GAIN

GUIDELINES AND AUDIT
IMPLEMENTATION NETWORK

NORTHERN IRELAND GUIDELINES FOR MANAGEMENT OF CHRONIC KIDNEY DISEASE

Practical points for use of estimated GFR + quality outcome framework indicators

Developed by GAIN and the Northern Ireland Nephrology Forum

February 2010

PREFACE

Northern Ireland Guidelines for Management of Chronic Kidney Disease.

These guidelines have been published by the Guidelines & Audit Implementation Network (GAIN), which is a team of health care professionals established under the auspices of the Department of Health, Social Services & Public Safety in 2008. The aim of GAIN is to promote quality in the Health Service in Northern Ireland, through audit and guidelines, while ensuring the highest possible standard of clinical practice is maintained.

This guideline was produced by a sub-group of health care professionals from varied backgrounds and was chaired by Professor Peter Maxwell, Consultant in the Belfast HSC Trust. This guideline revises and updates the original guideline on Chronic Kidney Disease published in July 2006 under the auspices of CREST (Clinical Efficiency Support Team), the predecessor to GAIN.

GAIN wishes to thank clinicians from the Northern Ireland Nephrology Forum, General Practice, and all those who contributed in any way to the development of these guidelines.

Dr T Trinick
Chairman of GAIN

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Abbreviations

ACEi: angiotensin converting enzyme inhibitor
ACR: urine albumin/creatinine ratio
ARB: angiotensin-II receptor blocker
PCR: urine protein/creatinine ratio
NSAIDs: non-steroidal anti-inflammatory drugs
eGFR: estimated glomerular filtration rate
MDRD: modification of diet in renal disease

FOREWORD

Chronic kidney disease is common with approximately 5% of adults having an abnormal glomerular filtration rate of less than 60 mL/min/1.73m^2. Recognition of chronic kidney disease has improved with the routine reporting of an estimated glomerular filtration rate (eGFR) each time serum creatinine is measured. The introduction of kidney specific Quality Outcome Framework (QOF) indicators has helped to increase awareness of chronic kidney disease in primary care. The QOF indicators emphasize the importance of identifying persons with chronic kidney disease and treating associated risk factors for progressive kidney failure such as diabetes and hypertension.

These guidelines update the previous 2006 CREST Guidelines for the Management of Chronic Kidney Disease in Adults. The changes in the updated document reflect current NICE guidance and include advice on assessment of chronic kidney disease, appropriate referral of patients with declining kidney function for specialist help and the use of quantitative measures of proteinuria.

I would like to thank clinicians from the Northern Ireland Nephrology Forum, GP colleagues, Dr Joanne Shields, Specialist Registrar in Renal Medicine and the staff from GAIN for their enthusiastic help in producing this updated guidance.

Prof Peter Maxwell
Professor of Renal Medicine / Consultant Nephrologist

INTRODUCTION

Chronic kidney disease (CKD) is common, usually unrecognised and often exists in association with other conditions such as diabetes and cardiovascular disease.

CKD has emerged as a significant public health problem with up to 10% of adults having evidence of underlying CKD or risk factors for CKD. There is evidence that earlier treatment may delay or prevent progression of CKD. One challenging issue is that CKD is often not diagnosed because persons with kidney disease usually have no specific symptoms. Late diagnosis of advanced CKD is associated with increased morbidity and mortality.

CKD is now incorporated in the General Practice Quality and Outcomes Framework (QOF) with an increase in both the number and value of CKD QOFs since April 2006.

Specifically five QOF indicators (accounting for 38 points) are recorded based upon generation of a register of patients with chronic kidney disease, measurement of blood pressure, treatment of blood pressure to target, use (if appropriate) of ACEi or ARB medication in patients with CKD and quantitative assessment of proteinuria.

This booklet provides brief guidance on investigation, monitoring and management of CKD in adults. It replaces the Northern Ireland CREST guidelines on the management of chronic kidney disease published in 2006.

