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Deprescribing as a Competing-Risk Intervention: Balancing Withdrawal Effects, Disease Recurrence, Treatment Burden, and Time to Benefit in Frail Adults

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ABSTRACT

Deprescribing in frail adults is commonly framed as the removal of medicines whose harms or burdens exceed their likely benefits. That formulation is clinically useful but incomplete because discontinuation itself changes risk. Medication withdrawal can relieve adverse effects, administration burden, monitoring demands, drug interactions, and treatment workload, yet the same action may provoke physiological withdrawal, rebound phenomena, recurrence of the treated disorder, or loss of future preventive benefit. These consequences operate on different time scales. Withdrawal may emerge within days, recurrence may become apparent over weeks or months, preventive benefits may require months or years to accrue, and competing illness or mortality may prevent some delayed benefits from ever being realized. Frailty further alters the decision by changing susceptibility to drug harm, functional reserve, treatment priorities, monitoring capacity, and the consequences of unsuccessful withdrawal. This Current Opinion therefore treats deprescribing as a time-dependent competing-risk intervention rather than a unidirectional reduction in medication exposure. The central clinical task is to distinguish the type of risk created by stopping, determine when that risk is likely to become observable, compare it with the timing of continued-treatment benefit and harm, and preserve reversibility where uncertainty is substantial. Evidence from deprescribing trials remains heterogeneous: medication counts and potentially inappropriate prescribing can often be reduced, but improvements in mortality, function, quality of life, hospitalization, or other patient-important outcomes are less consistent. A clinically defensible deprescribing decision consequently requires an explicit decision horizon, class-specific understanding of discontinuation effects, and post-deprescribing surveillance capable of distinguishing transient withdrawal from recurrent disease or loss of necessary treatment.

Keywords: Deprescribing, Frailty, Polypharmacy, Medication withdrawal, Time to benefit, Treatment burden

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Introduction

Deprescribing has moved from a narrow focus on medication discontinuation toward individualized reassessment of whether each treatment remains aligned with current benefit, harm, treatment burden, patient priorities, and feasible care. Contemporary guidance emphasizes that medication withdrawal is only one possible outcome of this reassessment and that decisions should be individualized rather than driven solely by medication number or potentially inappropriate medication lists [1]. This distinction is especially important in older adults with multimorbidity, for whom a medicine can remain pharmacologically effective while becoming less valuable because the indication, prognosis, treatment workload, adverse-effect susceptibility, or patient goals have changed.

The evidence base nevertheless leaves an important asymmetry. Deprescribing interventions can often reduce polypharmacy or inappropriate medication exposure, but evidence that these changes consistently improve mortality, function, hospitalization, quality of life, or other major clinical outcomes is less certain [2]. The problem is partly methodological and partly clinical. Trials differ in what they stop, why treatment is considered inappropriate, how medicines are tapered, which patients are selected, what outcomes are measured, and how long patients are followed. A single label such as "successful deprescribing" can therefore hide several distinct events. Recent evidence syntheses reinforce this point. Reductions in medication burden and potentially inappropriate prescribing are more consistently observed than uniform improvements across downstream clinical outcomes, while mortality findings remain heterogeneous rather than showing a single general effect [3, 4]. Community-based interventions similarly demonstrate that deprescribing can produce measurable reductions in polypharmacy or potentially inappropriate medication use, although the average medication-level change is often modest and should not be equated automatically with a clinically important patient-level benefit [5].

Frailty makes this interpretive problem more consequential. Direct evidence among frail older adults is substantially smaller and more heterogeneous than the broader deprescribing literature. A frailty-specific systematic review found only a limited number of eligible studies, and the largest direct randomized evidence has shown that medication exposure can be reduced without establishing a general survival or functional advantage [6, 7]. The Opti-med trial is particularly instructive: protocolized deprescribing achieved a meaningful difference in medication number, but under-recruitment limited certainty around major clinical outcomes. The appropriate conclusion is neither that deprescribing is inherently beneficial nor that it is ineffective. Rather, medication reduction and clinical benefit are different outcomes requiring separate evidence.

A further limitation of conventional benefit–harm reasoning is temporal. Continued therapy and treatment withdrawal do not generate their consequences at the same moment. An adverse drug effect or treatment workload may be experienced every day. Withdrawal may occur shortly after dose reduction. Recurrence of a treated condition may emerge after a longer interval. Preventive benefit may require years of continued exposure. Competing illness, progressive frailty, or death may occur before that delayed benefit is realized. A deprescribing decision in frailty is therefore not adequately represented by a static comparison of "benefits" and "harms." It is a decision about several competing clinical trajectories unfolding over different horizons.

