Patient Preference and Adherence

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REVIEW

Effectiveness of Pharmacist-Led Intervention on Medication Adherence in Chronic Diseases: A Systematic Review of Randomized Controlled Trials

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Background: Managing chronic diseases often requires long-term treatment to prevent complications. However, the effectiveness of treatment is often reduced due to poor medication adherence. Poor medication adherence has been associated with 1.1 million hospital days in France and contributes to 200,000 premature deaths in Europe. As primary providers of pharmaceutical care, pharmacists have implemented various intervention strategies to address the problem. Therefore, this study aims to systematically examine the effectiveness of pharmacist-led interventions in improving medication adherence among patients with chronic diseases.

Methods: Literature search was conducted using 2 databases (PubMed and EBSCO), focusing on RCTs published until October 2024. These RCTs analyzed the impact of pharmacist-led interventions on medication adherence in chronic diseases, such as hypertension, diabetes, dyslipidemia, asthma, cardiovascular disease, and COPD. Studies on multiple chronic, acute, or mental conditions were excluded. The Risk of Bias 2 tool (RoB2) was used to assess the quality of the studies.

Results: Among 75 studies, a total of 26 were included, with the majority conducted in Europe (42%). In addition, 4 types of interventions were identified, including counseling (53.8%), tailored (26.9%), technology-based monitoring (3.85%), and multiple interventions (15.4%). A total of 18 studies (69.2%) demonstrated a significant association between pharmacist-led interventions and medication adherence. The majority measured adherence using self-reported questionnaires. Bias assessment results showed that 7 studies had low risk of bias, 10 had high risk, and 9 had some concerns.

Conclusion: Pharmacist-led interventions, such as counseling, tailored, and multiple interventions, can improve medication adherence in chronic diseases. Although pharmacist-led interventions show promising potential, their effectiveness varies depending on the type of intervention and adherence measurements. Further studies are needed to focus on tailored interventions that address patient-specific barriers, ensuring higher efficiency in time, resources, and costs.

Keywords: chronic diseases, pharmacist-led intervention, medication adherence, randomized controlled trials, public health

Introduction

Chronic diseases are a group of conditions that serve as major contributors to global mortality.[1] In 2019, the World Health Organization showed that chronic diseases were responsible for 74% of deaths worldwide, increasing to 75% in 2021.[1,2] Several studies have shown that cardiovascular disease, diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), asthma, and dyslipidemia are among the most prevalent chronic diseases and remain the primary causes of morbidity and mortality worldwide.[3–5] These high-burden diseases typically require long-term or lifelong therapy, where medication adherence plays a significant role in determining patients' outcomes.[6–8] Globally, a large number of studies have

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been conducted to assess medication adherence and its impact on outcomes across several medical conditions, including diabetes, hypertension, cardiovascular diseases, cancer, and neurodegenerative diseases.[9–11]

According to previous studies, medication adherence plays an important role in ensuring effective treatment as well as influencing the rate of disease progression and patients' overall health-related quality of life.[12–15] Patients with low adherence to antihypertensives and statins showed a 28% reduction in blood pressure and a 25% increased hazard for mortality.[13,16,17] Medication adherence has also been estimated to prevent approximately 200,000 premature deaths and generate healthcare savings ranging from USD 3 to 13 for every additional dollar spent on medications. This was achieved by reducing avoidable emergency department visits and hospitalizations across Europe[18] However, approximately 50% of the patients with chronic diseases are non-adherent to their prescribed medication.[19–22] Many patients with chronic diseases experience difficulty adhering to their recommended regimen due to various factors. These include patients-centered, therapy-related, social and economic, healthcare system, and disease factors.[23–26]

Given the severe consequences of non-adherence, there is an urgent need for scalable solutions in the healthcare systems. Pharmacists, as the most accessible healthcare providers, are uniquely positioned to bridge this gap through tailored patients' engagement.[27,28] This includes identifying barriers to adherence and providing solutions.[27,29,30] Various interventions have been developed to enhance patients' adherence to prescribed medications, such as education,[31] counseling,[32] digital medication adherence systems,[33] reminder systems,[34] social supports, and follow-up.[35] Each of these interventions has its advantages and disadvantages, as well as varying levels of success.[36,37] Variability in adherence measurement methods (eg self-reports vs pill counts) also complicates cross-study comparisons and necessitates careful interpretation of effectiveness.[38,39]

Previous systematic reviews found that interventions could positively influence medication adherence and play a significant role in achieving treatment goals in chronic diseases management.[40–46] However, most of the evidence from previous systematic reviews is limited to studies published several years ago in a single country.[40–43] These studies focused on a single disease[44–46] and interventions led by healthcare professionals, such as doctors or nurses, rather than pharmacists[40] In medical practice, pharmacists have greater accessibility to patients[40–42,47] and are capable of providing more in-depth information and education tailored to their specific needs of patients.[48] Other systematic reviews also limit the interventions setting to community pharmacists services, despite their potential to practice in various health services, such as hospitals, clinics, or during home visits.[42,49,50] Therefore, this study aims to systematically assess the effectiveness of pharmacist-led interventions in improving medication adherence in patients with chronic diseases (hypertension, diabetes, COPD, asthma, cardiovascular disease, and dyslipidemia). Compared to previous reviews, this study provides an updated, global synthesis of pharmacist-led interventions across diverse healthcare settings (community pharmacies, hospitals, clinics), using rigorous RCTs inclusion criteria to minimize bias.

Materials and Methods

This systematic review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)[51] (Table S1). The protocol was registered on the PROSPERO: International Prospective Register of Systematic Reviews (CRD42024626668) and can be accessed at www.crd.york.ac.uk.

