

# Chronic kidney disease in adults: assessment and management

Clinical guideline

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[www.nice.org.uk/guidance/cg182](https://www.nice.org.uk/guidance/cg182)

## Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline replaces CG73.

This guideline is the basis of QS5.

## Introduction

This guideline updates and replaces NICE guideline CG73. The recommendations are labelled according to when they were originally published (see [about this guideline](#) for details).

Chronic kidney disease (CKD) describes abnormal kidney function and/or structure. It is common, frequently unrecognised and often exists together with other conditions (such as cardiovascular disease and diabetes). Moderate to severe CKD is also associated with an increased risk of other significant adverse outcomes such as acute kidney injury, falls, frailty and mortality. The risk of developing CKD increases with age. As kidney dysfunction progresses, some coexisting conditions become more common and increase in severity. CKD can progress to end-stage kidney disease in a small but significant percentage of people.

CKD is usually asymptomatic, but it is detectable, and tests for CKD are simple and freely available. There is evidence that treatment can prevent or delay the progression of CKD, reduce or prevent the development of complications, and reduce the risk of cardiovascular disease. However, CKD is often unrecognised because there are no specific symptoms, and it is often not diagnosed or diagnosed at an advanced stage.

The classification of CKD has evolved over time. In 2004, the Department of Health's [National service framework for renal services](#) adopted the 2002 US [National Kidney Foundation Kidney Disease Outcomes Quality Initiative](#) classification of CKD. This classification divides CKD into 5 stages and uses the combination of an index of kidney function, the glomerular filtration rate (GFR), and markers of kidney damage to define the stages. Stages 3–5 were defined by a GFR less than 60 ml/min/1.73 m<sup>2</sup> with or without markers of kidney damage, on at least 2 separate occasions separated by a period of at least 90 days. Stages 1 and 2 were defined by the presence of markers of kidney damage including albuminuria, urine sediment abnormalities, electrolyte and other abnormalities caused by tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging and a history of kidney transplantation.

To delineate an increased risk of adverse outcomes, the 2008 NICE guideline on chronic kidney disease suggested 2 key changes to this classification: the subdivision of stage 3 into 3a (GFR

45–59 ml/min/1.73 m<sup>2</sup>) and 3b (30–44 ml/min/1.73 m<sup>2</sup>), and the addition of the suffix 'P' to denote significant proteinuria at any stage. The 2008 NICE guideline defined significant proteinuria as a urinary albumin:creatinine ratio (ACR) of 30 mg/mmol or higher (roughly equivalent to a protein:creatinine ratio of 50 mg/mmol or higher). In 2013, the Kidney Disease: Improving Global Outcomes (KDIGO) guidance on [the evaluation and management of chronic kidney disease](#) adopted the subdivision of GFR categories suggested by the NICE guideline, but also included 3 ACR categories (ACR under 3 mg/mmol, 3–30 mg/mmol, and over 30 mg/mmol) for each GFR category in an updated classification (as shown in the following tables).

This update of the NICE guideline reviews the classification of CKD.

## Kidney Disease Improving Global Outcomes GFR categories

GFR category	GFR (ml/min/1.73 m <sup>2</sup> )	Terms
G1	>90	Normal or high
G2	60–89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure

\* Relative to young adult level

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate

Reprinted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) [KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease](#). Kidney International (Suppl. 3): 1–150

## Kidney Disease Improving Global Outcomes ACR categories

ACR category	ACR (mg/mmol)	Terms
A1	<3	Normal to mildly increased

A2	3–30	Moderately increased*
A3	>30	Severely increased**
<p>* Relative to young adult level</p> <p>** Including nephrotic syndrome (ACR usually &gt;220 mg/mmol)</p> <p>Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease</p> <p>Reprinted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) <a href="#">KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease</a>. Kidney International (Suppl. 3): 1–150</p>		

Late presentation of people with kidney failure increases morbidity, mortality and associated healthcare costs. Diagnosis of people with kidney disease has improved since the introduction of national estimated GFR reporting and CKD indicators in the primary care Quality and Outcomes Framework, and also because there is increased public and health professional awareness of CKD. However, late presentation was still reported as 19% overall in the Renal Association's 2013 [UK Renal Registry report](#).

The total cost of CKD in England in 2009–10 was estimated at between £1.44 and £1.45 billion, which was approximately 1.3% of all NHS spending in that year<sup>[1]</sup>. More than half of this amount was spent on renal replacement therapy for the 2% of people with CKD that progresses to kidney failure. It was estimated in the economic model that approximately 7000 excess strokes and 12,000 excess myocardial infarctions occurred in people with CKD in 2009–10 (relative to an age- and gender-matched population without CKD), with an estimated cost of between £174 and £178 million. Strategies aimed at earlier identification and prevention of progression to end-stage kidney disease are clearly needed.

This guideline seeks to address these issues by updating the 2008 NICE guidance in areas where new data have become available, and providing new guidance in areas where previously no evidence existed.

The new and updated areas include:

- identification and investigation of people who have or are at risk of developing CKD
- classification of CKD and identification of people at risk of CKD complications and progression
- the definition of CKD progression

- the relationship between acute kidney injury and CKD
- self-management of CKD
- pharmacotherapy for CKD.

## Drug recommendations

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

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<sup>[1]</sup> Kerr M, Bray B, Medcalf J et al. (2012) Estimating the financial cost of chronic kidney disease to the NHS in England. Nephrology Dialysis Transplantation. 27 (Suppl. 3): iii73–80

## Patient-centred care

This guideline offers best practice advice on the care of adults with chronic kidney disease.

Patients and healthcare professionals have rights and responsibilities as set out in the [NHS Constitution for England](#) – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. Healthcare professionals should follow the [Department of Health's advice on consent](#). If someone does not have capacity to make decisions, healthcare professionals should follow the [code of practice that accompanies the Mental Capacity Act](#) and the supplementary [code of practice on deprivation of liberty safeguards](#).

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in [patient experience in adult NHS services](#).

## Key priorities for implementation

The following recommendations have been identified as priorities for implementation. The full list of recommendations is in [section 1](#).

## Investigations for chronic kidney disease

- Clinical laboratories should:
  - use the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation to estimate  $\text{eGFR}_{\text{creatinine}}$ , using creatinine assays with calibration traceable to standardised reference material
  - use creatinine assays that are specific (for example, enzymatic assays) and zero-biased compared with isotope dilution mass spectrometry (IDMS)
  - participate in a UK national external quality assessment scheme for creatinine. [new 2014]
- Consider using  $\text{eGFR}_{\text{cystatinC}}$  at initial diagnosis to confirm or rule out CKD in people with:
  - an  $\text{eGFR}_{\text{creatinine}}$  of 45–59 ml/min/1.73 m<sup>2</sup>, sustained for at least 90 days and
  - no proteinuria (albumin:creatinine ratio [ACR] less than 3 mg/mmol) or other [marker of kidney disease](#). [new 2014]
- Do not diagnose CKD in people with:
  - an  $\text{eGFR}_{\text{creatinine}}$  of 45–59 ml/min/1.73 m<sup>2</sup> and
  - an  $\text{eGFR}_{\text{cystatinC}}$  of more than 60 ml/min/1.73 m<sup>2</sup> and
  - no other [marker of kidney disease](#). [new 2014]


- Offer testing for CKD using eGFRcreatinine and ACR to people with any of the following risk factors:
  - diabetes
  - hypertension
  - acute kidney injury (see [recommendation 1.3.9](#))
  - cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
  - structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
  - multisystem diseases with potential kidney involvement – for example, systemic lupus erythematosus
  - family history of end-stage kidney disease (GFR category G5) or hereditary kidney disease
  - opportunistic detection of haematuria. [new 2014]


## Classification of chronic kidney disease

- Classify CKD using a combination of GFR and ACR categories (as described in table 1). Be aware that:
  - increased ACR is associated with increased risk of adverse outcomes
  - decreased GFR is associated with increased risk of adverse outcomes
  - increased ACR and decreased GFR in combination multiply the risk of adverse outcomes. [new 2014]

