

## International exchange

# Management of chronic kidney disease in primary health care: position paper of the European Forum for Primary Care

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## Introduction

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Chronic kidney disease (CKD) is a worldwide public health problem that is often underdiagnosed and undertreated. CKD is a ‘silent’ disease and goes unnoticed because it may not be ‘felt’. Yet it affects many more people than we might imagine: 1 out of 10 adults in the world has some form of kidney damage.<sup>1</sup> However, as many as 90% of those who have CKD remain unidentified. High blood pressure and diabetes are the main causes of CKD. It is projected that diabetes will increase by 70% by 2025. Therefore, early detection and prevention of the progression of CKD for people who also have a very high cardiovascular risk are extremely important challenges and goals for general practitioners/family doctors (GPs/FDs).

CKD represents a progressive, irreversible decline in glomerular filtration rate (GFR).<sup>2</sup> Most chronic nephropathies unfortunately lack a specific treatment and progress relentlessly to end-stage renal disease (ESRD). Progressive renal function loss is a common phenomenon in renal failure, irrespective of the underlying cause of the kidney disease.<sup>3</sup> The kidney is able to adapt to damage by adaptive hyperfiltration – increasing the filtration in the remaining normal nephrons. As a result, a patient with mild renal insufficiency often has a normal or near-normal serum creatinine concentration. Adaptive hyperfiltration, although initially beneficial, appears to result in long-term damage to the glomeruli of the remaining nephrons, which is manifest by proteinuria and progressive renal insufficiency. This process appears to be responsible for

the development of renal failure among those in whom the original illness is either inactive or cured.<sup>4</sup> The cost of the advanced renal failure and renal replacement therapy is enormous.<sup>5,6</sup> Therefore, early diagnosis and optimal management of CKD affords many challenges for primary health care in helping to maintain health and quality of life among the population at risk.

This position paper is based on published reviews about CKD management in different stages, and focuses on key references published since the year 2000. This position statement also provides evidence-based screening recommendations and interventions for shared care between GPs/FDs and specialists.

## Chronic kidney disease: definition, classification and epidemiology

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### Definition

The National Kidney Foundation – Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) workgroup has defined CKD as the following,<sup>7</sup> which have been accepted internationally with some clarifications:<sup>8,9</sup>

- 1 the presence of markers of kidney damage for three months, as defined by structural or functional abnormalities of the kidney with or without decreased GFR, that can lead to decreased GFR, manifest by either pathological abnormalities or other markers

of kidney damage, including abnormalities in the composition of blood or urine, or abnormalities in imaging tests

or:

- 2 the presence of GFR  $<60$  ml/min/(1.73 m<sup>2</sup>) for three months, with or without other signs of kidney damage as described above.

Based upon representative samples of the US population,<sup>7</sup> the studies have estimated the prevalence of CKD in the general population through measurement of markers of kidney damage, such as elevated serum creatinine concentration, decreased predicted GFR and presence of albuminuria.

According to the *Kidney Disease: improving global outcomes* (KD:IGO) position statement, the use of the term 'disease' in CKD is consistent with:

- 1 the need for action to improve outcomes through prevention, detection, evaluation and treatment
- 2 providing a message for public, physician and patient education programmes
- 3 common usage
- 3 its use in other conditions defined by findings and laboratory tests, such as hypertension, diabetes and hyperlipidaemia.<sup>9</sup>

## Classification of CKD

CKD is classified according to severity, diagnosis, treatment and prognosis.<sup>9</sup> Five-stage classification is based on structural and functional criteria regardless of the cause and accounting for dialysis and transplantation (see Table 1). The suffix 'T' is used for all transplant recipients, at any level of GFR, and 'D' for dialysis, for CKD stage 5 patients treated with dialysis.

## Epidemiology of CKD

Clinical evaluation for CKD should include elucidation of the cause of disease. However, the cause of the disease cannot be ascertained in all cases. Also, renal function declines normally with age, and the exact level of decline at a given age that should be considered pathological is not known. The KD:IGO statement considers GFR less than 60 ml/min to be pathological at all ages.<sup>10</sup> Cross-sectional studies report a slow decline in GFR after the fourth decade of life of  $\sim 0.75$  ml/min/(1.73 m<sup>2</sup>)/year. These changes proceed slowly but in the presence of other diseases such as diabetes, hypertension and heart disease, the kidney becomes vulnerable to failure.<sup>11</sup>

Very few of the causes of chronic renal failure are completely curable. It is often not necessary to do extensive tests to find a cause, especially when symptoms of renal insufficiency are already present. However, for determining the stage and specific characteristics of the underlying disease, follow-up of patients and thorough diagnostic work-up is needed. Diabetes is one of the commonest causes of kidney failure after glomerulonephritis in many countries.<sup>12–15</sup> The major groups of diseases leading to ESRD are glomerulonephritis, diabetic nephropathy, hypertension, chronic pyelonephritis and polycystic kidney disease. In different countries the proportions of these diseases as a cause of renal failure vary: e.g. glomerulonephritis accounts for 22–24% of renal replacement therapy (RRT) patients in Estonia, Germany, Poland or Finland, but only 11–12% in France, Italy or England. Patients of diabetic nephropathy form 12% of RRT patients in Italy, 22% in Estonia, 24% in Finland and Poland, 23% in Germany, 12% in England, 30% in Japan, and 37% in the US.<sup>16–19</sup>

