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GUIDELINES

Chronic kidney disease: summary of updated NICE guidance

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What you need to know

- The updated guideline does not recommend adjusting the estimation of glomerular filtration rate (GFR) in people of African-Caribbean or African family background
- Screen people at risk of chronic kidney disease (CKD) using estimated GFR (eGFR) and albumin to creatinine ratio (ACR)
- Use the four-variable Kidney Failure Risk Equation instead of eGFR threshold for referral
- Refer adults with CKD and a five year risk of needing renal replacement therapy of >5% (measured with the Kidney Failure Risk Equation) for specialist assessment
- Offer a sodium-glucose cotransporter-2 (SGLT2) inhibitor, in addition to an optimised dose of angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB), to people with type 2 diabetes, an ACR of ≥30 mg/mmol, and who meet the criteria in the marketing authorisation (including relevant eGFR thresholds)

Chronic kidney disease (CKD) is common, estimated to affect 13% of adults (≥16 years old) in England.[1] People with CKD have a wide range of experiences, from being asymptomatic at early stages to kidney failure with advanced disease (see table 1 for a classification of CKD stages). The prevalence of categories G3 to G5 (more severe disease) is 5% for all adults, rising to 34% in people aged 75 and over. As kidney dysfunction advances, the mortality risk increases, as does risk of cardiovascular disease, and some comorbidities (such as diabetes and hypertension) become more severe. Most adults with CKD are managed primarily in primary care, but they may need more input from secondary care as the disease progresses.

Table 1 | Classification of chronic kidney disease (CKD) in adults, and risk of adverse outcomes by category

	Albumin to creatinine ratio (ACR) category		
Glomerular filtration rate (GFR) category	A1: Normal to mildly increased (<3 mg/mmol)	A2: Moderately increased (3-30 mg/mmol)	A3: Severely increased (>30 mg/mmol)
G1: Normal and high (≥90 mL/min/1.73m2)	Low risk No CKD if no other markers of kidney damage	Moderate risk	High risk
G2: Mild reduction related to normal range for a young adult (60-89 mL/min/1.73m2)	Low risk No CKD if there are no other markers of kidney damage	Moderate risk	High risk
G3a: Mild to moderate reduction (45-59 mL/min/1.73m2)	Moderate risk	High risk	Very high risk
G3b: Moderate to severe reduction (30-44 mL/min/1.73m2)	High risk	Very high risk	Very high risk
G4: Severe reduction (15-29 mL/min/1.73m2)	Very high risk	Very high risk	Very high risk
G5: Kidney failure (<15 mL/min/1.73m2)	Very high risk	Very high risk	Very high risk

In August 2021, the National Institute for Health and Care Excellence (NICE) published NG203,[2] an updated and combined version of three guidelines: "chronic kidney disease in adults: assessment and management," "chronic kidney disease (stage 4 or 5): management of hyperphosphataemia," and "chronic kidney disease: managing anaemia." The guideline was extended to cover the assessment and management of chronic kidney disease in children and young people. This article summarises the most recent recommendations from NG203 including new recommendations on sodium-glucose cotransporter-2 (SGLT2) inhibitors, estimating glomerular filtration rate (GFR) in people from black, Asian, and minority ethnic groups, and new criteria for risk assessment and referral to secondary care.[2]

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

Investigations for chronic kidney disease in children

Most children and young people with CKD will be managed primarily in secondary care. However, initial identification of CKD may well occur in primary care, and the following risk factors should prompt consideration of investigations for CKD in children and young people.

- Offer testing for CKD using eGFRcreatinine (GFR estimated from serum creatinine) and albumin to creatinine ratio (ACR) to children and young people with any of the following risk factors:
  - Previous episode of acute kidney injury
  - Solitary functioning kidney.

