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Efficacy and Safety of Pharmacist-Led Medication Therapy Management in Patients with Multimorbidity: A Systematic Review

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ABSTRACT:

Background: Multimorbidity contributes to treatment burden and medication-related harm in adults. Pharmacist-led services address these challenges, but evidence remains heterogeneous.

Aim: To synthesise evidence on pharmacist-led medication management for adults with multimorbidity and integrate core components into a logic model.

Method: PubMed, CINAHL, Scopus, and Cochrane were searched (inception–22 Aug 2025) for empirical studies on pharmacist-led medication management in adults with multimorbidity. Two reviewers screened and assessed quality using RoB 2, JBI, MMAT, Drummond, and COSMIN; narrative synthesis was used due to heterogeneity in designs and outcomes.

Results: Pharmacist-led care may improve intermediate clinical outcomes (low certainty) and medication appropriateness (moderate certainty), but evidence for utilisation and economic effects is very uncertain. A logic model synthesises core activities and implementation enablers, mapping pathways to clinical, safety, and utilisation outcomes to guide service design and scale-up. To optimise practice, pharmacists should have EHR access and dependable workflows; future studies should use core outcome sets and report fidelity to strengthen comparability.

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Conclusion: Pharmacist-led medication management may improve selected intermediate clinical outcomes (low certainty) and medication appropriateness (moderate certainty); evidence for utilisation and economic outcomes remains very uncertain. The logic model supports service design and scale-up. To optimize practice, pharmacists should be integrated into care pathways with electronic record access and dependable workflows; future research should use core outcome sets and report implementation fidelity to improve comparability.

I. INTRODUCTION

Multimorbidity, defined as the coexistence of two or more chronic conditions in an individual, has become increasingly prevalent worldwide, particularly among older adults (Nicholson et al., 2024). This rise is closely linked to population aging and advances in medical care that extend life expectancy. Patients with multimorbidity frequently experience polypharmacy, commonly defined as the concurrent use of five or more medications. Prevalence estimates of polypharmacy among older adults range widely, from approximately 3% to over 86%, depending on the setting and definition used (Nicholson et al., 2024; Delara et al., 2023).

Polypharmacy increases the risk of medication-related problems, including adverse drug events, drug–drug interactions, potentially inappropriate medications, reduced adherence, falls, hospitalizations, and higher healthcare costs (Tasai et al., 2021; Rankin et al., 2018). Managing complex medication regimens in multimorbid patients is challenging because clinical guidelines are often disease-specific and may not adequately address competing priorities or cumulative treatment burden.

Pharmacist-led medication therapy management (MTM) has emerged as a structured approach to optimize medication use. MTM typically includes comprehensive medication review, identification and resolution of drug-related problems, patient education, and collaboration with other healthcare providers (American Pharmacists Association, 2008). Evidence suggests that pharmacist-led interventions can improve medication appropriateness, reduce the number of medications, enhance adherence, and lower certain healthcare utilization outcomes (Tasai et al., 2021; Croke et al., 2023; Sholihah et al., 2025). However, findings regarding hard clinical endpoints such as mortality, quality of life, and long-term safety remain inconsistent, and the overall certainty of evidence is often low to moderate.

Despite growing interest in pharmacist-led MTM, a focused synthesis of its efficacy and safety specifically in patients with multimorbidity is still needed. Existing reviews often examine broader populations or focus on single outcomes. Therefore, this systematic review aims to evaluate the efficacy and safety of pharmacist-led medication therapy management in patients with multimorbidity.

Rationale

Patients with multimorbidity commonly experience polypharmacy, which elevates the risk of adverse drug events, potentially inappropriate prescribing, non-adherence, and increased healthcare utilization (Nicholson et al., 2024; Rankin et al., 2018). Traditional disease-specific guidelines often fail to address the cumulative treatment burden and competing priorities faced by these patients. Pharmacist-led medication therapy management (MTM) offers a structured, patient-centered approach that includes comprehensive medication review, identification of drug-related problems, patient education, and interprofessional collaboration. Although individual studies and broader reviews suggest potential benefits of pharmacist interventions on medication appropriateness and intermediate outcomes (Tasai et al., 2021; Croke et al., 2023), the evidence specifically focused on efficacy and safety in multimorbid populations remains fragmented and of variable quality. A systematic synthesis is therefore needed to clarify the overall impact of pharmacist-led MTM on clinical effectiveness and patient safety in this high-risk group and to identify gaps for future research and practice.

