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BURDEN OF POLYPHARMACY AND DRUG–DRUG INTERACTIONS IN HAEMODIALYSIS PATIENTS WITH CHRONIC KIDNEY DISEASE: IMPLICATIONS FOR MEDICATION SAFETY AND CLINICAL PHARMACY PRACTICE

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ABSTRACT

Background: Chronic kidney disease (CKD) patients undergoing haemodialysis are exposed to complex pharmacotherapy due to multiple comorbidities, resulting in a high prevalence of polypharmacy. This significantly increases the risk of drug–drug interactions (DDIs), adverse drug reactions (ADRs), and medication-related complications, posing major challenges to medication safety. **Objective:** This review aims to evaluate the burden of polypharmacy and drug–drug interactions in haemodialysis patients with CKD and to examine their implications for medication safety and clinical pharmacy practice. **Methods:** A systematic-style literature review was conducted using PubMed, Scopus, and Web of Science databases. Relevant studies published in the last decade were identified using predefined keywords related to CKD, haemodialysis, polypharmacy, and DDIs. Study selection followed PRISMA guidelines, and data were synthesized qualitatively, focusing on prevalence, mechanisms, clinical outcomes, and pharmacy interventions. **Results:** The review identified a high prevalence of polypharmacy, affecting approximately 60–90% of haemodialysis patients, with an average of 8–12 medications per patient. DDIs were reported in 50–85% of cases, with a significant proportion classified as moderate to severe. Pharmacokinetic alterations, including reduced renal clearance, altered protein binding, and dialysis-related drug removal, contribute substantially to interaction risk. High-risk drug classes include cardiovascular agents, antidiabetics, antibiotics, and anticoagulants. DDIs were associated with increased ADRs, hospitalization, and mortality. Evidence suggests that clinical pharmacy interventions, including medication therapy management, reconciliation, and interaction screening, significantly improve medication safety and therapeutic outcomes. **Conclusion:** Polypharmacy and DDIs are highly prevalent and clinically significant in haemodialysis patients with CKD. Integrating clinical pharmacists into multidisciplinary care, along with structured medication review and pharmacovigilance systems, is essential to reduce medication-related harm and improve patient outcomes.

KEYWORDS: Chronic kidney disease; haemodialysis; polypharmacy; drug–drug interactions; medication safety; clinical pharmacy; adverse drug reactions; pharmacovigilance.

INTRODUCTION

Chronic kidney disease (CKD) is a major global public health concern characterized by progressive and irreversible decline in renal function. According to recent global burden estimates, CKD affects approximately 9–13% of the adult population worldwide and is among the leading causes of morbidity and premature mortality, particularly in low- and middle-income countries. [1,2] The rising prevalence is largely driven by increasing incidence of diabetes mellitus, hypertension, aging populations, and lifestyle-related risk factors. Importantly, CKD contributes significantly to healthcare expenditure due to long-term treatment requirements and complications.

Patients with advanced CKD frequently require renal replacement therapy, with haemodialysis being the most widely utilized modality. Haemodialysis patients

represent a clinically complex population due to the coexistence of multiple comorbid conditions such as cardiovascular disease, anaemia, mineral and bone disorders, and metabolic abnormalities.[3] The management of these conditions necessitates the use of multiple medications, often prescribed by different specialists, thereby increasing therapeutic complexity. Furthermore, dialysis procedures themselves influence drug disposition by altering drug clearance and necessitating post-dialysis dosing adjustments, adding a layer of pharmacotherapeutic challenge.

Polypharmacy, typically defined as the concurrent use of five or more medications, is highly prevalent among haemodialysis patients, with reported rates exceeding 80% in several observational studies. [4] Polypharmacy in CKD can be broadly categorized into appropriate polypharmacy, where multiple medications are clinically justified based on evidence-based guidelines, and inappropriate polypharmacy, characterized by unnecessary, duplicative, or potentially harmful medications. While appropriate polypharmacy is often unavoidable in CKD management, inappropriate polypharmacy significantly increases the risk of adverse drug events, medication non-adherence, and drug–drug interactions (DDIs).

Polypharmacy in haemodialysis patients can be categorized based on clinical appropriateness and associated risks, as summarized in Table 1.

Table 1: Classification of Polypharmacy in Chronic Kidney Disease Patients Undergoing Haemodialysis.

Type of Polypharmacy	Definition	Clinical Relevance in CKD	Implications for Medication Safety
Appropriate polypharmacy	Concurrent use of multiple medications that are clinically indicated and evidence-based for managing comorbid conditions	Common in haemodialysis patients requiring treatment for hypertension, diabetes, anaemia, and mineral bone disease	Enhances therapeutic outcomes when monitored appropriately; requires regular review to minimize cumulative toxicity
Inappropriate polypharmacy	Use of medications without a clear indication, or where potential harms outweigh benefits	May include unnecessary continuation of drugs, use of nephrotoxic agents, or suboptimal prescribing practices	Increases risk of adverse drug reactions (ADRs), drug–drug interactions (DDIs), and poor adherence
Hyper polypharmacy	Use of ten or more medications simultaneously	Frequently observed in patients with multiple comorbidities and complex therapeutic regimens	Associated with a higher risk of severe DDIs, medication errors, hospitalization, and reduced quality of life
Therapeutic duplication	Concurrent use of two or more drugs with similar pharmacological actions without a clear clinical justification	May occur due to multiple prescribers or a lack of medication reconciliation	Leads to additive toxicity, increased ADRs, and avoidable drug exposure
Potentially inappropriate medications (PIMs)	Drugs that pose a higher risk than benefit in CKD due to altered pharmacokinetics or pharmacodynamics	Includes drugs requiring dose adjustment or avoidance in renal impairment	Increases risk of drug accumulation, toxicity, and preventable adverse outcomes
Prescribing cascade	The addition of new medications to manage the adverse effects of existing therapy rather than addressing the root cause	Common in CKD, where symptoms of ADRs are misinterpreted as new clinical conditions	Contributes to unnecessary polypharmacy, increased pill burden, and medication-related harm

