Assessment of pain domain, quality of life, management and pharmacist-led intervention among chronic pain patients in Western Nepal

Report Submitted to

Nepal Health Research Council (NHRC)

Ram Shah Path

Kathmandu, Nepal

Submitted by

Parbati Thapa

ERB Registration Number 211/2020

Table of content

1 General overview

1.1 Chronic Pain

Chronic pain is a major public health problem characterized by pain that persists beyond the normal tissue healing time of 3 months or more.[1, 2] The International Association for the Study of Pain estimates that 1 in 5 patients experience pain, and 1 in 10 patients are diagnosed with chronic pain yearly, and is one of the most common reasons for seeking medical care.[3] Chronic pain affects patients' physical performance, reducing their physical activity and even causing disability, affecting other aspects of their daily activity.[4, 5] It often affects professional life as absenteeism, change of job responsibilities, or even losing a job is common among chronic pain patients resulting reduce productivity.[6] Likewise, chronic pain affects patients' social interactions restricting their leisure activities and social contacts.[7] All these factors ultimately result in a significant social and economic burden.[5] The impact of pain on economies is enormous and estimated to cost between $560 to $635 billion in the United States alone in 2008.[8]

The global prevalence of chronic pain ranges from 10.1 to 55.2 %. [9, 10] In the United States, the prevalence of chronic pain was reported as 20.4%,[11] while it was 18.4 in Germany,[12] 21.5% in Hongkong,[13] 24 % in Norway,[14] and 19% in European countries.[15] In low-middle-income counties (LMICs), 30% of adults and 56% of the elderly have chronic pain. [16] In Nepal, it was reported to be between 48-50%, while it is estimated to be between 24% and 41% in India[17] while its prevalence in China is 42.2%,[17] 10.4% in the Philippines, [18] and 38.9% in Iran.[19] The prevalence of pain varies between countries and is influenced by several factors.

Chronic pain is a multifaceted condition influenced by various physical and psychological factors.[20] Chronic pain is more prevalent among the population of advanced age and females. Women have lower pain thresholds and tolerance and are more likely to experience intensity and unpleasantness with pain. Multiple morbidities with advanced age are more likely to have the noxious stimuli that can trigger chronic pain.[2] Persistent chronic pain alters the physical function of individuals.[21] Deterioration in physical activities with chronic pain was reported among 31.7 to 50 % of the patients.[22, 23] Intensity, duration, and location of chronic pain also influence patients' physical activity. It gets worse with the pain severity leading to diminished activity and disability.[24]

Altered physical function and disability among chronic pain patients may predispose depression.[25] Depression and chronic pain co-exist and are reported to be prevalent among 60% of the patients.[26] Chronic pain and depression have a bidirectional relationship, Chronic pain and depression have a bidirectional relationship, and both might be risk factors for each other.[26, 27] Depression often goes unrecognized and remains untreated among chronic patients contributing to mental health issues and reduced quality of life.[5, 28] Identifying and treating depression is crucial in managing chronic pain, as chronic pain patients with depressive symptoms report higher pain, activity interference, and more pain behavior.[29] Patient self-reported questionnaires for depression can be used as a screening tool as the accuracy of detecting depression is evident even when used by nonpsychiatric physicians.[30] Figure 1.1.1 depicts the biopsychosocial model of pain and consequences on the quality of life.

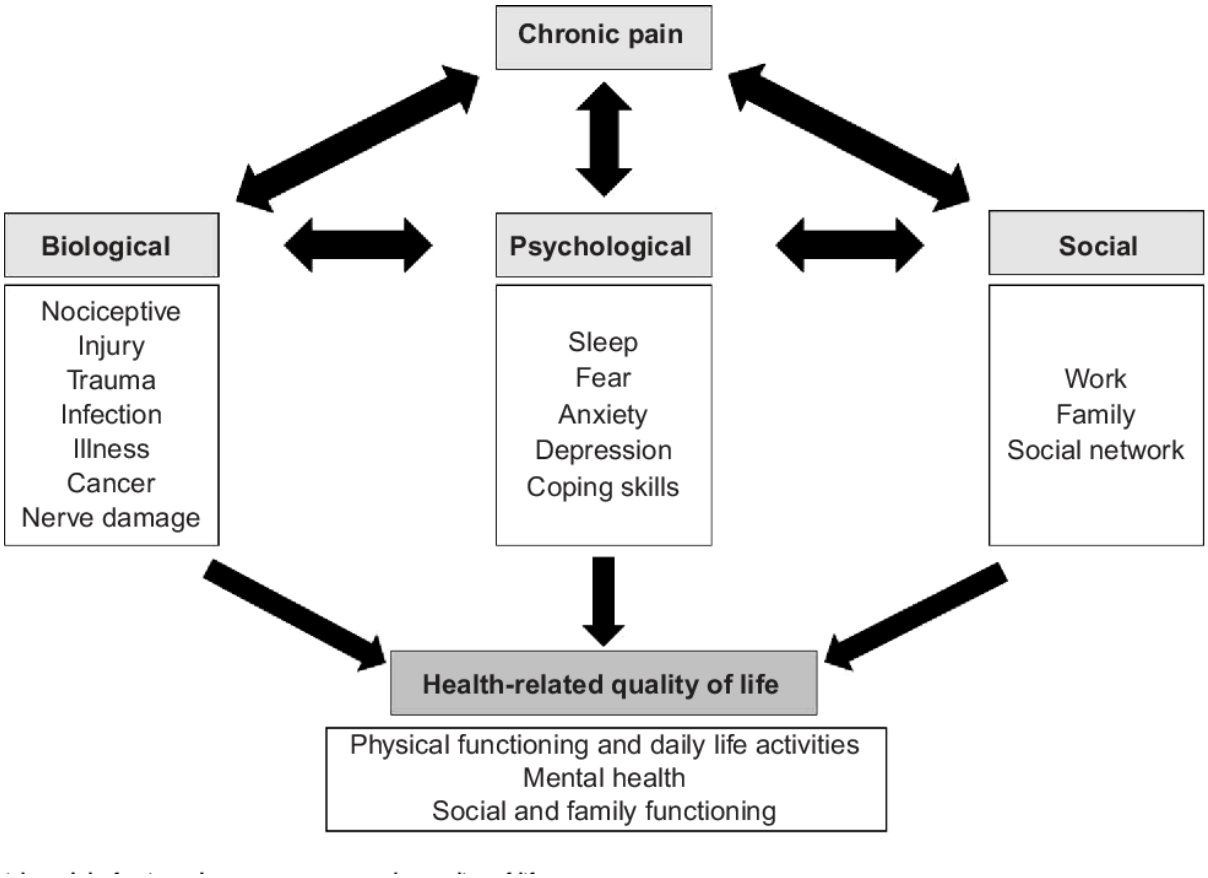

Figure 1.1 The biopsychosocial model of pain and consequences on the quality of life [5]

1.2 Chronic pain assessment and management

Chronic pain significantly affects individuals' physical, psychological, and social life. Chronic pain is complex and challenging to assess, as the experience of it varies between individuals.[31] A comprehensive person-centered assessment of the cause and effects of pain and possible management strategies, including self-management, is crucial.[32] Standardized self-reporting assessment tools effectively evaluate pain intensity, effects of pain on an individual's quality of life, functional abilities, and emotional distress.[33] The clinical guidelines for managing chronic pain recommend a multimodal approach combining pharmacological and non-pharmacological treatment. Its primary recommendation is assessing and planning care, self-management support, pharmacological management, psychological intervention, and physical therapy.[34]

Pharmacological management includes nonopioid and opioid analgesics, corticosteroids, antidepressants, anticonvulsants, and muscle relaxants.[35] Paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), or opiates are used individually or as a combination therapy for chronic pain management.[36] Topical formulations are also used for the management of chronic pain. Topical NSAIDs for musculoskeletal pain and who cannot tolerate oral NSAIDs, topical capsaicin for neuropathic pain when the first-line pharmacological treatment is ineffective.[34] Additionally, the use of antiepileptic drugs like gabapentin is effective in the treatment of neuropathic pain. Pregabalin is also used for neuropathic pain if first and second-line treatments are ineffective. Antidepressants, serotonin reuptake inhibitors, and tricyclic antidepressants are effective in the management of chronic pain as well as for the management of a prevailing condition like depression. However, patients with antidepressants should be regularly reviewed to confirm that the benefits outweigh the risk.[34]

Nonpharmacological treatment includes psychological therapies, mindfulness, exercise, physical therapy, osteopathic and spinal manipulation, and acupuncture.[37] Psychological intervention helps patients with chronic pain to increase their coping skills and improve their quality of life. These interventions aim to achieve increased self-management behavioral change, and cognitive change to manage pain rather than focusing on eliminating the pain locus.[38] Cognitive behavioral therapy, acceptance-based interventions, and psychophysiological techniques are examples of psychological interventions that have proven effective and promising in managing chronic pain.[39, 40] Psychological intervention improves patients' ability to control their pain and enables them to live as normal as possible

despite the pain. The skill learned will make patients more responsible and allow them to actively participate in managing their illness.[38]

Physical therapies, including manual therapy, exercise, and electric therapy, are also recommended for chronic pain management.[34] Guidelines on the management of chronic pain recommendations on the use of exercise and exercise therapies regardless of their form in the management of chronic pain. Individuals can easily adapt to physical activity and exercise and help themselves. It is assumed to have minimal adverse effects, no interactions with medication, and risk of abuse. However, simply giving an individual advice to exercise is insufficient to bring about the change, so a supervised and structural intervention might be required.[41] Integrating pharmacological and non-pharmacological interventions on an individualized based could be a practical approach to managing chronic pain. Figure 1.1.2 details the broad to specific chronic condition management, related to chronic pain as well.

The WHO analgesic ladder strategy is also used to manage chronic non-cancer and acute pain after several changes to the original one focused on cancer pain.[42] The original analgesic ladder has three steps, with the first step including nonopioids like NSAIDs or acetaminophen for mild pain. The second step includes weak opioids for moderate pain, and the third includes potent opioids with or without non-opioid analgesics and severe pain. Adjuvant medications are added when needed in each step.[43] A new analgesic ladder has been developed, with fourth steps including intervention and invasive procedure.[44]

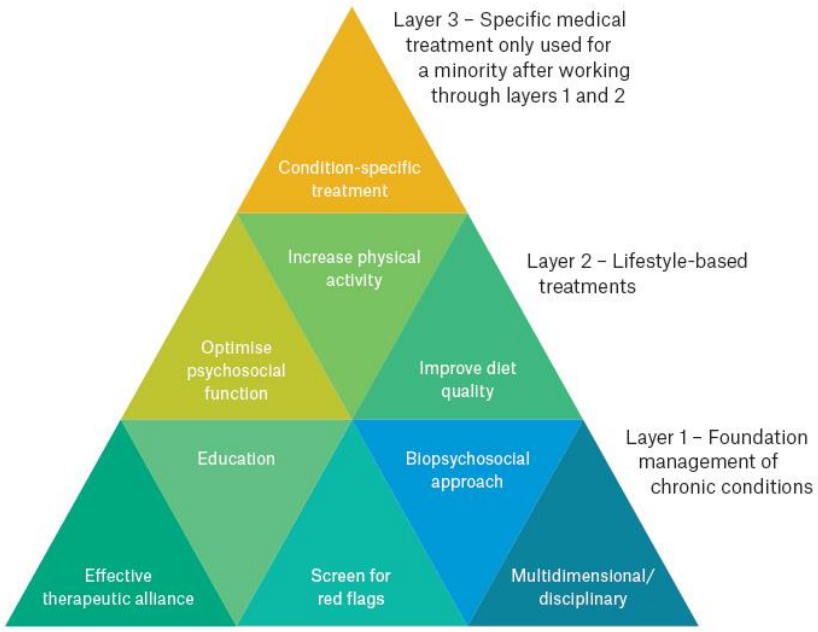

Figure 1.1.2 Reconceptualizing chronic condition management: Broad to specific [45]

1.3 Challenges in chronic pain management

Pain management is challenging and stressful as the complete elimination of pain is rarely attainable. Chronic pain generates psychological and social problems that are difficult for the physician and the patient.[46] Resource constraints, restriction on opioids, variation in the care, lack of communication, lack of proper assessment, inadequate knowledge, experience among staff, lack of time, perception about pain and therapeutic expectation and cost are some of the barriers for health care professionals and patients for effective pain management.[47, 48] These barriers are common in both High-Income and LMICs but are compounded by resource constraints in LMICs. Additionally, scarce data and research from LMICs in the areas of pain impose and important barrier to improving pain management in these countries.[49]

Advocacy, improving treatment availability, and education could improve pain management in LMICs. Advocacy is possible through the collaboration between national and local authorities to develop the guidelines and prioritize monitoring the impact of the intervention on pain management.[49] Improving access to pain care facilities and treatment options could improve pain management. Additionally, educating healthcare professionals as well as patients is important. Healthcare professionals should have adequate knowledge, positive attitudes, and efficient clinical decision-making skills about pain for effective management.[50] However, they have low to good knowledge of pain management, as reported by different studies.[51-53] Continuous professional development (CPD) pain management training could enhance healthcare professionals' knowledge and improve access to evidence-based pain care.[54]

Patient participation in the medical decision-making process also improves pain management.[55] Educating patients on self-management strategies is beneficial as they know skills and techniques that may help them cope when aiming to manage medical, emotional, cognitive, and behavioral facets accompanying their pain.[56] Education can be delivered in several ways: via media, leaflets, videos, face-to-face counseling, or a web-based application.[57] Applying a multimodal approach with patient active participation will allow to manage the pain holistically.[58]

1.4 Pharmacist in chronic pain management

Pharmacists are accessible healthcare team members who can provide services to patients with chronic pain and comorbidities.[59] The pharmacist has a role in different aspects of chronic pain management. The primary role is medication management, where they can provide pharmaceutical care, gather the best possible medication history, select medication and dosing, check for drug interaction, monitor and follow up, deprescribe, and discontinue.[60-62] Pharmacists can also provide services to chronic pain patients with opioid use disorder, where they observe doses, monitor for missed doses, adverse effects, and toxicity, and communicate essential treatment issues.[59] Figure 1.1.4 details on the consideration of patients factor for medications selection. Pharmacists' role in patient education and self-management is inevitable, where they help patients to adopt strategies to manage their symptoms, treatments better, and the physical and psychological challenges of their pain experience.[63-65] Pharmacist role in the interprofessional health care team of chronic pain management is other important aspects where they can screen, monitor and make treatment recommendations to the interprofessional team. This could be at community pharmacies, primary care teams, inpatient acute care and rehabilitation settings, long-term care, and specialty ambulatory pain clinics.[59]

Studies have confirmed medication review as the most common service provided by the pharmacist, followed by patient education, counseling, and opioid drug monitoring among patients with chronic pain.[66] Medication review was effective for drug optimization, identifying adverse drug effects, changing the drug if necessary, and reducing the dose. Likewise, it helps to minimize pain scores and improve physical functioning.[66, 67] Pharmacist roles in interdisciplinary pain management teams are also established, and it serves as a promising strategy in pain management.[68] It further helps to reduce the burden on primary care physicians and increase patient satisfaction.[69] Pharmacists provided intervention (either individually or in a multidisciplinary team) on chronic pain management was beneficial. However, most of these studies were centered in developed countries.[66] So, it is essential to highlight and study the importance of pharmacist contribution to pain management in LMICs as they are the frontline healthcare workers in the community.

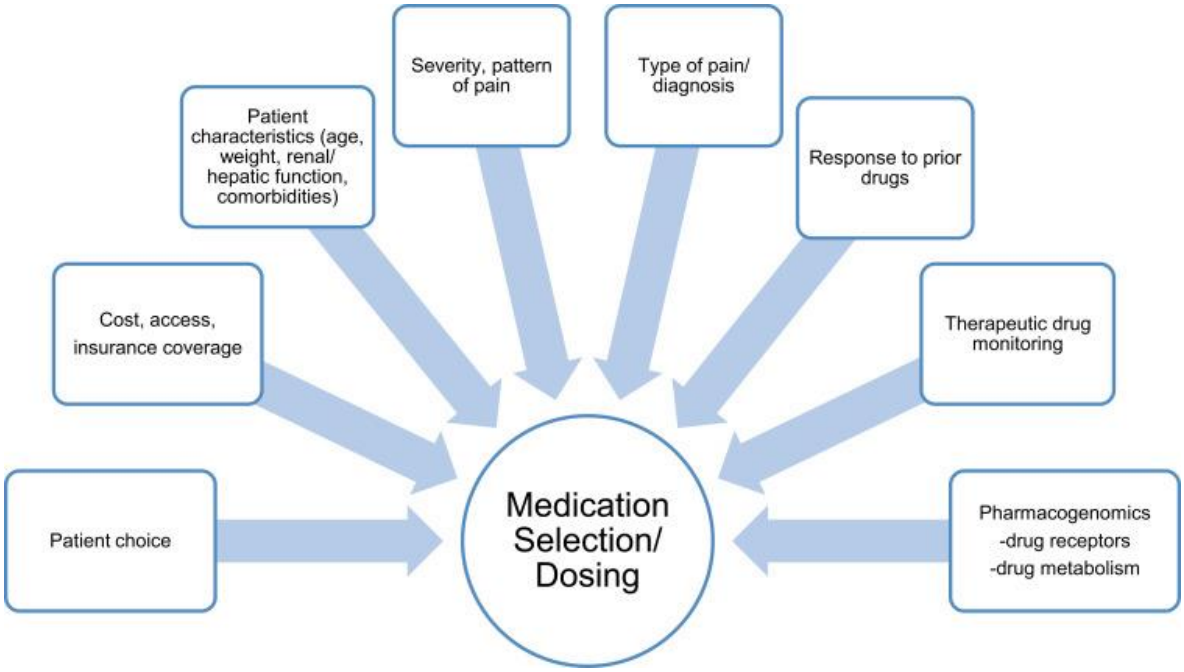

Figure 1.4 Patient factors for medication selection [59]

1.5 Health care system and pain management in Nepal

Nepal is a landlocked country in South Asia, bordered by China and India, and has a federal republic parliamentary government system. The population of Nepal is around 29 million, with the estimated life expectancy at birth being 67.44 years for females and 64.94 years for males. It is categorized as a low-middle-income country. Expenditure on health is 5.2 % of the GDP. Urbanization is a recent trend in Nepal, with 21 % of the population living in urban areas. Around 32.8 % of the people are below the poverty line. Poverty is more prevalent in rural areas with inadequate access to quality healthcare facilities.[70] The Constitution of Nepal declared the right to free primary healthcare services and emergency healthcare for all citizens. It covers the essential healthcare services program, including free primary care services, essential secondary care services, and a limited amount of free essential medications for the poor. However, health equity and universal coverage are deficient due to poverty, reduced government funding, pro-rich bias, poor demand-supply, lack of education, and poor access to healthcare services in rural areas.[71]

Nepal has a mixed healthcare system where the healthcare services to the people are provided by the government, private sectors, and non-governmental organizations (NGOs). Social health insurance policy has been introduced and is available in most districts. However, only 6 % of the population is utilizing the scheme.[72] Out-of-pocket (OOP) payment covers 57.4% of the health expenditure in Nepal.[73] Nepal has been unable to reduce the proportion of OOP, despite multiple intervention support, including a chronic disease support program, an impoverished citizens' program, and a national health insurance scheme.[74] Non-communicable diseases are the leading causes of death, with 66% of deaths, 9% of deaths due to injury, and 25% to communicable diseases. Low back pain, migraine, chronic obstructive pulmonary disease (COPD), and other musculoskeletal disorders were the leading causes of disability in 2017.[75] Musculoskeletal pain, including backache, multiple joint pain, generalized body ache, shoulder pain, knee pain, and abdominal pain due to peptic ulcer disease, were the most reported chronic pain conditions in Nepal.[76]

Though the concept of specialized pain management clinic was established in 1985, it is just emerging in Nepal,[77, 78] and most are localized to the capital city. Generally, people with chronic pain are treated in hospitals, clinics, or community pharmacies. A study conducted in one emergency department in Nepal reveals lack of protocol for pain management leads to inadequate analgesics being prescribed to needy patients. Failure to acknowledge and assess

initial pain, lack of pain management guidelines, and failure to document pain are problems for effective pain management.[79] However, the scenario is gradually changing, with more people interested in contributing to pain management. Subedi and colleagues reported several improvements after essential pain management training in Nepal. Trainees were inspired for advanced training, pain management services were established and strengthened in some academic services, assessment with the use of pain scale has been practiced, pain management training was made compulsory for first-year residents in one institution, chronic pain is more likely to recognize as a disease by healthcare professionals, use of opioids has been started, and non-pharmacological treatment of pain also increased.[80] Likewise, a multidisciplinary approach to pain management is also emerging in Nepal,[77] which shows a positive way for better improvement.

2. Rationale of the study

Chronic pain ranks among the most prevalent medical conditions affecting humans, among the ten most prevalent diseases worldwide.[81] Chronic pain, especially joint pain, is high in Nepal, as reported by one in five adults.[82] However, the pain has not received adequate focus regarding disease management in Nepal. There are not sufficient provisions for the treatment of pain in tertiary, secondary, and primary care settings. As a result, many people with chronic pain are compelled to live with inadequately managed pain. Managing pain as a specialized focus and via pain management clinics is a novel concept in Nepal. People with chronic pain usually visit hospitals and clinics, which often lack the specialized focus it needs. At the community level, people visit the community pharmacies to buy over-the-counter analgesics and other pain medications and for the repeat refill of their prescribed pain medications. However, the provision of care, guidelines, resources, infrastructure and training and support to pharmacist and other healthcare professionals in terms of pain management still needs to be developed in Nepal.

Information on prevalence of chronic pain, associated characteristics, and its impact on social and mental health is important to deliver or plan an effective pain management strategy. Likewise, regular assessment of healthcare professionals' knowledge, attitude and practice is equally important to update, intervene or introduce the pain management techniques. However, there is paucity of literature based on this context in Nepal. Overall, the information regarding the domains of chronic pain, healthcare professionals' perspectives, and pharmacist role in chronic pain management is lacking in Nepal.

To address all these issues, this Ph.D. thesis aimed to critically synthesize the literature on pharmacists' role in chronic pain management in different settings via a systematic review and meta-analysis and find out suitable interventions for chronic pain management by pharmacists in Nepalese healthcare settings. It aims to examine and document the effect of a pharmacist's services on chronic pain patients in Nepal and healthcare professionals' perspectives on pain management. Likewise, the pattern of chronic pain conditions, psychological aspects including depressive symptoms, quality of life of the patients, and treatment approach has been less explored in studies conducted in Nepal. So, this project also aimed to identify common pain conditions, depression, and quality of life together with other pain domains among chronic pain patients visiting hospitals.

The study's findings will help bridge the gap and provide essential insights about chronic pain, healthcare professionals' perspectives and most importantly, the effectiveness of community pharmacist intervention on chronic pain management. The available information will be helpful to healthcare professionals, stakeholders, and the overall healthcare system to devise guidelines, contribute to and promote an effective pain management practice in Nepal.

3. Aims and objective

This research aimed to assess the pain domain, healthcare professional perspective, and community pharmacists' interventions in chronic pain management.

3.1 Primary objective

- To assess the domain of chronic non cancer pain, management, quality of life with implications for

3.2 Secondary objectives

- To perform the systematic review on pharmacist led intervention on chronic pain management
- To assess the Knowledge, Attitude and Practice among health care workers (Physician, Pharmacist and Nurses)
- To translate and validate the McGill Pain Questionnaire in Nepalese language
- To assess domain of chronic pain (types, location, intensity of pain), anxiety and depression, quality of life
- To study the impact of pharmaceutical care intervention among patients with chronic pain through RCT

4. Research questions

Based on the study objectives, the research questions to which the dissertation will elucidate are as follows:

1) What roles could pharmacists take on in pain management, and what are the impacts of community pharmacist intervention on the management of osteoarthritic pain in Nepal?
2) What is the knowledge, attitude, and practice of pain management among healthcare professionals in Nepal?
3) What is the pattern of pain domain, quality of life, depression, and drug management among patients with chronic pain visiting hospitals in Nepal?

5. Research methodology

To address the above-mentioned research questions, multiple research techniques were applied.

1. A systematic review and meta-analysis were performed to determine pharmacist role in chronic pain management. It is the gold standard method to generate evidence for healthcare systems' decision-making. Systematic review collects all possible studies related to a given topic and design and reviews and analyzes their results[83], and meta-analysis is a valid, objective, and scientific method of analyzing and presenting quantitative summary of findings from different studies.[84]
2. Cluster randomized control trial was applied for the community pharmacist-led intervention among osteoarthritic pain, a type of chronic pain condition. It is also a gold standard method to assess the effectiveness of new interventions or treatments. The randomization methods reduce bias and provide a rigorous tool to examine the cause-effect relationships between intervention and outcome. The process balances the participants' characteristics between groups allowing attribution to any differences in the outcome of the study intervention.[85] Cluster randomized trials effectively avoid contamination of the participants. Additionally, it offers logistical convenience for researchers and are acceptable study design, especially for community pharmacies-based interventional studies.
3. To assess healthcare professionals' knowledge, attitude and practice on pain management and chronic pain patients visiting hospitals, a cross-sectional study design was selected. Cross-sectional study design is convenient and the best method to assess sample population at one time point. These studies generate hypotheses and provide information about the healthcare professionals' perspective and different domains of chronic pain, which are helpful to design the randomized control trial.

Objective 1

- **To perform the systematic review on pharmacist led intervention on chronic pain management.**

  A systematic review was conducted to evaluate the pharmacist's provided intervention in chronic non-cancer pain management and the impact of such intervention. We excluded chronic cancer pain because chronic cancer pain is complex and depends on several physiological, biological, and clinical processes, cancer staging, presence of metastasis, and treatment compared to chronic noncancer pain." An extensive database search was performed to retrieve studies and grey literature that describe pharmacists' involvement in chronic pain management. Initially, randomized controlled trials (RCTs) were prioritized for inclusion. However, very limited RCTs were identified. Therefore, all non-randomized and observational studies were also included. Studies in non-English were excluded because of the lack of expertise of researchers in languages other than English. The studies from the database inception until June 2020 that fulfilled the inclusion criteria were included in the review. The findings from the review provide insight into pharmacist intervention in chronic pain management.

  This systematic review has been accepted and published online in the *British Journal of Clinical Pharmacology* (Impact Factor: *3.716*). The printed version publication was in press. The publication's citation is as follows: Thapa P, Lee SWH, KC B, Dujaili JA, Mohamed Ibrahim MI, Gyawali S. Pharmacist-led intervention on chronic pain management: A systematic review and meta-analysis. *British Journal of Clinical Pharmacology*, 2021; in press. doi: https://doi.org/10.1111/bcp.14745

  Article available appendix 1

Objective 2

- **To assess the Knowledge, Attitude and Practice among health care workers (Physician, Pharmacist and Nurses)**

  A cross-sectional study was conducted at five hospitals in Pokhara, Nepal. The knowledge and attitude assessment items regarding pain were adapted from "The Knowledge and Attitudes Survey Regarding Pain (KASRP)," developed by Ferrel and McCaffery, revised in 2014. Practice-related questionnaires were developed based on the literature. Frequencies and descriptive statistics were used to describe the sample characteristics and responses to each item of KASRP and the practice-based question. Mann-Whitney U-test and Kruskal-Wallis H-test were used to analyze the association between the mean rank of the KASRP score and sample characteristics.

  The results showed that healthcare professionals have low to moderate knowledge and attitude regarding pain management. In comparison, doctors scored higher score to pharmacists and nurses. Professional category, age, department, and experience influence the perceived score. Practice assessment reveals that very few healthcare professionals use pain assessment tools, opioid risk assessment tools, and assess allergic reactions to the prescribed medications. Very few of them have attended the training for pain management. However, most of them either agreed or strongly agreed that standard pain management guidelines should be followed and training related to pain management is needed for healthcare professionals in Nepal. In summary, the findings highlight the need for improvement of knowledge and attitude regarding pain among healthcare professionals in Nepal for better practice.

The manuscript has been accepted and published online in the *Journal of pain research* (Impact Factor: *2.581*). The printed version publication was in press. The publication's citation is as follows: Thapa P, KC B, Lee SWH, Dujaili JA, Gyawali S, Mohamed Ibrahim MI, and Alrasheedy AA (2022). Managing Pain in Low Resource Settings: Healthcare Professionals' Knowledge, Attitude and Practice Regarding Pain Management in Western Nepal. *Journal of Pain Research*, 1587-1599; in press

Article available appendix 2

Objective 3

- **To translate and validate the McGill Pain Questionnaire in Nepalese language**

Background

Patient-reported outcome measures (PROMs) are reports from the patient's perspective of their health status. PROMs can tailor treatment and helps monitor the progress of clinical conditions. [86]It is widely used in clinical settings and research. Appropriate translation in the preferred language with cross-culturally adapted, and measurement properties (validity, reliability, and responsiveness) is necessary for its proper use. [87]

The International Association for the study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage." [88] It estimates that 1 in 5 patients experience pain, and 1 in 10 patients are diagnosed with chronic pain yearly.[89] Effective management of pain is possible through proper assessment. The numeric rating scale and visual analog scale are the commonly used unidimensional measure of pain in clinics and research. [90]

Mc Gill pain questionnaire (MPQ) is a reliable and valid tool widely used to evaluate pain's intensity, sensory, and affective components. The short form of the McGill pain questionnaire (SF-MPQ) and the short form of McGill pain questionnaire-2 (SF-MPQ-2) are simplified versions of MPQ. SF-MPQ-2 was developed to address the component of neuropathic pain, which was not included in SF-MPQ. It consists of 22 descriptors of pain and a 0-10 numeric rating scale for each descriptor. It has shown good reliability, validity, and responsiveness among different populations, [91] including US veterans,[92] patients at multidisciplinary pain clinics,[93] pain after cesarean delivery,[94] and cancer pain.[95] The SFMPQ-2 has also been translated into different languages and validated in different cultures, Arabic,[96], Chinese,[97] Thai,[98] Japanese,[99] Irani[93], and Norwegian populations[100]. The results of these studies have shown that the SFMPQ-2 is valid and reliable in these cultures. However, the Nepalese version of SFMPQ-2 is unavailable, so we attempted to develop the culturally

appropriate Nepalese SFMPQ-2 and evaluate its reliability and validity among chronic pain patients.

