Chronic kidney disease: early identification and management of chronic kidney disease in adults in primary and secondary care

NICE guideline

Draft for consultation, February 2014

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence for the 2014 recommendations is contained in the full version of the 2014 guideline. Evidence for the 2008 recommendations is in the full version of the 2008 guideline.

Contents

Introduction

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 established renal failure 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 National service framework for renal services adopted the 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^2 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, Chronic kidney disease (NICE clinical guideline 73) suggested 2 key changes to this classification: the sub-division of stage 3 into 3a (GFR 45–59 ml/min/1.73 m^2) and 3b (30–44 ml/min/1.73 m^2), and the addition of the suffix ‘P’ to denote significant proteinuria at all stages. The 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) CKD guidance[1] 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), with each GFR category in an updated classification (as demonstrated in the following 2 tables). This update of the NICE guideline reviews the classification of CKD.

Kidney Disease Improving Global Outcomes GFR categories for CKD

GFR category	GFR (ml/min/1.73 m^2)	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 Supplements 3: 1–150.

[1] Kidney Disease: Improving Global Outcomes (KDIGO) (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 for CKD

ACR category	ACR (mg/mmol)	Terms
A1	<3	Normal to mildly increased
A2	3–30	Moderately increased*
A3	>30	Severely increased**

*Relative to young adult level

** Including nephrotic syndrome (ACR usually >220 mg/mmol)

Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease.

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 Supplements 3: 1–150.

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 2013 UK Renal Registry report[2]. 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[3]. More than half of this amount was spent on renal replacement therapy for the 2% of people with CKD who progress to renal 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 established renal failure are clearly needed.

[2] Gilga J, Raoa A, Fogarty D. UK Renal Registry 16th Annual Report: Chapter 1 UK Renal Replacement Therapy Incidence in 2012: National and Centre-specific Analyses. Available from: http://www.renalreg.com/Reports/2013.html

[3] Kerr M, Bray B, Medcalf J, O'Donoghue DJ, Matthews B. Estimating the financial cost of chronic kidney disease to the NHS in England. Nephrol Dial Transplant. 2012 Oct;27 Suppl 3:iii73-80.

This guideline seeks to address these issues by updating NICE clinical guideline 73 in areas where new data has 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.

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.

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 shaded in grey and ending [2008] (see 'Update information' box below 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.

Update information

This guidance is an update of NICE clinical guideline 73 (published September 2008) and will replace it.

New recommendations have been updated or added for the investigation, diagnosis, monitoring and management of adults with chronic kidney disease.

You are invited to comment on the new and updated recommendations in this guideline. These are marked as **[2014]** if the evidence has been reviewed but no change has been made to the recommendation, or **[new 2014]** if the evidence has been reviewed and the recommendation has been added or updated.

You are also invited to comment on recommendations that NICE proposes to delete from the 2008 guideline, because either the evidence has been reviewed and the recommendations have been updated, or NICE has updated other relevant guidance and has replaced the original recommendations. Appendix A sets out these recommendations and includes details of replacement recommendations. Where there is no replacement recommendation, an explanation for the proposed deletion is given.

Where recommendations are shaded in grey and end **[2008]**, the evidence has not been reviewed since the original guideline. We will not be able to accept comments on these recommendations. Yellow shading in these recommendations indicates where wording changes have been made for the purposes of clarification only.

Where recommendations are shaded in grey and end **[2008, amended 2014]**, the evidence has not been reviewed but changes have been made to the recommendation wording that change the meaning (for example, because of equalities duties or a change in the availability of drugs, or incorporated guidance has been updated). These changes are marked with yellow shading, and explanations of the reasons for the changes are given in appendix A for information. We will not be able to accept comments on these

recommendations.

The original NICE guideline and supporting documents are available here.

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 GFRcreatinine, 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 the UK National External Quality Assessment Service scheme for creatinine. **[1.1.2] [new 2014]**

- Consider using eGFRcystatinC to confirm the diagnosis of CKD in people with:
  - an eGFRcreatinine of 45–59 ml/min/1.73 m^2, sustained for at least 90 days **and**
  - no proteinuria (albumin:creatinine ratio [ACR] less than 3 mg/mmol). **[1.1.14] [new 2014]**

- Do not diagnose CKD in people with:
  - an eGFRcreatinine of 45–59 ml/min/1.73 m^2 **and**
  - an eGFRcystatinC of more than 60 ml/min/1.73 m^2 **and**
  - no other marker of kidney disease[4]. **[1.1.15] [new 2014]**

- Offer testing for CKD to people with any of the following risk factors:
  - diabetes
  - hypertension

[4] Markers of kidney disease include albuminuria (ACR more than 3 mg/mmol), urine sediment abnormalities, electrolyte and other abnormalities caused by tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging and previous kidney transplantation.

