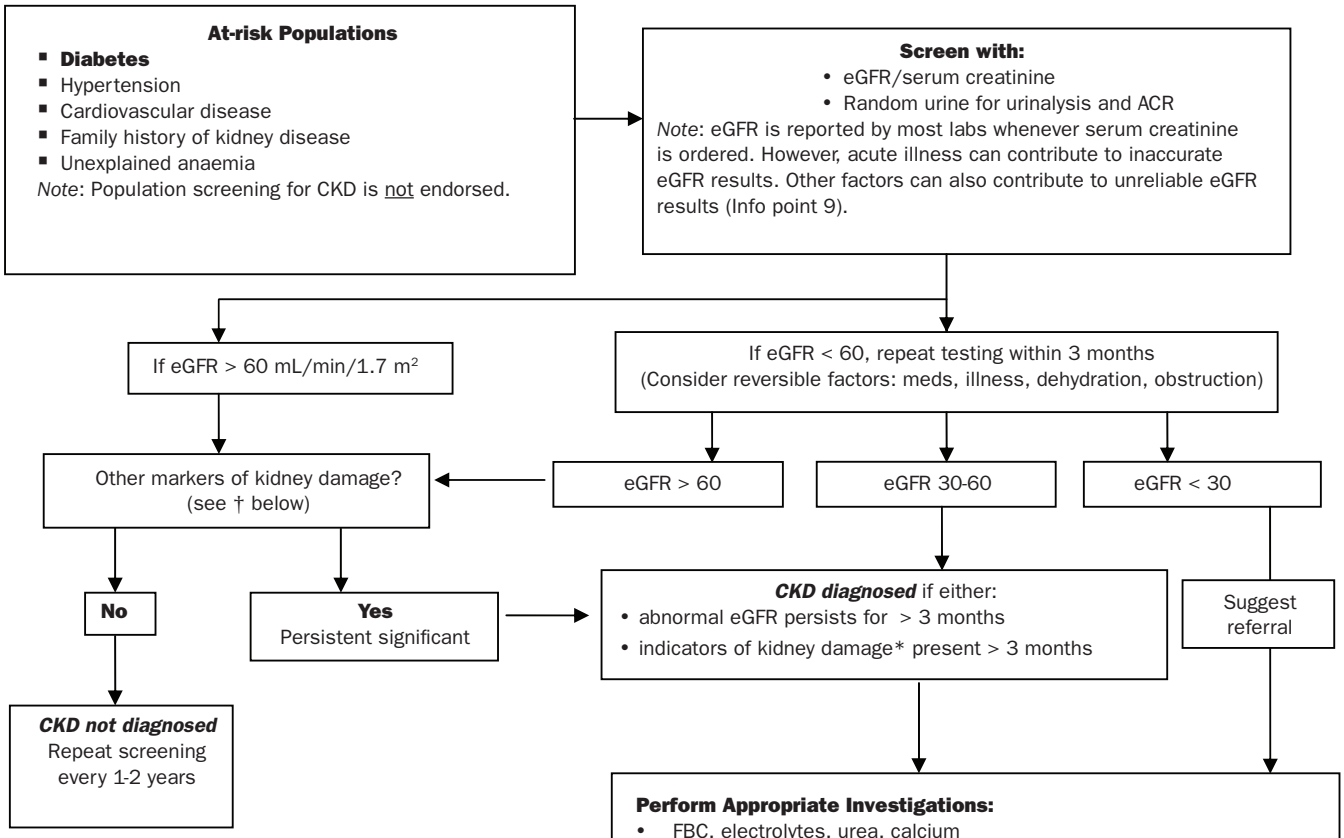
APPENDIX 1. CKD SCREENING AND DIAGNOSIS



Classify the Stage of CKD

eGFR	Stage	Description
≥ 90	1	Markers of kidney damage* but normal or raised eGFR
60-89	2	Markers of kidney damage* with mild decrease in eGFR
30-59	3	Moderately reduced kidney function
15-29	4	Severely reduced kidney function
< 15	5	Kidney failure

* **Markers of kidney damage**

- Persistent proteinuria (significant = 2 of 3 samples with positive urine dipstick or ACR > 2.5 mg/mmol in men or > 3.5 mg/mmol in women done 2-8 weeks apart), *or*
- Abnormalities in urine sediment (persistent presence of erythrocytes or leukocytes or presence of casts) *or*
- Abnormal results in imaging studies (scarring or small kidneys on ultrasound or bilateral cystic changes consistent with polycystic kidney disease).

