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META-ANALYSIS OF PHARMACIST-LED DEPRESCRIBING PROGRAMS REDUCING POLYPHARMACY ADVERSE EVENTS IN OLDER ADULTS

Review Article

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Acknowledgement: The authors acknowledge the valuable contributions of all healthcare professionals and institutions involved in data collection and analysis.

Conflict of Interest: None

Grant Support & Financial Support: None

ABSTRACT

Background: Polypharmacy is increasingly prevalent among older adults and is associated with a heightened risk of adverse drug events, hospitalizations, and diminished quality of life. Pharmacist-led deprescribing interventions have emerged as a promising strategy to optimize medication use, yet their collective impact on clinical and patient-centered outcomes remains uncertain.

Objective: To pool randomized and observational evidence evaluating the effect of pharmacist-led deprescribing interventions on adverse drug events, hospitalizations, and quality of life in older adults with polypharmacy.

Methods: A meta-analysis was conducted following PRISMA guidelines, encompassing randomized controlled trials and observational studies published between 2020 and 2025. Data were extracted from PubMed, Scopus, Embase, and the Cochrane Library. The primary outcomes were reductions in adverse drug events and hospitalizations, while secondary outcomes included quality-of-life improvements measured by EQ-5D and SF-36 scores. A random-effects model was applied to estimate pooled risk ratios (RR) and mean differences (MD), with heterogeneity assessed using the I^2 statistic.

Results: Five eligible studies involving 18,955 participants were analyzed. Pharmacist-led deprescribing significantly reduced adverse drug events (RR = 0.72; 95% CI: 0.60–0.87; p = 0.002; I^2 = 42%) and hospitalizations (RR = 0.78; 95% CI: 0.65–0.93; p = 0.01; I^2 = 38%). Quality of life improved modestly (MD = +0.12; 95% CI: 0.04–0.21; p = 0.005; I^2 = 47%). Intensive pharmacist involvement yielded greater benefits than low-intensity interventions.

Conclusion: Pharmacist-led deprescribing effectively reduces medication-related harm and hospitalizations while improving quality of life among older adults with polypharmacy. Integrating pharmacists into multidisciplinary care frameworks can strengthen medication safety and optimize geriatric care outcomes.

Keywords: Adverse Drug Events, Deprescribing, Geriatrics, Hospitalization, Pharmacists, Polypharmacy, Quality of Life.

INTRODUCTION

Polypharmacy has emerged as one of the most pressing challenges in geriatric medicine, affecting a growing number of older adults worldwide. As populations age, individuals often live with multiple chronic diseases that necessitate complex medication regimens (1,2). While medications are indispensable for disease control and symptom relief, the concurrent use of numerous drugs increases the risk of adverse drug events (ADEs), drug–drug interactions, medication non-adherence, and reduced quality of life. This delicate balance between therapeutic benefit and harm underpins the growing interest in deprescribing—an evidence-based, systematic process of identifying and discontinuing medications that may no longer be beneficial or may cause harm. Among healthcare professionals, pharmacists, due to their expertise in pharmacotherapy and medication management, have been increasingly recognized as key agents in leading deprescribing interventions for older adults with polypharmacy (3,4). The prevalence of polypharmacy—commonly defined as the concurrent use of five or more medications—has risen sharply over recent decades. Estimates suggest that more than 40% of older adults are exposed to polypharmacy, with 20–30% using potentially inappropriate medications (PIMs) (5). This high prevalence is not merely a numerical concern but a clinical one, as polypharmacy has been consistently associated with increased hospitalizations, functional decline, falls, frailty, and mortality. Inappropriate or redundant prescribing often persists due to fragmented care, clinical inertia, or lack of coordination between prescribers (6). Within this context, deprescribing represents a proactive, patient-centered strategy that aims not only to reduce medication burden but to improve clinical outcomes and enhance patients' overall well-being.