Eligibility Criteria

This study systematically reviewed randomized controlled trials (RCTs) published in English until October 2024, focusing on pharmacist-led interventions to improve medication adherence in patients with chronic diseases (hypertension, diabetes, dyslipidemia, asthma, cardiovascular disease, or COPD). Pharmacist-led interventions were defined as structured healthcare strategies or programs delivered by pharmacists to improve patients' medication adherence. Studies conducted among patients with severe mental illness (schizophrenia, other psychoses, and bipolar disorder), tuberculosis, HIV, and substance abuse were excluded because interventions for these diseases were more specific.[52–54] In addition, studies that addressed multiple chronic diseases, lacked a comparison group, and not original studies (eg, study protocol, review, abstracts, case reports, commentaries, or editorials) were excluded.

Search Strategy

An extensive search for published literature was conducted on PubMed and EBSCO. This study design was developed using the PICO framework. 1) Population, namely those with chronic diseases (hypertension, diabetes, dyslipidemia, asthma,

cardiovascular disease, or COPD), 2) Interventions carried out by pharmacists to improve medication adherence and outcomes. All selected studies had a control group receiving usual care. The full search strategy is presented in Table S2.

Study Selection

The selection process was carried out in 2 stages. In the first stage, 2 reviewers (LF, SS) independently screened studies based on title and abstract. In the second stage, a full-text review was conducted on the selected studies. The reviewers (LF, SS) independently assessed the studies for applicability to the inclusion and exclusion criteria. Disagreements between the 2 reviewers were resolved by consensus with a third reviewer (FPR).

Data Extraction

For each eligible study, a reviewer (LF) extracted features of the publication details (title, author, year, and country), type of diseases, setting, time and duration, sample size, intervention group, control group, adherence measurement, and effectiveness of intervention. Each extraction was confirmed by another reviewer (SS).

Quality Assessment

Study quality was assessed using The Cochrane Risk-of-Bias (RoB) 2 tool for RCTs study. The RoB 2 is a tool used to assess a single trial result, which represents the estimated relative effect of 2 interventions on a particular outcome. This consisted of 5 domains of bias aimed at eliciting information about features of the trial that were relevant to the risk of bias. The domains in the RoB 2 tool were the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results. Based on the answers to the signaling questions, an algorithm generated a risk of bias assessment for each domain. The assessment was categorized as "Low risk", "High risk", or "Some concerns".[55] RoB assessment was conducted independently by 2 reviewers for each study (LF, FPR), and any disagreements across domains were resolved through consensus with a third reviewer (SS).

Results

Study Characteristics

From the literature search, 65 studies were identified from PubMed, while 72 were identified from EBSCO. After removing 62 duplicates, 75 were screened, and 38 were excluded during title and abstract screening. A total of 37 full-text studies were assessed for eligibility. Among these, 11 were excluded because the studies were not RCTs,[56,57] the intervention was not specifically delivered by pharmacists,[58,59] medication adherence was not measured,[60–63] focused on multimorbidity,[64,65] and addressed acute disease.[66] Consequently, this systematic review comprised 26 studies, and the PRISMA flow diagram was shown in Figure 1.

Characteristics of the studies were summarized in Table 1. Most of the studies were conducted in America,[67–70] and European countries such as Portugal,[71] Spain,[72,73] Norway,[74] Belgium,[75–78] the Netherlands,[79] Denmark,[80] and Ireland.[81] A total of 9 studies were conducted in Asian countries.[32,82–89] Diabetes was the most frequently studied disease featured in 6 studies,[68,75,83,85,87,89] followed by hypertension (n=5), cardiovascular diseases (n=5), asthma (n=4), COPD (n=4), dyslipidemia (n=1), and 1 study assessed medication adherence for each disease independently in patients with hypertension, COPD, or asthma (n=1). The majority of the studies had a follow-up period of 3 to 6 months,[69,72,73,75–77,79–81,87–90] and only 5 studies included more than 500 participants.[70,72,74,77,80]

Interventions and Control Groups

Of the 26 interventions, 14 studies implemented counselling,[71,73,75,77,79,81,82,84–89] 7 studies implemented tailored interventions,[68,70,72,74,78,80,91] and 2 studies implemented both counselling and tailored interventions,[32,76] as summarized in Table 2. Counselling provided by pharmacists included both educational and behavioral elements[71,75,77,82–85,87–89] or focused only on educational elements.[73,79,81,86] Information provided in educational elements was about medications[79,87] (doses/frequencies,[82] side effects,[77] names of medications, indications, time to take medications),[85] the importance of medication adherence,[82] and information about disease.[71,75,83–86,88] Counselling intervention in 5 studies was delivered

