

Research Article

Deprescribing to Reduce Harm From Polypharmacy in Chronic Disease: What Works, for Whom, and at What Cost

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Abstract:

Background: Polypharmacy is common in chronic disease and can increase adverse drug events, prescribing cascades, and regimen complexity. Deprescribing is the planned, supervised reduction or discontinuation of medicines where harms outweigh benefits in a patient's current context. This review compares deprescribing strategies, focusing on what works, for whom, and at what cost.

Methods: A focused evidence synthesis was conducted using PubMed and targeted cross-checking (January 1, 2000 to January 31, 2026). Priority was given to systematic reviews/meta-analyses and pragmatic randomised or cluster randomised trials evaluating deprescribing or structured medication review with deprescribing intent in chronic disease and polypharmacy contexts.

Results: Deprescribing interventions consistently improve prescribing outcomes and reduce exposure to high-risk medicines. Patient-activated education can produce substantial discontinuation for targeted drug classes, exemplified by EMPOWER (27% discontinuation versus 5% at 6 months). Pharmacist-led interventions reduce inappropriate medication exposure and can support simplification. Disease-specific medication reduction can maintain short-term disease control in carefully selected patients, exemplified by OPTIMISE where systolic blood pressure control remained noninferior at 12 weeks after antihypertensive reduction. Effects on admissions and mortality vary and appear more likely when interventions target high-risk patients and high-harm medicines.

Conclusions: Deprescribing reliably improves prescribing quality and can meaningfully reduce exposure to high-risk medicines, particularly through patient activation and pharmacist-integrated workflows. Clinical endpoint benefits depend on targeting, implementation fidelity, and monitoring capacity.

Keywords: chronic diseases, polypharmacy, deprescribing

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Introduction

Chronic disease care often accumulates medicines over years. Each addition may be sensible at the moment it is started, yet the combined regimen can drift away from the patient's current goals, organ function, frailty status, and risk tolerance. Polypharmacy increases the probability of adverse drug events, drug-drug interactions, therapeutic duplication, and prescribing cascades. In older adults with multimorbidity, these risks often converge with fall risk, cognitive vulnerability, renal impairment, and low physiologic reserve. When the same patient is treated by several clinicians, or when the drug list spans multiple care settings, the probability that at least one medicine is now low-value or harmful rises sharply.

Deprescribing is the planned, supervised reduction or discontinuation of medicines that may no longer be beneficial or may be causing harm. It is not synonymous with undertreatment. Instead, it is a method to re-balance benefit versus risk using the patient's current prognosis, preferences, and functional reserve. A practical deprescribing workflow generally follows a repeatable sequence: confirm the full medication list and indications; estimate the patient's overall risk of drug-related harm; assess each medicine's current benefit, time-to-benefit, and risk; prioritise candidates to stop; taper when necessary; and monitor for withdrawal, rebound, or symptom recurrence. This approach is well described in the modern deprescribing literature and remains a useful anchor for real-world implementation (1).

The shift from “more treatment is better” to “better treatment is better” has created a need for explicit tools to identify potentially inappropriate medications in older adults. The American Geriatrics Society updated Beers Criteria and the STOPP/START criteria provide structured prompts for medicines and patterns that are more likely to be harmful in older people, especially when frailty, kidney disease, or cognitive impairment is present (3,4). These tools do not replace clinical judgement, but they reduce omission bias and help teams start the deprescribing conversation on high-yield targets.

This article compares deprescribing strategies as intervention classes, rather than as a single technique. It focuses on what works, for whom, and at what cost. Because adherence is tightly linked to regimen complexity and side effects, the synthesis also highlights simplification as an adherence mechanism, even when adherence is not directly measured. Throughout, citations use numeric style in parentheses. References are restricted to PubMed-indexed and equivalent peer-reviewed sources, with stable identifiers where available.

Methods

Search sources and time frame

A focused evidence synthesis was performed using PubMed and targeted cross-checking. The search window was January 1, 2000 to January 31, 2026. Because deprescribing is a broad intervention class with many setting-specific variants, priority was given to (i) systematic reviews and meta-analyses, (ii) pragmatic randomised trials and cluster randomised trials with clinically interpretable endpoints, and (iii) trials that reported key implementation components such as training, structured review, shared decision-making, taper protocols, or follow-up.