Material and methods

The study was conducted in two phases: Phase 1- the translation and cross-cultural adaptation of SFMPQ-2, with pretesting of the translated version and Phase 2- study of the psychometric properties of SF-MPQ2. The permission to translate the SF-MPQ-2 to Nepalese version was granted by the Mapi research trust, official distributor. The study protocol was approved by Nepal Health Research council, Nepal and Institutional review committee of Manipal medical college and teaching hospital , Pokhara, Nepal.

Participants

Participants for the study were patients visiting the outpatient orthopaedic ward of hospital. To be eligible to participate, participants were required to be (i)18 years or above, (ii) a Nepalese citizen able to speak and understand Nepalese language, (iii) chronic pain patients (pain that persist for 3 months or more), (iv) willing to particate in the study. Exclusion criteria were (i) patient with terminal illness (ii) patients having psychiatric problem. For the pretesting of the questionnaire a total of 30 participants were enrolled and for the assessment of psychometric properties a total of 116 participants were enrolled with consideration of respondents to item ratio (5:1). [101]

Instruments

Short form of McGill Pain Questionnaire-2

The SFMPQ-2 consists of 22 descriptors for pain with a numeric rating scale of 0-10, with “0” indicating “no pain” and “10” indicating “worst possible pain.” It has four subclasses: one affective and three sensories, namely continuous, intermittent, and neuropathic pain. Four descriptors of affective subscales are “tiring-exhausting”, “sickening”, “fearful”, and “punishing-cruel.” Descriptors of continuous pain include “throbbing pain,” “cramping pain,” “gnawing pain,” “aching pain,” “heavy pain,” and “tender.” Intermittent pain includes “shooting pain,” “stabbing pain,” “sharp pain,” “splitting pain,” “electric shock pain,” and “piercing.” Predominantly neuropathic pain includes “hot burning pain,” “cold-freezing pain,” “pain caused by slight touch,” “itching,” “tingling,” and “numbness.” Subscale scores can be calculated by adding the numeric values of the items, and the total scores equal the sum of all values. [91]

Numeric pain rating scale NPRS

Numeric pain rating scale (NPRS) is the most common, reliable and valid scale to assess the intensity of pain. [102] It has a 11-point scale to self-report pain, between 0 to 10, where 0 equals no pain and 10 equals to extreme or worst pain. It can be administered verbally or can be done over telephone. [103] It has been translated and cross-culturally adapted in Nepalese language. It has shown a good reliability, validity and ability to measure the change in pain intensity over time. [104]

Patient-Reported Outcomes Measurement Information System (PROMIS) Short Form Depression 8b items

PROMIS Short form depression 8b items is a set of person-centred measures that evaluates and monitors physical, mental, and social health in adults and children. It can be used to assess depression among general population and with individuals living with chronic conditions. It has eight items and each item on the measure is rated on a 5-point scale (1=never; 2=rarely; 3=sometimes; 4=often; and 5=always) with a range in score from 8 to 40 with higher scores indicating greater severity of depression. A total raw score is the summed-up response of 8 items. The raw scores on the 8 items should be summed to obtain a total raw score. Then it is converted to the T-score using a T-score table. A T-score of less than 55 is interpreted as "None to slight", 55-59.9 as "mild", 60-69.9 as "moderate" and 70 and over as "severe".[105] The Nepalese version of PROMIS Short form depression items are reliable and valid for clinical and research purpose. [106]

Phase 1

Translation and procedures

The SFMPQ-2 was translated into a Nepalese version according to the linguistic validation guidelines of the Mapi Research Trust under a translation agreement and Beaton's guidelines. [107] Forward translation of the English version to the Nepalese version of SFMPQ 2 was performed by two translators who were bilingual native speakers of Nepalese languages, and one was a clinical pharmacist. These two translators independently produced two initial Nepalese versions of SFMPQ-2. The instruction, items, and response options were translated into the Nepalese version. These versions were thoroughly discussed, and a reconciled version was developed by

consensus. It was also compared with the previously translated version developed by another group of researchers (Nil) with their permission. Then the backward translation was performed by two bicultural and bilingual English speakers. One was Nepalese, working and residing in English speaking countries for more than 10 years and other was the professor of English and professional translator residing in Nepal. Expert opinion was collected over the backward translated version. One was physiotherapist and expert researcher on pain semantics another anaesthesiologist from Nepal. Clinician and scientist from United States working in development and evaluation of pain measures, pain beliefs and psychological pain intervention and expert clinical on palliative medicine from Germany. A meeting was held with consideration of the opinion from all experts and reconciled version of the SFMPQ-2 was developed.

Pre-testing

The questionnaire was pretested among 30 patients with chronic pain. During the pretesting the participants were requested to rate the quality of the pain and associated symptoms accordingly. Upon completion they were asked if they understood the instructions, items, have they faced any difficulties in rating the items and time to complete the questionnaire was also noted. The participants were asked for response options where two words were proposed for the same items and majority preference were adopted. In response to the participants a minor corrections were made to improve the questionnaire and final Nepalese version of the questionnaire was developed.

Phase 2: SFMPQ-2 psychometric properties testing

For the psychometric properties assessment, participants were provided the information sheet, consent form, demographic details form, SFMPQ-2, NPRS, and PROMIS short form depression 8b items questionnaire. Majority of the participants had no formal education, so to maintain the consistency, the data collector read out the instructions of the questionnaire to the participants and asked for their response. SFMPQ-2 questionnaire was administered at 2 points, initial assessment and 2 weeks after. However only 39 participants were available for the retest of SPMPQ-2.

Data analysis

Data were entered in Statistical Package for Social Sciences (SPSS) version 26 and were analysed. Continuous data were presented as mean, standard deviation (SD) and

categorical data as frequencies and percentages. Cronbach's alpha coefficient was calculated to evaluate the internal consistency of each subscale of the SFMPQ-2. A value between 0.50 and 0.69 were considered poor, 0.70 and 0.79 acceptable, 0.08 and 0.89 good and value above 0.90 excellent. Intraclass correlation coefficient (ICC) between the initial and follow up SFMPQ-2 were used to determine the test and retest reliability. Concurrent validity was examined by comparing the total score of SFMPQ2 and PROMIS depression score, NRS using pearson correlation coefficients (r).

Result

The intraclass correlation (ICC) value for all items was between 0.809 to 0.998 and Cronbach's alpha coefficient value was 0.871 suggesting good reliability and internal consistency. The correlation of SF-MPQ-2 with pain score and Patient-Reported Outcomes Measurement Information System (PROMIS) depression questionnaire was 0.410 and 0.543 with good construct validity. The factor loading matrix of the SF-MPQ-2-CN forms subscales; continuous, intermittent, neuropathic, and affective, revealing four components similar to the original scale.

Conclusion

The Nepalese version of SFMPQ-2 showed good reliability and internal consistency. It is a valid and reliable instrument for measuring pain quality in chronic pain patients.

Table 1: Demographic details

Age (mean±SD)	49.14±15.48
Gender	n (%)
Male	43 (37.1)
Female	73 (62.9)
Pain site	
Shouder pain	19 (16.4)
Low back pain	42 (36.2)
Multiple joints pain	10 (8.6)
Knee pain	32 (27.6)
Elbow	8 (6.9)
Neck pain	2 (1.7)
Ankle	3 (2.6)
Education	
No formal education	46 (39.7)
Primary	13 (11.2)
Secondary	24 (20.7)
Higher secondary	16 (13.8)
Bachelor	14 (12.1)
Master and postgraduate	3 (2.6)
Pain duration (Range)	(3 months – 10 years)
3-11 months	52 (44.8)
1-3 year	48 (41.4)
4-6 year	11 (9.5)
7 years or more	5 (4.3)

Domain	Original SF-MPQ-2	T1 (n=) mean SD	T1 (n=) mean SD	ICC	95% CI	p-Value
Continuous	Throbbing pain	2.32±2.96	2.54±2.87	0.851	0.715-0.922	< 0.001
Continuous	Cramping pain	2.55±3.16	2.98±3.05	0.881	0.773-0.938	< 0.001
Continuous	Gnawing pain	3.09±3.08	3.36±3.24	0.755	0.532-0.871	< 0.001
Continuous	Aching pain	2.48±3.01	3.36±3.24	0.976	0.955-0.988	< 0.001
Continuous	Heavy pain	1.93±2.82	1.95±2.91	0.936	0.878-0.967	< 0.001
Continuous	Tender	1.77±2.82	1.05±2.39	0.815	0.647-0.903	< 0.001
Intermittent	Shooting pain	2.31±2.66	1.69±2.40	0.831	0.678-0.911	< 0.001
Intermittent	Stabbing pain	1.28±2.13	0.87±1.80	0.721	0.468-0.854	< 0.001
Intermittent	Sharp pain	1.12±1.89	0.85±2.13	0.807	0.631-0.899	< 0.001
Intermittent	Splitting pain	1.07±2.12	0.77±1.54	0.975	0.952-0.987	< 0.001
Intermittent	Electric-shock pain	0.85±1.91	0.31±1.34	0.954	0.912-0.976	< 0.001
Intermittent	Piercing	1.05±2.05	0.59±1.25	0.917	0.842-0.957	< 0.001
Neuropathic	Hot-burning pain	1.93±2.70	1.62±2.56	0.970	0.943-0.984	< 0.001
Neuropathic	Cold-freezing pain	1.05±2.27	0.64±1.72	0.989	0.979-0.994	< 0.001
Neuropathic	Pain caused by light touch	0.78±2.04	0.46±1.57	0.989	0.980-0.994	< 0.001
Neuropathic	Itching	0.76±1.93	0.46±1.46	0.991	0.984-0.996	< 0.001
Neuropathic	Tingling	1.99±3.0	1.03±2.30	0.942	0.889-0.970	< 0.001
Neuropathic	Numbness	0.98±2.27	0.46±1.66	0.991	0.984-0.996	< 0.001
Affective	Tiring-exhausting	1.82±2.44	1.31±1.88	0.898	0.805-0.946	< 0.001
Affective	Sickening	1.40±2.35	1.26±2.35	0.967	0.937-0.983	< 0.001
Affective	Fearful	1.27±2.28	0.79±1.83	0.970	0.942-0.984	< 0.001
Affective	Punishing-cruel	1.36±2.60	0.85±3.03	0.994	0.989-0.997	< 0.001

Table 2: Interclass correlation between the test and retest on the SF-MPQ-2

Table 3: Internal consistency and Correlation coefficients between the SF-McGill pain items with pain and depression score

	Cronbach's alpha	Pain score	p-value	Depression score	p-value
SF-MPQ-2 (Continuous pain)	0.927	0.347	<0.001	0.277	0.003
SF-MPQ-2 (Intermittent pain)	0.772	0.257	0.005	0.204	0.028
SF-MPQ-2 (Neuropathic pain)	0.762	0.308	0.001	0.265	0.004
SF-MPQ-2 (Affective pain)	0.878	0.274	0.003	0.345	<0.001
SF-MPQ-2 (Total)	0.828	0.501	<0.001	0.448	<0.001

Table 4: Rotated Component Matrix

	Component			
	Continuous	Neuropathic	Intermittent	Affective
Throbbing pain	.873			
Cramping pain	.871			
Gnawing pain	.720			
Aching pain	.846			
Heavy pain	.906			
Tender	.857			
Shooting pain			.534	
Stabbing pain			.696	
Sharp pain			.630	
Splitting pain			.814	
Electric-shock pain			.718	
Piercing			.714	
Hot-burning pain		.519		
Cold-freezing pain		.533		
Pain caused by light touch		.740		
Itching		.850		
Tingling		.691		
Numbness		.664		
Tiring-exhausting				.749
Sickening				.840
Fearful				.873
Punishing-cruel				.824

Extraction Method: Principal Component Analysis.

Rotation Method: Varimax with Kaiser Normalization.

a. Rotation converged in 5 iterations.

Objective 4

- **To assess domain of chronic pain (types, location, intensity of pain), anxiety and depression, quality of life**

Background

Pain is an unpleasant sensory and emotional experience associated with or resembling that associated with actual or potential tissue damage.[108] Pain, particularly chronic pain, is a prevalent reason for seeking medical attention and a significant contributor to disability.[2] Osteoarthritis pain, back pain, and headache are three of the top ten reasons for seeking care for pain.[109] Chronic pain prevalence rates differ across countries, with a pooled chronic prevalence estimate of 43.5% in the UK and a lower prevalence of 20.4% in the United States. Low-middle-income countries have a prevalence range of 33.9% to 41.1%, while Nepal has a higher prevalence of 48-50%.[110]

As pain is a dynamic consequence of psychological, biological, and social factors, guidelines have recommended an interdisciplinary treatment using a personalized approach.[111] The US Veteran Health Administration advocates that care should begin with the least intensive service and slowly progress towards more specialized care via patient-centred care.[112] However, many chronic pains are inadequately managed, negatively affecting patients' physical and emotional well beings, work efficiency, and quality of life.[113] The prevalence of depression among chronic pain patients has been reported to range from 13 to 85%. Hence, proper assessment of depression among chronic pain patients is crucial for effective and timely management.[114]

Pain management as a discipline by itself is still evolving in Nepal. Patients with pain are either treated in the outpatient department or the emergency department of the hospitals. Likewise, there is a lack of appreciation when it comes to the impact of chronic pain on the quality of life and mental health of patients. There is scant literature on chronic pain, its types and quality of life, and the patient's mental health. Against this backdrop, this study aims to determine the type of chronic pain patients visiting the hospitals in Nepal and the associated factors such as depression, quality of life, and the medication used for the management.

Methods

This study follows The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations for reporting observational studies.[115]

Study design and study site

This cross-sectional study was conducted in outpatient departments of two tertiary care hospitals in Pokhara, Nepal, from June 2021 to November 2021. These hospitals are well-equipped to provide affordable healthcare services to the public. They have a high patient flow and are accessible to patients from rural and urban areas.

Study Population

The study population included patients with chronic pain complaints visiting outpatient departments of the hospitals.

Inclusion Criteria

Patients with complaints of chronic pain (pain persists for three months and more), aged 18 years and above, and willing to participate in the study were included.

Exclusion Criteria

Patients with cancer pain, cognitive impairment, and those who could not understand the questionnaire were excluded.

Sample size

The sample size was calculated using the previously reported prevalence of chronic pain in Nepal, 50%.[116] The minimum required sample size for this study was estimated to be 385 responses.

Data collection tool and scoring system

Information on chronic pain and its management was assessed using a battery of questionnaires to identify the sociodemographic information, pain characteristics (duration of pain and pain site), and medications used. This was supplemented with questionnaires to assess pain score, depression, and quality of life, as described below.

Face pain scale

A Nepalese-translated version of the face pain scale was used to measure the pain score. It consists of a facial pictorial representation, with each face showing more pain from left to right. Each face was represented by a score of 0, 2, 4, 6, 8, and 10, where "0" means "no pain" and "10" represents "very much pain.". [3] Participants were requested to point out the face that shows how bad their pain is at present and the scores were recorded accordingly.

Patient-Reported Outcomes Measurement Information System Depression Questionnaire

Depression was assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS) Depression 8b short-form questionnaire. A Nepalese-translated version of the questionnaire was used. The reliability and validity of the questionnaire have been described previously.[106] The tool assesses the self-reported negative mood (sadness, guilt), views of self (self-criticism, worthlessness), social cognition (loneliness, interpersonal alienation), and decreased positive affect (loss of interest, meaning, and purpose). It has eight items with five responses, options ranging in value from one to five on the Likert scale. A depression score of below 55 was considered "within normal limit," 55 to 59.9 as "mild," 60 to 69.9 as "moderate," and 70 and above as "severe."[117]

Quality of life

The Nepalese version of the EQ-5D-3L (EUROQOL) measure was used for the health-related quality of life.[118, 119] It assesses the Quality of life based on five dimensions mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels: no problems, some problems, and extreme. A single index value was calculated in the "EQ-5D-3L Crosswalk Index Value Calculator" using weights of the UK as the reference from the five dimensions of EQ-5D. [120, 121]The EQ-5D index ranges from 0 to 1, where 0 represents severely ill, and 1 indicates perfect health. No problems on all five dimensions (11111) represent perfect health with the value assigned as 0, and severe health problems in all dimensions (33333) represent very severe health states with the value assigned as 1.

Process of Data collection

A pilot study was conducted among 30 participants to ensure the feasibility and appropriateness of the chosen tools. Although the questionnaires were deemed acceptable, poor literacy among participants was challenging. To ensure uniformity, it was decided that a data collector would administer all questionnaires.

Statistical analysis

Descriptive statistics were calculated for all variables. Univariate comparisons of Quality-of-life (EQ-5D-3L) and PROMIS depression scores were made using the Mann-Whitney U and Kruskal Wallis tests. Spearman's correlation coefficients (r) were used to test the association of two continuous measures: age, pain score, depression score, and quality of life score. Linear regression analysis was used to find the independent factor associated with the quality-of-life score (EQ-5D-3L). Standardized regression coefficients were performed to measure the effect of independent variables, and R squared was reported as the percent of the variance explained by the model. All data were analyzed using the SPSS (Statistical Package for Social Science, Version 26.0)

Ethical Consideration

Ethical approval for the study was obtained from Nepal (Registration number; 211/2020). Permission to collect the data was obtained from institutional review committees of the respective hospitals. All patients provided written informed consent.

Results

Descriptive data

A total of 400 participants were recruited for the study; after excluding 15 participants with missing data, 385 were included in the final analysis. Most participants were females (n=248; 64.4%), with a median age of 49 (range 18 to 91). The most common primary reason for seeking medical care was musculoskeletal pain, particularly back and knee pain. Abdominal pain and headache were among other commonly reported reasons. The mean pain score of the participants was 4.5 ± 1.97, with half of them (n=216; 56.1%) having pain complaints for at least 3 to 11 months. Participants were on a mean of 3.8 medications for pain, with non-steroidal anti-inflammatory drugs (NSAIDs) being the most prescribed medication, followed by a muscle relaxant,

steroids, and pregabalin. Further demographic and medication details are presented in Table 1 and Figure 1.

Depression among participants with chronic pain

About 50% of the participants have mild to moderate depression. The mean ± SD depression score among participants was 55.28 ± 9.22. According to the results of the univariate analysis, there was a significant positive correlation between depression and age ($r=0.19$, $p<0.001$), as well as pain score ($r=0.314$, $p<0.001$). Females, participants with no formal education, longer pain duration, and comorbidity reported higher depression scores ($p<0.001$), as shown in Table 2.

Quality of life among participants with chronic pain

Assessment of different components of quality of life revealed that the most common complaints by participants were related to their pain/discomfort (n=246; 63.9%), anxiety/depression (n=142; 36.9%), and mobility (n=105; 27.3%). Other complaints include issues with self-care (n=68; 17.7%) and usual activities (n=127; 33%) Table 3. We noted some differences in the self-reported quality-of-life, with poorer reported quality-of-life scores among females than males (0.73 versus 0.76; $p<0.001$). Likewise, participants with no formal education presented with comorbidity, longer pain duration, higher pain score, and depression score had a low self-reported quality of life ($p<0.001$). Multiple regression analysis showed that pain duration ($\beta=-0.208$, $p<0.001$), pain score ($\beta=-0.292$, $p<0.001$), and depression score ($\beta=-0.326$, $p<0.001$) were independently associated with the quality-of-life score. (Table 4)

Discussion

The current study assessed patient characteristics, the association of depression and quality of life with chronic pain, and medication management among those visiting tertiary care hospitals. Several studies have reported patient characteristics and pain severity among chronic pain patients.[17, 76, 110] However, to the best of our knowledge, this is the first study to explore the association of quality of life with depression and chronic pain in Nepal.

Three hundred and eighty-five participants were enrolled in this study. The chief complaint from the participants seeking care was musculoskeletal pain, followed by

abdominal pain and headache, especially among females. Low back pain (n= 96, 24.9%) and knee pain (n=85, 22.1%) were the commonly reported pain. This finding is similar to the one reported by Bhattarai and colleagues in the community-based study in Nepal, where most participants had musculoskeletal-related chronic pain and higher reporting among females.[76] Likewise, Dasgupta and colleagues reported a higher prevalence of musculoskeletal pain (knee pain) and preponderance among female patients visiting primary healthcare clinics in Malaysia.[122] Low back pain is a global problem; its prevalence was estimated at 7.5% of the worldwide population in 2017.[123] Low back and knee pain are common chronic pain problems in Nepal and are highly prevalent.[76, 82, 124] However, the higher prevalence of chronic pain among females is unclear. Laboratory research has revealed that women are more sensitive to experimental pain stimuli than men.[125] In their review study, Fillingim and colleagues reported that low intensity of different pain stimuli, pressure, heat, cold, electric, and ischemic, could easily provoke pain among females compared to males.[126] The exact mechanism to explain the gender difference is difficult; however, it is suggested that multiple factors, including endocrinological factors, cognitive and affective states, body size and functional capacity, and occupational status, might have some roles.[127]

The mean pain score of the participants was 4.5±1.97, considered moderate. Shaygan and colleagues from Iran reported the mean pain score of 4.04±2.49 and 4.26±2.86 among adults diagnosed with chronic pain in their study's control and treatment group, which is consistent with the finding of this study.[128] However, Nizar and colleagues in Malaysia reported pain intensity of 6.5±1.40 among patients visiting the pain clinic with either cancer or non-cancer pain.[129] While the exact reason for moderate pain scores among patients visiting the hospital is unclear, we postulate that this might be because patients with higher pain scores often visit the emergency department for its management. In a study by Baharuddin and colleagues, which examined the pain scores among Emergency Department (ED) patients, the authors found that most patients had a mean score of 6.8.[130] Most participants (n=216, 56.1 %) have a pain duration between 3 to 11 months, followed by 1 to 3 years. Majedi and colleagues reported five years of average pain duration among chronic pain patients.[131] Longer pain duration could be due to the delay in approaching treatment, the chronic nature of underlying conditions, delay in referral to the pain clinics, and inadequate pain management.

NSAIDs were the most prescribed medication to manage pain in our study. Naproxen and aceclofenac were used frequently for oral administration and diclofenac gel for topical application. These findings are consistent with one reported in the United States[132], Switzerland[133], India[134], and Nepal[135]. However, Zin and colleagues from Malaysia reported opioids as the most prescribed analgesics in public hospitals, contrasting our findings.[136] The center for disease control (CDC) guidelines 2016 recommend caution when initiating opioids and avoiding their use as a first-line therapy.[137] The use of opioids in our study was very minimal. Opioids are internationally controlled medications for their potential abuse. Consumption of opioids in Asia is much less than in the United States and Europe.[138] Its consumption in Nepal is significantly less; physicians are reluctant to prescribe it due to fear of abuse and lack of training on pain management.[139] So these might be the reason for the limited opioid prescriptions identified in our study. Antidepressants, anticonvulsants (pregabalin and gabapentin), steroids, and muscle relaxants were the other medications prescribed, and the prescription pattern aligns with the Scottish Intercollegiate Guidelines Network (SIGN) guidelines 2019 for chronic pain management, which recommends using this medication for short to the medium-term treatment of chronic pain.[140] Intraarticular steroids were used in a few patients with knee pain, and it has been shown to reduce pain and tenderness, especially in knee osteoarthritis.[141] Aroll and colleagues, in their meta-analysis study, reported the short-term improvement in knee osteoarthritis symptoms after intra-articular corticosteroids injection.[142] Muscle relaxants were combined with NSAIDs, and evidence suggests they are effective for acute or chronic low back pain.[143]

Our study confirmed the negative impact of higher pain scores and depression on patients' quality of life. A significant negative correlation was found between quality of life, pain score, and depression. Patients with high pain scores and more depressive symptoms have a lower quality of life. Several studies support these findings, establishing the reciprocal relationship between chronic pain and depression with quality of life.[144, 145] Tsuji and colleagues reported depression and lower health-related quality of life scores among patients with chronic low back pain.[146] Elliott and colleagues reported an association of depression with health-related quality of life

among chronic pain patients.[147] Likewise, Garnaes and colleagues, in a cross-sectional study among patients with musculoskeletal pain, reported the reduced health-related quality of life to be prevalent among females receiving a disability pension and several psychosocial factors.[148]

Univariate analysis of depression among patients with chronic pain revealed a positive correlation with pain scores. Chronic pain and depression are related and can co-occur.[149, 150] About fifty percent of the participants in our study have mild to moderate levels of depression. Brooks and colleagues in England; Muhammad and colleagues in India reported that participants with higher pain frequency and intensity have elevated depressive symptoms, consistent with our study's findings.[151, 152] Depression enhances the adverse effects on patients' outcomes, worsens functioning, and reduces the response to treatment.[153] Bair and colleagues reported depression to be prevalent among 56% of patients with pain in orthopaedic clinics, while Zuraida and colleagues reported it to be 27% among patients with headaches.[154, 155] Likewise, Mallen et al., and Suija et al., reported 23% to 35.5% among patients with musculoskeletal pain.[156, 157]

Depression and low self-reported quality of life were more prevalent among the elderly, females, and patients with comorbidity and longer duration of pain. Females with chronic pain conditions are more prone to develop depression as contributed by social and biological factors. [158, 159] The co-occurrence of chronic pain and depression among elderly patients is well-established, given their high prevalence in this population. Specifically, research has shown that approximately 13% of elderly individuals suffer from chronic pain and depression. Therefore, it is crucial to properly manage these co-morbid conditions using a combination of pharmacological and non-pharmacological approaches.[27] Depression among chronic pain patients is also often associated with severity, frequency, duration, and number of symptoms.[144] In managing chronic pain, mental healthcare plays a critical role. Addressing comorbid conditions such as depression is crucial to achieving effective pain management outcomes. It can improve pain severity, overall functioning, and pain perception and improve the quality of life. [160] Hadi and colleagues emphasized that poor pain management owing to failure to identify the multidimensional nature of chronic pain

might be the reason for the poor quality of life among patients with chronic pain. So strategies to improve the quality of life and pain relief are crucial, especially in low and middle-income countries where pain management is still challenging.[161]

Conclusion

Musculoskeletal pain was the primary complaint, followed by headache and abdominal pain to visit the outpatient department of hospitals. Females were found to have a higher prevalence of chronic pain, with most participants reporting moderate pain. The most frequently prescribed medication for managing chronic pain was NSAIDs. Participants with increased pain and depression scores reported a lower quality of life.

Study Limitation

This study has some limitations. Firstly, the data were collected from only two study sites, which limits generalizability. Secondly, the findings are based solely on quantitative data, and including a qualitative approach would have provided a better understanding of depression and quality of life among chronic pain patients. A more rigorous study design that includes multiple approaches, sites, and a large sample size is necessary to accurately assess pain and related domains and confirm the adequacy of treatment.

