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# **Chronic Kidney Disease (CKD)**

Chronic kidney disease means that the kidneys are not working as well as would be expected. Various conditions can cause chronic kidney disease. Severity can vary but most cases are mild or moderate, occur in older people and do not cause symptoms. Chronic kidney disease tends to become worse gradually over months or years.

# What is chronic kidney disease?

Chronic kidney disease (CKD) means that the kidneys are not working as well as they used to, either due to being diseased or damaged in some way, or due to ageing. A range of conditions can cause chronic kidney disease (see later).

Chronic means ongoing, persistent and long-term.

Chronic kidney disease used to be called chronic renal failure but chronic kidney disease is now considered a better term. The word "failure" implies that the kidneys have stopped working but in most cases of chronic kidney disease this is not the case - they are not working as well as would be expected.

In most people who have chronic kidney disease there is only a mild or moderate drop in kidney function.

### Acute kidney injury (AKI)

An acute kidney injury occurs when the function of the kidneys is rapidly affected - over hours or days. For example, the kidneys may go into acute kidney injury if there is a serious blood infection which can affect the kidneys.

This is in contrast to chronic kidney disease where the decline in function of the kidneys is gradual - over months or years.

For more information, see the separate leaflet called What do kidneys do?

### What causes chronic kidney disease?

A number of conditions can cause long-term damage to the kidneys and affect their function, leading to chronic kidney disease. The three most common causes in the UK are:

- Diabetes. Diabetic kidney disease is a common complication of diabetes.
- **High blood pressure**. Untreated or poorly treated high blood pressure is a major cause of CKD. However, CKD can also *cause* high blood pressure as the kidney has a role in blood pressure regulation. About nine out of ten people with CKD stages 3-5 have high blood pressure.
- Ageing kidneys. There is often an age-related decline in kidney function. About half of people aged over 75 have some degree of CKD. In most of these cases, the CKD does not progress beyond the moderate stage unless other problems of the kidney, such as diabetic kidney disease, develop.

These conditions account for three in four cases of chronic kidney disease in adults.

Other less common conditions that can cause chronic kidney disease include:

- Certain medications, including non-steroidal anti-inflammatory drugs (if they are used long-term, especially at high doses), lithium, ciclosporin and tacrolimus. People taking one of these medicines should have a blood test to check kidney function at least once a year.
- Diseases of the tiny filters in the kidneys (glomeruli), such as inflammation of the glomeruli (glomerulonephritis).
- Narrowing of the artery taking blood to the kidney (renal artery stenosis)
- Polycystic kidney disease. See the separate leaflet called Polycystic Kidney Disease.
- Blockages to the flow of urine, and repeated kidney infections.
- Previous injury to the kidney. After an acute kidney injury, blood tests should be done regularly for at least three years to check the kidney function.
- Having only one functioning kidney. Even though most people with a single kidney do not have any problems, the kidney function should be monitored once a year.

This list is not complete and there are many other causes.

# What are chronic kidney disease symptoms?

There are usually no symptoms with mild-to-moderate chronic kidney disease - that is, stages 1 to 3. Chronic kidney disease is usually diagnosed by a blood test before any symptoms develop.

Symptoms tend to develop when chronic kidney disease becomes severe (stage 4) or worse. The symptoms at first tend to be vague and nonspecific, such as feeling tired, having less energy than usual or just not feeling well. With more severe chronic kidney disease, symptoms that may develop include:

- Difficulty thinking clearly.
- A poor appetite.
- Weight loss.
- Dry, itchy skin.
- Muscle cramps.
- Fluid retention which causes swollen feet and ankles.
- Puffiness around the eyes.
- A need to pass urine more often than usual.
- Being pale due to anaemia.
- Feeling sick.

If the kidney function declines to stage 4 or 5 then various other problems may develop - for example, anaemia or an imbalance of calcium, phosphate and other chemicals in the bloodstream. These can cause various symptoms, such as tiredness due to anaemia, and bone thinning (osteoporosis) or fractures due to calcium and phosphate imbalance. End-stage kidney failure (stage 5) is eventually fatal unless treated.

