NHS South West London

Investigation and Management of Chronic Kidney Disease (CKD) in Adults in Primary Care

Contents

Introduction

This guideline covers the care and treatment for adults with, or at risk, of chronic kidney disease (CKD) in South West London. It aims to prevent or delay the progression of the disease and reduce the risk of complications and cardiovascular disease. See visual flow chart for a summary of pathway for managing and treating CKD for adult patients in primary care.

Definition of Chronic Kidney Disease

Chronic kidney disease is defined as abnormalities of kidney function or structure present for more than 3 months, with implications for health. This includes all people with markers of kidney damage and those with an estimated glomerular filtration rate (eGFR) of less than 60ml/min/1.73m² on at least two occasions separated by a period of at least 90 days (with or without markers of kidney damage)

Markers of CKD include albuminuria defined as an albumin to creatinine ratio (ACR) 3mg/mmol or more, urine sediment abnormalities, electrolyte, and other abnormalities due to tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging, and a history of kidney transplantation.

Who should be tested for CKD?

- Monitor eGFR at least annually in adults who are taking medicines that can adversely affect kidney function, such as calcineurin inhibitors (for example, ciclosporin or tacrolimus), lithium or long-term chronic use of non-steroidal anti-inflammatory drugs (NSAIDs).
- Offer testing for CKD using eGFR creatinine and ACR to adults with any of the following risk factors:
  - Diabetes
  - Hypertension (every 1-5 years, yearly if BP uncontrolled)
  - Previous episode of acute kidney injury
  - Cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease, or cerebral vascular disease)
  - Structural renal tract disease, recurrent renal calculi, or prostatic hypertrophy
  - Multisystem diseases with potential kidney involvement for example, systemic lupus erythematosus
  - Gout
  - Family history of end-stage renal disease (GFR category G5) or hereditary kidney disease
  - Incidental detection of haematuria or proteinuria

- Monitor adults, for the development or progression of CKD for at least 3 years after acute kidney injury (longer for people with acute kidney injury stage 3) even if eGFR has returned to baseline.
- To aid diagnosis of CKD, see the following resources:
    - London Kidney Network's '3 within 3 - LKN CKD Optimisation Pathway'
    - NICE identifying CKD in adults

Investigations

Measuring and interpreting kidney function:

- Interpret eGFR creatinine with caution in adults with extremes of muscle mass, for example, in bodybuilders, people who have had an amputation or people with muscle wasting disorders. (Reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR)
- Advise adults not to eat any meat in the 12 hours before having a blood test for eGFR creatinine. Avoid delaying the despatch of blood samples to ensure that they are received and processed by the laboratory within 12 hours of venepuncture.
- If eGFR is greater than 90 ml/min/1.73m^2, use an increase in serum creatinine concentration of more than 20% to infer significant reduction in kidney function.
- Interpret eGFR values of 60 ml/min/1.73m^2 or more with caution, bearing in mind that estimates of GFR become less accurate as the true GFR increases.

Confirming an eGFR result:

- Confirm an eGFR result of less than 60 ml/min/1.73m^2 in an adult 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.

Investigations for proteinuria:

- Do not use reagent strips to identify proteinuria in adults unless they are capable of specifically measuring albumin at low concentrations and expressing the result as an ACR.
- To detect proteinuria in adults, use urine ACR rather than protein to creatinine ratio (PCR) because of the greater sensitivity for low levels of proteinuria
- Check an ACR between 3 mg/mmol and 70 mg/mmol in a subsequent early morning sample to confirm the result.
- A repeat sample is not needed if the initial ACR is 70 mg/mmol or more.
- A confirmed ACR of 3 mg/mmol or more is clinically significant proteinuria.
- When ACR is 70 mg/mmol or more, PCR can be used as an alternative to ACR

Recommended groups for measuring proteinuria with urine ACR:

- Adults with diabetes (type 1 or type 2)
- Adults with an eGFR of less than 60 ml/min/1.73 m²
- Adults with an eGFR of 60 ml/min/1.73 m² or more if there is a strong suspicion of CKD

Incidental findings of proteinuria on reagent strips:

- If unexplained proteinuria is an incidental finding on a reagent strip, offer testing for CKD using eGFRcreatinine and ACR.

