The role of pharmacists in the management of patients with atrial fibrillation: A systematic review and meta-analysis

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ABSTRACT

Background: Pharmacist-led interventions have demonstrated benefits across various medical conditions; however, their impact on atrial fibrillation (AF) remains unexplored. This study aims to synthesize the available evidence regarding the pharmacist's role in AF management.

Methods: A systematic review with searches in PubMed, Scopus, and Web of Science was performed (PROSPERO: CRD42025647848). Randomized and non-randomized trials, as well as cohort studies reporting clinical, process, and humanistic outcomes, were included. Findings were pooled through pairwise meta-analyses. Dichotomous outcomes were reported as risk ratios (RRs) and continuous variables as standardized mean differences (SMDs) with 95% confidence intervals (CIs). The quality of the randomized and non-randomized studies was assessed using RoB 2.0 and ROBINS-I tools, respectively. Evidence was graded using the GRADE approach.

Results: Seventeen studies ($n = 11,428$ participants) published between 2008 and 2024, predominantly as non-randomized trials/cohorts (77%), were included. Pharmacist-led interventions varied widely in scope, including anticoagulation management services, medication therapy management, and prescribing. Meta-analyses showed that pharmacists improved time in therapeutic range (SMD 0.35; 95% CI, 0.13–0.56) and reduced major bleeding events (RR 0.76; 95% CI, 0.61–0.95) and strokes (RR 0.65; 95% CI, 0.44–0.94) compared with usual care. Pharmacist care also increased appropriate prescription rates (RR 1.36, 95% CI, 1.18–1.56). No significant differences were found for other outcomes. Evidence was of low-to-moderate certainty.

Interpretation: Pharmacist-led interventions have been shown to improve certain clinical and process outcomes in AF.

Conclusions: High-quality randomized studies with well-defined interventions are still needed to better refine the pharmacist's role in AF care and to identify the most effective intervention in practice (see Graphical Abstract). *Can Pharm J (Ott)* 2025;158:351-367.

FERNANDA S. TONIN

Pharmacist-led interventions have demonstrated substantial benefits across various cardiovascular diseases. Therefore, the lack of a systematic review and meta-analysis on their impact on atrial fibrillation was somewhat surprising to us. We thought to close this evidence gap using an international network of pharmacists and a cardiologist.

Il a été démontré que les interventions menées par les pharmaciens apportent un bénéfice considérable dans le traitement de diverses maladies cardiovasculaires. Nous avons donc été très étonnés de constater qu'il n'existait aucune revue systématique ni méta-analyse sur leur impact sur la fibrillation auriculaire. Pour combler cette lacune, nous avons décidé de faire appel à un réseau international de pharmaciens et à un cardiologue.

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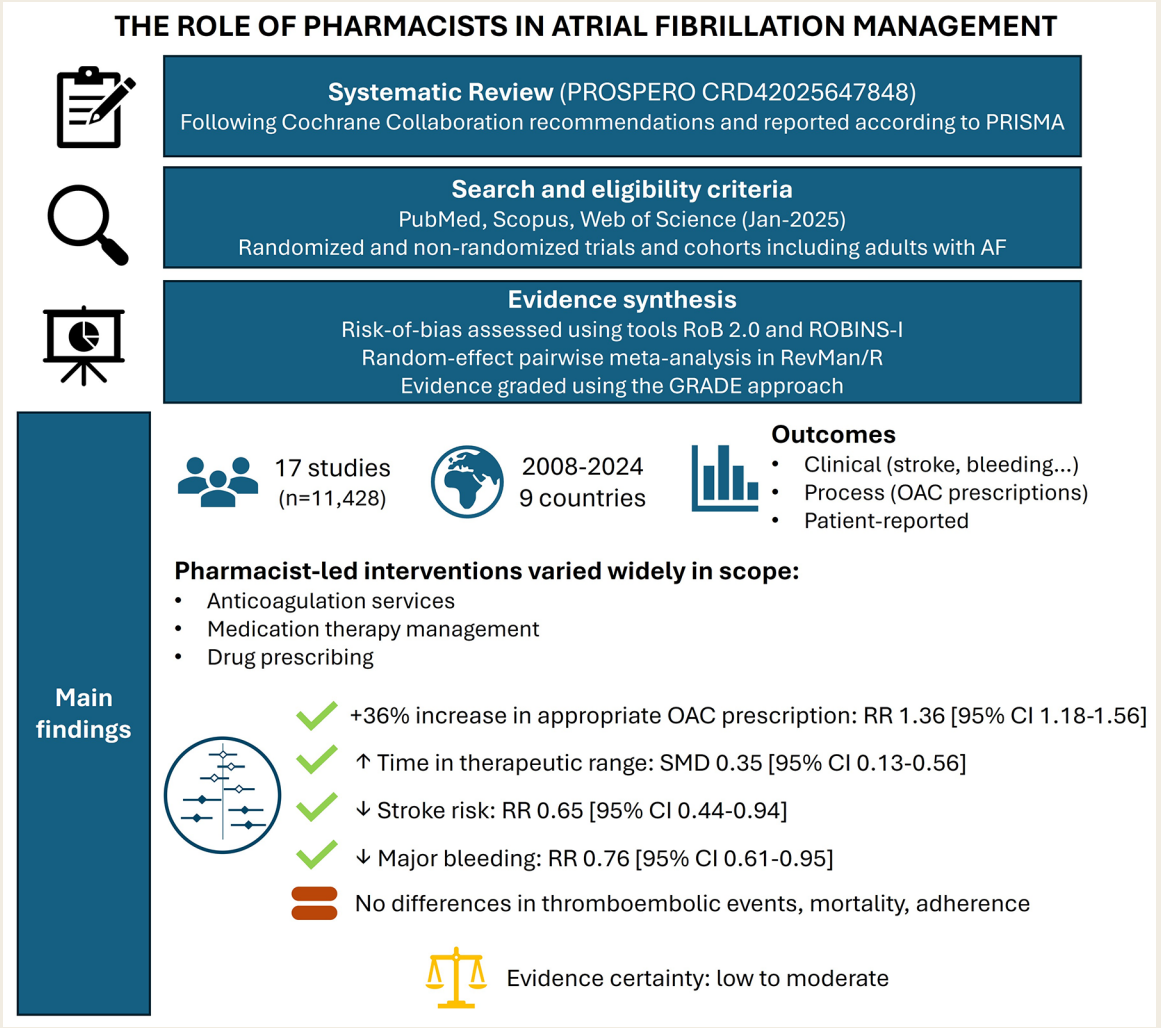
GRAPHICAL ABSTRACT



AF, atrial fibrillation; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; OAC, oral anticoagulants; RR, relative risk; SMD, standard mean difference.

