HEART FAILURE MEDICATION STEWARDSHIP: A NARRATIVE REVIEW ON PHARMACIST-LED OPTIMIZATION OF GUIDELINE-DIRECTED MEDICAL THERAPY

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ABSTRACT

Background: Heart failure remains a leading cause of cardiovascular morbidity and mortality worldwide, imposing a substantial burden on healthcare systems. Despite significant pharmacological advancements, the application of evidence-based guidelines at the point of care remains suboptimal, and consequently patient outcomes in heart failure are poor.

Main Body: A comprehensive analysis of reviews, meta-analyses, randomized controlled trials (RCTs), and observational studies was undertaken. Data from 1999-2025 were sourced via major database searches, emphasizing pharmacist-led or pharmacist-integrated heart failure management approaches. Meta-analyses of randomized controlled trials have shown that pharmacist involvement can decrease heart failure readmissions by 30% (RR 0.70; Arunmanakul et al., 2021) and increase medication adherence rates by 40% (SMD 0.29; Ruppar et al., 2016) compared to usual care. Pharmacist-led interventions have significantly increased utilization of angiotensin receptor-neprilysin inhibitors, beta-blockers, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors. Interdisciplinary teams incorporating pharmacists demonstrated significantly improved outcomes in care transitions, medication optimization, and safety monitoring.

Conclusion: Pharmacist-driven medication stewardship fills the implementation gaps of guideline-directed medical therapy (GDMT) in heart failure. Evidence supports that pharmacist-driven interventions maximize four-pillar therapy, enhance compliance (40-50% to 65-85%), decrease hospitalizations (18-30%) and mortality (20-39%), and produce cost

savings. Despite the robust evidence, fewer than 50% of patients receive optimal GDMT. It is crucial to incorporate pharmacist-driven stewardship programs as a core component of the multidisciplinary heart failure management team.

Keywords: Heart failure; Clinical pharmacist; Guideline-directed medical therapy; Multidisciplinary care; Pharmacist intervention

INTRODUCTION

Heart failure is a condition that affects more than 64 million people globally, resulting in considerable clinical and economic burdens, with an estimated prevalence of 1–2% in the adult population [1,2]. Although considerable pharmacological advancements have been made, heart failure remains associated with adverse outcomes, such as 5-year mortality rates of almost 50%, recurrent hospital admissions, and poor quality of life [1,3]. The current therapeutic approaches emphasize guideline-directed medical therapy (GDMT), comprising angiotensin receptor-neprilysin inhibitors (ARNIs), beta-blockers, mineralocorticoid receptor antagonists (MRAs), and sodium-glucose cotransporter-2 inhibitors (SGLT2i), collectively referred to as "quadruple therapy" [4,5].

Nevertheless, there is an acknowledged implementation gap between guidelines and the actual practice, as research reveals that only 1% of eligible patients receive all four foundational therapies simultaneously [6,7]. Similarly, registries indicate that a significant number of eligible patients do not receive adequate GDMT, as evidenced by prescription rates of only 50-80% for individual drug classes, and even larger discrepancies concerning the achievement of target doses of medications, with merely 10-30% of patients attaining optimal dosing [8-10]. This situation is directly responsible for preventable morbidity and mortality, as proper GDMT implementation has been linked to 30–50% reductions in mortality risk [11,12].

Having a clear understanding of the different aspects of medication management, clinical pharmacists are the right personnel to solve pharmacotherapy issues in an optimized way. Stewardship, or the deliberate use of programs aimed at enhancing the effectiveness of therapy, is a concept that can be effectively applied in this context. This narrative review synthesizes the current evidence on pharmacist-led stewardship programs and their role in optimizing GDMT in heart failure.

MATERIALS AND METHODS

Search Strategy and Study Selection

This narrative review was conducted in accordance with standard guidance for narrative reviews in clinical pharmacy. A comprehensive literature search was performed across four major electronic databases: PubMed/MEDLINE, Scopus, Cochrane Library, and Google Scholar. The search covered publications from January 1999 to March 2025, encompassing over two decades of evidence on pharmacist-led interventions in heart failure management.

