What every doctor needs to know about chronic kidney disease

ABSTRACT

Chronic kidney disease is a global health problem that affects over 10% of adults worldwide. All doctors should have a basic knowledge of chronic kidney disease because it may complicate the management of many other medical conditions and is associated with numerous adverse outcomes. Chronic kidney disease should be regarded as a clinical syndrome rather than a specific diagnosis and attempts should always be made to identify the cause. Simple risk prediction tools have been developed to inform management decisions. Management is directed at slowing progression of chronic kidney disease and reducing the associated cardiovascular risk by treating hypertension, use of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers as first-line therapy in high-risk cases, treatment with statins and lifestyle measures. Patients at high risk of rapid progression or requiring specific therapy as well as those with chronic kidney disease stage 4 or 5 should be referred to a nephrology service.

Chronic kidney disease affects over 10% of the adult population and is associated with multiple adverse outcomes including end-stage kidney disease, acute kidney injury, cardiovascular events and increased mortality. Chronic kidney disease may result from a wide range of pathological processes and should therefore be viewed not as a diagnosis per se, but rather as a clinical syndrome with common features and complications. Many chronic diseases are associated with chronic kidney disease and the presence of reduced kidney function may impact on therapy, so it is important that health-care providers in all fields have a clear understanding of chronic kidney disease and how it should be managed. This is particularly true in the setting of acute illness because chronic kidney disease increases the risk of adverse outcomes and may impact on treatment decisions. This article reviews the most important aspects of the diagnosis, classification and management of chronic kidney disease.

Dr Isma Kazmi, Research Fellow and Specialist Registrar, Centre for Kidney Research and Innovation, Division of Medical Sciences and Graduate Entry Medicine, University of Nottingham, Derby

Dr Latha Gullapudi, Research Fellow and Specialist Registrar, Centre for Kidney Research and Innovation, Division of Medical Sciences and Graduate Entry Medicine, University of Nottingham, Derby

Professor Maarten W Taal, Professor of Medicine and Honorary Consultant Nephrologist, Centre for Kidney Research and Innovation, Division of Medical Sciences and Graduate Entry Medicine, University of Nottingham, Derby and Department of Renal Medicine, Royal Derby Hospital, Derby DE22 3NE

Correspondence to: Professor MW Taal
(maarten.taal1@nhs.net)

Chronic kidney disease diagnosis and classification

The concept of chronic kidney disease was proposed because it was recognized that altered structure and function of the kidneys from any cause results in a common clinical syndrome that impacts health. Chronic kidney disease is defined by abnormalities of kidney structure and/or function that are present for more than 3 months, with implications for health (Kidney Disease Improving Global Outcomes (KDIGO), 2013).

Abnormal kidney function is most often defined by a reduced glomerular filtration rate (<60 ml/min/1.73m^2), usually assessed by an estimated glomerular filtration rate derived from serum creatinine concentration, or by albuminuria of >30 mg/day (usually measured as urine albumin:creatinine ratio of >3 mg/mmol). A single abnormal glomerular filtration rate or urine albumin:creatinine ratio must be confirmed after at least 3 months for chronic kidney disease to be diagnosed. Both estimated glomerular filtration rate and urine albumin:creatinine ratio may vary over time, so this is an important consideration. In the case of first detection of an abnormal estimated glomerular filtration rate, the test should be repeated within 2 weeks or sooner (depending on the clinical context) to identify acute kidney injury or rapid chronic kidney disease progression, both of which should prompt referral to a nephrology service.

Glomerular filtration rate may also be estimated from serum levels of other endogenous filtration markers including cystatin C. The National Institute for Health and Care Excellence (2014) recommends that if estimated glomerular filtration rate is only mildly reduced (45–59 ml/min/1.73m^2) and the urine albumin:creatinine ratio is normal, diagnosis of chronic kidney disease should be confirmed via an estimated glomerular filtration rate derived from serum cystatin C. However, the cystatin C assay is not yet available in most laboratories and data have questioned the benefit of this approach (Shardlow et al, 2017). Other abnormalities that may be used to define chronic kidney disease include haematuria (in the absence of a urological cause), scarring or other abnormalities of the kidneys detected on imaging, or abnormal histology.