Table 1: Demographic details, Pain, Quality of life, and Depression score

Demographic Details	Number	Percentage
Gender		
Male	137	35.6
Female	248	64.4
Age (Median) (range)	49 (18-91)	
Age Category		
18-25	31	8.1
26-35	36	9.4
36-45	89	23.1
46-55	89	23.1
56-64	72	18.7
65-74	44	11.4
75 and more	24	6.2
Education		
No formal education	152	39.5
Primary	47	12.2
Middle school/High school	144	37.4
University	42	10.9
Occupation		
Housewife	154	40.0
Teacher	13	3.4
Office employ	13	3.4
Farmer	79	20.5
Student	25	6.5
Retired	32	8.3
Business	37	9.6
Others	32	8.3
Smokers		
Yes	27	7.0
No	358	93.0
Alcohol		
Yes	45	11.7
No	340	88.3
Pain Duration		
3-11 months	216	56.1
1-3 years	123	31.9
4-5 years	24	6.2
6 years and more	22	5.7
Pain sites		
Knee pain	85	22.1
Low back pain	96	24.9
Multiple sites pain	36	9.4
Shoulder pain	44	11.4
Leg/foot pain	23	6.0

Neck pain	13	3.4
Wrist/forearm/hand pain	15	3.9
Elbow pain	17	4.4
Hip pain	23	6.0
Abdomen	26	6.7
Headache	7	1.8
Comorbid condition		
No	263	68.3
Yes	122	31.7
Pain score Mean ± SD 0=no pain,10=very much pain	4.5 ± 1.97	
2.00	75	19.5
4.00	196	50.9
6.00	71	18.4
8.00	27	7.0
10.00	16	4.2
Depression score Mean ± SD	55.28 ± 9.22	
None to slight (less than 55)	177	46.0
Mild (55-59.9)	97	25.2
Moderate (60-69.9)	98	25.5
Severe (70 and over)	13	3.4
Quality of life (QoL)score (Mean ± SD)	0.59 ± 0.37	
QoL Visual Analog Scale (0-100) Mean ± SD	64.57 ± 22.93	

Table 2: Univariate analysis results for EQ-5D and PROMIS depression score

	EQ5D score Median (IQR)	p-value	PROMIS Depression score Median (IQR)	p-value
Gender				
Male	0.76(0.16)	<0.001^{+}	54.3 (10.6)	<0.001^{+}
Female	0.72 (0.28)		57.1 (10.1)	
Age, r	-0.29$^{\pm}$	<0.001$^{\pm}$	0.19$^{\pm}$	<0.001
Education				
No formal education	0.68(0.50)	<0.001^{++}	57.9 (8)	<0.001^{++}
Primary	0.72(0.81)		57.1(9.3)	
Middle/High School	0.72(0.14)		54.3(9)	
University	0.79(0.27)		51.2 (12)	
Smoking				
Yes	0.68 (1.34)	0.109^{+}	57.1(8.2)	0.136^{+}
No	0.72 (1.34)		55.3 (11.8)	
Alcohol				
Yes	0.72(0.40)	0.820^{+}	55.3 (11.8)	0.334^{+}
No	0.72(0.21)		56.2 (11.8)	
Comorbid				
Yes	0.59(0.17)	<0.001^{+}	57.1(10.1)	<0.001^{+}
No	0.68(0.75)		54.3 (9.9)	
Pain Duration				
3-11 months	0.79 (0.10)	<0.001^{++}	54.3(9)	<0.001^{++}
1 -3 year	0.72(0.28)		57.9 (11.3)	
4-5 year	0.60 (0.87)		61(10.2)	
6 years and more	-0.05 (0.87)		62 (9.9)	
Pain scale, r	-0.374	<0.001$^{\pm}$	0.314	<0.001
Depression, r	-0.540	<0.001$^{\pm}$		

±Spearman's correlation; + Mann-Whitney U test; ++Kruskal-Wallis test

Table 3: Quality of life EQ-5D-3L

	Mobility N (%)	Self-care N (%)	Usual Activities N (%)	Pain/Discomfort N (%)	Anxiety/ Depression Pain/Discomfort N (%)
No problem	279 (72.5)	310 (80.5)	248 (64.4)	67 (17.4)	171 (44.4)
Some problem	105 (27.3)	68(17.7)	127 (33.0)	246 (63.9)	142 (36.9)
Extreme problem	1 (0.3)	7(1.8)	10 (2.6)	72 (18.7)	72 (18.7)
Visual analogue scale	Mean ± SD 64.57 ± 22.93 Range (10-90)				

Table 4: Multiple linear regression analyses for EQ-5D

	Regression Coefficient	Standard Error (SE)	Standardize Regression Coefficient (β)	p-value
Dependent variable: EQ-5D				
Pain duration	-0.094	0.019	-0.208	<0.001
PROMIS Depression score	-0.013	0.002	-0.326	<0.001
Pain score	-0.056	0.008	-0.292	<0.001
R square of the model 33%				

Table 5: Medications prescribed for management of pain

Medications		n	%
NSAIDS	Naproxen	136	35.3
	Aceclofenac	128	33.2
	Diclofenac Gel	229	59.5
	Etoricoxib/Celecoxib	46	11.9
	Piroxicam	1	0.2
Opioids	Tramadol	2	0.5
Analgesic and CNS stimulant/muscle relaxant	Paracetamol and caffeine	3	0.8
	Paracetamol and Chlorzoxazone	17	4.4
Anti-inflammatory	Diacerein	30	7.8
Steroids	Dexamethasone/ Methylprednisolone	44	11.4
Antidepressant	Duloxetine / Amitriptyline	22	5.7
Anticonvulsants	Pregabalin	41	10.6
	Gabapentin	3	0.7
Muscle relaxants	Tizanidine	82	21.3
Vitamins and supplements	Calcium supplements	155	40.3
	Calcium and Vitamin D	7	7
	Vitamin D	24	6.2
	Vitamin B12	22	5.7
	Multi-vitamin	18	4.7
Gastrointestinal agents	Sucralfate	17	4.4
	Antacids	4	1
	Hyoscine-N-butylbromide	10	2.6
	Rabeprazole	108	28
	Pantoprazole	222	57.7

Objective 5

- **To study the impact of pharmaceutical care intervention among patients with chronic pain through RCT**

A cluster randomized trial study was conducted among osteoarthritic patients visiting community pharmacies in Pokhara, Nepal. According to the pharmacy's assignment, Participants were recruited into intervention or control groups. Participants in the intervention group received patient education in the form of a leaflet and a video. Further, their medication was also reviewed. However, control group participants received as usual care. Participants were followed up after 3 months and 6 months at the end of the study period. The primary outcomes of the study were the knowledge score of osteoarthritis pain management, pain score [162], and The Western Ontario and McMaster Universities Arthritis Index (WOMAC)[163], and the secondary outcomes were the depression and quality of life score (EQ-5D-Qol).[164]

The result showed encouraging support towards community pharmacy intervention in osteoarthritic patients. Pharmacist-led intervention providing education and medication review improved pain scores at 3 months (mean difference 0.473, 95% CI 0.047 to 0.900) and end of the study, 6 months (mean difference 0.469, 95% CI 0.047 to 0.891) when compared to the control group. Similarly, improvement in knowledge score was observed among the intervention group at 3 months (mean difference 5.320, 95% CI 4.982 to 5.658) and 6 months (mean difference 5.411, 95% CI 5.086 to 5.735) compared to the control group. However, WOMAC score, depression score[105, 165], and EQ-5D-Qol did not improve significantly at 3 months or the end of the study period.

This study showed the important role of community pharmacists in improving osteoarthritis patients' knowledge and pain management via targeted education interventions and comprehensive medication reviews. While our interventions did not significantly impact physical functioning, quality of life, or depression, the findings highlight the importance of counseling and supporting individuals with osteoarthritis in community settings.

This manuscript has been accepted and published online in the *Research in Social and Administrative Pharmacy* (Impact Factor: *3.9*). The printed version publication was in press. The publication's citation is as follows: Thapa P, Bhuvan KC, Gyawali S, Leong SL, Ibrahim MI, Lee SW. Effectiveness of community pharmacist-led interventions in

osteoarthritis pain management: A cluster-randomized trial. Research in Social and Administrative Pharmacy. 2023; in press. doi https://doi.org/10.1016/j.sapharm.2023.10.012

Manuscript available in Appendix 3

6. Conclusion and future directions

Chronic pain is pain that persists for 3 months or more. It is a major global health problem and a cause of disability. Managing chronic noncancer pain is a major challenge for clinicians and patients who suffer because the complete elimination of pain is rarely obtainable. The treatment goals should be planned for reducing pain, maximizing function, and improving quality of life. The best outcomes can be expected when chronic pain management focuses on co-occurring mental disorders (anxiety, depression) and includes nonpharmacological and complementary therapies for symptom management. Clinical practice guidelines, and the role of healthcare professionals, and the healthcare facilities are pretty well defined and implemented in developed countries, making the pain management process effective. However, the scenario is different in LMICs as several barriers exist, including low prioritization of pain relief, patients' expectations and attitudes, staff knowledge and attitudes, access to analgesic treatment and issues related to opioids, and lack of data and research on pain management. So, this project was designed to explore the different aspects of chronic pain management in Nepal and the impact of pharmacist intervention.

Despite growing interest in chronic pain management, there needs to be more evidence and research in LMICs. Thus, this thesis addresses the gap in chronic pain management research and generates the evidence for further implementation and consideration. The systematic review on pharmacist-led intervention on chronic pain management reported the impact of pharmacists contributing to chronic pain management individually or in a multi-disciplinary team. Medication review and patient education was the most common intervention strategy applied by the pharmacists. The studies included in the review were from developed countries. However, the pharmacist role could be adapted to our settings. Likewise, the cross-sectional studies among chronic pain patients visiting tertiary care hospitals found the knee pain and low back pain as the common chronic pain conditions. It further reported the prevalence of depression and lower health-related quality of life among individuals. These findings emphasize for the intervention that incorporates the psychological aspects of chronic pain management. Assessment of the perspectives of healthcare professionals on pain management revealed the suboptimal level of knowledge, attitude, and practice. This finding

highlights the need for training and support to healthcare professionals to enhance their knowledge, philosophy and better practice.

Based on the reference to the findings mentioned above a cluster randomized trial evaluating the community pharmacist's role in managing osteoarthritis pain was devised with medication review and education counseling using leaflet and video as an intervention tool. The community pharmacist-led intervention enhances the patient's knowledge of osteoarthritis pain management and pain score; however no significant improvement was observed in physical functioning, depression, and quality of life. This highlights the need for advanced training for community pharmacist and comprehensive intervention for the patients with osteoarthritis for better health outcomes.

Overall, the research provides significant insights into chronic pain management and pharmacist's role and its impact in terms of outcomes measures which would be helpful for the pharmacist, other healthcare professionals, policymakers, and patients. Based on the research findings and discussion, the following suggestions for future research could be summarised as follows:

1. The nature of the cross-sectional study including healthcare professionals' knowledge, attitudes, and practices on pain management and assessment of chronic pain patients visiting tertiary care hospitals, poses several limitations, including convenience sampling methods, limited study site, quantitative approach for data collection. A multicentre study with a larger sample size and inclusion of mixed methods; qualitative and quantitative approach would be essential to generate more precise evidence in this area.

2. Pharmacist-led intervention in pain management studies is sparse in LMICs, so pharmacists can explore the different aspects of chronic pain management individually or in collaboration with other healthcare professionals and conduct the research. The findings will determine current research's reproducibility and generate more information essential for pain management.

3. The current research was conducted in tertiary care hospitals and community pharmacies in one urban part of the country. Chronic pain is a common problem in Nepal and is associated with the occupation and lifestyle of rural people, so more comprehensive research in this area is warranted to get the exact scenario of pain and related factors in Nepal.
4. Further studies to investigate the cost-effectiveness of chronic pain management are mandated. Health economics analysis will help in medical decision-making.

5. Further studies on the effectiveness of non-pharmacological intervention like exercise is warranted, as it has significant role in preventing disability related to chronic pain.

6. The reports generated from this research could be submitted to the hospital authority, key stakeholders, and the Nepal pharmacy council for implementation consideration. We could further advocate training and continuous professional development module for pharmacists to enhance their pain management knowledge and skills in hospital and community settings.

7. Pain management is not well covered in the undergraduate curriculum; we could further provide suggestions to the curriculum development committee at the Universities of Nepal during the revision process to incorporate pain management in their syllabus, so the students get aware of the concept before they start their professional career.

This research project can serve as an initial study that provides important insights and better understanding of chronic pain management in Nepal, but there is a long way to go.

References

1. Treede, R.-D., et al., *Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11).* PAIN, 2019. 160(1).
2. Mills, S.E.E., K.P. Nicolson, and B.H. Smith, *Chronic pain: a review of its epidemiology and associated factors in population-based studies.* British journal of anaesthesia, 2019. 123(2): p. e273-e283.
3. IASP. *International Association for the Study of Pain*. Available from: https://www.iasp-pain.org/PublicationsNews/NewsDetail.aspx?ItemNumber=8340.
4. Jones, J., et al., *Self-assessed physical function levels of women with fibromyalgia: a national survey.* Women's Health Issues, 2008. 18(5): p. 406-412.
5. Dueñas, M., et al., *A review of chronic pain impact on patients, their social environment and the health care system.* Journal of pain research, 2016. 9: p. 457-467.
6. Blyth, F.M., et al., *Chronic pain, work performance and litigation.* PAIN®, 2003. 103(1-2): p. 41-47.
7. Porter, L.S., et al., *Pain communication in the context of osteoarthritis: patient and partner self-efficacy for pain communication and holding back from discussion of pain and arthritis-related concerns.* The Clinical journal of pain, 2008. 24(8): p. 662-668.
8. Gaskin, D.J. and P. Richard, *The economic costs of pain in the United States.* J Pain, 2012. 13(8): p. 715-24.
9. El-Metwally, A., et al., *The prevalence of chronic pain and its associated factors among Saudi Al-Kharj population; a cross sectional study.* BMC Musculoskelet Disord, 2019. 20(1): p. 177.
10. Harstall, C. and M. Ospina, *How prevalent is chronic pain.* Pain clinical updates, 2003. 11(2): p. 1-4.
11. Dahlhamer, J., et al., *Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults - United States, 2016.* MMWR Morb Mortal Wkly Rep, 2018. 67(36): p. 1001-1006.
12. Hensler, S., et al., *Chronic pain in German general practice.* Pain Medicine, 2009. 10(8): p. 1408-1415.
13. Wong, W.S. and R. Fielding, *Prevalence and characteristics of chronic pain in the general population of Hong Kong.* The Journal of Pain, 2011. 12(2): p. 236-245.
14. Rustøen, T., et al., *Prevalence and characteristics of chronic pain in the general Norwegian population.* European Journal of pain, 2004. 8(6): p. 555-565.
15. Breivik, H., et al., *Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment.* Eur J Pain, 2006. 10(4): p. 287-333.
16. Jackson, T., et al., *Prevalence of chronic pain in low-income and middle-income countries: a systematic review and meta-analysis.* The Lancet, 2015. 385: p. S10.
17. Walters, L.J., et al., *Chronic Pain and Associated Factors in India and Nepal: A Pilot Study of the Vanderbilt Global Pain Survey.* Anesthesia & Analgesia, 2017. 125(5).
18. Javier, F. and H. Lu, *Prevalence and treatment of chronic pain in the Philippines.* Philippine Journal of Internal Medicine, 2011: p. 61-69.
19. Zarei, S., et al., *Chronic Pain and Its Determinants: A Population-based Study in Southern Iran.* Korean J Pain, 2012. 25(4): p. 245-53.
20. Jensen, M.P., et al., *Psychosocial factors and adjustment to chronic pain in persons with physical disabilities: a systematic review.* Arch Phys Med Rehabil, 2011. 92(1): p. 146-60.

21. Taylor, A.M., et al., *Assessment of physical function and participation in chronic pain clinical trials: IMMPACT/OMERACT recommendations.* Pain, 2016. 157(9): p. 1836.
22. Bassols, A., F. Bosch, and J.E. Baños, *How does the general population treat their pain? A survey in Catalonia, Spain.* J Pain Symptom Manage, 2002. 23(4): p. 318-28.
23. Miró, J., et al., *Pain in older adults: a prevalence study in the Mediterranean region of Catalonia.* Eur J Pain, 2007. 11(1): p. 83-92.
24. Jones, J., et al., *Self-assessed physical function levels of women with fibromyalgia: a national survey.* Womens Health Issues, 2008. 18(5): p. 406-12.
25. García-Campayo, J., et al., *Relationship of somatic symptoms with depression severity, quality of life, and health resources utilization in patients with major depressive disorder seeking primary health care in Spain.* Prim Care Companion J Clin Psychiatry, 2008. 10(5): p. 355-62.
26. Roughan, W.H., et al., *Comorbid chronic pain and depression: shared risk factors and differential antidepressant effectiveness.* Frontiers in Psychiatry, 2021. 12: p. 643609.
27. Zis, P., et al., *Depression and chronic pain in the elderly: links and management challenges.* Clinical interventions in aging, 2017: p. 709-720.
28. Lee, H.-J., et al., *Prevalence of unrecognized depression in patients with chronic pain without a history of psychiatric diseases.* The Korean journal of pain, 2018. 31(2): p. 116-124.
29. Turner, J.A. and J.M. Romano, *Self-report screening measures for depression in chronic pain patients.* Journal of clinical psychology, 1984. 40(4): p. 909-913.
30. Geisser, M.E., R.S. Roth, and M.E. Robinson, *Assessing depression among persons with chronic pain using the Center for Epidemiological Studies-Depression Scale and the Beck Depression Inventory: a comparative analysis.* The Clinical journal of pain, 1997. 13(2): p. 163-170.
31. Howarth, A. and D. Poole, *Assessment and management of chronic pain.* Nurs Stand, 2019. 10.
32. guideline NG193, N., *Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain.* Methods, 2021.
33. Dansie, E.J. and D.C. Turk, *Assessment of patients with chronic pain.* BJA: British Journal of Anaesthesia, 2013. 111(1): p. 19-25.
34. SIGN, *SIGN 136 Management of chronic pain A national clinical guideline*. 2019.
35. Bonezzi, C., et al., *Pharmacological management of adults with chronic non-cancer pain in general practice.* Pain and therapy, 2020. 9: p. 17-28.
36. Roe, M. and A. Sehgal, *Pharmacology in the management of chronic pain.* Anaesthesia & Intensive Care Medicine, 2016. 17(11): p. 548-551.
37. Skelly, A.C., et al., *Noninvasive nonpharmacological treatment for chronic pain: a systematic review.* 2018.
38. Roditi, D. and M.E. Robinson, *The role of psychological interventions in the management of patients with chronic pain.* Psychology Research and Behavior Management, 2011. 4: p. 41-49.
39. Hoffman, B.M., et al., *Meta-analysis of psychological interventions for chronic low back pain.* Health psychology, 2007. 26(1): p. 1.
40. Kerns, R.D., J. Sellinger, and B.R. Goodin, *Psychological treatment of chronic pain.* Annual review of clinical psychology, 2011. 7: p. 411-434.
41. Geneen, L.J., et al., *Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews.* Cochrane Database Syst Rev, 2017. 4(4): p. Cd011279.
42. Jadad, A.R. and G.P. Browman, *The WHO analgesic ladder for cancer pain management: stepping up the quality of its evaluation.* Jama, 1995. 274(23): p. 1870-1873.

43. Araujo, A., et al., *Tratamiento del dolor en el paciente oncológico Treatment of pain in the oncology patient.* An. Sist. Sanit. Navar, 2004. 27(Suplemento 3).
44. Anekar, A.A. and M. Cascella, *WHO analgesic ladder.* 2020.
45. Bruggink, L., et al., *Chronic pain: Overlap and specificity in multimorbidity management.* Australian Journal for General Practitioners, 2019. 48: p. 689-692.
46. Thomas, M.A., *Pain management–the challenge.* Ochsner Journal, 2003. 5(2): p. 15-21.
47. Cate Polacek, M., et al., *Healthcare Professionals' Perceptions of Challenges to Chronic Pain Management.* The American journal of managed care, 2020. 26(4): p. e135-e139.
48. Bigen Man Shakya, S.S., Ninadini Shrestha, *Pain Management Practices and Perceived Barriers among the Health Professionals in Different Hospitals of Nepal.* Journal of Clinical and Diagnostic Research, 2020. 14(1): p. UC01-UC05.
49. Morriss, W. and C. Roques, *Pain management in low-and middle-income countries.* Bja Education, 2018. 18(9): p. 265-270.
50. Issa, M., A. Awajeh, and F. Khraisat, *Knowledge and attitude about pain and pain management among critical care nurses in a tertiary hospital.* J Intensive Crit Care, 2017. 3(1): p. 12.
51. Patel, T., et al., *Knowledge, perceptions and attitudes toward chronic pain and its management: a cross-sectional survey of frontline pharmacists in Ontario, Canada.* PloS one, 2016. 11(6): p. e0157151.
52. Nuseir, K., M. Kassab, and B. Almomani, *Healthcare providers' knowledge and current practice of pain assessment and management: How much progress have we made?* Pain Research and Management, 2016. 2016.
53. Shakya, B.M. and S. Shakya, *Knowledge and Attitude of Nurses on Pain Management in a Tertiary Hospital of Nepal.* Age (in years), 2016. 20(24): p. 21.
54. Rice, A.S., B.H. Smith, and F.M. Blyth, *Pain and the global burden of disease.* Pain, 2016. 157(4): p. 791-796.
55. Borders, T.F., et al., *Patient involvement in medical decision-making and pain among elders: physician or patient-driven?* BMC Health Services Research, 2005. 5(1): p. 1-8.
56. Varsi, C., et al., *Health care providers' experiences of pain management and attitudes towards digitally supported self-management interventions for chronic pain: a qualitative study.* BMC Health Services Research, 2021. 21(1): p. 275.
57. Tuong, W., E.R. Larsen, and A.W. Armstrong, *Videos to influence: a systematic review of effectiveness of video-based education in modifying health behaviors.* Journal of Behavioral Medicine, 2014. 37(2): p. 218-33.
58. Cuomo, A., et al., *Multimodal approaches and tailored therapies for pain management: the trolley analgesic model*. 2019, Taylor & Francis. p. 711-714.
59. Murphy, L., et al., *The role of the pharmacist in the care of patients with chronic pain.* Integrated Pharmacy Research and Practice, 2021: p. 33-41.
60. *Safer Healthcare Now. Best possible medication history interview guide.*
61. Busse, J.W., et al., *Guideline for opioid therapy and chronic noncancer pain.* Cmaj, 2017. 189(18): p. E659-E666.
62. Moulin, D., et al., *Pharmacological management of chronic neuropathic pain: revised consensus statement from the Canadian Pain Society.* Pain Research and Management, 2014. 19(6): p. 328-335.
63. Jessica Van Oosterwijck, M., et al., *Pain neurophysiology education improves cognitions, pain thresholds, and movement performance in people with chronic whiplash: a pilot study.* Pain, 2011. 48(1): p. 43-58.

64. Lee, H., et al., *Does changing pain-related knowledge reduce pain and improve function through changes in catastrophizing?* Pain, 2016. 157(4): p. 922-930.
65. Louw, A., et al., *The clinical application of teaching people about pain.* Physiotherapy theory and practice, 2016. 32(5): p. 385-395.
66. Thapa, P., et al., *Pharmacist-led intervention on chronic pain management: A systematic review and meta-analysis.* British Journal of Clinical Pharmacology, 2021.
67. Mishriky, J.S., Ieva: Chan, Vincent, *Expanding the role of Australian pharmacists in community pharmacies in chronic pain management - a narrative review.* Pharmacy Practice (1886-3655), 2019. 17(1): p. 1-6.
68. Giannitrapani, K.F., et al., *Expanding the role of clinical pharmacists on interdisciplinary primary care teams for chronic pain and opioid management.* BMC Family Practice, 2018. 19(1): p. 107.
69. Rapoport, A. and H. Akbik, *Pharmacist-managed pain clinic at a Veterans Affairs Medical Center.* American journal of health-system pharmacy, 2004. 61(13): p. 1341-1343.
70. Garha, M., *Health care in Nepal: An observational perspective.* J Nurs Educ Pract, 2017. 7(1): p. 114-117.
71. Mishra, S.R., et al., *National health insurance policy in Nepal: challenges for implementation.* Global health action, 2015. 8(1): p. 28763.
72. Ghimire, P., V.P. Sapkota, and A.K. Poudyal, *Factors Associated with Enrolment of Households in Nepal's National Health Insurance Program.* International journal of health policy and management, 2019. 8(11): p. 636-645.
73. Population, M.o.H.a., *Ministry of Health and Population. Nepal National Health Accounts Estimates 2017/18. Kathmandu: Ministry of Health and Population, Government of Nepal; 2022.*
74. Pandey, A.R., *Health financing reforms in the quest for universal health coverage: Challenges and opportunities in the context of Nepal.* J Glob Health, 2023. 13: p. 03021.
75. Nepal Health Research Council , M.o.H., M.E. Population , and O. Research, *Nepal Burden of Disease 2017: A Country Report based on the Globan Burden of Disease 2017 Study*. 2019, NHRC, MoHP and MEOR Kathmandu, Nepal.
76. Bhattarai, B., et al., *Chronic pain and cost: an epidemiological study in the communities of Sunsari district of Nepal.* Nepal Med Coll J, 2007. 9(1): p. 6-11.
77. Anil Shrestha, R.A., Ninadini Shrestha, *Evolution of pain management services in Nepal.* Anaesthesia & Intensive Care Medicine, 2020. 24(4).
78. Bal Bahadur Swar, D. and R. Senior, *Pain practice in Nepal thirty years ago: A practitioner's Quest.* Journal of Society of

Anesthesiologists of Nepal, 2017. 4(2): p. 49-53.
79. Bhandari, R., et al., *Use of analgesia in an emergency department.* Journal of Nepal Medical Association, 2013. 52(189): p. 224-228.
80. Subedi, A., et al., *Essential Pain Management: Perspective From Nepal.* Anesthesia & Analgesia, 2020. 131(5).
81. Sá, K.N., et al., *Prevalence of chronic pain in developing countries: systematic review and meta-analysis.* PAIN Reports, 2019. 4(6).
82. Poudyal, A., et al., *Prevalence and factors associated with joint pain in Nepal: findings from a countrywide cross-sectional STEPS survey.* BMJ Open, 2021. 11(10): p. e051536.
83. Kang, H., *Statistical considerations in meta-analysis.* Hanyang Medical Reviews, 2015. 35(1): p. 23-32.

84. Ahn, E. and H. Kang, *Introduction to systematic review and meta-analysis.* Korean J Anesthesiol, 2018. 71(2): p. 103-112.
85. Hariton, E. and J.J. Locascio, *Randomised controlled trials - the gold standard for effectiveness research: Study design: randomised controlled trials.* Bjog, 2018. 125(13): p. 1716.
86. Weinfurt, K.P. and B.B. Reeve, *Patient-Reported Outcome Measures in Clinical Research.* JAMA, 2022. 328(5): p. 472-473.
87. Kc, S., et al., *Nepali translation, cross-cultural adaptation and measurement properties of the Shoulder Pain and Disability Index (SPADI).* Journal of Orthopaedic Surgery and Research, 2019. 14(1): p. 284.
88. Raja, S.N., et al., *The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises.* PAIN, 9000. Articles in Press.
89. Enright, A. and R. Goucke, *The global burden of pain: the tip of the iceberg?* 2016, LWW.
90. Younger, J., R. McCue, and S. Mackey, *Pain outcomes: a brief review of instruments and techniques.* Current pain and headache reports, 2009. 13(1): p. 39-43.
91. Dworkin, R.H., et al., *Development and initial validation of an expanded and revised version of the Short-form McGill Pain Questionnaire (SF-MPQ-2).* Pain, 2009. 144(1-2): p. 35-42.
92. Lovejoy, T.I., D.C. Turk, and B.J. Morasco, *Evaluation of the psychometric properties of the revised short-form McGill Pain Questionnaire.* The Journal of Pain, 2012. 13(12): p. 1250-1257.
93. Adelmanesh, F., et al., *Reliability, validity, and sensitivity measures of expanded and revised version of the short-form McGill Pain Questionnaire (SF-MPQ-2) in Iranian patients with neuropathic and non-neuropathic pain.* Pain Medicine, 2012. 13(12): p. 1631-1638.
94. Ortner, C.M., et al., *The short-formmcgill pain questionnaire-revised to evaluate persistent pain and surgery-related symptoms in healthy women undergoing a planned cesarean delivery.* Regional Anesthesia & Pain Medicine, 2014. 39(6): p. 478-486.
95. Gauthier, L.R., et al., *Validation of the short-form McGill pain questionnaire-2 in younger and older people with cancer pain.* The Journal of Pain, 2014. 15(7): p. 756-770.
96. Farhat, B., F. Shebbo, and G. Kanazi, *Translation, Cross Cultural Adaptation and Validation of an Arabic Version of Short Form-2-Mcgill Pain Questionnaire (SF-MPQ-2).*
97. Wang, J.-L., et al., *A cross-cultural adaptation and validation of the short-form McGill Pain Questionnaire-2: Chinese version in patients with chronic visceral pain.* Journal of Pain Research, 2017: p. 121-128.
98. Buppha, P., et al., *Reliability and validity of the Thai short-form McGill pain questionnaire-2 (SF-MPQ-2).* Anesthesia & Clinical Research, 2016. 7(8): p. 1-6.
99. Maruo, T., et al., *Validity, reliability, and assessment sensitivity of the Japanese version of the short-form McGill pain questionnaire 2 in Japanese patients with neuropathic and non-neuropathic pain.* Pain Medicine, 2014. 15(11): p. 1930-1937.
100. Hasvik, E., et al., *Cross-cultural Adaptation and Validation of the Norwegian Short-form McGill Pain Questionnaire-2 in Low Back-related Leg Pain.* Spine (Phila Pa 1976), 2019. 44(13): p. E774-e781.
101. Tsang, S., C.F. Royse, and A.S. Terkawi, *Guidelines for developing, translating, and validating a questionnaire in perioperative and pain medicine.* Saudi journal of anaesthesia, 2017. 11(5): p. 80.

