CKD Made Easy – a guide for general practice

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Outline
In the past, kidney medicine was regarded as rare, complicated and best left to the specialists. Now it is an everyday part of primary care. This review demystifies chronic kidney disease. It uses real-life examples and gives practical suggestions for treating patients with chronic kidney disease (CKD) from stages 1 to 5. Citing recent trial evidence, it signposts you to information and educational resources for clinicians and patients.

Introduction
Good primary care, working in collaboration with secondary care, is crucial for the successful management of all stages of CKD (defined below). To confirm CKD, eGFR must be measured on two or more occasions at least three months apart. Most patients with CKD are at stage 3 and can be managed effectively in the community. Specialist care is more often needed for stages 4 and 5.

<table>
<thead>
<tr>
<th>Stage</th>
<th>eGFR ml/min/1.73m²</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>90+</td>
<td>Normal kidney function but urine findings or structural abnormalities or genetic trait point to kidney disease</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td>Mildly reduced kidney function and other findings point to kidney disease as for stage 1</td>
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<tr>
<td>3A</td>
<td>45-59</td>
<td>Moderately reduced kidney function</td>
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<tr>
<td>3B</td>
<td>30-44</td>
<td>Moderately reduced kidney function</td>
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<tr>
<td>4</td>
<td>15-29</td>
<td>Severely reduced kidney function</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15 or on dialysis</td>
<td>Very severe or end stage kidney failure</td>
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CKD that has worsened over years can suddenly decompensate to cause acute problems such as pulmonary oedema. If you identify such patients early, you will reduce the chances of an emergency hospital admission. Following an unplanned start of dialysis, mortality in the first year is doubled and time spent in hospital tripled compared to a planned start. Thanks to improved collaborative working, the proportion of patients starting dialysis without adequate predialysis nephrology care has fallen steadily in the UK.
Screening of the well population for albuminuria or eGFR is not cost effective, nor clinically appropriate. On the other hand, targeted screening is worthwhile. NICE recommends that you offer testing for CKD, i.e. blood for eGFR and urine for albumin:creatinine ratio, to people who have:

- diabetes, hypertension, ischaemic heart disease, heart failure, peripheral vascular disease or cerebrovascular disease
- structural urinary tract disease, kidney stones or an enlarged prostate
- a multisystem disease with potential kidney involvement (for example, systemic lupus erythematosus)
- a family history of stage 5 CKD or hereditary kidney disease
- blood or protein detected on urinalysis

Test for microscopic haematuria with reagent strips; there is no need to use urine microscopy to confirm a positive result. Confirm results of 1+ or more by a positive result on two out of three repeat tests. Investigate for urinary tract malignancy in appropriate patients, such as those aged over 50 years. Macroscopic haematuria always requires an explanation, whatever the age of the patient.
Patients with persistent microscopic haematuria who do not have proteinuria or a known urological cause are still at an increased risk of hypertension, proteinuria and reduced GFR in the future. They should be followed up annually with repeat testing for haematuria and proteinuria on urinalysis, eGFR and blood pressure, as long as the haematuria persists.

NICE recommends that people receiving long-term lithium have their eGFR checked at least every six months and those taking systemic NSAIDs at least annually.

Should I tell patients they have CKD?

The term ‘chronic kidney disease’ includes two words that mean different things to patients and clinicians. To lay people, ‘chronic’ implies severe, serious and possibly cancer; ‘disease’ relates to feeling ill. None of these applies to the early stages of CKD and it is important not to raise unnecessary alarm. However, no one wants to miss the opportunity of avoiding severe illness in the future.

When explaining CKD, you may find it helpful to use an everyday analogy - money. “At birth, your two kidneys normally have enough kidney function to last your whole life. This is like having a lot of money in your kidney savings account. As you get older, your kidney function slowly goes down and your savings are used up. If you do not have normal kidneys to start with, or they lose function more quickly than normal, you will run out of ‘savings’ and start to feel ill.”

How do I identify patients who are likely to be troubled by their kidney disease?

Simple urinalysis is the first step. The greater the amount of proteinuria or albuminuria, the greater is the risk that GFR will decline in future. Conversely, the absence of albuminuria in a patient with CKD is a good prognostic sign.

Patients who suffer one or more episodes of acute kidney injury (previously termed acute renal failure) have an increased risk of advanced CKD and death in the long term, even if their GFR recovers following the acute episode. Highlight this past medical history in their records.