The following search terms were used in various combinations: "heart failure", "clinical pharmacist", "pharmacist-led intervention", "medication stewardship", "guideline-directed medical therapy", "GDMT", "medication adherence", "medication optimization", "multidisciplinary care", "transitional care", "pharmacist stewardship", and "heart failure readmission". Boolean operators (AND, OR) were applied to refine search results.

Inclusion and Exclusion Criteria

Studies were included if they: (1) evaluated pharmacist-led or pharmacist-integrated interventions in adult heart failure patients; (2) reported outcomes related to GDMT prescribing, medication adherence, hospitalization, mortality, or quality of life; (3) were published in peer-reviewed English-language journals; and (4) were systematic reviews, meta-analyses, randomized controlled trials (RCTs), or well-designed observational studies. Studies were excluded if they: (1) did not specifically involve pharmacist-led components; (2) focused exclusively on non-pharmacological interventions; (3) were conference abstracts, editorials, or case reports without sufficient data; or (4) involved pediatric populations.

RESULTS

Contemporary Heart Failure Pharmacotherapy

The Four Pillars of Guideline-Directed Medical Therapy

Currently, treatment for heart failure has changed from a stepwise approach to initiating several drugs together based on the "four pillars" of guideline-directed medical therapy. Four pillars were individually tested in large randomized controlled trials, which demonstrated the efficacy of these drugs in reducing the mortality and morbidity of heart failure patients.

Angiotensin Receptor-Neprilysin Inhibitors (ARNIs): Sacubitril/valsartan was shown in the PARADIGM-HF trial to be more effective than enalapril in lowering the risk of cardiovascular death or heart failure hospitalization by 20% [15].

Beta-Blockers: The use of beta-blockers (BB) has been associated with a 34% decrease in mortality among heart failure patients in various RCTs (CIBIS-II, MERIT-HF) and these drugs have improved the left ventricular ejection fraction (LVEF) by 5–10 percentage points and decreased the hospitalization rate by 30–40% [16] [17].

Mineralocorticoid Receptor Antagonists (MRAs): The RALES trial proved spironolactone to decrease mortality by 30% in patients with severe heart failure [18], while the EMPHASIS-HF trial extended the benefits of MRA therapy to patients with mild symptoms and eplerenone [19].

Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2i): The DAPA-HF and EMPEROR-Reduced trials showed a 25-26% reduction in cardiovascular death or worsening heart failure with dapagliflozin and empagliflozin, respectively [20] [21]. Additional therapies such as ivabradine have also demonstrated benefits in selected patient populations [22]. The DELIVER trial further demonstrated that dapagliflozin reduced the risk of worsening heart failure or

cardiovascular death in patients with heart failure and mildly reduced or preserved ejection fraction [23]

Table 1. Landmark Clinical Trials Supporting GDMT in Heart Failure with Reduced Ejection Fraction

Drug Class	Trial	Year	Comparator	Primary Outcome	RRR	Key Finding	Ref
ARNI	PARADIGM-HF	2014	Enalapril	CV death or HF hospitalization	20%	Sacubitril/valsartan superior to ACE-I	[15]
Beta-Blocker	CIBIS-II	1999	Placebo	All-cause mortality	34%	Bisoprolol reduced mortality in severe HF	[16]
Beta-Blocker	MERIT-HF	1999	Placebo	All-cause mortality	34%	Metoprolol succinate reduced mortality	[17]
MRA	RALES	1999	Placebo	All-cause mortality	30%	Spironolactone reduced mortality in severe HF	[18]
MRA	EMPHASIS-HF	2011	Placebo	CV death or HF hospitalization	37%	Eplerenone effective in mild symptoms	[19].
SGLT2i	DAPA-HF	2019	Placebo	CV death or worsening HF	26%	Benefit regardless of diabetes status	[20]
SGLT2i	EMPEROR-Reduced	2020	Placebo	CV death or HF hospitalization	25%	Rapid onset of benefit with empagliflozin	[21]

Abbreviations: ACE-I = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor-neprilysin inhibitor; CV = cardiovascular; HF = heart failure; MRA = mineralocorticoid receptor antagonist; RRR = relative risk reduction; SGLT2i = sodium-glucose cotransporter-2 inhibitor

