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Does Clinical Pharmacy Improve What Matters to Patients? An Umbrella Review Separating Process Gains from Medication-Related Harm, Health-Care Use, Survival, and Quality of Life, 2017–2024

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ABSTRACT

Clinical-pharmacy interventions are frequently described as effective, yet the meaning of effectiveness changes substantially according to the outcome assessed. Improvements in medication appropriateness, adherence, prescribing quality, and medication-related problems may occur without corresponding reductions in hospital use, mortality, or deterioration in quality of life. Interpretation is further complicated when systematic reviews repeatedly include the same primary studies and are treated as independent corroborating evidence. To determine across systematic reviews of clinical-pharmacy interventions which benefits are concentrated in process and medication-related outcomes and which extend to health-care use, survival, or quality of life, while accounting for methodological quality, outcome heterogeneity, and overlap of primary studies across reviews. An umbrella review of systematic reviews published from 2017 through 2024 was conducted using review-of-reviews methodology informed by PRISMA 2020 and PRIOR principles. Eligible reviews evaluated pharmacist-led or pharmacist-integrated clinical interventions and reported process, medication-related harm, health-care use, mortality, or quality-of-life outcomes. Reviews were characterized by population, setting, intervention, comparator, outcome definitions, and methodological limitations. Methodological quality was assessed using AMSTAR 2 principles. Outcomes were coded into prespecified tiers. Primary-study overlap was examined using study-review membership information where ascertainable; quantitative overlap statistics were restricted to matrices sufficiently complete for reproducible calculation. The searches identified 146 review records, of which 42 duplicates were removed. After screening 104 unique records, 43 full-text reports were assessed and 20 systematic reviews met the formal umbrella-synthesis criteria. Evidence was most consistently favorable for medication appropriateness, medication-related problems, adherence, medication errors, and selected medication-harm outcomes. Effects on admission and readmission were more variable and appeared sensitive to setting and intervention intensity. Mortality was generally unchanged in broad medication-review programmes, although favorable associations occurred in selected high-risk settings. Quality-of-life findings were mixed, with stronger signals in some targeted counseling and pain-management interventions. Repeated primary studies across reviews reduced the extent to which concordant review conclusions could be interpreted as independent replication. Clinical pharmacy improves outcomes that matter to patients under some conditions, but the strength and consistency of benefit differ markedly by outcome. Evidence is strongest for outcomes close to medication management and less uniform for health-care use, survival, and quality of life. Review-level corroboration also requires adjustment for shared underlying primary evidence.

Keywords: Clinical pharmacy, Medication review, Adverse drug events, Hospital readmission, Mortality, Quality of life

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Introduction

Clinical pharmacy has accumulated a large secondary evidence base, but the question of whether it "works" remains poorly specified when outcomes with very different clinical meanings are collapsed into a single effectiveness judgment. A recent scoping review of pharmacist-led medication-review systematic reviews documented marked variation in intervention composition, outcome selection, and methodological confidence, with favorable and null conclusions occurring across the same broad service category [1]. Earlier review-of-reviews evidence in community practice similarly suggested that changes in medication-related or intermediate clinical measures were more consistently demonstrable than effects on mortality or health-service use [2]. The continued coexistence of positive and null findings makes the unit of outcome interpretation as important as the unit of intervention.

This distinction is visible in reviews that evaluate increasingly patient-important endpoints. Hospital medication review can reduce some forms of subsequent health-care use while leaving mortality essentially unchanged, and multidisciplinary polypharmacy interventions can improve medication appropriateness or adherence without producing consistent improvements in function, quality of life, mortality, or service utilization. Reviews of inpatient medication review and deprescribing show a similar separation between medication optimization and harder clinical endpoints [3–5]. A finding that pharmacists identify inappropriate therapy or improve prescribing quality therefore cannot by itself establish that patients experience fewer admissions, longer survival, or better health-related quality of life.

Variation in what pharmacists actually do further complicates interpretation. Pharmacist-led medication review can incorporate medication reconciliation, identification of drug-related problems, communication with prescribers, patient goal-setting, counseling, follow-up, monitoring, and implementation of recommended treatment changes in different combinations. Component-focused synthesis indicates that these configurations are not interchangeable and that the presence of a nominal "medication review" does not specify the intensity, authority, continuity, or patient participation embedded within the intervention [6]. Apparent disagreement between reviews may consequently arise before outcome measurement begins because their underlying interventions represent materially different clinical activities.

The outcomes themselves also require clearer boundaries. An international core outcome initiative for medication-review trials in multimorbid older adults identified patient-important domains including drug-related hospital admission and health-related quality of life rather than limiting evaluation to prescribing indicators [7]. At the same time, systematic examination of community-pharmacist medication-review trials identified extensive variation in outcome definitions and instruments, limiting direct comparison even among studies assigned the same broad label [8]. The present umbrella review therefore treats process measures, medication-related harm, health-care utilization, survival, and quality of life as analytically separate outcome tiers. These tiers describe differences in what is being measured; they are not assumed to form a deterministic causal progression.

