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Review Article

Safety Outcomes After Deprescribing in Maintenance Hemodialysis: A Narrative Review of Current Evidence and Research Gaps

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ABSTRACT

Patients receiving maintenance hemodialysis commonly experience substantial medication burden because of multiple comorbidities, complex treatment regimens, and pharmacokinetic changes associated with advanced kidney disease. Deprescribing may reduce unnecessary or potentially inappropriate medication use and treatment burden; however, medication discontinuation may also result in withdrawal effects, symptom recurrence, medication re-initiation, or other clinically important consequences. This narrative review examined available evidence regarding safety outcomes following intentional deprescribing interventions in adults receiving maintenance hemodialysis. The review focused on adverse drug events, adverse drug withdrawal events, withdrawal or rebound effects, symptom recurrence, medication re-initiation, hospitalization, emergency department utilization, mortality, and other clinically relevant harms. Relevant studies were identified through structured literature identification using concepts related to hemodialysis, deprescribing, medication discontinuation, withdrawal, symptom recurrence, and safety outcomes. Due to heterogeneity in study designs, interventions, targeted medications, follow-up periods, and outcome definitions, findings were synthesized descriptively. Available evidence consisted mainly of small randomized or controlled studies, quality-improvement studies, feasibility studies, and implementation-based interventions. Overall, the included studies did not demonstrate a clear increase in serious adverse outcomes following structured deprescribing, although adverse drug events were inconsistently assessed. Symptom recurrence and medication re-initiation were reported in some patients, while withdrawal-related outcomes were rarely assessed using standardized definitions. Current evidence suggests that carefully selected and monitored deprescribing may be feasible in maintenance hemodialysis, but evidence remains insufficient to establish long-term safety.

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Further studies should use standardized safety definitions, medication-specific approaches, longer follow-up, and systematic assessment of patient-important outcomes.

INTRODUCTION

Patients receiving maintenance hemodialysis commonly experience a substantial medication burden because of multiple comorbidities, complex therapeutic regimens, and the simultaneous management of kidney-related and non-kidney-related conditions. Polypharmacy is particularly prevalent in this population and may contribute to increased pill burden, treatment complexity, medication-related problems, and the use of potentially inappropriate or unnecessary medications. In addition, advanced kidney disease and dialysis-related physiological changes can alter drug disposition and complicate medication selection and monitoring.

Deprescribing has emerged as an important component of medication optimization in chronic kidney disease and maintenance hemodialysis. It refers to a planned and supervised process of reducing the dose or discontinuing medications when their potential risks, treatment burden, or limited expected benefit outweigh their ongoing clinical value. In patients receiving hemodialysis, deprescribing interventions may target medications for which the original indication is no longer present, medications with limited benefit in the current clinical context, or medications associated with potentially inappropriate use. Several structured medication-review and targeted deprescribing interventions have demonstrated reductions in potentially inappropriate or unnecessary medication use among patients receiving hemodialysis.^{1-3,5,6}

Despite these potential benefits, medication discontinuation may itself be associated with clinically important consequences. Depending on the medication and clinical context, dose reduction or discontinuation may result in adverse drug withdrawal events (ADWEs), withdrawal or rebound effects, recurrence or worsening of previously controlled symptoms, or subsequent medication re-initiation. Other outcomes, including emergency department visits, hospitalization, and mortality, may also be relevant when assessing the safety of deprescribing interventions.

An important consideration is that these outcomes are not synonymous. An adverse drug event (ADE) represents harm associated with medication use, whereas an adverse drug withdrawal event (ADWE) refers specifically to an adverse event occurring following medication reduction or discontinuation. Symptom recurrence may reflect loss of the medication's therapeutic effect rather than a withdrawal reaction, while medication re-initiation may occur because of recurrent symptoms, patient preference, or other clinical considerations. Distinguishing these outcomes is particularly important in maintenance hemodialysis, where substantial comorbidity and polypharmacy can complicate the attribution of clinical events to individual medication changes.^{7,8}