**Table 1** Classification of chronic kidney disease<sup>10</sup>

Stage	Description	GFR (ml/min/1.73 m <sup>2</sup> )	Related terms
1	Kidney damage with normal or $\uparrow$ GFR	$\geq 90$	Albuminuria; proteinuria; haematuria
2	Kidney damage with mild $\downarrow$ GFR	60–89	Albuminuria; proteinuria; haematuria
3	Moderate $\downarrow$ GFR	30–59	Chronic renal insufficiency; early renal insufficiency
4	Severe $\downarrow$ GFR	15–29	Chronic renal insufficiency; late renal insufficiency; pre-end-stage renal failure
5	Kidney failure	$<15$	Renal failure; uraemia; end-stage renal disease

The use of RRT varies in different countries. There is a rising incidence and prevalence of kidney failure,<sup>12–15</sup> and the worldwide epidemic of CKD shows no signs of abating in the near future. The exact reasons for the growth of ESRD are unknown. Changes in the demographics of the population, differences in disease burden among different racial groups and under-recognition of earlier stages and of risk factors for CKD may partially explain this growth.<sup>8</sup> Recent trends show that the rate of increase of new cases of both diabetic and all-cause ESRD has progressively levelled off in many countries.<sup>13,20</sup> It is therefore currently impossible to predict the long-term trend of RRT in Europe. The prevalence of RRT patients/million inhabitants in 2005 was very different worldwide: in Estonia it was 394, in Finland 722, in Sweden 818, in Germany 1057, in Spain 899, in England 668 and in the US 1590.<sup>16,17</sup>

It has been shown that CKD affects men more often than women. For example, according to the Finnish Registry for Kidney Diseases, the prevalence of RRT in men was 898 and in women 553/million inhabitants in 2006.<sup>17</sup> Since 1996, the prevalence of RRT has increased faster among men (63%) than among women (44%). The prevalence among the elderly is growing rapidly: in the age group 75+ years, the prevalence of RRT has increased by almost 250% during the past ten years and 70% during the past five years. In the younger age groups, the prevalence has increased 10–61% in ten years and 4–14% in five years.<sup>17</sup>

## Management of chronic kidney disease patients

### Risk groups and screening

Detection of CKD is believed to be a priority for primary care because early treatment of CKD and its complications may delay or prevent the development of ESRD. It would be ideal for GPs/FDs to carry out screening, as the majority of the population visits their GP/FD within a 3-year period and can be subject to screening. There are reports suggesting that CKD is often not detected, even when patients have access to primary care.<sup>21</sup> There is an overwhelming consensus that screening for CKD should include high-risk groups. Screening for asymptomatic persons beyond the above-mentioned patient groups has not yet found justification. Early detection of diabetes and hypertension as the most important reasons for CKD, and their appropriate treatment is a method of avoiding or postponing complications, including chronic kidney failure. Screening of hypertension by measurement of blood pressure at GP/FD surgery visits has found

support in many guidelines.<sup>22</sup> However, systematic diabetes screening of members of the general population without symptoms or risk factors has not been found to be effective.

Risk groups for chronic kidney disease are those with the following:

- a family history of diabetes or hypertension
- diabetes
- hypertension
- recurrent urinary tract infections
- urinary obstruction
- systemic diseases that affect kidneys
- past or family history of cardiovascular disease.

The most widely used methods for screening for kidney disease are:

- 1 an analysis of a random urine sample for albuminuria
- 2 a serum creatinine measurement to calculate an estimated GFR, which is an indication of functioning kidney mass.

It is recommended to use both of these methods, as significant kidney disease can present with diminished GFR or proteinuria, or both.<sup>23</sup> Detecting and quantifying proteinuria is essential to the diagnosis and treatment of CKD. Albumin, the predominant protein excreted by the kidney in most types of renal diseases, can be detected by urine dipstick testing. The protein-creatinine ratio in an early-morning random urine sample correlates well with 24-hour urine protein excretion, and is much easier to obtain.<sup>7</sup> Albuminuria often heralds the onset of diabetic nephropathy; thus this sample is therefore recommended for all patients at risk for kidney disease. The quantitative determination of protein in the urine in the lab is more economical and more correct than the use of microalbuminuria dipsticks, and should be the recommended method to detect proteinuria. The term ‘albuminuria’ should be substituted for the terms ‘microalbuminuria’ and ‘macroalbuminuria.’ These terms are commonly used but should be avoided because they are misleading.<sup>10</sup> Increased urinary excretion of albumin is the earliest manifestation of CKD due to diabetes, other glomerular diseases and hypertensive nephrosclerosis. Also, albuminuria may accompany tubulointerstitial diseases, polycystic kidney disease and kidney disease in transplant recipients.

