

SEN-semFYC Consensus Document on chronic kidney disease

R. Alcázar, M.^a I. Egocheaga¹, L. Orte, J. M.^a Lobos², E. González Parra, F. Álvarez Guisasola³, J. L. Górriz, J. F. Navarro and A. L. Martín de Francisco

Spanish Society of Nephrology (SEN). Spanish Society of Family and Community Medicine (semFYC). ¹On behalf of the Working Group on HBP. ²On behalf of the Working Group on Cardiovascular Disease. ³On behalf of the Working Group on Diabetes.

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INTRODUCTION

Chronic kidney disease (CKD) is a significant public health problem. According to the preliminary results of the EPIRCE study (Epidemiology of Chronic Kidney Disease in Spain), designed to ascertain the prevalence of CKD in Spain and sponsored by the Spanish Society of Nephrology (SEN) with the support of the Ministry of Health and Consumer Affairs, approximately 11% of the adult Spanish population has CKD of any severity.¹ CKD is associated to a significant cardiovascular morbidity and mortality, and also to highly significant costs. In Spain, the annual costs of treatment of the most advanced stages of CKD is estimated at more than 800 million euros.

There is a widespread idea that CKD is a rare and complex disease, but the actual fact is that, in its earlier stages, it is a common and easy to treat condition. Only a small proportion of patients evolve to end-stage renal failure with its associated complications and the need for renal replacement therapy. This evolution towards kidney function loss follows a progressive course in which we may influence by early intervention on its main causes, high blood pressure (HBP) and diabetes mellitus. Control of these two conditions should be strict and adequate to recommendations of the applicable guidelines,²⁻⁶ not only to minimise their progression and treat the complications inherent to renal failure, but also to reduce the vascular risk associated to CKD. A decreased kidney function is significantly associated to an increased cardiovascular risk.⁷⁻⁹

A significant number of patients with CKD are not diagnosed (it is estimated that approximately 20% of the population older than 60 years has renal failure, i.e. advanced CKD) either because kidney function controls are not made or because they have occult CKD (they have kidney disease despite the fact the serum creatinine levels are within the normal laboratory range).¹⁰⁻¹² In patients seen in primary care with such common diseases as HBP or diabetes mellitus, the prevalence of renal failure may be as high as 35%-40%.

Studies conducted over the past 5 years have confirmed that early detection and adequate referral to nephrology of patients with CKD improve long-term morbidity and decrease costs both for patients and the healthcare system¹³⁻¹⁷ because they allow for:

- Early identification of reversible causes of renal failure.
- Decreasing the progression rate of kidney disease.
- Reducing cardiovascular morbidity and mortality associated to renal failure.
- Adequately preparing patients for dialysis if this is required.
- Shortening hospital stay.
- Decreasing healthcare costs associated to CKD.

CKD care and prognosis should be improved by using early detection plans in the population at risk of developing CKD, which implies a close coordination and collaboration between primary care and nephrology.

OBJECTIVE AND APPLICATION SCOPE

The general objective of this document is to provide recommendations that allow for:

- Promoting optimum treatment of patients with CKD in the National Health System.
- Providing standardised and concise criteria for CKD definition and referral that may be easily accepted by all healthcare staff.

METHODOLOGY USED TO PREPARE THE DOCUMENT

Recommendations given in this document result from the search, critical evaluation, and synthesis of the available scientific evidence about CKD, its estimation using glomerular filtration rate (GFR), and the benefits of intervention on this. Whenever possible, the level of scientific evidence and the strength supporting each of the recommendations have been included in accordance with the criteria of the Kidney Disease Improving Global Outcomes (KDIGO), which are the Gra-

Correspondence: Roberto Alcázar Arroyo
Hospital de Fuenlabrada
Camino del Molino, 2
28942 Fuenlabrada. Madrid
ralcazar@senefro.org

special article

des of Recommendation, Assessment, Development, and Evaluation (GRADE), as modified for CKD. Annex I shows the meaning of the evidence levels and strength of recommendations used in this document.¹⁸

CONCEPT OF CHRONIC KIDNEY DISEASE (CKD)

CKD is defined as a decreased kidney function, as shown by a GFR < 60 mL/min/1.73 m² or the presence of persistent renal damage for at least 3 months. It therefore includes:

- Kidney damage diagnosed by a direct method (histological changes in a renal biopsy) or indirectly using markers such as albuminuria or proteinuria, urinary sediment changes, or imaging test changes.
- GFR impairment (< 60 mL/min/1.73 m²).

The following stages are distinguished based on the GFR calculated or estimated using different formulas:²

Stage	GFR (ml/min/1.73 m ²) (glomerular filtration rate)	Description
1	≥ 90	Kidney damage with normal GFR
2	60-89	Kidney damage, slight decrease in GFR
3	30-59	Moderate decrease in GFR
4	15-29	Severe decrease in GFR
5	< 15 or dialysis	Predialysis/dialysis

Stages 3-5 represent what is usually known as renal failure. These changes should be confirmed for at least 3 months.

RECOMMENDATIONS

1. Any patient with CKD (renal failure (GFR < 60 mL/min) and/or renal damage) should undergo studies to determine the evolution stage, potential reversibility, and prognosis of the disease, and to allow for optimisation of therapeutic options (*Strength of recommendation: C*).

