International Journal of Chronic Obstructive Pulmonary Disease

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REVIEW

Pharmacist-Led Integrated Management for Patients with Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis

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Purpose: Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality worldwide, and suboptimal medication management contributes to exacerbations and preventable healthcare utilization. Pharmacist-led integrated care has the potential to improve medication use and clinical outcomes. We conducted a systematic review and meta-analysis to evaluate the effects of pharmacist-led interventions in COPD.

Methods: This systematic review and meta-analysis was conducted and reported in accordance with PRISMA 2020. We searched PubMed, Embase, and Web of Science from inception until June 23, 2025. Randomized controlled trials (RCTs) assessing the effects of pharmaceutical care on clinical outcomes in COPD patients were included. A random-effects model was used to estimate pooled relative risks (RRs) or mean differences (MDs) with 95% confidence intervals (CIs). Risk of bias was assessed using the Cochrane Risk of Bias tool.

Results: A total of 11 randomized controlled trials involving 2313 participants were included. Pharmacist-led interventions were associated with a lower risk of exacerbation-related hospital admissions (RR = 0.43, 95% CI: 0.33–0.55). Improvements in medication adherence and higher smoking cessation rates were also observed. Improvements in health-related quality of life were reported; however, substantial heterogeneity was present. In contrast, effects on COPD Assessment Test scores and objective disease measures, including lung function, were non-significant. Overall study quality was variable, with many trials being small and at high risk of bias.

Conclusion: Pharmacist-led interventions in COPD may improve selected medication-related and patient-centered outcomes; however, the available evidence is heterogeneous and limited by study quality and inconsistent effects across outcomes. These findings should be interpreted cautiously, and well-designed, adequately powered trials with standardized outcomes are needed before robust conclusions regarding clinical effectiveness can be drawn.

Keywords: COPD, pharmacist-led integrated management, randomized controlled trials, meta-analysis

Introduction

Chronic obstructive pulmonary disease (COPD) is a common chronic airway disease characterized by persistent airflow limitation, chronic respiratory symptoms and structural pulmonary abnormalities.[1] It has become a major public health issue worldwide, with significant epidemiological impact.[2] COPD affects more than 400 million people globally and is the third leading cause of death worldwide,[3,4] responsible for over 3 million deaths annually.[5] The economic burden is equally substantial, with estimated global costs INT$4.326 trillion in 2020–50.[6] In China, the situation is particularly severe, with nearly 100 million people affected,[7] placing immense pressure on the healthcare system and society. Improving treatment outcomes for these patients is therefore urgently needed.

https://doi.org/10.2147/COPD.S589904
Received: 29 December 2025
Accepted: 22 March 2026
Published: 16 April 2026

To effectively manage symptoms, patients with COPD often require long-term adherence to inhalation therapy. However, despite considerable evolution in inhalation therapies, more than half of patients make critical errors in their use, and medication adherence remains poor.[8–10] Compounding this issue, COPD patients often face polypharmacy due to frequent comorbidities, which increases the risk of adverse drug reactions, interactions, and overall treatment complexity.[11] These challenges contribute to suboptimal disease control, reduced quality of life, and a higher risk of exacerbations and hospitalizations.[12,13] Consequently, enhancing inhaler technique, adherence, and overall medication management is essential to improving prognosis.

Given their expertise in pharmacotherapy, clinical pharmacists are well-positioned to deliver value-added services such as medication management and adherence support for patients with chronic conditions including COPD, potentially leading to improved health outcomes. For instance, pharmacists can provide structured education on proper inhaler use, explain the purpose of treatment, dosing frequency, potential side effects, and drug interactions. They can also offer counseling on lifestyle modifications and continuous adherence support.[14] Through improving effective drug delivery and persistence with maintenance therapy, such interventions may enhance real-world treatment effectiveness and reduce exacerbation-related utilization. Although randomized controlled trials (RCTs) have evaluated pharmacist-led interventions in COPD, existing evidence syntheses have limitations.

Several systematic reviews[15] and meta-analyses have examined pharmacist-led interventions in patients with COPD. Earlier reviews primarily focused on specific aspects of care, such as medication adherence, inhaler technique, or health-related behaviors, and many are now outdated.[16] More recent reviews have provided valuable summaries of pharmacist involvement in COPD management; however, these syntheses often included a limited range of outcomes,[17] placed less emphasis on exacerbation-related healthcare utilization, or did not comprehensively integrate multiple clinically relevant endpoints. In addition, prior reviews generally provided limited critical appraisal of between-study heterogeneity arising from differences in intervention components, follow-up duration, outcome measurement tools, and healthcare settings. As a result, uncertainty remains regarding the consistency and strength of evidence supporting pharmacist-led integrated management across key clinical outcomes.

To address these gaps, we conducted an updated systematic review and meta-analysis of randomized controlled trials to comprehensively synthesize evidence across exacerbation-related healthcare utilization, quality of life, symptom burden, medication adherence, and smoking cessation, while explicitly considering heterogeneity and study quality.

Methods

The protocol for this systematic review has been registered with PROSPERO (CRD420251274607). This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[18] See eTable 1 for details.

