thing is patient counseling... Pharmacists fg4 p5	That, a pharmacist who is sitting and working in the community pharmacy section or if he's sitting in the hospital in pharmacy section... Can give only this service... "the advice" which can be given to the patient that this medicine should be used in this way... These things should be avoided... These habits should be changed... These timings should be followed... You should take this food... And avoid that food...
	Pt 3			Pm2
Patient education	Yes a pharmacist in a medicine shop telling medicine information.. This will be very ideal... as such even now people are going .. And asking chemist for medicines.. If there is an authorized person.	"many of these people are less educated, so the pharmacists can help point them visually, how to use which medicine... Maybe differentiate with the help of colour of medicines... Shapes... it is essential" doctors focus group-1, p5	Dr prescribe .. Pharmacies sell.. Pharmacists counsel.. And cater it for patients... The benefit pt gets is immense. Similarly... for opioids.. The benefit can be immense pharmacists fg2 p2	If a person is using a painkiller medicine.... He should be told how many tablets he has to take.... How many times a day... Should you take it with food or without food... Should you take grapefruit juice with it should you not ... Are there other interactions... In so many months the blood levels should be checked.... The prescription should be reviewed, the need has to be re evaluated.. The side
	Pt1			

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	are able to guide the patients properly... Pt 3	Counsel the patients about medication dose, side effects, adverse effects. Fg1 drs p1	most important thing is patient counseling... Pharmacists fg4 p5	That, a pharmacist who is sitting and working in the community pharmacy section or if he's sitting in the hospital in pharmacy section... Can give only this service... "the advice" which can be given to the patient that this medicine should be used in this way... These things should be avoided... These habits should be changed... These timings should be followed... You should take this food... And avoid that food... Pm2
Patient education	Yes a pharmacist in a medicine shop telling medicine information.. This will be very ideal... as such even now people are going .. And asking chemist for medicines.. If there is an authorized person. Pt1	"many of these people are less educated, so the pharmacists can help point them visually, how to use which medicine... Maybe differentiate with the help of colour of medicines... Shapes... it is essential" doctors focus group-1, p5	Dr prescribe .. Pharmacies sell.. Pharmacists counsel.. And cater it for patients... The benefit pt gets is immense. Similarly... for opioids.. The benefit can be immense pharmacists fg2 p2	If a person is using a painkiller medicine.... He should be told how many tablets he has to take... How many times a day... Should you take it with food or without food... Should you take grapefruit juice with it should you not ... Are there other interactions... In so many months the blood levels should be checked... The prescription should be reviewed, the need has to re evaluated.. The side

	should be an authorized person... He should be watching... Pt 1			
Side effects /poly pharmacy monitoring		It can cause a lot of other problems.... It should not be dispensed... Without a proper check .. A review... The review can be done by the pharmacist.... The pharmacist can enforce the prescription system.... It is just checking that is the medicine working... Is the patient properly using it in the prescribed dose... Is the patient having any specific side effects.... Is the patient... Taking it as prescribed.... These are very small checks....drs fg2 p2	Pharmacists.. Are going to review if they're going to counsel if they're going to be standing in pharmacies performing different services.. They're going to see the polypharmacy problem.. Maybe adjust the dose.. Pharmacists fg3 p1	F in a community pharmacy a wrong prescription is filled for a patient.... Maybe there is an under dose.. Or an over dose... Or a wrong Medicine... Switched with another medicine... I am not talking about the brand I am talking about the generic... This is called medication error.... So being a pharmacist it's the responsibility of a community pharmacist to stop these things...ADR's...pm5
referral	Especially the pharmacist should be able to tell if the patient needs to go back to the doctor.. I think to make him understand and convince him to go to the doctor is also the role of a pharmacist.. Specially in those cases where we are buying the medicines. For the fourth or fifth time.. Without a doctor's review.. I	This is why pharmacist role is imp. If they keep dispensing without prescriptions, the people would be using it lifelong. Without drs review. So pharmacist review- an element of regular checkup should be there. And the should be told doctors are not making money out of you, they will determine whether you are getting		

	think a pharmacist can do this.. But the doctors.. They should also check and review properly.. Please.. just not make the money.. Pt 7	benefit or the medicine needs to be changed. Drs fg5 p6		
Flag up red flags		The question that detecting or making sure there is no misuse and opioid abuse... Is related to less knowledge about the medication... Either the dose is high... Maybe the patient is compromised hepatically or renally... Maybe they are using another medicine... That can induce an interaction.... So no such things are observed while dispensing an opioid medicine....drs fg1 p7	In liaison.. With the doctor he can... Increase the dose of the drug... So he can act as a mediator... Between the patient and between the doctor... And he can guide the doctor....pharmacists fg1 p2	When it comes into the pharmacy, the pharmacist can have a review.... That the right dose...right patient... right dosage form...pm5
Easy patient language	If they can help me understand these medicines.. And see whether they have any effect or not.. See i am educated but i do not understand...the medical terms..pt4			
Dose adjustments	A: As I am suffering from a liver disease so probably help me select the proper medicine for my condition.... If the doctor has not prescribed right medicine or maybe right dose... Dose adjustment... and...ummm..... A side effect of a medicine...			

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	Pt4			
substitution	<i>You know they can also tell you .. That this is the chemical name and which brands are available in which price range... And if there is not much difference in the prices.. But then i will see according to my own pocket.. So the pharmacist can advise that this is relatively cheap and this can be good for you.. This is more safe for you.. Then i would take it. Pt7</i>			<i>Being a pharmacist i can change their prescription right there... As per my knowledge... But this is not the way this is incorrect... The prescription is the property of the doctor..... The patient has trusted and gone to the doctor for his problem... So therefore he wrote the medicine.... Now he should be the one to change it if it is not according to the patient....pm5</i>
Need to talk to drs				<i>In my mind if we were to develop communication channels between community pharmacists and private clinics.. Will be to start with electronic systems... I do not think phone systems would work well as doctors are in their clinics in a specific time, whereas community pharmacies are open at least 16 hours or some are even open now for 24 hours..pm5</i>

Stakeholders identifying challenges and barriers for CP services

Theme Focus group/interviews	Sub themes (unsafe use of opioids)	Focus group/interviews (key interpretation) ¹	Strategies shared by stakeholders
Individual CP challenges and facilitators	Specialized knowledge	<p>Sufficient knowledge and ready:</p> <p><i>I think the community pharmacist have good knowledge regarding opioids sources and other pain medicines and can fairly review the opioids therapy and adjust according to patients individual profile. Drs fg1 p1</i></p> <p><i>So actually the pharmacist told him.. That you take these medicines with breakfast, so it's not right.. it will be an issue with its absorption.. But it is better to take them in midday.. It will be more beneficial... Then my colleague said that I've searched on the Internet.. And that's fact was present on Internet.. Patient 4</i></p> <p>Insufficient knowledge:</p> <p><i>We are talking about utilizing pharmacist to review a prescription used by the patients.... he does not know.. how can he review? drs fg2 p8 believe me even doing these simple tasks which other pharmacists are doing in a routine in other countries.... giving 5 extra minutes.. this will create their place in society and people will like to buy their medicine when they think that the doctor of pharmacy (name of degree) has seen and reviewed their medication.. obviously pharmacists would need immense knowledge.. for that.. and training in their specialised roles..patient 8</i></p>	<ul style="list-style-type: none"> • Improve advanced knowledge by curriculum redesign • Include clinical pharmacy and pharmacy practice experts • Maintain educational standards by identifying core competencies