Significant kidney dysfunction may be present despite a normal serum creatinine level. An estimated GFR based on serum creatinine level correlates better with direct measures of the GFR, and detects more cases of CKD than does the serum creatinine level alone. Clinically useful GFR estimates are calculated from the measured serum creatinine level after adjustments for age, sex and race.<sup>24,25</sup> The two most commonly used formulae for GFR estimation are the

MDRD (Modification of Diet in Renal Disease) study equation and the Cockcroft–Gault equation (see Table 2). Validation studies in middle-aged patients with CKD showed the MDRD study equation to be more accurate.<sup>24</sup> However, the MDRD study equation was found to systematically underestimate the GFR in patients without CKD. It is important to realise that the methodology used for determination of serum creatinine is of great importance in the interpretation of the results obtained with the MDRD formula, and that in fact only the IDMS-corrected serum creatinine can be used.<sup>26</sup> It should be kept in mind that these formulae do not result in correct GFRs when used in persons with abnormal body composition: the obese, patients with oedema, pregnant women, those in states of cachexia, or amputees. In most situations of FDs, and as long as kidney function is stable, a calculated GFR can replace measurement of a 24-hour urine collection for creatinine clearance, but this is still required in pregnant women, patients with extremes of age and weight, patients with malnutrition, patients with musculoskeletal diseases, paraplegia or quadriplegia and patients with a vegetarian diet or rapidly changing kidney function.<sup>27</sup> Also, creatinine clearance is preferred in pre-dialysis and transplant patients.

## Prevention

Screening of risk populations may help early detection of kidney disease by GPs/FDs and enable the use of primary prevention strategies to avoid the development of diabetic or hypertensive nephropathy that may occur over many years and decades.

Primary prevention interventions seek to delay or halt the development of CKD. This involves public health measures to influence smoking cessation, modification of wrong dietary habits, and reduction of the prevalence of obesity among the population. Secondary and tertiary prevention interventions include prevention strategies for individuals with CKD, and seeking to prevent (secondary) or control (tertiary) complications of renal insufficiency.

Primary and secondary prevention of cardiovascular disease (CVD) and CKD remain the main purpose in modern medicine, as the main cause of death in patients with CKD is cardiovascular disease. The risk of death in CKD stage 4–5 patients is 10–20-fold that of the general population.<sup>28,29</sup> CKD patients belong in the highest-risk group for subsequent atherosclerotic complications. Therefore, CKD should be recognised as early as possible, and all prevention interventions that may arrest the progression of kidney disease and cardiovascular disease should be used.<sup>30</sup>

When kidney disease progresses, CKD patients become hypertensive, and develop combined hyperlipidaemia and hyperhomocysteinaemia, increased oxidative stress and decreased physical activity and psychosocial stress. If patients choose to smoke, the additive risk is profound.<sup>31</sup> Diabetes mellitus is a major risk factor for both CVD and CKD progression.<sup>32</sup> Moreover, CKD patients are usually older and are often menopausal if female.<sup>33</sup> Finally, CKD patients have a dramatic tendency for vascular and cardiac calcification that is related to hyperphosphataemia and secondary hyperparathyroidism.<sup>34</sup> Therefore, modification of cardiovascular risk factors, both classical and those associated with renal insufficiency (uraemic toxins, hyperphosphatemia, prolonged oxidative stress, malnutrition, hyperuricemia etc) should be considered in the management of CKD patients.

Secondary prevention and management of several renal and CVD risk factors such as hypertension, being overweight, hypercholesterolaemia, hypertriglyceridaemia and others should begin early in the course of CKD, with renoprotective and vasoprotective medications.<sup>35</sup> Hypertensive diabetics and those with microalbuminuria or macroalbuminuria, whether hypertensive or not, should be treated with renin–angiotensin system (RAS) blockers of either an angiotensin converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB).<sup>36</sup> ACE inhibitor therapy also lowers the rate of progressive kidney disease in children and young adults with immunoglobulin A (IgA) nephropathy and moderate proteinuria.<sup>37</sup> In addition to

**Table 2** Estimated GFR mathematical formulae

Study	Formula
Abbreviated MDRD study equation <sup>24</sup>	$GFR \text{ (ml/min/(1.73 m}^2)) = 186 \times (S_{Cr})^{-1.154} \times (\text{age})^{-0.203} \times (0.742, \text{ if female}) \times (1.210, \text{ if black})$
IDMS traceable MDRD formula <sup>26</sup>	$GFR \text{ (ml/min/(1.73 m}^2)) = 175 \times \text{standardised } (S_{Cr})^{-1.154} \times (\text{age})^{-0.203} \times (0.742, \text{ if female}) \times (1.212, \text{ if black})$
Cockcroft–Gault equation <sup>25</sup>	$GFR \text{ (ml/min/(1.73 m}^2)) = [(140 - \text{age}) \times \text{weight} \times (0.85, \text{ if female})] \div (0.81 \times S_{Cr})$

GFR = glomerular filtration rate; MDRD = Modification of Diet in Renal Disease;  $S_{Cr}$  = serum creatinine concentration ( $\mu\text{mol/l}$ )

classical risk factors, patients with CKD have specific risk factors (see Table 3). Psychosocial factors, such as environmental stress and responsiveness to stress, should not go unmentioned, especially when the patient is referred late to a kidney clinic.

