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Effectiveness of Hospital Pharmacist Interventions for COPD Patients: A Systematic Literature Review and Logic Model

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Purpose: This review aimed to summarize empirical evidence about pharmacist-led interventions for chronic obstructive pulmonary disease (COPD) patients in hospital settings and to identify the components of a logic model (including input, interventions, output, outcome and contextual factors) to inform the development of hospital pharmacist's role in COPD management.

Methods: A systematic review of literature retrieved from four English databases (PubMed, Web of Science, Scopus, ScienceDirect) and one Chinese database (CNKI) were conducted to identify eligible studies published from inception to March 2022. Studies concerning pharmacist and COPD were identified to screen for randomized controlled studies that focused on pharmacist interventions for COPD at the hospital setting.

Results: Twenty-nine studies were included in this review. The components of interventions identified were categorized according to the six service domains in the International Pharmaceutical Federation's Basel Statements, and mainly concerned prescribing, preparation, administration and monitoring but not procurement and training. Extended interventions were also identified including life guidance, psychological counseling, and respiratory function exercise. The most common outputs reported were improvement in medication adherence, rational drug use, level of knowledge, and inhalation technique. The clinical outcomes (symptomatic control, lung function, rates of hospital readmission, length of hospital stay, and adverse drug adverse reactions), humanistic outcomes (quality of life and patient satisfaction), and economic outcomes (drug costs, hospitalization costs, antibiotic costs, and direct costs) were reported only in some studies. The contextual factors mainly included geographical factors, education level of patients, socio-economic factors, and no-smoking policy.

Conclusion: The evidence for hospital pharmacists' interventions in improving COPD patients' outcome is growing. However, considering the challenges of COPD management, hospital pharmacists should further leverage the advantages of cross-sector and multi-disciplinary collaboration in order to provide more comprehensive support to better address the needs of their patients.

Keywords: chronic obstructive pulmonary disease, hospital pharmacist, systematic review, intervention, output, outcome, logic model

Introduction

Chronic obstructive pulmonary disease (COPD) is a major health challenge typically associated with an irreversible decline in lung function, progressive functional disability, and a significant impact on the quality of life. Worldwide, it is estimated that COPD affects around 300 million people (4% of the world's population) causing at least 3 million deaths each year[1,2] and will become the fourth leading cause of death by 2030.[3] The high prevalence, severity and high mortality rates of COPD also cause great economic burden on the patients and the overall health system.[4] For instance, the annual direct medical cost per COPD patient was estimated as $10,367 in the US.[5] The mean hospitalization cost per COPD patient per admission was $3669 in China.[6] The hospitalization rates,[7] primary care visits,[8] length of hospital stay[8] and ICU admissions[9] were found to be associated with the severity of the illness.

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Many patients with COPD cannot control the progress of the disease effectively, which inevitably contributes to periodic exacerbations in which symptoms of breathlessness and sputum production deteriorate rapidly, requiring emergency room visits and hospitalizations.[10,11] In fact, acute exacerbation of COPD (AECOPD) is the principal reason for unscheduled hospital visits among COPD patients, and one of the most common reasons for hospitalization across the countries.[12–15] AECOPD exerts a significant impact on patients' health status and accelerates disease progression, leading to in-hospital mortality and post-discharge mortality. One of the important treatment goals during COPD hospitalization is to manage the symptoms and reduce the risk and severity of future exacerbations.

Pharmacist interventions at the hospital settings, both during hospitalization and at discharge, have been reported to be effective in improving the management of COPD for patients suffering from exacerbation or ready for discharge.[16] For instance, a pharmaceutical care programme initiated at the emergency department could reduce the number and prevalence of drug-related negative outcomes leading to clinical benefits for the patients.[17] Early in-hospital pharmacist-led medication review could optimize the pharmacotherapy and thus reduce the median length of hospital stay by at least 8% or up to 11% for patients >80 years of age).[18] The pharmacist-driven COPD bundled-care could also improve outpatient management in patients with COPD.[19] Pharmacists, as a member of a multidisciplinary team, also played a crucial role in hospital-based transitions of care (TOC) at the time of discharge to reduce COPD readmissions.[20]

Despite the emerging evidence for the benefits of improved patient outcomes associated with hospital pharmacist intervention, much of the current literature designates a prime focus on the role of pharmacist at the community level for COPD management.[21,22] Indeed, within the scope of COPD, the disease is deemed preventable should risk factors such as tobacco smoking and air pollution can be avoided, while under-diagnosis and mis-diagnosis are often common, which are areas best addressed at the community setting.[23] Nevertheless, COPD patients also receive care in the hospitals during specialist consultation, ICU admission and hospitalization. It is also important to systematically evaluate the role of hospital pharmacists in COPD management to supplement the current knowledge about the evidence-base approaches to the challenges of long-term COPD management and hospital readmissions.

The objective of this study was to analyze the current evidence about pharmacist-led interventions for COPD patients in hospital settings and to identify the corresponding input, output, outcome and contextual factors guided by the logic modelling framework. This will enable a better understanding of the contributions that hospital pharmacists can make and help inform strategies that support them developing their role in COPD management.

Methods

This systematic literature review was conducted and reported in compliance with the PRISMA 2020 statement.[24] For searching the literature. The literature search was completed in April 2022. Articles published from inception to March 2022 were included.

Search Strategy

A systematic search of peer-reviewed published literature was performed via five electronic databases, including four English databases (PubMed, Web of Science, Scopus, ScienceDirect) and one Chinese database (China National Knowledge Infrastructure (CNKI)), were searched. The three primary search concepts were "pharmacist", "COPD" and "hospital". To identify appropriate key words, in addition to Medical Subject Headings (MeSH) terms, common phrases used in the literature were utilized to develop a comprehensive search strategy (Table 1). The terms within "pharmacist", "COPD" and "hospital" were combined with OR, and the following results from each concept were combined with AND. The reference lists and citations of included articles were examined for any potential publications relevant to the objective of the current study.

Inclusion and Exclusion Criteria

To be considered eligible for inclusion in the study, the literature must comply with all of the following criteria: (1) the studies must be original research limited to randomized controlled trials (RCT); (2) the main intervention providers should be pharmacists in hospital settings; (3) the pharmacist intervention should be specifically described in the article; (4) the main target disease should be COPD; (5) the full text must be available; (6) the publications must be original

Table 1 Search Term Identifiers

Concept 1 Pharmacist	Concept 2 COPD	Concept 3 Hospital setting
• Pharmac*	• Chronic Obstructive Pulmonary Disease • COPD • Chronic Airflow Obstruction • Bronchial • Respiratory • Airway • AECOPD • Acute exacerbation	• Hospital • Clinical • Inpatient • Hospitalization • Intensive care unit • Emergency department • Patient discharge • Ambulatory care

articles published in English or Chinese; and (7) for papers identified in CNKI, only articles published in journals listed on the 2012 Institute of Scientific and Technical (S&T) Information of China (2013a) Core Journal List were included. Exclusion criteria were: (1) observational studies, reviews, commentaries and publication types other than RCT; and (2) the main target disease of the studies was other diseases or COPD combined with other diseases.

Study Selection Procedure

The screening process was separately completed by 2 of the authors (LG and ZJ) according to the inclusion and exclusion criteria outlined above. The whole study selection procedure is shown in Figure 1. First, we yielded 1670 articles from the English databases and 44 articles from the Chinese database. After removal of duplications, 1479 articles were further screened for inclusion based on title, abstract and full-text. This screening process was conducted separately by two of the authors separately and the screening results were compared for any discrepancies. Disputes were first discussed between these 2 authors and final agreement was made upon confirmation by the senior author (COLU).

