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Impact of pharmacist-delivered interventions on pain-related outcomes: An umbrella review of systematic reviews and meta-analyses

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ABSTRACT

Introduction: Pain is a significant healthcare challenge, impacting millions worldwide. Pharmacists have increasingly taken on expanded roles in managing pain, particularly in primary and ambulatory care contexts. This umbrella review aims to systematically evaluate evidence from published systematic reviews that explore the impact of pharmacist-delivered interventions on clinical, humanistic, and economic outcomes related to pain.
Methods: A systematic search was conducted across six electronic databases, including Ovid Embase, MEDLINE, CINAHL, Scopus, CENTRAL, APA PsycINFO, and DARE, from inception until June 2023. Prior to inclusion, two independent reviewers assessed study titles and abstracts. Following inclusion, an assessment of the methodological quality of the included studies was conducted. AMSTAR 2 was used to evaluate the methodological quality of the included SRs.
Results: From 2055 retrieved titles, 11 systematic reviews were included, with 5 out of 11 being meta-analyses. These SRs encompassed diverse pharmacist-led interventions such as education, medication reviews, and multi-component strategies targeting various facets of pain management. These findings showed favorable clinical outcomes, including reduced pain intensity, improved medication management, enhanced overall physical and mental well-being, and reduced hospitalization durations. Significant pain intensity reductions were found due to pharmacists' interventions, with standardized mean differences (SMDs) ranging from −0.76 to −0.22 across different studies and subgroups. Physical functioning improvements were observed, with SMDs ranging from −0.38 to 1.03. Positive humanistic outcomes were also reported, such as increased healthcare provider confidence, patient satisfaction, and quality of life (QoL). QoL improvements were reported, with SMDs ranging from 0.29 to 1.03. Three systematic reviews examined pharmacist interventions' impact on pain-related economic outcomes, highlighting varying cost implications and the need for robust research methodologies to capture costs and benefits.
Conclusion: This umbrella review highlights the effectiveness of pharmacist-delivered interventions in improving clinical, humanistic, and economic outcomes related to pain management. Existing evidence emphasises on the need to integrate pharamacists into multi-disciplinary pain management teams. Further research is needed to investigate innovative care models, such as pharmacist-independent prescribing initiatives within collaborative pain management clinics.

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1. Introduction

Acute and chronic pain presents a significant public health concern worldwide, affecting the well-being of millions.[1–3] As the prevalence of pain-related conditions rises, it becomes imperative to identify effective pain management strategies.[4–6] This necessitates a multi-disciplinary approach involving various healthcare professionals, each playing crucial roles in improving patient outcomes.[4,5,7] Among these healthcare professionals involved in pain management, pharmacists have emerged as valuable contributors, offering unique skills and expertise that can optimize pain outcomes.[4,5,7]

Acknowledged as medication experts, pharmacists play a pivotal role in pain management. Through evidence-based interventions and ensuring the safe and effective use of analgesics, they contribute significantly to improving patient care and outcomes.[7–11] Pharmacist roles include patient counseling, medication therapy management and collaborative decision-making with other healthcare professionals.[4,12–14] In addition, they are involved in medication optimization to help minimize adverse effects and enhance patient adherence to pain management plans.[4,12,13]

While numerous original research studies have investigated the role of pharmacists in pain outcomes across various clinical settings,[7,9,15–17] synthesizing the vast array of evidence reported throughout these studies is crucial for gaining comprehensive insights. These studies have evaluated diverse roles and outcomes summarized by several published SRs.[18–22] Therefore, this study adopts an umbrella review approach to systematically identify, evaluate and consolidate the findings from the published SRs in the field. By synthesizing evidence from multiple SRs, both with and without meta-analysis, we aim to provide a comprehensive overview of evidence-based regarding pharmacists' roles in pain management. This study aimed to systematically evaluate published SRs that explore the impact of pharmacist-delivered interventions on clinical, humanistic, and economic pain-related outcomes.

2. Methods

2.1. Study design

The review protocol was registered in International prospective register of systematic reviews (PROSPERO) [registration number CRD42023440803]. This study followed the principles outlined in the Cochrane Handbook for Systematic Reviews of Interventions version 6.4.[23] The Preferred Reporting Items for Overviews of Reviews (PRIOR)[24] were followed throughout this umbrella review's conduct and reporting to ensure transparency and rigor. A PRIOR checklist is available in Supplementary File 1.

2.2. Literature search

A comprehensive search strategy was developed and implemented to identify relevant SRs on the topic existing from inception to June 2023. The following electronic databases were searched: APA PsycINFO, Ovid MEDLINE®, Embase, Cochrane Central Register of Controlled Trials, CINAHL, Scopus and Database of Abstracts of Reviews of Effects (DARE). The search strategy included a combination of controlled vocabulary (e.g., MeSH terms) and keywords related to pharmacists, chronic non-cancer pain, acute pain, cancer pain, pain management and SRs. The search was limited to articles published in English due to resource constraints (lack of resources for hiring translator services). PROSPERO, reference lists of the identified SRs and relevant articles were manually searched to identify any additional studies. The search strategies employed for this umbrella review and the detailed literature search across various electronic databases can be found in supplementary files 2 Appendix S1 and S2, respectively.

2.3. Study selection

Two reviewers (SS and AI) independently screened the identified articles' titles and abstracts to determine their inclusion eligibility utilizing the Covidence™, the systematic review software (Veritas Health Innovation, Melbourne, Australia), to manage the screening process efficiently. Full-text articles of potentially relevant studies were retrieved and independently assessed for inclusion based on predetermined criteria provided below. Any discrepancies between the two reviewers were recorded in Microsoft 365 Excel and resolved through further discussion and consensus.

2.4. Inclusion and exclusion criteria

This study included SRs, with or without meta-analysis, that examined the effects of pharmacist-delivered interventions on pain outcomes. The reviews encompass studies conducted in any healthcare setting, reflecting a broad healthcare context. Additionally, reviews were included evaluating acute or chronic pain management and those assessing pain outcomes in cancer and non-cancer populations. To ensure uniformity in data extraction and synthesis, we focused only on reviews published in English. No restrictions on the publication year of the reviews were imposed to allow for a more comprehensive and up-to-date analysis. Exclusion criteria encompassed reviews that did not focus on pharmacist-delivered interventions, studies lacking pain outcomes assessment, or those unavailable in English.

2.5. Data extraction

Two reviewers (SS and AI) independently searched and extracted the data from the included SRs and subsequently recorded it into a standardized data extraction form.[25] All the eligible studies were exported to Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. The full-text papers were assessed against the inclusion criteria by author SS and AI, and all authors rechecked those identified as relevant. The extracted data was kept in Microsoft 365 Excel and included the following information: author(s), publication year, objectives, study design, types of pain, interventions evaluated, outcomes assessed, population characteristics and key findings. Any discrepancies were resolved through discussion and consensus.

2.6. Quality assessment

The methodological quality of the included SRs was assessed using A MeaSurement Tool to Assess Systematic Reviews (AMSTAR 2).[26] This tool employs a domain-based rating system consisting of seven critical and nine non-critical domains. Originally designed to evaluate SRs involving randomized controlled trials (RCTs), AMSTAR 2 underwent a fundamental revision to improve its effectiveness. Each review received an AMSTAR 2 score categorized as high, moderate, low, or seriously low based on the presence and severity of weaknesses. Discrepancies between the AMSTAR 2 scores for the articles were resolved by discussion between the review investigators. The updated version of the tool, released in 2017, comprises 16 items.[26] Two independent reviewers (VP and SLT) evaluated the methodological quality of the included reviews, with any disagreements resolved through further discussions to reach a mutual consensus. While the reliance on SRs with descriptive analysis may introduce uncertainty regarding the accuracy of findings, efforts were made to mitigate this limitation through rigorous assessment of the methodological quality of included reviews using AMSTAR 2. Discrepancies between AMSTAR 2 scores were resolved through discussion amongst team members to ensure consistency and reliability in the evaluation process.