**Table 1 Classification of chronic kidney disease using GFR and ACR categories**

GFR and ACR categories and risk of adverse outcomes			ACR categories (mg/mmol), description and range		
			<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73 m <sup>2</sup> ), description and range	≥90 Normal and high	G1	No CKD in the absence of markers of kidney damage		
	60–89 Mild reduction related to normal range for a young adult	G2			
	45–59 Mild–moderate reduction	G3a <sup>1</sup>			
	30–44 Moderate–severe reduction	G3b			
	15–29 Severe reduction	G4			
	<15 Kidney failure	G5			


  
Increasing risk


  
Increasing risk

<sup>1</sup> Consider using eGFR<sub>cystatinC</sub> for people with CKD G3aA1 (see recommendations 1.1.14 and 1.1.15)

Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate

Adapted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International (Suppl. 3): 1–150

## Frequency of monitoring

- Use table 2 to guide the frequency of GFR monitoring for people with, or at risk of, CKD, but tailor it to the person according to:
  - the underlying cause of CKD
  - past patterns of eGFR and ACR (but be aware that CKD progression is often non-linear)
  - comorbidities, especially heart failure
  - changes to their treatment (such as renin-angiotensin-aldosterone system [RAAS] antagonists, NSAIDs and diuretics)
  - intercurrent illness
  - whether they have chosen conservative management of CKD. [new 2014]

**Table 2 Frequency of monitoring of GFR (number of times per year, by GFR and ACR category) for people with, or at risk of, CKD**

		ACR categories (mg/mmol), description and range		
		A1 <3 Normal to mildly increased	A2 3–30 Moderately increased	A3 >30 Severely increased
GFR categories (ml/min/1.73 m <sup>2</sup> ), description and range	G1 ≥90 Normal and high	≤1	1	≥1
	G2 60–89 Mild reduction related to normal range for a young adult	≤1	1	≥1
	G3a 45–59 Mild–moderate reduction	1	1	2
	G3b 30–44 Moderate–severe reduction	≤2	2	≥2
	G4 15–29 Severe reduction	2	2	3
	G5 <15 Kidney failure	4	≥4	≥4

Increasing risk

Increasing risk

Abbreviations: GFR, glomerular filtration rate, ACR, albumin creatinine ratio

NB: ACR is an important indicator of cardiovascular risk and progression.

Adapted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International (Suppl. 3): 1–150

- Monitor people for the development or progression of CKD for at least 2–3 years after acute kidney injury, even if serum creatinine has returned to baseline. [new 2014]

# 1 Recommendations

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation). See [about this guideline](#) for details.

## Terms used in this guideline

### Chronic kidney disease (CKD)

Defined as abnormalities of kidney function or structure present for more than 3 months, with implications for health. This includes all people with markers of kidney damage and those with a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m<sup>2</sup> on at least 2 occasions separated by a period of at least 90 days (with or without markers of kidney damage).

### Classification of CKD

CKD is classified according to estimated GFR (eGFR) and albumin:creatinine ratio (ACR) (see [table 1](#)), using 'G' to denote the GFR category (G1–G5, which have the same GFR thresholds as the CKD stages 1–5 recommended previously) and 'A' for the ACR category (A1–A3), for example:

- A person with an eGFR of 25 ml/min/1.73 m<sup>2</sup> and an ACR of 15 mg/mmol has CKD G4A2.
- A person with an eGFR of 50 ml/min/1.73 m<sup>2</sup> and an ACR of 35 mg/mmol has CKD G3aA3.
- An eGFR of less than 15 ml/min/1.73 m<sup>2</sup> (GFR category G5) is referred to as kidney failure.

### Glomerular filtration rate (GFR)

This is abbreviated in the following way in this guideline:

- GFR: either a measured or an estimated GFR
- eGFR: estimated GFR (without indicating the method of estimation)

- eGFR<sub>creatinine</sub>: an estimation of GFR using serum creatinine
- eGFR<sub>cystatinC</sub>: an estimation of GFR using cystatin C.

## Markers of kidney disease

These include albuminuria (ACR more than 3 mg/mmol), urine sediment abnormalities, electrolyte and other abnormalities due to tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging, and a history of kidney transplantation.

## Renin–angiotensin–aldosterone system antagonist

A drug that blocks or inhibits the renin–angiotensin–aldosterone system including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), direct renin inhibitors and aldosterone antagonists.

## Renin–angiotensin system antagonist

A drug that blocks or inhibits the renin–angiotensin system including ACE inhibitors, ARBs and direct renin inhibitors. This group of drugs does not include aldosterone antagonists.

# 1.1 Investigations for chronic kidney disease

## Measuring kidney function

### Creatinine-based estimate of GFR

- 1.1.1 Whenever a request for serum creatinine measurement is made, clinical laboratories should report an estimate of glomerular filtration rate (eGFR<sub>creatinine</sub>) using a prediction equation (see recommendation 1.1.2) in addition to reporting the serum creatinine result<sup>[2]</sup>. [2014]
- 1.1.2 Clinical laboratories should:
  - use the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation to estimate GFR<sub>creatinine</sub>, using creatinine assays with calibration traceable to standardised reference material
  - use creatinine assays that are specific (for example, enzymatic assays) and zero-biased compared with isotope dilution mass spectrometry (IDMS)

- participate in a UK national external quality assessment scheme for creatinine. [new 2014]

For more information about implementing this recommendation, see [implementation: getting started](#).

- 1.1.3 Apply a correction factor to GFR values estimated using the CKD-EPI creatinine equation for people of African-Caribbean or African family origin (multiply eGFR by 1.159). [new 2014]
- 1.1.4 In people with extremes of muscle mass – for example, in bodybuilders, people who have had an amputation or people with muscle wasting disorders – interpret eGFR<sub>creatinine</sub> with caution. (Reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR.) [2008]
- 1.1.5 Advise people not to eat any meat in the 12 hours before having a blood test for eGFR<sub>creatinine</sub>. Avoid delaying the despatch of blood samples to ensure that they are received and processed by the laboratory within 12 hours of venepuncture. [2008]

## Cystatin C-based estimate of GFR

- 1.1.6 Whenever a request for serum cystatin C measurement is made, clinical laboratories should report an estimate of glomerular filtration rate (eGFR<sub>cystatinC</sub>) using a prediction equation (see recommendation 1.1.7) in addition to reporting the serum cystatin C result. [new 2014]
- 1.1.7 When an improved assessment of risk is needed (see recommendation 1.1.14), clinical laboratories should use the CKD-EPI cystatin C equation to estimate GFR<sub>cystatinC</sub>. [new 2014]
- 1.1.8 Clinical laboratories should use cystatin C assays calibrated to the international standard to measure serum cystatin C for cystatin C-based estimates of GFR. [new 2014]
- 1.1.9 Interpret eGFR<sub>cystatinC</sub> with caution in people with uncontrolled thyroid disease because eGFR<sub>cystatinC</sub> values may be falsely elevated in people with hypothyroidism and reduced in people with hyperthyroidism. [new 2014]

## Reporting and interpreting GFR values

- 1.1.10 Clinical laboratories should report GFR either as a whole number if it is 90 ml/min/1.73 m<sup>2</sup> or less, or as 'greater than 90 ml/min/1.73 m<sup>2</sup>'. [new 2014]
- 1.1.11 If GFR is greater than 90 ml/min/1.73 m<sup>2</sup>, use an increase in serum creatinine concentration of more than 20% to infer significant reduction in kidney function. [new 2014]
- 1.1.12 Interpret eGFR values of 60 ml/min/1.73 m<sup>2</sup> or more with caution, bearing in mind that estimates of GFR become less accurate as the true GFR increases. [2014]
- 1.1.13 Confirm an eGFR result of less than 60 ml/min/1.73 m<sup>2</sup> in a person not previously tested by repeating the test within 2 weeks. Allow for biological and analytical variability of serum creatinine ( $\pm 5\%$ ) when interpreting changes in eGFR. [2008]

## When to use a cystatin C-based estimate of GFR for diagnosis of CKD

- 1.1.14 Consider using eGFR<sub>cystatinC</sub> at initial diagnosis to confirm or rule out CKD in people with:
- an eGFR<sub>creatinine</sub> of 45–59 ml/min/1.73 m<sup>2</sup>, sustained for at least 90 days and
  - no proteinuria (albumin:creatinine ratio [ACR] less than 3 mg/mmol) or other marker of kidney disease. [new 2014]

For information about implementing this recommendation, see [implementation: getting started](#).

