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Clinical Pharmacist-Led Management of Medication-Related Acute Kidney Injury: Early Risk Detection, Drug Withdrawal, and Safe Reintroduction

Yasser JH Alyassery*

College of Pharmacy, Al-Zahraa University for Women, Karbala, Iraq.

https://orcid.org/0009-0002-7538-4478.

***Correspondence:**
Yasser JH Alyassery, College of Pharmacy, Al-Zahraa University for Women, Karbala, Iraq, E-mail: Yasseralyassery@alzahraa.edu.iq.

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ABSTRACT

Medication-related acute kidney injury (MR-AKI) is an important and potentially preventable cause of acute kidney injury in hospital and community settings. Its consequences may extend beyond the initial episode, contributing to persistent kidney dysfunction, chronic kidney disease (CKD), cardiovascular complications, and mortality. Clinical pharmacists can contribute throughout the MR-AKI care pathway by identifying patients at increased risk, supporting early detection, evaluating medication-related causality, recommending drug withdrawal or dose modification, optimizing supportive pharmacotherapy, and facilitating the appropriate reintroduction of essential treatments. This narrative review examines the epidemiology and principal mechanisms of MR-AKI and discusses pharmacist-led approaches to risk assessment, kidney function surveillance, medication review, and clinical management. Particular attention is given to the structured assessment of suspected drug-induced injury and to evidence-informed decisions regarding the temporary interruption, subsequent reintroduction, or avoidance of selected therapies, including renin–angiotensin system inhibitors, sodium–glucose cotransporter 2 inhibitors, immune checkpoint inhibitors, and other potentially nephrotoxic medications. The review also considers post-AKI monitoring, transitions of care, implementation challenges, and priorities for future research. By integrating risk identification, timely medication intervention, and individualized reassessment of treatment, this review proposes a practical pharmacist-led framework to support kidney safety while preserving access to therapies with established clinical benefits. Prospective studies are needed to evaluate the framework's feasibility and its effects on patient outcomes, medication-related harm, and continuity of evidence-based treatment.

Keywords

Acute kidney injury, Nephrotoxicity, Clinical pharmacist, Medication safety, Deprescribing, Drug rechallenge, Renal dosing, Stewardship.

Introduction

Acute kidney injury (AKI) affects roughly one in five hospitalised adults worldwide and a considerably higher proportion of critically ill patients, with associated increases in length of stay, cost, and mortality [1,2]. In multinational critical-care cohorts, nephrotoxic drugs have been recognised as a leading contributor to AKI, alongside sepsis and major surgery [3]. Estimates of the drug-attributable fraction vary with setting and case definition, but it is generally considered to account for a meaningful minority of hospital-acquired episodes and to be among the most modifiable causes [4,5].

AKI is defined by the Kidney Disease: Improving Global Outcomes (KDIGO) criteria as a rise in serum creatinine of at least 26.5 µmol/L (0.3 mg/dL) within 48 hours, a rise to at least 1.5 times baseline within 7 days, or urine output below 0.5 mL/kg/h for 6 hours [4]. These criteria are functional rather than aetiological and say nothing about whether a drug is responsible. Attributing injury to medication therefore requires clinical reasoning that integrates

pharmacology, timing, concomitant haemodynamic or septic insults, and the response to withdrawal. This reasoning is a core competence of the clinical pharmacist.

Medication-related AKI is distinctive among AKI aetiologies in three respects. First, exposure is often known in advance, creating a window for primary prevention. Second, the exposure can frequently be modified or stopped, which makes secondary prevention (limiting injury once it begins) feasible. Third, many implicated drugs are indispensable (antimicrobials, chemotherapy, cardio-renal protective agents), so the question is not simply whether to stop but how to continue safely, or restart safely, when benefit outweighs risk. The pharmacist's role spans all three phases, summarised in this review as detect, withdraw, and reintroduce. To provide a comprehensive and clinically relevant overview, this narrative review synthesizes current literature focusing on the intersection of clinical pharmacy practice, nephrotoxicity, and acute kidney injury management. A targeted literature search was conducted across major electronic databases, including MEDLINE/PubMed, Embase, and the Cochrane Library. Search terms and medical subject headings (MeSH) included combinations of "acute kidney injury", "nephrotoxicity", "clinical pharmacist", "medication safety", "deprescribing", "drug rechallenge", and "renal stewardship". English-language articles, consensus guidelines, systematic reviews, clinical trials, and observational studies examining pre-exposure risk stratification, electronic surveillance, causality assessment, medication withdrawal, and safe therapeutic reintroduction were evaluated. While this article is structured as a narrative review rather than a formal systematic review, studies were selected based on their methodological rigor, clinical impact, and relevance to establishing a practical, pharmacist-led framework for mitigating medication-related acute kidney injury.

Epidemiology and Mechanisms of Medication-Related AKI

Burden and risk factors

Risk of MR-AKI reflects the interaction of drug, patient, and context. Patient-level factors include older age, pre-existing CKD, diabetes, heart failure, cirrhosis, hypovolaemia, hypoalbuminaemia, and prior AKI. Drug-level factors include intrinsic nephrotoxic potential, dose, duration, and the number of concurrent nephrotoxins. Contextual factors include sepsis, major surgery, contrast administration, and inadequate monitoring [5,6]. Polypharmacy compounds these risks, and the combination of several individually modest nephrotoxic exposures is often more harmful than any single agent [5].