2.7. Data synthesis and analysis

The findings from the incorporated SRs were synthesized and presented descriptively. The characteristics of the reviews, including SRs with meta-analysis or without meta-analysis, interventions, and outcomes, were summarized. However, due to the heterogeneity and variance of original articles in different SRs, a quantitative analysis (meta-analysis) could not be conducted to estimate the overall effect sizes of pharmacist-delivered interventions on pain outcomes. Although meta-analyses offer quantitative estimates of effect sizes, SRs with descriptive analysis contribute valuable qualitative insights into the breadth and depth of the literature. Additionally, quantitative findings from primary studies included in some SRs were presented where available. These quantitative findings were incorporated into the synthesis to better understand the evidence base and formulate future research and practice recommendations.

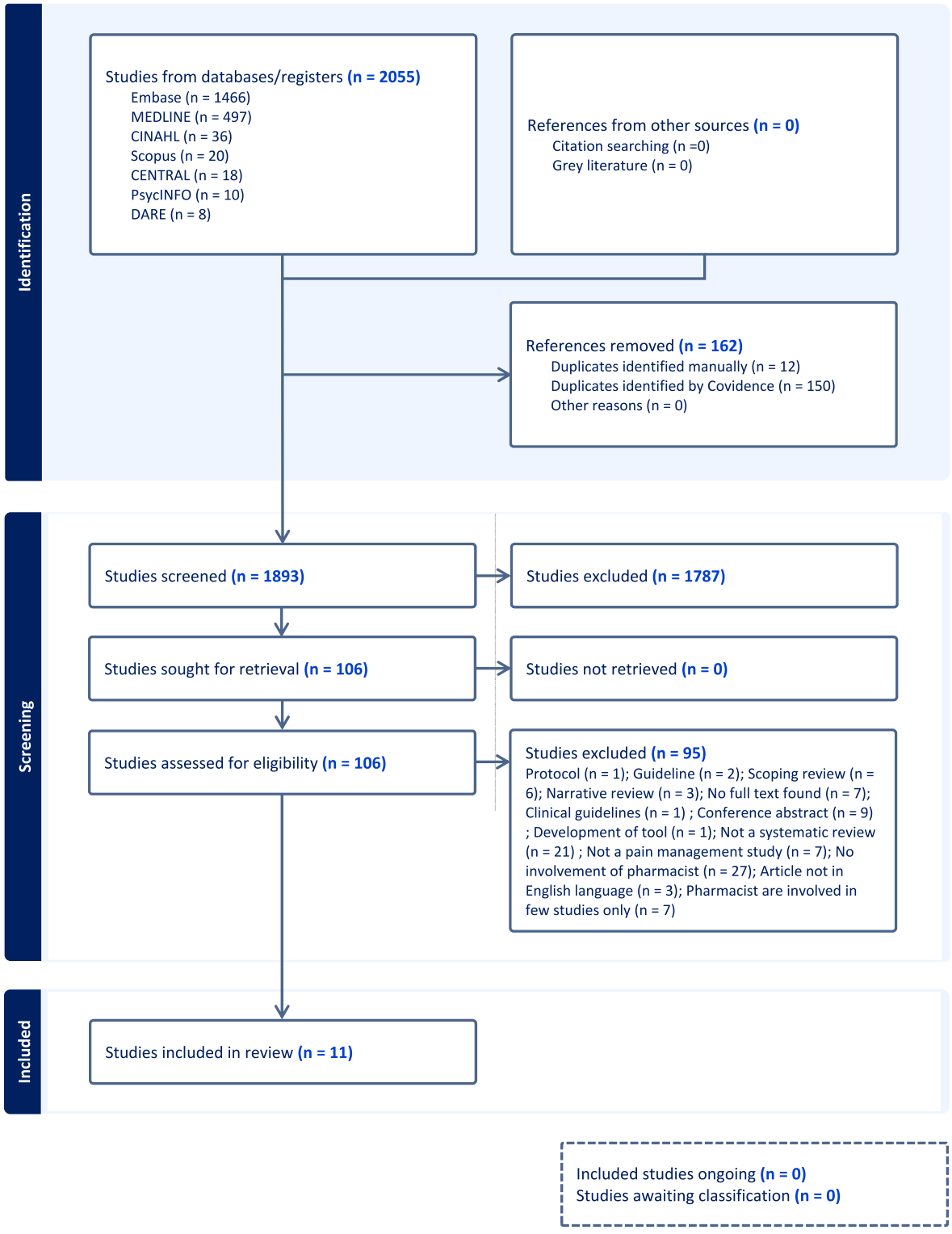

Fig. 1. Flow diagram of the study selection process.

2.8. Ethical considerations

Ethical approval was not required as this study is based on a review of existing published SRs.

2.9. Results

The initial search yielded 2055 results from various electronic databases, search engines and bibliography reviews. After screening and selection, a total of 11 SRs were included. Fig. 1 illustrates a PRISMA diagram showing the results of the entire search, screening, and selection process.

2.10. Characteristics of included systematic reviews

Eleven included SRs were published between 2011 and 2023. These SRs encompassed primary studies published from 1983 to 2020. They had original studies conducted in the USA, Canada, Australia, and other Asian, European, and African countries. Among these eleven SRs, five studies,[20–22,27,28] exclusively focused on RCTs, while the remaining included primary studies of different designs.[18,19,29–32] The eleven reviews comprised 281 primary studies, each including 4 to 64. Table 1 summarizes the study characteristics, including the author(s) list, publication year, objectives, study design, pain types, interventions evaluated, outcomes assessed, population characteristics, and key findings.

The included SR varies in their search periods, with some spanning from inception to specific dates, while others cover limited time frames. Diverse databases such as MEDLINE, EMBASE, CINAHL, and PsycINFO were utilized for literature searches. The comparators range from usual care to specific control groups or interventions. Funding sources for the studies include research grants, scholarships, and institutional support. Notably, the certainty of evidence varies across studies, with some demonstrating moderate certainty for certain outcomes while others exhibit low to very low certainty. The detailed information on the search period, database, comparator, funding, and certainty of evidence are available in Supplementary File 3 Supplementary Table 1. Out of 11 SRs, five SRs included a meta-analysis.[12,19–21,28] Table 2 presents a comprehensive overview of findings from SRs with meta-analyses across several studies examining various outcomes related to pain management interventions. Effect sizes and their corresponding 95% confidence intervals (CIs) are reported by including SRs for each outcome.

2.11. Methodological quality assessment

We identified areas of strength and potential biases within the included SRs. The majority of the included studies (7/11, 63.63%) were determined to be high, and the remaining (4/11, 36.36 %) were determined to be of moderate quality. Based on the AMSTAR 2 criteria, none of the investigations were graded as low quality (Table 3). Six SRs formulated research questions and inclusion criteria with clear population, intervention, comparison, and outcomes (PICO) components.[18,19,21,27,31,32] Four SRs explicitly documented the established methods before conducting the review and provided justifications for any deviations from the protocol.[18,21,30,31] Six SRs explained their criteria for selecting study designs for inclusion.[18,21,27,29,31,32] Regarding literature search strategies, ten SRs used comprehensive approaches,[18–22,27,29–32] while 9 SRs performed study selection in duplicate.[18–22,27,28,30,31] Table 3 presents the quality assessment findings for each SRs.

2.12. Summary of findings

The SRs investigated a range of pharmacist-delivered pain management interventions or pharmacist-involved pain management, targeting acute, chronic cancer and non-cancer pain in diverse healthcare settings. Table 1 summarizes the evaluated interventions and the reported outcomes (clinical, humanistic, and economic) across the included SRs and the types of pain, nature of interventions and associated outcomes described in the subsequent sections.

