eGFR; Whatever next?

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April 2006

eGFR hits the QoF

GFR =175 x ((creatinine(µmol/L))-intercept))/slope))$^{-1.154}$ x (Age)$^{-0.203}$ x [0.742 if patient is female] x [1.212 if African American]

Renal Bods: -

Joy!

" Greatest advance in renal medicine this century"

Lab Bods; -

Despair!

"Why didn't you speak to us first!"

Primary Care: -

Confusion!

"Not sure what it means, but we have to have it now!"

Staging as KDOQI

http://www.kidney.org/professionals/kdoqi/index.cfm

Among patients with chronic kidney disease, the stage of disease should be assigned based on the level of kidney function, irrespective of diagnosis,

according to the K/DOQI CKD classification: -

Table 10. Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	Kidney failure	<15 (or dialysis)

Normal

Mild

Moderate impairment

Severe impairment

Established renal disease

What to Measure: RCGP

Minimum frequency of testing		
CKD stage	**Tests**	**Frequency**
1 and 2	BP eGFR Urine PCR*	yearly
3	- also Hb, potassium calcium, phosphate	6 monthly (12 if stable **)
4 and 5	- also bicarbonate, PTH	3 monthly (6 if stable CKD stage 4 **)

* if dipstick protein present

** stable=<2mL/min change eGFR over 6months

Problem: Majority of patients with CKD have an eGFR >60 mL/min/1.73m²

Prevalence of CKD: NHANES III Adults >20

Stage	Description	eGFR MDRD ml/min/1.73m²	Prevalence %
1*	Kidney damage With "normal" GFR	≥ 90	3.3
2 *	Kidney Damage with mildly ↓ GFR	60-89	3.0
3	Moderate ↓ GFR	30-59	4.3
4	Severe ↓ GFR	15-29	0.2
5	Kidney Failure	<15	0.1

*** Albumin/creatinine ratio 1.9mg/mmol males; 2.8 mg/mmol female on 2 occasions.**

Problem: Equation not Universally Applicable

Steak Pie

Race = Cherub i.e. not white or African American

Under 18?

Pregnant or Obese?

One Leg

Strenuous Exercise
Creatine Supplements

Problems:

- **High and variable referral rates due to:-**
  - inaccuracy of creatinine measurements
  - Uncertainty as to correct course of action in primary care. (e.g. 80 year old lady eGFR = 56 ?)
  - Lack of guidance. SIGN & NICE to Report.
- **Increase in biochemistry workloads.**

Where are the Cavalry?

Scotland Forever! Lady Elizabeth Butler

UK Consensus Conference on Early Chronic Kidney Disease 6 and 7 February 2007.

Royal College of Physicians Edinburgh

Nephrol Dial Transplant. 2007 Sep;22(9):2455-7

Archibald G, Bartlett W, Brown A, Christie B, Elliott A, Griffith K, Pound S, Rappaport I, Robertson D, Semple Y, Slane P, Whitworth C, Williams B.

RCPE UK Consensus Statement on Diagnosis of Early CKD

Main Changes: -

- Report eGFR as > 60 ml/min/1.73/M^2 across the uk
- Stage 3 now: -
  - 3A 45 to 59
  - 3B 30 to 44
- Suffix P = proteinuria = PCR 100 mg/mmol creatinine = risk
- If ΔeGFR >4 mL/min/1.73M^2 refer?

Proteinuria not in QoF Yet!

Guidance for Labs: -

- **Enzymatic creatinine or slope and intercept adjusters**
- **Indicate on reports** that an eGFR greater than 60 does not exclude CKD stages 1 and 2; **urinalysis and further investigations where appropriate**
- **Report CKD 3a and 3B**
- provide **indicators of the significance of change** between serial results (e.g. reference change value).
- provide specific **recommendations on collection procedures** to minimise biological and other sources of variation.

Clear Guidance for GPs

Stage 1, 2 and 3A: -

- Manage cardiovascular risk factors
- Annual review with; -
  - eGFR,
  - Urinalysis
  - Blood pressure

Stage 3B

- 6 monthly review as above

Primary aim to reduce progression optimise blood pressure and reduce proteinuria.

Help for Lab workload!

Bone and Mineral Disorders

- Not common in early CKD. Recommend leaving the PTH measurements to the renal units.

Anaemia

- Uncommon unless diabetic or eGFR <45 mL/min/1.73m^2

Problem: eGFR >60 ?

