PrescQIPP Community Interest Company

Bulletin 281. Part 1 - Chronic kidney disease (CKD) in adults

This bulletin looks at the assessment and management of chronic kidney disease (CKD) in line with guidance from the National Institute for Health and Care Excellence (NICE). It is the first of two bulletins focusing on kidney health. Along with the associated support materials it provides advice and support to assist a range of primary care health professionals including GPs, nurses and pharmacists to improve the care of people with CKD.

Further PrescQIPP bulletins on Acute Kidney Injury (AKI) in children, young people and adults and the management of AKI and AKI - Sick day guidance are available.

Recommendations

- Ensure glomerular filtration rate (GFR) is monitored at least annually in people prescribed drugs that can adversely affect kidney function, such as oral non-steroidal anti-inflammatory drugs (long term chronic use of NSAIDS), calcineurin inhibitors (for example, ciclosporin or tacrolimus) and lithium. See appendix 1.
- Offer testing for CKD, using eGFRcreatinine (estimated GFR measurement based on serum creatinine) and urine albumin to creatinine ratio (ACR), to people with risk factors.
- Monitor for the development or progression of CKD for at least three years after AKI even if eGFR has returned to baseline.
- CKD should be classified using a combination of eGFR and urinary ACR.
- Systems should be in place to inform people of their diagnosis, in order to support shared decision-making, self-management and enable people to make informed choices.
- Patients should be offered tailored education and information about their condition, the associated complications and the risk of progression.
- The frequency of monitoring (eGFRcreatinine and ACR) should be agreed with the person with, or at risk of, CKD; taking into consideration an individual's clinical circumstances and bearing in mind that CKD is not progressive in many people.
- Ensure people with risk factors associated with CKD progression are supported to optimise their health.
- Do not offer a combination of renin-angiotensin system antagonists (angiotensin-converting enzyme (ACE) inhibitor, angiotensin-receptor blocker (ARB) or direct renin inhibitor therapy) to adults with CKD.
- Use caution and monitor the effects on GFR when treating people with CKD with potentially nephrotoxic drugs (see appendix 1) over prolonged periods of time. Regular review of the ongoing need and reassessment of the risk versus the benefit is appropriate.

Background

CKD is a reduction in kidney function or structural damage (or both) present for more than 90 days, with associated health implications. Kidney damage may cause fluid and electrolyte imbalance, and leakage of protein and/or blood into the urine, resulting in proteinuria and haematuria. There are multiple possible causes and risk factors for CKD and its progression, including:[1]

- Conditions associated with intrinsic kidney damage - hypertension, diabetes mellitus and glomerular disease, such as acute glomerulonephritis.
- Obesity with metabolic syndrome (metabolic syndrome is a combination of hypertension, diabetes mellitus and obesity, but obesity alone is not a risk factor for CKD).
- Current or previous history of AKI.
- Potentially nephrotoxic drugs such as aminoglycosides, ACE inhibitors, ARB, bisphosphonates, calcineurin inhibitors (such as ciclosporin or tacrolimus), diuretics, lithium, mesalazine, and oral NSAIDs. See appendix 1 for further examples.
- Conditions associated with obstructive uropathy – structural renal tract disease, bladder voiding problems, urinary diversion surgery and recurrent urinary tract calculi.
- Multisystem diseases with potential renal involvement - systemic lupus erythematosus (which may cause lupus nephritis), vasculitis and myeloma.
- A family history of CKD stage 5, or hereditary kidney disease such as autosomal dominant polycystic kidney disease, Alport's syndrome and familial glomerulonephritis.
- Cardiovascular disease
- Gout
- People with an incidental finding of haematuria or proteinuria.

CKD is usually asymptomatic, but it is detectable and easily tested for. 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, the lack of specific symptoms means it is often not diagnosed or is diagnosed at an advanced stage.[2] Diagnosis has improved since the introduction of the CKD indicator (to establish and maintain a register of patients aged 18 or over with CKD with classification of categories G3a to G5) in the primary care Quality and Outcomes Framework (QOF). Nonetheless, late presentation of patients with kidney failure increases morbidity, mortality and healthcare costs. Early identification and treatment of CKD is therefore important to slow or prevent the progression to more serious CKD, but also to highlight and manage the key associated risks related to patient safety and avoidable harm.[3]

National guidance

The NICE guideline on the assessment and management of CKD [NG203] covers care and treatment for people with, or at risk of, CKD. It aims to prevent or delay the progression, and reduce the risk of complications and cardiovascular disease. It also covers managing anaemia and hyperphosphataemia associated with CKD.[2] It is applicable in England and Wales. The Scottish Public Health Observatory lists NICE guidelines for the management of CKD and advises that the previous Scottish Intercollegiate Guidelines Network (SIGN) 103 guideline on CKD has not been updated and is no longer available.

