

Chronic kidney disease Frequently asked questions

April 2007



A part of the NHS Confederation
working on behalf of the 

Contents

About eGFR	3
About Chronic kidney disease	8
Testing for proteinuria and investigation of people with CKD	11
Referral in CKD	13
QOF issues, computer reporting and exception reporting	16

NHS Employers and the General Practitioners Committee of the British Medical Association have produced these frequently asked questions in response to queries received from primary care organisations and practices, in relation to the diagnosis and management of chronic kidney disease following its inclusion in the Quality and Outcomes Framework for 2006.

We would like to thank Dr Simon de Lusignan, Head of General Practice and Primary Care and Course Director Biomedical Informatics, Division of Community Health Sciences at St. George's University of London, for the help and support he has provided in the production of this publication.

About eGFR

1. What is estimated Glomerular Filtration Rate (eGFR)?

eGFR is the estimated glomerular filtration rate. It is used to assess renal function and is a more sensitive measure of renal impairment than serum creatinine. Patients can have significant renal impairment even with a serum creatinine in the normal range. It is possible to lose up to 50% of renal function before the creatinine becomes elevated, especially in the elderly.

2. Why is Glomerular Filtration Rate (GFR) being adopted?

It follows the recommendations in the Renal NSF. It is a more sensitive marker of kidney dysfunction than serum creatinine; it will allow earlier identification of patients with chronic kidney disease (CKD). This is particularly important as these patients are at increased cardiovascular risk compared with the general population and may benefit from risk factor modification. The use of eGFR will also facilitate identification of patients with more advanced CKD previously not recognised as such (for example an 80 year old with a creatinine of 160).

3. How is Glomerular Filtration Rate measured?

The eGFR is calculated from the serum creatinine, age, sex and ethnicity of the patient using a formula, called the MDRD formula. Over 75 per cent of chemical pathology laboratories are now reporting eGFR automatically alongside any request for creatinine. For the aficionado, the formula is available via the internet at: www.renal.org

Not all creatinine assays are equivalent. The laboratory may apply a correction factor which may make the eGFR calculated at the lab slightly different from the one you may get if you calculate it in your practice. The laboratory calculated eGFR should be given priority as it will standardise the creatinine assay.

Many labs have opted to report the numerical value for eGFR only if the eGFR is 60 or under. If eGFR is over 60 they will simply report it as >60 mL/min/1.73m².

4. What are the issues about lab reference ranges?

There are two issues about laboratory reference ranges:

- (1) UK laboratories don't have a standard creatinine assay. Creatinine in one place is not equivalent to that in another. However, they can apply a correction factor. The implications of this are that lab calculated eGFR is more accurate than practice calculated eGFR.
- (2) Some laboratories are only reporting numeric GFR when it is equal to or less than 60 mL/min/1.73m². The recommendation is to report numerical values up to 89 and then report >90 mL/min/1.73m². Changes in eGFR

within an individual patient are a highly reliable way of tracking changes in kidney function. Looking at all previous serum creatinine measurements, not just the last two or three, is important to get an idea of trend over time.

5. Why is ethnicity in the Glomerular Filtration Rate formula?

Afro-Caribbeans tend to have proportionally greater muscle mass than non Afro-Caribbeans and therefore produce more creatinine. Therefore, a creatinine of, for example, 150 in an Afro-Caribbean represents better renal function than the same creatinine in a non Afro-Caribbean patient.

The laboratory will generally not know the ethnicity of the patient. For that reason the eGFR will always be calculated for a non Afro-Caribbean patient, with instructions on the report to multiply by 1.21 for an Afro-Caribbean patient. There is no adjustment necessary for Asian or mixed race populations.

6. What is the influence of ethnicity on eGFR and how should this influence what GPs do?

For people of Afro-Caribbean origin, multiply the eGFR by the correction factor of 1.21. For people of other ethnic groups we will have to follow the emerging evidence. Many other ethnic groups appear to have lower levels of CKD but these increase as they adopt western lifestyles. As most of the major studies were carried out on the white population we do not as yet have a clear answer to this. For now the best advice is to treat Afro-Caribbean patients using the correction factor and everyone else without.