# What are the stages of chronic kidney disease?

Chronic kidney disease is diagnosed by blood tests including an eGFR test and is divided into five stages:

Stage of Chronic Kidney Disease	eGFR ml/min/1.73 m
Stage 1: the eGFR shows normal kidney <i>function</i> but you are already known to have some kidney damage or disease. For example, you may have some protein or blood in your urine, an abnormality of your kidney, kidney inflammation, etc.	90 or more
Stage 2: mildly reduced kidney function AND you are already known to have some kidney damage or disease. People with an eGFR of 60- 89 without any known kidney damage or disease are not considered to have chronic kidney disease (CKD).	60 to 89
Stage 3: moderately reduced kidney function. (With or without a known kidney disease. For example, an elderly person with ageing kidneys may have reduced kidney function without a specific known kidney disease.)	45 to 59 (3A) 30 to 44 (3B)
Stage 4: severely reduced kidney function. (With or without known kidney disease.)	15 to 29
Stage 5: very severely reduced kidney function. This is sometimes called end-stage kidney failure or established renal failure.	Less than 15

**Note**: it is normal for the eGFR to change slightly from one measurement to the next. In some cases these changes may actually be large enough to move from one stage of chronic kidney disease to another and then back again. These normal fluctuations are acceptable as long as the eGFR is not progressively getting worse.

# What if I have chronic kidney disease stage 3?

Stage 3 means moderate chronic kidney disease. People with stage 3 CKD do not usually need to see a kidney specialist (a nephrologist) but will need annual blood and urine tests at their GP practice.

Treatment will often be advised to reduce the risk of progressing to more severe chronic kidney disease. This includes managing the blood pressure aggressively to reduce it to below recommended levels. It also includes aggressively managing any other conditions such as diabetes. Other treatments might be suggested to reduce the risk of any other problems, particularly cardiovascular diseases (CVDs - see below).

Urine tests will look for leakage of protein from the kidneys. People with CKD who leak protein are more likely to develop progressive worsening of their condition. If there is leakage of protein then medications will usually be suggested to reduce this and to slow down the deterioration of the kidney function.

If regular blood and urine tests show that the chronic kidney disease is progressing to stage 4 then referral to a kidney specialist will often be needed.

# How is chronic kidney disease diagnosed?

Kidney function is assessed using a combination of:

- A blood test called the estimated glomerular filtration rate (eGFR); and
- A measure of the amount of protein in the urine (proteinuria).

Increased protein in the urine and decreased eGFR are both associated with an increased risk of progressive chronic kidney disease.

### Estimated glomerular filtration rate (eGFR)

A normal eGFR is 90 ml/minute/1.73 m or more. If some of the glomeruli do not filter as much as normal then the kidney is said to have reduced or impaired kidney function.

The eGFR test involves a blood test which measures a chemical called creatinine. Creatinine is a breakdown product of muscle. Creatinine is normally cleared from the blood by the kidneys. If the kidneys are not working very well and the glomeruli are not filtering as much blood as normal, the level of creatinine in the blood goes up.

The eGFR is calculated from age, sex and blood creatinine level. See the separate leaflets called Routine Kidney Function Blood Test and Estimated Glomerular Filtration Rate (eGFR).

### Proteinuria

Proteinuria means that the urine contains an abnormal amount of protein. Most proteins are too big to pass through the kidneys' filters and get into the urine. However, tiny amounts of a small protein called albumin is leaked into the urine.

If a kidney is damaged then increased amounts of albumin and other larger proteins from the blood can pass into the urine. This abnormal amount of protein in the urine is known as proteinuria. The amount of proteinuria is a good indicator of the extent of kidney damage. Proteinuria is also associated with an increased risk of the development of heart and blood vessel disease.

The amount of proteinuria is measured by a sample of urine sent to the laboratory to measure the ratio of the level of either albumin or total protein in the urine compared with the amount of creatinine in the urine.

Excess protein in the urine is called microalbuminuria.

# How common is chronic kidney disease?

About 1 in 10 people have some degree of chronic kidney disease. It can develop at any age and various conditions can lead to CKD. It becomes more common with increasing age and is more common in women.

Although about half of people aged 75 or more have some degree of chronic kidney disease; most of these people do not actually have diseases of their kidneys but have normal ageing of their kidneys.

Most cases of CKD are mild or moderate (stages 1-3).