A second problem concerns independence of the evidence. Systematic reviews in mature clinical-pharmacy fields frequently draw on overlapping pools of primary studies. Counting several concordant reviews as several independent confirmations can exaggerate the apparent breadth of replication when the same trial participants repeatedly contribute to those conclusions. Accordingly, this review evaluates not only whether conclusions agree, but also the extent to which apparent agreement reflects shared underlying evidence.

Aim

The primary aim was to determine, across systematic reviews of clinical-pharmacy interventions published from 2017 through 2024, which reported benefits are concentrated in process and medication-related outcomes and which extend to health-care utilization, survival, or quality of life.

A secondary aim was to examine whether apparently concordant or discordant review conclusions could be interpreted independently after considering intervention scope, comparator intensity, outcome definition, methodological quality, clinical context, and overlap of included primary studies.

Materials and Methods

Review design and review-unit eligibility

The review was conducted as an umbrella review of systematic reviews of health-care interventions. Reporting and selection procedures were informed by PRISMA 2020 principles [9] and by the PRIOR reporting guideline for overviews of reviews [10]. Methodological choices were additionally informed by established work on eligibility, searching, extraction, and synthesis in overviews [11].

The formal unit of inclusion was a completed systematic review, with or without meta-analysis, that synthesized primary evidence evaluating pharmacist-led or pharmacist-integrated clinical-pharmacy interventions and reported at least one eligible outcome. When different reviews addressed the same intervention domain, they were retained when they contributed meaningfully different populations, settings, intervention configurations, outcome domains, or evidence periods. Selection decisions were made explicitly because different rules for choosing among overlapping systematic reviews can materially alter both the comprehensiveness and complexity of an overview [12]. Empirical work demonstrating the sensitivity of overview findings to alternative review-inclusion strategies was used to inform this decision process [13].

Journal quartile was not an eligibility criterion for the umbrella synthesis. Review-of-review articles, methodological papers, consensus work, and realist syntheses could inform interpretation or methods but were not counted as additional independent effect-bearing systematic reviews.

Eligible interventions included medication review, medication optimization, medication counseling, deprescribing, clinical-pharmacy participation within multidisciplinary teams, pharmacist-led therapeutic management, transitional medication interventions, and related clinical services in which pharmacist activity was a substantive component. Purely educational descriptions, implementation reports without systematic outcome synthesis, protocols, editorials, and reviews without an eligible outcome tier were excluded.

The predefined outcome tiers were: process or medication-management outcomes; medication-related harm; health-care utilization; survival; and quality of life or closely related patient-reported health outcomes. A single review could contribute to more than one tier.

Search, selection, extraction, and methodological appraisal

The literature search used combinations of terms relating to clinical pharmacy, pharmacist intervention, medication review, medication management, deprescribing, adverse drug events, medication-related problems, hospital admission or readmission, mortality, quality of life, systematic review, and meta-analysis. Searches were supplemented by targeted review retrieval, citation-chain examination, journal and publisher searches, and methodological searches relevant to umbrella-review methods and primary-study overlap.

The searches identified 146 potentially relevant review records. Forty-two duplicate records were removed, leaving 104 unique records for title and abstract screening. Sixty-one records were excluded at this stage. Forty-three full-text review reports were assessed against the eligibility criteria.

Twenty-three full-text reports were excluded: seven were of an ineligible review design or evidence level; five did not contain a sufficiently central pharmacist or clinical-pharmacy intervention; four did not provide an extractable eligible outcome tier; three fell outside the 2017–2024 publication window; two were protocols, editorials, or otherwise lacked a completed extractable synthesis; and two represented duplicate or superseded review reports. Twenty systematic reviews were retained as formal effect-bearing evidence units.

For each included review, extraction covered population, setting, pharmacist role, intervention components, comparator, outcome definition, measurement approach, direction of findings, quantitative results where directly reported, authors' limitations, and features relevant to interpretation of heterogeneity. Review-level conclusions were not recoded simply as “positive” or “negative”; outcome-specific results and null findings were retained separately.

Methodological confidence was evaluated using AMSTAR 2 principles [14]. Appraisal was used to modify confidence in interpretation rather than to convert methodological quality into an effectiveness score. Primary-study risk of bias, certainty assessments, heterogeneity, intervention comparability, and limitations reported by the review authors were also retained because high-quality review conduct cannot compensate for weak or heterogeneous primary evidence.

The aggregate selection process is shown in **Figure 1**.