Existing studies have evaluated several approaches to deprescribing in patients receiving hemodialysis, including pharmacist-led, multidisciplinary, algorithm-guided, and structured medication-review interventions. However, the primary emphasis of many studies has been reduction of medication burden or potentially inappropriate medication use rather than systematic evaluation of safety outcomes. Reviews addressing deprescribing and medication-review interventions in chronic kidney disease have similarly highlighted the limited and heterogeneous nature of the available evidence. Consequently, the safety profile of intentional deprescribing specifically in adults receiving maintenance hemodialysis remains incompletely characterized.^{4-6,9}

The available safety evidence is further limited by differences in targeted medications, deprescribing approaches, follow-up periods, outcome definitions, and methods used to identify adverse events or symptom recurrence. Some studies report serious adverse events or healthcare utilization, whereas others provide limited safety information or report that no serious events occurred. Therefore, the absence of reported serious harm in an individual study should not necessarily be interpreted as definitive evidence of the absence of clinically relevant risks.^{7,8}

A focused assessment of safety outcomes is therefore important for understanding the potential consequences of deprescribing in maintenance hemodialysis. This narrative review aims to examine the available



evidence regarding safety outcomes following intentional deprescribing interventions in adults receiving maintenance hemodialysis, with particular emphasis on adverse drug events, adverse drug withdrawal events, withdrawal or rebound effects, symptom recurrence, medication re-initiation, hospitalization, emergency department utilization, mortality, and other clinically relevant harms. The review also aims to identify important gaps in the current evidence and areas requiring further investigation.

MATERIALS AND METHODS

2.1. Review Approach

This study was conducted as a narrative review to critically examine the available evidence regarding safety outcomes following intentional deprescribing interventions in adults receiving maintenance hemodialysis. The review focused on adverse drug events (ADEs), adverse drug withdrawal events (ADWEs), withdrawal or rebound effects, symptom recurrence, medication re-initiation, hospitalization, emergency healthcare utilization, mortality, and other clinically relevant safety outcomes.

A narrative review approach was selected because the available literature was limited and heterogeneous with respect to study designs, deprescribing interventions, medications targeted, follow-up periods, and definitions and assessment of safety outcomes. The available evidence included randomized or controlled studies, prospective controlled studies, quality-improvement studies, feasibility studies, and observational or implementation-based studies. Because of the methodological and clinical heterogeneity of the available evidence, findings were synthesized descriptively rather than through quantitative meta-analysis.

2.2. Review Population

The population of interest comprised adults receiving maintenance hemodialysis for advanced kidney disease. The review focused primarily on maintenance hemodialysis because the directly relevant literature was predominantly conducted in this population.

Studies involving adults with advanced chronic kidney disease were considered when their findings were directly relevant to medication deprescribing and safety

outcomes; however, the primary synthesis was centered on evidence generated specifically in maintenance hemodialysis populations. Pediatric populations were excluded. Kidney transplant populations were also excluded unless data relating specifically to patients receiving dialysis could be separately identified.

2.3. Intervention

The intervention of interest was intentional medication deprescribing. For this review, deprescribing was considered a planned and supervised process involving dose reduction, discontinuation, or withdrawal of a medication when continued treatment was considered potentially unnecessary, inappropriate, burdensome, or associated with an unfavorable benefit-risk balance.

Eligible approaches included pharmacist-led deprescribing, multidisciplinary deprescribing programs, structured medication-review interventions involving actual medication discontinuation, algorithm-guided deprescribing, clinical decision-support-assisted deprescribing, targeted deprescribing of potentially inappropriate medications, patient-partnership or shared-decision-making approaches, and other structured interventions in which one or more medications were intentionally reduced or discontinued.

Medication review alone was not considered sufficient for inclusion unless it resulted in an actual deprescribing or medication discontinuation process.

2.4. Outcomes of Interest

The principal focus of the review was the safety of deprescribing following medication reduction or discontinuation.

The primary safety outcomes included:

Adverse drug events (ADEs) occurring following deprescribing.

Adverse drug withdrawal events (ADWEs) associated with medication discontinuation or dose reduction.⁸

Clinically important withdrawal symptoms.

Rebound effects following medication discontinuation.

Recurrence or worsening of symptoms or disease previously controlled by the discontinued medication.



Medication re-initiation or restart because of recurrence, withdrawal effects, clinical deterioration, or other problems.