Younger patients with kidney disease, such as damage due to reflux in childhood, are at a high lifetime risk of progressing to advanced CKD. They may develop proteinuria and hypertension before the decline in GFR. Similarly, patients under the age of 40 years with idiopathic hypertension are at a higher risk, especially if they have proteinuria.

You should counsel younger women with CKD or proteinuria about their increased risk of complications during pregnancy. The lower the eGFR, the more likely they are to have pre-eclampsia, premature delivery and neonatal complications. In turn, the
increased kidney blood flow in pregnancy can accelerate the decline in GFR. Advise women about contraception and consider referring them to an obstetrician or nephrologist when they are planning a pregnancy.

**Which patients should I refer to a nephrologist?**

Patients without diabetes mellitus who have more than 1 gram per day of proteinuria (urine albumin:creatinine ratio >70 mg/mmol or protein:creatinine ratio >100 mg/mmol) are likely to have a significant glomerular disease. You should refer them for consideration of a renal biopsy.

In patients with diabetes, these levels of proteinuria put them at very high risk of progressive loss of GFR. They too should be referred to a nephrologist to make sure everything is being done to reduce this risk.

Patients with both haematuria and proteinuria (urine albumin:creatinine ratio >30 mg/mmol with dipstick haematuria) who do not have symptoms of urinary tract infection may have glomerulonephritis. This may be a kidney-limited disease with no other symptoms, or be part of a systemic disease such as SLE or vasculitis. A vasculitic illness may include low-grade fever, tiredness, weight loss, joint pains, rash and ENT symptoms. GFR may decline rapidly so repeat the eGFR measurement a week after the first detection. Discuss the details with a nephrologist at an early stage. By getting treatment started quickly, you may avoid the need for long-term dialysis.

Patients with poorly controlled blood pressure (>150/90 mmHg) have a higher risk of kidney failure and death. You may need specialist advice in a minority of patients whose blood pressure is not controlled even though they take the medication regularly.

Older men with reduced eGFR and symptoms such as frequency, dribbling and nocturia may have chronic urinary retention and hydronephrosis. These men may be unaware of the severity of the problem, assuming the symptoms are a sign of old age. If you find suprapubic dullness and a palpable bladder you should make an urgent hospital referral. Otherwise request an ultrasound scan to be performed within 4 weeks.

Patients with stage 4 CKD who are not unwell and whose eGFR is not deteriorating may not need to attend an outpatient appointment. However, it is a good idea to get the advice of your local nephrologist to make sure nothing important is being overlooked. Conversely, patients with stage 5 CKD should be reviewed in person by a nephrologist so that a long-term treatment plan can be discussed, unless they are too unwell or unwilling to travel to the clinic.

You may be asked to monitor patients with uncommon causes of CKD as part of a disease-specific management plan. This should include clear criteria for when to seek
advice from the nephrologist. All patients with CKD should take an active part in their care plan, monitoring their own blood pressure and keeping a track of their eGFR. Patients can access their own blood results securely via the Internet using Renal Patient View (www.renalpatientview.org). Patients with rare kidney diseases may wish to join a self-help group linked to Rare Disease UK (www.raredisease.org.uk).

**Monitoring kidney function – the power of the eGFR graph**

Having identified who is at risk of kidney failure, you and the patient need a simple and effective tool for monitoring the CKD. This is the eGFR graph.

Symptoms are of no help in tracking the early stages of CKD. Instead, the eGFR graph acts as a map of the kidney history. The following examples demonstrate its value in describing the natural history of kidney disease. See if you can work out from the graphs when the management could have been better.

![eGFR graph](image)

*This man was referred to a nephrologist in late 2005 because of a progressive decline in eGFR. He had diabetes and was feeling more tired but did not volunteer any new symptoms. On examination, he had a prominently distended bladder. eGFR improved following catheterisation to relieve his chronic urinary retention and bilateral hydronephrosis, but sadly not to its previous level.*
This woman had diabetes and macroscopic haematuria. An ultrasound scan revealed a renal cell carcinoma that was removed in April 2003. After the operation, her eGFR fell by 50% but then recovered slightly as some nephrons increased their filtration rate to compensate for the loss of one kidney.

