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OPTIMIZATION OF PHARMACOTHERAPY IN PATIENTS WITH MULTIPLE CHRONIC DISEASES

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Abstract

Background: Multimorbidity commonly leads to polypharmacy, fragmented prescribing, treatment burden, drug-drug interactions, prescribing cascades, and difficulty applying single-disease clinical guidelines. Pharmacotherapy optimization therefore requires a patient-centered approach that distinguishes appropriate from problematic polypharmacy and integrates evidence on medication review, deprescribing, precision dosing, pharmacogenomics, and clinical decision support. Objective: To synthesize contemporary evidence on strategies for optimizing pharmacotherapy in adults with multiple chronic diseases and to propose a practical framework for medication prioritization, individualized dosing, monitoring, and follow-up. Methods: A structured literature review was conducted using international peer-reviewed evidence and major clinical frameworks published predominantly between 2020 and 2026. Studies and guidance addressing multimorbidity, polypharmacy, medication review, deprescribing, multidisciplinary care, electronic decision support, model-informed precision dosing, therapeutic drug monitoring, and pharmacogenomics were prioritized. Results: The evidence consistently supports recurrent medication reconciliation, indication-by-indication review, identification of potentially inappropriate medicines, active deprescribing when harms outweigh benefits, shared decision-making, and explicit monitoring after regimen changes. Multidisciplinary interventions reliably improve medication appropriateness and reduce medication-related problems, although effects on mortality, hospitalization, and functional outcomes remain heterogeneous. Precision dosing and pharmacogenomic strategies can further reduce interindividual variability for selected drugs, but implementation depends on validated tools, informatics integration, and clinician expertise. Conclusion: Pharmacotherapy optimization in multimorbidity should be treated as a continuous clinical process rather than a one-time reduction in pill count. The most defensible model combines patient goals, disease priorities, medication necessity, interaction risk, organ function, adherence, evidence-based deprescribing, and precision tools within a structured follow-up cycle. (1,2,5,9,11,13)

Keywords: multimorbidity; polypharmacy; deprescribing; medication review; personalized pharmacotherapy; model-informed precision dosing; pharmacogenomics; clinical decision support.

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1. INTRODUCTION

Population ageing and improved survival from cardiovascular, metabolic, respiratory, oncological, and other chronic disorders have increased the number of patients living simultaneously with two or more long-term conditions. Multimorbidity changes the clinical meaning of prescribing because the therapeutic plan is no longer a simple sum of disease-specific recommendations. A medicine that is appropriate for one condition may aggravate another, interact with treatment for a competing condition, increase treatment burden, or offer benefits that are unlikely to be realized within the patient's remaining life expectancy. Consequently, pharmacotherapy optimization must reconcile guideline evidence with the total clinical context. (1,3,12)

Polypharmacy is often operationally defined as the concurrent use of five or more medicines, but medication count alone is an imperfect marker of quality. Appropriate polypharmacy may be necessary in patients with multiple evidence-based indications, whereas problematic polypharmacy describes regimens in which one or more medicines lack a valid indication, duplicate therapy, create excessive interaction risk, impose disproportionate burden, or are inconsistent with current goals of care. This distinction is essential because indiscriminate medicine reduction can lead to undertreatment, while failure to reassess legacy prescriptions exposes patients to preventable harm. (4,5,6)

The clinical consequences of problematic polypharmacy include adverse drug reactions, drug-drug and drug-disease interactions, falls, cognitive impairment, nonadherence, prescribing cascades, medication errors, emergency visits, and avoidable hospital admissions. Risk increases when renal or hepatic function changes, when frailty alters pharmacodynamic sensitivity, or when several prescribers modify the regimen independently. These factors are particularly important after hospitalization, when medication lists frequently change and continuity may be incomplete. (2,4,10)

Optimization strategies have therefore evolved beyond simple drug-count reduction. Contemporary models include structured medication review, deprescribing, explicit screening tools such as STOPP/START and the American Geriatrics Society Beers Criteria, shared decision-making, pharmacist-physician collaboration, electronic clinical decision support, therapeutic drug monitoring, model-informed precision dosing, and pharmacogenomic information for selected drug-gene pairs. These approaches differ in maturity and evidence strength, but they share a common objective: maximizing clinically meaningful benefit while minimizing preventable harm and treatment burden. (5,7,8,11,13)

The aim of this article is to synthesize current evidence on optimization of pharmacotherapy in adults with multiple chronic diseases and to provide a practical, integrated framework suitable for clinical pharmacology, internal medicine, geriatrics, and primary care. Particular attention is given to medication prioritization, deprescribing, individualized dosing, multidisciplinary implementation, monitoring, and the emerging role of digital and precision-medicine tools.