Approximate equivalent values of ACR, PCR and urinary protein excretion

ACR (mg/mmol)	PCR (mg/mmol)	Urinary protein excretion (g/24h)
30	50	0.5
70	100	1

WHAT IS CKD AND eGFR (ESTIMATED GLOMERULAR FILTRATION RATE)?

- CKD can manifest as either reduced kidney function (reduced GFR) or urinary abnormalities (haematuria/proteinuria) or a combination of both.

- The international classification of CKD, based largely on estimated Glomerular Filtration Rate (eGFR), has 5 classes of CKD. Patients with an eGFR < 60 ml/min/1.73m^2 have CKD stage 3, 4 or 5 and are the focus of these guidelines and the revised QOF indicators.

- GFR in healthy young adults is approximately 100 mL/min/1.73m^2. An eGFR result can be explained to patients as an approximate percentage of normal kidney function.

- eGFR is an estimate of renal function (GFR) based on serum creatinine but also accounting for differences in gender, ethnicity and age. Laboratories report it whenever any creatinine is requested.

- If the eGFR is 60 ml/min/1.73m^2 or greater, the diagnosis of CKD requires the presence of **other kidney damage** e.g. persistent proteinuria (albumin-creatinine ratio >30 mg/mmol), persistent non-visible (microscopic) haematuria or structural kidney disease e.g. polycystic kidney disease.

- In Northern Ireland laboratories do not routinely report eGFR > 60ml/min/1.73m^2. Thus, CKD stages 1 and 2 would require urinalysis or renal imaging to allow CKD definition.

Stage	**Description**	**eGFR (ml/min/1.73m^2)**	**Population Prevalence**
1	CKD with normal GFR + other kidney damage	>90	3.3%
2	Mild CKD and other kidney damage	60-89	3.0%
3a 3b	Mild to Moderate CKD Moderate to Severe CKD	45-59 30-44	4.3%
4	Severe CKD	15-29	0.2%
5	Established renal failure	<15 or on dialysis	0.2%

WHAT CAUSES CKD?

- No specific cause is found in the majority of patients.
- Specific causes include conditions such as diabetes, atheromatous renal vascular disease, glomerulonephritis, pyelonephritis and polycystic kidney disease.
- In the absence of a specific diagnosis, it is most likely related to hypertensive or ischaemic kidney damage both of which become more common with advancing age.

WHY DOES IT MATTER?

- The CKD staging system recognizes that patients with progressive kidney failure pass through a number of stages before reaching end-stage renal disease. Recognition of CKD allows earlier intervention to prevent dialysis and cardiovascular events.
- Persons with CKD stages 4 and 5 have higher risks for hospitalisation, cardiovascular events and premature death.
- Most persons with CKD stage 1-3 will be entirely asymptomatic.
- Very few persons with CKD 1-3 will end up on dialysis. Those at most risk of progression of kidney disease have higher blood pressure and more proteinuria.
- However, there is a substantial increased risk of cardiovascular events and premature death.

WHAT BASELINE INVESTIGATIONS SHOULD I DO IN CKD?

- In patients with newly identified reduced eGFR (i.e. <60 ml/min/1.73m^2), the first step is to exclude acute kidney failure. Review of previous serum creatinine tests may allow confirmation that this is chronic disease. Otherwise the patient should have a repeat creatinine (eGFR) within one week.

- Rapidly declining kidney function (over days to weeks) is acute kidney failure and urgent referral for assessment is advised.

- In all newly identified CKD patients the following should be checked at the earliest opportunity:

    - *blood pressure*
    - *dipstick urinalysis*
    - *random urine albumin-creatinine ratio or urine protein-creatinine ratio*
    - *glucose, cholesterol and full blood count.*

HOW DO I TEST FOR PROTEINURIA?

- Reagent strips for dipstick urinalysis provide a simple screening test but are not an accurate method of quantifying proteinuria. Reagent strips cannot detect low concentrations of albumin in the urine.