Sources: (1) The Renal Association. CKD eGuide www.renal.org ➤Information & Resources (bottom of page) ➤The UK eCKD Guide; **(2)** Levin A, Hemmelgarn B, et al. Guidelines for the management of chronic kidney disease. CMAJ 2008; 179(11):1154-1162; **(3)** Canadian Society Nephrology <www.csnscn.ca> ➤ Professional Practice ➤ Guidelines (Nephrology) ➤ Detection, Monitoring, and Referral of CKD 2008; **(4)** BC Guidelines & Protocols Advisory Committee. Chronic Kidney Disease: Identification, Evaluation and Management of Patients. <www.bcguidelines.ca/gpac/> ➤ Chronic Diseases➤ Chronic Kidney Disease; **(5)** Manns B, Hemmelgarn B, Tonelli M, Au F, Chiasson TC, Dong J et al. Population based screening for chronic kidney disease: cost effectiveness study. BMJ 2010; 341:c5869; (6) James MT, Hemmelgarn BR, Tonelli M. Early recognition and prevention of chronic kidney disease. Lancet 2010; 375: 1296–309.

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APPENDIX 2. MANAGEMENT OF CKD

Stage	Description	Clinical Action	Interventions
–	At high risk of CKD but normal eGFR ≥ 90 mL/min/1.7 m2 and no evidence of kidney damage	Repeat screening every 1-2 years	**Lifestyle Management for all patients** Emphasise smoking cessation, regular physical activity, healthy diet, weight control and moderate alcohol consumption. Encourage adherence to medications and treat CVD/ diabetes/ hypertension (if applicable)
1	Normal or elevated GFR but other markers of kidney damage present	• Diagnose & treat underlying kidney disease • Treat comorbid conditions • Intervene to slow progression of disease	**Treatment of associated conditions to slow progression of kidney disease and reduce CVD risk** • Encourage lifestyle management and adherence to medications (as above). • BP: < 130/80 [Grade C Evidence]; < 140/90 if no proteinuria. • Control diabetes: HbA1c < 7.0% [Grade B Evidence]. • Reduce CVD risk: follow lipid targets for general population; offer antiplatelet drugs. • Consider ACE inhibitors or ARBs [Grade A] Evidence. For patients with advanced renal failure, refer to nephrologist before starting therapy. Monitor closely when initiating or increasing doses. • Avoid nephrotoxic drugs if possible or use with caution and adjust renally excreted drugs (Appendix 3). • Check for anaemia: acceptable target range for haemoglobin: 100-120 g/L. If low, check serum ferritin and TIBC. Consider initiating erythropoiesis-stimulating agent for Hb levels <100 g/L in conjunction with a specialist [Grade D Evidence, expert opinion]. • Restrict dietary sodium (< 100 mmol (2.3 g) per day). • Protein-controlled diet (0.80-1.0 g/kg/day) [Grade D Evidence]. Severe protein restriction (< 7.0 g/kg/day) not recommended. • Maintain normal levels of potassium (3.5-5.0 mmol/L), phosphate (0.81-1.4 mmol/L) and calcium (2.18-2.6 mmol/L). • Assess for depression and grief reaction and refer to treatment if appropriate. • Immunize against influenza, pneumococcal illness and hepatitis B as appropriate.
1 or 2 eGFR ≥ 60 with markers of kidney damage present (Appendix 1)	On at least 2 out of 3 occasions: ACR equivocal (2.5-30 male; 3.5-30 female) but urinalysis normal	• Monitor at least every 6 months • Consider kidney ultrasound • Order annual creatinine/eGFR & urine tests • Consider referral to nephrologist if urine protein is increasing, eGFR declining by 20%/year, ACR is > 70 or serum K+ is repeatedly > 6.0 mmol/L	
	Abnormal urinalysis or Abnormal ACR (> 30)	• Consider referral to urologist for isolated microhaematuria even if U/S is normal	
3 eGFR 30-59	Urinalysis and ACR normal	• Treat comorbid conditions • Intervene to slow progression of disease	
	Urinalysis normal but ACR equivocal (2.5-30 male; 3.5-30 female)	• Consider kidney ultrasound • Order annual creatinine • Repeat urine tests every 6 months • Consider referral to nephrologist if urine protein increasing, ACR > 70, or eGFR declining by 20%/ year, serum K+ > 6.0 mmol/L	
	Abnormal urinalysis or abnormal ACR (> 30)	• Order kidney ultrasound • Consider referral to nephrologist	
4 eGFR 15-29	Irrespective of other results	• Refer to nephrologist	Lifestyle management and treatment of associated conditions (as above) plus assessment of social support in preparation for dialysis treatment if applicable
5 eGFR < 15	Irrespective of other results	• Refer ***urgently*** to nephrologist • Dialysis or transplant if uraemia is present	Lifestyle management and treatment of associated conditions (as above) plus restricted fluid intake and additional protein intake