Search Strategy

Two independent investigators conducted a systematic literature search in the following electronic databases: Embase, PubMed, and Web of Science. The search period spanned from the establishment of each database to June 23, 2025. The search strategy incorporated a combination of keywords and MeSH terms related to "pharmaceutical care" and "COPD", along with their synonyms and variations. The search was restricted to RCTs. Furthermore, the reference lists of all retrieved articles and relevant reviews were manually screened to identify additional eligible studies. The complete search strategies for each database are provided in eTable 2.

Eligibility Criteria

RCTs investigating the effects of pharmaceutical care on outcomes in patients with COPD were included. The exclusion criteria were as follows: (1) non-randomized studies; (2) studies involving non-pharmacist-led interventions; (3) duplicate publications.

Data Extraction and Quality Assessment

Two reviewers independently extracted data from each included study using a pre-designed data extraction form. The following information was collected: (1) first author, publication year, and country; (2) study design, duration, and all primary and secondary outcomes; (3) intervention and comparator group details, including number of patients and baseline characteristics (eg, mean age).

The methodological quality and risk of bias of the included studies were assessed independently by two reviewers using the Cochrane Risk of Bias Tool (RoB 1). The tool evaluates the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other potential sources of bias. Each domain was rated as having low, unclear, or high risk of bias.

Data Analysis

Meta-analyses were conducted using Review Manager (RevMan) software version 5.4 when at least three studies provided sufficient and comparable outcome data. Random-effects models were applied to incorporate potential between-study heterogeneity. For dichotomous outcomes, results were pooled and expressed as risk ratios (RR) with 95% confidence intervals (95% CIs). For continuous outcomes, mean differences (MD) and 95% CIs were calculated. When continuous outcomes were reported as medians and interquartile ranges (IQRs), means and standard deviations (SD) were estimated using validated methods[19,20] to enable inclusion in the meta-analysis.

Heterogeneity was assessed using the I^2 statistic. I^2 values were interpreted as follows: 0%-40% indicated negligible heterogeneity, 30%-60% moderate heterogeneity, 50%-90% substantial heterogeneity, and 75%-100% considerable heterogeneity.[21] A p value < 0.05 was considered statistically significant.

Results

Literature Screening

A total of 811 references were identified through electronic searches. From these references, 11 studies met the inclusion criteria and were selected for our study. The details of the selection process were summarized in Figure 1.

Study Characteristics

The pooled analysis included a total of 2313 patients with COPD. The mean age of participants was consistently greater than 60 years across all studies, indicating a geriatric population. In addition, the studies demonstrated a multicenter international representation, encompassing a total of 7 countries across Asia, Europe, and the Middle East. The majority of studies were

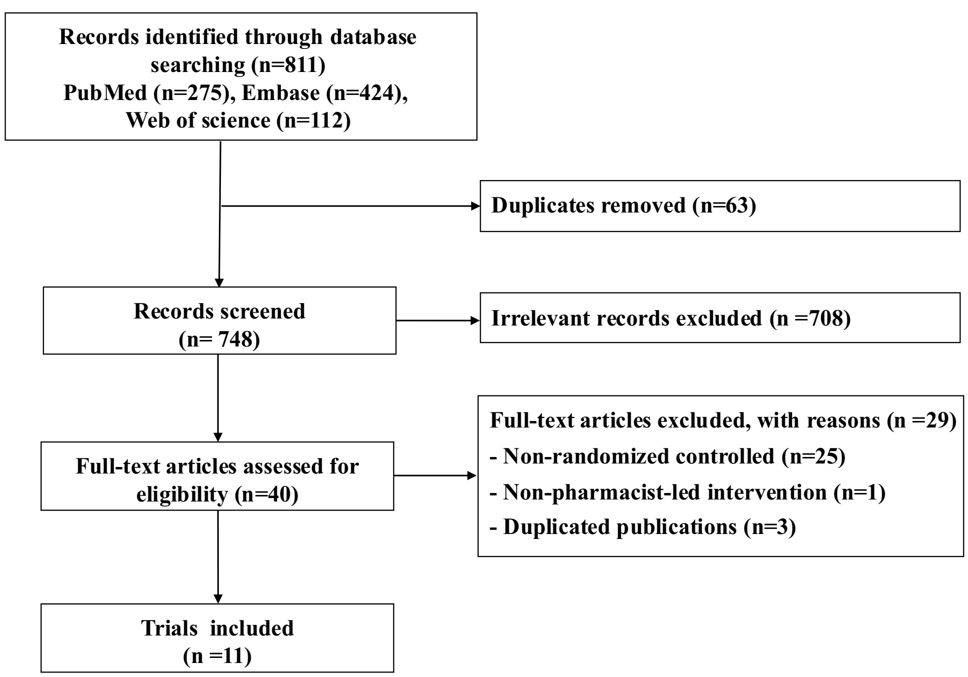

Figure 1 Flow diagram of studies that were assessed and included.

https://doi.org/10.2147/COPD.S589904

conducted in Asia (n=7), with specific contributions from China (n=3), India (n=2), and Vietnam (n=2). European countries (n=3), including Belgium, Norway, and Northern Ireland, and one study from Jordan in the Middle East were also represented. The sample sizes varied widely, ranging from 40 participants to 734 participants. The duration of the interventions and follow-up also differed considerably, spanning from short-term studies to long-term trials, with the most common durations being 6 and 12 months. The characteristics of the included trials are summarized in Table 1.