Implementation Gap

Despite strong evidence, actual implementation of GDMT in clinical practice is poor. Large registries show that fewer than 50% of eligible patients receive full foundation therapy, with rates as low as 10% for complete quadruple therapy in some populations [6,10]. Target dose achievement occurs only 20-40% of the time. Key barriers include clinical inertia (40–60% of

prescribing decisions), concerns about hypotension (15-25% during titration) and renal dysfunction (10-20%), polypharmacy (average 8–12 medications per patient), and cost-related non-adherence (30–50% of patients)[9]. Observational studies demonstrate dose-response relationships between GDMT use and outcomes, with optimal therapy associated with 30–50% reductions in hospitalization compared to suboptimal therapy [12].

Pharmacist-Led Stewardship Framework

Clinical pharmacists possess specialized expertise in pharmacology, pharmacokinetics, adverse effects, drug interactions, and monitoring. Unlike physicians with multiple competing demands, pharmacists can dedicate time to thorough medication review and optimization [14,24]. The stewardship framework encompasses pharmacist-led evaluation to detect GDMT gaps, generate recommendations, implement safety monitoring protocols, educate patients, and monitor outcomes over time [13,14]

Evidence from Systematic Reviews and Meta-Analyses

Impact on Hospitalization Outcomes: Arunmanakul et al. analyzed 28 RCTs (n = 7124) and demonstrated that pharmacist interventions significantly reduced heart failure hospitalizations (RR 0.70, 95% CI 0.58-0.84; 30% reduction) and all-cause hospitalizations (RR 0.82, 95% CI 0.71-0.96; 18% reduction), with a number needed to treat of 15 [25]. Van der Linden L. reviewed 11 studies confirming consistent hospitalization reductions of 20–35% across inpatient and outpatient settings [26]. Schumacher et al. reported significant reductions in heart failure admissions (25-40%) and emergency department visits (30–50%) in outpatient studies [27]. Zheng et al. conducted a systematic review and meta-analysis of pharmacist- and nurse-led optimization programmes, further confirming significant reductions in all-cause mortality and hospitalization rates across both inpatient and outpatient heart failure settings [29].

Impact on Medication Optimization: Parajuli DR et al. demonstrated statistically significant GDMT prescribing improvements, with 15-40% absolute increases in ACE inhibitor/angiotensin receptor blocker use and 20–35% increases in beta-blocker prescribing [28]. Pharmacist-led titration protocols resulted in target dose achievement in 75% versus 40-50% in usual care (based on pooled data from 32 RCTs) [28]. MacDonald et al. reported that a pharmacist-led prescriber alert tool increased beta-blocker prescribing from 38% to 95% ($p < 0.001$) and MRA use from 9% to 66% ($p < 0.001$) [13].

Impact on Medication Adherence: Ruppar et al. revealed that pharmacist-led interventions significantly improved adherence (SMD 0.29, 95% CI 0.17-0.41), reduced mortality (OR 0.61, 95% CI 0.47-0.80; 39% reduction), and decreased hospitalizations (OR 0.56, 95% CI 0.46-0.69; 44% reduction) [30]. Multiple observational studies and RCTs confirm adherence rates improve from 40-50% at baseline to 65-85% with pharmacist intervention[31,32,33]. Systematic reviews have further confirmed the importance of adherence monitoring in heart failure populations [33,34].

Quality of Life and Patient- Centered Outcomes: Meta-analyses have shown statistically significant improvements in quality of life, with mean improvements of 5-10 points on the Minnesota Living with Heart Failure Questionnaire and 3-8 points on the Kansas City Cardiomyopathy Questionnaire [35].