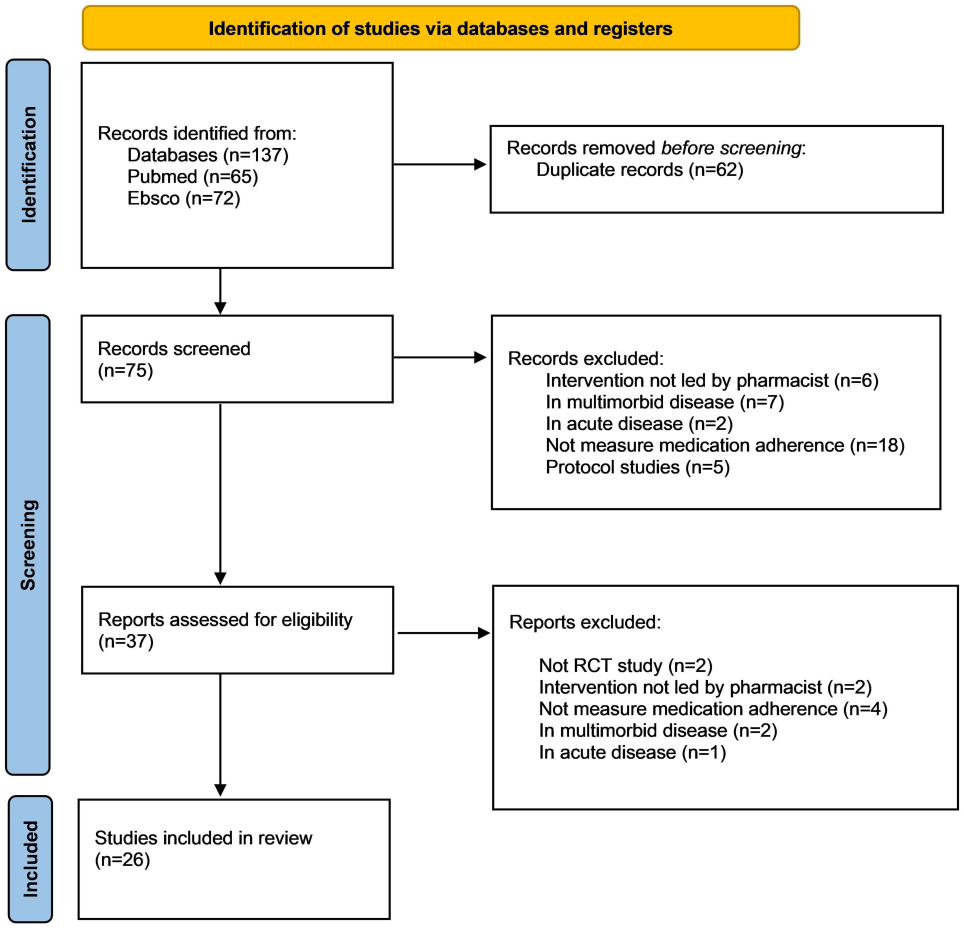

Figure 1 PRISMA flow diagram of the study selection process.

using information leaflets with or without follow-up.[71,82–84,89] In addition, 2 studies used verbal and written information,[77,85] while another 2 used physical demonstration and written information.[73,81] A total of 7 studies conducted a tailored intervention to identify nonadherent patients, detect barriers to medication adherence, and deliver potential solutions according to the patients' non-adherence reasons. Tailored interventions were delivered using motivational interviewing,[72,80] patients' beliefs,[91] semi-structured interviews,[74] diabetes care plan,[68] community pharmacists assisting in total cardiovascular health (CPATCH) model,[70] or personalized information.[78]

A study implemented technology-based interventions using home blood pressure monitoring.[69] Home measurements were evaluated by a clinical pharmacist every month and followed by regular follow-ups.[69] Stewart et al (2014) conducted motivational interview, medication use reviews, and prescription refill reminders.[90] According to Murray et al (2004) patient education was provided using verbal and written information tailored to the patients' barriers, as well as icon-based labeling of medication containers.[62] In addition, 2 studies implemented counselling and tailored interventions based on the General Medication Adherence Scale (GMAS)[32] and Asthma Control Test (ACT)[76] scores assessments. The interventions were delivered in a primary care setting, 12 in pharmacies,[70,72–78,81,85,87,90] 10 in a hospital,[32,62,79,80,82–84,86,89,91] 3 in a clinic,[68,71,88] and 1 during a home visit.[69] The control group in all studies implemented usual care.

Measure of Outcomes

Adherence was usually measured over a period and reported as a percentage, offering information about dose-taking behavior based on what was prescribed. Adherence assessment methods could be classified into direct and indirect methods. Direct methods included directly observing the patient taking the medication or measuring drug levels, metabolites, or biological

Table 1 Characteristic of the Studies

Characteristics	Number of Studies
Country	
India	2
Vietnam	3
Spanish	2
Pakistan	2
Portugal	1
Australia	2
Norway	1
Belgium	4
America	4
Netherlands	1
Iran	1
Jordan	1
Denmark	1
Ireland	1
Type of Disease	
COPD	4
Asthma	4
Diabetes	6
Hypertension	5
Cardiovascular disease	5
Dyslipidemia	1
Hypertension, asthma, or COPD	1
Participants number	
<250	15
250–500	6
>500	5
Outcome Measurement (in month)	
<3	5
3–6	13
7–12	7
>12	1

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Table 2 Details of the Intervention

Control	Interventions	Details	Number of Studies
Usual Care	Counselling	Educational and behavioral using patient information leaflets	5 studies[71,82–84,89]
		Educational and behavioral	3 studies[75,87,88]
		Educational and behavioral using verbal and written information	2 studies[77,85]
		Educational	2 studies[79,86]
		Educational using physical demonstration and written information	2 studies[73,81]
	Tailored intervention (a personalized approach according to a patient's specific barriers to medication adherence)	Motivational interviewing	2 studies[72,80]
		Discussing patients' beliefs using repertory grid	1 study[91]
		A semi structured interview	1 study[74]
		Diabetes care plan	1 study[68]
		Personalized support using Community Pharmacists Assisting in Total Cardiovascular Health (CPATCH) model	1 study[70]
		Personalized information	1 study[78]
	Technology based monitoring	Home blood pressure monitoring	1 study[69]
	Multiple intervention	Counselling including educational and behavioral elements, tailored intervention based on patients' specific problem	2 studies[32,76]
		Technology based intervention, medication regimen management, medication taking reminders, motivational interviewing	1 study[90]
		Counselling including educational using verbal and written information, icon-based labeling of medication containers, tailored intervention	1 study[62]