2. MATERIALS AND METHODS

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This article was designed as a structured evidence-based review organized in an IMRAD format. A focused literature search was performed for international peer-reviewed publications and recognized clinical frameworks addressing multimorbidity, polypharmacy, pharmacotherapy optimization, medication review, deprescribing, potentially inappropriate medications, multidisciplinary medication management, electronic clinical decision support, therapeutic drug monitoring, model-informed precision dosing, and pharmacogenomics. Priority was given to systematic reviews, meta-analyses, randomized clinical trials, position papers, guideline-oriented publications, and contemporary narrative reviews published predominantly from 2020 through September 2026.

Eligible evidence included adult populations with multimorbidity and/or polypharmacy in primary care, hospital, long-term care, and specialist settings. Studies limited to a single disease without a medication-optimization component were not used as primary evidence. Because the objective was conceptual and translational rather than quantitative, no pooled meta-analysis was undertaken. Findings were synthesized into six domains: identification of medication-related risk, comprehensive medication review, deprescribing and prescribing correction, individualized dosing, digital/precision tools, and longitudinal monitoring.

Outcomes of interest were medication appropriateness, number of medicines, potentially inappropriate medications, medication-related problems, adherence, adverse drug events, hospital utilization, quality of life, functional status, mortality, and feasibility of implementation. Where evidence was inconsistent, the synthesis emphasized the distinction between improvements in process outcomes (for example, fewer inappropriate medicines) and patient-important clinical outcomes (for example, hospitalization or mortality).

The proposed framework does not represent a new clinical trial and no patient-level data were generated. Tables and figures are evidence-informed conceptual summaries intended to support structured clinical reasoning.

3. RESULTS

3.1. Sources of pharmacotherapy complexity in multimorbidity

Multimorbidity creates several overlapping forms of therapeutic complexity. First, independent disease guidelines may generate a large cumulative treatment burden because each guideline is usually optimized for a single index condition. Second, disease interactions can create competing therapeutic targets; for example, tight blood-pressure or glycemic targets may become inappropriate in frailty, orthostatic hypotension, recurrent falls, or limited life expectancy. Third, age-related changes in renal clearance, hepatic metabolism, body composition, receptor sensitivity, and homeostatic reserve amplify the clinical impact of standard doses. (3,4,12)

Fourth, the risk of drug-drug interactions rises nonlinearly as medication count increases. Interactions may be pharmacokinetic, through altered absorption, enzyme inhibition or induction, or renal transport; or pharmacodynamic, through additive effects on

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bleeding, sedation, QT prolongation, blood pressure, glucose, potassium, or renal perfusion. Fifth, treatment burden itself is clinically relevant: complex schedules, multiple formulations, monitoring requirements, and competing instructions can reduce adherence even when each medicine is individually justified. (4,6,10)

Table 1. Major drivers of medication-related risk in patients with multiple chronic diseases

Risk domain	Typical mechanisms/examples	Optimization response
Indication mismatch	Legacy prescriptions; duplicate therapy; medicine continued after original indication resolved	Confirm current indication and expected benefit; discontinue non-beneficial therapy
Drug-drug interaction	Additive bleeding, hypotension, CNS depression, QT effects; CYP inhibition/induction	Interaction review; substitute, separate, dose-adjust, or intensify monitoring
Drug-disease interaction	NSAIDs in CKD/heart failure; sedatives in falls; anticholinergics in cognitive impairment	Prioritize competing risks and avoid drugs that worsen major comorbidities
Organ dysfunction	Reduced renal/hepatic clearance; altered volume of distribution	Recalculate dose using current renal/hepatic function; consider TDM/MIPD
Frailty and vulnerability	Greater PD sensitivity, falls, delirium, orthostatic symptoms	Relax overly aggressive targets; start low, titrate carefully, monitor function
Treatment burden	Complex schedules, multiple prescribers, high pill burden, frequent monitoring	Simplify regimen; synchronize doses; use shared medication plan
Adherence barriers	Cognitive, financial, behavioral, formulation-related problems	Assess adherence explicitly; simplify, educate, involve caregivers where appropriate
Prescribing cascade	New drug used to treat an adverse effect of another drug	Identify causal medicine before adding another long-term therapy