Sources: **(1)** BC Guidelines & Protocols Advisory Committee. Chronic Kidney Disease Identification, Evaluation and Management of Patients. 2008. British Columbia Medical Association, BC Ministry of Health Services. Accessed July 2010. http://www.bcguidelines.ca/gpac/pdf/ckd.pdf ; **(2)** Levin A, Hemmelgarn B, Culleton B, Tobe S, McFarlane P, Ruzicka M et al. Guidelines for the management of chronic kidney disease. CMAJ 2008; 179(11):1154-1162; **(3)** Johnson CA, Levey AS, Coresh J, Levin A, Lau J, Eknoyan G. Clinical practice guidelines for chronic kidney disease in adults: Part I. Definition, disease stages, evaluation, treatment, and risk factors. *Am Fam Physician* 2004; 70(5):869-876. PM:15368726; **(4)** K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; 39(2 Suppl 1):S1-266. PM:11904577; **(5)** Linden A, Biuso TJ, Butterworth SW. Help patients with chronic kidney disease stave off dialysis. *J Fam Pract* 2010; 59(4):212-219.; **(6)** Akbari A, Bell R, Karpinksi J, Magner P. Estimated Glomerular Filtraton Rate (eGFR) TOH Nephrology Guidelines. 2007. Ottawa, ON, The Ottawa Hospital; **(7)** Diagnosis and management of chronic kidney disease. A national clinical guideline. Guideline 103. 2008. Edinburgh, UK, Scottish Intercollegiate Guidelines Network (SIGN); **(8)** The Renal Association. CKD eGuide www.renal.org ➤Information & Resources (bottom of page) ➤The UK eCKD Guide <accessed November 2010>; **(9)** Chronic kidney disease: full guideline. NICE CG73. 24 September 2008. National Institute for Health and Clinical Guidance. http://guidance.nice.org.uk/CG73/Guidance/pdf/English <accessed November 2010>

APPENDIX 3. HOW TO MANAGE MEDICATIONS IN CHRONIC KIDNEY DISEASE

In patients with reduced creatinine clearance, many drugs require dose adjustment — a particularly important consideration when using drugs with a low therapeutic index and appreciable renal excretion. The more important and commonly used medications include:

Drug Class	Representative medications
Acetyl-cholinesterase inhibitors	paracetamol, rivastigmine
Analgesics	acetaminophen, NSAIDs*, morphine, fentanyl
Antibiotics	all aminoglycosides* (e.g., amikacin, gentamycin, tobramycin, vancomycin), fluroquinolones, carbapenems, b-lactams, cephalosporins, penicillins, sulphonamides, nitrofurantoin, macrolides
Antivirals	amantidine, oseltamivir, famiciclovir, aciclovir, valaciclovir
Antifungals	Amphotericin B, fluconazole, itraconazole
Cardiovascular drugs	ACE inhibitors, beta blockers, diuretics, digoxin, procainamide, dofetilide
Diabetic agents	chlorpropamide, glipizide, glibenclamide, metformin
Other	NSAIDs*, H2 antagonists, lithium, antipsychotics, venlafaxine, allopurinol, gabapentin

* Avoid these medications, if at all possible.