Secondary outcomes included hospitalization, emergency department visits, unplanned healthcare utilization, mortality, serious adverse events, patient-reported clinical deterioration, and other clinically important harms associated with deprescribing.

ADEs, ADWEs, withdrawal symptoms, and symptom recurrence were considered distinct outcomes whenever the original study allowed them to be distinguished. The absence of reported serious adverse events was not interpreted as evidence that deprescribing was completely free of clinically relevant consequences when other safety outcomes were not systematically assessed.

2.5. Eligibility Criteria

2.5.1. Inclusion Criteria

Studies were considered eligible when they:

included adults receiving maintenance hemodialysis;

evaluated an intentional deprescribing intervention or structured deprescribing process;

involved actual medication dose reduction or discontinuation;

reported at least one safety-related outcome following deprescribing;

included outcomes such as ADEs, ADWEs, withdrawal or rebound effects, symptom recurrence, medication restart, hospitalization, emergency department utilization, mortality, or other clinically relevant harms; and represented human clinical or implementation research.

Relevant study designs included randomized controlled trials, prospective controlled studies, quality-improvement studies, feasibility studies, cohort studies, and other relevant clinical or implementation research.

2.5.2. Exclusion Criteria

The following were excluded:

pediatric studies;

studies without chronic kidney disease or hemodialysis relevance;

studies evaluating medication use without an actual deprescribing intervention;

studies examining medication adherence without deprescribing;

studies involving renal dose adjustment without medication discontinuation or reduction;

studies of adverse drug reactions in chronic kidney disease unrelated to deprescribing;

studies examining drug–drug interactions or polypharmacy without a deprescribing intervention;

animal or experimental studies;

editorials, commentaries, letters, and opinion pieces without relevant original clinical data;

reviews and systematic or scoping reviews as sources of primary evidence;

duplicate reports from the same underlying study; and

studies for which relevant dialysis data could not be separately identified.

Reviews and methodological publications were retained as background sources where relevant to understanding deprescribing concepts, terminology, frameworks, and previously identified research gaps.

2.6. Literature Identification

Relevant literature was identified through a structured literature identification process using predefined concepts related to chronic kidney disease, maintenance hemodialysis, deprescribing, medication discontinuation, adverse drug events, adverse drug withdrawal events, withdrawal, rebound effects, symptom recurrence, medication re-initiation, and safety outcomes.

The literature identification process considered both primary clinical studies and relevant background literature. Retrieved publications were assessed to distinguish studies directly addressing intentional deprescribing in hemodialysis from studies addressing related but distinct topics, including general adverse drug reactions, drug–drug interactions, polypharmacy, and deprescribing tools.

Supplementary citation screening was also undertaken to identify additional relevant publications. Greater emphasis was placed on evidence published from 2017 to 2026, while earlier publications were considered



when relevant to background concepts, definitions, or established deprescribing principles.

2.7. Study Selection

Identified publications were initially assessed according to their relevance to the review question. Potentially relevant studies were subsequently assessed in greater detail against the predefined eligibility criteria. Studies were retained when they directly addressed intentional deprescribing in adults receiving maintenance hemodialysis and provided information relevant to at least one prespecified safety outcome.

Reports originating from the same underlying study were treated as a single study to avoid double counting. Where multiple publications described the same study, the most complete publication was used as the principal source where appropriate.

2.8. Data Extraction

The following information was extracted from eligible studies where available:

first author and year of publication;
country and clinical setting;
study design;
sample size and patient characteristics;
dialysis status;
medications or medication classes targeted for deprescribing;
deprescribing intervention;
healthcare professionals involved;
patient involvement or shared decision-making;
follow-up period;
primary study outcomes;
ADEs;
ADWEs;
withdrawal symptoms;
rebound effects;
symptom or disease recurrence;
medication re-initiation or restart;
hospitalization;

emergency department visits;
mortality;
other safety outcomes;
authors' conclusions regarding safety; and
study limitations.

When a particular safety outcome was not reported in a study, it was recorded as not reported (NR) rather than assuming that no event occurred. This distinction was considered important because some studies reported the absence of serious adverse events without systematically assessing withdrawal effects, symptom recurrence, or medication re-initiation.

