NICE National Institute for Health and Care Excellence

Chronic kidney disease

Early identification and management of chronic kidney disease in adults in primary and secondary care

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NICE clinical guideline 73

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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 (for example, cardiovascular disease and diabetes). When advanced, it also carries a higher risk of mortality. The risk of developing CKD increases with increasing age, and some conditions that coexist with CKD become more severe as kidney dysfunction advances. 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 detecting CKD are both 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, because of a lack of specific symptoms people with CKD are often not diagnosed, or diagnosed late when CKD is at an advanced stage.

The 'National service framework for renal services' adopted the US 'National Kidney Foundation kidney disease outcomes quality initiative' (NKF-KDOQI) classification of CKD. This classification divides CKD into five stages. Stages 3–5 may be defined by glomerular filtration rate (GFR) alone, whereas stages 1 and 2 also require the presence of persistent proteinuria, albuminuria or haematuria, or structural abnormalities.

On average 30% of people with advanced kidney disease are referred late to nephrology services from both primary and secondary care, causing increased mortality and morbidity. Over 2% of the total NHS budget is spent on renal replacement therapy (dialysis and transplantation) for those with established renal failure.

Strategies aimed at earlier identification and (where possible) prevention of progression to established renal failure are therefore clearly needed. This clinical guideline seeks to address these issues by providing guidance on identifying:

- people who have or are at risk of developing CKD
- those who need intervention to minimise cardiovascular risk and what that intervention should be
- those who will develop progressive kidney disease and/or complications of kidney disease and how they can be managed

- those who need referral for specialist kidney care.

Person-centred care

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

Treatment and care should take into account people's needs and preferences. People with chronic kidney disease should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If people who have the disease do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent and the code of practice that accompanies the Mental Capacity Act. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the person's needs. Treatment and care, and the information people are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the person agrees, families and carers should have the opportunity to be involved in decisions about treatment and care. Families and carers should also be given the information and support they need.

Key priorities for implementation

- To detect and identify proteinuria, use urine albumin:creatinine ratio (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.
- Offer angiotensin-converting enzyme inhibitors (ACE inhibitors)/ angiotensin-II receptor blockers (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)[i].
- 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).

Stages of chronic kidney disease (updated)

Stage[a]	GFR (ml/min/ 1.73 m2)	Description
1	90 or more	Normal or increased GFR, with other evidence of kidney damage
2	60–89	Slight decrease in GFR, with other evidence of kidney damage
3A	45–59	Moderate decrease in GFR, with or without other evidence of kidney damage
3B	30–44	
4	15–29	Severe decrease in GFR, with or without other evidence of kidney damage
5	< 15	Established renal failure
[a] Use the suffix (p) to denote the presence of proteinuria when staging CKD (recommendation 1.2.1).		

- 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 estimate of GFR (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 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.
- Offer people testing for CKD if they have any of the following risk factors:
  - diabetes
  - hypertension
  - cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease and 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 or proteinuria.
- 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 rate of decline.

- 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[2].

[1] Two different ACR thresholds are given in the guideline for initiating ACE inhibitor treatment in people with CKD and proteinuria. The potential benefit of ACE inhibitors in this context is greatly increased if the person also has diabetes or hypertension, and in these circumstances, a lower threshold is applied. The evidence base at present does not allow thorough analysis of all scenarios and the Guideline Development Group (GDG) based these decisions on clinical experience as well as what evidence there is.

[2] 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. 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. The GDG therefore set out a range of blood pressure targets, given in these recommendations, which in their clinical experience will inform good practice in CKD.

1 Guidance

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.

1.1 Investigation

Measurement of kidney function

1.1.1 Whenever a request for serum creatinine measurement is made, clinical laboratories should report an estimate of GFR (eGFR) using a prediction equation (see recommendation 1.1.2) in addition to reporting the serum creatinine result[3].

1.1.2 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).

1.1.3 Where indicated, apply a correction factor for ethnicity to reported GFR values (multiply eGFR by 1.21 for African-Caribbean ethnicity[4]).

1.1.4 Interpret reported values of eGFR 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.

1.1.5 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.

1.1.6 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 gold standard measure (inulin, ^{51}Cr-EDTA, ^{125}I-iothalamate or iohexol).

1.1.7 In cases where there are extremes of muscle mass – for example, in bodybuilders, amputees or people with muscle wasting disorders – interpret the eGFR with caution. (Reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR.)