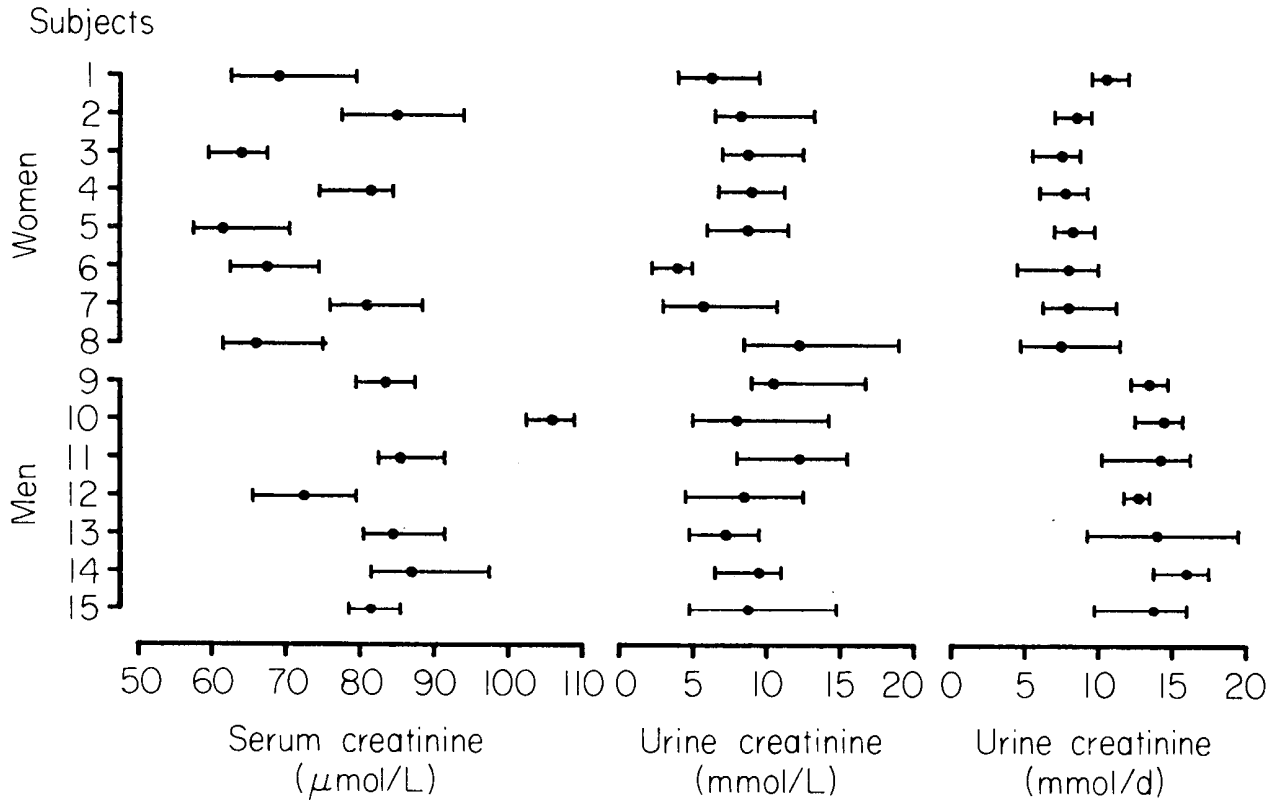
- Is it falling at a rate of greater than 4 mL/min/1.73m^2/year ?
- Creatinine measurement employing appropriate reference intervals and reference change values?

Significance of Change

Reference Change Values?

- eGFR or Creatinine.
- Biological Variation: Average within subject (CV_I) = 4.3%

Biological Variation



Gowans & Fraser. Ann Clin Biochem 1988:25:259-263

Reference Change Value

- Interpretation of serial results.
- Difference > than combined analytical and biological variation: -