3.2. Comprehensive medication review and reconciliation

A structured medication review is the central intervention around which other optimization strategies are organized. The process begins with creation of a single accurate medication list that includes prescribed medicines, over-the-counter products, supplements, intermittent medicines, and recently discontinued drugs. Medication reconciliation is

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particularly important at transitions of care, because duplicated or unintentionally omitted therapy can persist when hospital and outpatient records diverge.

Each medicine should then be assessed for current indication, evidence of benefit, time to benefit, dose appropriateness, adherence, adverse effects, interactions, monitoring requirements, and consistency with patient priorities. Recent position statements emphasize that medication review and deprescribing are complementary rather than competing concepts: review identifies the full set of medication-related problems, while deprescribing is one possible corrective action. (2,5,6)

The OPTICA cluster randomized trial evaluated an electronic clinical decision support-centered medication review in older adults with multimorbidity and polypharmacy. Although the intervention could be delivered safely, improvements in the trial's primary measures of medication appropriateness and prescribing omissions were not clearly superior to usual-care discussion, illustrating that digital support alone does not guarantee clinically meaningful optimization. (7)

3.3. Deprescribing and correction of inappropriate polypharmacy

Deprescribing is the supervised process of dose reduction or withdrawal when the balance of benefits and harms has shifted against continued treatment. It should not be equated with arbitrary medicine discontinuation. Appropriate candidates include drugs without a current indication, duplicate therapies, drugs producing clinically important adverse effects, preventive therapies with a time to benefit inconsistent with prognosis, and medicines that no longer match patient goals. (2,5,6)

Explicit tools such as STOPP/START criteria and the Beers Criteria can accelerate identification of potentially inappropriate medications, while implicit approaches require individualized clinical judgment regarding indication, effectiveness, safety, adherence, and patient preference. Explicit criteria improve standardization but cannot fully account for multimorbidity, patient priorities, underprescribing, or the risk-benefit trade-offs of complex regimens. (4,8,12)

Evidence syntheses suggest that multidisciplinary medication review and deprescribing can reduce medication count, improve medication appropriateness, resolve medication-related problems, and sometimes improve adherence. However, systematic reviews have not consistently demonstrated large improvements in mortality, hospitalization, cognition, or function. This gap emphasizes the need to select high-risk patients carefully and to measure patient-important outcomes rather than using drug count alone as a surrogate for success. (9,10,15)

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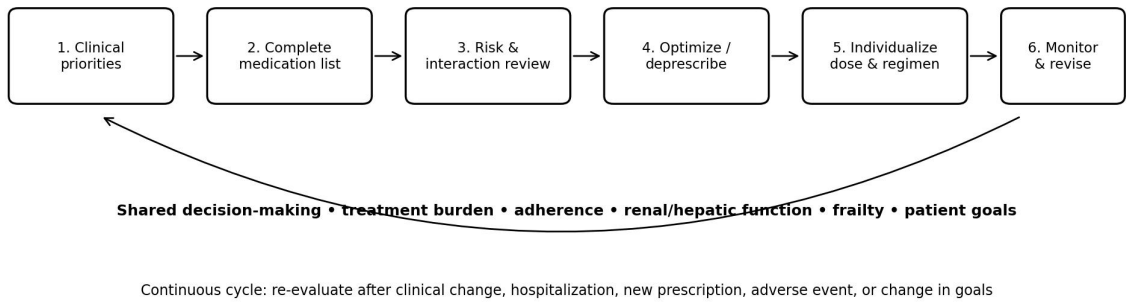


Figure 1. Continuous workflow for optimizing pharmacotherapy in multimorbidity.

3.4. Individualized dosing and therapeutic monitoring

Optimization is not limited to deciding whether a medicine should be continued. Many patients need the same medicines but at different doses or dosing intervals because of renal function, hepatic function, body composition, interacting drugs, inflammation, genetics, or variable adherence. Traditional dose adjustment based on creatinine clearance and clinical response remains essential, but therapeutic drug monitoring provides direct exposure information for drugs with narrow therapeutic windows.

