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Improving patient safety and access to healthcare: The role of pharmacist-managed clinics in optimizing therapeutic outcomes

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ABSTRACT

Contemporary patient care requires a multidisciplinary approach to monitoring, assessing, and managing diseases. Promoting multidisciplinary approaches encourages the purposeful participation of many healthcare professionals and harnessing their combined knowledge to provide tailored treatment plans. Pharmacists, skilled and knowledgeable professionals in medication management, drug-related problems, and disease prevention, can offer vital interventions that contribute to improved patient outcomes. Advances in healthcare and information technology have expanded pharmacists' professional roles and made them essential in healthcare. Pharmacist-managed clinics (PMCs), an innovative healthcare approach, could potentially improve patient safety, satisfaction, accessibility, and affordability to quality healthcare. Spread across the healthcare continuum, pharmacists have a well-defined role in providing comprehensive pharmaceutical care and interprofessional collaboration, further reinforcing the necessity of establishing PMCs. This narrative review aims to compile and summarize information on PMCs from PubMed, Scopus, Web of Science, and Google Scholar till December 2023. The PMC shortlist covers specialties such as cardiovascular, hematologic, endocrine, pain medicine, respiratory medicine, infectious diseases, gastrointestinal, nephrology, neurology, and oncology. Pharmacists in disease-specific PMCs have demonstrated improved treatment outcomes and access to specialty care. Additionally, based on peer-reviewed literature, the review also highlights how PMCs enhance the pharmacist's role in improving disease-specific outcomes, overall quality of care, and medication management. The inclusion criteria are randomized controlled trials, case-control studies, cohort studies, and pre-post studies involving patients from cardiology, hematology, endocrinology, pain medicine, respiratory medicine, infectious diseases, neurology, nephrology, gastroenterology, and oncology specialties, focusing on pharmacist-driven clinics, published in English, and covering any geographical location. The exclusion criteria include review articles, proposed models, commentaries, editorials, and those published in languages other than English. Our findings reveal that PMCs are underutilized globally. PMCs work better in developed countries, possibly on account of robust healthcare infrastructure, adequate healthcare budgets, availability of trained pharmacists, and supportive regulatory

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environments. The review found that pharmacist-led interventions, such as medication monitoring and patient education, significantly enhance therapeutic outcomes. Pharmacist Managed Clinics improve affordability and acceptability, expanding healthcare access in outpatient and inpatient settings. This review also highlights the critical need for implementing PMCs to improve healthcare delivery, particularly in providing comprehensive and accessible services in developing countries.

1. Introduction

Chronic illnesses dominate the contemporary healthcare scenario, aggravating susceptibility to long-term complications and mortality.[1–4] Cardiovascular diseases are among the most numerous globally, followed by cancer. Although chronic conditions predominantly affect geriatric populations, recent reports highlight the growing incidence of chronic diseases in younger people. A sedentary lifestyle and increased consumption of alcohol and intoxicants by youngsters can increase their susceptibility to chronic diseases.[5,6] Allopathy has dominated other systems of medicine and has demonstrated considerable therapeutic success in most disease conditions, both chronic and acute. However, drugs also have negative impacts. In a meta-analysis, the primary care sector encountered a total of 8 % adverse drug reactions, of which more than 30 % were considered preventable, implying a significant impact on patient's health status.[7] Additionally, the world is currently witnessing a rise in the incidence of drug-induced renal impairment. Nonsteroidal anti-inflammatory drugs (NSAID), some antibiotics, antiviral, antifungal, and oncology medications have a significant potential to cause renal damage unless the patient is appropriately monitored.[8]

Polypharmacy is prominent in the geriatric population. Inappropriate doses, unindicated drugs, and drug duplications are among medication errors identified by Rasool et al., covering multiple hospitals.[9] Such irrational drug use affects clinical outcomes and the quality of life of patients. Medication adherence may be compromised in such circumstances, persuading patients to opt for unproven alternative strategies, further aggravating disease progression.[10]

A multidisciplinary approach to monitoring, assessing, and managing diseases is pivotal in contemporary patient care. Multidisciplinarity promotes the involvement of different healthcare providers and the pooling of their collective expertise toward defining individualized treatment protocols.[11,12] Pharmacists, skilled medical professionals knowledgeable in medication management, drug-related problems, and disease prevention, can offer vital interventions for better patient outcomes. Pharmacists' professional role and essentiality has been steadily expanding with the advancement in healthcare.[13] This new avenue has promoted the establishment of pharmacist-managed clinics (PMCs) exclusively under different specialties to improve the quality of patient care. Considering PMCs' capability to ensure patient-centered care, we have consolidated evidence showcasing the global implementation and scope of PMC services. This narrative review describes pharmacist-driven clinics that offer pharmaceutical care to patients.

2. Methods

A comprehensive search was conducted on PubMed, Scopus, and Web of Science using the keywords 'Pharmacist' and 'Clinic' with suitable Boolean operators. The articles retrieved include randomized controlled trials, case-control studies, cohort studies, and pre-post studies published till December 2023. Additionally, a snowball search was conducted using Google and Google Scholar. Review articles, proposed models, commentaries, and editorials were excluded from the search criteria (Table 1).

The articles were sourced and retrieved independently by two researchers, followed by evaluation by a committee of subject matter experts from five different countries, each specializing in various fields. The experts critically assessed the literature, identified strengths, weaknesses, and challenges, and discussed the literature's implications for establishing PMC services. Articles were then categorized based on specialization, pharmacists' activities, and outcomes. The distribution of articles based on specialties are depicted in Fig. 1.

Fig. 1 illustrates the number of studies on Pharmacist-Managed Clinics that were included to synthesize this narrative review under 10 different clinical specialties.

2.1. Diverse expert panel

The expert panel consisted of authors with varying backgrounds in pharmacy practice, including academicians, researchers, clinical pharmacists, and pharmacists from five different countries: Saudi Arabia, the United Arab Emirates, Qatar, India, and Malaysia. Despite identifying multiple pharmacist-led or managed clinics across various specialties, only a limited number of articles were included to generate this review based on applicability and relevance.

3. Results

We identified PMCs specialized in cardiology, hematology, endocrinology, pain medicine, respiratory, infectious diseases, neurology, nephrology, gastroenterology, and oncology. Most studies were conducted in the USA. We tabulated the results by author's name, published year, country, type of clinic and specialty, the aim of the study, the significance of pharmacist interventions, prime findings and limitations ((Table 2).