# Do I need any further tests?

As mentioned, the eGFR test is done to diagnose and monitor the progression and severity of chronic kidney disease. For example, it should be done once a year in people with stages 1 and 2 CKD, and more frequently in some people with stage 3 and in everyone with stage 4 or 5 CKD.

Annual urine tests are needed to check for protein in the urine. Other blood tests may be done from time to time to check on your blood level of chemicals such as sodium, potassium, calcium and phosphate.

The need for other tests then depends on various factors. For example:

- An ultrasound scan of the kidneys or a kidney biopsy may be advised if certain kidney conditions are suspected.
- A scan or having a sample taken (a biopsy) is not needed in most cases. This is because most people with chronic kidney disease have a known cause for the impaired kidney function, such as a complication of diabetes, high blood pressure or ageing.
- If the chronic kidney disease progresses to stage 3 or worse then various other tests may be done. For example, blood tests
  might be required to check for anaemia and an altered level of parathyroid hormone (PTH). PTH is involved in the control of
  the blood level of calcium and phosphate.

### Chronic kidney disease treatment

Management of most cases of chronic kidney disease takes place in general practice. This is because most cases are mild-tomoderate (stages 1-3) and do not need more specialist treatment.

Referral will usually be needed at stages 4 or 5 CKD, at earlier stages in younger adults with no obvious risk factors or if there are other symptoms that might need further investigation.

Research studies have shown that, in many people, treatment at early stages of chronic kidney disease can prevent or slow down progression of the disease.

The aims of treatment include:

- If possible, to treat any underlying kidney condition.
- To prevent or slow down the progression of CKD and reduce the risk of developing kidney failure.
- To reduce the risk of developing cardiovascular disease.
- To relieve symptoms and problems caused by CKD.

### Treating any underlying kidney condition

There are various conditions that can cause CKD. For some of these there may be specific treatments for that particular condition - for example:

- Good blood sugar (glucose) control for people with diabetes.
- Blood pressure control for people with high blood pressure.
- Antibiotic medication for people with recurring kidney infections.
- Surgery for people with a blockage to urine flow.

### Preventing or slowing down the progression of chronic kidney disease

There are ways to stop chronic kidney disease becoming any worse or to slow down any progression.

These usually include:

- Blood pressure control. The most important treatment to prevent or delay the progression of chronic kidney disease, whatever the underlying cause, is to keep blood pressure very well controlled. Most people with CKD will require medication to control their blood pressure. Depending on the amount of albumin in the urine, a target blood pressure level of below 130/80 mm Hg or even lower will be advised. For children and young people with CKD and high levels of albumin in the urine, blood pressure should be kept less than average for their height.
- Review of medication. Certain medicines can affect the kidneys as a side-effect which can make CKD worse. For example, people with CKD should not take anti-inflammatory medicines unless advised to by a doctor. The dose of certain medicines may also need to be adjusted if CKD gets worse.
- Diet. People with more advanced CKD (stage 4 or 5) may be advised to follow a special diet. See the separate leaflet called Diet in Chronic Kidney Disease.

### Medication to protect your kidneys

- ACE inhibitors and ARBs. If there are high levels of protein in the urine then medication usually used to reduce blood pressure will be advised, even with normal blood pressure levels. Two related types of medication have been shown to be beneficial for many people with CKD. This is because they can prevent further worsening of the kidney function. These medicines are called:
  - Angiotensin-converting enzyme (ACE) inhibitors (for example, captopril, enalapril, ramipril, lisinopril); and
  - Angiotensin receptor blockers (ARBs), such as losartan, valsartan, candesartan, telmisartan).
- SGLT2 inhibitors. A group of medicines called the SGLT2 inhibitors (such as canagliflozin, dapagliflozin, empagliflozin and ertugliflozin) were originally used to keep blood sugar under control in type 2 diabetes. However, more recent studies show that some of them can significantly reduce decline in kidney function. Guidance now suggests that dapagliflozin should be considered and would be recommended for most people with CKD and high levels of protein in their urine. However, dapagliflozin is not advised for people with stage 5 CKD (and only on the advice of a specialist in people with stage 4 CKD).

