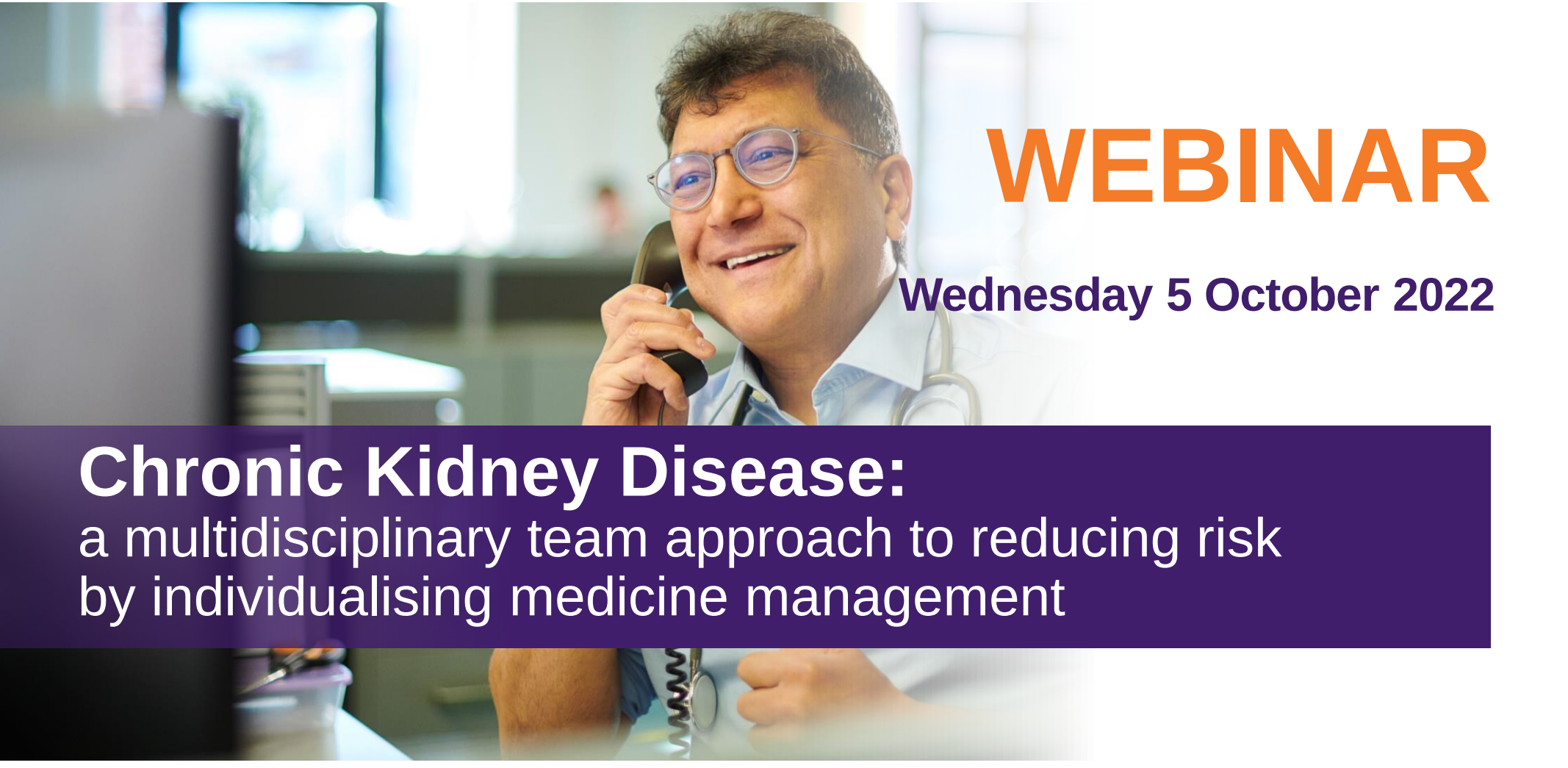

WEBINAR

Wednesday 5 October 2022

Chronic Kidney Disease:
a multidisciplinary team approach to reducing risk by individualising medicine management

This program is funded by the Australian Government Department of Health and Aged Care.