KNOWLEDGE INTO PRACTICE

- Pharmacist-led interventions in the management of patients with atrial fibrillation improve outcomes. To help change health care policy, a synthesis of the worldwide evidence is needed.
- In this study, pharmacist-led interventions improved time in therapeutic range, reduced major bleeding events and strokes, and increased appropriate prescription rates of oral anticoagulants.
- The study provides moderate-quality evidence supporting the role of pharmacists in improving both clinical and process-related outcomes in atrial fibrillation care.
- Expanding pharmacist-led services in community and hospital cardiovascular settings can enhance adherence to guidelines and reduce adverse outcomes.

Introduction

Atrial fibrillation (AF) is the most prevalent sustained arrhythmia, affecting more than 43 million people worldwide. It is a leading cause of cardiovascular complications, most notably including a 5-fold increased risk of ischemic stroke and heart failure and reduced quality of life.[1,2]

To improve patients' outcomes in AF, integrated and holistic care approaches have been strongly advocated over the past decade.[3] The Atrial fibrillation Better Care (ABC) pathway, first proposed in 2017 and currently endorsed by several international guidelines,[4-7] provides a structured framework to AF management through 3 core elements: "A" (Anticoagulation/Avoid stroke), "B" (Better symptom management), and "C" (Cardiovascular and other comorbidity optimization). The European "CC to ABC" model recently expanded this approach by incorporating steps for diagnostic confirmation and risk stratification (e.g., stroke risk, symptom severity).[6,7] By implementing this or similar strategies—focusing on risk factor

MISE EN PRATIQUE DES CONNAISSANCES

- Les interventions menées par les pharmaciens dans la prise en charge des patients atteints de fibrillation auriculaire contribuent à améliorer les résultats. Pour faire évoluer les politiques en matière de soins de santé, il faut d'abord réaliser une synthèse des données disponibles à l'échelle mondiale.
- Dans cette étude, les interventions menées par les pharmaciens ont permis de maintenir les patients dans la fourchette thérapeutique plus longtemps, de diminuer la fréquence des hémorragies majeures et des accidents vasculaires cérébraux, et d'améliorer le taux de prescription appropriée d'anticoagulants oraux.
- L'étude apporte des preuves de qualité modérée qui soutiennent le rôle des pharmaciens dans l'amélioration des résultats cliniques et des processus dans le traitement de la fibrillation auriculaire.
- L'élargissement des services menés par les pharmaciens dans les établissements de soins cardiovasculaires communautaires et hospitaliers peut contribuer à améliorer le respect des directives et à réduire les résultats indésirables.

modification, rate or rhythm control, and identifying patients who require oral anticoagulation—AF can be effectively managed. This approach significantly reduces cardiovascular morbidity, including more than 62% of AF-related strokes,[8,9] while also enhancing patients' functional capacity and reducing health care use.[10-12]

However, despite the availability of these frameworks, the access to safe and low-burden oral anticoagulants (OAC) and the relatively widespread use of left atrial appendage occlusion, a significant proportion of patients with AF, especially those with subclinical disease, often individuals older than 65 years with comorbidities, remain either undertreated or untreated.[13-15] Even among diagnosed patients, a substantial gap persists in appropriate anticoagulation therapy.[16] Barriers to this include bleeding risk concerns, therapy access, and medication non-adherence, among others.[17,18]

These persistent challenges demand a new approach. Pharmacists are widely recognized as the most accessible health care professionals in the community, positioning them ideally for the early detection and management of AF (e.g., medication optimization and patient education focused on anticoagulation therapy, improved medication adherence, and modified risk factors).[17,19] Moreover, pharmacists with added prescribing authority can also initiate, adjust, and monitor treatments.[17,20] However, despite growing recognition of the role of pharmacist-led care in cardiovascular diseases—including conditions such as hypertension, heart failure, and stroke,[21-26] which have led to significant improvements in clinical outcomes, medication adherence, and health care cost reductions—their specific impact on AF care remains underexplored. Existing systematic reviews and ongoing studies are mostly limited to evaluating pharmacist management of OAC, regardless of patients' clinical condition,[27-30] or focus on the role of other professionals.[31-33]

To address this gap, we aimed to critically evaluate and synthesize the available evidence on the impact of pharmacist-led interventions on clinical, process-related, and patient-reported outcomes in AF management.

Methods

This systematic review was registered with the International Prospective Register of Systematic Reviews—PROSPERO (CRD42025647848)[34]; the protocol is also available at Open Science Framework (DOI: 10.17605/OSF.IO/MX5QB) and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; see the checklist in Appendix 1, available online under Supplementary Materials) and Cochrane Collaboration recommendations.[35,36] Meta-analyses followed Bonetti et al.[37] All study selection stages, data extraction, and risk-of-bias analyses were performed by 1 expert author and independently verified by another.

Search strategy and eligibility criteria

Searches were performed in MEDLINE (PubMed), Scopus, and Web of Science (January 25, 2025) without publication filters. Clinicaltrials.gov and reference lists of included studies were manually searched (Table 1 in Appendix 2, available online under Supplementary Materials). Studies written in English, Spanish, Portuguese, French, or German were eligible if they included the following:

- Population: patients ≥18 years old diagnosed with AF (with or without comorbidities)
- Intervention: pharmacist-led care or management services of any type delivered by pharmacists alone or in collaboration with other health care professionals
- Comparator: usual care
- Outcomes: clinical outcomes (all-cause mortality, stroke, bleeding, other thromboembolic events); secondary outcomes such as process indicators (appropriate prescription or use of OAC), patient-reported outcomes, adherence, quality of life, and satisfaction were also extracted
- Study design: interventional studies (randomized controlled trials [RCTs] or quasi-experimental studies) and observational cohorts with published results in peer-reviewed journals.

Studies focusing exclusively on populations younger than 18 years, those not distinguishing results for the target population

(i.e., AF), or without a clear definition of the pharmacist's role were excluded. Commentaries, cross-sectional studies, feasibility studies, and protocols were excluded.

Selection of studies, data extraction, and methodological quality assessment

Records retrieved from the searches were exported to EndNote X21 (Clarivate-London) for duplicate removal. Reference management and data extraction were performed using Excel spreadsheets (Microsoft, Redmond, WA, USA). Titles and abstracts were screened to identify potentially eligible studies. Full texts of these studies were retrieved and reviewed for final eligibility confirmation.

Data extraction was performed using a standardized Excel form, including general article information (authors, year, country, sample size), study design, participant characteristics (age, sex, diagnosis, comorbidities), details of the intervention, and controls and outcomes.