Model-informed precision dosing (MIPD) extends conventional therapeutic drug monitoring by combining population pharmacokinetic/pharmacodynamic models with individual patient variables and, when available, measured drug concentrations. Contemporary reviews describe applications in anti-infective therapy, oncology, transplantation, and inflammatory disease, while noting that broad implementation requires validated models, reliable software, workflow integration, and prospective evidence of clinical benefit. (11,13,14)

In patients with multiple chronic diseases, precision dosing is particularly relevant when one therapy has a narrow therapeutic index and the patient simultaneously has organ dysfunction or interacting medications. Examples include immunosuppressants, selected anti-infectives, anticoagulants, antiepileptic drugs, lithium, and some oncology agents. The practical goal is not technological complexity for its own sake, but avoidance of both underexposure and toxicity.

3.5. Pharmacogenomics and electronic decision support

Pharmacogenomic information can be clinically useful when actionable gene-drug relationships influence metabolism, transport, or pharmacodynamic response. In polypharmacy, a single patient may receive several medicines affected by CYP2D6, CYP2C19, CYP2C9, SLCO1B1, TPMT, NUDT15, or other genes. Pre-emptive panel testing has demonstrated the feasibility of integrating multiple gene-drug recommendations,

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but uptake depends on interpretability, reimbursement, informatics infrastructure, and availability of alternative therapies. (13)

Electronic clinical decision support can combine drug-drug interaction alerts, renal dosing, potentially inappropriate medication criteria, duplication checks, pharmacogenomic rules, and disease-specific targets. However, poorly calibrated alerts create fatigue and may be ignored. The most useful systems prioritize high-severity, patient-specific risks and embed recommended actions directly into the prescribing workflow rather than producing generic warnings. (7,11,14)

Table 2. Evidence-informed interventions for pharmacotherapy optimization

Intervention	Primary purpose	Strengths	Key limitations
Medication reconciliation	Establish one accurate medication list	Prevents duplication/omission; foundational for all other steps	Resource-intensive; depends on reliable sources
Structured medication review	Assess indication, benefit, harm, interactions, adherence	Comprehensive and patient-centered	Effectiveness depends on follow-through and clinician time
Deprescribing	Stop or reduce medicines with unfavorable benefit-risk balance	Reduces treatment burden and inappropriate therapy	Withdrawal/rebound risk; requires monitoring
STOPP/START or Beers criteria	Identify potentially inappropriate prescribing	Rapid, standardized case finding	Cannot replace individualized clinical judgment
Pharmacist-physician intervention	Use multidisciplinary expertise	Improves medication appropriateness and problem resolution	Clinical outcome effects heterogeneous
eCDSS	Automate interaction, dosing, and appropriateness checks	Scalable; can integrate EHR data	Alert fatigue; rule quality and workflow integration are critical
TDM / MIPD	Individualize exposure for selected drugs	Supports dose precision in high-variability or narrow-index drugs	Requires assays, models, software, and validation
Pharmacogenomics	Identify actionable drug-gene interactions	Potentially useful across repeated prescribing decisions	Implementation cost, coverage, and clinical interpretation vary

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3.6. Multidisciplinary and patient-centered optimization

Pharmacotherapy optimization is more effective when medication decisions are shared across clinicians, pharmacists, nurses, and the patient rather than performed in parallel by isolated prescribers. Pharmacists contribute expertise in interactions, dosing, adherence, and reconciliation; physicians integrate diagnosis, prognosis, and competing disease priorities; nurses and caregivers often identify practical administration problems, orthostatic symptoms, hypoglycemia, falls, and cognitive changes that may not be visible in the prescription record.

Patient goals should determine the hierarchy of treatment objectives. For some patients, prevention of long-term vascular events is the dominant priority; for others, symptom control, maintenance of independence, avoidance of dizziness or falls, reduction of pill burden, or preservation of cognition is more important. A regimen that is pharmacologically rational but impossible for the patient to follow is not optimized therapy.