$$RCV = 2^{½} * Z * (CV_A^2 + CV_I^2)^{½}$$

The Z score determines the level of significance of the change: -

e.g. 1 tailed 95% = 1.65

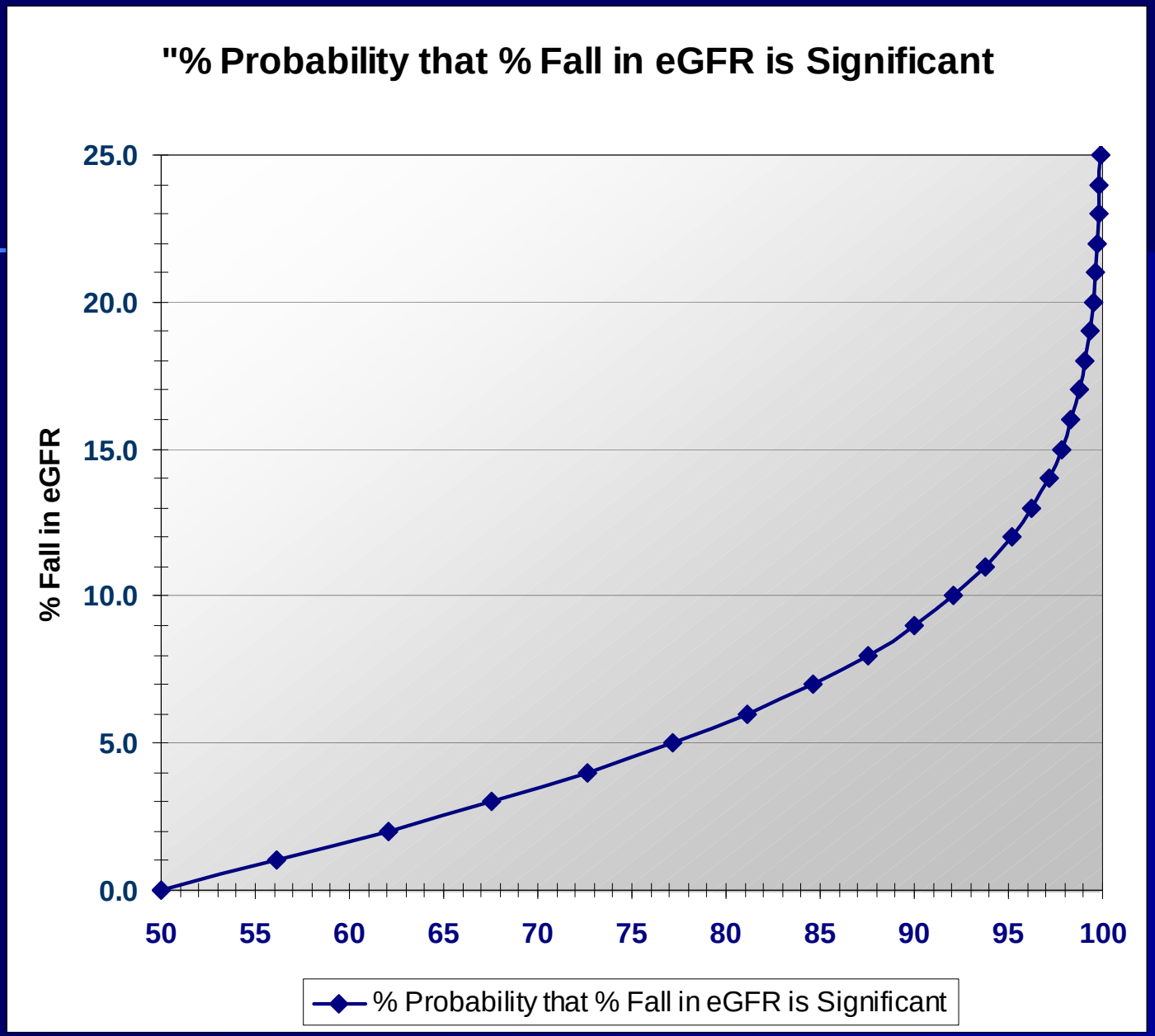
99% = 2.33

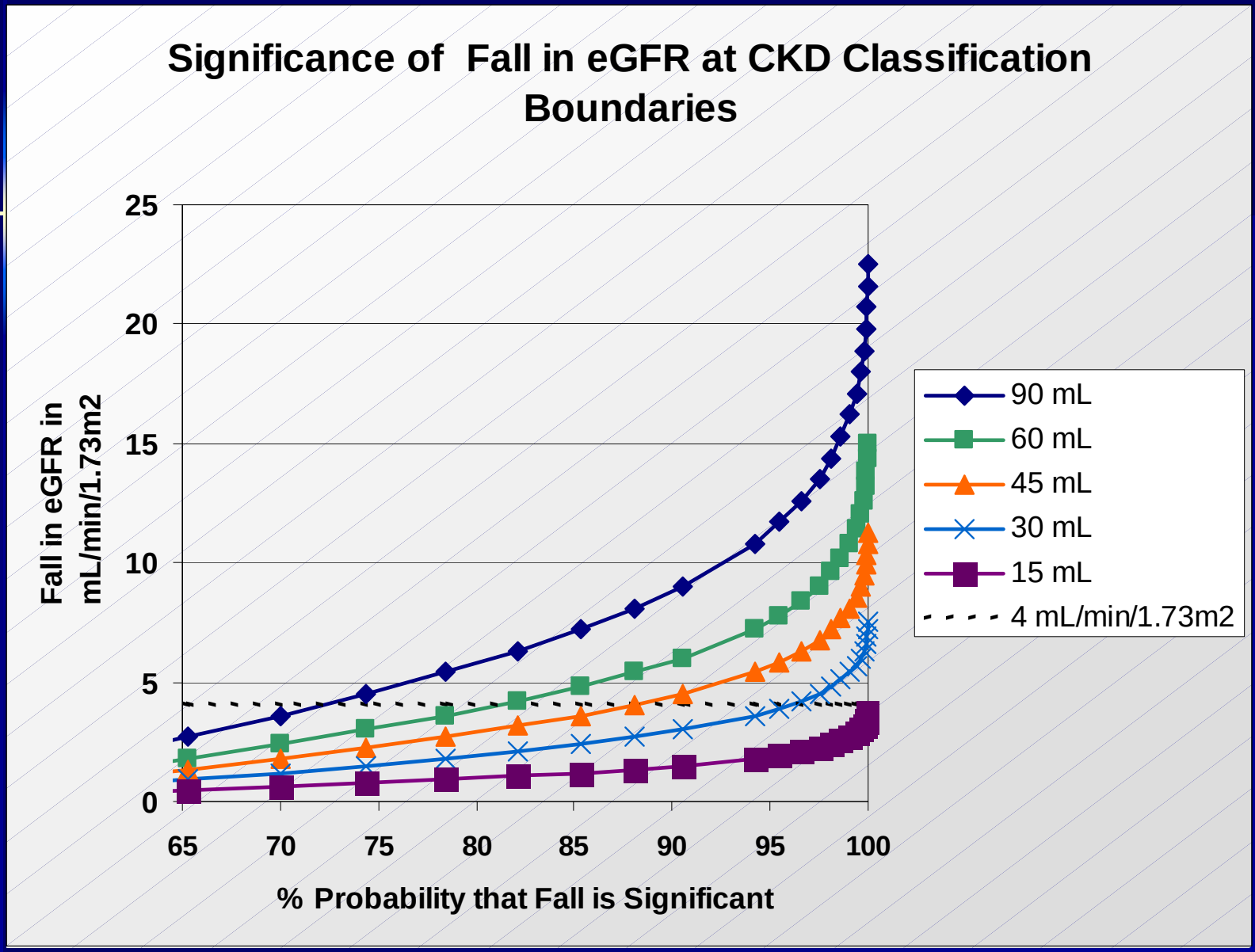
RCV eGFR.