102. Ashby, M., *Essentials of pain medicine and regional anesthesia.* Anaesthesia and Intensive Care, 2005. 33(4): p. 548.
103. Dworkin, R.H., et al., *Core outcome measures for chronic pain clinical trials: IMMPACT recommendations.* Pain, 2005. 113(1-2): p. 9-19.
104. Sharma, S., et al., *Translation, cross-cultural adaptation and psychometric properties of the Nepali versions of numerical pain rating scale and global rating of change.* Health and quality of life outcomes, 2017. 15(1): p. 236.
105. PROMIS-DEPRESSION, *Health measures PROMIS Depression Scoring Manual PDF*.
106. Sharma, S., et al., *Psychometric properties of nepali versions of PROMIS short from measures of pain intensity, pain interference, pain behaviour, depressions, and sleep disturbance.* The Journal of Pain, 2018. 19(3): p. S59.
107. Beaton, D.E., et al., *Guidelines for the process of cross-cultural adaptation of self-report measures.* Spine (Phila Pa 1976), 2000. 25(24): p. 3186-91.
108. Raja, S.N., et al., *The revised International Association for the Study of Pain definition of pain: concepts, challenges, and compromises.* Pain, 2020. 161(9): p. 1976-1982.
109. Toblin, R.L., et al., *A population-based survey of chronic pain and its treatment with prescription drugs.* Pain, 2011. 152(6): p. 1249-1255.
110. Baxter, K., *Abstract PR284: Pain in Nepal Analysis of Prevalence, Impact and Treatment in the Kathmandu District.* Anesthesia & Analgesia, 2016. 123(3S_Suppl): p. 360.
111. Gatchel, R.J., et al., *Interdisciplinary chronic pain management: past, present, and future.* American psychologist, 2014. 69(2): p. 119.
112. Cohen, S.P., L. Vase, and W.M. Hooten, *Chronic pain: an update on burden, best practices, and new advances.* The Lancet, 2021. 397(10289): p. 2082-2097.
113. Cheung, C.W., et al., *Inadequate Management of Chronic Non-cancer Pain and Treatment-Related Adverse Events in Asia: Perspectives from Patients from 10 Countries/Regions.* SN Comprehensive Clinical Medicine, 2019. 1(6): p. 442-450.
114. Meda, R.T., et al., *Chronic Pain-Induced Depression: A Review of Prevalence and Management.* Cureus, 2022. 14(8): p. e28416.
115. Von Elm, E., et al., *The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies.* Annals of internal medicine, 2007. 147(8): p. 573-577.
116. Walters, J.L., et al., *Chronic pain and associated factors in India and Nepal: a pilot study of the Vanderbilt global pain survey.* Anesthesia & Analgesia, 2017. 125(5): p. 1616-1626.
117. Cella, D., et al., *The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008.* J Clin Epidemiol, 2010. 63(11): p. 1179-94.
118. Brooks, R. and E. Group, *EuroQol: the current state of play.* Health policy, 1996. 37(1): p. 53-72.
119. Bhattarai, P., et al., *Health related quality of life of adults in Nepal with respiratory symptoms using WHOQOL and EQ-5D*. 2005, Thesis Samir Kumar, K C.[University of Groningen] 2009:[Sn].
120. Van Hout, B., et al., *Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets.* Value in health, 2012. 15(5): p. 708-715.
121. Ghimire, S., et al., *Factors Associated With Health-Related Quality of Life among Hypertensive Patients in Kathmandu, Nepal.* Frontiers in cardiovascular medicine, 2017. 4: p. 69-69.

122. Dasgupta, E., et al., *Prevalence of musculoskeletal pain in two primary care clinics in a mid-sized town's urban population in Malaysia.* Malaysian family physician: the official journal of the Academy of Family Physicians of Malaysia, 2021. 16(1): p. 93.
123. Wu, A., et al., *Global low back pain prevalence and years lived with disability from 1990 to 2017: estimates from the Global Burden of Disease Study 2017.* Annals of translational medicine, 2020. 8(6).
124. Kshetri, D.B.B., *Knee pain and knee pain related disability in adults of the Western Development Region of Nepal*. 2017, University of Central Lancashire.
125. Riley III, J.L., et al., *Sex differences in the perception of noxious experimental stimuli: a meta-analysis.* Pain, 1998. 74(2-3): p. 181-187.
126. Fillingim, R.B., et al., *Sex, gender, and pain: a review of recent clinical and experimental findings.* The journal of pain, 2009. 10(5): p. 447-485.
127. Alabas, O.A., et al., *Gender role affects experimental pain responses: a systematic review with meta-analysis.* Eur J Pain, 2012. 16(9): p. 1211-23.
128. Shaygan, M. and A. Jaberi, *The effect of a smartphone-based pain management application on pain intensity and quality of life in adolescents with chronic pain.* Scientific Reports, 2021. 11(1): p. 6588.
129. Jalil, N.A., et al., *Retrospective review of outcomes of a multimodal chronic pain service in a major teaching hospital: A preliminary experience in Universiti Sains Malaysia.* 2009.
130. Baharuddin, K.A., et al., *Assessing patient pain scores in the emergency department.* The Malaysian journal of medical sciences : MJMS, 2010. 17(1): p. 17-22.
131. Majedi, H., et al., *Predicting Factors of Pain Duration in Patients with Chronic Pain: A Large Population-based Study.* Anesth Pain Med, 2020. 10(1): p. e95776.
132. Clark, J.D., *Chronic Pain Prevalence and Analgesic Prescribing in a General Medical Population.* Journal of Pain and Symptom Management, 2002. 23(2): p. 131-137.
133. Di Gangi, S., et al., *Prescribing patterns of pain medications in unspecific low back pain in primary care: a retrospective analysis.* Journal of clinical medicine, 2021. 10(7): p. 1366.
134. Bhaskar, R., et al., *Prescription pattern of analgesics in orthopedics outpatient department at a tertiary care hospital.* Int J Basic Clin Pharmacol, 2015. 4(2): p. 250-253.
135. Bhattarai, A.K., K.R. Khanal, and J.P. Bharati, *Non-Steroidal Anti-Inflammatory Drugs in Orthopedic Outpatient Cases in a Tertiary Care Teaching Hospital: A Descriptive Cross-sectional Study.* JNMA: Journal of the Nepal Medical Association, 2021. 59(243): p. 1116.
136. Zin, C.S., et al., *Trends and patterns of analgesic prescribing in Malaysian public hospitals from 2010 to 2016: tramadol predominately used.* Journal of pain research, 2018: p. 1959-1966.
137. Goldstick, J.E., et al., *Patterns in nonopioid pain medication prescribing after the release of the 2016 Guideline for Prescribing Opioids for Chronic Pain.* JAMA Network Open, 2022. 5(6): p. e2216475-e2216475.
138. Richards, G.C., et al., *Global, regional, and national consumption of controlled opioids: a cross-sectional study of 214 countries and non-metropolitan territories.* British journal of pain, 2021: p. 20494637211013052.
139. Paudel, B.D., et al., *Opioid Availability and Palliative Care in Nepal: Influence of an International Pain Policy Fellowship.* Journal of Pain and Symptom Management, 2015. 49(1): p. 110-116.
140. Network, S.I.G., *SIGN 136: management of chronic pain: a national clinical guideline (revised edition). 2019.*

141. Singh, S., et al., *A Comparative study of intra-articular injection of steroid versus prolotherapy for pain relief in patients of osteoarthritis knee.* Indian Journal of Pain, 2019. 33(1): p. 25.
142. Arroll, B. and F. Goodyear-Smith, *Corticosteroid injections for osteoarthritis of the knee: meta-analysis.* Bmj, 2004. 328(7444): p. 869.
143. Chang, W.J., *Muscle Relaxants for Acute and Chronic Pain.* Physical Medicine and Rehabilitation Clinics of North America, 2020. 31(2): p. 245-254.
144. Rapti, E., et al., *Patients with chronic pain: evaluating depression and their quality of life in a single center study in Greece.* BMC psychology, 2019. 7(1): p. 86-86.
145. Silva, S.M.C., et al., *Impairment of quality of life due to anxiety and depression in patients with chronic pain.* BrJP, 2021. 4: p. 216-220.
146. Tsuji, T., et al., *The impact of depression among chronic low back pain patients in Japan.* BMC musculoskeletal disorders, 2016. 17: p. 1-9.
147. Elliott, T.E., C.M. Renier, and J.A. Palcher, *Chronic pain, depression, and quality of life: correlations and predictive value of the SF-36.* Pain Med, 2003. 4(4): p. 331-9.
148. Garnaes, K.K., et al., *What factors are associated with health-related quality of life among patients with chronic musculoskeletal pain? A cross-sectional study in primary health care.* BMC musculoskeletal disorders, 2021. 22(1): p. 1-12.
149. Hannerz, H., A. Holtermann, and I.E.H. Madsen, *Musculoskeletal pain as a predictor for depression in the general working population of Denmark.* Scand J Public Health, 2021. 49(6): p. 589-597.
150. Donnet, A., et al., *Chronic cluster headache: a French clinical descriptive study.* Journal of Neurology, Neurosurgery & Psychiatry, 2007. 78(12): p. 1354.
151. Brooks, J.M., et al., *Pain intensity, depressive symptoms, and functional limitations among older adults with serious mental illness.* Aging & mental health, 2019. 23(4): p. 470-474.
152. Muhammad, T. and M. Rashid, *Prevalence and correlates of pain and associated depression among community-dwelling older adults: Cross-sectional findings from LASI, 2017–2018.* Depression and anxiety, 2022. 39(2): p. 163-174.
153. Rayner, L., et al., *Depression in patients with chronic pain attending a specialised pain treatment centre: prevalence and impact on health care costs.* Pain, 2016. 157(7): p. 1472-1479.
154. Bair, M.J., et al., *Depression and pain comorbidity: a literature review.* Archives of internal medicine, 2003. 163(20): p. 2433-2445.
155. Zuraida, N. and R. Parameswaran, *Prevalence of depression among patients with headache in Kuala Lumpur, Malaysia.* Malaysian Journal of Psychiatry, 2007. 16(2).
156. Mallen, C.D. and G. Peat, *Screening older people with musculoskeletal pain for depressive symptoms in primary care.* British Journal of General Practice, 2008. 58(555): p. 688-693.
157. Suija, K., R. Kalda, and H.-I. Maaroos, *Depression and musculoskeletal problems.* British Journal of General Practice, 2009. 59(558): p. 51-51.
158. Munce, S.E. and D.E. Stewart, *Gender differences in depression and chronic pain conditions in a national epidemiologic survey.* Psychosomatics, 2007. 48(5): p. 394-399.
159. Ang, D.C., et al., *Predictors of Pain Outcomes in Patients with Chronic Musculoskeletal Pain Co-morbid with Depression: Results from a Randomized Controlled Trial.* Pain Medicine, 2010. 11(4): p. 482-491.
160. Mullins, P.M., R.J. Yong, and N. Bhattacharyya, *Associations between chronic pain, anxiety, and depression among adults in the United States.* Pain Practice, 2023.

161. Hadi, M.A., G.A. McHugh, and S.J. Closs, *Impact of Chronic Pain on Patients' Quality of Life: A Comparative Mixed-Methods Study.* Journal of Patient Experience, 2019. 6(2): p. 133-141.
162. Sharma, S., et al., *Translation, cross-cultural adaptation and psychometric properties of the Nepali versions of numerical pain rating scale and global rating of change.* Health Qual Life Outcomes, 2017. 15(1): p. 236-236.
163. Nakarmi, S., S.A. Haq, and B. Vaidya, *Translation, validation and cross-cultural adaptation of the Nepali version of WOMAC® LK 3.1.* International journal of rheumatic diseases, 2019. 22(10): p. 1877-1883.
164. EQ-5D-3L and *EuroQol Research Foundation. EQ-5D-3L User Guide,*. 2018. .
165. Cella, D., et al., *The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years.* Medical care, 2007. 45(5 Suppl 1): p. S3.

Received: 19 August 2020 | Revised: 5 January 2021 | Accepted: 17 January 2021

DOI: 10.1111/bcp.14745

SYSTEMATIC REVIEW AND META-ANALYSIS

Pharmacist-led intervention on chronic pain management: A systematic review and meta-analysis

Parbati Thapa[1] | Shaun Wen Huey Lee[1] | Bhuvan KC[1,2] | Juman Abdulelah Dujaili[1] | Mohamed Izham Mohamed Ibrahim[3] | Sudesh Gyawali[4]

[1]School of Pharmacy, Monash University Malaysia, Subang Jaya, Selangor, Malaysia

[2]College of Public Health, Medical & Veterinary Sciences, James Cook University, Townsville, QLD, Australia

[3]Social and Administrative Pharmacy, College of Pharmacy, Qatar University, Doha, Qatar

[4]Department of Pharmacology, Manipal College of Medical Sciences, Pokhara, Nepal

Correspondence
Bhuvan KC, School of Pharmacy, Monash University Malaysia, Jalan Lagoon Selatan, 47500 Bandar Sunway, Selangor, Malaysia.
Email: bhuvan.kc@monash.edu

Aims: Pharmacists have been contributing to the management of chronic pain, ensuring the quality use of medicine. However, there is diversity in the interventions provided by pharmacists and their impact.

Methods: Six electronic databases were searched from inception until June 2020 for articles published in English examining the intervention provided by the pharmacist in chronic pain management. Studies investigating the impact of pharmacist intervention individually or multidisciplinary teams including pharmacists for chronic pain management were included.

Results: Fourteen studies (2365 participants) were included in the current review. Six studies were randomized controlled trials while the remainder were observational studies in which pharmacists provided intervention individually or in collaboration with other healthcare professionals. Medication review was the most common intervention provided by the pharmacist. The pooled analysis found that pharmacist-led interventions reduced the pain intensity (−0.22; 95% confidence interval [CI]: −0.35 to −0.09; moderate certainty) among participants with chronic pain. Opiate stewardship provided by pharmacists was effective; however, mixed results were noted on the impact of the intervention on physical functioning, anxiety, depression and quality of life. Pharmacist intervention was more expensive than treatment as usual.

Conclusions: Pharmacists contribute substantially to chronic pain management, ensuring the quality use of medicine, resulting in reduced pain intensity. Further studies with rigorous design are needed to measure the impact of pharmacist-provided intervention individually or in a multidisciplinary team on the economic benefit and other health outcomes.

KEYWORDS
chronic pain, medication review, pain intensity, pain management, pharmacist, systematic review

1 | INTRODUCTION

Chronic pain is defined as pain that persists beyond the normal tissue healing time of 3 months or more.[1] It is a major global health problem and cause of disability.[2] Studies indicate a high prevalence of chronic pain ranging between 13% and 51% of the population in developing countries and up to 60% of the population in developed countries.[3] The impact of pain on economies is enormous, and is estimated to cost between $560 to $635 billion in the United States alone.[4] Chronic pain is also associated with mental health issues such as depression and anxiety, which affect an individual's quality of life.[5] The high prevalence and refractory nature of chronic

pain have led to a surge in research on how to best manage this condition.

Current guidelines recommend the management of chronic pain via the adoption of a multimodal approach using both pharmacological and non-pharmacological treatments.[6] These include paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs) or opiates used individually or as a combination therapy.[7] However, despite available evidence, there are various barriers to effective pain management. Lack of clearly defined pain management protocols, inadequate knowledge and skills among healthcare workers, lack of teamwork among healthcare staff, patients' fear of adverse effects, and reluctance to take analgesics are some of the barriers to effective pain management. Pharmacists' involvement in a medication review and pain education is a promising strategy to reduce pain intensity and enhance physical functioning.[7] The potential benefits of involving clinical pharmacists specialized in pain management include reducing the burden on physicians as well as better use of opioids.[8]

To date, several reviews have examined the impact of pharmacist-led intervention on chronic pain management. In the earliest review by Bennett et al. in 2011, the authors reported that the provision of pain education by pharmacists was effective in reducing the adverse effects of medication and pain intensity.[9] Hadi and colleagues in their review reported that pharmacist-led medication review reduces pain intensity, improves physical functioning and patient satisfaction.[10] A narrative review by Mishriky et al. in 2019 highlighted that pharmacist-led chronic pain education and medication management were effective in alleviating pain and adverse events related to drug use in community pharmacies.[11] Nevertheless, these reviews focused on only one aspect of intervention or setting and were not a comprehensive review focusing on the roles of pharmacist-led management of chronic pain. The current review aims to comprehensively summarize pharmacist-led intervention on pain management, either individually or in a multidisciplinary team, irrespective of setting.

2 | METHODS

2.1 | Search strategy

We searched for articles describing pharmacist-led intervention on pain management from database inception to June 30, 2020. The electronic search was performed in MEDLINE, Embase, CINAHL, PsycINFO, International Pharmaceutical Abstracts, and Cochrane Central Register of Controlled Trials. Search terms included pharm*, medication review, counselling, patient education, pharmaceutical care, chronic pain, and chronic pain management (Table S1). This was supplemented with hand-search of reference lists of the retrieved articles.

2.2 | Study selection

Retrieved articles were screened by title and abstract independently by two reviewers (P.T. and S.W.H.L). Studies were included if: (i) they involved pharmacist-delivered intervention either alone or within a multidisciplinary team (medication review, pharmaceutical care, patient education or counselling); (ii) intervention was delivered to an adult patient aged 18 years and above; and (iii) patient had complaints of chronic noncancer pain (defined as pain persisting for 3 months or more). All study designs were eligible for inclusion in the review. However, review articles and conference poster abstracts were excluded.

2.3 | Data extraction

Data were extracted independently using the standardized data extraction form. All relevant information required for the systematic review was extracted including author names, year of publication, the country where the study was performed, study demographics, intervention details, as well as outcome measures. The extracted data were verified by two authors (B.K.C. and S.W.H.L) for any inconsistencies and were resolved by discussion and consensus. The outcomes of interest were pain intensity, physical functioning and mental health.

2.4 | Risk of bias (quality assessment)

Quality was independently assessed by two authors (P.T. and B.K.C) using the Cochrane Risk of Bias (ROB 2.0) for randomized controlled trials[12] and Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) assessment tool for non-randomized studies.[13] The quality assessment was checked by a third reviewer (S.W.H.L). We subsequently used the GRADE criteria to assess the quality of evidence for each outcome reported. Any disagreements between the reviewers were resolved through discussion and consensus.

2.5 | Data analysis

All studies were described narratively. Data were pooled if comparable outcome data from two or more studies were available. In the meta-analysis, we used the random effect meta-analysis model, as we assumed that clinical and methodological heterogeneity was likely to exist and have an effect on the result. Comparable data studies with multiple arms were combined to create a single pairwise comparison. Results are presented as mean differences and their 95% confidence interval for continuous outcomes. Statistical heterogeneity was assessed using I^2 statistics. As a priori, we also performed subgroup analyses by activities performed by pharmacist, pain aetiology as well as study duration. All analyses were performed using Review Manager version 5.4 (The Nordic Cochrane Centre, Copenhagen).[14]

2.6 | Study protocol registration

The study protocol was registered with PROSPERO (CRD42020164445).

3 | RESULTS

3.1 | Study characteristics

A total of 517 articles were identified and 31 articles underwent further review. Fourteen articles, including six randomized controlled trials (RCT),[15–20] three retrospective chart reviews,[21–23] two before and after studies,[24,25] one retrospective cohort study,[26] one prospective cohort study[27] and one cross-sectional study,[28] were included (Figure 1). These studies were conducted in the United States (*n* = 6), United Kingdom (*n* = 4), Canada (*n* = 2), Germany (*n* = 1) and Japan (*n* = 1), either in general practices, hospitals or specialized settings such as pain clinics and rehabilitation centres. These studies had recruited a total of 2365 participants, with a median sample size of 120 participants (range 23–410). The mean age of participants was between 42.7 and 68.2 years old and the majority (81.9%) of the participants were females. Participants in these studies had reported chronic pain originating from the musculoskeletal systems (knee, spine, joint, back), neurological system (headache and migraine) and unspecified chronic pain. Pain measurement tools used in these studies were the Chronic Pain Grade Scale (CPGS),[18,28] Numeric Pain Rating Scale (NPRS),[15,26] Western Ontario and McMaster Universities osteoarthritis index (WOMAC),[16,17] Brief Pain Inventory (BPI),[23–25] pharmacotherapeutic pain inventory,[20] and the Pain, Enjoyment of Life and General Activity score (PEG).[27]

3.2 | Quality of studies

3.2.1 | Randomized controlled studies

The six included RCTs had a low risk of bias for most of the criteria assessed (Figures S1 and S2). However, there was some concern about risk of bias in deviation from intended intervention in all studies due to blinding of participants and personnel, as most of the studies were open label in nature. Two studies were judged to have a high risk due to the measurement of the outcome[20] and the selection of reported results.[17]

3.2.2 | Observational studies

Most of the studies were judged to be of average quality. Two of the studies were judged to have a serious risk of bias,[21,26] five moderate,[22–25,27] and only one low risk of bias.[28] The studies were judged to have a serious risk of bias due to participant selection and confounding (Table S2).

3.3 | Pharmacist intervention

3.3.1 | Medication review

Medication review was the most common intervention provided by the pharmacist, which was performed in eight studies.[15,17–20,22,26,28]

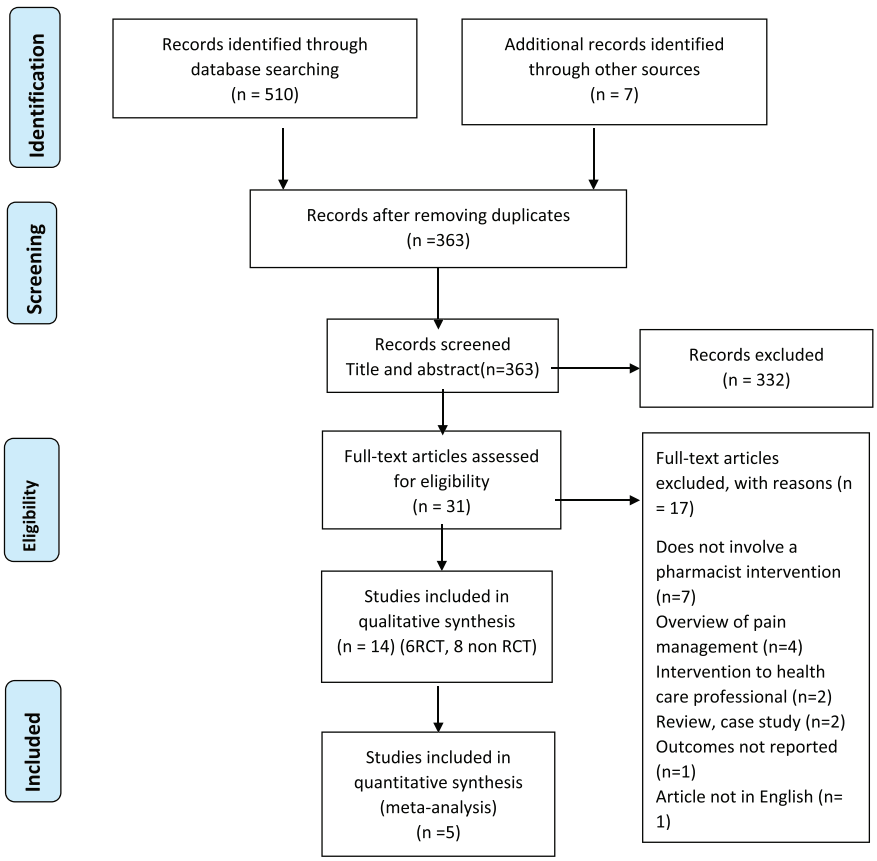

FIGURE 1 Flowchart of selection of articles in the study

In these reviews, pharmacists assessed for allergies and adverse drug reactions (ADRs), reviewed medication and made recommendations for medication changes.[15,17–19,26,28] Pharmacists also individualized drug therapy, assessed for drug-related problems and untreated symptoms.[20,22] Three studies described how pharmacists devised a pharmaceutical care plan including medication review[15,18,20] (Tables 1–3).

3.3.2 | Multidisciplinary team for the management of pain

We also identified five studies where pharmacists were involved in the multidisciplinary or interdisciplinary team for the management of pain.[16,21,23–25] Pharmacists reviewed patient medications,[16] performed opiate stewardship, where they screened and evaluated the use of opioids to support its judicious use,[21,23,24] and provided patient education.[25] These approaches led to improvements in pain score,[16] pain disability index,[24] symptoms of anxiety and depression,[23–25] self-efficacy,[25] pain severity and interference, as well as reduced need for morphine use[21,23] (Table 4).

3.3.3 | Intervention through educational video

One study used educational videos as an intervention aid followed by group discussion with pharmacists and physicians. Each video was 10 minutes long and educated patients on pain management and pain medications. At the end of the study, the patients' knowledge of pain was improved, but no impact was observed on patients' functional status[27] (Table 3).

3.4 | Outcome measures of RCT studies

3.4.1 | Pain score/intensity

Five studies reported the impact of pharmacist intervention on pain intensity.[15–18,20] Pooled estimates of the five studies found that pharmacist involvement reduced pain intensity scores among participants with chronic pain compared to control (SMD: −0.22; 95% confidence interval [CI]: −0.35 to −0.09; I^2 = 0%, P = 0.001, Figure 2). Subgroup analyses showed that pharmacist intervention was more effective if the intervention was at least 3 months or longer, among those with musculoskeletal pain as well as if it involved a medication review process or pharmaceutical care with the medication review group and among different pain aetiology (Table 1).

3.4.2 | Physical functioning

Five studies reported physical functioning as an outcome measure of their intervention.[15–18,20] Pharmacist-led intervention had a mixed impact on the physical functioning of participants. Pooled estimates found that pharmacist-provided intervention had minimal effect on

TABLE 1 Subgroup analysis on pain intensity: duration of intervention, pain aetiology and intervention type

Outcome/subgroup	No. of studies	No. of participants	Statistical method	Effect size (95% CI)
Pain intensity (overall)	5 [15–18, 20]	876	Std. mean difference (IV, random, 95% CI)	−0.22[−0.35, −0.09]
1. Subgroup: By duration of intervention				
1.1 Three months	1 [20]	41	Std. mean difference (IV, random, 95% CI)	−0.44[−0.16, 0.19]
1.2 More than three months	4 [15–18]	835	Std. mean difference (IV, random, 95% CI)	−0.21 [−0.35, −0.07]
2. Subgroup: By pain aetiology				
2.1 Musculoskeletal pain	2 [16, 17]	332	Std. mean difference (IV, random, 95% CI)	−0.32[−0.59, −0.04]
2.2 Neurological pain	1 [15]	357	Std. mean difference (IV, random, 95% CI)	−0.15[−0.35, 0.06]
2.3 Chronic pain (unspecified)	2 [18, 20]	187	Std. mean difference (IV, random, 95% CI)	−0.21[−0.15, 0.09]
3. Subgroup: By types of intervention				
3.1 Medication review	2 [16, 17]	332	Std. mean difference (IV, random, 95% CI)	−0.32[−0.59, −0.04]
3.2 Pharmaceutical care with medication review	3 [15, 18, 20]	544	Std. mean difference (IV, random, 95% CI)	−0.17[−0.34, 0.00]

TABLE 2 Subgroup analysis on physical functioning: duration of intervention, pain aetiology and intervention type

Outcomes/subgroup	No. of studies	No. of participants	Statistical method	Effect size (95% CI)
Physical functioning (overall)	5 [15–18, 20]	851	Std. mean difference (IV, random, 95% CI)	−0.16[−0.38, 0.06]
1. Subgroup: By duration of intervention				
1.1 Three months	1 [20]	41	Std. mean difference (IV, random, 95% CI)	−0.50[−1.12, 0.13]
1.2 More than three months	4 [15–18]	810	Std. mean difference (IV, random, 95% CI)	−0.13[−0.36, 0.10]
2. Subgroup: By pain aetiology				
2.1 Musculoskeletal pain	2 [16, 17]	327	Std. mean difference (IV, random, 95% CI)	−0.27[−0.62, 0.08]
2.2 Neurological pain	1 [15]	354	Std. mean difference (IV, random, 95% CI)	−0.14[−0.35, 0.07]
2.3 Chronic pain (unspecified)	2 [18, 20]	170	Std. mean difference (IV, random, 95% CI)	−0.09[−0.79, 0.61]
3. Subgroup: By types of intervention				
3.1 Medication review	2 [16, 17]	327	Std. mean difference (IV, random, 95% CI)	−0.27[−0.62, 0.08]
3.2 Pharmaceutical care with medication review	3 [15, 18, 20]	524	Std. mean difference (IV, random, 95% CI)	−0.08[−0.41, 0.24]

improving the physical functioning of the participants (SMD: −0.16; 95% CI: −0.38 to 0.06; I^2 = 54%, P = 0.15, Figure 3). No difference was observed when studies were stratified by study duration, pain aetiology or pharmacist-led activities (Table 2).

3.4.3 | Mental health

In two studies that reported mental health of participants,[15,20] pooled estimates found that pharmacist-led intervention had minimal effect on their mental health (SMD: −0.01; 95% CI: −0.21 to 0.19; I^2 = 0%, P = 0.94, Figure 4).