Haematuria:

- Reagent strips should be used to test for haematuria in adults
    - Evaluate further for results of 1+ or higher.
    - Do not use urine microscopy to confirm a positive result.

Managing isolated invisible haematuria

- 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.
- Persistent invisible haematuria, with or without proteinuria, should prompt investigation for urinary tract malignancy in appropriate age groups (see Suspected cancer: recognition and referral NICE guideline NG12

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

- Agree a plan to establish the cause of CKD during an informed discussion with the person with CKD, particularly if the cause may be treatable (for example, urinary tract obstruction, medicines that can adversely affect kidney function or glomerular disease).
- Use the person's GFR and ACR categories 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. This is summarised in the NICE table 1 Risk of adverse outcomes in adults by GFR and ACR category, which is also available in the SWL CKD pathway and described below:

GFR category G1: Normal and high (90 ml/min/1.73 m²)
ACR category A1: Normal to mildly increased (less than 3 mg/mmol): Low risk. No CKD if there are no other markers of kidney damage

ACR category A2: Moderately increased (3 to 30 mg/mmol): Moderate risk

ACR category A3: Severely increased (over 30mg/mmol): High risk

GFR category G2: Mild reduction related to normal range for a young adult (60-89 ml/min/1.73m²)
ACR category A1: Normal to mildly increased (less than 3 mg/mmol): Low risk. No CKD if there are no other markers of kidney damage

ACR category A2: Moderately increased (3 to 30 mg/mmol): Moderate risk

ACR category A3: Severely increased (over 30mg/mmol): High risk

GFR category G3a: Mild to moderate reduction (45 to 59 ml/min/1.73m²)
ACR category A1: Normal to mildly increased (less than 3 mg/mmol): Moderate risk

ACR category A2: Moderately increased (3 to 30 mg/mmol): High risk

ACR category A3: Severely increased (over 30mg/mmol): Very high risk

GFR category G3b: Moderate to severe reduction (30 to 44 ml/min/1.73m²)
ACR category A1: Normal to mildly increased (less than 3 mg/mmol): High risk

ACR category A2: Moderately increased (3 to 30 mg/mmol): Very high risk

ACR category A3: Severely increased (over 30mg/mmol): Very high risk

GFR category G4: Severe reduction (15 to 29 ml/min/1.73m²)
ACR category A1: Normal to mildly increased (less than 3 mg/mmol): Very high risk

ACR category A2: Moderately increased (3 to 30 mg/mmol): Very high risk

ACR category A3: Severely increased (over 30mg/mmol): Very high risk

GFR category G5: Kidney failure (under 15 ml/min/1.73m²)
ACR category A1: Normal to mildly increased (less than 3 mg/mmol): Very high risk

ACR category A2: Moderately increased (3 to 30 mg/mmol): Very high risk

ACR category A3: Severely increased (over 30mg/mmol): Very high risk

Frequency of monitoring

- For guidance on the minimum frequency of eGFRcreatinine monitoring, see NICE table 2: Minimum number of monitoring checks (eGFRcreatinine) per year or the SWL CKD pathway (CKD classification by eGFR and albuminuria)
- ACR monitoring should be individualised based on a person's individual characteristics, risk of progression and whether a change in ACR is likely to lead to a change in management.

Coding CKD in primary care

- Standardised coding updated in real time reflecting both GFR and ACR categories is important to inform CKD datasets tracking prevalence, incidence and progression; inform prognosis; and to facilitate in-house monitoring, optimisation of care, and support structured medication reviews.
- Since diagnosis of CKD requires demonstration of a sustained reduction in eGFR and/or elevation in uACR over 3 months, GFR and ACR status should be sought both at diagnosis and during routine monitoring to ensure all the data required for full classification is available.
- A wide variety of CKD SNOMED codes exist.
- The following GFR/ACR combination SNOMED codes are used for this purpose which are also recognised by the Quality and Outcomes Framework and contribute to the Quality and Outcomes Framework CKD prevalence register.

