NHS
National Institute for Health and Clinical Excellence

Quick reference guide

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Chronic kidney disease

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

NICE clinical guideline 73
Developed by the National Collaborating Centre for Chronic Conditions

About this booklet

This is a quick reference guide that summarises the recommendations NICE has made to the NHS in 'Chronic kidney disease: early identification and management of chronic kidney disease in adults in primary and secondary care' (NICE clinical guideline 73).

Who should read this booklet?

This quick reference guide is for healthcare professionals and other staff who care for adults with chronic kidney disease. If you are a diabetologist you may find the sections marked D particularly helpful.

Who wrote the guideline?

The guideline was developed by the National Collaborating Centre for Chronic Conditions, which is based at the Royal College of Physicians. 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.

For more information on how NICE clinical guidelines are developed, go to www.nice.org.uk

Where can I get more information about the guideline?

The NICE website has the recommendations in full, reviews of the evidence they are based on, a summary of the guideline for patients and carers, and tools to support implementation (see inside back cover for more details).

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

This guidance represents the view of the Institute, 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.

Contents

Introduction

Chronic kidney disease (CKD) 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.

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.

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.

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.

Person-centred care

Treatment and care should take into account people's individual needs and preferences. Good communication is essential, supported by evidence-based information, to allow people to reach informed decisions about their care. Follow Department of Health advice on seeking consent if needed. If the person agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Key priorities for implementation

D 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.

- Offer ACE inhibitors/ARBs to non-diabetic people with CKD and hypertension and ACR ≥ 30 mg/mmol (approximately equivalent to PCR ≥ 50 mg/mmol, or urinary protein excretion ≥ 0.5 g/24 h)[1].
- Stage 3 CKD should be split into two subcategories (see the table on page 6) defined by:
  - GFR 45–59 ml/min/1.73 m^2 (stage 3A)
  - GFR 30–44 ml/min/1.73 m^2 (stage 3B).

D 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, approximately equivalent to PCR ≥ 100 mg/mmol, or urinary protein excretion ≥ 1 g/24 h) unless known to be due to diabetes and already appropriately treated
- proteinuria (ACR ≥ 30 mg/mmol, approximately equivalent to PCR ≥ 50 mg/mmol, or urinary protein excretion ≥ 0.5 g/24 h) together with haematuria
- rapidly declining eGFR (> 5 ml/min/1.73 m^2 in 1 year, or > 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.

D 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] 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 GDG based these decisions on clinical experience as well as what evidence there is.

- 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 > 5 ml/min/1.73 m^2 within 1 year, or > 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].

Abbreviations and terms used

D: implications for diabetes

ACE inhibitor: angiotensin-converting enzyme inhibitor

ACR: albumin:creatinine ratio

ARB: angiotensin-II receptor blocker

eGFR: estimated glomerular filtration rate

GDG: Guideline Development Group

IDMS: isotope dilution mass spectrometry

MDRD: modification of diet in renal disease

NSAIDs: non-steroidal anti-inflammatory drugs

PCR: protein:creatinine ratio

Approximate equivalent values of ACR, PCR and urinary protein excretion[a]

ACR (mg/mmol)	PCR (mg/mmol)	Urinary protein excretion (g/24 h)
30	50	0.5
70	100	1

[a] The approximate equivalent values in this table are based on GDG consensus.

[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 (see page 13), which in their clinical experience will inform good practice in CKD.

Stages of CKD[a] and frequency of eGFR testing

Stage[b]	eGFR (ml/min/ 1.73 m^2)	Description	Typical testing frequency[c]
1	≥ 90	Normal or increased GFR, with other evidence of kidney damage	12 monthly
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	6 monthly
3B	30–44		
4	15–29	Severe decrease in GFR, with or without other evidence of kidney damage	3 monthly
5	< 15	Established renal failure	6 weekly

Test eGFR[c]:

- Annually in all at risk groups.
- During intercurrent illness and perioperatively in all patients with CKD.
- The 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.

[a] This updates stage 3 of the classification of CKD adopted by the 'National service framework for renal services' (the US 'National Kidney Foundation kidney disease outcomes quality initiative' [NKF-KDOQI]).

[b] Use the suffix (p) to denote the presence of proteinuria when staging CKD, and define proteinuria as urinary ACR ≥ 30 mg/mmol, or PCR ≥ 50 mg/mmol.