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Meet the panel

Dr Kate Annear
Medical Advisor at NPS MedicineWise

Dr Tim Senior
GP at Tharawal Aboriginal Corporation, and chronic kidney disease expert in general practice

Graeme Turner
Chronic Kidney Disease Nurse Practitioner

Tim Perry
Consultant pharmacist in general practice

Margaret Sugden
Living with CKD

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Disclosure

Graeme Turner: Received honoraria payments June 2021 and Nov 2021 for educational meeting speaker Astra Zeneca

Learning outcomes

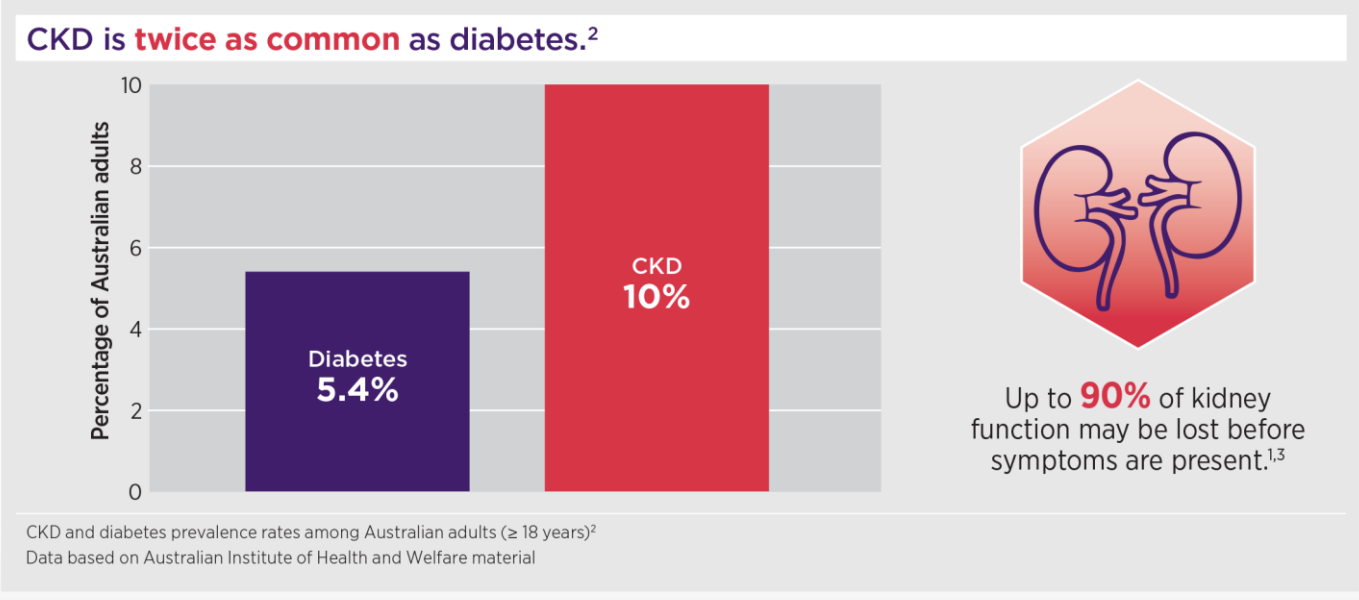
1. Develop a plan with the patient that optimise pharmacological treatments for the management of chronic kidney disease (CKD) and related comorbidities

2. Implement a patient-centred multidisciplinary team approach to care to improve patient outcomes

3. Identify when referral to experts or support services is advisable to reduce patient hospitalisations and improve patient outcomes

CKD is a major public health problem

- CKD is a silent disease[1]
- CKD is common, harmful and treatable[2,3]



Australian Institute of Health and Welfare. Cardiovascular disease, diabetes and chronic kidney disease - Australian facts: Prevalence and incidence. Cardiovascular, diabetes and chronic kidney disease series no. 2. Canberra: AIHW, 2014.
Australian Institute of Health and Welfare. Chronic kidney disease. Canberra: AIHW, 2020 Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney Health Australia, 2020

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What is CKD?

Definition of CKD[1]

Reduced kidney function for ≥ 3 months as demonstrated by:		Kidney damage for ≥ 3 months as demonstrated by:
▸ estimated or measured glomerular filtration rate (GFR) < 60 mL/min/1.73m^2	**and/ or**	▸ albuminuria (abnormal urine albumin-to-creatinine ratio [ACR]), or ▸ haematuria after the exclusion of urological causes, or ▸ structural abnormalities, such as those found on kidney imaging tests, or ▸ pathological abnormalities, such as those found on kidney biopsy

1. Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney Health Australia, 2020. 'Used with permission from Kidney Health Australia, 2022'

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Multidisciplinary team approach

- Patient and carer
- GP
- Pharmacist
- Nurse practitioner
- Aboriginal health worker
- Nephrologist
- Psychologist
- Dietitian

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Staging CKD

Combine eGFR stage, albuminuria stage and underlying diagnosis to specify CKD stage[1]

		Albuminuria stage		
Kidney function stage	GFR (mL/min/1.73m²)	Normal (urine ACR mg/mmol) Male: < 2.5 Female: < 3.5	Microalbuminuria (urine ACR mg/mmol) Male: 2.5–25 Female: 3.5–35	Macroalbuminuria (urine ACR mg/mmol) Male: > 25 Female: > 35
1	≥ 90	Not CKD unless haematuria, structural or pathological abnormalities present	moderate	very high
2	60–89		moderate	very high
3a	45–59	moderate	high	very high
3b	30–44	high	high	very high
4	15–29	very high	very high	very high
5	< 15 or on dialysis	very high	very high	very high