Quality Assessment of the Included Studies

A prevalent limitation across the included RCTs was the high risk of blinding due to the inherent challenges in blinding the intervention, as the nature of pharmacist-led education and counseling precludes complete masking. The result of the risk of bias assessment is shown in eFigures 1 and 2.

Interventions

A review of the literature reveals that pharmaceutical interventions for COPD, despite being implemented across diverse countries, consistently employ a highly similar and comprehensive model of care. The cornerstone of this model is inhaler technique training, which typically involves pharmacist demonstration, patient practical operation, and assessment using standardized checklists, supplemented with written instructions. This core component is systematically integrated with other essential elements, including disease and medication education, medication adherence counseling, and respiratory self-management training. In addition, the interventions are further supported by lifestyle counseling on smoking cessation, physical activity, and diet, and conclude with follow-up visit education to ensure continuity of care. A detailed breakdown of these interventions is provided in Table 2.

Outcomes

The findings suggest potential benefits of pharmaceutical care interventions across several outcome domains, although effects varied by endpoint. The detailed results for each outcome are presented below.

Clinical Measures

Pharmaceutical care interventions were associated with reductions in severe exacerbations across contributing trials, a key clinical endpoint in COPD management. The number of patients experiencing one or more severe exacerbations was significantly lower in the intervention groups compared to usual care as evidenced by individual study results (Tommelein 2013:[24] 19/371 vs 33/363, $p = 0.038$; Xin 2016:[26] 14/114 vs 28/113, $p = 0.024$). In contrast, the interventions showed a limited effect on objective physiological measures. Although Forced Expiratory Volume in 1 second (FEV1) values were numerically higher in the intervention groups across studies, these differences did not reach statistical significance (Khdour 2009:[22] 1.19 vs 1.05, $p = 0.13$; Jarab 2012:[23] 1.15 vs 1.06, $p = 0.55$).

The effects on patient-reported symptoms were mixed. One study found a reduction in the proportion of patients experiencing significant dyspnea (Modified Medical Research Council (mMRC) ≥ 2) following the intervention (Nguyen 2024:[33] 46/91 vs 65/89, $p = 0.002$), while another found no between-group difference (Tommelein 2013:[24] 130/346 vs 125/346, $p = 0.973$). The pooled estimate suggested no consistent improvement in COPD Assessment Test (CAT) score (Mean difference = −2.61, 95% CI: −7.38 to 2.15; $I^2 = 98\%$; $p = 0.28$; 3 studies[24,30,33]). The extremely high heterogeneity indicates that the pooled result may not reflect a common underlying treatment effect and should therefore be interpreted with considerable caution (Figure 2). The effects of pharmaceutical care on clinical measures of COPD patients were summarized in eTable 3.

Healthcare Utilization

Pharmaceutical care was associated with reductions in selected healthcare resource utilization outcomes. Meta-analysis showed that hospital admissions for acute exacerbations of COPD (AECOPD) were significantly reduced in the intervention groups (RR = 0.43, 95% CI: 0.33 to 0.55; $I^2 = 0\%$; $p < 0.001$; N = 5 studies[22–26]) with no heterogeneity observed (Figure 3). In contrast, the evidence regarding emergency department (ED) visits was less conclusive, with one

Table 1 Characteristics of the Included Studies

Study	Country	Study Design	Duration	Primary Outcome	Secondary Outcome	Interventions Arms	N	Age (y), Mean (SD) or Median (IQR)
Khdour 2009[22]	Northern Ireland	RCT	12	1) Hospital admissions for AECOPD 2) ED visits for AECOPD	1) QoL assessed by SGRQ 2) Medication adherence assessed by MMAS-4 3) FEV1 4) Knowledge scores assessed by COPD knowledge questionnaire developed by Scherer et al 5) BMI 6) Number of quit smoking	1) Inhaler technique training 2) Disease & medication education 3) Medication adherence counseling 4) Respiratory self-management training 5) Lifestyle counseling	86	65.63 (10.1)
						Usual care	87	67.3 (9.2)
Jarab 2012[23]	Jordan	RCT	6	QoL assessed by SGRQ	1) Hospital admissions for AECOPD 2) ED visits for AECOPD 3) Medication adherence assessed by MMAS-4 4) FEV1 5) Knowledge scores assessed by COPD knowledge questionnaire developed by Scherer et al 6) BMI	1) Disease & medication education 2) Medication adherence counseling 3) Respiratory self-management training 4) Lifestyle counseling	66	61 (14) †
						Usual care	67	64 (15) †
Tommelein 2013[24]	Belgium	RCT	3	1) Inhalation technique assessed by checklist 2) Medication Adherence assessed by MRA	1) Hospital admissions for AECOPD 2) QoL assessed by EQ-5D 3) Dyspnoea assessed by mMRC 4) COPD-specific health status assessed by CAT 5) Patients with Severe exacerbations 6) Number of quit smoking	1) Inhaler technique training 2) Disease & medication education 3) Medication adherence counseling 4) Lifestyle counseling	371	68.4 (9.6)
						Usual care	363	68.9 (9.7)
Wei 2014[25]	China	RCT	12	Medication adherence assessed by pill counts plus direct interview	1) Hospital admissions for AECOPD 2) QoL assessed by SGRQ	1) Inhaler technique training 2) Disease & medication education 3) Medication adherence counseling	58	65.2 (8.1)
						Usual care	59	63.9 (6.2)
Xin 2016[26]	China	RCT	12	1) Medication Adherence assessed by MRA 2) QoL assessed by SGRQ	1) Hospital admissions for AECOPD 2) Patients with Severe exacerbations 3) Number of quit smoking	1) Inhaler technique training 2) Disease & medication education 3) Medication adherence counseling 4) Lifestyle counseling 5) Follow-up visit education	114	64.2 (14.2)
						Usual care	113	64.6 (14.5)