SNOMED codes

CKD stage 1 and:

- **uACR less than 3mg/mmol**
  SNOMED description: CKD G1A1 (if non proteinuric markers of CKD)
  SNOMED code: 2426331000000114
- **uACR 3mg/mmol to 30mg/mmol**
  SNOMED description CKDG1A2
  SNOMED code: 2426381000000113
- **uACR greater than 30mg/mmol**
  SNOMED description: CKD G1A3
  SNOMED code: 242651100000014

CKD stage 2 and:

- **uACR less than 3mg/mmol**
  SNOMED description: CKD G2A1 (if non proteinuric markers of CKD)
  SNOMED code: 2426601000000111
- **uACR 3mg/mmol to 30mg/mmol**
  SNOMED description CKDG2A2
  SNOMED code: 2426691000000116
- **uACR greater than 30mg/mmol**
  SNOMED description: CKD G2A3
  SNOMED code: 2426821000000118

CKD stage 3a and:

- **uACR less than 3mg/mmol**
  SNOMED description: CKD G3aA1 (if non proteinuric markers of CKD)
  SNOMED code: 2427381000000110
- **uACR 3mg/mmol to 30mg/mmol**
  SNOMED description CKDG3aA2
  SNOMED code: 2427401000000110
- **uACR greater than 30mg/mmol**
  SNOMED description: CKD G3aA3
  SNOMED code: 2427451000000111

CKD stage 3b and:

- **uACR less than 3mg/mmol**
  SNOMED description: CKD G3bA1
  SNOMED code: 24227751000000117
- **uACR 3mg/mmol to 30mg/mmol**
  SNOMED description CKDG3bA2
  SNOMED code: 24227801000000112

- **uACR greater than 30mg/mmol**
  SNOMED description: CKD G3bA3
  SNOMED code: 2427851000000113

CKD stage 4 and:

- **uACR less than 3mg/mmol**
  SNOMED description: CKD G4A1
  SNOMED code: 2428021000000111
- **uACR 3mg/mmol to 30mg/mmol**
  SNOMED description CKDG4A2
  SNOMED code: 24228091000000114
- **uACR greater than 30mg/mmol**
  SNOMED description: CKD G4A3
  SNOMED code: 242814100000

- On occasion GFR data may be available in the absence of ACR data and vice versa and recommend the following interim SNOMED codes are applied until ACR or GFR status is confirmed when they should be replaced with the appropriate GFR and ACR combination code.

Interim SNOMED codes for uACR

- **uACR between 3 to 30mmol/ml**
  SNOMED code for albuminira: 410631017
- **uACR is more than 30mg/mmol**,
  SNOMED code for Grade 3 albuminuria: 3515025016

Interim SNOMED codes for Chronic Kidney Disease

- **eGFR 90 ml/min/1.73m² or more**
  SNOMED description: chronic kidney disease stage 1(if non proteinuric markers of CKD):
  SNOMED code: 2767383018
- **eGFR 60-89 ml/min/1.73m²**
  SNOMED description: chronic kidney disease stage 2(if non proteinuric markers of CKD):
  SNOMED code: 2767384018
- **eGFR 45-59 ml/min/1.73m²**
  SNOMED description: chronic kidney disease stage 3a
  SNOMED code: 2773184015
- **eGFR 30-44 ml/min/1.73m²**
  SNOMED description: chronic kidney disease stage 3b
  SNOMED code: 2773184015
- **eGFR 15-29 ml/min/1.73m²**
  SNOMED description: chronic kidney disease stage 4
  SNOMED code: 2767385013

- When eGFR has fallen below 15ml/min/1.73m^2 patients may be coded with the code 'Chronic Kidney Disease Stage 5' as they will be regularly monitored in secondary care and are all at high risk of cardiovascular disease irrespective of ACR status