## Principles of management of CKD: role of the GP/FD and shared care

As the population with chronic renal failure grows, primary care physicians will increasingly be involved in the management of these patients. GPs/FDs have an important role in detecting CKD early, in taking measures to slow the disease progression and in providing timely referral to a nephrologist.<sup>38</sup> However, who is responsible for CKD patients, whether the GP/FD or the specialist, depends on the stage of CKD and often on the organisation of the healthcare system. Several models of care of CKD patients are possible: a primary care-based model (conventional shared care between GPs and hospital-based nephrologists), secondary care-based model, or a model of specialised kidney centres besides routine primary and secondary care. International evidence indicates that health systems based on well-structured and organised primary care with adequately trained GPs provide both more cost-effective and more clinically effective care than those with a low primary care orientation. However, there is no specific evidence for the cost-effectiveness and clinical effectiveness of primary care in the specific case of CKD.<sup>39</sup> There are few data about management of CKD in primary care, and the data vary a lot from excellent to poor quality of care.<sup>40–43</sup> In addition, high total quality of care was achieved in most of the studies on CKD management in nephrological centres.<sup>44,45</sup>

The few studies that directly compared primary and nephrological care in advanced CKD supported management of CKD in nephrological centres.<sup>42,46</sup> In the guidelines of the UK, Canada and Australia, co-management of patients referred to a nephrologist with their primary care physician and other healthcare providers, to enable a shared care model is suggested,<sup>47</sup> which defines the roles and the ways of communication, but their implementation may be problematic.

The most important role of GPs/FDs in the management of CKD patients is detecting and treating possible reversible causes of renal dysfunction, and preventing the progression of CKD and CVD.<sup>4</sup> It is important to consider the patient's renal function in prescribing and, nowadays more importantly, in planning radiological investigations with contrast media. However, when symptoms of renal insufficiency become more pronounced, referral to and shared care with a nephrologist is essential (see Table 3).

The gradual decline in function in patients with CKD is initially asymptomatic. Different signs and

symptoms may be observed with advanced renal dysfunction, including volume overload, hyperkalaemia, metabolic acidosis, hypertension, anaemia and bone disease. A shared care, including involvement of a nephrologist, primary care physician, renal dietician, nurse and social worker, should be initiated early in the course of CKD, with close patient follow-up.

Management should include measurements of serum creatinine concentration and estimated GFR, haemoglobin, calcium, phosphate, potassium, bicarbonate and parathyroid hormone (PTH) concentrations, dietary assessment, treatment of anaemia with intravenous iron  $\pm$  erythropoiesis-stimulating agents, treatment of hyperparathyroidism and phosphate retention, correction of acidosis, counselling and education about the options for RRT and conservative (non-dialytic) management. Conservative (palliative) treatment may still include drug treatment of hypertension, anaemia, phosphate retention, hyperparathyroidism and acidosis if the patient chooses not to undergo RRT.

## Early referral to a nephrologist

Patients with CKD stage 1 and 2 should be treated in primary care, while the nephrologist's task is seen to be providing RRT. Late referral to specialist care for renal failure is associated with increased morbidity, mortality and cost. The criteria for referral to a nephrologist are shown in Box 1.<sup>48,49</sup>

## Pre-dialysis and renal replacement therapy: role of primary care and nephrologists

The availability of RRT forces the nephrologist to consider its application in every patient in whom it might be indicated. As kidney disease progresses, patients cannot get help only from GPs/FDs because of pre-dialysis activities and preparations for RRT, which take several months. Patients often feel that the nephrologist is the only doctor who should manage all medical problems.

There are many clinical problems in patients with CKD during the pre-dialysis and RRT period; these can be associated with CKD, but not always. Therefore, nephrologists often provide primary care or non-renal-related medical care to pre-dialysis patients or to patients undergoing chronic haemodialysis, because these patients visit the centre often. Patients also often feel that the nephrologist should manage even their acute illness, because the nephrologist is the first person who makes the diagnosis of acute illness. On the other hand, comparison of haemodialysis and peritoneal dialysis (HD, PD) patients showed that PD patients depended upon their nephrologists less.<sup>50</sup>

**Table 3** Principles of management of CKD patients

Management of CKD	Symptoms	Treatment of CKD, medical/non-medical	Monitoring of CKD patient by GP/FD/internist/ endocrinologist/cardiologist/ other	Monitoring of CKD patient by nephrologist
Treatment of reversible causes of renal dysfunction	Decreased renal perfusion (vomiting, diuretic use, diarrhoea, hypotension, etc) Administration of nephrotoxic drugs (aminoglycosides, non-steroidal anti-inflammatory drugs (NSAIDs), etc) Urinary tract obstruction	Diagnosis and treatment of pre-renal causes of renal dysfunction The administration of nephrotoxic drugs should be avoided or used with caution Urinary tract obstruction should always be considered in the patient with unexplained worsening renal function	Diagnosis and treatment by GP Urologic consultation if needed	If CKD progresses nephrologist consultation may be needed
Preventing or slowing the progression of CKD	Hypertension Proteinuria Diet Hyperlipidaemia Metabolic acidosis Anaemia Smoking Being overweight Low physical activity	RAS blockade Diet: low-protein, low-salt and low-fat Exclusion of risk factors (smoking, being overweight, low physical activity)	Diagnosis and treatment mostly by GP/FD when GFR >60 ml/min If GFR <60 ml/min(1.73 m <sup>2</sup> ): referral to nephrologist GFR <60–30 ml/min/ (1.73 m <sup>2</sup> ): equal shared care with GP/FD	Nephrologist consultation if needed for diagnosis clarification or when GFR <60 ml/min