A 2024 systematic review and meta-analysis of multidisciplinary polypharmacy interventions in community-dwelling older adults found improvements in medication appropriateness, medication-related problems, medication count, costs, and adherence, but did not demonstrate consistent benefits for functional or cognitive status, mortality, falls, or healthcare use. These findings support multidisciplinary care while also underscoring the need for better targeting and outcome selection. (9)

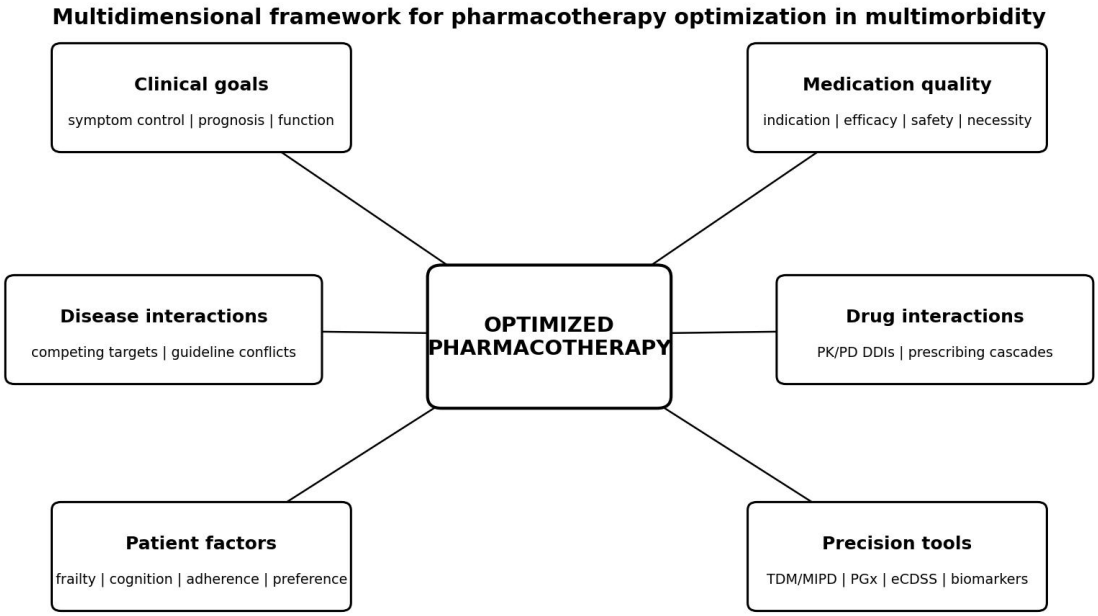


Figure 2. Multidimensional framework for individualized pharmacotherapy optimization.

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3.7. Monitoring after medication changes

Every optimization decision should be paired with a monitoring plan. After deprescribing, clinicians should monitor for recurrence of the treated condition, withdrawal phenomena, and changes in function or quality of life. After dose reduction or substitution, a prespecified interval for review should be defined. After initiation of a new medicine, expected benefit, common adverse effects, laboratory monitoring, and stop criteria should be documented.

Review intensity should be proportional to risk. High-risk transitions include discharge from hospital, acute kidney injury, major weight loss, new frailty, new cognitive impairment, initiation of anticoagulants or sedating drugs, and addition of strong metabolic inhibitors or inducers. These events should trigger a focused medication review even if the next routine visit is months away.

Success should be measured with a balanced set of indicators: fewer inappropriate medicines, resolution of medication-related problems, improved adherence, symptom control, functional stability, adverse-event reduction, patient satisfaction, and avoidance of undertreatment. A lower medicine count is useful only when it reflects better therapeutic alignment.

Table 3. Practical monitoring indicators after pharmacotherapy optimization

Domain	**Suggested indicators**	**Typical reassessment trigger**
Clinical benefit	Symptoms, BP, glycemia, angina burden, exacerbations, pain, function	After initiation/titration; disease-specific interval
Safety	Falls, dizziness, bleeding, sedation, delirium, hypoglycemia, edema	Within days-weeks for high-risk changes
Laboratory	Renal/hepatic function, electrolytes, INR, drug concentrations, blood counts	According to drug risk and organ function
Adherence	Missed doses, refill gaps, administration errors, regimen complexity	At every medication review
Treatment burden	Pill count, dosing frequency, monitoring load, cost	After any major regimen change
Patient goals	Preference, quality of life, functional priorities, willingness to continue	At scheduled reviews and major health changes
Medication appropriateness	Unnecessary/duplicate therapy, underprescribing, interactions	At least annually and after transitions of care