The central question is consequently how deprescribing decisions in frail adults should account simultaneously for withdrawal effects, recurrence risk, treatment burden, competing morbidity and mortality, and delayed time to benefit. The analysis that follows separates the mechanisms created by stopping, then examines how time horizon and prognosis alter their relative importance. The purpose is not to construct a universal deprescribing score. It is to make explicit which consequences are being compared, when they are expected to occur, and whether an unsuccessful withdrawal can be detected and corrected. Here, competing consequences may coexist; the term does not imply that withdrawal, recurrence and treatment burden are mutually exclusive events in a statistical competing-risks model.

Stopping changes more than exposure: withdrawal, rebound, recurrence, and lost preventive benefit

The safety of deprescribing cannot be judged only by whether a medicine was successfully removed from a prescription list. Clinical trials have used inconsistent approaches to detect adverse drug withdrawal events, and a recent systematic review found that only a small minority of eligible deprescribing trials explicitly reported such events [8]. This creates an important evidentiary problem. If withdrawal is not prospectively defined, monitored, and distinguished from the natural course of illness, an apparently uncomplicated discontinuation may reflect incomplete ascertainment rather than genuine absence of post-withdrawal effects.

Withdrawal is the first of several clinically distinct post-deprescribing phenomena. It refers to symptoms or physiological consequences attributable to removal or reduction of drug exposure rather than to return of the treated disorder itself. Antidepressants provide a well-characterized example. A recent systematic review and meta-analysis confirmed that discontinuation symptoms occur after antidepressant cessation, although estimates depend on study design, comparator, drug characteristics, and how symptoms are defined [9]. This phenomenon should not be collapsed into recurrence of depression because the mechanisms, expected timing, and appropriate response may differ.

Recurrence can nevertheless coexist with withdrawal. In a randomized primary-care trial, adults assigned to discontinue long-term antidepressant therapy experienced more depressive relapse over 52 weeks than those

assigned to maintenance treatment, while withdrawal symptoms were also more frequent after discontinuation [10]. The same patient can therefore deteriorate after stopping for more than one reason. A clinician who interprets every early symptom as recurrent disease may restart treatment unnecessarily, whereas attributing every deterioration to transient withdrawal may delay treatment of genuine recurrence.

Some medicines create withdrawal through direct physiological dependence on continued exposure. Chronic systemic glucocorticoid treatment may suppress hypothalamic–pituitary–adrenal function, making cessation potentially hazardous when endogenous cortisol production has not recovered [11]. Here the clinical problem is neither return of the original inflammatory disease alone nor a nonspecific "discontinuation syndrome." It is a physiological consequence of prior treatment that can require tapering, assessment of recovery, and protection against adrenal insufficiency.

Opioid deprescribing illustrates another configuration in which withdrawal risk, symptom recurrence, and treatment burden interact. In older adults, reducing long-term opioid therapy may decrease sedation, constipation, falls risk, cognitive burden, or other adverse effects, yet uncontrolled pain and opioid withdrawal can make an otherwise rational reduction clinically unsuccessful [12]. Evidence from large observational cohorts also warns against assuming that dose reduction is intrinsically safe. Opioid tapering has been associated with subsequent overdose and mental-health crisis, although confounding and treatment selection prevent these associations from proving that tapering itself caused every adverse event [13]. The implication is narrower but clinically important: an inadequately supported taper can itself become a period of heightened vulnerability.

Disease recurrence becomes even more explicit when the medicine suppresses a condition with potentially serious episodic consequences. Antiseizure medication withdrawal in seizure-free patients requires individualized assessment because recurrent seizure risk persists after treatment discontinuation and current evidence does not support a single withdrawal rule that applies across epilepsy syndromes or patients [14]. The observation that a patient has remained event-free while treated does not establish that the underlying propensity has disappeared.

A similar distinction applies to symptomatic therapy in dementia. Evidence from withdrawal trials suggests that stopping cholinesterase inhibitors can worsen cognition, function, or neuropsychiatric symptoms in some patients, although certainty is limited and the available evidence is concentrated largely in Alzheimer disease [15]. Such deterioration is better interpreted as loss of symptomatic treatment effect or disease-related worsening than as a generic pharmacological withdrawal syndrome. The practical response may still be to restart treatment, but the clinical reasoning is different.

