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Safety and Efficacy of Antihypertensive Deprescribing in Frail Geriatric Patients: A Narrative Review of Contemporary Clinical Trial Evidence

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ABSTRACT: Polypharmacy with antihypertensive agents in frail older adults presents a clinical dilemma: continuing therapy may preserve cardiovascular protection, yet it simultaneously increases the risk of orthostatic hypotension, falls, and drug-related adverse events. This narrative review synthesizes contemporary clinical evidence on the safety and efficacy of antihypertensive deprescribing (gradual withdrawal or dose reduction) in frail geriatric populations, particularly those residing in long-term care facilities. Literature searches were conducted in PubMed/MEDLINE, Cochrane Library, and Google Scholar (2011–2025).
Key findings include: the OPTIMISE randomized trial, which demonstrated that withdrawing one antihypertensive agent in patients aged ≥80 years was non-inferior to usual care for systolic blood pressure control over 12 weeks, with 66% sustaining the reduction. The DANTE trial found no cognitive benefit from discontinuation in older adults with mild cognitive impairment. Observational data from the PARTAGE study revealed that low systolic blood pressure combined with ≥2 antihypertensives was associated with increased two-year mortality in frail nursing home residents, supporting the rationale for deprescribing in this subgroup. A Cochrane systematic review (2020, updated 2023) encompassing six trials (1,073 participants) found no significant association between antihypertensive withdrawal and mortality, myocardial infarction, stroke, or hospitalization, though evidence on falls and quality of life remains limited.
Overall, current evidence supports selective, closely monitored deprescribing in frail geriatric patients. However, long-term outcomes and data specific to Asian populations, including Indonesia, remain scarce, underscoring the need for further research.

KEYWORDS: antihypertensives, deprescribing, geriatrics, frailty, orthostatic hypotension, polypharmacy.

INTRODUCTION

Hypertension is highly prevalent among geriatric populations, with most older adults requiring two or more antihypertensive agents for long-term management. In frail patients characterized by diminished physiological reserve, multimorbidity, and vulnerability to stressors the benefits of strict blood pressure control may not outweigh the risks. Age-related changes in pharmacodynamics and pharmacokinetics increase susceptibility to orthostatic hypotension, falls, renal impairment, and drug-related complications.
Deprescribing, defined as the systematic identification and withdrawal of medications whose risks outweigh their benefits in the context of patient goals and life expectancy, has emerged as a strategy to mitigate polypharmacy in geriatrics. Yet, clinicians often hesitate to deprescribe antihypertensives due to concerns about rebound hypertension and cardiovascular events. This review synthesizes recent randomized and observational evidence to inform clinical decision-making.

METHODS

This review was conducted as a narrative synthesis, rather than a new systematic review. Literature searches were performed in PubMed/MEDLINE, Cochrane Library, and Google Scholar for publications between 2011 and 2025, using combinations of the following keywords: “antihypertensive deprescribing,” “frail elderly,” “orthostatic hypotension,” “polypharmacy,” and “nursing home.”
Priority was given to Randomized controlled trials (RCTs) evaluating deprescribing interventions, Systematic reviews published in high-impact journals (e.g., JAMA, JAMA Internal Medicine, Lancet Healthy Longevity, Cochrane Database of Systematic Reviews). Large observational cohort studies relevant to frail geriatric populations. To provide contextual relevance for Indonesia, additional epidemiological data were retrieved from official reports of the Ministry of Health of the Republic of Indonesia (Riskesdas) and regional health profiles from West Java Province and Majalengka District. This review did not follow the PRISMA protocol in full, nor did it perform new statistical pooling. All effect sizes and outcome measures were cited directly from the original studies. The synthesis was qualitative, aiming to integrate findings across diverse study designs and healthcare settings.

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EVIDENCE FROM RANDOMIZED CONTROLLED TRIALS

The most relevant randomized controlled trial (RCT) evidence derives from the OPTIMISE study (Optimising Treatment for Mild Systolic Hypertension in the Elderly), a non-inferiority, open-label RCT conducted across 69 primary care facilities in the United Kingdom. A total of 569 patients aged ≥80 years with systolic blood pressure (SBP) <150 mmHg while receiving ≥2 antihypertensive agents were randomized either to the withdrawal of one antihypertensive drug or to usual care, with a follow-up period of 12 weeks.