- 1.1.15 Do not diagnose CKD in people with:
- an eGFR<sub>creatinine</sub> of 45–59 ml/min/1.73 m<sup>2</sup> and
  - an eGFR<sub>cystatinC</sub> of more than 60 ml/min/1.73 m<sup>2</sup> and
  - no other marker of kidney disease. [new 2014]

## When highly accurate measures of GFR are required

- 1.1.16 Where a highly accurate measure of GFR is required – for example, during monitoring of chemotherapy and in the evaluation of renal function in potential living donors – consider a reference standard measure (inulin,  $^{51}\text{Cr}$ -EDTA,  $^{125}\text{I}$ -iothalamate or iohexol). [2008]

## Proteinuria

- 1.1.17 Do not use reagent strips to identify proteinuria unless they are capable of specifically measuring albumin at low concentrations and expressing the result as an ACR. [2008]
- 1.1.18 To detect and identify proteinuria, use urine ACR in preference to protein:creatinine ratio (PCR), because it has greater sensitivity than PCR for low levels of proteinuria. For quantification and monitoring of levels of proteinuria of ACR 70 mg/mmol or more, PCR can be used as an alternative. ACR is the recommended method for people with diabetes. [2008, amended 2014]
- 1.1.19 For the initial detection of proteinuria, if the ACR is between 3 mg/mmol and 70 mg/mmol, this should be confirmed by a subsequent early morning sample. If the initial ACR is 70 mg/mmol or more, a repeat sample need not be tested. [2008, amended 2014]
- 1.1.20 Regard a confirmed ACR of 3 mg/mmol or more as clinically important proteinuria. [2008, amended 2014]
- 1.1.21 Quantify urinary albumin or urinary protein loss as in recommendation 1.1.18 for:
- people with diabetes
  - people without diabetes with a GFR of less than  $60 \text{ ml/min/1.73 m}^2$ . [2008, amended 2014]
- 1.1.22 Quantify by laboratory testing the urinary albumin or urinary protein loss of people with a GFR of  $60 \text{ ml/min/1.73 m}^2$  or more if there is a strong suspicion of CKD (see also recommendation 1.1.28). [2008]

## Haematuria

1.1.23 When testing for the presence of haematuria, use reagent strips rather than urine microscopy.

- Evaluate further if there is a result of 1+ or more.
- Do not use urine microscopy to confirm a positive result. [2008]

## Managing isolated invisible haematuria

1.1.24 When there is the need to differentiate persistent invisible haematuria in the absence of proteinuria from transient haematuria, regard 2 out of 3 positive reagent strip tests as confirmation of persistent invisible haematuria. [2008]

1.1.25 Persistent invisible haematuria, with or without proteinuria, should prompt investigation for urinary tract malignancy in appropriate age groups. [2008]

1.1.26 Persistent invisible haematuria in the absence of proteinuria should be followed up annually with repeat testing for haematuria (see recommendations 1.1.24 and 1.1.25), proteinuria or albuminuria, GFR and blood pressure monitoring as long as the haematuria persists. [2008]

## Who should be tested for CKD

1.1.27 Monitor GFR at least annually in people prescribed drugs known to be nephrotoxic, such as calcineurin inhibitors (for example, cyclosporin or tacrolimus), lithium and non-steroidal anti-inflammatory drugs (NSAIDs). [2008, amended 2014]

1.1.28 Offer testing for CKD using eGFRcreatinine and ACR to people with any of the following risk factors:

- diabetes
- hypertension
- acute kidney injury (see [recommendation 1.3.9](#))

- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
- structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement – for example, systemic lupus erythematosus
- family history of end-stage kidney disease (GFR category G5) or hereditary kidney disease
- opportunistic detection of haematuria. [new 2014]

1.1.29 Do not use age, gender or ethnicity as risk markers to test people for CKD. In the absence of metabolic syndrome, diabetes or hypertension, do not use obesity alone as a risk marker to test people for CKD. [2008, amended 2014]

## 1.2 Classification of chronic kidney disease


1.2.1 Classify CKD using a combination of GFR and ACR categories (as described in table 1). Be aware that:


- increased ACR is associated with increased risk of adverse outcomes
- decreased GFR is associated with increased risk of adverse outcomes
- increased ACR and decreased GFR in combination multiply the risk of adverse outcomes. [new 2014]

For information about implementing this recommendation, see [implementation: getting started](#).

**Table 1 Classification of chronic kidney disease using GFR and ACR categories**

GFR and ACR categories and risk of adverse outcomes			ACR categories (mg/mmol), description and range		
			<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73 m <sup>2</sup> ), description and range	≥90 Normal and high	G1	No CKD in the absence of markers of kidney damage		
	60–89 Mild reduction related to normal range for a young adult	G2			
	45–59 Mild–moderate reduction	G3a <sup>1</sup>			
	30–44 Moderate–severe reduction	G3b			
	15–29 Severe reduction	G4			
	<15 Kidney failure	G5			


  
Increasing risk


  
Increasing risk

<sup>1</sup> Consider using eGFRcystatinC for people with CKD G3aA1 (see recommendations 1.1.14 and 1.1.15)

Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate

Adapted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International (Suppl. 3): 1–150

## 1.2.2 Do not determine management of CKD solely by age. [new 2014]

## Investigating the cause of CKD and determining the risk of adverse outcomes

- 1.2.3 Agree a plan to establish the cause of CKD during an informed discussion with the person with CKD, particularly if the cause may be treatable (for example, urinary tract obstruction, nephrotoxic drugs or glomerular disease). [new 2014]
- 1.2.4 Use the person's GFR and ACR categories (see table 1) to indicate their risk of adverse outcomes (for example, CKD progression, acute kidney injury, all-cause mortality and cardiovascular events) and discuss this with them. [new 2014]

## Indications for renal ultrasound

- 1.2.5 Offer a renal ultrasound scan to all people with CKD who:
- have accelerated progression of CKD (see recommendation 1.3.3)
  - have visible or persistent invisible haematuria
  - have symptoms of urinary tract obstruction
  - have a family history of polycystic kidney disease and are aged over 20 years
  - have a GFR of less than 30 ml/min/1.73 m<sup>2</sup> (GFR category G4 or G5)
  - are considered by a nephrologist to require a renal biopsy. [2008, amended 2014]
- 1.2.6 Advise people with a family history of inherited kidney disease about the implications of an abnormal result before a renal ultrasound scan is arranged for them. [2008]

## 1.3 Frequency of monitoring

- 1.3.1 Agree the frequency of monitoring (eGFRcreatinine and ACR) with the person with, or at risk of, CKD; bear in mind that CKD is not progressive in many people. [new 2014]
- 1.3.2 Use table 2 to guide the frequency of GFR monitoring for people with, or at risk of, CKD, but tailor it to the person according to:

- the underlying cause of CKD
- past patterns of eGFR and ACR (but be aware that CKD progression is often non-linear)
- comorbidities, especially heart failure
- changes to their treatment (such as renin–angiotensin–aldosterone system [RAAS] antagonists, NSAIDs and diuretics)
- intercurrent illness
- whether they have chosen conservative management of CKD. [new 2014]

**Table 2 Frequency of monitoring of GFR (number of times per year, by GFR and ACR category) for people with, or at risk of, CKD**

		ACR categories (mg/mmol), description and range		
		A1 <3 Normal to mildly increased	A2 3–30 Moderately increased	A3 >30 Severely increased
GFR categories (ml/min/1.73 m <sup>2</sup> ), description and range	G1 ≥90 Normal and high	≤1	1	≥1
	G2 60–89 Mild reduction related to normal range for a young adult	≤1	1	≥1
	G3a 45–59 Mild–moderate reduction	1	1	2
	G3b 30–44 Moderate–severe reduction	≤2	2	≥2
	G4 15–29 Severe reduction	2	2	3
	G5 <15 Kidney failure	4	≥4	≥4

Increasing risk

Increasing risk

Abbreviations: GFR, glomerular filtration rate, ACR, albumin creatinine ratio

NB: ACR is an important indicator of cardiovascular risk and progression.