Conversely, some treatments can be reduced without immediate loss of control when patients are carefully selected. In the OPTIMISE randomized trial, adults aged 80 years or older with controlled systolic blood pressure who were receiving at least two antihypertensive agents could have one medicine removed while largely maintaining short-term blood-pressure control [16]. This provides an important counterexample to the assumption that withdrawal necessarily destabilizes the treated condition. It also demonstrates why reversibility matters: reduction can be approached as an observable clinical trial when the relevant outcome can be monitored and treatment can be reinstated if control deteriorates.

Preventive therapies add a fourth category that may not produce an obvious early recurrence at all. Discontinuation can instead remove protection against future events. Among older long-term statin users in Denmark, stopping therapy was associated with higher rates of major adverse cardiovascular events compared with continuation [17]. Because the study was observational, residual confounding remains possible, but its interpretation differs from withdrawal or rebound. The potential consequence is loss of future preventive benefit, not necessarily an immediate post-cessation syndrome.

These distinctions matter because identical observations can arise through different mechanisms. Fatigue after stopping a medicine could represent withdrawal, return of disease, another illness, or relief from adverse treatment effects followed by unrelated deterioration. A fall after antihypertensive reduction could reflect persistent frailty rather than the medication change itself. A cardiovascular event years after statin withdrawal cannot be interpreted using the same causal assumptions as symptoms appearing days after antidepressant cessation. Deprescribing therefore requires mechanism-specific surveillance rather than a generic question of whether the patient is "better" after stopping.

The clinically relevant differences across medicine classes concern what can happen after withdrawal, how quickly it may become visible, whether the underlying indication remains active, and what corrective action remains available.

Table 1. Distinct post-deprescribing risks and monitoring logic across representative medication classes

Medication class or treatment context	Principal reason withdrawal may be considered	Withdrawal or physiological cessation effect	Rebound or early destabilization concern	Disease or symptom recurrence	Potential loss of preventive benefit	What should be observed after reduction	Reversibility considerations
Antidepressants	Adverse effects, treatment burden, changed indication or preference	Discontinuation symptoms may occur	Early symptom intensification may be difficult to attribute	Depressive relapse can occur after cessation	Usually not the dominant mechanism	Timing and character of new symptoms, mood trajectory, function	Gradual dose reduction and reassessment can help distinguish transient withdrawal from persistent relapse
Systemic glucocorticoids	Cumulative adverse effects or resolved indication	Adrenal suppression may make cessation physiologically unsafe	Clinical deterioration can occur if endogenous cortisol response is inadequate	Original inflammatory or endocrine indication may also recur	Context dependent	Symptoms compatible with adrenal insufficiency and activity of the treated disease	Tapering and recovery assessment are central; abrupt cessation may be inappropriate after relevant exposure
Long-term opioids	Sedation, constipation, falls risk, cognitive effects, reduced benefit or patient preference	Opioid withdrawal may occur	Pain and distress may worsen during reduction	Persistent pain may re-emerge or remain inadequately treated	Not principally preventive	Withdrawal symptoms, pain, function, mental health, evidence of destabilization	Reduction should remain adjustable; alternative analgesic and non-drug strategies may be required
Antiseizure medicines	Sustained seizure freedom, adverse effects, changing goals	Drug-specific withdrawal effects are not the principal concern in most decisions	Abrupt withdrawal may create avoidable instability	Seizures may recur	Protection against future seizures is lost when effective therapy is withdrawn	Seizure recurrence, neurological status, safety consequences	Restart may restore protection, but recurrent seizure can have immediate consequences; candidate selection is therefore critical
Cholinesterase inhibitors	Limited benefit, adverse effects, advanced disease, treatment burden	Classical physiological withdrawal is not usually the principal issue	Neuropsychiatric or functional worsening may emerge after stopping	Cognitive, functional, or behavioral deterioration may become apparent	Loss of symptomatic benefit rather than distant prevention	Cognition, daily function, behavior, caregiver-observed change	A monitored withdrawal can permit reinstatement when clinically important deterioration follows cessation
Antihypertensive therapy in selected very old adults	Hypotension, falls risk, pill burden, changed targets or limited marginal benefit	Drug-specific; cessation effects cannot be inferred from the antihypertensive class label alone	Blood pressure can rise after reduction	Hypertension may again require treatment	Reduced long-term cardiovascular protection is possible	Blood pressure, orthostatic symptoms, falls, relevant cardiovascular symptoms	One-drug reduction can be tested in selected patients with prompt reassessment if control deteriorates
Statins used for prevention	Treatment burden, adverse effects, changing prognosis or goals	No characteristic acute withdrawal syndrome is expected	No typical rebound syndrome is required to explain risk	Not a recurrence model in the usual symptomatic sense	Future cardiovascular protection may be reduced	Cardiovascular risk context, evolving prognosis, adverse-effect resolution	Restart is possible, but the consequences of temporary discontinuation are less directly observable than with symptom-targeted therapy