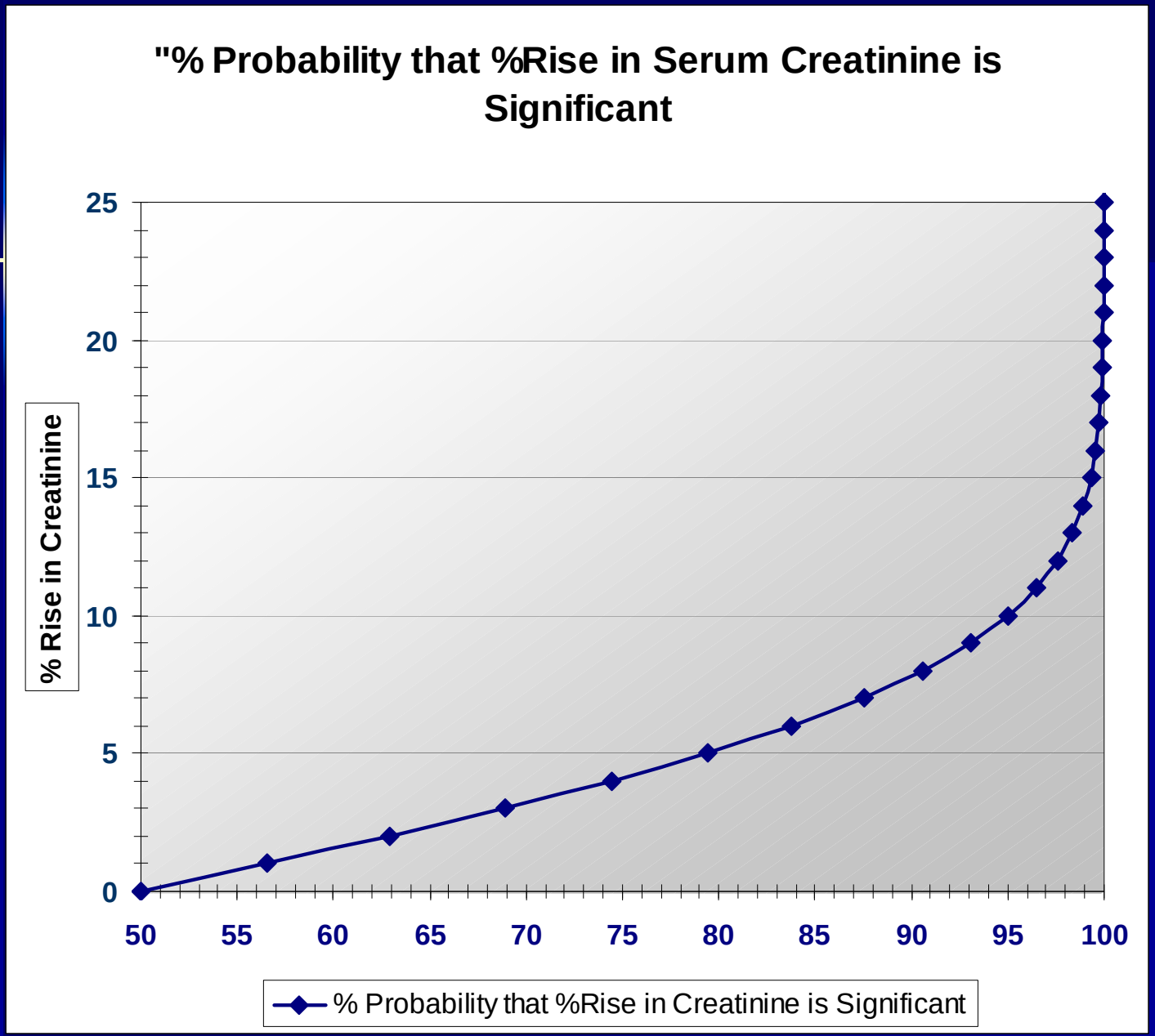
GFR = 175 x (creatinine)$^{-1.154}$ x (Age)$^{-0.203}$ x [0.742 if patient is female] x [1.212 if African American]

Confidence limits?

- Only analytical Variable is the Creatinine with a CV_I of 4.3 % the impact of this is increased by the power function in the equation to an average of 5.4%.
- Non linear relationship between eGFR and [Creatinine] = non linear relationship between probability of change and starting eGFR.


"% Probability that % Fall in eGFR is Significant
% Fall in eGFR
25.0
20.0
15.0
10.0
5.0
0.0
50
55
60
65
70
75
80
85
90
95
100
% Probability that % Fall in eGFR is Significant


Significance of Fall in eGFR at CKD Classification Boundaries
Fall in eGFR in mL/min/1.73m2
25
20
15
10
5
0
65
70
75
80
85
90
95
100
% Probability that Fall is Significant
90 mL
60 mL
45 mL
30 mL
15 mL
4 mL/min/1.73m2


"% Probability that %Rise in Serum Creatinine is Significant
% Rise in Creatinine
25
20
15
10
5
0
50
55
60
65
70
75
80
85
90
95
100
% Probability that %Rise in Creatinine is Significant

Observation: -

- The significance of a change depends on starting eGFR
- Single cut off of 4 mL maybe clinically useful, but carries different significance at different levels of eGFR
- Complicated story to tell GPs

Question being Asked?

- Has the patient got reduced renal function?
- Has the function deteriorated?

Answer?

- Use eGFR for initial classification of CKD stage.
- Use creatinine to follow patients with RCV indicator flag?
  - More Precise?