Drug–drug interactions represent a critical and often under-recognized challenge in CKD patients undergoing haemodialysis. The altered physiological state in CKD profoundly affects pharmacokinetics and pharmacodynamics, thereby modifying drug response. Reduced renal clearance leads to accumulation of renally excreted drugs, while uraemia can alter hepatic metabolism and protein binding, increasing the free fraction of drugs.[5] Additionally, haemodialysis can remove certain drugs from circulation, resulting in subtherapeutic levels if not appropriately managed. These factors collectively increase the susceptibility of CKD patients to clinically significant DDIs, which may manifest as toxicity, therapeutic failure, or exacerbation of comorbid conditions.

The clinical consequences of DDIs in haemodialysis patients are substantial. Studies have demonstrated that DDIs contribute to increased incidence of adverse drug reactions (ADRs), electrolyte imbalances such as hyperkalaemia, cardiovascular events, and hospital admissions. [6] Importantly, a significant proportion of these interactions are preventable, highlighting the need for proactive medication management strategies.

From a medication safety perspective, the identification, prevention, and management of DDIs are central to improving therapeutic outcomes in CKD. Clinical pharmacists are uniquely positioned to address these challenges through medication therapy management (MTM), comprehensive medication review, reconciliation, and the use of evidence-based interaction screening tools. Despite strong evidence supporting the

role of clinical pharmacists in reducing medication-related harm, their integration into nephrology care teams remains inconsistent, particularly in resource-constrained healthcare settings.[7]

Existing literature on polypharmacy and DDIs in haemodialysis patients is fragmented, with variability in definitions, methodologies, and reported outcomes. Moreover, there is limited emphasis on translating these findings into clinical pharmacy practice and medication safety frameworks. Therefore, a comprehensive synthesis of current evidence is essential to bridge this gap and inform clinical decision-making.

Rationale of the study

Given the high burden of polypharmacy and the increased risk of DDIs in haemodialysis patients, there is a critical need to systematically evaluate their clinical implications and identify strategies to enhance medication safety through clinical pharmacy interventions.

AIM OF THE STUDY

This review aims to evaluate the burden of polypharmacy and drug–drug interactions in patients with chronic kidney disease undergoing haemodialysis and to explore their implications for medication safety and clinical pharmacy practice.

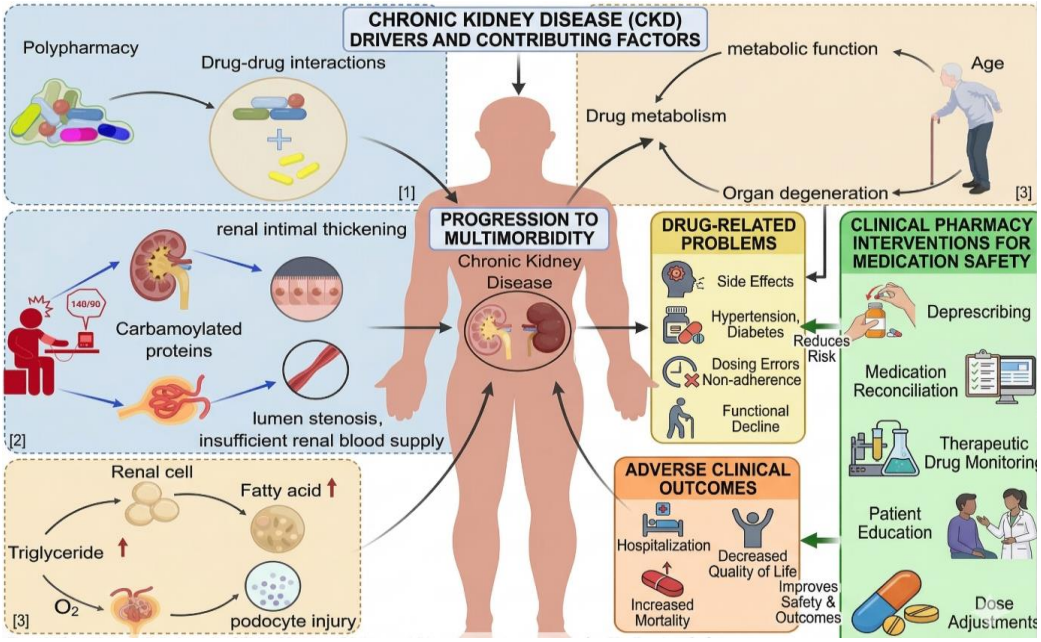

Figure 1: Pathway Linking CKD, Polypharmacy, and Drug–Drug Interactions.

Figure 1 illustrates the progression from chronic kidney disease to comorbidities, leading to polypharmacy, drug–drug interactions, and adverse drug reactions.

MATERIALS AND METHODS

Study Design and Review Framework

This review was conducted using a systematically structured narrative approach to comprehensively evaluate the burden of polypharmacy and drug–drug interactions (DDIs) in patients with chronic kidney disease (CKD) undergoing haemodialysis. Although the study did not involve quantitative meta-analysis, it incorporated key methodological elements of systematic reviews to enhance transparency, reproducibility, and methodological rigor.