[c] The information on testing frequency is based on GDG consensus and not on evidence.

Investigation

Testing kidney function

- Report eGFR as well as serum creatinine result[3].
- Use IDMS-traceable simplified MDRD equation to estimate GFR, using creatinine assays with calibration traceable to a standardised reference material.
- Correct for ethnicity: multiply eGFR by 1.21 for African-Caribbean or African ethnicity.
- Where a highly accurate measure of GFR is required – for example, during monitoring of chemotherapy – use a gold standard measure.
- Interpret eGFR with caution for people with extremes of muscle mass.
- Make an allowance for biological and analytical variability of serum creatinine (± 5%) when interpreting changes in eGFR.
- Advise the person not to eat meat for at least 12 hours before the eGFR blood test.
- If eGFR is:
  - < 60 ml/min/1.73 m^2 in first test: retest within 2 weeks. Quantify urinary albumin/protein excretion and confirm first abnormal result on an early morning sample (if not previously obtained)
  - ≥ 60 ml/min/1.73 m^2: interpret with caution as estimates of GFR become less accurate as the true GFR increases. Quantify urinary albumin/protein excretion if there is strong suspicion of CKD
  - reported simply as ≥ 60 ml/min/1.73 m^2: consider significant reduction in renal function if rise in serum creatinine concentration of > 20%.

D For all people with diabetes, quantify urinary albumin/protein excretion and confirm first abnormal result on an early morning sample (if not previously obtained).

[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).

Testing for proteinuria

D To detect and identify proteinuria, use 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.

- 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.
- If the initial ACR is ≥ 30 mg/mmol and < 70 mg/mmol, confirm by a subsequent early morning sample. If the initial ACR is ≥ 70 mg/mmol a repeat sample need not be tested.
- In people without diabetes consider clinically significant proteinuria to be present when the ACR is ≥ 30 mg/mmol.

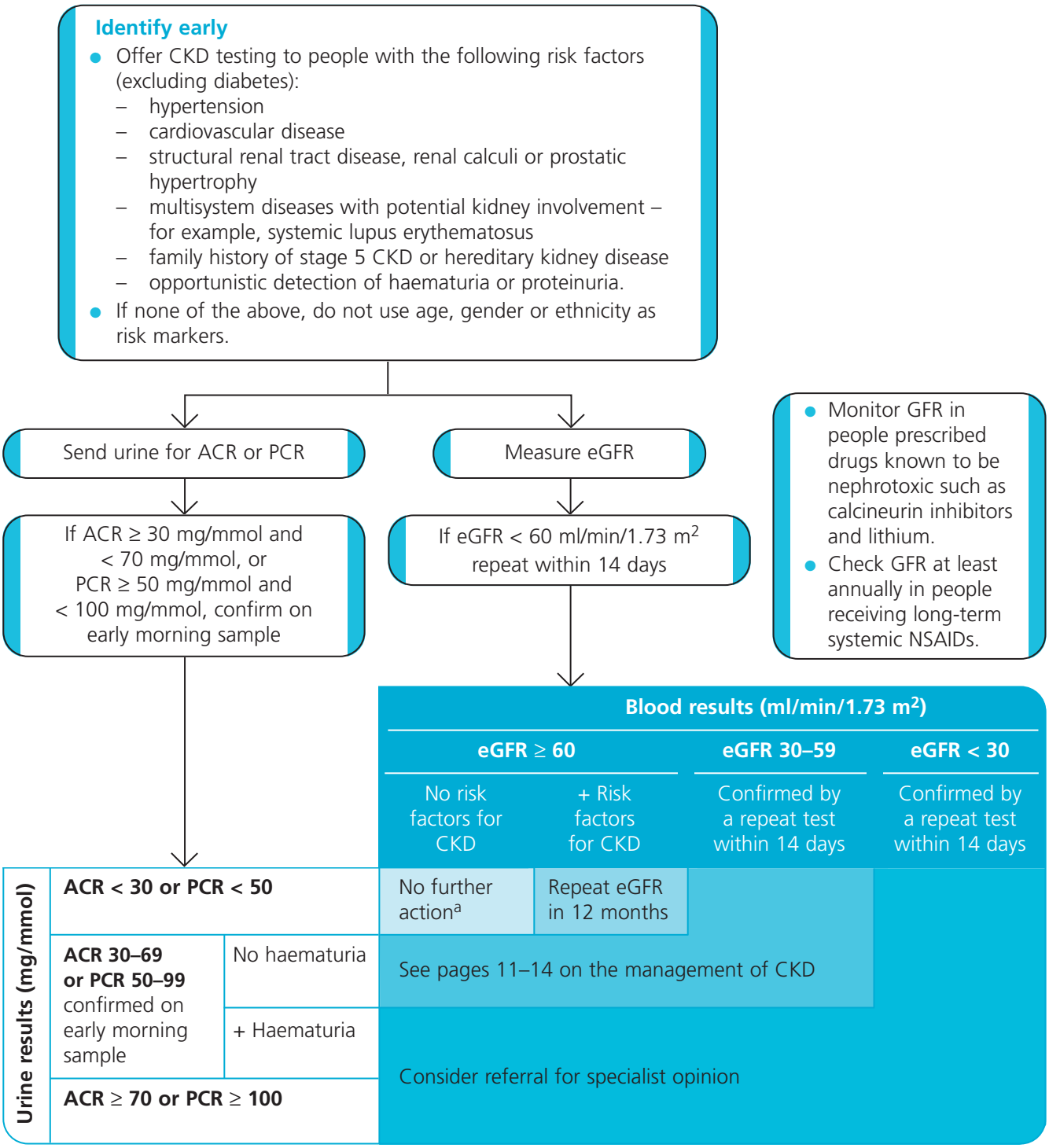
D In people with diabetes consider microalbuminuria (ACR > 2.5 mg/mmol in men and ACR > 3.5 mg/mmol in women) to be clinically significant.