RCV for eGFR and Creatinine: -

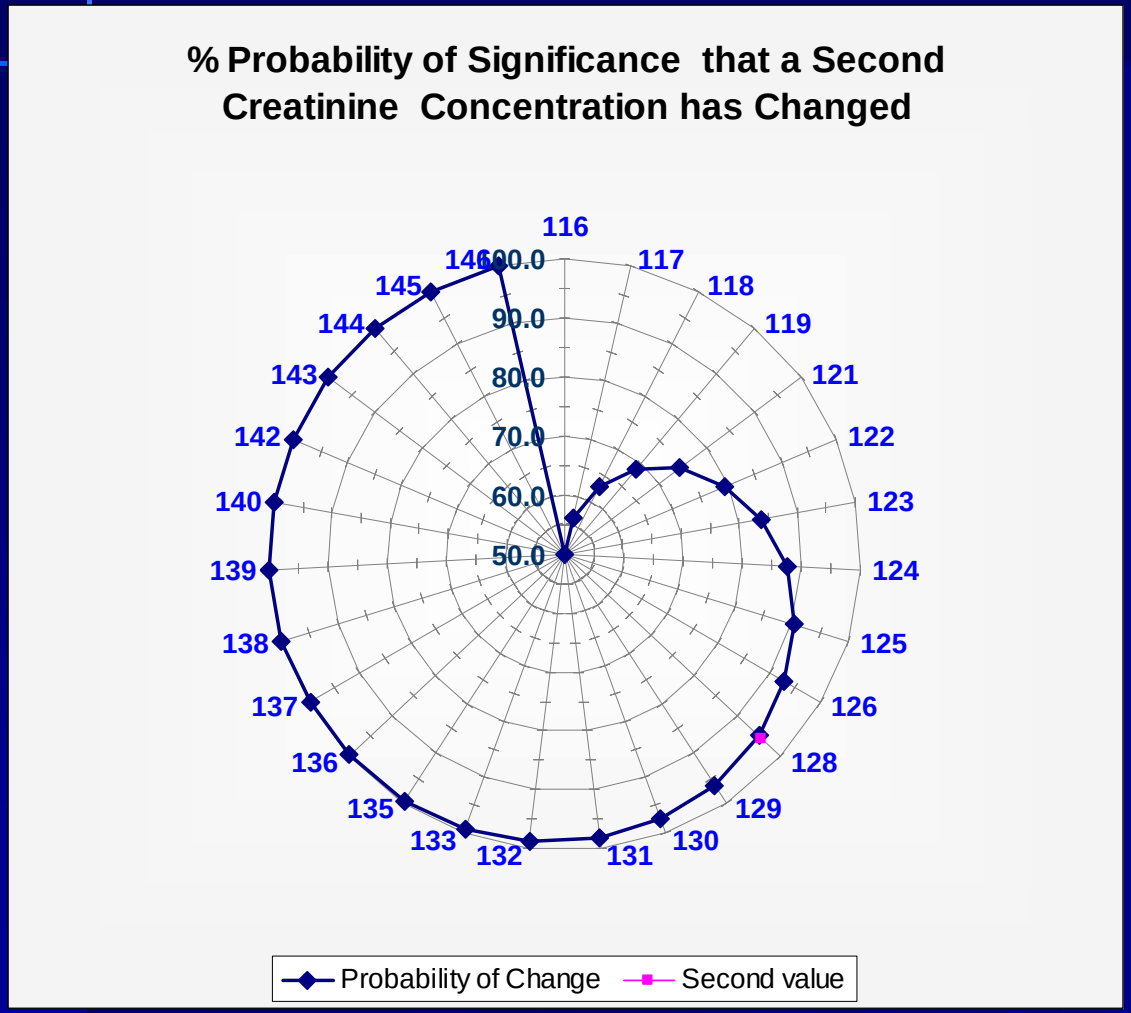
	% Change at % Probability	
	95%	99%
Rise in Creatinine	10.3%	14.6%
Fall in eGFR	12.8%	15.4%

Assumes a CV_A = 1%
CV_I = 4.3 % creatinine
CV_I = 5.4 % eGFR

How do we communicate the significance

- Use graphs?
- Report probabilities?
- Flags?

55 year old white male



Creatinine rise from 116 to 128

Change = 10.3%

95% probability of significant rise

eGFR at baseline = 60mL/min/1.73m^2

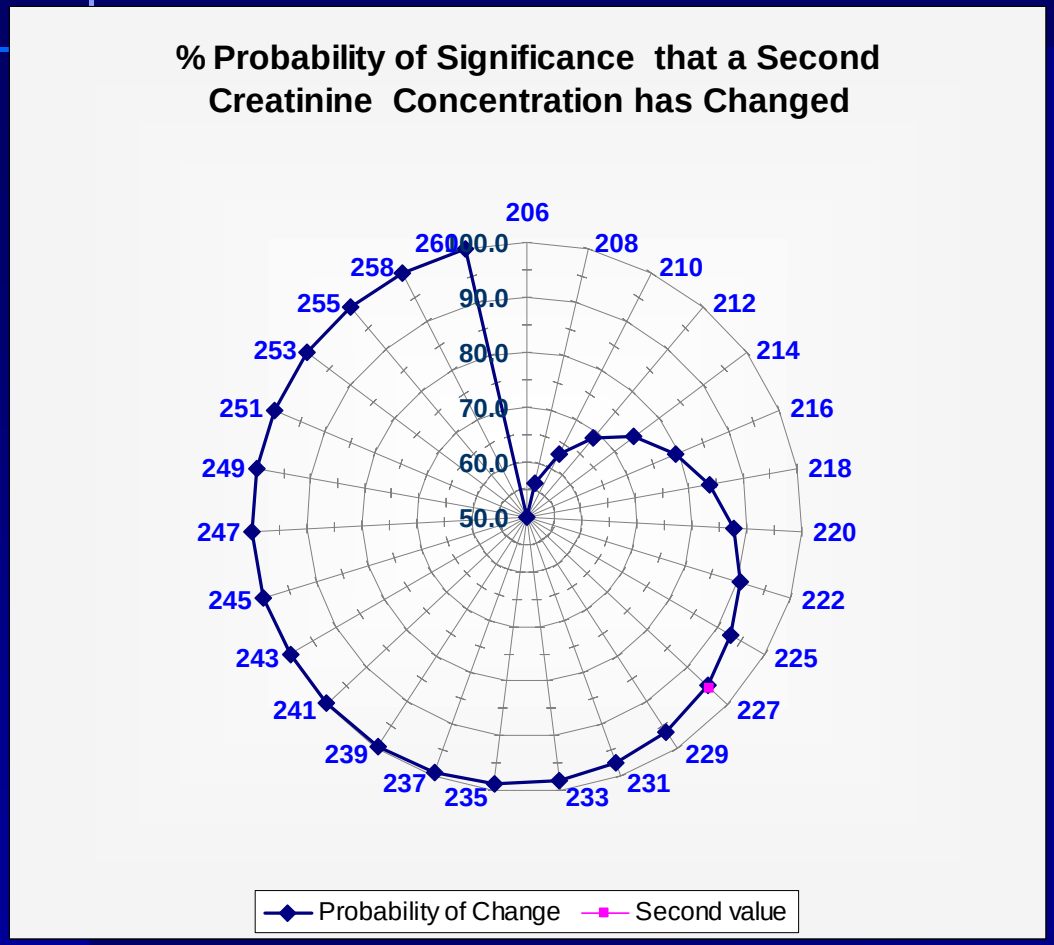
eGFR now = 53 mL/min

Change = 11.6% = 7 mL

93.5% probability significant fall in eGFR

Patient referral?

