The 21st Budapest Nephrology School

Nephrology, Hypertension, Dialysis, Transplantation

Estimation and Measurement of GFR

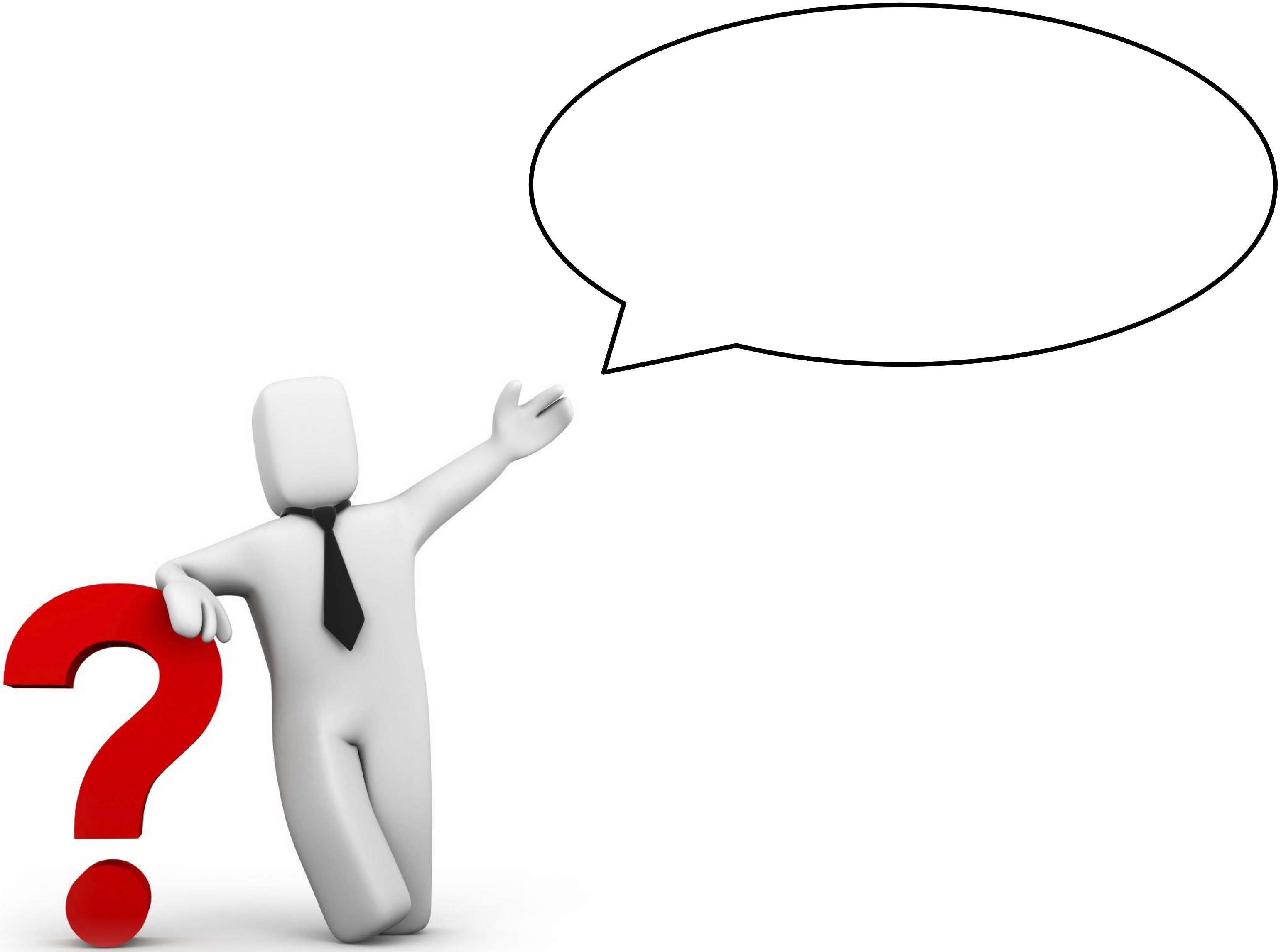
Past, Present and Future

Prof. Mustafa ARICI, MD

Hacettepe University, Ankara-TURKEY

Member of Science Academy, TURKEY

Let me start with a question



Glomerular Filtration Rate (GFR)

- GFR estimates are used to:
  - Estimate measured GFR
  - Predict risk for adverse outcomes
    - Staging of CKD
    - ESRD risk
    - CV risk
    - Overall mortality risk

Glomerular Filtration Rate (GFR)

But, what is the **best** **way** to find exact GFR ?