Eligibility approach

Included evidence primarily involved adults with chronic disease and polypharmacy, with emphasis on older adults and those with multimorbidity. Interventions had to include active deprescribing (discontinuation or dose reduction) or structured medication review with explicit deprescribing intent. Disease-specific trials were included when the core intervention was medication reduction with monitoring, even if the trial framed this as “medication reduction” rather than “deprescribing.”

Synthesis strategy

Given heterogeneity in populations, intervention intensity, and outcome definitions, evidence was synthesised narratively with structured comparison across intervention classes. Where a trial provides a clear, widely cited effect estimate (for example, discontinuation rate or noninferiority margin), that estimate is reported as an exemplar. Where reviews aggregate broader outcome patterns, directionality and consistency were prioritised over pooling additional estimates.

Figure 1. Schematic selection flow (conceptual)

- Records identified (PubMed + targeted cross-checking)
- Screened for deprescribing intent and chronic disease/polypharmacy context
- Prioritised: systematic reviews/meta-analyses + pragmatic RCTs/cluster RCTs

→ Included: high-signal evidence supporting comparative conclusions

Results

Deprescribing strategies can be grouped into five practical classes: (A) patient-directed education and behavioural activation, (B) pharmacist-led or clinician-led structured medication review, (C) multidisciplinary transitional care deprescribing, (D) algorithm-supported optimisation and electronic decision support, and (E) disease- or drug-class targeted deprescribing. Across these classes, the most reliable outcomes are medication outcomes: stopping target drugs, reducing potentially inappropriate medications, and simplifying regimens. Effects on downstream clinical endpoints such as hospitalisation and mortality are more variable, largely because event rates are lower, follow-up is often limited, and trials are rarely powered for hard endpoints.

A. Patient-directed education and behavioural activation

Patient activation interventions change the default interaction. Instead of the clinician being the sole owner of the medication list, the patient is prompted to ask whether a medicine is still needed. This tends to work best when the target medication has a recognised harm profile in older adults, when the patient can recognise side effects or dependence concerns, and when tapering guidance is explicit.

The EMPOWER cluster randomised trial is the clearest exemplar. Community pharmacy patients received direct education designed to trigger patient-clinician conversations about benzodiazepine cessation. At 6 months, 27% of the intervention group discontinued benzodiazepines compared with 5% in the control group, yielding an absolute risk difference of 23% and a number needed to treat of 4. Dose reduction occurred in an additional 11% (7). This discontinuation magnitude is large for a low-intensity intervention and is clinically relevant because benzodiazepines are consistently associated with falls, sedation, and cognitive impairment in older people.

Mechanistically, patient activation reduces inertia. It also shifts the emotional framing of stopping. Patients can treat discontinuation as a proactive health choice rather than as “losing” a medicine. The limitation is scope. Patient-driven deprescribing is most scalable for one or two targeted classes. It is less suited to complex polypharmacy without structured clinician workflows, because patients may not have the bandwidth to manage trade-offs across a dozen medicines.

B. Pharmacist-led deprescribing and structured medication review in primary care

Pharmacist integration is one of the most consistently supported strategies for medication optimisation. Pharmacists contribute time, medication knowledge, taper planning, and follow-up. Effectiveness depends on the pathway from recommendation to prescription change and on communication with prescribers.

The D-PRESCRIBE cluster randomised trial demonstrates an actionable model. Community pharmacists delivered structured deprescribing recommendations and education targeting inappropriate prescriptions in older adults. The intervention reduced inappropriate medication use compared with usual care, supporting the concept that a pharmacist-led approach can deliver measurable deprescribing outcomes at scale (6). Beyond the immediate medication outcomes, these models are important because they operationalise deprescribing into a repeatable service rather than a one-off conversation.

Regimen simplification is often bundled into medication review programmes. Simplification matters because it reduces dosing frequency, cognitive load, and logistical friction. In residential aged care, the SIMPLER cluster randomised trial used a structured regimen simplification guide. At 12 months, the intervention reduced daily medication administration times compared with usual care, without signal of harm in major outcomes, indicating that simplification is feasible and can reduce operational burden in care facilities (23). Even when adherence is not measured directly, reduced administration times and reduced schedule complexity are credible mediators of improved adherence and fewer administration errors.

C. Multidisciplinary transitional care deprescribing

Transitions are high-risk moments. Admissions and discharges often expose renal function changes, delirium risk, hemodynamic instability, and medication duplications. Multidisciplinary models aim to embed deprescribing into transition workflows, using structured review to reduce medication harms that cluster around transitions.