2.13. Pain type

The findings of the umbrella review encompass a comprehensive analysis of pain-related studies conducted through various SRs. These reviews[18–22,27–32] investigated a wide array of pain types and management strategies. Two SRs focused on cancer pain, contributing to understanding pain management strategies and examining methodologies to alleviate pain and enhance the quality of life (QoL) of individuals with cancer.[18,22] Additionally, Iqbal (2022) examined chronic non-malignant pain, exploring potential interventions and approaches for those experiencing persistent pain unrelated to cancer.[31]

Thapa (2021) covered a broad spectrum of pain types, including musculoskeletal systems such as knee, spine, joint, back pain, headache and migraine,[19] thereby providing a comprehensive overview.[19] Karp (2022) conducted a SR encompassing various non-cancer pain etiologies, such as low back pain, medication-induced headache, migraine, knee osteoarthritis, fibromyalgia, osteoarthritis, slipped disc, compression fracture, headache, tendonitis and[27] chronic pain linked to opioid use.[27] Hadi (2014) investigated multiple pain domains, including knee pain, headache and migraine, contributing valuable understandings into pharmacists' role in managing or helping to manage these specific pain conditions.[28] Veetil (2022) covered pain stemming from musculoskeletal and neurologic systems, cancer-related pain, postoperative pain, and unspecified chronic pain, thus expanding understanding of effective pain management strategies.[21] Alenezi (2021) explored various pain types, including low back pain, neuropathic pain, fibromyalgia, arthritis and multiple forms of chronic pain, suggesting further understanding.[29]

Buckley (2023) shed light on pain management considerations mechanically ventilated critically ill patients, providing crucial insights.[30]

Bennett (2011) focused on chronic pain associated with knee pain, arthritis and cancer, contributing additional strategies for managing specific health conditions.[20] Perrot (2019) collectively examined various pain domains (chronic non-malignant pain, unspecified joint pain, neuropathy, unspecified back pain, chronic pain cancer-related pain and acute pain),[32] offering a broad perspective on pain management approaches.[32]

2.14. Role of the pharmacist and nature of the pharmacist interventions

The results of this umbrella review identified several key interventions made by pharmacists to support pain management. The interventions delivered by the pharmacists are broadly categorized as follows.

2.14.1. Educational interventions

Pharmacists provided educational interventions, including informational booklets, pamphlets and educational videos, to enhance patients' understanding of their pain conditions and treatment options.[18–20,22] Group educational sessions led by pharmacists focused on equipping patients with essential knowledge for self-management and covered disease education, as well as both pharmacologic and non-pharmacologic education.[18] The education also included information, behavioral instructions, or advice about managing chronic pain.[20] Pharmacist-led medication review sessions included patient counseling and consultations to ensure proper medication adherence and compliance.[18] A SR reported that pharmacists provide education to prevent pain medication misuse.[32] The pharmacists also provided appropriate education and training to pharmacy staff and patients.[18,32]

2.15. Medication review and adjustment

Pharmacists played a critical role in medication review and

Table 1
Study characteristics of included studies in umbrella review.

Author (s) Year	Number of primary studies included	Study design of original studies	Countries of original studies	Period of publication of original studies	Total number of patients (Sample size range)	Type of pain	Population	Settings	Pharmacist Intervention	Clinical outcomes studied	Humanistic outcomes studied	Economic outcomes studied
Edwards 2019	4	RCTs (n = 4)	China (n = 3) UK (n = 1)	1983–2015	944 (16–542)	Cancer pain	Cancer patients	Hospital in-patient population and continuing the interventions in the community (n = 3) hospital out-patient population (n = 1)	Educational intervention dosage adjustment non-prescription drug recommendation and supportive counseling a series of educational interventions	Pain intensity Pain relief Number of side effects Pain Interference and severity Pain interference – daily activity, mood, walking ability, normal working, relationships with others, sleep, enjoyment of life Opioid administration Pain assessment before therapy Dose titration before therapy, before slow-release formulation, before dosage increase Opioid – Morphine slow release, Oxycodone SY, Fentanyl patches Pain score – bone, body, visceral, and nerve Gastrointestinal side effects – constipation, nausea, vomiting Psychological problems – delirium, excess sedation, itchy skin, addiction Symptom scales – fatigue, nausea and vomiting, pain, dyspnoea, changes in sleep, appetite loss, constipation, diarrhea Inappropriate conversion – change in drug	Patient feedback – familiarity with clinical pharmacist, how they contributed, satisfaction with outcome, would you request their help in the future Patient satisfaction Patient feedback – familiarity with clinical pharmacist, how they contributed, satisfaction with outcome, would you request their help in the future QoL – Global, physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning QoL score Knowledge Attitude Practice Pain knowledge Analgesic knowledge Total pain-related knowledge	Symptom scale - financial difficulties

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Table 1 (*continued*)

Author (s) Year	Number of primary studies included	Study design of original studies	Countries of original studies	Period of publication of original studies	Total number of patients (Sample size range)	Type of pain	Population	Settings	Pharmacist Intervention	Clinical outcomes studied	Humanistic outcomes studied	Economic outcomes studied
										without reason, incorrect conversion		
Iqbal 2022	14	Exploratory study (n = 2) Prospective cohort study (n = 5) Pilot study (n = 2) Retrospective chart review (n = 2) Exploratory RCT (n = 1) Uncontrolled trial (n = 1) Mixed methods Quasi experimental study (n = 1)	USA, UK and Canada	2005–2020	1237	chronic non-malignant pain	People with pain originating from any origin except cancer pain	outpatient clinical settings, primary care services, community pharmacy settings	Detailed review of medication charts.	Dose of opioid medicines Changes in pain intensity Opioid medicine knowledge Type of analgesic medicine and doses Number of visits for inadequate pain management or referral Adherence to standard treatment guidelines Alteration in the number of prescription medicines Decreased frequency of medication-related problems (MRPs)	- QoL - Patient and physician acceptance and -satisfaction	–
Thapa 2021	14	RCT (n = 6 Retrospective chart reviews (n = 3) before and after studies (n = 2) Retrospective Cohort Study (n = 1) Prospective Cohort Study (n = 1) cross-sectional study (n = 1)	United States (n = 6) United Kingdom (n = 4) Canada (n = 2) Germany (n = 1) Japan (n = 1)	2000–2019	2365 (range 23–410)	Musculoskeletal systems (knee, spine, joint, back), neurological system (headache and migraine) and unspecified chronic pain.	Chronic pain	Various settings, including general practices, hospitals, and specialized settings such as pain clinics and rehabilitation centers	Medication reviews individualized drug therapy, assessed for drug-related problems and untreated symptoms Intervention through educational video	Pain score/ intensity Physical functioning Mental health Anxiety and depression	- QoL - Satisfaction and acceptability of pharmacist intervention	Costs and benefits
Shrestha 2022	64	RCTs (n = 7) NRSIs (n = 5) observational studies (n = 52)	US (n = 21) Japan (n = 13) China (n = 9) Canada (n = 5) Other countries	1983–2020	12684 (18–90)	Cancer pain	Cancer patients with pain	hospital settings (n = 36) clinic, palliative, and outpatient settings (n = 17) home care settings (n =	Medication review Patient education, counseling, consultation Detection and management of ADRs/ side effects Recommendations (e.g., adjustment in dosing and	Adverse drug reaction (ADR) Cancer patients' chemotherapy-related knowledge Pain knowledge Analgesics knowledge Total pain-related knowledge	- QoL - Patient satisfaction - Improvement in the attitude and practice of patients	–

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Table 1 (*continued*)

Author (s) Year	Number of primary studies included	Study design of original studies	Countries of original studies	Period of publication of original studies	Total number of patients (Sample size range)	Type of pain	Population	Settings	Pharmacist Intervention	Clinical outcomes studied	Humanistic outcomes studied	Economic outcomes studied
								4) community pharmacy (n = 1) hospital and community (n = 3) hospital and clinic (n = 2) hospital and home care setting (n = 1)	pharmacotherapy) made by pharmacist to the physician, Pain assessment	Identifying drug-related problems (DRPs) and rectifying them Incidence of ADRs Improvement in medication adherence Acceptance of the recommendations (e.g., adjustment in dosing and pharmacotherapy) made by the pharmacist Decreased pain interference. Pain intensity Pain relief		
Karp 2022	Total studies = 13 Depression studies (n = 7 studies) Pain studies (n = 6)	RCT	Canada (n = 4) USA (n = 1) Germany (n = 1) Australia (n = 1)	1999–2020	935	low back pain, medication-induced headache, migraine and headache, knee osteoarthritis, non-cancer pain of multiple etiologies such as fibromyalgia, low back pain, osteoarthritis, slipped disc, compression fracture, headache, and tendonitis, and chronic pain associated with opioid use	Knee OA Chronic non cancer pain headache migraine	community pharmacy	Medication management with review of participants' medications and medication counseling, and a pharmacist-led collaborative care approach which included the pharmacist, physiotherapist, and patients' primary care physician. The pharmacist coordinated faxing information about the participants' diagnosis and medication recommendations to the participants' PCP in addition to generating referrals for physiotherapy Referral patient education regarding pain medication and alternatives and made care plan recommendations often related to medications and	Pain intensity, Frequency, duration, and location of pain; Pain frequency and duration (number of days with headache and number and severity of headaches)	- Use of analgesics - Self-efficacy - QoL	