markers in blood or urine to confirm medication use. However, indirect methods relied on secondary information sources, such as patient questionnaires, self-reports, pill counts, prescription refill rates, clinical response evaluations, electronic medication monitoring, physiological marker measurements, or patient diaries. All studies in this systematic review used indirect measurement methods, both subjective,[32,68,71,72,78,82–90] objective measures,[62,69,70,77,79–81] or a combination of both measurements[74–76,91] (Table 3). Subjective methods assessed adherence based on patient perceptions, while objective methods relied on measurable data like pharmacy records, dose counts, or clinical outcomes for more accurate evaluation[92] A total of 7 studies used objective indirect measures of adherence, such as pill counting,[69] medication refill adherence (MRA),[77] medication event monitoring systems (MEMS),[62,79] proportion of days covered (PDC),[70] medication possession ratio (MPR),[80] and the inhaler compliance assessment (INCA).[81] Of the 16 studies that used indirect methods, the use of questionnaires and patient self-reports were the main tools used to measure medication adherence. Questionnaires measuring adherence included Medication Adherence Questionnaire (MAQ),[72,82] GMAS,[32,84] Morisky,[71,74,83,85,87,88,90] Drug Attitude Inventory (DAI),[86] and Medication Adherence Rating Scale (MARS).[73,89] Odegard et al (2005) measured medication adherence in diabetes patients using self-reporting techniques.[56] A study conducted by Aslani et al (2011) used 2 questionnaires, the Beliefs Medicines Questionnaire (BMQ) and the Medication Adherence Report Scale (MARS), to assess adherence in patients with dyslipidemia.[78] Subjective adherence measurements were applied due to their simplicity, adaptability for different patients, and relatively low cost.

Table 3 Details of Outcomes Measurement

Measure of Outcomes	Details	Number of Studies
Objective measures	Pill Counts	1 study[69]
	Medication Refill Adherence (MRA)	1 study[77]
	Medication Event Monitoring Systems (MEMS)	2 studies[62,79]
	Proportion of Days Covered (PDC)	1 study[70]
	The Inhaler Compliance Assessment (INCA)	1 study[81]
	Medication Possession Ratio (MPR)	1 study[80]
Subjective measures	Medication Adherence Questionnaire (MAQ)	2 studies[72,82]
	General Medication Adherence Scale (GMAS)	2 studies[32,84]
	Morisky	6 studies[71,83,85,87,88,90]
	The Drug Attitude Inventory (DAI)	1 study[86]
	Medication Adherence Rating Scale (MARS)	2 studies[73,89]
	Self-reports	1 study[68]
	Belief Medication Questionnaire (BMQ) dan MARS	1 study[78]
Objective and subjective measures	Prescription refill rates dan self-reporting	1 study[75,76]
	MARS and MPR	1 study[91]
	MMAS-8 and MPR	1 study[74]

Effectiveness of Pharmacist-Led Interventions for Improving Medication Adherence

Based on the results of testing the relationship between interventions and adherence, 18 studies showed significant findings that pharmacist-led interventions enhanced patient adherence in chronic diseases,[32,67,71–73,76,77,80–90] while 7 other studies did not show results.[68–70,75,78,90,91] Table 4 presented the results of studies on intervention by pharmacists. Mehuys et al (2008) stated that adherence rates significantly increased in the intervention (90.3%) compared to the control group (74.6%) (p=0.016), and there was no difference between the control and intervention groups when adherence was measured using self-reporting (p=0.108).[76] A study by Bouvy et al (2003) demonstrated that adherence measured using MEMS was higher in the intervention group (163.3 days) than the control group (143.6 days). However, this study did not further analyze the significance of this difference.[79] The impact of interventions to improve medication adherence in chronic conditions varied in effectiveness across different clinical contexts.

Risk of Bias Assessment

The results of the bias assessment using risk of bias (RoB 2) were summarized in Figure 2. Out of 26 included studies, 7 were "low risk",[70,73,74,76,77,80,81] while 10 were assessed as "high risk" of bias,[62,68,69,78,79,82,85–87,91] and 9 studies were assessed as "some concerns".[32,71,72,75,83,84,88–90] The results of the risk of bias assessment for each study were shown in Figure 3. A previous study was deemed "high risk",[79] and 4 studies were deemed "some concerns"[68,78,85,89] for bias arising in the "randomization process". This was because some of these studies only stated the use of the randomization method without explaining in detail how the process was carried out. "Deviations from intended intervention" exhibited the greatest proportion of "high risk" scores.[62,69,78,82,85–87,91] This was primarily due to the lack of proper analysis in many studies to evaluate the effects of the provided interventions. A total of 13 studies showed "some concerns" in the "measurement of outcome" domain.[32,71,72,78,79,82,84–90] This issue arose primarily because many studies did not implement blinding for outcome assessors. In addition, several studies relied on subjective measurement tools, which were

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Table 4 Results of Studies on Pharmacist-Led Intervention