3.4.4 | Anxiety and depression

Pharmacist-led intervention had mixed results on anxiety and depression. In the study by Bruhn et al., intervention by pharmacists reduced anxiety and depression,[18] but no improvements were seen in another study by Hay et al. in 2006.[17]

3.4.5 | Quality of life

Pharmacist-led intervention had a mixed impact on the quality of life of participants. While the study by Hoffmann et al. in 2008 and Marra et al. in 2012[15,16] reported an improvement in the quality of life, no changes were observed in the study by Bruhn et al. in 2013.[18]

3.4.6 | Satisfaction and acceptability of pharmacist intervention

Three studies reported that patients were satisfied with the involvement of pharmacists in their chronic care management, as they felt they received better service delivery.[17,18,20] Similarly, the healthcare providers were also positive about the involvement of pharmacists in a pharmaceutical care plan delivery with medication review and agreed upon the provided recommendation in a study by Bruhn et al. in 2013.[18]

3.4.7 | Costs and benefits

Only one study assessed the costs and benefits of pharmacist-led intervention.[19] Intervention cost was calculated based on pharmacist training, intervention delivery and pharmacist follow-up appointments together with medication, primary and secondary care utilities. Compared with treatment as usual, pharmacist-led intervention was more expensive, mainly due to the higher cost related to salaries, with an incremental cost of £54 to £77 per patient in the intervention group relative to the treatment as usual group.[19]

3.5 | Outcome measures of observational studies

Eight observational studies were included in this review. Six studies reported pain intensity scores.[23–28] Pharmacist intervention or

TABLE 3 Summary of studies that involved medication review and educational video

RCT studies							
Author, year, country	**Study design and study site**	**Pain aetiology**	**No. of participants**	**Intervention**	**Intervention frequency**	**Follow-up period**	**Conclusion**
Neilson et al., 2015, UK[19]	Randomized control trial, general practices	Chronic pain	Total (*n* = 196) • Pharmacist prescribing arm (*n* = 70) • Pharmacist review arm (*n* = 63) • Treatment as usual (*n* = 63)	Medication review whereby pharmacist reviewed medications, provided face to face consultation and generated report to GP	Not mentioned	3 or 6 months	Pharmacist-led intervention was more expensive compared with treatment as usual.
Bruhn et al., 2013, UK[18]	Randomized controlled trial, pharmacy practices	Chronic pain	Total (*n* = 196) • Pharmacist prescribing arm (*n* = 70) • Pharmacist review arm (*n* = 63) • Treatment as usual (*n* = 63)	Medication review with pharmaceutical care plan whereby pharmacist reviewed the medication devised and implemented pharmaceutical care plan and generated report to GP	Not mentioned	3 or 6 months	Pharmacist-led intervention improved the chronic pain grade, anxiety and depression score.
Hoffmann et al., 2008, Germany[15]	Randomized controlled trial, pharmacies	Headache and migraine	Total (*n* = 410) • Control (*n* = 209) • Intervention (*n* = 201)	Medication review with pharmaceutical care plan whereby pharmacist reviewed the medication, prioritized patient's problem, and devised a pharmaceutical care plan	Each pharmacy counselled 4.6 ± 3.01 patients on average, 2 hours/ patient	4 months	Short-term pharmaceutical care programme intervention improved mental health and self- efficacy.
Hay et al., 2006, UK[17]	Randomized clinical trial, general practices	Knee pain	Total (*n* = 325) • Intervention (*n* = 108) • Enhanced pharmacy review (*n* = 108) • Community physiotherapy (*n* = 109)	Medication review whereby pharmacist assessed adverse events from NSAIDs, monitored the effectiveness of drugs and recommended changes if required	Three to six sessions of 20 minutes duration over the 10 weeks	3, 6 or 12 months	Pharmacist-led intervention improved health outcomes, reduced use of NSAIDs, and achieved high patient satisfaction.
Gammaitoni et al., 2000, USA[20]	Randomized controlled trial, pain clinic	Chronic pain	Total (*n* = 74) • Control (*n* = 36) • Intervention (*n* = 38)	Medication review with pharmaceutical care programme whereby pharmacist monitored	81 phone calls; 45 to patient and 36 to clinical staff; average time: 12 min/patient	3 months	The pharmaceutical care model was beneficial. Patients perceived better access to

(Continues)

TABLE 3 (Continued)

Author, year, country	Study design and study site	Pain aetiology	No. of participants	Intervention	Intervention frequency	Follow-up period	Conclusion
RCT studies							
				pharmacotherapy for potential and actual drug-related problem and implemented pharmaceutical care programme			medicine, efficient prescription processing, and satisfaction with the pharmacist's service.
Observational studies							
Semerjian et al., 2019, USA[22]	Retrospective chart review, pain clinic at an academic centre	Back pain, myofascial pain	Total (*n* = 67)	Medication review whereby pharmacist identified and resolved any medication-related problem	In 2 years, 67 patients had 380 visits to pharmacist; initial visit 30 minutes (294 visits) and follow-up 15 minutes (86 visit)	Not mentioned	A clinical pharmacist can identify medication-related problems and implement interventions to resolve it in chronic pain management.
Mathew et al., 2016, USA[26]	Retrospective cohort study, academic medical centre	Pain due to skin and soft tissue infection, sickle cell crisis, neuropathic pain	Total (*n* = 100)	Medication review whereby pharmacist comprehensively assessed pain, functional status, substance abuse, medication usage and side effects	821 interventions in the 2 years, each patient followed for 3 days	3 days	The pharmacy pain team in pain management had a positive impact on pain score and improved functionality.
McDermott et al., 2006, UK[28]	Cross-sectional study, general practice	Chronic pain	Total (*n* = 230)	Medication review whereby pharmacist reviewed the medicine and prepared the prescribing recommendation to the GP	192 recommendations for 113 patients	6 months	Pharmacist-led intervention was accepted and most of the recommendations provided to the GP were implemented.
Vogler et al., 2017, USA[27]	Prospective cohort design, academic general medicine practice	Chronic pain	Total (*n* = 35)	Education video on chronic pain was displayed whereby pharmacists participated in education group visit with doctor and nurse	20 group visits over the 18-month study period (each group visit lasted 90 minutes)	Immediately after	Group visits providing education on chronic pain enhanced patient's knowledge and satisfaction.

GP: General Practitioner.

TABLE 4 Summary of studies that involved multidisciplinary/interdisciplinary pain management team

Author, year, country	Study design and study site	Pain aetiology	No. of participants	Intervention	Intervention frequency	Other health care professionals involved	Follow-up period	Conclusion
RCT study								
Marra et al., 2012, Canada[16]	Cluster randomized trial, community pharmacies	Knee osteoarthritis	Total (n = 139) • Control (n = 66) • Intervention (n = 73)	Multidisciplinary pain management programme whereby pharmacist was involved in medication review, provided education, recommended to primary care physician, and referred to physiotherapist if needed	297 follow-ups by the pharmacist and 355 recommendations to GP	Physician, physiotherapist	3 or 6 months	Pharmacist-initiated multidisciplinary intervention improved the pain, function and quality of life of patients with knee osteoarthritis
Observational studies								
Boren et al., 2019, USA[21]	Retrospective chart review, out-patient physical medicine and rehabilitation clinic	Musculoskeletal pain, neuropathic pain	Total (n = 383)	Interdisciplinary team managing chronic opioid therapy whereby pharmacist was involved in medication review, recommended for screening of drug in urine, initiated noncontrolled medications	Pharmacist completed 1197 visits, non- opioid Medication initiated to 209 patients	Physician, physical therapist, nurse	Every 3 months	The addition of clinical pharmacists helped to optimize opioid and nonopioid therapy, improved adherence to best practice standards.
Takahashi et al., 2019, Japan[25]	Before and after study, hospital	Musculoskeletal pain	Total (n = 23)	Multidisciplinary pain management programme whereby pharmacist provided patient education related to side effects of drugs	Education session lasted for 30–60 minutes, patients received 20 sessions in total	Orthopaedic surgeons, psychiatrists, nurses, physical therapists, clinical psychologists, nutritionists	3 weeks, 3 or 6 months	The multidisciplinary intervention improved physical function, ability to cope with pain, and enhanced quality of life.

(Continues)

TABLE 4 (Continued)

RCT study								
Author, year, country	**Study design and study site**	**Pain aetiology**	**No. of participants**	**Intervention**	**Intervention frequency**	**Other health care professionals involved**	**Follow-up period**	**Conclusion**
White et al., 2018, Canada[23]	Retrospective chart review, hospital	Myofascial pain, musculoskeletal pain, neuropathic pain	Total (*n* = 102)	Interdisciplinary pain management programme whereby pharmacist was involved in medication management and recorded opioid analgesic	Patients spent 150 clinic hours and 90 minutes of pain neurophysiology education	Physician, physical therapist, occupation therapist, psychologist, kinesiologist	6 weeks	The interdisciplinary intervention improved pain interference, knowledge, severity, depression and opioid intake.
Chelminski et al., 2005, USA[24]	Before and after study, academic general medicine clinic	Chronic pain	Total (*n* = 85)	Multidisciplinary pain management programme whereby pharmacist was involved in medication review and monitored substance misuse	Monthly follow-up by a clinical pharmacist	Physician, psychiatrist, nurse	3 months	The multidisciplinary intervention improved pain, depression and disability score, and identified substance misuse.

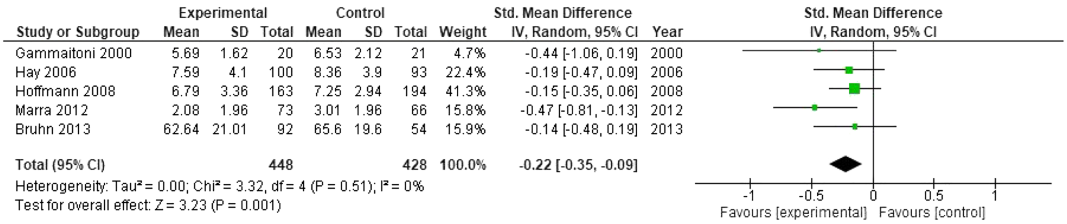

FIGURE 2 Forest plot showing the standard mean difference (SMD) in pain intensity among participants following the pharmacist intervention and the control group. The size of the data marker is determined by weight from random effect analysis. CI, confidence interval

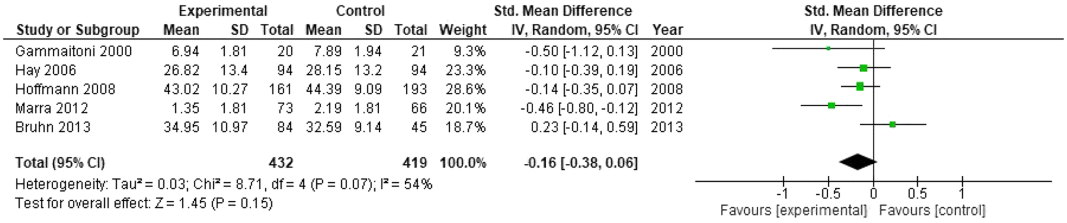

FIGURE 3 Forest plot showing the standard mean difference (SMD) among participants on physical functioning following the pharmacist intervention and the control group. The size of the data marker is determined by weight from random effect analysis. CI, confidence interval

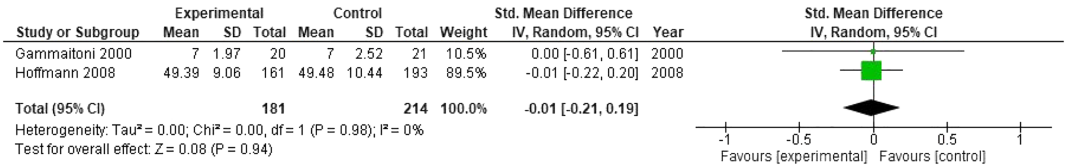

FIGURE 4 Forest plot showing the standard mean difference (SMD) among participants on mental health following the pharmacist intervention and the control group. The size of the data marker is determined by weight from random effect analysis. CI, confidence interval

multidisciplinary pain management programmes involving pharmacists had a mixed impact on the patients' reported pain scores. Improvement in score was recorded in four studies,[23–26] while studies by Vogler et al. in 2017, and McDermott et al. in 2006 reported otherwise.[27,28] Similarly, among five of the reported studies,[23–27] physical functioning was improved in four studies[23–26] while no impact was observed in the study by Vogler et al. in 2017.[27]

Pharmacists conducted opiate stewardship and optimized the dose of morphine, with dose reduction in two studies[21,23] and dose increment in a study by Chelminski et al. in 2005.[24] Pharmacists identified and resolved medication related problems in two studies.[22,26] Several studies identified in the review had also reported outcomes such as depression,[23–25] quality of life,[25] satisfaction and acceptability of the intervention.[27,28] These studies reported a positive impact on these outcomes with the provided intervention.

3.5.1 | Certainty of evidence

Based upon the GRADE assessment, the certainty of evidence was rated as moderate for the outcome of pain intensity and quality of life. However, the other outcomes were rated as "low" to "very low" owing to imprecisions and heterogeneity (Table S3).

4 | DISCUSSION

Chronic pain is a complex phenomenon and managing chronic pain is a challenging issue due to its multifactorial nature. A collaborative care model of healthcare professions including pharmacists has been shown to be essential for better health outcomes.[29] Our review showed that most of the interventions carried out by pharmacists were focused on appropriate medication use for better pain control. However, there was diversity in how these interventions were delivered including medication review, implementation of the pharmaceutical care plan, use of educational videos, and multidisciplinary or interdisciplinary team effort.

Medication review was the most common intervention provided by the pharmacist in chronic pain management in our review. It includes review of overall prescription, review of medicine with associated adverse effects, review of dose only, pharmaceutical care plan with medication review and review forwarded to the general practitioner for further implementation. In studies by Bruhn et al. and

Neilson et al., a pharmaceutical care plan was agreed between the patient and pharmacist where the pharmacist assessed and documented relevant medical history and current condition, including known allergies and adverse drug reactions, relevant laboratory results, pain-related medications prescribed in the previous 10 years, current pain-related prescription medication, current symptoms, lifestyle issues, including units of alcohol consumption, and recommended changes in medication if required.[18,19] Likewise, the pharmacist provided pharmaceutical care and monitored patient pharmacotherapy for actual or any potential drug-related problem in a study by Gammaitoni et al.[20] The pharmacist counselled the patient on application and possible adverse effects of the drugs and optimized the drugs based on the patient's need in a study by Hoffmann et al.,[15] whereas the pharmacist distributed information leaflet on arthritis, self-help measures, monitored effectiveness and acceptability of the drugs, assessed risk for NSAID use and recommended changes as necessary in studies by Hay et al. and Marra et al.[16,17] In a study by McDermott et al., the pharmacist reviewed the analgesic prescribed and made recommendations for changes to the treatment based on a protocol and forwarded it to the general practitioner.[28] While there is no universally accepted method for a medication review, systematic assessment and approaches are utilized to optimize drug therapy and prescribing.[30] Medication review by pharmacists is important to achieve outcomes in chronic pain management. Suboptimal use of analgesics, inappropriate use of repeat prescriptions, and self-medication with over-the-counter drugs together with prescribed analgesics, non-adherence and adverse drug effects are some of the common issues that need a medication review.[31] The value of pharmacists in conducting medication reviews has been well established to optimize drug therapy and reduce drug-related problems.[30,32–34] Pharmacist-implemented pharmaceutical care plans[15,18,20] or use of educational videos[27] are some of the additional interventions to medication review that have been noted in this review. All these interventions have a positive impact on one or the other outcome of measures. The findings of this study also concur with the previous review by Hadi and colleagues[10] and Bennett and colleagues[9] which found that medication review and education provided by pharmacists reduced pain intensity and enhanced patient satisfaction.

Studies included in this review were conducted in general practices, pharmacies, specialist clinic, rehabilitation centre and hospitals. In the specialist pain clinic, the pharmacist provided pharmaceutical care with a focus on prescription services and monitored patient pharmacotherapy for actual or any potential drug-related problems. The pharmacist assessed the effectiveness of the medication and recommended discontinuation (especially when opioids for long-term users were ineffective), and adjusted dose. Pharmacists identified and managed side effects through counselling and by addition of therapy. Patients were satisfied with the pharmacist intervention as they had better access to medicine, more efficient processing of prescriptions, and fewer stigmatizing experiences. Similarly, a higher number of pharmacist recommendations were followed by staff of the pain clinic, which indicates the effectiveness of the intervention. Clinically meaningful improvement was observed in pain score, percent relief from medication and physical functioning, which indicates the positive impact on the pharmacist intervention in a specialist pain clinic.[20,22] Incorporation of a pharmacist in the pain and opioid practice management team in outpatient physical medicine and rehabilitation centres led to best practice standards being followed, optimized opioid and non-opioid medication therapy, and enhanced patients' access and safety.[21]

This review noted the contribution of pharmacists in a multidisciplinary or interdisciplinary team to chronic pain management. The pharmacist provided counselling and education, and conducted medication review. In hospitals, pharmacist worked as a member of an interdisciplinary/multidisciplinary team and the results showed that the collaborative pain management effort was effective as it improved pain severity, physical functioning and opioid intake. As a part of the multidisciplinary team, pharmacists provided education on side effects of drugs and conducted medication management including opioid dose adjustment.[23,25] Pharmacists were accepted by the general physician as a team member in pain management. A study by Read and Krska also reported similar findings regarding pharmacists' contribution to pain management and acceptance of their role by other health professionals.[35] Giannitrapani and colleagues reported that pharmacists were identified by primary care providers to have a central role and contribute to opioid stewardship. Similarly, the concept of an interdisciplinary team base model with the expansion of the role of the clinical pharmacist in the management of chronic conditions is being explored.[8]

We found that pharmacist intervention was successful in improving one of the most important outcomes, namely reducing the pain intensity among the patients. Besides pain intensity and physical functioning, this review also noted that the pharmacist-led medication review has a positive impact on the quality of life, anxiety, depression and patient satisfaction. Some observational studies in this review noted the positive impact of pharmacist intervention on opioid use.[21,23,24] Nevertheless, we have noted that while the pharmacist intervention reduced the pain intensity, there was limited impact on physical functioning and mental health. This might be because patients with chronic pain tend to report more impaired physical function than they can perform. It was further suggested that patient beliefs might have influenced the perceived physical function.[36] Associated psychological factors like depression and anxiety also lowers physical functioning. Besides, the choice of outcome measure may also have impacted the results.[37] Self-report together with performance measures could be useful in assessing the physical functioning over time during the treatment process.[38]

Recent NICE (National Institute for Health and Care Excellence) guidelines recommend the use of very few medicines for the management of chronic primary pain, but a wide range of pharmacological management is required for chronic secondary pain.[39] As an integral member of the healthcare system, pharmacists can provide a substantial contribution to effective pain management. The effect size of pharmacist intervention in the included studies seems to be low to medium and pharmacists' involvement increases the total healthcare expense. However, benefit to the patient by the pharmacist involvement should also be considered. Among the studies investigating pharmacists' intervention in chronic pain, only one

study in this review covered cost-effectiveness of such services.[19] Compared with treatment as usual, the pharmacist-led intervention was more expensive. Nevertheless, the economic evaluation of the service provided should be studied with the use of a reliable tool. This will be important to guide health authorities to further plan and implement such services. Studies have confirmed pharmacist intervention to have a positive impact in chronic pain management. Pharmacists are considered trustworthy and responsible advocates for medication treatment and management; however, the role requires further exploration.[11] In a study by Bruhn et al., pharmacists were involved in prescribing in general practice. The ageing population and rise in chronic conditions has tremendously increased demand for primary care with General Practitioners already burdened with both chronic and elderly patients. To bridge this gap, pharmacist's involvement can expand the supply of primary care workforce and ease the burden on General Practitioners as well. With the involvement of clinical pharmacists in an interdisciplinary pain management team, clinics have reported a decreased burden on primary care physicians and improved patient satisfaction.[8] Various medication-related problems were identified and resolved by pharmacists in a study by Semerjian et al.[22] In a study by Mathew et al., patients benefited, and the quality of the service was improved with the implementation of pharmacy pain consultation services.[26] So, it is essential to identify the pharmacist contribution in chronic pain management through economic appraisal of the provided service, adequate training, collaboration of pharmacist with physician and other healthcare professionals.

This study offers several strengths. We included both RCT and observational studies, thus providing a more comprehensive overview of the literature compared to previous studies. The previous reviews by Hadi and Bennett were based on RCT studies only. We also assessed the quality of evidence using GRADE. Nevertheless, this needs to be viewed in light of the limitations. Firstly, our search strategy may have omitted studies that did not state pain as an outcome. Furthermore, most of the studies included in this review were conducted in high-income countries, and thus the results might not be applicable to populations in other countries. Although this review was focused on pharmacist-provided intervention, the selected interventions were still diverse, particularly in terms of intervention components (including intensity of intervention, frequency and total duration), study location and study design. Nevertheless, we believe that the information provided by this review are in concurrence with the previous reviews,[9,10] and provides evidence for policymakers in formulating future professional services for chronic pain management.

4.1 | Implications for research and practice

Pharmacists contribute substantially to patient care and, in chronic pain management, take on the roles of educators, medication reviewers and researchers in ensuring safe and effective use of medicine. In particular, they ensure that the medicines best meet the patients' needs, treatment is economical, advise on medication management (which helps patients with knowledge and skills for self-management), and ultimately achieve optimal clinical outcomes.[11] The role of a pharmacist in chronic pain management needs to be expanded to low- and middle-income countries and more research based on it is anticipated. Training pharmacists and developing a country-specific best practice model for pharmacist-led chronic pain management is needed. Expanding the role of pharmacists in chronic pain management in an interdisciplinary team is necessary. Specific barriers to it include limitation of the scope of practice, inadequate institutional support, challenges, and opportunities for disseminating the pharmacist's expanded role.[8] Another aspect that needs further examination is the impact and potential financial cost to the healthcare system of introducing pharmacist services and evaluating the impact through valid patient-related outcome measures.

5 | CONCLUSION

This review noted mixed results on the impact of pharmacist intervention on the management of chronic pain, but there was some promising evidence to suggest that the intervention reduced the intensity of pain, and medication review as the most adopted interventional strategy. The impact on physical functioning and mental health was not so significant, which might be due to the heterogeneity of the interventional approach, its description, as well as the settings. As such, there is a need for better research and reporting of these studies measuring the important patient-reported outcomes.

COMPETING INTERESTS

There are no competing interests to declare.

CONTRIBUTORS

P.T., S.W.H.L., and B.K.C. contributed to study concept, article screening, data extraction, quality assessment of the studies, and manuscript writing. J.A.D. and M.I.M.I. contributed to analysis of the data, and had input to the writing of the manuscript. S.G. contributed to interpretation of the data and provided critical feedback on the manuscript. All authors contributed to the revision and final approval of the manuscript.

ORCID

Shaun Wen Huey Lee https://orcid.org/0000-0001-7361-6576
Bhuvan KC https://orcid.org/0000-0002-9135-962X

REFERENCES

1. Treede RD, Rief W, Barke A, et al. Chronic pain as a symptom or a disease: the IASP Classification of Chronic Pain for the International Classification of Diseases (ICD-11). *Pain*. 2019;160(1):19-27.
2. Mills SEE, Nicolson KP, Smith BH. Chronic pain: a review of its epidemiology and associated factors in population-based studies. *Br J Anaesth*. 2019;123(2):e273-e283.
3. Sá KN, Moreira L, Baptista AF, et al. Prevalence of chronic pain in developing countries: systematic review and meta-analysis. *PAIN Reports*. 2019;4(6):e779.

4. Gaskin DJ, Richard P. The economic costs of pain in the United States. *J Pain*. 2012;13(8):715-724.
5. Woo AK. Depression and anxiety in pain. *Reviews in Pain*. 2010;4(1):8-12.
6. Yang J, Bauer BA, Wahner-Roedler DL, Chon TY, Xiao L. The modified WHO analgesic ladder: is it appropriate for chronic non-cancer pain? *J Pain Res*. 2020;13:411-417.
7. Roe M, Sehgal A. Pharmacology in the management of chronic pain. *Anaesth Intensive Care Med*. 2016;17(11):548-551.
8. Giannitrapani KF, Glassman PA, Vang D, et al. Expanding the role of clinical pharmacists on interdisciplinary primary care teams for chronic pain and opioid management. *BMC Fam Pract*. 2018;19(1):107.
9. Bennett MI, Bagnall AM, Raine G, et al. Educational interventions by pharmacists to patients with chronic pain: systematic review and meta-analysis. *Clin J Pain*. 2011;27(7):623-630.
10. Hadi AM, Alldred DP, Briggs M, Munyombwe T, Closs SJ. Effectiveness of pharmacist-led medication review in chronic pain management: systematic review and meta-analysis. *Clin J Pain*. 2014;30(11):1006-1014.
11. Mishriky J, Stupans I, Chan V. Expanding the role of Australian pharmacists in community pharmacies in chronic pain management—a narrative review. *Pharm Pract (Granada)*. 2019;17(1):1410.
12. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898.
13. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919.
14. *Cochrane, Review Manager (RevMan) [Computer program]. Version 5.4*. Copenhagen: The Nordic Cochrane Centre; 2020.
15. Hoffmann W, Herzog B, Mühlig S, et al. Pharmaceutical care for migraine and headache patients: a community-based, randomized intervention. *Ann Pharmacother*. 2008;42(12):1804-1813.
16. Marra CA, Cibere J, Grubisic M, et al. Pharmacist-initiated intervention trial in osteoarthritis: a multidisciplinary intervention for knee osteoarthritis. *Arthritis Care Res*. 2012;64(12):1837-1845.
17. Hay EM, Foster NE, Thomas E, et al. Effectiveness of community physiotherapy and enhanced pharmacy review for knee pain in people aged over 55 presenting to primary care: pragmatic randomised trial. *BMJ*. 2006;333(7576):995.
18. Bruhn H, Bond CM, Elliott AM, et al. Pharmacist-led management of chronic pain in primary care: results from a randomised controlled exploratory trial. *BMJ Open*. 2013;3(4):e002361.
19. Neilson AR, Bruhn H, Bond CM, et al. Pharmacist-led management of chronic pain in primary care: costs and benefits in a pilot randomised controlled trial. *BMJ Open*. 2015;5(4):e006874.
20. Gammaitoni AR, Gallagher RM, Welz M, Gracely EJ, Knowlton CH, Voltis-Thomas O. Palliative pharmaceutical care: a randomized, prospective study of telephone-based prescription and medication and counseling services for treating chronic pain. *Pain Med*. 2000;1(4):317-331.
21. Boren LL, Locke AM, Friedman AS, Blackmore CC, Woolf R. Team-based medicine: incorporating a clinical pharmacist into pain and opioid practice management. *PM&R*. 2019;11(11):1170-1177.
22. Semerjian M, Durham MJ, Mirzaian E, Lou M, Richeimer SH. Clinical pharmacy services in a multidisciplinary specialty pain clinic. *Pain Pract*. 2019;19(3):303-309.
23. White LD, Summers P, Scott A. Changes in clinical status after completion of an interdisciplinary pain management programme incorporating pain neurophysiology education. *Physiother Can*. 2018;70(4):382-392.
24. Chelminski PR, Ives TJ, Felix KM, et al. A primary care, multidisciplinary disease management program for opioid-treated patients with chronic non-cancer pain and a high burden of psychiatric comorbidity. *BMC Health Serv Res*. 2005;5:1-3.
25. Takahashi N, Takatsuki K, Kasahara S, Yabuki S. Multidisciplinary pain management program for patients with chronic musculoskeletal pain in Japan: a cohort study. *J Pain Res*. 2019;12:2563-2576.
26. Mathew S, Chamberlain C, Alvarez KS, Alvarez CA, Shah M. Impact of a pharmacy-led pain management team on adults in an academic medical center. *Hosp Pharm*. 2016;51(8):639-645.
27. Vogler CN, Sattovia S, Salazar LY, Leung TI, Botchway A. Assessing outcomes of educational videos in group visits for patients with chronic pain at an academic primary care clinic. *Postgrad Med*. 2017;129(5):524-530.
28. McDermott M, Smith BH, Elliott AM, Bond CM, Hannaford PC, Chambers WA. The use of medication for chronic pain in primary care, and the potential for intervention by a practice-based pharmacist. *Fam Pract*. 2006;23(1):46-52.
29. Aryani FMY, Lee SWH, Chua SS, Kok LC, Efendie B, Paraidathathu T. Chronic care model in primary care: can it improve health-related quality of life? *Integr Pharm Res Pract*. 2016;5:11-17.
30. Lee SWH, Mak VSL, Tang YW. Pharmacist services in nursing homes: a systematic review and meta-analysis. *Br J Clin Pharmacol*. 2019;85(12):2668-2688.
31. Hadi MA, Alldred DP, Closs SJ, Briggs M. Effectiveness of pharmacist-led medication reviews in improving patient outcomes in chronic pain: a systematic review protocol. *Can Pharm J/Revue des Pharmaciens du Canada*. 2012;145(6):264-266.
32. Chua SS, Kok LC, Yusof FAM, et al. Pharmaceutical care issues identified by pharmacists in patients with diabetes, hypertension or hyperlipidaemia in primary care settings. *BMC Health Serv Res*. 2012;12(1):388.
33. Kua C-H, Yeo CY, Tan PC, et al. Association of deprescribing with reduction in mortality and hospitalization: a pragmatic stepped-wedge cluster-randomized controlled trial. *J Am Med Dir Assoc*. 2020;22(1):82-89.
34. Lee S, Chong C, Chong D. Identifying and addressing drug-related problems in nursing homes: an unmet need in Malaysia? *Int J Clin Pract*. 2016;70(6):512.
35. Read RW, Krska J. Potential roles of the pharmacist in chronic pain management: a multidisciplinary perspective in primary care. *Int J Pharm Pract*. 1998;6(4):223-228.
36. Estévez-López F. Assessment of physical function: considerations in chronic pain populations. *Pain*. 2017;158(7):1397.
37. Karayannis VN, Sturgeon JA, Chih-Kao M, Cooley C, Mackey SC. Pain interference and physical function demonstrate poor longitudinal association in people living with pain: a PROMIS investigation. *Pain*. 2017;158(6):1063-1068.
38. Guildford BJ, Jacobs CM, Daly-Eichenhardt A, Scott W, McCracken LM. Assessing physical functioning on pain management programmes: the unique contribution of directly assessed physical performance measures and their relationship to self-reports. *Br J Pain*. 2017;11(1):46-57.
39. NICE. Chronic pain in over 16s: assessment and management. NICE draft guideline, August, 2020.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Thapa P, Lee SWH, KC B, Dujaili JA, Mohamed Ibrahim MI, Gyawali S. Pharmacist-led intervention on chronic pain management: A systematic review and meta-analysis. *Br J Clin Pharmacol*. 2021;87:3028–3042. https://doi.org/10.1111/bcp.14745

APPENDIX

Section/topic	#	PRISMA checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: Background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4,5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., web address), and, if available, provide registration information including registration number.	7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9, S1,S2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9,10
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11–16
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11–15

(Continues)

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15).	9,10
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see item 16]).	12, 14
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	20
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

Journal of Pain Research

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Managing Pain in Low Resource Settings: Healthcare Professionals' Knowledge, Attitude and Practice Regarding Pain Management in Western Nepal

Parbati Thapa[1], Bhuvan KC[1,2], Shaun Wen Huey Lee[1], Juman Abdulelah Dujaili[1], Sudesh Gyawali[3], Mohamed Izham Mohamed Ibrahim[4], Alian A Alrasheedy[5]

[1]School of Pharmacy, Monash University Malaysia, Subang Jaya, Selangor, Malaysia; [2]College of Public Health, Medical, and Veterinary Sciences, James Cook University, Townsville, Queensland, Australia; [3]Department of Pharmacology, Manipal College of Medical Sciences, Pokhara, Nepal; [4]Department of Clinical Pharmacy and Practice, College of Pharmacy, QU Health, Qatar University, Doha, Qatar; [5]Department of Pharmacy Practice, College of Pharmacy, Qassim University, Buraidah, Qassim, Saudi Arabia

Correspondence: Bhuvan KC, School of Pharmacy, Monash University Malaysia, Jalan Lagoon Selatan, Subang Jaya, Selangor, 47500, Malaysia, Email kcbhuvan@gmail.com; Alian A Alrasheedy, Department of Pharmacy Practice, College of Pharmacy, Qassim University, Buraidah, Qassim, Saudi Arabia, Email aarshiedy@qu.edu.sa

Background: Pain is a public health problem and affects millions of people globally. Effective pain management is possible through comprehensive pain management guidelines, adequate facilities, and trained healthcare professionals. Therefore, this study aims to analyze the healthcare professionals' knowledge, attitude, and practice regarding pain management in Western Nepal.

