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Medicines and Kidneys

Medicines Advice Initiative Australia

CATAG Council of Australian Therapeutic Advisory Groups

Medicines and the kidney

CATAG Practice Tool

Key Points

Medicine dosage adjustments in people with reduced kidney function should be anticipated at the point of prescribing. This consideration takes into account the clinical situation of the person, including trends, rather than rigid calculations based on reported numbers alone.

Educate people with reduced kidney function, and their carers, about their diagnosis and the possible need for medicine dosage adjustments.

Provide a complete and accurate discharge summary to guide ongoing treatment and care for people whose renal function has declined during hospitalisation.

Medicines and Therapeutics Advisory Committees should endorse and implement:

- → Local protocols for the estimation of kidney function and application to medicine dosage adjustments
- → Local guidance for standards of communication at transitions of care when reduced kidney function has been identified.

Purpose

The Council of Australian Therapeutic Advisory Groups (CATAG) has developed this practice tool to increase awareness of the safe and effective use of medicines in reduced kidney function. It promotes effective communication at discharge around the diagnosis or occurrence of reduced kidney function and provision of a clear medicines plan.

Implementation of these recommendations may be used as evidence towards achievement of The National Safety and Quality Health Service (NSQHS) Standards: Clinical Governance, Partnering with Consumers, Medication Safety, Comprehensive Care, and Communicating for Safety.

Background

Reduced kidney function is a commonly identified problem in hospitals, and a major risk factor for serious adverse reactions to medicines.[1, 2] 1 in 3 people with reduced kidney function are prescribed medicines that are either contraindicated, or prescribed dosages that are inappropriately high.[3]

Medicines can have a profound effect on the kidneys, and reduced kidney function can impact the safety and effectiveness of many medicines.

Chronic Kidney Disease (CKD)

In Australia, approximately 1.7 million adults (1 in 10 adult Australians and 1 in 5 adult First Nations Australians) have CKD.[4, 5, 6] Yet fewer than 10% of people with CKD are aware they have the condition.[6]

CKD is defined as:[5]

- An estimated or measured glomerular ltration rate (GFR) <60 mL/min/1.73m^2 that is present for ≥3 months with or without evidence of kidney damage.

Or

- Kidney damage, with or without decreased GFR that is present for ≥3 months, as evidenced by the following:
  - Albuminuria
  - Haematuria (after exclusion of urological causes)
  - Structural abnormalities (e.g. on kidney imaging tests)
  - Pathological abnormalities (e.g. kidney biopsy).

CKD is commonly asymptomatic and is often overlooked in the community.[5] 75% of Australian adults have a risk factor for developing CKD[5] (see Table 1).

At-risk people also have an increased likelihood of inappropriate medicine dosage, which may predispose to acute kidney injury (AKI).[4]

Acute Kidney Injury (AKI)

AKI affects 8–20% of adults admitted to hospital and approximately 50% of patients in intensive care units.[7] It is independently and strongly associated with increased morbidity and mortality.[5]

The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines define AKI as:[7, 8, 9]

- an increase in serum creatinine by ≥26.5 micromol/L within 48 hours
- an increase in serum creatinine by ≥50% within the prior 7 days, or
- a urine volume <0.5 mL/kg/hour for 6 hours.

Without recent creatinine measurements, differentiating AKI from unrecognised CKD can be difficult, and urine output is often imprecisely measured.[7]

AKI in Australian hospitalised patients is significantly under-reported.[10] Medication-induced AKI accounts for up to 20% of AKI cases and can contribute to the development of incident CKD or progression of existing CKD.[4]

Table 1: Risk factors for CKD and AKI[5]

CKD	AKI	
• History of AKI • Anatomical factors (e.g. single kidney or congenital abnormalities of the urinary tract)[11] • Age >60 years • Age >18 years in First Nations Australians • Diabetes • Hypertension • Established cardiovascular disease • Family history of kidney failure • Obesity (body mass index ≥30 kg/m^2) • Current or past smoker	**Pre-existing risk factors**	
	• CKD • Advanced age • Other chronic diseases (e.g. diabetes, cancer, anaemia, and heart, lung or liver disease)	
	Potentially modifiable kidney insults	
	Pre-renal	Hypovolaemia, Blood loss, Hypotension
	Intra-renal	Critical illness, Drug toxicity, Rhabdomyolysis[12]
	Post-renal	Obstruction