Study	Disease of Interest	Setting	Sample size	Intervention vs Usual Care	Follow-Up Intervention	Follow-Up Outcome Measurement	Adherence Measure	Results
Abdulsalim et al (2017)[82]	COPD	Hospital	130 (CG) 130 (IG)	Counselling sessions (15–20 minutes), patient information leaflets (PILs), and monthly telephone calls	Monthly via telephone calls	6 months 12 months 18 months 24 months	MAQ	Medication adherence improved significantly after pharmacist intervention in IG at all follow-up time points ($P < 0.001$)
Nguyen T et al (2023)[32]	Asthma	Hospital	124 (CG) 123 (1G)	Counselling, education, intervention based on the patient's non-adherence reasons, and medication regimen management	No follow up	1 months	GMAS	Adherence rate was higher among the intervention group than the control group (94.3% vs 82.8%, $P = 0.001$)
Torres-Robles et al (2022)[72]	Hypertension Asthma COPD	Community pharmacy	569 (CG) 653 (IG)	Tailored intervention using motivational interviewing	Monthly scheduled visits	6 months	MGL-MAQ	Percentage of adherent patients during the study was higher in the IG (51.8%) than in the CG (22.2%) ($P < 0.05$).
Abubakar M et al (2021)[85]	Diabetes	Community pharmacy	80 (CG) 80 (IG)	Counselling (education and behavioral) and medication regimen management. These interventions were based on an array of charts and verbal communication	No follow-up	1 months	MMAS-8	A high level of self-reported medication adherence was seen in the intervention group (95%) as compared to the control group (46%) after the completion of one month of the trial ($P < 0.001$)
Morgado L et al (2011)[71]	Hypertension	Clinic	99 (CG) 98 (IG)	Counselling (hypertension education, BP self-monitoring recommendation, goal BP to achieve, lifestyle education and counselling, medication education and counselling tips to enhance adherence)	At 3 and 6 months	9 months	Morisky	Medication adherence was significantly higher in the intervention group at the end of the study (74.5% vs 57.6%, $P = 0.012$)
Nguyen T et al (2024)[84]	COPD	Hospital	89 (CG) 92 (IG)	Counselling (education and behavioral) and information leaflet describing COPD symptoms, medication, and inhaler techniques.	No follow-up	1 months	GMAS	After the intervention, the results indicated a significant improvement in medication adherence rate between the two groups, IG 90.1% vs CG 66.3% ($P < 0.001$)
Gujral G et al (2014)[91]	STEMI Non STEMI	Hospital	100 (CG) 100 (IG)	Interventions tailored to patient beliefs about treatments	Monthly when patients collected prescriptions	12 months	MARS and MPR	There was no significant difference between the number of patients categorized as non-adherent between the control group and the intervention group as measured by the MPR ($P = 0.605$) and MARS ($P = 0.932$)
García-Cárdenas V et al (2013)[73]	Asthma	Community pharmacy	150 (CG) 186 (IG)	A protocol-based intervention addressing individual needs related to asthma control, inhaler technique and medication adherence.	At baseline, 3 months, and 6 months	3 months 6 months	MARS-4	The intervention resulted in improved medication adherence by 40.3% ($P < 0.001$) at all follow-up time points

Nguyen T et al (2022)[83]	Diabetes	Hospital	83 (CG) 82 (IG)	Counselling intervention (educational and behavioral) and leaflets about diabetes.	No follow-up	1 months	MMAS	Medication adherence improved significantly after pharmacist intervention in IG 14.5% (P = 0.001)
Hovland R et al (2020)[74]	Cardiovascular disease	Community pharmacy	754 (CG) 726 (IG)	Participants in the intervention group received two consultations with a pharmacist 1–2 and 3–5 weeks after filling the prescription using a semi-structured interview.	At 1–2 weeks and 3–5 weeks after filling their prescription for the first time	7 weeks 18 weeks 52 weeks	MMAS-8 and MPR	91.3% of the patients in the intervention group were adherent after 7 weeks versus 86.8% in the control group (P = 0.017), and 88.7% versus 83.7% after 18 weeks (P = 0.021). According to MPR data there were no significant difference in adherence after 52 weeks (P = 0.24)
Mehuys E et al (2008)[76]	Asthma	Community pharmacy	94 (CG) 107 (IG)	Counselling (educational and behavioral), tailored intervention based on the ACT score	At 1 months and 3 months	6 months	Prescription refill rates dan self-reporting	Medication adherence as judged by the prescription refill rates, was higher in the intervention group compared with the control group (mean adherence rate 90.3 versus 74.6%; P = 0.016). However, there was no significant between-group difference in medication adherence as assessed by self-reporting (P = 0.108)
Odegard P et al (2005)[68]	Diabetes	Clinic	34 (CG) 43 (IG)	Tailored intervention using diabetes care plan (DCP)	Weekly in person or telephone meetings	6 months 12 months	Self-reported	Self-reported adherence was not significantly improved by the intervention.
Mehuys E et al (2011)[75]	Diabetes	Community pharmacy	135 (CG) 153 (IG)	Counselling (educational and behavioral)	At each prescription-refill visit	6 months	Prescription refill rates dan self-reporting	There was no significant difference between interventions carried out by pharmacists and the medication adherence
Stewart K et al (2014)[90]	Hypertension	Community pharmacy	188 (CG) 207 (IG)	Package comprising BP monitor, training on BP, self-monitoring, motivational interviewing, medication use review, and prescription refill reminders.	At baseline, 3 months, and 6 months	6 months	Morisky	The proportion of adherent participants increased in both groups but was not significantly different between groups [57.2% to 63.6% (control) vs 60.0% to 73.5% (intervention), P = 0.23]
Saleem F et al (2015)[86]	Hypertension	Hospital	192 (CG) 193 (IG)	Educational module	Twice per month	9 months	DAI-10	Medication adherence improved in the intervention group, as the post-intervention analysis revealed an increase in medication adherence scores (P < 0.001).
Mehos B et al (2000)[69]	Hypertension	Home	18 (CG) 18 (IG)	Home blood pressure monitoring	Monthly scheduled visits	6 months	Pill counts	There was no significant difference between the group (P = 0.29)
Tommelein E et al (2014)[77]	COPD	Community pharmacy	363 (CG) 371 (IG)	Counselling (educational and behavioral) in two session with verbal and written form	At the start of the study and at the 1 month follow-up visit	3 months	MRA	Medication adherence (8.51%; 95% CI, 4.63–12.4; P < 0.001) were significantly higher in the intervention group compared with the control group.

(*Continued*)

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Table 4 (Continued).