(*Continued*)

https://doi.org/10.2147/COPD.S589904

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Table 1 (Continued).

Study	Country	Study Design	Duration	Primary Outcome	Secondary Outcome	Interventions Arms	N	Age (y), Mean (SD) or Median (IQR)
Abdulsalim 2016; 2018[27,28]	India	RCT	24	1) QoL assessed by SGRQ[27] 2) Medication adherence assessed by MMAS-4[28]	-	1) Inhaler technique training 2) Disease & medication education 3) Medication adherence counseling 4) Respiratory self-management training 5) Lifestyle counseling 6) Follow-up visit education	130	60.6 (7.9)
						Usual care	130	61.1 (8.4)
Bui 2020[29]	Vietnam	RCT	3	QoL assessed by validated Vietnamese version of the CCQ	-	1) Inhaler technique training 2) Disease & medication education 3) Medication adherence counseling 4) Lifestyle counseling	92	63.80 (9.96)
						Usual care	93	66.08 (8.67)
Liu 2021[30]	China	RCT	6	DDDs of antibacterials	1) Length of stay 2) Costs of hospitalization 3) Cases of adverse drug reactions 4) Medication adherence assessed by MMAS-8 5) COPD-specific health status assessed by CAT	Comprehensive MTM	96	75.13 (8.03)
						Usual care	97	73.25 (7.45)
Vastrad 2021[31]	India	RCT	1	QoL assessed by WHOQOL	-	Pharmaceutical care	35	-
						Usual care	35	-
Kebede 2022[32]	Norway	RCT	12	Time to readmission	COPD-specific health status assessed by CAT	Inhaler technique training	20	Female 73.1 (9.1) Male 73.4 (7.4)
						Usual care	20	Female 74.4 (9.7) Male 74.5 (6.1)
Nguyen 2024[33]	Vietnam	RCT	1	Medication adherence assessed by General Medication Adherence Scale	1) Dyspnoea assessed by mMRC 2) COPD-specific health status assessed by CAT 3) Inhalation technique assessed by checklist	1) Inhaler technique training 2) Disease & medication education 3) Medication adherence counseling 4) Respiratory self-management training 5) Lifestyle counseling 6) Follow-up visit education	92	65.2 (9.5)
						Usual care	89	66.6 (7.0)

Notes: †Values are presented as median (interquartile range). References[27,28] and report different outcomes from the same randomized controlled trial conducted by Abdulsalim et al.
Abbreviations: RCT, Randomized Controlled Trial; AECOPD, Acute Exacerbation of COPD; ED, Emergency Department; QoL, Quality of Life; SGRQ, St. George's Respiratory Questionnaire; MMAS, Morisky Medication Adherence Scale; FEV1, Forced Expiratory Volume in 1 second; BMI, Body Mass Index; MRA, Medication Refill Adherence; mMRC, Modified Medical Research Council; CAT, COPD Assessment Test; CCQ, Clinical COPD Questionnaire; DDD, Defined Daily Dose; MTM, Medication Therapy Management; WHOQOL, World Health Organization Quality of Life.

Table 2 Summary of Pharmacist-Led Interventions in Included Trials

Intervention	Items
Inhaler technique training	1) Pharmacist demonstration 2) Patient practical operation 3) Register patient's inhaler technique through Standardized checklists 4) Written information for inhaler technique
Disease & medication education	1) Disease knowledge encompasses the definition of COPD, the disease's pathophysiology, the interpretation of medical tests, and the rationale behind medications 2) The types, indications, doses, frequency of administration, as well as the recognition and prevention of possible side effects for each prescribed medication, along with the potential effects of drug combinations
Medication adherence counseling	1) The importance of adherence 2) Current problems with adherence
Comprehensive MTM	Standard services provided by clinical pharmacists, such as pharmacy consulting, medication monitoring, and medication education for patients
Respiratory self-management training	1) Self-efficacy in managing dyspnea 2) Upper and lower limb exercises and relaxation techniques 3) Symptom management such as pursed-lip breathing technique 4) Sputum expectoration technique such as huff cough technique 5) Importance of basic exercises, symptom management and sputum expectoration techniques
Lifestyle counseling	1) Smoking cessation 2) Exercise habit 3) The importance of a well-balanced diet with sufficient intake of fresh fruits and vegetables
Follow-Up visit education	1) The necessity of timely follow-up by physicians 2) How to prevent covid-19 when follow-up visiting

study reporting significant reductions (Khdour 2009,[22] $p = 0.02$), although another study found no significant difference (Jarab 2012,[23] $p = 0.79$).