2.9. Evidence Synthesis

Because the included studies differed substantially in study design, interventions, populations, medications targeted, follow-up periods, and outcome definitions, the evidence was synthesized descriptively and qualitatively.

The findings were organized into the following major safety domains:

Adverse drug events;
Adverse drug withdrawal events;⁸
Symptom recurrence and rebound;
Medication re-initiation;
Hospitalization and emergency healthcare utilization; and
Mortality and other safety outcomes.

The synthesis emphasized patterns of findings, consistency between studies, methodological limitations, and gaps in safety reporting rather than calculating pooled effect estimates.

2.10. Assessment of Evidence Limitations

2.11. Ethical Considerations

This review used previously published literature and did not involve the collection or analysis of new patient-level data. Therefore, institutional ethical approval was not required.

RESULTS AND DISCUSSION

3.1. Characteristics of the Available Evidence



The available evidence regarding safety outcomes following deprescribing in adults receiving maintenance hemodialysis remains limited and heterogeneous. The identified literature includes randomized or controlled studies, prospective controlled studies, quality-improvement initiatives, feasibility studies, and implementation-based interventions. Most studies were primarily designed to evaluate the feasibility of deprescribing, reduction of potentially inappropriate medications, medication burden, or implementation of structured medication-review interventions rather than safety outcomes as their principal endpoint.

The deprescribing approaches differed considerably between studies. Interventions included pharmacist-led medication reviews, multidisciplinary deprescribing programs, structured medication reconciliation, algorithm-guided approaches, and targeted discontinuation of potentially inappropriate medications. The medications targeted also varied according to the clinical setting and individual patient characteristics and included proton pump inhibitors, α 1-adrenergic blockers, quinine, statins, gabapentinoids, antiplatelet agents, and other medications considered potentially inappropriate or of limited ongoing benefit.

The duration and nature of follow-up also varied between studies. Some investigations included structured follow-up after medication discontinuation, whereas others focused primarily on implementation or medication reduction. Safety assessment was similarly inconsistent. Some studies specifically reported adverse events, serious adverse events, symptom recurrence, or medication re-initiation, while others provided limited information regarding clinical consequences following deprescribing.

3.2. Adverse Drug Events

Evidence regarding adverse drug events following deprescribing in maintenance hemodialysis remains limited. Only a small proportion of the available studies were specifically designed to evaluate ADEs as a primary outcome. Consequently, the available evidence provides more information about the feasibility and implementation of deprescribing than about the comparative incidence of adverse events.

One of the most directly relevant studies evaluated hospitalized patients with end-stage kidney disease receiving chronic hemodialysis. The intervention involved medication reconciliation, individualized deprescribing recommendations, clinician review, and post-discharge follow-up. Thirty-day ADEs were assessed after discharge. Three ADEs occurred in the control group compared with two in the intervention group, with no statistically significant difference between groups. Gastrointestinal bleeding was the most frequently identified event, with three events attributed to antiplatelet therapy. No significant difference in readmission was observed between the groups.¹²

A prospective controlled quality-improvement study involving patients receiving hemodialysis evaluated a structured multidisciplinary deprescribing intervention. The intervention substantially increased the proportion of patients in whom at least one potentially inappropriate medication was deprescribed compared with the control group. However, the study was not primarily designed or statistically powered to determine the effect of deprescribing on ADEs. Its findings therefore provide stronger evidence regarding the feasibility and implementation of medication deprescribing than regarding comparative safety.¹⁴

Similarly, an outpatient hemodialysis quality-improvement study evaluating targeted deprescribing of potentially inappropriate medications reported no adverse events during the intervention period. However, because adverse events were not the primary focus and were not prospectively adjudicated as a principal outcome, the absence of reported events should be interpreted cautiously.¹⁰

More recent multidisciplinary deprescribing interventions have also reported no serious adverse events during follow-up. Nevertheless, some deprescribing plans were discontinued because of recurrent symptoms or patient preference. These findings demonstrate that the absence of serious ADEs does not necessarily mean that medication discontinuation produces no clinically relevant consequences.¹⁵⁻¹⁷