François-Marie Arouet (November 21, 1694 – May 30, 1778)

Which one of the following does show your patient's GFR **most** accurately ?

A) Measured GFR

B) Estimated GFR

Does anyone of you measured GFR at any time?

A) Yes

B) No

Which one of the following markers does represent the gold standard for measuring GFR?

A) Inulin

B) 51Cr-EDTA

C) 99Tc-DTPA

D) Iothalamate

E) Ioxehol

Do you know what is inulin?

A) A synthetic sugar

B) A muscle breakdown product

C) A naturally occuring polysaccharide

D) A natural alcohol derivative

E) A metabolic by-product of intestinal bacteria

What **will** I tell ?

- GFR and concept of renal clearance
- Measuring GFR: From past to present
- Estimating GFR: From past to present
- Measured vs Estimated GFR: Advantages vs disadvantages and clinical use
- Future prospects

Renal Clearance

- Renal clearance of a substance is defined as the volume of plasma cleared from this substance per time unit (mL/min).

$$C_x = \frac{U_x \times \dot{V}}{P_x^a}$$

- Clearance is thus a virtual volume but will permit to apprehend GFR and renal function.

Pierre Delanaye (2012). How Measuring Glomerular Filtration Rate? Comparison of Reference Methods, http://www.intechopen.com/books/basic-nephrology-and-acute-kidney-injury/how-measuring-glomerularfiltration-rate-comparison-of-reference-methods

The concept of clearance: History

- The Danish physiologist, Poul Brandt **Rhehberg** was the first to use and define the concept of clearance in **1926** even if this author did not use the word “clearance”.
- Rhe **crea** has acti

LX. STUDIES ON KIDNEY FUNCTION.

I. THE RATE OF FILTRATION AND REABSORPTION IN THE HUMAN KIDNEY.

BY POUL BRANDT REHBERG.

From the Laboratory of Zoophysiology, University of Copenhagen.

(Received April 26th, 1926.)

The concept of clearance: History

- The term clearance was used for the first time by **Möller in 1929** and was then concerning the urea clearance which was proposed as the first e

STUDIES OF UREA EXCRETION. II.

RELATIONSHIP BETWEEN URINE VOLUME AND THE RATE OF UREA EXCRETION BY NORMAL ADULTS[1]

BY EGGERT MÖLLER, J. F. McINTOSH AND D. D. VAN SLYKE

(From the Hospital of the Rockefeller Institute for Medical Research, New York)

(Received for publication August 21, 1928)

THE EXCRETION OF URINE IN THE DOG

III. THE USE OF NON-METABOLIZED SUGARS IN THE MEASUREMENT OF THE GLOMERULAR FILTRATE

NORMAN JOLLIFFE, JAMES A. SHANNON AND HOMER W. SMITH

From the Department of Physiology, University and Bellevue Hospital Medical College, New York City

Received for publication December 29, 1931

"No substance is known to be present normally in the plasma and urine of vertebrates which can be safely used to evaluate the quantity of glomerular filtrate under physiological conditions"

Homer W. Smith

THE EXCRETION OF URINE IN THE DOG

III. The Use of Non-metabolized Sugars in the Measurement of the Glomerular Filtrate

NORMAN JOLLIFFE, JAMES A. SHANNON and HOMER W. SMITH

From the Department of Physiology, University and Bellevue Hospital Medical College, New York City

Received for publication December 29, 1931

- "**Creatinine** of exogenous origin has been recommended for this purpose by Rehberg, (1926) but when it is recognized that this substance is **secreted by the renal tubules** of the lower vertebrates (Marshall and Grafflin, 1932; Clarke and Smith, 1932) and that it is not present normally in significant quantities in the blood of mammals (Behre and Benedict, 1922; Gaebler and Keltch, 1928; Gaebler, 1930) **its use is open to question**."

THE EXCRETION OF URINE IN THE DOG

III. THE USE OF NON-METABOLIZED SUGARS IN THE MEASUREMENT OF THE GLOMERULAR FILTRATE

NORMAN JOLLIFFE, JAMES A. SHANNON AND HOMER W. SMITH

From the Department of Physiology, University and Bellevue Hospital Medical College, New York City

Received for publication December 29, 1931

The properties which we believe such a substance should possess are as follows:

1. It must be determinable in plasma and urine with quantitative accuracy.
2. It must be non-toxic and it must exert no local stimulating or depressing action upon the kidney.
3. It must be completely filtrable from plasma.
4. It must not be secreted by the renal tubules.
5. It must not be reabsorbed by the renal tubules.