Testing for 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.

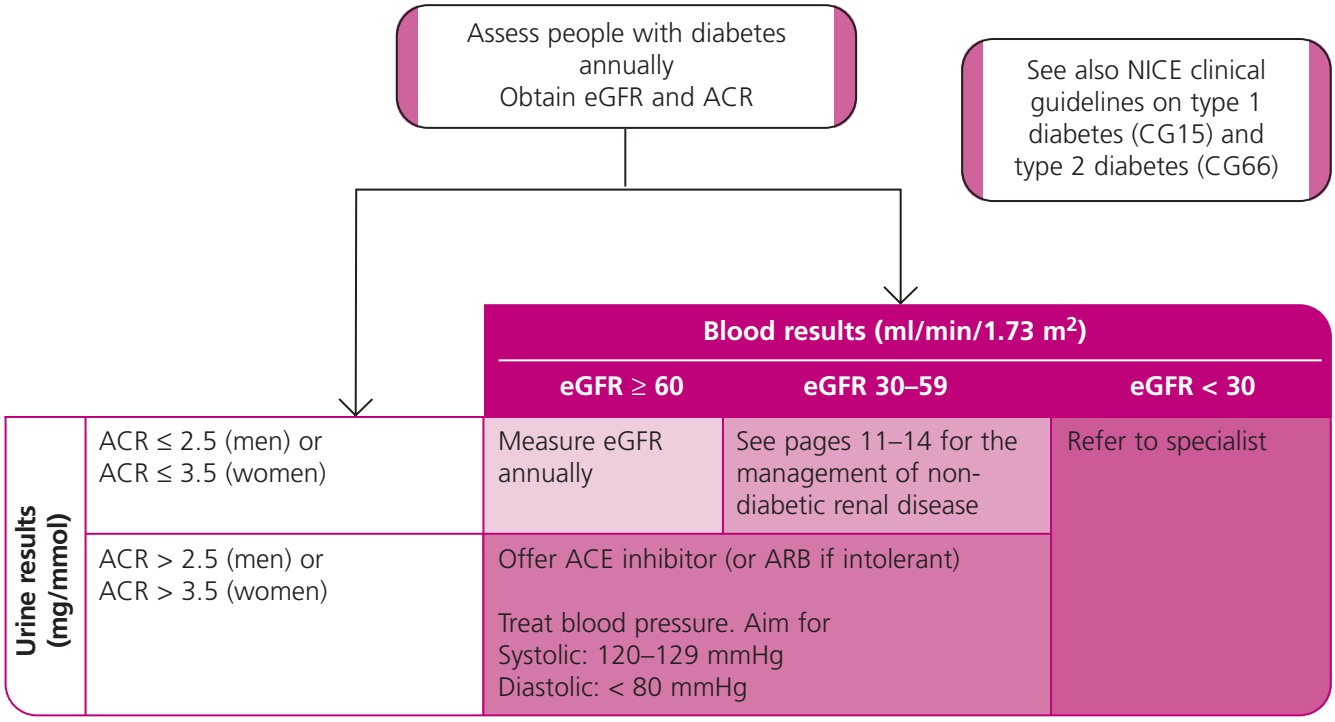
Persistent invisible haematuria	Action
To differentiate, in the absence of proteinuria, from transient haematuria	Confirm persistent invisible haematuria by two out of three positive reagent strips
With or without proteinuria	Investigate for urinary tract malignancy in appropriate age groups
Without proteinuria	Follow up annually with repeat testing for haematuria, proteinuria/albuminuria, GFR and blood pressure monitoring as long as the haematuria persists