Another intervention reported no serious adverse events but documented medication re-initiation in some patients because of recurrent symptoms. Four proton pump inhibitors were restarted following recurrent



heartburn, while one gabapentinoid was restarted following recurrence of neuropathic pain. These events were not necessarily ADEs, but they represent clinically relevant consequences occurring after medication discontinuation.¹⁵

A recent feasibility study conducted in dialysis clinics similarly reported no serious adverse events. Symptom recurrence occurred in a subset of participants, although the reported events did not result in unplanned healthcare utilization. This further illustrates the importance of evaluating safety beyond serious ADEs alone.¹⁷

Overall, the available studies have not demonstrated a clear increase in serious ADEs following structured deprescribing interventions in maintenance hemodialysis. However, this observation should not be interpreted as proof that deprescribing is universally safe. Most studies were small, several were not adequately powered to detect differences in ADEs, follow-up was relatively limited, and adverse events were not consistently defined or systematically assessed.

3.3. Adverse Drug Withdrawal Events and Withdrawal

Adverse drug withdrawal events represent a distinct safety consideration when medications are reduced or discontinued. Withdrawal-related consequences may include physiological withdrawal symptoms, rebound phenomena, recurrence of symptoms, or other clinical changes that become apparent after medication reduction.⁸

The identification of withdrawal-related events can be particularly challenging in patients receiving maintenance hemodialysis because these individuals frequently have multiple comorbidities and symptoms that may arise from advanced kidney disease, dialysis treatment, or other concurrent medications. Consequently, establishing whether a symptom is directly related to medication withdrawal may require careful temporal and clinical assessment.

The available evidence suggests that withdrawal-related consequences have more commonly been described as symptom recurrence or medication restart rather than formally assessed ADWEs. Most studies did not use standardized definitions or systematic

assessment methods for withdrawal events. Therefore, the current literature should primarily be interpreted as evidence regarding clinically relevant consequences following medication discontinuation rather than as a reliable estimate of ADWE incidence.^{8,15-17}

In several studies, deprescribing plans were discontinued because of recurrent symptoms or patient preference. These events are clinically relevant but cannot automatically be classified as ADWEs because sufficient information may not be available to establish a direct causal relationship with medication withdrawal.

Withdrawal-related consequences may be medication-specific; findings for one medication class should therefore not automatically be generalized to others.⁸

3.4. Symptom Recurrence and Rebound Effects

Symptom recurrence and rebound effects represent important but incompletely characterized consequences of deprescribing in maintenance hemodialysis. Although these outcomes do not necessarily constitute conventional ADEs, they may determine whether a medication can remain discontinued and may lead to modification or reversal of the deprescribing plan.

Symptom recurrence has been reported in several interventions. Recurrent heartburn led to re-initiation of proton pump inhibitors, while recurrent neuropathic pain led to gabapentinoid re-initiation, showing that initial discontinuation does not always result in sustained discontinuation.¹⁵

Other multidisciplinary deprescribing interventions similarly reported discontinuation of some deprescribing plans because of recurrent symptoms or patient preference. Although these events were not necessarily serious adverse events, they were clinically important because they altered the treatment plan and limited sustained medication discontinuation.

Symptom recurrence has also been observed in feasibility research among dialysis patients without resulting in unplanned healthcare utilization. This suggests that recurrence of symptoms does not necessarily lead to serious clinical deterioration and may sometimes be managed through outpatient reassessment, modification of treatment, or medication re-initiation.



The clinical meaning of symptom recurrence may depend on the medication being discontinued. Discontinuation of a medication used primarily for symptomatic control may result in return of the underlying symptoms without representing a pharmacological withdrawal syndrome. In contrast, discontinuation of certain medications may result in physiological withdrawal or rebound effects. These situations should therefore be distinguished whenever sufficient clinical information is available.

3.5. Medication Re-initiation and Restart

Medication re-initiation is an important downstream outcome following deprescribing. A medication may be restarted because of recurrence or worsening of the original symptoms, withdrawal or rebound effects, clinical deterioration, or patient preference.^{15,16}

Medication re-initiation occurred in a subset of patients; four proton pump inhibitors were re-initiated for recurrent heartburn and one gabapentinoid for recurrent neuropathic pain.¹⁵

Medication restart has also been reported when deprescribing plans could not be maintained because of recurrent symptoms or patient preference. These observations support the concept that deprescribing should be viewed as a dynamic clinical process rather than a one-time discontinuation decision. Continued follow-up allows clinicians to determine whether a medication remains unnecessary after discontinuation or whether its therapeutic benefit remains clinically important.