NICE has also produced COVID-19 rapid guidelines on chronic kidney disease [NG176] and dialysis service delivery [NG160] which recommends changes to usual practice to maximise the safety of patients, while protecting staff from infection and enable services to make the best use of NHS resources.

Who should be tested for CKD?

- Monitor glomerular filtration rate (GFR) at least annually in adults, children and young people who are taking medicines that can adversely affect kidney function, such as calcineurin inhibitors (for example, ciclosporin or tacrolimus), lithium or NSAIDs (long-term chronic use of NSAIDs).[2]
- Offer testing for CKD using eGFRcreatinine and urine albumin to creatinine ratio (ACR) to adults with any of the following risk factors:
  - Diabetes
  - Hypertension
  - Previous episode of AKI
  - 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 (SLE)
  - Gout
  - Family history of end-stage kidney disease (GFR category G5) or hereditary kidney disease
  - Incidental detection of haematuria or proteinuria.
- Offer testing for CKD using eGFRcreatinine and ACR to children and young people with any of the following risk factors:*
  - Previous episode of AKI
  - Solitary functioning kidney.
- Consider testing for CKD using eGFRcreatinine and ACR in children and young people with any of the following risk factors:
  - Low birth weight (2,500 g or lower)
  - Diabetes
  - Hypertension
  - Cardiac disease
  - Structural renal tract disease or recurrent renal calculi
  - Multisystem diseases with potential kidney involvement, for example, SLE
  - Family history of end-stage renal disease (GFR category G5) or hereditary kidney disease
  - Incidental detection of haematuria or proteinuria.
- Do not use any of the following as risk factors indicating testing for CKD in adults, children and young people:
  - Age
  - Gender
  - Ethnicity
  - Obesity in the absence of metabolic syndrome, diabetes or hypertension.
- Monitor adults, children and young people for the development or progression of CKD for at least three years after acute kidney injury (longer for people with acute kidney injury stage 3) even if eGFR has returned to baseline.

*For children and young people, the evidence showed that acute kidney injury and solitary functioning kidney were clinically significant risk factors for developing CKD. Solitary functioning kidney was not due to kidney donation but to nephrectomy secondary to congenital anomalies of the kidney and urinary tract or to a lack of a kidney at birth or a non-functioning kidney.

Investigations for CKD

Measuring kidney function - creatinine-based estimate of GFR (eGFRcreatinine):[2]

- When serum creatinine is requested, clinical laboratories should report an estimate of eGFRcreatinine using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation in addition to reporting the serum creatinine result.
- Interpret eGFRcreatinine 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 or using protein supplements.
- Reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR.
- eGFRcreatinine may also be less reliable in certain other situations, for example, acute kidney injury, pregnancy, oedematous states, and in adults who are malnourished.
- eGFRcreatinine has not been well validated in certain ethnic groups (for example, black, Asian and other minority ethnic groups with CKD living in the UK).
- Advise adults not to eat meat for at least 12 hours before the eGFRcreatinine test.
- Avoid delaying the despatch of blood samples to ensure that they are received and processed by the laboratory within 12 hours of venepuncture.

Reporting and interpreting GFR values:[1,2]

- Report eGFR as a whole number if it is less than 90ml/min/1.73 m^2, or as >90ml/min/1.73m^2 if it is above.
- Confirm an eGFR result of less than 60ml/min/1.73m^2 in an adult not previously tested, by repeating the test within two weeks.
- If the eGFR remains less than 60ml/min/1.73m^2 on repeat, with no evidence of sudden deterioration in renal function suggesting AKI, repeat the eGFR within 3 months.[1]

Investigations for proteinuria:[1,2]

- Do not use reagent strips to identify proteinuria in children and young people.
- 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 albumin:creatinine ratio ACR.
- For the initial detection of proteinuria in adults, children and young people use an early morning urine sample to measure the urinary ACR rather than protein:creatinine ratio (PCR) because of the greater sensitivity for low levels of proteinuria.
- Measure proteinuria with urine ACR in the following groups:
  - Adults, children and young people with diabetes (type 1 or type 2).
  - Adults with an eGFR of less than 60ml/min/1.73m^2.
  - Adults with an eGFR of 60ml/min/1.73m^2 or more if there is a strong suspicion of CKD.
  - Children and young people without diabetes and with creatinine above the upper limit of the age-appropriate reference range.
- If the result is:
  - Less than 3mg/mmol (no proteinuria), no action is needed.
  - Between 3 and 70mg/mmol, check an ACR in a subsequent early morning sample to confirm the result.

  - 70mg/mmol or more, a repeat test is not needed as this indicates significant proteinuria.
- Regard a confirmed ACR of 3mg/mmol or more as clinically important proteinuria.
- If the ACR is 70mg/mmol or more, protein:creatinine ratio (PCR) can be used as an alternative to ACR.

Haematuria:[1,2]

- Use reagent strips to test for haematuria in adults, children and young people.
  - Evaluate further for results of 1+ or more of blood on dipstick, arrange a mid-stream urine sample (MSU) to exclude a UTI, and manage accordingly.
  - Do not use urine microscopy to confirm a positive result.