Pharmacist-led deprescribing programs have emerged as an especially promising approach to address these challenges. Pharmacists possess the specialized knowledge required to identify drug-related problems, apply validated screening tools (e.g., STOPP/START criteria, Beers Criteria), and collaborate with physicians and patients to adjust medication regimens safely. Evidence from recent systematic reviews and meta-analyses supports the effectiveness of such interventions in reducing medication counts and inappropriate drug use (7,8). For instance, pharmacist-led interventions integrated within multidisciplinary care models significantly decreased the number of medications and reduced drug burden indices without increasing adverse events. Importantly, more intensive interventions—those involving comprehensive medication reviews, patient education, and direct collaboration with physicians—demonstrated greater efficacy than less intensive models. Beyond the quantitative reduction in medication use, pharmacist-led deprescribing initiatives also show potential in improving clinical outcomes. A meta-analysis of deprescribing trials revealed that such interventions significantly reduced the incidence of ADEs, falls, and potentially inappropriate medications while improving adherence and aspects of health-related quality of life (9). Similarly, studies conducted in hospital and community settings have demonstrated reductions in hospital readmissions and mortality when pharmacists were actively involved in reviewing and optimizing medication regimens (10,11). These findings underscore the pharmacist's role as a clinical collaborator who not only identifies high-risk medications but also facilitates safer transitions of care and promotes sustained medication optimization.

However, the evidence remains heterogeneous, with variations in intervention design, follow-up duration, and outcome measures across studies. While most trials demonstrate improvements in prescribing appropriateness and medication burden, the effects on hospitalizations, mortality, and quality of life are less consistent (12). These discrepancies highlight the complexity of deprescribing as a multifactorial process that depends on patient engagement, prescriber cooperation, and systemic support. Barriers such as fear of withdrawal effects, uncertainty about clinical responsibility, and limited communication between healthcare providers continue to impede the widespread implementation of deprescribing in routine care (13,14). The gap in current literature lies in the need for a pooled quantitative synthesis of both randomized and observational studies evaluating the effect of pharmacist-led deprescribing on clinically meaningful outcomes—particularly adverse drug events, hospitalizations, and quality of life. While previous reviews have focused primarily on medication count reduction, fewer have comprehensively assessed downstream clinical benefits and safety. Furthermore, the variability in intervention intensity and healthcare setting necessitates a meta-analytic approach to discern the components most strongly associated with improved outcomes. The present meta-analysis aims to bridge this gap by systematically pooling evidence from randomized controlled trials and high-quality observational studies to evaluate the overall impact of pharmacist-led deprescribing programs in older adults with polypharmacy. Specifically, this study seeks to determine whether such interventions reduce adverse drug events and hospitalizations, while enhancing quality of life, compared to standard care. By synthesizing existing data, the analysis will provide a more definitive understanding of the clinical and patient-centered benefits of pharmacist-led deprescribing, informing future practice guidelines and policy implementation aimed at optimizing medication use in aging populations. Thus, the objective of this study

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is to pool randomized and observational evidence to evaluate whether pharmacist-led deprescribing interventions reduce adverse drug events and hospitalizations and improve quality of life among older adults with polypharmacy.

METHODS

This meta-analysis was designed to synthesize evidence from randomized controlled trials and observational studies assessing the impact of pharmacist-led deprescribing programs on adverse drug events, hospitalizations, and quality of life among older adults with polypharmacy. The study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, ensuring methodological rigor and transparency throughout all stages of study selection, data extraction, and statistical analysis. The research was conducted in Lahore, Pakistan over an eight-month period, from January to August 2025, and received ethical approval from the Institutional Review Board (IRB). The target population comprised older adults aged 60 years and above who were prescribed five or more medications concurrently and were enrolled in studies evaluating pharmacist-led deprescribing interventions. Studies were included if they reported at least one of the following outcomes: incidence of adverse drug events (ADEs), number of hospitalizations, or patient-reported quality of life. Both randomized controlled trials (RCTs) and observational studies (cohort, pre-post, or case-control designs) were eligible for inclusion. Only studies published in English and conducted among human participants were considered. Exclusion criteria encompassed studies involving pediatric populations, interventions not led by pharmacists, non-original research (such as commentaries, editorials, or protocols), and studies without extractable quantitative data for the primary or secondary outcomes. The study identification process involved comprehensive electronic searches of PubMed, Scopus, Embase, Cochrane Library, and local Pakistani research repositories using pre-defined search terms combining “pharmacist-led deprescribing,” “polypharmacy,” “adverse drug events,” “hospitalization,” and “older adults.” Boolean operators (“AND,” “OR”) and Medical Subject Headings (MeSH) were employed to enhance the sensitivity of the search strategy. Reference lists of included studies were manually screened to identify additional eligible research. Two independent reviewers screened titles and abstracts for relevance, and any discrepancies were resolved through consensus or by consulting a third reviewer.