55 year old White Male



Creatinine rise from 206 to 227

Change = 10.3%

95% probability of significant rise

eGFR at baseline = 30mL/min/1.73m^2

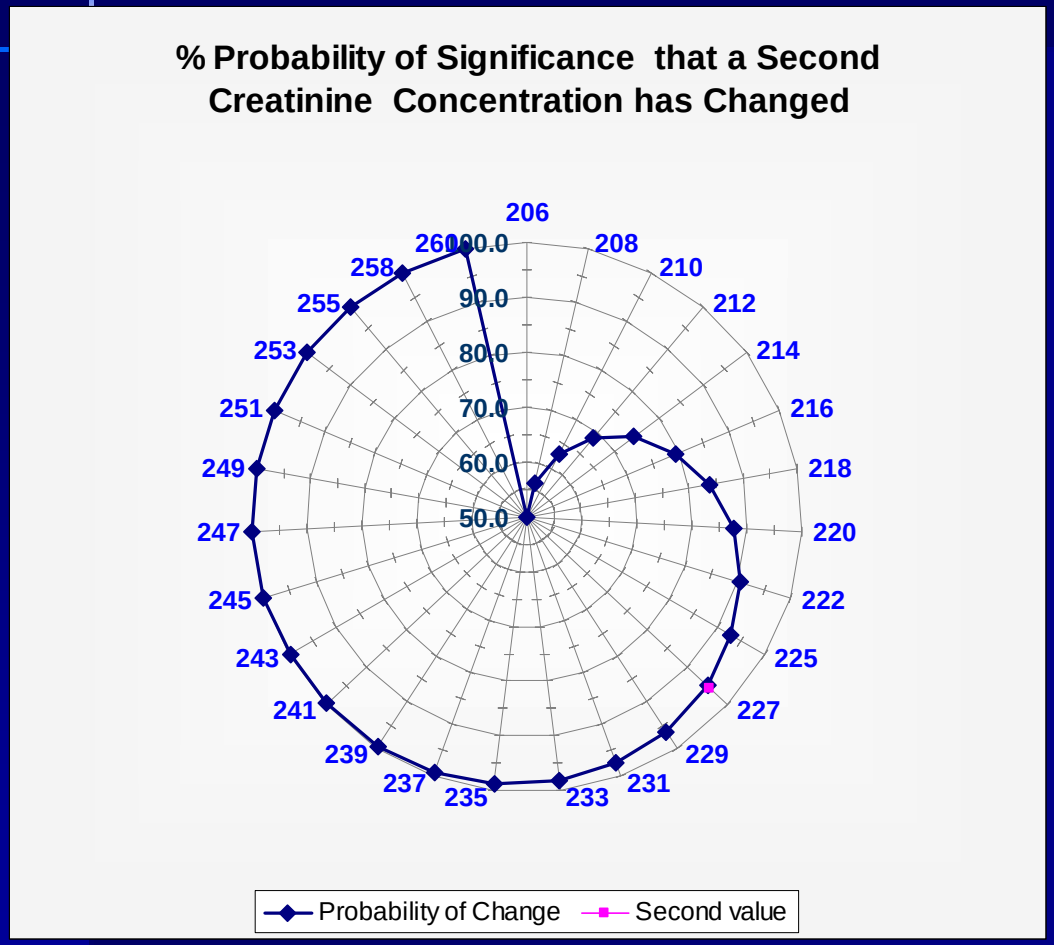
eGFR now = 27 mL/min

Change = 10 % = 3 mL

90% probability significant fall in eGFR

Patient referral?

55 year old White Female



Creatinine rise from 206 to 227

Change = 10.3%

95% probability of significant rise

eGFR at baseline = 23 mL/min/1.73m^2

eGFR now = 20 mL/min

Change = 10 % = 3 mL

90% probability significant fall in eGFR

Patient referral?

Keep it simple? Use Flags

Tayside Clinical Laboratory Services — Telephone 01738 473223 (PRI) 01382 632602 (NW)

Name:

N/W Ward 3

SODIUM	130	**	mmol/L	(	135-147)
POTASSIUM	4.8		mmol/L	(	3.5-5.0)
UREA	25.2	**	mmol/L	(	3.3-6.6)
CREATININE	212	**	umol/L	(	44-80)
ESTIMATED GFR	24		mL/min		
CKD Stage	4		.		
ALT	47	**	U/L	(	12-40)
BILIRUBINS	12		umol/L	(	0-15)
ALKALINE PHOSPHATASE	603	**	U/L	(	20-80)
ALBUMIN	34	<	g/L	(	36-50)
GGT	651	>>	U/L	(	5-35)

Lab.Comments:

Sample Date/Time
18 Aug 2007 07:34

Clin.Details: CF, bilateral lung transplant

Request Entered: 18 Aug 2007 09:54 Report Printed: 18 Aug 2007 11:19

30 year old white female: Highly significant change in renal function: - ** indicates highly significant change

Tayside Clinical Laboratory Services — Telephone 01738 473223 (PRI) 01382 632602 (NW)

