Pharmacist-Led Management of Congestive Heart Failure: Improving Treatment Adherence and Patient Outcomes: A Systematic Review

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ABSTRACT

Research showed that congestive heart failure (CHF) patients receiving pharmacist-participated management interventions have improved clinical and non-clinical benefits. This is a systematic review study evaluating the impact of pharmacists' interventions in improving adherence and patient outcomes in CHF. Randomized controlled trials (RCTs) peer-reviewed in English-language assessing the pharmacist-participated collaborated care intervention in CHF were included. PubMed/MEDLINE database was searched for relevant literature published from January 1997 until October 2024. The systematic search strategy yielded 557 articles from PubMed/MEDLINE. Using the relevant title and or abstract review as a basis, 465 papers in total didn't meet inclusion criteria. The remaining 92 full-text articles were assessed manually. Finally, 24 RCTs were identified for inclusion with a total of 9,785 patients. The 24 RCT articles reported six different impacts of the pharmacist-participated interventions. In most of the articles, 16 (66.7%) pharmacist-led intervention was the type of pharmacist-participated intervention in multidisciplinary team management of CHF patients. Pharmacists' interventions had significant effects on medication adherence and reduction of medication errors among CHF patients. However, rates of hospitalization, mortality, and quality of life of the intervention groups were not significantly different compared to the control groups. The findings of this review suggest that pharmacist-led interventions improved medication adherence and reduced medication errors among patients with CHF. Pharmacists ought to be a member of the collaborative care team of CHF patients for better clinical and non-clinical outcomes.

Keywords: Congestive heart failure; Hospitalization; Adherence; Multidisciplinary team; Pharmacist intervention; systematic review

INTRODUCTION

Congestive heart failure (CHF) is a prevalent disease affecting 23 million people globally. CHF is associated with an increased risk of death after one year in elderly adults[1,2]. Nevertheless, a guideline directed medical therapy (GDMT) for heart failure with reduced ejection fraction (HFrEF) has been demonstrated to improve health clinical symptoms, reduce number of hospital visits, patients' quality of life, and reduce mortality[3]. Examples of these internationally recognized guidelines include those developed by the European Society of Cardiology (ESC), American College of Cardiology (ACC), and the American Heart Association (AHA). These guidelines provide appropriate recommendations regarding drugs choice and dosage regimens for heart failure patients with reduced ejection fraction. The guidelines recommend the inclusion of the following drug classes for the initial therapy: angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), angiotensin receptor-neprilysin inhibitor (ARNI), beta blockers (BBs), mineralocorticoid receptor antagonists (MRA), and sodium-glucose cotransporter 2 inhibitors (SGLT2I)[3].

Despite the clear advantages of GDMT in randomized clinical trials, available data reveals that the majority of patients with HFrEF in real-world clinical settings are not receiving appropriate doses of drug therapy[4]. Studies demonstrated that within 30 days of being discharged from the hospital, about 2% of patients with HFrEF receive no GDMT prescription and approximately 45% of patients receive monotherapy rather than oral GDMT[5,6]. Even still, community-based management of HFrEF patients often lacks target doses of oral GDMT, and does not make changes even after one year, in spite of discharge on underdoses or no GDMT[6–8]. The inconsistent and inappropriate administration of medications following GDMT has been associated with adverse health outcomes. For example, a 29% increased risk of mortality after a 2-year follow-up was associated with insufficient GDMT in a real-world sample of HFrEF patients[9]. Furthermore, some studies have linked the discontinuation of an initiated oral GDMT with higher mortality risk even after achieving clinical stability [4–6, 9,10].

The issue of inadequate or ineffective utilization of GDMT for CHF continues despite its proven effectiveness in enhancing patient outcomes. Pharmacists are becoming more and more valued members of the healthcare team due to their particular knowledge of drugs.[12] Recent studies showed that pharmacists make a significant impact in improving medication adherence, regimen optimization, quality of life, and symptom control among patients requiring care for CHF.[13,14] They can be part of a multidisciplinary team or manage interventions independently. However, the holistic impact and efficacy of pharmacist-led interventions in enhancing GDMT consumption among CHF patients remains largely unclear. Therefore, this systematic review sought to examine the available published data on the impact of pharmacists' interventions in improving adherence and patient outcomes in CHF.