¹ The + indicates a factor which was a current facilitator for CP services whereas the – indicates it to be a barrier

Theme Focus group/interviews	Sub themes (unsafe use of opioids)	Focus group/interviews (key interpretation) ¹	Strategies shared by stakeholders
	General knowledge	<i>see as long as I've already shared that academic curriculum is sufficient enough... the only thing missing is.. they've already learned it , it just needs to be polished.. once they come in through to practical field.. And we have to develop them and upgrade them according to different specialties... they need to have general understanding and skills but then they need to have specialized skills in order for to go in-depth in disease management and chronic condition management or in specific problematic drugs like opioids.. because it is a specialized field .. the community pharmacy itself is a specialized and dedicated field.. it needs skill .. and then we need advanced skills as well.. PM9</i>	<ul style="list-style-type: none"> • Improve advanced knowledge by curriculum redesign • Launch professional trainings (CPD) • Develop community pharmacy clerkships • Include clinical preceptors and field experts for content development
	Pharmacy professional body role	<p><i>but in regards of clinical pharmacy and pharmacy process practice aspect... the core area the entire topic is missing.. So it is not specific just to pain management... pharmacists fg3 p2</i></p> <p><i>For particular medicines where it is important to go and check every patient use of medicines individually... or the conditions like they need dose adjustment or maybe injectable medicines like opioids pain killer... they require monitoring... and individuality... if you want like really good expertise then they (CPs) need to further get trained in those areas..." Patient 10-interview</i></p>	<ul style="list-style-type: none"> a. CP Knowledge (+/-) b. CP training (+/-) c. Lack of community pharmacy clerkships (-) d. Lack of advanced clinical knowledge and skills (-) e. CPD has been launched for training CPs (+)

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Theme Focus group/interviews	Sub themes (unsafe use of opioids)	Focus group/interviews (key interpretation) ¹	Strategies shared by stakeholders	
		<i>"A lot of things are missing in our curriculum that we recognize during our practical and fieldwork. And it is one of that missing objects... opioid medicines... and pain management..." Pharmacists Focus Group-3, P8</i>		
	CPs perception and competency about their role	<i>Pharmacist is the bridge between doctors and patients who counsel and advise the patient to maximize the desired effect of drugs and minimize adverse effect. Today most drug from pharmaceutical company are in standard dose and packed forms and therefore very often argue and debate the necessity of pharmacists in retailing of drugs ignoring the fact that pharmacist assume more importance in the context of Pakistani health care system not just in compounding and manufacturing but in patient counselling, safety. drs fg5 p1 See being pharmacist we have a role in patient safety.. in avoiding interactions.. and other problems in patients... pharmacists fg5 p5 you can also say that they give proper medication counseling.. educate the patient about the medicines.. to this extent actually.. only the pharmacist community have this know how.. how to do these roles.. other license holders like B and C cannot do this.. pm9</i>	Introducing community pharmacy clerkships in undergraduate and training for pharmacists	a. Lack of knowledge, skills and competencies (-) b. Lack of confidence (-) c. Perceived their role is important in opioid safety (+)
	CP interpersonal skills			
	CP technical skills	a. Lack of technical expertise (-) b. Lack of training opportunities (-) c. Pharmacy council support and CPD development launched in pilot phase (+)	Launch professional trainings (CPD) On-job training	

Theme Focus group/interviews	Sub themes (unsafe use of opioids)	Focus group/interviews (key interpretation) ¹	Strategies shared by stakeholders	
	CP interest to join pharmacies	a. Unwilling due to social stigma (-) b. Lack of career growth options (-) c. Lack of motivation due to management (-) d. Less remuneration (-) e. CP landscape changing and some organisations respect and value their contributions (+)	a. Interdisciplinary care models b. Service remuneration c. Supportive CP laws and policies	
	CPs insecurity	<i>"Security as well, job security is not here.. Payment is not there... respect is not there..." Pharmacists Focus Group-3, P2</i>	a. Improving CP communication with their professional bodies and regulatory authorities b. Remuneration models c. Pharmacy policy makers support in helping CP career development pathways	a. Motivation (+/-) b. Lack of CPs workforce (-) c. Allied staff support (+/-) d. Lack of payment of service (-) e. Lack of complaint channels (-) f.
	Lack job description	Lack of defined CP responsibilities might impact CP service provision	Clearly defined job responsibilities/ job description	
Organisational facilitators and barriers for CPs Community level challenges and facilitators for CPs	Location	a. Location of an organisation directly translates it the number of people arriving within a pharmacy (+/-) b. Location might also impact the implementation of laws and the support of managers towards hiring and facilitating CPs for delivering the service (+/-)	a. Developing and implementing CP strict laws and policies b. Supportive pharmacy management c. Improve CP capability by pharmacy management support	
	Organisational capacity for communications	a. Lack of communication (-) b. Existing computers, IT systems, software (+)	a. New interdisciplinary models of health care b. Developing and switching to digital health systems c. Improving CP knowledge and skills to	

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Theme Focus group/interviews	Sub themes (unsafe use of opioids)	Focus group/interviews (key interpretation) ¹	Strategies shared by stakeholders
			inspire CP confidence to talk to doctors and gain their acceptance
	Organisation culture and vision	a. Aim and vision of organisation or individuals owning the pharmacies define the reason for hiring CPs (+/-) b. Profit making (+/-) c. Business reputation, loyalty of customers (+/-) d. Substantial benefits of hiring CPs, short term or long term (+/-)	Enable support of pharmacy managers/ proprietors through law enforcement, awareness of CP benefits to businesses
	Benefits of service for organisation CP autonomy	a. Lack of CP autonomy (-) b. Lack of legislative support (-)	Laws and policies providing legislative support and regulation to CPs
	Organisational layout and workflow Duration of intervention	a. CPs visibility to public will impact the CP capability to deliver the service (+/-) b. Lack of electronic medical records (-), non-standard prescriptions, health illiteracy (-), lack of public awareness (+/-), physical space to accommodate people (-) c. Existing IT resources (+), Schedule-G amendment (+), increased public awareness (+)	Improving the visibility of the CP in pharmacies need to be focused and pharmacy management and allied staff should actively participate in signposting people acquiring opioid medication towards CPs Improve public awareness
	Community perception and awareness of CP roles	a. Public perception of CPs and their roles would affect the utilisation and acceptance of future service (+/-) b. Public lack of awareness of CP roles (-) c. People's individual characteristics like: health literacy, social norms, past medication experience, motivation to self-care, doctor's guidance to consult CPs, CP awareness as well	Improving public awareness about role of CPs