Mechanistic classification

Mechanism-based thinking helps pharmacists predict injury, choose monitoring, and interpret urine findings. Awdishu and Mehta's '6 Rs' framework (Rhabdomyolysis, Renal haemodynamics, Resistance to drug excretion, Reactions such as hypersensitivity, Renal tubular toxicity, and Residual precipitation/crystal nephropathy) offers a practical aide-memoire [7]. Perazella has described the pharmacological basis of tubular injury, including the role of tubular transporters in concentrating drugs within proximal tubular cells [6,8].

Selected high-risk exposures

NSAIDs, RAS inhibitors, and diuretics. Concurrent use of an NSAID with a RAS inhibitor and a diuretic (the 'triple whammy') is associated with a significantly increased risk of hospitalisation for AKI, particularly in the first 30 days after initiation [9]. Because these drugs are frequently bought over the counter or prescribed by different clinicians, pharmacists in community and hospital settings are the professionals most likely to see the whole picture.

Vancomycin and piperacillin-tazobactam. Meta-analyses indicate that the combination is associated with a higher incidence of AKI than vancomycin combined with other anti-pseudomonal beta-lactams, although the mechanism, and the degree to which creatinine rises reflect true tubular injury rather than altered tubular secretion, remain debated [10]. Current guidelines favour area-under-the-curve (AUC)-guided vancomycin dosing over trough-only monitoring to reduce nephrotoxicity risk [11].

Acute interstitial nephritis (AIN). Drug-induced AIN is under-diagnosed because the classic triad of rash, fever, and eosinophilia is uncommon [12]. Proton pump inhibitors, antibiotics, and NSAIDs account for a large proportion of biopsy-proven cases, and delay in withdrawing the offending drug is associated with incomplete renal recovery [12,13].

Mechanism	Representative drugs	Typical features	Key pharmacist actions
Hemodynamic (functional)	NSAIDs, ACE inhibitors/ARBs, calcineurin inhibitors, diuretics, SGLT2 inhibitors (early dip)	Rapid creatinine rise, bland urinary sediment, often reversible	Review volume status and combination therapy; hold or reduce; plan restart
Acute tubular injury	Aminoglycosides, vancomycin, cisplatin, amphotericin B, contrast, zoledronate	Muddy-brown casts, subacute onset, slower recovery	Dose by exposure targets; avoid combinations; hydration where indicated
Acute interstitial nephritis	Beta-lactams, PPIs, NSAIDs, sulfonamides, immune checkpoint inhibitors, allopurinol	Pyuria, white-cell casts, rash/ eosinophilia in a minority	Stop culprit promptly; avoid cross-reacting agents; document reaction type
Crystal nephropathy / obstruction	Acyclovir, methotrexate, sulfonamides, indinavir	Crystalluria, rapid onset with high dose or volume depletion	Hydrate, adjust dose, consider alternative agents
Thrombotic microangiopathy	Gemcitabine, calcineurin inhibitors, anti-VEGF agents, quinine	Haemolysis, thrombocytopenia, hypertension	Early recognition, withdraw, specialist referral
Rhabdomyolysis	Statins (especially with interacting drugs), daptomycin, propofol (infusion syndrome)	Markedly raised creatine kinase	Review interacting drugs, stop offending agent

Immune checkpoint inhibitors (ICIs). ICI-associated AKI, most often acute interstitial nephritis, occurs in a minority of treated patients and is strongly associated with concomitant PPI use and other drugs that may prime the immune response [14,15]. Medication review at ICI initiation is therefore a high-yield pharmacist intervention.

Cisplatin and other chemotherapy. Cisplatin accumulates in proximal tubular cells via organic cation transporters, producing tubular injury that is dose-dependent and cumulative [16]. Pharmacist-led hydration, magnesium supplementation, and avoidance of co-administered nephrotoxins are established mitigation strategies.

Iodinated contrast. Contrast-associated AKI is a recognised risk in patients with reduced baseline eGFR, but the risk attributable to intravenous contrast itself appears lower than historically feared when patients are appropriately hydrated [17]. The PRESERVE trial showed no benefit of sodium bicarbonate over saline or of N-acetylcysteine over placebo in high-risk patients undergoing angiography, reinforcing isotonic volume expansion as the main preventive measure [18].

Early Risk Detection: The Pharmacist's Surveillance Role

Pre-exposure risk stratification

Prevention is most effective before a nephrotoxin is prescribed. Pharmacists can apply a structured pre-exposure assessment at prescribing, verification, or admission medication reconciliation:

1. **Baseline kidney function.** Review recent creatinine, eGFR, urine albumin-to-creatinine ratio, and trend. Recognise that creatinine-based estimates are unreliable in unstable kidney function, at extremes of body composition, and in acute illness, and that dose adjustment for drugs with a narrow therapeutic index may require individualised estimates and drug-level monitoring [19].
2. **Volume and haemodynamic status.** Hypovolaemia, hypotension, and recent vomiting, diarrhoea, or poor intake are often modifiable precipitants.
3. **Cumulative nephrotoxin burden.** Count concurrent agents, including over-the-counter NSAIDs, herbal products, and contrast exposure.
4. **Indication and alternatives.** Ask whether a less nephrotoxic option exists (for example, avoiding an aminoglycoside when equivalent alternatives are available) and whether the shortest effective duration can be used.
5. **Monitoring plan.** Define baseline and follow-up creatinine and electrolytes, therapeutic drug monitoring where relevant, and who will act on the results.