This man had peripheral vascular disease. An ultrasound scan in 2001 showed a small left kidney that had become ischaemic over the preceding two years, leading to a decline in the combined GFR of both kidneys.
This lady had diabetes and poorly controlled blood pressure despite taking an ACE inhibitor. At her first consultation with a nephrologist in 2005, she was shown her eGFR graph and encouraged to measure her own blood pressure at home, with a target systolic pressure of less than 140mmHg. A diuretic was added to the ACE inhibitor. Following control of her blood pressure, the decline in her eGFR was arrested.

This lady had diabetes and normal kidney function until she suffered a myocardial infarction (MI) in 2009. This was complicated by acute kidney injury (AKI), which only partially resolved. In 2011 she suffered a second MI, again complicated by AKI. She was left with moderate to severe CKD and at risk of needing dialysis in the future.
This man had type 1 diabetes and his eGFR was slowly declining. In late 2009, his eGFR dropped much more rapidly and urinalysis was positive for blood and protein. A kidney biopsy showed crescentic glomerulonephritis. His GFR responded well to high dose steroids and cyclophosphamide.

Making sense of variation in eGFR.
NICE guidance suggests that a decline in eGFR of >5 ml/min/1.73m² per year or >10ml/min/1.73m² within 5 years should prompt a search for remediable causes. These numerical rules are hard to apply when the eGFR is varying month by month. The eGFR graph makes it easy to see whether a drop is part of a consistent downward trend, as in the example below.

This man suffered with bipolar disorder and was taking long-term lithium therapy. Lithium can cause both reversible changes in fluid balance and irreversible damage to renal tubules. Reviewing the results over six years makes the declining trend due to irreversible damage obvious.
Judge the most recent result against the previous range of variation in eGFR for that patient. Variation is greatest when the eGFR is >60 ml/min/1.73 m$^2$. eGFR values at this level are calculated from near normal levels of serum creatinine. Variation at lower levels of serum creatinine leads to large variation in the eGFR because the two are inversely related. Conversely, variations in eGFR below 45 ml/min/1.73 m$^2$ are more likely to represent important changes in GFR.

**Misleading estimates of GFR**

Estimated GFR (eGFR) is calculated from the serum creatinine concentration. Changes in the serum creatinine concentration may not always be due to changes in the true GFR.

Variation in the laboratory creatinine assay is proportionally greatest in or near the normal range. Hence most laboratories do not report an exact figure for eGFR >60 ml/min/1.73 m$^2$ because the confidence interval at this level is so wide.

Changes in meat intake can lead to small short-term changes in the serum creatinine concentration. However, you do not usually need to ask the patient to starve before the blood test.

Body builders and athletes have a large muscle mass. This produces a lot of creatinine, increases the serum creatinine level and gives a misleadingly low eGFR. In addition, some take dietary protein and creatine supplements. These are digested to release urea and creatinine into the bloodstream and so further reduce the estimated GFR. To give a more consistent estimate of GFR, take blood samples after a week without supplements.

Take care to use the eGFR correction factor for African-Caribbean race where appropriate – this increases the estimate by 21%.

Some drugs can alter the serum creatinine level without affecting the true GFR. Trimethoprim inhibits the secretion of creatinine by the kidney tubules, leading to a rise in serum creatinine concentration. Fibrates can alter muscle creatinine metabolism and increase serum creatinine. As the true GFR is unaltered, these effects do not alter the serum urea - a helpful pointer to this explanation.

Finally, if a change in eGFR seems inexplicable, check whether the patient’s gender has changed between male and female, either surgically or inadvertently on the blood test request form.

If you suspect that a persistently reduced eGFR may not reflect the true GFR, check for other signs of kidney disease such as proteinuria, hypertension and abnormalities on ultrasound.
What does proteinuria mean?
Proteinuria results from damage to the endothelial cells and basement membranes of the glomeruli. It is also a sign of damage to the vascular endothelium elsewhere in the body. Hence, proteinuria is an important risk marker for future worsening of kidney function and for cardiovascular events such as heart attack and stroke. The greater the amount of proteinuria, the greater is the risk of loss of GFR and the faster it is likely to decline.

Day-to-day variation in the amount of proteinuria can be large, 100% or more, due to the effects of exercise, diet and blood pressure. However, longer-term trends in the amount of proteinuria are useful guides to changes in the risk of kidney damage. In patients with CKD and high blood pressure, a sustained reduction in proteinuria is an encouraging sign that improved control of blood pressure is giving long-term benefits.