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METHODS

Database Search and Selection of Studies: Using PubMed/ MEDLINE database, a thorough literature search was carried out. All relevant literature published from January 1997 until October 2024, were included in the search. The search was restricted to randomized clinical trials (RCTs) published in English and utilized the terms "pharmacist" and "heart failure". To broaden the search, the author identified and included MeSH terms such as “congestive heart failure”, “hospitalization”, “adherence”, “multidisciplinary team”, and “pharmacist intervention”. The synonyms or other possible description of the key words were used to develop a robust search strategy in this review. The search strategy used in the database was “heart failure” [MeSH] OR “congestive heart failure” [Text Word] AND “hospitalization” [Text Word] OR “hospitalized” [Text Word] OR “outpatient” [Text Word] AND “medication adherence” [Text Word] OR “medication persistence” [MeSH]“drug compliance” [MeSH] OR “concordance” [Text Word] OR “medication non-adherence” [MeSH] AND “multidisciplinary team” [Text Word] OR “healthcare team” [Text Word] OR “healthcare professionals” [Text Word] OR “patient care team” [Text Word] Or “interdisciplinary team” [Text Word] AND “pharmacist intervention” [Text Word] OR “medication review” [Text Word] OR “patient counselling” [Text Word] OR ‘medication reconciliation” [Text Word]. Studies were included if the patients were at least 18 years and assessed the type and or impact of pharmacist-led, pharmacist-involved or pharmaceutical care interventions in the management of CHF patients. The author excluded any non-RCTs, studies with abstract and protocol only, and studies focusing on non-CHF populations.

The author manually examined the reference lists of the included articles and eliminated any duplicate entries. Approval from the Institutional Review Board was not necessary for this research, as it is considered a secondary analysis.

Classification of the Pharmacist-Participated Interventions

The interventions reported by the 24 RCTs articles analysed were classified into the following categories:

Pharmacist-led interventions: Either with doctors in the clinic, pharmacist provides interventions on education, medication reconciliation, and optimization, or in an inpatient setting.

Nurse or pharmacist home visit: To evaluate clinical assessment and education visits made to the patient's home.

Telephone support: To evaluate the clinical status of the patient and help, structured telephone conversations are used without remote telemonitoring.

Pharmacist transitions coordinator (PTC): This involves collaboration with community-based and inpatient pharmacists to offer 30 days of drugs upon release as well as pre-discharge medication reconciliation.

Telemonitoring: To assess weight, vitals, or other indicators of functional condition are monitored remotely using phone calls to follow-up.

Pharmacist and nurse intervention: This involves intervention made by pharmacist or nurse including medication education, optimizing medication adherence, and counseling.

Study Outcomes: The primary outcome of interest in this systematic review was medication adherence among CHF patients who received any form of pharmacists’ intervention. The secondary outcomes were rate of rehospitalization, all-cause mortality, rate of medication error, promotion of GDMT, and quality of life.

Data Extraction and Quality Assessment: Relevant data were extracted from the included full-text articles using the data extraction form. The data obtained included publication year and country, number of participants, type of pharmacists’ interventions, and their impacts on patients’ outcomes. Cochrane quality assessment tool was utilized in evaluating the quality of the eligible studies. This tool is designed for the purpose of evaluating the quality of RCTs before their inclusion in systematic reviews. It assesses the methodological rigors of the paper based on seven distinct domains. The domains are generation of random sequence, concealment of allocations, blinding of the participants and the researchers, completeness of the outcome data reported, selective reporting, and other biases that may take place during the conduct of the study. The quality of each paper was adjudged as having either low risk or unclear risk or high risk of bias in each of the seven domains evaluated. Following the evaluation of bias in each of these domains, the author combine the data to produce an overall risk of bias verdict for each article. The overall outcome was classified as "high risk of bias" if one or more domains are judged to have a high risk, or as "low risk of bias" if all domains are thought to have a low risk.

Data analysis: A summary of the articles that reported each type of intervention was presented as frequencies and percentages. On the other hand, the impact of the interventions was reported in terms of the number of articles reported.

RESULTS

The systematic database search yielded 557 articles from PubMed/ MEDLINE. A total of 465 articles were eliminated based on the relevance of the title of the study and review of the abstract. The remaining 92 full-text articles were assessed manually. Finally, 24 RCTs were identified for inclusion. The final included 24 articles were studies conducted in 10 different countries, cutting across North America, Europe, Middle East, and Oceania. Specifically, most of the studies were conducted in the North America (United States of America [9] and Canada [2]), followed by Europe (Netherland [3], United Kingdom [2], Spain [1], Sweden [1], Slovenia [1], and Germany [1]). Three papers originated from Oceania as represented by Australia, and one paper originated from the United Arab Emirates. Overall, a total of 9,785 patients with heart failure participated in the reviewed studies (Table 1).