- acute kidney injury (see recommendation 1.3.8)
- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
- structural renal tract disease, renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement - for example, systemic lupus erythematosus
- family history of stage 5 CKD or hereditary kidney disease
- opportunistic detection of haematuria. **[1.1.28] [new 2014]**[5]

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 progression
  - decreased GFR is associated with increased risk of progression
  - increased ACR and decreased GFR in combination multiply the risk of progression. **[1.2.1] [new 2014]**

[5] This recommendation has been updated. However, only diabetes, hypertension and acute kidney injury were included in the evidence review. The other bullet points were not reviewed for this update and so we will not be able to accept comments on these.

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

GFR and ACR categories (including stages of CKD from previous guideline)			Albuminuria categories (mg/mmol)		
			<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73 m²)	≥90 Normal and high	G1 (Stage 1)	No CKD*	G1 A2	G1 A3
	60–89 Mild reduction related to normal range for a young adult	G2 (Stage 2)		G2 A2	G2 A3
	45–59 Mild–moderate reduction	G3a (Stage 3a)	G3a A1^	G3a A2	G3a A3
	30–44 Moderate–severe reduction	G3b (Stage 3b)	G3b A1	G3b A2	G3b A3
	15–29 Severe reduction	G4 (Stage 4)	G4 A1	G4 A2	G4 A3
	<15 Kidney failure	G5 (Stage 5)	G5 A1	G5 A2	G5 A3

Increasing risk

Increasing risk

** By definition, in the absence of evidence of kidney damage, these categories are not CKD.*

^ Consider using eGFRcystatinC to confirm the diagnosis of CKD in people with an eGFRcreatinine of 45–59 ml/min/1.73 m2, sustained for at least 90 days ***and*** *no proteinuria (albumin:creatinine ratio [ACR] less than 3 mg/mmol).*

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

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 progression of CKD 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. **[1.3.2] [new 2014]**

Table 2 Frequency of monitoring of GFR for people with, or at risk of, CKD

Frequency of monitoring (number of times per year)		Albuminuria categories (mg/mmol)		
		<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
GFR categories (ml/min/1.73 m^2)	G1 ≥90 (Stage 1)	≤1	1	≥1
	G2 60–89 (Stage 2)	≤1	1	≥1
	G3a 45–59 (Stage 3a)	1	1	2
	G3b 30–44 (Stage 3b)	≤2	2	≥2
	G4 15–29 (Stage 4)	2	2	3
	G5 <15 (Stage 5)	4	≥4	≥4

Abbreviations: GFR, glomerular filtration rate

- 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. **[1.3.8] [new 2014]**

1 Recommendations

The following guidance is based on the best available evidence. The full guideline [hyperlink to be added for final publication] gives details of the methods and the evidence used to develop the guidance.

Terms used in this guideline

The term glomerular filtration rate (GFR) is abbreviated in the following way within the recommendations in this guideline:

- eGFR: estimated GFR (used when the recommendation relates specifically to an estimated GFR and does not indicate the method of estimation)
- mGFR: measured GFR
- eGFRcreatinine: an estimation of GFR using serum creatinine
- eGFRcystatinC: an estimation of eGFR using cystatin C
- GFR: is used alone when the recommendation relates to either a measured GFR or an estimated GFR.

1.1 Investigations for chronic kidney disease

Measuring kidney function

Serum creatinine 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 (eGFRcreatinine) using a prediction equation (see recommendation 1.1.2) in addition to reporting the serum creatinine result.[6] **[2014]**

1.1.2 Clinical laboratories should:

- use the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation to estimate GFRcreatinine, 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 the UK National External Quality Assessment Service scheme for creatinine. **[new 2014]**

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 eGFRcreatinine with caution.

[6] 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).