OPERAM, a large pragmatic cluster randomised trial, evaluated a structured medication review intervention in multimorbid older adults with the goal of reducing avoidable hospital admissions. The trial is important as an implementation template, even though hard endpoint effects are not uniformly dramatic. It shows that complex medication review interventions can be delivered at scale in real-world settings and that outcomes may depend on targeting, fidelity, and patient risk stratification (9). Economic work linked to OPERAM highlights that implementation costs can be non-trivial and that savings depend on whether the intervention meaningfully reduces high-cost events in the highest-risk patients (18).

D. Algorithm-supported optimisation and electronic decision support

Algorithm-supported deprescribing attempts to reduce variability and embed best practice into workflow. This can take the form of explicit deprescribing algorithms delivered through training, structured templates, or electronic decision support that flags potentially inappropriate medications and suggests alternatives or taper plans.

In Swiss primary care, a cluster randomised trial evaluated a patient-centred deprescribing procedure supported by training and a validated algorithm with shared decision-making. The intervention reduced medication count immediately after intervention, but effects were not sustained at 6 or 12 months, and there were no significant differences in safety or quality of life at follow-up (24). This trial illustrates a practical truth: deprescribing is often not a one-time event. Sustainable effects may require repeated review cycles, monitoring, and reinforcement.

Recent long-term care evidence also suggests that electronic decision support can reduce inappropriate medication exposure, but the magnitude and the clinical impact depend on baseline prescribing quality and on the scope of authority for implementation (17).

E. Disease- or drug-class targeted deprescribing

Disease-specific trials clarify where deprescribing can be safe without loss of disease control and where the safety margin is narrower. These trials are often easier to interpret because they use measurable monitoring endpoints.

Antihypertensive deprescribing is a high-value example because blood pressure offers a short-term, measurable endpoint. The OPTIMISE randomised clinical trial enrolled adults aged 80 years and older taking multiple antihypertensives. Medication reduction was compared with usual care. At 12 weeks, systolic blood pressure below 150 mm Hg was maintained in 86.4% of the reduction group and 87.7% of the control group, meeting the prespecified noninferiority criteria. Medication reduction was sustained in a substantial fraction of participants (8). This supports a carefully selected approach where deprescribing is paired with clear monitoring and thresholds for reintroduction.

Another exemplar is discontinuation of preventive medicines near the end of life. In a randomised trial of patients with advanced, life-limiting illness, discontinuing statin therapy did not worsen short-term survival and was associated with potential improvements in quality of life and reduced medication burden (10). While generalisability depends on patient selection and prognosis, the trial provides concrete evidence that time-to-benefit and life expectancy should explicitly shape deprescribing decisions for preventive therapies.

Guideline-driven deprescribing in primary care also provides disease- or class-specific scaffolding. Evidence-based deprescribing guidelines exist for proton pump inhibitors and for antihyperglycemic agents in older adults, with structured recommendations for tapering, monitoring, and re-escalation when needed (11,12). These guidelines help reduce clinician uncertainty and can improve implementation safety.

What Works For Whom: Matching Strategies To Patient Profiles

A common error is to treat deprescribing as a uniform intervention with uniform effects. Deprescribing is a strategy class. Its value depends on the patient's baseline risk of medication harm, the time-to-benefit of each drug, and the feasibility of tapering and follow-up. This section operationalises “for whom” into practical matching rules.

Patients most likely to benefit

First, older adults with frailty or functional impairment often have reduced physiologic reserve, making adverse effects more consequential. Deprescribing can reduce dizziness, orthostatic hypotension, sedation burden, and fall risk when high-risk central nervous system medicines and other culprit classes are targeted.

Second, patients with polypharmacy plus prior adverse drug events or a recent hospitalisation are on a higher-risk trajectory. These events create a window where discontinuation is more acceptable to clinicians and patients because the harm is recent, observable, and attributable.

Third, long-term care residents with limited life expectancy may have less to gain from long-term preventive medicines and more to lose from pill burden, drug interactions, and adverse effects. Tools such as STOPPFrail explicitly target potentially inappropriate prescribing in frail older adults with limited life expectancy and can support consistent decision-making across clinicians (13).