Indications for renal ultrasound in adults:

- Offer a renal ultrasound scan to all adults with CKD who:
  - have accelerated progression of CKD (fall in GFR by 25% or more in 1 year or by more than 15 mL/min/1.73m^2)
  - have a new diagnosis of CKD with a GFR of less than 30 ml/min/1.73 m² (GFR category G4 or G5) if not known to CKD services
  - have visible or persistent invisible haematuria (see SWL London Urology Pathways)
  - have symptoms of urinary tract obstruction e.g., urinary retention, decreased or altered urine flow, hesitancy, loin pain increased urgency and nocturia, incontinence
  - have a family history of polycystic kidney disease and are older than 20 years old
- Advise adults with a family history of hereditary kidney disease about the implications of an abnormal result before a renal ultrasound scan is arranged for them.

Pharmacotherapy for blood pressure control

Blood pressure control principles:

See the SWL - diagnosis and management of blood pressure in primary care

Blood Pressure targets

NICE recommends the following targets for blood pressure control:

- In adults with CKD and an ACR under 70 mg/mmol, aim for a clinic systolic blood pressure below 140 mmHg (target range 120 to 139 mmHg) and a clinic diastolic blood pressure below 90 mmHg.
- In adults with CKD and an ACR of 70 mg/mmol or more, aim for a clinic systolic blood pressure below 130 mmHg (target range 120 to 129 mmHg) and a clinic diastolic blood pressure below 80 mmHg.

Medication for blood pressure control

- For patients diagnosed with hypertension and an ACR of 30 mg/mmol or less (ACR categories A1 and A2). Follow the recommendations in the treating hypertension in SWL hypertension guideline,
- Offer an angiotensin-converting enzyme (ACE) inhibitor (e.g. Ramipril) **OR** an angiotensin-receptor blocker (ARB) (e.g. Losartan or irbesartan) (titrated to the highest licensed dose that the person can tolerate- refer to SWL hypertension guideline on dose titration and monitoring recommendations) to adults with CKD who have hypertension and an ACR over 30 mg/mmol (ACR category A3 or above).

Note: Ramipril is currently the only licensed ACE inhibitor for treating renal disease and losartan and irbesartan are the only licensed ARBs for treating renal disease.

Pharmacotherapy for CKD in adults with related persistent proteinuria

- For adults with CKD and diabetes (type 1 or type 2)
  - offer ramipril, losartan (titrated to the highest licensed dose that the person can tolerate) if ACR is 3 mg/mmol or more.
- For adults with CKD but without diabetes:
  - Refer for nephrology assessment and offer ramipril or losartan or irbesartan titrated to the highest licensed dose that they can tolerate), if ACR is 70 mg/mmol or more.
- See NICE for recommendations in monitoring. If ACR is above 30 but below 70 mg/mmol; consider discussing with a nephrologist if eGFR declines or ACR increases.
- When offering medicines to lower proteinuria to people with frailty, comorbidities or who are taking many other prescribed medicines, follow the recommendations in NICE's guideline on medicines optimisation to ensure the best possible outcomes. Seek specialist advice if needed, for example from a consultant in care of the elderly, or from a kidney physician if the person asks about contraception

Renin-angiotensin system antagonists

- Do not offer a combination of renin–angiotensin system antagonists to adults with CKD.
- Explain to adults with CKD (and their family members or carers, as appropriate) 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.
- Measure serum potassium concentrations and estimate the GFR before starting renin–angiotensin system antagonists in people with CKD. Repeat these measurements between 1 and 2 weeks after starting renin–angiotensin system antagonists and after each dose increase.
- Do not routinely offer a renin–angiotensin system antagonist to adults with CKD if their pre-treatment serum potassium concentration is greater than 5.0 mmol/litre.
- If an adult cannot use renin-angiotensin system antagonists because of hyperkalaemia:
  - assess for and treat any other factors that promote hyperkalaemia **and**
  - recheck serum potassium concentration
  - more frequent monitoring of serum potassium concentration may be needed if medicines known to promote hyperkalaemia are prescribed for use in people alongside renin–angiotensin system antagonists.