THE AMERICAN

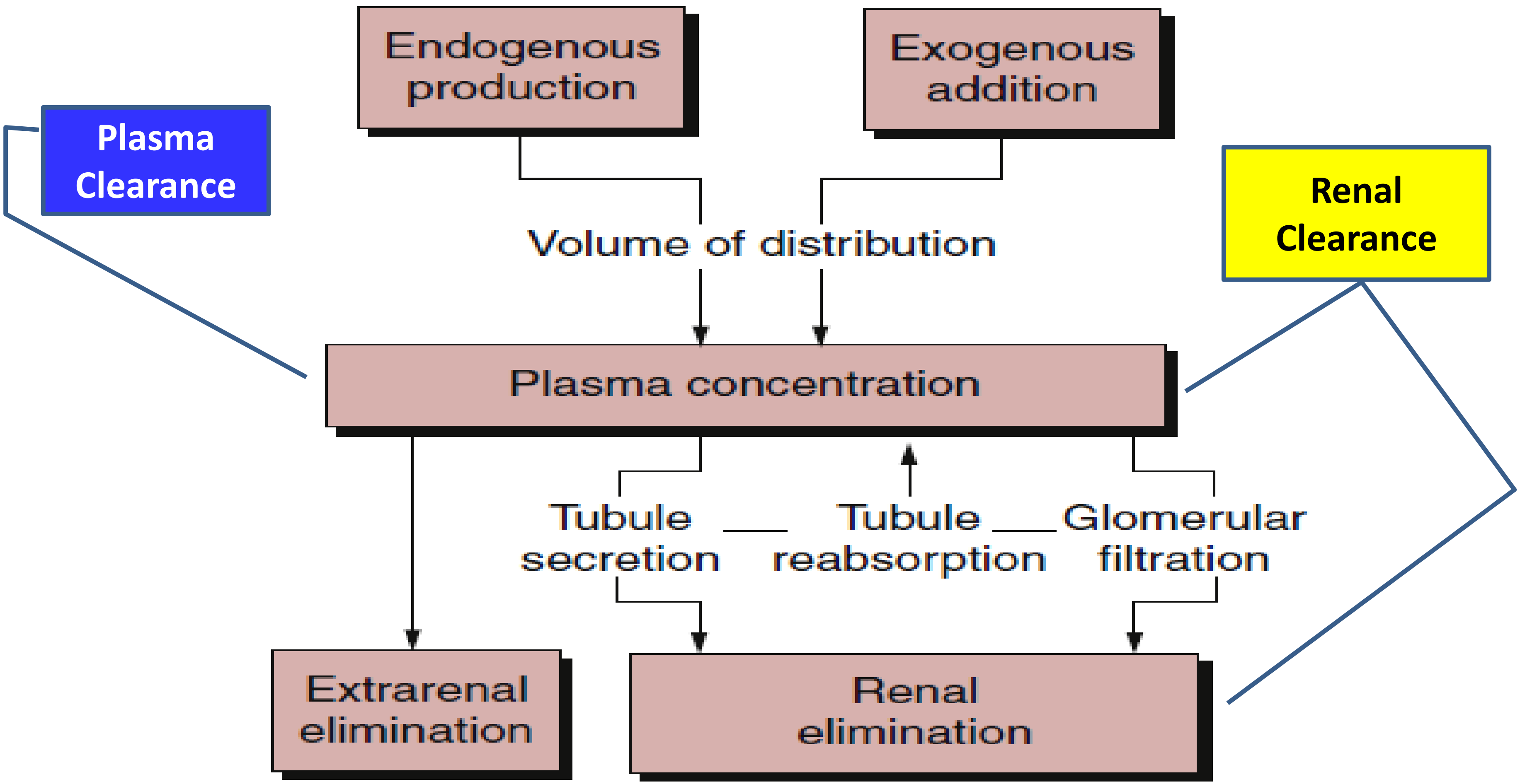
JOURNAL OF PHYSIOLOGY

- They concluded that **inulin was a near perfect filtration marker**, which was eventually verified conclusively by micropuncture and tracer studies.
- **It remains the standard against which filtration markers are gauged.**

(Received for publication February 13, 1935)

Hostetter and Meyer. Am J Physiol Renal Physiol 287: F868–F870, 2004.

