

# Timing Referral for CKD

NBIMU 2018

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Nephrologist

Horizon Health

# Alternative Title

“What should I do with this annoying eGFR calculation that is constantly changing and appears to be indicating impending doom despite the fact that my 80yr robust patient continues to volunteer 3X a week as well as playing golf and otherwise seems to be fine....”



I'M TIRED,  
GRANDDAD!  
CARRY ME?

# Referrals for CKD- A Indirect Path

- 2 Important slides
- CKD definition, eGFR calculations, CKD staging
- Review of renal disease progression
- What does a nephrologist do?
- Maybe a funny cartoon
- 2 important slides
- Question

# Suggestions

- Share uncertainty about appropriateness of diagnostic thresholds and reliability of measurements
- Look for changes that support the diagnosis of disease (beyond GFR)
- Be aware of variability
- Be careful of labeling (Age >65, GFR30-60, No albuminuria...CKD?)

# Nephrology referral suggestions

- To assist with diagnostic challenge (e.g. decision to biopsy)
- To assist with therapeutic challenge (e.g. blood pressure)
- Rapid decay of estimated GFR
- Most primary kidney diseases, (e.g. glomerulonephritides)
- Preparation for renal replacement therapy, especially when GFR less than 30

# Definition of CKD

Structural or functional abnormalities of the kidneys for  $\geq 3$  months, as manifested by either:

1. Kidney damage, with or without decreased GFR, as defined by
  - pathologic abnormalities
  - markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in imaging tests
2. GFR  $< 60$  ml/min/1.73 m<sup>2</sup>, with or without kidney damage

# Glomerular Filtration rate (GFR)

- ***Glomerular filtration rate (GFR):***  
*is the volume of fluid filtered from the renal glomerular capillaries into the Bowman 's space per unit time.*
- *Normal for a 20 year old is ~ 120ml/min*

# Methods to assess GFR

- Serum urea
- Serum creatinine
- Serum cystatin C
- Timed urine collections
  - Creatinine clearance
  - Inulin clearance
- Calculated GFR calculations
  - based on serum creatinine
  - many formulas including Cockcroft Gault and MDRD
- Nuclear medicine methods

# Creatinine based approximations

## 1) Cockcroft-Gault equation

$$\text{CrCl (ml/min)} = \frac{(140 - \text{age}) \times \text{actual weight (kg)} \times 1.2 \text{ (if male)}}{\text{SCreat } (\mu\text{mol/L})}$$

**Weight probably not available for lab to calculate**

## 2) MDRD (Modification of Diet in Renal Disease)

6 variable or abbreviated version

$$\text{GFR (ml/min/1.73m}^2\text{)} = 170 (\text{PCr})^{-0.999} \times (\text{Age})^{-0.176} \times (0.762 \text{ if female}) \times (1.21 \text{ if African American}) \times (\text{serum urea})^{-0.170} \times (\text{Albumin})^{+0.318}$$

**Lab has patient age and gender – can do abbreviated version**

# eGFR equation provisos

- eGFR calculations may be less reliable in:
  - individuals with near normal GFR ( $>60$  ml/min/1.73m<sup>2</sup>)
  - individuals with markedly abnormal body composition
    - extreme obesity
    - cachexia
    - paralysis
    - amputations
- *Controversies exist as to the applicability of these formulae to various ethnic groups and the very elderly*

# Is it just about GFR?

## Should also assess urine protein losses

- 24 hour urines are no longer recommended
  - For same reasons as with GFR
- Urine dipsticks are affected by hydration status

### **Quantify protein excretion with random urine for:**

- **Urine albumin to creatinine ratio** or
- **Urine protein to creatinine ratio**

# Importance of Proteinuria in CKD

Interpretation	Explanation
Marker of kidney damage	Spot urine albumin-to-creatinine ratio >30 mg/g or spot urine total protein-to-creatinine ratio >200 mg/g for $\geq 3$ months defines CKD
Clue to the type (diagnosis) of CKD	Spot urine total protein-to-creatinine ratio >500-1000 mg/g suggests diabetic kidney disease, glomerular diseases, or transplant glomerulopathy.
Risk factor for adverse outcomes	Higher proteinuria predicts faster progression of kidney disease and increased risk of CVD.
Effect modifier for interventions	Strict blood pressure control and ACE inhibitors are more effective in slowing kidney disease progression in patients with higher baseline proteinuria.
Hypothesized surrogate outcomes and target for interventions	If validated, then lowering proteinuria would be a goal of therapy.