The primary outcome demonstrated that the proportion of patients maintaining SBP <150 mmHg at 12 weeks was 86.4% in the deprescribing group versus 87.7% in the control group, thereby meeting non-inferiority criteria. Furthermore, 66.3% of patients in the intervention arm sustained medication reduction through the end of follow-up. No significant differences in serious adverse events were observed during this short-term monitoring period. Long-term follow-up, published in *Lancet Healthy Longevity* (2024), subsequently evaluated the impact of deprescribing on hospitalization and mortality.

THE DANTE STUDY: COGNITIVE FUNCTION AND TREATMENT WITHDRAWAL

The DANTE study (Discontinuation of Antihypertensive Treatment in Elderly People) was an RCT specifically designed to assess the effects of antihypertensive withdrawal on cognitive performance in older adults with mild cognitive impairment. Unlike OPTIMISE, which focused on blood pressure control and general safety, DANTE tested the hypothesis that excessively low blood pressure in frail elderly patients may impair cerebral perfusion and worsen cognition. The study found no improvement in cognitive outcomes following discontinuation, underscoring the importance of incorporating cognitive status into deprescribing decisions alongside cardiovascular endpoints.

A. OBSERVATIONAL EVIDENCE: THE PARTAGE COHORT AND RISKS OF OVERTREATMENT

The PARTAGE study (Predictive Values of Blood Pressure and Arterial Stiffness in Institutionalized Very Aged Population) was a large observational cohort conducted among nursing home residents. Although not an interventional deprescribing trial, it examined associations between achieved blood pressure, number of antihypertensive medications, and mortality. Findings revealed that residents with SBP ≤130 mmHg while receiving ≥2 antihypertensives had significantly higher two-year mortality compared with those on fewer medications. Additional analyses reported a prevalence of orthostatic hypotension of 18% in very old nursing home residents, linked to arterial stiffness parameters.

While causality cannot be inferred from observational data, these results reinforce the biological rationale that low SBP combined with polypharmacy may constitute overtreatment in frail institutionalized populations. They highlight the need for careful reassessment of therapeutic regimens in this subgroup.

B. SYSTEMATIC REVIEW EVIDENCE: THE COCHRANE ANALYSIS

A Cochrane systematic review (Reeve et al., 2020; updated 2023) synthesized evidence from six RCTs involving 1,073 participants aged ≥50 years. The review found no significant association between antihypertensive withdrawal and mortality, myocardial infarction, stroke, or hospitalization. However, mean blood pressure increased by approximately 10/4 mmHg in the deprescribing groups compared with continued therapy. Importantly, data on adverse events, falls, and quality of life were limited, and follow-up durations were relatively short (4–56 weeks).

This synthesis provides valuable context: while short-term deprescribing appears feasible without increasing major cardiovascular events, definitive conclusions regarding long-term safety and patient centered outcomes particularly falls and quality of life remain elusive due to the paucity of robust evidence.

C. CLINICAL IMPLICATIONS AND PRACTICAL CONSIDERATIONS

Based on the available evidence, several practical implications emerge for clinicians in internal medicine and geriatrics:

- Deprescribing appears to be safely considered in the short term (up to 12 weeks) for selected geriatric patients with well-controlled blood pressure and relatively low cardiovascular risk, based on evidence from the OPTIMISE trial.
- In very frail populations with already low systolic blood pressure (≤130 mmHg) who are receiving multiple antihypertensive medications, reassessment of the therapeutic regimen should be considered in light of associative findings from the PARTAGE study, although causal evidence is not yet available.

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- Deprescribing decisions should ideally be individualized, taking into account life expectancy, goals of care, functional and cognitive status, fall history, and patient/family preferences rather than applied as a blanket policy across all geriatric populations.
- Close monitoring after deprescribing (blood pressure, symptoms of orthostatic hypotension, cognitive function) remains crucial given the limitations of long-term data.
- Data on falls and quality of life two outcomes most clinically relevant for frail patients remain major evidence gaps identified in the Cochrane review. Therefore, interpretation of findings from OPTIMISE and other studies must remain cautious in these domains.