1.1.8 Advise people not to eat any meat in the 12 hours before having a blood test for GFR estimation. Avoid delaying the despatch of blood samples to ensure that they are received and processed by the laboratory within 12 hours of venepuncture.

1.1.9 An eGFR result less than 60 ml/min/1.73 m^2 in a person not previously tested should be confirmed by repeating the test within 2 weeks. Make an allowance for biological and analytical variability of serum creatinine (± 5%) when interpreting changes in eGFR.

Measurement of eGFR: how often? [a]		
Annually in all at risk groups.		
During intercurrent illness and perioperatively in all patients with CKD.		
Exact frequency should depend on the clinical situation. The frequency of testing may be reduced where eGFR levels remain very stable but will need to be increased if there is rapid progression.		
Stage	eGFR range (ml/min/1.73 m^2)	Typical testing frequency
1 and 2	≥ 60 + other evidence of kidney disease	12 monthly
3A and 3B	30–59	6 monthly
4	15–29	3 monthly
5	<15	6 weekly
[a] The information in this table is based on GDG consensus and not on evidence.		

Proteinuria

Albumin is the principal component of proteinuria in glomerular disease. Reagent strips in current clinical practice predominantly detect albumin, not total protein, but are not reliably quantitative. ACR has far greater sensitivity than PCR for the detection of low levels of proteinuria and enhances early identification of CKD. However, there may be clinical reasons for a specialist to subsequently use PCR to quantify and monitor significant levels of proteinuria.

1.1.10 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.

1.1.11 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.

1.1.12 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.

1.1.13 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).

1.1.14 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.

1.1.15 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).

1.1.16 Quantify by laboratory testing the urinary albumin/protein excretion of people with an eGFR 60 ml/min/1.73 m^2 or more if there is a strong suspicion of CKD (see also recommendation 1.1.22).

Haematuria

1.1.17 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.

1.1.18 When there is the need to differentiate persistent invisible haematuria in the absence of proteinuria from transient haematuria, regard two out of three positive reagent strip tests as confirmation of persistent invisible haematuria.

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

1.1.20 Persistent invisible haematuria in the absence of proteinuria should be followed up annually with repeat testing for haematuria, proteinuria/albuminuria (see recommendations above), GFR and blood pressure monitoring as long as the haematuria persists.

Early identification

1.1.21 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.

1.1.22 Offer people testing for CKD if they have any of the following risk factors:

- diabetes
- hypertension

- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease and 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 or proteinuria.

1.1.23 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.

1.2 Classification

1.2.1 Use the suffix (p) to denote the presence of proteinuria when staging CKD.

1.2.2 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 h or more).

1.2.3 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).

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5	< 15	Established renal failure
[a] Use the suffix (p) to denote the presence of proteinuria when staging CKD (recommendation 1.2.1).		

1.2.4 At any given stage of CKD, management should not be influenced solely by age[5].

1.3 Information and education

1.3.1 Offer people with CKD education and information tailored to the stage and cause of CKD, the associated complications and the risk of progression.

1.3.2 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 when they attend clinic?
- 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.

1.3.3 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.

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

1.3.5 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.

1.4 Indications for renal ultrasound

1.4.1 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.

1.4.2 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.

1.5 Progression

1.5.1 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 rate of decline.

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

- cardiovascular disease
- proteinuria
- hypertension
- diabetes
- smoking
- black or Asian ethnicity
- chronic use of NSAIDs
- urinary outflow tract obstruction.

1.5.3 In people with CKD the chronic use of NSAIDs may be associated with progression and acute use is associated with a reversible fall 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.

1.6 Referral criteria

1.6.1 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 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.

1.6.2 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.

1.6.3 Once a referral has been made and a plan jointly agreed, 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.

1.6.4 Take into account the individual's wishes and comorbidities when considering referral.

1.6.5 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.

1.7 Lifestyle advice

1.7.1 Encourage people with CKD to take exercise, achieve a healthy weight and stop smoking.

1.7.2 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.

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

1.7.4 Offer dietary advice to people with progressive CKD concerning potassium, phosphate, protein, calorie and salt intake when indicated.

1.8 Pharmacotherapy

Blood pressure control

1.8.1 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[6].

1.8.2 In people with CKD and diabetes, and also in people with an 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) aim to keep the systolic blood pressure below 130 mmHg (target range 120–129 mmHg) and the diastolic blood pressure below 80 mmHg[6].