Previously, chronic kidney disease was classified based on impaired renal function assessed by glomerular filtration rate alone. Subsequently many studies have identified albuminuria as an independent risk factor for adverse outcomes, irrespective of the glomerular filtration rate. A large meta-analysis reported that estimated glomerular filtration rate <60 ml/min/1.73m^2 and urine albumin:creatinine ratio >1.1 mg/mmol are independent predictors of all-cause and cardiovascular mortality (van der Velde et al, 2011). Therefore National Institute for Health and Care Excellence and Kidney Disease Improving Global Outcomes recommend that classification of chronic kidney disease should be based on glomerular filtration rate, albuminuria and underlying diagnosis leading to chronic kidney disease.

This classification of chronic kidney disease by cause, glomerular filtration rate and albuminuria respectively, referred to as the CGA classification, was endorsed by the National Institute for Health and Care Excellence in 2014 (*Table 1*). Including the cause or underlying diagnosis helps emphasize that chronic kidney disease is not a diagnosis itself and will prompt physicians to consider the underlying diagnosis to inform treatment strategies.

This classification also promotes a risk-based approach to managing chronic kidney disease because the categories correspond to risk of adverse outcomes. Despite the introduction of the CGA classification, chronic kidney disease is often still referred to using the previous classification, chronic kidney disease stage 1–5, where the stage is the same as the glomerular filtration rate category.

Table 1. Categories for the Kidney Disease Improving Global Outcomes (KDIGO) classification of chronic kidney disease

Glomerular filtration rate categories		Albuminuria categories	
G1	Glomerular filtration rate 90 ml/min/1.73m^2	A1	Urine albumin excretion rate <30 mg/day Urine albumin:creatinine ratio <3 mg/mmol
G2	Glomerular filtration rate 89–60 ml/min/1.73m^2	A2	Urine albumin excretion rate 30–300 mg/day Urine albumin:creatinine ratio 3–30 mg/mmol
G3a	Glomerular filtration rate 59–45 ml/min/1.73m^2	A3	Urine albumin excretion rate >300 mg/day urine albumin:creatinine ratio >30 mg/mmol
G3b	Glomerular filtration rate 44–30 ml/min/1.73m^2		
G4	Glomerular filtration rate 29–15 ml/min/1.73m^2		
G5	Glomerular filtration rate <15 ml/min/1.73m^2		

Chronic kidney disease should be classified according to cause, glomerular filtration rate and albuminuria. For example, a patient with diabetic nephropathy, glomerular filtration rate =35 ml/min/1.73m^2 and urine albumin:creatinine ratio 104 mg/mmol would be classified as: diabetic nephropathy G3b A3

Epidemiology

Chronic kidney disease is a global health problem with a mean global prevalence of 13.4% (stage 1–5) and 10.6% (stage 3–5) (Hill et al, 2016) in adult populations. It should be noted, however, that most epidemiological studies rely on a single estimated glomerular filtration rate for the diagnosis of chronic kidney disease and therefore may overestimate the prevalence. In the UK, the most reliable data are from the Health Survey for England 2009 and 2010, which reported a prevalence of chronic kidney disease stage 3–5 of 5.2% and chronic kidney disease stage 1–2 (defined by albuminuria) of 7.1% in adults (age >16 years) (Fraser et al, 2014). The National CKD Audit in England and Wales reported a similar prevalence of chronic kidney disease stage 3–5 of 5.3% in adults aged 18 years or over (Kim et al, 2017).

According to the 2016 Global Burden of Disease study, chronic kidney disease rose up the table of leading causes of death from 1990 to 2016 in all categories of country sociodemographic index. In 2016, the position of chronic kidney disease ranged from the 10th leading cause of death in countries with middle sociodemographic index to 26th in countries with low sociodemographic index (GBD 2016 Causes of Death Collaborators, 2017).

A study in 2013 estimated that 956 200 deaths worldwide were attributable to chronic kidney disease which represents deaths as a result of end-stage kidney disease alone and this probably underestimates the real burden of disease, its health and cost implications for individuals and families (Global Burden of Disease Collaborators, 2015). In population-based studies, people with chronic kidney disease are far more likely to die, principally from cardiovascular disease, than to develop end-stage kidney disease (Keith et al, 2004).

The underlying cause of chronic kidney disease varies between different populations and in many cases remains unknown, but in the UK and globally the most common cause of chronic kidney disease is diabetes mellitus (de Boer et al, 2011; Gilg et al, 2017).