Managing isolated invisible haematuria:[2]

- 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.
- Persistent invisible haematuria, with or without proteinuria, should prompt investigation for urinary tract malignancy in appropriate age groups.
- Persistent invisible haematuria in the absence of proteinuria should be followed up annually with repeat testing for haematuria, proteinuria or albuminuria, GFR and blood pressure monitoring as long as the haematuria persists.

Renal tract ultrasound:[1,2]

If a diagnosis of CKD is suspected, consider arranging a renal tract ultrasound if indicated, for example if the person has suspected urinary tract stones or obstruction, or a family history of polycystic kidney disease and is aged over 20 years.[1] Offer a renal ultrasound scan to all people with CKD who:[2]

- Have accelerated progression of 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 years.
- Have a GFR of less than 30ml/min/1.73m^2 (GFR category G4 or G5).
- 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 a renal ultrasound scan is arranged for them.[2]

Classification of CKD

CKD should be classified using a combination of eGFR and urinary ACR:[1,2]

- Increased ACR is associated with increased risk of adverse outcomes.
- Decreased eGFR is associated with increased risk of adverse outcomes.
- Increased ACR and decreased GFR in combination multiply the risk of adverse outcomes.

Table 1: Classification of CKD using eGFR and urinary ACR categories (reproduced from NICE NG203)[2]

	ACR category A1: normal to mildly increased (less than 3mg/mmol)	ACR category A2: moderately increased (3 to 30mg/mmol)	ACR category A3: severely increased (over 30mg/mmol)
GFR category G1: normal and high (90ml/min/1.73m^2 or over)	Low risk No CKD if there are no other markers of kidney damage	Moderate risk	High risk
GFR category G2: mild reduction related to normal range for a young adult (60 to 89ml/min/1.73m^2)	Low risk No CKD if there are no other markers of kidney damage	Moderate risk	High risk
GFR category G3a: mild to moderate reduction (45 to 59ml/min/1.73 m^2)	Moderate risk	High risk	Very high risk
GFR category G3b: moderate to severe reduction (30 to 44ml/min/1.73m^2)	High risk	Very high risk	Very high risk
GFR category G4: severe reduction (15 to 29ml/min/1.73 m^2)	Very high risk	Very high risk	Very high risk
GFR category G5: kidney failure (under 15ml/min/1.73 m^2)	Very high risk	Very high risk	Very high risk

Some examples of classifications would be:

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

Diagnosis and management of CKD

If a person has a confirmed diagnosis of CKD, arrange monitoring for disease progression and associated complications, and arrange specialist referral if appropriate.[1]

A plan to establish the cause of CKD should be agreed during an informed discussion with the person with CKD, particularly if the cause may be treatable (for example, urinary tract obstruction, nephrotoxic drugs or glomerular disease).[2] When checking for nephrotoxic drugs, health professionals should ask about the use of non-prescription items, e.g. over-the-counter oral NSAIDs or herbal remedies.

Systems should be in place to support shared decision-making and self-management (this includes providing information about blood pressure, smoking cessation, exercise, diet and medicines) and enable people to make informed choices. NICE recommends that people with CKD are offered tailored education and information about their condition, the associated complications and the risk of progression. They also advocate giving people with CKD access to their medical data (including diagnosis, comorbidities, test results, treatments and correspondence) through information systems, to promote self-management.[2]

The following websites provide patient information, and some have helplines for patients about CKD and other kidney disorders:

- Chronic kidney disease: assessment and management. NICE guideline [NG203]. Information for the public
- Kidney Care UK
  (01420 541424) for information, advice and support.
- Kidney Research UK
  (0300 303 1100) for information, advice and support.
- The National Kidney Federation
  (0800 1690936) for information, advice and support.
- Polycystic Kidney Disease (PKD) Charity
- UK Kidney Association
- NHS Chronic Kidney Disease
- Patient Chronic Kidney Disease
- Think Kidneys
- Kidney Wales (Aren Cymru)
  (02920 343940) for information, advice and support.
- Infokid has information about kidney disease in babies, children and young people.

The management of CKD should not be determined solely by age. Use the person's GFR and ACR categories (see table 1 above) to indicate their risk of adverse outcomes (for example, CKD progression, AKI, all-cause mortality and cardiovascular events) and discuss this with them. The frequency of monitoring (eGFRcreatinine and ACR) should be agreed with the adult, child or young person with, or at risk of, CKD; bearing in mind that CKD is not progressive in many people. Table 2 (below) can be used to guide the frequency of monitoring, but this should be tailored to the person according to:[2]

- The underlying cause of CKD.
- The rate of decline in eGFR or increase in ACR (but be aware that CKD progression is often non-linear).
- Other risk factors, including heart failure, diabetes and hypertension.
- Changes to their treatment (such as renin–angiotensin–aldosterone system [RAAS] antagonists (ACE inhibitors, ARBs, direct renin inhibitors and aldosterone antagonists), oral NSAIDs and diuretics).
- Intercurrent illness (for example acute kidney injury).
- Whether they have chosen conservative management of CKD.