Measuring GFR



Brenner & Rector's the kidney / [edited by] Maarten W. Taal ... [et al.]. -- 9th ed., 2012

Measured GFR Methods

- 1) Inulin
- 2) 51Cr-EDTA (Ethylenediaminetetra-acetic acid)
- 3) 99Tc-DTPA (Diethylenetriaminepenta-acetic acid)
- 4) Iothalamate
- 5) Ioxehol

Pierre Delanaye (2012). How Measuring Glomerular Filtration Rate? Comparison of Reference Methods, http://www.intechopen.com/books/basic-nephrology-and-acute-kidney-injury/how-measuring-glomerularfiltration-rate-comparison-of-reference-methods

Inulin

- Inulin is a polymer of fructose which is found in some plants
- Its molecular weight is 5200 Da (Gaspari et al., 1997).
- Humans are not able to metabolize inulin.
- Inulin was freely and fully filtrated through the glomerulus
- Absence of both tubular absorption and secretion

Pierre Delanaye (2012). How Measuring Glomerular Filtration Rate? Comparison of Reference Methods, http://www.intechopen.com/books/basic-nephrology-and-acute-kidney-injury/how-measuring-glomerularfiltration-rate-comparison-of-reference-methods

Inulin

- **Limitations to its use** in daily practice.
  - Because its relatively **high molecular weight** (5200 Da), the molecule is relatively viscous and don't quickly reach its volume of distribution. Therefore, only methods using **urinary clearance** with constant infusion rate seem accurate
  - **Difficulty linked to its measurement** in urine and plasma
  - There is **no standardization** in inulin measurement.

Pierre Delanaye (2012). How Measuring Glomerular Filtration Rate? Comparison of Reference Methods, http://www.intechopen.com/books/basic-nephrology-and-acute-kidney-injury/how-measuring-glomerularfiltration-rate-comparison-of-reference-methods

Inulin

The scarcity, cumbersome methodology and high cost of inulin all but eliminated its routine use.

Pierre Delanaye (2012). How Measuring Glomerular Filtration Rate? Comparison of Reference Methods, http://www.intechopen.com/books/basic-nephrology-and-acute-kidney-injury/how-measuring-glomerularfiltration-rate-comparison-of-reference-methods

Which one is the best ?

AJKD

Am J Kidney Dis. 2014;64(3):411-424

Original Investigation

Measuring GFR: A Systematic Review

*Inga Soveri, MD, PhD,[1] Ulla B. Berg, MD, PhD,[2] Jonas Björk, PhD,[3] Carl-Gustaf Elinder, MD, PhD,[4] Anders Grubb, MD, PhD,[5] Ingegerd Mejare, PhD,[6] Gunnar Sterner, MD, PhD,[7] and Sten-Erik Bäck, MSc, PhD,[5] on behalf of the SBU GFR Review Group**

Direct measurement of glomerular filtration rate (GFR) is impossible because the filtration process simultaneously takes place in millions of glomeruli and filtrate composition and volume change when passing through the kidney.

Swedish Council on Health Technology Assessment

Which one is the best for measuring GFR ?

Index Tests

- Endogenous creatinine clearance
- ^{51}Cr-EDTA
  * Renal * Plasma
- DTPA
  * Renal * Plasma
- Ioxehol
  * Renal * Plasma
- Iothalamate
  * Renal * Plasma
- Inulin (plasma)

Reference Test

Renal inulin clearance measured under continuous inulin infusion and urine collection

Am J Kidney Dis. 2014;64(3):411-424

- Endogenous creatinine clearance

  Inaccurate method (strong evidence)