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Table 1 (*continued*)

Author (s) Year	Number of primary studies included	Study design of original studies	Countries of original studies	Period of publication of original studies	Total number of patients (Sample size range)	Type of pain	Population	Settings	Pharmacist Intervention	Clinical outcomes studied	Humanistic outcomes studied	Economic outcomes studied
									activity. patient education through a 2-h group pain education class led by a pharmacy student or resident consisting of 2, 20-min videos with time for questions. The videos include education on different types of pain, treatment options (both pharmacologic and non-pharmacologic), and the nature of an opioid contract. Medication therapy management visit which covered pain assessment and treatment history. A care plan was then formulated and shared with the referring provider.			
Hadi 2014	5	RCTs (n = 5)	United Kingdom (n = 2) Canada (n = 1) Germany (n = 1) United States (n = 1)	2000–2012	1144 (74–410)	Multiple (n = 2) Knee pain (n = 2) Headache and migraine (n = 1)	chronic non cancer pain	University pain clinic (n = 1) General practice (n = 2) Community pharmacy (n = 2)	Medication review patient education referred patients to a physiotherapist-guided exercise program Education-related recommendations to patients' primary care physicians	Pain Intensity Physical Functioning Adverse Effects Severity and functional disability related to pain	- QoL	
Veetil 2022	12	RCTs (n = 12)	United States (n = 2), United Kingdom (n = 2), China (n = 2), Canada (n = 1), Germany (n = 1), Bulgaria (n = 1), Malta (n = 1), Australia (n = 1), and Iraq (n = 1)	1983–2020	1710 (range 16–410)	pain originating from the musculoskeletal and neurologic systems, cancer-related pain, postoperative pain, and unspecified chronic pain	individuals with pain of any etiology	community pharmacy setting (n = 4), community clinic (n = 3), tertiary hospitals (n = 3), specialized ambulatory settings such as pain clinics (n = 3)	Pharmacist-led medication review combined with some form of patient education, such as counseling or the use of a leaflet. medication review as part of a multicomponent intervention, pharmacist-patient consultation, telephone interviews, and specialized	Pain Intensity Physical Functioning Adverse Effects	- QoL	Medication adherence

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Table 1 (*continued*)

Author (s) Year	Number of primary studies included	Study design of original studies	Countries of original studies	Period of publication of original studies	Total number of patients (Sample size range)	Type of pain	Population	Settings	Pharmacist Intervention	Clinical outcomes studied	Humanistic outcomes studied	Economic outcomes studied
									prescription delivery services dosage adjustment, nonprescription drug recommendation, and supportive counseling through face-to-face interactions followed by telephone counseling a series of educational interventions through informational booklets, pamphlets, and telephone calls educational sessions as a group run by pharmacists. These sessions covered disease education, nonpharmacologic and pharmacologic education. 3-month lifestyle modification program run by a clinical pharmacist pharmaceutical care plan, discharge education, and dosing schedule for patients after surgery			
Alenezi 2020	21	RCTs (n = 3), prospective cohort design (n = 9) retrospective cohort (n = 7) cross sectional (n = 1) per-post interventional without control art (n = 1)	USA (n = 18) Denmark (n = 1) Germany (n = 1) Netherlands (n = 1)	2003–2018	6011 (32–1487_	Low back pain, neuropathic pain. Back pain, mixed aetiologies, chronic headache. chronic pain. Back pain, Fibromyalgia Joint Diseases. Back pain Arthritis, skeletal muscle disease. Back or neck pain. Lower back and legs Upper back	Chronic non cancer pain	outpatient's pain clinics (n = 7) primary care settings (n = 6) pain center (n = 4) primary care and pain clinics (n = 2) primary care and an internet site (n = 1)	Single component interventions 1. Opioid treatment contract (OTC) with or without urine drug screening (UDS) 2. Behavioral interventions: Cognitive, emotional 3. Educational interventions: specific medication education on patients' adherence to their medication using a brief video	Medicine optimization Appropriate use of pain medication Inappropriate use of pain medication Self-discharge from chronic opioid treatment Provider confidence in managing CNMP (Chronic Non-Malignant Pain) patients Compliance with universal precautions	- Pain intensity or functional improvement - Depression and anxiety - QoL - Patient satisfaction - Provider satisfaction	Reduction in utilization of healthcare services Healthcare costs

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Table 1 (*continued*)

Author (s) Year	Number of primary studies included	Study design of original studies	Countries of original studies	Period of publication of original studies	Total number of patients (Sample size range)	Type of pain	Population	Settings	Pharmacist Intervention	Clinical outcomes studied	Humanistic outcomes studied	Economic outcomes studied
						and arms low back, neuropathic, or viscera back pain, fibromyalgia, arthritis, Low back pain. Neck, back, Shoulder and knee pain, peripheral neuropathy : Neck, back, Shoulder pain, neuropathy			and w itten instruction about the medication name, dosage, and frequency Multi-component interventions 1. Urine drug screening and opioid treatment contract within multi-component intervention 2. Monthly clinical/ pain assessment 3. Risk assessment 4. Prescription monitoring program (PMP) 5. Opioid dose adjustments: Average daily Morphine Equivalent Daily Dose (MEDD) adjustment as an intervention to optimize medication use 6. Prescribing/ dispensing small quantities/pill count 7. Team-based approach 8. Patient education within a multi-component intervention: printed educational material 26 and group sessions 11. 9. Provider education within a multi-component intervention: pain management education and monitoring techniques.	Adherence to clinical guidelines		

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Table 1 (*continued*)

Author (s) Year	Number of primary studies included	Study design of original studies	Countries of original studies	Period of publication of original studies	Total number of patients (Sample size range)	Type of pain	Population	Settings	Pharmacist Intervention	Clinical outcomes studied	Humanistic outcomes studied	Economic outcomes studied
									10. Behavioral interventions within a multi-component intervention: structured motivational and cognitive behavioral training program to prevent substance misuse 11. Psychiatric consultation as support for patients at high risk of misuse, abuse and addiction, assessment of patient risk, stability and the presence of contraindications of using an opioid/BZD combination to treat CNMP 12. Electronic diaries			
Buckley 2023	9	Retrospective, before-after design (n = 6) Not specified (n = 3)		2008–2020	3769 (60–2151)	Mechanically ventilated critically ill patients.	mechanically ventilated critically ill patients.	ICU	Continuous infusion sedation dosing requirements and/or duration, medication reconciliation, protocol development and implementation, medication dose adjustment, and patient education.	Mechanical ventilation duration In-hospital mortality ICU length of stay Overall hospital stay	- Quantity of analgesia (pain medication) - Opioid continuous infusion dosing requirement	Estimated hospital cost saving Drug expenditures
Bennett 2011	4	RCT (n = 4)	USA (n = 2) UK (n = 1) Bulgaria (n = 1)	1983–2009	400 (range 20–216)	Chronic pain associated with knee pain, arthritis, cancer	chronic pain associated with knee pain, arthritis, cancer and various types of pain	Pain Clinic, Community Settings	Educational intervention as information, behavioral instructions, or advice in relation to the management of chronic pain Medication Review supply service (which included same day delivery of prescriptions by	Intensity and interference from pain on daily activities Resolution or reduced risk of side effects or drug interactions	- Self-efficacy and adherence to medication - Knowledge and attitudes toward pain and analgesics - Mood - Patient satisfaction	–

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Table 1 (*continued*)

Author (s) Year	Number of primary studies included	Study design of original studies	Countries of original studies	Period of publication of original studies	Total number of patients (Sample size range)	Type of pain	Population	Settings	Pharmacist Intervention	Clinical outcomes studied	Humanistic outcomes studied	Economic outcomes studied
									courier) to remove barriers to accessing medications.T elephone monitoring by a palliative trained pharmacist who assessed and advised on potential DRPs and monitored patient outcomes and QoL. Pain assessment, medication advice and review, and adjustment according to patient preference			
Perrot 2019	20	RCTs, Surveys	More than 50 countries, with specific national surveys in United Kingdom, Germany, France, India, Brazil, Australia, the Netherlands, Croatia, Slovenia, Iran, Belgium and Columbia.	2009–2018	NA	Chronic nonmalignant painU nspecified joint painN europathyU nspecified Back painC hronic pain (including some patients with cancer related pain) Acute pain	Patients with pain	Various setting.	Reviewing prescriptions or providing education to prevent misuse Playing a primary and crucial role in improving benefits of pain management and reducing misuse-associated risks Providing appropriate education and training to pharmacy staff Encouraging and developing pharmacist-led medication as an important "chain link" in pain management Offering interventions for consumers about prescribed and over-the-counter medications	pain intensity, physical functioning	- Risks associated with self-medication in pain management - Outcome expectations of OTC pain medications and behavioral capabilities - Chronic pain health literacy in students - Patient Satisfaction - Drivers of self-medication in pain management	

Table 2
Summary of Findings from SRs with meta-analysis.