Methods: A cross-sectional study was carried out in hospitals of Pokhara, Nepal. Healthcare professionals, including doctors, pharmacists, and nurses, were enrolled. Tools for the study were "The Knowledge and Attitudes Survey Regarding Pain (KASRP)" and a validated practice-based questionnaire. Frequencies and descriptive statistics were used to describe the outcomes. Kruskal–Wallis *H*-test and Mann-Whitney *U*-test were used to analyze the association between the mean rank of KASRP score and sample characteristics. A p-value of <0.05 was considered significant for all statistical tests.

Results: A total of 336 healthcare professionals were enrolled in this study (108 medical doctors, 150 nurses, and 78 pharmacists). The mean KASRP scores (% ± SD) obtained by doctors, pharmacists, and nurses were 58.48±8.98, 53.01±7.80, and 52.26±6.39, respectively. A significant difference was found between the KASRP score and sample characteristics (p<0.001). The pain assessment tool is used by 96 (29%) healthcare professionals every time they meet the patients. Doctors and nurses used it more frequently as compared to pharmacists. Many of the pharmacists, 40 (51%), reported that they counsel the patients on the prescribed medicine (analgesics, NSAIDs, and opioids) every time. As only few participants had already attended a training on pain management, most healthcare professionals, 110 (33%), agreed and 198 (59%) strongly agreed that training related to pain management is needed in Nepal

Conclusion: Adequate training and support are required to enhance the knowledge, attitude and ultimately better practice for healthcare professionals regarding pain management in Nepal.

Keywords: pain management, knowledge, attitude, practice, healthcare professionals, Nepal

Background

Pain is a common healthcare problem that affects millions of people globally and contributes to seeking medical care for patients.[1] Acute pain is initiated by a specific injury or disease coupled with activation of the sympathetic nervous system and self-limited. In contrast, chronic pain is a disease state that outlasts the average healing time and persists or recurs for three months or more.[2,3] The International Association for the Study of Pain (IASP) estimates that 1 in 5 patients experience pain and 1 in 10 patients are diagnosed with chronic pain every year.[1] The prevalence of chronic pain in low-

Received: 3 February 2022
Accepted: 14 May 2022
Published: 2 June 2022

and middle-income countries (LMICs) varies between 34 and 41%. It causes a high clinical, financial and humanistic burden on people where the public health systems are inadequate and underfunded.[4] In Nepal, the prevalence of chronic pain was estimated to be 48–50%, while 24–41% in India.[5]

Effective pain management requires a comprehensive approach comprising national strategy and guidelines on pain management, adequately trained human resources, and proper healthcare facilities/settings. Pain management in LMICs, especially in developing countries, is inadequate. The infrastructure, human resources, and clinical systems to manage pain are lacking in developing countries.[6,7] Access to information and specialist pain service is limited in Nepal.[8] Like in other chronic disease management, people often rely on medical care that one can access via out-of-pocket spending at private healthcare facilities.[9]

Adequate pain management needs a national strategy that recognizes pain as an essential aspect of secondary and long-term care. Institutional guidelines and policies on pain management are formed based on the federal system. In line with this goal, the IASP has recommended various methods to improve pain care including access to pain education for healthcare providers and the general population, coordination of care, quality improvement program, and funding for pain research.[10]

Proper pain management needs healthcare professionals to be appropriately trained on pain management, which involves appropriately assessing pain and selecting the right medicines and approaches. Therefore, the knowledge and training of healthcare professionals on pain education form the backbone of improved pain care. Studies carried out among healthcare professionals in several countries have revealed varied responses ranging from sufficient to inadequate level of knowledge, attitude, and practice on pain management. Low scores were obtained on key aspects of pain management, including initial assessment, treatment plan, reassessment, and knowledge of the pharmacology of medications, especially narcotics.[11,12] Studies have also reported poor knowledge and attitudes regarding pain relief among healthcare professionals, lack of access to medicines and proper pain treatment, financial and socioeconomic factors among patients as the main barriers to effective pain management.[13] These studies highlight the need to assess healthcare providers' knowledge regarding pain management in each country and provide training and support as per the local needs.

In Nepal, patients with acute or chronic pain visit hospitals (both public and private), clinics, and other available healthcare facilities that could provide pain management. For minor ailments, including mild to moderate pain, patients prefer self-medication with the available over-the-counter medications.[14] Many patients visit tertiary care hospitals or hospitals because of the availability of multiple facilities at low cost and the available insurance policy. Some institutions have pain management clinics that provide outpatient services and interventions. A multidisciplinary approach to pain management is gradually emerging in Nepal, especially in the private sector. There are very few specialized pain management clinics in the country,[8] and most of them are localized in the capital city Kathmandu. A study by Shakya et al has reported strict opioid regulation, lack of knowledge among patients about pain management, insufficient staff, and the least priority for pain management services as barriers to pain management in Nepal.[15] Furthermore, Nepal lacks a comprehensive pain management strategy at the national level that deals with procedures, policies, systems, and human resources required to manage chronic pain. There is inadequacy in terms of proper training of healthcare professionals on pain management, availability of therapeutic resources, and dedicated pain management programs in hospitals.[16] Very few studies have been conducted in Nepal regarding the knowledge, attitude, and practice of healthcare professionals on pain management, and the studies focused only on nurses.[15,17]

There have not been any attempts to assess and compare the knowledge, attitude, and practice (KAP) of doctors, nurses, and pharmacists in pain management in Nepal. Such studies would contribute to pain management policy and improve pain management practice. Consequently, in this study, we aimed to assess the knowledge, attitude, and practice of pain management among medical doctors, pharmacists, and nurses in hospitals in Western Nepal.

Methods

Study Design and Setting

A cross-sectional study was carried out from June to August 2020 at five hospitals in Pokhara, Western Nepal.

Study Population, Sample Size, and Sampling methods

Registered doctors, pharmacists, and nurses who have been working as full-time employees at the hospitals were included in the study. The sample size for the study was 334, calculated by the Raosoft sample size calculator,[18] with a margin of error of 5%, confidence level of 95%, the population of 2500, and response distribution of 50%. Healthcare professionals meeting the inclusion criteria and willing to participate in the study were enrolled. A convenience sampling method was used, and all healthcare professionals available during data collection were enrolled until the required sample size was reached.

The Study Instrument

The questionnaire consisted of 3 main parts: the demographic and participants' data, knowledge and attitude regarding pain, and participants' practices for pain management. The items for knowledge and attitude regarding pain were adapted from "The Knowledge and Attitudes Survey Regarding Pain (KASRP)," developed by Ferrel and McCaffery, revised in 2014.[19] The tool's content was based on the standards of pain management such as the American Pain Society and the World Health Organization guidelines etc. Internal consistency reliability for this tool was established (alpha $r > 0.7$). In our study, we have adopted 31 items from the KASRP based on the study objectives. Out of these, 18 were true or false questions, 11 were multiple-choice questions with four options and 2 items from the case study. We did not include some questions/items, especially those related to cancer pain (n=5), pediatric pain (n=2), culture (n=1), and the 2nd case study (n=2). The response to each item of KASRP was scored as "1" for the correct response and a "0" for the incorrect response. The total score was the sum of all correctly answered questions. The percentage score is calculated by dividing the number of correct responses by the total number of items in the survey. Healthcare professionals were considered to have adequate knowledge and attitude if the score was 80% and above, a level identified by McCaffery and Robinson 2002.[20] However, the percentage called "adequate" varies among different studies, as some used 80% or above as representing adequate knowledge and attitudes,[21] whereas others used 70% as a minimum score.[22] Some studies did not even indicate the pass rate.[23] According to Ferrel et al, items should be differentiated with the least correct responses and those with the best scores for better response analysis.[19] For the participants' perspectives on the practice of pain management, eight questions were developed to assess their practices based on the literature review,[6,12,24] with six questions on a 4-point Likert scale and two yes/no questions. Consequently, the final questionnaire consisted of 39 items and demographic information. The practice was assessed based on the response provided by the healthcare professionals on the Likert scale.

The final questionnaire was checked by a panel of experts comprising pharmacists, physicians, senior nurses, and academicians to ensure clarity and suitability in the Nepalese healthcare system. In addition, pretesting of the questionnaire was conducted among 17 healthcare professionals: six doctors, six nurses, and five pharmacists. They were requested to fill up the form and provide feedback on the questionnaire. The questionnaire was examined for reliability, and its internal consistency was established (Cronbach alpha of 0.73 was obtained for the practice-based questionnaire, and for the KASRP tool, it was 0.7).

Data Collection

The questionnaire was developed in a google form. Department heads of medical, nursing and pharmacy facilities were contacted and requested coordination among staff to fill out the questionnaire. Healthcare professionals working full time in hospitals, registered in respective professional councils, and consented to participate in the study were enrolled.

Data Analysis

Data from the google forms were checked for completeness and accuracy. Data were retrieved on an excel sheet and were transferred to IBM SPSS Statistics for Windows, version 26.0. Frequencies and descriptive statistics were used to describe the sample characteristics and responses to each item of KASRP and the practice-based question. Mann-Whitney *U*-test and Kruskal-Wallis *H*-test were used to analyze the association between the mean rank of KASRP score and sample characteristics as data were non-normally distributed. A p-value of <0.05 was considered significant for all statistical tests.

Ethical Consideration

Ethical approval for the study was obtained from the Nepal Health Research Council (Reg no. 211/2020). Permission to collect the data was obtained from institutional review committees of the respective hospitals.

Results

Participants' Characteristics

A total of 336 questionnaire were completed, mostly by nurses (n=150, 44.6%), followed by medical doctors (n=108, 32.1%) and pharmacists (n=78, 23.2%) from different hospitals. Most of the respondents were female (n=230, 68.5%), and more than two-thirds of them (n=240, 71.4%) were young adults aged 25–35 years old. The demographic characteristics are shown in Table 1.

Table 1 Demographic Details and the mean Knowledge and Attitudes Survey Regarding Pain (KASRP) Score

Characteristics	Frequency	Percent	Mean KASRP Score (%)	p-value
Profession				
Doctor	108	32.1	58.48	<0.001
Nurse	150	44.6	52.26	
Pharmacist	78	23.2	53.01	
Gender				
Male	106	31.5	59.26	<0.001
Female	230	68.5	53.46	
Age				
20–24	82	24.4	51.75	<0.001
25–35	240	71.4	56.47	
36–45	10	3.0	53.40	
46–55	4	1.2	61.50	
Department				
Medicine	98	29.2	52.91	<0.001
Orthopaedics	22	6.5	60.72	
Gynaecology and obstetrics	46	13.7	54.34	
Pharmacy	78	23.2	53.64	
Surgery	32	9.5	60.68	
Others	60	17.85	63.43	
Experience				
Less than 5 years	200	59.5	54.58	<0.001
5–10 years	122	36.3	58.01	
11–15 years	4	1.2	54.50	
More than 15 years	10	3	58.60	

Note: p< 0.05 is considered statistically significant. The Knowledge and Attitudes Survey Regarding Pain (KASRP) Others: ENT, ICU, Dermatology, Emergency, Paediatric.

Knowledge and Attitude of Health Care Professionals (HCPs) Regarding Pain

The mean percentage KASRP score obtained was 55.29±8.66 for correct responses. The mean score (% ± SD) obtained by doctors, pharmacists, and nurses were 58.48±8.98, 53.01±7.80, and 52.26±6.39, respectively. The maximum score obtained was 24 (77%), and the minimum was 10 (32%). Most healthcare professionals, 63.1%, have their scores between 40–60%. Details of the score obtained are depicted in Table 2.

Items of the KASRP were classified into assessment, medication, intervention, addiction, and spiritual categories. More than 80% of the healthcare professionals showed a correct response to 5 items of the medication category and 1 item of the addiction category. These items assessed knowledge on respiratory depression due to opioids, the effectiveness of combining analgesics, adjustment of opioid doses, the definition of "equianalgesic," the peak effect of morphine after intravenous administration, and assessment of sedation during pain management using opioids; however, knowledge and attitude were found poor on using placebo to determine whether the pain is real, initiation of opioid when the source of the pain is not known, use of opioids among patients with substance abuse and symptoms of physical dependency on opioid withdrawal. Details of the correct responses to different items are shown in Table 3.

Kruskal Wallis tests showed a statistically significant difference in the KASRP score between the professional category ($p<0.001$), age ($p<0.001$), department ($p<0.001$), and their experience ($p<0.001$). Further pairwise comparison showed a significant difference between doctor and pharmacist, doctor and nurse. For department wise the differences included medicine and surgery, gynaecology/obstetrics and surgery, pharmacy and surgery. A significant difference in score was observed between the gender, as shown by the Mann Whitney *U*-test ($p<0.001$). The details are presented in (Table 1).

The Practice of HCPs Regarding Pain Management

Assessment of the practice of healthcare professionals on pain management reveals that only 96 (29%) of them used the pain assessment tool every time during their consultation. Doctors (37%) and nurses (32%) used it more frequently as compared to pharmacists (10%). The verbal/graphic rating scale was reported as the most used tool to assess pain (n=132, 39%). Counselling on the use of analgesics, NSAIDs, opioids, and assessment of allergic response or adverse drug reaction to the prescribed drugs was conducted every time by 128 (38%) healthcare professionals. Similarly, only 100 (31%) of them used opioid risk assessment tools before prescribing, administering, or dispensing. Pharmacist involvement was higher in counselling as 51% reported counselling the patient every time. However, only a few, 10%, assessed the allergic responses and adverse drug reactions. In addition, 30% of the doctors and 41% of the nurses provided the counselling every time, and 44% and 48% assessed allergic responses, respectively.

The majority of them either agreed or strongly agreed that standard pain management guidelines should be followed, and training related to pain management is needed for healthcare professionals in Nepal. However, more than three-quarters of the healthcare professionals (n=254, 76%) reported that they do not follow any specific pain management guidelines. Likewise, the majority (n=284, 85%) of them had never attended any training regarding pain management. Details of the response of healthcare professionals on the practice-based questions are shown in Table 4.

Table 2 Distribution of the Knowledge and Attitudes Survey Regarding Pain (KASRP) Score

	≥60 %	>40 and <60 %	≤40%
Doctors n (%)	52 (48.1)	56 (51.9)	0 (0)
Nurses n (%)	24 (16.0)	120 (80.0)	6 (4.0)
Pharmacists n (%)	28 (35.9)	36 (46.2)	14 (17.9)
Total n (%)	104 (31.0)	212 (63.1)	20 (6.0)

Note: Maximum score 77% and minimum score 32%.
Abbreviation: n, frequency.

Table 3 Frequency of Correctly Answered Questions; the Knowledge and Attitudes Survey Regarding Pain (KASRP)

S. No.		Doctors		Nurse		Pharmacist		Overall	
	Assessment Category	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
1	Vital signs are always reliable indicators of the intensity of a patient's pain.	82	76	28	19	56	72	166	49
2	Patients may sleep despite severe pain.	86	80	116	77	50	64	252	75
3	Giving patients sterile water by injection (placebo) is a useful test to determine if the pain is real.	36	33	32	21	22	28	90	27
4	If the source of the patient's pain is unknown, opioids should not be used during the pain evaluation period, as this could mask the ability to correctly diagnose the cause of pain.	24	22	22	15	4	5	50	15
5	The most accurate judge of the intensity of the patient's pain is the patient.	64	59	140	93	54	69	258	77
6	Case Study A. Andrew is 25 years old and this is his first day following abdominal surgery. As you enter his room, he smiles at you and continues talking and joking with his visitor. Your assessment reveals the following information: BP = 120/80; HR = 80; R = 18; on a scale of 0 to 10 (0 = no pain/discomfort, 10 = worst pain/discomfort) he rates his pain as 8. A. On the patient's record you must mark his pain on the scale below. Circle the number that represents yourassessment of Andrew's pain.	20	19	10	7	0	0	30	9
Medication Category									
7	Respiratory depression rarely occurs in patients who have been receiving stable doses of opioids for months.	84	78	130	87	64	82	278	83
8	Combining analgesics that work by different mechanisms (eg, combining an NSAID with an opioid) may result in better pain control with fewer side effects than using a single analgesic agent.	92	85	126	84	70	90	288	86
9	The usual duration of analgesia of 1–2 mg morphine IV is 4–5 hours.	26	24	48	32	10	13	84	25
10	Opioids should not be used in patients with a history of substance abuse.	30	28	26	17	46	59	102	30
11	Elderly patients cannot tolerate opioids for pain relief.	84	78	58	39	50	64	192	57
12	Patients should be encouraged to endure as much pain as possible before using an opioid.	76	70	72	48	16	21	164	49
13	After an initial dose of an opioid analgesic is given, subsequent doses should be adjusted by the individual patient's response.	108	100	136	91	54	69	298	89
14	(Hydrocodone 5 mg + acetaminophen 300 mg) PO is approximately equal to 5–10 mg of morphine PO.	76	70	110	73	36	46	222	66
15	Anticonvulsant drugs such as gabapentin (Neurontin) produce optimal pain relief after a single dose.	68	63	50	33	10	13	128	38
16	Benzodiazepines are not effective pain relievers and are rarely recommended as part of an analgesic regiment.	60	56	114	76	62	79	236	70
17	The term "equianalgesic" means approximately equal analgesia and is used when referring to the doses of various analgesics that provide approximately the same amount of pain relief.	108	100	144	96	74	95	326	97
18	The recommended route administration of opioid analgesics for patients with brief, severe pain of sudden onsets such as trauma or postoperative pain is Intravenous.	72	67	130	87	54	69	256	76

(*Continued*)

Table 3 (Continued).

S. No.		Doctors		Nurse		Pharmacist		Overall	
	Assessment Category	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
19	A 30 mg dose of oral morphine is approximately equivalent to Morphine 10 mg IV.	68	63	68	45	46	59	182	54
20	Analgesics for postoperative pain should initially be given around the clock on a fixed schedule.	100	93	90	60	54	69	244	73
21	The most likely reason a patient with pain would request increased doses of pain medication is experiencing increased pain.	70	65	92	61	54	69	216	64
22	The time to peak effect for morphine given IV is 15 min.	108	100	138	92	76	97	322	96
23	The time to peak effect for morphine given orally is 1–2 hours.	52	48	50	33	56	72	158	47
24	Which statement is true regarding opioid-induced respiratory depression: Obstructive sleep apnea is an important risk factor.	74	69	64	43	40	51	178	53
Intervention Category									
25	Patients who can be distracted from pain usually do not have severe pain.	42	39	80	53	22	28	144	43
26	Case Study A, b Your assessment, above, is made two hours after he received morphine 2 mg IV. Half hourly pain ratings following the injection ranged from 6 to 8, and he had no clinically significant respiratory depression, sedation, mor other untoward side effects. He has identified 2/10 as an acceptable level of pain relief. His physician's order for analgesia is "morphine IV 1–3 mg q1h PRN pain relief." Check the action you will take at this time. 1. Administer no morphine at this time. 2. Administer morphine 1 mg IV now. 3. Administer morphine 2 mg IV now.	14	13	8	5	2	3	24	7
Addiction Category									
27	Narcotic/opioid addiction is defined as a chronic, neurobiological disease characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.	88	81	106	71	66	85	260	77
28	Sedation assessment is recommended during opioid pain management because excessive sedation precedes opioid-induced respiratory depression.	108	100	150	100	78	100	336	100
29	How likely is it that patients who develop pain already have an alcohol and/or drug abuse problem? 5–15%	74	69	64	43	40	51	178	53
30	Following abrupt discontinuation of an opioid, physical dependence is manifested by the following sweating, yawning, diarrhea, and agitation with patients when the opioid is abruptly discontinued.	42	39	30	20	12	15	84	25
Spiritual Category									
31	Patients' spiritual beliefs may lead them to think pain and suffering are necessary.	56	52	96	64	56	72	208	62

Abbreviation: n, frequencies.

Table 4 Response to Practice-Based Question

		Doctor (N=108)		Nurse (N=150)		Pharmacist (N=78)		Total (N=336)	
		n	%	n	%	n	%	n	%
1. How often do you use the pain assessment tools to assess the pain level of the patients?	Never	4	4	32	21	32	41	68	20
	Rarely	16	15	44	29	34	44	94	28
	Often	48	44	26	17	4	5	78	23
	Every time	40	37	48	32	8	10	96	29
If you use, select the one you prefer often:	Face pain scale	30	28	16	11	26	33	72	21
	Numeric rating scale	28	26	10	7	0	0	38	11
	Verbal rating scale/ graphic rating scale	24	22	88	9	20	26	132	39
	Visual analog scale	22	20	4	3	0	0	26	8
2. How often do you provide counselling to the patient on analgesics, NSAIDs, or opioids?	Never	4	4	12	8	0	0	16	5
	Rarely	6	6	40	27	4	5	50	15
	Often	66	61	36	24	34	44	142	42
	Every time	32	30	62	41	40	51	128	38
3. How often do you assess allergic response/ adverse drug reaction to drugs prescribed for chronic pain?	Never	0	0	10	7	2	3	12	4
	Rarely	26	24	30	20	52	67	108	32
	Often	34	31	38	25	16	21	88	26
	Every time	48	44	72	48	8	10	128	38
4. How often do you use opioid risk assessment tools before prescribing/ administering /dispensing opioids?	Never	6	6	22	15	14	18	42	13
	Rarely	28	26	44	29	38	49	110	33
	Often	34	31	24	16	24	31	82	24
	Every time	40	37	60	40	2	3	102	30
5. Do you agree that standard pain management guidelines should be followed to manage pain?	Strongly disagree	4	4	10	7	0	0	14	4
	Disagree	2	2	0	0	0	0	2	1
	Agree	38	35	76	51	34	44	148	44
	Strongly agree	64	59	64	43	44	56	172	51
6. Do you agree pain management-related training is needed for a healthcare professional in Nepal?	Strongly disagree	6	6	14	9	4	5	24	7
	Disagree	4	4	0	0	0	0	4	1
	Agree	22	20	56	37	32	41	110	33
	Strongly agree	76	70	80	53	42	54	198	59

(*Continued*)

Table 4 (Continued).

		Doctor (N=108)		Nurse (N=150)		Pharmacist (N=78)		Total (N=336)	
		n	%	n	%	n	%	n	%
7. Do you follow any guidelines for the management of pain?	Yes	30	28	42	28	10	13	82	24
	No	78	72	108	72	68	87	254	76
8. Have you attended any training related to pain management?	Yes	20	19	28	19	4	5	52	15
	No	88	81	122	81	74	95	284	85

Discussion

The current study assessed doctors, pharmacists, and nurses' knowledge, attitude, and practice regarding pain management in hospitals of Western Nepal. In general, our study indicated that the performance of healthcare professionals on the selected aspect of knowledge and attitude was low to moderate. Healthcare professionals were considered to have adequate knowledge and attitude if the score was 80% and above.[20] However, in comparison, doctors' scored higher than pharmacists and nurses. These results align with several other studies' outcomes where doctors scored higher than pharmacists or nurses on these aspects.[11,12,25] Furthermore, a pairwise comparison shows a significant difference in scores between doctors and nurses, consistent with the results of the studies by Nuseir et al, 2016, Fallatah et al, 2017 and Alkhatib et al, 2020.[12,25,26] Doctors' better knowledge and attitude scores in our study may be due to their experience and prior education on pain management. Doctors lead the current pain management paradigm with only a supportive role for nurses and a minor role/involvement for pharmacists. However, these discrepancies could be resolved through continuing education and the development of multidisciplinary pain management team in an organization.[11,27] The low percentage and variation of correct response among the healthcare professionals might be due to inadequate pain management content in the educational curriculum and insufficient training regarding pain management, especially in low resources settings like Nepal.[6] Similarly, a lack of institutional policy and guidelines regarding pain management, limited interprofessional education, and knowledge sharing between healthcare professionals could also contribute to the variability in the pain management knowledge and attitude score.

The concept of pain management in Nepal dates to 1970. However, it could not progress much due to a resource crunch, an inadequate public health system, and a lack of comprehensive pain management policy and training system in healthcare institutions. Over the recent years, pain management as a specialized discipline has been increasing as more and more training, fellowship, and practice environments are being provided to healthcare professionals in Nepal.[8] However, our study shows that there is still a need for institutional policy and environmental support for pain management, especially in public hospitals outside the Kathmandu valley and other healthcare settings.

A significant difference in KASRP score was observed between different professions ($p<0.001$), genders ($p<0.001$), age ($p<0.001$), department ($p<0.001$), and experience ($p<0.001$). Differences in gender might be because almost all nurses were female, and their score was relatively lower than doctors and pharmacists. More than half of the doctors were male and obtained higher scores. This finding is similar to Al-Quliti and Alamri, where there was a statistical difference in scores obtained by physicians compared to nurses.[28] In the study findings of Alkhatib et al, there was no significant difference observed based on gender.[26] A gender skewed scenario can be observed among healthcare professionals in Nepal as more females work as nurses and more males as doctors. However, the impact of gender differences in KASRP scores between departments and professionals needs further study to see the effect of gender on collaborative practice and knowledge sharing among professionals regarding pain management.

Our study showed that the healthcare professionals scored low (ie, 30% and below) on three items of the assessment category and these items were about the use of sterile water (placebo) to determine whether the pain is real using placebo, use of opioids during the pain evaluation period and pain assessment based on patient medical history and facial

expression. Items from the medication category which were less scored were the duration of action of 1–2 mg morphine and the use of opioids among substance abusers. Likewise, one item from the intervention category that dealt with a selection of morphine dose based on pain rating and clinical condition, and one item from the addiction category about symptoms of physical dependency on abrupt cessation of morphine, were also scored low. Most of these items were related to opioids. This result was consistent with the study's findings by Kheshti et al, where the narcotic questions get the lowest percentage of correct responses.[29] Another survey by Nuseir et al, also reported a deficit in knowledge of the pharmacology of narcotics among healthcare professionals.[12] The poor knowledge regarding opioids (narcotic analgesics) could probably be due to low use of narcotics, policy constraints, and training regarding its use among healthcare professionals. In hospitals, all healthcare professionals do not have the same privilege /opportunities to prescribe and dispense narcotics which could also be a reason for inadequate knowledge. Narcotics are considered controlled drugs due to their abuse potential.[30] Morriss et al reported the poor knowledge and attitude about pain relief and access to opioids as a barrier to pain management in LMICs.[13] Nepal has ranked in the bottom three countries in the WHO Regional Office for Southeast Asia (SEARO) between 1996 and 2005 for the consumption of morphine.[31] Physicians were reluctant to prescribe opioids due to a lack of education and training in pain management, which led to the expiration of 49% of the sustained release morphine products in 2011. Likewise, though Nepal's national drug policy promotes the rational use of medicines, there is no specific mention or details, or guidance for opioids for pain management.[30] Consequently, adequate training and proper guidelines regarding opioids in pain management are crucial for Nepalese healthcare professionals.

Participants had inadequate knowledge of pain assessment and drug dosing, as reflected by their response to the case study-based question. A small number of healthcare professionals provided the correct response (< 10%). These are similar to the finding of Kahsay et al, where the nurses from resource-limited settings scored least for pain assessment and drug dosing.[32] The deficit in pain assessment and management knowledge was also identified among healthcare providers in Saudi Arabia, and the study suggested the requirement of pain education among the providers.[25] The lack of comprehensive pain management guidelines that outline a routine assessment of pain in clinical settings and its appropriate might have resulted in low scores on pain assessment and drug dosing.[28] Likewise, the selection of minimum doses shows a reluctance from healthcare professionals to prescribe higher doses of analgesics. It also shows that the patients, mostly with moderate to severe pain, might not be receiving adequate analgesics. Healthcare professionals were quite aware of the possible adverse effects of opioids, as depicted by the response to item "22," where all of them correctly answered the questions about the sedation assessment during opioid management to prevent respiratory depression. So, a fear of side effects from a higher dose of opioids and other factors might have contributed to using a low dose of analgesics (narcotic analgesics). Inadequate pain treatment is a grave issue, and we need studies to identify possible reasons for the use of analgesics with low doses.