The design and reporting of the review were guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 framework, ensuring a standardized approach to literature identification, screening, and synthesis. This hybrid methodology enables both breadth of evidence exploration and critical thematic interpretation, which is particularly relevant for complex clinical pharmacy topics such as medication safety and pharmacovigilance.

Data Sources and Search Strategy

A comprehensive and systematic literature search was conducted across three major biomedical databases: PubMed/MEDLINE, Scopus, and Web of Science, which collectively provide extensive coverage of peer-reviewed clinical and pharmacy practice literature.

The search was restricted to studies published between January 2015 and March 2025, to ensure inclusion of contemporary evidence reflecting current prescribing practices, dialysis protocols, and pharmacotherapeutic advancements.

A combination of Medical Subject Headings (MeSH) and free-text keywords was employed to maximize retrieval sensitivity. Boolean operators (“AND,” “OR”) and truncation techniques were used to refine the search strategy and capture relevant variations in terminology.

Core Search Strategy

("chronic kidney disease" OR "CKD" OR "end-stage renal disease" OR "renal failure")
AND
("haemodialysis" OR "haemodialysis" OR "renal dialysis")
AND
("polypharmacy" OR "multiple drug therapy" OR "medication burden")
AND
("drug–drug interactions" OR "drug interactions" OR "DDIs")
AND
("medication safety" OR "adverse drug reactions" OR "pharmacovigilance" OR "medication errors")

To enhance comprehensiveness, manual screening of reference lists (snowballing) and citation tracking of key articles were also performed.

ELIGIBILITY CRITERIA

Inclusion Criteria

Studies were considered eligible if they met the following criteria:

- Included adult patients (≥18 years) diagnosed with CKD undergoing haemodialysis
- Reported outcomes related to polypharmacy prevalence, drug–drug interactions, or medication safety parameters
- Employed observational (cross-sectional, cohort, case-control) or interventional study designs, as well as systematic reviews
- Published in peer-reviewed journals indexed in recognized databases
- Available in the English language

Exclusion Criteria

Studies were excluded based on the following:

- Studies involving non-dialysis CKD populations without separate haemodialysis subgroup analysis
- Research focusing exclusively on paediatric populations
- Case reports, editorials, commentaries, conference abstracts, and grey literature lacking methodological rigor
- Studies with insufficient or unclear reporting of polypharmacy or DDI-related outcomes

Study Selection Process

All retrieved citations were imported into a reference management software (e.g., EndNote/Zotero), where duplicate records were identified and removed.

The study selection process was conducted in two sequential phases:

1. Title and abstract screening: Studies were screened for relevance based on predefined eligibility criteria.
2. Full-text review: Potentially eligible articles were assessed in detail to confirm inclusion.

To minimize selection bias, discrepancies in study inclusion were resolved through consensus-based discussion. The entire selection process was systematically documented and presented using a PRISMA flow diagram, ensuring methodological transparency and reproducibility.

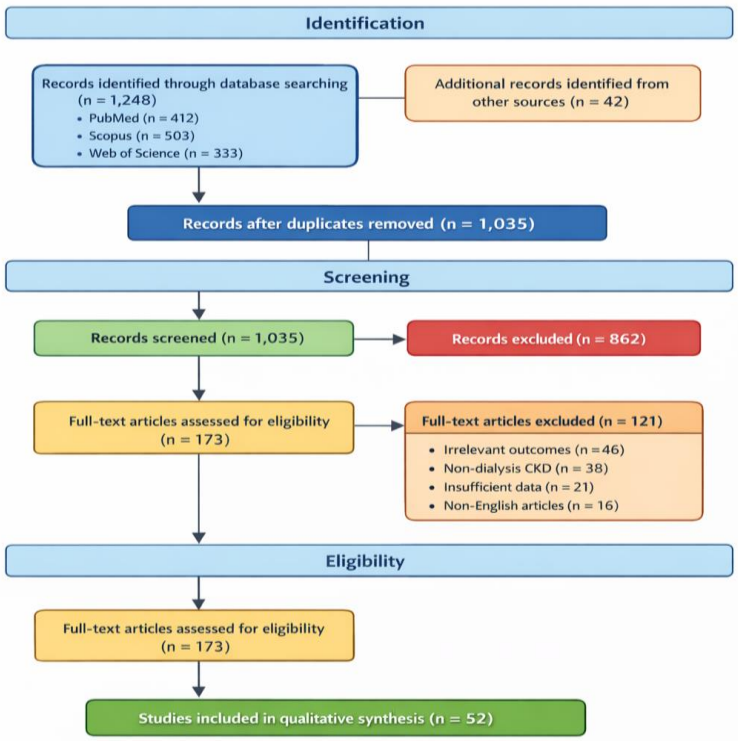

Figure 2: PRISMA 2020 Flow Diagram Illustrating Study Selection Process for the Review of Polypharmacy and Drug–Drug Interactions in Haemodialysis Patients with Chronic Kidney Disease.

The study selection process, as illustrated in Figure 2, presents a systematic process of study identification, screening, eligibility assessment, and final inclusion in accordance with PRISMA 2020 guidelines. A total of 1,248 records were initially identified through database searching, including PubMed (n = 412), Scopus (n = 503), and Web of Science (n = 333), along with 42 additional records identified through manual searching of reference lists and other sources.

Following the removal of duplicate records, 1,035 unique studies remained and were subjected to title and abstract screening, of which 862 records were excluded based on irrelevance to the study objectives. A total of 173 full-text articles were subsequently assessed for eligibility.