Adapted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International (Suppl. 3): 1–150

## Defining progression

### 1.3.3 Define accelerated progression of CKD as:

- a sustained decrease in GFR of 25% or more and a change in GFR category within 12 months or
- a sustained decrease in GFR of 15 ml/min/1.73 m<sup>2</sup> per year. [new 2014]

### 1.3.4 Take the following steps to identify the rate of progression of CKD:

- Obtain a minimum of 3 GFR estimations over a period of not less than 90 days.
- In people with a new finding of reduced GFR, repeat the GFR within 2 weeks to exclude causes of acute deterioration of GFR – for example, acute kidney injury or starting renin-angiotensin system antagonist therapy. [2008, amended 2014]

### 1.3.5 Be aware that people with CKD are at increased risk of progression to end-stage kidney disease if they have either of the following:

- a sustained decrease in GFR of 25% or more over 12 months or
- a sustained decrease in GFR of 15 ml/min/1.73 m<sup>2</sup> or more over 12 months. [2008, amended 2014]

### 1.3.6 When assessing CKD progression, extrapolate the current rate of decline of GFR and take this into account when planning intervention strategies, particularly if it suggests that the person might need renal replacement therapy in their lifetime. [2008, amended 2014]

## Risk factors associated with CKD progression

### 1.3.7 Work with people who have any of the following risk factors for CKD progression to optimise their health:

- cardiovascular disease
- proteinuria
- acute kidney injury
- hypertension

- diabetes
- smoking
- African, African-Caribbean or Asian family origin
- chronic use of NSAIDs
- untreated urinary outflow tract obstruction. [new 2014]

1.3.8 In people with CKD the chronic use of NSAIDs may be associated with progression and acute use is associated with a reversible decrease in GFR. Exercise caution when treating people with CKD with NSAIDs over prolonged periods of time. Monitor the effects on GFR, particularly in people with a low baseline GFR and/or in the presence of other risks for progression. [2008]

## Acute kidney injury and CKD

- 1.3.9 Monitor people for the development or progression of CKD for at least 2–3 years after acute kidney injury, even if serum creatinine has returned to baseline. [new 2014]
- 1.3.10 Advise people who have had acute kidney injury that they are at increased risk of CKD developing or progressing. [new 2014]

## 1.4 Information and education

- 1.4.1 Offer people with CKD education and information tailored to the severity and cause of CKD, the associated complications and the risk of progression. [2008]
- 1.4.2 When developing information or education programmes, involve people with CKD in their development from the outset. The following topics are suggested.
- What is CKD and how does it affect people?
  - What questions should people ask about their kidneys?
  - What treatments are available for CKD, what are their advantages and disadvantages and what complications or side effects may occur as a result of treatment/medication?
  - What can people do to manage and influence their own condition?

- In what ways could CKD and its treatment affect people's daily life, social activities, work opportunities and financial situation, including benefits and allowances available?
- How can people cope with and adjust to CKD and what sources of psychological support are available?
- When appropriate, offer information about renal replacement therapy (such as the frequency and length of time of dialysis treatment sessions or exchanges and pre-emptive transplantation) and the preparation required (such as having a fistula or peritoneal catheter).
- Conservative management and when it may be considered. [2008]

1.4.3 Offer people with CKD high-quality information or education programmes as appropriate to the severity of their condition to allow time for them to fully understand and make informed choices about their treatment. [2008]

1.4.4 Healthcare professionals providing information and education programmes should ensure they have specialist knowledge about CKD and the necessary skills to facilitate learning. [2008]

1.4.5 Healthcare professionals working with people with CKD should take account of the psychological aspects of coping with the condition and offer access to appropriate support – for example, support groups, counselling or a specialist nurse. [2008]

## Lifestyle advice

1.4.6 Encourage people with CKD to take exercise, achieve a healthy weight and stop smoking. [2008]

## Dietary interventions

1.4.7 Offer dietary advice about potassium, phosphate, calorie and salt intake appropriate to the severity of CKD. [2008, amended 2014]

1.4.8 Where dietary intervention is agreed this should occur within the context of education, detailed dietary assessment and supervision to ensure malnutrition is prevented. [2008]

## Low-protein diets

- 1.4.9 Do not offer low-protein diets (dietary protein intake less than 0.6–0.8 g/kg/day) to people with CKD. [new 2014]

## Self-management

- 1.4.10 Ensure that systems are in place to:

- inform people with CKD of their diagnosis
- enable people with CKD to share in decision-making about their care
- support self-management (this includes providing information about blood pressure, smoking cessation, exercise, diet and medicines) and enable people to make informed choices. [new 2014]

- 1.4.11 Give people access to their medical data (including diagnosis, comorbidities, test results, treatments and correspondence) through information systems, such as [Renal PatientView](#), to encourage and help them to self-manage their CKD. [new 2014]

## 1.5 Referral criteria

- 1.5.1 Take into account the individual's wishes and comorbidities when considering referral. [2008]

- 1.5.2 People with CKD in the following groups should normally be referred for specialist assessment:

- GFR less than 30 ml/min/1.73 m<sup>2</sup> (GFR category G4 or G5), with or without diabetes
- ACR 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated
- ACR 30 mg/mmol or more (ACR category A3), together with haematuria
- sustained decrease in GFR of 25% or more, and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m<sup>2</sup> or more within 12 months

- hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses (see also [Hypertension](#) [NICE guideline CG127])
- known or suspected rare or genetic causes of CKD
- suspected renal artery stenosis. [2008, amended 2014]

1.5.3 Consider discussing management issues with a specialist by letter, email or telephone in cases where it may not be necessary for the person with CKD to be seen by the specialist. [2008]

1.5.4 Once a referral has been made and a plan jointly agreed (between the person with CKD or their carer and the healthcare professional), it may be possible for routine follow-up to take place at the patient's GP surgery rather than in a specialist clinic. If this is the case, criteria for future referral or re-referral should be specified. [2008]

1.5.5 People with CKD and renal outflow obstruction should normally be referred to urological services, unless urgent medical intervention is required – for example, for the treatment of hyperkalaemia, severe uraemia, acidosis or fluid overload. [2008]

## 1.6 Pharmacotherapy

### Blood pressure control

1.6.1 In people with CKD aim to keep the systolic blood pressure below 140 mmHg (target range 120–139 mmHg) and the diastolic blood pressure below 90 mmHg<sup>[3]</sup>. [2008]

1.6.2 In people with CKD and diabetes, and also in people with an ACR of 70 mg/mmol or more, aim to keep the systolic blood pressure below 130 mmHg (target range 120–129 mmHg) and the diastolic blood pressure below 80 mmHg<sup>[3]</sup>. [2008]

### Choice of antihypertensive agent

1.6.3 Offer a low-cost [renin-angiotensin system antagonist](#) to people with CKD and:

- diabetes and an ACR of 3 mg/mmol or more (ACR category A2 or A3)
  - hypertension and an ACR of 30 mg/mmol or more (ACR category A3)
  - an ACR of 70 mg/mmol or more (irrespective of hypertension or cardiovascular disease)<sup>[4]</sup>. [new 2014]
- 1.6.4 Do not offer a combination of renin–angiotensin system antagonists to people with CKD. [new 2014]
- 1.6.5 Follow the treatment recommendations in [Hypertension](#) (NICE guideline CG127) for people with CKD, hypertension and an ACR of less than 30 mg/mmol (ACR categories A1 and A2), if they do not have diabetes. [new 2014]
- 1.6.6 To improve concordance, inform people who are prescribed renin–angiotensin system antagonists about the importance of:
- achieving the optimal tolerated dose of renin–angiotensin system antagonists and
  - monitoring eGFR and serum potassium in achieving this safely. [2008]
- 1.6.7 In people with CKD, measure serum potassium concentrations and estimate the GFR before starting renin–angiotensin system antagonists. Repeat these measurements between 1 and 2 weeks after starting renin–angiotensin system antagonists and after each dose increase. [2008]
- 1.6.8 Do not routinely offer a renin–angiotensin system antagonist to people with CKD if their pretreatment serum potassium concentration is greater than 5.0 mmol/litre. [2008, amended 2014]
- 1.6.9 When hyperkalaemia precludes use of renin–angiotensin system antagonists, assessment, investigation and treatment of other factors known to promote hyperkalaemia should be undertaken and the serum potassium concentration rechecked. [2008]
- 1.6.10 Concurrent prescription of drugs known to promote hyperkalaemia is not a contraindication to the use of renin–angiotensin system antagonists, but be aware that more frequent monitoring of serum potassium concentration may be required. [2008]