Theme Focus group/interviews	Sub themes (unsafe use of opioids)	Focus group/interviews (key interpretation) ¹	Strategies shared by stakeholders
		as dependence on medications like opioids (+/-)	
	Public demand	Public demand to speak to CP increasing public interest in getting medicine information, convenience and potential benefits it might offer (+)	
	Perception of pharmacists	People lack awareness about CP roles in medicines information, counselling and review	Improving public awareness about CPs
	Uncontrolled chronic pain	a. May try to use opioids more than the recommended dose and won't comply to CPs	Developing the role of CPs can help guide people about pain management, possible expectations Patient counselling Improved public awareness
	Resistance of pharmacy technicians	Resistant to CPs presence in pharmacies due to unclear roles (-)	Clearly defined job responsibilities/ job description
System	Laws and policies	a. Lack of laws regarding supporting and utilising CPs (-), roles and definition of CP missing (-), lack of pharmacy policy makers (-)	CP favourable laws should be established
	Pharmacist policy makers	b. Weak implementation of existing laws (-), lack of strict penalties (-), lack of adequate number of regulatory workforce (-)	
	Strategic policy alignment	c. Government strategic focus to improve health and inclusion of pharmacy policy makers, amended rules (+), increased regulators (+)	
	Community pharmacy sector privatised	a. Lack of government remuneration system (-) leads to CP motivation (-), privatised	a. Enable support and advocacy of policy makers

Theme Focus group/interviews	Sub themes (unsafe use of opioids)	Focus group/interviews (key interpretation) ¹	Strategies shared by stakeholders
	Cost of intervention	pharmacies, non-supportive pharmacy managements (-)	b. Developing remuneration systems
	Pharmacist policy makers	b. Supportive government strategic focus to develop pharmacy services (+), inclusion of pharmacist policy makers (+)	c. Pharmacy policy makers advocacy for assortment of health budget
	Pharmacy workforce	a. Lack of CPs in medicine shops (-), CP missing in rural areas (-), lack of CP motivation (-), brain drain (-), lack of community pharmacy career progression or service structure (-), privatised sector and job insecurity (-), CP social stigma of being less competent/shopkeeper (-) b. Increased number of pharmacists due to increased number of pharmacy schools (+), increasing trend to join pharmacies, Schedule-G amendments facilitating CP hiring	Developing remuneration system, enhanced regulation, and enabling the support of pharmacy managements might help increasing the CP motivation and capability to deliver opioid service
	Quality assurance system	a. Lack of pharmacy regulator (-) b. Lack of check on regulators (-)	a. Improved regulatory system b. Advocacy and support of policy makers
	Lack of communication systems	a. Lack of communication doctor and CP (-), lack of medical and medication history (-), b. Government interest in developing digital health (+)	Develop Digital health systems

Appendix 9b: Case studies raw data observations, possible themes and its interpretation

Table 9.2: Reasons observed for unsafe use of opioids

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Themes/sub-themes (inductive analysis)	Observations in case study 1	Observations in case study 2	Observations in case study 3	Observations in case study 4	Observations in case study 5	Observations in case study 6	Perceived interpretation of relations/themes amongst all case studies	Interpretation of how an observed phenomenon can be overcome
Pharmacy factors causing unsafe use of opioids								
Reasons for opioid dispensing (unauthorised)	Allied staff focused on sale of medicines	Sale of medicines high, refusal NA because people had prescriptions	Sale of medicines high, refusal problematic by people/suspected manager	Sale of medicines high, refusal problematic by people/customer loyalty (brand focused)	No compromise acceptable on sale of medicines-dispensing took place in each interaction	Prime focus selling more/extra medicines	Business focused, customer happiness and loyalty focused	Implementation of schedule-G laws and strict regulation
Opioid medicine dispensing by dispensers	Dispensers did not have access to narcotic cabinet; however, they had access to warehouse, from where they would dispense opioids after CP left. (possible limitation-as researcher could not see what they usually	Dispensers did not have access to narcotic cabinet when CP was present. After she left, they had access and were observed to keep records/scans, which were handed over to the CP next day (pharmacist owner/manager)	Dispensers had access to the narcotic cabinet which was right besides the manager seat (billing counter) CP had no role in refusing opioids, however each person was told next time they will need a prescription.	Dispensers did not have the key to narcotic cabinet; however CP handed them the key every time, they will take out medicine, inform CP, hand prescription for scanning and record entering in narcotic register and go. During rush hours both CPs and staff were assessing	Dispensers had full access to opioids which were displayed on a shelf	Dispensers had full access to opioids which were displayed on a shelf	CPs in their presence might be able to enforce strict implementation of laws, however, the lack of autonomy to refuse opioids might be a challenge for CPs.	Implementation of schedule-G laws and strict regulation

	brought out of the warehouse as was already in a bag)			narcotic cabinet and keeping scans. No records written in narcotic register during those times				
Impact of patient load on CP/staff	Dispensers handling all patients, unless opioids. There is no rush hour so CPs can easily manage and update narcotic dispensing records with each prescription	Staff seemed adequate to handle incoming prescriptions	Staff seemed adequate to handle incoming prescriptions	Staff seemed inadequate to handle incoming prescriptions at rush hours. Day time CP was found on main counter and helped with dispensing all medications similar to allied staff. Narcotic records were not updated/kept during those hours in the register however each prescription was scanned and stamped by CP	Staff seemed adequate to handle incoming prescriptions	Cannot be inferred-single chemist	Lack of adequate staff in pharmacy might impact CP capability to engage with people and properly engage with them	Management support to hire adequate staff to handle prescriptions so CP might be able to counsel/educate/revise w/maintain record as applicable
IT/equipment	Manual systems despite having computer	Computer system used only for billing despite having software	Computer system used only for billing despite having software	having computer software/capacity and all computers were connected even	Pharmacist manager using for billing	Lack of minimum logistic-infrastructure	Advanced software systems are not being used to their full potential	Laws and policies implementation for a standardised pharmacy Government support and guidelines needed

	software/capacity			though pharmacy counter was far away			Softwares used for managing pharmacy had an inbuilt function of flagging up possible drug interactions/warnings/special checks however that feature was disabled and was being used to only process billing and stocking/dispensing	to help record equal record keeping in a universal format, which can be easily accessible Using software systems might help flag up possible drug interactions
People reluctant to go back to drs	Some were reluctant, some were not, cannot infer why	Mostly no referral information given, however next doctor review was reminded	Some were reluctant, some were not, cannot infer why	Some were reluctant, some were not. Those people who were reluctant thought this is another tactic for doctors to make money	Cannot be inferred as no referral	Cannot be inferred as no referral	Patient lack of reviews, lack of compliance or refusal of reviews. Preference towards self-medication	Patient counselling might help improve their review visits and adherence to drs advice
Telephonic activities (by staff/CP)	Medicine home delivery service available over phone. Staff asked to send the prescription over phone.	Not observed	Not observed	Not observed	Not observed	Not observed	Opioid medicines dispensed over phone call and bypassed the narcotic record maintenance	Proper laws and regulations need to be enforced