2. In any male over 60 years of age with CKD, the presence of obstructive urinary disease should be ruled out using ultrasonography (*Strength of recommendation: A*).

3. Patient groups at risk of developing CKD who should be screened include: patients over 60 years of age, patients with HBP, diabetes or cardiovascular disease, or relatives of patients with renal failure (Annex II) (*Strength of recommendation: B*). Screening consists of assessment of GFR and albuminuria at least once a year.

4. Serum creatinine measurements should not be used as the only parameter to assess kidney function. GFR estimation through equations is the best index available in clinical practice to assess kidney function. Measurement of creatinine clearance by collection of 24-hour urine does not improve, except in certain circumstances, the GFR estimation obtained from equations (*Strength of recommendation: A*).

5. The formula of the MDRD study (Modification of Diet in Renal Disease) is recommended to estimate GFR. The Cockcroft-Gault formula may be used as an alternative.

MDRD

$$\text{Estimated GFR} = 186 \times (\text{creatinine (mg/dL)}/88.4)^{-1.154} \times (\text{age})^{-0.203} \\ \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$$

Cockcroft-Gault

$$\text{CrCl} = [(140 - \text{Age}) \times \text{Weight (kg)}] / [\text{SCr (mg/dL)} \times 72] \times 0.85 \text{ if female}$$

Predictive equations recommend giving the numerical result only if GFR is less than 60 mL/min, but not for higher levels.

6. Equations are not adequate under the following circumstances.

- Extreme body weight: body mass index (BMI) under 19 kg/m² or over 35 kg/m².
- Significant muscle mass changes (amputations, muscle mass loss, muscle diseases or paralysis).
- Acute renal failure.
- Pregnancy.
- Severe liver disease, generalised oedema, or ascites.

In these cases, it is recommended to use other methods to estimate GFR, such as conventional creatinine clearance (24-hour urine) or isotopic methods.

7. Urinary protein excretion should preferably be assessed as the albumin/creatinine ratio in a random urine sample (normal < 30 mg/g), preferably in first morning urine. This ratio represents a good estimate of proteinuria and avoids use of 24-hour urine collection (*Strength of recommendation: A*).

8. CKD represents an independent and additive vascular risk factor. The risk of cardiovascular morbidity and mortality increases with the progression stage of CKD and is much higher than the risk of progression to advanced renal failure.

CKD detection and control is therefore recommended in the setting of overall assessment and management of vascular risk (*Strength of recommendation: A*).

9. In the overall approach to patients with CKD, special attention should be paid to control of classical vascular risk factors (Strength of recommendation: B). Therapeutic objectives include:

- Control of BP < 130/80 mmHg (125/75 mmHg if the albuminuria/creatininuria ratio is > 500 mg/g).
- Reduction of proteinuria (with the objective of achieving an albuminuria/creatininuria ratio < 300 mg/g) with angiotensin converting enzyme inhibitors (ACEIs) or angiotensin II receptors blockers (ARBs).
- Control of dyslipidemia: low density lipoprotein (LDL) levels < 100 mg/dL, high density lipoprotein (HDL) levels > 40 mg/dL.
- Control of diabetes: HbA1c < 7%.

10. In overall management of patients with CKD 3-5 (renal failure), special attention should also be paid to avoiding iatrogenics (Strength of recommendation: A).

- Adjusting drugs to GFR, particularly in the elderly.
- Avoiding use of NSAIDs as much as possible.
- Using with caution metformin and oral antidiabetics excreted by the renal route (most of them) and avoiding their use with GFR values < 30 mL/min.
- Avoiding uncontrolled association of potassium-retaining drugs, such as ACEIs, ARBs, potassium-sparing diuretics, NSAIDs, beta-blockers.

11. Referral to nephrology will be made based on CKD stage, patient age, rate of progression of kidney failure, degree of albuminuria, and the presence or occurrence of warning signs* (fig. 1) (Strength of Recommendation: C). In general:

- Age > 70 years, stable stage 1-3 CKD (GFR > 30 mL/min) and albuminuria < 500 mg/g, may be followed up in primary care without the need for referral, provided adequate control of BP and all other vascular risk factors is maintained.
- Age < 70 years, GFR > 45 mL/min: Refer if albuminuria is increasing or > 500 mg/g, or complications occur (anaemia: Hb < 11 g/dL after correcting iron deficiency, or impossibility of controlling vascular risk factors, such as refractory HBP). Primary care or joint follow-up, as appropriate.
- GFR < 45 mL/min: Referral to nephrology. Joint follow-up or, in selected cases, primary care follow-up.
- Stages 4-5: Referral to nephrology in all cases.
- Warning signs: Non-urological haematuria associated to proteinuria, serum creatinine increase by > 1 mg/dL in less than one month.

12. Referral of diabetic patients to nephrology for assessment will be based on prior criteria, but is mandatory in any patient with: (Strength of recommendation: C):

Table I. Joint follow-up of patients with CKD by nephrology and primary care

	Glomerular filtration rate estimated by MDRD (mL/min)			
	> 60 (CKD 1-2)	45-60 (CKD 3)	30-45 (CKD 3)	< 30 (CKD 4-5)
Primary care	6 months	4-6 months	3-6 months	Individualised*
Nephrology	1 year or no revision	1 year or no revision	6 months	1-3 months

* Joint follow-up, particularly at nephrology, except for advanced CKD not amenable to start of renal replacement therapy (revision every 1-2 months) or in the event of any other non-nephrological concomitant condition.