Table 3 Continued

Management of CKD	Symptoms	Treatment of CKD, medical/non-medical	Monitoring of CKD patient by GP/FD/internist endocrinologist/cardiologist/other)	Monitoring of CKD patient by nephrologist
Treatment of the complications of renal dysfunction	Hypertension	RAS blockade and other antihypertensive drugs if needed	GP visits rarely, shared care with nephrologist	GFR <30 ml/min/(1.73 m <sup>2</sup> ): pre-dialysis care at kidney centre
Pre-dialysis care	Hyperphosphataemia	Diet	Identification, referral and adequate preparation of the CKD patient in whom RRT will be required	
	Osteodystrophy	Phosphate binders		
	Anaemia	Iron, erythropoietin		
	Disorders of fluid and electrolyte balance (volume overload)	Statins		
	Hyperkalaemia	Pre-dialysis care		
	Metabolic acidosis			
	Dyslipidaemia			
	Hormonal dysfunction			
Adequate preparation of the patient in RRT	Uraemic pericarditis, neuropathy	Haemodialysis	GP visits very rare, only if acute problems arise	Nephrologist: leads the treatment
	Bleeding	Peritoneal dialysis		
	Malnutrition	Kidney transplantation		
	Thyroid dysfunction			

### Box 1 Criteria for referral to a specialist

#### Services depending on GFR

- *Estimated GFR less than 15 ml/min/(1.73 m<sup>2</sup>):* immediate referral
- *Estimated GFR 15–29 ml/min/(1.73 m<sup>2</sup>):* urgent referral (routine referral if known to be stable)
- *Estimated GFR 30–59 ml/min/(1.73 m<sup>2</sup>):* routine referral if:
  - progressive fall in GFR/increase in serum creatinine
  - microscopic haematuria present
  - urinary protein to creatinine ratio greater than 45 mg/mmol
  - unexplained anaemia (haemoglobin below 11 mg/l)
  - abnormal potassium, calcium or phosphate
  - suspected systemic illness
  - uncontrolled blood pressure (above 150/90 mm/Hg on three occasions)
- *estimated GFR 60–89 ml/min/(1.73 m<sup>2</sup>):* referral not required unless other problems present

#### Services irrespective of GFR

- *Immediate referral* for: malignant hypertension, hyperkalaemia (potassium >7.0 mmol/l)
- *Urgent referral* for: proteinuria with oedema and low serum albumin (nephrotic syndrome)
- *Routine referral* for: dipstick proteinuria present and urine protein/creatinine ratio above 100 mg/mmol, proteinuria and microscopic haematuria present, macroscopic haematuria but urological tests negative

A paucity of objective data exist concerning the nephrologist's role as a primary care provider: the volume and type of practice provided by the nephrologist for patients with ESRD may be similar to that of the GP/FD.<sup>51–54</sup> During the pre-dialysis period and especially during RRT, patients visit the kidney centre more often than the GP/FD surgery. Therefore, as well as the RRT, nephrologists also have to deal with other general health problems (infections, traumas, drug prescription, social problems etc), which may or may not be associated with the CKD. Examples are a pre-dialysis diabetic patient with CKD and leg ischaemia, a peritoneal dialysis patient with abdominal pain, a transplanted patient with fever, or a haemodialysis patient with oedema.

The results of a recent study that estimates the annual cost of implementation of the guidelines on newly identified CKD cases among family doctors show significant increases in nephrology referral and additional investigation. The projected cost per practice of investigating stable stage 3 CKD patients was lower than for nephrology referral.<sup>54</sup> More studies

should be performed to compare long-term life quality and economic aspects in different managed care practices. It is possible that although in the first year CKD patient management costs are higher in specialised care settings, the long-term costs may be lower because of the better care.

Some nephrologists feel that the GP/FD should be the first to encourage the use of home-based dialysis therapies such as peritoneal dialysis. In practice, however, most GPs/FDs seem to be afraid of such methods. Once a patient is already undergoing dialysis therapy, the role of the GP/FD differs from country to country. In the UK, haemodialysis patients are seen by their nephrologist only once every month, so here the GP/FD might have an important role. In other countries, for example Belgium, haemodialysis patients are seen three times a week by their nephrologist.

### Social support

Social support is an understudied, yet important, modifiable risk factor in a number of chronic illnesses, including CKD and ESRD. Increased social support has the potential to positively affect outcomes through a number of mechanisms, including decreased levels of depressive effect, increased patient perception of quality of life, increased access to health care, increased patient compliance with prescribed therapies, and direct physiological effects on the immune system. Higher levels of social support have been linked to survival in several studies of patients with and without renal disease.<sup>55</sup> CKD patient education during the pre-dialysis period also involves management of future social needs. In patients who are students or still working, a suitable RRT method will usually be considered.

CKD occurs in patients with complex medical and social problems. CKD management requires that multidisciplinary professionals provide patient education, disease management and psychosocial support. To remain cost-efficient, many physicians are training and supervising mid-level practitioners in the delivery of specialised health care.<sup>56</sup> In the US and other countries, CKD clinics have been organised to better meet the specific needs of CKD patients. Multi-disciplinary collaboration among physicians (GP/FD, nephrologist, cardiologist, endocrinologist, vascular surgeon and transplant physician) and participating caregivers (nurse, pharmacist, social worker and dietician) is also critical. There are several potential barriers to the successful implementation of a CKD/ESRD programme, including lack of awareness of the disease state among patients and healthcare providers, late identification and referral to a nephrologist, and complex fragmented care delivered by multiple providers in many different sites of care.<sup>57</sup> Whether the multi-disciplinary team is built around specialist services or



primary care will depend on the particular healthcare system. However, primary care is an environment that permits better co-ordination of medical and social care.