- 1.6.11 Stop renin–angiotensin system antagonists if the serum potassium concentration increases to 6.0 mmol/litre or more and other drugs known to promote hyperkalaemia have been discontinued. [2008]
- 1.6.12 Following the introduction or dose increase of renin–angiotensin system antagonists, do not modify the dose if either the GFR decrease from pretreatment baseline is less than 25% or the serum creatinine increase from baseline is less than 30%. [2008]
- 1.6.13 If there is a decrease in eGFR or increase in serum creatinine after starting or increasing the dose of renin–angiotensin system antagonists, but it is less than 25% (eGFR) or 30% (serum creatinine) of baseline, repeat the test in 1–2 weeks. Do not modify the renin–angiotensin system antagonist dose if the change in eGFR is less than 25% or the change in serum creatinine is less than 30%. [2008]
- 1.6.14 If the eGFR change is 25% or more, or the change in serum creatinine is 30% or more:
- investigate other causes of a deterioration in renal function, such as volume depletion or concurrent medication (for example, NSAIDs)
  - if no other cause for the deterioration in renal function is found, stop the renin–angiotensin system antagonist or reduce the dose to a previously tolerated lower dose, and add an alternative antihypertensive medication if required. [2008]

## Statins

- 1.6.15 Follow the recommendations in [Lipid modification](#) (NICE guideline CG181) for the use of statins in CKD. [new 2014]

## Oral antiplatelets and anticoagulants

- 1.6.16 Offer antiplatelet drugs to people with CKD for the secondary prevention of cardiovascular disease, but be aware of the increased risk of bleeding. [new 2014]
- 1.6.17 Consider apixaban in preference to warfarin in people with a confirmed eGFR of 30–50 ml/min/1.73 m<sup>2</sup> and non-valvular atrial fibrillation who have 1 or more of the following risk factors:

- prior stroke or transient ischaemic attack
- age 75 years or older
- hypertension
- diabetes mellitus
- symptomatic heart failure. [new 2014]

## 1.7 Other complications

### Bone metabolism and osteoporosis

- 1.7.1 Do not routinely measure calcium, phosphate, parathyroid hormone (PTH) and vitamin D levels in people with a GFR of 30 ml/min/1.73 m<sup>2</sup> or more (GFR category G1, G2 or G3). [2008]
- 1.7.2 Measure serum calcium, phosphate and PTH concentrations in people with a GFR of less than 30 ml/min/1.73 m<sup>2</sup> (GFR category G4 or G5). Determine the subsequent frequency of testing by the measured values and the clinical circumstances. Where doubt exists, seek specialist opinion. [2008]
- 1.7.3 Offer bisphosphonates if indicated for the prevention and treatment of osteoporosis in people with a GFR of 30 ml/min/1.73 m<sup>2</sup> or more (GFR category G1, G2 or G3). [2008]

### Vitamin D supplements in the management of CKD–mineral and bone disorders

Detailed advice on the management of CKD–mineral and bone disorders is beyond the scope of this guideline. If uncertain, seek advice from your local renal service.

- 1.7.4 Do not routinely offer vitamin D supplementation to manage or prevent CKD–mineral and bone disorders. [new 2014]
- 1.7.5 Offer colecalciferol or ergocalciferol to treat vitamin D deficiency in people with CKD and vitamin D deficiency. [new 2014]
- 1.7.6 If vitamin D deficiency has been corrected and symptoms of CKD–mineral and

bone disorders persist, offer alfacalcidol (1-alpha-hydroxycholecalciferol) or calcitriol (1-25-dihydroxycholecalciferol) to people with a GFR of less than 30 ml/min/1.73 m<sup>2</sup> (GFR category G4 or G5). [new 2014]

- 1.7.7 Monitor serum calcium and phosphate concentrations in people receiving alfacalcidol or calcitriol supplements. [2014]

## Anaemia

- 1.7.8 If not already measured, check the haemoglobin level in people with a GFR of less than 45 ml/min/1.73 m<sup>2</sup> (GFR category G3b, G4 or G5) to identify anaemia (haemoglobin less than 110 g/litre [11.0 g/dl], see [Anaemia management in people with chronic kidney disease](#) [NICE guideline CG114]). Determine the subsequent frequency of testing by the measured value and the clinical circumstances. [2008]

## Oral bicarbonate supplements in the management of metabolic acidosis

Detailed advice on the management of metabolic acidosis is beyond the scope of this guideline. If uncertain, seek advice from your local renal service.

- 1.7.9 Consider oral sodium bicarbonate supplementation for people with both:
- a GFR less than 30 ml/min/1.73 m<sup>2</sup> (GFR category G4 or G5) and
  - a serum bicarbonate concentration of less than 20 mmol/litre. [new 2014]

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<sup>[2]</sup> eGFRcreatinine may be less reliable in certain situations (for example, acute kidney injury, pregnancy, oedematous states, muscle wasting disorders, and in people who are malnourished or have had an amputation) and has not been well validated in certain ethnic groups (for example, in people of Asian family origin).

<sup>[3]</sup> The GDG searched for and appraised evidence on blood pressure control, and did not set out to establish definitive safe ranges of blood pressure in CKD. The evidence presented in the full guideline does not therefore include safety of low blood pressure, but some such evidence does exist. The GDG set out a range of blood pressure targets, given in these recommendations, which in their clinical experience will inform good practice in CKD.

<sup>[4]</sup> The evidence to support these criteria is limited in people aged over 70 years.

## 2 Implementation: getting started

This section highlights some important changes to practice that may result from implementing this guideline, which were identified at the time of publication in July 2014. With input from stakeholders, experts and health professionals, 3 areas were identified that may have a big impact on practice or could be challenging to implement. However, other changes to practice may be needed to fully implement the guideline.

Primary care providers, laboratory services and their respective commissioners may be particularly affected by these changes.

### 2.1 Calculating estimates of creatinine-based glomerular filtration rate (GFR)

See [recommendation 1.1.2](#).

#### Potential impact of implementation

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation is more accurate than the Modification of Diet in Renal Disease (MDRD) Study equation, is less biased at a GFR of more than 60 ml/min/1.73 m<sup>2</sup> and performs better in people aged 75 years and over. The use of the MDRD Study equation may over-diagnose CKD. Using the CKD-EPI equation instead could benefit patients and clinicians by reducing unnecessary appointments, reducing patients' concerns and reducing the overall burden of CKD in the population.

#### Challenges for implementation

- Laboratories using the MDRD Study equation to estimate GFR may need to change their practice.
- Using the CKD-EPI creatinine equation to estimate GFR may make it difficult to assess trends over time in people with previous GFR estimates calculated using other equations.
- Laboratories may need to update their software to include the CKD-EPI creatinine equation so that it is used automatically.

## Support for implementation

- Online tools can be used to give estimates of GFR using the MDRD Study equation (for example, those produced by the [UK Renal Association](#) the [National Kidney Disease Education Program](#) and at [MDRD.com](#)), for comparison with CKD-EPI results.
- The Association of Clinical Biochemistry and Laboratory Medicine, [Lab Tests Online UK](#) and the UK National External Quality Assessment Service are raising awareness of the change and include it in laboratory inspection frameworks.
- Local clinical commissioning groups could contact their local laboratory to help ensure that this change is incorporated into practice.

## 2.2 Using cystatin C-based estimates of GFR

See [recommendation 1.1.14](#).