Importantly, medication re-initiation should not automatically be interpreted as evidence that the original deprescribing decision was inappropriate. A medication may initially appear to have limited ongoing benefit, while the patient's response following discontinuation may reveal a clinically meaningful therapeutic effect. Similarly, restarting a medication because of patient preference does not necessarily indicate pharmacological failure.

3.6. Hospitalization and Emergency Department Utilization

Hospitalization and emergency department utilization are important patient-centered outcomes when

evaluating the safety of deprescribing. Clinically significant deterioration following medication discontinuation may result in urgent medical assessment or hospital-based care. However, evidence concerning these outcomes following deprescribing in maintenance hemodialysis remains limited.

In the study involving hospitalized patients with end-stage kidney disease receiving maintenance hemodialysis, an individualized medication-deprescribing intervention was implemented together with medication reconciliation, clinician review, and post-discharge follow-up. No significant difference in readmissions was observed between the intervention and control groups. The number of ADEs also did not differ significantly between groups.¹²

These findings do not indicate an apparent increase in short-term readmission following the intervention, but the relatively small sample limits the ability to exclude clinically important differences in uncommon events.

Other deprescribing studies have primarily focused on medication reduction, feasibility, or implementation rather than hospitalization or emergency department utilization as predefined safety outcomes. Consequently, hospitalization and unplanned healthcare utilization were either not reported or were insufficiently powered to determine whether deprescribing influenced healthcare use.

Importantly, symptom recurrence does not necessarily result in hospitalization or emergency care. In one feasibility study, some participants experienced symptom recurrence following medication discontinuation, but these events did not result in unplanned healthcare utilization. Some consequences of deprescribing may therefore be managed through outpatient reassessment, medication modification, or re-initiation.

The absence of an observed increase in hospitalization should nevertheless be interpreted cautiously. Hospitalization is relatively infrequent and may require larger populations and longer follow-up to detect meaningful differences. Furthermore, patients receiving maintenance hemodialysis may be hospitalized for numerous reasons unrelated to deprescribing, making causal attribution difficult.

3.7. Mortality and Other Safety Outcomes



Mortality represents an important clinical outcome when evaluating medication deprescribing in maintenance hemodialysis. However, the available evidence provides very limited information regarding mortality following deprescribing interventions. Most studies were small, had relatively short follow-up periods, and were primarily designed to evaluate medication reduction, feasibility, implementation, or potentially inappropriate medication use rather than mortality.^{7,12,14-17}

Consequently, the current evidence does not permit a reliable assessment of the effect of deprescribing on mortality in patients receiving maintenance hemodialysis. The absence of reported mortality differences should not be interpreted as evidence that deprescribing has no effect on survival because most available studies were not powered to detect mortality differences.

Patients receiving maintenance hemodialysis also have multiple competing causes of morbidity and mortality, making attribution of an individual death to medication discontinuation particularly challenging.

Other safety outcomes were similarly inconsistently reported. Several studies reported no serious adverse events during the intervention or follow-up period. Although this provides some information regarding the feasibility of deprescribing, interpretation is limited when adverse events are not systematically defined or adjudicated.

The absence of serious events does not exclude less severe but clinically meaningful consequences such as withdrawal symptoms, symptom recurrence, reduced treatment tolerance, or medication re-initiation. Patient preference and treatment acceptability were also relevant to some interventions. Although patient preference is not itself a safety outcome, it may influence the sustainability of deprescribing and should therefore be considered alongside clinical outcomes.