## Prognosis of CKD by GFR and albuminuria category

### Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

				Persistent albuminuria categories		
				Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (mL/min/1.73 m <sup>2</sup> ) Description and range	G1	Normal or high	≥90	Green	Yellow	Orange
	G2	Mildly decreased	60-89	Green	Yellow	Orange
	G3a	Mildly to moderately decreased	45-59	Yellow	Orange	Red
	G3b	Moderately to severely decreased	30-44	Orange	Red	Red
	G4	Severely decreased	15-29	Red	Red	Red
	G5	Kidney failure	<15	Red	Red	Red

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

## I.2 When to refer to a nephrology clinic

### Guideline I.2.1

A. Referral to nephrology should be considered when the GFR is  $<60$  ml/min and is mandatory when the GFR is  $<30$  ml/min.

B. If a GFR prediction or measurement is not available, patients with chronic renal failure should be referred to a nephrologist when on two consecutive measurements, plasma creatinine exceeds 150 mmol/l in men and 120 mmol/l in women, corresponding to a GFR of  $\sim 50$  ml/min. These patients should be referred whether or not there are other indications of chronic renal disease, such as proteinuria.

## 2002 NKF Framework for defining and classifying CKD

National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. Executive summary. *Am J Kidney Dis* 2002;39:S17-31.

## There are dangers in becoming too “GFR-centric”

- *Increased testing*
- *Increased procedures*
- *Psychological stress*
- *Medicalization*



Reception

Dr. P. Sohi Dr. N. Gogan

Réception

Dr. C. Pippy Dr. M. MacKinnon

Nephrology &  
Hypertension Services

Services de néphrologie  
et d'hypertension



# Chronic kidney disease controversy: how expanding definitions are unnecessarily labelling many people as diseased

Ray Moynihan *senior research fellow*<sup>1</sup>, Richard Glasscock *emeritus professor, department of medicine*<sup>2</sup>, Jenny Doust *professor*<sup>1</sup>

## Suggestions for clinicians

Be informed about the controversy and debate over methods used to define chronic kidney disease

Share uncertainty about appropriateness of diagnostic thresholds and reliability of measurements with patients

Look for other changes that support the diagnosis—for example, is there evidence of anaemia, abnormal urinalysis results, or abnormalities on renal ultrasonography?

Be aware of the variability in measures of kidney function (eGFR and albuminuria) and the need to repeat the test to confirm reduced renal function

Don't routinely use the label chronic kidney disease for people aged 65 years and older with eGFR stage 3A and no albuminuria

Older people with stable but modestly reduced eGFR (45-59 ml/min/1.73 m<sup>2</sup>) are unlikely to have a high risk of future adverse events unless they have persistent overt albuminuria

The ultimate goal of a nephrologist is to maintain renal function and manage associated metabolic changes and prolong time till dialysis



Educate about, and prepare for, renal replacement therapy

## When assessing for the presence and significance of CKD what do I worry about...

- CKD stage
- Creatinine / eGFR trajectory
- Presence and degree of proteinuria / urinary abnormalities
- Support for CKD “disease” – anemia, Ca/Pi/PTH abn, structural abn
- Risk of CV disease

## CLASSIFICATION OF CHRONIC KIDNEY DISEASE

Stage	Estimated GFR (mL/min/1.73 m <sup>2</sup> )	Comment
1	≥90	Normal GFR w/ proteinuria
2	60–89	Age-related decline in GFR w/proteinuria
3A	30–59	Low risk of progression to kidney failure
3B*		
4	15–29	High risk of progression to kidney failure
5	<15	Kidney failure
5D		
5T		

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# Renal Function Trajectory Is More Important than Chronic Kidney Disease Stage for Managing Patients with Chronic Kidney Disease