Measuring kidney function

GFR is accepted as the best overall marker of kidney function but specific tests to quantitate GFR are not always feasible.[13] Validated prediction equations that estimate GFR (eGFR) are routinely used in clinical practice, however these are indexed for a standardised body surface area (BSA) of 1.73m^2 and may need to be adjusted for a person's actual BSA before clinical application.[4, 13, 14] Historically, the Cockcroft-Gault formula has been used to estimate creatinine clearance (eCrCl) for medicine dosage adjustment in people with reduced kidney function, however it overestimates GFR, is not adjusted for BSA, and has not been validated with newer standardised creatinine assays.[13, 14]

More information

A more detailed discussion of the different equations and their application is available at:

- Estimation of kidney function for medication dosing in adult patients with chronic kidney disease: a practice update[4]
- How to adjust drug doses in chronic kidney disease[14]
- Frequently asked questions about GFR estimates[13]

Estimation of kidney function for medication dosing in adult patients with chronic kidney disease: a practice update

How to adjust drug doses in chronic kidney disease

Frequently asked questions about GFR estimates

Australian Medicines Handbook

Table 2: Formulae used in estimating glomerular filtration rates[14]

	Equation
Adjusted eGFR (mL/min)	$\frac{\text{eGFR (mL/min/1.73 m}^2\text{) x BSA}}{1.73}$
BSA (m^2)	refer to Australian Medicines Handbook for calculator and equation
Cockcroft-Gault eCrCl (mL/min)	$\frac{\text{(140 – age) x weight}}{\text{serum creatinine x 0.814}}$ (x 0.85 if female)

Table 3: Examples of clinical situations where eGFR or eCrCl results may be unreliable or misleading[4, 5]

eGFR is misleading but serum creatinine concentration is a better marker	eGFR is falsely reduced due to other reasons for increased serum creatinine	eGFR is falsely increased due to other reasons for decreased serum creatinine
• Acute changes in kidney function (e.g. AKI) • People under 18 years of age • Severe liver disease present • eGFR values above 90 mL/min/1.73m^2 • Pregnancy	• Extremes of body size – very big • High muscle mass • Medicines interacting with creatinine excretion (e.g. trimethoprim, cimetidine) • Medicines which increase creatinine production (e.g. fenofibrate)	• Extremes of body size – very small • Significant loss of muscle mass • Myopathies • Paraplegia • Amputees

Medicines in reduced kidney function

Reduced kidney function alters the pharmacokinetics of many medicines.[2] This causes some medicines to:[4, 14]

- accumulate to toxic concentrations causing adverse effects (e.g. pethidine) and in some cases, lead to further kidney damage (e.g. lithium, vancomycin, methotrexate)[15]
- require dosage reductions or potentially be contraindicated below certain thresholds (e.g. dabigatran, metformin)[15]
- become less effective (e.g. nitrofurantoin, furosemide).[15]

The need for, and extent of, medicine dosage adjustment depends on:[14]

- the severity of kidney disease
- the proportion of the medicine eliminated by the kidney
- the risk of adverse effects from the medicine
- the duration of treatment
- if the medicine has active or toxic metabolites that rely on the kidney for elimination
- For people on dialysis, serum creatinine concentration is not reliable and eGFR is always < 15 mL/min.

Medicine dosage adjustments should be based on advice included in the Australian Medicines Handbook, Renal Drug Database or Therapeutic Guidelines.

Applying eGFR to medicines

Medicine dosage adjustments in people with reduced kidney function should be anticipated at the point of prescribing,[14] and must take into consideration the clinical situation of the person, including trends, rather than rigid calculations based on reported numbers alone.

→ Use adjusted eGFR (Table 2) to estimate kidney function for medicine dosage.[4]

→ Applying eGFR where eCrCl is recommended for medicine dosage adjustments, is not likely to result in a clinically significant difference.[4, 14]

→ Use therapeutic monitoring for medicines with a narrow therapeutic index, when available.[14]

→ In AKI, eGFR calculations are not reliable and should not be used to dose medicines.[16] The trend in serum creatinine concentrations over multiple measurements should instead be used to judge the degree of decline or improvement in GFR (see Table 4).[16]

Table 4: Application of serum creatinine trend to guide medicine dosage adjustments in AKI[16]

Serum creatinine trend in AKI	Medicine dosage adjustment
Rising rapidly, or only single initial elevated value available	GFR should be assumed to be 0 mL/min and medicines dosed accordingly
Falling	eGFR likely underestimates the true GFR. Medicines should be dosed according to a GFR greater than the calculated GFR and re-evaluated daily
Plateau reached and stable for at least several days	eGFR may be used to guide medicine dosage

Australian Medicines Handbook

Renal Drug Database

Therapeutic Guidelines

Effective communication at discharge

A complete and accurate discharge summary is essential for people and their ongoing treatment and care.[17] Despite AKI being commonly identified in hospital settings,[7] a recent study found that only half of laboratory-identified AKI were documented,[10] which is a barrier to effective communication at discharge. Following AKI, Kidney Health Australia recommends a Kidney Health Check (eGFR, urine albumin/creatinine ratio, and blood pressure) every year for the first 3 years, then every 2 years thereafter.[5] It is crucial that AKI, even if completely resolved, is communicated appropriately to people and their general practitioners and other relevant members of their healthcare team for comprehensive follow-up care.