### Potential impact of implementation

Estimates of GFR (eGFR) based on serum cystatin C have a higher specificity for significant disease outcomes than those based on serum creatinine. For people with a borderline diagnosis, eGFR<sub>cystatinC</sub> is an additional diagnostic tool that may reduce over diagnosis. Using this tool may result in a significant proportion of people classified as having stage 3 CKD being reclassified as not having CKD (G1A1 or G2A1). This could benefit patients and clinicians by reducing unnecessary appointments, reducing patients' concerns and reducing the overall burden of CKD in the population. This additional test may have a cost impact, but there will be financial benefits, with fewer diagnoses leading to reduced management costs.

### Challenges for implementation

- Cystatin C testing is a new recommendation and so primary care teams may not be aware of when to request this test.
- Cystatin C testing may not be widely available. Laboratories may need to invest in training and, in some cases, equipment.
- Using cystatin C as an additional test will have a financial impact. Based on estimated demand, decisions might need to be made about whether all laboratories or designated laboratories offer this test. Costs will vary, and should be assessed locally depending on the model of provision.

## Support for implementation

- This test only needs to be performed in a defined population (as recommended in [1.1.14](#)) and generally only once for each person.
- The assay for cystatin C can be performed using existing analysers.
- Clinicians are likely to welcome the introduction of a more accurate test for eGFR because many of them doubt the previously recommended diagnostic criteria for early CKD.
- See the NICE [costing statement](#) for further information and advice on costs.

## 2.3 Classifying chronic kidney disease

See [recommendation 1.2.1](#).

### Potential impact of implementation

Both albumin:creatinine ratio (ACR) and GFR indicate the risk of adverse events and CKD progression, but when used together, risk stratification and accuracy is increased. More accurate classification of CKD may lead to more targeted treatment and monitoring.

### Challenges for implementation

- Testing for both eGFR and ACR may add extra burden and cost to diagnosis and monitoring.
- The addition of ACR makes classification of CKD more complex and those using CKD stages will need to change their practice.

## Support for implementation

- The [classification table](#) shows how the GFR categories (G1–G5, which have the same GFR thresholds as the CKD stages 1–5 recommended previously), and ACR categories (A1–A3) should be combined, for example:
  - A person with an eGFR of 25 ml/min/1.73 m<sup>2</sup> and an ACR of 15 mg/mmol has CKD G4A2.
  - A person with an eGFR of 50 ml/min/1.73 m<sup>2</sup> and an ACR of 35 mg/mmol has CKD G3aA3.
- An algorithm is available to help healthcare professionals understand how the category of CKD should determine the next steps for management (see [algorithm B](#) in the NICE resources for local practice).

- Raised ACR is a powerful independent marker of the risk of adverse outcomes in CKD, and the use of ACR and GFR in combination will allow better risk stratification.

## 2.4 Further resources

Further [resources](#) are available from NICE that may help to support implementation.

A [clinical knowledge summary](#) on chronic kidney disease (not diabetic) is available with details of the evidence and guidance for primary care.

The [National Chronic Kidney Disease Audit](#) pilot (December 2014) aims to improve diagnosis in primary care, to understand the standard of patient care and map its variation, and to drive improvements using electronic patient management systems.

NICE produces indicators annually for use in the Quality and Outcomes Framework (QOF) for the UK. The [process for this and the NICE menu](#) are available.

[Uptake data](#) about guideline recommendations and quality standard measures are available on the NICE website.

## 3 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

### 3.1 Self-management

Does the provision of educational and supportive interventions to people with chronic kidney disease (CKD) by healthcare professionals increase patients' skills and confidence in managing their conditions and improve clinical outcomes?

#### Why this is important

CKD is a common long-term condition that frequently coexists with other long-term conditions, including diabetes, cardiovascular disease and depression, and is associated with reduced quality of life. Through greater understanding of their conditions and provision of the information needed to support lifestyle change, people with CKD may be better able to live well with their long-term condition(s). Self-management may also improve their biomedical markers, for example, blood pressure.

People with advanced CKD may benefit from education and support on particular issues, such as preparation for renal replacement, symptom management and specific dietary modifications. However, the current evidence base for self-management support in the CKD population is very limited.

### 3.2 Antiplatelet therapy

For people with CKD at the highest risk of cardiovascular disease, what is the clinical effectiveness of low-dose aspirin compared with placebo for primary prevention of cardiovascular disease?

#### Why this is important

CKD is a common long-term condition and a powerful independent predictor of cardiovascular disease. The risks are increased as the estimated glomerular filtration rate (eGFR) decreases and level of albuminuria increases. Kidney Disease: Improving Global Outcomes (KDIGO) classifies people with CKD as being at moderate risk, high risk or very high risk of cardiovascular disease according to their eGFR and albumin:creatinine ratio (ACR). However, the current evidence base

for reducing cardiovascular risk in the CKD population is very limited.

### 3.3 Renin–angiotensin–aldosterone system

For people aged over 75 years with CKD, what is the clinical effectiveness of renin–angiotensin–aldosterone system (RAAS) antagonists?

#### Why this is important

RAAS antagonists are among the most commonly used drugs. They are recommended for people with CKD to reduce the rate of disease progression and mortality. The evidence for the use of RAAS antagonists is not specific to older people, so these recommendations are the same for all adults, regardless of age. However, there is a clinical suspicion that older people have a higher incidence of adverse effects from using RAAS antagonists, and uncertainty as to the balance of benefits and harm of using these agents in older people.

### 3.4 Uric acid-lowering agents

In people with CKD who are at high risk of progression, what is the clinical and cost effectiveness of uric acid-lowering agents on the progression of CKD and on mortality?

#### Why this is important

Observational data have suggested that uric acid is an independent predictor of both progression and new incidence of CKD. It has also been proposed that elevated uric acid may have a role in initiating hypertension, arteriolosclerosis, insulin resistance and hypertriglyceridaemia. Hyperuricaemia is also associated with type 2 diabetes. It is difficult to infer causation from the observational data; is hyperuricaemia nephrotoxic or a marker of reduced eGFR? Is the relationship due to residual confounding?

The current randomised evidence for reducing uric acid in CKD patients is very limited and of poor quality, especially relating to the major outcomes of end-stage kidney disease needing renal replacement therapy and mortality.

### 3.5 Vitamin D supplements in the management of CKD–mineral and bone disorders

In people with hyperparathyroidism secondary to CKD, does treatment with vitamin D or vitamin D

analogues improve patient-related outcomes?

### Why this is important

Changes in bone and mineral metabolism and alterations in calcium and phosphate homeostasis occur early in the course of CKD and progress as kidney function declines. The prevalence of hyperparathyroidism increases from 5.5% in people with a GFR over 90 ml/min/1.73 m<sup>2</sup> to 23%, 44% and 73% in people with a GFR of 45–59, 30–44 and under 30 ml/min/1.73 m<sup>2</sup> respectively. 25-Hydroxyvitamin D deficiency is twice as prevalent in people with a GFR under 30 ml/min/1.73 m<sup>2</sup> compared with those with a normal GFR. Decreased bone mass and changes in bone microarchitecture occur and progress early in CKD increasing the risk of bone fracture. Replacing vitamin D in people with CKD is known to reduce hyperparathyroidism but there is little data to suggest any benefit on clinical outcomes (including CKD progression measured by change in eGFR, all-cause mortality, cardiovascular mortality, cardiovascular events, fractures and hypercalcaemia). Potential benefits of vitamin D therapy in people with CKD include increased bone mineral density and muscle strength, reduced risk of falls and fractures, and reduction in hyperparathyroidism. Potential adverse effects are hypercalcaemia and extraskeletal (vascular) calcification, and increased cardiovascular risk.

## 4 Other information

### 4.1 Scope and how this guideline was developed

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

#### How this guideline was developed

NICE commissioned the National Clinical Guideline Centre to develop this guideline. The Centre established a Guideline Development Group (see [section 5](#)), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

# The Guideline Development Group, National Collaborating Centre and NICE project team

## 4.2 Guideline Development Group

The Guideline Development Group members listed are those for the 2014 update. For the composition of previous Guideline Development Groups, see the [full guideline](#).

