Nice CKD Clinical Guidelines 2014
The challenges and benefits they may bring to primary care

Paula D'Souza
Senior CKD Nurse Specialist
Royal Devon and Exeter Healthcare Trust

Introduction

- Background
- What are the main aims of the guideline
- Overview of the new recommendations incorporating some of the perceived challenges and benefits of implementation
- Amended guidelines and other recommendations
- Summary

Background

* Moderate to severe CKD is associated with an increased risk of other significant adverse outcomes such as: acute kidney injury, falls, frailty and mortality
* The risk of developing CKD increases with age
* There is evidence that treatment can prevent or delay the progression of CKD, reduce or prevent the development of complications, and reduce the risk of cardiovascular disease
* CKD can progress to established renal failure, in a small but significant percentage of people

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What is the aim of the guideline

* Update NICE clinical guideline CG73 in areas where new information has become available
* Provide new guidance in areas where previously no evidence existed
* Promote strategies aimed at earlier identification and prevention of progression

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New Recommendations

- Identification and investigation of people who have or are at risk of developing CKD
- Classification of CKD and identification of people at risk of CKD complications and progression
- The definition of CKD progression
- Self-management of CKD
- The relationship between acute kidney injury and CKD
- Pharmacotherapy for CKD

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Identification and investigation of people who have or are at risk of developing CKD

Clinical laboratories are recommended to:

- Use the Chronic Kidney Disease Epidemiology Collaboration (**CKD-EPI**) creatinine equation to estimate GFRcreatinine, using creatinine assays with calibration traceable to standardised reference material
- Use creatinine assays that are specific (for example, **enzymatic assays**) and zero-biased compared with isotope dilution mass spectrometry (IDMS)
- Participate in UK national quality assessment schemes for creatinine

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Why change from MDRD to CKD-EPI?

Modification of Diet in Renal Disease study equation or MDRD uses serum creatinine to estimate GFR (2006)

- Easy to use
- It does not require weight or height variables because the results are reported normalised to 1.73m2 body surface area which is an accepted average adult surface area.
- It provides an **estimated** GFR measurement **but not** an actual GFR measurement
- It uses four variables age, sex, race and serum creatinine

Problems with MDRD

Not validated:

- < 18years of age
- Individuals with serious co-morbid conditions and hospitalised patients especially with AKI where you get rapidly changing creatinine levels
- People with extremes of muscle mass
- Less accurate in people with near normal kidney function eGFR≥90ml/min/m2
- It is also not validated in the older person

MDRD equation was developed in a population with sub-optimal kidney function its accuracy in predicting GFR is best reflected in those with mild kidney impairment (category G2) → **group not routinely monitored in primary care**

In severe renal impairment eGFR<15ml/min its less sensitive

CKD-EPI

CKD-EPI equation (2009) like the MDRD was developed to estimate GFR from serum creatinine

Difference: CKD-Epidemiology Collaboration group developed equation to match the accuracy of the MDRD **but** at lower GFR <60 mL/min/1.73m² (**category ≥G3**)

- Uses the same variables as MDRD but different coefficients
- Limitations similar to the MDRD group (e.g. elderly and extremes of muscle mass)

However:

- It is also considered a more accurate way of estimating GFR in those with **higher** level of GFR (>60ml/min) than the MDRD minimizing the over-diagnosis of CKD seen with MDRD equation → **fewer classifications**
- More accurate in young individuals, women and whites
- Predictor of mortality and ESKD in a broad range of populations

What are the challenges for primary care in relation to the use of either MDRD or CKD-EPI

No challenges but continued education is needed regarding the accuracy of theses equations in certain sub-groups

Education should include messages such as:

If eGFR is greater than 90ml/min/1.73m2, use an increase in serum creatinine concentration of more than 20% to infer significant reduction in kidney function (**new 2014**) Chronic Kidney Disease: NICE guideline CG 182 2014

Interpret eGFR values of 60ml/min/1.73m2 or more with **caution**, bearing in mind that estimates of GFR become less accurate as true GFR increases (**new 2014**) Chronic Kidney Disease: NICE guideline CG 182 2014

Encourage looking at trends of eGFR / serum creatinine

New reporting criteria

Clinical laboratories should report GFR either as a whole number if it is 90 ml/min/1.73 m2 or less

If > 90 ml/min/1.73 m2 report as this

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The 'new boy' on the block Cystatin C

Low molecular weight (13.3 kilodaltons) → protein freely filtered in the glomerulus

Not secreted, fully reabsorbed and broken down in the renal tubules making it an excellent marker of GFR