Surveillance and trigger tools

Pharmacist-led surveillance has its strongest evidence in paediatrics. The Nephrotoxic Injury Negated by Just-in-time Action (NINJA) programme used the electronic record to identify non-critically ill children exposed to three or more nephrotoxic medications, or to intravenous aminoglycosides for more than three days, and prompted daily creatinine monitoring and medication review. In the original and sustained implementation, this approach reduced nephrotoxic medication exposure and the rate of medication-associated AKI [20,21], and a multicentre evaluation reported reductions in AKI rates across several paediatric centres [22].

Evidence in adults is more mixed. Electronic alerts for AKI alone have not consistently improved outcomes: a randomised trial of automated alerts found no overall benefit, with signals of potential harm at some non-teaching-hospital sites [23], and a later multicentre trial likewise found that alerts alone did not improve clinical outcomes [24]. In contrast, organisation-level programmes that combine alerts with education, care bundles, and clinician engagement have shown more promise. The Tackling AKI stepped-wedge trial improved processes of care and reduced length of stay, although it did not demonstrate a significant effect on 30-day mortality [25]. A biomarker-guided implementation of the KDIGO bundle reduced AKI after cardiac surgery in high-risk patients [26], and care bundles in general hospital settings have improved recognition and management [27]. Collectively these data suggest that the response to an alert, rather than the alert itself, produces benefit, and pharmacists are well placed to own that response.

Practical components of a pharmacist-led surveillance model include:

- Daily review of patients with a new creatinine rises of at least 26.5 μmol/L (0.3 mg/dL), falling urine output, or a flagged nephrotoxin combination.
- Nephrotoxin stewardship rounds, analogous to antimicrobial stewardship rounds, focused on high-risk units such as intensive care, hematology-oncology, and transplant services.
- Targeted review of at-risk groups: patients starting ICIs, platinum chemotherapy, vancomycin, aminoglycosides, or high-dose methotrexate, and patients receiving contrast.
- Integration of pharmacist review into medication reconciliation at admission, transfer, and discharge, which is associated with fewer medication discrepancies and improved clinical outcomes at transitions [28].

Systematic reviews of pharmacist participation in multidisciplinary intensive care teams report reductions in adverse drug events and, in some analyses, improved clinical outcomes, supporting the embedding of pharmacists in critical-care teams [29].

Responding to Suspected MR-AKI: Assessment and Drug Withdrawal

A structured pharmacist assessment

When creatinine rises or urine output falls, the pharmacist can contribute a rapid, structured medication-focused assessment alongside the clinical team. The following sequence is proposed:

1. **Confirm and stage AKI** using KDIGO criteria, and verify that the rise is not a laboratory artefact or an expected haemodynamic change (for example, an early eGFR dip after RAS inhibitor or SGLT2 inhibitor initiation) [4].
2. **Compile a complete exposure timeline**, including prescribed, over-the-counter, herbal, recreational, and