Choice of antihypertensive agents

1.8.3 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.

1.8.4 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].

1.8.5 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].

1.8.6 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].

1.8.7 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.

1.8.8 When using ACE inhibitors/ARBs titrate them to the maximum tolerated therapeutic dose before adding a second-line agent[8].

1.8.9 To improve concordance, inform people who are prescribed ACE inhibitors or ARB therapy about the importance of:

- achieving the optimal tolerated dose of ACE inhibitor/ARB, and
- monitoring eGFR and serum potassium in achieving this safely.

Practicalities of treatment with ACE inhibitors/ARBs

1.8.10 In people with CKD, measure serum potassium concentrations and estimate the GFR before starting ACE inhibitor/ARB therapy. Repeat these measurements between 1 and 2 weeks after starting ACE inhibitor/ARB therapy and after each dose increase.

1.8.11 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).

1.8.12 When hyperkalaemia precludes the use of ACE inhibitors/ARBs, assessment, investigation and treatment of other factors known to promote hyperkalaemia should be undertaken and the serum potassium concentration rechecked.

1.8.13 Concurrent prescription of drugs known to promote hyperkalaemia is not a contraindication to the use of ACE inhibitors/ARBs, but be aware that more frequent monitoring of serum potassium concentration may be required.

1.8.14 Stop ACE inhibitor/ARB therapy if the serum potassium concentration rises to 6.0 mmol/litre or more and other drugs known to promote hyperkalaemia have been discontinued.

1.8.15 Following the introduction or dose increase of ACE inhibitor/ARB, do not modify the dose if either the GFR decrease from pretreatment baseline is less than 25% or the plasma creatinine increase from baseline is less than 30%.

1.8.16 If there is a fall in eGFR or rise in plasma creatinine after starting or increasing the dose of ACE inhibitor/ARB, but it is less than 25% (eGFR) or 30% (serum creatinine) of baseline, the test should be repeated in a further 1–2 weeks. Do not modify the ACE inhibitor/ARB dose if the change in eGFR is less than 25% or the change in plasma creatinine is less than 30%.

1.8.17 If the change in eGFR is 25% or more or the change in plasma 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 ACE inhibitor/ARB therapy or reduce the dose to a previously tolerated lower dose, and add an alternative antihypertensive medication if required.

1.8.18 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.

Statins and antiplatelet drugs

1.8.19 The use of statin therapy for the primary prevention[9] of cardiovascular disease (CVD)[8],[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.

1.8.20 Offer statins to people with CKD for the secondary prevention of CVD irrespective of baseline lipid values.

1.8.21 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.

1.8.22 There is insufficient evidence to recommend the routine use of drugs to lower uric acid in people with CKD who have asymptomatic hyperuricaemia.

1.9 Other complications

Bone metabolism and osteoporosis

1.9.1 The routine measurement of calcium, phosphate, parathyroid hormone (PTH) and vitamin D levels in people with stage 1, 2, 3A or 3B CKD is not recommended.

1.9.2 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.

1.9.3 Offer bisphosphonates if indicated for the prevention and treatment of osteoporosis in people with stage 1, 2, 3A or 3B CKD.

1.9.4 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.

1.9.5 Monitor serum calcium and phosphate concentrations in people receiving 1-alpha-hydroxycholecalciferol or 1,25-dihydroxycholecalciferol supplementation[11].

Anaemia

1.9.6 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 39]). Determine the subsequent frequency of testing by the measured value and the clinical circumstances.

[3] eGFR may be less reliable in certain situations (for example, acute renal failure, pregnancy, oedematous states, muscle wasting disorders, amputees and malnourished people) and has not been well validated in certain ethnic groups (for example, Asians and Chinese).

[4] In practice this correction factor should also be applied to those of African ethnicity.

[5] 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.

[6] 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. 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. The GDG therefore set out a range of blood pressure targets, given in these recommendations, which in their clinical experience will inform good practice in CKD.

[7] Two different ACR thresholds are given here for initiating ACE inhibitor treatment in people with CKD and proteinuria. The potential benefit of ACE inhibitors in this context is greatly increased if the person also has diabetes or hypertension, and in these circumstances, a lower threshold is applied. The evidence base at present does not allow thorough analysis of all scenarios and the GDG based these decisions on clinical experience as well as what evidence there is.