If kidney function and GFR rate decline the cystatin C levels will rise

Compared to creatinine the production of Cystatin C is less influenced by a persons age, gender and size ∴ its considered a better reflection of GFR than serum creatinine

Alone it has not been shown to be superior to the formula-adjusted estimations of kidney function, but combined with eGFRCreatinine studies have shown it improves the estimation accuracy of GFR

Challenges for Primary Care

Clinical

When to test:

Suggest **consideration** should be given to using eGFRcystatinC at **initial** diagnosis to confirm **or** refute CKD in people with: an eGFRcreatinine of 45–59 ml/min/1.73 m2, sustained for at least 90 days **AND** no proteinuria (albumin:creatinine ratio) [ACR] <3 mg/mmol **or** any other marker of kidney damage (**new 2014**)

Message: Do not diagnose CKD in people with**:** an eGFRcreatinine of 45–59 ml/min/1.73 m2 **AND** an eGFRcystatinC of more > 60 ml/min/1.73 m2 **AND** no other marker of kidney disease **(new 2014)**

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Interpret with caution

Cystatin C levels have been reported to alter in some people with cancer and thyroid dysfunction

Cigarette smoking and CRP may also influence levels

Cost

Locally available for clinicians to request but commissioning needs to be agreed

Benefits

Correct Classification both patient and financial

Predictor of new onset and or developing CVD

Classification of CKD and identification of people at risk of CKD complications and progression

- **Who should be tested:**
- Diabetes
- Hypertension
- Cardiovascular disease
- Vascular disease or cerebral vascular disease
- Structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
- Multisystem diseases with potential kidney involvement e.g. systemic lupus erythematosus
- Family history of end-stage kidney disease (GFR category G5) or hereditary kidney disease
- Opportunistic detection of hematuria
- **Acute Kidney Injury (new 2014)**

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Classification of CKD using a combination of GFR and ACR

GFR and ACR categories (including stages of CKD from previous guideline)			Albuminuria categories (mg/mmol)		
			<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73 m²)	≥90 Normal and high	G1 (Stage 1)	No CKD*	G1 A2	G1 A3
	60–89 Mild reduction related to normal range for a young adult	G2 (Stage 2)		G2 A2	G2 A3
	45–59 Mild–moderate reduction	G3a (Stage 3a)	G3a A1^	G3a A2	G3a A3
	30–44 Moderate–severe reduction	G3b (Stage 3b)	G3b A1	G3b A2	G3b A3
	15–29 Severe reduction	G4 (Stage 4)	G4 A1	G4 A2	G4 A3
	<15 Kidney failure	G5 (Stage 5)	G5 A1	G5 A2	G5 A3

Increasing risk

Increasing risk

** By definition, in the absence of evidence of kidney damage, these categories are not CKD.*
*^ Consider using eGFRcystatinC to confirm the diagnosis of CKD in people with an eGFRcreatinine of 45–59 ml/min/1.73 m2, sustained for at least 90 days **and** no proteinuria (albumin:creatinine ratio [ACR] less than 3 mg/mmol).*
Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate

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Key Message

* Increased ACR is associated with increased risk adverse outcomes
* Decreased GFR is associated with increased risk of adverse outcomes
* Increased ACR and decreased GFR in combination **multiply** the risk of adverse outcomes

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Challenges and Benefits of the new classification system

Challenges:

Primary care may see it as too complicated → getting used to stages rather than categories

Not all practitioners have the discussion about CKD

Benefits:

A visual tool (heat map)

ACR measurements have changed

Working together

Investigating the cause of CKD:

* After having an informed discussion with the person with CKD **agree a plan** to establish the cause, particularly if the cause is thought to be treatable (e.g. urinary tract obstruction, nephrotoxic drugs or glomerular disease)
* Use the person's GFR and ACR categories to **indicate** their risk of adverse outcomes (e.g. CKD progression, acute kidney injury, all-cause mortality and cardiovascular events) and discuss this with them

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Monitoring

Agree the frequency of monitoring (eGFRcreatinine and ACR) with the person, with or at risk of CKD

Bear in mind that CKD is not progressive in many people

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Guide to frequency of monitoring of GFR for people with, or at risk of CKD

Frequency of monitoring (number of times per year)		Albuminuria categories (mg/mmol)		
		<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
GFR categories (ml/min/1.73 m²)	G1 ≥90 (Stage 1)	≤1	1	≥1
	G2 60–89 (Stage 2)	≤1	1	≥1
	G3a 45–59 (Stage 3a)	1	1	2
	G3b 30–44 (Stage 3b)	≤2	2	≥2
	G4 15–29 (Stage 4)	2	2	3
	G5 <15 (Stage 5)	4	≥4	≥4