7. Will eGFR replace serum creatinine?

No. Creatinine will continue to be reported, but will be supplemented by eGFR.

8. What is the difference between creatinine clearance and glomerular filtration rate?

Measurement of creatinine clearance gives an estimate of the actual glomerular filtration rate, as does eGFR. However, eGFR is less cumbersome than performing creatinine clearance. There is no longer any need to perform creatinine clearance on 24 hour urine collections.

9. What is the normal range for eGFR?

An eGFR >90 mL/min/1.73m² is considered normal.

An eGFR of 60 to 90 ml/min does not in itself indicate chronic kidney disease (CKD) – for a formal diagnosis of CKD additional markers of damage are required as well. These markers can either be on imaging (for example polycystic kidneys) or abnormal urine findings (for example microalbuminuria or microscopic haematuria). The finding of an eGFR of 60 to 90 mL/min/1.73m² should not prompt investigations looking for these markers.

An eGFR of <60ml/min, however, does represent chronic kidney disease.

10. Does eGFR change with age?

Yes. Beyond the age of 40 a progressive loss of GFR of up to 1 ml/min/year is commonly seen, particularly amongst patients with hypertension or vascular disease. Whether this should be considered 'normal' is controversial.

Women generally have a higher prevalence of CKD. Half of women over 75 years old have an eGFR of under 60 ml/min/1.73m².

Although eGFR can decline with increasing age, this in itself should not preclude these patients from receiving care as outlined by the QOF indicators. The decision to treat CKD should be made in conjunction with the patient and where appropriate their carer and take into account issues such as their general health and quality of life that they feel they have.

In reaching this clinical decision it should be remembered that the care outlined in QOF seeks to protect these patients from experiencing preventable cardiovascular complications to which they are more vulnerable. Therefore it is not possible to give an age cut off after which CKD should not be diagnosed or hypertension treated.

The eGFR calculation is not valid in children (those under 16 years). The Schwartz formula is valid for use in this age group. However, should kidney disease be suspected in children this would be a reason for referral.

11. Is eGFR useful in acute renal failure?

No. However, if an unexpected eGFR <60 is reported it is worth looking at historic creatinine values. If there has been a sudden rise or there are no historic creatinine values, then a repeat creatinine should be requested to exclude any sudden increase in creatinine which might indicate acute renal failure.

12. What should practices do if they do not have access to eGFR?

Practices without access to eGFR should calculate it using one of the available calculators. Practices can adopt one of two strategies or a mixture of the two. The two suggested strategies are:

- (1) Calculate eGFR for each creatinine result that comes into the practice. This can be done using an online calculator www.renal.org.
- (2) Export age, gender and creatinine from your GP computer system into a spreadsheet which will run the calculation for you. This can be downloaded from www.pcel.info/gfr/ (N.B. You must "enable macros" if asked to do so when you download this; full instructions are available via a tab at the bottom of the spreadsheet). Once in the spreadsheet the data can be sorted by stage of CKD. We would recommend that you flag patients for a blood pressure review at their next visit.

Some of the software manufacturers have developed options which allow eGFR to be estimated for the whole population. Practices should contact their computer system supplier about this. Remember that because there is no standard reference range yet – where locally calculated eGFR differs from the lab result please give the lab result priority. This is because they will have corrected their creatinine to take account for any differences in their assay technique.

There is no easy way of defining a creatinine cut off as an alternative to using eGFR. This is because creatinine is a poor measure of renal function – it is possible to have a decline in renal function of around 50 per cent before creatinine starts to rise.