The following is recommended at each primary care revision:

Monitor BP and adjust treatment to achieve the goal (BP < 130/80 mmHg or < 125/75 mmHg if albumin/creatinine ratio > 500 mg/g. More than 2 drugs, including adequate diuretic therapy, will be required in many cases to achieve this goal. This measure must be cautiously and carefully individualised in elderly patients.

- **Monitor for anaemia.** If CKD 3-5 and Hb < 11 g/dL, consider referral or advance revision at nephrology to consider treatment with erythropoiesis stimulating factors.
- **Review medication,** with dose adjustment according to GFR. In CKD 3-5, avoid use of NSAIDs, oral antidiabetics excreted by the renal route, and iodinated contrast agents.
- **Review dietary habits,** guiding patients on the type of diet to be followed based on GFR:
 - CKD 1-3: Low sodium diets are only advised in the event of HBP.
 - CKD 4-5: Dietary recommendations about sodium, phosphorus, and potassium.
- **Laboratory tests at each revision for CKD stage 3 or higher*:** A 24-hour urine test is not needed (test required as a minimum in **bold**):
 - **Complete blood test.**
 - Blood chemistry: **glucose, Scr, urea, Na, K, Ca, P, albumin, and cholesterol. GFR estimated by MDRD equation.**
 - Urine chemistry (in spot sample of first morning urine): **albumin/creatinine ratio.**
 - Urine sediment, if prior changes should be monitored.

* An attempt will be made to avoid repeat sampling. Patients must be given a report or a copy of test results. In the event of monthly revisions at nephrology, tests need not be repeated in primary care visits.

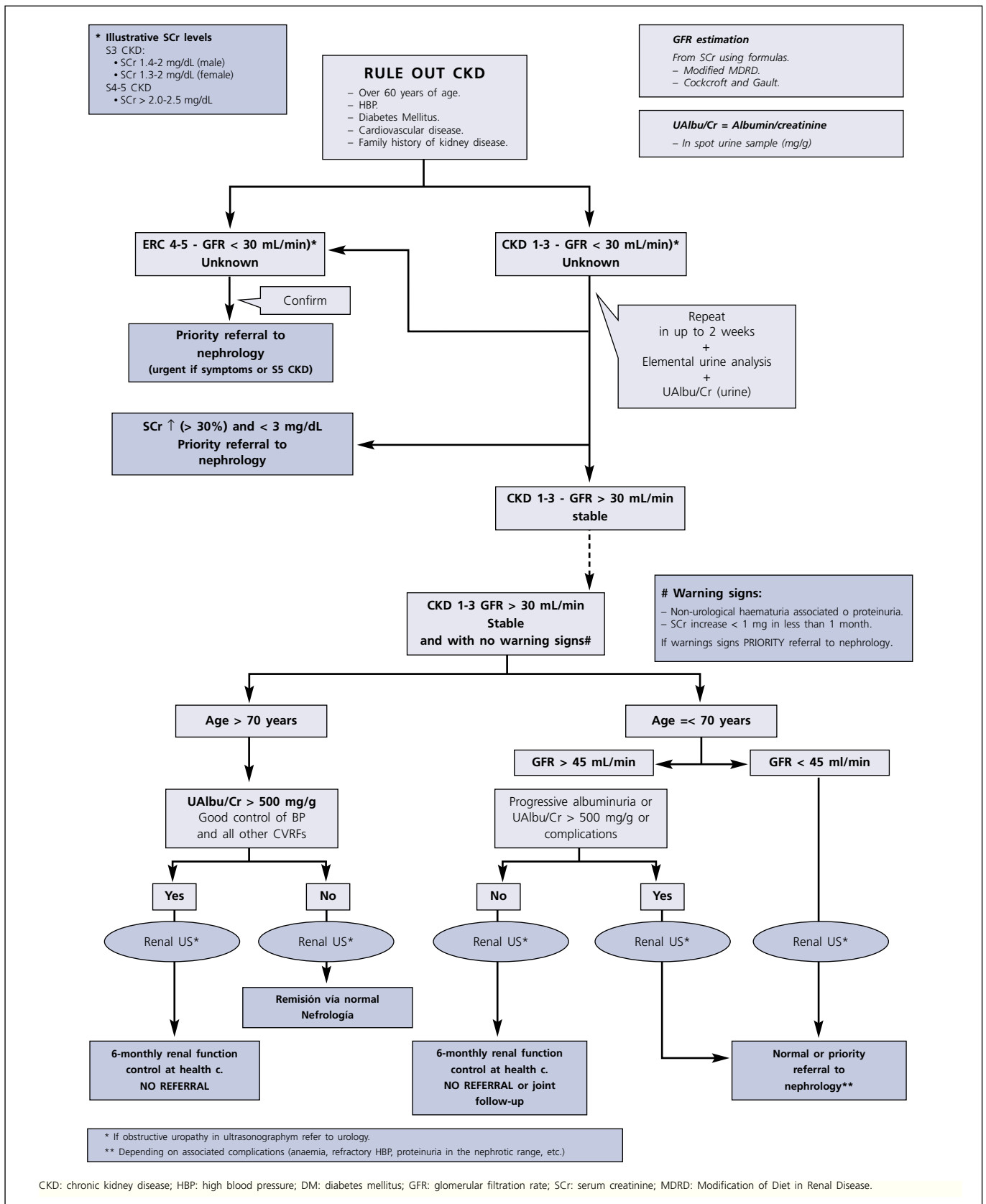


Figure 1. Diagnóstico y seguimiento de la ERC.

