

Mate tākihi ukiuki

Making a difference in chronic kidney disease

Part 1: Catching renal impairment early

He matenga ohorere, he wairua uiui, wairua mutunga kore

The grief of a sudden, untimely death will never be forgotten

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Key concepts

- Chronic kidney disease (CKD) and end-stage renal failure is much more common in Māori, Pacific, Asian people and people from the Indian subcontinent
- CKD is a silent condition but can be readily detected with eGFR and urinalysis
- Early intervention gives the opportunity to slow progression to end-stage renal disease and reduce cardiovascular risk

www.bpac.org.nz keyword: earlyrenal

Chronic kidney disease (CKD) is the modern term for chronic renal impairment, diagnosed using estimated glomerular filtration rates (eGFR) and markers of kidney damage, detected with urinalysis, imaging or biopsy (Table 1).

Renal impairment has traditionally been diagnosed using serum creatinine. However serum creatinine does not show an abnormal rise until at least 50% of renal function is lost. Diagnosis is often delayed until symptoms or complications of renal failure develop, missing the opportunity for early protective intervention. Using eGFR facilitates early diagnosis of CKD before any change to serum creatinine.

Chronic kidney disease is common

CKD is estimated to affect approximately 10% of the population. It appears that Māori, Pacific peoples, Asian people and people from the Indian subcontinent have a higher burden of this disease. Māori with diabetes are three and a half times more likely to have renal failure than non-Māori with diabetes.¹

Only a small proportion of patients with CKD progress to end-stage renal disease. However Māori and Pacific peoples are much more likely to have end-stage renal disease than other ethnic groups in New Zealand. The higher incidence of diabetic and hypertensive end-stage renal disease in Māori and Pacific peoples cannot be fully explained by the underlying disease prevalence. Other factors that may contribute to this difference in incidence are socio-economic disadvantage, which is a known risk factor for end-stage renal disease, and underutilisation of medical services.

People with end-stage renal disease commonly have a progressive fall in eGFR, marked proteinuria and hypertension. Early recognition and management, and appropriate referral can prevent end-stage renal disease in some cases and greatly improve the outcome for others.²

Markers of kidney damage include:

- Persistent proteinuria/albuminuria
- Persistent haematuria/WBC in urine
- Red blood cell casts/dysmorphic cells on urine microscopy
- Ultrasound/other radiological abnormalities

Table 1: CKD staging based on eGFR and markers of kidney damage

eGFR (mL/min/1.73 m ²)	Markers of kidney damage (see box)	CKD staging	Description
>60	No	No chronic kidney disease	Renal function declines with age
	Yes	1 = eGFR >90	Normal kidney function but urine findings or structural abnormalities or genetic trait point to kidney disease
		2 = eGFR 60–89	Mildly reduced kidney function, and other findings (as for stage 1) point to kidney disease
<60	Not required for staging	3 = eGFR 30–59	Moderately reduced kidney function
		4 = eGFR 15–29	Severely reduced kidney function
		5 = eGFR <15, or needing dialysis	Very severe, or end-stage renal disease

It is important to note that CKD is an independent cardiovascular risk factor and more people with CKD die from cardiovascular disease than end-stage renal disease.³

Being able to detect CKD early allows:⁴

- Early protective intervention to reduce progression towards end-stage renal disease (CKD stage 5)
- Monitoring and treatment of cardiovascular risk factors to reduce cardiovascular disease
- Monitoring and treatment of complications

Quick clinical assessment for kidney health check

History including:

- Any risk factors, particularly hypertension
- Prescribed, OTC and alternative medication
- Symptoms of cardiovascular disease e.g. breathlessness, oedema, chest pain, claudication
- Symptoms suggestive of underlying systemic diseases such as vasculitis, lupus or myeloma e.g. fever, weight loss, fatigue, general aches and pains

Examination:


- Dipstick urine
- Blood pressure
- Weight
- Fluid status (JVP, signs of pulmonary oedema, peripheral oedema)
- Enlarged bladder or kidneys
- Renal bruits
- PR in male with lower urinary tract symptoms