3.1. Key findings from the review on PMCs across medical specialties

Therapeutic and clinical outcomes of PMCs are categorized across the following specialties:

3.1.1. Cardiovascular diseases

Pharmacist-led programs for monitoring ambulatory blood pressure succeeded significantly in improving blood pressure management. Khazan E et al. reported that an average of 1.4 medication recommendations per patient had imparted positive clinical outcomes. Moreover, they could recommend at least one medication to 60 % of patients through their clinic.[14] Okamoto MP et al. found that the involvement of pharmacists in a hypertension clinic notably optimized systolic and

Table 1
The inclusion and exclusion criteria for the selection of articles.

	Inclusion criteria	Exclusion criteria
Study designs	Randomized controlled trials, case-control studies, cohort studies, and pre-post studies	Review articles, proposed models, commentaries, and editorials.
Patient/ Population/ Problem:	Patients from cardiology, hematology, endocrinology, pain medicine, respiratory, infectious diseases, neurology, nephrology, gastroenterology, and oncology specialties	–
Intervention	Pharmacist-driven clinics	Other
Language	English only	Studies published in languages other than English
Geographical location of study	Any	–

diastolic blood pressure, which enhanced overall quality of life and increased patient satisfaction.[15]

Patients enrolled in the pharmacist-managed heart failure (HF) medication titration clinics achieved a greater success rate in reaching optimal dosages of β-blockers and ACE inhibitors.[16,17] Patients managed in pharmacist-led heart failure bridge clinics experienced fewer deaths within 90 days and fewer readmissions for any cause. Additionally, these clinics minimized initial follow-up time for patients.

Dolder NM et al. in their pharmacist-managed lipid clinic, performed in-person and phone-based interventions. The majority of the patients enrolled in the in-person clinic (75 %) and the phone clinic (78 %) attained optimum low-density lipoprotein (LDL) cholesterol serum levels.[18] A similar clinic, set up by Gerrald KR et al. in an ambulatory hospital-based setting, ensured the attainment of the LDL-C goal in 83 % of patients compared to only 55 % at baseline, coupled with a mean reduction of LDL-C from 103 ± 45 mg/dL to 82 ± 28 mg/dL ($P < 0.01$).[19] Further, patients with cardiovascular conditions in the secondary prevention lipid clinic were subjected to twice the influenza vaccination rate (24 % to 54 %) because of pharmacist intervention.[20]

Patients referred to a pharmacist-managed weight management clinic in the cardiology department experienced significant weight loss using Glucagon-like peptide-1 receptor agonists (GLP-RA). Yates M et al. found that all patients enrolled in the pharmacist-managed weight management clinic within the cardiology department achieved a minimum of 5 % weight loss within six months, with an average weight reduction of 12.6 %.[21]

3.1.2. Hematology diseases

Shin-Yi Lin et al. found that over 95 % of patients showed an improved understanding of warfarin use after receiving interventions from the pharmacist-managed anticoagulation clinic (ACC), resulting in a significant increase in average time in therapeutic range (TTR). The study highlighted the essentiality of enhancing the participants' educational level and baseline knowledge scores in improving clinical outcomes.[22] Perhaps Garwood CL et al. identified better anticoagulation-associated care from their pharmacist-managed anticoagulation clinic than the corresponding physician-managed care (target INR range dropped from 76 % to 48 %). Moreover, patient's satisfaction rate was also significantly higher.[23] Deanne Hall et al. found that pharmacist-managed anticoagulation services saved over $6.5 million in hospital admission and medication therapy costs compared to standard medical care.[24] Yates NY. et al. investigated the impact of clinical pharmacy services on the selection and dosing of direct-acting oral anticoagulants (DOACs). Their study showed that more than 84 % of pharmacist recommendations, including dose adjustments or medication changes, were accepted by treating physicians. This underscores the valuable contribution of pharmacists in optimizing medication regimens, especially in the context of anticoagulant therapy.[25] Clapp SE et al. reported that both hemoglobin levels and patient compliance, associated with erythropoietin stimulating agent (ESA), improved with the intervention of pharmacist-managed patients' clinic.[26] Similarly, Ferro-López L et al.'s report suggests that pharmacist-led hematology clinic had excellent patient satisfaction due to team-based medical care.[27]

3.1.3. Endocrine diseases

Nadia J. Aneese et al. demonstrated that pharmacist-managed diabetes clinics (PMDCs) significantly improved diabetes-related parameters and achieved A1C goals more frequently. They also enhanced nephropathy screening rates.[28] In a similar study, Mohammad I et al. reported that among pharmacist-managed diabetic patients, by using sodium-dependent glucose cotransporters (SGLT2) inhibitors and GLP-1RA, 20 % more patients achieved targeted A1C than usual care patients.[29] A comparison between PMDC and routine care from primary care providers (PCPs) showed that PMDC achieved better clinical outcomes in the patients.[30]

3.1.4. Pain medicine

Keke Liu et al. compared the value of physician and pharmacist collaboration in pain management with physician-only clinics. Pharmacist involvement improved the degree of pain, effectiveness of pain management, drug compliance, and health-related quality of life.[31] Similarly, Stacy Mathew et al. evaluated an inpatient pain management service in terms of the degree of the patient's pain and functioning. Pharmacists' intervention reduced pain post-consultation and before discharge. Pain relief lasted during the complete hospital stay ($p < 0.001$). It was accompanied by a significant fall in opioid use, in addition to 87 % of patients showing general functional improvement, especially in sleep, mobility, and appetite.[32] On the other hand, in a headache clinic, Kristin Wiisanen et al. conducted a detailed medication history review followed by therapeutic recommendations, which improved both the frequency and severity of headaches in most patients at follow-up. Moreover, they reduced the number of follow-ups in the following year due to improved patient quality of life.[33] In a Canadian study led by Jorgenson et al., a pharmacist-led chronic pain clinic effectively reduced morphine-equivalent doses among patients with Chronic Non-Cancer