Risk of progressive CKD: low moderate high very high

1. Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney Health Australia, 2020. 'Used with permission from Kidney Health Australia, 2022'

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Managing CKD in primary care

Kidney function stage	GFR (mL/min/1.73m²)	Albuminuria stage: Normal (urine ACR mg/mmol) Male: < 2.5 Female: < 3.5	Microalbuminuria (urine ACR mg/mmol) Male: 2.5–25 Female: 3.5–35	Macroalbuminuria (urine ACR mg/mmol) Male: > 25 Female: > 35
1	≥ 90	Not CKD unless haematuria, structural or pathological abnormalities present		
2	60–89			
3a	45–59			
3b	30–44			
4	15–29			
5	< 15 or on dialysis			

Risk of progressive CKD: low moderate high very high

Follow the corresponding colour-coded action plan found in the handbook

Recognise that CKD is part of integrated care for chronic conditions

TABLE 1

Assessment and management for people with CKD based on colour-coded clinical action plans[1]

CKD clinical action plans[c]	eGFR ≥ 60 with microalbuminuria or eGFR 45–59 with normoalbuminuria	eGFR 30–59 with microalbuminuria or eGFR 30–44 with normoalbuminuria	Macroalbuminuria irrespective of eGFR or eGFR < 30 irrespective of albuminuria

1. Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney Health Australia, 2020. 'Used with permission from Kidney Health Australia, 2022'

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Focus on medicine management

Pharmacological management of CKD involves three key areas

PRESCRIBE
medicines shown to slow progression of CKD and/or reduce cardiovascular risk

REDUCE
doses of medicines cleared by the kidneys according to current kidney function and individual product information

AVOID
nephrotoxic medicines where possible

1. Dwyer KD, Robson B, Sum C. How to treat chronic kidney disease. AusDoc. How to Treat. Australian Doctor, 2021
2. Bezabhe WM, Kitsos A, Saunder T, et al. Medication prescribing quality in Australian primary care patients with chronic kidney disease. J Clin Med 2020;9:783.
3. Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney
4. 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.
5. Usherwood T, Lee V. Advances in chronic kidney disease pathophysiology and management. Aust J Gen Pract 2021;50:188-92 Australia, 2020

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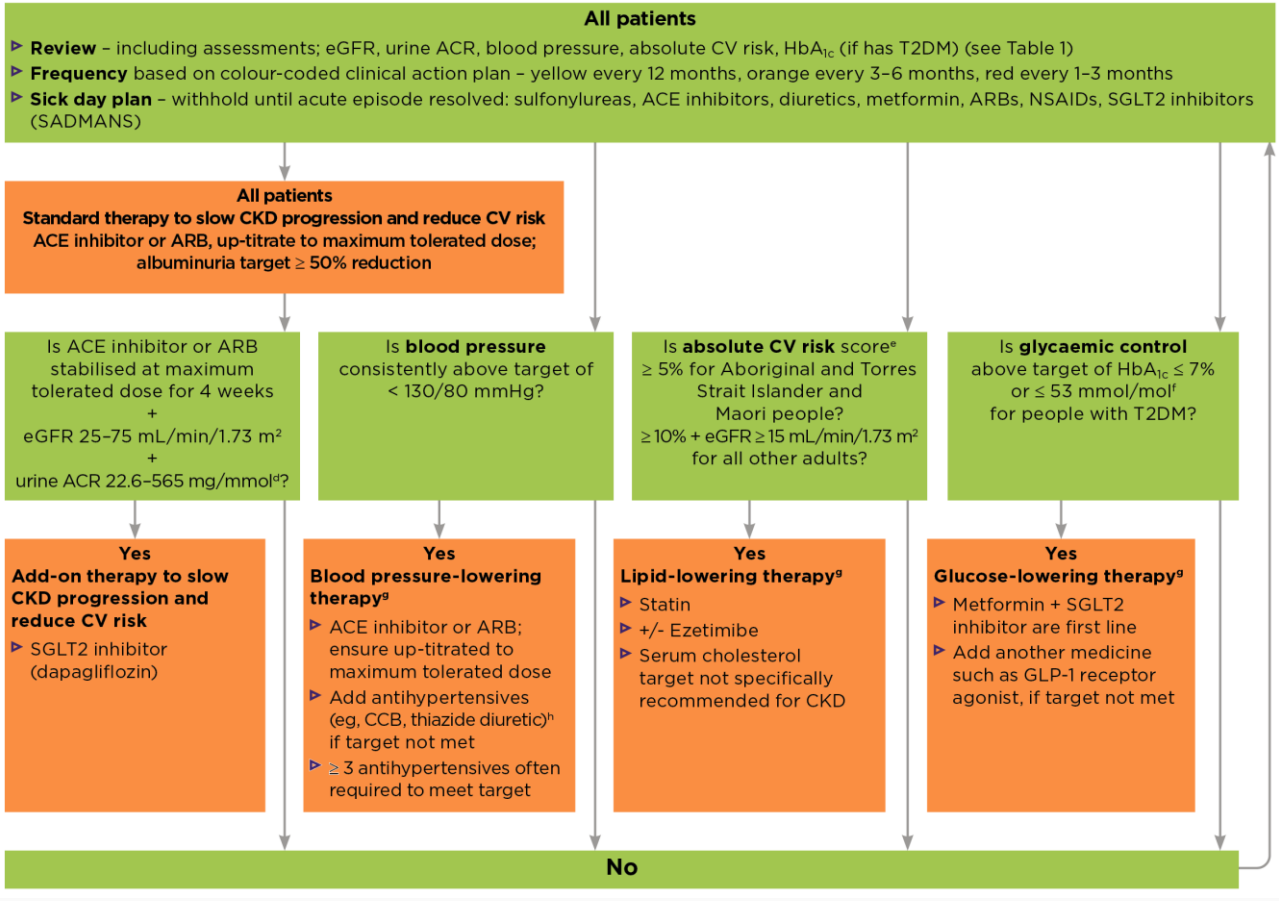
Algorithm for medicines that slow CKD progression and reduce CV risk