The strength of the correlation between proteinuria and the risk of kidney failure has led to it being used as a surrogate outcome in drug trials of patients with CKD. Unfortunately, not all ways of reducing proteinuria also reduce the risk of kidney failure. Combining drugs that inhibit the renin-angiotensin system (such as ACE inhibitors, angiotensin receptor blockers and renin inhibitors) reduces proteinuria but longer-term trials have shown an increase in the risk of kidney failure in some patients.

Proteinuria is a guide to the long-term risk of kidney and cardiovascular disease so there is little value in measuring it repeatedly in elderly patients with limited life expectancy.

Management of patients with CKD
Your two main roles in the management of patients with kidney disease are: 1) to minimize the cardiovascular risk associated with CKD, and 2) to reduce the rate of loss of kidney function. The actions required for both are similar. Complex management of kidney diseases, such as immunosuppressive drugs, should remain in secondary care.

The CKD QOF encourages practices to develop a CKD register of patients with stage 3-5 disease, record BP and urine ACR measurements at least annually, control blood pressure (target <140/85) and use Angiotensin Converting Enzyme Inhibitors (ACE-I) or Angiotensin Receptor Blockers (ARB) in patients with proteinuria. You may wish to expand your QOF CKD register to include patients with abnormal kidneys or albuminuria and eGFR >60ml/min/1.73m².

Most patients with CKD are on at least one other chronic disease register, such as diabetes, coronary heart disease or hypertension. You may wish to operate a combined vascular disease clinic to avoid duplication of effort. Organise primary and
secondary prevention of cardiovascular disease according to the usual guidelines. Most patients will need to be reviewed every 6-12 months depending on their clinical need.

Get the results of tests for serum urea and electrolytes, eGFR, corrected calcium, phosphate, HbA1c if diabetic, lipids, full blood count, and urine ACR (preferably an early morning sample) and share them with the patient a week or two before the clinical review. During the face-to-face consultation, discuss the test results and home blood pressure readings, and agree goals for the future. Carry out a general health check, and assess any lower urinary tract symptoms and cardio-respiratory symptoms such as breathlessness and swelling.

**Blood pressure – the number one priority**

Effective blood pressure control is the top priority in CKD. For patients without diabetes, NICE recommends a systolic BP in the range 120-139 mmHg and diastolic BP <90 mmHg. In those with diabetes or significant proteinuria (urine ACR >70 mg/mmol), systolic BP should be in the range 120-129 mmHg and diastolic BP <80 mmHg.

Emphasise ways that the patient can take control of their own blood pressure. Home blood pressure meters are inexpensive. Most arm cuff meters have been validated as accurate but wrist meters do not give reliable readings. Patients do not become anxious from measuring their own blood pressure. They may become insistent that their blood pressure is not adequately controlled but that is to be welcomed.

Even though few doctors wear white coats, the ‘white coat’ effect can be very marked and lead to inappropriate escalation of medication. Home readings are a much better guide to long-term outcomes. Set a simple blood pressure goal: “The top number should be less than 140 almost every time you check it.”

Patients often ask about possible dietary changes that may lower blood pressure. There is strong evidence that reducing daily salt intake increases the antihypertensive effect of drugs such as ACE inhibitors. In patients with CKD, lower salt intake is associated with a lower risk of ESRD (Vegter S et al., 2012). Patients should not add salt at the table and should avoid processed foods with a high salt content. Salt substitutes may contain large amounts of potassium chloride, which is contraindicated in some CKD patients.

Advise patients to reduce their salt intake over a period of weeks. A rapid and large reduction will mean food suddenly tastes bland and your advice will probably be ignored. Reduce slowly and the taste buds will adapt to the new diet and food will continue to be enjoyable. Indeed, a variety of subtle flavours will emerge when the overwhelming taste of salt is removed.
Patients with CKD and hypertension lose the usual night-time ‘dip’ in blood pressure. Advise them to take at least one of the blood pressure agents at bedtime to maximise the blood pressure-lowering effect during sleep. Simply changing the time the tablets are taken can reduce the risk of cardiovascular events by two-thirds (Hermida RC et al., 2011).

Apart from blood pressure control, there is no convincing evidence to support other interventions for slowing the decline in GFR. Low protein diet was studied in the Modification of Diet in Renal Disease study. The MDRD eGFR formula was the main product of this study - low protein diet did not have a significant effect. Similarly, lowering cholesterol does not slow the rate of decline in GFR.