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## 4.3 National Clinical Guideline Centre

**Caroline Blaine (until November 2013)**

Research Fellow

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Editor

## About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions.

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

This guideline was developed by the National Clinical Guideline Centre, which is based at the Royal College of Physicians. The Centre worked with a Guideline Development Group, comprising healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, which reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in [the guidelines manual](#).

NICE produces guidance, standards and information on commissioning and providing high-quality healthcare, social care, and public health services. We have agreements to provide certain NICE services to Wales, Scotland and Northern Ireland. Decisions on how NICE guidance and other products apply in those countries are made by ministers in the Welsh government, Scottish government, and Northern Ireland Executive. NICE guidance or other products may include references to organisations or people responsible for commissioning or providing care that may be relevant only to England.

## Update information

January 2015: New section, [implementation: getting started](#), added.

This guideline updates and replaces NICE guideline CG73 (published September 2008).

Recommendations are marked as [2008], [2008, amended 2014], [2014] or [new 2014]:

- [2008] indicates that the evidence has not been reviewed since 2008
- [2008, amended 2014] indicates that the evidence has not been reviewed since 2008, but changes have been made to the recommendation wording that change the meaning
- [2014] indicates that the evidence has been reviewed but no change has been made to the recommended action
- [new 2014] indicates that the evidence has been reviewed and the recommendation has been updated or added.

## Recommendations from NICE guideline CG73 (2008) that have been amended

Recommendations are labelled [2008, amended 2014] if the evidence has not been reviewed but changes have been made to the recommendation wording that change the meaning.

Recommendation in 2008 guideline	Recommendation in current guideline	Reason for change
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<p>To detect and identify proteinuria, use urine ACR in preference, as it has greater sensitivity than PCR for low levels of proteinuria. For quantification and monitoring of proteinuria, PCR can be used as an alternative. ACR is the recommended method for people with diabetes. (1.1.11)</p>	<p>To detect and identify proteinuria, use urine ACR in preference to protein:creatinine ratio (PCR), because it has greater sensitivity than PCR for low levels of proteinuria. For quantification and monitoring of high levels of proteinuria (ACR 70 mg/mmol or more), PCR can be used as an alternative. ACR is the recommended method for people with diabetes. (1.1.18)</p>	<p>'High levels of proteinuria' and the ACR category was added for clarification on quantification and monitoring.</p>
<p>For the initial detection of proteinuria, if the ACR is 30 mg/mmol or more (this is approximately equivalent to PCR 50 mg/mmol or more, or a urinary protein excretion 0.5 g/24 h or more) and less than 70 mg/mmol (approximately equivalent to PCR less than 100 mg/mmol, or urinary protein excretion less than 1 g/24 h) this should be confirmed by a subsequent early morning sample. If the initial ACR is 70 mg/mmol or more, or the PCR 100 mg/mmol or more, a repeat sample need not be tested. (1.1.12)</p>	<p>For the initial detection of proteinuria, if the ACR is between 3 mg/mmol and 70 mg/mmol, this should be confirmed by a subsequent early morning sample. If the initial ACR is 70 mg/mmol or more, a repeat sample need not be tested. (1.1.19)</p>	<p>The criteria for clinically significant proteinuria have been changed from an ACR of 30 mg/mmol or more to 3 mg/mmol or more. Although this question was not directly included in the update, the change came from evidence reviewed for the markers of kidney damage and classification of CKD sections. The GDG agreed that the risk of adverse outcomes is a continuum and starts at an ACR well below 30 mg/mmol.</p> <p>The equivalences to PCR and urinary protein excretion were removed because the evidence showed that ACR was more accurate.</p>

In people without diabetes consider clinically significant proteinuria to be present when the ACR is 30 mg/mmol or more (this is approximately equivalent to PCR 50 mg/mmol or more, or a urinary protein excretion 0.5 g/24 h or more).(1.1.13)	Regard a confirmed ACR of 3 mg/mmol or more as clinically important proteinuria. (1.1.20)	Replaced with recommendation 1.1.20.  The criteria for clinically significant proteinuria have been changed from an ACR of 30 mg/mmol or more to 3 mg/mmol or more. Although this question was not directly included in the update, the change came from evidence reviewed for the markers of kidney damage and classification of CKD sections. The GDG agreed that the risk of adverse outcomes is a continuum and starts at an ACR well below 30 mg/mmol.
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<p>In people with diabetes consider microalbuminuria (ACR more than 2.5 mg/mmol in men and ACR more than 3.5 mg/mmol in women) to be clinically significant. (1.1.14)</p>	<p>Regard a confirmed ACR of 3 mg/mmol or more as clinically important proteinuria. (1.1.20)</p>	<p>Replaced with recommendation 1.1.20</p> <p>The criteria for clinically significant proteinuria have been changed from an ACR of 30 mg/mmol or more to 3 mg/mmol or more. Although this question was not directly included in the update, the change came from evidence reviewed for the markers of kidney damage and classification of CKD sections. The GDG agreed that the risk of adverse outcomes is a continuum and starts at an ACR well below 30 mg/mmol. There is a general move away from the term 'microalbuminuria' (ACR between 3 and 30 mg/mmol) and the GDG wanted the latest recommendations to reflect this.</p> <p>Additionally it was no longer felt appropriate to have different criteria for gender. The GDG was not aware of any evidence on which the gender differences were based.</p>
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<p>All people with diabetes, and people without diabetes with a GFR less than 60 ml/min/1.73 m<sup>2</sup>, should have their urinary albumin/protein excretion quantified. The first abnormal result should be confirmed on an early morning sample (if not previously obtained).(1.1.15)</p>	<p>Quantify urinary albumin or urinary protein loss as in recommendation 1.1.18 for:</p> <ul style="list-style-type: none"> <li>• people with diabetes</li> <li>• people without diabetes with a GFR less than 60 ml/min/1.73 m<sup>2</sup> (1.1.21)</li> </ul>	<p>The second part of the original recommendation (regarding confirming on an early morning sample) was removed because modified criteria are provided in recommendation 1.1.19.</p> <p>Other changes for clarification only – see clarification table.</p>
<p>Monitor GFR in people prescribed drugs known to be nephrotoxic such as calcineurin inhibitors and lithium. Check GFR at least annually in people receiving long-term systemic non-steroidal anti-inflammatory drug (NSAID) treatment. (1.1.21)</p>	<p>Monitor GFR at least annually in people prescribed drugs known to be nephrotoxic, such as calcineurin inhibitors (for example cyclosporin or tacrolimus), lithium and non-steroidal anti-inflammatory drugs (NSAIDs). [2008, amended 2014]</p>	<p>The frequency of monitoring was added for nephrotoxic drugs based on the British National Formulary, which no longer indicates a difference in monitoring needs between NSAIDs and other nephrotoxic drugs. Annual monitoring was agreed by the GDG as appropriate for all of these drugs. Examples of calcineurin inhibitors were added for clarification.</p>

<p>In the absence of the above risk factors, do not use age, gender or ethnicity as risk markers to test people for CKD. In the absence of metabolic syndrome, diabetes or hypertension, do not use obesity alone as a risk marker to test people for CKD. (1.1.23)</p>	<p>Do not use age, gender or ethnicity as risk markers to test people for CKD. In the absence of metabolic syndrome, diabetes or hypertension, do not use obesity alone as a risk marker to test people for CKD. (1.1.29)</p>	<p>The initial part of the sentence 'In the absence of the above risk factors' was removed.</p> <p>The 2008 recommendation implied that if risk factors were present then age, gender and ethnicity could be considered as risk factors. The GDG did not find any evidence for this and agreed that rewording the recommendation promotes equality.</p>
<p>For the purposes of this classification define proteinuria as urinary ACR 30 mg/mmol or more, or PCR 50 mg/mmol or more (approximately equivalent to urinary protein excretion 0.5 g/24 hours or more). (1.2.2)</p>	<p>Regard a confirmed ACR of 3 mg/mmol or more as clinically important proteinuria. (1.1.20)</p>	<p>The criteria for clinically significant proteinuria have been changed from an ACR of 30 mg/mmol or more to 3 mg/mmol or more. Although this question was not directly included in the update, the change came from evidence reviewed for the markers of kidney damage and classification of CKD sections. The GDG agreed that the risk of adverse outcomes is a continuum and starts at an ACR well below 30 mg/mmol. The equivalences to PCR and urinary protein excretion were removed because the evidence showed that ACR was more accurate.</p>