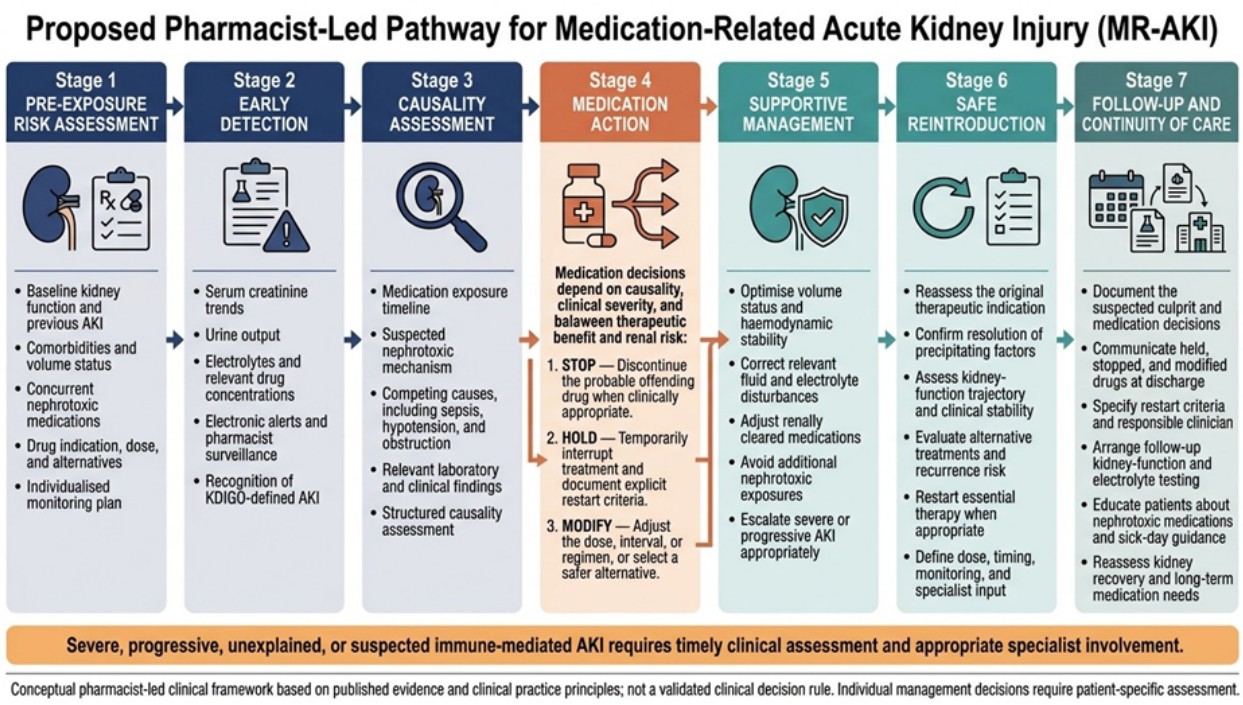


Figure 1: Proposed pharmacist-led pathway for the prevention and management of medication-related acute kidney injury (MR-AKI). The framework integrates pre-exposure risk assessment, early detection, medication-causality assessment, appropriate drug withdrawal or modification, supportive management, safe reintroduction of essential therapies, and post-AKI follow-up. Clinical pharmacists contribute through medication reconciliation, nephrotoxin surveillance, renal-dose optimisation, interdisciplinary communication, and structured documentation of treatment interruptions and restart plans. Decisions regarding withdrawal and reintroduction should consider the suspected mechanism of injury, AKI severity, the strength of the therapeutic indication, clinical recovery, alternative treatments, and recurrence risk. Severe, progressive, unexplained, or suspected immune-mediated AKI warrants timely clinical assessment and specialist involvement. This figure represents a proposed practice framework and has not been prospectively validated as a clinical decision rule.

procedural exposures (contrast, bowel preparation) with start dates, doses, and recent changes.

3. **Identify likely mechanisms** (Section 2.2) and match them to the clinical picture: urinalysis and microscopy, urine output, volume status, drug levels, creatine kinase, and imaging where relevant.
4. **Consider competing causes** such as sepsis, hypotension, obstruction, and contrast, recognising that most hospital AKI is multifactorial.
5. **Assess causality** using a structured tool.
6. **Recommend actions** on withdrawal, dose modification, monitoring, and supportive therapy.

Causality assessment

Structured causality tools reduce reliance on intuition and improve documentation. The Naranjo adverse drug reaction probability scale scores temporal relationship, dechallenge response, alternative causes, objective evidence (for example drug levels), and rechallenge, and categorises the likelihood of an adverse drug reaction as doubtful, possible, probable, or definite [30]. Its limitations are well known: it was not designed for nephrotoxicity specifically, it weights rechallenge heavily although rechallenge is often unethical or unsafe, and it can underestimate the role of multiple interacting drugs. Pharmacists should therefore apply it alongside mechanistic reasoning and, where the diagnosis is uncertain (for example suspected AIN), advocate for nephrology input and, when appropriate, kidney biopsy rather than prolonged empirical exposure to a possible culprit.

Principles of withdrawal and modification

The central pharmacist recommendation in confirmed or probable MR-AKI is to stop or modify the offending agent promptly. KDIGO recommends discontinuing nephrotoxic agents where possible, ensuring volume status and perfusion pressure, and monitoring creatinine and urine output [4]. Practical principles include:

- **Stop the most likely and least essential agents first.** Non-essential agents (NSAIDs, PPIs without a firm indication, over-the-counter supplements) are removed without hesitation. Essential agents are replaced by lower-risk alternatives where available.
- **Do not stop reflexively when the drug is essential and the evidence of causality is weak.** For example, withdrawing an effective antimicrobial during sepsis on the basis of a creatinine rise alone may expose the patient to greater harm. In such cases, modify (dose, interval, formulation, or monitoring strategy) and document the risk-benefit reasoning.
- **Hold, do not delete.** Temporarily holding a drug (for example an ACE inhibitor in volume depletion) with an explicit restart plan prevents inadvertent permanent discontinuation, a recognised cause of lost long-term benefit.

- **Address the whole regimen.** Review other renally cleared drugs for accumulation, including opioids, gabapentinoids, direct oral anticoagulants, low-molecular-weight heparins, metformin, and antimicrobials, and adjust dosing accordingly [19].
- **Avoid further insults.** Defer non-essential contrast, avoid hypotension, and avoid unnecessary nephrotoxic co-prescription during recovery.
- **Prevent cross-reactivity and labelling errors.** In suspected AIN, record the culprit and drug class in the allergy or intolerance record with details of the reaction type, so that the label is neither lost nor inappropriately broadened.

Dosing in AKI deserves particular care. Creatinine-based estimates lag behind true kidney function: when creatinine is rising they overestimate it, and during recovery they underestimate it. Dosing decisions for renally cleared and narrow-therapeutic-index drugs should integrate clinical judgement, trajectory, urine output, and drug-level monitoring rather than a single eGFR value [19].

Supportive care and monitoring

Beyond drug withdrawal, pharmacists contribute to optimising fluid and electrolyte management, nutritional support, glycaemic control, and avoidance of hyperkalaemia-promoting drugs. They also support timely referral to nephrology when AKI is severe, progressive, unexplained, or suspected to be immune-mediated, and contribute to drug dosing decisions when kidney replacement therapy is required [4,19].

Safe Reintroduction of Medications after AKI

Withdrawal is only half of the pharmacist's task. Many drugs that precipitate AKI also provide major long-term benefit, and failure to restart them is a form of avoidable harm. A structured reintroduction framework is therefore essential.