[d] PBS criteria for dapagliflozin for CKDt;
[e] Moderate or severe CKD (eGFR < 45 mL/min/1.73 m² or persistent ACR > 25 mg/mmol [males] or > 35 mg/mmol [females]) already considered highest risk of CV event (> 15% probability in 5 years);
[f] Cut off level needs individualising according to patient circumstances;
[g] Therapy for underlying cause/comorbidity to slow CKD progression and reduce CV risk;
[h] Antihypertensive choice depends on patient preferences, comorbidities, eGFR and cost.

ACE = angiotensin-converting enzyme; ACR = albumin-to-creatinine ratio; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; GLP-1 = glucagon-like peptide-1; ; HbA_{1c} = glycated haemoglobin; NSAIDs = non-steroidal anti-inflammatory drugs; PBS = Pharmaceutical Benefits Scheme; SGLT2 = sodium-glucose co-transporter 2; T2DM = type 2 diabetes mellitus

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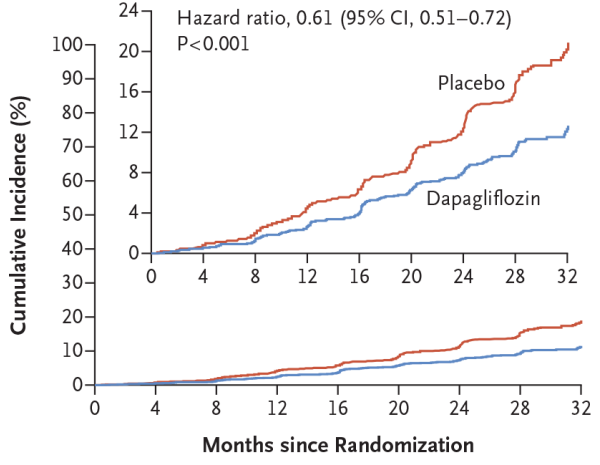
DAPA-CKD

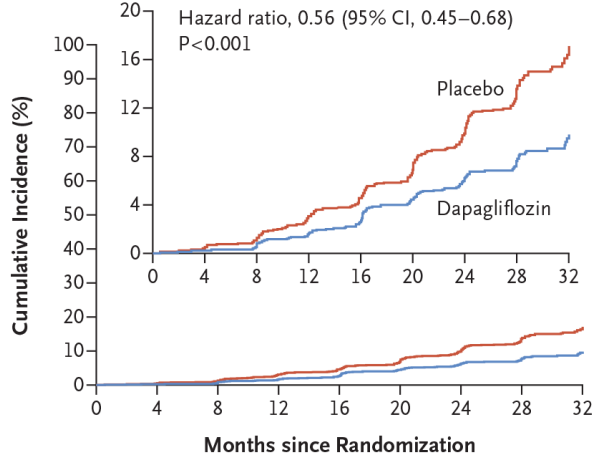
Dapagliflozin is TGA indicated to reduce the risk of progressive decline in kidney function in patients with CKD in stages 2–4 & macroalbuminuria

A Primary Composite Outcome



No. at Risk									
Placebo	2152	1993	1936	1858	1791	1664	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309

B Renal-Specific Composite Outcome



No. at Risk									
Placebo	2152	1993	1936	1858	1791	1664	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309

Dapaglifozin is now PBS listed for the treatment of CKD in addition to standard care

Heerspink et al NEJEM 2020; 383

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Evidence from the DAPA- CKD Trial

For people with CKD **+/-** type 2 diabetes:

39% reduction with dapagliflozin vs placebo (9.2% with dapagliflozin vs 14.5% with placebo) for primary composite outcome:

- Worsening kidney function decline (eGFR decline ≥ 50%) or
- Onset of kidney failure (dialysis, kidney transplant or GFR < 15mL/min/1.73m^2) or
- Death due to kidney disease or cardiovascular disease

Heerspink et al NEJEM 2020; 383

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Dapagliflozin – New PBS Authority Required (streamlined) for CKD

The new indication for dapagliflozin is chronic kidney disease (CKD). According to the clinical criteria, the patient must have:

- ✓ a diagnosis of CKD, defined as abnormalities of kidney structure or function present for 3 months or more, prior to initiating treatment with dapagliflozin, **and**
- ✓ an estimated glomerular filtration rate (eGFR) 25–75 mL/min/1.73 m^2 inclusive, prior to initiating treatment with dapagliflozin, **and**
- ✓ a urine ACR 22.6–565 mg/mmol (200–5000 mg/g) inclusive, prior to initiating treatment with dapagliflozin, **and**
- ✓ stabilised disease for at least 4 weeks on the maximum tolerated dose of an:
  - angiotensin-converting enzyme (ACE) inhibitor, **or**
  - angiotensin receptor II blocker (ARB)

that is continued as a combination treatment with dapagliflozin, unless contraindicated.

Role of SGLT2 inhibitors in CKD

Diabetes CKD population[6]

- Initially designed for diabetes treatment, reduce blood glucose and HbA_{1c}
- SGLT2 inhibitor added to ACE inhibitor or ARB protects the kidneys

Non- diabetes CKD population[7]

- Same protection of the kidneys observed as with the diabetic population when SGLT2 inhibitor added to ACE inhibitor or ARB
- SGLT2 inhibitors work to slow deterioration of kidney function irrespective of diabetic status

- Dapagliflozin
- Empagliflozin
- Ertugliflozin

6. Perkovic V et al NJEM 2019; 380 (24): 2295-2306
7. Heerspink HJL et al, NEJM 2020; (15) 1436-1446

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Referral to a nephrologist

Nephrology referral recommended

- **eGFR <30** mL/min/1.73m² (Stage 4 or 5 CKD of any cause).
- **Persistent significant albuminuria** (urine ACR ≥30 mg/mmol).
- A **sustained decrease** in **eGFR** of 25% or more within 12 months OR a sustained decrease in eGFR of 15 mL/min/1.73m² per year.
- **CKD with hypertension** that is hard to get to target despite **at least three anti-hypertensive agents.**

Referral not necessary*

- **Stable eGFR ≥30** mL/min/1.73m².
- **Urine ACR <30** mg/mmol (with no haematuria).
- **Controlled blood pressure.**

A quality referral includes:

- Current eGFR
- Previous renal imaging (if available)
- Reason for referral

Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney, 2020. 'Used with permission from Kidney Health Australia, 2022'

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Managing medicines with CKD

- Promote adherence- discuss the ‘why’ of medicines with patients
- Up-titrating an ACE inhibitor or ARB
  - Monitoring BP, fluids, K+
  - Predictable reduction in eGFR when starting an ACE inhibitor or ARB
  - Tolerate up to 25% decrease
- No dose titration needed for an SGLT2 inhibitor
  - Monitoring for dehydration
  - Predictable reduction in eGFR when starting an SGLT2 inhibitor
  - Tolerate up to 30% decrease

Managing potential adverse effects of up-titrating an ACE inhibitor / ARB

Result/ Adverse effect	Action
eGFR decrease **< 25% (within 2 months of starting treatment)**	Continue therapy
eGFR decrease **> 25% (below baseline value)**	Stop ACE inhibitor or ARB Seek nephrologist advice
Hyperkalaemia **Serum K+ (potassium)** **> 6.0- 6.5 mmol/L**	Refer patient to an Accredited Practising Dietician to discuss low K+ diet Correct metabolic acidosis (target serum HCO3 >22 mmol/L). Initiate potassium wasting diuretics (eg, thiazides) Avoid salt substitutes which may be high in K+ Consider a cation exchange resin (eg, Resonium A). Stop ACE inhibitor/ARB/spironolactone if K+ is persistently > 6.0 mmol/L and not responsive to above therapies
Hyperkalaemia **Serum K+(potassium)** **>6.5 mmol/L**	Refer to nearest Emergency Department if K+ due to the lethal risk of arrhythmia.

- ACE inhibitors and ARBs can be safely prescribed at all stages of CKD and should not be deliberately avoided just because GFR is reduced.

Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney, 2020

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Patient Action Plans

- Individualise treatment goals
- Sick day management
- Patient follow-up

All patients with CKD should have an acute kidney injury prevention and management plan

Table 3: Medicines to avoid on a sick day or when dehydrated[3,5]

S	A	D	M	A	N	S
Sulfonylureas	ACE inhibitors	Diuretics	Metformin	ARBs	NSAIDs	SGLT2 inhibitors

[g] Medicines withheld need to be recommenced when acute episode has resolved

3. Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney Health Australia, 2020. 'Used with permission from Kidney Health Australia, 2022'
5. Usherwood T, Lee V. Advances in chronic kidney disease pathophysiology and management. Aust J Gen Pract 2021;50:188-92

Pharmacists in different settings

- Community pharmacist
- Accredited pharmacist – HMRs
- GP practice pharmacist (including Aboriginal health services)
- Pharmacists working in aged care facilities

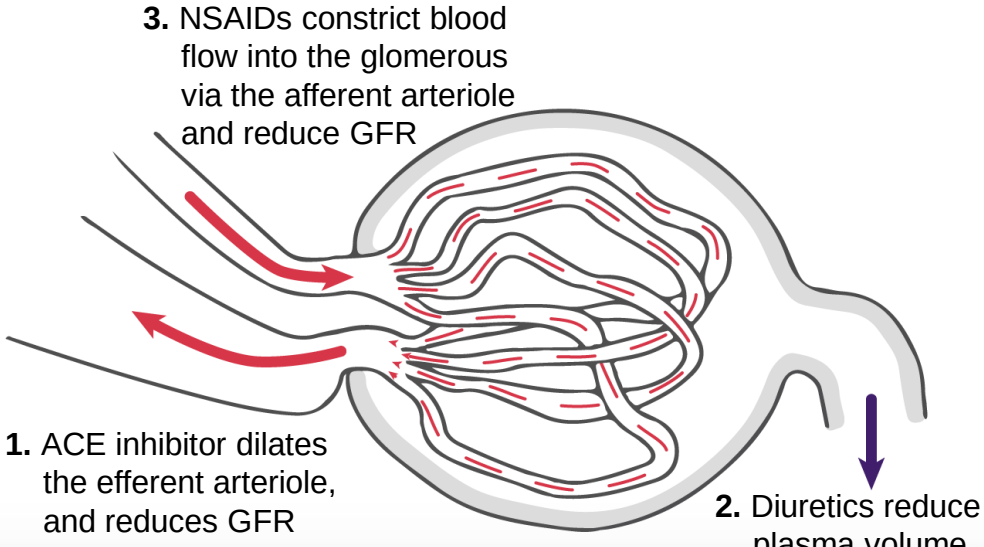
Medicines that can adversely affect kidney function in CKD

Table 4: Nephrotoxic medicines that can adversely affect kidney function in CKD[3,5,20]

Nephrotoxic medicines	
▸ aminoglycosides (eg, gentamicin) ▸ calcineurin inhibitors (eg, tacrolimus) ▸ lithium	▸ NSAIDs/COX-2 inhibitors ▸ radiographic contrast agents

TRIPLE WHAMMY

The combination of **ACE inhibitor/ARB**, any **diuretic** and **NSAID/COX-2 inhibitor** (except low-dose aspirin) – the '**triple whammy**' – can result in acute kidney injury, especially if the patient is volume depleted or CKD is present.[3,28] **Avoid combination** where possible.



3. Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney Health Australia, 2020
5. Usherwood T, Lee V. Advances in chronic kidney disease pathophysiology and management. Aust J Gen Pract 2021;50:188-92
20. Australian Medicines Handbook. Adelaide: AMH Pty Ltd, 2022.
28. Manski-Nankervis JA, McMorrow R, Nelson C, et al. Prescribing and deprescribing in chronic kidney disease. Aust J Gen Pract 2021;50:183-7.

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Medicine considerations in CKD

Consider:

- eGFR
- Absorption
- Distribution
- Metabolism
- Elimination

Commonly prescribed medicines cleared by the kidney

Table 4: Medicines cleared by the kidney that may require dose reduction in people with CKD following the orange and red clinical action plans[d,3,21,26]

Anti-infective	Diabetes		Pain
▸ famciclovir	▸ acarbose	▸ **metformin**[e]	▸ gabapentin
▸ trimethoprim	▸ gliptins	▸ SGLT2 inhibitors[16,17]	▸ **NSAIDs**
▸ nirmatrelvir[27]	● saxagliptin	● empagliflozin	▸ opioid analgesics
▸ valaciclovir	● sitagliptin	● ertugliflozin	▸ pregabalin
Cardiovascular	● vildagliptin	▸ sulfonylureas[f]	**Other**
▸ **apixaban**	▸ GLP-1 receptor agonists	● glibenclamide	▸ allopurinol
▸ dabigatran	● exenatide	● gliclazide	▸ benzodiazepines
▸ digoxin	▸ insulin	● glimepiride	▸ colchicine
▸ fenofibrate		● glipizide	▸ denosumab
▸ **rivaroxaban**			▸ lithium
▸ sotalol			
▸ spironolactone			