Practice related to pain management among healthcare professionals revealed that still few doctors, pharmacists, and nurses do not use any assessment tool to assess the patient's pain level, which is consistent with the findings of Shakya et al, 2020 and Nuseir et al, 2016.[6,12] Limited consultation time of the physician's 5.26±2.31 minutes[33] due to several contributing factors; higher patient flow, workload and lack of clear protocol on patient assessment could also have impacted the pain assessment. Likewise, inadequate training and inappropriate nurse-to-patient ratios were considered barriers to implementing the nursing process, which could relate to pain assessment as well.[34]

The verbal or graphical rating scale is the most widely used tool to assess pain in the current study, in contrast to the study by Shakya et al, 2020 where the visual analog scale was primarily used almost by 84% of healthcare professionals.[6] However, there is still variation in the choice of pain assessment tool between healthcare professionals. A common practice for pain assessment of outpatients in Nepal is to verbally ask the patient the intensity and types of pain and note the patient's response. This could be due to the lack of implementation of pain management guidelines and knowledge of the available pain assessment tools. However, nurses use different pain assessment tools in the in-patient hospital settings, including the numeric pain rating scale[35] and The Wong-Baker Faces Pain Rating Scale.[10] These pain assessment tools are available in Nepalese languages, and they can be used in hospital and clinical settings for better practice. Likewise, pain characterization with an appropriate tool like McGill pain questionnaire could help in better pain assessment and management.[36]

Most pharmacists reported that they never or rarely used the pain assessment tool. Clinical pharmacy practice is a recent establishment in Nepalese hospital settings as per the government's directive (2015 hospital pharmacy guidelines).[37] Nepalese hospital pharmacists are primarily involved in dispensing medications and counselling. Their involvement in pain management activities such as pain assessment, pain medication education, and pharmacotherapy review of pain medications are still lacking in Nepalese hospitals. Therefore, pharmacists have less opportunity to deal with the patient's symptoms as they meet the patient only after the assessment is complete. This trend might change if more clinical pharmacists are well trained and involved in multidisciplinary pain management teams involving nurses, physicians, and pharmacists are set up at Nepalese hospitals in the near future. These pharmacists can help with pain management via medication review, pain assessment, discharge counselling, medication reconciliation, and medication education.[38]

Most healthcare professionals provide counselling on the use of NSAIDs and opioids, assess allergic responses, and use the opioid risk assessment tool. Patients managing their pain via self-medication practice with paracetamol and NSAIDs is high in Western Nepal, where this study was carried out.[39] These NSAIDs are over-the-counter drugs and may benefit mild to moderate pain or manage chronic pain. However, OTC analgesics, without proper consideration, could result in adverse effects and serious complications such as gastrointestinal bleeding and kidney diseases.[14] Pharmacists need to promote the safe use of OTC analgesics in Nepal via appropriate dispensing and medication safety education.[40]

More than three-quarters of the healthcare professionals (76%) reported that currently, they do not follow any standard pain management guidelines, and very few follow the WHO pain management guidelines. Likewise, 85% of the healthcare professionals have not attended any training regarding pain management. However, they agreed that standard protocol should be followed, and pain-related training should be provided to the healthcare professionals in Nepal. Comprehensive pain management guidelines are essential as they promote evidence-based practice. Many international and national pain management guidelines are available. However, there are no specific pain management guidelines formulated or made mandatory to follow in Nepal. Pain management has not been given priority in secondary and tertiary care settings.[6] This could be the barrier to optimal practice. The treatment gap in pain management is prevalent in Nepal and many developing countries. Inadequate education and training of health professionals coupled with limited resources and facilities for pain management and limited access to medicines for pain relief are the significant reasons for this gap. In addition to the government policies, fear of opioid addiction, patient noncompliance, and the high cost of medication are the barriers to effective pain management in developing countries, as per the International Association for the Study of pain study.[16] So, it is necessary for the hospital management and healthcare professional's organization to be aware of the status of pain management and provide the essential training and support to enhance the knowledge, attitude, and improve practice.

Overall, the study findings emphasize the need for developing a national pain management strategy and comprehensive institutional guidelines for hospitals, primary care centers, and community pharmacies. A systematic assessment and management of pain can be carried out at Nepal's different healthcare facilities. Revision of the healthcare professionals teaching curriculum with the addition of modules on pain management could have positive impact on the practice. Continuing Professional Development training modules for doctors, nurses, and pharmacists will help them enhance their knowledge and equip them with the right tools and approaches for pain management.[32]

Strength and Limitations of the Research

This study depicts healthcare professionals' current knowledge, attitude, and practice in pain management in Western Nepal. It opens the opportunity for the development and implementation of intervention programs to strengthen the ability of healthcare professionals and healthcare institutions in pain management. Limitations include the study site, only one part of Nepal, so studies with multiple healthcare facilities and a larger sample could provide a better representation of the situations. Data were collected using a self-reported questionnaire which could limit the identification of the problem, so further studies with quantitative and qualitative component could better portray the scenario.

Conclusions

This study highlights the need of improvement in knowledge and attitude toward pain management among healthcare professionals in Western Nepal. Variation of practice exists among healthcare professionals in the implementation of pain assessment tools, opioid risk assessment tools, counselling, and assessing allergic reactions. Only a few participants reported having and following pain management guidelines, and the majority agreed that pain management training is crucial.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Goldberg DS, McGee SJ. Pain as a global public health priority. *BMC Public Health*. 2011;11(1):1–5. doi:10.1186/1471-2458-11-770
2. Grichnik KP, Ferrante FM. The difference between acute and chronic pain. *Mt Sinai J Med*. 1991;58(3):217–220.
3. Treede R-D, Rief W, Barke A, et al. Chronic pain as a symptom or a disease: the IASP classification of chronic pain for the international classification of diseases (ICD-11). *Pain*. 2019;160(1):19–27. doi:10.1097/j.pain.0000000000001384
4. Enright A, Goucke R. The global burden of pain: the tip of the iceberg? *Anesth Analg*. 2016;123:529–530. doi:10.1213/ANE.0000000000001519
5. Walters LJ, Baxter K, Chapman H, et al. Chronic pain and associated factors in India and Nepal: a pilot study of the Vanderbilt global pain survey. *Anesth Analg*. 2017;125(5):1616–1626. doi:10.1213/ANE.0000000000002360
6. Shakya BM, Ninadini Shrestha SS. Pain management practices and perceived barriers among the health professionals in different hospitals of Nepal. *J Clin Diagn Res*. 2020;14(1):UC01–UC05.
7. Goucke R, Morriss W. Pain management in Low and Middle Income Countries (LMIC) just put up with it? *Egypt J Anaesth*. 2012;28(1):1–2. doi:10.1016/j.egja.2011.11.005
8. Anil Shrestha RA, Shrestha N. Evolution of pain management services in Nepal. *Anaesth Intensive Care Med*. 2020;24(4):463–466.
9. Sapkota T, Houkes I, Bosma H. Vicious cycle of chronic disease and poverty: a qualitative study in present day Nepal. *Int Health*. 2020;13:30–38.
10. IASP. International association for the study of pain. Available from: https://www.iasp-pain.org/PublicationsNews/NewsDetail.aspx?ItemNumber=8340. Accessed May 18, 2022.
11. Lalonde L, Leroux-Lapointe V, Choinière M, et al. Knowledge, attitudes and beliefs about chronic noncancer pain in primary care: a Canadian survey of physicians and pharmacists. *Pain Res Manag*. 2014;19(5):241–250. doi:10.1155/2014/760145
12. Nuseir K, Kassab M, Almomani B. Healthcare providers' knowledge and current practice of pain assessment and management: how much progress have we made? *Pain Res Manag*. 2016;2016:1–7. doi:10.1155/2016/8432973
13. Morriss W, Roques C. Pain management in low-and middle-income countries. *BJA Educ*. 2018;18(9):265–270. doi:10.1016/j.bjae.2018.05.006
14. Thapa S, Shankar P, Palaian S, et al. Promoting rational self. medication of nonsteroidal anti. inflammatory drugs in Nepal. *Arch Pharm Pract*. 2016;7(2):61–66. doi:10.4103/2045-080X.181035
15. Shakya BM, Shakya S. Knowledge and attitude of nurses on pain management in a tertiary hospital of Nepal. *Age*. 2016;20(24):21.
16. Bond M. Pain education issues in developing countries and responses to them by the International Association for the Study of Pain. *Pain Res Manag*. 2011;16(6):404–406. doi:10.1155/2011/654746
17. Thapa RD, Gurung G. Nurses'knowledge, attitude and practice regarding postoperative pain management at selected hospitals, Bharatpur, Nepal. *J Chitwan Med Coll*. 2020;10(1):64–68. doi:10.3126/jcmc.v10i1.28074
18. Raosoft I. Sample size calculator by Raosoft, Inc; 2020.
19. Ferrell BM. "Knowledge and attitudes survey regarding pain" developed by Betty Ferrell, RN, PhD, FAAN and Margo McCaffery, RN, MS, FAAN; 2012. Available from: http://prc.coh.org. Accessed May 18, 2022.
20. McCaffery M, Robinson ES. Your patient is in pain—here's how you respond. *Nursing 2019*. 2002;32(10):36–45.
21. Latina R, Mauro L, Mitello L, et al. Attitude and knowledge of pain management among Italian nurses in hospital settings. *Pain Manag Nurs*. 2015;16(6):959–967. doi:10.1016/j.pmn.2015.10.002
22. Yava A, Çicek H, Tosun N, Özcan C, Yildiz D, Dizer B. Knowledge and attitudes of nurses about pain management in Turkey. *Int J Caring Sci*. 2013;6(3):494.
23. Keen A, McCrate B, McLennon S, et al. Influencing nursing knowledge and attitudes to positively affect care of patients with persistent pain in the hospital setting. *Pain Manag Nurs*. 2017;18(3):137–143. doi:10.1016/j.pmn.2017.04.002
24. Louriz M, Belayachi J, Madani N, et al. Practices and perceived barriers regarding pain management among emergency department physicians: a nationwide multicenter survey in Moroccan hospitals. *Acute Med Surg*. 2016;3(4):360–363. doi:10.1002/ams2.201
25. Fallatah SMA. Pain knowledge and attitude survey among health-care professionals at a university hospital in Saudi Arabia. *Saudi J Med Med Sci*. 2017;5(2):155–159.
26. Alkhatib GS, Al Qadire M, Alshraideh JA. Pain management knowledge and attitudes of healthcare professionals in primary medical centers. *Pain Manag Nurs*. 2020;21(3):265–270. doi:10.1016/j.pmn.2019.08.008
27. Hammick M, Freeth D, Koppel I, et al. A best evidence systematic review of interprofessional education: BEME guide no. 9. *Med Teach*. 2007;29(8):735–751. doi:10.1080/01421590701682576
28. Al-Quliti KW, Alamri MS. Assessment of pain. Knowledge, attitudes, and practices of health care providers in Almadinah Almunawwarah, Saudi Arabia. *Neurosciences*. 2015;20(2):131–136. doi:10.17712/nsj.2015.2.20140546
29. Kheshti R, Namazi S, Mehrabi M, et al. Health care workers' knowledge, attitude, and practice about chronic pain management, Shiraz, Iran. *Anesthesiol Pain Med*. 2016;6(4):e37270–e37270. doi:10.5812/aapm.37270
30. Paudel BD, Ryan KM, Brown MS, et al. Opioid availability and palliative care in Nepal: influence of an international pain policy fellowship. *J Pain Symptom Manage*. 2015;49(1):110–116. doi:10.1016/j.jpainsymman.2014.02.011
31. Foley KM, et al. Pain control for people with cancer and AIDS. *Disease Control Priorities in Developing*. World Bank; 2006.

32. Kahsay DT, Pitkäjärvi M. Emergency nurses knowledge, attitude and perceived barriers regarding pain management in resource-limited settings: cross-sectional study. *BMC Nurs*. 2019;18(1):1–13. doi:10.1186/s12912-019-0380-9
33. Paudel S, Krishna Bahadur GC, Subedi M, Arjyal A, Daha SK, Lamichhane B, Sharma PK.Communication skills of physicians during consultation in out-patient settings at a tertiary hospital in Nepal. *Middle East J Fam Med*. 2017;7(10):28.
34. Katel K. Nursing process application in Nepal teaching hospital. *RUDN J Med*. 2022;26(1):79–87. doi:10.22363/2313-0245-2022-26-1-79-87
35. Sharma S, Palanchoke J, Reed D, et al. Translation, cross-cultural adaptation and psychometric properties of the Nepali versions of numerical pain rating scale and global rating of change. *Health Qual Life Outcomes*. 2017;15(1):236. doi:10.1186/s12955-017-0812-8
36. Melzack R. The short-form McGill Pain Questionnaire. *Pain*. 1987;30(2):191–197. doi:10.1016/0304-3959(87)91074-8
37. Hospital pharmacy guideline 2072. Kathmandu (Nepal): Government of Nepal, Ministry of Health and Population. Available from: http://www.dda.gov.np/content/hospital-pharmacy-guideline-2072
38. Thapa P, Lee SWH, KC B, et al. Pharmacist-led intervention on chronic pain management: a systematic review and meta-analysis. *Br J Clin Pharmacolog*. 2021;87:3028–3042. doi:10.1111/bcp.14745
39. Shankar P, Partha P, Shenoy N. Self-medication and non-doctor prescription practices in Pokhara valley, Western Nepal: a questionnaire-based study. *BMC Fam Pract*. 2002;3(1):1–7. doi:10.1186/1471-2296-3-17
40. Phueanpinit P, Pongwecharak J, Krska J, et al. Evaluation of community pharmacists' roles in screening and communication of risks about non-steroidal anti-inflammatory drugs in Thailand. *Prim Health Care Res Dev*. 2018;19(6):598–604. doi:10.1017/S1463423618000142

Research in Social and Administrative Pharmacy xxx (xxxx) xxx

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

journal homepage: www.elsevier.com/locate/rsap

Effectiveness of community pharmacist-led interventions in osteoarthritis pain management: A cluster-randomized trial

Parbati Thapa [a], Bhuvan KC [b,c], Sudesh Gyawali [d], Siew Lian Leong [a], Mohamed Izham Mohamed Ibrahim [e], Shaun Wen Huey Lee [a,f,g,h,*]

[a] School of Pharmacy, Monash University Malaysia, Subang Jaya, Selangor, Malaysia
[b] School of Clinical Sciences, Queensland University of Technology, Brisbane, Australia
[c] College of Public Health, Medical, and Veterinary Sciences, James Cook University, Townsville, Queensland, Australia
[d] Department of Pharmacology, Manipal College of Medical Sciences, Pokhara, Nepal
[e] Clinical Pharmacy and Practice Department, College of Pharmacy, Qatar University, Doha, Qatar
[f] School of Pharmacy, Faculty of Health and Medical Sciences, Taylor's University, Subang Jaya, Selangor, Malaysia
[g] Asian Centre for Evidence Synthesis in Population, Implementation and Clinical Outcomes (PICO), Health and Well Being Cluster, Monash University Malaysia, Bandar Sunway, Selangor, Malaysia
[h] Global Asia in the 21st Century (GA21) Platform, Monash University Malaysia, Bandar Sunway, Selangor, Malaysia

ARTICLE INFO

Keywords:
Education
Medication review
Nepal
Osteoarthritis
Pharmacist

ABSTRACT

Background: Community pharmacists contribute in osteoarthritis management via evidence-based pain management services. However, their roles and impacts on osteoarthritis management in low- and middle-income countries have yet to be explored.
Objective: This study aims to evaluate the effectiveness of community pharmacist-led educational intervention and medication review among osteoarthritis patients.
Methods: A 6-month cluster-randomized controlled study was conducted in 22 community pharmacies of Nepal. Patients clinically diagnosed with osteoarthritis, aged 18 years and above, with a poor knowledge level of osteoarthritis and pain management were enrolled in the study. The intervention groups were educated on osteoarthritis and pain management, and had their medications reviewed while control group received usual care. Primary outcomes evaluated for the study were the change in pain levels, knowledge, and physical functional scores at 3 and 6 months. Repeated analyses of covariance were performed to examine the outcomes.
Results: A total of 158 participants were recruited for the study. The intervention group reported improvements in pain score (mean difference 0.473, 95 % CI 0.047 to 0.900) at 3 months and the end of the study (mean difference 0.469, 95 % CI 0.047 to 0.891) as compared to control. Similarly, improvement in knowledge scores were observed in the intervention group at 3 months (mean difference 5.320, 95 % CI 4.982 to 5.658) and 6 months (mean difference 5.411, 95 % CI 5.086 to 5.735). No differences were observed in other outcomes, including physical functional score, depression, and quality of life.
Conclusion: Community pharmacist-led intervention improved patients' knowledge of osteoarthritis and pain management. While pain scores improved, physical functional score, depression, and quality of life score remained unchanged.
Trial registration: ClinicalTrials.gov identifier: NCT05337709.

1. Introduction

Osteoarthritis is one of the most prevalent chronic diseases globally and is a leading cause of disability, especially in low-middle-income countries (LMICs). Studies have determined that osteoarthritis affects one in six to seven individuals globally.[1] Osteoarthritis is characterized by the progressive destruction of the cartilage, accompanied by pain, immobility, muscle weakness, and reduced ability to perform activities of daily living.[2] In people with osteoarthritis, it typically affects the hand, knee, hip, and feet; knee being the most commonly affected part.[3]

* Corresponding author. School of Pharmacy, Monash University, Malaysia, Subang Jaya, Selangor, Malaysia.
E-mail address: shaun.lee@monash.edu (S.W.H. Lee).

https://doi.org/10.1016/j.sapharm.2023.10.012
Received 30 June 2023; Received in revised form 4 September 2023; Accepted 26 October 2023
Available online 4 November 2023

Effective osteoarthritis management requires long-term treatment strategies for symptom management (pain and limitations in physical function) and joint structure changes, that can lead to disability.[4] Current clinical guidelines prioritize non-surgical procedures with appropriate pharmacological care, including patient education, advice, physical activity, and weight management in osteoarthritis.[4,5] However, there exists a gap in effective osteoarthritis management attributed to the complexity of health priorities, limited access to quality conservative care, underutilization of non-pharmacological therapies, resource constraints, and variation in models of care.[6,7]

Health inequities, unaffordable osteoarthritis management, failure to recognize osteoarthritis as an important disease, lack of coordinated care, knowledge and skills among health care professionals, and low health literacy among people with osteoarthritis are the challenges in implementing osteoarthritis evidence-based care especially in LMICs.[8,9] In particular, health literacy plays a pivotal role in patients engagement in self-management strategies for osteoarthritis, as it improves personal responsibility with corresponding behavior change.[10,11] This can be partly explained using the biopsychosocial model, where a multidimensional, dynamic integration among physiological, psychological, and social factors reciprocally influence one another, resulting in chronic and complex pain syndromes.[12] To address this, the model recommends improving a person's functional capacity, resulting in better physical strength and mobility and thus improving affective state and self-esteem.

Patients must be educated on various self-management strategies in osteoarthritis as it enhances the patients' ability to manage diseases, symptoms, treatments, lifestyle, and cope with mental and physical changes.[13] This can be achieved in several ways: via media, leaflets, videos, face-to-face counselling, or a web-based application.[14] Studies have consistently shown that patient education improves health literacy, especially among people with chronic diseases such as diabetes, hypertension, and osteoarthritis.[15–17] Among all the strategies, educational videos are the most widely used as they provide a multisensory approach that could deliver a better health education, especially among patients with low literacy skills.[18] Egerton and colleagues reported that patients with osteoarthritic knee pain positively rated the education video in enjoyment, helpfulness, relevance, believability, and intentions for behavior change.[15] Likewise, Lopez and colleagues reported that education videos improved patients' knowledge on osteoarthritis impact, medication and associated side effects, and self-care activities.[19]

Recently, several studies have examined the impact of pharmacists working collaboratively with a multidisciplinary pain management team to educate patients and conduct medication reviews.[7,10,20,21] Darlow and colleagues evaluated the impact of providing an informational booklet to knee osteoarthritis patients in community pharmacies, which was reportedly influential in increasing patient knowledge of osteoarthritis.[22] Hanson et al. in their study, provided patient education to osteoarthritic patients, which improved self-perceived health and function.[23] These encouraging results suggest that community pharmacists can help address the gap in osteoarthritis patient care,[20] especially in LMICs, via education and medication review.[1]

Nepal is a LMIC located in South Asia where healthcare is provided through a two-tier system consisting of the publicly funded healthcare with a co-existing private healthcare systems.[24] However, healthcare is unequally distributed, and mostly concentrated in urban areas of the nation. As such, community pharmacies are often the first point of contact for most patients in Nepal due to their low costs for service, easy accessibility, and trust on provided health information.[25,26] However, there are limited pharmacy services available in most community pharmacies of Nepal. Against this backdrop, this study aims to investigate the impact of a community pharmacist-led medication reviews and educational intervention on pain score, physical function, knowledge, depression, and quality of life among people with osteoarthritis.

2. Methods

2.1. Study design

This study was a multicenter, open-label cluster-randomized study of 22 community pharmacies located in Pokhara, Nepal. The study was conducted from February 2022 to November 2022. Community pharmacies (clusters) were randomized as the intervention involved the training of pharmacists and staffs at each of the community pharmacy. This design reduced the risk of contamination of the intervention effect.

2.2. Participating community pharmacies

Community pharmacies in the Pokhara Valley were randomly approached via telephone or in-person to inquire on their interest to participate in the study. In the event the community pharmacy was interested, information related to their daily customer load was obtained. Details of the study and its intervention was explained to the pharmacist. Community pharmacies who agreed to participate were then stratified into blocks according to the daily customer load; and randomly allocated 1:1 to intervention or control using a computer-generated permuted block design. Randomization was blinded and performed by an independent researcher. Owing to the nature of the study, blinding was not possible for participants or researcher.

2.3. Participants and recruitment

We recruited adults aged 18 years and above who had been clinically diagnosed with osteoarthritis and experienced chronic pain persisting for three months or more. Only individuals willing to participate in the study were included, while those unable to provide informed consent, individuals with a terminal illness, and individuals with a good osteoarthritis knowledge score (>80 % on the assessment tool) were excluded.

Potential participants were recruited using advertisements placed in community pharmacies. All potential participants were provided with an explanation of the study's purpose, procedures and detailed information about the study itself. Those who expressed willingness to enroll were asked to sign a written informed consent form specifically developed in Nepalese language to ensure easy comprehension.

2.4. Intervention group

In this study, education and medication review interventions were designed to promote behavioral change and aid in the appropriate use of medications among osteoarthritis patients, over a period of six weeks, for the management of pain. Our educational intervention (aided by leaflet and video) was anticipated to enhance the physical and psychological capabilities of the participants by improving their knowledge to manage the pain and associated symptoms of osteoarthritis. Community pharmacists from respective pharmacies were trained by the first author (PT) to deliver the intervention (counselling and medication review).

All participants assigned to the intervention group received individualized education counselling on osteoarthritis and pain management. In addition, participants had their medications reviewed. Patients were also inquired about their knowledge on medications(e.g., indication, appropriate use, adverse drug reactions, adherence issues, and self-medication practices). They were further assessed for the risk of development of adverse effects with NSAIDs. Patients were counselled and referred to the physician if any medication overuse, inappropriate dose, or risk of developing adverse effects with NSAIDs were identified.

Participants also watched a video vignette on osteoarthritis management between a patient and pharmacist to reinforce the educational content. During the six weeks period, participants had weekly calls with the community pharmacist to clarify any doubts on the educational materials and were counselled if needed (Appendix Tables 1 and 3).

2.5. Control group

Participants in the control group received as usual care provided by the community pharmacies. This included the dispensing of medications and instructions on when and how to take the medicines and basic counselling on osteoarthritis management. To ensure participants received the best available care, all participants received intervention education counselling materials (leaflet and video) and medication review at the end of the trial period.

2.6. Primary outcomes

The primary outcome of interest was the change in pain score, assessed using a numeric pain rating scale (NRS) on the 11-point scale from baseline to three months and the end of the study.[27,28] In addition, we evaluated the change in physical functionality using the Western Ontario and McMaster Universities Arthritis Index (WOMAC),[29] which measures the pain, stiffness, and difficulties in performing daily activities among patients with osteoarthritis. This was supplemented with a change in participants' knowledge of osteoarthritis assessed using a knowledge assessment questionnaire developed by performing a thorough literature search[30,31] and questions adapted from the validated osteoarthritis patient knowledge questionnaire (PKQ-OA) by Hill and colleagues.[32] The final questionnaire was composed of 12 multiple choice questions; three questions each assessed the knowledge on osteoarthritis, risk factors for osteoarthritis, medication use, the importance of exercise, and self-care activities. To ensure content validity, expert opinions were obtained from the physicians and pharmacists, and the questionnaire was modified as suggested. A pilot study was conducted among 12 patients with osteoarthritis, and its internal consistency was established; a Cronbach alpha value of 0.825 was obtained.

2.7. Secondary outcome

Secondary outcomes of interest were the change in participants' depression scale and quality of life. Depression was assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS) depression 8b short-form questionnaire.[33] The tool assesses the self-reported negative mood (sadness, guilt), views of self (self--criticism, worthlessness), social cognition (loneliness, interpersonal alienation), and decreased positive affect (loss of interest, meaning, and purpose). Quality of life was measured using the EuroQoL-five-dimension 3 levels instrument (EQ-5D-3L) and a visual analog scale.[34] (Appendix Table 2).

2.8. Sample size

We assumed that our intervention would result in a medium effect, with a reduction of 0.46 points on the pain score and 0.47 points on the physical functioning based upon results from a previous study.[7] Assuming an 80 % power, a sample size of 128 patients was determined to achieve a significance level of 0.05.[35] After accounting for a 20 % dropout, a sample size of 154 participants was finalized (77 in each control and intervention groups).

2.9. Statistical analysis

All analyses were performed using a modified intention-to-treat (mITT). Descriptive analysis was used across the randomized groups, with categorical variables presented as frequencies and percentages. In contrast, continuous variables were presented as mean and standard deviation. A repeated measure of analysis of covariance (ANCOVA), was used to examine the differences in effects for both primary and secondary outcomes. Multiple imputation technique was used to replace the missing data in the follow-up periods. All analyses were conducted in the SPSS version 26.0 (Statistical Package for Social Science)).[36]

2.10. Fidelity monitoring

Adherence and fidelity were monitored using the phone call record and the data collection sheets. The principal investigator scheduled regular visits and meetings with the community pharmacists to ensure that the intervention was well delivered, and the data collection procedure followed the proposed protocol.

2.11. Ethics and dissemination

Ethical approval for the trial was obtained from Nepal Health Research Council (Reg. no. 211/2020). The protocol was registered at ClinicalTrials.gov, NCT05337709.

3. Results

3.1. Baseline demographic and clinical characteristics

A total of 158 participants (n = 80 for control group and n = 78 for intervention group) were recruited in the study(Fig. 1). The mean age of the participants was 58.8 years with majority females (n = 124, 78.5 %). More than half of the participants reported pain related to knee osteoarthritis (n = 90, 57.0 %) and had a low knowledge regarding osteoarthritis and pain management (mean score: 5.16 ± 1.92; range 0–12). The participants' pain and WOMAC scores (mean ± standard deviation) were 6.36 ± 1.71 and 63.85 ± 18.12, respectively. No significant differences in the baseline demographic and clinical characteristics were observed between groups (Tables 1 and 2).

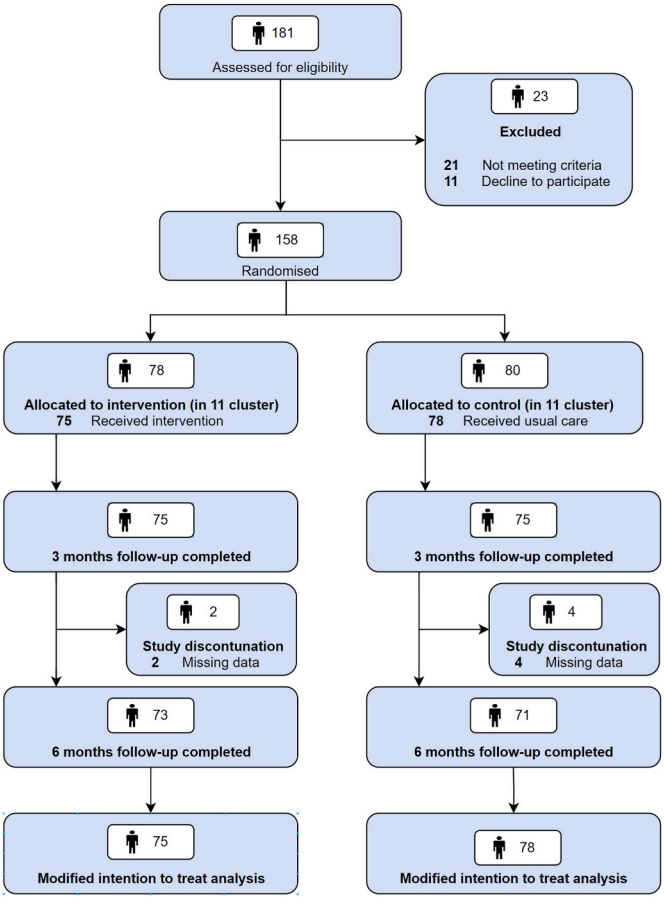

Fig. 1. Flow of participants through study.