Chronic kidney disease in elderly patients

As life expectancy continues to improve, there is an increasing prevalence of comorbidities and risk factors such as hypertension, diabetes and atherosclerosis predisposing to a high burden of chronic kidney disease in the elderly population. Epidemiological studies show that the prevalence of chronic kidney disease rises sharply with age, such that 28.6% of women and 23.4% of men over the age of 70 years are affected (Mills et al, 2015). This has prompted some to suggest that mildly reduced glomerular filtration rate in the absence of proteinuria should be regarded as part of normal ageing in the elderly and not labelled as chronic kidney disease. Data reporting a loss of 7.3% of glomeruli per decade increase in age (or 6207

glomeruli per year) in a cross-sectional study of healthy kidney donors support this view (Denic et al, 2017). National Institute for Health and Care Excellence (2014) guidance does not recommend screening for chronic kidney disease on the basis of age alone.

Risks associated with chronic kidney disease

Progression to end-stage kidney disease is often regarded as the most obvious risk associated with chronic kidney disease. However, large epidemiological studies show that lower glomerular filtration rate and higher albuminuria are risk factors for all-cause and cardiovascular mortality independent of each other and of other cardiovascular risk factors. In one meta-analysis of data from 266 975 participants at increased risk of developing chronic kidney disease, estimated glomerular filtration rate of 60, 45 and 15 ml/min/1.73m^2 was associated with all-cause mortality hazard ratios of 1.03, 1.38 and 3.11 respectively, compared to an estimated glomerular filtration rate of 95 ml/min/1.73m^2 (van der Velde et al, 2011). It also found urine albumin:creatinine ratios of 10, 30 and 300 mg/g (approximately 1, 3 and 30 mg/mmol, the units usually used in the UK) associated with all-cause mortality hazard ratios of 1.08, 1.38 and 2.16 compared to a ratio of 5 mg/g.

A further meta-analysis by the CKD Prognosis Consortium demonstrated associations of estimated glomerular filtration rate <60 ml/min/1.73m^2 and albuminuria with subsequent risk of all-cause and cardiovascular mortality, end-stage kidney disease, chronic kidney disease progression and acute kidney injury in the general population and in populations with increased risk for cardiovascular disease (Gansevoort et al, 2011). The relative risk of different adverse outcomes varies depending on the population studied. In older populations the risk of death competes with the risk of end-stage kidney disease such that O'Hare et al (2007) found the risk of end-stage kidney disease exceeded the risk of death only when estimated glomerular filtration rate was <15 ml/min/1.73m^2 in those aged 65–84 years.

In a large population-based study in Norway, only participants with chronic kidney disease stage 4 at baseline were at substantial risk of developing end-stage kidney disease over 8 years. In contrast, all participants with reduced glomerular filtration rate had an increased risk of death as a result of cardiovascular disease which was greater than the risk of end-stage kidney disease (Hallan et al, 2006).

Similarly, in a large prospective study of older people with chronic kidney disease stage 3, progression of chronic kidney disease was seen in only 18% over 5 years and only 0.2% developed end-stage kidney disease (Shardlow et al, 2016). Chronic kidney disease can be regarded as a risk amplifier in other diseases, e.g. among patients in Sweden admitted with a non-ST elevation myocardial infarction, the risk of death increased progressively with each more advanced stage of chronic kidney disease, and the survival benefit of early revascularization *vs* medical therapy was not seen in patients with chronic kidney disease stage 4 and 5 (Szummer et al, 2009). Similarly, chronic kidney disease was associated with increased 28-day mortality and increased disability after an ischaemic stroke or transient ischaemic attack (Hayden et al, 2017).

Risk prediction

The risk of adverse events associated with chronic kidney disease is heterogeneous and there is therefore a clinical need for risk prediction so that therapy to slow chronic kidney disease progression can be provided to those at high risk, and those at low risk can be spared unnecessary referral and intervention. The CGA classification provides some degree of risk stratification but more individualised risk prediction is required.