(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 eGFRcreatinine. 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 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 (eGFRcystatinC) 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 GFRcystatinC. **[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 eGFRcystatinC with caution in people with uncontrolled thyroid disease as eGFRcystatinC 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^2 or less, or as 'greater than 90 ml/min/1.73 m^2'. **[new 2014]**

1.1.11 If GFR is greater than 90 ml/min/1.73 m^2, use an increase in serum creatinine concentration of more than 20% to infer significant reduction in renal function. **[new 2014]**

1.1.12 Interpret eGFR values of 60 ml/min/1.73 m^2 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^2 in a person not previously tested by repeating the test within 2 weeks. Allow for biological and analytical variability of serum creatinine (±5%) when interpreting changes in eGFR. **[2008]**

When to diagnose CKD

1.1.14 Consider using eGFRcystatinC to confirm the diagnosis of CKD in people with:

- an eGFRcreatinine of 45–59 ml/min/1.73 m^2, sustained for at least 90 days **and**
- no proteinuria (albumin:creatinine ratio [ACR] less than 3 mg/mmol). **[new 2014]**

1.1.15 Do not diagnose CKD in people with:

- an eGFRcreatinine of 45–59 ml/min/1.73 m^2 **and**
- an eGFRcystatinC of more than 60 ml/min/1.73 m^2 **and**
- no other marker of kidney disease[7]. **[new 2014]**

[7] Markers of kidney disease include albuminuria (ACR more than 3 mg/mmol), urine sediment abnormalities, electrolyte and other abnormalities caused by tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging and previous kidney transplantation.

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}Cr-EDTA, ^{125}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, as it has greater sensitivity than protein:creatinine ratio (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. **[2008]**

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 less than 60 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 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 to people with any of the following risk factors:

- diabetes
- hypertension
- acute kidney injury (see recommendation 1.3.8)
- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
- structural renal tract disease, renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement - for example, systemic lupus erythematosus
- family history of stage 5 CKD or hereditary kidney disease
- opportunistic detection of haematuria. **[new 2014][8]**

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]**

[8] This recommendation has been updated. However, only diabetes, hypertension and acute kidney injury were included in the evidence review. The other bullet points were not reviewed for this update and so we will not be able to accept comments on these.

1.2 Classification of CKD

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

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

GFR and ACR categories (including stages of CKD from previous guideline)			Albuminuria categories (mg/mmol)		
			<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73 m²)	≥90 Normal and high	G1 (Stage 1)	No CKD*	G1 A2	G1 A3
	60–89 Mild reduction related to normal range for a young adult	G2 (Stage 2)		G2 A2	G2 A3
	45–59 Mild–moderate reduction	G3a (Stage 3a)	G3a A1^	G3a A2	G3a A3
	30–44 Moderate–severe reduction	G3b (Stage 3b)	G3b A1	G3b A2	G3b A3
	15–29 Severe reduction	G4 (Stage 4)	G4 A1	G4 A2	G4 A3
	<15 Kidney failure	G5 (Stage 5)	G5 A1	G5 A2	G5 A3

Increasing risk

Increasing risk

** By definition, in the absence of evidence of kidney damage, these categories are not CKD.*

^ Consider using eGFRcystatinC to confirm the diagnosis of CKD in people with an eGFRcreatinine of 45–59 ml/min/1.73 m2, sustained for at least 90 days ***and*** *no proteinuria (albumin:creatinine ratio [ACR] less than 3 mg/mmol).*

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

1.2.2 For any given stage of CKD, do not determine management solely by age. **[new 2014]**

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

1.2.3 After an informed discussion with the person with CKD, agree a plan to establish the cause (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 to all people with CKD who:

- have progressive CKD (a sustained decrease in GFR of 25% or more and a change in GFR category, or a sustained decrease in GFR of 15 ml/min/1.73 m^2 or more)
- 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 stage 4 or 5 CKD
- 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 kidney function monitoring (eGFR and ACR) with the person with, or at risk of, CKD, recognising 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 for people with, or at risk of, CKD

Frequency of monitoring (number of times per year)		Albuminuria categories (mg/mmol)		
		<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
GFR categories (ml/min/1.73 m^2)	G1 ≥90 (Stage 1)	≤1	1	≥1
	G2 60–89 (Stage 2)	≤1	1	≥1
	G3a 45–59 (Stage 3a)	1	1	2
	G3b 30–44 (Stage 3b)	≤2	2	≥2
	G4 15–29 (Stage 4)	2	2	3
	G5 <15 (Stage 5)	4	≥4	≥4

Abbreviations: GFR, glomerular filtration rate

Defining progression

1.3.3 Take the following steps to identify progressive 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]**

1.3.4 Be aware that people with CKD are at increased risk of progression to end-stage renal 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^2 or more over 12 months. **[2008, amended 2014]**

1.3.5 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

1.3.6 Work with people who have risk factors for CKD progression to optimise their health. These risk factors are:

- 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]**[9]

1.3.7 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]**

[9] This recommendation has been updated. However, only acute kidney injury was included in the evidence review. The other bullet points were not reviewed for this update and so we will not be able to accept comments on these.