## Concomitant major health problems in CKD patients

### Infection

Different infections are associated with CKD. The occurrence of urinary tract infection (UTI) is frequent and may complicate the course of CKD. Despite the frequency of renal impairment as a result of diabetes, the management of UTI in patients with CKD or renal failure has not been a focus of published literature.<sup>58</sup> Hepatitis- and human immunodeficiency virus (HIV)-infected patients can develop different types of CKD. At the time of HIV diagnosis, all patients should be assessed for existing kidney disease with a screening urine analysis for proteinuria and a calculated estimate of renal function.<sup>20,59,60</sup> Infectious diseases are the second most common cause of death in ESRD patients.<sup>61</sup> Hepatitis C is a complicating factor among patients with ESRD. The source of hepatitis C virus (HCV) infection in these patients can be nosocomial. Screening

and careful attention to infection control precautions are mandatory for dialysis units to prevent the spread of HCV.<sup>62</sup>

Regardless of age and the presence of other comorbid illnesses, it is recommended that patients with CKD receive regular vaccinations. Responsiveness to vaccination in patients with CKD can be diminished, but adequate seroresponse with standard or augmented regimens for vaccinations against influenza, hepatitis B, pneumococcus and other infections have been documented (see Table 4).<sup>63</sup> Live vaccines (yellow fever, polio, varicella and measles, mumps and rubella (MMR) vaccines) are generally avoided because they present a theoretical risk of vaccine-induced infection.<sup>63</sup>

### Nutrition

Dietary recommendations are important in the management of CKD and the maintenance of broader health in CKD patients. In early stages of CKD, dietary protein restriction is the first recommendation for preventing its progression.<sup>64,65</sup> However, the effects of dietary protein restriction in humans are controversial.<sup>66–69</sup> Guidelines suggest that the protein content of the diet should not be lower than 0.75 g/kg/day and should not exceed 0.8–1.0 g/kg/day.<sup>70</sup> The desire to maintain adequate nutrition among patients with

**Table 4** Recommended vaccines for CKD patients

Infection	Vaccine	Existing evidence and recommendations for CKD patients
Hepatitis B virus	Non-infectious recombinant DNA hepatitis B vaccine (Engerix B®)	Seroconversion rates were found in 60–91% of ESRD patients with higher doses of vaccine with 40 µg on a four-shot schedule
Hepatitis A virus	Inactivated non-infectious hepatitis A vaccine (Havrix®)	Hepatitis A virus vaccination in ESRD patients is well tolerated and immunogenic
Influenza	Inactivated influenza vaccines (Vaxigrip®, Influvac®)	Influenza vaccination was safe and effective in patients with CKD despite an impaired antibody response
Diphtheria and tetanus	Diphtheria and tetanus toxoids	Diphtheria and tetanus vaccine can be used in ESRD patients, but monitoring of antibody levels is recommended and a booster may be used in non-responding patients
Haemophilus influenza	Haemophilus influenza type B conjugate vaccine	ESRD patients should receive the same doses as for healthy subjects
Pneumococcal infection	23-valent pneumococcal polysaccharide vaccine (Pneumo 23®)	Vaccination is recommended standard doses of 23-valent pneumococcal polysaccharide vaccine, but revaccination should be performed within 3–5 years

chronic renal failure clearly competes with attempts to slow the progression of renal dysfunction with the use of a low-protein diet, since this level of restriction avoids protein malnutrition and may slow progressive disease.<sup>4</sup> All patients with stage 4–5 CKD should undergo regular nutritional screening by a dietician. Nutritional assessment should include a minimum of a record of body weight prior to the onset of sickness, current body weight and ideal body weight; body mass index (weight/height<sup>2</sup>); and subjective global assessment. Other measures of nutritional state are: serum creatinine, serum lipids, serum albumin and handgrip strength.<sup>65,71</sup> The dietary recommendations are different in all countries, but all guidelines agree that the energy intake in CKD patients of 30–35 kcal/kg/day may be sufficient. Sodium, total fat, cholesterol, carbohydrate, protein, phosphorus and potassium are restricted for all CKD patients.

## Anaemia

Anaemia is an early and common complication of CKD.<sup>72</sup> The GP's/FD's role should involve measurement of haemoglobin (Hb) concentration, mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) to assess the type of anaemia, absolute reticulocyte count to assess erythropoietic activity, plasma/serum ferritin concentration to assess iron stores, plasma/serum C-reactive protein (CRP) to assess inflammation, and assessment of occult gastrointestinal blood loss. GPs can usually treat most causes of anaemia.<sup>73</sup> Patients with a GFR <60 ml/min/(1.73 m<sup>2</sup>) should have their Hb level checked, and if it is found to be low then their anaemia should be further investigated and treated,<sup>73</sup> usually by a nephrologist. The recommended Hb levels at which therapy with an erythropoietic agent should be initiated is <110 g/l.<sup>74</sup>