**Healthy living - healthy kidneys**

Lifestyle advice for people with CKD is no different to general healthy living advice: stop smoking, drink alcohol in moderation and not every day, eat more fruit and vegetables, take regular exercise and, if obese, lose weight.

Smoking is a risk factor for the development CKD and is associated with more rapid decline in GFR and increased mortality. Knowledge that the kidneys are affected may help motivate a patient to quit. Signpost patients to smoking cessation support at every review.

Excess alcohol consumption contributes to CKD through its link with obesity and cardiac disease. Incorporate brief intervention, including an alcohol screening questionnaire such as the AUDIT C, into the review (www.alcohollearningcentre.org.uk/_library/AUDIT-C.doc).

Drinking two or more cola drinks per day, diet or regular, has been associated with a doubling of the risk of CKD. Other carbonated drinks showed no association. This may be due to the phosphoric acid in cola.

Many fruits and vegetables have an important acid-neutralising effect. If taken in sufficient amounts, they are as effective as sodium bicarbonate tablets in reducing urinary albumin excretion and other markers of kidney injury (Gorayal N et al., 2012).

30 minutes of moderately intense physical activity should be taken on a regular basis, ideally 5 times a week. Kidney disease is not worsened by exercise and the health benefits of exercise extend even to patients on dialysis. Some kidney dialysis units offer exercise programmes that patients can do during the dialysis treatment.

Obesity has mixed associations with kidney disease and outcomes. It leads to increased proteinuria, and extreme obesity can cause glomerular damage (focal segmental glomerulosclerosis). On the other hand, in patients with end stage kidney
disease, obesity loses its association with mortality. This is possibly because it protects against malnutrition in patients with severe chronic disease.

**How can I use ACE inhibitors and ARBs safely?**

Drugs that inhibit the renin-angiotensin-aldosterone system (RAAS) are used frequently in patients with CKD. They include angiotensin converting enzyme inhibitors (ACE-I, drug names ending in '-pril'), angiotensin II receptor blockers (ARB, ending in '-sartan') and renin inhibitors, all of which act to reduce the effect of angiotensin-II (A-II). A-II is a potent vasoconstrictor that also stimulates the adrenal glands to produce aldosterone. Aldosterone stimulates potassium excretion by the kidney tubules and is blocked by drugs such as spironolactone.

If you used them appropriately, ACE-I and ARBs can protect kidney function and reduce the risks of heart failure and mortality; use them inappropriately and they can cause acute kidney injury, severe hyperkalaemia and precipitate dialysis. How can you get the balance right?

To understand how these drugs can heal and harm, you need to understand how angiotensin-II (A-II) affects the kidney. A-II acts on the small muscular blood vessels that take blood away from the glomeruli (the efferent arterioles). Vasoconstriction of these vessels is needed to maintain pressure in the blood vessels behind them, i.e. within the glomeruli. This hydrostatic pressure forces fluid through the pores in the endothelial cells and across the glomerular basement membrane, in other words causes glomerular filtration.

Imagine you are using a garden hose on a summer’s day, spraying your flowerbeds and anybody nearby. To get a strong spray you need the tap turned full on. This is like a high arterial blood pressure. To vary the spray you change the resistance on the end of the hose. The harder you press with your thumb, the greater the resistance, the higher the pressure and the further the spray goes. This is like varying the resistance in the efferent arterioles – vasoconstriction increases glomerular filtration.

So if you block A-II with an ACE-I, you allow vasodilatation of the efferent arterioles and relieve the pressure within the glomeruli. If this pressure was damaging the glomerular cells and membranes, reducing the pressure will reduce the damage and preserve kidney function in the long term. Proteinuria is a sign of membrane damage and so ACE-I’s are particularly suitable for hypertensive patients with proteinuria.

The following is an example of how effective an ACE-I can be.
This man with type 1 diabetes presented to the renal clinic in May 2009 with gross peripheral oedema, proteinuria 10g/24 hours and serum albumin 21g/L, i.e. nephrotic syndrome. His eGFR had dropped from 114ml/min/1.73m² in March 2007 to 38ml/min/1.73m² in May 2009. His blood pressure was poorly controlled by a calcium channel blocker and he had not been taking an ACE-I. A renal biopsy confirmed diabetic nephropathy. Ramipril 5mg per day was started. Proteinuria reduced to <3.5g/24hours, oedema cleared, serum albumin returned to normal and the rate of decline in eGFR was greatly reduced.