Furthermore, the intervention led to more efficient and safer use of resources. The intervention group had a significantly shorter mean length of hospital stay (11.27 vs 13.46 days, $p < 0.05$[30]), lower hospitalization costs (13405.45 vs 14856.51 RMB, $p < 0.05$[30]), reduced antibacterial consumption (121 vs 189 defined daily doses [DDDs], $p < 0.05$[30]), and fewer cases of adverse drug reactions (9 vs 23, $p < 0.01$[30]) (Liu 2021). There was no statistically significant effect on the time to readmission (Kebede 2022:[32] 41 vs 95 days, $p = 0.16$). The effects of pharmaceutical care on healthcare utilization and costs of COPD patients were summarized in eTable 4.

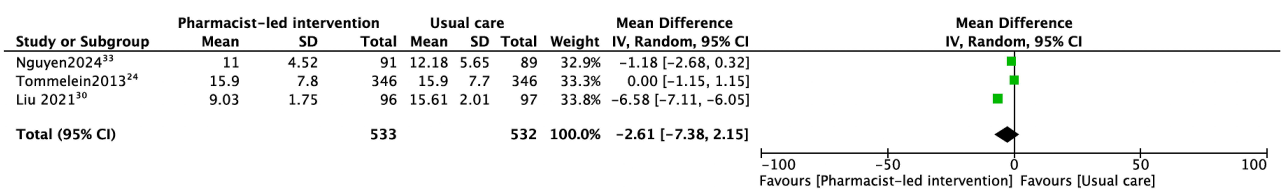

Figure 2 Forest plot of comparison on COPD-specific health status assessed by CAT. Mean differences (MD) with 95% confidence intervals (CI) were pooled using the inverse variance (IV) method under a random-effects model. The size of each square reflects the weight assigned to each study, and horizontal lines indicate 95% CIs. The diamond represents the pooled estimate of the overall effect. Between-study heterogeneity was high ($Tau^2 = 17.40$; $Chi^2 = 130.95$, $df = 2$, $P < 0.00001$; $I^2 = 98\%$). The overall effect was not statistically significant ($Z = 1.08$, $P = 0.28$).
Abbreviations: CI, confidence interval; df, degrees of freedom; IV, inverse variance; SD, standard deviation; MD, mean difference.

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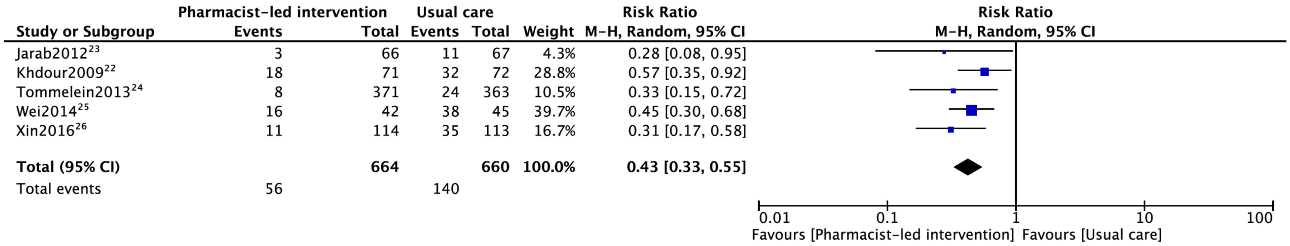

Figure 3 Forest plot of comparison on hospital admissions for AECOPD. Risk ratios (RR) with 95% confidence intervals (CI) were pooled using the Mantel–Haenszel (M–H) method under a random-effects model. The size of each square reflects the weight assigned to each study, and horizontal lines represent 95% CIs. The diamond represents the pooled estimate of the overall effect. Between-study heterogeneity was low ($Tau^2 = 0.00$; $Chi^2 = 3.56$, $df = 4$, P = 0.47; $I^2 = 0\%$). The pooled analysis showed a statistically significant reduction in risk in the intervention group (RR = 0.43, 95% CI 0.33–0.55; Z = 6.49, P < 0.00001).
Abbreviations: CI, confidence interval; df, degrees of freedom; M–H, Mantel–Haenszel; RR, risk ratio.

QoL

Improvements in QoL were reported in several trials; however, heterogeneity across instruments and studies was substantial. The pooled analysis using the St. George's Respiratory Questionnaire (SGRQ) showed improvement (Mean difference = −6.04, 95% CI: −11.10 to −0.98; $I^2 = 80\%$; $p = 0.02$; 3 studies[22,25,26]). However, substantial heterogeneity was observed, indicating considerable between-study variability and limiting the certainty of the pooled estimate (Figure 4). Two additional SGRQ studies not included in the meta-analysis due to insufficient statistical data showed mixed findings, with one[27] reporting a significant between-group difference and the other[23] showing no statistically significant improvement.

Improvements in QoL were also reported in individual studies using the World Health Organization Quality of Life (WHOQOL) (Vastrad 2021:[31] 64.10 vs 46.05, $p < 0.001$) and the Clinical COPD Questionnaire (CCQ) (Bui 2020:[29] 0.81 vs 1.24, $p = 0.001$). In contrast, one study using the EQ-5D found no significant difference between groups (Tommelein 2013,[24] $p = 0.190$). The effects of pharmaceutical care on health-related quality of life of COPD patients were summarized in eTable 5.