Table II. What is expected from each specialist at each revision?

CKD Stage	Primary care	Nephrology
1 and 2 (GFR > 60 mL/min)	<ul style="list-style-type: none"> - Identification of risk factors for CKD. - Detect CKD progression. <ul style="list-style-type: none"> • GFR impairment. • Increased proteinuria. - Control associated CVRFs. 	<ul style="list-style-type: none"> - Look for renal diseases amenable to specific treatment: <ul style="list-style-type: none"> • Primary or secondary glomerulonephritis. • Ischaemic nephropathy. - Detect CKD progression. - Assess suitability of combinations of specific drugs (including ACEIs + ARBs).
3 (GFR 30-60 mL/min)	<ul style="list-style-type: none"> - Detect CKD progression. - Control associated CVRFs. - Drug adjustment to GFR Review of nephrotoxic drugs (e.g. NSAIDs). - Hygienic and dietary advice. - Vaccinate against pneumococcus, influenza, and HBV. - Detect CKD complications: <ul style="list-style-type: none"> • Anaemia. • Electrolyte disorders. 	<ul style="list-style-type: none"> - Look for renal diseases amenable to specific treatment. - Assess and treat CKD complications: <ul style="list-style-type: none"> • Renal osteodystrophy. • Anaemia. • Electrolyte disorders. - Control associated CVRFs.
4-5 (GFR < 30 mL/min)	<ul style="list-style-type: none"> - Hygienic and dietary advice. - Drug adjustment to GFR Avoid nephrotoxic agents (NSAIDs, iodinated contrasts). - Detect CKD complications: <ul style="list-style-type: none"> • Anaemia. • Electrolyte disorders. 	<ul style="list-style-type: none"> - Prepare for renal replacement therapy if appropriate. - Organise palliative treatment if replacement therapy not appropriate. - Assess and treat CKD complications: <ul style="list-style-type: none"> • Renal osteodystrophy. • Anaemia. • Acidosis. • Electrolyte disorders.

Care is cumulative (e.g. in stage 3, actions recommended for stages 1 and 2 should also be taken).

- Albuminuria: albumin/creatinine ratio (confirmed) > 300 mg/g despite adequate BP treatment and control.
- Increase in albuminuria despite adequate treatment.
- Refractory HBP (three drugs at full doses and lack of control).

13. In each health area, primary care and nephrology should establish *joint follow-up procedures* including objectives to be met depending on CKD stage (tables I and II), (*Strength of recommendation: C*).

RATIONALE FOR RECOMMENDATIONS

CKD is a progressive condition with a variable impairment rate depending on the etiology of kidney disease and on patients themselves. Observational studies have consistently shown increases in morbidity, hospital stay, and costs in patients in advanced CKD stages (CKD 4-5) referred late to nephrology clinics.¹⁹⁻²⁵

It is also known that patients in earlier stages (CKD 1-3) may also benefit from early diagnosis and start of measures to prevent CKD progression and vascular disease.²⁶⁻²⁹ Eleven percent of the adult population has some degree of CKD, and approximately 5% already have renal failure (stage 3-5 CKD).¹

The expert group writing this consensus document therefore thinks that any patient with CKD should undergo

tests that establish the stage, potential reversibility, and prognosis of the disease and allow for optimising therapeutic options (*Recommendation 1*) (*Strength of recommendation: C*)

Final evaluation of any patient with CKD should be made based on changes in laboratory tests over time. Any prior control allows for optimising differential diagnosis between a stable or slowly progressive CKD and an acute or subacute CKD, or an exacerbation of CKD.

Obstructive uropathy is a common cause of CKD, particularly in males over 60 years of age.³⁰ A recent epidemiological study confirmed a clear association between symptoms and signs of urinary flow obstruction and risk of CKD.³¹ It is also a treatable cause, as correction of obstruction delays progression of CKD. An ultrasonography is therefore *recommended* in any male over 60 years of age with CKD (*Recommendation 2*) (*Strength of recommendation: A*).

Various epidemiological studies have shown an increased risk of CKD in subjects with any of the following: age over 60 years, HBP, diabetes, or cardiovascular disease, patients with autoimmune diseases or a history of acute renal failure, or relatives of patients with renal failure (Annex II). Thus, according to K/DOQI and KDIGO guidelines on CKD,^{2,32} screening tests for CKD should be performed in all these patients. (*Recommendation 3*) (*Strength of recommendation: B*).

GFR should be estimated using equations that take into account serum creatinine levels. The Spanish Society of Nephrology has jointly prepared with the Spanish Society of Clinical Chemistry a consensus document defining equations to be used and the circumstances in which these estimations are not useful³³ (*Recommendations 4, 5, and 6*) (*Strength of recommendation: A*).