Figure 1 showed the PRISMA flow chart of the study screening and selection criteria.

Articles reporting pharmacist-led intervention, 16 (66.7%) were the majority, followed by those that reported nurse or pharmacist home visits, 3 (12.5%) as the type of pharmacist-participated interventions in multidisciplinary team management of CHF patients (Table 2).

The 24 RCT articles reported six different outcomes evaluating the impact of pharmacist-participated interventions. The primary outcome, medication adherence, was reported in nine studies (37.5%). The secondary outcomes were reported as the following: rate of rehospitalization in 14 studies (58.3%), all-cause mortality in seven studies (29.2%), rate of medication errors in three studies (12.5%), quality of life in five studies (20.9%), and GDMT promotion in one study (4.2%). The impact of pharmacist interventions was significantly associated with reduced medication error (100%), improved quality of life (40%), improved medication adherence (75%), better GDMT promotion (100%), reduced rehospitalizations (35.7%), and lower mortality rate (14.3%) (Table 3).

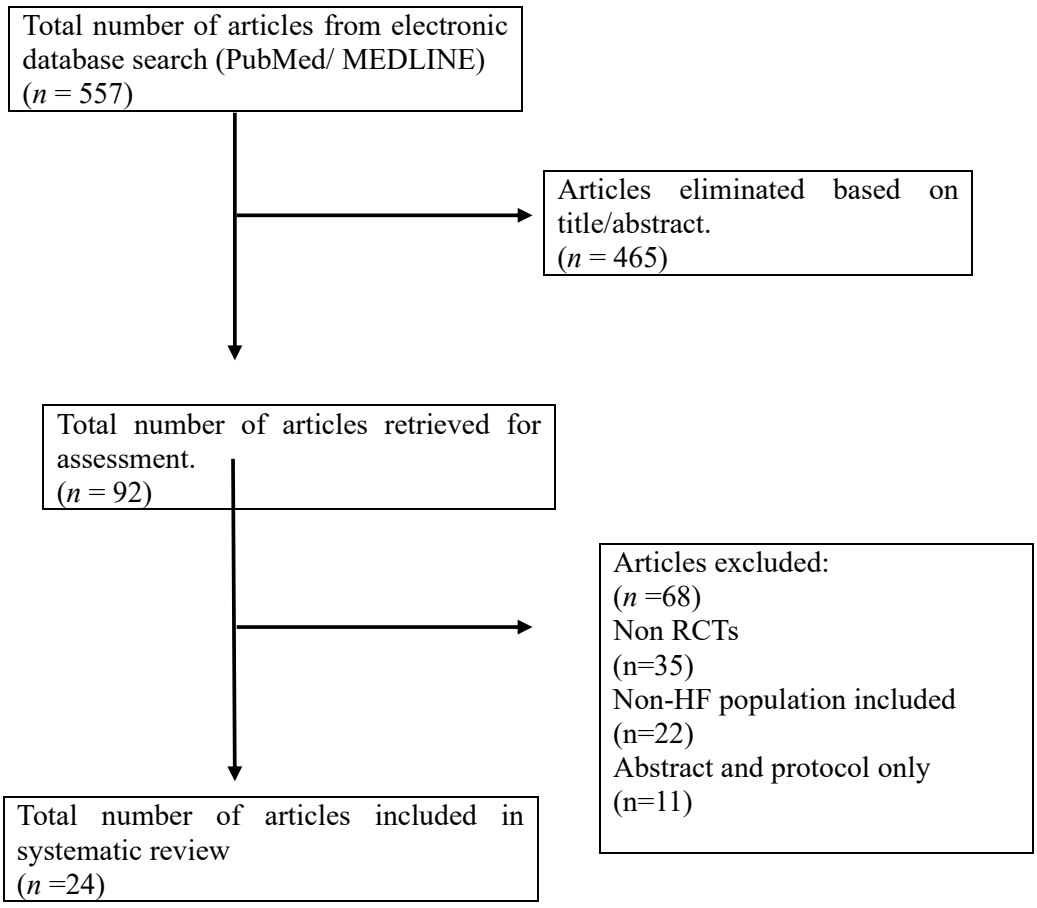

Figure 1. Systematic Review Flow Chart

Table 4 shows the risk of bias assessment of the included studies. The findings revealed slight variations across methodological domains. Most of the studies demonstrated a generally low risk of bias in domains such as random sequence generation and selective reporting bias, indicating adequate randomization processes and appropriate outcome assessment. However, unclear and high risk of bias were observed in three studies regarding allocation concealment [23,26,33], possibly due to insufficient reporting of methods used to prevent foreknowledge of treatment assignments. Four studies had unclear risk of performance bias[16,22,29,32], as blinding of participants and personnel was either not feasible or inadequately described in many trials, which may have influenced outcome measurement. Attrition bias was largely low, with most studies providing complete outcome data and clear explanations for participant withdrawals, although two studies had incomplete reporting that resulted in unclear judgments.[17,26] Overall, the majority of the included studies were rated as having a low to moderate risk of bias. While methodological quality was acceptable for most trials, the primary concerns related to performance bias, detection bias and incomplete descriptions of allocation concealment. These limitations should be considered when interpreting the results of this review.

DISCUSSION

The present review sought to evaluate the impact of pharmacists' interventions on medication adherence and other health outcomes of patients with CHF. The findings demonstrated that pharmacists' intervention significantly improved medication adherence in most of the studies reviewed[17,26,27,31,34,38]. However, in a few studies, there were no significant difference in medication adherence between pharmacists' associated interventions and control groups[18,24,37].

The most prominent secondary outcomes that were significantly improved by pharmacist interventions were rate of rate of medication errors as well as GDMT promotion[19,20,30,32]. On the other hand, there were controversy regarding the impact of pharmacist's intervention on rate of hospitalization, all-cause death, and quality of life. Most of the included articles reported no significant difference in CHF hospitalization rate or hospital readmission rate over different timeline ranging from 30 days up to 5 years[15,16,20,22,23,25,28,32,36]. On the other hand, five studies found a significant difference in the rate of hospitalization between pharmacists' intervention group and usual care group[21,27,31,35,37]. Almost all the included papers that evaluated the impact of pharmacists associated interventions found no significant influence of the interventions on the rate of death as