Among the key frameworks for data reporting,[38-40] the Template for Intervention Description and Replication (TIDieR) checklist was used to systematically collect details of the included interventions (components, providers, models of delivery, dosage, fidelity).[38] The methodological quality of RCTs and non-randomized studies of interventions or cohort studies was assessed using the Cochrane's tools RoB 2.0 and ROBINS-I, respectively.[35]

Statistical analysis

Findings were synthesized structured around the type of intervention, target population characteristics, and outcome. Whenever possible, results were pooled using pairwise meta-analyses. For these analyses, different statistical methods (Mantel-Haenszel, inverse of variance) and models (random or fixed effects) were tested. Dichotomous outcomes were reported as risk ratio (RR), while continuous data were reported as standard mean difference (SMD), both with a 95% confidence interval (CI).[35,36] p-values < 0.05 (2-tailed) indicated statistical significance. Between-study variance was estimated using DerSimonian and Laird moment-based method or restricted maximum likelihood method considering the fit of the model. Between-study heterogeneity was estimated using the inconsistency relative index I^2; values >50% were considered heterogeneous.[35,36] Tau and Tau^2 were used to estimate the distribution of true effect sizes and to compute the prediction intervals (PIs) when heterogeneity was present ($I^2 \neq 0$).[41,42] Summary CIs were calculated using Wald-type or Hartung-Knapp-Sidik-Jonkman methods.[35,36] Sensitivity analyses to evaluate the impact of individual studies on the meta-analyses were also performed. The number needed to treat (NNT) was calculated according to Altman.[43,44] The fragility index (FI), a measure of the robustness of a meta-analysis using dichotomous outcomes, was also calculated.[37,44] Analyses were performed in RevMan[35] and confirmed in R/RStudio.

GRADE

The certainty of the evidence at the outcome level was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group[45] approach.

Results

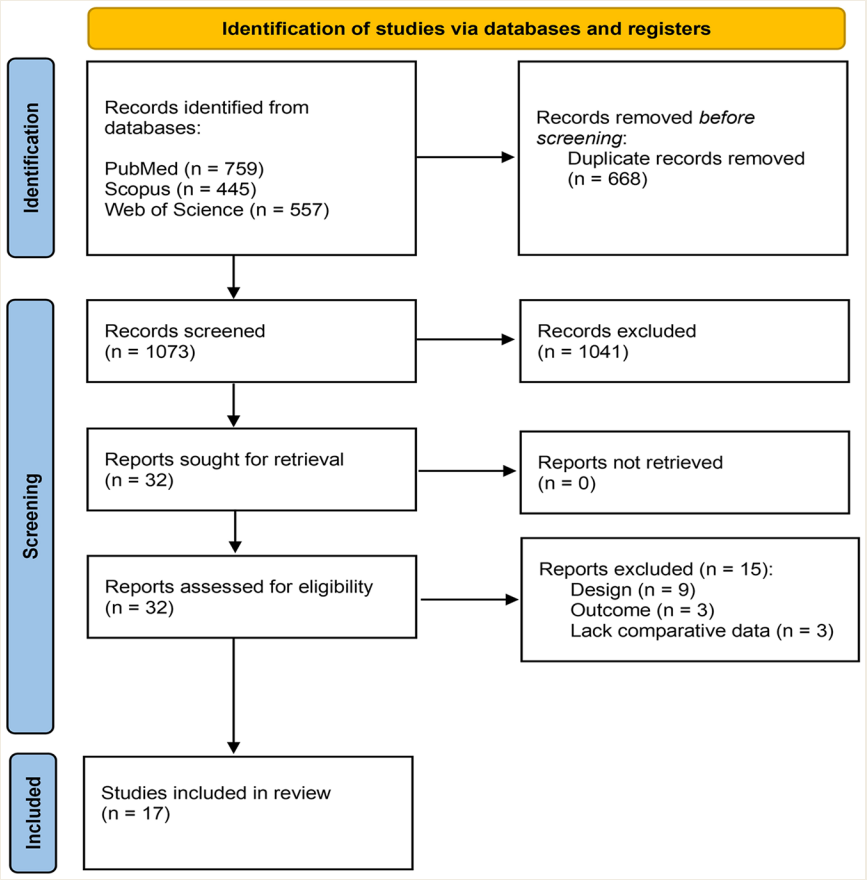
The search strategy retrieved 1073 records after removal of duplicates, of which 1041 were excluded during screening. Fifteen articles were excluded after full-text appraisal (Table 2 in Appendix 2); the remaining 17 studies[46-62] were included for data extraction and analyses (Figure 1). No additional study was found through manual searches.

These 17 studies (11,428 patients) were published between 2008 and 2024, with most of them (65%) conducted in or after 2020. The studies covered 11 different countries, with the United States being the most represented ($n = 4$; 24%), followed by China and Japan (each $n = 3$; 18%). Most studies ($n = 13$; 77%) were non-randomized trials (NRCT) or cohorts[46-56,58,61]; 4 (24%) were RCTs.[57,59,60,62] Ten studies (59%) were performed in hospitals, and 6 (35%) within health care systems; 1 study[57] was conducted in community pharmacies. See Tables 1 and 2.

Most studies ($n = 10$; 59%) evaluated all types of AF regardless of underlying valvular conditions. The mean proportion of male participants was 57.4%. Patients' mean age ranged from 65 to 80 years, with an overall trend toward elderly populations. Hypertension was the most frequent comorbidity (68% of patients), followed by diabetes (30%) and dyslipidemia (30%). A history of stroke or thromboembolic events was reported in about 20% of the sample, with most CHA_2DS_2-VASc [Congestive heart failure, Hypertension, Age (≥75 years), Diabetes, Stroke/TIA (doubled score), Vascular disease, Age (65-74 years), and Sex (female)] median scores of about 2 to 3 (i.e., moderate-to-high stroke risk for most patients). HAS-BLED [Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly] scores indicated moderate bleeding risk (medians 1–2). Seven studies (41%)[46,47,51,52,55,56,61] assessed warfarin as the primary pharmacologic intervention, while 7 (41%) focused on the use of direct oral anticoagulants (DOAC).[48,49,53,54,58-60] Three studies[50,57,62] included patients treated with either warfarin or DOAC, although the former represented only a small portion of these cohorts (10%–20%).

Although pharmacist-led interventions in the included studies consistently focused on anticoagulation management, medication therapy, and patient education and counselling, the specific nature of these interventions and the level of pharmacist involvement varied considerably (Table 1). Seven studies (41%) assessed anticoagulation management services, in which pharmacists played a broader role in overseeing multiple anticoagulant therapies, monitoring patient responses, and providing long-term follow-up through face-to-face consultations or remote services. Studies on medication therapy management ($n = 6$; 35%) were often structured around a single

FIGURE 1 Flow diagram of the systematic review



anticoagulant (warfarin or DOAC), with pharmacists primarily responsible for ensuring proper dosing and adjustments. Two studies (12%), performed in the United Kingdom and Canada, explored the role of pharmacists with anticoagulant prescribing authority.[57,58] In all studies, "usual care" (e.g., standard or routine care provided by a physician) was the comparator.

According to the Template for Intervention Description and Replication (TiDIER) checklist, all studies reported key intervention elements and the rationale of the intervention; however, most ($n = 9$, 52.9%) lacked details on materials, delivery procedures, modifications/adaptations, adherence, or real-world implementation strategies (Table 3 in Appendix 2).