Evaluation of patients with documented or suspected CKD should include GFR estimation, urine sediment, and measurement of albuminuria in a spot urine sample.⁵ Calculations made in a spot sample (albumin/creatinine ratio) are adequately correlated to 24-hour albuminuria (Annex III). Various studies in both diabetic and non-diabetic patients have shown this correlation.³⁴⁻³⁹ (*Recommendation 7*) (*Strength of recommendation: A*).

The importance of detecting patients with CKD lies in intervention not only to prevent progression of kidney disease, but to decrease the associated cardiovascular risk. Indeed, a much greater proportion of CKD patients die from cardiovascular complications during follow-up as compared to those who progress to a CKD stage amenable to renal replacement therapy.⁸ CKD is a treatable and potentially preventable independent vascular risk factor. Patients with CKD should be considered the group with the highest risk for developing cardiovascular events, as stated in the most recent HBP guidelines of the Joint National Committee and in the guidelines of the American Heart Association and National Kidney Foundation.⁴⁰⁻⁴⁴ (*Recommendation 8*) (*Strength of recommendation: A*).

Therapeutic measures to be taken in CKD patients should be adapted to CKD grade. Classical vascular risk factors (HBP, dyslipidemia, diabetes, and obesity) should be controlled in all patients. The therapeutic goals of such control are given in the SEN guidelines on kidney and cardiovascular disease.⁵ (*Recommendation 9*) (*Strength of recommendation: B*).

The main complications of stage 3-5 CKD include those derived from iatrogenics, particularly in elderly patients. This is one of the aspects requiring closer attention in monitoring of these patients. There are three essential considerations: (*Recommendation 10*) (*Strength of recommendation A*).

1. Avoid drug-related hyperkalemia.⁴³ Special caution should be taken with the association of a potassium-sparing diuretic (spironolactone, amiloride, eplerenone) and a potassium-retaining drug (ACEIs, ARBs, NSAIDs, beta-blockers). Frequent monitoring of serum potassium levels is mandatory in these cases.
2. Avoid diagnostic tests using iodinated contrast agents and unnecessary use of NSAIDs, because of the risk of kidney function impairment.
3. Adjust drugs to GFR, particularly in elderly and diabetic patients. Metformin and oral antidiabetics excreted

by the renal route (most of them) should be used with caution in these patients, and avoided if GFR is < 30 mL/min.

In each health area, primary care physicians and the reference nephrology department should reach a consensus about patient referral to a nephrologist, including written action plans and regular reviews. In this document, the expert group is of the opinion that referral should be based on CKD stage, age, progression rate of renal failure, degree of proteinuria, and the presence or absence of warning signs. In patients over 70 years of age, and particularly in those older than 80 years, the mortality risk associated to stage 1-3 CKD is not as consistent or high as in patients younger than 70 years,⁴⁵ and it is therefore advisable that age is a very significant aspect to be considered in referral (*Recommendation 10*) (*Strength of recommendation: C*). Other important recommendations for referral are given in Annex IV.

STATEMENT OF INTENTION

These recommendations are not intended to be a reference standard. Treatment standards are established based on all clinical data available for a specific case and change with progress in technical advances and scientific knowledge. This publication is an opinion of experts from two scientific societies, SEMFYC and SEN, based on the evidence available at the time of its preparation. Adherence to these recommendations may not ensure an effective outcome in each particular case, nor does imply that all appropriate care methods are included, or that other acceptable methods for achieving the same results are excluded. Physicians have the ultimate responsibility for treatment of their patients based on individual clinical data and on the diagnostic and therapeutic options available.

CONFLICTS OF INTEREST

None.

ABBREVIATIONS

ACEIs: Angiotensin converting enzyme inhibitors.

ARBs: Angiotensin II receptor blockers.

BMI: Body mass index.

BP: Blood pressure.

CKD: Chronic kidney disease.

CVRFs: Cardiovascular risk factors.

GFR: Glomerular filtration rate.

HBV: Hepatitis B virus.

HDL: High density lipoprotein.

LDL: Low density lipoprotein.

MDRD: Modification of Diet in Renal Disease.

NSAIDs: Non-steroidal anti-inflammatory drugs.

SCr: Serum creatinine.

UACR: Albumin/creatinine ratio in a spot urine sample.

ANNEX I: LEVELS OF EVIDENCE

Sources of information

High evidence: Subsequent research is unlikely to change confidence in effect estimation.

Moderate evidence: Subsequent research may have an impact on effect estimation and this estimation may change.

Low or very low evidence: Subsequent research is very likely to have a significant impact on effect estimation.

Strength of recommendations included in the document

Strength of recommendation A. Strong recommendation. The quality of the available evidence is high, which together with other considerations leads to strongly advising that this recommendation is followed. This recommendation is expected to be followed and to serve as the basis for a quality indicator.

Strength of recommendation B. Weak recommendation. The quality of the available evidence is high or moderate, which together with other considerations leads to suggest that this recommendation is followed. It is expected to be followed by most clinicians.

Strength of recommendation C. Opinion. The quality of the available evidence is low or very low. This is a recommendation based on the opinion of experts.

Modified from: Unlig K, Macleod A, Craig J, et al: Grading evidence and recommendations for clinical practice guidelines in nephrology. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int.* 2006 70: 2058-65.