Table 1: Summary of the included RCTs studies evaluating pharmacy-led management of congestive heart failure

Author	Year	Sample size (intervention vs control)	Country	Intervention	Control	Primary outcome(s)	Secondary outcome(s)
Barker, Anna et al.[15]	2012	120 (64 vs 54)	Australia	Pharmacist-led intervention	Standard care	Mortality and congestive heart failure (CHF) rehospitalization over 6-month (no significant difference between the two arms in both outcomes). There was no difference between groups in mortality (HR = 1.41, 0.50 - 3.97; P = 0.51) or CHF rehospitalizations (incidence rate ratio [IRR] = 1.74 95% CI: 0.85-3.60; P = 0.13) over the 6-month follow-up period.	NA
Bloodworth, Lauren S et al. [16]	2019	477 (96 vs 381)	USA	Pharmacist transitions coordinator (PTC)	Standard care	30-day and all-cause rehospitalizations (no significant difference between the two arms in both outcomes). 30-day rehospitalization were 5.8% in the intervention group and 6.9% in the control group (OR = 0.82; P= 0.761). All-cause rehospitalization were 10.5% in the intervention group and 16.2% in the control group (OR = 0.59; P= 0.242).	NA
Bouvy, Marcel L et al.[17]	2003	152 (74 vs 78)	Netherlands	Pharmacist-led intervention	Standard care	Medication adherence (significantly better in intervention arm). Patients in the intervention group had 140/7656 days without use of loop diuretics compared with 337/6196 days in the usual care group (RR= 0.33 [CI 95% 0.24–0.38]).	Rehospitalizations, mortality, and quality of life. All secondary outcomes showed no significant differences between the two groups.
Bucci, Claudia et al.[18]	2003	80	Canada	Pharmacist-led intervention	Standard care	Medication adherence by using the Medication Appropriateness Index (MAI) and Purdue Directive Guidance (DG) scale (significantly better MAI score in intervention arm, but no significant difference in DG score) The change in MAI score from baseline was 0.74 and 0.49 for the intervention and control groups, respectively; P= 0.605).	NA
Eggink, Rixt Nynke et al.[19]	2010	85 (44 vs 41)	Netherlands	Pharmacist-led intervention	Standard care	Prescription errors and medication discrepancies after discharge (significantly less error and discrepancies in intervention arm). 68% of patients in the control group had at least one discrepancy or prescription error vs 39% in the intervention group (RR 0.57 (95% CI, 0.37-0.88)) The percentage of medications with a discrepancy or prescription error in the control group was 14.6% and 6.1% in the intervention group (RR= 0.42 (95% CI, 0.27–0.66)).	NA
Freeman, Christopher R et al.[20]	2021	306 (129 vs 177)	Australia	Pharmacist-led intervention	Standard care	One-year rehospitalization (no significant difference between the two arms). By 12 months, 282 rehospitalizations among control patients and 136 among intervention patients (fully adjusted IR ratio [IRR], 0.79; 95% CI, 0.52–1.18).	NA
Gattis, W A et al.[21]	1999	181 (90 vs 91)	USA	Pharmacist intervention and telemonitoring	Standard care	Combined all-cause mortality and non-fatal heart failure rehospitalization (significantly lower in intervention arm). All-cause mortality and non-fatal heart failure rehospitalization up to one year were significantly lower in the intervention group compared with the control group odds ratio [OR], 0.22; 95% confidence interval [CI], 0.07-0.65; P= 0.005).	NA