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3.8. Prioritizing competing therapeutic goals

An additional challenge in multimorbidity is that therapeutic targets can conflict even when each individual recommendation is evidence-based. A patient with diabetes, heart failure, chronic kidney disease, osteoarthritis, and recurrent falls may simultaneously receive glucose-lowering therapy, diuretics, renin-angiotensin system blockade, analgesics, antithrombotic therapy, and sedating agents. Optimization requires ranking the expected magnitude and timing of benefit for each therapy against the probability and severity of harm. The clinically relevant question is therefore not simply whether a medicine is guideline-concordant, but whether it remains the highest-value choice for this particular patient at this particular stage of illness.

A practical prioritization strategy begins by identifying therapies that prevent near-term catastrophic events, such as anticoagulation for a strong indication or disease-modifying treatment for unstable heart failure, and distinguishing them from interventions whose principal benefit emerges only after years. Symptom-relieving medicines should be judged by observable benefit, while preventive therapies should be judged by baseline risk, time to benefit, treatment burden, and competing mortality. When two targets conflict, the plan should explicitly document which target takes precedence and why.

Treatment targets should also be recalibrated after major changes in health status. Frailty, recurrent falls, advanced cognitive impairment, progressive renal disease, terminal illness, or repeated hospitalization may change the relative value of intensive glycemic, blood-pressure, lipid, or preventive targets. Conversely, undertreatment must be actively considered; deprescribing should never become a rationale for omitting therapies with clear current benefit. This dual focus on overprescribing and underprescribing is a major strength of structured optimization frameworks. (5,8,12)

Table 4. Clinical questions for prioritizing medicines when treatment goals compete

Clinical question	**Interpretation**	**Possible action**
Is there a current indication?	The original indication may have resolved or changed	Stop if no valid indication remains
What is the expected time to benefit?	Long time-to-benefit may be less relevant in limited prognosis	Reconsider preventive therapy if benefit is unlikely to be realized
Is benefit observable?	Symptom-directed treatment should produce measurable improvement	Reduce/stop if no meaningful response
What is the absolute harm risk?	Falls, bleeding, hypoglycemia, renal injury, delirium may dominate benefit	Dose-reduce, substitute, or intensify monitoring
Does the medicine conflict with another disease?	Single-disease recommendations can worsen a comorbid condition	Prioritize the condition with greater current risk

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Clinical question	Interpretation	Possible action
Can the regimen be simplified?	Complexity itself reduces adherence and increases error risk	Use once-daily options, combination products, synchronized dosing
Does the patient value the expected outcome?	Benefits not aligned with goals may not justify burden	Use shared decision-making and document preference

3.9. Adherence, treatment burden, and transitions of care

Adherence should be treated as a pharmacologic variable because apparent treatment failure may reflect missed doses, incorrect administration, financial barriers, cognitive limitations, or an impractical schedule rather than inadequate drug efficacy. Escalating treatment without assessing adherence can create a prescribing cascade in which additional medicines are added to compensate for inconsistent exposure. A structured review should therefore ask how medicines are actually taken, not merely how they are prescribed.

Regimen simplification is one of the most underused optimization strategies. Consolidating dosing times, selecting once-daily formulations when clinically equivalent, discontinuing duplicate supplements, removing unnecessary PRN medicines, aligning refill dates, and using combination products can reduce cognitive workload and administration errors. Simplification should be balanced against flexibility; for example, fixed-dose combinations can reduce pill burden but may complicate dose adjustment in renal impairment or when one component causes adverse effects.

Transitions of care are high-risk periods because medicines may be started temporarily in hospital, withheld during acute illness, or duplicated when pre-admission therapy is restarted. Discharge documentation should specify which medicines were stopped, which were newly initiated, the intended duration, and the monitoring plan. The first post-discharge review should focus on reconciliation, organ function, adherence, and whether acute-phase prescriptions remain necessary. Communication failures at this stage can convert short-term treatment into indefinite polypharmacy.