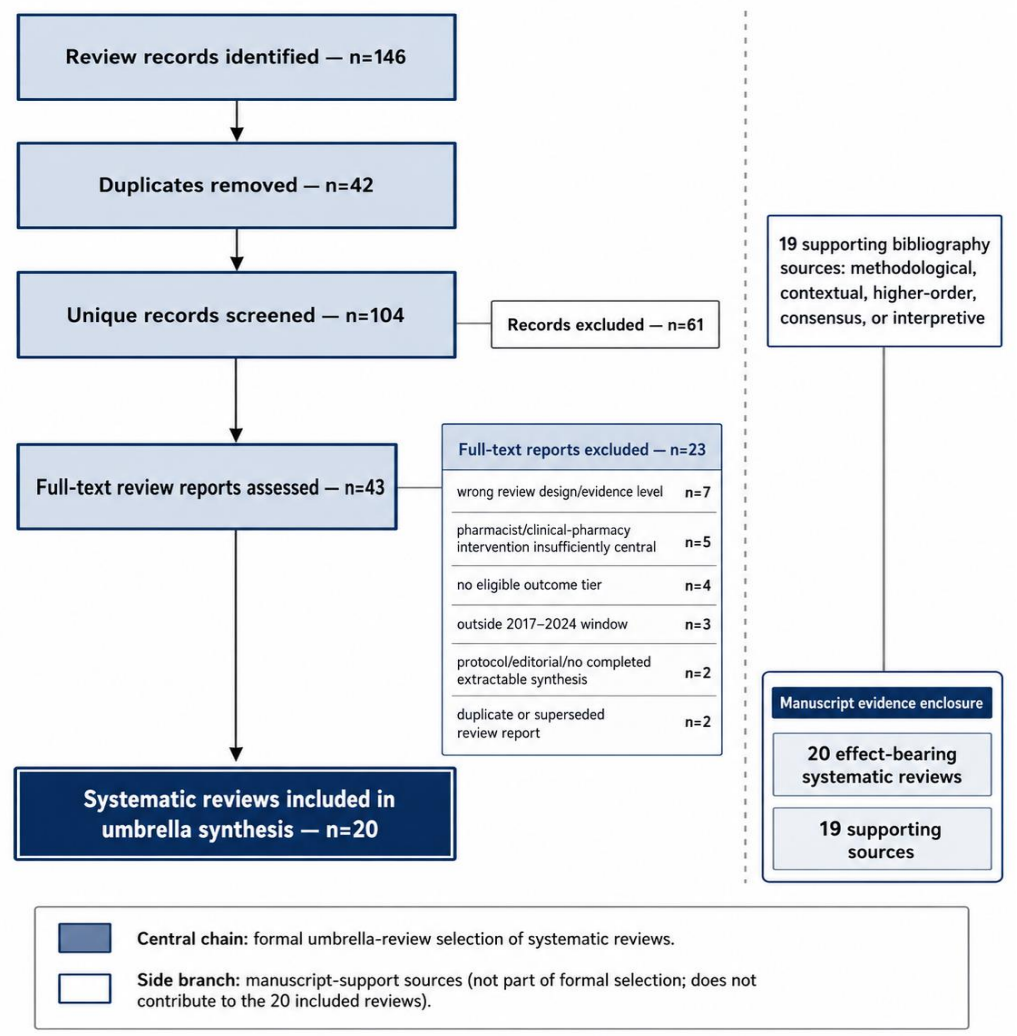

Figure 1. Review selection and separation of effect-bearing reviews from supporting evidence

Outcome-tier coding, primary-study overlap, and synthesis

Outcome coding was established before comparative interpretation. Process and medication-management outcomes included measures such as medication appropriateness, prescribing quality, medication reconciliation, medication errors, implementation of treatment changes, adherence, and resolution of medication-related problems when these did not themselves constitute patient harm. Medication-related harm comprised adverse drug events and other realized clinically important pharmacotherapy harms. Health-care utilization included hospital admission, readmission, emergency-department attendance, length of stay, and comparable service-use measures. Survival comprised mortality outcomes. Quality of life was restricted to explicitly measured patient-reported health or health-related quality-of-life outcomes.

These categories were analytically separate rather than sequential causal stages. An intervention could plausibly alter a proximal medication measure without producing a detectable change in mortality because downstream outcomes depend on baseline risk, competing causes, implementation fidelity, follow-up duration, statistical power, and factors outside medication management.

Primary-study dependence was evaluated because repeated inclusion of the same studies can make review-level evidence appear more extensively replicated than it is. Corrected covered area and related overlap measures provide methods for describing this problem [15–17]. Overall and pairwise displays were considered because overlap concentrated between particular review pairs may be obscured by a single global statistic [18]. Reproducible implementation of corrected covered area was informed by available methodological software and algorithms [19]. Recent methodological evidence demonstrating that overall overlap and pairwise overlap may lead to different interpretations was therefore treated as particularly relevant [20]. Review-size imbalance and other structural features of citation matrices were also considered when interpreting pairwise estimates [21].

A global corrected covered area was not calculated when complete primary-study membership could not be established across all 20 included reviews. Quantitative overlap values were restricted to review pairs or clusters with sufficiently complete study-level identification. Elsewhere, overlapping primary studies were treated qualitatively as a source of non-independence. No review received additional evidential weight merely because its primary studies had already appeared in another included review.