Evidence on the prevalence of antihypertensive polypharmacy and deprescribing practices among frail geriatric populations in Indonesia remains extremely limited. Given the projected demographic shift toward an aging population and the high prevalence of hypertension among older adults, there is an urgent need for local research evaluating prescribing patterns, frailty prevalence, and deprescribing outcomes in both primary care and long-term care facilities.

Hypertension is the most common non-communicable disease among older adults in Indonesia. According to the 2018 National Basic Health Survey (Riskesdas), prevalence increases with age, reaching 63.2% in individuals aged 65–74 years and 69% in those aged ≥75 years. Overall, 32.5% of Indonesian older adults are affected, a figure surpassing other chronic conditions such as arthritis (18%) and obesity (14.6). Epidemiological projections anticipate further increases in hypertension prevalence among the elderly in the coming decade.

West Java represents one of the provinces with the highest burden of hypertension. Riskesdas 2018 reported a prevalence of 39.6%, rising to 41.6% in the 2019 West Java Health Profile. More recent data from the West Java Provincial Health Office (2023) documented 3,212,072 cases of hypertension, reflecting a 39.09% increase compared with the previous year. In Majalengka District, hypertension ranks among the top ten non-communicable diseases in older adults at the primary care level, according to the Majalengka Health Profile (2023). These figures align with increasing life expectancy and evolving dietary and lifestyle patterns.

The high prevalence of hypertension among Indonesian older adults correlates with widespread polypharmacy. Elderly patients with hypertension typically receive two or more antihypertensive agents long-term to achieve target blood pressure <140/90 mmHg. This practice increases the risk of adverse drug reactions, drug–drug interactions, and poor adherence. Consequently, the development of safe deprescribing strategies is particularly relevant for internal medicine and geriatric practice in Indonesia. The burden of hypertension and polypharmacy in West Java, especially among individuals aged ≥60 years, underscores the urgency of evaluating deprescribing safety within the Indonesian healthcare context.

1) RESEARCH GAPS

- Long-term follow-up (>1 year) in deprescribing RCTs remains scarce; most available trials are limited to 12 weeks or several months.
- Patient-centered outcomes (quality of life, falls, functional status) are inconsistently reported compared with biomedical endpoints (blood pressure, major cardiovascular events).
- Non-Western populations, including Southeast Asia and Indonesia, are underrepresented; most evidence originates from European cohorts (UK, France, Netherlands).
- No consensus exists on optimal patient selection criteria for antihypertensive deprescribing (frailty thresholds, blood pressure cut-offs, or biomarker combinations), and prospective validation is lacking.

LIMITATIONS OF THIS REVIEW

This review was conducted as a narrative synthesis rather than a systematic review. As such, study selection may be subject to author bias. The synthesis was qualitative, without new statistical pooling, and therefore cannot provide precise effect size estimates. Furthermore, the studies discussed were conducted in diverse healthcare systems (UK, France, Netherlands), limiting direct generalizability to the Indonesian context.

CONCLUSION

Available evidence consistently indicates that antihypertensive deprescribing can be safely implemented in frail geriatric patients under close monitoring, with short-term success rates exceeding 60% (OPTIMISE study: 66,3% in 12 weeks) and no increase in

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major cardiovascular events. Nonetheless, long-term safety, patient-centered outcomes, and region-specific data remain critical gaps. Clinical practice should adopt individualized deprescribing strategies rather than blanket policies, while future research must address these evidence deficits to guide geriatric care in Indonesia and beyond.

AUTHOR CONTRIBUTIONS, FUNDING, AND CONFLICTS OF INTEREST

The author was responsible for the conceptualization of the review question, development of the search strategy, selection and critical appraisal of relevant studies, synthesis and interpretation of findings, drafting of the manuscript, and subsequent revisions. As a practicing physician in primary care, the author also contributed to contextualizing the evidence within local epidemiological patterns and clinical practice implications, particularly in relation to healthcare delivery in West Java.

In addition, the author undertook the structuring of the review, methodological refinement, verification of citation accuracy, and comprehensive editorial oversight of the final manuscript.

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