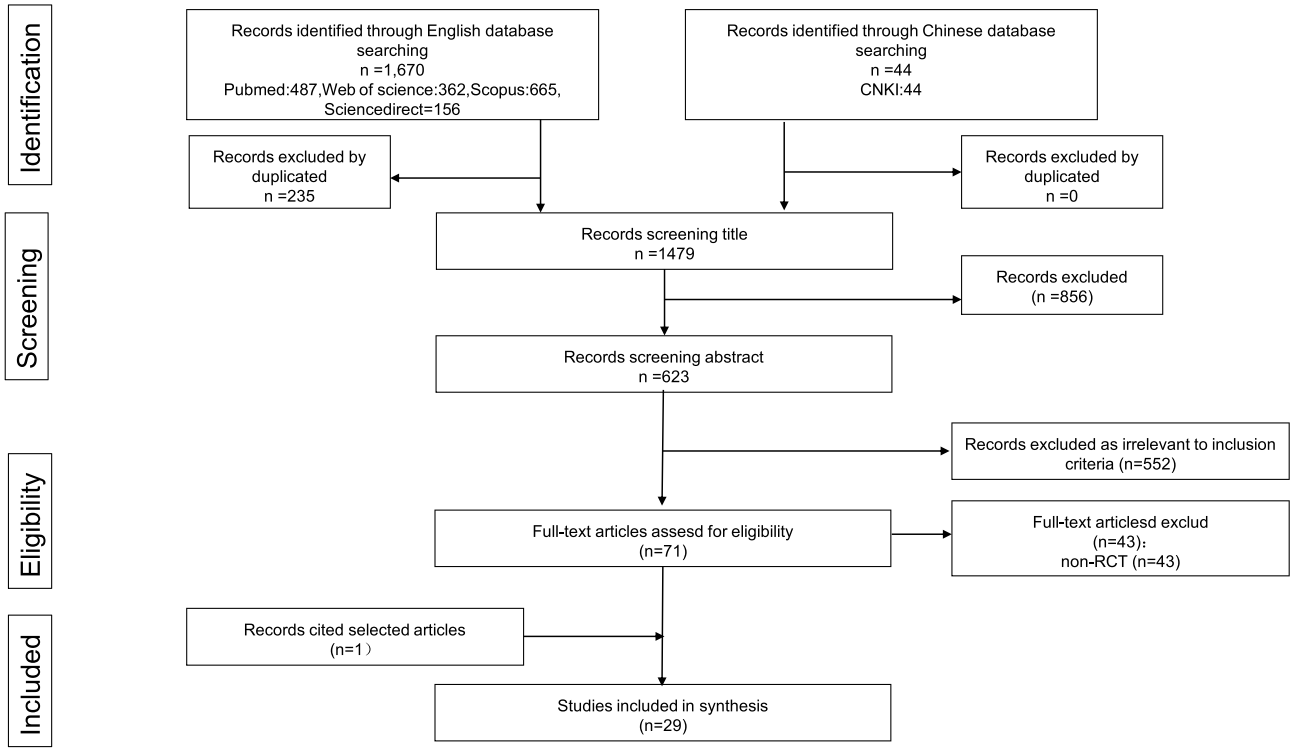

Figure 1 PRISMA flow chart of systematic review.
Note: Adapted from Page MJ, Moher D. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ*. 2021;372:23. Open Access.[24]

Data Extraction and Analysis

A standard extraction form was used to extract relevant data from the eligible trials, which contained the name of the first author, study location, sample size, intervention from pharmacists, outputs, and outcomes. The types of interventions were classified according to the 2015 version of the Basel Statements hosted by the Global Conference on the Hospital Pharmacy Section of the International Pharmaceutical Federation (FIP) (the Basal Statements), which covered all areas of the medicine use process in hospitals (including: (1) Procurement, (2) Prescribing, (3) Preparation and Delivery, (4) Medicine administration, (5) Monitoring of Medicine Use, and (6) Human Resources, Training and Development. The category "(7) Others" was added to accommodate any possible interventions beyond the 6 areas of the medicine use process described in the Basal Statements. Moreover, for the purpose of this study, the output of interventions referred to observations not directly related to disease conditions or management such as medication adherence, changes in blood test results, improvement of inhalation technique, etc. Patient outcomes were defined according to the ECHO model and might be grouped into economic outcomes, clinical outcomes, and/or humanistic outcomes.

Study Appraisal

For quality evaluation, we chose the CONSORT 2010 checklist[25] as an evaluation tool to evaluate the validity of the results of each article. The CONSORT 2010 checklist contains 25 items to cover all important aspects of the experiment, some of which are divided into sub-items a and b. If the item was fully met, we defined it as "Fully satisfied", and if only a sub-item was met, we defined it as "Partially satisfied". We aggregated the numbers of "Fully satisfied", "Partially satisfied", "Not satisfied", and "Not applicable" per study to assess the quality of the study. The greater the number of "fully satisfied", the better the quality of the article. Two authors (LG and ZJ) independently appraised the quality of the included studies based on the CONSORT 2010 checklist. When there were differences and conflicts in the evaluation results, the third researcher (COLU) participated in the evaluation process and made the final evaluation.

Results

According to the inclusion and exclusion criteria, 15 English articles and 14 articles in Chinese were included in this evaluation (Table 2). The research covered ten countries and regions with China being the most common study country (n=19), followed by the United States (n=4),[26,27,32,44] India (n=3),[37,41,48] Jordan (n=1),[29] Spain (n=1)[17] and Thailand (n=1).[52] The research site was mainly based on a single hospital (n=28) and only 1 study were conducted based on a collaboration of hospital[44] and community pharmacy. In all studies, hospital pharmacists participated in the intervention, either as the sole healthcare profession (n=25) or as a member of a multi-disciplinary team (n=4).[28,32,36,44] The duration of intervention ranged from 1 month to two years, and all the interventions were directed at patients.

Types of Interventions for COPD Patients Provided by Hospital Pharmacists

As shown in Table 3, pharmacists played multiple roles in COPD management in the hospital setting, most of which focused on prescribing,[17,27–29,32,34,35,39,40,43,44,50,52,53] medicine administration,[17,26,27,29–53] monitoring of medicine use[17,26,27,29–43,46,47,50,52,53] and other non-pharmacologic therapy management.[27,29,30,35,37–39,41–43,46–48,50,52] As a member of the medical team, hospital pharmacists collaborated with clinicians to formulate treatment plans. They provided recommendations for the types, indications, doses, frequency of administration, and possible side effects for each prescribed medication. Furthermore, COPD was usually complicated by a variety of primary conditions, such as diabetes and heart disease. The combination use of medications was complex, and pharmacists reviewed and adjusted the medications according to the patients' conditions. For COPD patients requiring transition of care to primary care institutions after discharge, hospital pharmacists also ensured that the transfer of accurate information about the medication used by the patients at discharge.[32,44]

Most of the pharmacist services related to medicine administration included in this review were through education. Such education intervention was primarily directed at patient instruction, including information about: 1) COPD, COPD medicines, administration and dosing, management of COPD symptoms, possible adverse reactions;[27,29–33,35–53] 2) rational use of specific antibiotics;[27,39] and 3) proper inhaler use.[27,36–39,41,48,49,51,52] In terms of educational methods,

Table 2 Summary of Basic Information of Selected Articles

No.	Authors	Study Location	Sample Size	Numbers of Hospitals	Key Components of the Intervention	Duration of Intervention	Pharmacist Only?
1	De et al[26]	USA	IG: 30 patients CG: 30 patients	1 hospital	Comprehensive verbal instruction on how theophylline works and the importance of drug compliance	6 months	√
2	Khdour et al[27]	USA	IG: 86 patients CG: 87 patients	1 hospital	A structured education programme on disease state, medications and breathing techniques	12 months	√
3	Shen et al[28]	China	IG: 176 patients CG: 178 patients	1 hospital	Pharmacist interventions on rational antibiotic use	10 months	Hospital Pharmacist and doctors
4	Jarab et al[29]	Jordan	IG: 66 patients CG: 67 patients	1 hospital	A structured education on COPD and management of its symptoms	6 months	√
5	Wei et al[30]	China	IG: 75 patients CG: 75 patients	1 hospital	Pharmaceutical care plan on knowledge of drugs and diseases	6 months	√
6	Wei et al[31]	China	IG: 58 patients CG: 59 patients	1 hospital	A comprehensive pharmaceutical care program composed of individualized education (including effective use of respiratory devices, pathophysiology of the disease, interpretation of medical testing and rationale for medication) and a series of telephone counseling	6 months	√
7	Farris et al[32]	USA	Enhanced:314 Minimal:315 Usual care:316	1 hospital	Pharmacist case manager project composed of admission medication reconciliation, pharmacist visits for patient education, discharge counseling and discharge medication list	90 days	Hospital Pharmacists and inpatient physicians, primary care physicians and community pharmacists
8	Wei et al[33]	China	IG: 150 patients CG: 150 patients	1 hospital	Medication guidance and medication education, including drug use methods and precautions	Not specified	√
9	Yan et al[34]	China	IG: 50 patients CG: 46 patients	1 hospital	Pharmaceutical care plan including monitoring the whole process of medication, putting forward adjustment opinions, preventing and treating adverse drug reactions and drug interactions, and conducting pharmaceutical follow-up for some patients	Not specified	√
10	Wang et al[35]	China	IG: 100 patients CG: 92 patients	1 hospital	Pharmaceutical care plan including reviewing medical orders, pharmaceutical education, and monitoring of non-medication treatment	Not specified	√
11	Lin et al[36]	China	Pharmacist education: 34 Nursing education: 35 Self-medication: 32	1 hospital	Education about oxygen-driven aerosol inhalation	Not specified	Hospital Pharmacist and other health care professionals apart from doctors

(*Continued*)

Table 2 (Continued).