A framework for rechallenge

The following questions can guide reintroduction decisions:

1. **Was the drug causal, contributory, or incidental?** Probable or definite immune-mediated reactions (such as AIN) carry a different rechallenge risk than haemodynamic, dose-related, or context-dependent injury.
2. **Is the original precipitant resolved?** For example volume depletion, sepsis, or an interacting drug.
3. **Has kidney function stabilised or recovered?** Reintroduction is usually considered once creatinine has plateaued or returned toward baseline and the patient is euvolaemic and haemodynamically stable.
4. **How strong is the ongoing indication?** Compelling indications (for example heart failure, post-myocardial infarction, proteinuric CKD, or life-saving anticancer therapy) justify greater willingness to rechallenge.
5. **Is there an equally effective, safer alternative?** If so, prefer it, particularly after a probable immune-mediated reaction.
6. **Can the risk be mitigated?** Options include a lower starting dose, slower titration, avoiding interacting drugs, sick-day guidance, and close early monitoring.
7. **Has the patient agreed?** Shared decision-making and clear communication of risks and warning signs are essential.

RAS inhibitors

RAS inhibitors produce an expected, haemodynamically mediated rise in creatinine, and a rise of up to about 30% is generally considered acceptable in stable patients. In AKI driven by volume depletion or hypotension, temporary withdrawal is appropriate, but prolonged omission is common. Observational data from a large Canadian cohort found that use of ACE inhibitors or ARBs after AKI was associated with lower mortality, though confounding by indication cannot be excluded [31]. Caution is needed when extrapolating from chronic disease: the STOP-ACEi trial showed that discontinuing RAS inhibitors in stable advanced CKD did not slow eGFR decline, which indicates that routine withdrawal in chronic disease offers no kidney benefit, but it does not directly address reintroduction after an acute episode [32]. A reasonable pharmacist-supported approach is to restart at a low dose once the patient is euvolaemic and creatinine has stabilised, titrate gradually, recheck creatinine and potassium within one to two weeks, and provide explicit sick-day advice.

SGLT2 inhibitors

SGLT2 inhibitors reduce progression of CKD and cardiovascular events in people with and without diabetes [33,34], and they cause a small initial, reversible eGFR decline that should not by itself prompt discontinuation. During acute illness with dehydration they should be paused (sick-day rule) because of volume depletion and, in diabetes, ketoacidosis risk, and restarted once the patient is eating, drinking, and clinically stable. Pharmacists should ensure that the hold is communicated with a clear restart trigger, since omitted restarts after hospital discharge are common.

Immune checkpoint inhibitors

For ICI-associated AKI, management usually involves holding the ICI, withdrawing contributory drugs such as PPIs, and administering corticosteroids when the diagnosis is probable or confirmed. Decisions about rechallenge should be multidisciplinary and consider the severity of AKI, the degree of renal recovery, the availability of effective alternatives, and the patient's oncological prognosis. Cohort data suggest that a proportion of patients can be rechallenged successfully, while a minority develop recurrent kidney injury [14,15]. Pharmacist roles include reviewing the medication list for other AIN-associated agents, supporting steroid tapering and prophylaxis (gastric, bone, infection), and ensuring creatinine monitoring at each treatment cycle.

Antimicrobials

When an antibiotic has been implicated in AKI, rechallenge depends on mechanism. For dose-related tubular toxicity (for example vancomycin or aminoglycosides), the same drug can often be used again with AUC- or level-guided dosing, shorter duration, and avoidance of nephrotoxic combinations [11]. For suspected immune-mediated AIN, avoidance of the culprit and structurally related drugs is usually recommended, and the reaction should be documented precisely [12].

NSAIDs and contrast

NSAIDs generally should not be reintroduced in patients who have had NSAID-related AKI, particularly those with CKD, heart failure, or concurrent RAS inhibitor and diuretic therapy [9]. Alternative analgesic strategies should be provided. For contrast, reassessment is indicated whenever imaging is clinically necessary: the decision should weigh the diagnostic value of the study against baseline risk, using isotonic volume expansion in high-risk patients and avoiding duplicate or closely spaced exposures [17,18].

Documentation

Every reintroduction decision should be recorded in a way that persists across care transitions: the drug, the reason it was held, the suspected role in AKI (causal, contributory, or unlikely), criteria for restart, the monitoring plan, and who is responsible. This reduces both inappropriate rechallenge and inappropriate permanent avoidance.

Follow-Up and Transitions of Care

AKI is not a self-limited event for many patients. Survivors have an increased long-term risk of CKD, end-stage kidney disease, cardiovascular events, and death [35,36]. Acute kidney disease (AKD), the period of up to 90 days after the initiating insult, is a recognised window in which recovery, persistent impairment, or progression is determined, and consensus statements advocate structured follow-up during this window [35].

Pharmacists can contribute at discharge and after discharge by:

- Reconciling medications and clearly distinguishing drugs that are stopped, held, and changed, with reasons and restart criteria.
- Communicating AKI as a diagnosis in the discharge summary, including suspected nephrotoxic culprits, so that primary care and community pharmacists are aware.
- Arranging a creatinine and potassium check within one to two weeks, and sooner after RAS inhibitor or diuretic changes.
- Providing patient education on avoiding over-the-counter NSAIDs, maintaining hydration, and recognising warning symptoms.
- Delivering sick-day guidance for drugs such as RAS inhibitors, diuretics, metformin, and SGLT2 inhibitors. A scoping review found that guidance exists in many forms but evidence of effectiveness is limited, highlighting the need for standardised, evaluated materials [37].
- Contributing to deprescribing of inappropriate or renally unsafe medications, as inappropriate prescribing in CKD is common and linked to adverse outcomes [38].

Implementation: Building a Pharmacist-Led MR-AKI Service

Implementation lessons from the paediatric and adult literature suggest several enablers.