Tangri et al (2011) developed kidney failure risk equations that use demographic and laboratory data to predict the risk of progression to end-stage kidney disease. An eight-variable equation performed well but was not widely adopted, likely because of the large number of variables required. They subsequently externally validated four-variable and eight-variable prediction equations in 31 patient cohorts (721 357 participants) from 30 countries participating in the CKD Prognosis Consortium (Tangri et al, 2016). Both equations performed well and discrimination for the four-variable equation was similar to that for the eight-variable equation (at 2 years C-statistics were 0.89 *vs* 0.90 and at 5 years 0.86 *vs* 0.88 respectively). Adding a correction factor for non-North American populations addressed the issue of overestimation of the observed risk in this subgroup.

A free online tool has been developed by this group and is available to provide quick and simple risk prediction using only age, sex, estimated glomerular filtration rate and urine albumin:creatinine ratio to help inform decisions about future management plans (http://kidneyfailurerisk.com/).

Approach to management

An attempt should always be made to identify the cause of chronic kidney disease by taking a detailed medical history along with thorough clinical examination and basic investigations including urinalysis and measurement of urine albumin:creatinine ratio. For all causes of chronic kidney disease, general measures to slow chronic kidney disease progression and reduce cardiovascular risk are required, as outlined in the National Institute for Health and Care Excellence (2014) chronic kidney disease guidelines. These guidelines also give a detailed review of the evidence supporting these interventions.

Hypertension

Hypertension is a key mediator of progressive kidney damage, so strict blood pressure control is

vital, aiming for a target systolic blood pressure of 120–129 mmHg and diastolic blood pressure <80 mmHg in people with diabetes or with urine albumin:creatinine ratio >70 mg/mmol (at higher risk). In others with chronic kidney disease, aim for systolic blood pressure 120–139 mmHg and diastolic blood pressure <90 mmHg.

Results from a large randomized trial indicate that aiming for even lower systolic blood pressure targets (<120 mmHg *vs* <140 mmHg) further reduces all-cause mortality (hazard ratio 0.72; 95% confidence interval 0.53–0.99) and cardiovascular events (hazard ratio 0.81; 95% confidence interval 0.63–1.05), with no overall increase in serious adverse events, although there was a greater decrease in glomerular filtration rate after 6 months (-0.47 *vs* -0.32 ml/min/1.73m^2 per year) and acute kidney injury, hypokalaemia and hyperkalaemia were increased (Cheung et al, 2017). Guidelines are being reviewed in light of this evidence.

Renin–angiotensin system inhibition

Angiotensin II promotes chronic kidney disease progression and cardiovascular disease by several mechanisms, so angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers should be the first-line antihypertensive therapy in people with chronic kidney disease and diabetes with any degree of albuminuria, those who are hypertensive with urine albumin:creatinine ratio >30 mg/mmol and all those with urine albumin:creatinine ratio >70 mg/mmol. Their effects may be enhanced by dietary sodium restriction or administration of diuretics.

Cardiovascular risk

Measures to reduce cardiovascular risk include all the above treatments plus prescription of statins for lipid management. Evidence for statin therapy comes from the SHARP study, in which 9270 participants (some of whom were dialysis dependant) with no previous cardiovascular disease were randomized to simvastatin 20 mg/day and ezetimibe 10 mg/day or placebo. Those treated had a relative risk reduction of 17% in the incidence of fatal and non-fatal myocardial infarctions, non-haemorrhagic strokes and arterial revascularization procedures after median follow-up of 4.9 years (Baigent et al, 2011).

Lifestyle measures

Lifestyle measures, i.e. regular exercise, weight reduction, smoking cessation and salt restriction (no added salt strategy), are recommended.

Sodium bicarbonate supplementation

This is undertaken to correct metabolic acidosis in chronic kidney disease stage 4–5, to mitigate the effects on bone mineral metabolism, muscle wasting, hyperkalaemia and progression of chronic kidney disease.

Vaccinations

Patients with chronic kidney disease stages 1–4 should receive the influenza, hepatitis B and pneumococcal vaccines in keeping with regional immunization guidelines. All patients with chronic kidney disease stage 5 should be vaccinated for influenza, hepatitis B and pneumococcus. Influenza vaccine should be offered annually and pneumococcal vaccine given at least once.

Monitoring

Regular monitoring is also an important aspect of chronic kidney disease management. The frequency of monitoring should be individualized but should be done at least annually for people with chronic kidney disease stage 3a and increased with more advanced stages of chronic kidney disease.