The methodological quality of the RCTs demonstrated an overall low risk of bias, with only 1 study (25.0%) classified as having a moderate risk of bias due to subjective outcome assessment and lack of full report of secondary outcomes data.[60] All 4 RCTs were considered to have adequate randomization and centralized allocation. Although 2 studies[57,60] reported loss rates exceeding 15%, both mitigated this risk of bias by using intention-to-treat analyses. Among the 13 NRCTs, most (62%) were classified as having a moderate risk of bias. Only 1 study[54] was judged as having a low risk of bias. The most common sources of bias were inadequate assessment of confounding factors (54%), missing data (31%), and selection bias (31%) (Tables 4 and 5 in Appendix 2).

It was possible to build 8 pairwise meta-analyses comparing pharmacist-led interventions vs usual care for process outcomes (appropriate prescription rate), clinical outcomes (time in therapeutic range [TTR]; major bleeding, minor bleeding, stroke, thromboembolic event, all-cause mortality), and patient-reported outcomes (patients' adherence to treatment).

Pharmacist-led care was associated with improved TTR for patients on warfarin use (5 NRCT[46,47,51,52,56] with a pooled SMD of 0.35 [95% CI 0.13–0.56]; $I^2 = 27\%$; 95% PI [0.02–0.67]; $p < 0.0001$) and a reduction in major bleeding events in the entire cohort (6 NRCT[47-49,51,53,56] and 2 RCT[59,62] with a pooled RR of 0.76 [95% CI 0.61–0.95]; $I^2 = 0\%$; $p = 0.02$). The NNT for major bleeding was 178. No significant differences between intervention and usual care were observed for minor bleedings ($p = 0.15$) (Figure 2). In addition, pharmacists' interventions showed potential benefits in reducing stroke (5 NRCT[48,49,53,54,56] and 1 RCT[57] with a pooled RR 0.65 [95% CI 0.44–0.94]; $I^2 = 0\%$: $p = 0.03$), with an NNT of 324. No significant effects were observed for other thromboembolic events ($p = 0.11$) or all-cause mortality ($p = 0.15$), although the magnitude of effect varied across studies (Figure 3). Yet, meta-analyses on clinical outcomes were considered of modest clinical significance (low FI; varying from 2–3) (Table 6 in Appendix 2). It is worth noting that, except for TTR, DOAC-based studies constituted

TABLE 1 Characteristics of the included studies ($N = 17$)

First author, year	Study design	Country	Follow-up	Intervention definition[a]	Pharmacist role[b]
Aidit, 2017[46]	Retrospective study with pre–post design[c]	Malaysia	2009–2014	Warfarin medication therapy adherence protocol led by a pharmacist in a specialized clinic	Patient education and counselling, implementation of warfarin protocol, recommendation of any dosage adjustment or continuation of warfarin therapy
An, 2017[47]	Retrospective study with pre–post design[c]	Japan	2011–2013	Warfarin medication therapy management led by a pharmacist	Patient education and counselling, confirmation of drugs, drug–drug interactions, monitoring, recommendation of any dosage adjustment or continuation of warfarin
Emad, 2024[48]	Retrospective study with pre–post design[c]	Saudi Arabia	2018–2019	Apixaban medication therapy management led by a pharmacist	Patient education and counselling, medication therapy management
Jones, 2020[49]	Retrospective cohort	United States	2013–2016	DOAC management services led by a pharmacist	Patient education and counselling by phone calls and chart reviews
Khalil, 2021[50]	Prospective study with pre–post design[c]	Australia	2017–2018	Anticoagulation management services and decision-making led by a pharmacist	Patient education and counselling
Kose, 2018[51]	Retrospective study with pre–post design[c]	Japan	2011–2013	Warfarin medication therapy management led by a pharmacist	Patient education and counselling, confirmation of drugs, drug–drug interactions, monitoring, recommendation of any dosage adjustment
Leal, 2021[52]	Prospective study with pre–post design[c]	Chile	2019	Warfarin medication therapy management led by the pharmacist	Patient education and counselling, confirmation of drugs, drug–drug interactions, medication adherence
Lee, 2013[53]	Retrospective study with pre–post design[c]	United States	2011–2012	DOAC management services led by a pharmacist	Patient education and counselling
Li, 2020[54]	Prospective cohort	China	2019	Rivaroxaban medication therapy management led by a pharmacist	Patient education and follow-up service managed remotely by a pharmacist

(continued)

TABLE 1 (continued)

First author, year	Study design	Country	Follow-up	Intervention definition[a]	Pharmacist role[b]
Marcatto, 2018[55]	Prospective study with pre–post design[c]	Brazil	2017–2018	Warfarin medication therapy management led by the pharmacist	Patient education and counselling, confirmation of drug, drug–drug interactions, monitoring, recommendation of any dosage adjustment
Phelps, 2018[56]	Prospective cohort	United States	2006–2013	Warfarin medication therapy management led by the pharmacist	Patient education and counselling, confirmation of drugs, drug–drug interactions, monitoring, recommendation of any dosage adjustment
Sandhu, 2024[57]	Randomized, open-label, controlled trial	Canada	2019–2022	Anticoagulation prescribing led by the pharmacist	Patient education and counselling, anticoagulants prescribing, monitoring
Sharma, 2024[58]	Retrospective cohort with pre–post design	United Kingdom	2018–2019	DOAC prescribing led by the pharmacist	Patient education and counselling, anticoagulants prescribing, monitoring
Shiga, 2022[59]	Randomized, single-blind, controlled trial	Japan	2018	DOAC management services led by the pharmacist	Patient education and counselling, monitoring
Sun, 2021[60]	Randomized, single-blind, controlled trial	China	2018–2019	Evidence based on rivaroxaban management services led by the pharmacist	Patient education and counselling
Touchette, 2008[61]	Prospective cohort	United States	2001–2002	Warfarin medication therapy management led by the pharmacist	Patient education and counselling
Xu, 2024[62]	Randomized, single-blind, controlled trial	China	2019–2020	Anticoagulation management services led by the pharmacist	Patient education and counselling

Abbreviations: DOAC, direct oral anticoagulants.

[a]As briefly defined by the authors following the TiDIER framework. TiDIER, Template for Intervention Description and Replication.

[b]As briefly defined by the authors.

[c]Pre–post quasi-experimental study design.