Acute kidney injury and CKD

1.3.8 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]**

1.3.9 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 stage 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 may be considered where appropriate. **[2008]**

1.4.3 Offer people with CKD high-quality information or education programmes at appropriate stages 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 appropriate to the stage of CKD about potassium, phosphate, calorie and salt intake. **[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:

- enable people with CKD to share in decision-making about their care
- support self-management (this includes providing information about blood pressure, 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 Patient View, to encourage and help them to self-manage their CKD. **[new 2014]**

1.5 Referral criteria

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

- GFR less than 30 ml/min/1.73 m^2 (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, 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^2 or more
- hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses (see Hypertension [NICE clinical guideline 127])
- known or suspected rare or genetic causes of CKD
- suspected renal artery stenosis. **[2008, amended 2014]**

1.5.2 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]**

1.5.3 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]**

1.5.4 Take into account the individual's wishes and comorbidities when considering referral. **[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.[10] **[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

[10] 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.

below 130 mmHg (target range 120–129 mmHg) and the diastolic blood pressure below 80 mmHg[11]. **[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
- hypertension and an ACR of 30 mg/mmol or more
- an ACR of 70 mg/mmol or more (irrespective of hypertension or cardiovascular disease).[12] **[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 clinical guideline 127) for people with CKD, hypertension and an ACR of less than 3 mg/mmol, 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

[11] 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.

[12] The evidence to support these criteria is limited in people aged over 70 years.

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 clinical guideline; publication expected July 2014) 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 15-50 ml/min/1.73 m^2 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 stage 1, 2, 3a or 3b CKD. **[2008]**

1.7.2 Measure serum calcium, phosphate and PTH concentrations in people with stage 4 or 5 CKD (GFR less than 30 ml/min/1.73 m^2). 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 stage 1, 2, 3a or 3b CKD. **[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 cholecalciferol 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 stage 4 or 5 CKD. **[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 stage 3b, 4 and 5 CKD to identify anaemia (Hb less than 11.0 g/dl, see Anaemia management in people with chronic kidney disease, NICE clinical guideline 114). 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:

- stage 4 or 5 CKD **and**
- a serum bicarbonate concentration of less than 20 mmol/litre. **[new 2014]**

2 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.

2.1 Self-management

Does the provision of educational and supportive interventions to people with 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 co-exists 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 we would expect people with CKD to 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.

2.2 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 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 ACR. However the current evidence base for reducing cardiovascular risk in the CKD population is very limited.

2.3 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.

2.4 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 has 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 requiring renal replacement therapy and mortality.

2.5 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^2 to 23%, 44% and 73% in people with a GFR of 45-59, 30-44 and under 30 ml/min/1.73 m^2, respectively. 25-Hydroxyvitamin D deficiency is twice as prevalent in people with a GFR under 30 ml/min/1.73 m^2 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.

3 Other information

3.1 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 4), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in The guidelines manual.

3.2 Related NICE guidance

Details are correct at the time of consultation on the guideline (21 February 2014). Further information is available on the NICE website.

Published

General

- Patient experience in adult NHS services. NICE clinical guidance 138 (2012).
- Medicines adherence. NICE clinical guidance 76 (2009).

Condition-specific

- Apixaban for preventing stroke and systemic embolism in people with nonvalvular atrial fibrillation. NICE technology appraisal guidance 275 (2013).
- Acute kidney injury. NICE clinical guideline 169 (2013).