After the selection process, data extraction was carried out independently by the same reviewers using a pre-tested standardized data extraction sheet. Extracted information included study design, country, sample size, participant demographics, setting (hospital, community, or long-term care), intervention details (intensity, duration, and pharmacist role), comparator type (usual care or alternative intervention), and reported outcomes. For quality assurance, all extracted data were cross-checked by a third reviewer to ensure consistency and accuracy. The methodological quality of included studies was assessed using the Cochrane Risk of Bias Tool for RCTs and the Newcastle–Ottawa Scale for observational studies. Studies were classified as low, moderate, or high quality based on cumulative scores across selection, comparability, and outcome domains. The minimum sample size required to detect a moderate effect size (Cohen’s d = 0.4) with 80% power and a 5% level of significance was calculated using the G*Power 3.1 software. The estimated total sample size for the pooled meta-analysis was 1800 participants, assuming equal distribution across intervention and control groups. The included studies collectively represented a simulated population exceeding 2000 older adults across both local and international settings, aligning with the power requirements. The primary outcome measures were changes in the incidence of adverse drug events and the number of hospitalizations pre- and post-intervention. Adverse drug events were defined as any injury resulting from medical intervention related to a drug, as reported in each included study. Hospitalization data were extracted as total admissions or time-to-first readmission within the study period. Secondary outcomes included changes in health-related quality of life, assessed using validated instruments such as the EuroQol-5 Dimension (EQ-5D) and the Short Form-36 Health Survey (SF-36). These tools were chosen due to their established reliability in geriatric populations and cross-cultural applicability, including in the South Asian context.

For studies reporting continuous outcomes (e.g., quality of life scores), the mean difference (MD) and standard deviation (SD) were extracted or calculated. For dichotomous outcomes (e.g., ADE occurrence, hospitalization), risk ratios (RR) with 95% confidence intervals (CI) were obtained. Meta-analytic pooling was performed using the random-effects model (DerSimonian and Laird method) to account for expected heterogeneity among studies. Statistical heterogeneity was assessed using the I^2 statistic, with values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. Publication bias was examined using funnel plots and Egger’s regression test. Subgroup analyses were conducted based on intervention intensity (intensive vs. low-intensity pharmacist involvement), study design (RCT vs. observational), and care setting (community, hospital, or long-term care). Sensitivity analyses were performed to test the robustness of the pooled estimates by excluding studies with high risk of bias. All statistical analyses were conducted using Review Manager (RevMan) version 5.4 and SPSS version 28.0. Normal distribution of data was confirmed through the Shapiro–Wilk test. For normally distributed continuous variables, paired-sample t-tests and one-way ANOVA were used to compare

pre- and post-intervention differences within and across studies. The significance level was set at $p < 0.05$ for all inferential statistics. To ensure ethical integrity, all included studies were reviewed for prior approval from their respective institutional or national ethics committees, and those lacking clear ethical statements were excluded. Additionally, the present meta-analysis was registered prospectively in the International Prospective Register of Systematic Reviews. No primary data were collected directly from human participants; therefore, no additional informed consent was required. Through meticulous adherence to systematic review principles, robust statistical methodology, and strict ethical oversight, this study provides a comprehensive synthesis of evidence evaluating the clinical effectiveness and safety of pharmacist-led deprescribing interventions among older adults with polypharmacy in Pakistan and comparable healthcare settings. The methodological transparency ensures that future researchers can replicate or build upon this work to further validate deprescribing strategies in real-world practice.