TABLE 2 Baseline clinical data of the included studies ($N = 17$)

First author, year	AF diagnosis	*n*	Male (%)	Age (years)[a]	Comorbidities (%)					CHA_2DS_2VASc score[a,b]	HAS-BLED score[a,c]
					Hypertension	Diabetes	Dyslipidemia	Prior stroke	Heart failure		
Aidit, 2017[46]	AF	151	47	66.1 ± 10.8	79.5	38.4	15.9	19.2	15.2	Median 3	Median 1
An, 2017[47]	NVAF	57	61.4	71 [64–77]	64.9	21.1	36.8	15.8	—	Median 3 (IQR 2–3)	—
Emad, 2024[48]	NVAF	215	53	65	63.2	52.1	36.3	9.3	—	Median 3	Median 1
Jones, 2020[49]	AF	460	62	68.0 ± 11.5	—	—	—	—	—	Median 3	—
Khalil, 2021[50]	AF	126	53.2	74.1	—	—	—	—	—	—	—
Kose, 2018[51]	NVAF	39	71.8	72.1 ± 2.0	64.1	20.5	20.5	5.1	—	Mean 2.1 ± 1.3	—
Leal, 2021[52]	AF	41	56.1	70.8 ± 11.2	73.2	46.3	51.2	—	26.8	—	—
Lee, 2013[53]	AF	68	98.5	75 [67–83]	91.1	33.8	—	17.6	29.4	Median 2 (IQR 2–3)	—
Li, 2020[54]	AF	381	61.0	75.8 ± 7.5	66.3	19.9	6.0	22.0	—	Median 3	Mean 2.0 ± 0.8
Marcatto, 2018[55]	NVAF	268	52.4	66.6 ± 0.7	81.6	31.5	56.2	—	—	—	—
Phelps, 2018[56]	AF	8405	45.6	74.3 ± 10.3	51.9	24.6	—	10.3	24.8	Mean 1.8 ± 1.3	—
Sandhu, 2024[57]	AF	80	43.8	79.7 ± 7.4	82.5	22.5	—	18.8	35.0	Median 2 (IQR 1–3)	—
Sharma, 2024[58]	NVAF	470	54.7	67.3 ± 9.5	—	—	—	7.7	—	Mean 4.0 ± 1.8	Mean 1.9 ± 0.8
Shiga, 2022[59]	NVAF	268	61.1	73.0 ± 9.5	63.1	40.7	—	11.6	42.1	Mean 2.2 ± 1.4	—
Sun, 2021[60]	NVAF	199	54.3	75.9 ± 9.0	70.4	21.6	—	65.8	25.6	Mean 4.6 ± 1.4	—
Touchette, 2008[61]	NVAF	252	47.2	78.8 ± 10.2	59.5	32.5	—	33.3	—	—	—
Xu, 2024[62]	AF	376	52.4	65.6 ± 10.0	52.7	21.8	—	16.2	19.7	Mean 2.7 ± 1.8	Mean 1.5 ± 1.1

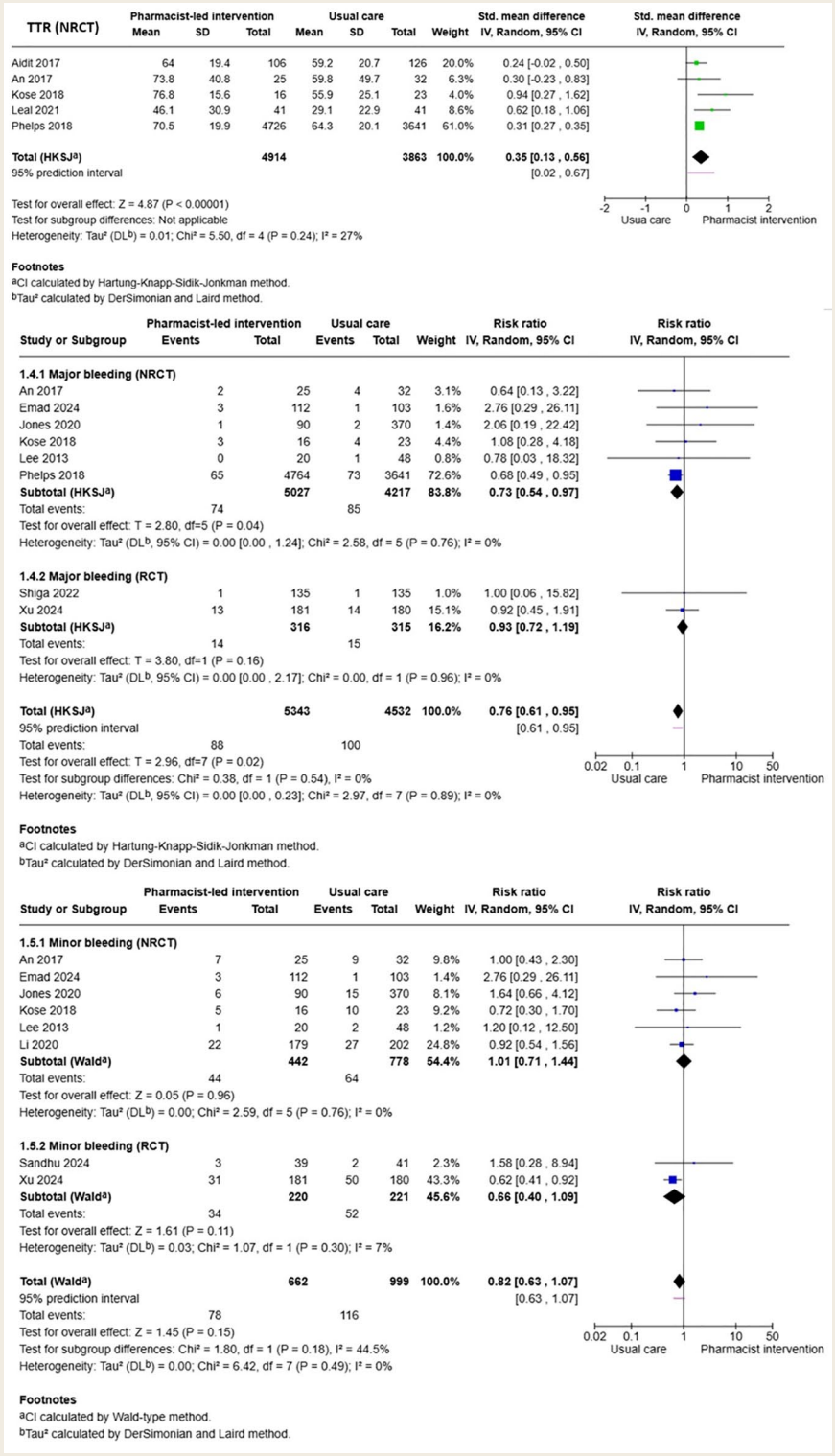
Abbreviations: AF, atrial fibrillation; HAS-BLED, Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly; I, intervention group; IQR, interquartile range; NVAF, non-valvular atrial fibrillation; UC, usual care; ±, standard deviation; —, not reported.

[a]Data represent combined values, including means with standard deviations and medians with interquartile ranges, calculated from the intervention and usual care groups.

[b]CHA_2DS_2-VASc score calculates thromboembolic/ischemic stroke risk for decisions on initiating oral anticoagulation for patients with AF.

[c]HAS-BLED score estimates the 1-year risk of major bleeding for patients on anticoagulation.

FIGURE 2 Meta-analyses of time in therapeutic range (TTR) and bleeding events



Subgroups by study design whenever possible. CI, confidence interval; DL, DerSimonian-Laird method; HKSJ, Hartung-Knapp-Sidik-Jonkman method; IV, inverse variance; NRCT, non-randomized trials/cohorts; RCT, randomized controlled trials; REML, Restricted Maximum Likelihood; SD, standard deviation.

the majority of the clinical outcome data in the meta-analyses, with warfarin users representing only a minority (10%–25%) of the included cohorts.