Reducing the pressure within the glomeruli can cause a drop in GFR. This may recover towards the previous level over subsequent weeks but sometimes the drop is greater and does not recover. To understand why this happens, let’s return to our garden hose.

If the tap attached to the hose is turned down, the spray becomes less powerful. This is like having a lower systemic arterial pressure due to cardiac failure, vasodilator drugs or salt and water depletion by diuretics or diarrhoea. If someone stands on the hose, the spray becomes even weaker. This is like narrowing the main renal arteries or the smaller arteries within the kidney, which reduces the pressure in the glomeruli. Glomerular filtration then becomes critically dependent upon there being a lot of resistance to blood flowing out of the glomeruli. If you stop pressing hard with your thumb, the spray drops to a trickle.
Patients at risk of harm from ACE-I and ARBs are those with low blood pressure due to cardiac failure and those with vascular disease who have narrowing in the renal arteries or afferent arterioles. If the eGFR drops by >25%, the ACE-I or ARB should be stopped and the eGFR rechecked after 1-2 weeks.

A critical ACE-I or ARB effect can be identified from the pattern of changes in serum potassium, urea and creatinine. Aldosterone normally increases potassium excretion into the urine. When it is blocked, serum potassium rises, often to >6mmol/L. With the drop in GFR, urea increases to a greater extent than creatinine, perhaps doubling compared to a 50% rise in creatinine. This is because urea diffuses back into the blood stream from the filtered fluid within the tubules. Creatinine cannot diffuse back and is actively pumped out by the tubules, so its rise is comparatively smaller than that of urea.

Patients who initially tolerate an ACE-I or ARB may, after years of taking them, develop the distinctive abnormalities in serum potassium, urea and creatinine, as illustrated in the next case.

This man with diabetes was treated for many years with the ACE-I lisinopril. Because his home blood pressure remained too high and eGFR was falling, irbesartan (an ARB) was added in 2004. (NB. This preceded evidence that combination therapy can be harmful.) In 2008 there was sudden drop in eGFR, with a rise in urea to 22mmol/L and potassium to 7.5mmol/L.
The ARB and ACE-I were stopped. Potassium returned to normal and the eGFR rose towards the previous baseline. Blood pressure was controlled with other drugs. Proteinuria appeared for the first time, presumably due to increased pressure within the glomeruli.

**Systematic care of the CKD population**

Many patients fail to get access to treatments that would reduce their risk of kidney damage. Those who have the biggest problems with managing their own health and in accessing healthcare are also at the highest risk of kidney failure. This is particularly an issue with CKD because it is asymptomatic. However, patients at high risk of kidney failure can be identified from their eGFR and ACR result in existing computer databases.

Having sought these patients out, refer them to a specialist clinic at the earliest signs of progressive damage, such as heavy proteinuria or declining eGFR. Personalised education and support for self-care can then reduce their risk of kidney failure (Rayner HC et al. 2011). Such organised systems can be operated within a general practice or from a hospital laboratory and kidney unit.

GP, practice nurses, hospital and community-based diabetes nurses and doctors can be integrated using information technology. Shared electronic patient records can increase the efficiency and effectiveness of care. In Bradford, the number of traditional nephrology referrals has been halved, improving the lives of patients who no longer have to attend the hospital (Stoves J et al., 2010).

**Management of CKD patients who become unwell**

Intercurrent illness in patients with CKD may lead to acute worsening of kidney function (‘acute-on-chronic kidney injury’). Patients taking diuretics are vulnerable, especially if they have high fever, sweating, vasodilatation and low blood pressure. Diarrhoea and vomiting can rapidly cause salt and water depletion. Patients with an ileostomy are at high risk of acute kidney injury due to fluid loss.

Community nurses monitoring frail and elderly patients need to be alert to these risks and seek a medical review at an early stage. A drop in blood pressure to ‘low-normal’ levels (e.g. 110/60 mmHg) in an elderly hypertensive person with CKD may lead to a marked drop in GFR due to reduced pressure within the glomeruli.

If the blood pressure is low, suspend any drug that may be contributing to the drop (e.g. diuretics, ACE-I, ARB, or other antihypertensives) and keep the patient under close review. Stop non-steroidal anti-inflammatory drugs (NSAIDs) - they can reduce kidney blood flow by blocking the action of vasodilatory prostaglandins.
Stop metformin in patients with diabetes if the eGFR falls below 30ml/min/1.73m². Metformin is not nephrotoxic and does not affect eGFR. However, metformin increases the risk of lactic acidosis in patients with acute kidney injury.