<p>Offer a renal ultrasound to all people with CKD who:</p> <ul style="list-style-type: none"> <li>• have progressive CKD (eGFR decline more than 5 ml/min/1.73 m<sup>2</sup> within 1 year, or more than 10 ml/min/1.73 m<sup>2</sup> within 5 years)</li> <li>• have visible or persistent invisible haematuria</li> <li>• have symptoms of urinary tract obstruction</li> <li>• have a family history of polycystic kidney disease and are aged over 20</li> <li>• have stage 4 or 5 CKD</li> <li>• are considered by a nephrologist to require a renal biopsy. (1.4.1)</li> </ul>	<p>Offer a renal ultrasound scan to all people with CKD who:</p> <ul style="list-style-type: none"> <li>• have accelerated progression of CKD (see recommendation 1.3.3)</li> <li>• have visible or persistent invisible haematuria</li> <li>• have symptoms of urinary tract obstruction</li> <li>• have a family history of polycystic kidney disease and are aged over 20 years</li> <li>• have a GFR of less than 30 ml/min/1.73 m<sup>2</sup> (GFR category G4 or G5)</li> <li>• are considered by a nephrologist to require a renal biopsy. (1.2.5)</li> </ul>	<p>The first bullet point was modified to reflect the updated guideline definition of progression based on the evidence reviewed in the frequency of monitoring section (see recommendation 1.3.5).</p>
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<p>Take the following steps to identify progressive CKD.</p> <ul style="list-style-type: none"> <li>• Obtain a minimum of three GFR estimations over a period of not less than 90 days.</li> <li>• In people with a new finding of reduced eGFR, repeat the eGFR within 2 weeks to exclude causes of acute deterioration of GFR – for example, acute kidney injury or initiation of ACE inhibitor/ARB therapy.</li> <li>• Define progression as a decline in eGFR of more than 5 ml/min/1.73 m<sup>2</sup> within 1 year, or more than 10 ml/min/1.73 m<sup>2</sup> within 5 years.</li> <li>• Focus particularly on those in whom a decline of GFR continuing at the observed rate would lead to the need for renal replacement therapy within their lifetime by extrapolating the current rate of decline. (1.5.1)</li> </ul>	<p>Take the following steps to identify the rate of progression of CKD:</p> <ul style="list-style-type: none"> <li>• Obtain a minimum of 3 GFR estimations over a period of not less than 90 days.</li> <li>• In people with a new finding of reduced GFR, repeat the GFR within 2 weeks to exclude causes of acute deterioration of GFR – for example, acute kidney injury or starting renin–angiotensin system antagonist therapy. (1.3.4)</li> </ul> <p>Be aware that people with CKD are at increased risk of progression to end-stage kidney disease if they have either of the following:</p> <ul style="list-style-type: none"> <li>• a sustained decrease in GFR of 25% or more over 12 months or</li> </ul>	<p>The first 2 bullet points of the 2008 recommendation were made into a separate recommendation (1.3.4) to emphasise the process to identify progressive CKD.</p> <p>The third bullet point was updated (1.3.5) based on evidence derived from the frequency of monitoring review, which identified thresholds for progression.</p> <p>The GDG made a separate recommendation (1.3.6) from the fourth bullet point to give it additional focus, and clarified the wording according to NICE house style.</p>
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	<ul style="list-style-type: none"> <li>• a sustained decrease in GFR of 15 ml/min/1.73 m<sup>2</sup> or more over 12 months. (1.3.5)</li> </ul> <p>When assessing CKD progression, extrapolate the current rate of decline of GFR and take this into account when planning intervention strategies, particularly if it suggests that the person might need renal replacement therapy in their lifetime. (1.3.6)</p>	
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<p>People with CKD in the following groups should normally be referred for specialist assessment:</p> <ul style="list-style-type: none"> <li>• stage 4 and 5 CKD (with or without diabetes)</li> <li>• higher levels of proteinuria (ACR 70 mg/mmol or more, approximately equivalent to PCR 100 mg/mmol or more, or urinary protein excretion 1 g/24 h or more) unless known to be due to diabetes and already appropriately treated</li> <li>• proteinuria (ACR 30 mg/mmol or more, approximately equivalent to PCR 50 mg/mmol or more, or urinary protein excretion 0.5 g/24 h or more) together with haematuria</li> <li>• rapidly declining eGFR (more than 5 ml/min/1.73 m<sup>2</sup> in 1 year, or more than 10 ml/min/1.73 m<sup>2</sup> within 5 years)</li> </ul>	<p>People with CKD in the following groups should normally be referred for specialist assessment:</p> <ul style="list-style-type: none"> <li>• GFR less than 30 ml/min/1.73 m<sup>2</sup> (GFR category G4 or G5), with or without diabetes</li> <li>• ACR 70 mg/mmol or more (ACR category A3), unless known to be caused by diabetes and already appropriately treated</li> <li>• ACR 30 mg/mmol or more (ACR category A3), together with haematuria</li> <li>• sustained decrease in GFR of 25% or more and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m<sup>2</sup> or more within 12 months</li> </ul>	<p>The first bullet point was amended to give GFR values rather than the stages to help clarify the criteria.</p> <p>In the second bullet point the equivalence to PCR value was removed to ensure consistency of ACR use.</p> <p>In the fourth bullet point the definition of progression was amended to the 2014 definition (see recommendation 1.3.5).</p> <p>The fifth bullet point was amended to cross reference the current NICE guideline on hypertension.</p>
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<ul style="list-style-type: none"> <li>• hypertension that remains poorly controlled despite the use of at least four antihypertensive drugs at therapeutic doses (see also 'Hypertension: management of hypertension in adults in primary care' [NICE guideline CG34])</li> <li>• people with, or suspected of having, rare or genetic causes of CKD</li> <li>• suspected renal artery stenosis. (1.6.1)</li> </ul>	<ul style="list-style-type: none"> <li>• hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses (see also Hypertension [NICE guideline CG127])</li> <li>• known or suspected of rare or genetic causes of CKD</li> <li>• suspected renal artery stenosis. [2008, amended 2014] (1.5.2)</li> </ul>	
<p>Offer dietary advice to people with progressive CKD concerning potassium, phosphate, protein, calorie and salt intake when indicated. (1.7.4)</p>	<p>Offer dietary advice about potassium, phosphate, calorie and salt intake appropriate to the severity of CKD. (1.4.7)</p>	<p>Protein was removed because this was subject to a new evidence review.</p> <p>The GDG reworded the recommendation to state that advice should be appropriate to the stage of CKD because 'progressive CKD' was considered to be ambiguous as it could refer to anyone with CKD.</p>

ACE inhibitor/ARB therapy should not normally be started if the pretreatment serum potassium concentration is significantly above the normal reference range (typically more than 5.0 mmol/litre). (1.8.11)	Do not routinely offer a renin-angiotensin system antagonist to people with CKD if their pretreatment serum potassium concentration is greater than 5.0 mmol/litre. (1.6.8)	The recommendation was amended for clarity and to reduce the uncertainty implied by changing 'significantly above the normal reference range' to 'greater than 5.0 mmol/litre'.
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## Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also [patient-centred care](#)).

## Interventions that must (or must not) be used

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

## Interventions that should (or should not) be used – a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer...') when we are confident that an intervention will not be of benefit for most patients.

## Interventions that could be used

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

## Recommendation wording in guideline updates

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations ending [2008] (see [update information](#) for details about how recommendations are labelled). In particular, for recommendations labelled [2008], the word 'consider' may not necessarily be used to denote the strength of the recommendation.

## Other versions of this guideline

The full guideline, [Chronic kidney disease](#), contains details of the methods and evidence used to develop the guideline. It is published by the National Clinical Guideline Centre.

The recommendations from this guideline have been incorporated into a [NICE pathway](#).

We have produced [information for the public](#) about this guideline.

## Implementation

[Implementation tools and resources](#) to help you put the guideline into practice are also available.

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## Accreditation