Author	Year	Sample size (intervention vs control)	Country	Intervention	Control	Primary outcome(s)	Secondary outcome(s)
Heaton, Pamela C et al.[22]	2019	400 (213 vs 187)	USA	Pharmacist-led intervention	Standard care	30-day rehospitalization (no significant difference between the two arms; significant difference was noticed only in the per-protocol analysis). There was no significant difference in 30-day rehospitalization between intervention and control groups (11.3% vs. 10.7%; P= 0.49). In a per protocol (PP) analysis for patients who showed up in their appointment, there was a significant difference in 30-day rehospitalization (1.6% vs. 10.7%; P= 0.02).	NA
Holland, Richard et al.[23]	2007	293 (149 vs 144)	UK	Pharmacist-led intervention	Standard care	Six months rehospitalization (no significant difference between the two arms). 134 admissions at six months occurred in the intervention group compared with 112 in the control group (rate ratio=1.15, (95% confidence interval CI= 0.89-1.48; P= 0.28)).	Mortality and quality of life. No statistical difference in both outcomes were noted.
Israel, Emily N et al.[24]	2013	732 (486 vs 246	USA	Pharmacist-led intervention	Standard care	Medication adherence at discharge, 30 days after discharge, and 90 days after discharge (no significant difference between the two arms in any outcome).	NA
Lee, Keane K et al[25]	2020	2091 (1027 vs 1064)	USA	Pharmacist intervention and telephone support	Standard care	30-days rehospitalization and all-cause mortality (no significant difference between the two arms). There were no significant differences in 30-day heart failure rehospitalization (8.6% intervention group vs 10.6% control group; P= 0.11). All-cause rehospitalization (18.8% intervention group vs 20.6% control group; P= 0.30). All-cause mortality (4.0% intervention group vs 4.6% control group; P= 0.49).	NA
Linné, A B et al.[26]	1999	130 (64 vs 66)	Sweden	Nurse or pharmacist home visit	Standard care	Medication adherence and knowledge after 6 months using an interactive Kodak Photo-CD Portfolio technique (significantly better points in intervention arm). The intervention group attained 17.2 points (mean) vs 14.3 points (mean) in control group, 95% CI of difference 1.0–4.7 points; P= 0.0051)	NA
López Cabezas, C et al.[27]	2006	134 (70 vs 64)	Spain	Pharmacist intervention and telephone support	Standard care	Medication adherence, 6 months rehospitalization, and quality of life (significantly better adherence and lower rehospitalization in intervention arm; but no significant difference in quality of life). Medication adherence was significantly better in intervention group than in the control group 88.2% vs. 60.5% at 2 months; P= 0.002, 91.1% vs. 69.0% at 6 months; P= 0.015. Intervention group had a lower risk of rehospitalization (Hazard ratio 0.56; 95% CI: 0.32-0.97). No differences were recorded in quality of life between groups.	NA