ANNEX II. CONDITIONS LEADING TO AN INCREASED RISK OF CHRONIC KIDNEY DISEASE

- Age \geq 60 years.
- HBP.
- Diabetes mellitus.
- Cardiovascular disease.
- Obesity.
- Autoimmune diseases.
- History of acute renal failure.
- Family history of renal failure or disease (polycystic kidney disease).
- Heart failure
- Neoplasm

- Long-term treatment with any of the following drugs:
 - Lithium carbonate.
 - Mesalazine and other 5-aminosalicylic drugs.
 - Calcineurin inhibitors (cyclosporin, tacrolimus).
 - NSAIDs.
- Recurrent urinary tract infections.
- Urinary stones.
- Obstructive urinary tract disease.
- Low birth weight.
- Low socioeconomic level.
- Afroamerican ethnicity.

In bold, conditions with a high prevalence in the population.

ANNEX III. DEFINITIONS OF ALBUMINURIA DEPENDING ON THE TYPE OF SAMPLE USED

	ALBUMINURIA		
	Spot urine sample Albumin/creatinine ratio (mg/g)	24-hour urine (mg)	Timed urine (μ g/min)
Normal	< 30	< 30	< 20
Albuminuria	30-299	30-299	20-199
Proteinuria	\geq 300	\geq 300	\geq 200

Albumin/creatinine ratio is mg/g is advised.

Albuminuria should always be confirmed in at least two of three samples within 3-6 months.

ANNEX IV. SUGGESTIONS ABOUT PATIENT REFERRAL TO NEPHROLOGY

1. Confirm laboratory test data.

2. When should patients be referred to nephrology?

In the event of:

- Any stage 4-5 CKD (GFR < 30 mL/min). This corresponds to SCr > 2-2.5 mg/dL. Referral should be preferential/urgent depending on the waiting list in each health area.
- Stage 3-4 CKD (GFR < 60 mL/min) that progresses (serum creatinine increase by more than 0.5 mg/dL every 2-3 months in successive controls).
- For stable CKD, the following age criteria will apply:
 - Age > 70 years, stable stage 1-3 CKD and albuminuria < 500 mg/g (in a spot urine sample), may be followed up in primary care without the need for referral, provided adequate control of all other vascular risk factors is maintained.
 - Age > 70 years, stage 1-3 CKD. If GFR is higher than 45 mL/min and albuminuria is < 500 mg/g, referral to nephrology

may not be required, and patients may be monitored in primary care with a consensus on follow-up and treatment. GFRs under 45 mL/min should be assessed at nephrology, with joint follow-up with primary care.

- In diabetic patients, the above criteria will apply, but any patient with the following conditions must be referred to nephrology:
 - Macroalbuminuria: albumin/creatinine ratio (confirmed) > 300 mg/g despite adequate BP treatment and control.
 - Increase in albuminuria despite adequate treatment.
 - Refractory HBP.

Referral to the nephrology department is recommended for patients with grades of renal failure lower than those previously discussed in the presence of active sediments (micro and macrohaematuria) and associated systemic signs such as fever, malaise, joint pain, paraesthesia, or skin lesions, as they may suggest conditions such as vasculitis, among others. A rapid increase in serum creatinine levels (> 1 mg/dL in one month) is an indication for preferential/urgent referral to nephrology.

3. How should patients be referred?

It is advised to refer patients with a short report including laboratory tests (recent and old), examinations performed, and current medication.

4. Indications for requesting renal ultrasonography (a short report with the clinical judgment must be included in the request form).

- Renal failure (GFR < 60 mL/min).
- Persistent haematuria or proteinuria.
- Recurrent urinary tract infections with renal involvement.
- Difficult to control HBP with target organ lesion.

Shared approaches to CKD and priorities in responsibility

Once CKD diagnosis is established, the primary care physician (PCP) and the nephrologist should agree on a plan of action and regular monitoring aimed at:

- Treating the underlying disease if amenable to treatment (systemic diseases, primary glomerulonephritis,...) (nephrologist).
- Identifying and treating factors related to progression of kidney disease (PCP and nephrologist):
 - HBP, preferably with ACEIs or ARBs and diuretics from the start. BP goal: 130/80 mmHg (125/75 mmHg if the albuminuria/creatininuria ratio is > 500 mg/g). Monitoring of serum creatinine and potassium levels one week after treatment start is mandatory.
 - Proteinuria: Use ACEIs or ARBs and a low sodium diet.
 - Metabolic control in diabetic patients: HbA1C < 7%.
- Identifying and treating conditions secondary to CKD (anaemia, secondary hyperparathyroidism, hyperphosphoremia, dyslipidemia, malnutrition, metabolic acidosis) (PCP and nephrologist).
- Preparing patients for renal replacement therapy in advanced CKD (nephrologist).