## Education and quality of care

### Education

Education about the CKD, risk factors of the CKD progression and treatment with RRT should be viewed at different levels: medical professionals (nephrologists, internists, primary care doctors, nurses), patients, relatives and public health professionals. A modern approach to CKD and the concept that CKD is a risk factor for cardiovascular disease and needs to be managed (as does diabetes and dyslipidaemia) should be included in the undergraduate and postgraduate curriculum of physicians everywhere. The free movement of doctors

throughout the European Community has led to harmonisation of medical education to ensure common standards of care.<sup>75</sup>

Awareness of CKD risk factors among GPs/FDs who treat high-risk populations, such as persons with diabetes, persons with hypertension and family members of dialysis patients, should be excellent. Only GPs/FDs can diagnose the disease early and give advice to patients about the management of the risk factors that may lead to CKD progression. Primary care physicians and nurses need targeted education to increase awareness of populations at high risk for CKD.<sup>76</sup>

Timely education of CKD patients, their family members and close friends and/or primary care providers is critical for both HD and PD. Studies have shown that this can both improve outcomes and reduce costs. Nephrology nurses are often crucial for educating patients with CKD, patients with ESRD, family members and caregivers.

Hypertension and diabetes care guidelines have recently been updated. Many guidelines have also been worked out exceptionally for nephrologists.<sup>48</sup> A nephrologist's conformity to guidelines has been shown to be systematically better than that of non-nephrologists. Published analyses reveal that a large number of patients with advanced CKD are being treated solely by non-nephrologists, and that nephrologists treat patients with more-advanced disease.<sup>77</sup>

In order to improve patient outcomes, there is a need to take a more holistic approach to the problem, by co-ordinating the efforts of policymakers, those involved in healthcare system redesign, clinicians and researchers. In doing so, there should be an improvement in both identification and management of patients with impaired kidney function, whether cared for by primary care physicians, specialists, or nephrologists, and irrespective of the healthcare system.<sup>78</sup>

## Quality of care in CKD

Monitoring quality, particularly when clinically detailed measures are combined with appropriate incentives, may be one of the most effective ways to improve performance on targeted measures.<sup>79</sup> However, quality monitoring is only one aspect of quality management. Training of health staff, promoting the use of guidelines, having a database of chronically ill patients, call/recall systems, early recognition and referral, improved information systems, etc, are other very important tools in improving the quality of care of chronic patients.<sup>80</sup> Wagner worked out the widely accepted model of improvement of chronic disease management, which includes several components that are also important when talking about CKD management.<sup>81</sup>

### ***Training of health staff***

Several studies have shown that there is a lack of awareness of evidence-based guidelines for CKD, a large variability in the treatment of complications of CKD, and uncertainty of timing for referral to a nephrologist. The need for targeted training to raise the awareness of clinical practice guidelines and recommendations for patients with CKD among primary care physicians is emphasised.<sup>42,82,83</sup>

### ***Existence and implementation of evidence-based guidelines for management of CKD patients***

For optimal management of patients with CKD in primary care, good guidelines are needed, including identification of those who would benefit from referral to specialist services. Formulating and implementing specific treatment strategies are key factors in the success of achieving quality patient outcomes. Evidence-based guidelines for management of CKD have been developed in several countries.<sup>47,48,84</sup> As a variety of models have been proposed and implemented to improve CKD care, careful evaluation of what works and what does not work in the current clinical environment is needed. Guidelines need to be adapted to local situations in order to be acceptable and implemented.

### ***Information system facilitating the development of disease registries, tracking systems and reminders***

Early identification of CKD is important as it allows appropriate measures to be taken to slow or prevent the progression to more serious CKD and also to combat the major risk of illness or death due to cardiovascular disease. Studies of general practice computerised medical records show that it is feasible to identify people with CKD,<sup>85</sup> and that computer records are a valid source of data.<sup>86</sup> The UK Quality and Outcomes Framework has a very good example in having a valuable database of chronic patients and improving the quality of care. This system also consists of indicators for monitoring CKD, e.g. the percentage of patients on the CKD register in whom the last blood pressure reading, recorded in the previous 15 months, is 140/85 mmHg or less; the percentage of patients in the CKD register with hypertension who are treated with an ACE inhibitor or ARB.<sup>22</sup>

### ***Reorganising team function and practice systems to meet the needs of CKD patients and ensuring access to services that are proven to improve outcomes***

Recognition of CKD by the treating physician, and timely nephrology referral are shown to be essential

components for providing adequate care to patients with CKD.<sup>27,84</sup> Several authors believe that patients with CKD require a multidisciplinary team approach that focuses on early diagnosis of CKD, identifying and managing the complications of CKD, co-morbid conditions and smoothing transition to RRT. There should be integrated services with primary care, specialist services (nephrologist, endocrinologist, cardiologist, surgeon), nurses, a dietician and a palliative care team.<sup>47,57,87,88</sup>

## **Recommendations and issues for policymakers**

- 1 Health systems should guarantee the access of the population to primary care, with referral to secondary care, if needed.
- 2 Primary care should have a leading position in implementing the screening programmes for CKD in risk groups, and health systems should provide resources for this.
- 3 Primary care is in an ideal position to implement primary and secondary prevention of CKD. It is important to realise that CKD adds significantly to the overall cardiovascular risk; therefore, its prevention should be looked at within the framework of cardiovascular prevention.
- 4 Optimal co-operation between primary and secondary care should be developed for CKD patients. Shared-care models permit better co-ordination of services and are more cost-effective.
- 5 In primary health care, teams of GPs and other specialists should be involved. It is important to collect evidence of the role of primary care in prevention and care for patients with CKD. For advanced CKD cases when renal replacement therapies are used, nephrology teams have a major role. Even in this phase, good co-operation between primary and secondary care permits the best results for patients and for society. Educational programmes for different levels of patients, nurses and doctors are of utmost importance for achieving the best outcomes.