13. What are GPs expected to do when they find someone with a low eGFR?

If the low eGFR is a new unexpected finding – look at historic creatinine to see if there has been a sudden change. If there is a big change or no historic creatinine records, repeat the test in one week. If the patient is acutely unwell consider Acute Renal Injury (previously called Acute Renal Failure) and repeat the test immediately or discuss/ refer for a specialist opinion.

If eGFR is low:

- the first priority is to check the patient's blood pressure.

The target for blood pressure should be 130/80. However, if there is proteinuria a lower target of 120/75 is recommended. We recognise that the QOF target has been set at 140/85 because of the very real difficulty in controlling blood pressure in many of these patients – the best way to get most patient's blood pressure below the audit threshold is to aim for the 'target' of 130/80. However, the evidence base is for the 130/80 target. Treat with an ACE-I or ARB and other agents to reduce blood pressure measurements to target. Check potassium before starting and recheck along with creatinine after two weeks of starting, after changes in dose or if any severe intercurrent illness. ACE-I or ARBs are the best drugs to treat hypertension in proteinuric CKD although they can sometimes reduce renal profusion. These agents are often used in non-proteinuric patients to achieve the target blood pressure as part of combination therapy. It is not justified to change patients who have good blood pressure control on other agents and no proteinuria to an ACEi/ARB just because of CKD Stage 3.

If the patient's blood pressure is >150/90 and they are on at least three anti-hypertensive agents they should be referred, though this may initially be to the appropriate medical specialist, rather than a renal specialist if the patient has diabetes or heart disease.

- Next test for proteinuria and check the patient is not anaemic. Anaemia is generally defined in CKD as Hb<11g/dL. Please see Question 23 on how anaemia is defined in CKD in the investigations section.

- Manage other cardiovascular risk by controlling cholesterol and encouraging smokers to quit.
- Improve control of heart failure and diabetes. Conduct a medication review for drugs which impair renal function. In men consider whether prostatic disease may be causing outflow problems.

Please see how CKD is classified for information on how often to re-check creatinine. Please also see referral guidance.

About chronic kidney disease

14. What is chronic kidney disease?

Chronic kidney disease (CKD) is the term for what used to be called chronic renal failure. It is classified into 5 stages according to the eGFR as follows:

Stage	GFR (ml/min)	Description	Prevalence (%)
1	> 90	Kidney damage with normal or ↑GFR	3.3
2	60-89	Kidney damage with mild ↓GFR	3.0
3	30-59	Moderate ↓GFR	4.3
4	15-29	Severe ↓GFR	0.2
5	< 15	Kidney failure	0.2

People with CKD may go on to develop end stage renal disease (ESRD – requiring dialysis or transplantation) but a much greater problem is the increase in cardiovascular and all cause mortality and morbidity. Control of cardiovascular risk, especially blood pressure control slows progression and improves outcome.

15. How is CKD classified?

CKD is classified into five stages based on eGFR. The lower the eGFR the worse the stage of CKD. The diagnosis requires the abnormalities to be present for at least three months. People with eGFR over 60 mL/min/1.73m² should not be considered to have CKD unless there is other evidence of kidney damage.

Stage	GFR (ml/min)	Description	Frequent complications	Testing frequency
1	> 90	Kidney damage with normal or ↑GFR	Hypertension	Yearly
2	60-89	Kidney damage with mild ↓GFR	Hypertension (Parathyroid hormone elevation)	Yearly
3	30-59	Moderate ↓GFR	Hypertension, Changed in Calcium and phosphate metabolism, renal anaemia, left ventricular hypertrophy	6 months
4	15-29	Severe ↓GFR	As above, plus hyperkalaemia	3 months; 6 monthly once stable
5	< 15	Kidney failure	All above plus salt and water retention causing apparent heart failure, anorexia, vomiting, pruritis	3 months

16. What are the most important facts about chronic kidney disease for primary care clinicians?

- It is very common (at least five per cent population have Stage 3 to 5 disease)
- Common causes include diabetes, vascular disease, and in males, obstructive renal disease
- The majority (>80%) of patients have stable CKD (i.e. eGFR falling by 4 ml/min/year or less) and are at far higher risk from cardiovascular disease than they are of ever requiring renal replacement therapy.
- The presence of proteinuria indicates a higher cardiovascular and progressive kidney disease risk.
- The mainstays of management are:
 - to identify patients requiring nephrology referral (see below) ;
 - to assess stability of disease (by monitoring creatinine, typically every six to 12 months);
 - to assess any functional consequences of disease;
 - to address cardiovascular risk;
 - to avoid nephrotoxic drugs.