Table 2: Minimum number of monitoring checks (eGFRcreatinine) per year for adults, children and young people with or at risk of CKD - reproduced from NICE NG203[2]

	ACR category A1: normal to mildly increased (less than 3mg/mmol)	**ACR category A2: moderately increased (3 to 30mg/mmol)**	**ACR category A3: severely increased (over 30mg/mmol)**
GFR category G1: normal and high (90ml/min/1.73m^2 or over)	0 to 1	1	1 or more

	ACR category A1: normal to mildly increased (less than 3mg/mmol)	ACR category A2: moderately increased (3 to 30mg/mmol)	ACR category A3: severely increased (over 30mg/mmol)
GFR category G2: mild reduction related to normal range for a young adult (60 to 89ml/min/1.73m^2)	0 to 1	1	1 or more
GFR category G3a: mild to moderate reduction (45 to 59ml/min/1.73m^2)	1	1	2
GFR category G3b: moderate to severe reduction (30 to 44ml/min/1.73m^2)	1 to 2	2	2 or more
GFR category G4: severe reduction (15 to 29ml/min/1.73m^2)	2	2	3
GFR category G5: kidney failure (under 15ml/min/1.73m^2)	4	4 or more	4 or more

Management should include lifestyle advice such as encouraging people with CKD to take exercise, achieve a healthy weight and stop smoking. Also, dietary advice about potassium, phosphate, calorie and salt intake (e.g. low salt and potassium diet) appropriate to the severity of CKD. Dietary intervention if needed should occur within the context of education, detailed dietary assessment and supervision to ensure malnutrition is prevented. Do not offer low-protein diets (i.e. dietary protein intake less than 0.6–0.8g/kg/day) to people with CKD.[2]

Progression of CKD and modifying risk factors

Accelerated progression of CKD is defined as a sustained decrease in GFR of 25% or more and a change in GFR category within 12 months or a sustained decrease in GFR of 15ml/min/1.73m^2 per year. A minimum of three GFR estimations over 90 days or more should be obtained to identify the rate of progression. In people with a new finding of reduced GFR, the GFR should be repeated within two weeks to exclude causes of acute deterioration, for example, AKI or starting renin–angiotensin system antagonist therapy (ACE inhibitors, ARBs or direct renin inhibtors).[2]

The NICE guideline [NG203] recommends working with people with risk factors associated with CKD progression to optimise their health. Risk factors for progression are:[2]

- Cardiovascular disease
- Proteinuria
- Previous episode of AKI
- Hypertension
- Diabetes
- Smoking
- African, African-Caribbean or Asian family origin
- Chronic use of oral NSAIDs
- Untreated urinary outflow tract obstruction.

Give adults with CKD and their family members or carers (as appropriate) information about their 5-year risk of needing renal replacement therapy.[2]

Cardiovascular risk factors – blood pressure

Managing cardiovascular risk and delaying the progression of kidney disease are central to CKD management. NICE guideline on chronic kidney disease: assessment and management [NG203] advises reducing the cardiovascular risk by controlling blood pressure, prescribing an antiplatelet where indicated and lipid modification.[2]

- In adults with CKD and an ACR under 70mg/mmol, aim for a clinic systolic blood pressure below 140 mmHg (target range 120 to 139mmHg) and a clinic diastolic blood pressure below 90mmHg.
- In adults with CKD and an ACR of 70mg/mmol or more, aim for a clinic systolic blood pressure below 130mmHg (target range 120 to 129mmHg) and a clinic diastolic blood pressure below 80mmHg.
- In children and young people with CKD and an ACR of 70mg/mol or more, aim for a clinic systolic blood pressure below the 50th percentile for height.

For adults with CKD, hypertension and an ACR of 30mg/mmol or less (ACR categories A1 and A2) follow hypertension treatment recommendations in Hypertension in adults: diagnosis and management NICE guideline [NG136].[2,4]

For adults, children and young people with CKD who have hypertension and an ACR over 30mg/mmol (ACR category A3 or above) offer an ARB, (e.g. losartan, candesartan) or an ACE inhibitor, (e.g. lisinopril, ramipril) titrated to the highest licensed dose that the person can tolerate.[2]

To improve concordance, inform people of the need to optimise the dose of ARB or ACE inhibitor and the need for eGFR and serum potassium monitoring to do this safely. NICE recommends both of these tests are performed before starting treatment and one to two weeks after initiation or subsequent dose increase and regularly throughout treatment.[1,2] More frequent monitoring of serum potassium may be needed if there is concurrent prescription of other drugs known to promote hyperkalaemia, for example spironolactone, trimethoprim, oral NSAIDs.[2] NICE gives specific advice on managing renin-angiotensin system antagonists (ACE inhibitor, ARB or direct renin inhibitors) where eGFR and serum potassium test results are abnormal. NICE advises not to routinely offer a renin–angiotensin system antagonist to people with CKD if their pre-treatment serum potassium concentration is greater than 5.0mmol/litre.[2] See attachment 1 - Pharmacotherapy for blood pressure control and proteinuria in CKD.