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	software/capacity			though pharmacy counter was far away			Softwares used for managing pharmacy had an inbuilt function of flagging up possible drug interactions/warning/special checks however that feature was disabled and was being used to only process billing and stocking/dispensing	to help record equal record keeping in a universal format, which can be easily accessible Using software systems might help flag up possible drug interactions
People reluctant to go back to drs	Some were reluctant, some were not, cannot infer why	Mostly no referral information given, however next doctor review was reminded	Some were reluctant, some were not, cannot infer why	Some were reluctant, some were not. Those people who were reluctant thought this is another tactic for doctors to make money	Cannot be inferred as no referral	Cannot be inferred as no referral	Patient lack of reviews, lack of compliance or refusal of reviews. Preference towards self-medication	Patient counselling might help improve their review visits and adherence to drs advice
Telephonic activities (by staff/CP)	Medicine home delivery service available over phone. Staff asked to send the prescription over phone.	Not observed	Not observed	Not observed	Not observed	Not observed	Opioid medicines dispensed over phone call and bypassed the narcotic record maintenance	Proper laws and regulations need to be enforced

				CP that such people mostly present at late pm times			reported by CPs that people with abuse/misuse intention of opioids arrived at late times. Usually dispensers are available at that times who have been observed to be more relaxed/non-compliant to follow schedule-G laws	control unauthorised dispensing (done by dispensers) by properly following laws
People with CNMP								
Doctor shopping	Many people found handing more than one prescription, acquired both prescriptions having opioids	People acquired medicine using one prescription, however insisted on more quantity of medicines	Many people found handing more than one prescription, acquired both prescriptions having opioids- Pharmacist intervened and counselled the patient to use only one at a time however dispensing done for all	Many people found handing more than one prescription, acquired both prescriptions having opioids. Pharmacist intervened and counselled the patient to use only one at a time. Did not refuse dispensing of duplicate	Many people found handing more than one prescription, acquired both prescriptions having opioids	Not observed as no prescriptions	People were observed to be acquiring opioids for the same patient name having similar opioid medicines simultaneously. With the conversations it can be inferred that people might even be using the two Dr medications at the same times.	Need digital systems to flag up medical/medication history CPs can help identify a possible interaction/duplication (while review) and counsel patients how to use their medications CPs can let prescribers know of a possible interaction/duplication happening due to multiple drs
Dose adjustments	Not observed	People asked more medication	People found that the medication	People were observed to ask CPs to adjust	Not observed	Not observed	Lack of patient medical history, laboratory profiles,	CPs should discuss/reach the

		than the ones prescribed	was not helping relieve pain so they asked how much medicine they can use. CPs recommended the maximum dose, however advised they need to talk to Dr, who might change their medicine. Person refused and said, 'he will add another medicine, I will do it myself'.	their doses, where they had enquired about using sedative medicines along with opioids, to which CP adjusted sometimes/mostly asked them to talk to drs. Most people remained reluctant to go back and pay the doctor fee again. Very high dose was observed where CP expressed their need to talk to their Dr and ask the doctor, however, mentioned many challenges as Dr would not like, he will ask who you are to question my authority as well as timings of the clinic which would have closed down.			medication records, other diseases information might be causing unintended prescribing errors/ADRs/avoidable side effects	doctors to help dose adjustments Having digital health systems can help CPs review the prescriptions properly
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People question about opioids	Few people were observed talking to CPs, however did not have specific questions about medicine, interested in how medicine will help with pain.	Not observed	Most people observed asking staff about dose, medicine to take with food, timings (from conversations it was inferred people have used a different brand before and had no idea it was same generic)	Most people observed asking staff about dose, medicine to take with food, timings (layman type information of prescription (barrier-hand writing of drs). With CP people were more aware (highly health literate, had met a CP before and sked drug interactions, side effects, drug allergies.	Most people observed asking staff about dose, duration	No questions observed	People in general did not ask anything specific to opioid medication e.g side effects, addiction or tolerance	Public awareness about opioids CPs have a potential role in educating people about opioids when people ask about medicine information
Persistent uncontrolled pain	Many people asked for strong medications to help with their persistent pain which was not responding to 'normal pain medicines'	Not observed any pain conversation	Many people asked for strong medications to help with their persistent pain	Many people asked for strong medications to help with their persistent pain. Health literate people took names of medicines and discussed with CP they had used this before with no effect. (pharmacist had to look in	Many people asked recommendation for multiple medicines to help with their persistent pain	People would ask a name or say "I need a good/strong painkiller".	Most people seem unsatisfied with their pain medications. It could not be inferred from the conversations if people had used opioids in past. People believe to think different brand name of medicine are actually different medicine despite	CPs have a potential role in educating people about opioids when people ask about medicine information Improving public awareness about medicines

				mobile/ask allied staff for brand names-skill deficiency)			having same generic which shows an overall lack of health literacy	
Lack of patient medical/medication history	People usually arrived without any prescription, usually asking for opioids, where CP asked what medicines, they had used was reliant on a person memory. People even mentioned the colour of box and medicines	Cannot be inferred	CP/staff did not ask any patient pas medication history or tried to establish any risk assessments.	CP before dispensing without prescription did ask people if they knew the side effects of the medications. Also asked if they are taking any medications for sleeping. All information relayed depended on a person health literacy and understanding of medicines/self-management	CP/staff did not ask past medication history	CP/staff did not ask past medication history	A lack of medication/medical history and dispensing/prescribing opioids leaves an opportunity for medication errors, side effects, poly pharmacy, therapeutic duplication, synergism etc	Developing digital systems might help CPs review and flag up high risk people
Public perception of opioids medication/perception of opioid as common OTC	Cannot be inferred if people knew they were using opioid analgesics	Cannot be inferred if people knew they were using opioid analgesics	Cannot be inferred if people knew they were using opioid analgesics	Some people knew they were using opioid painkillers and were concerned for addiction. Some people reading the box/leaflet also	Cannot be inferred if people knew they were asking for opioid analgesics	Cannot be inferred if people knew they were asking for opioid analgesics	Opioid medicine demand without a prescription was done. Upon refusal of opioids they asked why this medicine cannot be dispensed and	Public awareness CP educating/counselling people about medicines and their possible side effects when used unsupervised

Self-medication with opioids	Public demand medicines (no hospital clinic near posh residential)	Mostly had prescriptions only asked more quantity which was dispensed (up to 6 months without its indication on prescriptions) (near hospital)	Medicine demand/aggressive (commercial)	asked about addiction Medicines demand/aggressive (Near hospital/commercial)	Medicine demand no hospital clinic, commercial)	Medicines demand (no hospital clinic near average economy residential)	needed a prescription. It was evident majority people arriving without prescriptions were self-medicating with opioids	CP educating/counselling people about medicines and their possible side effects when used unsupervised CP making sure opioid dispensing is followed after a valid prescription and help implement laws and control unauthorised dispensing CP referring/guiding/convincing people for a visit to a doctor
Demand more medicine (non-adherent/non-compliant)	Cannot be inferred from	People asked for more medication, then the prescribed	Poly pharmacy, doctor shopping could be observed from their communication	Poly pharmacy, doctor shopping could be observed from their communication	Cannot be inferred	Cannot be inferred	People demand more medications. The reasons stated in their communication for this behaviour were that they lived far away, or they have a lot of pain and take medicines as required, somebody else also needs pain medicine	CP can help educate people about the possible harms and risks associated with increased dose CP can help ensure opioids are dispensed as per prescription