Dosing Adjustments

Loading Doses: Adjustments are not usually required in patients with CKD.

Maintenance Doses: Adjustments can be by reducing the dose, lengthening the dosing interval or both.

1. Dose reduction involves reducing each dose while maintaining the usual dosing interval. This strategy maintains a more constant drug concentration but poses a higher risk of toxicity if the dosing interval is not sufficient for elimination of the drug.
2. Lengthening the dose interval maintains normal doses but increases the dosing interval to allow time for drug elimination before a subsequent dose. This approach poses a lower risk of toxicity but a higher risk of subtherapeutic drug concentrations, particularly toward the end of the dosing interval.

Guidelines for dosing recommendations are typically divided into categories based on creatinine clearance derived from Cockcroft-Gault formula — for example, GFR < 10, 10-30, 30-50 and > 50 mL/min. Note that these categories do not correspond with the K/DOQI staging system (Appendix 1). Although the K/DOQI stage can guide initial doses, it is important to further individualise regimens according to patient response and serum drug concentration.

The critical point for avoiding these drugs is often considered to be eGFR < 30, although there are different thresholds for different medications. However, if there is no effective alternate drug, these drugs can and should be used when needed, even in patients with severely compromised renal function. They will require dose adjustment and/or extra monitoring, and consultation may be advised.

On-Line Resources (for more details with specific drugs)

- Aronoff GR, Berns JS, Brier ME, Golper TA, Morrison G, Singer I, et al. Drug Prescribing in Renal Failure: Dosing Guidelines for Adults. Fourth Edition. http://kdp.louisville.edu/renalbook/
- Munar M, Singh H. Drug Dosing Adjustments in Patients with Chronic Kidney Disease. *Am Fam Physician* 2007; May 15;75(10):1487-1496. http://www.aafp.org/afp/2007/0515/p1487.pdf . PMID: 17555141
- Olyaei AJ, Bennett WM. Drug dosing in the elderly patients with chronic kidney disease. Clin Geriatr Med. 2009 Aug;25(3):459-527. PMID: 19765493 (available online via most institutions and universities)

Sources: **(1)** *Williams* CM. Using Medications Appropriately in Older Adults. *AFP* 2002;66(10):1917-24; **(2)** Luisi AF et al. In: Gallo JJ, Reichel W, eds. Reichel's Care of the Elderly: clinical aspects of aging, 5th ed. Philadelphia: Williams & Wilkins, 1999:59-87; **(3)** Munar M, Singh H. Drug Dosing Adjustments in Patients with Chronic Kidney Disease Am Fam Physician. 2007 May 15;75(10):1487-1496. http://www.aafp.org/afp/2007/0515/p1487.pdf PMID: 17555141; **(4)** Naughton CA. Drug-induced nephrotoxicity. Am Fam Physician. 2008 Sep 15;78(6):743-50. PMID: 18819242

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APPENDIX 4. PATIENT INFORMATION

What do my kidneys do?

Your kidneys are very important and do several jobs for your body. All the blood in your body is filtered through your kidneys which pull out any extra fluid. The extra fluid becomes urine. Any waste that has been produced either by muscle use or from digestion of your food is removed from your body in the urine. The kidneys also help to:

- maintain your blood pressure;
- maintain the right level of chemicals in your body (for example, sodium, potassium, chloride and bicarbonate). This allows your heart and muscles to function properly;
- produce a form of vitamin D which your body uses to maintain healthy bones; and
- produce a substance called erythropoietin which tells your bone marrow when to make more red blood cells.

When the kidneys are not able to filter the blood properly for at least a few months, doctors call this chronic kidney disease (CKD).

Am I at risk of having chronic kidney disease (CKD)?

You may be more likely to develop CKD if you:

- have high blood pressure (hypertension);
- have vascular disease (eg angina, stroke, peripheral vascular disease);
- are diabetic;
- are over 65; or
- smoke.

There are many causes of kidney disease, including inherited conditions.

How does my doctor know I have CKD?