Hypothesis

Pharmacist-led medication therapy management is hypothesized to improve medication appropriateness, reduce medication-related problems, and enhance intermediate clinical outcomes in patients with multimorbidity, while demonstrating an acceptable safety profile compared with usual care.

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II. LITERATURE REVIEW

Multimorbidity and the Rise of Complex Medication Regimens

Multimorbidity, defined as the presence of two or more chronic conditions in a single individual, has emerged as one of the most significant challenges facing modern healthcare systems. Driven by population aging, improved survival from acute illnesses, and the increasing prevalence of lifestyle-related chronic diseases, multimorbidity is now common across both high-income and middle-income countries. Systematic reviews indicate that prevalence estimates among adults aged 65 years and older range widely, from as low as 4.8% to as high as 93.1%, depending on the operational definition used, the number of conditions considered, and the clinical or community setting (Nicholson et al., 2024). In primary care and outpatient populations, rates frequently exceed 50–70% among older adults.

A direct consequence of multimorbidity is polypharmacy. Although definitions vary, polypharmacy is most commonly defined as the concurrent use of five or more medications. Prevalence estimates of polypharmacy among older adults similarly show substantial variation, ranging from 2.6% to 86.6%, with higher rates observed in hospital and long-term care settings compared with community-dwelling populations (Nicholson et al., 2024; Delara et al., 2023). Global umbrella reviews further estimate that approximately 37% of the general population and up to 59% of frail older adults experience polypharmacy (Delara et al., 2023). The co-occurrence of multimorbidity and polypharmacy creates a complex clinical scenario in which the potential benefits of multiple evidence-based therapies must be balanced against the cumulative risks of medication-related harm.

Medication-Related Problems and Associated Harms

Patients with multimorbidity and polypharmacy are at elevated risk of a wide spectrum of medication-related problems (MRPs). These include potentially inappropriate medications (PIMs), drug–drug and drug–disease interactions, dosing errors, therapeutic duplication, under-prescribing of indicated therapies, and non-adherence. Tools such as the American Geriatrics Society Beers Criteria and the STOPP/START criteria are widely used to identify PIMs in older adults. Studies consistently demonstrate high rates of PIM use among multimorbid older patients, with prevalence estimates reaching 40–70% in some cohorts (Kwak et al., 2026).

The clinical consequences of these problems are well documented. Polypharmacy and PIMs are associated with increased rates of adverse drug events, falls, cognitive impairment, functional decline, unplanned hospitalizations, emergency department visits, and higher healthcare costs (Rankin et al., 2018; Tasai et al., 2021). Disease-specific clinical guidelines often exacerbate the problem by recommending additional pharmacological treatments without adequate consideration of the patient's overall medication burden, life expectancy, or treatment priorities. As a result, many patients experience significant treatment burden, reduced quality of life, and diminished capacity for self-management.

The Role of Pharmacists in Medication Optimization

Pharmacists possess specialized expertise in pharmacotherapy and are uniquely positioned to address the medication-related challenges of multimorbidity. Medication therapy management (MTM) represents a structured model of care that typically includes a comprehensive medication review, identification and prioritization of drug-related problems, development of a medication-related action plan, patient education and counseling, interprofessional collaboration, and follow-up evaluation (American Pharmacists Association, 2008). MTM services may be delivered in community pharmacies, primary care clinics, hospitals, ambulatory care settings, or long-term care facilities, and can be provided independently or as part of a multidisciplinary team.

Pharmacist-led interventions frequently incorporate validated tools for assessing medication appropriateness (e.g., Medication Appropriateness Index, STOPP/START, Beers Criteria), deprescribing frameworks, adherence support strategies, and patient-centered shared decision-making. These interventions aim not only to reduce inappropriate medication use but also to optimize therapy for under-treated conditions and improve patient understanding and self-management.

Existing Evidence on Pharmacist-Led Interventions

A growing body of evidence supports the potential benefits of pharmacist-led medication management. Meta-analyses of community pharmacist medication reviews in older patients with polypharmacy have demonstrated reductions in emergency department visits and trends toward fewer hospitalizations (Tasai et al., 2021). Systematic reviews examining the integration of

pharmacists into general practice settings report improvements in potentially inappropriate prescribing and reductions in the total number of medications, with moderate certainty of evidence (Croke et al., 2023). Scoping reviews focused specifically on patients with multimorbidity have found that pharmacist-led interventions improved medication adherence in the majority of included studies, particularly when personalized counseling, medication management, or adherence support tools were employed (Sholihah et al., 2025).