Please see national guideline documents for more details, available at:

The Renal Association

www.renal.org/JSCRenalDisease/JSCRenalDisease.html

Northern Ireland NHS guidance:

www.crestni.org.uk/publications/chronic%2Dkidney%2Ddisease.html

Brief guidance for GPs distributed by RCGP:

Blades S, Burden R. Introducing eGFR. Promoting good CKD Management. CKD Guidelines Development Committee. URL:

www.renal.org/eGFR/resources/eGFRnatInfoLft0406.pdf

17. What is the expected prevalence of CKD in a practice with a list size of 10,000 patients

A practice of 10,000 will have at least 500 patients with Stage 3 to 5 CKD, with around 20 of these in stage 4 and 10 in stage 5. A more elderly and more deprived practice population are likely to have a higher prevalence.

About 90 per cent of people with stage 3 to 5 CKD will have hypertension, 40 per cent will have vascular disease and 30 per cent will have diabetes.

People with CKD are roughly twenty times more likely to die from cardiovascular disease than progress to end stage renal failure. The all causes mortality rate in CKD is 30 to 60 times higher than in the general population.

18. What drugs can make CKD worse

All patients with CKD should have a medication review. The advice of a current copy of the BNF should be followed. The priorities for this medication review should be:

- First, stop unnecessary medication which may impair renal function. For example, many patients may be on non-steroidal anti-inflammatory drugs which might be discontinued.
- Angiotensin converting enzyme inhibitors (ACE-I) and angiotensin II receptor blockers (ARB) are the best drugs to treat hypertension in proteinuric CKD, although they can sometimes reduce renal perfusion.
- Renal metabolism and excretion of drugs might be impaired. For example, patients on analgesics, B-blockers, digoxin and allopurinol may all need their dose reducing.
- In diabetes sulphonylureas may accumulate and therefore short acting drugs are preferred. Metformin should only be used under specialist advice when eGFR is below 30 mL/min/1.73m² (Stage 4 and 5 CKD). When eGFR is between 30 and 60 mL/min/1.73m² the risk-benefit of metformin should be assessed on an individual basis.

19. When should Angiotensin Converting Enzyme Inhibitors ACE-I and Angiotensin Receptor blockers be used OR not used in CKD?

ACE-I and ARBs are the best drugs to use to control blood pressure in proteinuric CKD. They give the best outcome for patients.

Very occasionally where a patient has hypovolemia or renal artery stenosis they can make things worse. Therefore it is important to check electrolytes two weeks after starting, after increasing dose and during any intercurrent illness likely to cause hypovolemia (including acute sepsis).

These agents are often used in non-proteinuric patients to achieve the target blood pressure as part of combination therapy. It is not justified to change patients who have good blood pressure control on other agents to an ACE-I or an ARB just because of CKD Stage 3.

Testing for proteinuria and investigation of people with CKD

20. Who should have their urine tested and responding to positive tests?

Everyone who has CKD should have their urine dip-stick tested annually. Patients with diabetes, who are having annual tests as part of their screening process, don't need to be additionally checked.

A change in blood pressure, fluid retention (oedema) or systemic disease is an indication for dip-stick testing.