Other actions to be considered:

- Drug adjustment to kidney function (particularly aminoglycosides, cephalosporins, quinolones, digoxin, acyclovir, vancomycin, and ethambutol).
- Avoid, if possible, nephrotoxic agents (aminoglycosides) and radiological contrast agents.
- Regular monitoring of kidney function according to the protocol.
- Avoid if possible NSAID use. If administered, NSAIDs with a short half-life should preferably be used for only a few days.
- If CKD exists, avoid concomitant administration of ACEIs or ARBs with potassium-sparing diuretics (spironolactone, eplerenone, amiloride) due to the risk of hyperkalemia, particularly when NSAIDs are concomitantly take.
- If advanced renal failure exists (GFR < 30 mL/min), potassium salts should not be replaced and salt substitutes should not be recommended.
- Give the drugs strictly necessary, at the adequate doses and intervals, for the necessary time.
- Monitor potentially dangerous treatments (potassium and creatinine monitoring after start of treatment with ACEIs-ARBs in risk patients).
- Any elderly subject should be considered as a patient with mild to moderate CKD.

Any question regarding diagnosis or treatment in a patient with CKD should be asked to the nephrologist, for which adequate contact means for each circumstance will be provided.

Note: A summary of the Consensus Document may be downloaded from the web site of the Spanish Society of Nephrology at <http://www.senefro.org>, section **Acción Estratégica**

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REFERENCES

- Otero A, Gayoso P, García F, De Francisco AL. Epidemiology of chronic renal disease in the Galician population: results of the pilot Spanish EPIRCE study. *Kidney Int Suppl* 2005; S16-S19.
- National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39 (Supl. 1): S46-S75.
- KDIGO: Kidney Disease: improving global outcomes. Disponible en: <http://www.kdigo.org/>
- Documento de consenso 2002 sobre pautas de detección, prevención y tratamiento de la nefropatía diabética en España. Asociación Española de Nefrología Pediátrica (AEN-PED). Sociedad Española de Diabetes (SEDIAB). Sociedad Española de Endocrinología y Nutrición (SEEN). Sociedad Española de Hipertensión Arterial, y Liga Española para la Lucha Contra la HTA (SEH-LELHA). Sociedad Española de Medicina Familiar y Comunitaria (SEMFYC). Sociedad Española de Medicina Rural y Generalista (SEMERGEN). Sociedad Española de Nefrología (SEN). *Nefrología* 2002; 22: 521-530.
- Guías SEN: Riñón y Enfermedad Cardiovascular. *Nefrología* 2004; 24 (Supl. 6): 13-235.
- Marín R, Goicoechea MA, Gorostidi M et al. en representación del Comité de Expertos de la Guía de la Sociedad Española de Nefrología (SEN) Riñón y Enfermedad Cardiovascular. Guía de la Sociedad Española de Nefrología sobre Riñón y Enfermedad Cardiovascular. Versión abreviada. *Nefrología* 2006; 26: 31-44.
- Go AS, Chertow GM, Fan D McCulloch CE, Hsu C. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization. *N Eng J Med* 2004; 351: 1296-1305.
- 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; 164: 659-663.
- Brosius FC III, Hostetter TH, Kelepouris E et al. Detection of Chronic Kidney Disease in Patients With or at Increased Risk of Cardiovascular Disease: a Science Advisory From the American Heart Association Kidney and Cardiovascular Disease Council; the Councils on High Blood Pressure Research, Cardiovascular Disease in the Young, and Epidemiology and Prevention; and the Quality of Care and Outcomes Research Interdisciplinary Working Group: Developed in Collaboration With the National Kidney Foundation. *Circulation* 2006; 114: 1083-1087.
- Otero A, Abelleira A, Camba MJ et al. Prevalencia de insuficiencia renal oculta en la provincia de Ourense. *Nefrología* 2003; 23 (Supl. 6): 26.
- Simal F, Martín JC, Bellido J et al. Prevalencia de la enfermedad renal crónica leve y moderada en población general. *Nefrología* 2004; 24: 329-337.
- Gorostidi M, Alonso JL, González de Cangas B et al. Prevalencia de insuficiencia renal en población de edad avanzada y factores asociados. Resultados preliminares. XXXIV Congreso Nacional de la SEN. *Resumen en Nefrología* 2004; 24 (Supl. 6).
- Ifudu O, Dawood M, Homel P, Friedman EA. Excess morbidity in patients starting uremia therapy without prior care by a nephrologist. *Am J Kidney Dis* 1996; 28: 841-845.
- Ismail N, Neyra R, Hakim R. The medical and economical advantages of early referral of chronic renal failure patients to renal specialists. *Nephrol Dial Transplant* 1998; 13: 246-250.
- Obrador GT, Ruthazer R, Arora P, Kausz A, Pereira BJG. Prevalence and factors associated with suboptimal care before initiation of dialysis in the United States. *J Am Soc Nephrol* 1999; 10: 1793-1800.
- Powe NR. Early referral in chronic kidney disease: an enormous opportunity for prevention. *Am J Kidney Dis* 2003; 41: 505-507.
- Aguilar MD, Orte L, Lázaro P, Gómez-Campderá F, Fernández E, Sanz D, en representación del Grupo INESIR, Pastor V. Eficiencia de implantar en atención primaria un programa dirigido a conseguir la referencia precoz al nefrólogo de los pacientes con insuficiencia renal crónica. *Nefrología* 2006; 26 (Supl. 3): 114-120.
- Unlig K, MacLeod A, Craig J et al. Grading evidence and recommendations for clinical practice guidelines in nephrology. A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2006; Sep 27 [Epub ahead of print].
- Cass A, Cunningham J, Snelling P, Ayanian JZ. Late referral to a nephrologist reduces access to renal transplantation. *Am J Kidney Dis* 2003; 42: 1043-9.
- Winkelmayer WC, Owen WF Jr, Levin R, Avorn J. A propensity analysis of late versus early nephrologists referral and mortality on dialysis. *J Am Soc Nephrol* 2003; 14: 486-92.
- Caskey FJ, Wordsworth S, Ben T, de Charro FT et al. Early referral and planned initiation of dialysis: what impact on quality of life? *Nephrol Dial Transplant* 2003; 18: 1330-8.
- Kessler M, Frimat L, Panescu V, Briancon S. Impact of nephrology referral on early and midterm outcomes in ESRD: Epidémiologie de l'Insuffisance Rénale chronique terminale en Lorraine (EPIREL): results of a 2-year, prospective, community-based study. *Am J Kidney Dis* 2003; 42: 474-85.
- Huisman RM. The deadly risk of late referral. *Nephrol Dial Transplant* 2004; 19: 2175-80.
- Khan SS, Xue JL, Kazmi WH, Gilbertson DT et al. Does predialysis nephrology care influence patient survival after initiation of dialysis? *Kidney Int* 2005; 67: 1038-46.
- Stack AG, Molony DA, Rahman NS, Dosekun A, Murthy B. Impact of dialysis modality on survival of new ESRD patients with congestive heart failure in the United States. *Kidney Int* 2003; 64: 1071-9.
- Levey AS, Coresh J, Balk E y cols. National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. *Ann Intern Med* 2003; 139: 137-147.
- Keane WF, Eknoyan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. *Am J Kidney Dis* 1999; 33: 1004-1010.
- Locatelli F, Del Vecchio L, Pozzoni P. The importance of early detection of chronic kidney disease. *Nephrol Dial Transplant* 2002; S1: S2-S7.
- Remuzzi G, Ruggenti P, Perico N. Chronic renal diseases: renoprotective benefits of renin-angiotensin system inhibition. *Ann Intern Med* 2002; 136: 604-615.
- National Institute for Clinical Excellence. Referral advice: a guide to appropriate referral from general to specialist services, December 2001. www.nice.org.uk/pdf/Referraladvice.pdf
- Rule AD, Jacobson DJ, Roberts RO, Girman CJ et al. The association between benign prostatic hyperplasia and chronic kidney disease in community-dwelling men. *Kidney Int* 2005; 67: 2376-82.
- Levey AS, Eckardt KU, Tsukamoto Y et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2005; 67: 2089-100.
- Gracia S, Montañés R, Bover J, Cases A, Deulofeu R, Martín de Francisco AL y Orte LM. Recomendaciones sobre la utilización de ecuaciones para la estimación del filtrado glomerular en adultos. *Nefrología* 2006; 26: 658-665.
- Nathan DM, Rosenbaum C, Protasowicki VD. Single-void urine samples can be used to estimate quantitative microalbuminuria. *Diabetes Care* 1987; 10: 414-418.
- Zelmanovitz T, Gross JL, Oliveira JR, Paggi A, Tatsch M, Azevedo M. The receiver operating characteristics curve in the evaluation of a random urine specimen as a screening test for diabetic nephropathy. *Diabetes Care* 1997; 20: 516-519.
- Ahn CW, Song YD, Kim JH, Lim SK, Choi KH, Kim KR et al. The validity of random urine specimen albumin measurement as a screening test for diabetic nephropathy. *Yonsei Med J* 1999; 40: 40-45.
- Ng WY, Lui KF, Thai AC. Evaluation of a rapid screening test for microalbuminuria with spot measurement of urine albumin-creatinine ratio. *Ann Acad Med Singapore* 2000; 29: 62-65.
- James MA, Fotherby MD, Potter JF. Screening tests for microalbuminuria in non-diabetic elderly and their relation to blood pressure. *Clin Sci* 1995; 88: 185-190.