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Using more than 6 months old prescription (lack of review by Dr)	After CP refused dispensing, some people returned with old prescription. Upon refusal again, people got angry and manager had to intervene and ask CP to dispense. CP looked exasperated and demotivated.	Not observed, people usually coming from hospital clinic would stop to buy medicine	Prescriptions not visible/shared with researcher	Scanned prescription shared with me, observed at many instances- CP dispensed medication in some cases when people seemed genuine, or were politely asking	Lack of prescriptions in most cases, available prescriptions not visible/shared with researcher	Lack of prescription	People might be using an old prescription for repeatedly obtaining medicines which indicates a lack of Dr review and a potential self medication/self management	CP can guide people and refer them back for a review with a Dr before dispensing more medications
Literacy	Educated people seem to be interested in talking to a CP about medication	No communications recorded with CP	Most people seem interested to talk to CPs (cannot infer their education as seemed both)	Both educated/uneducated people seem interested to talk to CPs when told 'there was a medicine expert in the pharmacy'	Cannot be inferred	Cannot be inferred	Mostly a question beyond (dose, food, frequency) was offered to take to CP ("medicine doctor") which, then interested people to talk and discuss more about their medicine	Improved public awareness of CPs might influence people to talk to CPs and understand their medicine better which might help guide them to use their medications in an optimised manner, get frequent reviews and understand any possible side effects
People reluctant to go back to drs	Some were reluctant, some were not, cannot infer why	Mostly no referral information given, however next	Some were reluctant, some were not, cannot infer why	Some were reluctant, some were not. Those people who were reluctant thought this is	Cannot be inferred as no referral	Cannot be inferred as no referral	People might be reluctant to go back to drs and wanted to keep purchasing medicines either	Patient counselling might help improve their review visits and adherence to drs advice

		doctor review was reminded		another tactic for doctors to make money			without a prescription or wanted to use the prescription(some people got angry when CP stamped the prescription to indicate dispensing)	
Educated people asking/reading leaflet	yes	Not observed	yes	yes	Not observed	Not observed	Some people were observed to read medicine leaflets which indicates they want to understand/find out more about the medication	CPs can help provide them knowledge about their medicine or help answer their queries
Possible actions/activities undertaken by CPs that can help optimise the use of opioids								
Information given on side effects (by whom, what)/ CP knowledge to give advice	Information given on side effects in some cases	No information given on side effects; people also did not ask	Information given on side effects in some cases	Information given on side effects to some people	No information given on side effects; people also did not ask	No information given on side effects; people also did not ask	Where people asked, CPs were able to give medication information either directly(memory) or by looking it up on their mobile	Opioid medication knowledge can be given to people
Pharmacist intervention/activity which was done	Followed laws	Patient counselling/medicine dosage form changed, brand substitution	Patient counselling/medicine dosage form changed, brand substitution, dispensing, prescribing	Patient counselling/medicine dosage form changed, brand substitution, dispensing, prescribing	No CP patient engagement	Not observed	CPs might be able to counsel, provide medicine information, identify pharmacy, help guide people for regular reviews and educate people about possible side	Developing mandated CP opioid optimisation service

							effects of medications	
Reduction in therapeutic duplication	Not observed (business focussed)	Not observed	Observed (management supportive)	Observed (management supportive)	Not observed	More medicines added in most cases (OTC)	CPs could recognise poly pharmacy with the same medicine within/across prescriptions	Might be able to reduce/refuse unnecessary duplications especially when there are two or more prescriptions and help educate people
Therapeutic substitution	Was done by pharmacy technicians based on availability of medicine- did not lose a potential sale	Not observed	Was done by pharmacy technicians based on availability of medicine- did not lose a potential sale	Was done by pharmacy technicians/CPs based on availability of medicine- did not lose a potential sale	Was done by pharmacy technicians based on request of people (low price)-did not lose a potential sale/customer	Was done by chemist based on availability of medicine, did not lose a potential sale	Alternates of medicines were offered, not just brand substitutions but also generic substitutions. CP and allied staff are not authorised to prescribe/amend	Sufficient knowledge and skills would be required for therapeutic/brand substitutions required as per patient request- would need legislation to authorise this action New legislation would be required to allow CPs to prescribe
OTC added	OTC + prescription only analgesics without prescription (in absence of CP)	OTC analgesic added sometimes	OTC + prescription only analgesics without prescription	OTC + prescription only analgesics without prescription	OTC + prescription only analgesics without prescription	OTC + prescription only analgesics without prescription		CPs can help overcome illegal prescribing and help with controlled opioid dispensing by following laws and maintaining a proper dispensing record
CP Risk assessment/ Information asked	No past medication/ medical history taken		Patient brief medication history especially in cases having two prescriptions/	Patient brief medication history especially in cases having two prescriptions/pe	Patient past history obtained sometimes (patient counselling)	Not observed	With lack of medication history/ medical history it will be really difficult for CPs to make a judgement on the	CPs might be able to identify therapeutic duplication, help cheaper substitutions to make it budget friendly, identify polypharmacy and able

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			or when people shared they are having persistent pain	resistant pain/drug interactions asked			appropriateness of the prescribed medication.	to identify drug-drug interaction within the same prescription
CP Advice offered	Referral offered to a Dr No medicine advice given except dose	Offered adherence, dose mostly, OTC added	patient counselling done on dose, frequency, adherence, repeat dose, missed dose	patient counselling done on dose, frequency, adherence, repeat dose, missed dose, side effects (drowsiness)	CP did not engage with patients	No engagement of CP	CPs can possibly provide advice to patients about medicine, their disease or simple what could be the next step in their course of action	Patient education and counselling
Record keeping	record maintained by CP-outside CP hours no record	Record maintained by CPs and off hours by dispensers	record not maintained by CP-staff- does claim has a narcotic register, was not seen	Record maintained, narcotic stamping, faked records	Record not maintained	Record not maintained	CP maintaining opioid dispensing records is variable and was found to be dependent on pharmacy management, location, and the chances of regulatory visits	Help maintain legal requirements and implement new laws
Narcotic dispensing stamp	no	no	Says has a stamp, never seen it used	Prescription stamping done with proper remaining amount; however, some people were observed to be very upset about this	no	no	CP could possibly help enforce opioid dispensing with prescription and help follow doctors' advice	Help control unnecessary/overuse of opioids by people by dispensing the prescribed amount