- Use a random urine albumin-creatinine ratio (ACR) to detect albuminuria.

- The urine ACR result may be normal (< 3 mg/mmol).

- The urine ACR may indicate microalbuminuria (3-30mg/mmol). Persistent microalbuminuria is the earliest clinical indicator of development of nephropathy in persons with diabetes.

- The urine ACR may indicate 'dipstick' positive proteinuria (>30mg/mmol).

- A urine protein-creatinine ratio (PCR) >50mg/mmol also indicates 'dipstick' positive proteinuria.

- Progression of renal failure (decline in GFR) and cardiovascular events are more common if albuminuria (or proteinuria) is present.

Approximate equivalent values of ACR, PCR and urinary protein excretion

ACR (mg/mmol)	PCR (mg/mmol)	Urinary protein excretion (g/24h)
30	50	0.5
70	100	1

WHAT SHOULD I DO IF HAEMATURIA IS PRESENT?

Haematuria is a very common presentation in general practice with a prevalence of 2%.

There is currently no evidence to justify screening of the general population.

In 2008, excellent short clinical guidelines on assessment of haematuria were published by the British Association of Urological Surgeons and Renal Association and should be read in association with the summary in this GAIN document (web link listed in Appendix).

The causes of haematuria vary with clinical presentation and age and in many such patients, particularly young adults, haematuria is transient and may be of no consequence.

The most common causes are urological such as kidney or urinary tract malignancy, stones, inflammation, infection or hyperplasia of the prostate or bladder. Only 10% of patients with haematuria will have a renal parenchymal cause. In up to 60% no diagnosis will be found despite complete assessment.

The following steps should be taken in the assessment of patients with haematuria:

1) **Urinary tract infection** should be excluded by absence of nitrite and leucocyte on dipstick and negative MSU. Urinalysis should be repeated following treatment of a UTI to ensure haematuria is not persistent.

2) **History/Examination** – are there any findings that suggest a particular diagnosis?

3) **Investigations:** serum creatinine /eGFR, urinary ACR, bone profile.

4) **Referral criteria:** Referral for **urological evaluation** including renal imaging and cystoscopy is required in all patients with significant haematuria as defined by:

a) Any single episode of **Visible Haematuria**, otherwise known as macroscopic or gross haematuria, at any age.

b) **Non-Visible Haematuria**, otherwise referred to as microscopic or dipstick positive haematuria, is significant if a single episode is symptomatic at any age (hesitancy, frequency, urgency, dysuria) or if it is persistent (defined as 2 out of 3 dipsticks positive) and aged over 40.

If a urological cause is excluded a nephrology referral should be considered if the patient meets any of the CKD criteria for referral or has:

- Significant proteinuria (ACR ≥30mg/mmol or PCR ≥50mg/mmol =0.5g/24hr).
- Evidence of declining GFR (by >10ml/min at any stage within the previous 5 years or by >5ml/min within the last 1 year).
- Stage 4 or 5 CKD (eGFR <30ml/min).
- Isolated haematuria (i.e. in the absence of significant proteinuria) with hypertension in those aged <40.
- Visible haematuria coinciding with intercurrent (usually upper respiratory tract) infection.

In the event the above criteria are not met, haematuria itself (visible or non-visible) does not require nephrology referral.

WHICH CKD PATIENTS SHOULD I CONSIDER REFERRING TO THE RENAL SERVICE?

General points

- Take into account the individual's wishes and comorbidities when considering referral to a specialist.

- Some individuals with advanced CKD (and their families) would not wish to consider renal replacement therapy e.g. dialysis and therefore referral may not be appropriate.

- Consider discussing management issues with a specialist (virtual referral) where it may not be necessary for a patient to attend for hospital-based assessment.

- Patients who seem too frail for dialysis may still be discussed as there are some non-dialytic management options.

Based on eGFR

- Patients with new **CKD 5 (eGFR <15 ml/min)** should be discussed **immediately**.

- Patients with new **CKD 4 (eGFR 15 - 29 ml/min)** should be **referred or discussed**.