Author	Year	Sample size (intervention vs control)	Country	Intervention	Control	Primary outcome(s)	Secondary outcome(s)
Lowrie, Richard et al.[28]	2012	2164 (1090 vs 1074)	UK	Pharmacist-led intervention	Standard care	A composite of mortality or rehospitalization up to five years (no significant difference between the two arms in any outcome). The primary outcome occurred in 35.8% of patients in the intervention group and 35.4% in the usual care group (hazard ratio 0.97, 95% CI 0.83-1.14; P= 0.72).	NA
McCarren, Madeline et al.[29]	2013	220 (122 vs 98)	USA	Pharmacist-led intervention	Standard care	GDMT promotion (significantly better guideline concordance in intervention arm). Eligible patients had a beta-blocker prescription that was not guideline concordant. Level 1 intervention included information to a pharmacist on facility guideline concordance. Level 2 also provided a list of patients not meeting guideline goals. Compared with level 1, the level 2 intervention was associated with 1.9-fold greater odds of improvement in prescribing (95% confidence interval [CI] 1.1-3.2).	NA
Murray Michael D et al,[30]	2009	800 (366 vs 434	USA	Pharmacist-led intervention	Standard care	Medication errors (significantly lower medication error in intervention arm). Compared with the control group, the risk of medication error was lower in the intervention group by 37% (risk ratio, 0.63; 95% CI, 0.40-0.98).	NA
Murray, Michael D et al.[31]	2007	314 (122 vs 192)	USA	Pharmacist-led intervention	Standard care	Medication adherence and nine months rehospitalization (significantly better adherence and lower rehospitalization in intervention arm). During the 9-month intervention period, medication adherence was 67.9% and 78.8% in the usual care and intervention groups, respectively (difference, 10.9 percentage points [95% CI, 5.0 - 16.7 percentage points]). Rehospitalization was 19.4% less in the intervention group (incidence rate ratio, 0.82 [CI, 0.73 - 0.93]).	NA
Roblek, Tina et al.[32]	2016	51 (26 vs 25)	Slovenia	Pharmacist-led intervention	Standard care	Drug-drug interactions (DDIs) at discharge, six months rehospitalization, and mortality (significantly lower DDIs in intervention arm; no significant difference in the other outcomes). DDIs were significantly lower in the intervention group at discharge: 8 cases vs. 18 cases; P= 0.003. Over a 6-month follow-up period, 11 control and 9 intervention patients were re-hospitalized or died; p > 0.2 for all.	NA
Sadik, A et al.[33]	2005	208 (104 vs 104)	United Arab Emirates	Pharmacist-led intervention	Standard care	Quality of life by using the Minnesota living with heart failure questionnaire (significantly better quality of life in intervention arm). Intervention patients showed significant (P < 0.05) improvements in health-related quality of life, [463.5 (433.2, 493.9) unit.month in intervention patients vs. 637.5 (597.2, 677.7) in control patients.	NA

Author	Year	Sample size (intervention vs control)	Country	Intervention	Control	Primary outcome(s)	Secondary outcome(s)
Schulz, Martin et al.[34]	2019	237 (110 vs 127)	Germany	Pharmacist-led intervention	Standard care	Medication adherence (significantly better adherence in intervention arm). Intervention group compared with control group resulted in an absolute increase in mean adherence to three heart failure medications for 365 days [adjusted difference 5.7%, 95% confidence interval (CI) 1.6–9.8, P= 0.007].	Quality of life by using Minnesota Living with Heart Failure Questionnaire, rehospitalization and death. Intervention group improved quality of life after 2 years (adjusted difference in scores −7.8 points (−14.5 to −1.1; P= 0.02), compared to control group. No difference between the two groups for rehospitalization and death.
Stewart, S et al.[35]	1998	97 (49 vs 48)	Australia	Nurse or pharmacist home visit	Standard care	Six months rehospitalization (significantly lower rehospitalization in intervention arm). The intervention group had less readmissions within 6 months (36% vs 63%; P= 0.03).	Mortality. No difference in mortality between the intervention group and control group, respectively 12.2% vs 25%; P= 0.11
Triller, Darren M, and Robert A Hamilton.[36]	2007	154	USA	Nurse or pharmacist home visit	Standard care	The composite of rehospitalization and death up to one year (no significant difference between the two arms). Intervention group had similar rate of the composite primary endpoint compared to usual care (61% vs. 62%, RR= 0.98; p= 1),	NA
Tsuyuki, Ross T et al.[37]	2004	276 (140 vs 136)	Canada	Pharmacist and nurse intervention	Standard care	Medication adherence and rehospitalization up to six months (significantly lower rehospitalization rate in intervention arm; but no significant difference in the adherence rate). There was no significant difference in medication adherence between the two groups; P= 0.69. There was less reduction in cardiovascular rehospitalization in the intervention group compared to the control group 14.3% vs 36%; P= 0.03.	NA
Varma, S et al.[38]	1999	83 (42 vs 41)	Netherlands	Pharmacist-led intervention	Standard care	Medication adherence by using drug use profiles (significantly better adherence in intervention arm). Patients in the intervention group showed improved adherence with drug therapy compared to the control group; P= 0.039.	NA