Do not offer a combination of renin-angiotensin system antagonists to adults with CKD.[2] The MHRA has also advised against using a combination of medicines from different classes of renin-angiotensin system blocking agents, other than under specialist supervision in a selected group of people with heart failure for whom other treatments are unsuitable.[5]

Cardiovascular risk factors – statins

The NICE clinical guideline on cardiovascular disease: risk assessment and reduction, including lipid modification [CG181] includes specific advice for those with CKD.[2,6] They advise against using a risk assessment tool to assess CVD risk in those with CKD (i.e. with an eGFR less than 60ml/min/1.73m^2 and/or albuminuria), as this group is at increased risk of cardiovascular disease. For people with CKD:[6]

- Offer atorvastatin 20mg daily, for the primary and secondary prevention of cardiovascular disease.
- Increase the dose if a greater than 40% reduction in non-HDL cholesterol is not achieved and eGFR is 30ml/min/1.73m^2 or more.
- Agree the use of higher doses with a renal specialist if eGFR is less than 30ml/min/1.73m^2.

Cardiovascular risk factors – oral antiplatelets and anticoagulants

Antiplatelet drugs should be offered to people with CKD for the secondary prevention of cardiovascular disease, but be aware of the general increased risk of bleeding in those with CKD.[2]

The NICE guidelines on atrial fibrillation: diagnosis and management [NG196] and venous thromboembolic diseases: diagnosis, management and thrombophilia testing [NG158] should be followed for people with CKD who require an anticoagulant.[2,7,8]

Encourage people with CKD to take exercise, achieve a healthy weight and stop smoking.[2]

Persistent proteinuria

CKD with diabetes:[2]

- For adults with CKD and diabetes (type 1 or type 2) offer an ARB or an ACE inhibitor (titrated to the highest licensed dose that the person can tolerate) if ACR is 3mg/mmol or more.
- For adults with CKD and type 2 diabetes, offer an SGLT2 inhibitor, in addition to an ARB or an ACE inhibitor at an optimised dose if:
  - ACR is more than 30mg/mmol, **and** they meet the criteria in the marketing authorisation (including relevant eGFR thresholds).
  - ACR is between 3 and 30mg/mmol **and** they meet the criteria in the marketing authorisation (including relevant eGFR thresholds).

Not all SGLT2 inhibitors are licensed for these indications, currently just dapagliflozin is licensed.[2,9,10]

- For children and young people with CKD and diabetes (type 1 or 2), offer an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate) if ACR is 3mg/mmol or more.[2]

For the treatment of blood glucose control follow NICE recommendations for:

- NICE's guideline on type 1 diabetes in adults
- NICE's guideline on type 2 diabetes in adults
- NICE's guideline on type 1 and type 2 diabetes in children and young people

The Kidney Disease: Improving Global Outcomes (KDIGO) 2020 Clinical Practice Guideline for Diabetes Management in CKD includes topics such as comprehensive care, glycemic monitoring and targets, lifestyle and antihyperglycemic interventions, and approaches to self-management and optimal models of care.

The PrescQIPP diabetes webkit pulls together all the PrescQIPP resources on diabetes in one webpage.

CKD without diabetes:[2]

- For adults with CKD but without diabetes:
  - Refer for nephrology assessment and offer an ARB or an ACE inhibitor (titrated to the highest licensed dose that they can tolerate), if ACR is 70mg/mmol or more.
  - Monitor in line with the agreed frequency if ACR is above 30 but below 70mg/mmol; consider discussing with a nephrologist if eGFR declines or ACR increases.
- For children and young people with CKD but without diabetes:
  - Offer an ARB or an ACE inhibitor if ACR (titrated to the highest licensed dose that they can tolerate) is 70mg/mol or more.
  - Monitor in line with the agreed frequencies if ACR is above 30 but below 70mg/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.

AKI

After AKI, monitor adults, children and young people for the development or progression of CKD for at least three years after acute kidney injury (longer for people with acute kidney injury stage 3) even if eGFR has returned to baseline.[2]

Chronic use of oral NSAIDs

Chronic use of oral NSAIDs may be associated with progression of CKD and acute use is associated with a reversible decrease in GFR. The NICE guideline chronic kidney disease: assessment and management [NG203] advises caution and monitoring of the effects on GFR when treating people with CKD with oral NSAIDs over prolonged periods of time.[2] Regular review of the ongoing need for an oral NSAID and reassessment of the risk versus the benefit is appropriate. An NSAID deprescribing algorithm is available to support decision making in the PrescQIPP Polypharmacy and deprescribing resources.