Suspected opioid abuse by CP	Cannot be inferred	Cannot be inferred	Refused or dispensed minimal to aggressive people	Everyday an average 2 to 3 people came at late pm times to ask medicines without a prescription	Cannot be inferred	Cannot be inferred	CPs might be able to identify people with aberrant use of opioids	CPs can ensure opioids are dispensed only after a valid prescription and help educate people to be aware of potential side effects
Stop dispensers prescribing	Unauthorised opioid prescribing (by allied staff)	No unauthorised opioid prescribing of opioids OTC only added	Unauthorised opioid prescribing by CP/allied staff	Unauthorised prescribing by CP/allied staff	Unauthorised opioid prescribing by CP/allied staff	Unauthorised opioid prescribing by chemist	Opioid prescribing and unauthorised dispensing was observed. The effect of presence of CP was variable and were bypassed in most organisations due to management intention to make potential sales and keep customers happy	CPs if supported properly with law, might be able to enforce schedule-G laws
Mention of CAM/referral to CAM	Observed in 3 instances	Cannot be inferred	Recommendation and usually herbal supplements sold out along with opioids	Cannot be inferred, although has the capacity for compounding too	Cannot be inferred	Cannot be inferred	CPs was observed to recommend herbal and CAM treatments to people	
Advice for CBT/physio/dentist /migraine specialist/ Referral to drs	Referred to physiotherapist for knee pain	Referred to physiotherapy department of near by hospital (knee replacement patients with	Herbal supplements advised	Upon discussion with patient, CP said to use migraine medicines for pain. In another	Medications, combo prescribed	Not observed any advice	CPs were able to guide people according to their specific needs and give them information about possible treatment	CPs might offer alternative therapies/treatments/referrals information to people with CNMP

		chronic pain)		patient, having uncontrolled pain CP advised to visit a pain specialist.			places/services which might help with their condition	CPs become a source of information
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Please note: All the blue colour texts show possible actions that can be undertaken specifically by CPs which help optimise the use of opioids by overcoming existing barriers contributing to unsafe use of opioids

Table xx: Barriers, facilitators and strategies for CPs to help implement future services

Themes/sub-themes (inductive analysis)	Observations in case study 1	Observations in case study 2	Observations in case study 3	Observations in case study 4	Observations in case study 5	Observations in case study 6	Perceived interpretation of relations	Interpretation of how an observed phenomenon can be overcome
Autonomy to refuse medicines (laws implementation)	CP strictly following laws, however after CP goes, the staff on managers instruction dispenses opioids (from stocks-not	CPs strictly following laws of dispensing medicines on prescription. Pharmacist manager supportive of CP activity	Manager supportive of implementation of laws, male CP following strictly, however female CPs dispenses to people	Manager full supportive however implementation of law weak, narcotics dispensed both with and without prescription. No	CP is manager, opioids dispensed without prescription by salesperson	No role of CP in implementation of law. Chemist (owner) dispensing without prescriptions/no records/no narcotic register	Whether CP can refuse opioid unauthorised dispensing is dependent on management/manager	improving legislation/strict drug inspector visits

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	narcotic cabinet)		perceived in need (old age)	narcotic register entries done during this period				Pharmacy management support
dispensing medicines	No dispensing-pharmacist attitude	dispensing Pharmacist+ allied staff	dispensing Pharmacist+ allied staff	dispensing Pharmacist+ allied staff	dispensing Pharmacist+ allied staff	Dispensing only allied staff	CP needs allied staff to help with opioid dispensing in rush hours however, each person should be offered an opportunity to speak to CP	Clearly defined internal job descriptions
People access/approach to CPs (direct/reliant on staff)	CP located on side, not directly approachable (staff brings people)	CP can be directly approached although located on side	CP can be directly approached as mostly remains on front counter	CP can be directly approached, although located on side (staff usually brings people)	CP can be directly approached however perceived people lack awareness/there is no indication that he is a CP	CP not available in pharmacy, even when available only does stocks/procurement	CPs are usually found at remote locations due to either own reasons or management decision or narcotic cabinet, so people have to be guided/brought to CPs, so support of allied staff is necessary. However their support might be reliant on their interpersonal relationship or management instructions	Better CP signposting, visibility, support staff support, CP uniform/badge, CP counselling counter might all help improve visibility and provide a place for CP-public interaction

								n for opioids
Positioning of pharmacist	Corner, due to narcotic cabinet, due to lack of allied staff/manager relationships	Narcotic cabinet	Narcotic cabinet near the manager. CP mostly found on counter helping with dispensing of medicines. No female gender barrier felt.	CP acting as a manager, that's why stationed at the back at a special counter. Narcotic cabinet is in visible distance, however staff accesses it every time.	CP owner so found at the billing counter	Cannot be inferred as CP only stays for a short time per week	Because of narcotic controlled dispensing, opioids are found in narcotic cabinets, which are at a side of a pharmacy and CPs are usually stationed near them to help facilitate dispensing/record keeping	No matter where CPs are stationed, there can be internal changes/SOPs where people can be given a chance to interact with CPs. Requires management and allied support staff
Visibility of CP	Low visibility/interaction (demotivated CP, staff issues)	Wears uniform makes them distinct from staff	No signposting/uniform/badge however good visibility of CP (pronounced due to good relationship with	visibility CP (pronounced-pharmacist manager, chain pharmacy highlighting CP(counter))	No CP specific distinction	No CP visibility (owner pharmacy technician, low chances of drug regulator, part time pharmacist)	Visibility of CP is pronounced where CPs are motivated, or in pharmacies where management want to highlight the role of CPs especially for improved customer	Counselling counter Uniform/badge Which requires

			staff/supportive manager)				satisfaction, brand recognition.	management and allied support staff
Self-medication by people-impact on CP trying to stop	People get angry	Not observed	People aggressive	Aggressive people	Not observed	Not observed	CP when tried to stop/guide people against self-medication or referred to drs, people due to lack of awareness of CP roles, inconvenience of going back to drs, economic and cultural norms of having always gotten a medicine were reluctant and refused to comply. This also resulted in managers getting offended because was perceived to decrease customer satisfaction as well as a declined opioid sale. Even allied staff dispensing of opioids from stock was observed (bypassed CP implementing schedule-G)-no check and balance on pharmacies	Improving public awareness
Weak implementation of	Not following laws because of manager	Following laws because of manager/chances	Weak implementation (no records)	Following laws because of manager/chance	Not following laws because of manager	Not following laws because of manager	Lack of regulatory checks, less chances of regulators arriving	Better implementation

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laws/policies (reason)		of arrival of drug inspector more	properly maintained) although chances of arrival of drug inspector moderate	es of arrival of drug inspector more	friendship with local drug inspector		allowed pharmacies to operationalise within business/customer loyalty perspectives(result unauthorised sale of opioids)	of laws and policies Increase regulator workforce Better regulatory systems
CP owners' impact on implementation of laws	Following laws against manager support has resulted in CP demotivation, broken relationship, friction between staff	Not observed	Good relationship which might have motivated CP to follow organisational aim of following medicine sales (CP relaxed to follow laws)	Good relationship, full support to CP to follow implementation of laws (organisation focus is to project proper pharmacy)	CP owner but focussed on business/customer loyalty-weak implementation	CP not engaged in dispensing	CP managers can either follow laws if it helps them be more credible than neighbouring pharmacies (reputed brands) or they can choose to bypass especially when there is less changes of drug arriving/possible friendship with drug inspector	CP lack autonomy to refuse medication on or follow laws or give patient services unless CP management will provide them a supportive environment