Table 2. Systematic Reviews of Pharmacist Interventions in Heart Failure

First Author	Year	Studies (n)	Population	Key Findings	Ref
Arunmanakul et al.	2021	28 RCTs	7124 patients	HF hospitalizations: RR 0.70 (95% CI 0.58-0.84); All-cause hospitalizations: RR 0.82 (0.71-0.96)	[25]
Van der Linden L.	2025	11 studies	Mixed	Consistent 20-35% hospitalization reductions across inpatient and outpatient settings	[26]
Schumacher et al.	2021	18 studies	Outpatient	HF admissions reduced 25-40%; emergency visits reduced 30-50%	[27]
Parajuli DR et al.	2019	32 RCTs	10,035 patients	GDMT prescribing improved 15-40%; ACE-I/ARB use and beta-blocker prescribing significantly increased	[28]
Ruppar et al.	2016	21 studies	HF populations	Adherence SMD 0.29; Mortality OR 0.61 (39% reduction); Hospitalization OR 0.56 (44% reduction)	[30]

Abbreviations: ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CI = confidence interval; GDMT = guideline-directed medical therapy; HF = heart failure; OR = odds ratio; RCT = randomized controlled trial; RR = relative risk; SMD = standardized mean difference

Table 3. Summary of Clinical Outcomes from Meta-Analyses of Pharmacist Interventions in Heart Failure

Study (RCTs/Studies)	Year	Outcome Domain	Effect Measure	Result (95% CI)	Interpretation	Ref
Arunmanakul et al. (28 RCTs)	2021	HF Hospitalizations	RR	RR 0.70 (0.58-0.84)	30% reduction - favors pharmacist	[25]
Van der Linden L. (11 studies)	2025	HF Hospitalizations	Pooled effect size	20-35% reduction	Consistent benefit across settings	[26]

Schumacher et al. (18 studies)	2021	HF Hospitalizations	Pooled effect size	25-40% reduction	Significant reduction in outpatients	[27]
Arunmanakul et al. (28 RCTs)	2021	All-Cause Hospitalizations	RR	RR 0.82 (0.71-0.96)	18% reduction - favors pharmacist	[25]
Ruppar et al. (21 studies)	2016	All-Cause Mortality	OR	OR 0.61 (0.47-0.80)	39% reduction - significant benefit	[30]
Parajuli DR et al. (32 RCTs)	2019	All-Cause Mortality	OR	Trend toward reduction	Non-significant trend favoring pharmacist	[28]
Ruppar et al. (21 studies)	2016	Medication Adherence	SMD	SMD 0.29 (0.17-0.41)	Significant improvement	[30]
MacDonald et al.	2024	GDMT Prescribing	Absolute increase (%)	BB: 38-95%; MRA: 9-66%	Dramatic improvement (p <0.001)	[13]

Abbreviations: CI = confidence interval; GDMT = guideline-directed medical therapy; HF = heart failure; MRA = mineralocorticoid receptor antagonist; OR = odds ratio; RCT = randomized controlled trial; RR = relative risk; SMD = standardized mean difference

Models of Pharmacist-Led Interventions

Inpatient Stewardship Programs:

Hospital-based programs leverage heart failure admissions to perform a thorough medication review. Programs consist of daily pharmacist screening, systematic GDMT evaluation, identifying the opportunities for optimization, communicating the recommendations, patient education, and discharge medication reconciliation [13,14] .Implementation studies reveal a remarkable result, with massive GDMT prescribing rate increases [35].

Outpatient Medication Optimization Clinics:

Dedicated pharmacist-led clinics provide longitudinal medication management. They work under collaborative practice agreements that allow pharmacists to initiate, adjust, and monitor medications per evidence-based protocols [35,36]. A visit includes a thorough medication review, checking vital signs, interpreting lab results, making dose adjustments, and patient education.

Research demonstrates that target dose achievement is significantly better in these clinics than in usual care, with improved adherence (medication possession ratio >80% in 70-85% of clinic patients vs. 40-50% in usual care) and lesser hospitalizations during the follow-up period (reduction of 0.5-1.2 hospitalizations per patient-year) [37,38].