Among these, 121 studies were excluded for specific reasons, including lack of relevant outcomes (n = 46), absence of haemodialysis-specific data (n = 38), insufficient methodological or outcome data (n = 21), and non-English language publications (n = 16).

Ultimately, 52 studies met the predefined inclusion criteria and were included in the qualitative synthesis. This structured selection process ensured methodological transparency and minimized selection bias, thereby enhancing the reliability of the evidence included in this review.

Data Extraction and Management

Data from included studies were systematically extracted using a standardized and pilot-tested data extraction form to ensure consistency and completeness.

The following variables were collected

- Study characteristics (author, publication year, country, study design)
- Patient demographics (sample size, age, comorbidities)
- Definitions and thresholds used for polypharmacy
- Number and categories of medications prescribed
- Identification and classification of DDIs (mechanism, severity)
- Clinical outcomes (e.g., adverse drug reactions, hospitalization, mortality)
- Description of clinical pharmacy interventions, where applicable

Data extraction focused on both quantitative outcomes and qualitative insights, enabling comprehensive thematic synthesis.

Quality Assessment and Risk of Bias

The methodological quality of included studies was critically appraised using validated tools appropriate to study design:

- Newcastle–Ottawa Scale (NOS) for observational studies
- Cochrane Risk of Bias Tool for interventional studies

Each study was evaluated for

- Selection bias
- Comparability of study groups
- Outcome assessment reliability
- Adequacy of follow-up

Rather than excluding studies solely based on quality scores, methodological limitations were contextualized during data synthesis, allowing balanced interpretation of findings.

Data Synthesis and Thematic Analysis

Given the heterogeneity in study designs, patient populations, and outcome measures, a qualitative thematic synthesis approach was adopted.

Extracted data were organized into the following key domains

- Prevalence and patterns of polypharmacy
- Epidemiology and severity of DDIs
- Pharmacokinetic and pharmacodynamic interaction mechanisms
- Clinical outcomes associated with DDIs
- Role and impact of clinical pharmacy interventions
- Medication safety and pharmacovigilance perspectives

A comparative analytical approach was employed to identify consistencies, discrepancies, and emerging trends across studies. Emphasis was placed on translating findings into clinically actionable insights, particularly in the context of medication therapy management and patient-centered care.

Methodological Strengths and Limitations

This review incorporates a robust, PRISMA-aligned methodology, enhancing reliability and transparency. The inclusion of multiple databases and structured search strategies minimizes selection bias and improves evidence coverage.

However, certain limitations should be acknowledged

- Restriction to English-language publications may introduce language bias
- Heterogeneity in study methodologies limits quantitative synthesis
- Variability in definitions of polypharmacy and DDI severity across studies

Despite these limitations, the structured approach provides a comprehensive and clinically relevant synthesis of current evidence.

RESULTS AND DISCUSSION

Study Selection (PRISMA-Based Results)

The systematic search identified 1,248 records from electronic databases (PubMed: n = 412; Scopus: n = 503; Web of Science: n = 333), along with 42 additional records obtained through manual searches. After removal of duplicates, 1,035 studies remained for screening.

Following title and abstract screening, 862 studies were excluded due to irrelevance to polypharmacy, drug–drug interactions (DDIs), or haemodialysis-specific outcomes. Subsequently, 173 full-text articles were assessed for eligibility. Of these, 121 studies were excluded for predefined reasons, including irrelevant outcomes (n = 46), non-haemodialysis CKD populations (n = 38), insufficient data (n = 21), and non-English publications (n = 16).

Ultimately, 52 studies were included in the qualitative synthesis, comprising cross-sectional, cohort, and interventional designs.

Burden of Polypharmacy in Haemodialysis Patients

Polypharmacy is a defining feature of pharmacotherapy in haemodialysis populations, with global prevalence estimates ranging from 60% to 90%, and an average medication count of 8–12 drugs per patient.[8] Higher prevalence has been reported in high-income settings due to broader implementation of guideline-directed therapies. In contrast, underreporting may occur in low- and middle-income countries (LMICs) due to fragmented prescribing systems.[9]

The primary drivers of polypharmacy include multimorbidity, particularly coexisting cardiovascular disease, diabetes mellitus, anaemia, and mineral bone disorders, all of which necessitate long-term pharmacotherapy.[10] In addition, adherence to disease-specific clinical guidelines often results in additive prescribing without sufficient integration across specialties, contributing to therapeutic complexity.[11]

A critical distinction exists between appropriate polypharmacy, which is evidence-based and clinically justified, and inappropriate polypharmacy, characterized by unnecessary, duplicative, or potentially harmful medications. Several studies indicate that up to 30–50% of prescribed medications in dialysis patients may be potentially inappropriate, highlighting a substantial opportunity for deprescribing and optimization.[12] From a clinical pharmacy perspective, this underscores the need for structured medication review processes to balance therapeutic benefit against cumulative risk.

Table 2: Prevalence of Polypharmacy and DDIs in Haemodialysis Patients.

Study Region	Polypharmacy Prevalence (%)	Average No. of Drugs	DDI Prevalence (%)	Key Findings
North America	75–90	10–12	65–85	High due to guideline-based therapy
Europe	70–85	8–11	60–80	Moderate-to-severe DDIs common
Asia	60–80	7–10	50–75	Underreporting possible
Middle East	65–85	8–12	55–80	High comorbidity burden
Africa	50–70	6–9	45–65	Limited pharmacovigilance systems

Table 2 presents the regional distribution of polypharmacy and drug–drug interactions (DDIs) among haemodialysis patients. The prevalence of polypharmacy is highest in North America (75–90%) and Europe (70–85%), where patients typically receive a higher number of medications due to guideline-based management of multiple comorbidities. These regions also report a high prevalence of DDIs (60–85%), indicating an increased risk associated with complex pharmacotherapy.