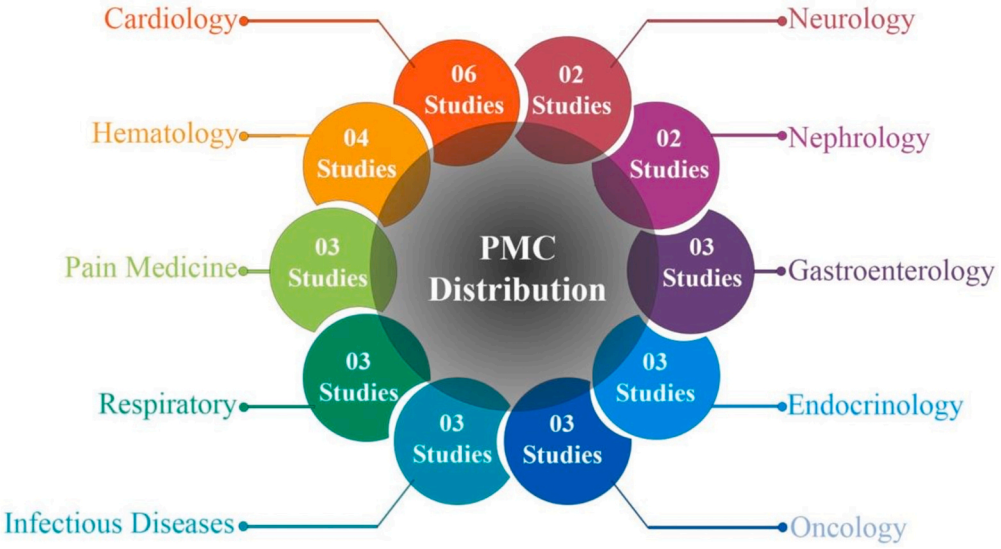

Fig. 1. Distribution of different types of Pharmacist Managed Clinics under various clinical specialties.

Table 2
Description of different PMCs across various clinical specialities.

Authors, Year & Country	Specialty	Type of clinic	Study objective	Pharmacist Interventions	Primary Findings of Pharmacist-Managed Clinical Interventions	Limitations of the study
Martinez et al., 2013, USA	Cardiovascular	Heart failure	• The development, execution, and evaluation of preliminary outcomes of a pharmacist-run medication titration clinic for heart failure.	• Medication reconciliation. • Medication titration. • Patient counseling.	• Target ACEI and ARB doses were achieved in a significantly higher percentage of pharmacist-managed titration clinic enrollees. • Patients enrolled in the pharmacist-managed HF medication titration clinic also had a significantly higher attainment rate of optimal β-blocker doses.	• Small sample size (n = 27) • Not blinded. • Retrospective data. • The results did not include hospital readmission related to heart failure and mortality rates.
Gerrald et al., 2010, USA	Cardiovascular	Dyslipidemia	• To document the effects of an outpatient lipid clinic using point-of-care testing on the achievement of LDL-C goals.	• Pharmacist consultation. • Medication management.	• Improved LDL-C target attainment observed in patients undergoing pharmacist-managed lipid management.	• The retrospective, pre-post-study design prevented determining the superiority of this patient care model over standard care and attributing results directly to pharmacist interventions. • This analysis does not address logistical and economic barriers that may limit this patient care model's generalizability. • Small sample size (n = 81)
Okamoto et al., 2001, USA	Cardiovascular	Hypertension	• Pharmacoeconomic evaluation of a pharmacist-managed hypertension clinic.	• BP measurements (automated). • Determination of the most appropriate regimen. • Patient counseling.	• Improved BP measurements were observed in the pharmacist-managed clinic compared to the physician-managed clinic alone.	• Included not only newly diagnosed patients. • Selective antihypertensive only. • Used only two BP readings to determine effectiveness: baseline and 6 months later.
Cording et al., 2002, USA	Cardiovascular	Dyslipidemia	• To outline the establishment of a lipid clinic run by pharmacists inside a primary care facility and to assess its outcomes.	• Medication recommendation. • Patient education.	• By effectively managing lipid-lowering therapy, pharmacists can aid in achieving LDL objectives.	• Single center study. • Small sample size (n = 115)
Loughlin et al., 2007, USA	Cardiovascular	Vaccination, dyslipidemia	• To ascertain if a vaccine campaign in a high-risk population raised influenza immunization rates in a secondary prevention lipid clinic run by pharmacists.	• Treatment optimization. • Offering influenza vaccination.	• The vaccination program run by pharmacists improved vaccination rates.	• Information related to vaccinations was extracted from the diagnostic tracking database. • Vaccination administered beyond the clinic's premises would not have been documented. • It is possible that errors in vaccination coding occurred, leading to an inaccurate representation of the vaccination rates.
Yates et al., 2023, USA	Cardiovascular	Weight management	• To assess the effects of a weight-loss program run by a pharmacist at a cardiology clinic on overweight/obese individuals by administering GLP-1 RAs and lifestyle counseling.	• Effective weight management using GLP-1 receptor agonists.	• Clinically significant weight loss and improvements in weight-related comorbidities were associated with pharmacist-led GLP-1 receptor agonist management in obese or overweight patients.	• Small sample size (n = 59). • Only 50 % of study population completed the required duration of 6 months treatment at the time of study completion.
Shin-Yi Lin et al.,	Hematology	Anticoagulation	• To assess the extent to which the introduction of an anticoagulation clinic	• Determined the effect of anticoagulation	• Over 90 % of surveyed individuals considered the pharmacist services	• Only outpatients with AF.

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Table 2 (*continued*)