Untreated urinary outflow tract obstruction

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.[2]

Pharmacotherapy for other complications

Bone metabolism and osteoporosis

Do not routinely monitor calcium, phosphate, parathyroid hormone (PTH) and vitamin D levels in adults with a GFR ≥30ml/min/1.73m^2 (GFR category G1, G2 or G3). Where GFR is <30ml/min/1.73m^2 (GFR category G4 or G5) serum calcium, phosphate and PTH concentrations should be measured. The subsequent frequency of testing should be determined by the measured values and the clinical circumstances. Where doubt exists, seek specialist opinion. Prescribe bisphosphonates if indicated for the prevention and treatment of osteoporosis in people with a GFR of ≥30ml/min/1.73m^2 (GFR category G1, G2 or G3).[2]

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

Detailed advice on this subject is beyond the scope of the guideline, and NICE recommends seeking advice from the local renal service where there is doubt. They advise:[2]

- Do not routinely offer vitamin D supplementation to manage or prevent CKD-mineral and bone disorders.
- Offer colecalciferol or ergocalciferol to treat vitamin D deficiency in people with CKD and vitamin D deficiency.

The PrescQIPP Bulletin 275: Vitamin D provide further detailed guidance and implementation resources.

Anaemia of CKD

When haemoglobin (Hb) levels fall to 110g/litre or less (or 105g/litre or less if younger than two years) or anaemia symptoms develop (e.g. tiredness, shortness of breath, lethargy and palpitations) consider investigating and managing anaemia in adults, children and young people with CKD.[2]

If eGFR is above 60ml/min/1.73m^2, anaemia is unlikely to be caused by CKD, so other causes of anaemia should be investigated. Clinical judgement is needed on how extensively to look for other causes of anaemia when eGFR is between 30 and 60ml/min/1.73m^2 balancing the risks of missing the real cause of anaemia if assumed caused by CKD and putting people through unnecessary and extensive

investigations when their anaemia is caused by CKD. When eGFR is below 30ml/min/1.73m^2, anaemia is more likely to be caused by CKD.[2]

People with anaemia of CKD should have access to a designated contact person or people who have principal responsibility for their anaemia management and who have the skills for:

- Prescribing medicines related to anaemia management and monitoring their effectiveness.
- Coordinating an anaemia service for people with CKD, working between secondary and primary care and providing a single point of contact, to ensure people receive a seamless high standard service.
- Providing information, education and support to empower people and their families and carers to participate in their care.
- Monitor and manage a caseload in line with locally agreed protocols.[2]

When offering erythropoietic stimulating agent (ESA) therapy to adults, children and young people with anaemia of CKD, they and their GP should be given information about:

- Why ESA therapy is needed
- How it works
- What benefits and side effects may be experienced.[2]

The designated contact person or people who have principal responsibility for their anaemia management should discuss the choice of ESA with the person with anaemia of CKD when starting treatment and at subsequent review, taking into account:

- The person's dialysis status
- The route of administration
- The local availability of ESAs
- The lack of evidence comparing the efficacy of ESAs.[2]

Review treatment in all people started on ESA therapy after an agreed interval to decide whether or not to continue using ESAs.[2]

Do not prescribe supplements of vitamin C, folic acid or carnitine as adjuvants specifically for the treatment of anaemia of CKD.[2]

Do not use androgens to treat anaemia in people with anaemia of CKD.[2]

Oral bicarbonate supplements in the management of metabolic acidosis

Consider oral sodium bicarbonate supplementation for people with both:[2]

- A GFR less than 30ml/min/1.73m^2 (GFR category G4 or G5) and
- A serum bicarbonate concentration of less than 20mmol/litre.

Referral criteria

The NICE guideline on the assessment and management of CKD [NG203] recommends that the individual's wishes and comorbidities are taking into account when considering referral, however the following adults should normally be referred for specialist assessment:[2]

- A five year risk of needing renal replacement therapy of greater than 5%.
- An ACR of 70mg/mmol or more, unless known to be caused by diabetes and already appropriately treated.
- An ACR of more than 30mg/mmol (ACR category A3), together with haematuria.
- A sustained decrease in eGFR of 25% or more and a change in eGFR category within 12 months.

- A sustained decrease in eGFR of 15ml/min/1.73m^2 or more per year.
- Hypertension that remains poorly controlled (above the person's individual target) despite the use of at least four antihypertensive medicines at therapeutic doses.
- Known or suspected rare or genetic causes of CKD.
- Suspected renal artery stenosis.

Refer children and young people with CKD for specialist assessment if they have any of the following:[2]

- An ACR of 3mg/mmol or more, confirmed on a repeat early morning urine sample.
- Haematuria.
- Any decrease in eGFR.
- Hypertension.
- Known or suspected rare or genetic causes of CKD.
- Suspected renal artery stenosis.
- Renal outflow obstruction.