Abbreviations: GFR, glomerular filtration rate

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Tailor individual monitoring according to:

- The underlying cause of CKD
- Past patterns of eGFR and ACR
- Comorbidities, especially heart failure
- Changes to their treatment (such as renin-angiotensin-aldosterone system [RAAS] antagonists, NSAIDs and diuretics)
- Inter-current illness
- Whether they have chosen conservative management of CKD (**new 2014**)

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Challenges and benefits of the new monitoring criteria

Challenges:

Slightly different from monthly to times per year

Benefits:

Visual reminder

The clinician and person with CKD decide on frequency according to clinical need

Aim: identify progressive CKD

Be aware that people with CKD are at increased risk of progression to end-stage renal disease if they have **either** of the following:

* a sustained decrease in GFR of 25% or more over 12 months

or

* a sustained decrease in GFR of 15 ml/min/1.73 m2 or more over 12 months (**new 2014**)

In people with an new finding of reduced GFR, repeat the GFR with 2 weeks to exclude causes of acute deterioration of GFR e.g. **AKI** or renin-angiotensin system antagonist (RASA) therapy **(amended 2014)**

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Risk factors associated with progression

- Cardiovascular disease
- Proteinuria
- **Acute Kidney Injury**
- Hypertension
- Diabetes
- Smoking
- African, African-Caribbean or Asian family origin
- Chronic use of NSAIDs

  Untreated urinary outflow tract obstruction

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Acute Kidney Injury and CKD

Monitor people for the development or progression of CKD for at least 2-3 years after acute kidney injury, even if serum creatinine has returned to baseline (**new 2014**)

Advise people who have had acute kidney injury that they are at increased risk of CKD developing or progressing (**new 2014**)

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Challenges and Benefits

Challenges:

Getting used to the new criteria

Not all AKI is documented or recognised

Is it 2 or 3 years?

Benefits:

Realistic position → kidney function does fluctuate and may not necessitate referral

Following AKI closer monitoring

Self management

Ensure that systems are in place to:

* Enable people with CKD to share in decision-making about their care
* Support self-management (this includes providing information about blood pressure, exercise, diet and medicines) and enable people to make informed choices
* Give people access to their medical data (including diagnosis, comorbidities, test results, treatments and correspondence) through information systems such as Renal Patient View, to encourage and help them to self-manage their CKD

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Challenges and Benefits

Challenges:

* Having the discussion → time and knowledge
* People having access to their medical data

Benefits:

Encourage practitioners to be up to date

Prompt discussion about treatment plan +/- referral

Ensure all information is correct → classification

Informed cohort → improve concordance

Proteinuria: amended guidelines

To detect and identify proteinuria use a urine ACR in preference to protein:creatinine ratio (PCR) → ACR has greater sensitivity at low levels of proteinuria

* For quantification and monitoring of high levels of proteinuria (ACR > 70mg/mmol) PCR can be used as an alternative
* ACR is recommended for people with diabetes

People without diabetes with a GFR of <60ml.min/1.73m2 quantify urinary albumin or urinary protein loss

* For initial detection of proteinuria if ACR 3mg/mmol-70mg/mmol a subsequent early morning urine should completed for confirmation
* If initial ACR is ≥70mg/mmol a repeat sample is not required
* **Regard a confirmed ACR of ≥ 3mg/mmol as clinically important proteinuria**

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Other Recommendations:

Blood pressure → No change to parameters

Offer a **low-cost** renin-angiotensin system antagonist to people with CKD and:

- diabetes and an ACR of 3 mg/mmol or more
- hypertension and an ACR of 30 mg/mmol or more
- an ACR of 70 mg/mmol or more (irrespective of hypertension or cardiovascular disease)(**new 2014**)

Do not offer a combination of renin-angiotensin system antagonists to people with CKD (**new 2014**)

Do not routinely offer a RASA therapy to people with a pre-treatment potassium of >5.0mmol/litre (**amended 2014**)

Follow the treatment recommendations in Hypertension (NICE clinical guideline 127) for people with CKD, hypertension and an ACR of <3 mg/mmol, if they do not have diabetes (**new 2014**)

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Vitamin D supplement in the management of CKD-MBD

- Do not routinely offer vitamin D supplementation to manage or prevent CKD-mineral and bone disorders (**new 2014**)
- Offer cholecalciferol or ergocalciferol to treat vitamin D deficiency in people with CKD and vitamin D deficiency (**new 2014**)
- If vitamin D deficiency has been corrected and symptoms of CKD-mineral and bone disorders persist, offer alfacalcidol (1-alpha-hydroxycholecalciferol) or calcitriol (1-25-dihydroxycholecalciferol) to people with stage 4 or 5 CKD (**new 2014**)
- Monitor serum calcium and phosphate concentrations in people receiving alfacalcidol or calcitriol supplements (**new 2014**)