- **Define the target population and triggers.** For example nephrotoxin-exposure thresholds, KDIGO stage 1 or higher, or specific high-risk drugs.
- **Use the electronic health record.** Decision support, dashboards, and automated lists allow pharmacists to focus time on patients at greatest risk, with the evidence cautioning that alerts alone are insufficient [23-25].

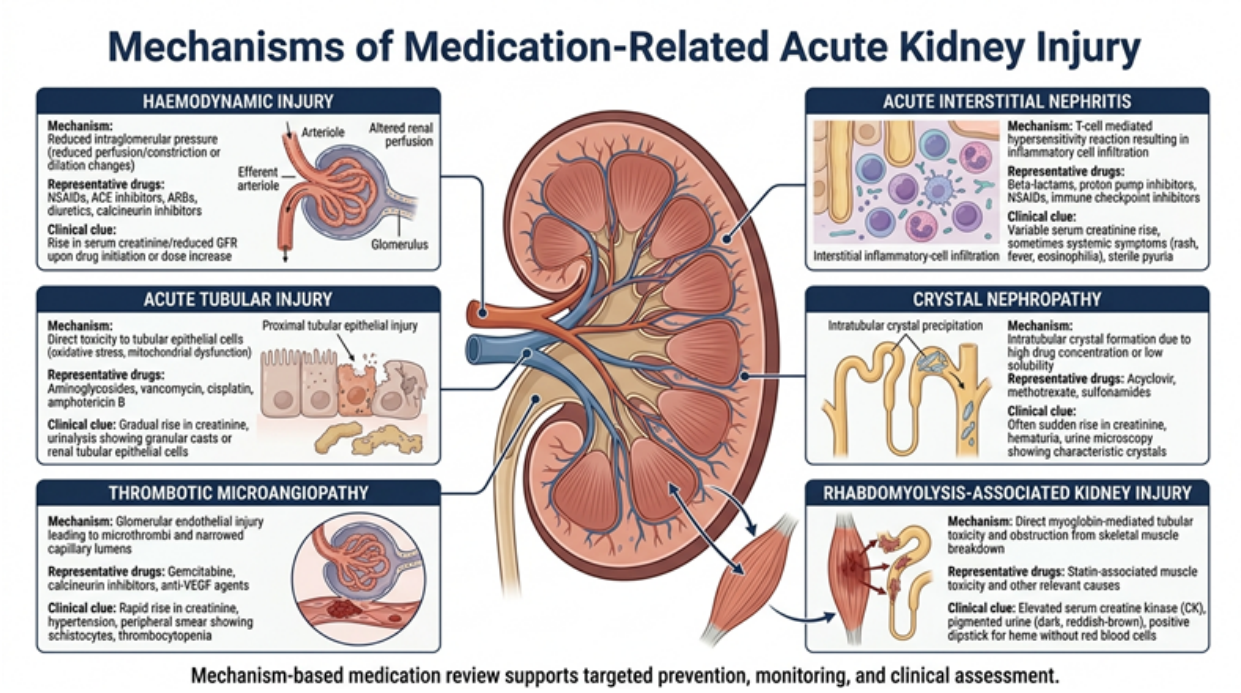


Figure 2: Principal mechanisms of medication-related acute kidney injury and representative drug exposures. Medication-related kidney injury may arise through altered renal haemodynamics, direct tubular toxicity, interstitial inflammation, intratubular crystal precipitation, thrombotic microangiopathy, or pigment-associated tubular injury. The mechanisms and clinical manifestations may overlap, particularly in patients with multiple comorbidities and concurrent nephrotoxic exposures. The drugs listed are representative examples and should not be interpreted as having a single exclusive mechanism of kidney injury.