Medication Adherence

Pharmaceutical care consistently resulted in substantially improved medication adherence, as measured by a variety of tools. The proportion of patients exhibiting high adherence on the MMAS-4 was greater in the intervention groups based on the pooled analysis (RR = 1.45, 95% CI: 1.24 to 1.68; $I^2 = 14\%$; $p < 0.001$; 3 studies[22,23,28]) with low heterogeneity (Figure 5). This finding was corroborated by studies using the MMAS-8 (Liu 2021:[30] 7.31 vs 6.05, $p < 0.05$), Medication Refill Adherence (MRA) (Tommelein 2013:[24] 93.9 vs 85.7, $p < 0.001$; Xin 2016:[26] 93.1 vs 83.2, $p = 0.003$), General Medication Adherence Scale (Nguyen 2024,[33] 32 vs 31, $p < 0.001$) and pill counts (Wei 2014:[25] 66.5 vs 54.4, $p = 0.039$). The effects of pharmaceutical care on medication adherence of COPD patients were summarized in eTable 6.

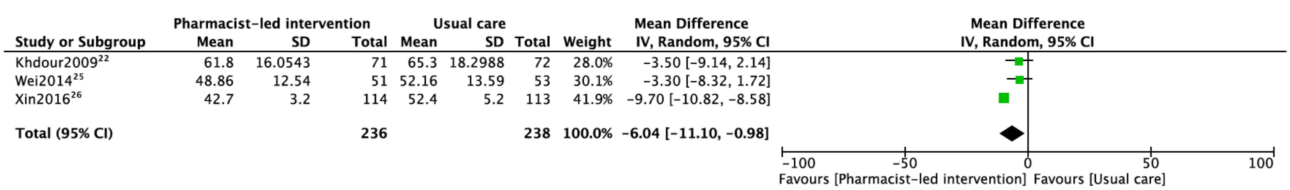

Figure 4 Forest plot of comparison on QoL assessed by SGRQ. Mean differences (MD) with 95% confidence intervals (CI) were pooled using the inverse variance (IV) method under a random-effects model. The size of each square reflects the weight assigned to each study in the meta-analysis, and horizontal lines indicate 95% CIs. The diamond represents the pooled estimate of the overall effect. Between-study heterogeneity was substantial ($Tau^2 = 15.59$; $Chi^2 = 9.98$, $df = 2$, P = 0.007; $I^2 = 80\%$). The pooled analysis showed a statistically significant improvement in SGRQ scores in the intervention group (MD = −6.04, 95% CI −11.10 to −0.98; Z = 2.34, P = 0.02).
Abbreviations: CI, confidence interval; df, degrees of freedom; IV, inverse variance; MD, mean difference; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire.

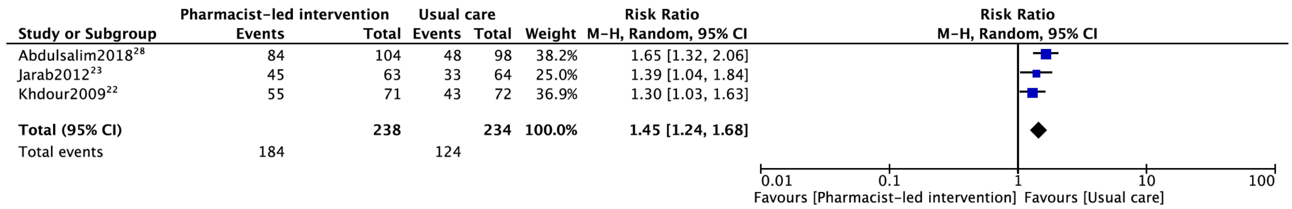

Figure 5 Forest plot of comparison on medication adherence assessed by MMAS-4. Risk ratios (RR) with 95% confidence intervals (CI) were pooled using the Mantel–Haenszel (M–H) method under a random-effects model. The size of each square reflects the weight assigned to each study in the meta-analysis, and horizontal lines represent 95% CIs. The diamond represents the pooled estimate of the overall effect. Between-study heterogeneity was low ($Tau^2 = 0.00$; $Chi^2 = 2.32$, $df = 2$, $P = 0.31$; $I^2 = 14\%$). The pooled analysis showed a statistically significant increase in medication adherence in the intervention group (RR = 1.45, 95% CI 1.24–1.68; Z = 4.81, P < 0.00001).
Abbreviations: CI, confidence interval; df, degrees of freedom; M–H, Mantel–Haenszel; RR, risk ratio.