Study	Disease of Interest	Setting	Sample size	Intervention vs Usual Care	Follow-Up Intervention	Follow-Up Outcome Measurement	Adherence Measure	Results
Bouvy M et al (2003)[79]	Heart Failure	Hospital	78 (CG) 74 (IG)	Counselling with pharmacists about drug use, reasons for noncompliance such as possible adverse drug reactions and difficulties to integrate medication use in daily life.	Monthly scheduled visits	6 months	MEMS	The average duration of MEMS use was 143.6 days in the usual care group and 163.3 days in the intervention group.
Aslani P et al (2011)[78]	Dyslipidemia	Community pharmacy	49 (CG) 48 (IG)	Targeted individualized interventions to address barriers to patient adherence	At baseline, 3 months, and 6 months	9 months	BMQ, MARS	There was no significant difference between intervention group and control group.
Jahangard-Rafsanjani Z et al (2015)[87]	Diabetes	Community pharmacy	40 (CG) 45 (IG)	Counselling and education about medications, clinical goals, self-care activities, and self-monitoring of blood glucose.	Monthly scheduled visits	5 months	Morisky	Medication adherence was significantly improved in the intervention group at the end of study (P = 0.02)
Jarab A et al (2012)[88]	COPD	Clinic	67 (CG) 66 (IG)	A structured education about COPD and management of its symptoms.	No follow-up	6 months	Morisky	There was a significant difference in the percentage (P < 0.05) of low medication adherence between the intervention group (28.6%) and the control group (48.4%) after the intervention.
Blackburn D et al (2016)[70]	Cardiovascular disease	Community pharmacy	999 (CG) 907 (IG)	Tailored intervention using the Community Pharmacists Assisting in Total Cardiovascular Health (CPATCH) protocol	Monthly scheduled visits	12 months	PDC	There was no significant differences in mean adherence were observed between those receiving the intervention and those receiving usual care (70.9% vs 71.6%, P = 0.64)
Hedegaard U et al (2015)[80]	Hypertension	Hospital	285 (CG) 231 (IG)	Medication review and tailored intervention including motivational interviewing and telephone follow-ups	Two or more follow-up telephone calls	12 months	MPR	There was a significant difference in the percentage (P = 0.01) of low medication adherence between the intervention group (20.3%) and the control group (30.2%) after administering the intervention.
Simon M et al (2021)[89]	Diabetes	Hospital	48 (CG) 49 (IG)	Counselling session (20 minutes) including patients education and patient information leaflets.	No follow-up	6 months	MARS	There was significant increase of mean MARS score during follow-up in intervention group when compared to control group (P < 0.05)
Murray M et al (2007)[62]	Heart Failure	Hospital	192 (CG) 120 (IG)	A pharmacist providing verbal and written education, icon-based labeling of medication containers, and therapeutic monitoring.	Monthly by telephone calls	12 months	MEMS	There was a difference in the level of adherence in patients in the control group (67.9%) compared to the intervention group (78.8%) after 9 months of intervention [95% CI, 5.0 to 16.7]
O'Dwyer S et al (2020)[81]	Asthma	Community pharmacy	22 (CG) 74 (BG) 56 (DG)	A biofeedback group received personalized inhaler training informed by data recorded by the device. The demonstration group received inhaler training, by physical demonstration with a placebo inhaler.	Beginning of month 1, end of month 1, and end of month 2	2 months 6 months	INCA	During month 6, adherence was 14% higher (95% CI, −1 to 30; P = 0.07) in the biofeedback group than in the demonstration group and 31% higher (95% CI, −3 to 48; P = 0.001) than in the control group.

Abbreviations: CG, control group; IG, intervention group; BG, biofeedback group; DG, demonstration group; MAQ, medication adherence questionnaire; GMAS, general medication adherence scale; MGL-MAQ, morisky green levine medication adherence questionnaire; MMAS, morisky medication adherence scale; GMAS, general medication adherence scale; MARS, medication adherence rating scale; MPR, medication possession ratio; DAI, drug attitude inventory; MRA, medication refill adherence; MEMS, medication event monitoring systems; BMQ, belief medication questionnaire; PDC, proportion of days covered; INCA, inhaler compliance assessment; CI, confidence interval.

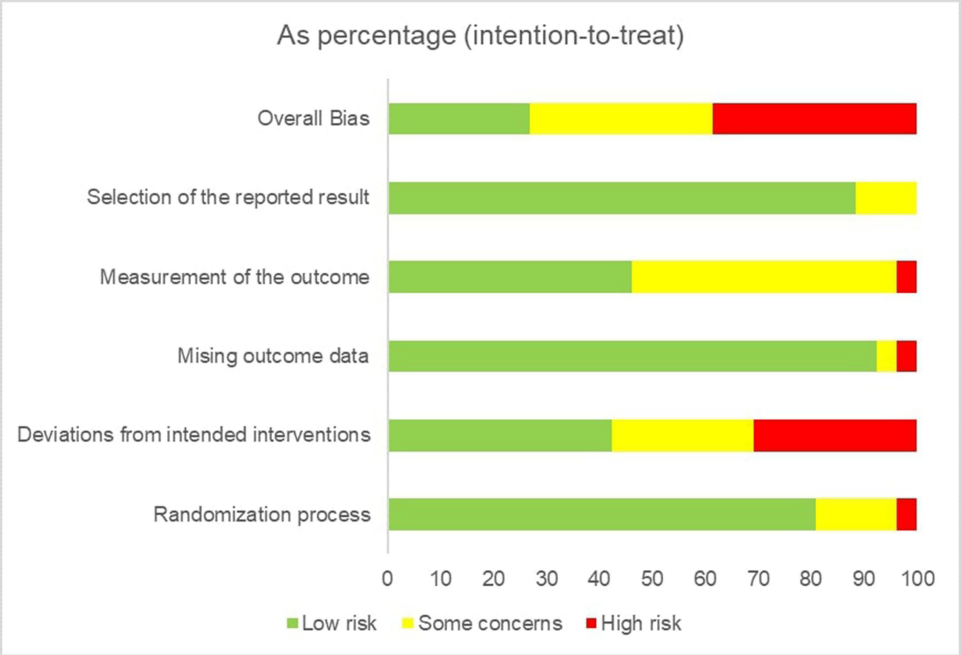

Figure 2 Overall risk of bias.

prone to being influenced by patients' knowledge resulting from the interventions received. The use of an objective measurement tool was recommended to minimize potential bias in assessments. In this study, the evaluation revealed that only 11 out of 26 studies had registered their study protocols.[32,69,70,72,77,80–82,85,87,89]

Discussion

This systematic review summarized the evidence from RCTs collectively evaluating pharmacist-led interventions to improve medication adherence in patients with chronic diseases. Of the 26 studies included, 18 demonstrated that pharmacist-led interventions significantly improved medication adherence.[32,67,71–73,76,77,80–90] A total of 7 studies indicated that the intervention was not effective.[68–70,75,78,90,91] Meanwhile, a study reported that pharmacist-led intervention made a difference, though the level of significance was unknown.[79] The characteristics of these interventions varied, but there were some consistencies between the studies selected for review.

