Diabetes and chronic kidney disease: What does the new NICE guidance say?

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Article points

1. NICE guidance on early detection and management of chronic kidney disease was published in September 2008.
2. The guidance contains specific recommendations for people with diabetes.
3. There have been changes made to the staging of chronic kidney disease.
4. Blood pressure targets for those with diabetes now have a range rather than an upper limit.

Key words

- Chronic kidney disease
- NICE guidance
- Blood pressure control
- Proteinuria
- Self-management

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In 2008, NICE published guidance on early identification and management of chronic kidney disease (CKD), with some changes to the way in which people with diabetes and kidney damage should be cared for. This article provides an overview of the main changes that have been made and will discuss prevention, ongoing management and referral for those with diabetic renal disease. NICE guidance for CKD has reinforced the message that people with diabetes at risk of renal disease can work together with their primary care or specialist nurse to slow the progression of the disease.

Diabetes is the leading cause of established renal failure in the Western world (Kiberd, 2006). The cause of chronic kidney disease (CKD) in 22% of new patients requiring dialysis in the UK is diabetes, with this figure increasing to around 30% in some areas of high ethnic diversity (UK Renal Registry, 2007). However, CKD can be prevented, or its progression slowed, by strict control of blood glucose levels (Diabetes Control and Complications Trial Research Group, 1993; UK Prospective Diabetes Study Group, 1999) and blood pressure (Gaede et al, 2003) using medications that modify the renin–angiotensin system (Lewis et al, 1993) and by the adoption of lifestyle changes, such as smoking cessation (Egede, 2003).

A number of important initiatives and publications regarding the care of people with CKD have appeared in the UK in recent years. The National Service Framework (NSF) for renal services was published in two parts in 2004–5 (Department of Health [DH], 2004; 2005). Commencing in April 2006, it recommended that estimated glomerular filtration rate (eGFR) be the standard measure of kidney function in hospital laboratories (DH, 2005). Several local and national guidelines on managing CKD in primary care appeared in 2005–6 (Joint Specialty Committee on Renal Medicine et al, 2006), and the General Medical Services contract for 2006 (with amendments in 2008 and 2009) included a new Quality and Outcomes Framework (QOF) domain for CKD. Most recently, NICE published guidance on early identification and management of adults with CKD (NICE, 2008). Collectively, these initiatives and publications have impacted the

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1. It is now recommended that kidney function should be assessed using the estimated glomerular filtration rate (eGFR).
2. Almost all hospital laboratories in the UK now report eGFR alongside serum creatinine. Some ethnicities require adjustment of their eGFR. For example, those of African or Caribbean ethnicity (not mixed race) must have their eGFR value multiplied by 1.21.
3. It is important to avoid inappropriately diagnosing chronic kidney disease (CKD) when an eGFR of 60–89 mL/min/1.73 m2 is returned; an eGFR in this range is only indicative of CKD in the presence of other laboratory or clinical indicators.
4. It is important to note that kidney disease is a risk factor for cardiovascular disease, and few people progress to stage 5 CKD in comparison with those who die of cardiovascular causes.

provision of care for those with diabetes who have, or are at risk of developing, CKD.

This article gives an overview of the recent NICE guidance on CKD and highlights the central recommendations with reference to those with diabetes. Prevention, ongoing management and referral for those with diabetic renal disease is discussed in the light of the guideline.

Identifying people at risk: Measuring kidney function

Traditionally, kidney function has been measured by serum creatinine levels alone. The value of serum creatinine is determined by the rate of production of creatinine, which is dependent on muscle mass, as well excretion rate (Thomas and Gallagher, 2007). Because of wide variation in body size, weight and muscle mass, serum creatinine is an inaccurate measure of kidney function, and a normal serum creatinine result is not necessarily indicative of normal kidney function.

In 2005, the NSF made some important recommendations on how to measure kidney function (DH, 2005). It is now recommended that kidney function should be assessed using eGFR. This more sensitive test allows for early detection of CKD and enables prompt intervention to slow the deterioration of kidney function.

The NSF recommended the use of the four-variable modification of diet in renal disease (MDRD) formula in the interpretation of eGFRs (DH, 2004; 2005). The formula uses the sex, age, serum creatinine level and ethnicity of the person being tested to better reflect their true eGFR.