Decision value changes over time: time to benefit, time to harm, and competing prognosis

Stopping and continuing treatment generate consequences on different time scales. This temporal mismatch is especially important for preventive medicines, for which benefit may accumulate gradually while burden or

adverse effects are experienced immediately. Time to benefit therefore provides a clinically useful complement to conventional estimates of relative risk reduction. In a survival meta-analysis of primary-prevention statin trials involving adults aged 50–75 years, approximately 2.5 years of treatment were required to prevent one major cardiovascular event per 100 people treated in the source population [18]. That estimate should not be converted into a universal discontinuation threshold. It depends on baseline risk, outcome definition, treatment class, and population. It describes the time required to reach a specified absolute benefit at population level, not a period during which no individual can benefit.

Bisphosphonate therapy provides a second example. A meta-analysis of randomized trials estimated that approximately 12.4 months of treatment were required before one nonvertebral fracture was prevented per 100 treated postmenopausal women within the analytical assumptions used by the authors [19]. Again, the number should not be transported to other therapies or patient groups. The broader implication is that a treatment can be evidence-based and still offer little realizable benefit to an individual whose clinically relevant decision horizon is substantially shorter than the period over which benefit is expected to emerge.

This does not mean that limited prognosis automatically justifies withdrawal. Prognosis changes the value of delayed benefit only in relation to the risks created by stopping and the harms or burdens of continuing. STOPPFrail version 2 provides an established example of prognosis-sensitive medication review in frail older people approaching the end of life, where treatment burden, goals, symptom control, and the likelihood of future benefit are explicitly considered [20]. The criteria are a consensus tool rather than proof that every listed medicine should be discontinued. Their value is that they make remaining life expectancy and care goals clinically relevant to medication appropriateness.

Frailty also changes the meaning of treatment benefit because maintaining function, independence, comfort, cognition, and the ability to perform daily activities may become as important as preventing a distant disease-specific endpoint. Contemporary work on drugs and healthy aging emphasizes that pharmacotherapy can either support or undermine functional ability depending on the medicine, patient susceptibility, interactions, and treatment burden [21]. A preventive medicine with delayed population-level benefit can remain worthwhile in a robust older adult with substantial life expectancy, whereas the same treatment may carry a different value in a patient with advanced frailty, frequent adverse effects, limited physiological reserve, and a strong preference to reduce medication workload.

Potentially inappropriate medication criteria can inform this assessment but cannot resolve it. The 2023 AGS Beers Criteria identify medicines and clinical circumstances associated with elevated risk in older adults, yet they remain screening and decision-support criteria rather than automatic instructions to stop treatment [22]. The decisive question is whether the medication's expected benefit remains relevant within the patient's horizon and whether stopping creates a greater immediate risk than continuation.

The longer-term follow-up of OPTIMISE illustrates why such reasoning must remain class- and context-specific. Among selected adults aged 80 years or older with controlled blood pressure, a strategy of removing one antihypertensive was sustained in approximately half of participants and was not associated with evidence of increased hospitalization or mortality over a median follow-up of four years [23]. The finding does not show that antihypertensive deprescribing is safe for all frail adults, nor does it establish that more extensive withdrawal would produce the same result. It shows that, in a carefully selected population, reduction can remain clinically acceptable over a substantially longer horizon than the original short-term blood-pressure trial suggested.

A competing-risk interpretation follows from these observations. Continued treatment can provide future protection while imposing current adverse effects, interactions, monitoring, administration workload, or loss of function. Deprescribing can remove some of those immediate burdens while introducing withdrawal or recurrence risk. Competing illness or mortality may prevent delayed preventive benefit from being realized, but they do not erase the possibility of an early cessation-related event. The decision therefore changes as the expected timing of these outcomes changes.

This temporal reasoning is particularly important when the harms of continuation and cessation are asymmetric. If continued therapy produces a daily adverse effect while its preventive benefit is expected only after years, a shorter decision horizon shifts the balance toward withdrawal, provided cessation itself does not create an important near-term hazard. Conversely, a medicine that prevents a rapidly recurrent and serious condition may remain valuable even when prognosis is limited because the benefit is immediate and the consequences of withdrawal are severe. The relevant unit of reasoning is therefore not simply “life expectancy” but the relationship

among the patient's remaining horizon, the medicine's time to benefit, the medicine's time to harm, the expected timing of withdrawal or recurrence, and the practical possibility of detecting and correcting an unsuccessful reduction.