In Asian and Middle Eastern regions, polypharmacy and DDI prevalence remain substantial, although slightly lower than in Western countries. These differences may be influenced by variations in prescribing practices and healthcare systems. In contrast, lower reported rates in African settings may reflect limited pharmacovigilance systems and underreporting rather than a true lower burden.

Overall, the table highlights that polypharmacy and DDIs are common across all regions, emphasizing the need for improved medication review and safety monitoring in haemodialysis patients.

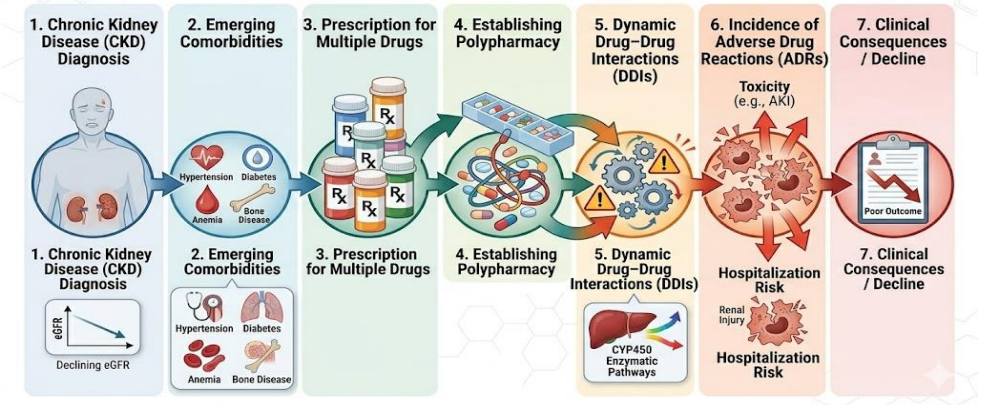

Figure 3: Polypharmacy Pathway in Chronic Kidney Disease.

Figure 3 illustrates how CKD leads to multiple comorbidities requiring multiple medications, resulting in polypharmacy and increased risk of drug–drug interactions and adverse drug reactions.

Epidemiology of Drug–Drug Interactions

The prevalence of potential drug–drug interactions (DDIs) in haemodialysis patients is consistently reported between 50% and 85%, with approximately 20–30% classified as clinically significant (moderate to severe).[13-15] The high burden reflects both the extent of polypharmacy and the altered physiological milieu of CKD.

DDIs are commonly categorized based on severity into minor (limited clinical relevance), moderate (requiring monitoring or dose adjustment), and major interactions (potentially life-threatening).[16] Evidence suggests that major DDIs account for a substantial proportion of preventable adverse outcomes in dialysis populations.[17]

High-risk groups include elderly patients, individuals with multiple comorbidities, and those receiving ≥10 medications (hyperpolypharmacy).[18] Notably, the absence of routine interaction screening tools in many healthcare settings contributes to under-detection and delayed intervention.

Table 3: Severity Classification of Drug–Drug Interactions.

Severity Level	Definition	Clinical Impact	Example
Minor	Limited clinical significance	Minimal monitoring required	Mild antihypertensive interactions
Moderate	Requires monitoring or dose adjustment	May affect therapy outcomes	Beta-blocker + insulin
Major	Potentially life-threatening	Requires avoidance or intervention	Warfarin + antibiotics

Table 3 classifies drug–drug interactions (DDIs) based on their severity and clinical significance. Minor interactions have limited clinical impact and usually require minimal monitoring. Moderate interactions may influence therapeutic outcomes and often require dose adjustment or closer monitoring, such as the combination of beta-blockers with insulin. Major interactions are potentially life-threatening and require avoidance or immediate intervention, as seen with combinations like warfarin and certain antibiotics.

Mechanisms of Drug–Drug Interactions

DDIs in CKD patients are mediated through complex pharmacokinetic and pharmacodynamic mechanisms, further influenced by dialysis-related factors.

Pharmacokinetic interactions involve alterations in drug absorption, distribution, metabolism, and excretion. Reduced renal clearance leads to accumulation of renally eliminated drugs, while uraemia-associated changes may impair hepatic cytochrome P450 (CYP450) enzyme activity and transporter function (e.g., P-glycoprotein).[19,20] Pharmacodynamic interactions occur when drugs exert additive, synergistic, or antagonistic effects. For example, concurrent use of ACE inhibitors and potassium-sparing agents may precipitate hyperkalaemia, while combined anticoagulant and antiplatelet therapy increases bleeding risk.[21]

Additionally, dialysis-related interactions play a unique role, as certain drugs are removed during haemodialysis depending on molecular weight, protein binding, and volume of distribution. Failure to account for dialysis clearance can result in subtherapeutic exposure or toxicity.[22]