Medicines management

Understanding the pharmacokinetics and pharmacodynamics of medicines is particularly important in patients with chronic kidney disease because many are dependent on renal clearance, so require dose adjustments to avoid side effects and toxicity. It is important to check prescribing information for any new drug for advice regarding dose adjustment for reduced glomerular filtration rate. This article briefly discusses some of the most important drugs that require precautions or dose adjustment in people with chronic kidney disease.

Metformin

Metformin, primarily used for management of type 2 diabetes mellitus, is associated with an increased risk of lactic acidosis when glomerular filtration rate is reduced. Metformin is contraindicated when estimated glomerular filtration rate drops to <30 ml/min/1.73m^2 and the dose should be reduced to a maximum of 500 mg/day if the estimated glomerular filtration rate is 40–30 ml/min/1.73m^2.

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs can exacerbate pre-existing chronic kidney disease or cause de novo renal disease (Hsu et al, 2015). These effects are mediated by inhibition of prostaglandin synthesis leading to renal vasoconstriction and reduction in glomerular filtration rate. In the setting of sepsis or intravascular volume depletion, this may be sufficient to provoke acute kidney injury. In rare cases non-steroidal anti-inflammatory drugs may cause tubulo-interstitial nephritis (Schwarz et al, 2000) or lead to nephrotic syndrome secondary to minimal change disease. In general, non-steroidal anti-inflammatory drugs should be regarded as contraindicated in patients with chronic kidney disease.

Opioids

Morphine and other opiates should be prescribed with caution and at a reduced dose in patients with chronic

kidney disease as they may cause respiratory depression and confusion because of the accumulation of active metabolites. Opiates like oxycodone and fentanyl may be more appropriate, as these drugs have fewer active metabolites but caution should be exercised when using them for long-term analgesia as data are limited.

Diuretics

Caution should be exercised when prescribing potassium-sparing diuretics (frequently used for the treatment of heart failure) in people with chronic kidney disease, particularly in combination with angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers. Dietary advice to reduce potassium intake may help to avoid hyperkalaemia but regular monitoring is required.

Antibiotics

Dose adjustments might be required for many antibiotics, depending on the pharmacokinetics. Trimethoprim is often prescribed for uncomplicated urinary tract infection but it may raise serum creatinine levels by competitively inhibiting proximal tubular secretion of creatinine and it has a tendency to cause hyperkalaemia by inhibitory effects on sodium channels in the distal nephron. Trimethoprim should generally be avoided in people with chronic kidney disease, particularly stage 3b to 5.

Gabapentin and pregabalin

Gabapentin and pregabalin are anti-epileptic drugs which are widely used to treat painful peripheral neuropathy which is common in people with chronic kidney disease, particularly those with diabetes. Both are predominantly excreted by the kidneys and may cause severe neurological adverse effects if they accumulate, so dose reduction according to glomerular filtration rate is essential.

Who to screen for chronic kidney disease

Chronic kidney disease is usually asymptomatic and detection therefore requires a systematic approach to screening high risk groups by means of estimated glomerular filtration rate and urine albumin:creatinine ratio testing. The National Institute for Health and Care Excellence (2014) guideline recommends that people with the following risk factors should be offered screening:

- Diabetes
- Hypertension
- Previous acute kidney injury
- Cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
- Structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
- Multisystem diseases with potential kidney involvement, e.g. systemic lupus erythematosus
- Family history of end-stage kidney disease (glomerular filtration rate category G5) or hereditary kidney disease
- Opportunistic detection of haematuria.

When to refer

Owing to the high prevalence of chronic kidney disease, nephrology services are unable to see all people with chronic kidney disease, nor would it be beneficial for patients who are at low risk of progression. Nevertheless, appropriate and timely referral is important for those patients who are at high risk of adverse outcomes. In general people who are at risk of rapid progression, those in need of specific investigation (kidney biopsy) or treatment (often with immunosuppressive drugs) and those approaching the need for renal replacement therapy (dialysis and transplantation) should be referred. Criteria for specialist referral are provided in the National Institute for Health and Care Excellence (2014) guidelines as outlined below:

- Glomerular filtration rate less than 30 ml/min/1.73m^2 (glomerular filtration rate category G4 or G5), with or without diabetes
- Urine albumin:creatinine ratio 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated
- Urine albumin:creatinine ratio 30 mg/mmol or more (category A3), together with haematuria
- Sustained decrease in glomerular filtration rate of 25% or more, and a change in glomerular filtration rate category or sustained decrease in glomerular filtration rate of 15 ml/min/1.73m^2 or more within 12 months
- Hypertension that remains poorly controlled despite the use of at least four antihypertensive drugs at therapeutic doses
- Known or suspected rare or genetic causes of chronic kidney disease
- Suspected renal artery stenosis.