Pharmacist interventions also significantly increased the rate of appropriate prescriptions, with an NNT of 5 (5 NRCT[48,50,54,58,61] and 1 RCT[57] with pooled RR of 1.36 [95%

FIGURE 3 Meta-analysis of stroke, thromboembolic events, and mortality

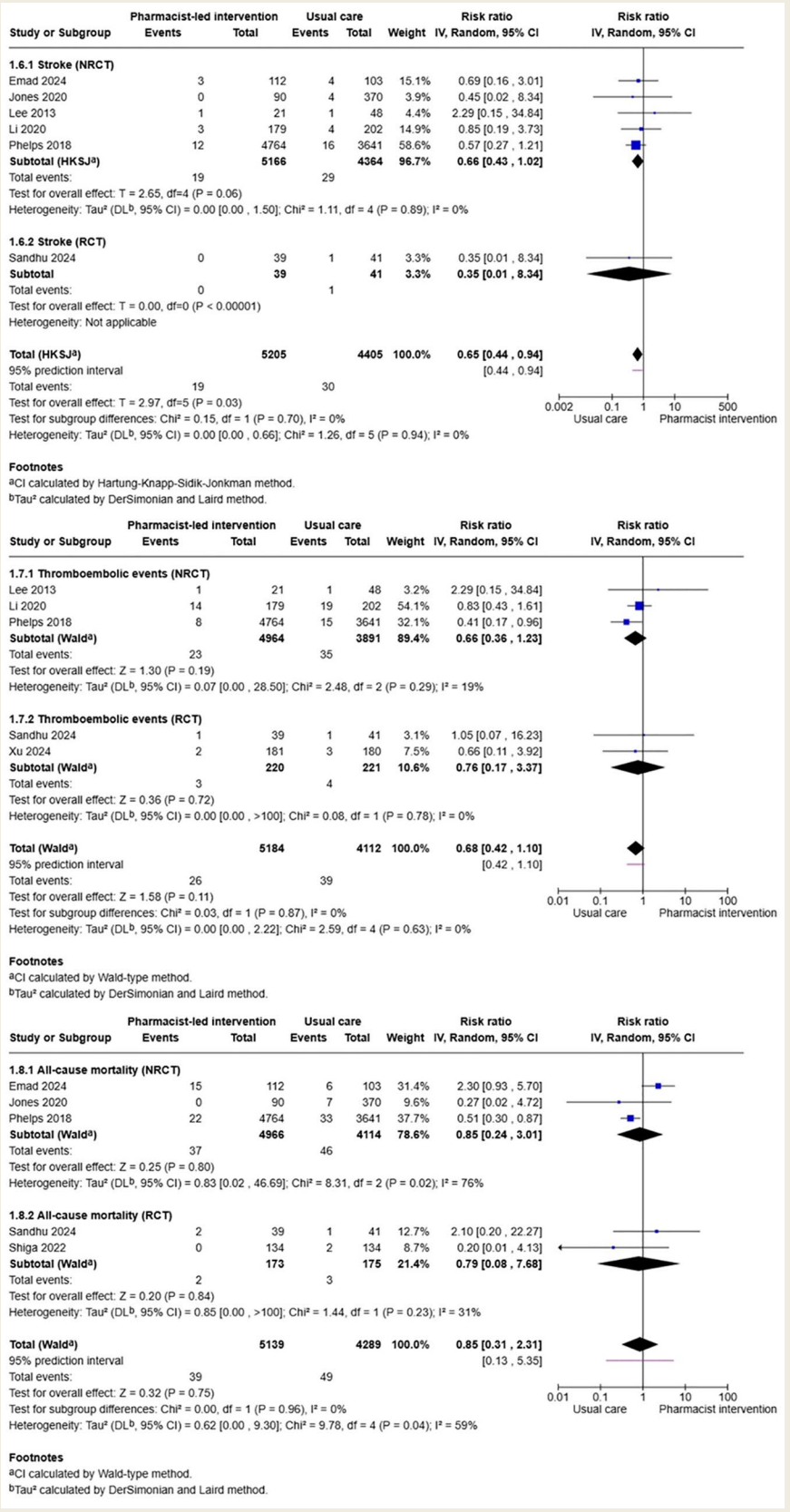


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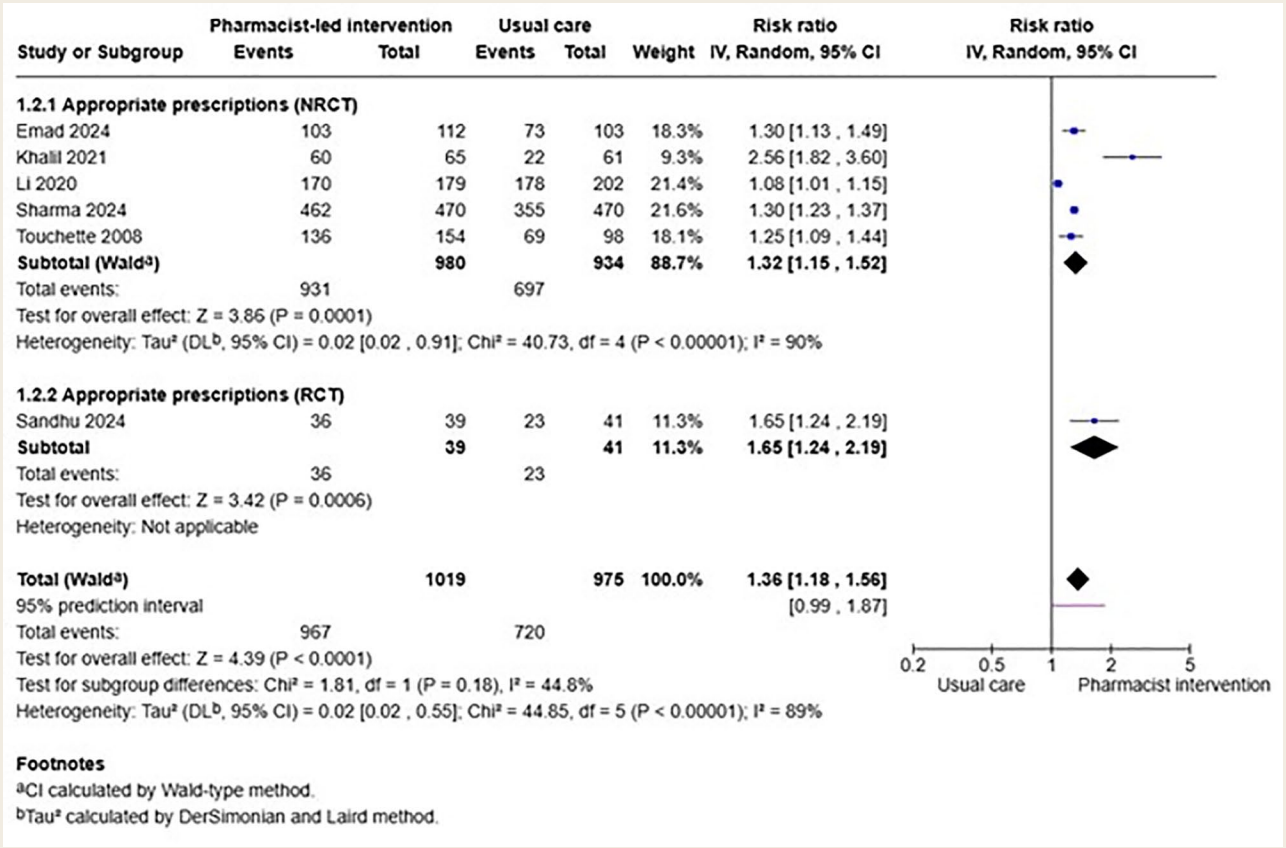
FIGURE 4 Meta-analysis of appropriate prescription rates