Following AKI, almost a third of people are readmitted to hospital within 90 days.[7] At discharge, health care practitioners need to explain critical information, such as diagnoses and treatment, while integrating people's conditions, perceptions, and needs at the same time.[18] A recent systematic review and meta-analysis found that educating people at discharge regarding their medication, diagnoses, or therapeutic regimen is associated with a lower risk of readmissions and increased rates of adherence.[18] Effective communication strategies must be in place to inform people and their carers of any reduced kidney function and the necessary adjustments to their medicines. This includes the need for ongoing monitoring to prevent adverse outcomes.

Discharge communication for people who have reduced kidney function during hospitalisation should include:[7, 17]

- A clear diagnosis of AKI or CKD, or a clear plan for obtaining a diagnosis
- When to recheck eGFR
- Anticipated outcomes (e.g. when the eGFR is expected to improve to baseline)
- Medicines administered during the hospital stay, where relevant
- Medicines plan:
  - All medicines listed alphabetically
  - Clear indication of which medicines are new, continued, or discontinued
  - Clear reasons for any changes to medicines
  - Action plan for medicines according to anticipated outcomes (e.g. once eGFR > 60 mL/min/1.73m^2, increase dose of metformin to previous regular dose of 2 g daily)
- A recommendation for a post-discharge comprehensive medicines review once kidney function has stabilised.

These communications should be issued in writing, together with verbal education to people and their carers.

Clinicians are encouraged to educate and empower people with reduced kidney function by taking the time to explain their diagnosis, providing their eGFR results and a current medicines list, educating on the risk of further kidney injury, and advising to seek medical attention in the event of acute illness or dehydration. Provision of a sick day action plan is also recommended; this provides information to the person about what to do when they are sick including which medicines that may need to be temporarily withheld.[5]

Next steps

For Medicines and Therapeutics Committees

Integrate renal dosage considerations into medicines policy frameworks.

Consider how the health service obtains estimates for renal function and provide guidance on the use of eGFR or eCrCl to facilitate best practice across the health service.

Consider endorsing local protocols for the estimation of kidney function and application to medicine dosage adjustments.

Foster educational initiatives to raise awareness of reduced kidney function and its impact on medicines management.

For Clinicians

Document clearly in medical records any diagnosis of reduced kidney function to improve discharge communications.

Anticipate medicine dosage adjustments in people with reduced kidney function at the point of prescribing.

Be mindful of the limitations of kidney function estimates such as eGFR and eCrCl, and consider the clinical situation of the person, including trends, to undertake medicine dosage adjustments.

Access Medicines and Therapeutics Advisory Committee-endorsed resources to ensure safe and effective medicine use in people with reduced kidney function.

Provide people affected by reduced kidney function, and their carers, with a clear diagnosis and medicines plan.

Following AKI in the hospital setting; recommend in discharge communications a Kidney Health Check every year for the first 3 years, then every 2 years.[5]

Educate and empower people with CKD to be active members of their healthcare team.

Recommend a post-discharge comprehensive medicines review for people whose renal function has declined during hospitalisation.

Resources

Tools and further information for implementation:

Medicine dosage adjustments

Australian Medicines Handbook (subscription required)

Renal Drug Database (subscription required)

Therapeutic Guidelines (subscription required)

CARI guidelines

AKI

Acute Kidney Injury toolkit – RCGP Learning

CKD

Kidney health: looking after your kidneys – NPS Medicinewise

Chronic Kidney Disease (CKD) Management in Primary Care 5th Edition – Kidney Health Australia

Medicines for chronic kidney disease: A practical guide – NPS Medicinewise

Discharge communication

Transfers of care – Professional Record Standards Body (UK)

Appendix 1: How this was developed

CATAG has developed this practice tool as part of the Medicines Advice Initiative Australia (MAIA); Supporting quality use of medicines consortium. This practice tool aims to assist good governance and decision-making for health service organisations, medicines governance committees and health professionals.