No.	Authors	Study Location	Sample Size	Numbers of Hospitals	Key Components of the Intervention	Duration of Intervention	Pharmacist Only?
12	Suhaj et al[37]	India	IG: 98 patients CG: 104 patients	1 hospital	Pharmacist intervention on importance of medication compliance, need for smoking cessation, simple exercise, proper use of inhaler devices and need for timely follow-up	24 months	√
13	Xin et al[38]	China	IG: 122 patients CG: 122 patients	1 hospital	A structured education on definition of COPD, pathophysiology of the disease, the importance of medication adherence, the importance of smoking cessation, drug use, use of respiratory devices, the possible ADR, the possible effect of drug combination, the importance of a well-balanced diet, and the necessity of timely follow-up by physicians	12 months	√
14	Qin et al[39]	China	IG: 128 patients CG: 128 patients	1 hospital	Pharmaceutical care including medication guidance, telephone follow-up and outpatient follow-up	6 months	√
15	Zhang et al[40]	China	IG: 63 patients CG: 62 patients	1 hospital	Pharmaceutical care including review of prescriptions, medication monitoring, patient medication education, discharge medication guidance, and telephone follow-up	Not specified	√
16	Abdulsalim et al[41]	India	IG: 98 patients CG: 104 patients	1 hospital	Pharmacist intervention on compliance, smoking cessation, exercise, inhaler use and need for timely follow up	24 months	√
17	Juanes et al[17]	Spain	IG: 59 patients CG: 59 patients	1 hospital	A pharmaceutical care programme focusing on resolving potential drug-related problems	12 months	√
18	Chen et al[42]	China	IG: 100 patients CG: 100 patients	1 hospital	Pharmaceutical care focusing on education on the etiology and symptoms of COPD, drug classification, correct use of various devices, lifestyle guidance, and smoking cessation	6 months	√
19	Song et al[43]	China	IG: 34 patients CG: 26 patients	1 hospital	Integrated pharmaceutical care including in-hospital guidance, classroom teaching, regular follow-up, life guidance, and psychological counseling	12 months	√
20	Bloodworth et al[44]	USA	IG: 96 CG: 160	1 hospital and 2 community pharmacies	Pharmacist care including telephonic and face-to-face consultation on indication, effectiveness, safety, and compliance	6 months	Hospital pharmacist and community pharmacist

(*Continued*)

Table 2 (Continued).

No.	Authors	Study Location	Sample Size	Numbers of Hospitals	Key Components of the Intervention	Duration of Intervention	Pharmacist Only?
21	Chen et al[45]	China	First time users: 64 Long-term users: 79	1 hospital	Pharmacist medication education on use of inhaler devices	Not specified	√
22	Li et al[46]	China	IG: 45 patients CG: 45 patients	1 hospital	Pharmaceutical intervention including medication guidance, education on inhaler device use and follow-up	40 days	√
23	Yang et al[47]	China	IG: 43 patients CG: 43 patients	1 hospital	Pharmaceutical education including disease knowledge, drug treatment, smoking cessation, introduction of common misunderstandings, guidance on living habits, and the necessity and importance of adherence to medication	1 month	√
24	Abdulsalim et al[48]	India	IG: 104 patients; CG: 98 patients	1 hospital	Structured pharmacist-led interventions on improving medication adherence	24 months	√
25	Wang et al[49]	China	IG: 133 patients CG: 126 patients	1 hospital	Multidimensional pharmaceutical care including establishment of a special dispensing window, face-to-face demonstration and education, brochure education, video education, online consultation and education, and follow-up reeducation	3 months	√
26	Wang et al[50]	China	IG: 64 patients CG: 65 patients	1 hospital	Medication management services including patient education, formulation of personal drug list, formulation of rehabilitation plan, and follow-up	6 months	√
27	Wang et al[51]	China	IG:88 patients CG:88 patients	1 hospital	Pharmaceutical care focusing on education of inhaler device use	3 months	√
28	Prasungriyo et al[52]	Thailand	IG: 23 patients CG: 21 patients	1 hospital	Pharmacist counseling on basic knowledge of COPD, the health consequences of smoking cigarettes, the technique for using inhalers, the importance of medication adherence, self-management and lifestyle modification, and breathing exercises	90 days	√
29	Liu et al[53]	China	IG: 96 patients CG: 97 patients	1 hospital	Medication therapy management services focusing on medication education	6 months	√

Abbreviations: IG, intervention group; CG, control group.

Table 3 Interventions Implemented by Hospital Pharmacists for COPD Patients

No.	Study	Components of Intervention							Description
		Areas of the Medicine Use Process in Hospitals According to the Basel Statement (A=Procurement; B=Prescribing; C=Preparation; D=Administration; E=Monitoring; F=Training)						Others	
		A	B	C	D	E	F		
1	De et al[26]			√	√	√			***C = Preparation***: • Labeling - Prescription containers carried both conventional and auxiliary labels. • Delivery - All medications were refillable by mail. ***D = Administration***: • Instruction to patients (theophylline therapy, medication questions, other related drugs). ***E = Monitoring***: • Serum level - The serum levels for the experimental group patients were drawn on their next regularly scheduled clinic visit after the consultation (a few months apart). • Refills - Prescription records for patients were reviewed for the 6-month period following the recorded drug level to determine how often patients received refills on theophylline products
2	Khdour et al[27]		√		√	√		√	***B=Prescribing***: • Antibiotics - Give advice to general practitioners to provide a prescription for an antibiotic ***D=Administration***: • Education o content - Disease, prescribed medication, the importance of adherence, inhaler technique and the management of COPD symptoms. o materials - Booklet to take home, a customized action plan for acute exacerbations. o programme - Reinforcement of the education on COPD and its treatment at each outpatient clinic visit (every 6 months arranged) by the clinical pharmacist. ***E=Monitoring***: • Follow-up telephone calls - Telephone calls by the clinical pharmacist at 3 and 9 months, ie between outpatient clinic appointments. • Assessment - SGRQ, Morisky scale, COPD knowledge questionnaire, BMI values at 6 and 12 months. ***Others***: • A special smoking cessation programme. • Simple exercises that patients can do at home.

3	Shen et al[28]		√						***B=Prescribing***: • Antibiotics - Collaboration with general practitioners to provide a prescription for an antibiotic, including: indication, choice, dosage, dosing schedule, duration and oral therapy.
4	Jarab et al[29]		√		√	√		√	***B=Prescribing:*** • A medication table - Discuss types, indications, doses, frequency of administration, and possible side effects for each prescribed medication. ***D=Administration***: • Education: o content - COPD and management of its symptoms, symptoms control and the technique for expectoration. o materials - Booklet to take home. o Adherence - Clinical pharmacist used the motivational interviewing technique to improve adherence. ***E=Monitoring***: • Assessment - Quality of life improvement, healthcare utilization, COPD knowledge and medication adherence were repeated at 6 months. ***Others***: • Smoking cessation programme. • Giving advice of simple exercises.
5	Wei et al[30]				√	√		√	***D=Administration***: • Education: o Outpatient medication consultation - Introduced the main effects, undesirable applications, and taking methods of the medication. o Telephone follow-up - Solve the doubts in the medication process, and remind the patient when to return to the clinic. o Lecture - Introduce the pharmacological effects, taking methods, side effects and treatment methods of related drugs. ***E=Monitoring***: • Follow-up phone calls - Record the patient's adverse drug reactions and the number of acute attacks. ***Others***: • Lecture - Suggest the healthy diet and living habits of COPD needs.

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Table 3 (Continued).

No.	Study	Components of Intervention						Description
		Areas of the Medicine Use Process in Hospitals According to the Basel Statement (A=Procurement; B=Prescribing; C=Preparation; D=Administration; E=Monitoring; F=Training)					Others	
		A	B	C	D	E	F	
6	Wei et al[31]				√	√		***D=Administration:*** • Education: o Interview - Use of respiratory devices, pathophysiology of the disease. o Telephone follow-up - Solve the doubts in the medication process, and remind the patient when to return to the clinic. ***E=Monitoring***: • Medication management records - Evaluated each participant's preferences and analyzed possible barriers to medication adherence.
7	Farris et al[32]		√		√	√		***B=Prescribing***: • Admission medication reconciliation. ***D=Administration***: • Education- Pharmacist visits every 2–3 days for patient education during inpatient stay. • Discharge counseling - Focused on goals of therapy, medication administration, barriers to adherence including cost and patient concerns. • Telephone follow-up - Participants received a telephone call at 3–5 days post-discharge. • Discharge care plan - Primary care physician and community pharmacist received a discharge care plan, including the discharge medication list, plans for dosage adjustments and monitoring, recommendations for preventing adverse drug events, with patient specific concerns such as adherence or cost issues highlighted. ***E=Monitoring***: • Usual care - The usual care discharge summary was transcribed and received in the mail by the primary care physician several days or weeks after discharge. • Adverse events and healthcare utilization - At 30 and 90 days post-discharge, all participants were phoned to gather self-reported adverse events and symptoms and self-reported healthcare utilization.