- ^{51}Cr-EDTA

  ✓ Sufficient accuracy

  ✓ Sufficient accuracy

✓Renal clearance of iothalamate

✓Renal clearance of 51Cr-EDTA

✓Plasma clearance of 51Cr-EDTA

✓Plasma clearance of iohexol

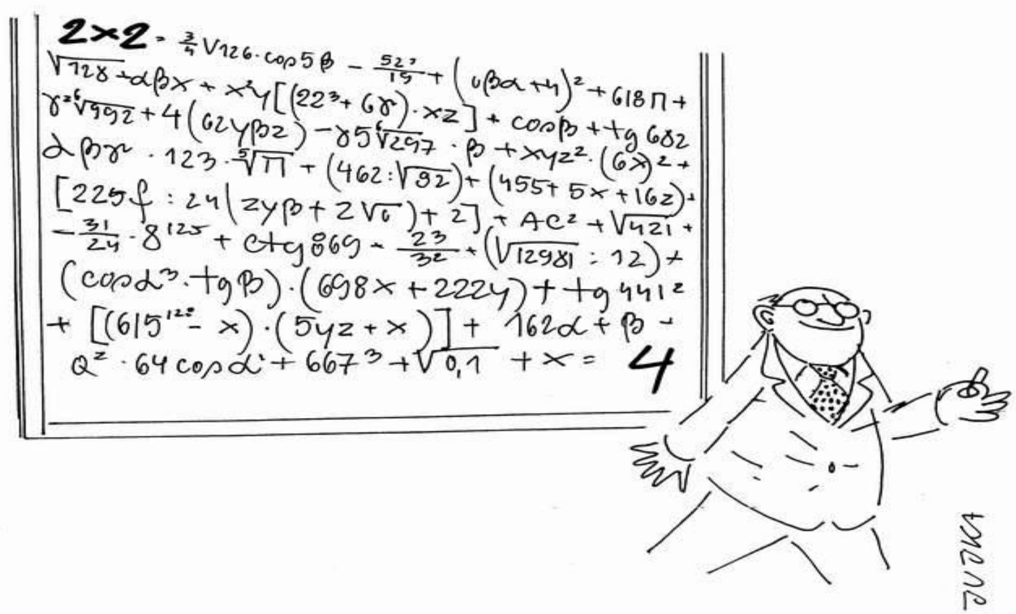
- Iothalamate

  * Renal **✓ Sufficient accuracy (strong evidence)**

  * Plasma **Evidence was insufficient**

- Inulin (plasma) **Sufficient accuracy (limited evidence)**

Estimated GFR Methods

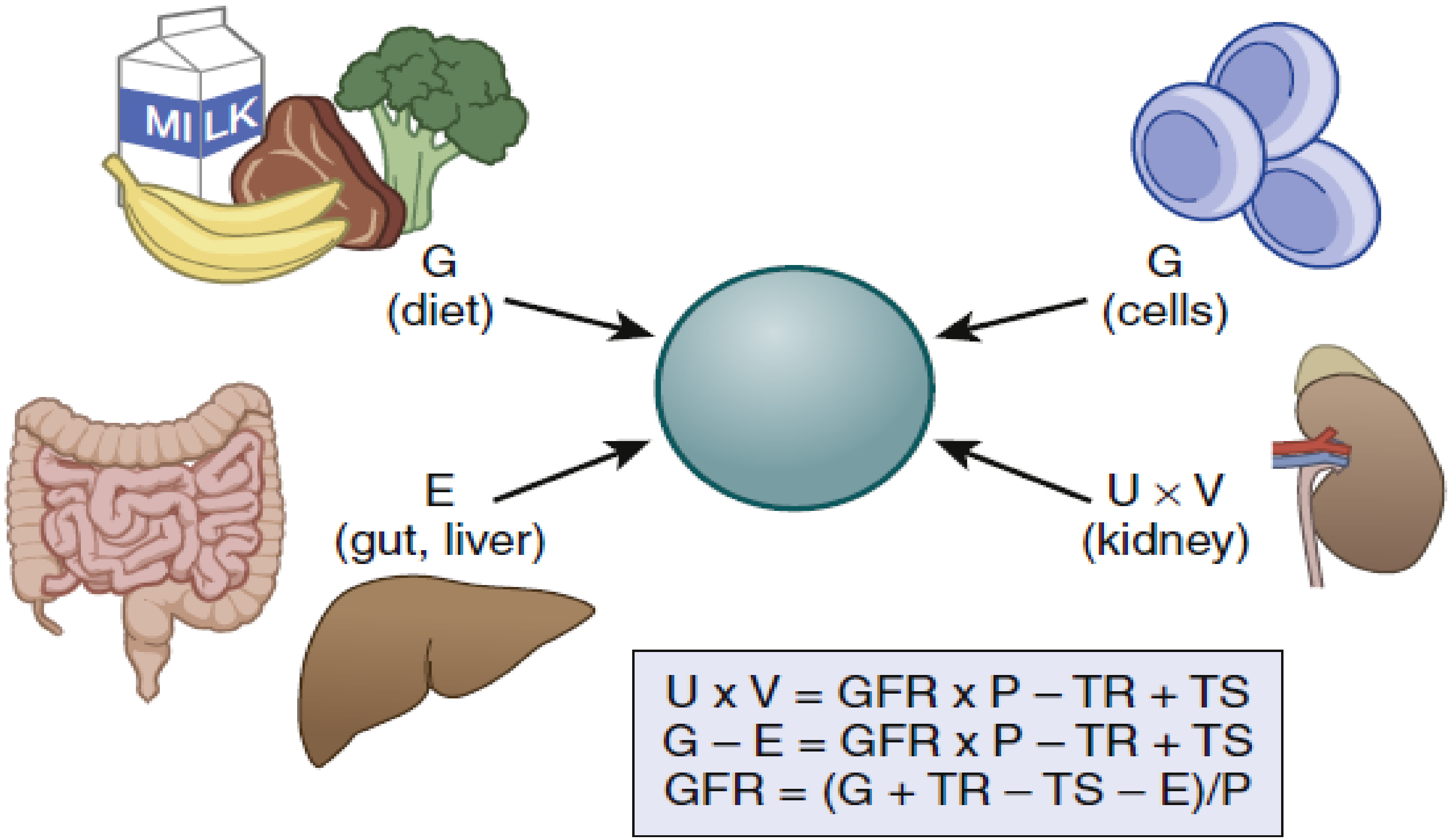


Estimated GFR Methods

- Clinically, GFR is often estimated from the serum concentration of endogenous filtration markers.
- Endogenous markers
  - Urea (used widely in the past)
  - Creatinine (most commonly used)
  - Cystatin C (promising new one)

Inker LA, Levey AS. National Kidney foundation's Primer on Kidney Diseases , Elsevier Saunders, 2014.
Arici M. Management of Chronic Kidney Disease, Springer, 2014.