People with CKD without diabetes



[a] See page 8 for the management of persistent invisible haematuria.

People with CKD and diabetes



Management

- At any given stage of CKD, management should not be influenced solely by age[4].

Information and education

- Offer high quality education at appropriate stages of the person's condition to enable understanding and informed choices about treatment. Tailor information to their stage and cause of CKD, any complications and the risk of progression.
- Involve people with CKD in the development of information/education programmes[5].
- Healthcare professionals providing information and education programmes should ensure they have specialist knowledge about CKD and skills to facilitate learning.
- Take account of the psychological aspects of the condition and offer support.

Lifestyle advice

- Where dietary intervention is indicated:
  - an appropriately trained professional should discuss the risks and benefits of dietary protein restriction
  - it should occur within the context of education, detailed dietary assessment and supervision
  - offer dietary advice concerning potassium, phosphate, protein, calorie and salt intake to people with progressive CKD.
- Encourage the person to take exercise, achieve a healthy weight and stop smoking.

Progressive CKD

- Define progression as a decline in eGFR of > 5 ml/min/1.73 m^2 within 1 year, or > 10 ml/min/1.73 m^2 within 5 years.
  - Take at least 3 eGFRs over at least 90 days.
  - For a new finding of reduced eGFR, repeat test within 2 weeks to exclude acute kidney injury (acute renal failure).
  - Consider whether the progression continuing at the observed rate would mean renal replacement therapy within the person's lifetime.
- Chronic use of NSAIDs may be associated with progression; exercise caution and monitor GFR.

D Work to optimise the health of people with risk factors for progressive CKD:

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

[4] In people aged > 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.
[5] See the NICE version of the guideline for suggested topics.

Renal ultrasound

- Offer a renal ultrasound to all people with CKD who:
  - have progressive CKD
  - 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.
- Advise people with a family history of inherited kidney disease about the implications of an abnormal result before arranging the scan.

Referral to specialist

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

D 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) unless known to be due to diabetes and already appropriately treated
  - proteinuria (ACR ≥ 30 mg/mmol) together with haematuria
  - rapidly declining eGFR (> 5 ml/min/1.73 m^2 in 1 year, or > 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 NICE clinical guideline 34)
  - people with, or suspected of having, rare or genetic causes of CKD
  - suspected renal artery stenosis.
- People with CKD and renal outflow obstruction should normally be referred to urological services, unless urgent medical intervention is required.
- Consider discussing management issues with a specialist in cases where it may not be necessary for the person with CKD to be seen by the specialist.
- Once a referral has been made and a plan jointly agreed, consider routine follow-up at the person's GP surgery rather than in a specialist clinic and specify criteria for future referral or re-referral.

Other complications

Control blood pressure

- Aim to keep systolic blood pressure below 140 mmHg (target range 120–139 mmHg) and diastolic blood pressure below 90 mmHg[6].

D In people with diabetes and CKD or when the ACR is ≥ 70 mg/mmol aim to keep systolic blood pressure below 130 mmHg (target range 120–129 mmHg) and diastolic blood pressure below 80 mmHg[6].

Reduce cardiovascular disease risk

- Use statins for the primary prevention of cardiovascular disease in the same way as in people without CKD[7].
- Offer statins for the secondary prevention of cardiovascular disease irrespective of baseline lipid values.
- Offer antiplatelet drugs for the secondary prevention of cardiovascular disease. Low dose aspirin can be used but there is increased risk of minor bleeding in people with CKD given multiple antiplatelet drugs.