Almost all hospital laboratories in the UK now report eGFR alongside serum creatinine. Some ethnicities require adjustment of their eGFR. For example, those of African or Caribbean ethnicity (not mixed race) must have their eGFR value multiplied by 1.21. Assumption of Caucasian ethnicity can be made when using the MDRD if ethnicity is unknown.

Changes to the staging of CKD

The staging of CKD is now recognised internationally and is based on the Kidney Disease Outcome Quality Initiative study (Levey et al, 2006). However, the NICE (2008) guidance suggests an alteration to the staging of CKD to include two sub-categories within stage 3:

- Stage 3a (eGFR 45–59 mL/min/1.73 m^2)
- Stage 3b (eGFR 60–44 mL/min/1.73 m^2; NICE, 2008).

This is because the evidence reviewed by the NICE guideline development group suggested that the risk of mortality and cardiovascular events increased considerably when the eGFR was less than 45 ml/min/1.73m^2. This led to the proposal to adopt the sub-division of stage 3 CKD into stages 3a and 3b. In practice, this means that it is important to assess people identified as having stage 3b CKD more closely for cardiovascular risk and also for other conditions related to CKD, such as anaemia. The prevalence of anaemia rises sharply from CKD stage 3b onwards (Stevens et al, 2007), therefore people with stage 3b should have a haemoglobin test. Subsequent frequency of testing is dependent on the measured value and the clinical circumstances. The CKD stages as recommended by NICE (2008) are shown in *Table 1*.

It is important to avoid inappropriately diagnosing CKD when an eGFR of 60–89 mL/min/1.73 m^2 is returned; an eGFR in this range is only indicative of CKD in the presence of other laboratory or clinical indicators (NICE, 2008). However, most hospital laboratories only report eGFR as ">60 mL/min/1.73 m^2", rather than giving a specific value in the range of 60–90 mL/min/1.73 m^2.

NICE (2008) also recommends using the suffix "p" to denote the presence of proteinuria when staging people with CKD. Proteinuria is defined by NICE as a urinary albumin:creatinine ratio (ACR) >30 mg/mmol and is discussed below. It is important to note that kidney disease is a risk factor for cardiovascular disease, and few people progress to stage 5 CKD in comparison with those who die of cardiovascular causes. A retrospective cohort study found that only 4% of 1076 individuals progressed to end-stage kidney disease over a 5.5 year follow-up period, while

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1. It is not clear how many people in the UK have chronic kidney disease (CKD) at stages 3–5 as data have not been routinely collected until recently.
2. Not all reduced estimated glomerular filtration rates indicate CKD.
3. Microalbuminuria is an early indicator of chronic kidney disease risk, and the albumin: creatinine ratio of people with diabetes should be checked as part of their annual review.

69% had died at the end of follow-up; the cause of death was cardiovascular in 46% of cases (Drey et al, 2003).

Prevalence and differential diagnosis of CKD

It is not clear how many people in the UK have CKD at stages 3–5 as data have not been routinely collected until recently. It is estimated that the prevalence of CKD is currently around 10%, with 5% having CKD at stages 3–5, although only around 0.4% of the population may eventually require dialysis or a renal transplant (Stevens et al, 2007).

Not all reduced eGFRs indicate chronic kidney disease. While rare, the possibility of a lowered eGFR being indicative of acute renal failure should be considered, especially in individuals with new signs and symptoms. For this reason, following documentation of a reduced eGFR, a comparison with a previous reading must be made to ensure that renal function is not rapidly deteriorating.

Age-related decline in the glomerular filtration rate is common. A loss of up to 1 mL/min/1.73 m^2/year after 40 years of age is possible (Eriksen and Ingebretsen, 2006). The eGFR of a healthy 80-year-old person can be as low as 60 mL/min/1.73 m^2 (Thomas and Gallagher, 2007). This decline is probably a result of vascular disease rather than a "normal" finding, and intervention should be as for other cardiovascular risk factors. Indeed, the NICE (2008) guideline development group reviewed the evidence and identified that in people aged >70 years, an eGFR in the range 45–59 ml/min/1.73m^2, if stable over time and without any other evidence of kidney damage, is unlikely to be associated with CKD-related complications. Even in conjunction with the MDRD formula, eGFRs identify a high proportion of older women as having CKD, and an appreciation of an individual's age is therefore essential in interpretation.

Specific NICE guidance for people with diabetes at risk of CKD

NICE (2008) recommendations for CKD are summarised in *Table 2*.