Figure 1 contrasts the timing of these competing clinical consequences without assigning probabilities or universal thresholds.

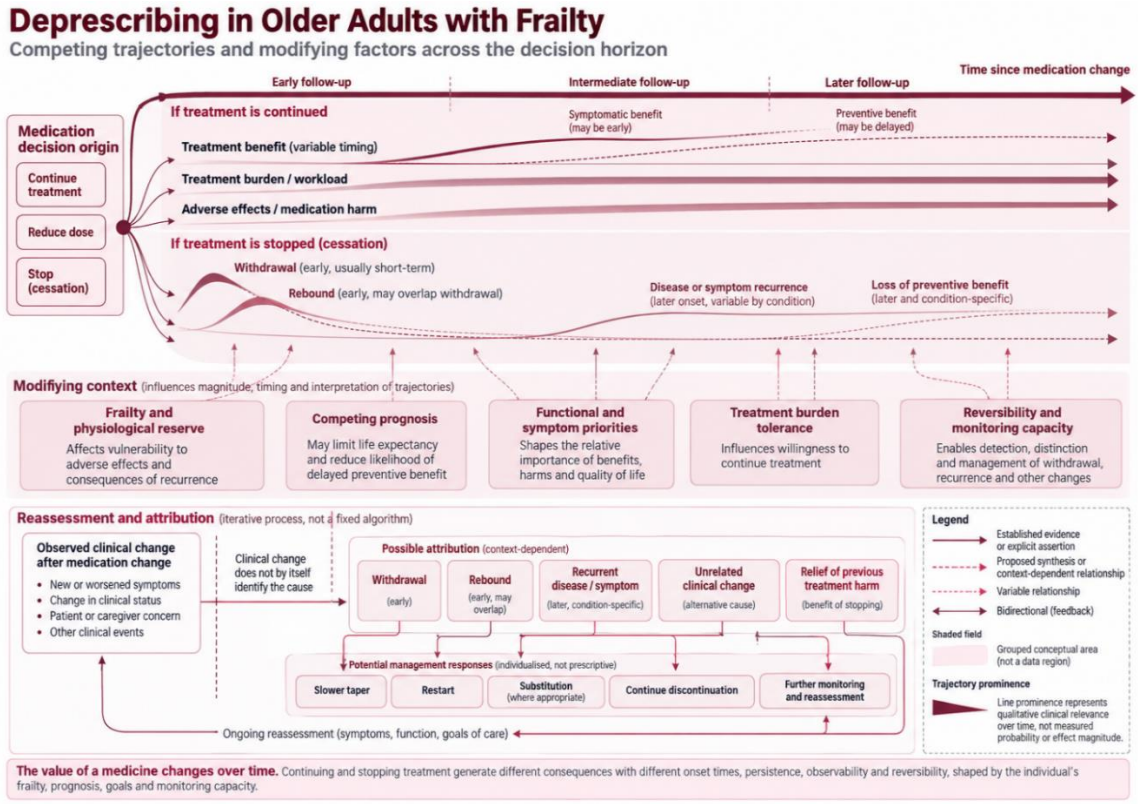

Figure 1. Competing clinical consequences of deprescribing across the decision horizon in frailty

Frailty makes the decision horizon patient- and state-dependent

Frailty does not convert deprescribing into a default treatment objective. It changes the clinical consequences of both continuation and cessation. Reduced physiological reserve can increase vulnerability to hypotension, sedation, renal or metabolic perturbation, falls, delirium, anorexia, and other medication-related harms, but the same reduction in reserve can also make recurrence of a previously controlled condition more consequential. The relevant question is therefore not whether a patient is "frail enough" to deprescribe. It is how frailty changes the probability, timing, detectability, and recoverability of the outcomes being compared.

The direct evidence base remains limited. Studies specifically enrolling older people living with frailty are relatively few, heterogeneous, and often too small to establish effects on mortality, hospitalization, disability, or quality of life with precision [6]. Opti-med further illustrates the distinction between feasibility and proven clinical superiority: medication reduction was achievable, but incomplete recruitment constrained inference about major health outcomes [7]. Frailty should therefore be used as a modifier of clinical reasoning rather than as a surrogate outcome or automatic indication for medication withdrawal.