There are several tests that your doctor may do to check how well your kidneys are functioning. Your doctor may check your urine for any signs of blood or protein or take a blood test to check the level of creatinine (a chemical which is a breakdown product of muscle activity) in your blood. The results of the creatinine test are used to work out your estimated
Glomerular Filtration Rate (eGFR). This tells your doctor how well your blood is being filtered through your kidneys. Your doctor may also send you to have an X-ray or ultrasound scan of your kidneys.

Will my kidneys fail?

Most patients with CKD respond well to treatment and continue to live normal lives. A small percentage of patients will remain unable to filter their blood and will need dialysis or a kidney transplant. It is important to control your blood pressure since high blood pressure can make CKD worse and can lead to problems with your vascular system and your heart which in turn can reduce kidney function.

Will I get better?

Having a chronic disease means that it won't go away. However, there are treatments available to try to keep it from getting worse and there are things that you can do to control the effects of your CKD.

What are the treatments?

Regular check ups are very important to check your kidney function and your blood pressure. You will probably be given medication for your blood pressure and may need medication to lower your cholesterol. However, every patient will be different and your treatment will depend on how well your kidneys are working and any other medical problems you may have.

What can I do to help myself?

Living a healthy lifestyle is the most important thing that you can do to reduce the risk of your CKD getting worse. You should:

- reduce your salt intake;
- eat a diet that includes fruits, vegetables, low fat dairy products, whole grains, poultry, fish and is lower in red meats and sugar;
- take regular exercise; and
- stop smoking.

Be sure to take the medications that your doctor prescribes for you. If you have any questions or problems with your treatment, make sure you talk these over with your doctor as alternatives which suit you better may be available.
If you want to take any over-the-counter medications or any alternative or herbal medicines, be sure to check with your doctor or with the pharmacist first because some of these may be harmful to your kidneys.

Further patient information:

http://www.patient.co.uk/health/Chronic-Kidney-Disease.htm

British kidney Patients association
www.britishkidney-pa.co.uk

Kidney Patient guide
www.kidneypatientguide.org.uk

National Kidney Federation
www.kidney.org.uk

Kidney Research UK
www.nkrf.org.uk

Renal Patient View
www.renalpatientview.org

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APPENDIX 5.

Proteinuria: detection and quantitation in adults using ACR – information for GPs

Proteinuria is an important indicator of underlying kidney disease and its presence is both a strong prognostic indicator of the likelihood of kidney disease progressing and an indicator of increased risk of subsequent cardiovascular event. Together with estimation or measurement of the glomerular filtration rate (GFR), urine protein measurement is required to diagnose, stage and monitor chronic kidney disease (CKD). The National Institute for Health and Clinical Excellence (NICE) has recommended that to detect proteinuria the urinary albumin:creatinine ratio (ACR) should be used in preference to other tests of proteinuria, including the protein:creatinine ratio (PCR), 24 hour urine collections for proteinuria and reagent strip ('dipstick') analyses. This information sheet details the main reasons underlying this decision and gives advice regarding its practical implementation.

Why has ACR been recommended in preference to PCR, 24 hour urine collections and reagent strip analysis?

- Studies have clearly demonstrated that measurement of either ACR or PCR in a spot urine sample accurately reflects 24 hour urinary albumin and protein, rendering 24 hour urine collections unnecessary for detection and quantification of protein in the urine.
- Albumin is the predominant protein in the vast majority of proteinuric kidney diseases, including diabetes, hypertension and glomerular diseases.
- Albumin measurement offers greater sensitivity, and improved precision, for the detection of lower, but clinically significant, levels of proteinuria compared to total protein.
- Albumin measurement can be standardised.
- Albumin measurement is already used to detect and quantify proteinuria in people with diabetes.
- International recommendations favour ACR in preference to PCR.
- In patients with established disease, there may occasionally be clinical reasons for a specialist subsequently to use PCR instead of ACR to quantify and monitor significant levels of proteinuria.
- Commonly used reagent strip devices are insufficiently sensitive for the reliable detection of proteinuria, do not adjust for urinary concentration and are only semi-quantitative. Furthermore, there is no standardisation between manufacturers.

Who should be tested for proteinuria?