- Hyperphosphataemia in chronic kidney disease. NICE clinical guideline 157 (2013).
- Osteoporosis fragility fracture risk. NICE clinical guideline 146. (2012).
- Rivaroxaban for the treatment of deep vein thrombosis and prevention of recurrent deep vein thrombosis and pulmonary embolism. NICE technology appraisal guidance 261 (2012).
- Rivaroxaban for the prevention of stroke and systemic embolism in people with atrial fibrillation. NICE technology appraisal guidance 256 (2012).
- Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation. NICE technology appraisal guidance 249 (2012).
- Peritoneal dialysis. NICE clinical guideline 125 (2011).
- Hypertension. NICE clinical guideline 127 (2011).
- Anaemia management in people with chronic kidney disease. NICE clinical guideline 114 (2011).
- Chronic heart failure. NICE clinical guideline 108 (2010).
- Prevention of cardiovascular disease. NICE public health guidance 25 (2010).
- Depression in adults with a chronic physical health problem. NICE clinical guideline 91 (2009).
- Lipid modification. NICE clinical guideline 67 (2008).
- Type 2 diabetes. NICE clinical guideline 87 (2008).
- Febuxostat for the management of hyperuricaemia in people with gout. NICE technology appraisal guidance 164 (2008).
- Cinacalcet hydrochloride for the treatment of secondary hyperparathyroidism in patients with end stage renal disease on maintenance dialysis therapy. NICE technology appraisal guidance 117 (2007).
- Atrial fibrillation. NICE clinical guideline 36 (2006)
- Brief interventions and referral for smoking cessation. NICE public health guidance 1 (2006).
- Type 1 diabetes. NICE clinical guideline 15 (2004).
- Guidance on home compared with hospital haemodialysis for patients with end-stage renal failure. NICE technology appraisal guidance 48 (2002).

Under development

NICE is developing the following guidance (details available from the NICE website):

- Lipid modification (update). NICE clinical guideline. Publication expected July 2014.
- Suspected cancer (update). NICE clinical guideline. Publication expected May 2015.
- Anaemia management in people with chronic kidney disease (update). NICE clinical guideline. Publication expected July 2015.
- Type 1 diabetes (update). NICE clinical guideline. Publication expected August 2015.
- Type 2 diabetes (update). NICE clinical guideline. Publication expected August 2015.

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

4.1 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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4.2 National Clinical Guideline Centre

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Appendix A: Recommendations from NICE clinical guideline 73 (2008) that have been deleted or changed

Recommendations to be deleted

The table shows recommendations from 2008 that NICE proposes deleting in the 2014 update. The right-hand column gives the replacement recommendation, or explains the reason for the deletion if there is no replacement recommendation.

Recommendation in 2008 guideline	Comment
Use the IDMS (isotope dilution mass spectrometry)-traceable simplified MDRD (modification of diet in renal disease) equation to estimate GFR, using creatinine assays with calibration traceable to a standardised reference material. Ideally use creatinine assays that are specific and zero biased compared with IDMS (for example, enzymatic assays). When non-specific assays are used (for example, Jaffe assays), employ appropriate assay-specific adjustment factors to minimise between-laboratory variation (for example, those provided by national external quality assessment schemes).(1.1.2)	Replaced by recommendation 1.1.2. Clinical laboratories should: • use the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation to estimate GFRcreatinine, 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 the UK National External Quality Assessment Scheme for creatinine.
Where indicated, apply a correction factor for ethnicity to reported GFR values (multiply eGFR by 1.21 for African-Caribbean ethnicity). (1.1.3)	Replaced by recommendation 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).
Where eGFR is simply reported as 60 ml/min/1.73 m^2 or more, use a rise in serum creatinine concentration of more than 20% to infer significant reduction in renal function.(1.1.5)	Replaced by recommendation 1.1.11. If GFR is greater than 90 ml/min/1.73 m^2, use an increase in serum creatinine concentration of more than 20% to infer significant reduction in renal function.
Use the suffix '(p)' to denote the presence of proteinuria when staging CKD. (1.2.1)	Recommendation deleted because recommendation 1.2.1 recommends using both GFR and ACR to stage CKD and so use of additional 'p' is not required.
Stage 3 CKD should be split into two subcategories defined by: GFR 45–59 ml/min/1.73 m^2 (stage 3A) GFR 30–44 ml/min/1.73 m^2 (stage 3B). (1.2.3)	Recommendation deleted because it is now in common use and so the recommendation was not considered to be necessary. CKD stage information is also given in recommendation 1.2.1.
At any given stage of CKD, management should not be influenced solely by age* * In people aged over 70 years, an eGFR in the range 45–59 ml/min/1.73 m^2, if stable over time and without any other evidence of kidney damage, is unlikely to be associated with CKD-related complications. (1.2.4)	Replaced by recommendation 1.2.2 The footnote on the 2008 recommendation was removed as the evidence reviewed did not support it. The wording of the recommendation was also modified to improve clarity.
Work with people who have risk factors for progression of CKD to optimise their health. These risk factors are: • cardiovascular disease	Replaced by recommendation 1.3.6. 'Acute kidney injury' was added based on the 2014 evidence review. Modified wording for ethnicity based on