[8] There is insufficient evidence to recommend the routine use of spironolactone in addition to ACE inhibitor and ARB therapy to prevent or ameliorate progression of CKD.

[9] There is insufficient evidence to support the routine use of statins to prevent or ameliorate progression of CKD.

[10] The use of statins for the primary prevention of CVD in people with CKD should be informed by the SHARP study: Baigent C, Landry M (2003) Study of heart and renal protection. Kidney International 63: S207–S210.

[11] Detailed advice concerning the management of bone and mineral disorders in CKD is beyond the scope of this guideline. Where uncertainty exists seek advice from your local renal service.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available.

This guideline is for the early detection/identification of adults with CKD (including diagnostic tests). It covers best practice advice on the care of adults with a diagnosis of CKD and their referral to specialist renal services. It also covers the general management of CKD resulting from a variety of causes including diabetes, hypertension, cardiovascular disease and genetic causes.

It does not cover children (aged under 16 years), people receiving renal replacement therapy, people with acute kidney injury (acute renal failure) and rapidly progressive glomerulonephritis, the treatment of each of the specific causes of CKD, the management of pregnancy in women with CKD and the management of anaemia in people with CKD.

How this guideline was developed

NICE commissioned the National Collaborating Centre for Chronic Conditions to develop this guideline. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see appendix B).

There is more information about how NICE clinical guidelines are developed on the NICE website. A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' is available.

3 Implementation

The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health', issued in July 2004. Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website.

- Slides highlighting key messages for local discussion.
- Costing tools:
    - costing report to estimate the national savings and costs associated with implementation
    - costing template to estimate the local costs and savings involved.
- Guide to resources, which signposts a selection of resources available from NICE, government and other national organisations.
- Audit support to monitor local practice.

4 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. The Guideline Development Group's full set of research recommendations is detailed in the full guideline (see section 5).

4.1 Measurement of kidney function

It is recommended that research is undertaken to identify more accurate and cost effective methods of monitoring kidney function, especially in patients with GFR 60 ml/min/1.73 m^2 or more.

Why this is important

The use of prediction equations to estimate GFR from serum creatinine has proved to be a simple and cheap method for detecting abnormal kidney function. However, the limitations of serum creatinine as a marker of kidney disease are well known. Creatinine is an endogenous marker of kidney disease but it only fulfils some, not all, of the essential criteria for assessment of kidney function. We know that there are several other endogenous markers – for example, cystatin C – that can be potentially used as measures of kidney function. Research needs to be directed towards finding an endogenous marker that reliably and accurately reflects underlying GFR, is simple and cheap to assay, but crucially also has low biological and analytical variability.

4.2 Cardiovascular risk in people with CKD

Evidence is needed to better determine the mechanisms leading to increased risk of CVD in people with CKD and to thus enable the CVD risk to be calculated in people with CKD.

Why this is important

People with CKD have an increased prevalence of CVD and they are far more likely to die from a CVD-related cause than they are to progress to established kidney failure. But the mechanisms driving this increased cardiovascular risk are still poorly understood. Although some traditional CVD risk factors such as hypertension clearly play a role, the prediction of cardiovascular risk using existing risk prediction models developed in people without CKD is flawed. Research is

urgently needed to determine the mechanisms that increase CVD risk in people with CKD and to determine the relative contribution of the key factors.

4.3 ACE inhibitor/ARB therapy for low levels of proteinuria

There is an urgent need to clarify the benefits of treatment with ACE inhibitors/ARBs in non-diabetic CKD patients with lower levels of proteinuria.

Why this is important

The benefits of ACE inhibitor/ARB therapy for people with diabetes with microalbuminuria and all levels of macroalbuminuria are well established. It is also established that ACE inhibitor/ARB therapy for people with significant proteinuria (ACR 30 mg/mmol or more, equivalent to total urinary protein excretion 0.5 g/24 h or more) without diabetes is beneficial. However, it is not yet known whether ACE inhibitor/ARB therapy in people without diabetes and with lower levels of proteinuria in the absence of cardiovascular indications is of additional benefit over and above good blood pressure control. It is also possible that use of ACE inhibitor/ARB therapy in this group of people with CKD may have an overall detrimental effect. There is a need for well conducted randomised controlled trials to establish the risk:benefit ratio in this group.

4.4 Does age or gender matter in CKD?

Further research is required to determine the impact of age and gender on outcomes stratified by the level of GFR and the presence or absence of proteinuria.