Table 2: Type of pharmacist-participated interventions in the management of CHF patients

Type of intervention	Studies n (%)	Components of care
Pharmacist-led intervention	16 (66.7)	Medication review[15,19,20,28,34], patient education and counselling on disease state, drug therapy, & lifestyle modifications[15,22–24,29–33], facilitation of appointments with physicians,[15] medication adherence support,[17] medication reconciliation on discharge,[19,22] telephone monitoring and follow-up,[20,24,31,33] home visit (drug therapy monitoring)[23]
Nurse or pharmacist home visit	3 (12.5)	Patient education on disease state and drug therapy[26,35,36]
Pharmacist intervention and telephone support	2 (8.4)	Patient education and counselling,[25,27] telephone monitoring and follow-up[25,27]
Pharmacist transitions coordinator	1 (4.2)	Medication therapy management, medication reconciliation, comprehensive medication review, telephone monitoring of patients on drug therapy[16]
Pharmacist intervention and telemonitoring	1 (4.2)	Patient education and counselling[21]
Pharmacist and nurse intervention	1 (4.2)	Patient education on disease and drug therapy, medication adherence support, telephone monitoring and follow-up[37]

CHF = Congestive Heart Failure

Table 3: Impact of pharmacist-participated interventions in the management of CHF patients

Impact of Intervention	No. of Studies reporting significant impact (n, %)	References
Reduced hospitalization & readmission	5 out of 14 (35.7%)	15, 16, 20, 21, 22, 23, 25, 27, 28, 31, 32, 35, 36, 37
Improved medication adherence	6 out of 9 (75%)	17, 18, 24, 26, 27, 31, 34, 37, 38
Reduced all-cause mortality	1 out of 7 (14.3%)	15, 21, 25, 28, 32, 35, 36
Improved medication error	3 out of 3 (100%)	19, 30, 32
Improved quality of life	2 out of 5 (40%)	17, 23, 27, 33, 34
GDMT promotion	1 out of 1 (100%)	29

GDMT = Guideline Directed Medical Therapy

Table 4: Risk of bias assessment for included articles

Authors	Random sequence generation	Allocation concealment	Performance	Detection	Attrition	Selective reporting	Overall
Barker et al., 2012	•	•	•	•	•	•	•
Bloodworthet al., 2019	•	•	•	•	•	•	•
Bouvy et al., 2003	•	•	•	•	•	•	•
Bucci et al., 2003	•	•	•	•	•	•	•
Eggink et al., 2010	•	•	•	•	•	•	•
Freeman et al., 2021	•	•	•	•	•	•	•
Gattis et al., 1999	•	•	•	•	•	•	•
Heaton et al., 2019	•	•	•	•	•	•	•
Holland et al., 2007	•	•	•	•	•	•	•
Israel et al., 2013	•	•	•	•	•	•	•
Lee et al., 2020	•	•	•	•	•	•	•
Linné et al., 1999	•	•	•	•	•	•	•
López et al., 2006	•	•	•	•	•	•	•
Lowrie et al., 2012	•	•	•	•	•	•	•
McCarren et al., 2013	•	•	•	•	•	•	•
Murray et al., 2009	•	•	•	•	•	•	•
Murray et al., 2007	•	•	•	•	•	•	•
Roblek et al., 2016	•	•	•	•	•	•	•
Sadik et al., 2005	•	•	•	•	•	•	•
Schulz et al., 2019	•	•	•	•	•	•	•
Stewart et al., 1998	•	•	•	•	•	•	•
Triller et al., 2007	•	•	•	•	•	•	•
Tsuyuki et al., 2004	•	•	•	•	•	•	•
Varma et al., 1999	•	•	•	•	•	•	•

Green = Low risk of bias; Red = High risk of bias; Yellow = Unclear risk of bias

a result of heart failure and its complications or even in terms of all-cause mortality rate[15,25,28,32,35,36]. Nevertheless, the study conducted Gattis and colleagues reported significantly lower all-cause mortality rate and heart failure events in the intervention group compared to the control group; however, the statistical difference was mainly due to readmission to heart failure events[21]. Two out of five studies found a significant impact of pharmacists' intervention on the quality of life compared to control group[33,34.]