• proteinuria • hypertension • diabetes • smoking • black or Asian ethnicity • chronic use of NSAIDs • urinary outflow tract obstruction.(1.5.2)	NICE house style. Clarified that not all urinary outflow tract obstructions are risk factors, only those that are untreated (treatment will eliminate the risk of CKD progression). Work with people who have risk factors for CKD progression to optimise their health. These risk factors are: • 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. (1.3.6)
Where the clinician in discussion with the patient has decided that dietary intervention to influence progression of CKD is indicated, an appropriately trained professional should discuss the risks and benefits of dietary protein restriction, with particular reference to slowing down the progression of disease versus protein-calorie malnutrition.(1.7.2)	Replaced by recommendation 1.4.9 after review of the evidence on low-protein diets. Do not offer low-protein diets (dietary protein intake less than 0.6–0.8 g/kg/day) to people with CKD.
When implementing blockade of the renin–angiotensin system start treatment with an ACE inhibitor first then move to an ARB if the ACE inhibitor is not tolerated. (1.8.3)	Recommendation deleted because the evidence reviewed highlighted that the drugs should not be used together.
Offer ACE inhibitors/ARBs to people with diabetes and ACR more than 2.5 mg/mmol (men) or more than 3.5 mg/mmol (women) irrespective of the presence of hypertension or CKD stage[7]. (1.8.4)	Replaced by recommendation 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 • hypertension and an ACR of 30 mg/mmol or more • an ACR of 70 mg/mmol or more (irrespective of hypertension or cardiovascular disease).
Offer ACE inhibitors/ARBs to non-diabetic people with CKD and hypertension and 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)[7]. (1.8.5)	Replaced by recommendation 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

	• hypertension and an ACR of 30 mg/mmol or more • an ACR of 70 mg/mmol or more (irrespective of hypertension or cardiovascular disease).
Offer ACE inhibitors/ARBs to non-diabetic people with CKD and 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) irrespective of the presence of hypertension or cardiovascular disease[7]. (1.8.6)	Replaced by recommendation 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 • hypertension and an ACR of 30 mg/mmol or more • an ACR of 70 mg/mmol or more (irrespective of hypertension or cardiovascular disease).
Offer non-diabetic people with CKD and hypertension and ACR less than 30 mg/mmol (approximately equivalent to PCR less than 50 mg/mmol, or urinary protein excretion less than 0.5 g/24 h) a choice of antihypertensive treatment according to the NICE guidance on hypertension (NICE clinical guideline 34) to prevent or ameliorate progression of CKD. (1.8.7)	Replaced by recommendation 1.6.5. Follow the treatment recommendations in Hypertension (NICE clinical guideline 127) for people with CKD, hypertension and an ACR of less than 3 mg/mmol, if they do not have diabetes.
When using ACE inhibitors/ARBs titrate them to the maximum tolerated therapeutic dose before adding a second-line agent[8]. (1.8.8)	Recommendation deleted because the evidence reviewed highlighted that the drugs should not be used together.
Where indicated, the use of ACE inhibitors/ARBs should not be influenced by a person's age as there is no evidence that their appropriate use in older people is associated with a greater risk of adverse effects. (1.8.18)	Recommendation deleted. Content of the recommendation is already covered in recommendation 1.2.2.
The use of statin therapy for the primary prevention[9] of cardiovascular disease (CVD)[9],[10] in people with CKD should not differ from its use in people without CKD and should be based on existing risk tables for people with and without diabetes. It should be understood that the Framingham risk tables significantly underestimate risk in people with CKD. (1.8.19)	Replaced by recommendation 1.6.15. Follow the recommendations in Lipid modification (NICE clinical guideline; publication expected July 2014) for the use of statins in CKD. The NICE 'Lipids modification' guideline provides guidance on the use of statins in people with CKD and a reference to this guideline was considered appropriate.
Offer statins to people with CKD for the secondary prevention of CVD irrespective of baseline lipid values. (1.8.20)	Replaced by recommendation 1.6.15. Follow the recommendations in Lipid modification (NICE clinical guideline; publication expected July 2014) for the use of statins in CKD. The NICE 'Lipids modification' guideline