Summary

CKD is a common disorder for which key portions of care are delivered in primary care. The NICE guideline on the assessment and management of CKD [NG203] puts a strong focus on early identification, accurate diagnosis and tailored monitoring in order to minimise the associated morbidity and mortality. CKD, along with AKI represent a large clinical area and the assessment and management in practice may need substantial input from a range of health care professionals and commissioners in primary (and secondary) care to plan and commission NHS renal services for the local population. However, the potential impact, in terms of improving patients' outcomes, is significant.

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Additional PrescQIPP resources

Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-281-implementing-nice-guidance-in-ckd-and-aki/
Implementation tools	

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Support with any queries or comments related to the content of this document is available through the PrescQIPP help centre https://help.prescqipp.info

This document represents the view of PrescQIPP CIC at the time of publication, which was arrived at after careful consideration of the referenced evidence, and in accordance with PrescQIPP's quality assurance framework.

The use and application of this guidance does not override the individual responsibility of health and social care professionals to make decisions appropriate to local need and the circumstances of individual patients (in consultation with the patient and/or guardian or carer). Terms and conditions

Appendix 1 – Potentially nephrotoxic drugs

Potentially nephrotoxic drugs are one of multiple causes and risk factors for CKD and its progression.[1] When checking for nephrotoxic drugs, health professionals should ask about the use of non-prescription items, e.g., 'over-the-counter' oral NSAIDs or herbal remedies. Estimated glomerular filtration rate should be monitored at least annually in those prescribed drugs known to be nephrotoxic.[2] Systemic potentially nephrotoxic drugs include:[1,3,4]

Aminoglycosides

- **Amikacin**
- Amikin®
- **Gentamicin**
- Cidomycin®
- **Neomycin sulfate**
- **Streptomycin**
- **Tobramycin**
- Tobi Podhaler®
- Munuza®
- Tobi®
- Tymbrineb®
- Bramitob®
- Vantobra®

Angiotensin-converting enzyme inhibitors

- **Captopril**
- Noyada®
- **Enalapril**
- Innovace®
- **Enalapril/hydrochlorothiazide**
- Innozide®
- **Fosinopril**
- **Imidapril**
- Tanatril®
- **Lisinopril**
- Zestril®
- **Lisinopril/hydrochlorothiazide**
- Lisoretic®
- Zestoretic 10®
- Zestoretic 20®
- **Perindopril arginine**
- Coversyl® Arginine
- **Perindopril/indapamide**
- Coversyl® Arginine Plus
- **Perindopril erbumine**
- **Quinapril**
- Accupro® (Quinapril)
- **Quinalapril/hydrochlorothiazide**
- Accuretic®
- **Ramipril**
- Tritace®
- **Ramipril/felodipine**
- Triapin®
- **Trandolapril**

Angiotensin-receptor blockers (ARBs)

- **Azilsartan**
- Edarbi®
- **Candesartan**
- Amias®
- **Eprosartan**
- Teveten®
- **Irbesartan**
- Aprovel®
- Ifirmasta®
- **Irbesartan/hydrochlorothiazide**
- CoAprovel®
- **Losartan potassium**
- Cozaar®
- **Losartan/hydrochlorothiazide**
- Cozaar-Comp 100/12.5®
- Cozaar-Comp 100/25®
- Cozaar-Comp 50/12.5®
- **Olmesartan**
- Olmetec®
- **Olmesartan/amlodipine**

Angiotensin-receptor blockers (ARBs)

- Sevikar®
- **Olmesartan/hydrochlorothiazide**
- Olmetec Plus®
- **Olmesartan/amlodipine/hydrochlorothiazide**
- Sevikar HCT®
- **Telmisartan**
- Micardis®
- Tolura®
- **Telmisartan/hydrochlorothiazide**
- Micardis Plus®
- Tolucombi®
- **Valsartan**
- Diovan Oral Solution®
- **Valsartan/hydrochlorothiazide**
- Co-Diovan®
- **Valsartan/amlodipine**
- Exforge®
- **Valsartan/sacubitril**
- Entresto®

Bisphosphonates

- **Alendronic acid**
- Fosamax Once Weekly®
- Binosto®
- **Alendronic acid/colecalciferol**
- Fosavance®
- Bentexo®
- **Ibandronic acid**
- Bondronat®
- Bonviva®
- Iasibon®
- Quodixor®
- **Pamidronate disodium**
- **Risedronate sodium**
- Actonel®
- Actonel Once a Week®
- **Risedronate/calcium carbonate/colecalciferol**
- Actonel Combi®
- **Sodium clodronate**
- Loron®
- Clasteon®
- **Zoledronic acid**
- Aclasta®
- Zometa®

Calcineurin inhibitors

- **Ciclosporin**
- Capimune®
- Capsorin®
- Deximune®
- Neoral®
- Sandimmun®
- Vanquoral®
- **Tacrolimus**
- Adoport®
- Advagraf®
- Dailiport®
- Envarsus®
- Modigraf®
- Prograf®