39. Mosca A, Paleari R, Ceriotti F, Lapolla A, Fedele D. Biological variability of albumin excretion rate and albumin to-creatinine ratio in hypertensive type 2 diabetic patients. *Clin Chem Lab Med* 2003; 41: 1229-1233.
40. Sarnak MJ, Levey AS, Schoolwerth AC et al. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation* 2003; 108: 2154-2169.
41. Chobanian AV, Bakris GL, Black HR et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure: The JNC 7 Report. *JAMA* 2003; 289: 2560-2573.
42. National Kidney Foundation: K/DOQI Clinical Practice Guidelines on Hypertension and antihypertensive Agents in Chronic Kidney Disease. *Am J Kidney Dis* 2004; 43 (Supl. 1): S1-S290.
43. Joint Specialty Committee on Renal Medicine of the Royal College of Physicians and the Renal Association, and the Royal College of General Practitioners. Chronic kidney disease in adults: UK guidelines for identification, management and referral. London: Royal College of Physicians, 2006.
44. Brosius III FC, Hostetter TH, Kelepouris E et al. Detection of chronic kidney disease in patients with or at increased risk of cardiovascular disease. *Circulation* 2006; 114: 1083-1087.
45. O'Hare AM, Bertenthal D, Covinsky KE et al. Mortality risk stratification in chronic kidney disease: One size for all ages? *J Am Soc Nephrol* 2006; 17: 846-853.