- Stop renin–angiotensin system antagonists in adults if the serum potassium concentration increases to 6.0mmol/litre or more and other medicines known to promote hyperkalaemia have been discontinued.
- After introducing or increasing the dose of renin-angiotensin system antagonists in adults, do not modify the dose if either:
    - the GFR decrease from pre-treatment baseline is less than 25% or
    - the serum creatinine increase from baseline is less than 30%.
- 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 to 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%.
- If an adult's eGFR change is 25% or more, or the change in serum creatinine is 30% or more:
    - investigate other causes of a deterioration in kidney function, such as volume depletion or concurrent medication (for example, NSAIDs)
- If no other cause for the deterioration in kidney 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 needed.

Sodium-glucose co-transporter-2 (SGLT2) inhibitor use in adults with CKD

- NICE (Type 2 diabetes guidance) suggests:
    - offer a SGLT2 inhibitor for adults with type 2 diabetes and CKD who are taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate) in addition to the ARB or ACE inhibitor) if ACR is over 30 mg/mmol **and** they meet the criteria in the marketing authorisation (including relevant eGFR thresholds).
    - considering a SGLT2 inhibitor for adults with type 2 diabetes and CKD who are taking an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate) in addition to the ARB or ACE inhibitor) if ACR is between 3 and 30 mg/mmol **and** they meet the criteria in the marketing authorisation (including relevant eGFR thresholds).
- Dapagliflozin is recommended as an option for treating chronic kidney disease (CKD) in adults. NICE TA775 recommends prescribing dapagliflozin only if:
    - it is an add-on to optimised standard care including the highest tolerated licensed dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), unless these are contraindicated, **and**
    - people have an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m^2 to 75 ml/min/1.73 m^2 at the start of treatment **and**:
        - have type 2 diabetes **or**

    - have a urine albumin-to-creatinine ratio (uACR) more than or equal to 22.6 mg/mmol
- Dapagliflozin is the SGLT2 inhibitor of choice, however if the patient is already established on another SGLT2 inhibitor for type 2 diabetes or heart failure (e.g., canagliflozin or empagliflozin), switching to dapagliflozin is not recommended. Refer to SPC to ensure SGLT2 inhibitors dose is adjusted for renal impairment
  We recommend following the SWL CKD pathway and the SWL dapagliflozin information sheet for the initiation of these therapies

Statin treatment for adults

The NICE guideline on cardiovascular disease risk assessment and reduction, including lipid modification details the use of statins in adults with CKD.

- Do not use a risk assessment tool to assess cardiovascular disease (CVD) risk in people with an eGFR less than 60 ml/min/1.73 m^2 and/or albuminuria. These people are at increased risk of CVD.
- It should be noted that people on renal replacement therapy are outside the scope of this guideline
- Adults with CKD should be offered atorvastatin 20 mg for the primary or secondary prevention of CVD
    - Increase the dose if a greater than 40% reduction in non-HDL cholesterol is not achieved and eGFR is 30 ml/min/1.73 m^2 or more.
    - Agree the use of higher doses with a renal specialist if eGFR is less than 30 ml/ min/1.73 m^2.

Measure total cholesterol, HDL cholesterol and non-HDL cholesterol in all people who have been started on high-intensity statin treatment (both primary and secondary prevention, including atorvastatin 20 mg for primary prevention) at 3 months of treatment and aim for a greater than 40% reduction in non-HDL cholesterol. If a greater than 40% reduction in non-HDL cholesterol is not achieved

- discuss adherence and timing of dose
- optimise adherence to diet and lifestyle measures
- consider increasing the dose if started on less than atorvastatin 80 mg and the person is judged to be at higher risk because of comorbidities, risk score or using clinical judgement.