Authors	Outcomes/subgroup	No. of studies	No. of participants	Statistical method	Effect size (95% CI)
Bennett 2011	**Pain Intensity at 3 months or less**				
	BPI (Average)	3	335	(IV, Fixed, 95% CI)	MD -0.49 [-0.79, −0.20] $I^2 = 0\%$ ($P = 0.001$)
	BPI (Worst)	2	127	(IV, Fixed, 95% CI)	MD -011 [-0.40, 0.18] $I^2 = 0\%$ ($P = 0.45$)
	BPI (Current)	2	127	(IV, Fixed, 95% CI)	MD -0.03 [-0.21, 0.16] $I^2 = 74\%$ ($P = 0.79$)
	Western Ontario and McMaster Universities Arthritis Index (WOMAC pain scores)	1	187	(IV, Fixed, 95% CI)	MD -1.50 [-2.60, −0.40] ($P = 0.008$)
	Visual Analogue Scale	1	16	(IV, Fixed, 95% CI)	1.07 (−0.00, 2.14] ($P = 0.005$)
	Satisfaction with Services Questionnaire	1	86	(IV, Fixed, 95% CI)	0.71 [0.27, 1.15] ($P = 0.001$)
	Treatment Helpfulness Questionnaire	1	41	(IV, Fixed, 95% CI)	0.16 [-0.46, 0.77] ($P = 0.62$)
	Total			(IV, Fixed, 95% CI)	0.58 (0.24, 0.92] $I^2 = 32.8\%$ (P = 0.23)
	Overall satisfaction with treatment	1	184	Risk ration M − H, Fixed 95% CI	1.43 [1.10, 1.86]
	Treatment reduces pain	1	186	Risk ration M − H, Fixed 95% CI	1.53 [1.05, 2.24]
	Return to usual activity	1	183	Risk ration M − H, Fixed 95% CI	1.72 [1.09, 2.72]
	Practical advice	1	184	Risk ration M − H, Fixed 95% CI	1.41 [1.12, 1.78]
Hadi 2014	Pain intensity at 3-month	3	367	(IV, Fixed, 95% CI)	SMD –0.37 [-0.58, −0.16]
	Pain intensity at 6 -month	2	330	(IV, Fixed, 95% CI)	SMD –0.31 [–0.53, −0.09]
	Physical Functioning at 3-month	3	366	(IV, Fixed, 95% CI)	SMD –0.38 [–0.58, −0.18]
	Physical functioning at 6-month	2	325	(IV, Fixed, 95% CI)	SMD –0.30 [–0.51, −0.09]
	Patient satisfaction	2	225	(IV, Fixed, 95% CI)	SMD –0.39 [–0.68, −0.10]
Thapa 2021	Pain intensity (overall)	5	876	(IV, random, 95% CI)	SMD -0.22 [-0.35, −0.09]
	Subgroup: By duration of intervention				
	Three months	1	41	(IV, random, 95% CI)	SMD -0.44 [-0.16, 0.19]
	More than three months	4	835	(IV, random, 95% CI)	SMD -0.21 [-0.35, −0.07]
	Subgroup: By pain etiology				
	Musculoskeletal pain	2	332	(IV, random, 95% CI)	SMD -0.32 [-0.59, −0.04]
	Neurological pain	1	357	(IV, random, 95% CI)	SMD -0.15 [-0.35, 0.06]
	Chronic pain (unspecified)	2	187	(IV, random, 95% CI)	SMD -0.21 [-0.15, 0.09]
	Subgroup: Intervention Types				
	Medication review	2	332	(IV, random, 95% CI)	SMD -0.32 [-0.59, −0.04]
	Pharmaceutical care with medication review	3	544	(IV, random, 95% CI)	SMD -0.17 [-0.34, 0.00]
	Physical functioning (overall)	5	851	(IV, random, 95% CI)	SMD -0.16 [-0.38, 0.06]
	Subgroup: Intervention duration				
	Three months	1	41	(IV, random, 95% CI)	SMD -0.50 [-1.12, 0.13]
	More than three months	4	810	(IV, random, 95% CI)	SMD -0.13 [-0.36, 0.10]
	Subgroup: Pain etiology				
	Musculoskeletal pain	2	327	(IV, random, 95% CI)	SMD -0.27 [-0.62, 0.08]
	Neurological pain	1	354	(IV, random, 95% CI)	SMD -0.14 [-0.35, 0.07]
	Chronic pain (unspecified)	2	170	(IV, random, 95% CI)	SMD -0.09 [-0.79, 0.61]
	Subgroup: Intervention types				
	Medication review	2	327	(IV, random, 95% CI)	SMD -0.27 [-0.62, 0.08]
	Pharmaceutical care with medication review	3	524	(IV, random, 95% CI)	SMD -0.08 [-0.41, 0.24]
Veetil 2022	**Pain Intensity**	12		(IV, random, 95% CI)	SMD - 0.22 [-0.31 to −0.12]
	Subgroup: Type of pain				
	Chronic pain	10	1253	(IV, random, 95% CI)	−0.26 (−0.37 to −0.14)
	Acute pain	2	457	(IV, random, 95% CI)	−0.14 (−0.40 to 0.12)
	Subgroup: Pain etiology				
	Cancer-related pain	3	402	(IV, random, 95% CI)	−0.37 (−0.57 to −0.17)
	Musculoskeletal pain	4	578	(IV, random, 95% CI)	−0.14 (−0.30 to 0.03)
	Subgroup: Setting				
	Community pharmacy	4	754	(IV, random, 95% CI)	−0.08 (−0.22 to 0.07)
	Community clinic	4	324	(IV, random, 95% CI)	−0.30 (−0.52 to −0.08)
	Hospital	3	486	(IV, random, 95% CI)	−0.36 (−0.53 to −0.18)
	Subgroup: Income country level				
	High-income countries	9	1224	(IV, random, 95% CI)	−0.15 (−0.27 to −0.04)
	Low- and middle-income countries	3	486	(IV, random, 95% CI)	−0.37 (−0.55 to −0.20)
Shrestha 2022	Pain Intensity (RCTs)	3	402	(IV[a], Random, 95% CI)	SMD -0.35 [-0.55, −0.16] $I^2 = 0\%$, $P = 0.0005$
	Pain Intensity (NRSIs)	3	297	(IV[a], Random, 95% CI)	SMD -0.55 [-1.33, 0.23] $I^2 = 91\%$, $p < 0.0001$
	Pain Intensity (NRSIs)	2	199	(IV[a], Random, 95% CI)	SMD -0.76 [-1.90, 0.38] $I^2 = 93\%$, $p = 0.0001$
	Pain Intensity (NRSIs)	2	214	(IV[a], Random, 95% CI)	SMD -0.74 [-1.91, 0.44] $I^2 = 94\%$, $P < 0.0001$

(*continued on next page*)

Table 2 (*continued*)