- Patients with **deteriorating renal function confirmed on repeat testing** (eGFR decline by > 5 ml/min/1.73m^2 within 1 year or > 10 ml/min/1.73 m^2 within 5 years) should be referred **routinely**.

- Patients with **eGFR <60 ml/min/1.73m^2 + inadequately controlled blood pressure** despite 2-3 antihypertensive agents should be referred **routinely**.

Based on proteinuria

- Patients with an **ACR or PCR >300 mg/mmol** and/or the nephrotic syndrome should be referred **urgently**.

- Patients with an **ACR or PCR 100-300 mg/mmol** should be referred **routinely**.

- Patients with an **ACR or PCR 30-100 mg/mmol AND haematuria** should be referred **routinely**.

Clinical judgement may suggest other patients who should be referred, or a different degree of urgency.

WHEN SHOULD A KIDNEY ULTRASOUND BE PERFORMED IN PERSONS WITH CKD?

A kidney ultrasound is recommended for persons with CKD who:

- have progressive CKD
- have visible or non-visible haematuria
- have symptoms of urinary tract obstruction,
- have a family history of polycystic kidney disease and are aged over 20
- have stage 4 or 5 CKD.

WHAT TREATMENTS ARE APPROPRIATE FOR CKD?

- Review existing **medication**. Stop NSAIDs. Adjust other medication dose(s) according to eGFR using Appendix 3 in BNF.

- Treat **blood pressure** ideally to <130/80 mmHg. Multiple agents may be required and the threshold for starting treatment is 140/90 mmHg **[140/85 mmHg is QOF target]**.

- If urine albumin-creatinine ratio >100 mg/mmol treat blood pressure ideally to <125/75 mmHg. ACEi/ARBs are first choice therapy.

- Serum creatinine/eGFR should be checked 7-10 days after starting, or increasing the dose of an **ACE-i / ARB**. These drugs may cause a rise in serum creatinine or fall in eGFR. If serum creatinine increase is < 30% or eGFR decrease is < 25% then the current dose can be tolerated, as long as it stabilises thereafter. Serum potassium up to 5.9 mmol/l can also be tolerated.

- Consider anti-platelet agents and statins to **reduce cardiovascular risk**.

- Standard cardiovascular risk tables markedly underestimate risk in CKD. Treat as an equivalent CHD risk factor as having diabetes.

- Advise **lifestyle changes** as appropriate: smoking cessation, reduction of obesity, increased exercise and reduce dietary salt intake to < 6 grams/day.

- In patients with diabetes mellitus HbA1c ideally should be <7%.

A NOTE OF CAUTION:

Decline in GFR with age is incompletely understood at present and there is a need to refine and validate the MDRD based eGFR equation especially when considering elderly (> 70 yr) patients with low eGFR.

The new CKD classification system will identify many elderly subjects with low eGFR who do not have "true" kidney disease (as defined by steadily progressive kidney failure in association with other abnormal features such as proteinuria). Most CKD in the elderly is due to the cumulative effect of other disease states, especially hypertension and atherosclerosis. It is important not to unduly alarm elderly patients with a misplaced diagnosis of advanced kidney failure.

HOW SHOULD I MONITOR NON-REFERRED CKD?

A majority of patients with CKD do not need to be referred and are well managed in primary care. A CKD register should be established for CKD stages 3, 4 and 5 (QOF indicator) to allow re-call arrangements.

This would include patients with mild proteinuria (ACR 30-100 mg/mmol or PCR 50-100 mg/mmol), isolated non-visible haematuria (after assessment by urology if appropriate see RA/BAUS guidelines 2008) and stable CKD 3/4. The attached table indicates suggested monitoring for these patients and some of the associated targets.

WHAT ABOUT A RISE IN SERUM CREATININE OR A FALL IN eGFR?

- Large rises in creatinine (>30%) and the commensurate fall in eGFR are associated with underlying renal vascular disease, heart failure treatment and the elderly. A falling eGFR will require closer monitoring.