Proteinuria

Microalbuminuria is an early indicator of CKD risk. The ACR of people with diabetes should be checked as part of their annual review. The ACR is taken from a reasonably concentrated urine sample (plain pot with no preservative; sample taken in the early morning is recommended but not essential).

An ACR >2.5 mg/mmol in a male or >3.5 mg/mmol in a female indicates microalbuminuria. Those who return an abnormal ACR should be offered angiotensin-

Table 1. Staging of chronic kidney disease (CKD) as given by NICE (2008).

CKD stage	eGFR (mL/min/1.73m^2)	Description	eGFR test frequency
1	>90	Normal or increased eGFR, with other evidence of kidney damage.	12 monthly
2	60–89	Slight decrease in eGFR with other evidence of kidney damage.	12 monthly
3a	45–59	Moderate decrease in eGFR with or without other evidence of kidney damage.	6 monthly
3b	30–44	Moderate decrease in eGFR with or without other evidence of kidney damage.	6 monthly
4	15–29	Severe decrease in eGFR, with or without other evidence of kidney damage.	3 monthly
5	<15	Established renal failure. Dialysis or transplantation may be required.	6 weekly

eGFR = estimated glomerular filtration rate.

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1. The 2008 NICE guidance has brought the way in which urinary protein among people with diabetes is quantified in line with the way urinary protein is measured for those who do not have diabetes.
2. In people with diabetes, NICE (2008) now recommends that systolic blood pressure be kept below 130 mmHg (target range 120–129 mmHg) and diastolic blood pressure below 80 mmHg.
3. It is particularly important that people with diabetes and poor kidney function are referred to a renal team in a timely way.

Table 2. A summary of NICE (2008) chronic kidney disease guidance on the care and management of people with diabetes.

- Screen for microalbuminuria annually using using ACR.
- Prescribe angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers if ACR results are abnormal, even if the person is normotensive.
- Maintain systolic blood pressure below 130 mmHg (target range 120–9 mmHg) and diastolic blood pressure below 80 mmHg.
- Optimise glycaemic control.
- Measure, assess and manage cardiovascular risk factors aggressively and educate about smoking cessation.
- Use eGFR to monitor renal function annually or more frequently if eGFR is falling by >5 mL/min/1.73 m^2/year.
- Refer the person to a renal unit if eGFR is <30 mL/min/1.73 m^2, or if their kidney function is decreasing rapidly.

ACR = albumin : creatinine ratio; eGFR = estimated glomerular filtration rate.

converting enzyme inhibitors or angiotensin-receptor blockers, even if normotensive (see the discussion of blood pressure). Importantly, the presence of protein in the urine is an independent risk factor for cardiovascular disease (Wali and Henrich, 2005).

The 2008 NICE guidance has brought the way in which urinary protein among people with diabetes is quantified in line with the way urinary protein is measured for those who do not have diabetes. ACR is now the recommended method for detecting and identifying proteinuria for everyone as it has greater sensitivity than the protein : creatinine ratio (PCR) for low levels of proteinuria.

As mentioned previously, an indicator related to ACR (or PCR) is included in the Quality and Outcomes Framework from 1 April 2009. Information sheets have been produced for GPs that summarise the benefits of using ACR and provide practical guidance on its use (see http://tinyurl.com/c3zggo).

Blood pressure control

In people with diabetes, NICE (2008) now recommends that systolic blood pressure be kept below 130 mmHg (target range 120–129 mmHg) and diastolic blood pressure below 80 mmHg. This guidance marks a change to the previous blood pressure targets by providing a range, rather than only an upper limit. Similar guidelines, such as the NICE (2006) hypertension guideline, give a range and clinicians may find this useful.

Referral

NICE (2008) suggests that people in the following groups should be referred for specialist assessment:

- Those with stage 4–5 CKD.
- Those with heavy proteinuria (ACR ≥70 mg/mmol), unless known to be due to diabetes and already appropriately treated.
- Those with an ACR ≥30 mg/mmol together with haematuria.
- Those with a rapidly declining eGFR (>5 mL/min/1.73 m^2 in a year or >10 mL/min/1.73 m^2 within 5 years).
- Those with hypertension that remains poorly controlled despite the use of at least four antihypertensive drugs at therapeutic doses (see NICE, 2006).
- Those with, or suspected of having, rare or genetic causes of CKD such as suspected renal artery stenosis.