Authors	Outcomes/subgroup	No. of studies	No. of participants	Statistical method	Effect size (95% CI)
	Pain Intensity (NRSIs)	2	183	(IV[a], Random, 95% CI)	SMD -0.15 [-0.45, 0.14] $I^2 = 0\%$, $P = 0.90$
	Pain Relief (RCT)	1	16	(IV[b], random, 95% CI)	MD 3.14 [0.31, 5.97]
	Number of Side Effects (RCT)	1	16	(IV[b], random, 95% CI)	MD -3.63 [-5.73, −1.53]
	ADRs (NRSIs)	2	3936	(M − H, Random, 95% CI)	OR 0.69 [0.61, 0.79] $I^2 = 0\%$, $P < 0.0001$
	Constipation	2	656	(M − H, Random, 95% CI)	OR 0.68 [0.50, 0.93]
	Nausea	2	656	(M − H, Random, 95% CI)	OR 0.62 [0.41, 0.92]
	Vomiting	2	656	(M − H, Random, 95% CI)	OR 0.63 [0.41, 0.96]
	Pruritis (Skin Itching)	2	656	(M − H, Random, 95% CI)	OR 1.05 [0.65, 1.71]
	QoL (RCT)	1	149	(IV[b], Random, 95% CI)	MD 8.38 [2.33, 14.43] I^2=NA, $P = 0.007$ (Overall effect)
	QoL (NRSIs)	2	628	(IV[a], Random, 95% CI)	SMD 0.80 [0.29, 1.32] $I^2 = 80\%$, $P = 0.03$
	QoL (NRSIs)	1	542	(IV[a], Random, 95% CI)	SMD 1.03 [0.85, 1.21] I^2=NA, $P < 0.00001$ (Overall effect)
	QoL (NRSIs)	1	86	(IV[a], Random, 95% CI)	SMD 0.50 [0.07, 0.93] I^2=NA, $P = 0.02$ (Overall effect)
	Patient Satisfaction (NRSIs)	2	621	(IV[a], random, 95% CI)	SMD 2.70 [-1.22, 6.63] $I^2 = 100\%$, $P = 0.18$
	Patient Satisfaction (NRSIs)	1	531	(IV[a], random, 95% CI)	SMD 4.70 [4.37, 5.03] I^2=NA, $P < 0.00001$
	Patient Satisfaction (NRSIs)	1	90	(IV, random, 95% CI)	SMD 0.70 [0.27, 1.13] I^2=NA, $P = 0.001$

SMD: Standardized mean difference; MD: Mean difference; OR: Odds Ratio; CI: Confidence intervals; IV[a]: weighted standard mean difference; IV[b]: weighted standard mean difference; M-H: Mantel Haenszel; I^2: Heterogeneity; NA: Not available as only study is included; p: p-value RCT: Randomized Control Trial, NRSIs: non-randomized studies of interventions; BPI: Brief Pain Inventory; ADRs: Adverse drug reactions

adjustment throughout the studies examined. Pharmacists conducted thorough medication chart reviews,[18–20,31] assessing for drug-related problems and untreated symptoms. Additionally, pharmacist evaluated and checked to prevent misuse of opioids.[32] Dosage adjustments[18–20,22] and recommendations for non-prescription drugs[22] were made to optimize pain management effectiveness and minimize adverse effects. Furthermore, pharmacists performed medication reconciliation to ensure the safe and appropriate use of medications, while considering potential drug interactions.[18]

2.15.1. Multi-component interventions

The SRs included in the analysis highlighted the collaborative efforts of pharmacists with other healthcare professionals, such as physiotherapists and primary care physicians, in developing comprehensive care plans and coordinating patient management.[18,19,29] These collaborations involved implementing activities such as urine drug screening, opioid treatment contracts, and risk assessments to prevent substance misuse and ensure safe opioid therapy.[29] Additionally, prescription monitoring programs and opioid dose adjustments were utilized to optimize medication use and enhance patient safety.[18,29,31] Structured motivational and cognitive behavioral training programs addressed behavioral aspects related to pain management and substance misuse.[29]

2.15.2. Pain assessment and supportive counseling

Pharmacists also conducted pain assessments to gain a better understanding patients' pain experiences[18,20] and tailor treatment plans accordingly.[19] Supportive counseling was provided to address various patients' concerns[22] and provide emotional support throughout their pain management journey.

2.15.3. Other interventions delivered by the pharmacist

Pharmacists played a crucial role in providing supply service, including same-day delivery of prescriptions by courier, to remove barriers to accessing medications.[20] Pharmacists were also reported to be vital in improving pain management benefits while simultaneously reducing misuse-associated risks.[32]

2.16. Outcomes

The outcomes were categorized into three main types: clinical, humanistic, and economic outcomes.

3. Clinical outcomes

3.1. Pain intensity and pain relief

Several SRs[18–22,27,28,31] focused on pain intensity and the degree of pain relief achieved via different interventions by the pharmacist or the involvement of the pharmacist. Pain intensity was commonly measured using standardized pain scales, allowing authors to gauge the effectiveness of treatments in reducing pain perception. Pain intensity was shown to decrease with the pharmacist's involvement.[18–20,22] The results of the meta-analysis of various SRs indicated significant reductions in pain intensity, with standardized mean differences (SMDs) ranging from −0.76 to −0.22 across different studies and subgroups (Table 2). Bennett (2011) examines pain intensity at three months or less, employing measures such as the Brief Pain Inventory (BPI) and the Western Ontario and McMaster Universities Arthritis Index, demonstrating significant reductions in pain intensity across different scales.[20] The BPI (Average) showed a moderate effect size (mean differences (MD): −0.49, 95% CI [−0.79, −0.20]), while the BPI (Worst) displayed a negligible effect size (MD = −0.11, 95% CI [−0.40, 0.18]). BPI (Current) didn't show a significant effect size (MD = −0.03, 95% CI [−0.21, 0.16]). The WOMAC pain scores indicated a substantial effect size (MD = −1.50, 95% CI [−2.60, −0.40]) in one study with 187 participants. The Visual Analogue Scale showed a significant effect size (MD = 1.07, 95% CI [−0.00, 2.14]). Hadi (2014) investigated pain intensity at three and six months, indicating consistent improvements in pain management over time.[28] Pain intensity at the three-months showed a SMD of −0.37 (95% CI [−0.58, −0.16]) and at six months, showed a SMD of −0.31 (95% CI [−0.53, −0.09]). Thapa (2021) explores pain intensity, categorizing it by duration of intervention, pain etiology, and intervention types, showing the effectiveness of different approaches.[19]

Table 3
Methodological quality assessment of included studies using AMSTAR 2.

Author(s)	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Item 15	Item 16	Total Score (Overall Rating)
Edwards 2019	1	1	1	0	0	1	1	0	0	1	0	0	0	0	1	1	8 (High)
Iqbal 2022	0	0	0	0	0	0	1	0	0	1	1	1	0	1	1	1	9 (High)
Thapa 2021	0	1	1	0	0	0	0	0	0	1	0	0	1	0	1	0	11 (High)
Shrestha 2022	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	12 (High)
Karp 2022	0	1	0	0	0	0	0	0	0	1	1	1	0	0	1	1	10 (High)
Hadi 2014	1	1	1	1	0	0	1	1	0	1	0	1	1	0	1	1	5 (Moderate)
Veetil 2022	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	16 (High)
Alenezi 2020	1	1	0	0	1	0	0	0	0	1	1	1	1	1	1	1	6 (Moderate)
Buckley 2023	1	0	1	0	0	0	0	0	0	1	0	0	0	0	0	1	12 (High)
Bennett 2011	1	1	1	0	0	0	1	0	0	1	0	1	1	0	1	1	7 (Moderate)
Perrot 2019	0	1	0	0	1	1	1	0	1	1	1	1	1	0	1	0	7 (Moderate)

AMSTAR 2 employs sixteen criteria to evaluate the methodological quality of systematic reviews, focusing on aspects such as review design validity, literature screening, data extraction, and assessment of individual study quality. Within these criteria, seven were designated as "critical domains" which have significant implications for the review's validity (e.g., items 2, 4, 7, 9, 11, 13, and 15). For a meta-analysis to be deemed of high quality, it must satisfy all "critical domains" in addition to meeting at least eight other criteria. Meta-analyses fulfilling all "critical domains" were categorized as medium quality. Conversely, those with one unsatisfied critical domain were classified as low quality, while meta-analyses with multiple unsatisfied critical domains were deemed to be of critically low quality. The specific criteria are outlined as follows.
Item 1: Did the research questions and inclusion criteria for the review include the components of PICO?
Item 2: Did the report of the review contain an explicit statement that the review methods were established prior to conduct of the review and did the report justify any significant deviations from the protocol?
Item 3: Did the review authors explain their selection of the study designs for inclusion in the review?
Item 4: Did the review authors use a comprehensive literature search strategy?
Item 5: Did the review authors perform study selection in duplicate?
Item 6: Did the review authors perform data extraction in duplicate?
Item 7: Did the review authors provide a list of excluded studies and justify the exclusions?
Item 8: Did the review authors describe the included studies in adequate detail?
Item 9: Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
Item 10: Did the review authors report on the sources of funding for the studies included in the review?
Item 11: If meta-analysis was justified, did the review authors use appropriate methods for statistical combination of results?
Item 12: If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
Item 13: Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?
Item 14: Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
Item 15: If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias (small-study bias) and discuss its likely impact on the results of the review?
Item 16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