Caregiver involvement may be appropriate when cognition, vision, dexterity, or health literacy interferes with safe self-administration. However, the patient should remain involved to the greatest extent possible. Medication organizers, clear written plans, teach-back, and a single updated medication list can reduce discrepancy between clinical intent and real-world use. These practical interventions are often as important as sophisticated pharmacokinetic tools in determining therapeutic success.

3.10. Implementation metrics and quality assurance

Health systems implementing pharmacotherapy optimization programs need explicit quality metrics. Process measures can include the proportion of high-risk patients receiving

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structured medication review, reconciliation completed after discharge, clinically significant interactions resolved, potentially inappropriate medicines addressed, and follow-up documented after deprescribing. Outcome measures should include adverse drug events, falls, bleeding, hypoglycemia, medication-related readmissions, patient-reported treatment burden, and adherence.

Quality assurance should also examine unintended consequences. Excessive focus on deprescribing can increase omission of beneficial medicines, while aggressive digital alerting can generate fatigue. Programs should therefore audit both overuse and underuse, stratify alerts by clinical severity, and periodically review whether accepted recommendations improve outcomes. Multidisciplinary case conferences can be especially useful for patients with repeated medication-related admissions or unresolved conflicts between disease-specific guidelines.

The strongest implementation model is iterative: identify high-risk patients, conduct structured review, agree on a limited number of prioritized changes, monitor predefined outcomes, and feed the result back into the next review. This creates a learning system in which local data improve future targeting and help determine which interventions provide meaningful benefit in the population being served.

4. DISCUSSION

The central finding of this review is that pharmacotherapy optimization in multimorbidity is best understood as a dynamic balancing process rather than a one-time exercise in reducing the number of medicines. The most consistent evidence supports repeated medication reconciliation, explicit assessment of indication and benefit, identification of problematic polypharmacy, careful deprescribing, and shared decision-making. These interventions reliably improve medication-level outcomes, but the evidence for large effects on hospitalization, mortality, function, or quality of life remains mixed. (5,7,9,10,15)

This apparent discrepancy is clinically plausible. Medication-related harm is only one determinant of outcomes in patients with multiple chronic diseases. Functional decline, hospitalization, and mortality are influenced by disease severity, frailty, social conditions, cognition, and access to care. Therefore, a successful medication intervention may meaningfully reduce prescribing risk without producing a measurable mortality signal. Studies may also be underpowered for patient-important outcomes or may enroll patients whose baseline treatment is already relatively appropriate.

Another important implication is that case finding should not depend exclusively on medication count. Recent scoping evidence shows substantial inconsistency in how problematic polypharmacy is identified, and simple numerical thresholds may fail to distinguish beneficial multi-drug therapy from harmful prescribing. More useful risk stratification combines medication number with high-risk drug classes, organ dysfunction, interaction burden, prior adverse drug events, frailty, adherence difficulty, and recent transitions of care. (12)

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Explicit tools such as STOPP/START and Beers criteria are valuable because they improve standardization and prompt clinicians to consider omissions as well as potentially inappropriate medicines. Nevertheless, they remain screening tools rather than automatic stop lists. In complex multimorbidity, a medicine identified as potentially inappropriate may still be the most reasonable option after competing risks, patient preference, prior treatment response, and alternatives are considered.

Precision approaches provide an additional layer of optimization. MIPD can support individualized dosing when interpatient pharmacokinetic variability is large, while pharmacogenomics can identify actionable inherited sources of variability. Their role is likely to expand as electronic health records, clinical decision support, biosensors, and longitudinal data become more integrated. However, implementation science is as important as pharmacology: poorly validated models, fragmented software, alert fatigue, unclear responsibility, and insufficient clinician training can negate theoretical benefit. (11,13,14)

The evidence also reinforces the importance of patient-centered prioritization. Applying every disease-specific target at maximum intensity may be incompatible with frailty, limited prognosis, orthostatic symptoms, or the patient's preference to reduce treatment burden. Optimization should therefore distinguish therapies that prevent near-term serious events, therapies that primarily offer long-term risk reduction, and therapies that mainly improve symptoms. This categorization helps clinicians decide which treatment goals should dominate when guidelines conflict.

From a health-system perspective, the most promising model is a recurrent medication-optimization cycle embedded in routine care. High-risk patients can be identified by electronic rules; pharmacists or trained clinicians can perform structured review; prescribers and patients can agree on prioritized actions; and follow-up can assess both benefits and harms. Such models should focus on clinically meaningful problems rather than maximizing the number of recommendations generated.