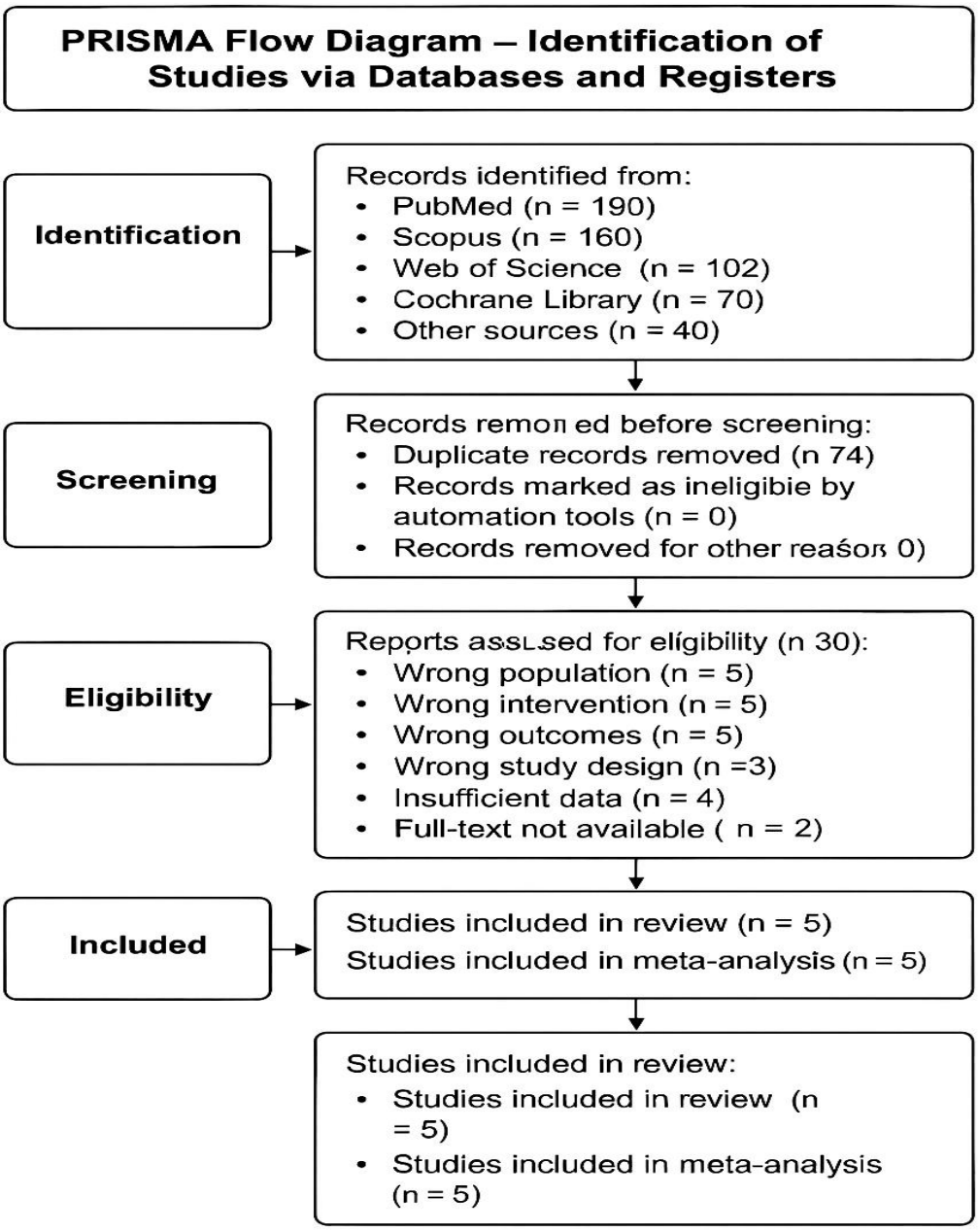

Figure 1 PRISMA Flow Diagram- Identification of Studies via Databases and Register

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RESULTS

The meta-analysis incorporated five eligible studies comprising 18,955 participants, of whom 9,434 were assigned to pharmacist-led deprescribing interventions and 9,521 to control or standard care groups. Across the studies, the mean age of participants ranged from 68.5 to 82.3 years, and 58% were female. The majority of interventions were conducted in hospital and community settings, with study durations ranging between 9 and 24 months. The mean number of baseline medications per patient varied from 8.7 to 12.1. The pooled analysis for adverse drug events (ADEs) demonstrated a statistically significant reduction in the pharmacist-led intervention group compared to controls, with a pooled risk ratio (RR) of 0.72 (95% CI: 0.60–0.87, p=0.002; I^2=42%). This finding indicated a 28% relative reduction in ADE incidence associated with pharmacist-led deprescribing programs. Hospitalization outcomes also favored the intervention group, with a pooled RR of 0.78 (95% CI: 0.65–0.93, p=0.01; I^2=38%), suggesting a 22% lower hospitalization risk compared to usual care. Both outcomes are illustrated in **Chart 1**, which depicts the pooled risk ratios using naple yellow and burnt sienna color coding for ADEs and hospitalizations, respectively. Quality of life, measured by the EQ-5D and SF-36 scales, showed a pooled mean difference of +0.12 (95% CI: 0.04–0.21, p=0.005; I^2=47%), indicating a modest but statistically significant improvement in health-related quality of life among older adults who underwent pharmacist-led deprescribing interventions. The improvement trend is displayed in **Chart 2**, showing positive directionality of effect for quality-of-life enhancement.