Patient state also matters more than chronological age alone. The short-term OPTIMISE trial showed that carefully selected adults aged 80 years or older with controlled systolic blood pressure could often tolerate withdrawal of one antihypertensive while maintaining blood-pressure control [16]. That finding is useful because it demonstrates testable reversibility. It does not establish that a similar strategy is safe in unstable hypertension, recent cardiovascular events, severe heart failure, or more complex multidrug withdrawal.

Prognosis modifies the decision most directly when expected medication benefit is delayed. STOPPFrail version 2 explicitly incorporates limited life expectancy, symptom burden, treatment goals, and the continuing value of preventive medication into structured medication review [20]. Its role is to support deliberation, not to replace it.

Prognosis is uncertain, frailty trajectories are non-linear, and a treatment whose preventive benefit is unlikely to be realized may still have important symptomatic or near-term effects.

Functional reserve provides another dimension. Medication value in later life includes effects on mobility, cognition, continence, balance, nutrition, participation, and treatment workload, not only disease-specific endpoints [21]. A small reduction in medication burden may be clinically meaningful when swallowing difficulty, administration complexity, monitoring requirements, or adverse effects consume a substantial fraction of a patient's remaining functional capacity. Conversely, stopping a medicine that preserves cognition, mobility, symptom control, or cardiovascular stability can worsen the very function that deprescribing is intended to protect.

Screening criteria can help identify situations requiring review but should not collapse this patient-specific reasoning into a binary classification. The Beers Criteria identify potentially inappropriate medication use in older adults and provide condition-specific cautions, yet appropriateness still depends on indication, alternatives, treatment history, goals, and the consequences of withdrawal [22].

Longer-term evidence from OPTIMISE is reassuring within its studied boundaries. Follow-up over a median of approximately four years found no evidence of increased hospitalization or mortality after the original one-drug antihypertensive reduction strategy, although medication reduction was not sustained in all participants and the population was selected [23]. The study supports the feasibility of reversible, monitored reduction in an appropriate subgroup; it does not justify generalization to extensive deprescribing or to medication classes with different withdrawal or recurrence profiles.

A practical decision horizon in frailty should therefore be individualized around four questions: what benefit is still realistically obtainable; what harm or burden is occurring now; what new risk is created by stopping; and whether deterioration can be detected and reversed before substantial injury occurs. Frailty influences all four.

Table 2. Patient-context features that reshape the deprescribing decision horizon

Patient-context feature	Why it matters for continuation	Why it matters for deprescribing	Effect on the decision horizon	Clinical implication
Frailty and physiological reserve	Adverse effects may produce larger functional consequences	Recurrence or withdrawal may also be less well tolerated	Often shortens tolerance for persistent harm while increasing the importance of cautious withdrawal	Avoid using frailty as an automatic stop signal; compare both continuation and cessation consequences
Prognosis and competing illness	Delayed preventive benefit may become less likely to be realized	Early withdrawal or recurrence can still occur despite limited prognosis	Reduces the relevance of benefits requiring a horizon substantially longer than the patient's likely course	Match expected benefit latency to the clinically meaningful horizon rather than using age alone
Current symptom burden	Continued treatment may preserve comfort or control symptoms	Treatment itself may contribute to fatigue, dizziness, cognitive effects, gastrointestinal symptoms, or other burden	Makes near-term outcomes more important	Clarify whether the medicine is causing, preventing, or merely coexisting with current symptoms
Functional reserve	Some medicines support mobility, cognition, or physiological stability	Drug effects and treatment workload can consume limited reserve	Increases the value of outcomes affecting day-to-day function	Include functional consequences alongside disease-specific endpoints
Treatment workload	Monitoring, administration, polypharmacy, swallowing, and regimen complexity can impose daily burden	Removing low-value treatment may create immediate practical benefit	Makes present burden clinically relevant even when long-term outcomes are uncertain	Consider workload as a legitimate outcome, not merely inconvenience
Patient priorities	Prevention, longevity, symptom relief, cognition, independence, and medication minimization may be valued differently	A technically defensible withdrawal may conflict with the patient's priorities	Determines which future outcomes are worth preserving	Explicitly establish the outcome the patient most wants treatment to protect
Reversibility	Continued treatment can usually be reconsidered later, but cumulative harms may persist	Some failed withdrawal attempts can be corrected; others may produce serious events before correction	Favors cautious trials when important outcomes are observable and restart is feasible	Prefer reversible changes when uncertainty is substantial

Monitoring capacity	Continued therapy may require laboratory, physiological, or clinical surveillance	Safe withdrawal may depend on detecting early deterioration	Poor monitoring capacity narrows the range of safely testable changes	Deprescribing plans should match available follow-up, caregiver support, and access to reassessment

What deprescribing evidence can—and cannot—establish

The contemporary deprescribing literature supports several conclusions with reasonable consistency. Medication review can reduce medication number and potentially inappropriate prescribing, and structured interventions can be implemented across community, hospital, and residential settings. The more difficult question is whether those changes reliably translate into patient-important benefit.