According to the current systematic review, pharmacists associated interventions were linked to improvement in medication adherence[17,26,27,31,34,38] even though in some studies, the investigators observed a downward spiral in the rate of medication adherence or compliance to prescribed treatment among heart failure patients shortly after the interventions were stopped[18,24,37]. According to the systematic investigation, there were several cases where pharmacist-led interventions improved medication adherence. Some studies have observed a decrease in medication adherence among patients with heart failure following the termination of these therapies. A dependence on the continuing assistance of pharmacists may be shown by the declining trend in adherence following the cessation of the intervention. It's possible that patients have become accustomed on the advice, prompts, or specific help provided by pharmacists to stick to their prescription schedule. The observed drop may have resulted from some patients' inability to maintain the same degree of adherence on their own once this support was removed. The importance of continued follow-up and support in helping heart failure patients continue to take their medications as prescribed is highlighted by this finding. In order to guarantee long-term adherence and treatment success, it emphasizes the difficulties that patients may encounter in sustaining adherence without ongoing care. This calls for prolonged interventions or other forms of ongoing support. Meanwhile, non-adherence to medications is considered among the chief factors that adversely affect drug therapy outcomes in patients with chronic diseases, including heart failure[39]. A previous systematic review among patients with heart failure identified several factors that promote medication non-adherence. These factors include social and economic factors (e.g., patients' age, level of education), patient-related factors (e.g., availability of social support), treatment-related factors (e.g., number of prescribed medications), and health-system related factors[39]. These determinants of medication adherence should be considered when designing robust strategies involving pharmacists aimed at maintaining high medication adherence levels among patients with health failure.

In the current review, pharmacists' interventions had no significant effect on the rate of hospitalization or readmission or mortality rate of patients with CHF. These findings were consistent with the results of a recent systematic review and meta-analysis of the impact of pharmacists' interventions on health outcomes of outpatients with heart failure[40]. According to the authors, there was no difference in rate of hospitalization and mortality rate[40]. However, an earlier systematic review of twelve RCTs studies reported that pharmacists care led to a reduction in the risk of all-cause deaths and rate of hospitalization in both inpatients and outpatients with heart failure in the intervention groups compared to the control groups, but had no significant impact on the rate of mortality[12]. This observed difference in the findings could be explained by the variation in the study population of interest and length of monitoring and follow-up. Thus, among patients with heart failure, the present review finding that pharmacist interventions had no discernible impact on hospitalization rates, readmissions, or mortality is remarkable. It implies that the examined pharmacist-led interventions did not appear to have a discernible effect on these crucial outcomes, based on the studies that made up the systematic review. The findings underscore the complexity of managing heart failure and the need for continued research, intervention refinement, and a patient-centered approach, even though they also suggest that the pharmacist-led interventions evaluated in the review did not produce statistically significant improvements in the rate of hospitalization or readmission and mortality rate for heart failure patients.

Pharmacists' intervention in the present review had no significant effect on the quality of life patients with CHF[17,23,27]. Nonetheless, the findings demonstrated that the quality of life scores of the intervention groups were higher than those of the control groups, but the difference were not statistically significance. The finding may indicate that, although there was no statistically significant difference in the quality of life between the intervention' groups and the control groups, there was a discernible trend, pointing to a probable beneficial effect accruing from the interventions provided. Even so, it is difficult to definitively link these benefits to the pharmacist-led interventions alone, given that the difference was not statistically significant. Therefore, to better understand the potential impact of pharmacists' interventions on improving the quality of life for CHF patients, this discovery may lead to additional research and modification of the intervention.

CONCLUSION

The findings of this review suggest that pharmacist-led interventions improved medication adherence and reduced medication errors among patients with CHF but had no effect on the rate of hospitalization or readmission, quality of life, and mortality rate. The findings of this analysis highlight how important pharmacist-led interventions are for improving medication adherence and decreasing medication errors in patients with CHF. It is important to highlight that, despite the interventions' favorable effects on medication adherence and medication errors, they had no significant effect on critical clinical endpoints including death, quality of life, or rates of hospitalization or readmission. Therefore, a more comprehensive and multidisciplinary approach involving the integration of pharmacist interventions with other healthcare strategies that address a wider range of factors affecting patient outcomes is recommended.

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