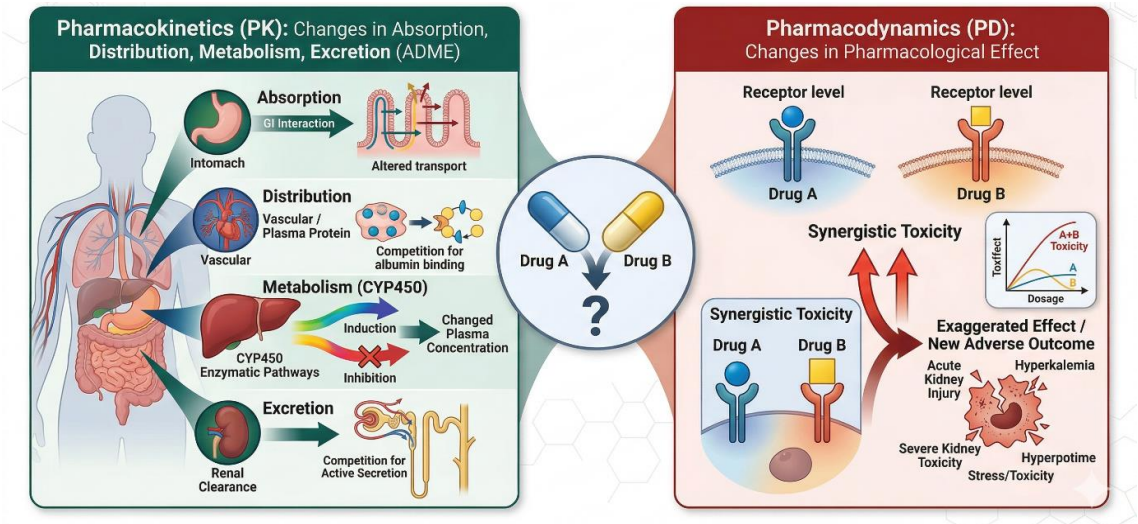

Figure 4: Mechanisms of Drug–Drug Interactions in Haemodialysis Patients.

Figure 4 illustrates pharmacokinetic mechanisms (absorption, metabolism, excretion) and pharmacodynamic interactions such as synergistic toxicity.

High-Risk Drug Classes

Certain drug classes are disproportionately associated with clinically significant DDIs in haemodialysis patients:

- **Cardiovascular drugs:** ACE inhibitors, beta-blockers, and diuretics are frequently implicated in electrolyte disturbances and hypotension.[23]
- **Antidiabetic agents:** Risk of hypoglycaemia is amplified due to reduced renal clearance of insulin and oral agents.[24]
- **Antibiotics:** Many require dose adjustment; interactions may alter drug levels or increase toxicity.[25]
- **Anticoagulants:** Warfarin and direct oral anticoagulants (DOACs) present significant bleeding risks when combined with interacting agents.[26]
- **Phosphate binders:** These agents can reduce the absorption of co-administered drugs through chelation mechanisms.

The clinical significance of these interactions is often magnified in CKD due to altered drug handling and narrow therapeutic windows.

Table 4: Common Drug Classes and Associated Risks in CKD.

Drug Class	Common Drugs	Risk in CKD	Clinical Concern
Cardiovascular	ACE inhibitors, beta-blockers	Hyperkalaemia, hypotension	Electrolyte imbalance
Antidiabetics	Insulin, metformin	Hypoglycaemia	Drug accumulation
Antibiotics	Aminoglycosides, fluoroquinolones	Nephrotoxicity	Dose adjustment needed
Anticoagulants	Warfarin, DOACs	Bleeding	INR variability
Phosphate binders	Calcium carbonate	Reduced drug absorption	Therapeutic failure

Table 4 summarizes commonly prescribed drug classes in CKD patients and their associated risks. Cardiovascular drugs such as ACE inhibitors and beta-blockers are linked to hyperkalaemia and hypotension, increasing the risk of electrolyte imbalance. Antidiabetic agents, including insulin and metformin, may cause hypoglycaemia due to reduced renal clearance and drug accumulation. Certain antibiotics, particularly aminoglycosides and fluoroquinolones, are associated with nephrotoxicity and require dose adjustment. Anticoagulants like warfarin and direct oral anticoagulants (DOACs) increase the risk of bleeding and require careful monitoring of coagulation parameters. Phosphate binders, such as calcium carbonate, may reduce the absorption of co-administered drugs, potentially leading to therapeutic failure.

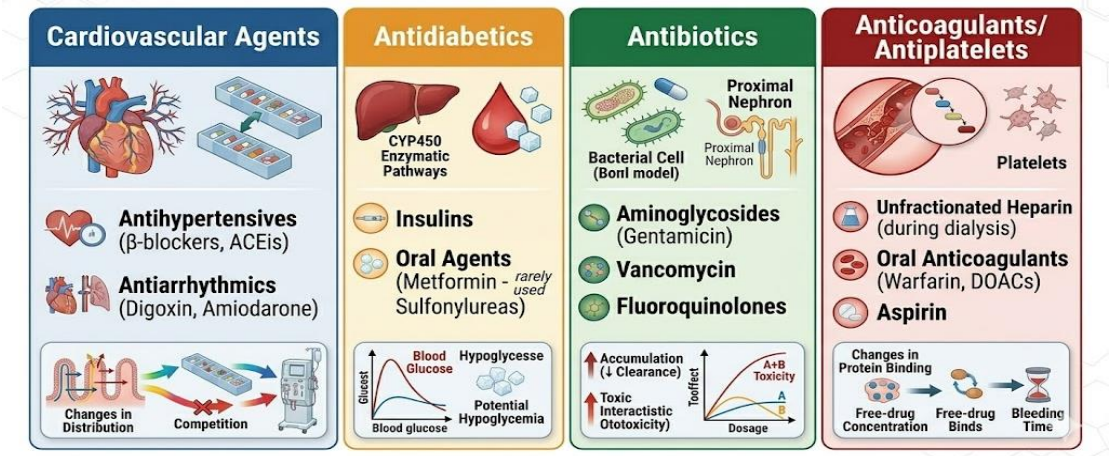

Figure 5: High-Risk Drug Classes Associated with Drug–Drug Interactions in Haemodialysis Patients.