Given the heterogeneity of populations, clinical-pharmacy interventions, comparators, outcome definitions, follow-up periods, review designs, and overlapping primary evidence, no second-order pooled estimate of an overall "clinical-pharmacy effect" was considered scientifically interpretable. Synthesis instead examined the distribution and consistency of findings within each outcome tier and then evaluated sources of discordance across reviews.

Results and Discussion

Review selection and profile of the evidence base

Twenty systematic reviews formed the formal effect-bearing umbrella-synthesis set. The included evidence covered hospital medication review, community medication review, deprescribing, multidisciplinary medication optimization, adverse-drug-event prevention, anticoagulation management, emergency-department services, pediatric hospital pharmacy, antimicrobial stewardship, mental-health pharmacy services, falls-related medication review, hospital-to-home medication interventions, ambulatory cardiology, and critical-care pharmacy.

The breadth of intervention labels concealed substantial clinical heterogeneity. In some reviews, pharmacists primarily identified medication discrepancies or inappropriate therapy and communicated recommendations to another prescriber. In others, pharmacists provided continuing counseling, therapeutic monitoring, deprescribing, anticoagulation management, post-discharge follow-up, or embedded multidisciplinary care. Comparator intensity ranged from routine care with limited pharmacist involvement to multidisciplinary services already containing substantial medication-management activity.

Outcome coverage was also uneven. Medication-related and process measures were common, whereas mortality and quality-of-life endpoints were less consistently reported. Some reviews contained large numbers of primary trials but relatively few events for individual patient-important outcomes. Others focused on high-risk clinical contexts where pharmacist participation was more tightly coupled to immediate treatment decisions.

The major characteristics relevant to interpretation are summarized in Table 1.

Table 1. Clinical and methodological profile of the systematic reviews contributing direct effect evidence

Review	Population/setting	Principal pharmacist exposure	Comparator	Main outcome span	Appraisal context relevant to interpretation
Bülow 2023	Hospitalised patients	Medication review	Usual care	Readmission, ED use, mortality, HRQoL	Outcome certainty varied; downstream endpoints not uniformly responsive
Roncal-Belzunce 2024	Community-dwelling older adults with polypharmacy	Multidisciplinary medication optimization	Usual care	Appropriateness, adherence, function, mortality, QoL, utilization	Most primary trials carried substantial risk-of-bias concerns
Carollo 2024	Older inpatients	Medication review/deprescribing	Usual care	Readmission, mortality	Primary-study limitations and clinical heterogeneity
Craske 2024	Adults across medication-review settings	Pharmacist medication-review components	Usual care	Medication and clinical outcomes	Component reporting and intervention composition varied
Vogt 2024	Community patients	Community-pharmacist medication review	Usual care	Approximately 40 reported outcome constructs	Marked intervention and measurement heterogeneity
Al-Babtain 2022	Community patients with long-term conditions	Pharmacist-led medication-review programme	Usual care	Intermediate clinical, medication, utilization outcomes	Trial interventions and endpoints heterogeneous

Kelly 2024	Multiple settings	Pharmacist intervention	No comparable pharmacist intervention	ADE and potential ADE	ADE estimate consistent; potential-ADE evidence heterogeneous
Fentie 2024	Patients receiving cancer treatment	Pharmacist intervention	Usual care	Medication-related problems	Disease- and therapy-specific evidence
Kefale 2024	Patients receiving anticoagulants	Pharmacist-led anticoagulation management	Usual care	Appropriateness, bleeding, hospitalization, thromboembolism, mortality	Mixed study designs and endpoint-specific heterogeneity
Kelly 2023	Multiple chronic-care populations	Pharmacist counseling	Usual care	Adherence, QoL	Intervention content and measurement instruments varied
Zaij 2023	Multidisciplinary clinical care	Pharmacist participation in team	Standard multidisciplinary care/usual care	Adverse drug events	Qualitative and clinically heterogeneous evidence
Atey 2023	Emergency departments	Pharmacist medication service	Usual care	Medication history, errors, appropriateness, quality use	Stronger evidence for proximal medication endpoints
Livori 2023	Cardiology ambulatory care	Pharmacist clinical care	Usual care	Clinical and patient-centered outcomes	Considerable variation in outcome measurement
Alcântara 2023	Hospitalized children	Clinical pharmacist service	Usual care	Length of stay, cost, quality indicators	Pediatric evidence base heterogeneous
Lambert 2022	Community antibiotic users	Pharmacist antimicrobial intervention	Usual care	Antibiotic supply/use, adherence	Methodological limitations across included studies
Bužančić 2022	Community adults	Pharmacist deprescribing	Usual care	Medication discontinuation and clinical outcomes	Considerable diversity of interventions and endpoints
Ng 2022	Severe and persistent mental illness	Multifaceted pharmacist intervention	Usual care	Medication, clinical and service outcomes	Heterogeneity and risk-of-bias concerns
Seppala 2022	Older adults	Medication review/deprescribing	Usual care	Falls and fall-related outcomes	Highly heterogeneous falls evidence
Daliri 2021	Hospitalised adults across discharge	Multicomponent medication intervention	Usual care	Readmission and medication outcomes	Attribution complicated by intervention bundles
Lee 2019	Critically ill patients	Pharmacist participation in ICU team	Team without comparable pharmacist participation	Mortality, length of stay, ADE	Mixed randomized and nonrandomized evidence limits causal certainty

Where benefit is most consistent: process and medication-related outcomes

The most reproducible favorable findings occurred in outcomes that directly reflected medication management. Community pharmacist-led medication-review programmes improved selected intermediate clinical and medication outcomes, although benefits did not extend consistently to every downstream endpoint [22]. This pattern supports distinguishing successful medication optimization from proof of broader health improvement.