Subgroups by study design whenever possible. CI, confidence interval; DL, DerSimonian-Laird method; HKSJ, Hartung-Knapp-Sidik-Jonkman method; IV, inverse variance; NRCT, non-randomized trials/cohorts; RCT, randomized controlled trials; REML, Restricted Maximum Likelihood; SD, standard deviation.

CI 1.18–1.56]; $I^2 = 45\%$; 95% PI [0.99–1.87]; $p < 0.0001$). This meta-analysis was considered more robust, with an FI of 184 (Figure 4). Conversely, no differences between groups were observed for medication adherence ($p = 0.26$) (Figure 5). Other outcomes, such as hospital admissions (intervention vs usual care rates of 4% vs 9%, respectively, $p = 0.403$) and patient acceptance or satisfaction (ranging from 60%–100%, with no significant differences between groups), were largely unavailable[46,50,57,59,60,62] and lacked standardized reporting (Table 7 in Appendix 2).

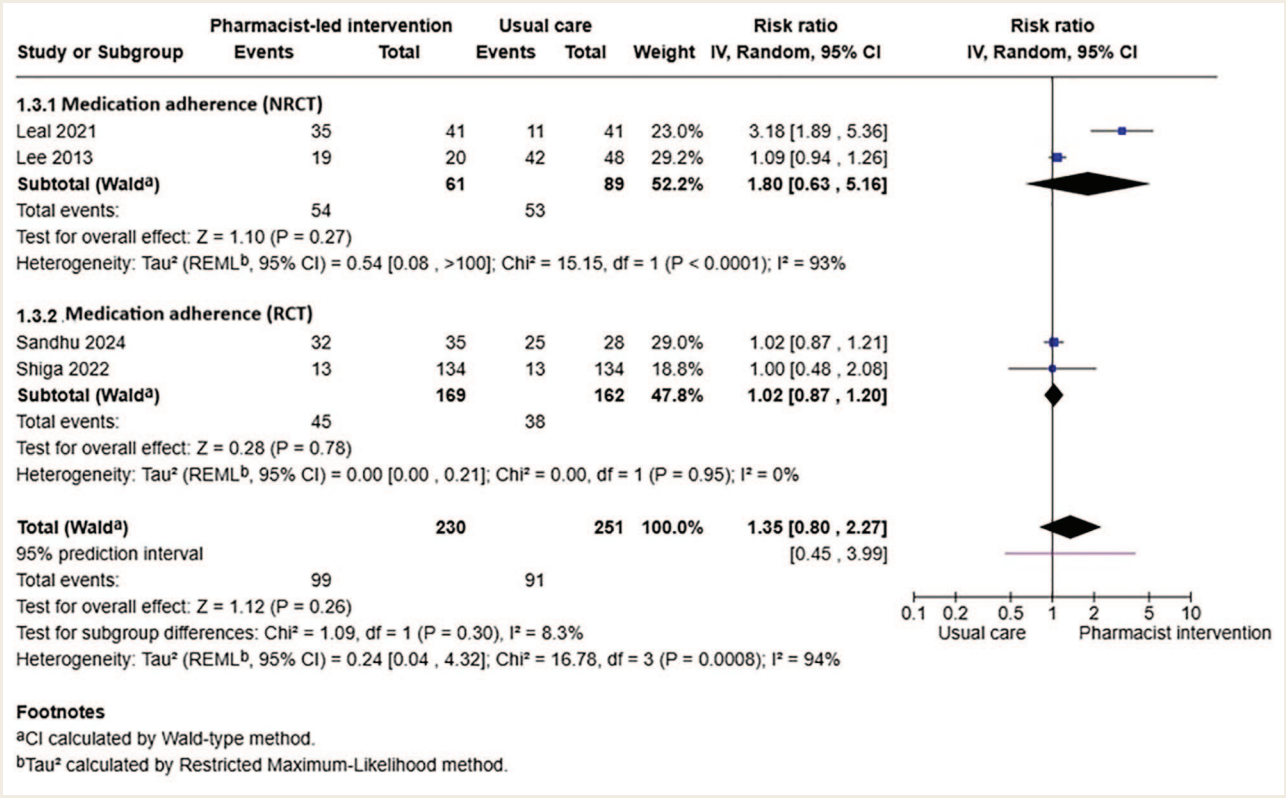
The certainty of the evidence (GRADE) varied from low to moderate for all outcomes of interest, especially due to the low methodological quality of some studies (risk of bias, lack of standard measures, subjective outcomes, and the imprecision of some results) (Table 8 in Appendix 2).

Discussion

AF is highly prevalent and contributes to significant morbidity and mortality. Despite the availability of effective therapies, AF management remains suboptimal. This systematic review and meta-analysis is the first to synthesize evidence from 17 studies evaluating the impact of pharmacist-led interventions compared with usual care in AF management. We demonstrated significant improvements in clinical outcomes, including a 10% to 15% increase in anticoagulation control (TTR) among warfarin users and a 25% to 35% reduction in major bleeding events and stroke, regardless of the anticoagulant used. In addition, pharmacist-led interventions led to a ~35% increase in prescription accuracy. These findings strongly suggest that pharmacists can play a pivotal role in optimizing AF care, especially in anticoagulation management. However, the overall strength of evidence remains limited compared with other cardiovascular conditions, due to fewer studies and a lack of RCTs.[63,64]

Pharmacists being accessible and trained in patient education,[49,53-56] medication monitoring, and dose adjustment[46,47,51,55,56] are well-positioned to support integrated AF care across health care settings. This aligns with the "CC to ABC" care model, as seen in National Health Service England's program, which has recruited practice-based pharmacists and achieved anticoagulation rates greater than 83%.[4,9] This project aims to reduce general practitioners' workload while ensuring the sustainable initiation and monitoring of anticoagulation therapy.[65] This initiative also addresses the