Authors, Year & Country	Specialty	Type of clinic	Study objective	Pharmacist Interventions	Primary Findings of Pharmacist-Managed Clinical Interventions	Limitations of the study
2021, Taiwan			service has improved patient satisfaction with pharmacists, patient understanding of warfarin use, and the standard of INR management.	intervention in warfarin patients.	in the Ambulatory Care Clinic (ACC) to be valuable.	• Failed to assess potential causes influencing patients' health-related behaviors. • Social history, such as smoking and drinking status, were not collected.
Garwood CL et al., 2012, USA	Hematology	Anticoagulation	• To evaluate the standard of anticoagulation care in a pharmacist-run clinic following stabilization of warfarin treatment.	• Anticoagulation care quality assessment.	• In all clinical care areas, statistically significant differences were observed that supported pharmacist-managed anticoagulation. • No statistically significant differences were found in answers to service-oriented questions.	• Nonrandomized. • Retrospective study • Short in duration of follow-up. • Small sample size (n = 40). • Not designed to differentiate clinical events such as significant bleeding/ new thromboembolic events.
Deanne Hall et al., 2011, USA	Hematology	Anticoagulation	• To compare healthcare costs and therapeutic outcomes between patients receiving warfarin therapy in a pharmacist-managed anticoagulation clinic with those receiving warfarin management by standard physician care.	• Cost-saving analysis related to drug therapy and hospital admissions.	• Compared to standard medical care, pharmacist-managed anticoagulation improved therapeutic outcomes and lowered healthcare costs.	• Matching was not done. • Individual cost analysis was not done for the usual care group. • Retrospective study. • Selection bias.
Yates et al., 2023 USA	Hematology	Anticoagulation	• To describe the impact of clinical pharmacist intervention on DOAC prescribing.	• Pharmacist recommendation for medication selection and dosing.	• The pharmacist selects and doses the appropriate direct oral anticoagulant medication.	• Retrospective study. • Single center study.
Nadia et al., 2018, USA	Endocrinology	Diabetes	• To examine how a diabetic clinic run by pharmacists affects quality measures.	• Multidisciplinary clinic assists the outpatient sector in attaining improved healthcare effectiveness data and providing information to high-risk diabetics. • Screening for diabetes complications and drug-related aspects.	• Advantageous in diabetes care. • The clinic achieved a reduction of 3.2 % in (Hb A1C) levels within six months.	• The study did not show a statistically significant difference in the percentage of patients reaching an A1C of <8 %.
Jordan et al., 2017, USA	Endocrinology	Diabetes	• To compare the standard care from primary care physicians with the effects of a diabetes clinic run by pharmacists on clinical outcomes.	• Consultation between the pharmacist and the diabetic patient before meeting with the physician.	• Following referral to the clinic managed by the pharmacist, glucose control significantly improved.	• Small sample size (n = 82). • Retrospective study. • Single-centre study. • Matching bias.
Mohammad et al., 2023 USA	Endocrinology	Diabetes	• To evaluate the impact of an ambulatory care pharmacist on HgbA1c among people with diabetes in a primary care clinic.	• Implementing pharmacy team recommendations to optimize diabetic therapy through medication initiation, modification, or discontinuation.	• Effective management of HbA1C in diabetic patients.	• Interventions made by other medical staff are not accounted. • Small sample size (n = 116) • Some uncontrolled diabetes patients are not included. • ~13 % of patients had baseline HgbA1c <7 %, affecting comparisons. • Only 88 of 116 patients were analyzed for secondary outcomes. • Medications, renal function, BMI, hypoglycemia, and timing of pharmacist encounters were not evaluated.
Kristin Wiisanen	Pain management	Headache	• To evaluate the effects of a pharmacy-based pain	• Pharmacist consultation.	• Drug therapy modifications	• Small number of patients and lack of outcomes

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Table 2 (*continued*)

Authors, Year & Country	Specialty	Type of clinic	Study objective	Pharmacist Interventions	Primary Findings of Pharmacist-Managed Clinical Interventions	Limitations of the study
et al., 2004, USA			management program on outcomes linked to pain in an adult inpatient population.	• Pharmacological and non-pharmacological management.	recommended by pharmacists helped minimize the frequency and severity of headaches.	data for patient satisfaction, quality of life, and headache-related disability, among other long-term outcomes.
Keke Liu et al., 2021, China	Pain management	Cancer	• To evaluate the effects of a physician-pharmacist joint clinic for cancer pain management	• Pain control assessment and optimization.	• Improving pain management and medication adherence in cancer patients is linked to pharmacists' involvement in outpatient care.	• The study was retrospective, which can introduce biases and limit the ability to establish causality • The results in the joint group may reflect the specific pharmacist intervention rather than a broader effect, complicating the interpretation of the findings. • Small sample size (n = 113) with a short (4-week) follow-up. • Some patients were excluded due to missing data, potentially affecting the representativeness of the sample.
Jorgenson et al., 2023, Canada	Pain management	Chronic pain clinic	• To evaluate the impact of an interprofessional pharmacist-led chronic pain clinic.	• Reduction in mean morphine equivalent dose.	• Switching morphine to buprenorphine or naloxone. • Reduction in mean morphine equivalent dose.	• Small sample size (n = 80). • Single-center study with a short follow-up period.
Pauley et al.,1995, USA	Respiratory medicine	Asthma	• To ascertain whether the frequency of ED visits for acute asthma exacerbations is lower in patients receiving a comprehensive program of asthma therapy administered by a doctor and pharmacist.	• ED visits for acute exacerbations of asthma were measured.	• ED visits were fewer (n = 6) in patients enrolled in the asthma program than in the previous year (n = 47).	• Small sample size (n = 25). • Small sample size limits the statistical power and generalizability of the findings • The absence of a control group receiving standard care makes it difficult to attribute the reduction in ED visits solely to the intervention
Sharette et al 1999, Australia	Respiratory medicine	Asthma	• Development and Evaluation of a Pharmacist-Managed Asthma Education Clinic and their capability to decrease complications.	• Patient education. • A self-management action plan for all patients.	• Following the intervention, 90 % of participants optimally utilized the metered dose inhaler. • 40 % reduction in hospitalization. • 67 % reduction in ED visit.	• Small sample size (n = 20). • The awareness of being part of a study may have influenced patients' behavior and adherence to the asthma management plan.
Liu et al., 2021, China	Respiratory medicine	COPD	• To assess how well patients with chronic obstructive pulmonary disease respond to medication therapy management services led by clinical pharmacists.	• Significant improvement in medication adherence. • Reduction in the number of ADRs.	• Significant improvement in medication adherence and COPD assessment test.	• Small sample Size = 138 • Study was limited to a single center in a given period of time. • Potential biases in random assignment affecting group comparability.
Last et al., 2009, USA	Infectious diseases	Tuberculosis	• To examine the effectiveness of a latent tuberculosis clinic run by a pharmacist.	• Improved adherence to the Latent Tuberculosis treatment.	• More patients completed treatment (74 %) than the previous years (26 %).	• Missing in documentation. • Lost to follow-up. • Small sample size (n = 80).
Chung et al., 2016, South Korea	Infectious diseases	Antimicrobial therapy	• To provide an overview of the development and implementation of an outpatient parenteral antibiotic therapy program overseen by	• Develop and install a parenteral antimicrobial therapy program for outpatients.	• Clinical cure was achieved in 93 % of cases. • Therapy adjustments due to ADRs occurred in 6 % of cases.	• Program in a locality with limited resources. • No evaluation of the added value through comparison with other

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Table 2 (*continued*)