Mineral metabolism is disturbed in most patients with advanced CKD.

- Parathyroid Hormone (PTH) and Vitamin D level testing is not recommended in primary care unless requested by a specialist.

Metabolic acidosis:

- Consider starting sodium bicarbonate capsules 500mg twice daily if acidaemia present (serum bicarbonate less than 20 mmol/L) and eGFR less than 30 mL/min. Recheck level at next routine CKD check.

Hyperkalaemia management in adults with categories G3b to G5

- If potassium is greater than 6 mmol/L check no haemolysis -refer to UKKA Management of hyperkalaemia in the community
- Check diet and offer diet sheet from Kidney Care UK on lowering potassium levels
- Stop Non-steroidal anti-inflammatory drugs (NSAIDs) and LoSalt®. Stop potassium retaining diuretics such as spironolactone.
- Consider reducing the dose of ACE inhibitor/ARB but the benefits of continuing the drugs may outweigh the potential risks of mild-moderate high potassium).
- Seek specialist advice if serum potassium persistently more than 6 mmol/L.
- Potassium binders (Sodium zirconium cyclosilicate and Patiromer) for hyperkalaemia treatment in adults with categories G3b to G5 chronic kidney disease have been recommended by NICE TA623 and NICE TA599. This may be initiated and continued in secondary care in line with trust guidance.

Diagnosing and assessing anaemia

Check Hb in target 100-120 g/L. If below target exclude other causes including iron deficiency, folate/B12 deficiency, haemolysis.

Diagnostic role of haemoglobin levels

Consider investigating and managing anaemia in adults with CKD if:

- their haemoglobin (Hb) level falls to 110 g/litre or less **or**
- they develop symptoms attributable to anaemia (such as tiredness, shortness of breath, lethargy, and palpitations).

Diagnostic role of glomerular filtration rate

In adults with anaemia:

- If eGFR is above 60 ml/min/1.73 m^2, investigate other causes of anaemia as it is unlikely to be caused by CKD.
- If eGFR is between 30 and 60 ml/min/1.73 m^2: investigate other causes of anaemia but use clinical judgment to decide how extensive this investigation should be, because the anaemia may be caused by CKD.
- If eGFR is below 30 ml/min/1.73 m^2, think about other causes of anaemia but note that anaemia is often caused by CKD.

Risk assessment for CKD

- Adults with CKD and their family members or carers (as appropriate) information about their 5-year risk of needing renal replacement therapy [measured using the 4-variable Kidney Failure Risk Equation (KFRE)].
- KFRE is also available as an Excel calculator.

Referral criteria and shared care

Refer adults with CKD for specialist assessment (considering their wishes and comorbidities) if they have any of the following:

- A 5-year risk of needing renal replacement therapy of greater than 5% (measured using the 4-variable Kidney Failure Risk Equation)
- An ACR of 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated
- An ACR of more than 30 mg/mmol (ACR category A3), together with nonvisible haematuria. If urological investigations not indicated/negative and uACR less than or equal to 30 mg/mmol then monitor and manage as CKD in primary care
- A sustained decrease in eGFR of 25% or more and a change in eGFR category within 12 months
- A sustained decrease in eGFR of 15 ml/min/1.73 m² or more per year
- Hypertension that remains poorly controlled (above the person's individual target) despite the use of at least 4 antihypertensive medicines at therapeutic doses (see SWL hypertension guideline)
- Known or suspected rare or genetic causes of CKD e.g. autosomal dominant polycystic kidney disease, SLE, vasculitis, myeloma
- Suspected renal artery stenosis: If ACE inhibitor or ARB induced fall in eGFR (eGFR falls by more than or equal to 30% or creatinine rises by more than or equal to 30%) during first 2 weeks on ACE inhibitor/ARB, repeat tests, stop drug, consider other causes (volume depletion, concurrent NSAID use) and seek specialist advice. If no other cause of deterioration identified, refer for further investigation of possible renal artery stenosis

References/resources

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