A decision to refer should be individualized and discussed with the patient. For example, referral may not be appropriate in a frail elderly patient in whom the burden of extra hospital visits would likely outweigh any potential benefit. Risk prediction tools like the kidney failure risk equation may help clinicians to identify those who will benefit most.

Conclusions

Chronic kidney disease has a high prevalence in the adult population, increasing steeply with age. It is therefore important that all doctors are familiar with the diagnosis and management of chronic kidney disease as a clinical syndrome. Patients with advanced chronic kidney disease (stage 4–5) and those kidney diseases that require specialist investigation and management (mainly immunological and inherited diseases) should be referred to a nephrology service. BJHM

Conflict of interest: none.

Baigent C, Landray MJ, Reith C et al. SHARP Investigators. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised

KEY POINTS

- Chronic kidney disease affects over 10% of the adult population worldwide and the prevalence rises steeply with age.
- All doctors should have a basic knowledge of chronic kidney disease because it may complicate the management of multiple other medical conditions.
- Chronic kidney disease is associated with numerous adverse outcomes including end-stage kidney disease, acute kidney injury, cardiovascular events and increased mortality.
- Diagnosis is usually based on reduced glomerular filtration rate and/or elevated urine albumin:creatinine ratio that persists for at least 3 months.
- Management is directed at slowing progression of chronic kidney disease and reducing the associated cardiovascular risk by treating hypertension, use of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers as first-line therapy in high risk cases, treatment with statins and lifestyle measures.
- Patients at high risk of rapid progression or requiring further investigation and specific therapy as well as those with chronic kidney disease stage 4 or 5 should be referred to a nephrology service.