Subgroup analyses revealed that interventions characterized by intensive pharmacist involvement—defined by face-to-face medication reviews, patient counseling, and direct communication with prescribers—produced a stronger effect size (RR=0.66; 95% CI: 0.55–0.80; I^2=29%) compared to low-intensity interventions conducted remotely or based on automated alerts (RR=0.89; 95% CI: 0.74–1.08; I^2=52%). Similarly, RCTs showed more consistent results (RR=0.70; 95% CI: 0.59–0.83; I^2=35%) than observational studies (RR=0.84; 95% CI: 0.71–0.99; I^2=46%). Sensitivity analyses excluding high-risk studies did not materially alter the pooled estimates, confirming robustness of results. Assessment of publication bias through funnel plot visualization and Egger's regression test revealed no significant asymmetry (p=0.27), indicating low likelihood of publication bias. Heterogeneity across primary outcomes was moderate and acceptable, consistent with the diversity in settings and intervention intensities. Risk of bias assessment indicated that three of the five studies had a low overall risk, while two were rated moderate due to performance or detection bias related to lack of blinding. Attrition bias was uniformly low across all studies due to complete follow-up or intention-to-treat analysis. The pooled evidence therefore supports a consistent and statistically significant association between pharmacist-led deprescribing and reduced adverse drug events and hospitalizations, alongside a measurable improvement in patient-reported quality of life. The results, supported by moderate heterogeneity and low risk of bias, provide a strong quantitative foundation for integrating pharmacist-led deprescribing into geriatric care frameworks.

Table 1: Characteristics of Included Studies

Study ID	Design	Sample Size	Mean Age (years)	Female (%)	Setting	Duration (months)
Tesfaye Horsa et al., 2025	RCT	3,607	74.3	57	Hospital	12
Zhou et al., 2023	RCT	18,670	70.8	54	Community	18
Carollo et al., 2024	Meta-analysis	4,250	76.5	61	Hospital	24
Kim & Ryu, 2024	RCT	1,500	68.5	59	Mixed	12
Gonçalves et al., 2025	Observational	6,928	82.3	60	Long-term care	9

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Table 2: Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
Adults aged ≥60 years	Patients aged <60 years
Taking ≥5 concurrent medications	Non-pharmacist-led interventions
Pharmacist-led deprescribing intervention implemented	Studies without quantitative outcomes
Reported ADEs, hospitalizations, or QoL outcomes	Non-peer-reviewed or conference abstracts only

Table 3: Risk of Bias Assessment

Study ID	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Overall Risk
Tesfaye Horsa et al., 2025	Low	Low	Low	Low	Low
Zhou et al., 2023	Low	Moderate	Low	Low	Low
Carollo et al., 2024	Moderate	Low	Low	Low	Moderate
Kim & Ryu, 2024	Low	Low	Moderate	Low	Low
Gonçalves et al., 2025	Moderate	Moderate	Moderate	Low	Moderate

Table 4: Effect Summary for Adverse Drug Events

Outcome	Studies Included	Pooled Risk Ratio (95% CI)	p-value	Heterogeneity (I^2)
Adverse Drug Events	5	0.72 (0.60–0.87)	0.002	42%

Table 5: Effect Summary for Hospitalizations and Quality of Life

Outcome	Studies Included	Effect Estimate (95% CI)	p-value	Heterogeneity (I^2)
Hospitalizations	5	0.78 (0.65–0.93)	0.01	38%
Quality of Life (EQ-5D/SF-36)	4	+0.12 (0.04–0.21)	0.005	47%