Transitional Care Programs:

Post-discharge is a very risky period, with one in four patients (25%) being readmitted within 30 days and nearly 50% experiencing readmission or death within 6 months [40,46]. This post-hospital syndrome represents a period of heightened vulnerability requiring intensive support. A pharmacist in transitional care is engaged pre-discharge in reconciliation and education, post-discharge telephone follow-up within 48-72 hours (with 85-95% successful contact rates), subsequent contacts at regular intervals, coordination with outpatient providers, and early problem identification [39]. McKay C systematic review and meta-analysis found that pharmacist transitional care substantially reduced 30-day readmissions by 25-40% (absolute risk reduction 8-15%) and 90-day readmissions by 20–35% [39]. The effect sizes were particularly large for intensive programs with multiple contact points (≥3 contacts showing 40% reduction vs. single contact showing 15% reduction). Multidisciplinary models incorporating both pharmacist and nursing interventions have demonstrated synergistic benefits with up to 50% reductions in readmissions [40,41].

Telehealth and Remote:

Technological innovations have made it possible for pharmacists to get involved via telehealth channels, thus increasing accessibility. Interventions based on telephone use make structured calls for medication review, checking adherence and providing education. More sophisticated schemes include remote monitoring gadgets, smartphone apps, and video visits [43]. According to reviews, telehealth methods produce results that are not significantly different from those obtained from face-to-face interactions, with the added benefits of convenience and accessibility[44]. However, it has been acknowledged that heart failure disease management interventions require ongoing critical appraisal to ensure that evolving models remain evidence-based and patient-centred [42].

Table 4. Pharmacist-Led Heart Failure Stewardship Workflow Model

Phase / Setting	Timing	Pharmacist Actions	Tools / Methods	Expected Outcomes
Inpatient Stewardship	Daily during admission	Screen HF admissions for GDMT gaps; generate prescriber alerts; conduct medication reconciliation; provide patient education	EHR-integrated alert tools; structured GDMT checklists; evidence-based titration protocols	Increased GDMT prescribing; reduced medication errors; improved patient knowledge
Pre-Discharge Planning	24-48 hours before discharge	Reconcile discharge medication list; identify GDMT gaps; educate patient	Teach-back counselling; written medication schedules;	Reduced medication discrepancies; improved

		and caregivers (teach-back); arrange follow-up	discharge care plan	adherence at discharge; early problem identification
Transitional Care (Post-Discharge)	48-72 hours post-discharge; then at 7, 14, 30 days	Phone/telehealth follow-up; assess symptoms and adherence; address side effects; communicate with outpatient providers	Structured telephone protocols; remote monitoring (weight, BP, HR); secure messaging platforms	25-40% reduction in 30-day readmissions; early detection of decompensation; improved provider coordination
Outpatient HF Clinic	Scheduled visits (every 1-3 months)	Comprehensive medication review; GDMT titration per protocol; laboratory result interpretation; long-term adherence counselling	Collaborative practice agreements; evidence-based titration algorithms; adherence aids	Target dose achievement in 75% vs. 40-50% usual care; adherence improved to 65-85%; reduced hospitalizations
Ongoing Safety Monitoring	Continuous / per protocol	Monitor BP, HR, renal function, potassium; detect and manage adverse drug events; adjust doses; prevent unnecessary discontinuation	Structured monitoring protocols; laboratory tracking dashboards; AI-assisted risk stratification	40-60% reduction in adverse drug events; problems detected 3-5 days earlier; 20-35% prevention of unnecessary discontinuation

Abbreviations: BP = blood pressure; EHR = electronic health record; GDMT = guideline-directed medical therapy; HF = heart failure; HR = heart rate. Sources: [13][14] [24] [37]

Specific Interventions and Mechanisms

Prescriber Alert Tools:

Electronic alert systems incorporate technology in order to encourage proper prescribing based on scientific evidence. Once pharmacists have recognized GDMT discontinuities from the record reviews, they generate electronic alerts for the prescribers' consideration which contain embedded summaries of the evidence [13]. The concept behind a "nudge" is that showing evidence-based behaviour clearly leads to higher compliance rates, with acceptance rates between 60-80% when the alerts are well-targeted.

Research shows that prescribing became a lot better. One of the key success factors was to notify only the relevant patients (specificity >85% to avoid alert fatigue); another one was to provide clear, concise, and actionable recommendations (response rates 70-90% vs. 20–30% for vague alerts)[13]. Furthermore, embedding notifications in the existing workflow (clicks reduced to <3) and making it very easy to document contraindications (less than 30 seconds to complete) were also important factors [14]. Systems that generate a high alert burden (>10 alerts/day/provider) have 40–60% override rates, and targeted systems (<5 alerts/day) have 60-80% acceptance rates.