Evidence concerning medication-related harm moved beyond purely procedural outcomes in several settings. A meta-analysis of randomized trials reported a reduction in adverse drug events associated with pharmacist interventions, whereas the pooled result for potential adverse drug events was less certain [23]. Pharmacist interventions in oncology similarly reduced medication-related problems, although these outcomes should not be interpreted as direct evidence of improved survival or quality of life [24]. Anticoagulation services provided a

particularly informative example of endpoint-specific effects: medication appropriateness, bleeding, and hospitalization were favorable while thromboembolism and mortality estimates did not establish statistically clear benefits [25].

The wider evidence base demonstrates why the label "pharmacist intervention" is too broad to function as a homogeneous exposure. Targeted pain interventions have generated favorable clinical and patient-reported signals in some reviews [26], whereas evidence in frail older adults suggests more consistent improvement in medication appropriateness than in hospitalization or frailty outcomes [27]. Pharmacist counseling can improve adherence and selected quality-of-life measures [28]. Pharmacist participation within multidisciplinary teams has been associated with reductions in adverse drug events [29], and emergency-department pharmacists consistently influence medication histories, prescribing appropriateness, and medication-error outcomes that occur close to the point of intervention [30]. Conversely, ambulatory cardiology reviews demonstrate that even clinically similar programmes may be difficult to compare when investigators select different outcome measures and instruments [31].

Taken together, the evidence supports a qualified process-to-harm distinction. Pharmacists can alter prescribing decisions, medication use, adherence, medication-problem resolution, and some realized medication harms. The consistency of these effects should not be used to imply that every intervention produces subsequent reductions in admission, mortality, or deterioration in patient-reported health. It does, however, indicate that the clinical-pharmacy evidence base contains effects more substantive than administrative completion of medication review alone.

Health-care use and survival do not move together

Health-care utilization showed greater contextual variation than process and medication outcomes. Pediatric inpatient evidence suggests that clinical-pharmacist services can influence selected quality indicators, length-of-stay measures, or costs, although the pediatric evidence base is heterogeneous and cannot be transferred directly to adults [32]. Community antibiotic interventions likewise demonstrate improvements in dimensions of medication use while adherence findings remain less uniform [33]. Community deprescribing reviews show that successful discontinuation of unnecessary treatment does not necessarily produce detectable changes in hospitalization, falls, mortality, or quality of life during the study periods available [34]. Similar interpretive caution applies to pharmacist-led interventions in severe mental illness, where some favorable clinical and medication effects coexist with substantial heterogeneity in intervention design and study quality [35].

Mortality was especially resistant to a uniform effectiveness claim. Medication review or deprescribing used as an isolated falls-prevention strategy did not clearly reduce falls across the heterogeneous older-adult literature [36], illustrating that modification of one pharmacological contributor may be insufficient when the final endpoint has multiple competing determinants. Hospital-to-home interventions produced more encouraging evidence for readmission when medication-related activities continued across discharge and incorporated several coordinated components [37]. Realist synthesis of post-discharge pharmacist medication review suggests that continuity, professional coordination, trust, clarity of responsibility, and patient preferences can alter whether the same nominal service produces useful action [38].

Critical care provides an important counterexample to a simple claim that pharmacist interventions cannot influence distal outcomes. Pharmacist participation in multidisciplinary intensive-care teams has been associated with improvements in mortality, length of stay, and adverse-drug-event outcomes [39]. The evidence base includes nonrandomized designs, however, so these associations do not establish that pharmacist participation alone caused the entire observed benefit. More importantly, the ICU findings indicate that absence of a consistent mortality effect across broad medication-review programmes should not be converted into a universal biological or service-level proposition. Baseline event risk, immediacy of medication decisions, intervention authority, team integration, and opportunity to prevent severe drug-related complications can differ substantially between routine medication review and critical-care pharmacotherapy.

Health-care utilization and survival must consequently remain separate outcome domains. Readmission can respond to coordination and continuity even when mortality does not change, while high-risk clinical environments may create a stronger pathway between pharmacist action and immediate clinical deterioration than lower-risk community settings. Treating all these outcomes as one category of "clinical benefit" obscures the conditions under which an intervention actually reaches a patient-important endpoint.