### Treating end-stage kidney failure

Only a small number of people with chronic kidney disease progress to end-stage kidney failure (stage 5 CKD) that requires kidney dialysis or kidney transplant. People with stage 4 or 5 CKD are likely to be referred to a kidney specialist (nephrologist) at a hospital.

Regular follow-up will be needed - how often depends on how severe the CKD is and how quickly it is getting worse. As well as monitoring the kidney function, the nephrology team is likely to carry out certain blood tests:

- Full blood count (for anaemia).
- Calcium.
- Phosphate.
- Vitamin D.
- Parathyroid hormone.

- Haemodialysis blood is removed from a vein in your arm, filtered to remove waste products and returned through another tube.
- Peritoneal dialysis a thin tube is inserted into the abdomen near the tummy button. Fluid is pumped into the abdominal cavity to filter waste products, and drained into a bag.
- A kidney transplant.

The National Institute for Health and Care Excellence (NICE) says that patients receiving dialysis should be offered the choice of having their treatment at home or in a hospital or clinic. It advises that patients, in discussion with doctors, should be able to decide which type of dialysis is right for them and where they will receive it, depending on local arrangements.

### Reducing the risk of developing cardiovascular diseases

People with chronic kidney disease have an increased risk of developing chronic vascular diseases, such as heart disease, stroke, and peripheral arterial disease.

People with CKD are twenty times more likely to die from cardiovascular-related problems than from kidney failure. This is why reducing any other cardiovascular risk factors is so important. See the separate leaflet called Cardiovascular Disease (Atheroma).

This typically includes:

- Excellent control of blood pressure.
- Excellent control of blood glucose level in diabetes.
- Medication to lower the cholesterol level (called statins), which is often given to people with CKD.
- Where relevant, to tackle lifestyle risk factors. This means to:
  - Stop smoking if smoking and cut back if drinking a lot of alcohol.
  - Eat a healthy diet which includes a low salt intake.
  - Keep weight and waistline in check.
  - Take regular physical activity.

### Relieving symptoms and problems caused by chronic kidney disease

If chronic kidney disease becomes severe, treatment might be needed to combat various problems caused by the poor kidney function. For example:

- Anaemia may develop which may need treatment with iron or erythropoietin a hormone normally made by the kidneys. A
  new medication called roxadustat has also been approved by NICE this can be used for people with stage 3-5 CKD who
  have symptomatic anaemia but who do not have iron deficiency and who are not on dialysis.
- Abnormal levels of calcium or phosphate in the blood may need treatment.
- Advice might be given about how much fluid to drink or how much salt to take.
- Other dietary advice may be given which can help to control factors such as the levels of calcium and potassium in the body.

If end-stage kidney failure develops, kidney dialysis or a kidney transplant are likely to be needed to survive.

People with stage 3 CKD or worse should be immunised against influenza each year, and have a one-off immunisation against pneumococcus. People with stage 4 CKD should also be immunised against hepatitis B.

# What is the outlook for chronic kidney disease?

Stage 1-3 chronic kidney disease (mild-to-moderate) is common, with most cases occurring in older people. It tends to become gradually worse over months or years. However, the rate of progression varies from case to case and often depends on the severity of any underlying condition.

For many people with CKD there is a much higher risk of developing serious CVD than of developing end-stage kidney failure.

The most important things that can affect the outlook (prognosis) are:

- Excellent blood pressure control.
- · Excellent diabetes control in people with diabetes
- Careful review of medications to make sure that the only ones used are those which have the least impact on the kidneys.
- Reducing the risk of developing CVDs for example, losing weight, exercising and reducing cholesterol.

# Further reading & references

- Chronic kidney disease: assessment and management; NICE guideline (last updated November 2021)
- Type 2 diabetes in adults: management; NICE Guidance (December 2015 last updated June 2022)
- Dapagliflozin for treating chronic kidney disease; NICE Technology appraisal guidance, March 2022
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- Kovesdy CP; Epidemiology of chronic kidney disease: an update 2022. Kidney Int Suppl (2011). 2022 Apr;12(1):7-11. doi: 10.1016/j.kisu.2021.11.003. Epub 2022 Mar 18.

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Last updated by: Dr Pippa Vincent	Peer reviewed by: Dr Surangi Mendis	
Last updated:	Next review date:	Document ID:
21/08/2023	19/08/2028	6961 (v47)

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