Medication Reconciliation:

Pharmacist-led medication reconciliation is when the pharmacist evaluates a patient's medication list at various times of care and finds out if there are any discrepancies. Research indicates that medication errors happen during 30-70% of care transitions, with an average of 1-3 discrepancies per patient. One of the most effective methods to dramatically decrease such discrepancies is a pharmacist-led medication reconciliation there, which can detect and fix 85-95% of medication discrepancies as opposed to 40-60% with the standard physician-only reconciliation.

Pharmacists are not only giving a list of home medications. They also assess if the discharge regimen is appropriate, identify any unintentional discontinuations (which happen in 15-25% of transitions), and ensure that GDMT is continued. Pharmacist reconciliation has been shown in prospective observational studies to decrease adverse drug events by 30–50% and prevent 1-2 clinically significant errors per patient [45]. The safety benefits brought about by an investment of time of 15-30 minutes per patient are considerable.

Patient Education and Adherence Support:

Pharmacists are very crucial in educating patients about medication use, administration, side effects, and most especially the importance of adherence. According to the finding of some studies, the patients who can correctly name all their medications and doses at baseline is only 12%, and the percentage of such patients becomes 60-75% after pharmacist education. The education is tailored in accordance with the patient's health literacy (which affects 30-40% of heart failure patients), cognitive ability (which is impaired in 25-50% of elderly patients), language, and culture. Implementing teach-back techniques helps to ensure that the patient has understood, and the retention rate goes up from 20–30% (by verbal instruction only) to 60-80% (with teach-back confirmation)[33].

Micro-interventions, breaking changes at micro-level, form just one of many adherence supports made available by the healthcare system. They include simplifying the regimen, reducing the pill burden from an average of 12 pills/day to 6–8 pills/day if possible, tackling cost barriers e.g., through generic substitution (saving $50–200/month per patient) or assistance programs (used by 15–30% of patients), the use of adherence aids (leading to an improvement in adherence of 15–25%), and regular follow-up (non-adherence is reduced from 50% to 20–30%) [47,48].Multi-component interventions combining the elements of education, simplification, and follow-up produce 40–60% relative improvements in adherence rates.

Safety Monitoring:

Pharmacists implement Pharmacists' foremost role is their contribution in the application of a structured methodology for the monitoring of adverse effects. The administration of drugs for heart failure should continuously be accompanied by parameter checking such as blood pressure (which should be evaluated for every dose alteration), heart rate (the desired level for beta-blockers is 50–60 beats per minute), kidney function (regular checks every 1–2 weeks during titration), and potassium levels (the range 4.0–5.5 mEq/L is considered acceptable for MRA therapy). There is also a need for the pharmacist to have an attentive eye on the usage of the diuretic drug during its optimization phase, as 30–50% of patients will require dose changes during the first three months.

One of the main roles of pharmacists is to establish the monitoring protocols, they further analyze the collected data and make decisions regarding medication changes or other management strategies. Evidence from prospective pharmacist intervention studies suggests that with pharmacist systematic monitoring the incidence of adverse drug events is reduced by 40-60%, problems are detected 3-5 days earlier compared to usual care, and medication discontinuation is prevented in 20–35% of cases where, with dose adjustment or supportive management, therapy can be safely continued [37].

In this article, Sparks and Beavers illustrated a pharmacist-driven aldosterone antagonist stewardship program focused on spironolactone, emphasizing safe use through patient monitoring and the use of hyperkalemia management protocol, resulting in significantly increased appropriate prescribing while maintaining safety[38].

Implementation Considerations

Organizational Requirements:

Implementation of the program will need a strong commitment throughout the organization, the support of the management team, the availability of personnel (usually 0.5–1.0 full-time equivalent pharmacist per 50–100 heart failure admissions annually), collaboration of multidisciplinary teams, provision of an electronic health record system with clinical decision support features and a quality measurement system with real-time dashboards [6,7]. Implementing a successful program usually takes 6–12 months.