The most common intervention to improve medication adherence was through counselling by pharmacists, including educational and behavioral elements. A larger number of studies indicated that adding a behavioral component (eg smoking cessation,[77] physical activity,[82] healthy diet[71,75,83–85,88,89]) to education could optimize effects on medication adherence. Similarly, Presley et al (2019) observed that the combined intervention strategy incorporating both educational and behavioral components was the most frequently used intervention approach and was effective in improving HbA1c levels in patients with diabetes mellitus.[44] Moreover, most included studies showed that pharmacist counselling was effective at improving medication adherence. This finding was consistent with a meta-analysis by Kelly et al (2023) which focused on counselling interventions and reported a significant increase in the odds of medication adherence among patient received counseling intervention (pooled odds ratio [OR] = 4.41; 95% confidence interval [CI] 2.46–7.91; $P < 0.01$)[93] The study conducted by Mehuys et al (2011) using the same type of intervention showed no significant improvement in adherence. This could occur because medication adherence during the study was very high in both groups (control=94.7%, intervention=99.7%), leaving minimal opportunity for further improvement.[75] However, counselling was easy to implement, being relatively low-cost and effective. Counselling could also positively influence patient satisfaction and knowledge.

Based on a previous study on technology-based monitoring, in the form of blood pressure monitoring and reminder-based systems using telephone calls by pharmacists, no significant effect on medication adherence was found.[69]

https://doi.org/10.2147/PPA.S530503

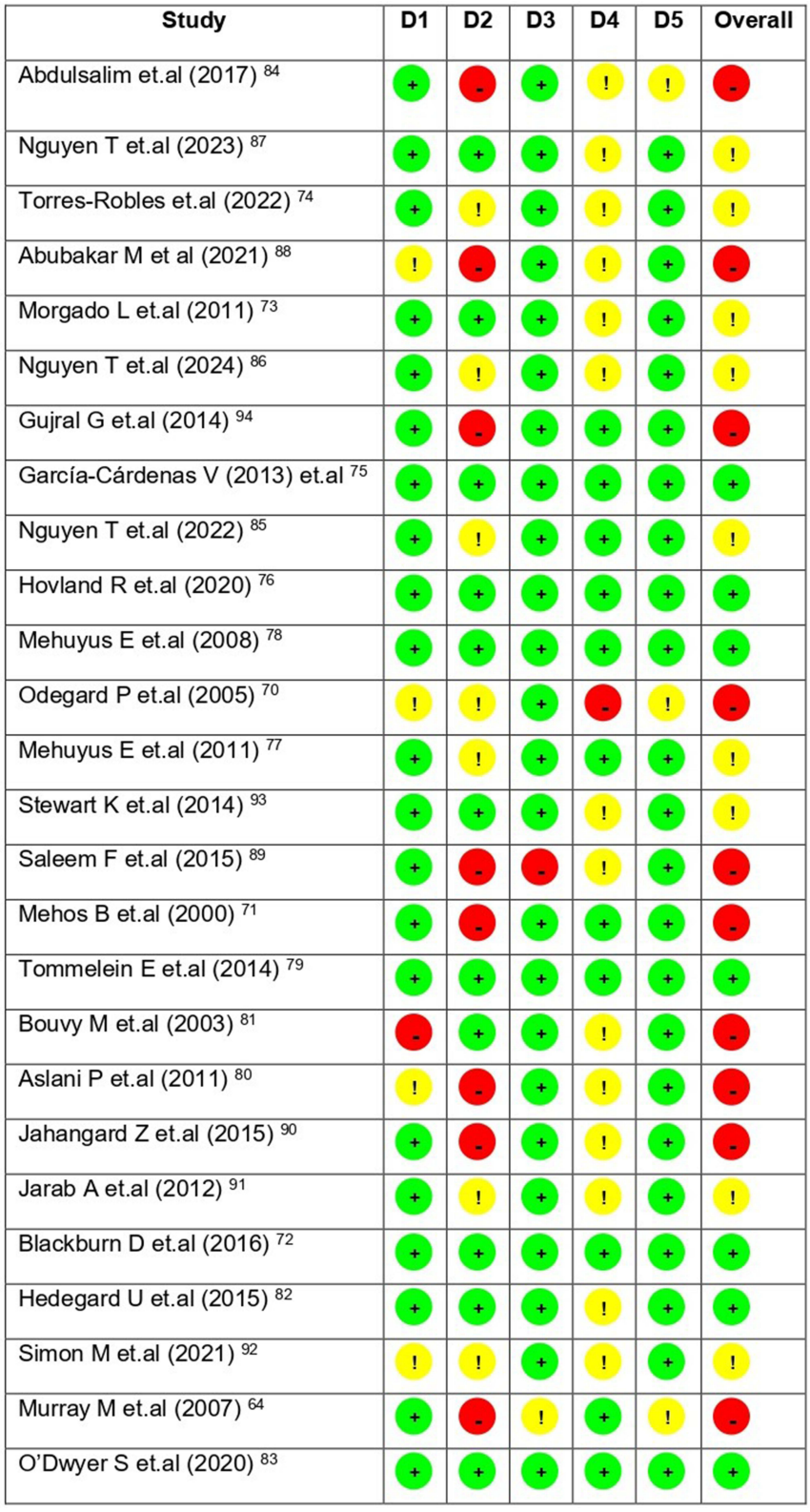

Figure 3 Risk of bias for individual studies.