Diuretics

- **Acetazolamide**
- Diamox®
- Diamox® SR
- **Amiloride**
- **Amiloride/bumetanide**
- **Co-amilofruse**
- Frumil LS®
- Frumil®
- **Co-amilozide**
- Moduretic®
- **Amiloride/cyclopenthiazide**
- Navispare®
- **Bendroflumethiazide**
- Neo-Naclex®
- **Bendroflumethiazide/timolol**
- **Bumetanide**
- **Chlortalidone**
- Hylaton®
- **Co-tenidone**
- Tenoret 50®
- Tenoretic®
- **Chlortalidone/triamterene**
- **Eplerenone**
- Inspra®
- **Furosemide**
- Diuresal®
- Frusol®
- **Furosemide/triamterene**
- Frusene®
- **Co-flumactone**
- Aldactide®
- **Indapamide**
- Natrilix®
- Alkapamid XL®
- Cardide SR®
- Indipam XL®
- Lorvacs XL®
- Natrilix SR®
- Rawel XL®
- Tensaid XL®
- **Perindopril/indapamide**
- Coversyl® Arginine Plus
- **Metolazone**
- Zaroxolyn®
- **Spironolactone**
- Aldactone®
- **Spironolactone/furosemide**
- Lasilactone®
- **Torasemide**
- Torem®
- **Triamterene**
- **Co-triamterzide**
- Dyazide®
- **Xipamide**
- Diurexan®

Lithium

- **Lithium carbonate**
- Camcolit®
- Liskonum®
- Priadel®
- **Lithium citrate**
- Li-Liquid® oral solution
- Priadel® liquid

Mesalazine

- **Mesalazine**
- Asacol®
- Mezavant XL®
- Octasa®
- Pentasa®
- Salofalk®
- Zintasa®

Non-steroidal anti-inflammatory drugs

- **Aceclofenac**
- Preservex®
- **Aspirin**
- Danamep®
- **Boots Aspirin**
- Disprin®
- Nu-Seals®
- **Co-codaprin**
- **Boots Aspirin and Codeine**
- Codis®
- **Aspirin/metoclopramide**
- MigraMax® oral powder sachets
- **Celecoxib**
- Celebrex®
- **Dexketoprofen**
- Keral®
- **Dexketoprofen/tramadol**
- Skudexa®
- **Diclofenac potassium**
- Voltarol Rapid®
- **Diclofenac sodium**
- Diclo-SR®
- Dicloflex SR®
- Dicloflex Retard®
- Diclomax Retard®
- Diclomax SR®
- Enstar XL®
- Fenactol®
- Fenactol SR®
- Fenactol Retard®
- Motifene®
- Akis®
- Voltarol®
- Econac®
- **Diclofenac sodium/misoprostol**
- Arthrotec 50®
- Arthrotec 75®
- Misofen®
- **Etodolac**
- Etolyn®
- Etopan XL®
- Lodine SR®
- **Etoricoxib**
- Arcoxia®
- **Flurbiprofen**
- Froben®
- **Ibuprofen**
- Anadin Ibuprofen®
- Anadin Joint Pain®
- Boots Rapid Ibuprofen lysine®
- Feminax Express®
- Nurofen®
- Nurofen Express®
- Nurofen Express Period Pain®
- Nurofen Joint & Back Pain Relief®
- Nurofen Migraine Pain®
- Brufen®
- Cuprofen®
- Nurofen Max Strength Joint & Back Pain Relief®
- Nurofen Max Strength Migraine Pain®
- Nurofen Meltlets®
- Brufen Retard®
- Anadin Ultra®
- Flarin®
- Nurofen for Children®
- Boots Ibuprofen Long Lasting®
- Lloydspharmacy Ibuprofen Long Lasting®
- Nurofen Back Pain SR®
- Brufen Granules®
- Boots Ibuprofen 3 Months Plus®
- Brufen Syrup®
- Calprofen®
- Care Ibuprofen for Children®
- Fenpaed®
- Nurofen for Children Cold, Pain and Fever®
- Nurofen for Children Singles®
- **Indometacin**
- Indocid®
- **Ketoprofen**
- Oruvail®
- Larafen CR®
- **Ketorolac**
- Toradol®
- **Mefenamic Acid**

Non-steroidal anti-inflammatory drugs

- Ponstan®
- Ponstan Forte®
- **Meloxicam**
- **Nabumetone**
- **Naproxen**
- Naprosyn®
- Stirlescent®
- Boots Period Pain Relief®
- Naprosyn EC®
- **Naproxen/ esomeprazole**
- Vimovo®
- **Parecoxib**
- Dynastat®
- **Piroxicam**
- Feldene Melt®
- Feldene®
- **Sulindac**
- **Tenoxicam**
- Mobiflex®
- **Tiaprofenic Acid**
- Surgam®
- **Tolfenamic acid**
- Clotam Rapid®

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