GLP-1 = glucagon-like peptide-1; NSAID = non-steroidal anti-inflammatory drug; SGLT2 = sodium-glucose cotransporter 2

[d] List is not exhaustive; always refer to current product information when prescribing for patients with CKD

[e] Metformin requires dose reduction if eGFR 30–60 mL/min/1.73m^2 and is contraindicated if eGFR < 30 mL/min/1.73m^2 [3,7]

[f] Sulfonylureas require dose reduction if eGFR < 30 mL/min/1.73m^2; glibenclamide is contraindicated if eGFR < 60 mL/min/1.73m^2 [3]

Adapted with permission from Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney Health Australia, 2020
3. Kidney Health Australia. Chronic kidney disease (CKD) management in primary care. Melbourne: Kidney Health Australia, 2020.
21. Australian Medicines Handbook. Adelaide: AMH Pty Ltd, 2022.
26. Manski-Nankervis JA, McMorrow R, Nelson C, et al. Prescribing and deprescribing in chronic kidney disease. Aust J Gen Pract 2021;50:183-7.

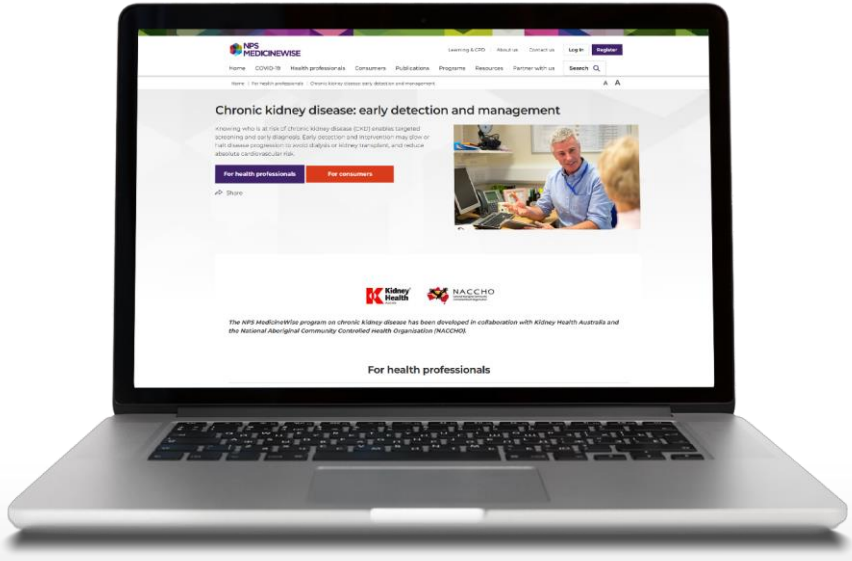
Margaret's story

- 68 years old
- Type 2 diabetes
- Hypertension
  (due to primary aldosteronism)
- Hypercholesterolaemia
- CKD (1 year)

NPS MedicineWise resources

Web content:

www.nps.org.au/professionals/chronic-kidney-disease



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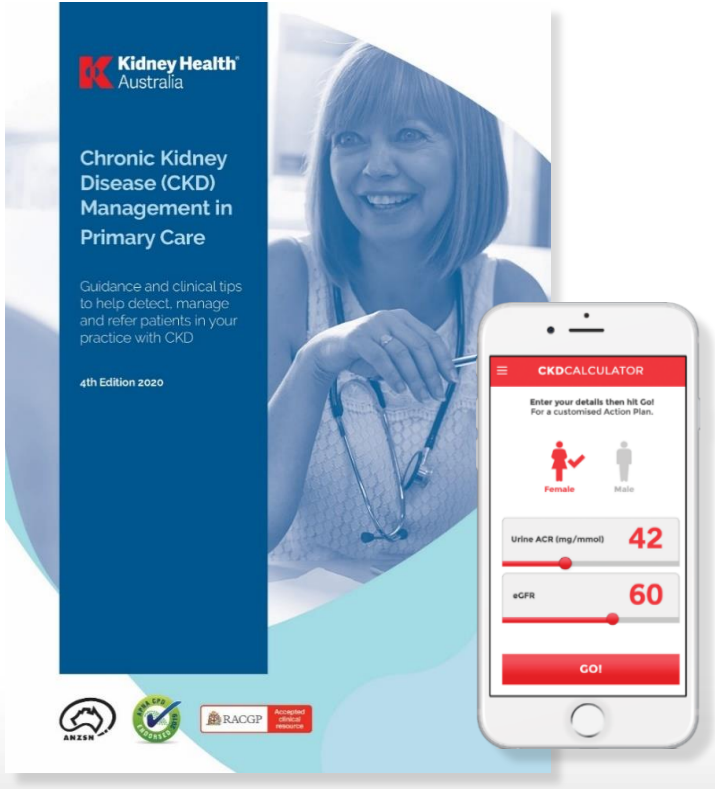