Authors, Year & Country	Specialty	Type of clinic	Study objective	Pharmacist Interventions	Primary Findings of Pharmacist-Managed Clinical Interventions	Limitations of the study
			pharmacists at a county teaching hospital.		• Hospitalization was necessary for 6 % of patients. • Reduced treatment costs and decreased unnecessary antibiotic use were observed.	conventional care and management strategies.
Meredith et al., 2021, USA	Infectious diseases	Staphylococcus-aureus Bacteremia	• To evaluate the effects of telemedicine versus on-site standard-of-care infectious disease consultation following the adoption of a *Staphylococcus aureus* bacteremia bundle guided by antibiotic stewardship.	• Initiation of AI-based infectious system Onsite/Telemedicine consultation. • Optimization of antimicrobial therapy.	• Virtual telemedicine consultations (89 %) were comparable to On-site consultations (86 %).	• Retrospective analysis. • Non-randomized. • Wider application is limited by the study's single health system methodology.
Huang et al., 2022, Taiwan	Neurology	Dementia	• To assess the effect of pharmacist-provided caregiver counseling on treatment persistence, adherence, and quality of life in dementia patients, as well as the caregiver's dementia knowledge and burden.	• Patients' treatment persistence and adherence assessment. • Patient counseling and education.	• Dementia knowledge scores improved significantly after counseling.	• Small sample size (n = 40) • Pilot study. • Single-center study • Due to self-reporting, caregiver knowledge, and burden scores could be biased.
Stefan et al., 2018, USA	Neurology	Parkinsonism	• To assess the pharmacologic and non-pharmacologic interventions offered by a neurology telephone clinic led by a clinical pharmacist in an effort to raise the standard of care for Parkinson disease patients.	• Treatment optimization. • Patient education.	• A total of 49 pharmacological and non-pharmacological interventions were administered across 10 patients.	• Small sample size (n = 10). • Short study duration. • Telephonic interactions may limit the depth of clinical assessment.
Owen et al., 2022, USA	Nephrology	Renal Transplant	• To assess the differences in therapeutic drug monitoring results between provider-driven and pharmacist-driven tacrolimus management protocols.	• Adjusting the dose of tacrolimus.	• There is no statistical difference between the patients initiated on a pharmacist-directed protocol (60.5 %) and prevailing patient management by provider (59.6 %). • Renal function, development of donor-specific antibodies, and rejection rate were similar in the two groups of patients.	• Small sample size (*n* = 124). • Single center study. • Retrospective design. • Short follow-up period.
Yang et al., 2019, China	Nephrology	Renal Transplant	• To evaluate the effectiveness of a pharmacist-run post-transplant medication management clinic.	• Treatment modulation. • Intervention analysis. • Cost-saving analysis.	• Physicians accepted 97 % of the interventions proposed by pharmacists. • The average cost of medication decreased by more than 30 %. • There was a significantly improved blood pressure control rate.	• Lack of randomization. • Retrospective study.
Walton et al., 2005, USA	Nephrology	Anemia	• To describe the anemia program run by pharmacists in an outpatient hemodialysis clinic and assess the program's effectiveness by contrasting the outcomes with the US average.	• Dose optimization by physician-reviewed protocol.	• There was improvement in ferritin and iron saturation at 6 months. • 8 % of patients had hemoglobin levels greater than 11 g/dL. • The dose of epoetin was minimal compared to the US average.	• Single center study. • Lack of control group. • Retrospective design.
Seko et al., 2021, Thailand	Gastroenterology	*H. pylori* irradiation	• To assess the efficacy of pharmacist-managed outpatient clinics and evaluate the cost-effectiveness of	• Cost-effectiveness. • Expert guidance for physician-led H Pylori eradication failure cases.	• Cost-effectiveness ratio was lower in the pharmacist intervention group compared to the lansoprazole and	• Bacterial factors were not assessed. • Disinfection rate was not compared with drug dosage.

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Table 2 (*continued*)

Authors, Year & Country	Specialty	Type of clinic	Study objective	Pharmacist Interventions	Primary Findings of Pharmacist-Managed Clinical Interventions	Limitations of the study
			lansoprazole and vonoprazan in *H. pylori* eradication therapy.		vonmoprazan-administered patient group.	
Bhat et al., 2020, USA	Gastroenterology	H pylori irradiation	• To evaluate the effects of a H pylori treatment program run by a pharmacist at a gastrointestinal clinic.	• Treatment optimization. • Medication adherence.	• The clinical pharmacist managed 60 referrals. • *H. pylori* was eradicated in 38 of these referrals. • The gastroenterologist expressed high levels of support and satisfaction.	• Small sample size (n = 60). • Missing eradication data. • Lack of control group.
Hunt et al., 2022, USA	Gastroenterology	Hepatitis C	• To assess the results of an HCV treatment program run by pharmacists within a regular screening program.	• Patient counseling on medication adherence and medical visits. • Ordering baseline laboratory tests and hepatitis immunizations.	• The program effectively identified patients with HCV, ensured completion of their treatment, and achieved SVR.	• Risk factors and birth cohort were not used to select the treatment population.
Lam et al., 2016, USA	Oncology	Cancer care	• To evaluate the impact of an oncology pharmacist-managed oral anticancer therapy program on oral medication adherence in chronic myelogenous leukemia patients versus usual care.	• Improvement in the efficacy of chemotherapy.	• Adherence rates to TKIs in CML patients significantly improved through an oral anticancer therapy program supervised by pharmacists.	• Retrospective design. • Results were compared with a previous study instead of the same patient population at the oncology clinic before and after implementing oncology pharmacist management. • Small sample size (45 patients treated with imatinib were evaluated). • Study assumed that the Medication Possession Ratio (MPR) reflected patient medication compliance.
Zhao et al., 2021 China	Oncology	Cancer care	• To describe and investigate the impacts of pharmacists-managed oncology outpatient clinic on ambulatory neoplasm patients.	• Resolving drug-related problems in chemotherapy.	• Pharmacist interventions effectively resolved drug-related problems and reduced adverse reactions in ambulatory neoplasm patients.	• The study assessed the frequency and type of DRPs and intervention acceptance rates, not the clinical outcomes or their significance. Secondly, the small number of patients and lack of a control group are limitations.
Homan et al., 2021, USA	Oncology	Cancer care	• To assess the results of a collaborative medication therapy management program for oncology symptom management by pharmacists.	• Effective management of gastrointestinal symptoms in chemotherapy patients.	• Following referral, the majority of patients (69.2 %) experienced improvement in symptom severity.	• Single-center study. • Small sample size (n = 62)

USA (United States of America), A1C (Hemoglobin A1c), ACC (American College of Cardiology), ACEI (Angiotensin-Converting Enzyme Inhibitor), ADRs (Adverse Drug Reactions), ARB (Angiotensin II Receptor Blocker), BP (Blood Pressure), COPD (Chronic Obstructive Pulmonary Disease), DOAC (Direct Oral Anticoagulant), ED (Emergency Department), GLP-RA (Glucagon-Like Peptide-1 Receptor Agonist), *H. pylori* (*Helicobacter pylori*), HbA1C (Hemoglobin A1c), HCV (Hepatitis C Virus), HF (Heart Failure), LDL (Low-Density Lipoprotein), LDL-C (LDL Cholesterol), TKIs (Tyrosine Kinase Inhibitors), SVR (Sustained Virologic Response).