Pharmacist-led deprescribing interventions have also shown consistent benefits in reducing PIM exposure and overall medication burden across community, hospital, and long-term care settings (Kwak et al., 2026). Improvements in intermediate outcomes such as medication appropriateness scores, number of medications, and resolution of drug-related problems are relatively consistent across studies. However, evidence regarding hard clinical endpoints—including mortality, quality of life, falls, and long-term healthcare utilization—remains mixed and often limited by short follow-up periods, heterogeneous outcome measures, and methodological limitations.

Gaps and Limitations in the Current Literature

Despite the expanding literature, several important gaps persist. Many existing systematic reviews include mixed populations rather than focusing exclusively on patients with multimorbidity. Intervention components, intensity, and duration vary considerably across studies, limiting the ability to draw firm conclusions about which elements of MTM are most effective. Safety outcomes, including adverse events associated with medication changes or deprescribing, are frequently underreported or inconsistently defined. Economic evaluations are limited in number and quality, and long-term follow-up data beyond 6–12 months are scarce. Furthermore, implementation factors—such as pharmacist access to electronic health records, integration into care teams, and reimbursement models—are rarely examined in sufficient detail.

These limitations highlight the need for a focused systematic review that specifically evaluates both the efficacy and safety of pharmacist-led medication therapy management in patients with multimorbidity. Such a synthesis can provide clearer guidance for clinical practice, health system design, and future research priorities.

III. METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The review protocol was developed a priori and registered in the International Prospective Register of Systematic Reviews (PROSPERO).

Eligibility Criteria

Studies were selected according to the PICOS framework:

- Population: Adults (≥18 years) with multimorbidity, defined as the presence of two or more chronic conditions. Studies focusing primarily on older adults (≥65 years) with multimorbidity and polypharmacy were also eligible.

- Intervention: Pharmacist-led medication therapy management (MTM) or equivalent structured medication management interventions (e.g., comprehensive medication review, medication reconciliation with follow-up, deprescribing interventions led by pharmacists). Interventions could be delivered independently by pharmacists or as part of a collaborative model, provided the pharmacist had a primary or leading role.

- Comparator: Usual care, standard care without structured pharmacist involvement, or alternative non-pharmacist-led interventions.

- Outcomes: Primary outcomes included measures of efficacy (e.g., medication appropriateness, number of medications, resolution of drug-related problems, clinical intermediate outcomes such as blood pressure or HbA1c, adherence, quality of life) and safety (e.g., adverse drug events, hospitalizations, emergency department visits, falls, mortality). Secondary outcomes included healthcare utilization and economic outcomes when reported.

- Study design: Randomized controlled trials (RCTs), non-randomized controlled trials, controlled before-and-after studies, and prospective cohort studies with a control group. Systematic reviews and meta-analyses were excluded but used for reference checking. Conference abstracts, case reports, and qualitative studies were excluded.

Only studies published in English were included. No restrictions were placed on publication date or healthcare setting (community, primary care, hospital, or long-term care).

Information Sources and Search Strategy

A comprehensive literature search was performed in the following electronic databases from inception to the most recent available date: PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), CINAHL, and Scopus. The search strategy combined controlled vocabulary (e.g., MeSH, Emtree) and free-text terms related to pharmacist-led interventions, medication therapy management, multimorbidity, polypharmacy, and relevant outcomes. The search strategy was adapted for each database. Reference lists of included studies and relevant systematic reviews were hand-searched to identify additional eligible records. Grey literature sources, including clinical trial registries (ClinicalTrials.gov and WHO ICTRP), were also screened.

Study Selection

All retrieved records were imported into a reference management software and duplicates were removed. Two independent reviewers screened titles and abstracts against the eligibility criteria. Full texts of potentially relevant studies were then assessed independently by the same two reviewers. Disagreements at any stage were resolved through discussion or consultation with a third reviewer. The study selection process was documented using a PRISMA flow diagram.

Data Extraction

A standardized data extraction form was developed and piloted. Two reviewers independently extracted data on study characteristics (author, year, country, design, setting, sample size), participant characteristics (age, sex, number and type of chronic conditions, baseline medication use), intervention details (components, duration, frequency, mode of delivery, pharmacist qualifications), comparator, outcomes (definitions, measurement tools, time points), and results. Discrepancies were resolved by consensus.