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www.kidney.org.au/health-professionals

CKD-GO! App

can be downloaded for FREE on the iPhone & Android app stores

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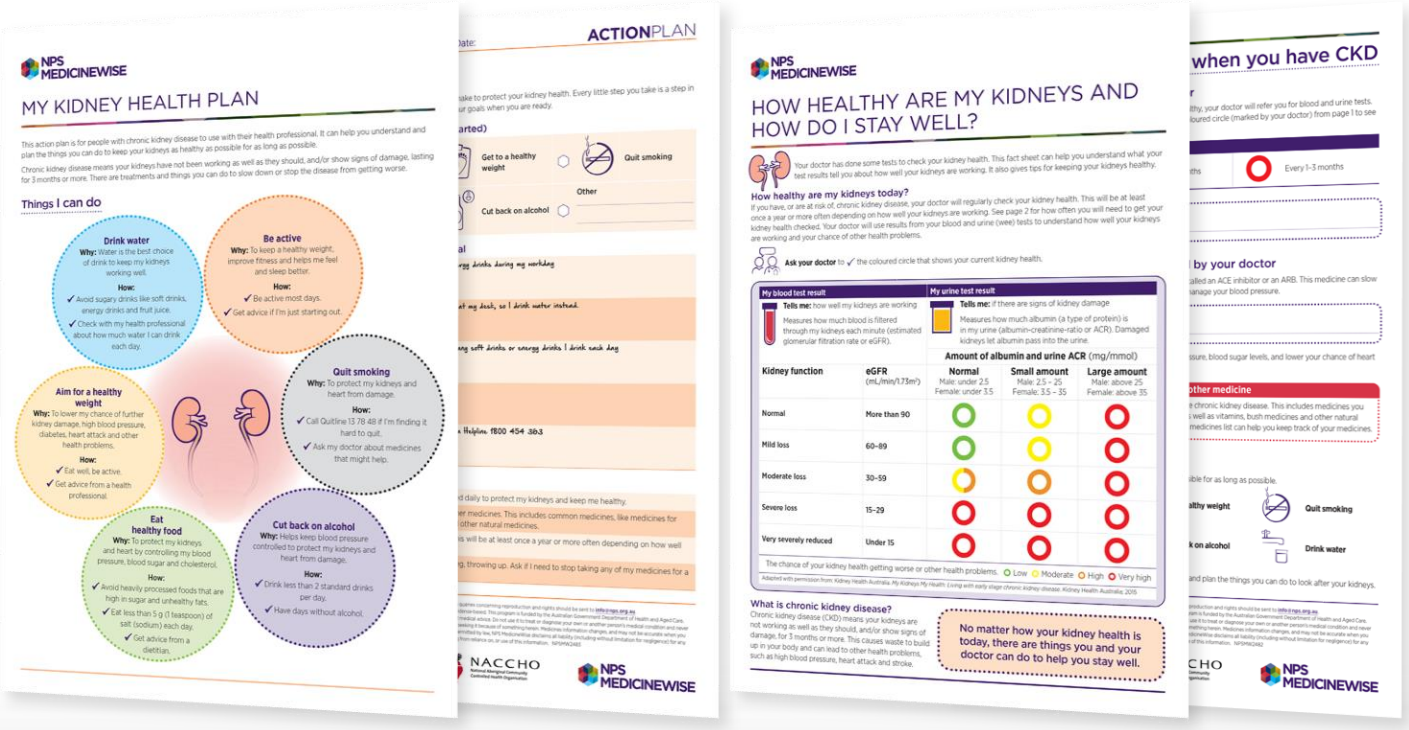
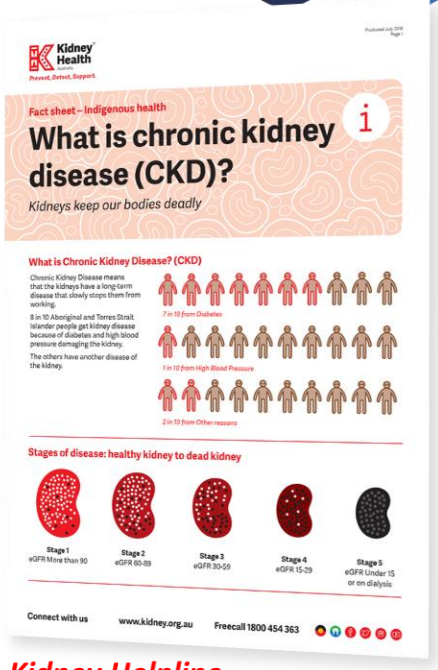
Patient resources



[Kidney health: looking after your kidneys (nps.org.au)](nps.org.au)



Kidney Helpline

Free call information service

Kidney questions?

Information or advice?

Contact 1800 454 363

kidneyhelpline@kidney.org.au

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