Table 1
Baseline demographic details of the study participants.

Age (mean ± SD)	Control (n = 80)		Treatment (n = 78)		Total		P value 0.297
	59.8 ± 11.3		57.7 ± 12.6		58.8 ± 12		
	n	%	n	%	n	%	
Gender							0.213
Male	14	17.5	20	25.6	34	21.5	
Female	66	82.5	58	74.4	124	78.5	
Education							
No formal education	31	38.8	31	39.7	62	39.2	0.291
Primary	14	17.5	10	12.8	24	15.2	
Secondary	22	27.5	20	25.6	42	26.6	
Higher secondary	5	6.3	11	14.1	16	10.1	
Bachelor	3	3.8	5	6.4	8	5.1	
Masters and above	5	6.3	1	1.3	6	3.8	
Occupation							
Housewife	52	65.0	50	64.1	102	64.1	0.437
Farmer	9	11.3	11	14.1	20	14.1	
Retired	5	6.3	1	1.3	6	1.3	
Administration/ Public services	3	3.8	1	1.3	4	1.3	
Teacher	4	5.0	4	5.1	8	5.1	
Others (Driver/ Labour)	2	2.5	1	1.3	3	1.3	
Business	5	6.3	10	12.8	15	12.8	
Pain Duration							
3 months-1 year	10	12.5	21	26.9	31	19.6	0.080
2–3 year	15	18.8	19	24.4	34	21.5	
4–5 year	24	30.0	20	25.6	44	27.9	
6–7 year	14	17.5	7	9.0	21	13.3	
8 years and more	17	21.3	11	14.1	28	17.7	
Pain sites							
Knee	40	50.0	50	64.10	90	57.0	0.214
Hip	28	35.0	23	29.49	51	32.3	
Hip and knee	10	12.5	4	5.13	14	8.9	
Multiple joints	2	2.5	1	1.28	3	1.9	
Presence of comorbidity							
Hypertension	21	26.3	16	20.1	37	23.0	0.291
Diabetes	6	7.5	8	10.3	14	8.9	
Asthma	3	3.8	4	5.1	7	4.4	
Thyroid disorder	7	8.8	7	9.0	14	8.9	
Cardiac problem	4	5.0	1	1.3	5	3.2	
GI disorder	8	10.0	1	1.3	9	5.7	

Table 2
Baseline primary and secondary outcomes of the study participants.

	Control (Mean ± SD)	Treatment (Mean ± SD)	Total (Mean ± SD)	P value
Knowledge score	5.19 ± 2.01	5.13 ± 1.83	5.16 ± 1.92	0.872
Pain score	6.56 ± 1.90	6.16 ± 1.48	6.36 ± 1.71	0.166
WOMAC score	66.17 ± 18.17	61.44 ± 17.87	63.85 ± 18.12	0.077
Depression score	51.77 ± 11.77	52.37 ± 9.54	52.05 ± 10.70	0.854
Quality of life score (EQ 5D)	0.61 ± 0.28	0.66 ± 0.25	0.64 ± 0.27	0.073
Visual Analog scale (EQ 5D)	57.75 ± 17.64	62.17 ± 21.35	59.80 ± 19.58	0.077

Pain scores: 0 = no pain,10 = very much pain.
Higher scores of knowledge represent better knowledge.
Higher WOMAC score indicative of poor function.
Higher score of PROMIS depression scores are indicative of greater severity of depression.
Higher EuroQol-5D is indicative of a better quality of life.

3.2. Primary outcomes

Pharmacist-led intervention for providing education and medication review to osteoarthritis patients improved pain scores at 3 months (mean difference 0.473, 95 % CI 0.047 to 0.900) and at the end of the study, 6 months (mean difference 0.469, 95 % CI 0.047 to 0.891) as compared to the control group. Similarly, improvement in knowledge score was observed in the intervention group at 3 months (mean difference 5.320, 95 % CI 4.982 to 5.658) and 6 months (mean difference 5.411, 95 % CI 5.086 to 5.735) compared to the control group. No statistically significant differences in the WOMAC score were noted between the intervention and control groups either at 3 months (mean difference 2.717, 95 % CI -0.300 to 5.734) or at the end of the study, 6 months (mean difference 2.717, 95 % CI -0.604 to 5.234) (Table 3, Fig. 2).

3.3. Secondary outcomes

At the end of the study at 6 months, no statistically significant differences in depression score (mean difference −0.181, 95 % CI -1.011 to 0.650)) the quality-of-life score EQ 5D(mean difference −0.018, 95 % CI -0.053to 0.018) and visual analog scale EQ 5D (mean difference −1.161, 95 % CI -3.236 to 0.017) were observed between the intervention and control groups (Table 3, Fig. 2).

3.4. Safety and adverse events

No adverse or severe adverse events related to our study were reported during the study period.

4. Discussion

In this randomized control trial, a community pharmacist-led intervention program was designed where the patients with osteoarthritis had their medications reviewed and received education on osteoarthritis and pain management that was compared to usual practice. The intervention effectively improved patient's knowledge and pain score, however physical functionality, depression, and quality of life remain unchanged.

Result of this study is consistent with the findings reported by Darlow and colleagues[22] and Marra and colleagues[21] which showed the effectiveness of education intervention and pharmacist-led intervention in improving the knowledge and pain score in osteoarthritic patients. This improvement in knowledge gained by the participants on osteoarthritis is important, as it might guide them in decision making, positive behavioral changes and improving health outcomes.[37] Against this, we attempted to reinforce the knowledge and self-care management practice of the participants in the intervention through the use of educational videos as well as counselling. Nevertheless, we do urge caution in the interpretation of the improvement in pain score as these changes were relatively small compared to the recommended minimum clinically importance difference of 1.41 points (versus 0.47 in our study).[38,39]

In contrast, we did not identify any statistically significant difference in WOMAC, depression, and quality of life score between intervention and control group participants at both study periods for 3 and 6 months. Studies to date have similarly reported a mixed impact on these outcomes. Coleman and colleagues and Marra and colleagues reported a significant improvement in WOMAC score after a self-management education program and pharmacist-initiated intervention trial in osteoarthritis.[21,40] Likewise, Hansson and colleagues also found a significant improvement in the quality of life of patients with osteoarthritis after education, contrary to our findings. While these studies had included the intervention modules relatively similar to us, the use of a multidisciplinary team approach with extensive exercise session might have resulted the positive outcomes as opposed to our study.[23]

Conversely, Lawford and colleagues and Allen and colleagues found that the pain coping skills training provided online and over the telephone for osteoarthritis patients shows no effect on physical functioning, measured by WOMAC score after the intervention.[41,42] Similarly, Taglietti and colleagues, in their randomized controlled trial, found no improvements in WOMAC score, quality of life score, and

Table 3
Comparisons of outcomes at 3 months and 6 months.

Outcomes	Mean Difference (I-J)	Std. Error	p-value	95 % Confidence Interval for Difference		Partial n square	Observed power
				Lower Bound	Upper Bound		
Pain score							
Three months	**.473***	.216	.030	.047	.900	.032	0.589
Six months	**.469***	.214	.030	.047	.891		
Knowledge score							
Three months	**5.320***	.171	.001	4.982	5.658	.882	0.998
Six months	**5.411***	.164	.001	5.086	5.735		
WOMAC SCORE							
Three months	1.789	1.524	.242	−1.223	4.800	.009	0.217
Six months	1.693	1.482	.255	−1.235	4.620		
Depression score							
Six months	−.181	.420	.668	−1.011	.650	.001	0.071
Quality of life score							
Six months	−.018	.018	.322	−.053	.018	.007	0.167
Visual Analog Score							
Six months	−1.61	.823	.052	−3.236	.017	.025	0.493

I = control, J = treatment, Analysis: Repeated measure Analysis of Co-variance (ANCOVA) with baseline value as covariates, * significant difference in scores between groups.

depressive symptoms score among participants assigned to the patient-education group,[43] similar to our findings. This could be attributed to the nature of the educational intervention which was insufficient to engage patients in physical activity and exercise, which have been found to be effective in improving physical function and, ultimately quality of life in osteoarthritis.[44]

Our study offers several strengths. Few studies to date have examined the effectiveness of community pharmacist-initiated intervention with education and medication review among osteoarthritis patients.[21,22] Acknowledging this gap, we designed a study which included verbal counselling, leaflet, and video for education and medication review for patients with osteoarthritis visiting community pharmacies. McLachlan and colleagues recently reported that the use of community pharmacist as the information source for osteoarthritis and pain management is limited and emphasized to train them for better management of the condition.[45] It is even more essential to strengthen the community pharmacy service in LMICs like Nepal to build trust in the community and expand the service beyond medication selling.[46] As such, continuous professional development modules on medication review and pain management in various conditions for community pharmacists might be beneficial to enhance the knowledge and skill for better patient services. To our knowledge, it is the first study on community pharmacist intervention among osteoarthritis patients in Nepal, a LMIC, where the services of community pharmacist may be a cost-effective option. This study serves as a reference for developing further interventions within community pharmacies for managing chronic conditions like osteoarthritis. However, further investigation is necessary to determine the sustainability and long-term effects of the intervention.

The coaching of osteoarthritis patients with multimedia for lifestyle changes, behavioral changes, and coping skill for pain to improve functioning and quality of life has been examined by several studies.[19,41,47] Most studies have suggested that the intervention potentially improves all major outcomes in osteoarthritis; this could be due to the ideal research setting compared with the pragmatic design in this study. Furthermore, most of the studies are conducted in high-income countries, where health literacy among individuals are higher compared with the population in LMICs like Nepal.[48] Inadequate health literacy hinders patients' adherence to health instructions and medicines.[49] As such, further osteoarthritis pain management programs should focus on the appropriate development and implementation of the intervention that is context specific and tailored to the needs of the target communities being examined for positive outcomes of the intervention.

Nevertheless, this has to be taken in light of some of the study limitations. Firstly, individual experience, beliefs, expectations, perceptions on health and illness and duration of pain can influence an individual's quality of life. As such, our intervention period of 6 months might not be sufficient to bring the changes on these factors resulting in insignificant changes in quality of life of the patients. Secondly, individualized and flexible exercise prescription with patient education and medication review have been suggested to provide optimal improvements in physical function and quality of life outcomes. Nevertheless, this design was not possible in our study due to the lack of expertise in our setting, which may have resulted in the indifference in WOMAC and quality of life scores. Likewise cognitive behavioral therapy, mind-body exercise, could help manage depressive symptoms in osteoarthritis,[50] which was lacking in our intervention. While a multimodal and multidisciplinary team approach with pharmacological and non-pharmacological intervention with patients' personal characteristics and preference could help better manage osteoarthritis and associated symptoms, this was not possible in our setting due to the healthcare resource constraints which may not have led to optimal results.[51] As such, future studies should also include and examine these aspects. Finally, due to limited internet connectivity and smartphone users, video could not be circulated to all the participants, which might have affected the intervention.

5. Conclusion

Our study demonstrated the important role of community pharmacists in improving osteoarthritis patients' knowledge and pain management via targeted education interventions and comprehensive medication reviews. While our interventions improved pain score albeit clinically insignificant, it did not significantly impact physical functioning, quality of life, or depression. The findings highlight the importance of providing counselling and support to individuals with osteoarthritis in community settings. By combining educational initiatives, medication management, and personalized guidance, community pharmacists can empower patients to better understand their condition, optimize self-care activities, and achieve positive health outcomes such as improved pain control and enhanced overall well-being.

Author statement

Conceptualization: Parbati Thapa, Shaun Wen Huey Lee, Bhuvan KC.

Methodology: Shaun Wen Huey Lee, Parbati Thapa, Bhuvan KC, Mohamed Izham Mohamed Ibrahim.

Formal analysis: Parbati Thapa, Shaun Wen Huey Lee, Siew Lian Leong.

Investigation: Parbati Thapa, Sudesh Gyawali, Bhuvan KC.

Data Curation: Shaun Wen Huey Lee, Parbati Thapa.

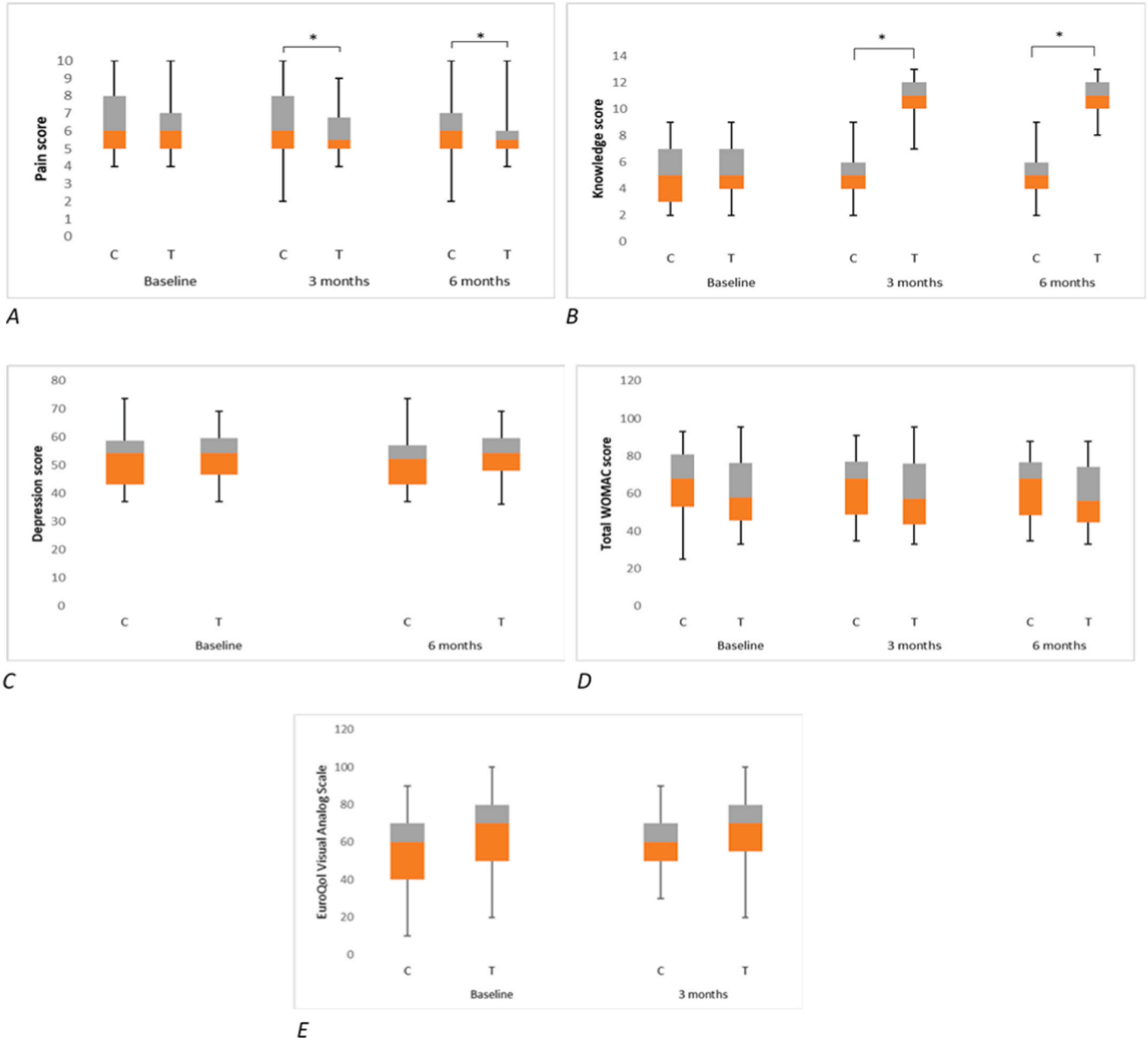

Fig. 2. Box plot on the changes on outcomes at baseline, 3 months and 6 months
A: pain score; B: Knowledge score; C: Depression score; D: Total WOMAC score; E: EuroQol Visual Analog Scale C = control, T = treatment, * significance at p value < 0.05.

Writing - Original Draft: Parbati Thapa, Shaun Wen Huey Lee, Bhuvan KC.

Writing - Review & Editing: Parbati Thapa, Mohamed Izham Mohamed Ibrahim, Sudesh Gyawali, Siew Lian Leong.

Appendix

Appendix Table 1
Description of intervention

Leaflet (Education)	
Osteoarthritis introduction	Brief introduction of osteoarthritis, risk factors, signs, and symptoms
Body mass index	Importance of BMI and formula to calculate, and interpretation with example
Treatment options for osteoarthritis	Enhance physical activity, medication to control inflammation and pain, physiotherapy, weight control, joint replacement therapy
Medication	Types of medication used (paracetamol and NSAIDs), side effects, duration, precaution to be applied, concern on prevalent comorbid condition, and concomitant medication use issued to be discussed with health care professionals.
Food to be consumed	Details on the food to be consumed

(*continued on next page*)

Appendix Table 1 (*continued*)

Leaflet (Education)	
Self-care activities	Importance of active life and exercise, hot and cold compression, avoidance of activities that intensify the pain, mental health, and meditation, seeking counselling from a health care professional.
Medication review	Listing medication regimens, assessing participants if they know the indication, developed any adverse effects, adherence issues, and self-medication practice. Assessment of risk for the development of adverse effects with NSAIDs. Counselling for the effective use of drugs, duration of therapy, probable side effects, and precautions to be applied. Patients were referred to the physician if any issues identified.
Video (Education)	The video was a role-play (simulated patient and pharmacist) at a community pharmacy. It was developed in the Nepalese language for better understanding. The contents were the same as in the leaflet. However, the pharmacist clarifies every piece of content by explaining and providing an opportunity for the patient to cross-questioning. It was 9 min long, starting with a brief introduction.

Appendix Table 2
An outcome measure

Variables	Domain	Measure
Descriptive/demographic	Participant characteristics	Structured questionnaire
Primary outcome	Pain score	Numeric pain rating scale
	Participants' knowledge	Participants' knowledge Questionnaire on osteoarthritis and pain management
	Physical function	Western Ontario and McMaster Universities Arthritis Index (WOMAC)
Secondary outcome	Depression	PROMIS Short form Depression Scale
	Quality of life	Euro Qol-five-dimension 3 levels (EQ-5D-3L)

Appendix Table 3
Data collection time points

Variables	Baseline (Both groups)	Intervention (treatment group)					Three months (Both groups)	Six months (Both groups)
		At enrollment Week 1	Week 2	Week 3	Week 4	Week 6		
Demographic detail	x	Medication review, educated counselling (leaflet)						
Pain score	x		Follow up phone calls				x	x
WOMAC score	x			Follow up phone calls			x	x
EQ-5D-3L	x				Follow up phone calls			x
PROMIS depression	x					Video Demonstration		x
Knowledge Assessment	x						x	x

Patient Reported Outcome Measures Information System (PROMIS); Western Ontario and McMaster Universities Arthritis Index (WOMAC); EuroQol-five-dimension 3 levels (EQ-5D-3L).

References

1. Yahaya I, Wright T, Babatunde OO, et al. Prevalence of osteoarthritis in lower middle- and low-income countries: a systematic review and meta-analysis. *Rheumatol Int*. 2021;41:1221–1231.
2. Newberry SJ, FitzGerald J, SooHoo NF, et al. *Treatment of Osteoarthritis of the Knee: An Update Review*. 2017.
3. Aboulenain S, Saber AY. *Primary Osteoarthritis. StatPearls*. StatPearls Publishing; 2022 [Internet].
4. National Clinical Guideline C. *National Institute for Health and Clinical Excellence: Guidance. Osteoarthritis: Care and Management in Adults*. London: National Institute for Health and Care Excellence (UK)Copyright © National Clinical Guideline Centre; 2014.
5. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage*. 2019;27:1578–1589.
6. Dziedzic KS, Allen KD. Challenges and controversies of complex interventions in osteoarthritis management: recognizing inappropriate and discordant care. *Rheumatology*. 2018;57:iv88–iv98.
7. Thapa P, Lee SWH, Kc B, Dujaili JA, Mohamed Ibrahim MI, Gyawali S. Pharmacist-led intervention on chronic pain management: a systematic review and meta-analysis. *Br J Clin Pharmacol*. 2021.
8. Goucke R, Morriss W. Pain management in low and middle income countries (LMIC) just put up with it? *Egypt J Anaesth*. 2012;28:1–2.
9. Eyles JP, Sharma S, Telles RW, Namane M, Hunter DJ, Bowden JL. Implementation of best-evidence osteoarthritis care: perspectives on challenges for, and opportunities from, low and middle-income countries. *Frontiers in Rehabilitation Sciences*. 2022;2.
10. McLachlan AJ, Carroll PR, Hunter DJ, Wakefield TAN, Stosic R. *Osteoarthritis Management: Does the Pharmacist Play a Role in Bridging the Gap between what Patients Actually Know and what They Ought to Know? Insights from a National Online Survey*. Health Expect; 2022.
11. Bensberg M, Kennedy M. A framework for health promoting emergency departments. *Health Promot Int*. 2002;17:179–188.
12. Gatchel RJ, Reuben DB, Dagenais S, et al. Research agenda for the prevention of pain and its impact: report of the work group on the prevention of acute and chronic pain of the federal pain research strategy. *J Pain*. 2018;19:837–851.
13. Wu Z, Zhou R, Zhu Y, et al. *Self-Management for Knee Osteoarthritis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials*. Pain Research and Management; 2022:2022.
14. Tuong W, Larsen ER, Armstrong AW. Videos to influence: a systematic review of effectiveness of video-based education in modifying health behaviors. *J Behav Med*. 2014;37:218–233.
15. Egerton T, McLachlan L, Graham B, et al. How do people with knee pain from osteoarthritis respond to a brief video delivering empowering education about the condition and its management? *Patient Educ Counsel*. 2021;104:2018–2027.
16. Sapkota S, Brien J-AE, Aslani P. Diabetes-related healthcare services in Nepal-A qualitative exploration of healthcare professionals' opinions. *Pharmacy*. 2020;8:131.
17. Lee JY, Wong CP, Lee SWH. *m-Health Views and Perception Among Malaysian: Findings from a Survey Among Individuals Living in Selangor*. vol. 6. Mhealth; 2020.
18. Murphy PW, Chesson AL, Walker L, Arnold CL, Chesson LM. Comparing the effectiveness of video and written material for improving knowledge among sleep disorders clinic patients with limited literacy skills. *South Med J*. 2000;93:297–304.

19. Lopez-Olivo MA, Ingleshwar A, Volk RJ, et al. Development and pilot testing of multimedia patient education tools for patients with knee osteoarthritis, osteoporosis, and rheumatoid arthritis. *Arthritis Care Res*. 2018;70:213–220.
20. Kielly J, Davis EM, Marra C. Practice guidelines for pharmacists: the management of osteoarthritis. *Can Pharm J*. 2017;150:156–168.
21. Marra CA, Cibere J, Grubisic M, et al. Pharmacist-initiated intervention trial in osteoarthritis: a multidisciplinary intervention for knee osteoarthritis. *Arthritis Care Res*. 2012;64:1837–1845.
22. Darlow B, Brown M, Hudson B, et al. Feasibility of a randomised controlled trial of two types of written information for people with knee osteoarthritis. *Osteoarthritis and Cartilage Open*. 2022;4, 100254.
23. Hansson EE, Jönsson-Lundgren M, Ronnheden A-M, Sörensson E, Å Bjärnung, Dahlberg LE. Effect of an education programme for patients with osteoarthritis in primary care-a randomized controlled trial. *BMC Muscoskel Disord*. 2010;11:1–7.
24. Khatri RB, Durham J, Assefa Y. Utilisation of quality antenatal, delivery and postnatal care services in Nepal: an analysis of Service Provision Assessment. *Glob Health*. 2021;17:102.
25. Jha N, Rathore DS, Shankar PR, et al. Effect of an educational intervention on knowledge and attitude regarding pharmacovigilance and consumer pharmacovigilance among community pharmacists in Lalitpur district, Nepal. *BMC Res Notes*. 2017;10:4.
26. Ojha A, Bista D, Kc B. Patients' perceptions on community pharmacy services of a ward (10) of kathmandu metropolitan. *Patient Prefer Adherence*. 2023;17: 1487–1499.
27. Sharma S, Palanchoke J, Reed D, Abbott JH. Translation, cross-cultural adaptation and psychometric properties of the Nepali versions of numerical pain rating scale and global rating of change. *Health Qual Life Outcome*. 2017;15:236.
28. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain*. 2005;113:9–19.
29. Nakarmi S, Haq SA, Vaidya B. Translation, validation and cross-cultural adaptation of the Nepali version of WOMAC® LK 3.1. *Int J Rheumatic Dise*. 2019;22:1877–1883.
30. Alyami AH, Alswat MM, Omer IA, et al. General population knowledge about osteoarthritis and its related risk factors in Jeddah Saudi Arabia. *Saudi Med J*. 2020; 41:516.
31. Mukharrib MS, Al-Sharif MN, Alshehri TK, Shaker A. Knowledge of knee osteoarthritis among general population in Aseer region. *J Fam Med Prim Care*. 2018; 7:1385–1389.
32. Hill J, Bird H. Patient knowledge and misconceptions of osteoarthritis assessed by a validated self-completed knowledge questionnaire (PKQ-OA). *Rheumatology*. 2006; 46:796–800.
33. Sharma S, Correia H, Pathak A, et al. Translation and cross-cultural adaptation of Nepali versions of the patient-reported outcomes measurement information system (PROMIS®) pain intensity, pain interference, pain behavior, depression, and sleep disturbance short forms in chronic musculoskeletal pain. *Qual Life Res*. 2021;30: 1215–1224.
34. Rabin R, Gudex C, Selai C, Herdman M. From translation to version management: a history and review of methods for the cultural adaptation of the EuroQol five-dimensional questionnaire. *Value Health*. 2014;17:70–76.
35. Faul F, Erdfelder E, Lang A-G, Buchner AG. * Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods*. 2007;39:175–191.
36. Released IC. *IBM SPSS Statistics for Windows*. Armonk, NY: IBM Corp; 2016. Version 24.0.
37. Kamsan SS, Singh DKA, Tan MP, Kumar S. The knowledge and self-management educational needs of older adults with knee osteoarthritis: a qualitative study. *PLoS One*. 2020;15, e0230318.
38. Kendrick DB, Strout TD. The minimum clinically significant difference in Patient-Assigned 11-Point numeric pain scale scores for pain. *Ann Emerg Med*. 2004;44: S86–S87.
39. Farrar JT, Young JPJ, LaMoreaux L, Werth JL, Poole MR. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain*. 2001;94:149–158.
40. Coleman S, Briffa NK, Carroll G, Inderjeeth C, Cook N, McQuade J. A randomised controlled trial of a self-management education program for osteoarthritis of the knee delivered by health care professionals. *Arthritis Res Ther*. 2012;14:R21.
41. Lawford BJ, Hinman RS, Kasza J, et al. Moderators of effects of internet-delivered exercise and pain coping skills training for people with knee osteoarthritis: exploratory analysis of the IMPACT randomized controlled trial. *J Med Internet Res*. 2018;20, e10021.
42. Allen KD, Somers TJ, Campbell LC, et al. Pain coping skills training for African Americans with osteoarthritis: results of a randomized controlled trial. *Pain*. 2019; 160:1297.
43. Taglietti M, Facci LM, Trelha CS, et al. Effectiveness of aquatic exercises compared to patient-education on health status in individuals with knee osteoarthritis: a randomized controlled trial. *Clin Rehabil*. 2018;32:766–776.
44. Focht BC. Move to improve: how knee osteoarthritis patients can use exercise to enhance quality of life. *ACSM's Health & Fit J*. 2012;16:24–28.
45. McLachlan AJ, Carroll PR, Hunter DJ, Wakefield TAN, Stosic R. Osteoarthritis management: does the pharmacist play a role in bridging the gap between what patients actually know and what they ought to know? Insights from a national online survey. *Health Expect*. 2022;25:936–946.
46. Sapkota S, Shrestha A. Community Pharmacy Practice in Nepal-An Underexploited Healthcare Domain. Vol vol. 172019:158-159.
47. Vogler CN, Sattovia S, Salazar LY, Leung TI, Botchway A. Assessing outcomes of educational videos in group visits for patients with chronic pain at an academic primary care clinic. *PGM (Postgrad Med)*. 2017;129:524–530.
48. Shrestha A, Singh SB, Khanal VK, Bhattarai S, Maskey R, Pokharel PK. Health literacy and knowledge of chronic diseases in Nepal. *HLRP: Health Literacy Research and Practice*. 2018;2:e221–e230.
49. Sorensen K, Van den Broucke S, Fullam J, Doyle G, Pelikan J, Slonska Z. i wsp.: health literacy and public health: a systematic review and integration of definitions and models. *BMC Publ Health*. 2012;12:80.
50. Wang ST, Ni GX. Depression in osteoarthritis: current understanding. *Neuropsychiatric Dis Treat*. 2022;18:375–389.
51. Veronese N, Cooper C, Bruyère O, et al. Multimodal multidisciplinary management of patients with moderate to severe pain in knee osteoarthritis: a need to meet patient expectations. *Drugs*. 2022;82:1347–1355.