The potential consequences of deprescribing are also likely to vary according to the pharmacological properties of the medication, duration of exposure, underlying indication, and individual patient characteristics. Findings from studies targeting a particular medication class therefore cannot necessarily be generalized to all medications used in maintenance hemodialysis.^{3,8}

4. RESEARCH GAPS

Despite increasing interest in deprescribing and medication optimization in patients receiving maintenance hemodialysis, evidence regarding the safety consequences of medication discontinuation remains limited and heterogeneous. Much of the available research has focused on reducing medication burden, identifying potentially inappropriate medications, evaluating feasibility, or implementing structured deprescribing interventions. In comparison, patient-important safety outcomes following medication discontinuation have received less systematic attention.

4.1. Limited Evidence on Adverse Drug Events

A major gap is the limited number of studies specifically designed to evaluate adverse drug events following deprescribing. Although some studies have reported adverse events, most were not primarily powered to detect differences in ADEs between deprescribing and usual-care groups. Safety assessment was frequently secondary to evaluation of medication reduction or intervention feasibility.^{7,8,12,14-17}

4.2. Inconsistent Assessment of Adverse Drug Withdrawal Events

Adverse drug withdrawal events remain poorly characterized in maintenance hemodialysis. Existing studies rarely use standardized definitions or systematic approaches for identifying withdrawal-related events. Instead, clinically relevant consequences are often described using terms such as withdrawal symptoms, rebound, symptom recurrence, or treatment failure.⁸

4.3. Inadequate Reporting of Symptom Recurrence and Rebound

Symptom recurrence emerged as an important consequence across several deprescribing interventions, yet it has not been consistently quantified. Some studies reported recurrent symptoms that resulted in modification or reversal of the deprescribing plan, whereas others provided insufficient information to determine whether symptoms occurred following medication discontinuation.

Future studies should systematically document the symptom that recurred, the medication that was



discontinued, the time between deprescribing and symptom recurrence, symptom severity and duration, whether medical intervention was required, and whether medication re-initiation resulted in improvement.

4.4. Limited Evidence on Medication Re-initiation

Medication re-initiation is an important but underreported outcome. Some studies demonstrated that medications may need to be restarted following deprescribing because of symptom recurrence or other clinical considerations. However, the frequency of medication restart and the reasons for re-initiation have not been consistently reported.^{15,16}

Future studies should prospectively document the medication restarted, reason for restarting, time to restart, severity of symptoms prompting re-initiation, and whether the patient subsequently remained on the medication. Such reporting would provide a more complete assessment of the sustainability of deprescribing.

4.5. Insufficient Evidence on Hospitalization and Emergency Healthcare Utilization

Evidence regarding hospitalization and emergency department utilization following deprescribing remains sparse. Most available studies were small and were not specifically designed to detect differences in healthcare utilization.

Future studies should include hospitalization and emergency department utilization as predefined outcomes and should assess whether each event is temporally and clinically related to medication discontinuation.

4.6. Lack of Long-term Safety Data

Most available deprescribing studies have relatively short follow-up periods. Consequently, the long-term consequences of medication discontinuation remain poorly understood.^{12,14-17}

Longer follow-up is necessary to determine whether deprescribing is associated with sustained medication discontinuation, delayed symptom recurrence, delayed withdrawal or rebound effects, changes in hospitalization, changes in quality of life, changes in treatment

burden, mortality, or subsequent medication re-initiation.

4.7. Lack of Standardized Safety Outcome Definitions

A major methodological limitation across the literature is heterogeneity in outcome definitions. Studies do not consistently distinguish among ADEs, ADWEs, withdrawal symptoms, rebound effects, symptom recurrence, medication restart, serious adverse events, and unrelated clinical events.^{7,8}

This makes direct comparison between studies difficult and limits the possibility of quantitative synthesis.

4.8. Limited Medication-specific Evidence

The potential consequences of deprescribing are likely to differ between medication classes. However, the current evidence base does not adequately establish which medications can be discontinued safely and which may require more cautious tapering and monitoring in maintenance hemodialysis.^{3,8}

Future research should examine medication classes separately and report the original indication, duration of prior treatment, deprescribing method, whether discontinuation was abrupt or gradual, tapering schedule where applicable, potential withdrawal risk, symptom recurrence, medication restart, and patient-important clinical outcomes.

4.9. Limited Evidence from Diverse Dialysis Populations

The available evidence is predominantly derived from selected hemodialysis populations and, in several cases, individual or limited healthcare settings. Evidence from different healthcare systems, geographical regions, socioeconomic settings, and patient populations remains limited.