Pain (CNCP). The clinic also successfully transitioned patients from morphine to alternative treatments.[34]

3.1.5. Respiratory diseases

Pett RG et al. demonstrated that pharmacists reduced asthma-related hospitalizations and visits to an emergency department or urgent care (ED) after appropriate patient education and treatment optimization.[35] Similarly, Pauley TR et al. highlighted the role of a comprehensive asthma management program in reducing ED visits for acute asthma exacerbations.[36] Meanwhile, Sharette C et al. emphasized pharmacist-provided education for asthmatic patients and their capability to decrease complications.[37] Liu M. et al. assessed clinical pharmacy-led medication therapy management (MTM) services for patients with chronic obstructive pulmonary disease (COPD). They found reduced antimicrobial use in hospitalized patients, improved medication adherence (MA), and higher chronic obstructive pulmonary disease (COPD) assessment test (CAT) scores compared to standard treatment, underscoring the benefits of integrating MTM into COPD care.[38]

3.1.6. Infectious diseases

Julie P et al. showed that implementing a pharmacist-managed latent tuberculosis clinic significantly improved treatment compliance and

outcomes. The treatment completion rate increased from 26 % to 74 %, reducing the risk of developing active disease, readmission, and tuberculosis transmission. In addition to public health benefits from reducing healthcare burden, the program also lowered the overall treatment cost. The study highlights the importance of pharmacists' involvement in managing tuberculosis and significantly improves patient outcomes.[39] The pharmacist-managed outpatient parenteral antimicrobial therapy program (OPAT) put forward by Eun Kyoung Chung et al. was highly effective in optimizing the management of infections. The program imparted clinical cure to 93 % of enrolled samples ($n = 203$). Structured monitoring and follow-up for patients requiring antimicrobials improved patient outcomes and reduced line-related complications. Additionally, there was an overall reduction in healthcare costs, along with an improvement in quality of care and patient satisfaction, which made OPAT services appear safe and effective for managing a variety of infections.[40] A study by Jacqueline Meredith et al. evaluated the effectiveness of a pharmacist-managed telemedicine service for *Staphylococcus aureus* bacteremia (SAB). A total of 576 patients received standard of care (SOC), and 162 received telemedicine ID consultations. There were no differences in overall bundle adherence and treatment outcomes for SAB administered by telemedicine compared to onsite ID consultation. Additionally, there was no difference in short-term outcomes like 30-day mortality, hospital readmission, and culture clearance. These findings suggest that telemedicine is a viable option for managing SAB and maintaining quality care while minimizing the need for onsite consultations.[41]

3.1.7. Neurological diseases

Stefan et al. studied a clinic offering consultations to Parkinson's disease (PD) patients and their caregivers. The patients ($n = 10$) received about 50 pharmacologic and nonpharmacologic interventions within three months, demonstrating a significant contribution from pharmacists in providing medical care.[42] Similarly, a telephone clinic capitalized on pharmacists' expertise, establishing a functional collaboration between health care providers, patients, and the electronic medical record, offering a multi-perspective evaluation of the anti-dementia therapy's effectiveness from a patient-centric view.[42] A pilot study by Hyang CY et al. highlighted low treatment persistence and adherence in dementia patients. Pharmacist counseling for these patients and their caregivers was found to be effective in enhancing caregiver knowledge.[43]

3.1.8. Kidney diseases

Hui Yang et al. investigated the impact of pharmacist-led post-transplant drug therapy management. The post-intervention group experienced a significant decrease in antibiotic usage and treatment duration. On the discharge day, the post-intervention group showed lower systolic blood pressure (SBP) and a greater BP control rate than the pre-intervention group.[44] Another study found that a pharmacist-managed anemia program allowed the initiation and adjustment of epoetin and iron therapy. Pharmacists could reduce the epoetin doses in kidney-impaired patients, saving $3000 per individual.[45] Kathryn Owen et al. demonstrated that transplant pharmacists were as effective as clinicians in maintaining tacrolimus TTR in kidney transplant patients, showing that pharmacist-led management is a viable alternative to primary outpatient care.[46]

3.1.9. Gastroenterological diseases

Bhat S et al. investigated pharmacist-managed H.pylori treatment in a gastroenterology clinic. The pharmacist received 55 patients, and upon treatment recommendation, 28 were cured, and 8 were scheduled for eradication evaluation (test). There were 10 patients who failed treatment, for which the pharmacist showed it to be associated with medication non-compliance. Accordingly, to minimize the barrier that affected the patient's treatment, the pharmacist reviewed the accuracy of prescriptions and ensured that medicines were dispensed.[47]

The pharmacist-led hepatitis C Virus (HCV) treatment model supported patients navigating through the treatment cycle and attaining sustained virologic response. Hunt BR et al. recommended the implementation of full-fledged pharmacist-led HCV treatment systems to accelerate its elimination goals.[48] The inappropriate use of proton pump inhibitors (PPI) was effectively tackled by a PMC by employing an algorithm-based, pharmacist-led PPI deprescribing practice.[49] Although counseling on medication by pharmacist-managed outpatient clinics costs more in terms of labor, such interventions can improve patients' quality of life and help accelerate *Helicobacter Pylori* (H.pylori) eradication therapy.[50]

3.2. Oncology

Oncology pharmacists are pivotal in cancer treatment, covering medication management, drug information, chemotherapy dosing and monitoring, supportive care, and patient education. Lam MS et al.'s study showcased notable advancements in reducing treatment failure linked to non-adherence to imatinib among chronic myelogenous leukemia (CML) patients.[51] Similarly, Zhao X et al. in a study to identify drug-related problems (DRPs) in oncology patients, demonstrated that pharmacist interventions effectively resolved DRPs and adverse reactions among ambulatory oncology patients.[52] A systematic review by Passey DG et al. revealed one or more favorable outcomes, encompassing improved patient adherence, enhanced safety, cost savings, and increased patient satisfaction.[53] Furthermore, oncology clinical pharmacists play a vital role in addressing gastrointestinal side effects associated with cancer and chemotherapy. Homan MJ et al. observed that when physicians referred patients to clinical pharmacists, 70 % of such patients experienced a reduction in the severity of symptoms associated with cancer.[54]

4. Discussion

The role of pharmacists in healthcare is rapidly evolving, and the concept of PMC is gaining momentum, providing better opportunities to support patient care and disease management. Pharmacists are trained to manage chronic diseases and to offer medication therapy management services.[44] Pharmacist Managed Clinics provide a holistic approach to patient care that can improve patient outcomes by offering a range of clinical services, such as health screening, immunization services, and medication counseling. Additionally, pharmacist-led interventions, especially medication reconciliation, have been shown to reduce the incidence of medication errors.[45] Another benefit of PMC is the potential for cost savings. Moreover, preventive care services from pharmacists can help reduce the burden of chronic diseases on the healthcare system and lower healthcare costs.[46]