Fourth, patients struggling with regimen complexity often benefit from simplification even if the number of medicines does not change dramatically. Simplification reduces administration times and may reduce missed doses and administration errors. Evidence from regimen simplification trials supports feasibility and operational benefit in residential care, which can translate into improved medication management quality (23).

Patients requiring caution or different sequencing

First, patients with tightly controlled diseases where withdrawal can cause rebound require careful sequencing. Examples include beta-blockers, certain psychotropics, corticosteroids, and some analgesics. These cases demand taper protocols and monitoring to avoid withdrawal syndromes and rebound symptoms.

Second, patients with high baseline cardiovascular risk where preventive therapies have near-term benefit require a more selective approach. In these patients, deprescribing should prioritise drugs with clear harm, duplications, or low benefit, rather than discontinuing cornerstone disease-modifying therapy with strong evidence of benefit over short time horizons.

Third, patients with limited access to follow-up should not be deprescribed without a monitoring plan. Deprescribing without monitoring can create avoidable risk if withdrawal symptoms, blood pressure increases, or symptom recurrence is not detected early. In such settings, lower-risk simplification strategies may be preferable until follow-up is reliable.

Matching strategy to patient profile

Patient activation works well when the target drug is a well-recognised harm class and tapering is manageable, as demonstrated by EMPOWER (7). Pharmacist-led deprescribing works best when there is a direct pathway for recommendations to become prescription changes and when follow-up is feasible, as in D-PRESCRIBE (6). Transitional care models have the highest yield when patients are high-risk and when medication changes are clinically justified by acute physiologic changes during admission or discharge (9). Disease-specific medication reduction works best when monitoring endpoints are clear and time-to-harm is short, as in antihypertensive reduction with blood pressure monitoring (8).

Cost And Resource Implications: What Deprescribing May Cost And What It May Save

Deprescribing is often assumed to save money by reducing drug costs and adverse events. That assumption can be correct, but it is not automatic. Deprescribing programmes require professional time, documentation, structured review, follow-up visits, and sometimes nonpharmacologic substitutes. Therefore, the relevant economic question is not “does deprescribing save money,” but “does it deliver enough harm reduction and patient-centred benefit to justify the resources used.”

Two cost patterns are common. First, targeted deprescribing interventions for a single high-risk drug class can be efficient because they have a narrow focus and clear taper pathways. In these cases, the time required per patient is often lower, and the probability of avoiding a known adverse event is higher. Economic evaluation linked to structured medication review programmes suggests that the cost-effectiveness profile depends heavily on baseline risk. If you target low-risk patients, benefits dilute and costs dominate. If you target high-risk patients, avoided events can offset programme costs (18).

Second, comprehensive structured medication review programmes can be resource-intensive and may not show rapid reductions in hospital utilisation at the population level. Even when prescribing quality improves, downstream savings can lag because many drivers of admission and mortality are not medication-related. This does not imply that the programmes have no value. It implies that value may be expressed through patient-centred outcomes, reduced adverse drug events, reduced administration burden, and safer prescribing. From a systems perspective, triage is therefore central. Risk stratification using prior adverse drug events, renal impairment, frailty indices, central nervous system burden, and recent transitions can identify the subgroup most likely to deliver a favourable cost-benefit profile.

Comparative Summary: What The Evidence Supports With The Highest Confidence

The strongest and most reproducible effects are on medication outcomes. Patient activation plus clinician engagement can produce substantial discontinuation of specific high-risk drug classes, as shown in EMPOWER (7). Pharmacist-led interventions reduce inappropriate medication exposure and support tapering and simplification, with D-PRESCRIBE and regimen simplification trials providing practical templates (6,23). Disease-specific medication reduction can be safe in carefully selected populations when monitoring endpoints are explicit, exemplified by OPTIMISE (8) and by discontinuation of statins in patients with limited life expectancy (10).

Evidence for hard endpoints is promising but inconsistent. Meta-analyses suggest that deprescribing and medication review may reduce mortality in some contexts, but effect size and certainty vary with setting and intervention design (15,16). Large pragmatic programmes show that implementation is feasible, but average effects on admissions can be modest if programmes are not tightly targeted to the highest-risk patients and medicines (9). Therefore, the most defensible summary is: deprescribing reliably improves prescribing quality; it may improve clinical outcomes when targeted to high-risk patients and high-harm medicines with strong implementation fidelity.