8	Wei et al[33]				√	√			***D=Administration:*** • Education - including medication usage, precautions, etc. ***E=Monitoring***: • Pharmacist rounds - Record the ward rounds and consultation content in the medical record in detail, and establish a record sheet for the patient to record the participation of clinical pharmacists in treatment.
9	Yan et al[34]		√		√	√			***B=Prescribing***: • Propose treatment plans. ***D=Administration***: • Follow-up - Pharmacological follow-up of some key patients. ***E=Monitoring***: • Adverse drug reactions - Monitor the whole process of patient medication, prevent and treat adverse drug reactions and drug interaction.
10	Wang et al[35]		√		√	√		√	***B=Prescribing:*** • Propose a personalized medication plan - join patient rounds, develop treatment plans. • Oversee physician prescriptions - Regarding the contraindications of the therapeutic drugs, the administration status, the combined medication status, and the presence or absence of repeated medications. ***D=Administration***: • Education - Admission education, in-hospital education, and discharge education. • Follow-up - Pharmacological follow-up of some key patients. ***E=Monitoring***: • Monitor the administration time, medication course, appropriate administration method, monitor drug-drug interactions, and record the ADR. • Non-medication monitoring - oxygen therapy, rehabilitation therapy, and monitoring of related common complications. ***Others***: • Healthy diet, strengthen their physique, and take appropriate physical exercise.
11	Lin et al[36]				√	√			***D=Administration***: • Inhalation technique education - Instruct the operation process of using the inhaler. ***E=Monitoring***: • Observe operating conditions and medication comfort, and record changes in pulse and oxygen saturation (SpO2).

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Table 3 (Continued).

No.	Study	Components of Intervention							Description
		Areas of the Medicine Use Process in Hospitals According to the Basel Statement (A=Procurement; B=Prescribing; C=Preparation; D=Administration; E=Monitoring; F=Training)						Others	
		A	B	C	D	E	F		
12	Suhaj et al[37]				√	√		√	***D=Administration***: • Education o Content - Symptom management, inhaler technique, to emphasized about medication compliance. o Method - Counselling sessions. o Materials - Patient information leaflets (PILs). • Follow up - Every six months, patients were trained for proper use of inhaler devices and were motivated for medication adherence. ***E=Monitoring***: • SGRQ assessment - Repeated at 6, 12, 18 and 24 months. ***Others***: • Smoking cessation programme. • Simple exercises that patients can do at home.
13	Xin et al[38]				√	√		√	***D=Administration:*** • Education - o Content - disease, prescribed medication, the importance of adherence, inhaler technique and drug combination. o Materials, telephone or network counseling - Remind the possible ADR and when to return to the clinic. ***E=Monitoring***: • SGRQ assessment -Reassessed every 6 months. ***Others***: • Smoking cessation programme. • Giving life health advice.

14	Qin et al[39]		√		√	√		√	***B=Prescribing***: • Review of prescriptions for special populations. • Adjustment of the treatment plan. ***D=Administration***: • Inhaler technique • Special drug consulting services. o The use of high-risk drugs. o Rationality of the use of special antibiotics. • Long-term medical advice on medication. • Interpretation of the instructions. • Checked the remaining amount of drug and the scale window of the inhalation device. ***E=Monitoring***: • Telephone follow-up - Evaluated adverse drug reaction. • Outpatient follow-up - MMAS-8 score and lung function monitoring - performed at 3 months and 6 months after the intervention. ***Others***: • Smoking cessation programme. • Healthy lifestyle suggestions.

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Table 3 (Continued).

No.	Study	Components of Intervention						Description
		Areas of the Medicine Use Process in Hospitals According to the Basel Statement (A=Procurement; B=Prescribing; C=Preparation; D=Administration; E=Monitoring; F=Training)					Others	
		A	B	C	D	E	F	
15	Zhang et al[40]		√		√	√		***B=Prescribing***: • Conducted evaluation of long-term, temporary and changed medical orders through the respiratory medicine medical order review platform. • Focused on the indications, drug selection, dosage and treatment course of antibacterial drugs, glucocorticoids, theophylline, proton pump inhibitors, adjuvant medications. ***D=Administration***: • Education o Patient medication education - In medical or pharmacy rounds, bedside explanations and educational materials are used to inform patients about disease-related knowledge, indications of commonly used drugs, pharmacological effects, usage and dosage, possible ADEs and precautions, etc. o Discharge medication guidance - provide medication guidance, including discharge medication treatment plan, discharge medication education (purpose of medication, usage and dosage, life precautions, ADE and treatment, drug storage, response measures after missed medication, Self-monitoring, etc. • Follow-up: In the first month after discharged, the designated clinical pharmacist will conduct a 20–30 minute telephone follow-up. ***E=Monitoring***: • The clinical pharmacist asks whether there is an increase, forgotten, discarded, or used off-prescription drugs. • Medication compliance - the patient reported whether the drug was used as prescribed by the doctor, whether there was a missed or wrong dose, whether patient mastered the correct use of the special dosage form, etc.

16	Abdulsalim et al[41]				√	√		√	***D=Administration***: • Counselling sessions and patient information leaflets (PILs) - the importance of medication compliance, dose and frequency of medications, proper use of inhaler devices and need for timely monitoring by the pulmonary medicine department. • Followed up - for a period of two years, and adherence was re-assessed after every six months. During follow up, patients in IG were trained for proper use of inhaler devices. • Medication adherence - Used monthly telephone calls for ensuring medication adherence. ***E=Monitoring***: • The medication adherence assessment - was repeated at 6, 12, 18 and 24 months in both the groups. ***Others***: • Smoking cessation programme. • Simple exercise.
17	Juanes et al[17]		√		√	√			***B=Prescribing***: • Medicine review and validation of physician prescriptions. • The indication for each medication in relation to the patient's condition. • The appropriateness of each medication, dose, schedule. • Duration of the treatment for the patient's age and/or clinical status (renal function or liver function). • Potential drug-related problems - The pharmacist reported the problem causing this problem and proposed an alternative prescription that would be available for the health team in the electronic health record. • Medication reconciliation - including drug name, dosage, frequency and route, and comparing that list against the physician's admission, transfer and/or discharge orders, with the goal of providing correct medications to the patient at all transition points within the hospital. ***D=Administration***: • Obtaining and recording the medication chart. By interviewing the patient or care-giver, the medication taken at home as listed in the electronic health records. • Follow-up. ***E=Monitoring***: • Therapeutic drug monitoring - was performed for drugs with a narrow therapeutic range.

(*Continued*)

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Table 3 (Continued).

No.	Study	Components of Intervention							Description
		Areas of the Medicine Use Process in Hospitals According to the Basel Statement (A=Procurement; B=Prescribing; C=Preparation; D=Administration; E=Monitoring; F=Training)						Others	
		A	B	C	D	E	F		
18	Chen et al[42]				√	√		√	***D=Administration***: • Education -The pharmacist personally demonstrated the correct use of inhalants, and informs patients of precautions, adverse reactions, etc. • WeChat interactive platform - Pushed publicity and education videos and popular science articles. • Brochure - Prepared and distributed the "Asthma and COPD Patients Chronic Disease Management Brochure". ***E=Monitoring***: • Within 6 months of treatment were recorded through telephone follow-up, and the incidence of adverse reactions was calculated to evaluate the drug safety. • After 3 or 6 months of enrollment, performed MMAS-8 score, CAT score (COPD), MasterScreen lung function test system, device use score, and recorded the number of acute attacks/exacerbations. ***Others***: • Smoking cessation programme • Scientific life style

19	Song et al[43]		√		√	√		√	***B=Prescribing***: • Ant-infective treatment plan - The clinical pharmacist determines the intervention points of antimicrobial treatment based on the patient's condition, and works with the clinician to formulate. ***D=Administration***: • Inhalation administration guidance - Established an education model for the use methods and precautions of commonly used inhalation preparations. • Education-Organized classroom teaching, with the help of slides, comic book propaganda books. • Nursing guidance - Informed the nurses of the precautions during drug infusion, including drug infusion speed, compatibility contraindications, etc. ***E=Monitoring***: • Followed up by telephone for a period of one year. • Assessed the use of common respiratory medicines and awareness of adverse reactions, the application of inhaled preparations, changes in lung function, and related medical expenses. ***Others***: • Life Guidance - During the follow-up period, explained the daily diet and life aspects of the patients that need to be noted and avoided, and encouraged the patients to increase exercise appropriately • Psychological counseling - Helped patients to correctly understand ACOS and reduced the negative emotions caused by the disease

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Table 3 (Continued).