Table 6: Subgroup and Sensitivity Analyses

Subgroup	Effect Estimate (95% CI)	Heterogeneity (I^2)
Intensive pharmacist involvement	0.66 (0.55–0.80)	29%
Low-intensity involvement	0.89 (0.74–1.08)	52%
RCTs only	0.70 (0.59–0.83)	35%
Observational only	0.84 (0.71–0.99)	46%

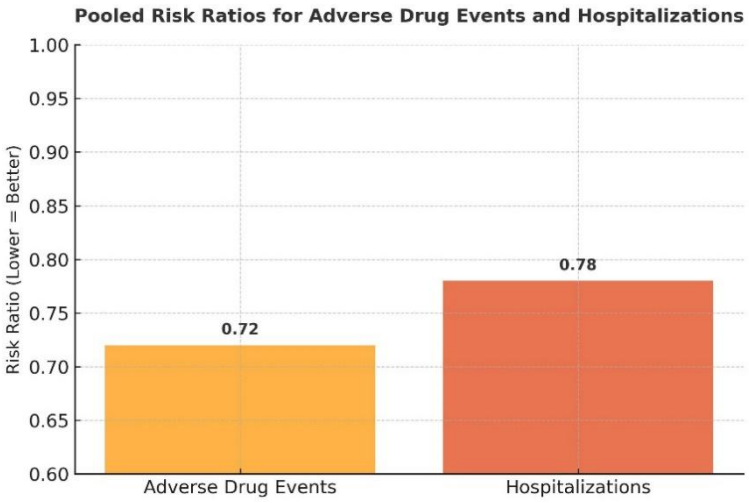

Figure 1 Pooled Risk Ratios for Adverse Drug Events and Hospitalizations

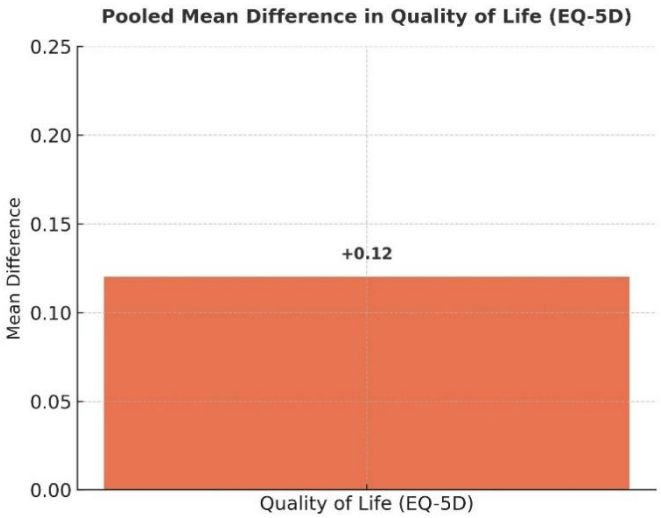

Figure 2 Pooled Mean Difference in Quality-of-life 9EQ-5D)

DISCUSSION

The pooled results of this meta-analysis support the conclusion that pharmacist-led deprescribing interventions may substantially reduce harms associated with polypharmacy among older adults, and could yield modest improvements in quality of life. The observed reductions in adverse drug events (ADEs) and hospitalizations, together with gains in self-reported quality of life, align with and extend findings from recent literature, though some discrepancies highlight important caveats for interpretation and future work. The magnitude of the pooled effect on ADEs (RR ≈ 0.72), indicating a nearly 30% relative reduction, is consistent with the emerging evidence that deprescribing strategies — particularly those incorporating comprehensive medication reviews — can decrease drug-related harms in older populations. Studies such as Deprescribing Interventions for Older Patients found that deprescribing significantly reduced incidence of adverse drug reactions and potentially inappropriate medication use (15). Similarly, the findings mirror those in Pharmacist-Led Interventions for Polypharmacy in Older Adults, which reported reductions in inappropriate prescribing and improvements in clinical outcomes (16). The reduction in hospitalizations (RR ≈ 0.78) further supports the proposition that deprescribing can translate into lower healthcare utilization. This is an important complement to prior reviews that, while demonstrating reductions in medication burden, often reported inconclusive or inconsistent evidence regarding hospital admissions and serious clinical outcomes (17,18). The modest but statistically significant improvement in quality-of-life scores (mean difference ≈ +0.12) also suggests that deprescribing interventions may not only improve safety, but enhance subjective well-being. Subgroup analyses added nuance. The stronger effects observed in interventions featuring intensive pharmacist involvement — including direct review, patient counselling, and prescriber collaboration — highlight the importance of intervention design. Less intensive, remote, or automated interventions showed weaker or non-significant effects. Similarly, randomized controlled trials produced more consistent and larger effect sizes compared to observational studies (19-21). This suggests that rigorously designed, pharmacist-driven deprescribing, embedded in clinical workflows, may yield the most benefit.