Quality of life and other patient-reported outcomes

Quality-of-life evidence was less consistent than medication-management evidence and was strongly dependent on intervention and measurement context. Broad hospital or community medication-review programmes frequently reported uncertain or null quality-of-life effects even when medication appropriateness or adherence improved [3, 4]. This discrepancy is plausible because many medication changes produce small, competing, delayed, or difficult-to-perceive effects on multidimensional health status. Generic quality-of-life instruments may also be insensitive to narrowly targeted improvements in medication burden, adverse effects, treatment confidence, or symptom control.

Patient-important measurement nonetheless remains central to judging the consequences of clinical pharmacy. International consensus work on medication-review outcomes explicitly included health-related quality of life among the outcomes that should be considered in trials involving multimorbid older adults [7]. Ambulatory cardiology evidence further shows that lack of consistent outcome definitions and instruments can impede comparison even where patient-centered evaluation is intended [31]. Community deprescribing studies similarly illustrate that successful medication discontinuation and changes in patient-reported health should be treated as separate outcomes [34].

Targeted services provide evidence that patient-reported benefit is achievable rather than intrinsically beyond the reach of pharmacist intervention. Pain-focused pharmacist services have reported improvements in pain-related functioning and quality-of-life measures in selected contexts [26]. Pharmacist-delivered counseling has also been associated with improved adherence and quality of life across randomized trials [28]. These findings do not justify transferring the same effect to medication review, deprescribing, emergency care, or multidisciplinary inpatient services. They instead suggest that quality-of-life effects may be more detectable when the pharmacist intervention directly addresses symptoms, treatment experience, understanding, or behaviors represented by the selected patient-reported instrument.

The resulting evidence pattern is therefore asymmetric. Process and medication-related benefits are comparatively common; some medication-harm outcomes also improve; effects on health-care use vary by service configuration and context; survival benefit is uncommon outside selected high-risk settings; and quality-of-life improvement is present in particular intervention classes but not consistently across broad medication-review programmes.

The outcome-tier synthesis is summarized in **Table 2**.

Table 2. Distribution of clinical-pharmacy evidence across outcome tiers

Outcome tier	Outcomes and favorable conditions	Evidence pattern and interpretive boundary
Process and medication-management outcomes	Outcomes: Medication appropriateness, medication reconciliation, prescribing quality, adherence, medication errors, implementation of recommendations, medication discontinuation	Pattern: Most consistently favorable tier
	Favorable conditions: Interventions with direct pharmacist action, clear treatment authority, follow-up, counseling, or repeated medication management	Interpretive boundary: Highly heterogeneous definitions; favorable process change does not establish downstream health benefit
Medication-related harm	Outcomes: Adverse drug events, bleeding, medication-related problems and clinically important medication complications	Pattern: Favorable in several targeted reviews, but less uniform than process outcomes
	Favorable conditions: High-risk medicines, active monitoring, integrated multidisciplinary care, clearly defined medication-harm endpoints	Interpretive boundary: Potential events, realized events, medication-related problems, and surrogate safety outcomes are not interchangeable
Health-care utilization	Outcomes: Admission, readmission, emergency-department use, length of stay and related service use	Pattern: Mixed and context-dependent
	Favorable conditions: Multicomponent hospital-to-home interventions, selected high-risk clinical services and strong continuity across care settings	Interpretive boundary: Intervention bundles complicate attribution; outcome windows and reasons for utilization differ

Survival and comparably distal clinical outcomes	Outcomes: Mortality and selected serious downstream events	Pattern: Usually null or uncertain in broad medication-review/deprescribing programmes; favorable signals in selected high-risk settings
	Favorable conditions: Immediate pharmacotherapy risk, intensive multidisciplinary integration and stronger opportunity for pharmacist action to alter severe deterioration	Interpretive boundary: Low event frequency, short follow-up, competing determinants and nonrandomized evidence in some favorable settings
Quality of life and patient-reported health	Outcomes: Generic or disease-specific HRQoL, pain-related functioning and related patient-reported outcomes	Pattern: Mixed overall, with clearer improvement in some targeted counseling and pain interventions
	Favorable conditions: Interventions closely aligned with symptoms, patient understanding, treatment experience or behaviors measured by the instrument	Interpretive boundary: Measurement heterogeneity and instrument insensitivity; medication optimization may not generate a detectable generic QoL change

Overlap-adjusted interpretation of apparent corroboration

Agreement between systematic reviews did not necessarily represent independent replication. Clinical-pharmacy reviews frequently covered similar intervention families, patient populations, and publication periods, creating substantial opportunity for the same primary studies to contribute to several secondary syntheses. This problem is especially important when several reviews reach concordant conclusions and the number of reviews is implicitly treated as the number of independent evidential confirmations.

Corrected covered area offers one approach to quantifying duplication, but its interpretation depends on a complete and correctly constructed study-by-review matrix [15]. Overlap must also be managed at the synthesis stage because merely acknowledging duplicate primary studies does not remove the resulting dependence [16]. Graphical and matrix-based representations can make repeated study membership more visible [17], while approaches that consider both overall and pairwise overlap provide additional information about concentrated duplication between particular reviews [18]. Reproducible calculation tools facilitate this process when complete membership data are available [19].