No.	Study	Components of Intervention						Description
		Areas of the Medicine Use Process in Hospitals According to the Basel Statement (A=Procurement; B=Prescribing; C=Preparation; D=Administration; E=Monitoring; F=Training)					Others	
		A	B	C	D	E	F	
20	Bloodworth et al[44]		√	√	√			***B=Prescribing***: • Medication issues -The pharmacist transitions coordinator worked with the decentralized clinical pharmacist, prescriber, or social worker to resolve identified medication issues. ***C=Preparation***: • Supply of discharge medications - On the day of discharge, a 30-day supply of discharge medications was offered to each patient at usual cost or co-pay and delivered to the bedside by the hospital's outpatient pharmacy. ***D=Administration***: • Duration - On hospital discharge, patients received telephonic and face-to-face interventions. Patients were contacted by telephone on post-discharge days 2, 9, and 25 by the pharmacist. • Content -The pharmacist completed a comprehensive medication review and assessed health status, identified any potential or actual drug therapy problems (DTPs), adverse drug events, or other concerns. • Adherence -The pharmacist answered any patient questions, assessed and reinforced adherence with medications, provided information on discharge instructions. • Transition -To facilitate communication during the transition, a pharmacist transitions coordinator uploaded the patient's discharge summary into the Health Navigator system for the pharmacists providing telephonic follow-up and faxed a copy of the summary to the community pharmacists providing the medication therapy management visits.
21	Chen et al[45]				√			***D=Administration***: • Education o Explanation o Demonstration o Exercise

22	Li et al[46]				√	√		√	***D=Administration***: • Education o Medication guidance o Inhalation device use o Medication compliance • Follow up -Asking about the drugs currently used and their usage and dosage, and correcting the medication deviation according to the discharge doctor's advice ***E=Monitoring***: • Follow up • Special reaction • Adverse reaction ***Others***: • Respiratory function exercise • Diet and lifestyle education
23	Yang et al[47]				√	√		√	***D=Administration***: • Education-disease knowledge, common misunderstandings, drug therapy, the necessity and importance of adhering to medication • Guiding medication - filled in the medication guidance card in detail, and explained the precautions ***E=Monitoring***: • Follow up - urged patients to adhere to medication and understood the improvement of patients' condition and the occurrence of adverse drug reactions. ***Others***: • Smoking cessation • Living habits
24	Abdulsalim et al[48]				√			√	***D=Administration:*** • Education-the dose and frequency of the prescribed medicines, the importance of medication compliance and the proper use of prescribed inhaler devices • Medication adherence - Patients were further contacted by telephone each month to enhance medication adherence and timely follow-up. • Counselling - were conducted during the 2-year follow-up period. ***Others***: • Smoking cessation • Simple exercise

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Table 3 (Continued).

No.	Study	Components of Intervention							Description
		Areas of the Medicine Use Process in Hospitals According to the Basel Statement (A=Procurement; B=Prescribing; C=Preparation; D=Administration; E=Monitoring; F=Training)						Others	
		A	B	C	D	E	F		
25	Wang et al[49]				√				***D=Administration***: • Inhalation Technical Guidance - A pharmacist demonstrated, observed the patient's inhaler technology, guided the incorrect steps until there were no errors in each step. • Education - Brochure, videos, popular science articles were regularly delivered to patients. • Consultation - Established an online consulting platform for online consultation and education • Telephone follow-up - Monthly telephone follow-ups were conducted for three months to guide correct operation.
26	Wang et al[50]		√		√	√		√	***B=Prescribing***: • Formulation of personal drug list - Listed the name, dosage, indications, usage, start time, stop time, and drug unit price of each drug used by the patient, which would be reviewed and updated by the pharmacist at the next return visit. ***D=Administration***: • Education- Provided education on the proper use of drugs and inhaled preparations ***E=Monitoring***: • Collect evaluation indicators at the first visit and follow-up for 3 months and 6 months: FEV1%, EQ-5D, CAT score, Morisky score • Identified DRPs in patients, recorded and proposed methods to resolve DRPs ***Others***: • Developed a rehabilitation plan- smoking cessation, exercise
27	Wang et al[51]				√				***D=Administration:*** • Education - Made videos and relevant popular science education articles. • Inhalation Technical - Demonstrated the operation steps of the inhaler device for the patients and corrected the operation error of the patients • Telephone follow-up - Repeatedly deepened the patient's impression of the precautions for the use of the inhaler device. • Online consultation - Established an online platform for online consultation and education.

28	Prasungriyo et al[52]		√		√	√		√	***B=Prescribing***: • Medication reconciliation - Together with medication dispensing, hospital pharmacists provided medication reconciliation. ***D=Administration***: • Counseling - Included basic knowledge of COPD, pathophysiology and risk factors in the development of the disease, a review of the technique for using inhalers, the importance of medication adherence • Education - Printed material containing succinct information regarding the disease, medications, and instructions on using the inhalers was made available to intervention patients. ***E=Monitoring***: • Patients were contacted by phone to investigate any adverse events. ***Others***: • Smoking cessation • Self-management and lifestyle modification • Breathing exercises
29	Liu et al[53]		√		√	√			***B=Prescribing***: • Analyzed the patient's prior use of medication and adjusted the prescription. ***D=Administration***: • Medication education for COPD patients. ***E=Monitoring***: • Recorded adverse drug events and misuse of drugs. • Two follow-up surveys were carried out 1 and 6 months after discharge (self-administering medication at home, CAT score, and patient medication adherence)

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in addition to face-to-face communication,[29–32,35–52] pharmacists also provided relevant reading materials for patients[27,29,37,38,40–43,49,51,52] or started a WeChat or online interactive platform,[42,49,51] or conducted follow-up phone calls,[30–32,38,40,41,44,49,51] in order to resolve doubts during medication administration, optimize compliance and monitor for drug-related problems.

Pharmacists recorded the patients' relevant responses to the drug treatment, COPD knowledge, medication adherence, drug-drug interactions, and adverse drug reactions for monitoring purposes.[17,26,27,29–43,46,47,50,52,53] Other non-pharmacologic therapy management responsibilities for pharmacists included human resources management, training, and development, in order to continuously improve their competence and knowledge. Besides, since COPD treatment was a process that required patient self-management, pharmacists also tried to help support patients improving their lifestyles and habits particularly with smoking cessation education.[27,29,37–39,41,42,47,48,50,52] More details about the intervention of hospital pharmacists are shown in Table 3.

Input of Hospital Pharmacist' Interventions for COPD Patients

The most common inputs included in the studies were educational materials, including booklets,[27,29] patient information leaflets,[37,41] videos,[42,49,52] popular science articles,[42,49,51] brochures[42,49] and printed materials.[52] In addition, various forms of face-to-face education were also common, including lectures,[30] interviews,[31] counselling sessions,[37,41] and classroom teaching.[43] Some studies played the role of the network, and input WeChat interactive platform,[42] online consulting platform.[49,51] In addition, the inputs in the studies also included labels,[26] mediation lists,[32,50] and special distribution window.[49]

Output and Outcome of Hospital Pharmacist' Interventions for COPD Patients

16 studies measured the output and outcome of COPD-intervention by hospital pharmacists among inpatients, 8 on outpatients[26,27,29–31,42,51,59] 5 on both.[17,32,39,48,53] The duration of intervention reported ranged from 1 month to 24 months. Only 4 studies[28,32,36,44] reported about multi-disciplinary intervention, while the others pharmacist-specific intervention.

A range of output had been reported including adherence, rational drug use, level of knowledge, drug serum level, health resources utilization, inhalation technique and success of smoking cessation. Among them, the most common change due to hospital pharmacist interventions was the improvement of patient medication adherence.[26,27,29–31,38–42,46,47,49–51] The second common output reported was improved rational use of drugs.[28,33,35,40,46,50,53] However, Farris et al[32] reported there were no statistically significant differences in medication appropriateness. Some studies which assessed changes in the knowledge of medication and knowledge of disease management[27,29,30,43,46] showed positive effects. The benefits of pharmacist intervention were also demonstrated in such areas as maintaining drug serum levels[26,] improving inhalation technique,[36,42,43,45,49,51] reducing health resource utilizations,[27,29] and promoting smoking cessation.[38]

All but three studies[26,41,45] also measured changes in the patient outcome (clinical, economic and humanistic) upon hospital pharmacist intervention. The most commonly used clinical tests were a reduction in CAT score or mMRC grading score, or an increase in SGRQ score in the intervention group to demonstrate a better clinical outcome after pharmacist involvement in the intervention.[34,35,37,38,47,49,50,52,53] An increase in the FEV1/ FEV1% was also a common test to demonstrate positive clinical outcomes.[27,29,42,43,47] Other clinical outcome measured included: reduced rates of hospital readmission,[27,30,32,35,39,43,45] the length of stay,[17,27,28,33,53] decrease in dyspnea[36,38,42] and reduced adverse drug adverse reactions.[30,35,39,40,43] Regarding humanistic outcomes, some related studies showed that pharmacists provided helpful services and improved patients' satisfaction with medical institutions.[36,40,46,49,51] Several studies showed positive effects in terms of quality of life.[27,31,49] However, two studies showed interventions by hospital pharmacists failed to improve patients' quality of life.[29,50] Regarding economic outcomes, five studies suggested that pharmacist services could help lower healthcare expenditures, including drug costs, costs of hospitalization, and antibiotic costs.[28,33,43,48,50] Two studies showed there were no statistically significant differences in total hospitalization costs, antibacterial drug costs, daily costs, and direct costs.[46,52] More details about the output and outcome of hospital pharmacist' interventions for COPD patients are shown in Table 4.