Endogenous Marker



Inker LA, Levey AS. National Kidney foundation's Primer on Kidney Diseases , Elsevier Saunders, 2014.

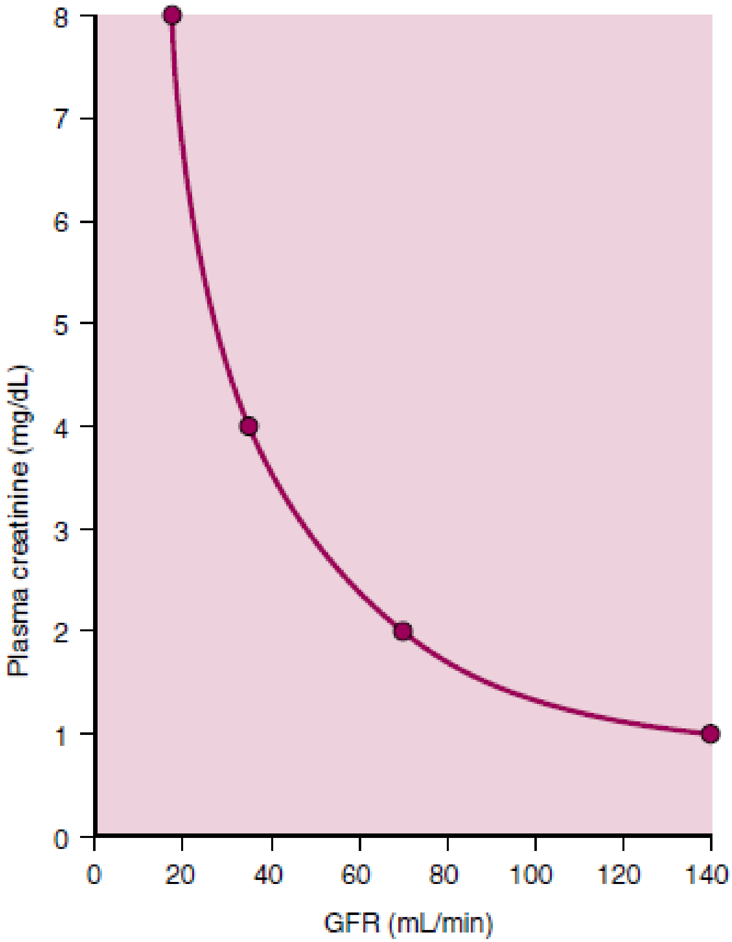
Serum Creatinine

- The **most commonly used** parameter to evaluate kidney function in routine clinical practice.
- Very **convenient, cheap, and readily available** technique