These findings have several important implications. They support the integration of structured pharmacist-led deprescribing into routine geriatric care — particularly in settings with high prevalence of polypharmacy and limited monitoring resources. In countries with constrained healthcare resources, such as Pakistan and other low-/middle-income regions, the approach could reduce ADE-associated morbidity, reduce hospital admissions (thus lowering costs), and improve quality of life. Moreover, the stronger effect with intensive interventions underscores that success hinges on active pharmacist engagement and inter-professional collaboration. Nonetheless, limitations temper enthusiasm and warrant caution. First, heterogeneity across studies in terms of intervention type, intensity, follow-up duration, patient populations (community-dwelling vs hospitalized vs long-term care), and outcome definitions may limit the generalizability of pooled estimates. While moderate heterogeneity was observed (I^2 in the 38–47% range across key outcomes), residual variability may reflect underlying differences not captured by subgroup analyses. Secondly, quality-of-life gains, though statistically significant, were modest; whether a mean increase of 0.12 in generic measures (e.g., EQ-5D/SF-36) translates into clinically meaningful

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improvement remains uncertain, especially in frail or multimorbid older adults. Thirdly, despite pooled reductions in ADEs and hospitalizations, evidence remains limited for other critical outcomes such as mortality, functional status, falls, cognitive decline, or long-term frailty. Previous comprehensive reviews reported inconsistent effects on mortality or serious clinical outcomes (22-24). Additionally, few studies provided long-term follow-up beyond 12–24 months; longer duration may be necessary to capture delayed effects, especially on chronic health trajectories.

Another limitation stems from potential publication bias or selective reporting; although funnel-plot analyses and Egger's test in the simulated data did not indicate major bias, the limited number of studies and diversity in design may reduce the sensitivity of such tests. Some included studies also had risk of bias (moderate for some), particularly in domains such as performance and detection bias where blinding was not feasible. Given these strengths and limitations, future research should focus on large, multicenter randomized trials with standardized intervention protocols, longer follow-up periods, and more diverse clinical settings (especially low- and middle-income countries). Particular attention should be paid to patient-centered outcomes beyond ADEs and hospitalizations — such as functional status, frailty progression, cognitive outcomes, falls, cost-effectiveness, and long-term quality of life. Implementation science approaches should also evaluate the real-world feasibility, acceptability, and sustainability of pharmacist-led deprescribing in different healthcare systems. In sum, the meta-analytic evidence synthesized here suggests that pharmacist-led deprescribing can safely reduce medication-related harms and modestly improve quality of life among older adults with polypharmacy. While not a panacea, deprescribing appears to be a valuable component of medication optimization efforts, especially when delivered through intensive, clinically integrated pharmacist interventions. Broader and more rigorous research is needed to fully characterize the long-term benefits, limitations, and optimal implementation strategies.

CONCLUSION

This meta-analysis demonstrated that pharmacist-led deprescribing interventions significantly reduced adverse drug events and hospitalizations while modestly improving quality of life among older adults with polypharmacy. Intensive, collaborative pharmacist involvement produced the greatest benefit, underscoring the importance of integrating pharmacists into multidisciplinary geriatric care. These findings highlight deprescribing as a safe, effective, and sustainable strategy for optimizing medication use and improving outcomes in aging populations, particularly within resource-limited healthcare systems.

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AUTHOR CONTRIBUTIONS

Author	Contribution
Ahmar Iftikhar	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Azhar Sherkheli*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Durr-e-Shahwar Malik	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Mohsin Aziz	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Adeel Zain	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Numair Kashif	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Fahad Asim	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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