Patient engagement is a crucial factor in the success of PMCs. Effective dissemination of information about the capabilities and responsibilities of pharmacists in healthcare, along with the potential benefits of pharmacist-led services, is essential for community awareness and participation. Moreover, PMCs should be conveniently located and easily accessible, particularly in underserved areas with limited access to healthcare.[55]

The United States of America hosts the majority of PMCs, while low and middle-income countries have few or none. Pharmacist Managed Clinics improve patient adherence, safety, efficacy, and medication affordability, serving as a model for others to follow. Healthcare authorities must establish PMCs cost-effectively to ensure quality care, as PMCs have become increasingly essential in recent years.[56] Pharmacist-managed clinics function at different standards in different clinical settings, depending on the availability of resources and public perceptions. Overall, disease burden (in terms of mortality, morbidity, disability, and economic burden) ascribable to a particular disease in a given population may be reduced by defining the nature and scope of PMC's involvement.[57] Pharmacist Managed Clinics with specialized

programs that address clinical and financial aspects of patients can facilitate optimal treatment for difficult-to-manage medical conditions.[26,58,59] Such a holistic approach further facilitates many aspects of patient's safe medication practices and efficient time-bound interventions.[60–62] This study shows that pharmacist-led interventions for chronic disease management, including medication monitoring, therapy review, patient education, and immunizations, significantly improve the attainment of therapeutic goals. Also, studies have shown that pharmacist involvement in clinical preventive services, (e.g. collecting complete medication histories, analyzing the clinical effects of ongoing treatment, and assisting with medication cost reduction) plays a significant role in patients' overall health and wellness. Pharmacist-managed clinics are highly beneficial in areas such as chronic disease management (e.g., diabetes, hypertension, asthma), anticoagulation therapy, medication therapy management, and preventive care. Another significant benefit of PMCs is wider healthcare access.[61] Increasing public demand for advanced healthcare services is compromising healthcare access. Pharmacist-managed clinics enhance affordability and acceptability, thereby broadening healthcare access in outpatient and inpatient settings.[63]

4.1. Practical implications for healthcare, policy, and research

Extensive reviews across specialties highlight PMCs' significant implications for healthcare practitioners, policymakers, and researchers. Pharmacists in these clinics offer specialized knowledge to optimize medication therapy and patient care. Collaborating with pharmacists helps practitioners enhance patient accessibility, reduce workload, improve outcomes, treatment effectiveness, patient empowerment, quality of life, and reduce healthcare costs.[64–70] Healthcare policymakers can use PMC data to develop policies, optimize resource allocation expenditure, and improve healthcare delivery.[71–73] Researchers may utilize PMCs to conduct comprehensive studies, identify trends, and establish evidence-based recommendations.

4.2. From PMC insights to action: implementing effective strategies

Translating insights from PMCs involves developing detailed care plans with specific drug regimens, lifestyle modifications, and follow-up sessions to attain therapeutic goals. Collaboration with healthcare providers or stakeholders ensures comprehensive and coordinated care, enhancing treatment effectiveness in practical settings.[3,4,74]

The creation of a conceptual framework that assesses clinical, financial, and holistic outcomes will make it easier to implement practice sites methodically and disseminate the data needed to support practice transformation, which will enhance healthcare delivery by making better use of pharmacists in primary care settings.[3,4,74] Furthermore, creating PMC guidelines with quantifiable criteria and standards can be universally applied in various clinical contexts, such as community pharmacies treating asthma and COPD patients or hospital pharmacies providing chemotherapy for cancer patients.[4,75] Providing dependable evidence that pharmacist-led patient education and counseling through PMCs not only improves patients' adherence but also has positive implications for clinical and humanistic outcomes and is cost-effective.[75,76]

Moreover, it's crucial to explore the PMC's outreach activity at the community level. Here, community and hospital pharmacists play pivotal roles in managing pharmacotherapy for chronic diseases, including cancer chemotherapy, which can enhance public awareness and appreciation.[4,74,77] The development and implementation of PMCs principally depend on the existing structure of healthcare systems. Organizations with an integrated healthcare system that facilitates interprofessional collaboration and legislations that support the expansion of pharmacy services and their roles, such as the ability to prescribe or manage chronic diseases, make the possible implementation of PMCs. Additionally, having a well-defined role in patient care and advanced training such as continuing education and professional development programs facilitates PMCs in healthcare settings. Understanding barriers and challenges in implementing and managing PMCs is critical for translating them into actionable strategies. This approach can help design effective ways to overcome barriers and challenges, such as financial constraints, lack of interprofessional collaboration, and resistance from healthcare practitioners.

4.3. Limitations and challenges in implementing PMCs

Although PMCs offer multiple benefits, acknowledging their limitations is crucial for optimizing patient outcomes. These clinics encounter challenges, including insufficient staff training, small sample sizes for impact assessment, high implementation cost, non-compliance with pharmacist recommendations, interference with appointment schedules, lack of patient participation, lack of time, and physical barriers. Other significant limitations include missing patient appointment rates and limiting the findings' generalizability.

Challenges include uncertainties on PMCs' financial sustainability due to poorly established reimbursement models for pharmacist-led services and questions on the cost-effectiveness of PMCs (currently under study). Another problem is establishing a mechanism to measure secondary outcomes, such as the safety and efficacy of the PMCs. Furthermore, there could be regulatory and legal barriers to implementing PMCs. Successful implementation and sustainability of PMCs depend on multiple factors, such as collaboration and coordination between pharmacists and other healthcare providers. Effective communication and shared decision-making among healthcare professionals can improve patient outcomes and reduce medication-related problems. Additionally, pharmacists must be adequately trained, staffed, and supported to provide clinical services and make therapeutic decisions.

4.4. Critical analysis of the studies included in the review

The review paper synthesizes various studies on PMCs in different specialties, each contributing differently to our understanding of these clinics' impact on patient care. Martinez AS et al. examined pharmacists' role in managing cardiovascular heart failure, specifically in counseling, dose titration, and drug reconciliation. The study showed progress in determining the optimal dosages for beta-blockers, ACE inhibitors, and ARBs. However, its retrospective approach and small sample size limited the generalizability of the results. The study did not include crucial outcomes such as hospital readmission and heart failure death rates.[17]

According to Gerrald KR et al., there was an improvement in achieving the LDL-C target when pharmacists managed dyslipidemia medication.[19] The study's retrospective, pre-post methodology, which did not examine financial or logistical barriers or establish causation, limited the conclusions' broader applicability. In contrast, hypertension clinics run by pharmacists had better blood pressure control than clinics overseen by physicians, according to Okamoto et al.[15] Patient counseling and automated blood pressure monitoring were two of the study's strengths. However, its breadth was limited since it focused solely on selected antihypertensives and relied on just two blood pressure readings. According to Cording et al., pharmacists could assist in reviewing and educating about managing lipid-lowering medications.[78] The study's single-center approach restricted its applicability, and concerns about clinic layout and physician support were raised but not thoroughly addressed.