If protein testing is positive send off a sample for microscopy and culture. If negative and the proteinuria persists, test total protein or albumin creatinine ratio in the urine and retest serum creatinine to obtain a further estimate of eGFR. If the total protein creatinine ratio (TPCR) is $>100\text{mg/mmol}$ or there is microscopic haematuria (not dip-stick test) and PCR $>45\text{mg/mmol}$ renal referral is indicated.

21. How should I measure proteinuria?

There is no longer any need to do 24-hour urine collections for protein in CKD. When a patient has newly recognised CKD the urine should be dip-stick tested. If there is more than a trace of proteinuria send a spot random urine (preferably early morning but not essential) in a white-topped plain bottle to the lab for a TOTAL PROTEIN:CREATININE RATIO (TPCR). It is worth sending an MSU at the same time if there is also blood or leucocytes/nitrites present.

You will get an answer in mg/mmol. Simply divide the value in mg/mmol by 100 to give the total daily 24-hour protein excretion in g/day. For example if TPCR = 100 mg/mmol , then total daily protein excretion = 100 divided by 100 = 1 g/day .

This is NOT the same as the albumin:creatinine ratio (ACR). There are other proteins in urine so the TPCR will always be greater than the ACR. The ACR is usually used to diagnose (and monitor) microalbuminuria, the first stage of diabetic nephropathy.

22. What is the normal range for total protein creatinine ratio (TPCR)?

Less than 15 mg/mmol .

23. Testing for anaemia in CKD

Patients who are due to be referred, are symptomatic, or who have heart failure as a co-morbidity should have their haemoglobin checked.

There are two definitions of renal anaemia used in CKD. The KDOQI¹ and European Best Practice Guidelines are recommended, i.e. using a threshold of 11g/Dl to define anaemia.

¹National Kidney Foundation (NKF) Kidney Disease Outcome Quality Initiative (K/DOQI) Advisory Board. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative – Am J Kidney Dis 2002; 39(Suppl 2): S1–246.

²European best practice guidelines for the management of anaemia in patients with chronic renal failure - Nephrol Dial Transplant 1999; 14(Suppl 5): 1–50.

24. Do all CKD patients need a renal ultrasound?

No. Ultrasound should be reserved for those with progressive disease, advanced (Stage 4 or 5) disease, refractory hypertension or palpable bladder/lower tract symptoms.

Practices should refer to local care pathways prior to making a referral for a renal ultrasound.

See also: Question 27 - What information is required in a referral to a nephrologist?

Referral in CKD

25. Which patients should be referred for a renal opinion?

Again, please refer to the guideline documents available at www.renal.org

This is not an exhaustive summary, but the patients who definitely should be seen are:

- Those with acute renal failure (the discovery of an abnormal eGFR should prompt a review of historical creatinine measurements)
- Those with significant (> 1 g/day) proteinuria, equivalent to a protein:creatinine ratio of 100 mg/mmol
- Those with microscopic haematuria (before urology referral if patient age < 45, after if > 45)
- Those with advanced disease (all Stage 5 should be seen, all Stage 4 should at least be discussed)
- Those with functional consequences of CKD; for example anaemia, bone disease or refractory hypertension (>150/90 on three agents).

In certain circumstances referral to another specialist would be appropriate initially. For example, we would recommend that people with poorly controlled diabetes and heart failure are referred to the appropriate specialist first. Men with outflow obstruction should be referred to an urologist. Elderly people with complex multiple problems may benefit from initial assessment by a geriatrician.

26. Who needs urgent referral?

Patients with newly diagnosed Stage 5 CKD should be referred urgently unless it is part of a known terminal illness or they are stable with a known management plan.

Immediate referral is required for acute renal failure, malignant hypertension, hyperkalaemia (K^+ >7mmol/L) and nephritic syndrome.

Advice should be sought from the renal clinic regarding people with newly diagnosed Stage 4 CKD unless renal function is known to be stable. People who are frail and stable in Stage 4 or 5 and thought to be in the last year of life or who choose the no dialysis option should be recorded as needing support and palliative care without referral. Normal decline in eGFR is up to 4 mL/min/1.73m² per year.