- A sustained fall in eGFR (reduction of >10 ml/min/1.73m^2) should be confirmed by repeating serum creatinine/eGFR within 1 month.

- Progressive CKD is usually defined by at least 3 eGFRs over at least 90 days.

- Many CKD patients exhibit minor fluctuations in their serum creatinine/eGFR (often linked to diuretic / ACE or ARB therapy or inter-current illness).

- Temporary cessation of ACEi or ARBs can often correct these changes if the patient is at risk of dehydration.

- However these agents are protective and should not be stopped indefinitely if vascular or renal protection is indicated.

- Chronic use of NSAIDs may be associated with progressive CKD; only use with caution and ideally only for short term.

- Patients with CKD should be referred if they have a SUSTAINED fall in GFR of > 5 ml/min/1.73m^2 per year.

DO I NEED TO SCREEN ANYONE FOR CKD?

- Any patient with diabetes mellitus, hypertension, ischaemic heart disease, heart failure, peripheral vascular disease, cerebrovascular disease or urinary tract abnormalities are more likely to have CKD and ideally should have their eGFR checked annually.

- Urinalysis should be checked in the initial assessment of hypertension, diabetes, peripheral oedema, heart failure and multi-system disease.

- Urine ACR should be checked annually in diabetes patients.

- If urinalysis shows one or more plus proteinuria, a spot sample in a plain (white cap) tube should be sent for ACR or PCR. A 24h urine collection is not required.

URGENCY OF REFERRAL TO A NEPHROLOGY SERVICE

All nephrology services should offer 24 h telephone access to qualified advice.
A guide to referral urgency is below:

Immediate

- Suspected ARF.
- ARF superimposed on CKD.
- Newly detected stage 5 CKD (GFR < 15 mL/min/1.73 m^2).
- Accelerated or malignant phase hypertension with suspicion of underlying kidney disease (or if there is no specialist hypertension service available locally).
- Hyperkalaemia, serum potassium >7.0 mmol/L.

Urgent outpatient

- Nephrotic syndrome.
- Newly detected stage 4 CKD (unless known to be stable) or stable stage 5 CKD.
- Multisystem disease (e.g. SLE, systemic vasculitis) with evidence of kidney disease.
- Hyperkalaemia, serum potassium 6.0-7.0 mmol/L (after exclusion of artefactual and treatable causes).

Routine outpatient

- Refractory hypertension (defined as sustained BP >160/90 mm Hg despite combination therapy with 3 drugs from complementary classes).
- Acute deterioration in kidney function (defined as a fall of eGFR of >25% or rise of serum creatinine concentration of >30% from baseline) associated with use of ACEIs or ARBs.
- Proteinuria (urine protein:creatinine ratio >100 mg/mmol) without nephrotic syndrome.
- Proteinuria with haematuria.
- Stage 3 CKD with haematuria.
- Urologically unexplained visible (macroscopic) haematuria (with or without proteinuria).
- Stable stage 4 CKD.

GP care +/- "virtual" nephrology support/advice

- Stable CKD stages 1, 2 and 3.
- Isolated non-visible (microscopic) haematuria (after negative urological evaluation).
- Isolated microalbuminuria in diabetes (albumin: creatinine ratio < 30mg/mmol).

VALUABLE INFORMATION TO INCLUDE WITH A HOSPITAL REFERRAL

- General medical history - particularly noting urinary symptoms, previous blood pressures, urine testing.

- Information on the patient's functional status and cognitive function is especially relevant if dialysis is being considered as a treatment option.

- Medication history.

- Examination e.g. blood pressure, presence of oedema, vascular disease findings.

- Urine dipstick result - and quantitation of dipstick positive proteinuria by urine albumin/creatinine ratio or protein/creatinine ratio.

- Blood tests - Full blood count, urea and electrolytes, calcium, albumin, phosphate, cholesterol. HbA1c (in diabetes).

- Previous tests of renal function with dates.