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

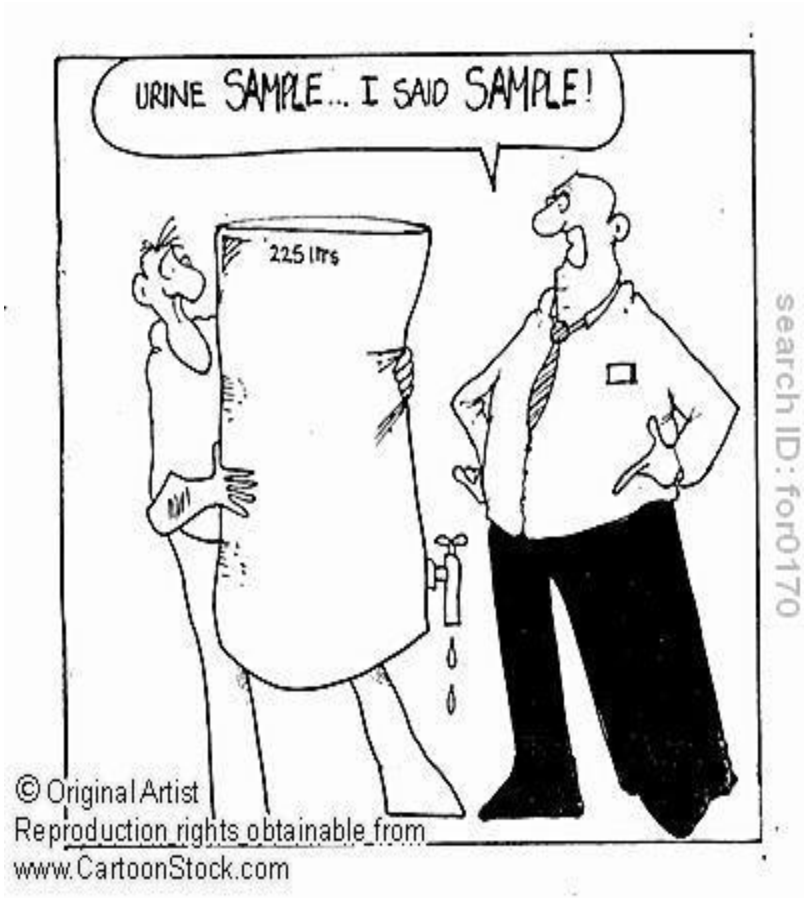
Serum Creatinine

- **Generation:** Muscle mass, dietary meat, age, gender, racial differences
- **Tubular secretion** (5-10 % of excreted creatinine)
- **Extrarenal elimination**
- **Measurement technique**
  - Alkaline picrate (Jaffe)
  - Enzymatic
  - HPLC
  - *IDMS (isotope dilution mass spectrometry) standardization*



Arici M. Management of Chronic Kidney Disease, Springer, 2014.

Creatinine Clearance



- 24 hour urine collection
  - Difficult
  - Less or much collection
- Tubular secretion
- Not accurate

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

Cockroft-Gault Equation

- The oldest (developed in **1973**) but simplest equation for everyday clinical use
- Derived using data from **249 men** with a creatinine clearance ranging from approximately 30–130 ml/min

$$eCrCl = \frac{(140 - Age) \times Weight\ (kg)}{72 \times Creatinine_{serum\ (mg/dL)}} \times 0.85 \text{ if female}$$

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

Cockroft-Gault Equation

- Derived when **standardized creatinine assays were not in use**.
- In labs where standardized creatinine assays were used, this equation will cause **an overestimation (10–40 %) of actual GFR.**
- Not adjusted for body surface area.
- **Less accurate in**
  - *obese* patients (overestimate),
  - in patients with *normal or mildly decreased GFR* (underestimates), and
  - in the *elderly* (underestimates).

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

This Week's Citation Classic®

CC/NUMBER 48
NOVEMBER 30, 1992

Cockcroft D W & Gault M H. Prediction of creatinine clearance from serum creatinine. *Nephron* 16:31-41, 1976. [Departments of Medicine, Queen Mary Veterans' Hospital, Montreal, Quebec, and Memorial University; St. John's, Newfoundland, Canada]

Donald W. Cockcroft

D.W. Cockcroft
Division of Respiratory Medicine
Royal University Hospital
Saskatoon, Saskatchewan S7N 0X0
Canada

- It is with amusement, that **after almost 20 years as an academic "asthmatologist,"** that house officers recognize my name as that attached to the widely used "Cockcroft-Gault" formula for predicting creatinine clearance.

MDRD Study Equation

- Develo… 1628 **CKD p**… s, with nondia… **FR range betwe**…

- The ec… for use with tl… **ne** assa s

$$GFR\ (ml/min/1.73\ m^2) = 186.3 \times Scr^{-1.154} \times age^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American}),$$
where Scr is expressed in mg/dl and age is expressed in years.

$$GFR\ (ml/min/1.73\ m^2) = 175 \times Scr^{-1.154} \times age^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American}),$$
where a standardized Scr (mg/dl) measurement is done.

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

MDRD Study Equation

- Most widely used formula
- Many laboratories automatically report
- **More accurate** in patients with **lower GFR levels** (<60 ml/min/1.73 m2)
- **Less accurate** in **obese** patients and in patients with **normal or mildly decreased GFR.**

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

CKD-EPI Equation

- Derived in **2009** from **a large study population** that included **patients with or without kidney disease** with a wide range of GFR.
- When compared with MDRD, CKD-EPI has found to be **more accurate in people especially with higher GFR levels**.