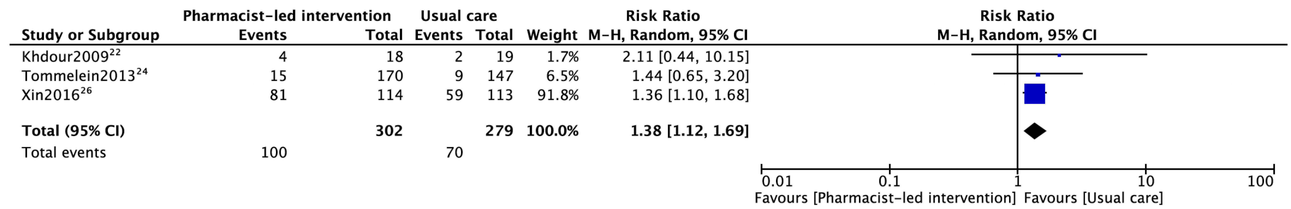

Figure 6 Forest plot of comparison on smoking cessation. Risk ratios (RR) with 95% confidence intervals (CI) were pooled using the Mantel–Haenszel (M–H) method under a random-effects model. The size of each square reflects the weight assigned to each study in the meta-analysis, and horizontal lines represent 95% CIs. The diamond represents the pooled estimate of the overall effect. Between-study heterogeneity was low ($Tau^2 = 0.00$; $Chi^2 = 0.32$, $df = 2$, $P = 0.85$; $I^2 = 0\%$). The pooled analysis showed a statistically significant improvement in the intervention group (RR = 1.38, 95% CI 1.12–1.69; Z = 3.08, P = 0.002).
Abbreviations: CI, confidence interval; df, degrees of freedom; M–H, Mantel–Haenszel; RR, risk ratio.

COPD-Related Knowledge Scores

The interventions successfully enhanced patients' understanding of their disease and treatment. Knowledge scores, assessed by a standardized COPD questionnaire, were significantly higher in the intervention groups compared to the controls (Khdour 2009:[22] 75.0 vs 59.3, $p = 0.001$; Jarab 2012:[23] 60.7 vs 43.6, $p = 0.007$). The effects of pharmaceutical care on COPD-related knowledge of COPD patients were summarized in eTable 7.

Inhalation Technique Assessed by Checklist

A direct and profound effect of the interventions was observed on the practical skill of inhaler use. The proportion of patients demonstrating correct inhalation technique was higher in the intervention group in one study (Tommelein 2013:[24] 237/346 vs 114/346, $p < 0.001$), a finding that was sustained in another (Nguyen 2024:[33] 90/91 vs 77/89, $p = 0.001$). The effects of pharmaceutical care on correct inhalation technique of COPD patients were summarized in eTable 8.

Other Secondary Outcomes: Smoking Cessation and BMI

The pooled analysis showed a higher quit rate in the intervention group (RR = 1.38, 95% CI: 1.12 to 1.69; $I^2 = 0\%$; $p = 0.002$; 3 studies[22,24,26]), although this estimate was based on a limited number of trials (Figure 6).

The interventions had no significant effect on Body Mass Index (BMI) at follow-up (Khdour 2009,[22] $p = 0.09$; Jarab 2012,[23] $p = 0.61$). The effects of pharmaceutical care on smoking cessation and BMI of COPD patients were summarized in eTable 9.

Discussion

In this updated systematic review and meta-analysis of 11 RCTs including 2313 patients with COPD, pharmacist-led integrated interventions were associated with improvements in selected domains of COPD management, although effects varied across outcomes. Among the evaluated outcomes, reductions in exacerbation-related hospital admissions were observed across several trials with low statistical heterogeneity; however, these findings should be interpreted in light of variability in study design and healthcare context. Improvements were observed in medication adherence and quality of

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life in several trials, and pooled analyses suggested higher smoking cessation rates; however, these effects varied across outcomes and studies.

The reduction in exacerbation-related hospitalization is particularly important because AECOPD is a major driver of disease progression, impaired functional status, and healthcare costs in COPD.[34] Pharmacist-led interventions are likely to reduce exacerbations through several complementary mechanisms. First, inhaler technique training improves effective drug delivery, which is essential for realizing the benefits of inhaled maintenance therapy.[35,36] Second, adherence counseling and reinforcement may increase persistence with long-term pharmacotherapy and reduce treatment gaps.[37] Third, pharmacists can identify and address medication-related problems in the context of polypharmacy, potentially reducing adverse drug reactions and optimizing regimens.[38,39] Finally, lifestyle counseling and follow-up support may facilitate smoking cessation and self-management behaviors, further mitigating exacerbation risk.[40] Together, these pathways may help explain the observed associations with utilization and selected patient-centered outcomes. A recent scoping review of pharmacist-physician collaborative models in COPD similarly highlighted substantial variability in intervention components, practice settings, and reported outcomes, underscoring the structural heterogeneity within this field and the need for standardized, trial-based evaluation of clinical effectiveness.[41]

In contrast, we did not observe a statistically significant improvement in COPD-specific health status measured by CAT, and heterogeneity was considerable. This finding should be interpreted cautiously given the limited number of CAT-contributing trials and the substantial differences among them. In addition, CAT is influenced by baseline disease severity, comorbidities, and concurrent clinical management, which likely differed across settings.[42] These considerations may explain the inconsistent CAT findings and underscore the need for harmonized outcome assessment and standardized follow-up time points in future trials.

Overall, the evidence regarding pharmacist-led interventions in COPD demonstrates both converging and diverging patterns across outcomes. Consistent benefits were observed for medication-related and behavioral outcomes, including medication adherence, inhaler technique, and smoking cessation, which were directionally favorable across most included trials. In contrast, effects on symptom burden and objective disease measures were inconsistent. Meta-analysis of CAT scores showed substantial heterogeneity, and lung function outcomes were reported in too few studies to permit reliable quantitative synthesis.