27. What information is required in a referral to a nephrologist?

- List of dates and results of previous serum creatinine measurements to assess stability
- Serum potassium
- Haemoglobin
- Past medical and full drug history
- Blood pressure

- Dipstick results and total protein-creatinine ratio if more than trace protein present
- Renal US if stage 4, refractory hypertension, progressive decline in eGFR or lower tract symptoms (if required under local protocols)
- If diabetic: HbA1c results and evidence of other diabetic complications
- If prostate disease: details.

28. When is it reasonable NOT to refer someone to the renal unit?

Referral needs to follow the appropriate guidance.

Key questions:

- Have you followed the guidance:
 - www.renal.org

Practices should also refer to any local guidance as to the information required to support referral.

In certain circumstances referral to another specialist would be appropriate initially. For example we would recommend that people with poorly controlled diabetes and heart failure and referred to the appropriate specialist first. Men with outflow obstruction should be referred to an urologist. Elderly people with complex multiple problems may benefit for initial assessment by a geriatrician.

People who are frail and stable in Stage 4 or 5 and thought to be in the last year of life or who choose the no dialysis option should be recorded as needing support and palliative care. As a minimum it is recommended that these patients are discussed formally with a nephrologist.

Where practices are experiencing difficulties accessing specialist renal advice then they should discuss this with the Commissioning Director.

29. How often do I need to measure eGFR?

eGFR should be measured annually in the following at-risk groups:

- Hypertension
- Diabetes mellitus
- Heart failure
- Vascular disease (coronary, cerebral, peripheral)
- Patients on ACEI/ARB or diuretics
- Bladder outflow obstruction until treated and the stability of the eGFR is established
- People with a family history of chronic kidney disease
- People with a genetic risk of kidney disease

In patients with known CKD, the frequency of measurement will depend upon the severity and stability of the kidney disease. As a rule of thumb:

Stage 1 and 2: annual (Not part of QOF and only diagnosed if known renal impairment)

Stage 3: six-monthly on diagnosis, annual once stable

Stage 4: three-monthly on diagnosis, six-monthly once stable

Stage 5: generally three-monthly

QOF issues, computer reporting and exception reporting

30. Why is CKD included in the GP contract Quality and Outcomes Framework (QOF)?

There is evidence that the management of the CVD risk factors of people with CKD is not always optimal. People with CKD can readily be identified if pathology labs estimate GFR when they measure creatinine. There is strong evidence that good blood pressure control in patients with CKD alters their outcome. Hence blood pressure control became one of the QOF targets from 1st April 2006

31. Who could/should be exception reported?

The usual categories of exception codes apply: "Patient unsuitable" and "Informed Dissent". There may be few situations where these apply other than in terminal illness where renal function may fail and there is no benefit to the patient in attempting to manage their renal impairment.

People who are intolerant to angiotensin converting enzyme inhibitors (ACE-I) and angiotensin II receptor blockers (ARB) are effectively exception reported as they are removed from the target population. The maximum tolerated dose of antihypertensive code has the same effect.

In the absence of proteinuria it is acceptable to exception report patients from the requirement for ACE-I/ARB prescription if their blood pressure control is satisfactory.

32. What should GPs record in their computer system?

Recording of all creatinine measures, cardiovascular risk factors (blood pressure, cholesterol and smoking habit) and evidence of renal damage including the presence of proteinuria are all important. Haemoglobin should be measured and recorded as some people with CKD become anaemic. A family history of CKD should also be recorded.

Negative results - particularly negative urine proteinuria tests and renal tract imaging results will help with more sophisticated sorting of patients at a later date.

33. How do I get more information?

Visit: www.renal.org for a comprehensive set of resources to help manage CKD, including links to calculators and guidelines.

34. Is any patient information available?

A patient information leaflet can be downloaded from:
www.renal.org/eGFR/resources/PatientCKDinf/an2007.pdf