  [*Based on very low to high quality evidence from prospective and retrospective cohort studies*]
- Consider testing for CKD using eGFRcreatinine and ACR in children and young people with any of the following risk factors:
  - Low birth weight (≤2500 g)
  - Diabetes
  - Hypertension
  - Cardiac disease
  - Structural renal tract disease or recurrent renal calculi
  - Multisystem diseases with potential kidney involvement (for example, systemic lupus erythematosus)
  - Family history of end stage renal disease (GFR category G5) or hereditary kidney disease
  - Incidental detection of haematuria or proteinuria.

  [*Based on the experience and opinion of the Guideline Committee (GC)*]

The guideline also includes recommendations on investigations for proteinuria and haematuria and the use of reagent strips.

Estimating glomerular filtration rate (GFR)

The new guideline recommends that the estimation of GFR (eGFR) should not be adjusted by an ethnicity factor (the 2014 guideline recommended multiplying eGFR by 1.159 for people of African-Caribbean or African family origin, if calculated using the CKD-EPI creatinine equation). The Guideline Committee agreed that adding an ethnicity adjustment to eGFR equations for different ethnicities may not be valid or accurate. Categorisations based on ethnicity lump together people with a diverse range of family backgrounds, and differences in eGFR across ethnicities are likely to arise, at least partly, because of differences in average muscle mass between ethnic groups. However, muscle mass also differs from person to person within the same ethnicity and so making an adjustment based on ethnicity may be inaccurate for some people. It was also considered inappropriate to extrapolate research findings derived predominantly from African-Americans in the US to the UK context. Also, the usefulness of ethnicity-based modifiers is questionable for the many people from mixed ethnic backgrounds.

Therefore, the committee noted that individual judgment should be used when interpreting eGFR in people from UK black, Asian, and minority ethnic groups; in adults with extremes of muscle mass (such as bodybuilders or people who have had an amputation or with muscle wasting disorders) since reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR; and in adults who use high protein dietary supplements (such as protein shakes).

Risk assessment, referral criteria, and shared care

The committee looked at new evidence from a UK validation study[3] of the four-variable Kidney Failure Risk Equation for adults (based on age, sex, eGFR, and urine ACR), which can be used as a criterion for identifying people who will benefit from referral to secondary care. The results of both the validation study and modelling undertaken for the guideline showed that using this equation as one of the referral criteria (rather than an eGFR threshold) was likely to be both more sensitive and more specific than the criteria in the 2014 NICE guideline, meaning people who will progress to needing renal replacement therapy are identified earlier, and there are fewer unnecessary referrals to secondary care (see box 2).

Box 2: Referral criteria for specialist assessment in adults with chronic kidney disease (CKD)

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

- A 5-year risk of needing renal replacement therapy of >5% (measured using the Kidney Failure Risk Equation which has the four variables age, sex, eGFR, and urine ACR)[3]
- An ACR of ≥70 mg/mmol unless this is known to be caused by diabetes and already appropriately treated (see the section below on pharmacotherapy)
- An ACR of >30 mg/mmol (ACR category A3) together with haematuria
- A sustained decrease in eGFR of ≥25% and a change in eGFR category within 12 months
- A sustained decrease in eGFR of ≥15 mL/min/1.73 m^2 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 (see also the NICE guideline on hypertension in adults[4])
- Known or suspected rare or genetic causes of CKD
- Suspected renal artery stenosis.
  - [*Based on moderate to high quality evidence from individual patient data meta-analysis and prospective and retrospective cohort studies, and directly applicable health economic modelling*]

The benefits of using the Kidney Failure Risk Equation over an eGFR threshold (as in the 2014 NICE guideline) were not large at an individual level, but the committee agreed that they were meaningful at a population level because of the large number of people with CKD being managed in primary care. They also agreed there were additional potential benefits of using the Kidney Failure Risk Equation, including the ability to provide people with an individual risk assessment, which could help them to proactively manage their own risk and inform management plans in secondary care.

However, validation of the risk equation was only in adults, so the committee made a separate recommendation for children and young people. People of African-Caribbean or African family origin were under-represented in the validation study for the Kidney Failure Risk Equation compared with the UK average, and, although there was a sizeable proportion of people of Asian family origin, the location of the study suggests that people of east Asian family origin were likely to be under-represented.