Name:

N/W

SODIUM	137	*	mmol/L	(	135-147)
POTASSIUM	4.0		mmol/L	(	3.5-5.0)
UREA	12.1	**	mmol/L	(	3.3-6.6)
CREATININE	79	*	umol/L	(	44-80)
ESTIMATED GFR	GT60		mL/min		
CKD Stage	IF HIGH RISK OF CKD, EXCLUDE STAGES 1 AND 2 BY CHECKING FOR HAEMATURIA AND PROTEINURIA.				
C-REACTIVE PROTEIN	16	>	mg/L	(	up to 5)
ALT	30		U/L	(	13-43)
BILIRUBINS	107	>>	umol/L	(	0-15)
ALKALINE PHOSPHATASE	202	>	U/L	(	40-150)
ALBUMIN	30	<	g/L	(	36-50)
CALCIUM	2.31	**	mmol/L	(	2.10-2.55)
CALCIUM (CORRECTED)	2.59	*	mmol/L	(	2.10-2.55)
AMYLASE	64		U/L	(	0-100)

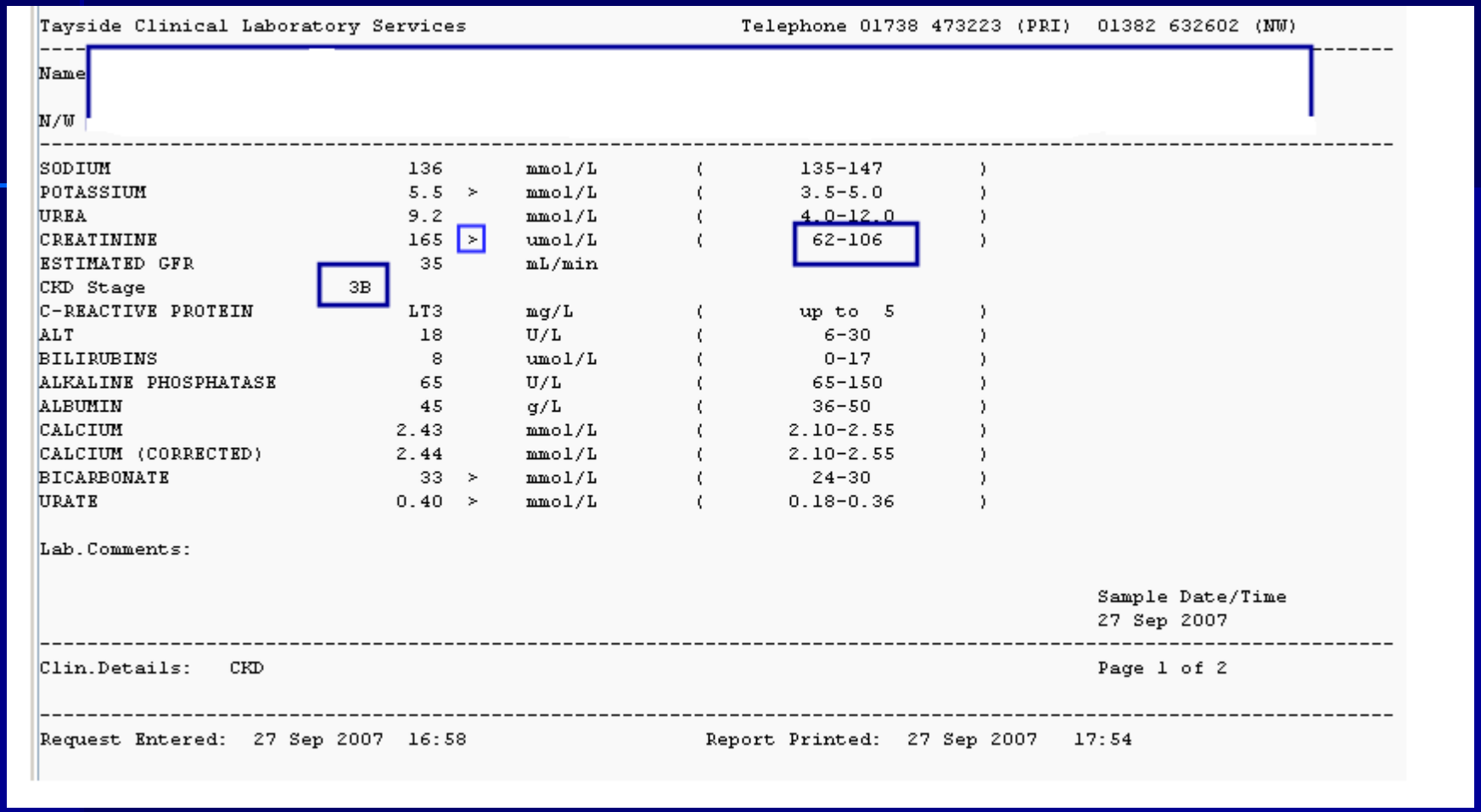
Lab.Comments:

Sample Date/Time
27 Sep 2007

Clin.Details:

Request Entered: 27 Sep 2007 19:21 — Report Printed: 27 Sep 2007 20:28

eGFR > 60 in a 30 year old white female: Changing renal function?
NB! Change has taken Place within the confines of the reference limits.
* indicates significant change



Tayside Clinical Laboratory Services Telephone 01738 473223 (PRI) 01382 632602 (NW)