	provides guidance on the use of statins in people with CKD and a reference to this guideline was considered appropriate.
Offer antiplatelet drugs to people with CKD for the secondary prevention of CVD. CKD is not a contraindication to the use of low dose aspirin but clinicians should be aware of the increased risk of minor bleeding in people with CKD given multiple antiplatelet drugs. (1.8.21)	Replaced by recommendation 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.
When vitamin D supplementation is indicated in people with CKD offer: • cholecalciferol or ergocalciferol to people with stage 1, 2, 3A or 3B CKD • 1-alpha-hydroxycholecalciferol (alfacalcidol) or 1,25-dihydroxycholecalciferol (calcitriol) to people with stage 4 or 5 CKD.(1.9.4)	Replaced by recommendations 1.7.5 and 1.7.6. Offer cholecalciferol or ergocalciferol to treat vitamin D deficiency in people with CKD and vitamin D deficiency. 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 stage 4 or 5 CKD.

Amended recommendation wording (change to meaning)

Recommendations are labelled **[2008, amended 2014]** if the evidence has not been reviewed but changes have been made to the recommendation wording (indicated by highlighted text) that change the meaning.

Recommendation in 2008 guideline	**Recommendation in current guideline**	**Reason for change**
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	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)	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

tested. (1.1.12)		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.
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 to 3 mg/mmol. 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 30mg/mmol.
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)	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 to 3 mg/mmol. 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 30mg/mmol. There is a general move away from the term 'microalbuminuria' (ACR between 3-30mg/mmol) and the GDG wanted the latest recommendations to reflect this. Additionally it was no longer felt appropriate to have different criteria for gender. The GDG were not aware of any evidence on which the gender differences were based.
All people with diabetes, and people without diabetes with a GFR less than 60 ml/min/1.73 m^2, 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)	Quantify urinary albumin or urinary protein loss as in recommendation 1.1.18 for: • people with diabetes • people without diabetes with a GFR less than 60 ml/min/1.73 m^2 (1.1.21)	The second part of the original recommendation (regarding confirming on an early morning sample) was removed as modified criteria are provided in recommendation 1.1.19 Other changes for clarification only see clarification table
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)	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]	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.
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)	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)	The initial part of the sentence 'In the absence of the above risk factors' was removed. The 2008 recommendation implied that if risk factors were present that 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.
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)	Regard a confirmed ACR of 3 mg/mmol or more as clinically important proteinuria. (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. The equivalences to PCR and urinary protein excretion were removed because the evidence showed

		that ACR was more accurate.

Offer a renal ultrasound to all people with CKD who: • have progressive CKD (eGFR decline more than 5 ml/min/1.73 m^2 within 1 year, or more than 10 ml/min/1.73 m^2 within 5 years) • 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 • have stage 4 or 5 CKD • are considered by a nephrologist to require a renal biopsy. (1.4.1)	Offer a renal ultrasound to all people with CKD who: • have progressive CKD (a sustained decrease in GFR of 25% or more and a change in GFR category or a sustained decrease in GFR of 15 ml/min/1.73 m^2 or more) • 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 stage 4 or 5 CKD • are considered by a nephrologist to require a renal biopsy. (1.2.5)	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 1.3.4).
Take the following steps to identify progressive CKD. • Obtain a minimum of three GFR estimations over a period of not less than 90 days. • 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. • Define progression as a decline in eGFR of more than 5 ml/min/1.73 m^2 within 1 year, or more than 10 ml/min/1.73 m^2 within 5 years. • 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	Take the following steps to identify progressive 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. (1.3.3) Be aware that people with CKD are at increased risk of progression to end-stage renal 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^2 or	The first two bullet points of the 2008 recommendation were made into a separate recommendation (1.3.3) to emphasise the process to identify progressive CKD. The third bullet point was updated (1.3.4) based on evidence derived from the frequency of monitoring review which identified thresholds for progression. The GDG made a separate recommendation (1.3.5) from the fourth bullet point to give it additional focus, and clarified the wording according to NICE