4.10. Insufficient Patient-centered Outcomes

Most studies have focused on medication-related or healthcare outcomes, whereas patient-reported outcomes have received comparatively less attention. Reduction in medication burden may be clinically beneficial only if it does not compromise symptom control, functional status, treatment satisfaction, or quality of life.^{7,14-17}



4.11. Lack of Adequately Powered Randomized Trials

Although randomized and controlled deprescribing studies have begun to emerge, the overall evidence remains dominated by small feasibility, quality-improvement, and implementation studies. These designs are useful for evaluating feasibility but are generally insufficient to determine uncommon safety outcomes.

12,16

4.12. Need for a Standardized Safety Framework

Taken together, the principal gap is not simply the absence of deprescribing interventions; rather, it is the limited and inconsistent evaluation of what happens after medications are discontinued.

Future studies should move beyond reporting the number of medications successfully discontinued and systematically evaluate the complete post-deprescribing trajectory:

Medication discontinuation → withdrawal/rebound → symptom recurrence → medication re-initiation → healthcare utilization → long-term clinical outcomes

A standardized framework incorporating these outcomes would allow future studies to generate more clinically meaningful evidence and help clinicians evaluate the potential benefits of reducing medication burden alongside the possible consequences of medication discontinuation.

CONCLUSIONS

Deprescribing may provide an important approach to reducing medication burden and potentially inappropriate medication use in adults receiving maintenance hemodialysis. The available evidence indicates that structured and monitored deprescribing interventions have generally been feasible and have not demonstrated a clear increase in serious short-term adverse outcomes. However, the evidence remains limited and heterogeneous, and most available studies were not specifically designed or adequately powered to establish the safety of deprescribing.

Adverse drug events have been inconsistently assessed, while adverse drug withdrawal events, withdrawal or rebound effects, symptom recurrence, and medication

re-initiation have rarely been evaluated using standardized definitions and methods. Symptom recurrence and medication restart appear to be clinically relevant consequences that should be considered when evaluating the sustainability of deprescribing. Evidence regarding hospitalization, emergency department utilization, mortality, and other long-term outcomes remains insufficient.

Therefore, current evidence supports careful and individualized deprescribing with appropriate clinical monitoring, rather than assuming that medication discontinuation is universally free of risk. Future studies should use standardized safety definitions, medication-specific approaches, predefined safety endpoints, longer follow-up, larger multicenter populations, and systematic assessment of patient-important outcomes.

A comprehensive evaluation of deprescribing should extend beyond the number of medications discontinued and consider what happens after discontinuation, including withdrawal or rebound effects, symptom recurrence, medication re-initiation, healthcare utilization, and long-term clinical outcomes. Such evidence will be important for developing safer and more patient-centered deprescribing strategies in maintenance hemodialysis.

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AUTHOR CONTRIBUTIONS

Riyad Hossain conceived the review topic, developed the review question and objectives, conducted the literature identification and study selection, extracted and interpreted the relevant evidence, and drafted the manuscript. Abhisek Chaudhary, Dhruva Narayan K, Shibankar Debnath, and Sayan Paul contributed to literature screening, evidence checking, interpretation of findings, and critical revision of the manuscript. All authors reviewed and approved the final version of the manuscript and agree to be accountable for all aspects of the work.



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COMPETING INTERESTS

The authors declare that they have no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable. This study was a narrative review based exclusively on previously published literature and did not involve the collection, use, or analysis of new human participant data.

CONSENT FOR PUBLICATION

Not applicable. This manuscript does not contain individual-level personal data or identifiable information from human participants.

AVAILABILITY OF DATA AND MATERIALS

Not applicable. No datasets were generated or analyzed during the current study.

AUTHORS' INFORMATION

Not applicable.

DECLARATION ON THE USE OF GENERATIVE AI IN SCIENTIFIC WRITING

During the preparation of this manuscript, the authors used ChatGPT (OpenAI) for language editing, organization of the manuscript, and assistance with drafting and refining text. The authors reviewed and critically evaluated all generated content and remain fully responsible for the accuracy, interpretation, and final content of the manuscript.

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