CP-pt engagement (yes/no why)	CP reluctant to public queries (overall non-motivated due to being alienated by management/allied staff behaviour)	Could not infer	Well established CP-Public engagement being used as a promotional technique to get more customers, improve customer loyalty, improve sales People interest to know medicines /talk to a CP was found to be enabling this	Public question welcomed. CP-Public engagement being used as a promotional technique to get more brand recognition amongst other competitors to get more customers improve customer loyalty, improve sales People interest to know medicines /talk to a CP was found to be enabling this	No patient centric CP engagement observed however CP was observed to be a good businessman trying to facilitate customer demand (filling prescriptions/prescribing medicines/no refusal on poly pharmacy)	CP kept at side from any patient activity. No patient engagement observed (CP license was the reason for hiring CP)	CP engagement depends upon the management behaviour for CP to facilitate them for the interaction by providing support (allied staff told to take people to CP, CP provided less work load, CP provided a separate place to talk to people, people interest/motivation/a awareness/health literacy impacting the CP-Pt engagement)	Management support Public awareness and acceptance CP improved motivation
Organization focus	Customer focused/ business/ profit making	Cannot infer	Customer loyalty focused/ business/ competing within market	Brand reputation focused	Customer loyalty focused/ establishing business within a competitive market	Profit making	Organisation focus/ manager focus influences what kind of environment will CPs get which will either support them to follow laws n deliver service or vice versa	
Display of new laws/explanation	No display, but explanation giving while refusing opioids	Not displayed	No display, but explanation giving while refusing opioids	Displayed and explanation also given while refusing opioids	Not displayed	Not displayed	Lack of people's awareness of laws creates problems for CP while refusing	Increasing medication

tion to people							opioids as part of implementing a mandatory requirement	awareness, medication laws awareness, CP role awareness might help with acceptance of new legislation and CP advice under that legislation
Avoiding problematic/shouting customers (skill/influence on implementation of law)-why	Dispensing still refused, which probably had caused relationship breakdown with the manager	Not observed	Dispensing done because focus of organisation was customer happiness to ensure they come here for medication	People say "other pharmacies are not making their life miserable", a possible hint to take their business elsewhere. Thus dispensing done with minimal medicine quantity (we are out of stock) as not to upset	Not observed	Not observed	CP management support/rules depends on whether CPs can strictly implement legislation	Improve public awareness Management support Improve regulation to inspire all pharmacists to follow

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				customer (to avoid awkwardness for CP, CP tasked for managing the pharmacy)				laws and help in getting management support
Pharmacist counter	No separate counter	No separate counter	No separate counter	Separate counter	Not observed	Not observed	Lack of CP separate counter might impact three aspects; visibility of CP, a separate place to talk to people to avoid influences of other dispensing going on and holding up a line, and to maintain patient confidentiality	Enabling smooth CP-pt interaction requires management support to assign CP counters /place to talk to people, have adequate staff to take care of other dispensing activities
Hiring of CP	Labelling License displayed/schedule-G displayed/narcotic	License displayed/schedule-G displayed/narcotic cabinet labelled	License displayed narcotic cabinet labelled	License displayed/schedule-G displayed/narcotic	License displayed/narcotic cabinet labelled	License displayed only	The hiring of CPs was observed because of their license and the new law that opioids	Improved regulation

	tic cabinet labelled			tic cabinet labelled			can be dispensed only in the presence of CP	Cp supportive laws/policies will enable service implementation
Narcotic cabinet	yes	yes	yes	yes	no	no	Weak implementation of law observed where chances of drug regulator arriving was low	Better regulation Implementation of laws and policies
Pharmacist relationship with allied staff	Not good as they perceive CPs has attitude, lack of skills, a lot of friction (manager has not tried to intervene or create internal rules)	No apparent relationship observed each one working within their own circles and supporting daily dispensing/procurement/record maintenance (internal rules clear)	Good relationship, both supportive towards each other towards daily tasks, clearly defined internal roles	Good relationship, clearly defined internal roles	Cp owner, keeps a hierarchy, relationship of employer/staff	Not observed	CPs need to rely on allied staff to get their support for CP-pt interaction by bringing/guiding/motivating people to talk to CPs, handling dispensing while CP are busy with people	Management support in clearly defining the internal roles and hierarchies helps with minimising friction
Opioid drug procurement	Allied staff	Allied staff	Allied staff+ CP	Allied staff+ CP	CP	CP	CPs (especially females) need help from allied staff with drug procurement,	Management support in clearly

							transportation from warehouse, shelving and dispensing	defining the internal roles and hierarchies helps with minimising friction Internal quality assurance and audit systems
Drug shelving	Allied staff	Allied staff	Allied staff	Allied staff	Allied staff	Chemist	CPs (especially females) need help from allied staff with drug procurement, transportation from warehouse, shelving and dispensing	Management support in clearly defining the internal roles and hierarchies helps with minimising friction
Manager	Relationship with manager broken (impact seen in the way allied staff was	Could not observe however had a pharmacist manager(owner)	Relationship with manager good (non-pharmacist manager)	Pharmacist acting as pharmacy branch manager, all	Pharmacist himself manager	Chemist manager	Implementation of laws/service/activities of CPs inside pharmacy are reliant on management, which is	CP management support vital to

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	behaving/talking about CP)	who never came during observation		branch manager also a CP- good relationship observed			usually derived from organisational aim	enable/provide Cps supportive environments to follow laws and deliver service
Groceries/other items	Yes (groceries)	Just a fridge with drinks	Yes (beauty, nutrition and cosmetics)	Yes but in another section having different staff	no	no	Having separate staff to handle dispensing medications and selling other items helps assign proper time and attention to each person	Implementation of laws and policies Management support
Public knowledge/awareness about CP	Public awareness about CP (due to uniform/badge)	Was not observed if anyone asked about CP	Public awareness about CP (due to uniform/badge/past interaction)	Public awareness about CP (due to pharmacist counter/past interaction)	Was not observed if anyone asked about CP	Was not observed if anyone asked about CP	Related to visibility of CP in the pharmacy Public health literacy Past experience/knowledge of people	Improved public awareness
Social behaviour of people	Arrive at front counters, usually talk to dispenser, buy meds and leave	Arrive at front counters, usually talk to person who is free, buy meds and leave	Arrive at front counters, usually talk to person who is free, buy meds and leave. People get random chance to talk to CPs as	Arrive at front counters, usually talk to person who is free, buy meds and leave/only brought to CPs when people ask or do not	Arrive at front counters, usually talk to person who is free, buy meds and leave	Only one person available to talk, one counter	Public health literacy and past experience/knowledge of people influences whether they will talk to CPs, accept their advice	Improved public awareness Allied staff support