Manage bone conditions

- Measure serum calcium, phosphate and parathyroid hormone concentrations in people with stage 4 or 5 CKD (but not routinely in stages 1–3B). Determine the subsequent frequency of testing by the measured values and the clinical circumstances. Where doubt exists seek specialist opinion.
- Offer bisphosphonates if indicated for the prevention and treatment of osteoporosis in people with stage 1, 2, 3A or 3B CKD.
- 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.
- Monitor serum calcium and phosphate concentrations in people receiving 1-alpha-hydroxycholecalciferol or 1,25-dihydroxycholecalciferol supplementation[8].

Test for anaemia

- If not already measured, check haemoglobin in people with stage 3B, 4 and 5 CKD to identify anaemia (Hb < 11.0 g/dl, see NICE clinical guideline 39). Continue appropriate testing.

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[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] The use of statins for the primary prevention of cardiovascular disease 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.

[8] 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.

Pharmacotherapy: antihypertensives in people with CKD

Indications	Action
D ***Diabetes***	
ACR > 2.5 mg/mmol (men) or > 3.5 mg/mmol (women) with or without hypertension[a]	Offer ACE inhibitors/ARBs
• ***No diabetes***	
Hypertension and ACR < 30 mg/mmol	Offer a choice of antihypertensive treatment according to NICE clinical guideline 34
Hypertension and ACR ≥ 30 mg/mmol[a]	Offer ACE inhibitors/ARBs
ACR ≥ 70 mg/mmol with or without hypertension or cardiovascular disease[a]	Offer ACE inhibitors/ARBs

[a] 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.

- Treat with ACE inhibitors first; move to ARBs if ACE inhibitors are not tolerated.
- Inform of the importance of reaching the optimal dose, and of monitoring to achieve this safely.
- Titrate ACE inhibitors/ARBs to the maximum tolerated therapeutic dose before adding a second-line agent.
- Test eGFR and serum potassium before treatment starts and repeat after 1–2 weeks of treatment and after each dose increase.

Potassium

- If serum potassium is significantly above the normal reference range (typically > 5.0 mmol/l):
  - do not start ACE inhibitors/ARBs
  - exclude and treat other factors that promote hyperkalaemia and recheck serum potassium.
- If also taking drugs that promote hyperkalaemia, more frequent monitoring of serum potassium may be required with ACE inhibitors/ARBs.
- If serum potassium rises to ≥ 6.0 mmol/l and other drugs that promote hyperkalaemia have been discontinued, stop ACE inhibitors/ARBs.

GFR

- If eGFR decrease is < 25% or plasma creatinine increase is < 30% following ACE inhibitor/ARB introduction or dose increase:
  - do not modify the dose
  - repeat the test after 1–2 weeks.
- If eGFR decrease is ≥ 25% or plasma creatinine increase is ≥ 30% following ACE inhibitor/ARB introduction or dose increase:
  - investigate other causes of deterioration in renal function, for example volume depletion or NSAIDs.

  If no other cause:
  - stop the ACE inhibitor/ARB therapy or reduce the dose to a previously tolerated lower dose
  - add alternative antihypertensive medication if required.

Implementation tools

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CG073).

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

Further information

Ordering information

You can download the following documents from www.nice.org.uk/CG073

- A quick reference guide (this document) – a summary of the recommendations for healthcare professionals.
- The NICE guideline – all the recommendations.
- 'Understanding NICE guidance' – information for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and reviews of the evidence they were based on.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote:

- N1686 (quick reference guide)
- N1687 ('Understanding NICE guidance').

Related NICE guidance

For information about NICE guidance that has been issued or is in development, see the website (www.nice.org.uk).

Published

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). Available from: www.nice.org.uk/CG067

Type 2 diabetes: the management of type 2 diabetes (update). NICE clinical guideline 66 (2008). Available from: www.nice.org.uk/CG066

Anaemia management in people with chronic kidney disease. NICE clinical guideline 39 (2006). Available from: www.nice.org.uk/CG039

Hypertension: management of hypertension in adults in primary care. NICE clinical guideline 34 (partial update of NICE clinical guideline 18) (2006). Available from: www.nice.org.uk/CG034

Brief interventions and referral for smoking cessation in primary care and other settings. NICE public health intervention guidance 1 (2006). Available from: www.nice.org.uk/PH001

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

- Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes (publication expected February 2009).

Updating the guideline

This guideline will be updated as needed, and information about the progress of any update will be posted on the NICE website (www.nice.org.uk/CG073).

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