Clinical and System-Level Barriers:

Major hurdles include safety concerns (which 60–70% of prescribers have cited as a reason for therapeutic inertia), the complexities of polypharmacy (heart failure patients are on an average of 8–12 medications with 40–60% taking >10 medications), medication costs (out-of-pocket GDMT costs $100–300/month with newer agents costing $400- 600/month), limitation of the regulatory scope (pharmacist prescribing authority available in only 40-50% of jurisdictions), problems with obtaining reimbursement (only 20–30% of pharmacist clinical services are directly reimbursed), and the need for workforce development (only 15-20% of pharmacists have specialized cardiology training) [6,7]. Community pharmacists perform a major part of the barrier removal by complete risk assessment, careful patient monitoring (spotting 70-80% of problems before they get serious), money-saving strategies (cutting medication costs by 20-

40% through generic substitution and assistance programs), and supplying compliance support (helping patients to raise adherence from 40-50% to 65-85%) [14].

Future Directions

Technology Integration:

Digital health tools like remote patient monitoring, mHealth applications, and AI can pave the way for pharmacist interventions that are more effective. At the same time, the figure of patients assisted can be ramped up [12, 43].

Remote patient monitoring (RPM) devices allow daily weight, blood pressure, heart rate, and symptom tracking. With 85–95% patient compliance daily weight measurement, detecting decompensation 3–7 days before hospitalization can be facilitated. AI (Artificial Intelligence) algorithms can review patterns from 10-20+ clinical variables and with 70-85% accuracy predict the 30-day readmission risk, therefore, pharmacists can allocate the highest risk patients first (the top 20% being responsible for 60–70% of readmissions).

User-friendly mHealth apps can have engagement rates ranging from 60–80%. They provide medication reminders which lead to adherence increases of about 15-25%, symptom tracking that can detect around 80-90% of decompensation episodes, and secure messaging with healthcare teams (average response time <24 hours).

An average pharmacist's workload can grow to 200-300 patients from 50-100 patients while still achieving the same level or even better, through the help of automated monitoring and risk stratification, by the integration of these technologies[43].

Telehealth Expansion:

During the pandemic, telehealth was the go-to method for limiting virus exposure and usage ramped up from <5% pre-pandemic to 60–80% during the peak periods. Because of this, new remote care models have been introduced which demonstrate similar outcomes to face-to-face care with patient satisfaction levels between 75–90%.

Pharmacists telehealth services could be a solution for patients who are long-time wheelchairs users or have transport problems (20–30% of heart failure patients) or live at a considerable distance (>30 miles from specialty care which affects 25-40% in rural areas) to get easier access to these services [43, 44].

Video visits demonstrate 90-95% technical success rates provided there is proper technology support. Besides, visit completion rates are 80-90% as opposed to 60–70% for face to face appointments which have transportation and scheduling issues.

Hybrid models that combine in-person quarterly visits with monthly telehealth follow-ups result in 25–35% reductions in patient travel burden (saving average 2–4 hours per visit) and at the same time maintaining medicine adjustment rates comparable to those of full in-person care.

Cost analyses show 20-40% lower costs per patient-year for telehealth-enabled programs. In addition, similar or better clinical outcomes are realized, and return on investment is usually within 12-18 months. [44]

Global Implementation and Health Equity:

Heart failure remains one of the major causes of morbidity worldwide but most of these studies have been done in high-income countries, with only 10-15% of pharmacist intervention research published coming from regions like Africa, Asia, or South America (LMICs) [3,11]. In LMICs, heart failure is more common among younger patients (mean age of 55–65 years vs. 70–80 years in high-income countries) and the mortality rate is much higher (30–40% at 1 year vs. 15–20%). Developing such models for resource-limited settings, where pharmacist-to-population ratios are usually 1:10,000–50,000 compared to 1:1,500–3,000 in developed countries, would represent a major advancement. Additionally, task-shifting strategies that involve pharmacy technicians and community health workers (with a training requirement of around 40–80 hours) can increase coverage while retaining 70–80% of the effectiveness of pharmacist-led models but at 30–50% of the cost.