This guidance was developed in consultation with the CATAG member organisations listed below:

ACT Health

Clinical Excellence Commission, NSW Health

NSW Therapeutic Advisory Group (NSW TAG)

Northern Territory Health Medicines and Therapeutics Committee (NTMTC)

Queensland Health Medicines Advisory Committee (QHMAC)

South Australian Medicines Advisory Committee (SAMAC)

Tasmanian Medicines Access and Advisory Committee (TMAAC)

Victorian Therapeutics Advisory Group (Vic TAG)

Western Australian Therapeutics Advisory Group (WATAG)

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Jennifer Nolan
CATAG QUM Project Officer

Lisa Pulver
CATAG National Coordinator

Subject Matter Experts

Dr Jessie Beaulieu

Dr Sally Fotheringham

Conjoint Associate Professor Darren Roberts

Carla Scuderi

Kristen Watson

References

1. Laville S, Gras-Champel V, Hamroun A, Moragny J, Lambert O, Metzger M, et al. Kidney Function Decline and Serious Adverse Drug Reactions in Patients With CKD. Am J Kidney Dis. 2024;83(5):601-14.
2. Roberts DM, Sevastos J, Carland JE, Stocker SL, Lea-Henry TN. Clinical Pharmacokinetics in Kidney Disease: Application to Rational Design of Dosing Regimens. Clin J Am Soc Nephrol. 2018;13(8): 1254-63.
3. Castelino R, Saunder T, Kitsos A, Peterson G, Jose M, Wimmer B, et al. Quality use of medicines in patients with chronic kidney disease. BMC Nephrol. 2020;21(1):216.
4. Mirkov S, Scuderi C, Lloyd J, Coutsouvelis J, O'Connor S, Potts S, et al. Estimation of kidney function for medication dosing in adult patients with chronic kidney disease: a practice update. Journal of Pharmacy Practice and Research. 2023;54(1): 94-106.
5. Chronic kidney disease (CKD) management in primary care (5th edition): Kidney Health Australia, Melbourne; 2024 [20 June 2024]. Available from: https://kidney.org.au/health-professionals/ckd-management-handbook
6. Australian Health Survey: Biomedical Results for Chronic Diseases: Australian Bureau of Statistics; 2011-12. 2013 [20 June 2024]. Available from: www.abs.gov.au/statistics/health/health-conditions-and-risks/australian-health-survey-biomedical-results-chronic-diseases/latest-release
7. Pianta TJ, Barakat Z, Langsford D. Care for survivors of acute kidney injury. Australian Journal of General Practice. 2021;50(7):450-6.
8. Palevsky PM. Definition and staging criteria of acute kidney injury in adults: UpToDate; 2023 [27 June 2024]. Available from: www.uptodate.com/contents/definition-and-staging-criteria-of-acute-kidney-injury-in-adults
9. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney inter., Suppl.2012; 2: 1-138 [24 July 2024]. Available from: https://kdigo.org/wp-content/uploads/2016/10/KDIGO-2012-AKI-Guideline-English.pdf
10. Campbell CA, Li L, Kotwal S, Georgiou A, Horvath AR, Westbrook J, et al. Under-detection of acute kidney injury in hospitalised patients: a retrospective, multi-site, longitudinal study. Intern Med J. 2020;50(3):307-14.
11. Life with a single kidney: Kidney Health Australia; 2020 [18 July 2024]. Available from: https://assets.kidney.org.au/resources/KHA-Factsheet-Life-with-a-single-kidney-2020.pdf
12. Candela N, Silva S, Georges B, Cartery C, Robert T, Moussi-Frances J, et al. Short- and long-term renal outcomes following severe rhabdomyolysis: a French multicenter retrospective study of 387 patients. Ann Intensive Care. 2020;10(1):27.
13. Frequently asked questions about GFR estimates: National Kidney Foundation; 2022 [11 July 2024]. Available from: www.kidney.org/sites/default/files/441-8491_2202_faqs_aboutgfr_v5.pdf
14. Stefani M, Singer RF, Roberts DM. How to adjust drug doses in chronic kidney disease. Australian Prescriber. 2019;42:163-7.
15. Australian Medicines Handbook: Australian Medicines Handbook Pty Ltd; 2024 [updated July 202417 July 2024]. Available from: https://amhonline.amh.net.au/auth
16. Okusa MD, Rosner MH. Overview of the management of acute kidney injury (AKI) in adults: UpToDate; 2023 [25 July 2024]. Available from: www.uptodate.com/contents/overview-of-the-management-of-acute-kidney-injury-aki-in-adults
17. Transfers of Care: Professional Record Standards Body; 2024 [10 July 2024]. Available from: https://theprsb.org/toolkits/transfersofcare/getting-to-grips/
18. Becker C, Zumbrunn S, Beck K, Vincent A, Loretz N, Muller J, et al. Interventions to Improve Communication at Hospital Discharge and Rates of Readmission. JAMA Network Open. 2021;4(8).

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