Table 1. High-signal deprescribing strategies and typical outcomes (selected evidence)

Strategy	Typical setting	Medication outcome signal	Implementation notes
Patient-directed education (single drug class)	Community pharmacy/primary care	High for stopping target drug (7)	Works best with clear harms and taper guides
Pharmacist-led deprescribing linked to prescribers	Community/primary care	Reduction in inappropriate medication exposure (6)	Requires authority pathways and follow-up

Regimen simplification using a structured guide	Residential aged care	Fewer daily administration times (23)	Reduces operational burden; monitor for unintended change
Disease-specific medication reduction with monitoring	Primary care	Short-term BP control maintained after reduction (8)	Requires thresholds for reintroduction
Structured medication review programmes	Hospital/community	Consistent prescribing improvement (9,15)	Benefits depend on targeting and repeated cycles

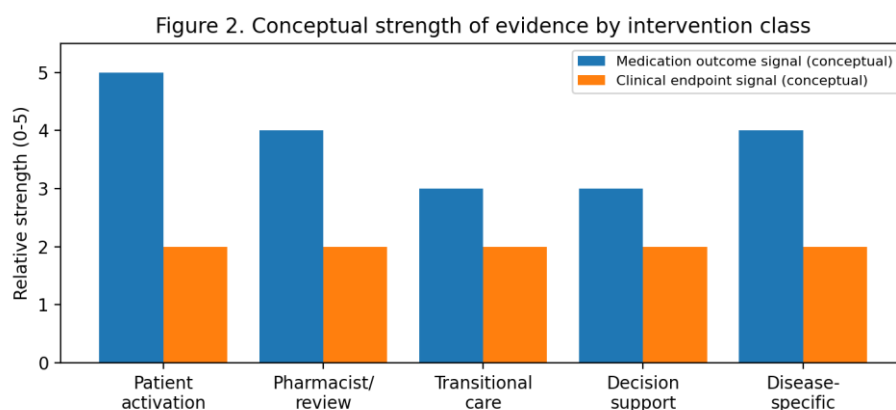
Discussion

Neutral results on admissions or mortality do not automatically refute deprescribing. Several factors explain why clinical endpoints can lag behind medication outcome improvements. First, many trials are underpowered for rare endpoints. A programme can stop inappropriate medicines yet not change mortality over 6 to 12 months because mortality drivers include disease severity, frailty, infections, and social determinants. Second, outcome selection can miss meaningful benefits. Reduced sedation, fewer minor adverse effects, improved sleep quality, reduced dizziness, and improved function can matter profoundly to patients, but they are not always captured in trial endpoints.

A constructive interpretation is to treat deprescribing as a safety intervention whose clinical impact depends on targeting. When deprescribing focuses on medicines strongly associated with harm in a particular patient, benefits are more plausible and more likely to be observed. When deprescribing is broad and not risk-targeted, average effects dilute. This parallels other safety interventions: a checklist applied to low-risk surgery yields smaller measurable effects than the same checklist applied in high-risk settings.

Implications for future research and publication-quality reporting

Future studies should consistently report baseline harm-risk profiles such as frailty, prior falls, renal function, and central nervous system burden; specify which medicines were stopped and why; describe taper protocols and monitoring schedules; and include patient-centred outcomes beyond admissions. Trials should also distinguish recommendations from achieved deprescribing, because implementation failure can otherwise be misinterpreted as intervention failure. Better reporting will make it easier to identify which intervention components are essential and which are optional.



Note: This figure is a conceptual visual aid, not a meta-analytic effect estimate. It summarises relative consistency of findings across intervention classes reported in the cited literature.

Conclusions

Deprescribing reliably improves prescribing quality and can reduce exposure to high-risk medicines, especially when interventions actively engage patients, pharmacists, and caregivers. The clearest evidence supports patient-activated deprescribing for specific high-risk drug classes, pharmacist-integrated deprescribing workflows, regimen simplification where complexity is a problem, and carefully selected disease-specific medication reduction strategies with explicit monitoring endpoints. Effects on admissions and mortality are more likely when interventions target patients at highest risk of medication harm and maintain strong follow-up and implementation fidelity.

For medication-focused journals and health systems, the most pragmatic near-term stance is simple: treat deprescribing as a core medication safety practice, measure medication outcomes rigorously, target high-risk patients and high-harm medicines, and evaluate downstream outcomes with adequate follow-up and appropriate endpoint selection.

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