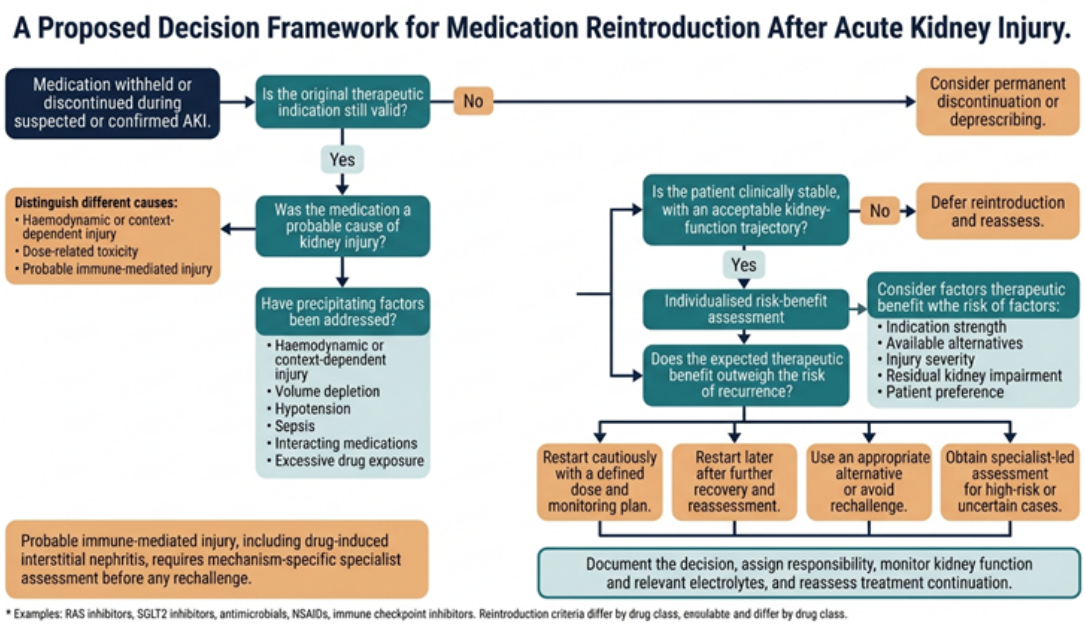


Figure 3: Proposed decision framework for medication reintroduction after AKI. Reintroduction decisions should integrate the continuing therapeutic indication, suspected drug causality and mechanism, resolution of precipitating factors, kidney-function trajectory, recurrence risk, alternative treatments, and patient preferences. Depending on the assessment, treatment may be restarted with monitoring, deferred pending further recovery, replaced with an alternative, or considered through specialist-led decision-making. The framework is conceptual and does not replace drug-specific guidance or individual clinical assessment.

- **Standardise protocols.** Agreed pathways for vancomycin dosing, contrast risk, ICI monitoring, and rechallenge reduce variability.
- **Secure prescribing authority or collaborative practice agreements** that allow timely action rather than recommendation alone.
- **Measure outcomes.** Track nephrotoxin exposure rates, AKI incidence and stage, recovery at discharge and at 90 days, appropriate restart of RAS or SGLT2 inhibitors, and readmissions.
- **Educate and communicate.** Pharmacist feedback to prescribers, plus patient-facing education, sustains behaviour change.
- **Invest in interdisciplinary collaboration.** Nephrologists, intensivists, oncologists, and primary care clinicians are partners rather than recipients of advice.

Limitations of the Evidence and Research Priorities

Several gaps limit confident practice. Most high-quality data on nephrotoxin surveillance derive from paediatric populations, and few randomised trials of pharmacist-led interventions in adults report kidney-specific outcomes. Definitions of drug-induced AKI vary, and creatinine-based criteria cannot distinguish haemodynamic changes from structural injury. Evidence on rechallenge is largely observational and subject to confounding by indication, and long-term outcomes of reintroduction versus permanent withdrawal are inadequately studied.

Priority research questions include:

- Pragmatic randomised or stepped-wedge trials of pharmacist-led nephrotoxin stewardship in adult medical, surgical, and oncology populations.
- Validation of kidney injury biomarkers to differentiate functional from structural injury and to guide rechallenge.
- Prospective studies of timing and dose strategies for restarting RAS and SGLT2 inhibitors after AKI.
- Predictive models, including machine learning, that integrate medication exposure, laboratory trends, and patient factors, with evaluation of whether they change outcomes when linked to pharmacist action.
- Patient-reported outcomes and implementation science on sick-day guidance and post-AKI follow-up.

Conclusion

Medication-related AKI is a high-burden but substantially modifiable condition. The pharmacist's contribution extends beyond renal dose adjustment to a coherent cycle of care: anticipate risk before exposure, detect injury early through surveillance, reason about causality, withdraw or modify offending drugs promptly, and reintroduce essential therapies deliberately, with monitoring and documentation that persist across transitions of care. Evidence from paediatric nephrotoxin stewardship and from multicomponent adult programmes supports this model, while the limitations of alert-only strategies emphasise the value of a skilled human response. Health systems seeking to reduce avoidable kidney harm should consider resourcing clinical pharmacists within protocolised, interdisciplinary MR-AKI pathways and evaluating them rigorously.

Declaration of Generative AI and AI-Assisted Technologies

Generative AI tools were used to assist in developing conceptual figure designs and generating illustrative visual elements for this review. AI-assisted tools were also used to improve language clarity, readability, and presentation. The author reviewed and critically evaluated the manuscript and all AI-assisted content, verified the scientific accuracy of the information, and takes full responsibility for the integrity, originality, and final content of the manuscript.

Author Contributions

The author was responsible for conceptualization, literature search, evidence synthesis, interpretation of the available literature, manuscript preparation, critical revision, and approval of the final manuscript. The author accepts full responsibility for the accuracy and integrity of the work.