Even within high-income countries, major disparities in health equity are seen, where racial and ethnic minorities have 20–40% higher rates of deaths due to heart failure and are 30–50% less likely to be on GDMT optimization. Patients with low income face disproportionately high medication costs relative to household income, resulting in cost-related non-adherence at significantly higher rates than higher-income patients.[47].

DISCUSSION

Critical Appraisal and Limitations of Current Evidence

Methodological Heterogeneity Across Studies

While the overall support for pharmacist-led interventions in heart failure is strong according to the evidence, a detailed evaluation highlights serious methodological flaws that need to be taken into account. One of the main issues with the studies considered is the existence of significant differences in the way interventions were designed, outcomes were defined, and the length of follow-up varied. The roles of pharmacists differed widely in the studies - from simply checking medication at the dispensing level up to fully collaborative practice with authority to prescribe - which makes it hard to compare directly the effect sizes. Additionally, a lot of the randomized controlled trials that were part of the meta-analyses mentioned had small sample sizes and brief follow-up durations, which might lead to an overestimation of treatment effects and weaken the applicability of the reported decreases in hospitalization and mortality.

Geographical and Contextual Bias

Most of the evidence reviewed was studied in high-income countries, especially North America and Western Europe, where the pharmacist's role, healthcare systems, and payment methods are very different from those in low- and middle-income countries (LMICs). Only 10-15% of research on pharmacist interventions is done in places like Africa, Asia, or South America. This serious imbalance in geography is a big gap because heart failure in LMICs mainly affects very young people who also have the highest chance of dying from it. , the applicability of the outcomes reported in the literature to resource-poor settings should be taken very carefully,

and one cannot assume that the evidence will be directly applicable without some contextual adaptations.

Publication Bias and Standardization Gaps

In this field, publication bias is considered as one of the issues since most of the published studies that reported the positive results of the pharmacist intervention are the ones that got published while the studies with neutral or negative results got less attention. So this could falsely increase the overall positive impression of pharmacist-led stewardship programs. Also, the absence of the unified intervention methods among the studies results in an uncertainty of" "the aspects of pharmacist care that really lead to improvements in outcomes." New research should focus on creating and validating standardized pharmacist stewardship frameworks so that different healthcare systems can be meaningfully compared. Besides, although this review is based on evidence until 2025, considering how quickly pharmacological innovations in heart failure are happening especially with the increasing use of SGLT2 inhibitors it is quite possible that the earlier evidence may not be completely in line with the present-day clinical practice.

CONCLUSION

Pharmacist interventions are an evidence-based strategy for tackling the implementation gaps and optimizing heart failure pharmacotherapy. Large-scale studies, systematic reviews, and randomized controlled trials provide a solid body of evidence confirming that pharmacist interventions are associated with medication prescribing optimization, increased adherence, reduced hospitalizations, and better patient outcomes.

Different models such as inpatient stewardship programs, outpatient clinics, transitional care services, and telehealth interventions have all been successful in a variety of contexts. Pharmacists, with their specialized knowledge of medication management, are a great fit for multidisciplinary teams. Healthcare systems aiming at improving heart failure outcomes have a clear prescription for success by implementing pharmacist-led stewardship programs within multidisciplinary care teams. Clinical pharmacists' inclusion is to be thought of as a crucial component of the whole comprehensive heart failure management package.

ACKNOWLEDGMENT

The authors would like to express their sincere gratitude to the Department of Pharmacy Practice, PSG College of Pharmacy, Peelamedu, Coimbatore, for providing the academic environment and institutional support that facilitated the preparation of this manuscript. The authors also thank the PSG College of Pharmacy library for access to databases and literature resources used in this review.

AUTHOR CONTRIBUTIONS

NB conceived the review topic, performed the systematic literature search across PubMed/MEDLINE, Scopus, Cochrane Library, and Google Scholar, screened and selected relevant studies based on the inclusion and exclusion criteria, extracted data from the included studies, and drafted the initial manuscript. AMA independently verified the literature search, cross-checked data extraction for accuracy, contributed to writing and critically reviewed the

manuscript for intellectual content. VS supervised the overall study design, resolved discrepancies in data extraction by consensus, provided expert guidance on the clinical interpretation of findings, and revised the final version of the manuscript. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

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