Thapa (2021) found an overall SMD of −0.22 (95% CI [−0.35, −0.09]), indicating reduced pain intensity. Among interventions, one lasting three months showed an SMD of −0.44 (95% CI [−0.16, 0.19]), while those exceeding three months exhibited an SMD of −0.21 (95% CI [−0.35, −0.07]). Veetil (2022) explored pain intensity across chronic and acute pain, diverse settings, and income country levels.[21] The overall pain intensity indicated a SMD of −0.22 (95% CI [−0.31 to −0.12]). Shrestha (2022) comprehensively examines pain intensity across various interventions and pain relief mechanisms.[18] In Shrestha's 2022 study, focusing on pain intensity, SMD was −0.35 (95% CI [−0.55, −0.16]). SRs have highlighted the potential of pharmacist-led educational interventions in reducing pain intensity for individuals experiencing both cancer-related pain[18,22] and non-cancer pain.[20] Other SRs have highlighted the potential of pharmacist-delivered medication review in reducing pain intensity.[18,19,28]

3.2. Medication management and adherence

The SRs conducted by Iqbal (2022)[31] and Alenezi (2021)[29] examined various facets of medication optimization, including the appropriate use of pain medication and patient adherence to prescribed regimens. Additionally, Buckley (2023) assessed the quantity of analgesia (pain medication) and the dosing requirement for continuous opioid infusion.[30]

3.3. Adverse drug reactions and drug-related problems

Shrestha (2022)[18] explored into the pharmacist's role in addressing adverse drug reactions (ADRs) associated with pain medications, highlighting the importance of identifying and mitigating potential drug-related problems (DRPs) in pain management. The SR encompassed three studies, including one RCT and two nonrandomized studies of interventions (NRSIs), which specifically examined pharmacist interventions for cancer patients with pain.

The RCT reported a notable reduction in ADRs (MD: 3.63; 95% CI: 5.73 to −1.53). When combining the findings of the NRSIs, it was shown that pharmacist interventions significantly decreased ADRs (OR: 0.69; 95% CI: 0.61–0.79) with low heterogeneity.[18] Shrestha (2022)'s review highlighted pharmacists' involvement in identifying drug-related problems and implementing necessary rectifications within pain management contexts.[18]

3.3.1. Physical functioning and mental health

Thapa (2021)[19] and Hadi (2014)[28] investigated the impact of pain on the physical functioning and mental health of patients experiencing chronic pain, thus emphasizing the need to address pain's broader impact on overall well-being.

In a study conducted by Hadi (2014), a meta-analysis demonstrated a notable enhancement in physical functioning among the intervention group compared to the control group during the 6-month follow-up with SMD: 0.30 (95% CI, −0.51 to - 0.09) corresponding to −3.82 points (95% CI, −6.49 to −1.14) on function subscale.[28] However, in a SR by Thapa (2021), pharmacist-led interventions had a mixed impact on physical functioning. Pooled estimates indicated a minimal effect (SMD: 0.16; 95% CI: 0.38 to 0.06), with moderate variability among studies (I^2 = 54%).[19] In these two studies,[19,28] pharmacists were primarily involved in medication review and pain education to improve physical functioning. SRs have found that pharmacist-led intervention had minimal effect on the mental health of patients with chronic pain[19]

3.4. Healthcare provider confidence

Alenezi (2021)[29] assessed healthcare providers' confidence in managing patients with chronic non-malignant pain, underscoring the significance of a well-informed and confident healthcare team for effective pain management. A team-based approach was led by one or multiple providers where pharmacists were also involved and helped support managing opioids in complex chronic pain patients.[29]

3.5. Healthcare utilization and length of stay

Buckley (2023)[30] explored the impact of critical care pharmacist-led interventions on pain, agitation and delirium on healthcare utilization, including duration of mechanical ventilation, in-hospital mortality, length of stay in the intensive care unit and the overall hospital stay. The types of pharmacist-delivered intervention strategies were inconsistent among the nine included SRs, such as recommending interventions [to physicians or nurses on the sedation plan during or after clinical rounds, pain management and sedative dose adjustments based on patient-specific parameters (organ function, duration of sedation and laboratory values)] as well as providing education.

4. Humanistic outcomes

4.1. Quality of life

Humanistic outcomes, including estimation of the QoL, were reported in nine SRs.[18,19,21,22,27–31] It was reported that the QoL of patients suffering from cancer pain was improved by pharmacists providing patient education or by conducting various combinations of interventions, including medication review, patient education, physician recommendation and pain assessment.[18,22] Thapa (2021) reported that pharmacist-led intervention had a mixed impact on the QoL of patients with chronic pain.[19] Shrestha (2022) examined pharmacist involvement's impact on cancer patients' QoL where one RCTs and 2 NRSIs. The RCT reported a significant MD of 8.38 (95% CI: 2.33, 14.43), and the pooled analysis from the 2 NRSIs showed a significant improvement, with SMD of 0.80 (95% CI: 0.29, 1.32).[18]

4.2. Perspectives of patients and physicians

Patient satisfaction either with pharmacist interventions or their pharmacy services, was reported in seven SRs[18–20,22,28,29,31,32] where overall, patients were generally satisfied. Physicians' satisfaction and acceptability of pharmacist intervention were reported.[19] Shrestha (2022) reported an increase in the chemotherapy knowledge score of cancer patients following a pharmacist's intervention.[18] The intervention included providing comprehensive pharmaceutical care, preparing a booklet which included information such as the purpose of chemotherapy, chemotherapy preparation and assessment, prevention and management of ADRs, and caution when using oral chemotherapy. In another SRs, Buckley (2023) assessed the quantity of analgesia and the requirement of a continuous infusion of opioids.[30] The pharmacist-delivered intervention group was associated with significant reductions in the use of opioid analgesia and had a greater than 50% reduction in continuous infusion requirements of opioid dose.

4.3. Patients' knowledge of pain and its management

Shrestha (2022)[18] and Iqbal (2022)[31] investigated patients' and healthcare providers' knowledge regarding pain, analgesics and opioids, highlighting the importance of education in promoting effective pain management strategies. Additionally, pharmacist involvement has been shown to enhance cancer patients' chemotherapy-related knowledge, pain and pain-related knowledge, and analgesics knowledge.[18] Improvements in patient knowledge about buprenorphine were reported, including increased awareness of its use for detox and/or opioid use disorder treatment.[31] In the SR by Bennett (2011), only one study was included in the analysis, which measured medication adherence, leading to the inability to draw reliable conclusions.[20]

Although researchers further assessed patients' knowledge and attitudes towards their pain and analgesics' use, none of the studies reported in the SR measured their effects on patient's knowledge or attitudes.[20] On the other hand, Perrot (2019) conducted a SR assessing the risks associated with self-medication and the potential drivers of self-medication in pain management.[32] This review also examined chronic pain health literacy among students suffering from pain, revealing that a short educational movie on recurrent and chronic pain could increase chronic pain health literacy.[32]

4.4. Financial difficulties of the patients

In another SR by Edwards (2019),[22] financial difficulties of cancer patients were studied, the specific impact of the pharmacist in assessing the financial difficulties of cancer patients was not specified. Further investigation of the study[33] included in SR revealed no significant changes within or between groups for financial difficulties ($p > 0.05$).