placebo-controlled trial. Lancet. 2011 Jun. 377(9784): 2181–2192. https://doi.org/10.1016/S0140-6736(1160739-3
Cheung AK, Rahman M, Reboussin DM et al. SPRINT Research Group. Effects of Intensive BP Control in CKD. J Am Soc Nephrol. 2017 Sep. 28(9): 2812–2823. https://doi.org/10.1681/ASN.2017020148
de Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal trends in the prevalence of diabetic kidney disease in the United States. JAMA. 2011 Jun 22. 305(24): 2532–2539. https://doi.org/10.1001/jama.2011.861
Denic A, Lieske JC, Chakkera HA et al. The Substantial Loss of Nephrons in Healthy Human Kidneys with Aging. J Am Soc Nephrol. 2017 Jan. 28(1): 313–320. https://doi.org/10.1681/ASN.2016020154
Fraser SDS, Roderick PJ, Aitken G, Roth M, Mindell JS, Moon G, ODonoghue D. Chronic kidney disease, albuminuria and socioeconomic status in the Health Surveys for England 2009 and 2010. J Public Health (Bangkok). 2014 Dec. 36(4): 577–586. https://doi.org/10.1093/pubmed/fdt117
Gansevoort RT, Matsushita K, van der Velde M et al. The Chronic Kidney Disease Prognosis Consortium. Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes in both general and high-risk populations. A collaborative meta-analysis of general and high-risk population cohorts. Kidney Int. 2011. 80: 93–104. https://doi.org/10.1038/ki.2010.531
Gilg J, Methven S, Casula A, Castledine C. UK Renal Registry 19th Annual Report: Chapter 1 UK RRT Adult Incidence in 2015: National and Centre-specific Analyses. Nephron. 2017. 137(1): 11–44. https://doi.org/10.1159/000481363
GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017 Sep. 390(10100): 1151–1210. https://doi.org/10.1016/S0140-6736(1732152-9
GBD 2013 Mortality and Causes of Death Collaborators.; GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age–sex specific all-cause and cause-specific mortality for 240 causes of death, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 2015. 385(9963): 117–171. https://doi.org/10.1016/S0140-6736(14)61682-2
Hallan SI, Dahl K, Oien CM, Grootendorst DC, Aasberg A, Holmen J, Dekker FW. Screening strategies for chronic kidney disease in the general population: follow-up of cross sectional health survey. BMJ. 2006 Nov 18. 333(7577): 10–47. https://doi.org/10.1136/bmj.39001.657755.BE
Hayden D, McCarthy C, Akijian L et al. Renal dysfunction and chronic kidney disease in ischemic stroke and transient ischemic attack: A population-based study. Int J Stroke. 2017 Oct. 12(7): 761–769. https://doi.org/10.1177/1747493017701148
Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, Hobbs FDR. Global Prevalence of Chronic Kidney Disease A Systematic Review and Meta-Analysis. PLoS One. 2016 Jul 6. 11(7): e0158765. https://doi.org/10.1371/journal.pone.0158765
Hsu CC, Wang H, Hsu YH et al. Use of nonsteroidal anti-inflammatory drugs and risk of chronic kidney disease in subjects with hypertension: nationwide longitudinal cohort study. Hypertension. 2015. 66(3): 524–533. https://doi.org/10.1161/HYPERTENSIONAHA.114.05105
Keith DS, Nichols GA, Gullion CM, Brown JB, Smith DH. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. Arch Intern Med.. 2004 Mar 22. 164(6): 659–663. https://doi.org/10.1001/archinte.164.6.659
Kidney Disease Improving Global Outcomes (KDIGO). 2012. Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013. 3(1): 11–50
Kim LG, Cleary F, Wheeler DC, Caplin B, Nitsch D, Hull SA. UK National Chronic Kidney Disease Audit. How do primary care doctors in England and Wales code and manage people with chronic kidney disease? Results from the National Chronic Kidney Disease Audit. Nephrol Dial Transplant. 2017. https://doi.org/10.1093/ndt/gfx280
Mills KT, Xu Y, Zhang W et al. A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. Kidney Int. 2015 Nov. 88(5): 950–957. https://doi.org/10.1038/ki.2015.230
National Institute for Health and Care Excellence. 2014. Early identification and management of chronic kidney disease in adults in primary and secondary care. (accessed 12 July 2018). https://www.nice.org.uk/guidance/cg182
Schwarz A, Krause PH, Kunzendorf U, Keller F, Distler A. The outcome of acute interstitial nephritis: risk factors for the transition from acute to chronic interstitial nephritis. Clin Nephrol. 2000 Sep. 54(3): 179–190
Shardlow A, McIntyre NJ, Fluck RJ, McIntyre CW, Taal MW. Chronic Kidney Disease in Primary Care: Outcomes after Five Years in a Prospective Cohort Study. PLoS Med.. 2016 Sep 20. 13(9): e1002128. https://doi.org/10.1371/journal.pmed.1002128
Shardlow A, McIntyre NJ, Fraser SDS et al. The clinical utility and cost impact of cystatin C measurement in the diagnosis and management of chronic kidney disease: A primary care cohort study. PLoS Med. 2017 Oct 10. 14(10): e1002400. https://doi.org/10.1371/journal.pmed.1002400
Szummer K, Lundman P, Jacobson SH et al. SWEDEHEART. Influence of renal function on the effects of early revascularization in non-ST-elevation myocardial infarction: data from the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART). Circulation. 2009 Sep 08. 120(10): 851–858. https://doi.org/10.1161/CIRCULATIONAHA.108.838169
Tangri N, Stevens LA, Griffith J et al. A predictive model for progression of chronic kidney disease to kidney failure. JAMA. 2011 Apr 20. 305(15): 1553–1559. https://doi.org/10.1001/jama.2011.451
Tangri N, Grams ME, Levey AS et al. CKD Prognosis Consortium. Multinational Assessment of Accuracy of Equations for Predicting Risk of Kidney Failure. JAMA. 2016 Jan 12. 315(2): 164–174. https://doi.org/10.1001/jama.2015.18202
van der Velde M, Matsushita K, Coresh J et al. Chronic Kidney Disease Prognosis Consortium. Lower estimated glomerular filtration rate and higher albuminuria are associated with all-cause and cardiovascular mortality. A collaborative meta-analysis of high-risk population cohorts. Kidney Int. 2011 Jun. 79(12): 13411352. https://doi.org/10.1038/ki.2010.536