A systematic review and meta-analysis of medication review and deprescribing among older inpatients found evidence of a small reduction in readmission, while mortality was not significantly reduced and many included studies had substantial risk of bias [24]. These findings are clinically relevant but do not support a general claim that deprescribing improves survival. They also illustrate the limits of aggregating interventions that differ in target medicines, populations, intensity, follow-up, and implementation.

A broader systematic review and meta-analysis likewise found that deprescribing interventions can reduce inappropriate medication exposure, but effects on other clinical outcomes vary across studies [25]. Such results are compatible with several possibilities: some medication reductions may be clinically valuable but too small or heterogeneous to alter broad outcomes; benefit may occur only in particular medication classes or patient subgroups; surveillance and implementation quality may determine whether benefit is realized; or medication-count outcomes may sometimes exaggerate the clinical importance of an intervention.

Frailty-specific randomized evidence reinforces the need for this restraint. In a community trial targeting anticholinergic and sedative medicines among frail older adults, the feasibility of reducing medication burden did not establish a universal functional benefit attributable to deprescribing [26]. A reduction in cumulative medication exposure is therefore best interpreted as an intermediate outcome unless the corresponding patient-level consequences are measured.

These limitations do not weaken the rationale for deprescribing. They define what evidence is required. A strong deprescribing study should identify why a medicine is being withdrawn, distinguish withdrawal from recurrence, specify the timing of expected benefit and harm, measure patient-important outcomes, report adverse drug withdrawal events, and describe how failed withdrawal was managed. Without those elements, two interventions producing the same reduction in medication count may have very different clinical meaning.

The competing-risk framework proposed here is therefore deliberately falsifiable. It would be weakened if clinically important outcomes proved unrelated to differences in benefit latency across therapies; if distinguishing withdrawal from recurrence did not improve interpretation of post-cessation deterioration; or if planned monitoring and reversibility provided no practical advantage over decisions without planned reassessment. These are empirical questions rather than assumptions.

Post-deprescribing surveillance is part of the intervention

Deprescribing is incomplete when the prescription is changed. The post-withdrawal period is the phase in which the consequences of the decision become observable and causal uncertainty is tested. Implementation research shows that deprescribing depends not only on identifying potentially inappropriate medication but also on communication, role clarity, follow-up, documentation, patient involvement, and the ability to respond when clinical status changes [27].

Transitions of care make these requirements more difficult. Older adults moving from post-acute settings to home may experience fragmented responsibility, medication-list discrepancies, delayed follow-up, inconsistent communication, and uncertainty about who should monitor a deprescribing plan [28]. Under these conditions, even a pharmacologically reasonable withdrawal can become unsafe if recurrent symptoms or withdrawal effects are not recognized.

Surveillance should therefore be medication-specific. After reduction of a drug capable of physiological withdrawal, monitoring should begin during the period in which withdrawal is biologically plausible. After withdrawal of symptom-control therapy, the outcome of interest may be function, behavior, pain, mood, or another patient-reported change rather than a laboratory value. After reducing antihypertensive treatment, blood pressure and orthostatic symptoms can provide observable signals. After stopping preventive therapy, however, the loss of

benefit may not be directly observable during a short follow-up period. Surveillance cannot eliminate that uncertainty; it can only monitor consequences that emerge within the available horizon.

Implementation models using pharmacists and telehealth illustrate how structured follow-up can support this process. A pilot pharmacist-led telehealth deprescribing intervention for people living with dementia and polypharmacy demonstrated the feasibility of medication review and follow-up within primary care, but its small sample and pilot design do not establish comparative efficacy [29]. Its relevance is operational: deprescribing requires a mechanism for reassessment rather than a one-time recommendation.

Recent work focused specifically on deprescribing in people with dementia similarly emphasizes a longitudinal process involving identification of treatment targets, shared decision-making, tapering where appropriate, monitoring, and reconsideration when important deterioration follows withdrawal [30]. This logic extends beyond dementia. Reassessment should be pre-specified whenever the likely post-withdrawal consequence is clinically important and potentially reversible.