Medication adherence in both groups were similar and high (>80%).[69] This could be explained in part because both groups received initial counseling by the clinical pharmacist after enrollment. However, patients with home blood pressure monitoring exhibited significant improvements in blood pressure control.[69] The findings of this study were consistent with the existing literature. Chun-Yun et al (2022) suggested that the use of a patient reminder system alone was not effective in improving adherence.[94] Emerging technology-based interventions like artificial intelligence (AI) and blockchain showed potential in medication adherence.[95–97] AI could enhance medication adherence through personalized education and reminders.[95–98] Meanwhile, blockchain supported patient-centered healthcare by improving data integrity, transparency, security, and interoperability.[96,97] RCT evidence remained limited at this stage.[95,97,99] Meta-analyses studies conducted by Miao et al (2024) observed that combined technology-based intervention was the most effective in improving medication adherence in patients with cardiovascular diseases.[100] This indicated the need for complementary strategies, such as counseling, to enhance the effectiveness of technology-based monitoring.[100]

A systematic review conducted by Dean et al (2010) revealed that single interventions were often insufficient to improve medication adherence.[47] Consequently, the use of multiple interventions had become increasingly common, as it was considered more effective in maximizing the success of adherence improvement programs. These approaches included counseling that incorporated educational and behavioral elements and tailored interventions.[32,62,76] Stewart et al (2014) used technology-based intervention, medication regimen management, medication taking reminders, and motivational interviewing to improve clinical outcomes for hypertension patients.[90] Several disadvantages were observed, while multiple interventions were considered more effective. Multiple interventions was complex and costly, making efficiency a key consideration.[101] Therefore, it was essential to ensure that the selected interventions were practical, easily implementable, and applicable in real-world settings.

Medication adherence was influenced by several factors, and the barriers experienced by patients were equally diverse. One of the approaches to addressing these challenges was through tailored interventions, which enabled pharmacists to effectively overcome barriers contributing to non-adherence and resolved misunderstandings. These interventions were provided based on the type of non-adherence,[72] barriers to medication use, drug-related problems,[80] patients' beliefs about their medications,[91] and protocol-based intervention.[68,70] In several studies, pharmacists used motivational interviewing to strengthen personal motivation and commitment toward achieving treatment goals.[72,80] Providing emotional support and motivation was shown to increase patients' desire to recover and strengthen their commitment to adhering to therapeutic recommendations.[91] Application of the transtheoretical model of behavioral change, where pharmacists assessed patients' readiness to change while discussing proposed strategies, could improve the effectiveness of tailored interventions.[72] Negative findings were reported in a study by Gujral et al (2014), which implemented a tailored intervention based on patients' medication beliefs.[91] Although the intervention was personalized to individual beliefs, the study did not identify the underlying reasons for non-adherence. As a result, the intervention did not lead to improvements in medication adherence.[91] The approach was more efficient because pharmacist-led interventions specifically targeted the barriers experienced by each patient, requiring less time and fewer resources compared to other interventions. Moreover, tailored interventions were proven to be cost-effective, making this strategy a solution for optimizing medication adherence.[102]

Although the majority of studies in this systematic review demonstrated that pharmacist-led interventions could improve adherence, 7 studies reported no significant difference between pharmacist interventions and adherence levels. Interestingly, 4 out of these 7 studies used objective adherence measurement methods,[69,70,75,91] which was an approach that did not rely on patient self-reports or subjective perceptions, thereby reducing the risk of patients overestimating their adherence levels. While more accurate than subjective methods, objective adherence measurement was less commonly used due to its relatively complex nature. Self-reported adherence resulted in overestimation of the patient's adherence, as patients often gave socially desirable answers. However, studies using subjective adherence measurement methods must not be automatically deemed biased, as some also evaluated other outcomes, such as blood pressure in hypertensive patients, which showed significant reductions.[71,72] This indicated that pharmacist-led interventions could contribute to improved disease management, likely associated with increased adherence to therapy. Meanwhile, the ineffectiveness of some interventions could be attributed to the limited time and skills of pharmacists in delivering these interventions.[41,103]

Strengths and Limitations

This systematic review provided a comprehensive and up-to-date overview of intervention strategies that could be used to improve adherence in patients with chronic diseases. Several limitations of this systematic review were observed. Initially, this systematic review included the diverse quality of the RCT studies. Due to the diversity of the studies included regarding the type of intervention, the results, design, methodological quality, as well as power and method of adherence measurement, it was impossible to assess the overall impact of adherence-enhancing interventions conducted by pharmacists. Second, geographic bias represented a notable limitation, as the majority of the included studies were conducted in Europe and the United States. This could be attributed to the more established and progressively expanding role of pharmacists in these regions. In addition, grey literature such as study reports, dissertations, and conference proceedings were not included in this review. By excluding these sources, the ability to fully capture the available evidence was limited.

Conclusion

In conclusion, this review confirmed that pharmacist-led interventions, particularly counseling with behavioral components and tailored strategies, could significantly improve medication adherence in chronic disease. Variability in outcomes existed due to differences in intervention design and adherence measurement methods. Notably, tailored interventions that addressed patient-specific barriers demonstrated higher efficiency, as more time, resources, and costs were saved, emphasizing the importance of tailored approaches. However, 38% of studies had a high risk of bias, revealing the importance of rigorous RCT designs in future studies. These findings supported integrating pharmacists into chronic disease management teams, potentially reducing complications and healthcare costs. Therefore, prioritizing tailored, scalable interventions and standardized adherence metrics was critical for advancing the field.

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Disclosure

The authors confirm that this study was conducted without any commercial or financial involvement that could be interpreted as a potential conflict of interest.

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