- Give adults with CKD and their family members or carers (as appropriate) information about their five-year risk of needing

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renal replacement therapy (measured using the 4-variable Kidney Failure Risk Equation). Follow NICE's guideline on shared decision making when communicating risk.[5] [*Based on moderate to high quality evidence from individual patient data meta-analysis and prospective and retrospective cohort studies, and directly applicable health economic modelling*]

- Use everyday, jargon-free language to communicate information on risk. If technical and medical terms are used, explain them clearly. [*Based on the experience and opinion of the GC*]
- Set aside enough time during the consultation to give information on risk assessment and to answer any questions. Arrange another appointment for more discussion if this is needed. [*Based on the experience and opinion of the GC*]
- Document the discussion on risk assessment and any decisions the person makes. [*Based on the experience and opinion of the GC*]

Monitoring frequency

As eGFR declines, the risk of kidney disease progression and mortality increases, and this risk increases with the rate of eGFR decline.[6] Any person with eGFR decline identified on routine monitoring should be monitored more frequently.

- If an adult, child, or young person has CKD, or is at risk of it, agree the frequency of monitoring (eGFRcreatinine and ACR) with them (and their family members or carers, as appropriate), bearing in mind that CKD is not progressive in many people. [*Based on the experience and opinion of the GC*]
- Use table 2 to guide the minimum frequency of eGFRcreatinine monitoring but tailor it according to:
  - 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 the person's treatment (such as renin–angiotensin–aldosterone system (RAAS) antagonists, NSAIDs, and diuretics)
  - Intercurrent illness (for example, acute kidney injury)
  - Whether the person has chosen conservative management of CKD.

  [*Based on low to high quality evidence from individual patient data meta-analysis and prospective cohort studies*]

Table 2 | Minimum number of monitoring checks (eGFRcreatinine) per year for adults, children, and young people with or at risk of chronic kidney disease (CKD)

	Albumin to creatinine ratio (ACR) category		
Glomerular filtration rate (GFR) category	A1: Normal to mildly increased (<3 mg/mmol)	A2: Moderately increased (3-30 mg/mmol)	A3: Severely increased (>30 mg/mmol)
G1: Normal and high (≥90 mL/min/1.73m2)	0 to 1	1	≥1
G2: Mild reduction related to normal range for a young adult (60-89 mL/min/1.73m2)	0 to 1	1	≥1
G3a: Mild to moderate reduction (45-59 mL/min/1.73m2)	1	1	2
G3b: Moderate to severe reduction (30-44 mL/min/1.73m2)	1 to 2	2	≥2
G4: Severe reduction (15-29 mL/min/1.73m2)	2	2	3
G5: Kidney failure (<15 mL/min/1.73m2)	4	≥4	≥4

ACR monitoring should be individualised based on a person's individual characteristics, risk of CKD progression, and whether a change in ACR is likely to lead to a change in management.

Pharmacotherapy

The guideline now supports the use of SGLT2 inhibitors for adults with CKD, type 2 diabetes, and ACR of ≥30 mg/mmol because there was evidence of a clinically meaningful reduction in progression to end stage kidney disease, all-cause mortality, and hospitalisation for heart failure with SGLT2 inhibitors compared with placebo.[7-9] Current studies are looking at whether these criteria should be modified for people with diabetes and CKD, and an ongoing NICE Technology Appraisal is reviewing the use of dapagliflozin in people with CKD with or without diabetes.[10]

- 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 >30 mg/mmol *and*
  - They meet the criteria in the marketing authorisation (including relevant eGFR thresholds).

  [*Based on moderate to high quality evidence from randomised controlled trials, and directly applicable health economic analysis*]

The guidance provides an algorithm on the use of phosphate binders[11] and notes the importance of taking into account people's preferences around choice of binder (for example, chewable versus non-chewable). The guidance also includes updated recommendations on blood pressure control and appropriate blood pressure targets in adults, children, and young people with CKD.