Targeted testing for chronic kidney disease in New Zealand

Targeted testing should be considered for people with the following risk factors:

- Aged over 50 years
- Hypertension
- Any cardiovascular disease (IHD, chronic heart failure, peripheral vascular disease and cerebral vascular disease)
- Diabetes
- Smoking
- Known personal or family history of kidney disease, including recurrent UTIs and lower urinary tract symptoms
- Māori, Pacific peoples, Asian people and people from the Indian subcontinent
- Long-term treatment with nephrotoxic medication such as lithium, cyclosporin, mesalazine (NSAIDs are not nephrotoxic but use increases the risk of kidney damage)

It is recommended to perform a kidney health check at a minimum of every five years. This should be done annually if diabetes, established cardiovascular disease or CKD is present.

 **Best practice tip:** link a kidney health check with a cardiovascular risk assessment by adding in urinalysis and serum creatinine.

Kidney Health Check

The kidney health check includes

- eGFR
- Urinalysis for proteinuria or microalbuminuria
- Blood pressure measurement

Further investigations depend on the results of these tests. Any abnormalities should prompt history-taking and examination.

eGFR results and action required

Laboratories provide the eGFR automatically when reporting serum creatinine results. If the eGFR is greater than 90 no further action is required unless there is suspicion of kidney disease. Levels less than 90 require urinalysis (Table 2).

The confirmation of a new CKD stage is based on a minimum of two eGFR values taken over three months. For newly diagnosed patients it is important to establish the rate of decline.

Table 2: Results of eGFR and required action

eGFR value	Action
>90	“No further action” unless known, or suspected, structural or urinalysis abnormalities.
60–89	Urinalysis required to check for evidence of kidney disease. If negative and no other markers of renal disease “no further action” required. If positive determine CKD stage.
<60	Exclude acute renal failure. Determine CKD stage. Urinalysis required to check for haematuria/proteinuria.


N.B. Most laboratories report the eGFR either as >90 mL/min/1.73m² or, if less than this, as an exact figure.⁵ Some laboratories only give exact figures if the result is less than 60.

If the eGFR is unexpectedly low, best practice is to exclude acute renal failure by a repeat serum creatinine/eGFR. If the patient is obviously ill with rising blood pressure, oedema, proteinuria, haematuria and an unexpected falling eGFR or rising creatinine, discuss urgently with the nephrology team as this may indicate acute kidney damage e.g. glomerulonephritis.

Urinalysis

Urinalysis can provide indirect evidence of kidney damage. Inflammation or abnormal function of the glomeruli can lead to leakage of red blood cells or protein into the urine, resulting in haematuria or proteinuria.

Urine dipstick testing is recommended as a screening test in general practice. Standard dipstick analysis is adequate to screen for proteinuria and haematuria, but will not detect microalbuminuria unless an albumin specific dipstick is used.

 **Best practice tip:** Most eGFRs in people with risk factors for CKD will be 60–89 and urinalysis will be required to decide if CKD is present. As proteinuria levels may fluctuate during the day an early morning urine for analysis is preferred.

Abnormal results should prompt:

- A mid-stream urine (MSU) looking for red blood cell casts or dysmorphic cells on microscopy or, if nitrates or leucocytes positive, culture for infection

and/or

- Early morning urinalysis for albumin:creatinine ratio (ACR) or protein:creatinine ratio (PCR) (Table 3). ACR and PCR have superseded 24 hour urine collection for quantification of proteinuria.

Table 3: Further tests required after dipstick urine

Dipstick result	MSU	ACR	PCR
No abnormality		✓ if diabetic or hypertensive	
Haemoglobin/blood +ve	✓		
Albumin +ve (albumin specific dipstick)	✓	✓ if diabetic or hypertensive	
Protein +ve	✓		✓

eGFR is an estimate

Although eGFR is now the basis of diagnosis of CKD it is only an estimate. The eGFR is calculated from the serum creatinine, using the four-variable Modification of Diet in Renal Disease (MDRD) equation, based on age and a standard adult body surface area. Results are reported as mL/min/1.73m². As it does not allow for any variation in body weight, a significant error is possible.

eGFR is not valid in pregnant women or in children (<18 years), nor accurate if the serum creatinine is changing rapidly as occurs in acute renal failure.