Steven J. Rosansky

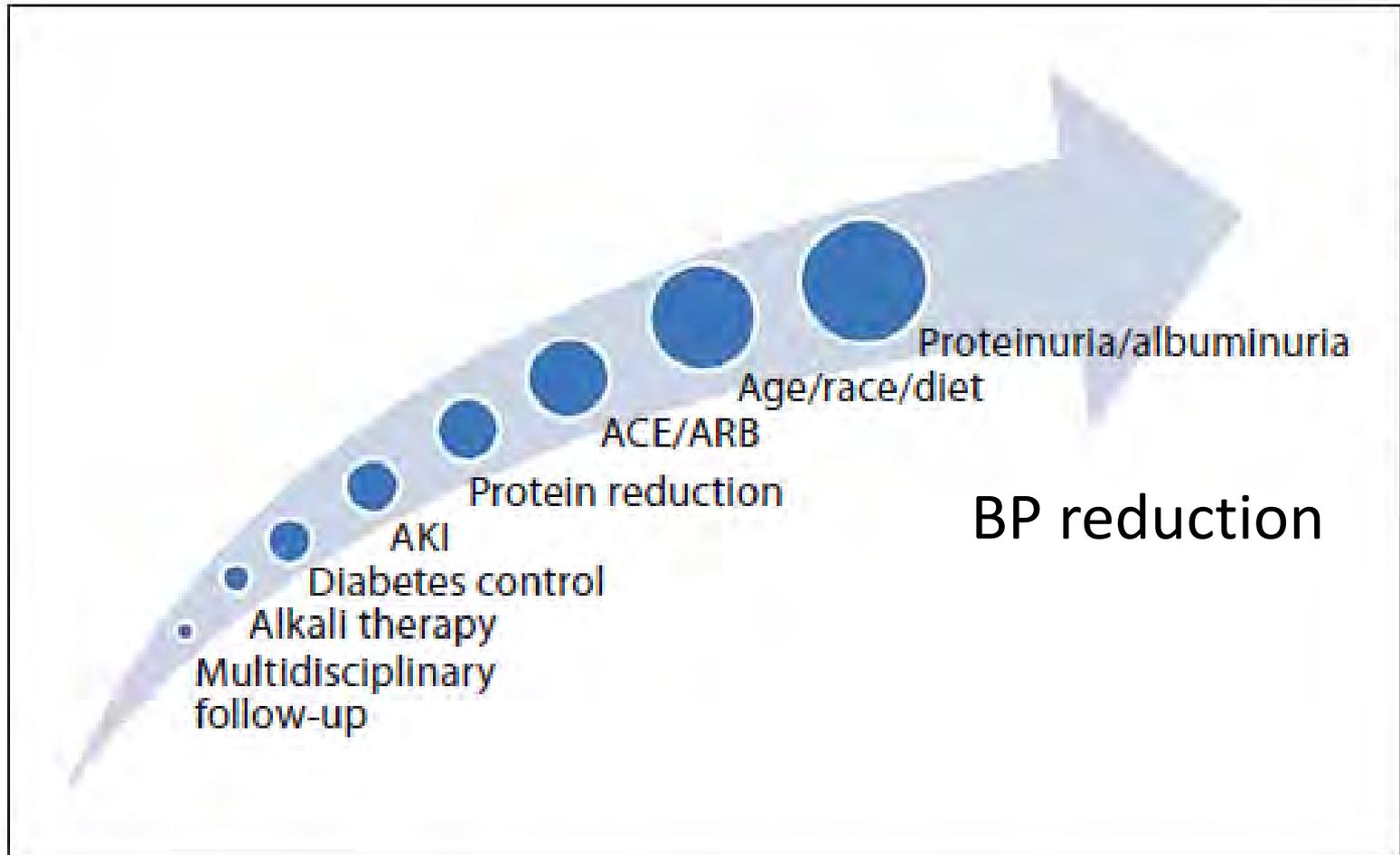
WJB Dorn Veteran's Hospital, Columbia, S.C., USA

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**Fig. 1.** Factors affecting renal function trajectory.