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Statins and oral antiplatelet and anticoagulant therapy

* Follow the recommendations in lipid modification (NICE CG 181) for the use of statins in CKD **(new 2014)**

* Offer antiplatelet drugs to people with CKD for the secondary prevention of cardiovascular disease, but be aware of the increased risk of bleeding **(new 2014)**

Consider **apixaban** in preference to warfarin in people with confirmed eGFR of 30-50ml/min/1.73m2 and non-valvular atrial fibrillation who have one or more of the following risk factors:

* Prior stroke or transient ischemic attack
* Age 75 years or older
* Hypertension
* Diabetes mellitus

Symptomatic heart failure (**new 2014**) (Chronic Kidney Disease: NICE guideline CG 182 2014)

Other recommendations

* Do not offer low-protein diets (dietary protein intake less than 0.6–0.8 g/kg/day) to people with CKD (**new 2014**)

* Consider oral sodium bicarbonate supplementation for people with both: a GFR less than 30ml/min/1.73m2 **AND** a serum bicarbonate concentration of less than 20 mmol/litre (**new 2014**)

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Referral Criteria

* GFR less than 30 ml/min/1.73 m2 (with or without diabetes)
* ACR 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated
* ACR 30 mg/mmol or more, together with hematuria
* **Sustained decrease in GFR of 25% or more and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 m2 or more**
* Hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses
* Known or suspected rare or genetic causes of CKD
* Suspected renal artery stenosis

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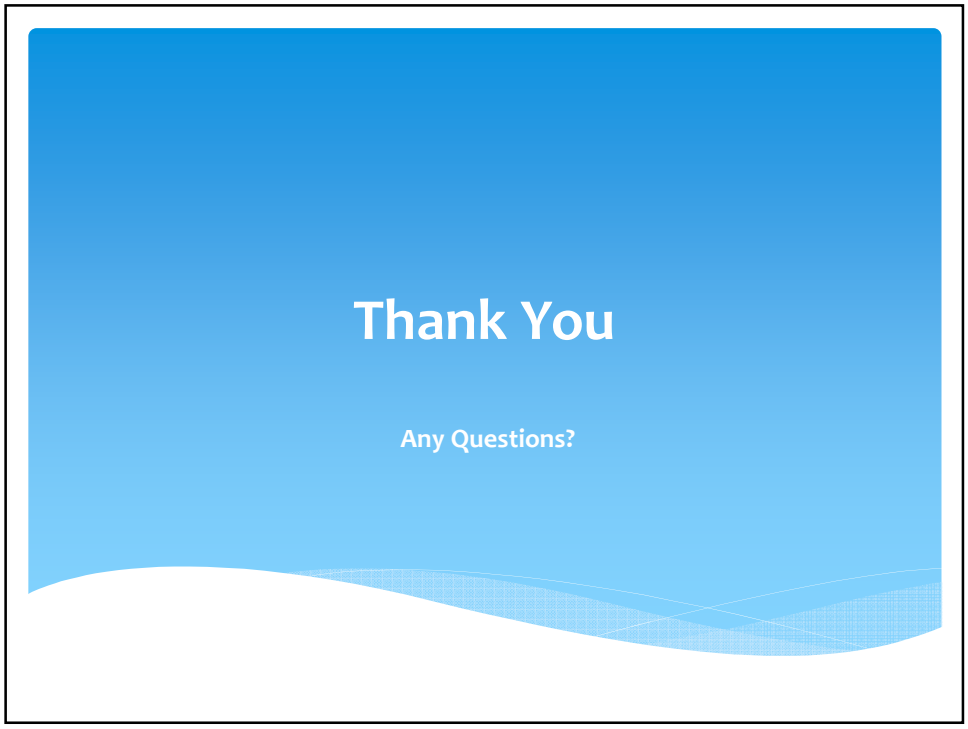
Summary

* Use CKD-EPI in preference to MDRD
* Combining eGFR using the CKD EPI equation and Cystatin C may classify less people with a CKD in a small but significant sub-group
* Commissioning of new tests will need to be agreed
* The new classification and monitoring grid should help practitioners with appropriate monitoring and assist them in identifying people who are increased risk of adverse outcome
* Practitioners are encouraged to discuss diagnosis and treatment plans with individuals
* Defining progression is more appropriate and may avoid inappropriate referrals
* Monitoring following AKI is recognised as important
* Access to medical data may create some challenges
* Gives practical advise on managing some of the complications associated with CKD


Thank You
Any Questions?