References

1. Hoste EAJ, Kellum JA, Selby NM, et al. Global epidemiology and outcomes of acute kidney injury. Nat Rev Nephrol. 2018; 14: 607-625.
2. Kellum JA, Romagnani P, Ashuntantang G, et al. Acute kidney injury. Nat Rev Dis Primers. 2021; 7: 52.
3. Uchino S, Kellum JA, Bellomo R, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA. 2005; 294: 813-818.
4. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int Suppl. 2012; 2: 1-138.
5. Kane-Gill SL, Goldstein SL. Drug-induced acute kidney injury: a focus on risk assessment for prevention. Crit Care Clin. 2015; 31: 675-684.
6. Perazella MA. Pharmacology behind common drug nephrotoxicities. Clin J Am Soc Nephrol 2018; 13: 1897-1908.
7. Awdishu L, Mehta RL. The 6R's of drug-induced nephrotoxicity. BMC Nephrol. 2017; 18: 124.
8. Perazella MA. Drug-induced acute kidney injury: diverse mechanisms of tubular injury. Curr Opin Crit Care. 2019; 25: 550-557.
9. Lapi F, Azoulay L, Yin H, et al. Concurrent use of diuretics, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers with non-steroidal anti-inflammatory drugs and risk of acute kidney injury: nested case-control study. BMJ. 2013; 346.
10. Luther MK, Timbrook TT, Caffrey AR, et al. Vancomycin plus piperacillin-tazobactam and acute kidney injury in adults: a systematic review and meta-analysis. Crit Care Med. 2018; 46: 12-20.
11. Rybak MJ, Le J, Lodise TP, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant Staphylococcus aureus infections: a revised consensus guideline and review. Am J Health Syst Pharm. 2020; 77: 835-864.
12. Perazella MA, Markowitz GS. Drug-induced acute interstitial nephritis. Nat Rev Nephrol. 2010; 6: 461470.
13. Muriithi AK, Leung N, Valeri AM, et al. Biopsy-proven acute interstitial nephritis, 1993–2011: a case series. Am J Kidney Dis. 2014; 64: 558-566.
14. Cortazar FB, Kibbelaar ZA, Glezerman IG, et al. Clinical features and outcomes of immune checkpoint inhibitor-associated AKI: a multicenter study. J Am Soc Nephrol. 2020; 31: 435-446.
15. Gupta S, Short SAP, Sise ME, et al. Acute kidney injury in patients treated with immune checkpoint inhibitors. J Immunother Cancer. 2021; 9: e003467.
16. Ozkok A, Edelstein CL. Pathophysiology of cisplatin-induced acute kidney injury. Biomed Res Int. 2014; 2014: 967826.
17. Mehran R, Dangas GD, Weisbord SD. Contrast-associated acute kidney injury. N Engl J Med. 2019; 380: 2146-2155.
18. Weisbord SD, Gallagher M, Jneid H, et al. Outcomes after angiography with sodium bicarbonate and acetylcysteine (PRESERVE). N Engl J Med 2018; 378: 603-614.
19. Matzke GR, Aronoff GR, Atkinson AJ Jr, et al. Drug dosing consideration in patients with acute and chronic kidney disease: a clinical update from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2011; 80: 1122-1137.
20. Goldstein SL, Mottes T, Simpson K, et al. A sustained quality improvement program reduces nephrotoxic medication-associated acute kidney injury. Kidney Int. 2016; 90: 212-221.
21. Goldstein SL, Kirkendall E, Nguyen H, et al. Electronic health record identification of nephrotoxin exposure and associated acute kidney injury. Pediatrics. 2013; 132: e756-767.
22. Goldstein SL, Dahale D, Kirkendall ES, et al. A prospective multi-center quality improvement initiative (NINJA) indicates a reduction in nephrotoxic acute kidney injury in hospitalized children. Kidney Int. 2020; 97: 580-588.
23. Wilson FP, Shashaty M, Testani J, et al. Automated, electronic alerts for acute kidney injury: a single-blind, parallel-group, randomised controlled trial. Lancet. 2015; 385: 1966-1974.
24. Wilson FP, Martin M, Yamamoto Y, et al. Electronic health record alerts for acute kidney injury: multicenter, randomized clinical trial. BMJ. 2021; 372. m4786.
25. Selby NM, Casula A, Lamming L, et al. An organizational-level program of intervention for AKI: a pragmatic stepped wedge cluster randomized trial (Tackling AKI). J Am Soc Nephrol. 2019; 30: 505-515.
26. Meersch M, Schmidt C, Hoffmeier A, et al. Prevention of cardiac surgery-associated AKI by implementation of the KDIGO guidelines in high-risk patients identified by biomarkers: the PrevAKI randomized controlled trial. Intensive Care Med. 2017; 43: 1551-1561.
27. Joslin J, Wilson H, Zubli D, et al. Recognition and management of acute kidney injury in hospitalised patients can be partially improved with the use of a care bundle. Clin Med (Lond) 2015; 15: 431-436.

28. Mekonnen AB, McLachlan AJ, Brien JA. Effectiveness of pharmacist-led medication reconciliation programmes on clinical outcomes at hospital transitions: a systematic review and meta-analysis. BMJ Open. 2016; 6: e010003.
29. Lee H, Ryu K, Sohn Y, et al. Impact on patient outcomes of pharmacist participation in multidisciplinary critical care teams: a systematic review and meta-analysis. Crit Care Med. 2019; 47: 1243-1250.
30. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981; 30: 239-245.
31. Brar S, Ye F, James MT, et al. Association of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use with outcomes after acute kidney injury. JAMA Intern Med. 2018; 178: 1681-1690.
32. Bhandari S, Mehta S, Khwaja A, et al. Renin-angiotensin system inhibition in advanced chronic kidney disease (STOP-ACEi). N Engl J Med. 2022; 387: 2573-2585.
33. Heerspink HJL, Stefansson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease (DAPA-CKD). N Engl J Med. 2020; 383: 1436-1446.
34. Herrington WG, Staplin N, Wanner C, et al. Empagliflozin in patients with chronic kidney disease. N Engl J Med. 2023; 388: 117-127.
35. Chawla LS, Bellomo R, Bihorac A, et al. Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. Nat Rev Nephrol. 2017; 13: 241-257.
36. Coca SG, Yusuf B, Shlipak MG, et al. Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. Am J Kidney Dis. 2009; 53: 961-973.
37. Watson KE, Dhaliwal K, McMurtry E, et al. Sick day medication guidance for people with diabetes, kidney disease, or cardiovascular disease: a systematic scoping review. Kidney Med. 2022; 4: 100491.
38. Tesfaye WH, Castelino RL, Wimmer BC, et al. Inappropriate prescribing in chronic kidney disease: a systematic review of prevalence, associated clinical outcomes and impact of interventions. Int J Clin Pract. 2017; 71.

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