4.5. Economic outcomes

No SR solely focused on evaluating economic evaluations in this research area. However, three SRs captured the economic outcomes as secondary or other outcomes.[19,29,30] One review[29] addressed interventions to optimize prescribed medicines and reduce their misuse in chronic non-malignant pain. Out of 21 included studies in SR, only two studies[34,35] reported that pharmacist intervention in optimizing medicine helps reduce healthcare costs, especially by saving pharmacy costs. The second SR, which evaluated nine studies about the impact of critical care pharmacist-led interventions on pain, agitation, and delirium in mechanically ventilated adults, reported that two included studies reported mixed information about the cost savings associated with the pharmacist intervention.[30] One study[36] included in this SR reported substantial annual savings of $7.2 million, with a significant portion attributed to drug expenditures, whereas another study failed to show a significant impact on total hospital stay costs.[37] However, the authors of

the SR advised caution in interpreting these financial estimates. The report lacked detailed information on specific cost estimates, financial assumptions, and the economic analytical approaches used in constructing their cost-savings model. This absence of comprehensive information raises valid concerns about the reliability of the published estimates, opening the possibility for debates on their validity. Yet, another included study centered on pharmacist-driven dexmedetomidine stewardship did not reveal a notable impact on total hospital stay costs.[37] The third SR[19] analyzing the impact of pharmacist-led intervention on chronic pain management included one study that evaluated cost and benefit. Although the SR did not report these outcomes in detail, we further researched the included study in this review.[38] This study utilized data from a pilot RCT to investigate the differences in mean costs and effects from the UK National Health Service perspective associated with pharmacist-led management of chronic pain in primary care.[38] It involved 125 patients across six practices, comparing three interventions: pharmacist medication review with face-to-face prescribing, pharmacist review with feedback to the general practitioner, and treatment as usual (TAU). Unadjusted mean costs per patient were £452 for prescribing, £570 for review, and £668 for TAU. Adjusted differences relative to TAU were £77 for prescribing and £54 for review. Quality-adjusted life years (QALYs) were similar to TAU. The authors concluded that pharmacist-led interventions for chronic pain were costlier but provided similar QALYs to TAU, urging larger trials for refined estimates.

5. Discussion

The included SRs collectively demonstrated a wide range of pharmacist-delivered interventions targeting pain management.[18–22,27–32] These interventions encompassed various aspects of patient care, including medication therapy management,[18–20,22,31] patient education,[18–20,22] collaborative decision-making with other healthcare professionals[18,19] and counseling on pain management strategies. Consistently, the SRs reported improved pain relief, reduced pain intensity,[18–22,27,28,31] improved QoL,[18,19,21,22,27–31] enhanced medication adherence[29,31] and increased patient satisfaction[13] indicating the value of pharmacist-delivered interventions. Moreover, the SRs highlighted the benefits of interdisciplinary teamwork, emphasizing the importance of pharmacists' involvement in collaborative care models.[18,19] Collaborative efforts enable comprehensive pain management strategies, combining pharmacological and non-pharmacological approaches to address the complex nature of pain.

However, our review also identified several significant gaps and challenges in existing literature. Firstly, the quality of the included SRs varied, indicating discrepancies in the design and execution. Secondly, differences in methods and measures employed across studies made comparing results challenging. Third, the lack of a consistent and universally accepted definition of a pharmacist-delivered intervention hindered the comprehensive assessment of their overall impact. These gaps underscore the need for further research to validate the effectiveness of pharmacist-delivered interventions and address the methodological limitations uncovered in this study. Variations in the specific populations, settings and types of pain addressed across the included SRs emphasize the critical nature of the umbrella review. By providing a consolidated and comprehensive perspective on this diverse field, this study aims to guide future research and practice in pharmacist-led pain management initiatives. This study also highlights the need for further research to explore the effectiveness of pharmacist-delivered interventions for specific pain conditions and patient populations. While this umbrella review encompassed a wide range of studies, future studies should focus on quantifying the combined effect sizes and assessing the detailed impacts of pharmacist-delivered interventions within specific pain conditions and amongst distinct patient populations. Another notable gap is the limited focus on economic outcomes and cost-effectiveness in the included SRs. Considering the rising healthcare costs associated with pain management, examining the economic impact of pharmacist-delivered interventions, and determining their cost-effectiveness is crucial. Additionally, incorporating economic evaluations into future research is essential in understanding the cost-effectiveness and sustainability of pharmacist involvement in pain management.

The interpretation of study quality based on the AMSTAR 2 checklist shows that majority of the included SRs (7/11) were classified as high quality, indicating a robust methodology and enhancing confidence in the reliability of their findings. Conversely, over a third (4/11) of SRs were deemed moderate quality. Notably, none of the included reviews were rated as low quality according to the AMSTAR 2 criteria.

There are some limitations in this umbrella review. Firstly, inclusion criteria encompass both SRs involving RCTs and observational studies. Recognizing variations in the strength of evidence between these two types of studies is essential. We understand that these differences in study design can significantly influence the evidence hierarchy. Additionally, variability in methodologies and reporting standards across SRs may introduce biases, while limitations in the search strategy and inclusion criteria could result in an incomplete representation of evidence. While it is acknowledged that most of the findings were derived from SRs with descriptive analysis, it's important to note that this approach was employed to provide a comprehensive overview of the available evidence in areas where meta-analyses were not feasible due to heterogeneity or limited data availability. This umbrella review only included the SRs published in English. Furthermore, the reliance on descriptive analysis rather than meta-analysis in SRs is noteworthy. This reliance may introduce uncertainty regarding the accuracy of synthesized findings despite efforts to ensure methodological rigor. Additionally, the inability to conduct meta-analyses for all included SRs limits comprehensive quantitative synthesis, potentially hindering the estimation of overall treatment effects. Therefore, caution is advised when interpreting findings due to the constraints associated with descriptive analysis and the absence of meta-analytical validation.

The findings of this umbrella review show that pharmacist-delivered interventions play a significant role in advancing pain management practices. Beyond the quantitative improvements reported, such as reduced pain intensity and enhanced medication adherence, this study emphasizes the broader implications for healthcare delivery. The emphasis on collaborative care models and interdisciplinary teamwork highlighted in the SRs demonstrates the effectiveness of pharmacist involvement and prompts a reevaluation of traditional healthcare roles. Integrating pharmacists into pain management strategies improves patient outcomes and suggests a transformative shift towards a more holistic, patient-centered care approach.

Moreover, identifying gaps in the existing literature, including variations in study quality and the absence of a standardized definition for pharmacist-delivered interventions, signals the need for a concerted effort in research standardization. Addressing these gaps is essential for building a more robust evidence base and has implications for developing guidelines and policies surrounding pharmacist-led initiatives in pain management. This study contributes to the knowledge of effective interventions and the ongoing discourse about reshaping healthcare paradigms to optimize patient care and outcomes in pain management.

6. Conclusion

Pharmacist-delivered interventions such as medication review and patient education can positively impact pain management. A critical implication of this umbrella review is an urgent need to establish standardized roles for pharmacists in pain management to optimize the delivery of these interventions. Further work is needed to investigate innovative care models, such as pharmacist-independent prescribing models in collaborative care clinics for pain management.

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Sunil Shrestha: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Ayesha Iqbal:** Data curation, Formal analysis, Methodology, Resources, Software, Writing – review & editing. **Siew Li Teoh:** Methodology, Project administration, Resources, Software, Supervision, Writing – review & editing. **Saval Khanal:** Conceptualization, Data curation, Formal analysis, Methodology, Validation, Visualization, Writing – review & editing. **Siew Hua Gan:** Conceptualization, Funding acquisition, Project administration, Supervision, Visualization, Writing – review & editing. **Shaun Wen Huey Lee:** Supervision, Validation, Visualization, Writing – review & editing. **Vibhu Paudyal:** Conceptualization, Data curation, Formal analysis, Supervision, Validation, Visualization, Writing – review & editing.

Declaration of competing interest

The authors declare that during the registration of this umbrella review in PROSPERO, it was indicated that the findings from the included studies would be reported following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020. However, once the review commenced, it was determined that the Preferred Reporting Items for Overviews of Reviews (PRIOR) would be more suitable for guiding umbrella reviews. This change in reporting guidelines may have influenced the review process and interpretation of the results. Additionally, some findings of this umbrella review were presented at the First Conference of the ISPOR Student Network Asia-Pacific Region on February 16–17, 2024. Apart from these, the authors have no competing interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sapharm.2024.03.005.

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