It is particularly important that people with diabetes and poor kidney function are referred to a renal team in a timely way. This is because there is a relentless decline of eGFR in people with diabetes and proteinuria at an average of 10–12 mL/min/year (Lee, 2005), so ample opportunities for considering choice of dialysis or transplant therapy must be made available. However, it is important to note

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1. At least two-thirds of people with overt nephropathy will die from cardiovascular disease before they require renal replacement, with a mortality rate 5- to 8-fold higher than in the average population.
2. In some cases, people with chronic kidney disease choose not to have dialysis, preferring "supportive care", or as it is sometimes termed "conservative management".
3. People with diabetes should be informed that their condition puts them at risk of CKD, and that providing an annual urine sample for microalbuminuria testing will help to identify if they are at risk.

that at least two-thirds of people with overt nephropathy will die from cardiovascular disease before they require renal replacement, with a mortality rate 5- to 8-fold higher than in the average population (Thomas and Viberti, 2005).

Ideally, the renal team needs at least a year to prepare people, both physically and emotionally, for dialysis (DH, 2004). People not referred to a renal team in good time are less likely to receive interventions that could alter the progression of their CKD (i.e. optimum blood pressure control), have a worse clinical state at the start of dialysis, have longer periods of hospitalisation and poorer survival rates (Lameire and Van Biesen, 1999; Roderick et al, 2002).

In some cases, people with CKD choose not to have dialysis, preferring supportive care, or as it is sometimes termed "conservative management". Refusing dialysis is a very difficult decision for people with CKD and their families to make, but often renal teams have specialist nurses and counsellors who can assist them during the decision-making process.

Education and self-management

NICE (2008) recommends that "high quality education at appropriate stages of the person's condition [should be offered] to enable understanding and informed choices about treatment". It is important to tailor the information to the stage and cause of CKD, and to explain associated complications and the risk of progression.

People with diabetes should be informed that their condition puts them at risk of CKD, and that providing an annual urine sample for microalbuminuria testing will help to identify if they are at risk. The link between high blood pressure and CKD should be highlighted, as should the fact that the drugs taken to control blood pressure also delay kidney disease progression. Importantly, people should be told that, to a large extent, the rate of kidney damage can be slowed through good self-management (e.g. good blood pressure and blood glucose control).

Self-management opportunities for people with CKD are summarised in *Table 3* and some educational resources are listed in *Box 1*.

Table 3. Opportunities for people with chronic kidney disease (CKD) to exercise self-management.

- **Urine test:** Explain the importance of returning an annual urine test (using ACR), which will help identify if at risk of CKD.
- **Blood test:** Explain the importance of attending for blood tests to monitor kidney function.
- **Blood pressure control**: Explain the importance of blood pressure tablets. These are not only for blood pressure control, but also delay the progression of CKD. Remind people to report side-effects.
- **Blood pressure monitoring:** Encourage people to monitor their own blood pressure and provide training on how to do this.
- **Lifestyle changes:** Encourage smoking cessation and suggest diet modifications (avoiding processed foods and those high in salt and fat). Encourage people to take exercise and keep to a healthy weight.
- **Diabetes control:** Explain that good blood sugar control will delay the progression of CKD.
- **Medicines management:** Give advice on buying over-the-counter tablets (particularly anti-inflammatories). Encourage people to disclose to their pharmacist that they have CKD.

ACR = albumin : creatinine ratio; CKD = chronic kidney disease.

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1. Recent NICE guidance for CKD reinforces that people with diabetes at risk of renal disease can work together with their primary care or specialist nurse to slow the progression of the condition.

Conclusion

Recent NICE guidance for CKD reinforces that people with diabetes at risk of renal disease can work together with their primary care or specialist nurse to slow the progression of the condition. This can be achieved by strict blood pressure and blood sugar control, prescription of medicines that modify the renin–angiotensin system and lifestyle changes. ■

Box 1. Web-based resources for healthcare professionals and people with chronic kidney disease.

An advanced online educational resource for GPs and practice nurses initiated by the Department of Health and the Chronic Kidney Disease Forum of the British Renal Society: www.ckdonline.org

Kidney Research UK and British Renal Society DVD. Can be purchased at: www.kidneyresearchuk.org/content/view/385/533

National Kidney Federation leaflets. Can be downloaded at: www.kidney.org.uk/Medical-Info/index.html or ordered by telephone.

Department of Health (2004) *The National Service Framework for Renal Services, Part One: Dialysis and Transplantation*. DH, London

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