Importantly, the observed heterogeneity was high for key patient-reported outcomes, reflecting marked differences in intervention components, intensity, follow-up duration, outcome measurement tools, and baseline patient characteristics across studies. These factors substantially limit the interpretability and generalizability of pooled estimates and suggest that pharmacist-led interventions may not uniformly translate into improvements in clinical symptoms or physiological measures. Taken together, these findings indicate that while pharmacist-led care may improve selected process-related and patient-centered outcomes, its impact on core disease outcomes remains uncertain. The present review therefore does not establish robust clinical effectiveness, but rather highlights variability in effects and identifies areas where evidence is inconsistent or limited.

Our findings are consistent with prior reviews that highlighted benefits of pharmacist involvement in COPD, particularly for medication-related behaviors and inhaler skills.[15–17,43,44] However, earlier syntheses were either outdated[16] or focused on selected outcomes.[17] By integrating more recent RCT evidence and evaluating multiple clinically meaningful endpoints, this study provides updated quantitative synthesis of available RCT evidence for pharmacist-led integrated care.

Pharmacists contribute to COPD management through multi-dimensional, medication-focused services that are relatively consistent across settings, including inhaler technique training, adherence support, and medication review. The reproducibility of these core components suggests potential feasibility of integrating pharmacists into routine COPD care, although contextual adaptation would be required. This perspective also aligns with the growing recognition of pharmacists' expanded role in chronic disease management.[45]

Several limitations warrant consideration. Many included trials were single-center and sample sizes varied substantially, including some small studies, which may limit generalizability. Blinding was frequently not feasible due to the behavioral nature of the interventions, introducing potential performance and detection bias, particularly for patient-reported outcomes. Intervention components, intensity, and follow-up durations varied widely, which likely contributed to heterogeneity for some endpoints. In addition, for several outcomes the number of available studies was limited, reducing precision and precluding robust exploration of effect modifiers and publication bias for specific endpoints. Accordingly, limitations related to small sample sizes, high risk of bias, lack of blinding, and substantial between-study heterogeneity should be considered integral to the interpretation of the findings, rather than ancillary concerns. Interpretation of pooled estimates for outcomes with very small numbers of studies warrants particular caution. Meta-analyses based on as few as three trials provide limited precision, and estimates of between-study heterogeneity may be unstable under such conditions. In such cases, pooled results should be interpreted with caution and should not be considered confirmatory evidence of treatment effect.

Future research should prioritize adequately powered, multi-center RCTs with standardized intervention frameworks and core outcome sets, including exacerbation-related utilization, QoL, and validated measures of adherence and inhaler technique assessed at harmonized time points. Technology-enabled approaches, such as smart sensors and digital monitoring of inhaler use, may provide objective and time-stamped measures of medication-taking and technique, enabling personalized feedback and reducing reliance on self-report.[46,47] Trials should also identify subgroups most likely to benefit,[48,49] such as patients with frequent exacerbations, poor adherence, high inhaler error rates, or complex comorbidity, and incorporate implementation and economic evaluations to inform scalable integration of pharmacists into COPD care pathways.

Conclusions

Pharmacist-led interventions in COPD were associated with reductions in exacerbation-related hospital admissions and improvements in medication adherence, with pooled analyses suggesting higher smoking cessation rates. However, these findings are derived from a limited number of studies, and the overall evidence base remains heterogeneous with variable methodological quality. Effects on symptom burden and objective disease measures were inconsistent or non-significant. Therefore, the results should be interpreted cautiously and do not establish robust or generalizable clinical effectiveness. Moreover, as most included trials were conducted in Asia and other low- to middle-income healthcare settings, differences in pharmacy practice scope and care pathways may further limit transferability to high-income systems.

Abbreviations

COPD, Chronic Obstructive Pulmonary Disease; RCT, Randomized Controlled Trial; RoB, Cochrane Risk of Bias Tool; RevMan, Review Manager; RR, Risk Ratio; CI, Confidence Interval; MD, Mean Difference; IQR, Interquartile Range; SD, Standard Deviation; FEV1, Forced Expiratory Volume in 1 second; mMRC, Modified Medical Research Council; CAT, COPD Assessment Test; AECOPD, Acute Exacerbation of Chronic Obstructive Pulmonary Disease; ED, Emergency Department; DDD, Defined Daily Dose; QoL, Quality of Life; SGRQ, St. George's Respiratory Questionnaire; WHOQOL, World Health Organization Quality of Life; CCQ, Clinical COPD Questionnaire; EQ-5D, EuroQol 5-Dimensions; MMAS, Morisky Medication Adherence Scale; MRA, Medication Refill Adherence; MTM, Medication Therapy Management; BMI, Body Mass Index.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was supported by the CAMS Innovation Fund for Medical Sciences (CIFMS) (2024-I2M-C&T-B-092). The funder had no role in the design of the study; the collection, analysis, or interpretation of data; the writing of the manuscript; or the decision to submit the manuscript for publication.

Disclosure

The authors declare that they have no competing interests in this work.

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