Figure 5 highlights major drug classes, including cardiovascular drugs, antidiabetics, antibiotics, and anticoagulants, associated with increased interaction risk.

Pharmacotherapeutic Challenges in CKD

CKD profoundly alters pharmacokinetics, necessitating individualized therapeutic strategies. Key challenges include:

- Reduced renal clearance, leading to prolonged drug half-life
- Altered protein binding due to hypoalbuminemia
- Increased volume of distribution for certain drugs
- Dialysis-related drug removal variability

Inadequate dose adjustment remains a persistent issue, with studies reporting inappropriate dosing in up to 40% of prescriptions.[27] Drugs with a narrow therapeutic index, such as digoxin and certain antibiotics, require careful monitoring to avoid toxicity.

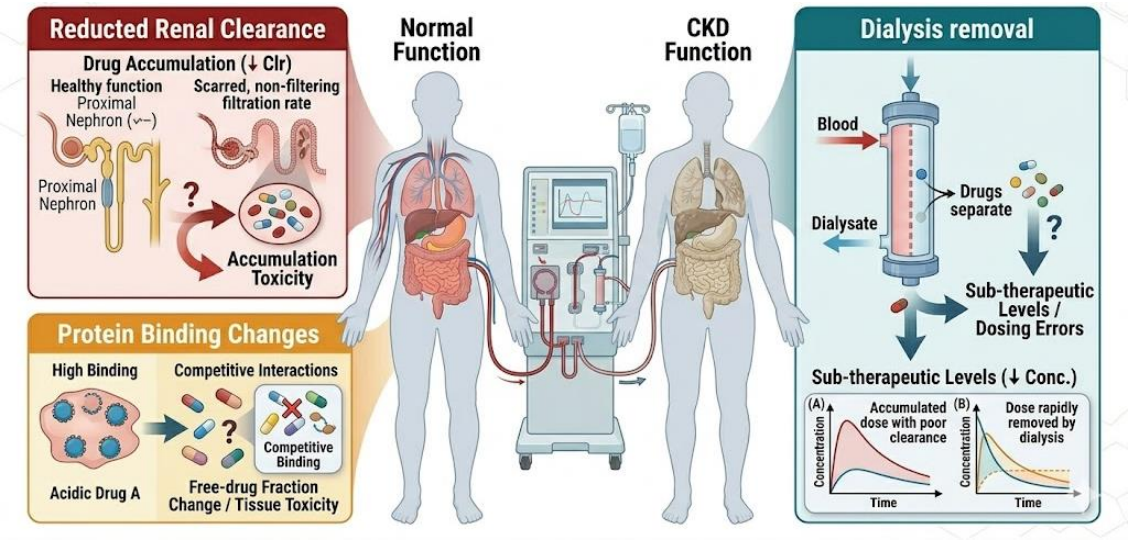

Figure 6: Pharmacokinetic Alterations in Chronic Kidney Disease.

Figure 6 illustrates reduced renal clearance, altered protein binding, and dialysis-related drug removal affecting drug exposure.

Clinical Outcomes Associated with DDIs

DDIs in haemodialysis patients are strongly associated with adverse clinical outcomes, including:

- Adverse drug reactions (ADRs)
- Electrolyte imbalances (e.g., hyperkalaemia)
- Increased hospitalization rates
- Higher mortality risk

Several cohort studies demonstrate a direct relationship between polypharmacy burden and adverse outcomes, with each additional medication increasing the risk of hospitalization and mortality.[28-30] Furthermore, DDIs contribute to a significant economic burden due to increased healthcare utilization.[31]

Clinical Pharmacy Interventions

Clinical pharmacists play a critical role in mitigating medication-related risks through targeted interventions:

- Medication therapy management (MTM)
- Medication reconciliation at transitions of care
- Use of DDI screening tools (e.g., Lexicomp, Micromedex)
- Patient education and adherence support

Evidence from interventional studies indicates that pharmacist-led services can reduce inappropriate prescribing, decrease DDI prevalence, and improve clinical outcomes.[32] However, the implementation of such services remains inconsistent, particularly in LMIC settings.