Restarting treatment should not automatically be interpreted as failure. If a medicine is withdrawn because its current value is uncertain, a monitored trial can generate patient-specific information unavailable from population averages. Recurrence of a clinically important symptom, deterioration in function, or emergence of a dangerous physiological consequence may demonstrate that continued treatment retains value. Conversely, absence of deterioration does not prove that all long-term preventive benefit was unnecessary, particularly when the expected benefit horizon is long.

The purpose of surveillance is therefore attribution as well as detection. Clinicians should ask whether a new event is temporally compatible with withdrawal, whether it reproduces the original disease phenotype, whether an alternative cause is more plausible, and whether improvement after reinstatement would meaningfully clarify the relationship. That reasoning is particularly important when withdrawal symptoms mimic recurrence.

A deprescribing plan is most defensible when it specifies in advance what will be monitored, when it will be assessed, what degree of deterioration is acceptable, and what finding would trigger reassessment or restart.

Table 3. Post-deprescribing surveillance and reasonable triggers for reassessment or restart

Clinical situation after deprescribing	What should be monitored	Typical interpretation problem	When reassessment is warranted	When restart or modification may be reasonable
New symptoms soon after dose reduction	Timing, severity, symptom pattern, functional effect	Withdrawal may be confused with recurrence or unrelated illness	Symptoms are persistent, severe, progressive, or inconsistent with the intended taper	When symptoms are plausibly treatment-related and clinically important, particularly if a slower taper is feasible
Return of the treated symptom or disorder	Original disease markers, patient-reported symptoms, function	Recurrence may be mistaken for transient withdrawal	The original clinical phenotype returns or meaningful control is lost	When recurrence causes clinically important harm and previous treatment remains consistent with current goals
Physiological instability	Relevant vital signs, laboratory measures, endocrine or neurological signs where appropriate	Deterioration may be silent until clinically significant	Predefined physiological limits are crossed or symptoms suggest instability	When the withdrawn medicine remains the safest effective means of restoring control
Improvement after withdrawal	Adverse effects, cognition, balance, function, treatment workload	Improvement may be attributed incorrectly if other treatments or illnesses changed simultaneously	Improvement is incomplete, temporary, or accompanied by new risk	Modification rather than full restart may be preferable if the original burden clearly improved
No early clinical change	Disease-specific status and relevant longer-term outcomes	Absence of early deterioration may falsely reassure when preventive benefit is delayed	The patient's prognosis, goals, or risk profile changes	Restart can be reconsidered if the indication becomes more important or the expected benefit horizon changes

Transition between care settings	Medication list, intended taper, monitoring responsibility, caregiver understanding	Deprescribing intent may be lost or the medicine may be unintentionally restarted	Responsibility for follow-up is unclear or medication records conflict	Reconciliation and clinical reassessment should precede automatic continuation or discontinuation
Cognitive impairment or limited self-monitoring	Caregiver observations, behavior, function, adherence, adverse effects	Clinically important change may not be self-reported	Caregivers identify meaningful deterioration or cannot safely supervise the plan	Restart or a simpler alternative may be reasonable when monitoring uncertainty becomes unacceptable
Multiple simultaneous medication changes	Symptoms, physiological markers, timing of each change	Causal attribution becomes difficult	New deterioration cannot be linked to a specific change	Reintroducing or sequencing medicines individually may be needed to recover interpretability

Conclusion

Deprescribing in frail adults is best understood as a time-dependent competing-risk intervention. Stopping treatment may reduce medication-related harm, administration burden, monitoring demands, and interference with daily function, but it can also create withdrawal, rebound, recurrence, or loss of future preventive benefit. These outcomes are mechanistically distinct and often occur over different time scales.

The central decision is therefore not whether a medicine is simply “appropriate” or “inappropriate.” It is whether the benefits expected from continued exposure remain relevant within the patient's clinical horizon, whether present treatment harm or burden justifies change, what new hazard stopping introduces, and whether that hazard can be observed and reversed. Frailty modifies each part of this comparison by altering physiological reserve, functional consequences, competing prognosis, treatment capacity, and recovery from destabilization.

Current deprescribing evidence supports medication reduction more consistently than it demonstrates improvements in broad patient-important outcomes. That uncertainty argues for better attribution and surveillance rather than therapeutic inertia. When uncertainty is substantial, a reversible, monitored reduction can function as a patient-specific therapeutic experiment. The quality of the decision then depends not only on what is stopped, but on what clinicians expect to happen next, when they look for it, and what they are prepared to do if the original treatment proves necessary.

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