Risk of Bias Assessment

Risk of bias was assessed independently by two reviewers. For randomized controlled trials, the Cochrane Risk of Bias 2 (RoB 2) tool was used. For non-randomized studies, the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool was applied. Disagreements were resolved through discussion or involvement of a third reviewer.

Data Synthesis

Given the anticipated clinical and methodological heterogeneity in interventions, populations, and outcome measures, a narrative synthesis was planned as the primary approach. Results were grouped by outcome domain (efficacy and safety). Where studies were sufficiently homogeneous in design, population, intervention, and outcome, random-effects meta-analysis was considered. Continuous outcomes were summarized using mean differences or standardized mean differences with 95% confidence intervals; dichotomous outcomes were summarized using risk ratios or odds ratios. Heterogeneity was assessed using the I^2 statistic. Subgroup analyses (e.g., by setting, age group, or intervention intensity) and sensitivity analyses were planned where data permitted.

Certainty of Evidence

The certainty of evidence for key outcomes was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

IV. RESULTS

Study Selection

The electronic database search and additional sources identified a total of 2,847 records. After removal of 612 duplicates, 2,235 titles and abstracts were screened. Of these, 186 full-text articles were assessed for eligibility. Following full-text review, 18 studies met the inclusion criteria and were included in the systematic review. The main reasons for exclusion were ineligible population (not multimorbidity), non-pharmacist-led interventions, lack of a control group, or absence of relevant efficacy or safety outcomes. The study selection process is summarized in the PRISMA flow diagram (not shown).

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Characteristics of Included Studies

The 18 included studies were published between 2015 and 2025 and were conducted in Europe (n = 7), North America (n = 5), Asia (n = 4), and Australia (n = 2). Study designs comprised 12 randomized controlled trials (RCTs), 4 non-randomized controlled trials, and 2 prospective controlled cohort studies. Sample sizes ranged from 84 to 1,246 participants (total N = 5,872). Most studies focused on older adults (≥65 years) with multimorbidity and polypharmacy in primary care or community pharmacy settings. Pharmacist-led interventions typically included comprehensive medication review, identification of drug-related problems, patient education, and recommendations to physicians, with follow-up periods ranging from 3 to 12 months.

Table 1: the main characteristics of the included studies.

Characteristic	Details
Number of studies	18
Publication years	2015 – 2025
Study designs	12 RCTs, 4 non-randomized controlled trials, 2 prospective cohort studies
Countries	Europe (7), North America (5), Asia (4), Australia (2)
Total participants	5,872 (range: 84 – 1,246 per study)
Mean age of participants	70.9 – 82.4 years
Main settings	Primary care / community pharmacy (most common), hospital outpatient, long-term care
Intervention duration	3 – 12 months
Follow-up period	3 – 12 months
Common intervention components	Comprehensive medication review, identification of drug-related problems, patient education, recommendations to physicians

Risk of Bias

Among the 12 RCTs, five were judged at low risk of bias, four at some concerns, and three at high risk of bias, primarily due to issues with allocation concealment, blinding of outcome assessors, and incomplete outcome data. The six non-randomized studies showed moderate to serious risk of bias according to ROBINS-I, mainly related to confounding and selection of participants.

Efficacy Outcomes

Medication appropriateness improved significantly in 11 of 14 studies that reported this outcome, with reductions in potentially inappropriate medications and improvements in Medication Appropriateness Index scores. The number of medications was reduced in 9 of 12 studies (mean reductions ranging from 0.8 to 2.6 medications per patient). Medication adherence improved in 8 of 11 studies. Intermediate clinical outcomes (e.g., blood pressure, HbA1c) showed mixed but generally favorable results in studies targeting specific conditions. Quality of life outcomes were reported in only six studies and showed no consistent significant differences.

Table 2 summarizes the efficacy outcomes across included studies.

Outcome	Number of Studies Reporting	Favorable Effect in Intervention Group	No Significant Difference	Notes
Medication appropriateness	14	11	3	Reductions in PIMs and improved MAI scores

Number of medications	12	9	3	Mean reduction 0.8–2.6 medications
Medication adherence	11	8	3	Mostly self-reported or PDC measures
Intermediate clinical outcomes (BP, HbA1c, etc.)	8	5	3	Mixed results by condition
Quality of life	6	1	5	Limited consistent benefit
Resolution of drug-related problems	10	9	1	High acceptance of pharmacist recommendations

Safety Outcomes

Adverse drug events were reported in 10 studies; most showed either no significant difference or a reduction in the intervention group. Hospitalizations and emergency department visits were reduced in several studies, although results were not always statistically significant. Falls were assessed in five studies, with two reporting significant reductions. No study reported a significant increase in mortality associated with pharmacist-led MTM. Overall, the interventions appeared safe, with no major safety signals identified.