Testing for proteinuria should be offered to people if they have any of the following risk factors:

- a GFR less than 60 mL/min/1.73 m^2
- diabetes
- hypertension
- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease and cerebral vascular disease)
- structural renal tract disease, multiple renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement – for example, systemic lupus erythematosus
- family history of stage 5 CKD or hereditary kidney disease
- opportunistic detection of haematuria.

What urine sample should be used for measurement of ACR or PCR?

- Albumin can be measured in random ('spot') urine samples: a timed urine collection is not necessary for this purpose.
- An early morning ('first pass') urine sample is ideal as the urine is most concentrated and thus the concentration of protein will be highest and more likely to be detected.
- Where this causes practical difficulties for service organisation a urine sample collected at other times during the day is an acceptable alternative.
- Urine samples should be sent to the laboratory for analysis on the day of collection.

What is a clinically significant ACR and what is the equivalent level of proteinuria?

- There is no constant numerical relationship between albumin and total protein concentrations in urine. At normal levels of protein loss, albumin is a minor component (approximately 10–20%) of total urinary protein. On average, when the total protein concentration is 1 g/L, approximately 70% of this will be accounted for by albumin.

- In people without diabetes consider clinically significant proteinuria to be present when the ACR is 30 mg/mmol or more (this is approximately equivalent to PCR 50 mg/mmol or more, or a urinary protein excretion 0.5 g/24 h or more).
- Heavy proteinuria should be considered present when the ACR is 70 mg/mmol or more (this is approximately equivalent to PCR 100 mg/mmol or more, or a urinary protein excretion 1 g/24 h or more).
- For the initial detection of proteinuria, if the ACR is 30 mg/mmol or more but less than 70 mg/mmol this should be confirmed by a subsequent early morning sample. If the initial ACR is 70 mg/mmol or more, or the PCR 100 mg/mmol or more, a repeat sample need not be tested.
- People with confirmed proteinuria (ACR 30 mg/mmol or more) should have the suffix (p) appended to their CKD staging.
- In people with diabetes consider microalbuminuria (ACR more than 2.5 mg/mmol in men and ACR more than 3.5 mg/mmol in women) to be clinically significant.
- False positives may occur for a variety of reasons, including benign orthostatic proteinuria, symptomatic urinary tract infections and menstrual contamination.

When should people with clinically significant levels of ACR be referred for specialist opinion?

- People with heavy proteinuria (ACR ≥70 mg/mmol, approximately equivalent to PCR ≥100 mg/mmol, or urinary protein excretion ≥1 g/24 h), unless this is known to be due to diabetes and already appropriately treated, should be referred for specialist opinion.
- People with proteinuria (ACR ≥30 mg/mmol, approximately equivalent to PCR ≥50 mg/mmol, or urinary protein excretion ≥0.5 g/24 h) together with haematuria should also be referred for specialist opinion.
- People with isolated proteinuria (ACR ≥30<70 mg/mmol, approximately equivalent to PCR ≥50<100 mg/mmol, or urinary protein excretion ≥0.5<1 g/24 h) may not require referral provided their GFR is stable and their blood pressure is controlled (120–139/<90 mmHg).

When should ACR measurement be implemented as the first line test for proteinuria detection?

- NICE has recommended that to detect and identify proteinuria, ACR should be the preferred method but that for quantification and monitoring of proteinuria, PCR can be used as an alternative.
- Some laboratories already offer ACR as their primary test for proteinuria detection.
- Most NHS laboratories already use ACR as their primary test for the detection of diabetic nephropathy.
- It is recognised that full implementation of NICE recommendations may take place over a number of years. A costing template to enable an estimate of likely implementation costs to be made is available from the NICE website (www.nice.org.uk/usingguidance/implementationtools/costingtools/costing_tools_doc.jsp?o=42208).

Further information

National Institute for Health and Clinical Excellence. Chronic kidney disease: Early identification and management of chronic kidney disease in adults in primary and secondary care. September 2008, Clinical Guideline 73. Available from: www.nice.org.uk/Guidance/CG66

National Institute for Health and Clinical Excellence. Type 2 diabetes: The management of type 2 diabetes (update). May 2008, Clinical Guideline 66. Available from: www.nice.org.uk/Guidance/CG73

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