			she spends half time o front counters (but was not found updating narcotic records)	have prescription (strictly updating narcotic records)			Allied staff behaviour to guide/refute people towards/from CPs Cps professional behaviour, knowledge and attitude can influence people behaviour	
People approaching CPs	Sometimes when asked for a CP	Not specifically	yes	yes	Not specifically	No CP available most times	Public health literacy and past experience/knowledge of people about CPs	Improved public awareness
Capacity for communication with drs	Yes (internal system, IT, phone)	yes	yes	yes	no	no	Sometimes prescriptions require clarification from doctors, however there are no existing systems or even culture of CP contacting the dr	Developing digital health systems
Dose adjustments require communication with drs	Not observed	People asked more medication than the ones prescribed	People found that the medication was not helping relive pain so they asked how much medicine they can use. CPs recommended the maximum dose, however advised they need to talk to	People were observed to ask CPs to adjust their doses, where they had enquired about using sedative medicines along with opioids, to which CP adjusted sometimes/mostly asked them to talk to drs.	Not observed	Not observed	Lack of patient medical history, laboratory profiles, medication records, other diseases information might be causing unintended prescribing errors/ADRs/avoidable side effects Cps anticipate drs reluctance to talk to drs	Interdisciplinary care models and strong legislation Having digital health systems can help

			Dr, who might change their medicine. Person refused and said, 'he will add another medicine, I will do it myself'.	Most people remained reluctant to go back and pay the doctor fee again. Very high dose was observed where CP expressed their need to talk to their Dr and ask the doctor, however, mentioned many challenges as Dr would not like, he will ask who you are to question my authority as well as timings of the clinic which would have closed down.				Cps review the prescriptions properly/also help communicate with drs
Pharmacy technicians feel entitled to dispensing	yes	yes	yes	yes	yes	Only one person	Allied staff job description is to dispense medications	Clearly defined internal rules and SOPs help with role distinction

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								between allied staff and CP
Skills of technicians	Good dispensing behaviour and knowledge about medications/brands/shelve place/alternate brands	Professional behaviour, however, not friendly. Good knowledge about medications/brands/shelve place/alternate brands	Good dispensing behaviour and knowledge about medications/brands/shelve place/alternate brands	Good dispensing behaviour and knowledge about medications/brands/shelve place/alternate brands	Good dispensing behaviour and knowledge about medications/brands/shelve place/alternate brands	Good dispensing behaviour and knowledge about medications/brands/shelve place/alternate brands	Allied staff was observed to be welcoming to every person and quickly dispensing medication. Their people skills, knowledge of medication places (as shelving done by them), and knowledge of brand names gives them confidence/motivation to deal with public and helps them quickly dispense and inspire public confidence	Appropriate skills, knowledge and training
Skills of pharmacists	Lack people skills, not approachable by people, has to see mobile for every drug query, asks brand names from allied staff	Cannot infer	Good people skills, good knowledge, checks mobile sometimes	Good people skills, good knowledge, asks brand names from allied staff, checks mobile for answering patient queries	Good people skills, knowledge skills not demonstrated however prescribing done without consulting mobile	Only involved in procurement so cannot infer	CPs currently were observed to lack skills required for opioid related counselling (clinical skills, brand name knowledge skills, opioid medication information) CPs lack of motivation to engage/welcome people's medication queries was perceived to be linked to their knowledge and skills	Appropriate CP skills, knowledge and training

CP (personal) reasons which could impact service provision:								
Pharmacist motivation/reasons	Non-motivated due to lack of support of manager for implementation of laws (refusing opioids) and allied staff	Cannot be inferred	CP motivated, happy, proactive which reflects in her patient engagement, behaviour due to supportive friendly environment. Manager seems to appreciate her patient counselling (which makes customer satisfied and they were observed to give positive feedback to manager while billing, which motivates her to engage and help more people	CP motivated, happy, proactive- due to good relationship with staff, clearly defined roles (due to supportive manager)- happy to be the pharmacy in-charge	CP owner, seems motivated to improve customer loyalty	CP demotivated- because his hiring/role was only because of his license and job included once a week procure/audit stocks, less salary- lack of patient engagement	CP motivation might be dependant upon the respect and treatment given to them inside pharmacies by the management and staff	Supportive management might help with CP motivation to deliver proper service

gender	Gender impact pronounced barrier for pt interaction	Gender impact (not pronounced)	Gender impact (not pronounced)	NA	NA	NA	The impact of female gender itself was not pronounced however, how management treats women, might be a source of motivation or demotivation for CPs	CP management might support the needs of individual pharmacists and enable them to overcome any gender related barriers
Outside factors affecting pharmacy:								
Locality impact on manager	Chances of regulator arriving less, dispensers dispense opioids from stock, CPs cannot be found after official hours	Chances of regulator arriving medium, pharmacy near hospitals, laws properly followed, Cps not found outside official hours	Drug regulator chances moderate, lack of implementation of schedule-G, Cps not found after official hours	Drug regulator chances high, manager supports proper implementation of schedule-G, where Cp does unauthorised dispensing (to help or in pressure of aggressive people) makes up by faking	Cannot be inferred	Drug regulator chances low (say never had an inspector visit), lack of implementation of schedule-G, lack of CP presence	The arrival of regulator influences how management/manager follows laws in the pharmacy (both sale of opioids, facilitating CPs to follow laws)	Enhanced regulation Strict laws and implementation

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				records. CPs found around the clock, however their hiring is related to brand reputation and not laws				
Patient time/impact on patient engagement	Ample parking, people not in rush, when knew CP was there, did talk	Cannot be inferred	People were observed not to be in a hurry	Insufficient parking, very crowded, people were almost always in a rush till 9 pm. In later hours people were more relaxed.	Could not be inferred, had no assigned parking. Shop was on main road.	Could not be observed no parking	Infrastructure like adequate parking, ample floor space, number of staff available to receive people might impact a CP-patient interaction	Standardised pharmacy requirements should be met according to laws Regulation Patient awareness
Locality impact on people	People coming from posh residential area sometimes had a prescription, people rush equal at all times	People coming near a private hospital have prescriptions, usually arrive in clinic running times, which translates into patient rush	Cannot be inferred	People coming near from a government hospital are usually in the am times, with most people arriving during OPD times, average dispensing time	Cannot be inferred	People from an average economical area usually did not have prescriptions. Medicine name usually written on a piece of paper. Mostly young boys	If people are coming from a hospital they had a prescription which infers, people directly go to pharmacies outside the hospitals, which translates into patient burden on specific times	

				reduced, more dispensers, CPs also supports dispensing to support		coming to get medicines, patient rush very low		
Learning resources/training locally available/ CP knowledge to give advice (whether used a resource to look up)	Mobile for information	Information mostly remembered-no technical questions	Mobile for information	Information mostly remembered/used mobile for drug interaction queries	General information	Prescribing done when asked information	CPs were searching for even (general) medication information using their personal devices. CP searched drug interactions too (advanced)	Pharmacy management support required to provide resources to CPs