Once the acute illness has resolved, review the patient’s medication and restart drugs when appropriate. Blood sugar control is often much worse when metformin is stopped so restart it once the eGFR is above 30ml/min/1.73m². If you omit diuretics and ACE-I/ARBs for too long in patients with heart failure they may slip into pulmonary oedema.

**Management of patients with CKD stages 4 and 5**

When the eGFR falls below 30ml/min/1.73m², complications of CKD become more common. These include acidosis, anaemia, falling serum calcium, and rising serum phosphate and parathyroid hormone.

Acidosis is diagnosed by serum bicarbonate <22 mmol/L. If this persists despite a diet high in fruit and vegetables, give sodium bicarbonate supplements to correct the serum level. The risk of sodium overload with these supplements is low. Correction of acidosis delays the progression of advanced CKD and the need for dialysis.

Renal anaemia can be treated with iron and erythropoietin. Do not fully correct the haemoglobin concentration with erythropoietin as this increases the risk of stroke. Treatment is not usually started until the Hb falls below 10g/dl. Treating anaemia does not slow down the decline in GFR.

Damaged kidneys are unable to activate vitamin D and this leads to a fall in serum calcium. Correct this with alfacalcidol or calcitriol as these forms of vitamin D are already activated. Over-treatment may cause hypercalcaemia, leading to an acute drop in GFR. Chronic moderate over-treatment may accelerate vascular calcification. Delay treatment until the serum calcium is near or below the lower limit of normal unless there are clear signs of osteomalacia such as a raised alkaline phosphatase level. A rise in serum phosphate probably signifies advanced kidney failure and should be managed in collaboration with a nephrologist.

At least a year before the predicted time when dialysis will be needed, care should be shared with a specialist multi-disciplinary predialysis clinic. Shared decision making is at the heart of care for patients in this clinic. Whilst a clinician can describe the symptoms and limitations likely to confront a patient, only the patient can decide how to cope with them and what adjustments they wish to make to their way of life. Patient autonomy is paramount, even if the course of action they choose may seem unreasonable to you.
Patients are given a choice of type of dialysis and are guided through the decision process. Informed patient choice requires information to be provided in a balanced and understandable way, clarifying how each treatment may help or hinder the patient in achieving the things that are most important to them. For most patients, retaining their independence is a high priority and so they are encouraged and supported in overcoming the hurdles of dialysing at home. Information for patients is available (www.patient.co.uk/health/Chronic-Kidney-Disease.htm) and NHS shared decision aids can be incorporated into the discussions (www.nhsdirect.nhs.uk/DecisionAids.aspx).

Symptoms of kidney failure such as lethargy, sleep disturbance, itching, nausea and vomiting become more severe when eGFR falls below 10 ml/min/1.73m². Dialysis can safely be delayed until symptoms of kidney failure justify the burden of treatment. There is no benefit from starting dialysis earlier based upon the eGFR alone.

Long-term outcomes are much better if patients start dialysis with a permanent modality such as CAPD or HD via an arteriovenous fistula. The high risk of morbidity and mortality associated with referral to a nephrologist less than 3 months before starting dialysis is largely due to the temporary vascular catheters needed for dialysis.

Older patients with CKD
CKD affects more than a third of those aged 75 years and over. The majority will not be aware they have a kidney ‘disease’ unless you tell them. Many will never be troubled directly by kidney disease. This raises the dilemma of whether you should inform elderly patients and risk causing anxiety and stress without any clear benefit.

Risk factors for progression in the elderly are proteinuria, hypertension and cardiovascular comorbidity. The decline in eGFR tends to be slower and older patients at stage 3 with none of these risk factors are unlikely to progress to stage 5. When discussing test results, it is reasonable not to emphasise the ‘chronic’ and ‘disease’ aspects of their CKD.

The risk of complications due to CKD (such as anaemia and hyperparathyroidism) is still present in the elderly but your response to this should be proportionate to the patient’s health and life expectancy. Conversely, you may recommend treatment of systolic blood pressure >160mmHg in people aged >80 years who are otherwise well (e.g. with indapamide SR 1.5mg ± perindopril 2 or 4mg to achieve BP 150/80) as it can reduce mortality, stroke and heart failure within a year or two of being started (Beckett NS et al., 2008).