Loughlin et al. reported that pharmacist-led programs increased vaccination rates; nonetheless, they ran into problems, including vaccine shortages and potential inaccuracies in documentation.[20] It is possible that the vaccinations given outside of the clinic were hidden due to the dependence on diagnostic tracking databases. GLP-1 RA was reported by Yates M. et al. to be an effective weight control tool with considerable benefits in weight-related comorbidities.[21] Despite these optimistic outcomes, other challenges remained, including a lack of

personnel, prescription scarcity, and insufficient insurance coverage. The smaller sample size further limited the applicability of the study results. According to Shin-Yi Lin et al., individuals on warfarin who had their anticoagulation managed well reported feeling satisfied with the services provided by pharmacists.[22] However, the study's emphasis was restricted to outpatients with atrial fibrillation, which may have reduced the findings' application. The study did not assess behavioral or social aspects influencing patient outcomes. Garwood CL et al. showed that involving pharmacists in treating anticoagulation enhanced the quality of care. However, the limited sample size, brief follow-up period, and non-randomized, retrospective methodology impacted the assessment of major clinical events and generalizability.[23] According to Deanne Hall et al., pharmacist-managed anticoagulation can lower costs and improve outcomes.[24]

However, the results were not as strong due to selection bias, restricted matching, and a focus on cost avoidance rather than income gain. Yates NY et al. discovered that pharmacist interventions enhanced drug selection and dose of DOAC drugs, although the results were restricted due to the small sample size and retrospective approach.[25] A multidisciplinary clinic improved diabetes care and reported lower A1C readings, according to Nadia J. Aneese et al.[28] Despite these optimistic results, concerns such as missed visits and the lack of significant changes in the A1C target-achieving range still need to be addressed. Jordan L. Schultz et al. discovered that seeing a pharmacist rather than a doctor improved glucose management; however, establishing a causal connection was problematic due to the retrospective design, small sample size, and potential referral bias.[30] Following the guidance of the pharmaceutical staff, it is feasible to manage HbA1c properly.[29] The study's failure to consider other staff interventions and the exclusion of individuals with uncontrolled diabetes limited its usefulness and comprehensiveness.

Although Kristin Wiisanen et al. demonstrated that headaches could be adequately managed with pharmacist consultations, the study's robustness was undermined by the small sample size and the absence of long-term outcome data.[33] The 2021 study by Keke Liu et al. showed that the involvement of pharmacists enhanced the adherence and pain management of cancer patients.[31] Nevertheless, the brief follow-up time, small sample size, and possible reporting bias impacted the data's generalizability and reliability. Jorgenson et al. saw reduced morphine equivalent doses following pharmacist interventions in assessing chronic pain treatment.[34] The limited sample size and measurement reliability issues restricted the generalizability of the results. Pauley TR et al. reported that asthma patients receiving pharmacist-managed therapy visited the ER less frequently; however, the small sample size and absence of a thorough challenge discussion limited the study's relevance.[36] With pharmacist-led asthma therapy, Sharette C. Sterné et al. reported lower hospitalization and ER visits; however, the limited cohort size may not fully reflect patient responses, which could affect extrapolation.[37]

The evaluated studies show that pharmacist-managed clinics can improve patient outcomes and safety. However, many factors limit them, including small sample sizes, retrospective designs, and a lack of long-term data. Future studies should overcome these shortcomings to produce more solid and broadly applicable proof of the efficacy of pharmacist-managed care.

4.5. Study limitations

Our review has several limitations. Firstly, it covered a limited range of research, generally focusing on certain regions, healthcare settings, or patient demographics, which may hinder the generalizability of the results. Secondly, the studies vary in methodological quality, sample size, and design, which could affect the dependability of the data and results. Furthermore, the absence of longitudinal data in some studies limits our knowledge of the ongoing impact of pharmacist-managed clinics on patient outcomes. Moreover, variations in the types of pharmacist-managed therapies, patient groups, and outcome measures among the studies make direct comparisons difficult. Furthermore, the continually changing healthcare delivery environment means that this evaluation may not fully encompass current innovations or newly developing care models. Thus, the study emphasizes the significance of further research to strengthen the evidence and provide a more complete role for pharmacist-managed clinics in enhancing patient outcomes.

5. Conclusions

Pharmacists are at the forefront of healthcare advancements, providing essential patient care services crucial in the fight against chronic diseases. The establishment of PMCs has empowered pharmacists to collaborate closely with patients and healthcare professionals, significantly enhancing patient satisfaction and improving the quality of life for those managing chronic disease patients. However, an urgent global imperative exists to establish PMCs across lower and middle-income countries, removing barriers that obstruct underserved populations from accessing quality healthcare services. This review demonstrated that pharmacists-led interventions in PMCs yield tangible benefits: improved treatment outcomes, cost-effective healthcare, enhanced access to care, greater patient adherence, and heightened knowledge about pharmacotherapy. Pharmacist Managed Clinics provide a pivotal platform for pharmacists to provide comprehensive pharmaceutical services, advancing healthcare on a broader scale. The overreaching aim of this study is to inspire the establishment of PMCs on a broader scale, thereby amplifying these benefits and improving healthcare delivery worldwide.

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Shabeer Ali Thorakkattil: Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **Sainul Abideen Parakkal:** Writing – review & editing, Writing – original draft, Formal analysis. **K.T. Mohammed Salim:** Writing – original draft. **Savera Arain:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis. **Gopika Krishnan:** Writing – original draft. **Hafees Madathil:** Writing – original draft. **Ajmal Karumbaru Kuzhiyil:** Writing – original draft, Investigation. **Ammad Aslam:** Data curation. **Suhaj Abdulsalim:** Writing – original draft, Data curation. **Mahmathi Karuppannan:** Writing – original draft, Formal analysis, Data curation. **Sathvik Belagodu Sridhar:** Writing – original draft, Data curation. **Javedh Shareef:** Writing – original draft, Data curation. **Mazhuvanchery Kesavan Unnikrishnan:** Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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