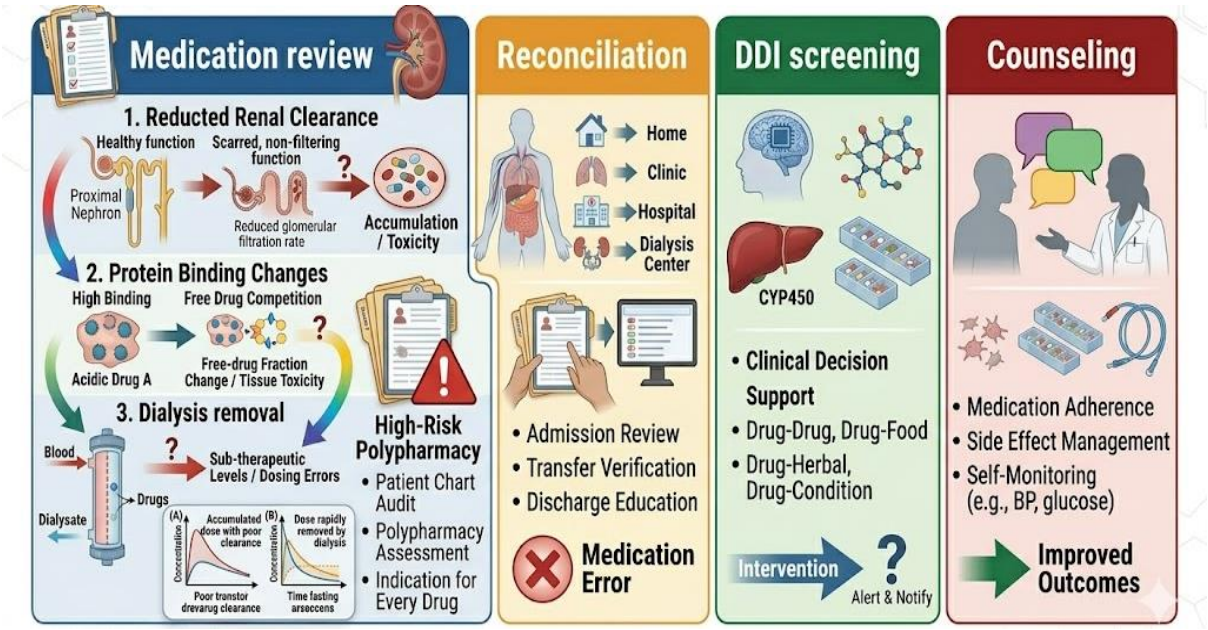

Figure 7: Role of Clinical Pharmacists in Enhancing Medication Safety in Haemodialysis Patients.

Figure 7 shows key pharmacist interventions, including medication review, reconciliation, interaction screening, and patient counselling.

Medication Safety and Pharmacovigilance

Pharmacovigilance is central to identifying and preventing DDIs, yet underreporting of ADRs remains a major challenge. Barriers include a lack of awareness, time constraints, and the absence of structured reporting systems.[33]

The integration of clinical decision support systems (CDSS) and electronic prescribing platforms has demonstrated potential in improving DDI detection and medication safety. However, issues such as alert fatigue and lack of contextual relevance limit their effectiveness.[34]

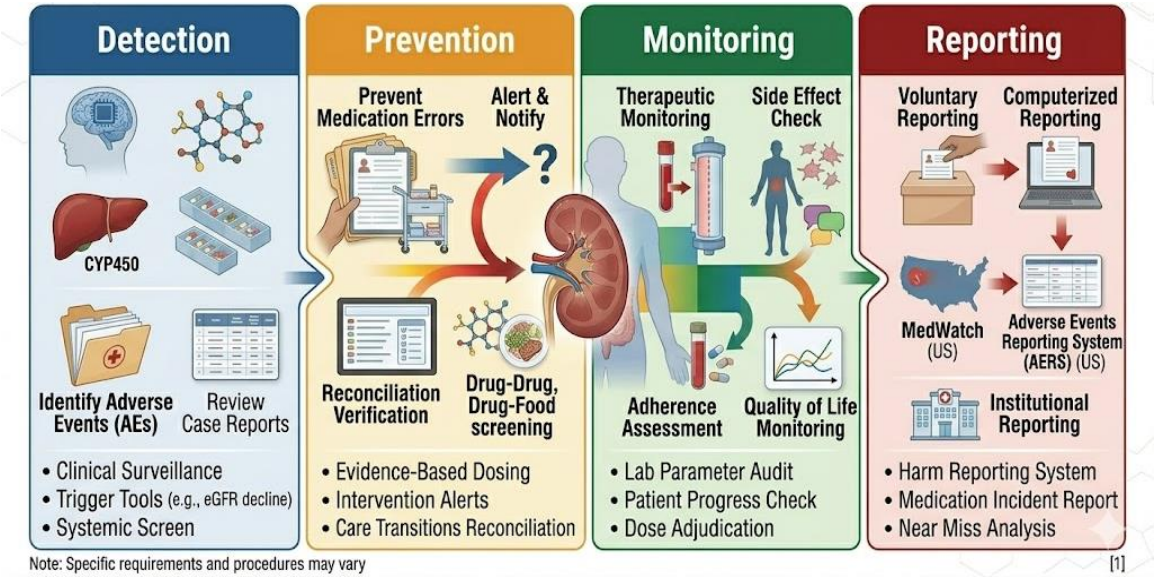

Figure 8: Medication Safety Framework for the Identification and Management of Drug-Related Problems in Haemodialysis Patients.

Figure 8 presents processes including detection, prevention, monitoring, and reporting of medication-related problems.

Research Gaps

Despite growing evidence, several gaps persist:

- Lack of standardized definitions of polypharmacy in CKD
- Limited randomized controlled trials evaluating clinical pharmacy interventions
- Underrepresentation of LMIC populations
- Absence of CKD-specific DDI prediction models

Addressing these gaps is essential for improving the generalizability and clinical applicability of research findings.

Future Directions

Future research should focus on:

- Artificial intelligence-based DDI prediction models to enhance risk stratification
- Pharmacogenomic approaches to personalize therapy
- Integration of clinical pharmacists into multidisciplinary care teams
- Development of CKD-specific prescribing guidelines and decision-support tools

These strategies have the potential to improve medication safety and patient outcomes significantly.

CONCLUSION

Polypharmacy and drug–drug interactions are highly prevalent and clinically significant challenges in haemodialysis patients with chronic kidney disease. The interplay between complex pharmacotherapy and altered drug handling increases the risk of adverse outcomes, including ADRs, hospitalization, and mortality.

Addressing these challenges requires a multifaceted approach, including rational prescribing, systematic medication review, and integration of clinical pharmacy services. Clinical pharmacists play a pivotal role in optimizing pharmacotherapy, preventing DDIs, and enhancing medication safety.

Strengthening pharmacovigilance systems and adopting evidence-based, patient-centered strategies are essential to reduce medication-related harm and improve healthcare outcomes in this high-risk population.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

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