Elderly patients with progressive stage 5 CKD do not always benefit from dialysis. (Dasgupta I, Rayner H. 2009). Those with multiple comorbidities such as ischaemic
heart disease, peripheral vascular disease, diabetes, poor intellectual capacity, functional dependence and low serum albumin have a very high mortality rate on dialysis. Their quality of life often gets worse when dialysis is started. Any prolongation of life is mitigated by the time they spend having and recovering from the treatments. Many such patients regret starting dialysis.

Conservative kidney management is a positive alternative to dialysis for such frail elderly patients. All symptomatic treatment is offered other than dialysis itself, avoiding inessential and unpalatable medications. You can refer a patient to the nephrology service specifically for such a care package to be arranged in partnership with your team.

The following graphs are from a report by the kidney unit in Stevenage. They show the survival of two groups of patients aged >75 years treated with either dialysis (renal replacement therapy, RRT; n=689) or conservative kidney management (n=155).

*Comparison of Kaplan–Meier survival curves by modality (renal replacement therapy RRT versus conservative kidney management) in patients > 75 years of age (Chandna SM et al., 2011).*

Patients with low comorbidity survived significantly longer with dialysis than with conservative care from two years after reaching stage 5 CKD. However for some patients, quality rather than quantity of life may be much more relevant to the decision about whether or not to start dialysis.

Patients with high comorbidity survived slightly longer with dialysis during the first three years of follow up. However, all who had dialysis died within four years of
reaching stage 5. Conversely, one in five patients with high comorbidity who received conservative kidney management had much longer survival.

These figures may be helpful when you are discussing treatment options with frail elderly patients and their families. It is very difficult to predict which patients are the ones likely to survive longer without dialysis.

As part of the conservative kidney management plan, you can play an important role in coordinating services, in improving continuity of care delivered by practice nurses, district nurses, community matrons and social workers, and in linking closely with the specialist team.

When patients with end stage kidney disease reach the terminal stage of their illness, they should have access to appropriate palliative care.

Patients with a kidney transplant
Patients who have had a kidney transplant must remain under follow up in secondary care. However, they will inevitably present to you and some familiarity with common issues that affect them is useful.

Immunosuppressive drugs must be taken throughout the life of the transplant. The immune response is most suppressed during the first year after transplantation. Have a low threshold for contacting the specialist unit during this time as the infection may be atypical and worsen rapidly. Infections of the respiratory and urinary tracts are not uncommon. The likely organism should guide your choice of antibiotic. Trimethoprim may lead to a rise in serum creatinine and hence drop in eGFR, as explained above. This can cause uncertainty about possible transplant rejection.

Immunosuppressive drugs should be initiated in secondary care. Once stable, you may accept responsibility for prescribing them under an Effective Shared-Care Agreement. The nephrologist will provide advice and monitor efficacy, side effects and drug levels. Many immunosuppressive drugs are now ‘off patent’ and available in a variety of generic formulations. These can have differing bioavailabilities so it is important not to switch preparations without close monitoring by the specialist unit.

Include medications prescribed in secondary care on the patient’s electronic record so that potential interactions are flagged up. You may need to alert the nephrologist about conditions that might interfere with drug absorption, e.g. diarrhoea and vomiting.

Joint pain is common in transplant patients. Avoid prescribing non-steroidal anti-inflammatory drugs because of their potential nephrotoxicity. When treating gout, do not start allopurinol in patients taking the immunosuppressant drug azathioprine. Allopurinol blocks the breakdown of the active metabolite of azathioprine
(mercaptopurine), which can lead to potentially fatal bone marrow suppression and low white blood cell count.

As a result of long-term immunosuppression, transplant patients have an increased risk of cancer. The commonest site is the skin and you should encourage pale skinned patients to wear a hat and use sunscreen, even when it is not sunny. The risk of lymphoma is also increased. This can present with weight loss, sweats, sickness abdominal pain and altered bowel habit. Other cancers are slightly more common and so it is worth reminding women to attend for regular breast and cervical cancer screening.

Conclusions
This review aims to give you the essential knowledge and understanding needed to treat chronic kidney disease in the community. Having read it, we hope you feel confident and ready to team up with your nephrology colleagues in supporting your CKD patients to manage their long-term condition.

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