FIGURE 5 Meta-analysis of medication adherence



Subgroups by study design whenever possible. CI, confidence interval; DL, DerSimonian-Laird method; HKSJ, Hartung-Knapp-Sidik-Jonkman method; IV, inverse variance; NRCT, non-randomized trials/cohorts; RCT, randomized controlled trials; REML, Restricted Maximum Likelihood; SD, standard deviation. *Studies by Lee (2013),[53] Sandhu et al. (2024),[57] and Shiga et al. (2022)[59] used measures related to medication possession ratio (MPR); Leal et al. (2021)[52] applied the Simplified Medication Adherence Questionnaire (SMAQ28).

global surge in OAC use, which nearly doubled between 2010 and 2018 following the introduction of DOACs. Despite this increase, approximately one-quarter of eligible AF patients remain without anticoagulation therapy.[16] Misuse, such as unnecessary acetylsalicylic acid co-prescription and undiagnosed AF remain concerns, highlighting the importance of proactive case finding through community pharmacy screenings (e.g., electrocardiogram devices, pharmacist-led tailored interventions).[17,66]

Most pharmacist-led AF studies primarily focus on anticoagulant management, reporting data on guideline-adherence appropriateness or prescription rates, and therapy optimization—especially for vitamin K antagonists and DOACs—as found in this review.[27,67] An audit by the International Pharmacists for Anticoagulation Care Taskforce across 22 countries confirmed that pharmacist involvement is often limited to care transitions and education, with some specific services such as point-of-care international normalized ratio/TTR testing.[68] Evidence on pharmacists' involvement in AF characterization or symptom management remains limited, potentially reflecting perceived competency gaps or a lack of confidence in prescribing therapies for rate and rhythm controls.[69]

The observed improvement in TTR (SMD 0.35) among patients using warfarin suggests that pharmacist involvement in dose adjustment and patient follow-up is clinically meaningful. Even modest gains in TTR have been associated with reduced stroke and hemorrhagic events in previous studies.[56,70] Yet, TTR alone does not fully account for the observed benefits, as significant reductions in major bleeding (RR 0.76) and stroke (RR 0.65) were identified across the overall cohort, even though warfarin users made up less than 25% of the dataset. These findings indicate that pharmacist-led interventions may benefit patients across different anticoagulant classes, including those on DOACs—potentially through improved prescribing, patient education, and early risk identification.[48,49,56] Nonetheless, differences between anticoagulant types remain unclear due to limited subgroup analyses, and the lack of direct comparisons between drugs warrants further research. Moreover, the observed increase in appropriate anticoagulant prescribing (RR 1.36, NNT = 5) may represent another key driver underlying these outcomes, as guideline-directed therapy remains suboptimal in many settings.[13,16] By addressing clinical inertia, pharmacist-led interventions can support better adherence to prescribing recommendations.[12,17]

Only 2 RCTs[57,58] evaluated pharmacist-led prescribing practices in AF. Nonetheless, this activity is expanding globally, with countries such as the United Kingdom, the United States of America, Canada, Australia, Poland, Switzerland, and Denmark allowing independent prescribing practice in community settings. Recent educational and regulatory reforms also aim to enhance pharmacist prescribing roles, although variations in terminology, legislation, and practice still persist.[71,72]

While pharmacist-led education improves patient knowledge, it may not alone improve clinical outcomes. Trials on integrated AF care have yielded mixed results. The recent AF-EduCare study found that intensive patient education led by the pharmacist did not reduce unplanned cardiovascular events in the general AF population, although certain subgroups may benefit.[73] A systematic review also indicated that pharmacist-managed anticoagulation models based solely on education had limited effects on patient safety and mortality.[74] In this context, direct comparisons to nurse-led interventions could further clarify the advantages and limitations of pharmacist-led strategies, as nurse-led services have significantly demonstrated improved anticoagulation control, medication adherence, and reduced adverse events.[74,75]

Conversely, this review found no significant effect of pharmacist services on certain outcomes, including mortality, medication adherence, and patient satisfaction. Interpreting these findings requires caution due to low statistical power (as many studies report low event rates) and lack of adequate adjustments for confounders. Moreover, the absence of well-defined interventions and standardized outcome measures may hinder data comparability and generalizability. More than half of the studies failed to provide sufficient details on intervention definition and materials, delivery procedures, adherence, and real-world implementation strategies, making it difficult to assess fidelity and transferability to broader health care settings.[76,77]

Standardizing intervention dosing and implementation is paramount for improving long-term medication adherence and persistence.[67,78] A recent meta-analysis found that only 1 in 3 patients adheres to DOACs at least 80% of the time,[78] with poor adherence linked to worse clinical outcomes, including stroke.[66] While DOACs offer the advantage of not requiring routine laboratory monitoring, additional efforts to detect and prevent medication non-adherence, such as technology-based strategies like mobile applications, may be necessary.[18] Implementation research is also important in this context for optimizing pharmacist-led AF management. A recent qualitative study using the Consolidated Framework for Implementation Research explored the feasibility of pharmacist-led anticoagulation services in primary care, ranking as key facilitators pharmacist competency, effective communication, and standardized operational protocols. Insights from such studies can inform future initiatives aimed at expanding pharmacist-led services.[79]

Limitations

This study has some limitations. Few clinical studies were included, most with small sample sizes and some risk of bias. Despite this, they represent the best available evidence on pharmacist-led interventions in AF management. Cross-sectional studies, including those on AF screening,[80] were excluded as they did not align with the research question, although they remain relevant for future analysis. Similarly, issues related to identifying untreated individuals and populations at risk of undertreatment fall outside the scope of this review and warrant further dedicated research in community pharmacy settings. Study heterogeneity, due to variations in design, populations, and outcome measures, limited statistical analyses. Due to the lack of stratified reporting by anticoagulant type, formal subgroup analyses comparing pharmacist-led interventions for DOACs vs warfarin were not performed. However, international guidelines were followed, efforts were made to minimize bias, and various statistical methods were applied to strengthen the findings. This remains an important limitation and warrants attention in future studies. In addition, while process indicators and supplementary measures were used to enhance result interpretation, accurately assessing the ultimate impact on clinical practice remains challenging.

Conclusions

We synthesized the current evidence on pharmacist-led interventions in AF management, revealing meaningful and promising improvements in both clinical and process-related outcomes. However, significant gaps remain—particularly regarding medication adherence and the standardization of intervention protocols, including key components such as dosing, follow-up schedules, and implementation strategies. Collaboration among clinicians, researchers, and patients is essential to develop a core outcome set, ensuring standardized outcome measurement and reporting. Integrating patient-reported outcome measures (e.g., quality of life, AF burden)[81] is also crucial to highlight patient-centred benefits. Lastly, developing and assessing new pharmacist prescribing models[57] should be a priority. Future high-quality RCTs should build on the findings of this review by exploring pharmacist-led models tailored to specific anticoagulants (especially contrasting DOAC and warfarin pathways) and by incorporating clearly defined intervention components. Emphasizing patient-centred outcomes and stratified results by drug type may help further clarify and refine the pharmacist's role in AF care.

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