Why this is important

CKD is increasingly prevalent with increased age, and the female gender is predominant in older age groups with CKD. Some suggest that this is largely a function of ageing and an epiphenomenon of the use of the MDRD equation to estimate GFR, whereas others maintain that this is a true effect. Studies are required to clearly determine the impact of age and gender on adverse outcomes in people with CKD. These studies should include stratification by level of GFR and the presence or absence of proteinuria in their design.

4.5 Validation of estimating equations in differing CKD populations

There is a need to validate eGFR equations in ethnic groups other than Caucasians and African-Caribbeans and among older people.

Why this is important

The use of the MDRD equation is recommended and indeed already widely applied, but the population it was developed in is not representative of all those with CKD. The same criticism may be levied for other prediction equations used to estimate GFR. There is therefore a need to validate these estimating equations in all populations with CKD, in particular those not represented in the MDRD study, such as the older population.

5 Other versions of this guideline

5.1 Full guideline

The full guideline, 'Chronic kidney disease: early identification and management in adults in primary and secondary care', contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Chronic Conditions, and is available from our website.

5.2 Information for the public

NICE has produced information for the public explaining this guideline.

We encourage NHS and voluntary sector organisations to use text from this booklet information in their own information materials.

6 Related NICE guidance

Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. NICE clinical guideline 67 (2008).

Type 2 diabetes: the management of type 2 diabetes (update). NICE clinical guideline 66 (2008).

Anaemia management in people with chronic kidney disease. NICE clinical guideline 39 (2006). [Replaced by NICE clinical guideline 114]

Hypertension: management of hypertension in adults in primary care. NICE clinical guideline 34 (partial update of NICE clinical guideline 18) (2006).

Brief interventions and referral for smoking cessation in primary care and other settings. NICE public health intervention guidance 1 (2006).

Type 2 diabetes: the management of type 2 diabetes. NICE clinical guideline 87 (2009).

7 Updating the guideline

NICE clinical guidelines are updated as needed so that recommendations take into account important new information. We check for new evidence 2 and 4 years after publication, to decide whether all or part of the guideline should be updated. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

Appendix A: The Guideline Development Group

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Dr David Stephens
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The following individuals were not full members of the Guideline Development Group but were invited to attend specific meetings.

Dr Claire Beeson
Consultant Geriatrician, East Kent Hospitals, attended as a deputy on behalf of Shelagh O'Riordan

Dr Indranil Dasgupta
Consultant Nephrologist, Birmingham Heartlands Hospital, attended on behalf of the 'Type 2 diabetes' Guideline Development Group

Dr Patrick Fitzgerald
General Practitioner, attended as a deputy on behalf of Ivan Benett

Dr Neil Iggo
Consultant Nephrologist, Royal Sussex County Hospital, attended as a deputy on behalf of Lawrence Goldberg

Dr Kanchana Imrapur
General Practitioner, attended as a deputy on behalf of David Stephens

Dr Marta Lapsley
Clinical Biochemist, Epsom and St Helier University Hospitals, attended as a deputy on behalf of Edmund Lamb

Ms Nicola Thomas
Senior Lecturer, St Bartholomew School of Nursing and Midwifery, attended as a deputy on behalf of Natasha McIntyre

National Collaborating Centre for Chronic Conditions

Ms Lina Bakhshi
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Mr Robert Grant
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Dr Suffiya Omarjee (from August 2007 until March 2008)
Health Economist

Ms Jaim Sutton (until March 2008)
Project Manager

Ms Meiyin Tok (until August 2007)
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Mr David Wonderling
Senior Health Economist

Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

Dr Robert Walker (Chair)
General Practitioner, Cumbria

Dr Mark Hill
Head of Medical Affairs, Novartis Pharmaceuticals UK

Dr John Harley
Clinical Governance and Prescribing Lead, North Tees PCT

Ailsa Donnelly
Lay member

Appendix C: The algorithms

The recommendations from this guideline have been incorporated into a NICE Pathway. The full guideline also contains a care pathway and algorithms.

About this guideline

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

The guideline was developed by the National Collaborating Centre for Chronic Conditions. The Collaborating Centre worked with a group of healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, who 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.

The recommendations from this guideline have been incorporated into a NICE Pathway. We have produced information for the public explaining this guideline. Tools to help you put the guideline into practice and information about the evidence it is based on are also available.

Changes after publication

January 2012: minor maintenance

October 2013: minor maintenance

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have

regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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