rate of decline. (1.5.1)	more over 12 months. (1.3.4) 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. (1.3.5)	house style.
People with CKD in the following groups should normally be referred for specialist assessment: • stage 4 and 5 CKD (with or without diabetes) • 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 • 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 • rapidly declining eGFR (more than 5 ml/min/1.73 m^2 in 1 year, or more than 10 ml/min/1.73 m^2 within 5 years) • hypertension that remains poorly controlled despite the use of at least four antihypertensive drugs at therapeutic doses (see 'Hypertension: management of	People with CKD in the following groups should normally be referred for specialist assessment: • GFR less than 30 ml/min/1.73 m^2 (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 together with haematuria • sustained decrease in GFR of 25% or more and change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m^2 or more • hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses (see Hypertension, NICE clinical guideline 127) • known or suspected of rare or genetic causes of CKD • suspected renal artery stenosis. [2008, amended 2014] (1.5.1)	The first bullet point was amended to give GFR values rather than the stages to help clarify the criteria. In the second bullet point the equivalence to PCR value was removed to ensure consistency of ACR use. In the fourth bullet point the definition of progression was amended to the 2014 definition (see recommendation 1.3.4). The fifth bullet point was amended to cross reference the current NICE guideline on hypertension.

hypertension in adults in primary care' [NICE clinical guideline 34]) • people with, or suspected of having, rare or genetic causes of CKD • suspected renal artery stenosis. (1.6.1)		
Offer dietary advice to people with progressive CKD concerning potassium, phosphate, protein, calorie and salt intake when indicated. (1.7.4)	Offer dietary advice, appropriate to the stage of CKD about potassium, phosphate, calorie and salt intake. (1.4.7)	Protein was removed because this was subject to a new evidence review. 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.
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'.

Changes to recommendation wording for clarification only (no change to meaning)

Recommendation numbers in current guideline	Comment
All recommendations except those labelled [new 2014]	Recommendations have been edited into the direct style (in line with current NICE style for recommendations in clinical guidelines) where possible. Yellow highlighting has not been applied to these changes.
1.1.1, 1.1.4, 1.1.5	Changes were made to these recommendations to reflect the terminology used for GFR in this guideline (see Terms used in this guideline). Yellow highlighting has not been applied to these changes.
1.3.7, 1.6.11, 1.6.13	The wording was changed throughout to say 'decrease' and 'increase' consistently rather than 'rise', 'fall' and 'drop' in line with NICE house style. Yellow highlighting has not been applied to these changes.
1.1.1	Changes were made to the footnote in line with NICE house style for describing people with conditions or who have had an amputation, and describing ethnicity.
1.1.4	Changes were made in line with NICE house style: 'cases' changed to 'people' and 'amputees' changed to 'people who have had an amputation'.
1.1.16	The wording was modified from 'gold standard' to 'reference standard' to highlight that there are a number of ways to measure GFR directly and that each of these methods is subject to variation and has limitations.
1.1.21	Addition of bullet points and clarification of wording to make the recommendation clearer. A reference to recommendation 1.1.18 regarding whether to use ACR or PCR has been added.
1.1.21, 1.1.22	The wording was changed from 'urinary albumin/protein excretion' to 'urinary albumin or urinary protein loss' as protein is lost rather than excreted and for clarity.
1.3.3, 1.6.6-1.6.14	The term 'ACE inhibitor/ARB therapy' was replaced with 'renin-angiotensin system antagonists' to include renin inhibitors in addition to ACE inhibitors and ARBs (the 3 classes of renin-angiotensin system antagonists are ACE inhibitors, ARBs and direct renin inhibitors).

1.4.2	The second bullet point (What questions should people ask about their kidneys when they attend clinic?) was changed to simplify and recognise that the provision of services has changed.
1.5.3	The text '(between the person with CKD or their carer and the healthcare professional)' was added to clarify who the plan should be agreed by.
1.6.1, 1.6.2	The text 'Existing hypertension guidelines such as the NICE hypertension guideline (NICE clinical guideline 34) give a range rather than just an upper limit and clinicians find this clear guidance useful.' was removed from the footnote because the current NICE guideline on hypertension does not provide ranges of blood pressure.
1.6.2	The PCR equivalence values were removed because the evidence suggests that ACR is more accurate.
1.6.12–1.6.14	The term 'plasma' was changed to 'serum' for consistency.
1.7.7	NICE house style change to give drug names rather than chemical names.
1.7.8	The reference to the NICE guideline on anaemia management in CKD guideline was updated.