# Reassurance

FROM THE FRONTLINE

## The power of doing nothing

Des Spence *general practitioner, Glasgow*



I recently booked a ticket on a sleeper train from Glasgow to London, and it was surprisingly cheap. At the station, I realised

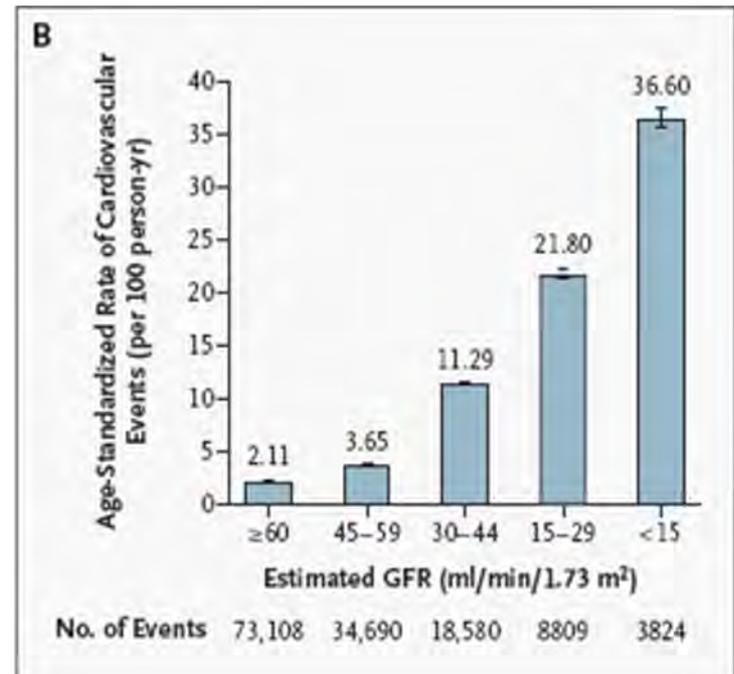


“Medicine is about comfort and reassurance, not about diagnostics, big machines, and glass fronted hospitals. In medicine, most patients present with anxiety, for the fear of illness is far, far greater than the risk of illness”

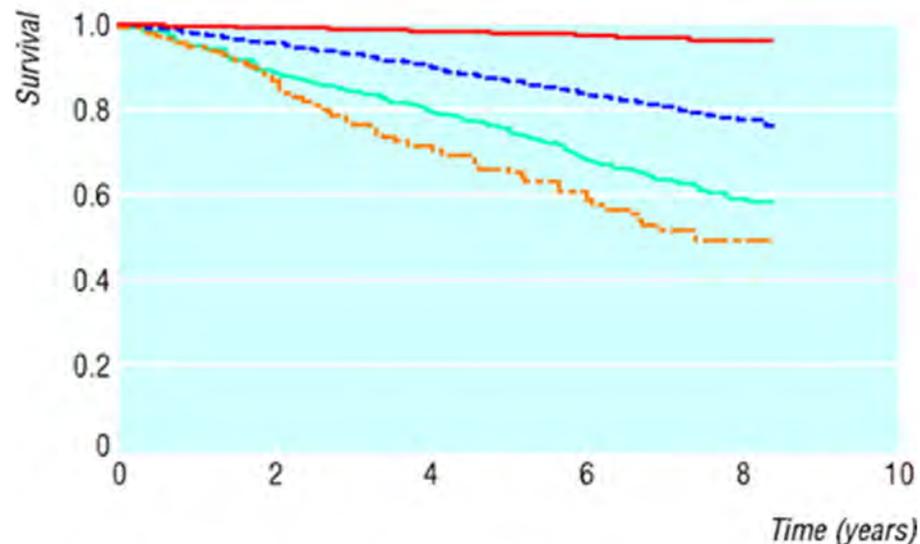
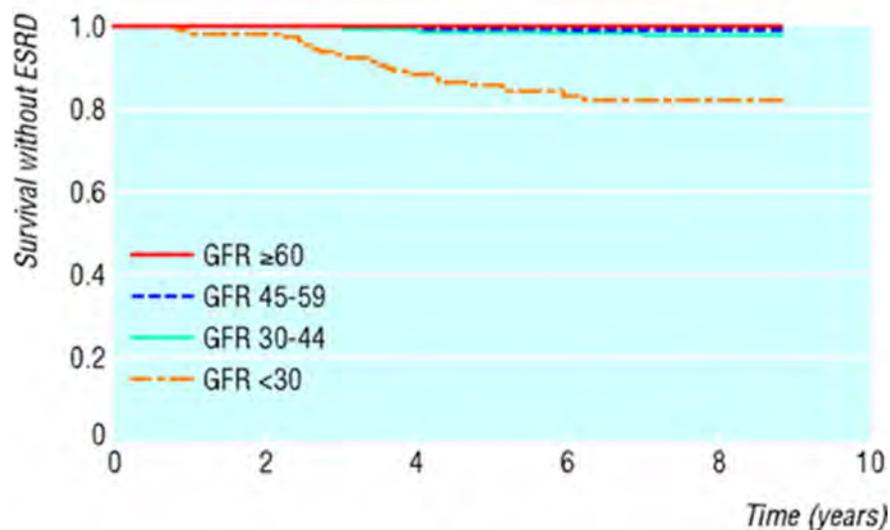
# ESRD is not the problem