No single overall overlap statistic was applied across the evidence base. Methodological evidence shows that low or moderate overall overlap can coexist with substantial duplication between particular review pairs [20]. Pairwise estimates can themselves be affected by review size and the configuration of the underlying evidence matrix [21]. Consequently, quantitative overlap was considered interpretable only where study-level membership could be reconstructed with sufficient completeness. Where this was not possible, reviews with substantially overlapping clinical scope were interpreted cautiously rather than assumed to provide fully independent corroboration. **Table 3** summarizes the limits on overlap interpretation across review clusters.

Table 3. Interpretability of primary-study overlap across recurrent clinical-pharmacy review clusters

Review configuration	Reason repeated primary studies are plausible	Study-membership completeness for this umbrella review	Quantitative overlap status	Interpretation permitted
Broad medication-review reviews spanning hospital or community care	Recurrent medication-review trials can enter reviews differing mainly by setting, population restriction, or outcome emphasis	Incomplete across the full cluster	Global CCA not calculated	Concordant review conclusions cannot automatically be counted as independent replications
Older-adult polypharmacy, medication review, and deprescribing reviews	Similar age, multimorbidity, polypharmacy, and prescribing-optimization eligibility criteria create overlapping candidate trial pools	Variable	Pairwise calculation only where complete study lists are reconstructable	Agreement should be interpreted alongside intervention and population differences

Medication-harm reviews	ADE, medication-related-problem, anticoagulation, and multidisciplinary-team syntheses may share individual trials while using different safety definitions	Variable	No universal overlap value assigned	Safety findings remain endpoint-specific even when individual studies recur
Hospital-to-home and utilization-focused reviews	Transitional interventions are often multicomponent and may appear in broader medication-review or readmission syntheses	Incomplete for some review pairs	Not quantified where membership cannot be verified	Repeated readmission evidence may reflect both genuine consistency and shared trials
Disease- or service-specific reviews	Cardiology, oncology, mental-health, antibiotic, pain, pediatric, emergency, or critical-care reviews draw from more restricted clinical pools	Generally lower expected scope overlap, but not assumed absent	Calculated only if complete study membership is available	Clinical specialization may provide more distinct evidence, but independence must be demonstrated rather than presumed

The practical consequence is that review count and corroboration count are different quantities. Twenty effect-bearing reviews can contain substantially fewer than twenty independent bodies of primary evidence. This distinction matters most when evidence appears strongest simply because multiple reviews repeatedly synthesize the same influential trials.

The relationship between outcome tier, methodological confidence, and evidential dependence is summarized in **Figure 2**.

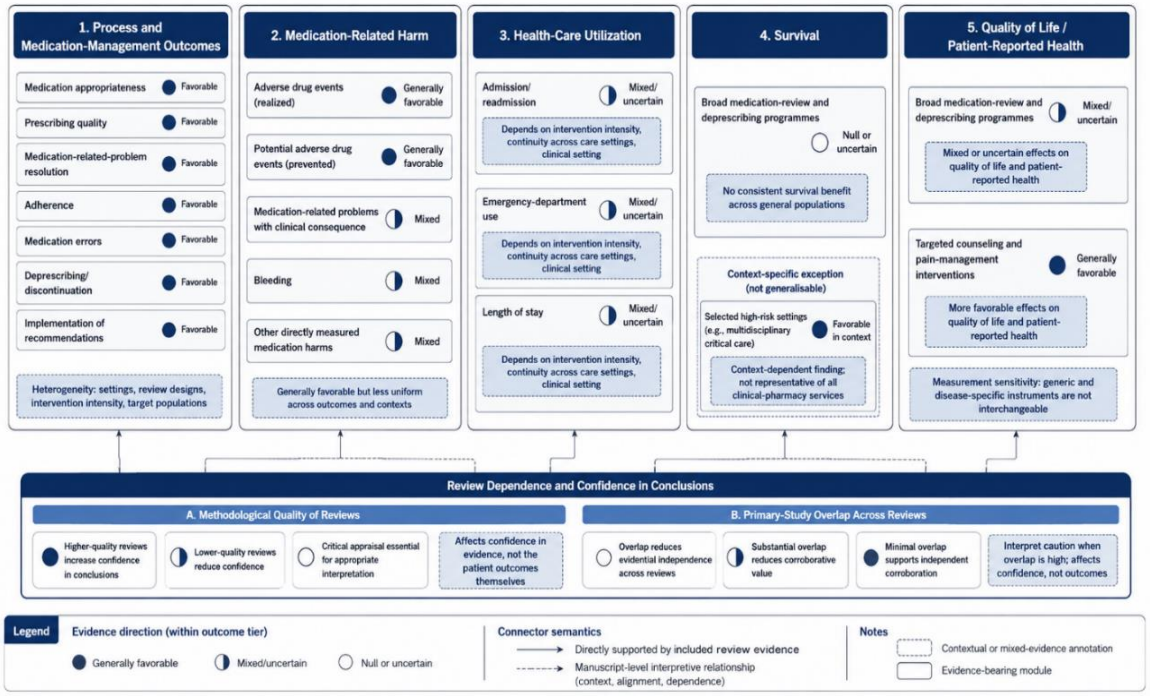

Figure 2. Uneven concentration of clinical-pharmacy evidence across patient-important outcome domains

Why apparently similar reviews reach different conclusions

Discordant systematic-review conclusions were not attributable to a single source of heterogeneity. Reviews using the same broad label—such as medication review—often evaluated interventions with different authority, intensity, follow-up, multidisciplinary integration, and opportunities to implement recommendations [6]. An intervention focused on identifying medication problems therefore differs clinically from one that also modifies treatment, monitors response, and follows the patient after discharge.