Table 4 Output and Outcome of Hospital Pharmacist Intervention

No.	Authors	Intervention Design				Output							Outcome		
		Service Components	Duration of Study (Months)	Duration of Intervention (Months)	Multi-Disciplinary	Adherence	Rational Drug Use	Knowledge	Serum Level	Health Resources Utilization	Inhalation Technique	Smoking Cessation	Patient		
													Economic	Humanistic	Clinical
Section 1: Inpatient															
1	Shen et al[28]	Prescribing	10	10	Yes		+						● Hospitalization cost (-) ● Antibiotics cost (-)		● Length of hospital stay (-)
2	Wei et al[33]	Administration Monitoring	N/A	N/A	No		+						● Hospitalization cost (-) ● Drug cost (-) ● Antibiotics cost (-)		● Length of hospital stay (-)
3	Yan et al[34]	Preparation Administration Monitoring	6	N/A	No										● CAT score (-) ● mMRC grading score(-)
4	Wang et al[35]	Prescribing Administration Monitoring Others	6	N/A	No		+								● CAT score(-) ● mMRC grading (-) ● Adverse drug reactions(-)
5	Lin et al[36]	Administration Monitoring	N/A	N/A	Yes						+			● Patients' satisfaction (+)	● Dyspnea phenomenon(-)
6	Suhaj et al[37]	Administration Monitoring Others	36	24	No										● SGRQ score (+)
7	Xin et al[38]	Administration Monitoring Others	12	12	No	+						+			● SGRQ score (+) ● Severe exacerbation (-) ● Hospitalizations(-)
8	Zhang et al[40]	Prescribing Administration Monitoring	N/A	N/A	No	+	+							● Patients' satisfaction (+)	● Adverse drug reactions(-)
9	Abdulsalim et al[41]	Administration Monitoring Others	36	24	No	+									
10	Song et al[43]	Prescribing Administration Monitoring Others	12	12	No			+			+		● Total medical cost (-) ● Antibiotics cost (-) ● cost of inhaled preparations (+)		● readmission %(+) ● Adverse drug reactions(-)

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Table 4 (Continued).

No.	Authors	Intervention Design				Output							Outcome		
		Service Components	Duration of Study (Months)	Duration of Intervention (Months)	Multi-Disciplinary	Adherence	Rational Drug Use	Knowledge	Serum Level	Health Resources Utilization	Inhalation Technique	Smoking Cessation	Patient		
													Economic	Humanistic	Clinical
11	Bloodworth et al[44]	Prescribing Preparation Administration Monitoring Others	6	6	Yes										• Readmission rates (-) • Time to readmission(-)
12	Chen et al[45]	Administration	N/A	N/A	No						+				
13	Li et al[46]	Administration Monitoring Others	N/A	40 days	No	+	+	+					• Hospitalization cost (=) • Drug cost (=) • Antibiotics cost (=) • Daily cost(=)	• Patients' satisfaction (+)	• Clinical symptom improvement (=) • Complication (=) • Prognosis (=) • Mortality (=)
14	Yang et al[47]	Administration Monitoring Others	6	1	No	+									• FEV1%(+) • 6MWD score (-) • CAT score (-) • mMRC grading(-) • Adverse drug reactions (-) • Hospital readmission rate(-)
15	Wang et al[49]	Administration	3	3	No	+					+			• Quality of life(+) • Patients' satisfaction (+)	• CAT score(-)
16	Prasungriyo et al[52]	Prescribing Administration Monitoring Others	3	3	No								• Direct costs(=)		1. Hospital readmissions(=) 2. CAT scores(-) 3. PDC scores(=)
Section 2: Outpatient															
1	De et al[26]	Preparation Administration Monitoring	6	6	No	+			+						
2	Khdour et al[27]	Prescribing Administration Monitoring Others	12	12	No	+		+		+				• Quality of life (HRQoL scores) (+)	• Hospital admissions (-) • ED visits (-) • Total of hospital days (-) • FEV1 (=) • BMI scores (=)
3	Jarab et al[29]	Prescribing Administration Monitoring Others	6	6	NO	+		+		+				• Quality of life (=)	• Hospital admission (-) • FEV1 (=) • BMI scores (=)
4	Wei et al[30]	Administration Monitoring Others	6	6	No	+		+							• Adverse drug reactions (-)

5	Wei et al[31]	Administration Monitoring	6	6	NO	+								● Quality of life (HRQoL scores) (+)	● Admission rate (-)
6	Chen et al[42]	Administration Monitoring Others	6	6	No	+					+				● FEV1% (+) ● Acute attacks/ exacerbations(-) ● Clinical effective control rate(+) ● Adverse drug reactions (=)
7	Wang et al[50]	Prescribing Administration Monitoring Others	6	6	No	+	+						● Drug cost(-)	● Quality of life (EQ-5D) (=)	CAT scores(-)
8	Wang et al[51]	Administration	3	3	No	+					+			● Patients' satisfaction(+)	● The clinical effective control rate(+) ● Adverse drug events(=) ● Acute exacerbation (-)
Section 3: Inpatient & Outpatient															
1	Farris et al[32]	Administration Monitoring	5 years	3	Yes		=			=					● Adverse events(=)
2	Qin et al[39]	Prescribing Administration Monitoring Others	6	6	No	+									● Clinical effect(+) ● Pulmonary function indicators(+) ● Acute exacerbation (-) ● Adverse drug reactions (-)
3	Juanes et al[17]	Prescribing Administration Monitoring	12	12	No										● Hospital stay (=) ● Mortality(=) ● Drug-related negative outcomes(-)
4	Abdulsalim et al[48]	Administration Monitoring Training Others	24	24	No								● Drug cost(-)		
5	Liu et al[53]	Prescribing Administration Monitoring	12	6	No	+	+						● Costs of hospitalization(-)		● CAT scores(+) ● length of stay (-) ● Adverse drug reactions (-)

Abbreviation: CAT, COPD assessment test.

Contextual Factors

Among the included literature, the contextual factors affecting the hospital pharmacists' interventions and their effectiveness can be summarized into four factors: geographical factors;[17,48] education level of patients;[45] socio-economic factors;[48,51] and no-smoking policy.[48] With different healthcare institutes in different areas, the professional skills of medical staff, patient management, and access to certain medications varied and might have affect the outcomes.[17,48] Besides, the education level of patients could affect the effect of pharmacist education, thus affecting the improvement in medication compliance.[45] The presence of policies that mandated the price of cigarettes and the prohibition of smoking in public places also aided in reducing COPD and its aggravation.[48]

Quality Assessment

Most of the studies included in this review fully satisfied 1/3 of the CONSORT items (Figure 2). The details were as follows: (1) *Title and abstract* - Few articles (n=7)[17,31,32,37,38,41,52] specified in their titles that they were RCTs, but most articles (n=22) provided structured abstracts; (2) *Introduction* - Almost all articles (n=27) reported the trial background and purpose; (3) *Methods* - The inclusion and exclusion criteria for study subjects were relatively well reported (n=26). Only 2 articles[39,44] clearly reported the trial design, 5 articles[27,32,37,40,52] fully described the details and timing of the trial intervention, 2 articles[32,53] specified the exact definition of the intended primary and secondary outcome indicators and their measurement methods, and 6 articles indicated the measurement time and sample size.[17,27,29,37,41,48] * In terms of randomization procedures, no articles were considered "fully satisfied", with the most common problems including not reporting the method used to generate the type of randomization (n=15),[29–33,35,36,41,45,46,49–53] allocation concealment mechanisms (n=10),[26,30,33,40,45,46,49,50,52,53] blinding and who was blinded after the implementation of the blinded allocation intervention (n=16);[27,29,30,33,35,39,40,43,45–47,49–53] (4) *Results* - Most papers described the baseline demographic and clinical characteristics (n=22), and the number of participants (denominator) included in each analysis (n=24); (6) *Discussion* - All articles (n=29) discussed the generalizability of the trial findings and considered other relevant evidence to make a reasonable interpretation of the trial findings. However, less than half of the articles considered trial limitations and analyzed them; (8) *Other information* - Few articles reported study registration (n=7),[17,27,32,37,38,41,42] study protocols (n=1),[44] and 14 articles reported funding.[27,29,31,32,37–40,42–45,50,52,53]