This review has limitations. It is a structured narrative synthesis rather than a formal systematic review with duplicate screening and quantitative meta-analysis. The evidence base is also heterogeneous in patient selection, intervention intensity, care setting, and outcome definitions. In addition, much of the literature focuses on older adults, although the principles of multimorbidity and polypharmacy apply to younger adults with complex chronic disease. These limitations should be considered when generalizing recommendations.

5. CONCLUSION

Optimization of pharmacotherapy in patients with multiple chronic diseases requires more than counting or removing medicines. A high-quality approach begins with an accurate medication list and a clear understanding of patient goals, then evaluates every drug for indication, effectiveness, safety, interactions, organ-function appropriateness, adherence, treatment burden, and time to benefit. Medication review and deprescribing should be routine components of care, while explicit prescribing tools, multidisciplinary

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collaboration, eCDSS, therapeutic drug monitoring, model-informed precision dosing, and pharmacogenomics can refine decision-making in selected patients. The most defensible endpoint is not the lowest possible number of medicines, but the simplest regimen that preserves necessary treatment, avoids preventable harm, remains feasible for the patient, and is continuously reassessed as diseases, physiology, and goals change. (2,5,9,11,13)

REFERENCES

1. NICE. Multimorbidity: Clinical Assessment and Management (NG56). National Institute for Health and Care Excellence; 2016, updated guidance accessed 2026.
2. Onder G, et al. Medication review and deprescribing in different healthcare settings: a position statement from an Italian scientific consortium. Drugs & Aging. 2024. PMID: 38459218.
3. Walker LE, Pirmohamed M. The status of drug evaluation in older adults in the United Kingdom: bridging the representation gap. Journal of the American Geriatrics Society. 2024;72(9):2933-2941. doi:10.1111/jgs.18817.
4. American Geriatrics Society Beers Criteria Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. Journal of the American Geriatrics Society. 2023;71(7):2052-2081.
5. van Poelgeest E, et al. Optimizing pharmacotherapy and deprescribing strategies in older adults living with multimorbidity and polypharmacy: EuGMS SIG on pharmacology position paper. European Geriatric Medicine. 2023;14(6):1195-1209. doi:10.1007/s41999-023-00872-0.
6. Zidan A, Awaisu A. Inappropriate polypharmacy management versus deprescribing: a review on their relationship. Basic & Clinical Pharmacology & Toxicology. 2024;134(1):6-14. doi:10.1111/bcpt.13920.
7. Streit S, et al. Optimising prescribing in older adults with multimorbidity and polypharmacy in primary care (OPTICA): cluster randomised clinical trial. BMJ. 2023;381:e074054.
8. O'Mahony D, et al. STOPP/START criteria for potentially inappropriate prescribing in older people: version 3. European Geriatric Medicine. 2023.
9. Martínez-Velilla N, et al. Systematic review and meta-analysis on the effectiveness of multidisciplinary interventions to address polypharmacy in community-dwelling older adults. Ageing Research Reviews. 2024;98:102317. doi:10.1016/j.arr.2024.102317.
10. Clinical impact of medication review and deprescribing in older inpatients: a systematic review and meta-analysis. 2024. PMID: 38822740.
11. Minichmayr IK, Dreesen E, Centanni M, Wang Z, Hoffert Y, Friberg LE, Wicha SG. Model-informed precision dosing: state of the art and future perspectives. Advanced Drug Delivery Reviews. 2024;215:115421. doi:10.1016/j.addr.2024.115421.
12. Defining, identifying and addressing problematic polypharmacy within multimorbidity in primary care: a scoping review. BMJ Open. 2024. doi:10.1136/bmjopen-2023-081698.

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13. Swen JJ, et al. A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study. The Lancet. 2023;401(10374):347-356. doi:10.1016/S0140-6736(22)01841-4.
14. Barriers and facilitators for bringing model-informed precision dosing to the patient's bedside: a systematic review. Clinical Pharmacology & Therapeutics. 2024. doi:10.1002/cpt.3510.
15. Interventions to optimize medication management in older adults: an umbrella review of systematic reviews. 2026. PMID: 42339921.