Creatinine level is dependant on muscle mass and the eGFR is most likely to be inaccurate in people at extremes of body type, e.g. reassuringly high in people with reduced muscle mass such as the frail elderly, amputees, people with chronic liver disease or on low protein diets (vegan).

The MDRD equation was originally validated in the United States. Although it has not been validated for Māori and Pacific peoples, Asian people or those from the Indian subcontinent, the eGFR is still recommended for screening for CKD in these populations.

An alternative calculation, that uses the individual's weight as an approximation of lean body mass, is the Cockcroft-Gault equation for calculating creatinine clearance as mL/min (the proxy measure for glomerular filtration rate). This equation is preferred for drug dosage adjustment, although it has similar disadvantages as the MDRD equation for people at extremes of body type.

$$\text{Creatinine clearance mL/min} = \frac{(140 - \text{age}) \times \text{weight(kg)} \times 0.85(\text{in females})}{815 \times \text{serum creatinine(mmol/L)}}$$

Transient proteinuria or haematuria is not unusual. Urine dipstick blood or protein that does not resolve should be followed up. Persistent haematuria requires referral to either urology or nephrology.

Other investigations

Ultrasound is the optimal first line test for imaging the renal tract in patients with CKD and identifies obstructive uropathy, renal size and symmetry, renal scarring and polycystic disease. It is recommended where there is lower urinary tract symptoms, eGFR < 60 mL/min/1.73m², progressively falling eGFR or refractory hypertension (blood pressure >150/90 mmHg despite three or more antihypertensives).

Further reading

The following guidelines were considered in the development of this article:

- Kidney Health New Zealand (KHNZ). Chronic kidney disease (CKD) management in general practice: summary guide. KHNZ 2009.

Available from www.kidneys.co.nz

- Kidney Health Australia (KHA). Chronic kidney disease (CKD) management in general practice: guidance and clinical tips to help identify, manage and refer CKD in our practice. KHA, Melbourne 2007.

Available from www.kidney.org.au or www.racgp.org.au

- Scottish Intercollegiate Guidelines Group (SIGN). Diagnosis and management of chronic kidney disease: a national clinical guideline. SIGN, Edinburgh 2008.


Available from www.sign.ac.uk

Definitions of microalbuminuria and proteinuria

Detection of an increase in protein excretion has both diagnostic and prognostic value in the initial detection and confirmation of renal disease.

Persistent higher-risk microalbuminuria is defined by an early morning ACR of >2.5 mg/mmol in men or >3.5 mg/mmol in women on two or more occasions.

In non-diabetic CKD significant proteinuria is regarded as >0.3 g/day on two separate occasions. This is equivalent to PCR >30 mg/mmol.

 **Best practice tip:** a PCR of 100 mg/mmol is equivalent to daily protein excretion of 1 g/24 hours.

- National Institute for Clinical Excellence (NICE). Chronic kidney disease: national clinical guideline for early identification and management in adults in primary and secondary care. NICE, London, 2008. Clinical Guideline 73.
Available from www.nice.org.uk
- Rosenberg M, Kalda R, Kasiulevicius V, Lember M. Management of chronic kidney disease in primary health care: position paper of the European Forum for Primary Care. Qual Primary Care 2008;16:279-94.

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2. Richards N, Harris K, Whitfiels M, et al. Primary care-based disease management of chronic kidney disease (CKD), based on estimated glomerular filtration rate (eGR) reporting, improves patient outcomes. Nephrol Dial Transplant 2008;23:549-55.
3. Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalisation. NEJM 2004;351(13):1296-1305.
4. Gomez GB, de Lusigan S, Gallagher H. Chronic kidney disease: a new priority for primary care. Brit J Gen Pract 2006;908-10.
5. Saleem M, Florkowski C for the Australasian Creatinine Consensus Working Group. Reporting of estimated glomerular filtration rate (eGFR) in New Zealand – what are the clinical laboratories doing? N Z Med J 2006;119(1246).