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## Appendix

### Consensus statements of the ISN (International Society of Nephrology) 2004 Consensus Workshop on Prevention of Progression of Renal Disease, Hong Kong, 29 June 2004 ( [www.nature.com/isn/education/guidelines/isn/full/ed\\_051027\\_4.html](http://www.nature.com/isn/education/guidelines/isn/full/ed_051027_4.html) )

The International Society of Nephrology recommends reference to these statements when formulating policy and guidelines for tackling chronic kidney disease (CKD), a disease with significant global impact.

- 1 It is recommended to establish a global surveillance centre (ISN Kidney Disease Data Center or ISN KDDC) to co-ordinate worldwide standardised screening studies with standardised screening techniques in appropriate target groups to allow for the collection of clearly comparable data.
- 2 It is recommended that patients diagnosed with diabetes and hypertension should have regular screening for development of kidney disease.
- 3 It is recommended that close relatives of patients with nephropathy due to diabetes, hypertension and glomerulonephritis should also be the primary targets for screening to detect clinically silent kidney disease.
- 4 No consensus was reached on an exact age 'cut-off' for initiating CKD screening.
- 5 It is recommended to develop standardised region- (or nation-) specific guidelines. It is envisaged that the 'tailor-made' tools for a particular region should provide reproducible and comparable results.
- 6 It is asserted that kidney disease is already a significant public health concern. There should be national policies for both public health and medical professionals to educate their societies on the importance of screening and early detection of kidney disease on prevention.
- 7 It is recommended to validate the current GFR estimation formulae based on ethnicities in different parts of the world.
- 8 It is recommended to use albumin–creatinine ratios (ACR) to quantify proteinuria and allow for follow-up. However, it is probably cost-prohibitive to use ACR as a tool for primary renal disease screening (except in diabetic patients).
- 9 It is strongly recommended to have the relevant screening for the development of CKD, recognising its close inter-relationship with cardiovascular, diabetic, and chronic metabolic diseases. Traditional cardiovascular disease risk factors should be screened in all patients with CKD. These include documentation of smoking history, measurement of blood pressure, body weight, body mass index, fasting plasma glucose, fasting lipid profile, serum uric acid level, and 12-lead electrocardiogram (ECG).
- 10 With the validation of GFR formulae in different ethnic groups, it is endorsed that GFR should be estimated from serum creatinine concentration at least yearly in patients with CKD. This should be done more often in patients with GFR below 60 ml/min/(1.73 m<sup>2</sup>), GFR decline greater than 4 ml/min/(1.73 m<sup>2</sup>), risk factors for faster progression, or exposure to risk factors for acute GFR decline, and in those undergoing treatment, to slow progression.
- 11 It is endorsed that CKD patients should be encouraged to reduce their body weight if overweight, adopt a healthy eating habit, restrict their dietary salt intake, cease smoking, moderate their alcohol consumption, and increase physical activity.
- 12 It is endorsed to achieve the target for blood pressure control in CKD patients of below 130/80 mmHg. It is recommended that adjunctive dietary salt restriction is invariably required. Diuretics and multiple medications in addition to ACE inhibitors/ARBs may also be used to achieve the blood pressure targets.
- 13 It is endorsed that glycaemic control in diabetic patients with CKD should be optimised to achieve a target fasting plasma glucose of <7.2 mmol/l and a hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) level of <7%. Hypertensive diabetics and those with microalbuminuria or macroalbuminuria, whether hypertensive or not, should be treated with either an ACE inhibitor or ARB.
- 14 It is recognised that further large-scale studies to substantiate the combined use of ACE inhibitor and ARB are needed, but that the cost of such combined therapy may be prohibitive for some countries.
- 15 It is recommended that patients with CKD should be referred to a nephrologist for evaluation when their creatinine clearance is <30 ml/min/(1.73 m<sup>2</sup>), or earlier in patients at risk of rapid progression or in whom doubt exists as to their diagnosis and prognosis.

## Guidelines

- ESH-ESC Task Force on the Management of Arterial Hypertension: *2007 ESH-ESC Practice Guidelines for the Management of Arterial Hypertension* [www.escardio.org/knowledge/cardiology\\_practice/ejournal\\_vol6/vol6n9.htm](http://www.escardio.org/knowledge/cardiology_practice/ejournal_vol6/vol6n9.htm)<sup>89</sup>
- European Renal Association: *European Dialysis and Transplantation Association guidelines* [www.era-edta.org/guidelines.htm](http://www.era-edta.org/guidelines.htm)
- International Society of Nephrology guidelines: [www.nature.com/isn/education/guidelines/guidelines.html](http://www.nature.com/isn/education/guidelines/guidelines.html)
- *Chronic Kidney Disease in Adults. UK guidelines for identification, management and referral*. London: RCP publications [www.rcplondon.ac.uk/pubs/books/kidney/ckd\\_clinical\\_guide.pdf](http://www.rcplondon.ac.uk/pubs/books/kidney/ckd_clinical_guide.pdf)