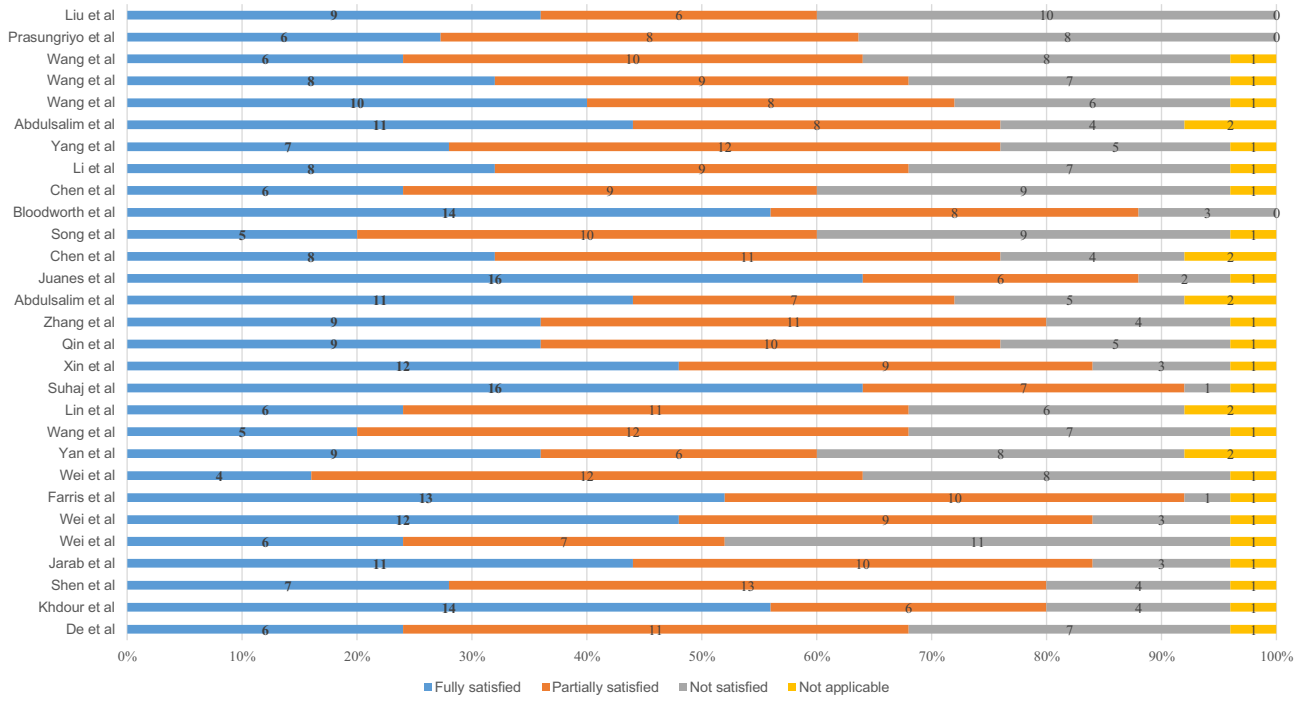

Figure 2 Reporting quality of the included studies according to the CONSORT Guideline (n=29).

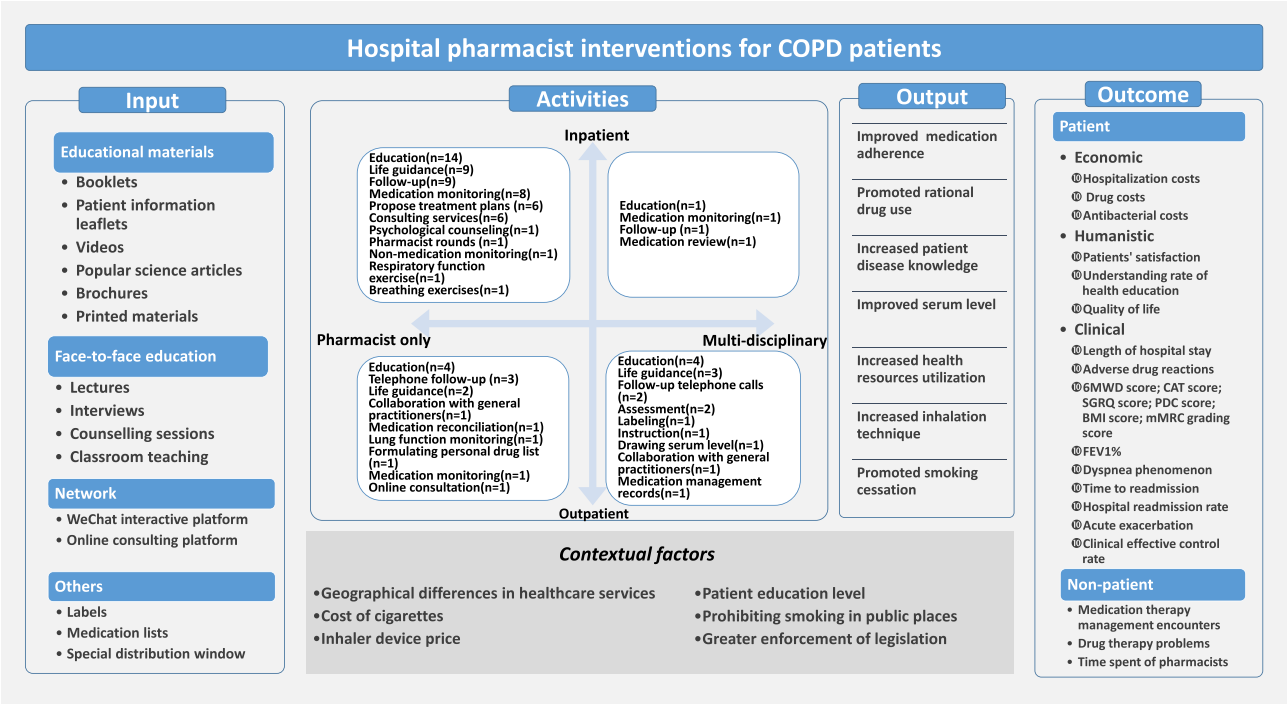

Figure 3 The logic model of hospital pharmacist interventions for COPD patients.

Discussion

This systematic literature review included 29 articles which reported the results of RCTs investigating the impact of interventions provided by hospital pharmacists on COPD patients. The findings provide a detailed summary of the evidence pertaining to the role hospital pharmacists could play in COPD management. An overview of the types of interventions, the output and outcome measures and the contextual factors identified was depicted following the logic modelling framework (Figure 3). In accordance with the general recommendations listed in the Basel statements, interventions by hospital pharmacists for COPD patients identified in this study mainly included preparation, prescribing, administration, and monitoring (but not so much about procurement and training). Extended interventions were also identified including lifestyle guidance, psychological counseling, and respiratory function exercise. Overall, hospital pharmacists' COPD-interventions had been shown to be beneficial to patient care in terms of a range of output (patient medication adherence,[26,27,29–31,38–42,46,47,49–51] rational use of drugs,[28,33,35,40,46,50,53] knowledge,[27,29,30,43,46] serum levels,[26] inhalation technique,[36,42,43,45,49,51] health resource utilizations,[27,29] and smoking cessation[38]), as well as clinical outcome (CAT score or mMRC grading score, SGRQ,[34,35,37,38,47,49,50,52,53] FEV1/FEV1%,[27,29,42,43,47] rates of hospital readmission,[27,30,32,35,39,43,45] the length of stay,[17,27,28,33,53] dyspnea[36,38,42] and adverse drug adverse reactions[30,35,39,40,43]), economic outcome (drug costs,[33,46,48,50] hospitalization costs,[28,33,46,53] antibiotic costs,[28,33,43,46] daily costs,[46] total costs,[43] and direct costs[52]) and humanistic outcome (patients' satisfaction,[36,40,46,49,51] quality of life[27,29,31,49,50]). This logic model may serve as a foundation for coordinating, promoting and evaluating hospital pharmacists' initiatives to strengthen COPD patient management.