*“Even in the absence of symptoms chronic kidney disease appears to add significantly to the burden of cardiovascular disease and death and for a important minority of patients progress to kidney failure”*

Go,A et al. NEJM 2004;351:1291-1305



**Fig 2 Survival without end stage renal disease (ESRD) and cardiovascular death by glomerular filtration rate (GFR) (ml/min/1.73 m<sup>2</sup>) at screening .**



GFR at screening	≥60	45-59	30-44	<30	Total
ESRD	13	9	7	22	51
Total No	62 066	2389	548	120	65 123
Log rank test (P value)	<0.001	0.001	<0.001		

GFR at screening	≥60	45-59	30-44	<30	Total
Cardiovascular death	1913	456	185	50	2604
Total No	62 099	2389	548	120	65 156
Log rank test (P value)	<0.001	<0.001	0.035		



**S** sulfonylureas  
**A** ACE-inhibitors  
**D** diuretics, direct renin inhibitors  
  
**M** metformin  
**A** angiotensin receptor blockers  
**N** non-steroidal anti-inflammatory  
**S** SGLT2 inhibitors



**Instructions for Healthcare Professionals:**

If patients become ill and are unable to maintain adequate fluid intake, or have an acute decline in renal function (e.g. due to gastrointestinal upset or dehydration), they should be instructed to hold medications which will:

1. Increase AKI Risk
2. Have reduced clearance



**Cochrane  
Library**

Cochrane Database of Systematic Reviews

## Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease (Review)

Smart NA, Dieberg G, Ladhani M, Titus T

# *Benefits of Early Referral to a Nephrologist*

**Early referral strategies for management of people with markers of renal disease: a systematic review of the evidence of clinical effectiveness, cost-effectiveness and economic analysis**

C Black,<sup>1</sup> P Sharma,<sup>1</sup> G Scotland,<sup>2</sup> K McCullough,<sup>3</sup> D McGurn,<sup>1</sup> L Robertson,<sup>1</sup> N Fluck,<sup>3</sup> A MacLeod,<sup>4</sup> P McNamee,<sup>2</sup> G Prescott<sup>1</sup> and C Smith<sup>1</sup>

<sup>1</sup>Section of Population Health, University of Aberdeen, Aberdeen, UK

<sup>2</sup>Health Economics Research Unit, University of Aberdeen, Aberdeen, UK

<sup>3</sup>NHS Grampian, Aberdeen, UK

<sup>4</sup>Grampian University Hospitals NHS Trust, Aberdeen, UK

# My interpretation of the data...

- Matched cohort studies suggest improved mortality and reduced hospitalizations in early referral group (bias? Driven by factors below?)
- Better hypertension control
- Better preparation for dialysis
  - Line versus fistula
  - Hgb support
  - Less crash starts

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*Delicate durability describes the human body, and nowhere is this more apparent than in the urinary tract. If the liver is all bulk and thunder, the heart fist and thrust and piston, and the brain a foamy paste of insubstantial electricity, the parts of the urinary tract — namely the kidneys, ureters, and bladder — are a tracery of tubules and ducts of such a fineness as would lay mad a master plumber, more, a Venetian glassblower.*

— RICHARD SELZER (1996)