- Imaging:- results of renal imaging if undertaken (according to local circumstances, pre-ordering may speed assessment).

APPENDIX

WHERE CAN I GET MORE INFORMATION?

- **http://guidance.nice.org.uk/CG73**
  National Institute for Health and Clinical Excellence guidelines for Chronic Kidney Disease (2008).

- **www.renal.org/ckd**
  Renal Association CKD eGuide that is derived from NICE, SIGN and Renal Association guidelines. Easy to navigate website with multiple useful points about CKD.

- **www.renal.org/eGFR**
  Renal Association website quick access to info about eGFR and CKD stages with links to management.

- **http://renux.demed.ed.ac.uk/EdREN/index.html**
  Website of the Edinburgh Renal Unit with may helpful articles on kidney disease that are suitable for both health care professionals and patients.

- **http://www.renal.org/pages/media/Guidelines/RA-BAUS%20Haematuria%20consensus%20guidelines%20July%202008.pdf**
  British Association of Urological Surgeons / Renal Association:
  Initial assessment of haematuria.

Access to these guidelines and any future updates

- **http://www.gain-ni.org/**
  Guidelines and Audit Implementation Network (Northern Ireland).

The Guidelines and Audit Implementation Network (GAIN) website also displays other topic guidelines with relevance to the management of chronic kidney disease.

These include:

- Guidance on the management of hypertension – FAQs (CREST 2007)
- Guidelines on the use of the laboratory (GAIN 2008)
- Hyperkalaemia guidelines (GAIN 2009).

WHO MAY I CONTACT FOR FURTHER ADVICE?

Contact your local nephrologist as listed below

Altnagelvin and Tyrone County Hospitals:

Dr PJ Garrett	Tel 028 8283 3520	peter.garrett@westerntrust.hscni.net
Dr Y Kuan	Tel 028 7134 5171	ying.kuan@westerntrust.hscni.net
Dr F Kelly	Tel 028 8283 3477	frank.kelly@westerntrust.hscni.net
Dr M Elawad	Tel 028 7134 5171	mamoun.elawad@westerntrust.hscni.net

Antrim Area Hospital:

Dr JC Harron	Tel 028 9442 4889	camille.harron@northerntrust.hscni.net
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Dr R Cunningham	Tel 028 9442 4887	ronan.cunningham@northerntrust.hscni.net

Belfast City Hospital:

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MANAGEMENT OF CHRONIC KIDNEY DISEASE (CKD)

A diagnosis of CKD should not be made on the basis of a single biochemistry value or an acute rise in serum creatinine. Likewise if a patient is unwell, with rapidly deteriorating kidney function, they should be discussed or referred urgently.

Stage	**1**	**2**	**3**	**4**	**5**
eGFR mls/min/1.73m^2	≥ 90 + albuminuria or haematuria	60 – 89 + albuminuria or haematuria	30 – 59	15 – 29	<15
Tests	Annual U+E (including eGFR) Annual urine ACR			As before but now 3 monthly	Check U&E 6 weekly
Treatment	• Treat BP to a target of < 130/80 (threshold to treat is 140/90 mmHg) • ACEi or ARB if urine ACR ≥ 30 mg/mmol in non-diabetic individual or ACR >3 in person with diabetes • Statin if cardiovascular disease risk ≥ 20% over 10 years • Aspirin 75mg (if no contraindication) • Advise lifestyle changes as appropriate				
Referral	Fall in eGFR by >5 ml/min/1.73m^2 per year Rise in serum creatinine >20% per year ± Urine ACR ≥ 70 mg/mmol ± Systolic BP ≥ 160 mmHg (despite treatment with multiple agents)			Discussion with or referral to renal unit is usual	Usually automatic (Unless not for active treatment based co-morbidity)

Approximate equivalent values of ACR, PCR and urinary protein excretion

ACR (mg/mmol)	PCR (mg/mmol)	Urinary protein excretion (g/24h)
30	50	0.5
70	100	1

NOTES

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