According to the National Institute of Clinical Excellence (NICE) clinical guideline,[54] COPD patients are in need of various support: advising patients about how to effectively use inhaled medications, educate patients about how to effectively manage their symptoms and exacerbations, support patients to quit smoking, promote healthy living and exercise, and help monitor antibiotic and corticosteroid use. As reported in the included studies in this review, which also echoed with the findings from a previous study,[55] hospital pharmacists were well-positioned to cover all these areas through the provision of pharmaceutical care to support the management and care of patients with COPD.[17,26,27,29–53] COPD patients seeking help at the hospital setting, whether it be for specialist consultation, ER visits or hospitalizations, were usually prone to more severe

cases of the disease requiring more complex medication use. Advising about pharmacotherapy regimen tailored to individual patients, taking into account their full medical and medication history and their most recent clinical presentations, were considered important to both prescribers and the patients.[17,27–29,32,34,35,39,40,43,44,50,52,53]

Hospital pharmacists were trained as a custodian of drug safety.[56] Having access to patients' full medical record, they were positioned to evaluate the rationale of drug use, determine and prevent any avoidable adverse drug reactions and drug interactions, and monitor for any unforeseeable drug related problems for timely management. This was especially the case when patients were prescribed to use medicines with narrow therapeutic index or great potentials to interact (eg theophylline).[28,33,35,40,46,50,53] Informing the patients about the importance of compliance with the use of preventer inhaler, and gargling after the use of inhaled corticosteroid medication to reduce the risks of common side effects (eg oral thrush) was some of the basic actions pharmacists should take when caring for COPD patients.[26,27,29–31,38–42,46,47,49–51] In 2 studies, pharmacists' monitoring of patient proper use of antibiotics and oral corticosteroids for acute exacerbations also demonstrated benefits in quality of life, severe exacerbations and hospitalizations.[27,39] Educating the patients about the technique of using different inhaled medications, and supporting the correct use of such medication even after discharge were also found to be important for symptomatic control and reducing readmission.[27,36–39,41,48,49,51,52]

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2022 report repeatedly emphasizes on the importance of compliance to COPD medications and the accuracy of inhaler technique for patients to achieve control of the disease.[57] However, incorrect use of the inhaled medications remain a long-standing challenge in the management of COPD and the prevalence of correct inhaler use remains unacceptably low,[58] which were associated with poor disease control and frequent disease exacerbation.[59] Critical errors in inhalation device technique for different types of inhalers (pressurized metered dose inhaler (pMDI), dry powder inhaler (DPI), soft mist inhaler (SMI)) had been well-documents for pharmacists to deliver more targeted counselling.[58,60] Moreover, hospital pharmacists could also offer advice to the prescribers about the choice of inhaler device considering individual patients preference, needs and abilities.[61,62] The benefits of improved adherence[26,27,29–31,38–42,46,47,49–51] due to hospital pharmacists' intervention were observed in both outpatients and inpatients.

Improvements in patient medication adherence were the most common outcome change.[26,27,29–31,38–42,46,47,49–51,53] The indicators for evaluating medication adherence were mixed. The Morisky scale was used most, and it was used in seven articles.[27,30,39,41,47,50,53] Besides, the Medication Adherence Questionnaire (MAQ),[41] the BMQ score,[49] medication refill adherence scores[38] and pill counts plus direct interview[26] were also used. However, one Chinese study[45] did not specify the method of measuring medication adherence. Although we believed that the care of hospital pharmacists could improve the compliance of patients, the standards for measuring the degree of improvement in medication adherence were different, making it challenging to compare study results and the effectiveness of different pharmacist interventions. Besides, we were unable to determine whether the patient's medication compliance may be improved for a longer period of time after the completion of the care plan. COPD generally requires long-term treatment time. The improvement of patient compliance must be sustained over a long period of time, and more studies on this topic are anticipated in the future.

This review also showed that hospital pharmacists' role in supporting the management and care of COPD patients extended beyond drug treatment. As recommended previously,[63,64] the hospital pharmacists involved in this review were often actively involved in patient counseling about the disease, drug use and control of symptoms,[17,26,27,29–35,37–44,46–53] lifestyles and habits particularly with smoking cessation education.[27,29,37–39,41,42,47,48,50,52] Smoking cessation, in particular, has a major influence on the disease course[65] and pharmacists could play an important role in the effective delivery of smoking cessation counseling.[66] As reported in one of the studies in this review, patients who attended the pharmacist-managed clinic were more likely to quit smoking. This is in line with other previous findings that even brief pharmacist-led counseling sessions were found to be associated with long periods of persistent quitting.[66] As such, even pharmacists in the hospital settings should take every opportunity to provide smoking cessation counseling and discuss with the patients about the tobacco cessation drug therapy.[67]

On contrary, this review also uncovered a number of areas about hospital pharmacists' role in COPD management that were under-researched. Firstly, only 1 study in this review investigated the effect of the cooperation by hospital pharmacists with pharmacies in the community setting.[44] Transition of care (TOC) refers to the various points where

a patient moves to, or returns from, a particular physical location for the purposes of receiving health care.[68] It had been estimated that about 60% of all medication errors occur during TOC.[69] It was of particular importance that hospital pharmacists were able to identify patients in need of post-discharge support and engage in communication and collaboration with their community pharmacists.[70] Upon patients' consent, programs that involved the sharing of information about medication therapy, monitoring requirements and other precautions between hospital pharmacists and community pharmacists. There is a need for more research to determine if such cross-sector collaboration would be beneficial to the patients' long-term disease control such as reduction in medication errors and even readmission in order to support the overall practices in COPD management during TOC.[71,72]

Secondly, the extent of physician-pharmacist collaboration for COPD management in the hospital setting was under-reported as only 2 studies in the review focused on multi-disciplinary intervention involving these 2 healthcare professions.[28,36] In a multidisciplinary approach, pharmacists played an important role in managing drug therapy and were thus integral members of healthcare professional (HCP) teams.[21] They were well-equipped to make inter-professional contribution by providing evidence-based pharmaco-therapeutic recommendations, and establishing and maintaining an effective medication reconciliation process in the hospital setting.[73] Patients being looked after via physician-pharmacist collaborative practices were likely to demonstrate improved disease control.[74] Program design involving physician-pharmacist collaboration required more research about its effect on patient outcome which would serve as evidence that further encouraged physicians' increased rate of acceptance of pharmacist interventions.

Thirdly, hospital pharmacists' role in pulmonary rehabilitation was not fully evaluated according to the findings of this review as only 3 studies explored this extended role.[46,50,52] Pulmonary rehabilitation is a specialized programme of exercise and education designed to help people with lung problems such as COPD and had been shown to effectively improve symptomatic control and reduce hospital readmissions, and improve patients' quality of life.[75] It had been suggested that pharmacists' participation in pulmonary rehabilitation for COPD patients might be beneficial with patient education about the use of medications, dosage, inhalation technique, symptoms and adverse drug reaction monitoring, and support to lifestyle changes leading to enhanced quality of life for the patients.[76] Fourthly, pharmacists' active role in improving the rates of vaccination against influenza through identifying predisposing factors and patient education might help to decrease the risk of lower respiratory tract infections triggering exacerbation of COPD.[76] However, no study in this review had explored the benefits of hospital pharmacists' involvement on vaccination intention. Further research is needed to allow the leverage of hospital pharmacists' contribution in promotion seasonal influenza vaccine in the overall COPD management.

This study has some limitations. Firstly, this study is a systematic literature review which included exclusively findings of RCTs. While the quality of evidence for hospital pharmacists' interventions derived from RCTs was considered the highest, this review was not able to capture any emerging trend or practice reported in other publication types. Future study could collect information from other sources, including cross-sectional studies and qualitative studies to validate and enrich the logic model developed in this study. Secondly, the included studies were heterogeneous in design and outcome of interest which made it difficult to compare results across studies. Thirdly, most of the studies included in this review were of moderate quality. However, the concerns about the quality of the included articles was not viewed to have significant import on the overall findings about the current landscape of hospital pharmacists' participation in COPD management. Despite the above-mentioned limitations, it is believed that this systematic review provided a comprehensive insight into a growing body of important literature that demonstrates the beneficial role of hospital pharmacists in COPD management.

Conclusion

Hospital pharmacists' interventions are effective for the management and care of COPD. Although the availability of high-quality, robust RCTs evaluating the impact of their interventions on patient outcomes is limited, the growing body of evidence identified in this study suggested that hospital pharmacists played a crucial role in the care of both COPD inpatients and outpatients, during their study in the hospital and even after discharge. Indeed, this current study has provided specific examples of interventions including pharmacists-only interventions and multi-disciplinary approach improving patients' clinical, humanistic and economic outcomes; however, study designs were highly variable highlighting a lack of standardized approach to COPD management by pharmacists at the hospital setting. Future research

should focus on providing strong evidence to support the development of standardized approach and thus good practices for pharmacists when caring for COPD patients in the hospital setting.

Data Sharing Statement

All the data for this systematic review has been included into the manuscript.

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.

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Disclosure

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