Comparator intensity also affects interpretation. Apparent benefits can be smaller when usual care already contains substantial medication-management expertise, whereas larger contrasts may occur when pharmacist involvement introduces services absent from the comparator. Transitional interventions illustrate this problem particularly clearly because favorable readmission findings often arise from multicomponent programmes extending across discharge [37]. Realist evidence indicates that continuity, trust, professional coordination, responsibility, and patient preference influence whether post-discharge review produces actionable change [38].

Outcome definitions generate another source of disagreement. Medication-related problems, adverse drug events, potential adverse drug events, prescribing appropriateness, hospitalization, and quality of life represent different constructs even when they are grouped under "clinical outcomes." Extensive measurement heterogeneity has been documented in medication-review trials [8], and ambulatory cardiology reviews similarly show that inconsistent clinical outcome measurement limits comparability [31].

Methodological confidence and evidential dependence further modify the strength of apparent agreement. A concordant conclusion from several critically weak reviews is not equivalent to concordance among methodologically rigorous reviews, and repeated synthesis of the same primary trials does not create new participants or independent replications. These dimensions explain why review conclusions must be interpreted as configurations of intervention, comparator, endpoint, setting, quality, and evidential independence rather than as interchangeable votes for or against clinical pharmacy. **Table 4** organizes these sources of discordance by clinical comparability, outcome measurement, and evidential confidence.

Table 4. Sources of discordance between apparently comparable clinical-pharmacy reviews

Discordance source	Apparent comparability	Interpretation-changing difference	Consequence for synthesis
Clinical comparability: intervention, comparator and context			
Intervention scope	Both use labels such as medication review or pharmacist intervention	One identifies problems; another also changes therapy, monitors response, or provides longitudinal follow-up	Intervention label alone is insufficient for cross-review comparison
Pharmacist authority and team integration	Both include pharmacists	Recommendation-only roles differ from prescribing, monitoring, or embedded multidisciplinary roles	Greater clinical proximity may alter opportunity to influence downstream outcomes
Comparator intensity	Both compare against "usual care"	Usual care may contain very different levels of pharmacy and multidisciplinary medication management	Smaller or larger effects may reflect comparator structure
Baseline clinical risk	Both evaluate pharmacist care	Routine community populations differ from anticoagulation, oncology, emergency, or intensive-care populations	Greater preventable-event risk can increase opportunity for measurable downstream benefit
Implementation context	Nominal intervention components are similar	Continuity, trust, professional coordination, patient participation, and organizational conditions differ	Context is retained as a possible explanation of heterogeneous effectiveness
Outcome comparability: construct and measurement			
Outcome definition	Both report "medication safety" or "clinical outcomes"	Appropriateness, medication-related problems, ADEs, admissions, mortality, and QoL are non-equivalent endpoints	Outcome-specific conclusions are retained rather than merged
Measurement and follow-up	Both measure the same nominal outcome	Instruments, event definitions, follow-up windows, and ascertainment differ	Apparent inconsistency may reflect measurement rather than opposing biological effects
Evidential confidence: methods and independence			
Methodological quality	Both report a systematic review	Search completeness, primary-study bias, synthesis methods, and confidence vary	Review conclusions receive different interpretive weight

Primary-study overlap	Several reviews reach the same conclusion	The same trials may be repeatedly included	Number of concordant reviews is not treated as number of independent confirmations

Conclusion

Clinical pharmacy improves medication management and can reduce selected medication-related harms, but the evidence does not support treating every favorable medication-process result as proof of improved hospitalization, survival, or quality of life. Benefits become less uniform when assessment moves to outcomes influenced by broader clinical, organizational, and patient factors.

The strongest interpretation is therefore conditional. Clinical-pharmacy interventions are most consistently effective for outcomes they can directly modify; downstream patient-important benefits occur in particular contexts where intervention intensity, authority, continuity, baseline risk, and outcome alignment create a credible opportunity for those benefits to emerge. Mortality and quality-of-life effects should not be inferred from prescribing improvement alone.

The apparent size of the evidence base also requires qualification. Multiple systematic reviews may reproduce the same primary evidence, so concordant review conclusions do not necessarily represent independent replication. Future evaluations should combine patient-important outcome selection with transparent intervention specification, consistent measurement, stronger primary-study reporting, and explicit assessment of review overlap.

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