Name

N/W

SODIUM	136		mmol/L	(	135-147)
POTASSIUM	5.5	>	mmol/L	(	3.5-5.0)
UREA	9.2		mmol/L	(	4.0-12.0)
CREATININE	165	>	umol/L	(	62-106)
ESTIMATED GFR	35		mL/min		
CKD Stage	3B				
C-REACTIVE PROTEIN	LT3		mg/L	(	up to 5)
ALT	18		U/L	(	6-30)
BILIRUBINS	8		umol/L	(	0-17)
ALKALINE PHOSPHATASE	65		U/L	(	65-150)
ALBUMIN	45		g/L	(	36-50)
CALCIUM	2.43		mmol/L	(	2.10-2.55)
CALCIUM (CORRECTED)	2.44		mmol/L	(	2.10-2.55)
BICARBONATE	33	>	mmol/L	(	24-30)
URATE	0.40	>	mmol/L	(	0.18-0.36)

Lab.Comments:

Sample Date/Time
27 Sep 2007

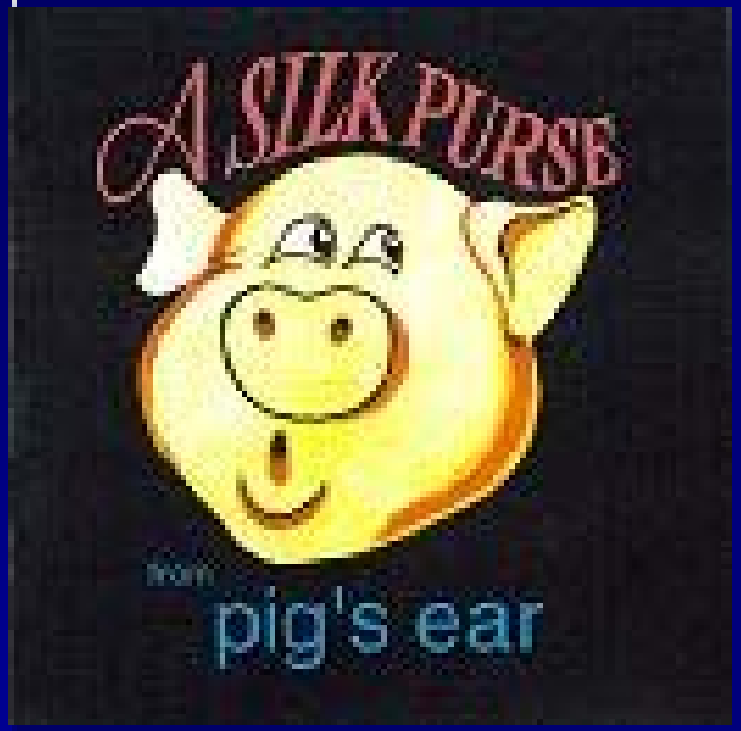
Clin.Details: CKD Page 1 of 2

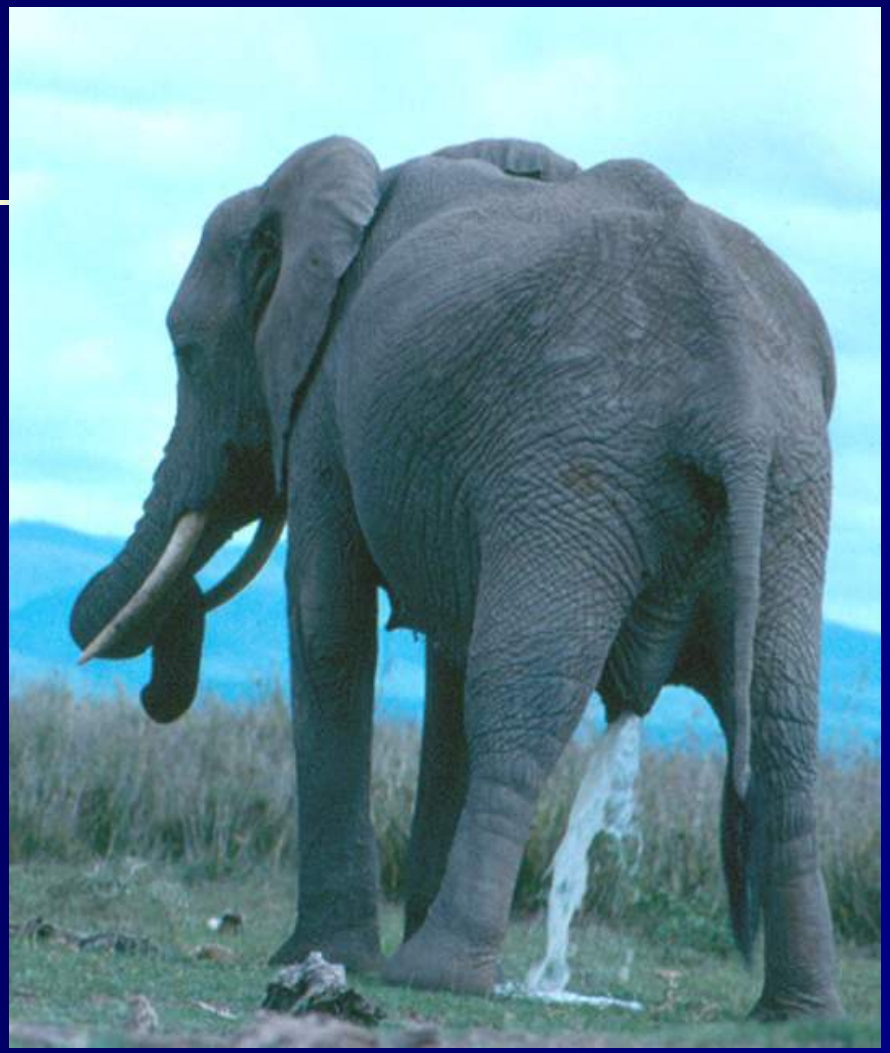
Request Entered: 27 Sep 2007 16:58 Report Printed: 27 Sep 2007 17:54

84 year old white male: Stable renal function

> Indicates value above reference interval

eGFR ?





eGFR?