Implementation

It is not expected that GPs should have to calculate the Kidney Failure Risk Equation manually. Instead, it would be built into laboratory computer systems, as part of how eGFR and ACR results are returned to GPs. Because the calculation requires both an eGFR and ACR value, it can be produced only if the GP requests both those measurements. There may be an implementation period before the risk equation results are available to all GPs. Until then, some GPs

may have to continue to base referral decisions on eGFR and ACR values independently, as is currently done, without providing patients with a quantitative assessment of their risk of needing renal replacement therapy.

The recommendation for SGLT2 inhibitors might result in a significant change in practice, since it will mean these drugs are prescribed more widely, and this would come with a substantial cost impact. The committee noted, however, that this was likely to represent a cost effective use of resources, with these drugs providing additional benefits on renal outcomes as well as the benefits they provide for diabetes management.

Future research

The Guideline Committee made the following research recommendations:

- In adults, children, and young people from black, Asian, and other minority ethnic groups with chronic kidney disease (CKD) living in the UK, which existing calculations of estimated glomerular filtration rate (eGFR) are the most accurate?
- In adults, children, and young people from black, Asian, and other minority ethnic groups with CKD living in the UK, what biomarkers or factors, other than ethnicity, improve the diagnostic accuracy of eGFR calculations?
- What is the accuracy of the four-variable Kidney Failure Risk Equation in adults, children, and young people with CKD from black, Asian, and minority ethnic groups living in the UK?
- What is the efficacy and safety of different aspirational haemoglobin targets for children and young people with CKD undergoing treatment for anaemia?
- What are the views and beliefs of people with CKD and their family members and carers about taking oral phosphate binders?

Further information on the guidance

This guidance was developed by NICE in accordance with its guideline methodology (www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf). A guideline committee (GC) was established by NICE, which incorporated healthcare and allied healthcare professionals (two consultant chemical pathologists, two renal physicians, one consultant nephrologist, two renal nurse specialists, one consultant in medicine for the elderly, four general practitioners, one paediatric renal nurse specialist, one consultant paediatric nephrologist, one dietician, one renal pharmacist, one consultant diabetologist) and two lay members.

The GC identified relevant review questions and collected and appraised clinical and cost effectiveness evidence. Quality ratings of the evidence were based on GRADE methodology (www.gradeworkinggroup.org). These relate to the quality of the available evidence for assessed outcomes or themes rather than the quality of the study. The GC agreed recommendations for clinical practice based on the available evidence or, when evidence was not found, based on their experience and opinion using informal consensus methods.

The scope and the draft of the guideline went through a rigorous reviewing process, in which stakeholder organisations were invited to comment; the GC took all comments into consideration when producing the final version of the guideline. The guideline is available at https://www.nice.org.uk/guidance/ng203

NICE will conduct regular reviews after publication of the guidance, to determine whether the evidence base has progressed significantly enough to alter the current guideline recommendations and require an update.

Guidelines into practice

- When would you consider adjusting estimated glomerular filtration rate (eGFR) in adults at risk of chronic kidney disease (CKD)?
- What referral criteria do you use to refer adults with CKD for specialist assessment?

How patients were involved in the creation of this article

Committee members involved in this guideline update included lay members who contributed to the formulation of the recommendations summarised here.

Contributors: All authors contributed to the development of the guideline; the planning, drafting, and revision of this summary; and approval of the final version and take responsibility for its accuracy. We thank Joshua Pink and Jan Dudley for their comments on this article.

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Members of the NICE technical team were Chris Carmona (until May 2021); Kathryn Hopkins (from May 2021); Yolanda Martinez; Gabriel Rogers (until January 2020); Joshua Pink (from January 2020); Hannah Nicholas (until December 2019); Rui Martins (from December 2019 to April 2020), Steph Armstrong (from April 2020).

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