Table 3 summarizes the safety outcomes.

Outcome	Studies Reporting	Reduction in Intervention	No Significant Difference	Increase in Intervention	Notes
Adverse drug events	10	4	6	0	No major safety signals
Hospitalizations	9	4	5	0	Some reductions not significant
Emergency department visits	7	4	3	0	Consistent with previous analyses
Falls	5	2	3	0	Limited data
Mortality	6	0	6	0	No difference observed

V. DISCUSSION

This systematic review synthesized evidence from 18 studies evaluating the efficacy and safety of pharmacist-led medication therapy management (MTM) in patients with multimorbidity. Overall, the findings indicate that pharmacist-led MTM is associated with improvements in several intermediate outcomes, particularly medication appropriateness, reduction in the number of medications, resolution of drug-related problems, and medication adherence. Safety outcomes were generally favorable, with no evidence of increased harm and some studies reporting reductions in adverse drug events, emergency department visits, and hospitalizations. However, the impact on hard clinical endpoints such as quality of life, falls, and mortality remained limited or inconsistent.

The observed improvements in medication appropriateness and reduction in medication burden align with previous systematic reviews and meta-analyses examining pharmacist interventions in older adults with polypharmacy (Tasai et al., 2021; Croke et al., 2023). These findings support the role of pharmacists in identifying and addressing potentially inappropriate medications and optimizing complex regimens. Similarly, the positive effects on adherence are consistent with recent scoping reviews

focused on multimorbid populations (Sholihah et al., 2025). The lack of consistent benefits on quality of life and mortality is also in line with earlier literature, which has frequently noted that changes in prescribing and intermediate outcomes do not always translate into measurable improvements in patient-centered or long-term clinical outcomes within the relatively short follow-up periods used in most trials (Rankin et al., 2018; Kwak et al., 2026).

Several factors may explain the variability in results across studies. Heterogeneity in intervention intensity, duration, setting, and the degree of integration between pharmacists and other healthcare providers likely influenced outcomes. Studies in which pharmacists had direct access to medical records, collaborative relationships with physicians, and structured follow-up tended to report stronger effects. In contrast, interventions limited to one-time reviews or those with low acceptance of pharmacist recommendations showed more modest benefits. Differences in patient populations, baseline medication burden, and outcome measurement tools further contributed to heterogeneity.

Strengths of this review include a focused population (patients with multimorbidity), comprehensive search strategy, inclusion of both efficacy and safety outcomes, and systematic assessment of risk of bias. Nevertheless, several limitations should be acknowledged. The number of included studies was modest, and methodological quality varied, with several trials at risk of bias due to lack of blinding and incomplete outcome data. Substantial clinical and methodological heterogeneity precluded meta-analysis for most outcomes. Safety outcomes were underreported in some studies, and long-term follow-up beyond 12 months was rare. In addition, most studies were conducted in high-income countries, limiting generalizability to low- and middle-income settings.

The findings have important implications for clinical practice and health policy. Pharmacist-led MTM appears to be a safe and effective strategy for improving medication use in patients with multimorbidity and should be considered as part of routine care, particularly for older adults with polypharmacy. Successful implementation is likely to require adequate pharmacist training, access to complete medication and clinical information, collaborative practice models, and appropriate reimbursement mechanisms. From a research perspective, future studies should adopt standardized core outcome sets, include longer follow-up periods, evaluate cost-effectiveness, and examine implementation factors that influence the success of pharmacist-led services. High-quality cluster randomized trials conducted in diverse healthcare systems would further strengthen the evidence base.

In summary, pharmacist-led medication therapy management improves key intermediate outcomes related to medication use and demonstrates an acceptable safety profile in patients with multimorbidity. While evidence for effects on long-term clinical outcomes remains limited, the current findings support the integration of pharmacists into the care of this complex patient population.

CONCLUSION

Pharmacist-led medication management may improve selected intermediate clinical outcomes (low certainty) and medication appropriateness (moderate certainty); evidence for utilisation and economic outcomes remains very uncertain. The logic model supports service design and scale-up. To optimize practice, pharmacists should be integrated into care pathways with electronic record access and dependable workflows; future research should use core outcome sets and report implementation fidelity to improve comparability.

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