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

This is the formula...

$$GFR\ (ml/min/1.73\ m^2) = 141 \times \min(SCr/\kappa, 1)^{\alpha} \times \max(SCr/\kappa, 1)^{-1.209} \times 0.993^{Age}$$
$$\times\ (1.018 \text{ if female}) \times (1.159 \text{ if African American}),$$

where SCr is serum creatinine (in mg/dl), κ is 0.7 for females and 0.9 for males, α is –0.329 for females and –0.411 for males, min indicates the minimum of SCr/κ or 1, and max indicates the maximum of SCr/κ or 1

Female

<0.7 mg/dl	$GFR = 144 \times (Scr/0.7)^{-0.329}$
>0.7 mg/dl	$GFR = 144 \times (Scr/0.7)^{-1.209}$

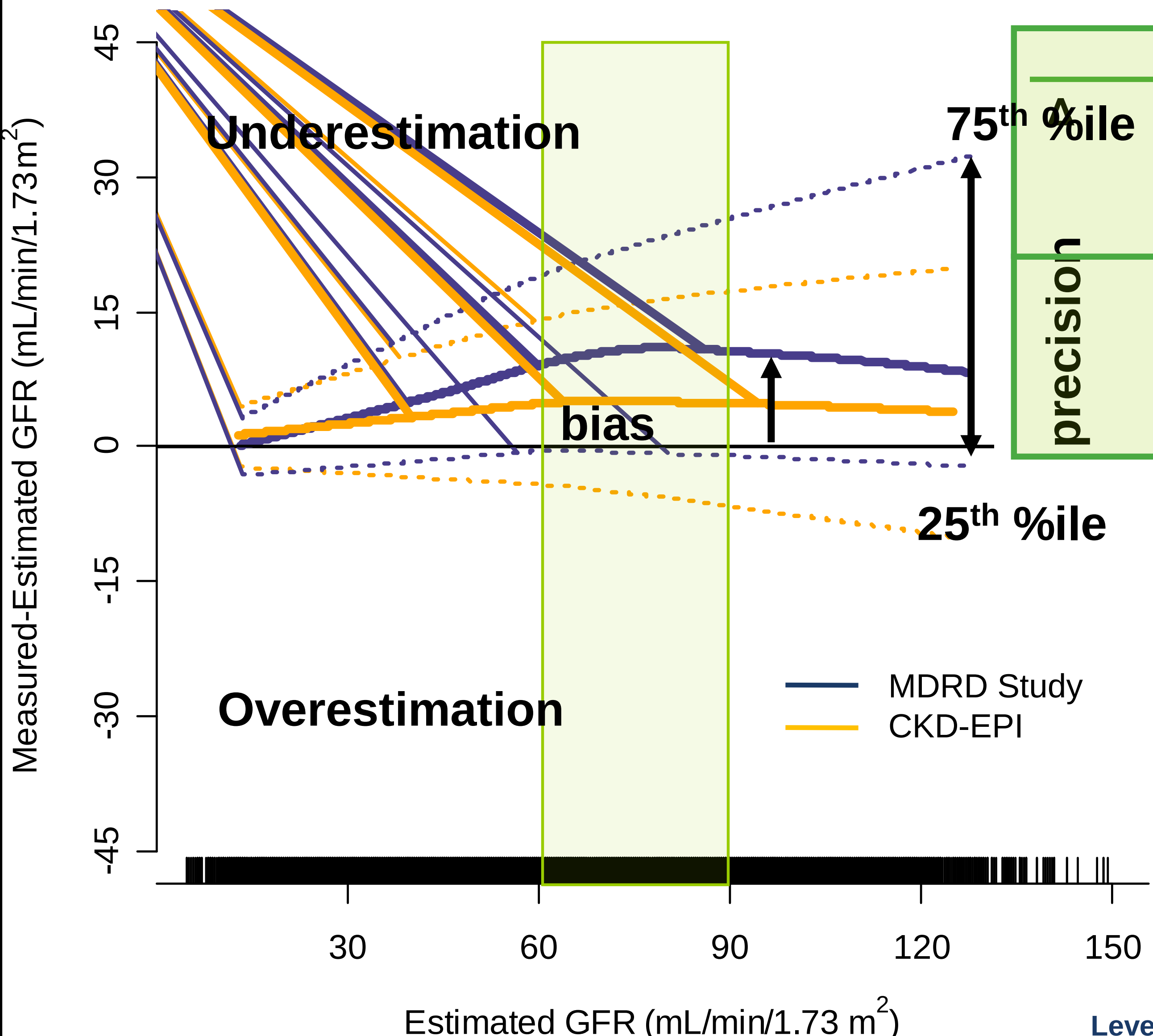
$\times\ (0.993)Age \times 1.157$ [if black]

Male

<0.9 mg/dl	$GFR = 141 \times (Scr/0.9)^{-0.411}$
>0.9 7mg/dl	$GFR = 141 \times (Scr/0.9)^{-1.209}$

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

Comparison of the Performance of the MDRD Study and CKD-EPI equations (Validation dataset)



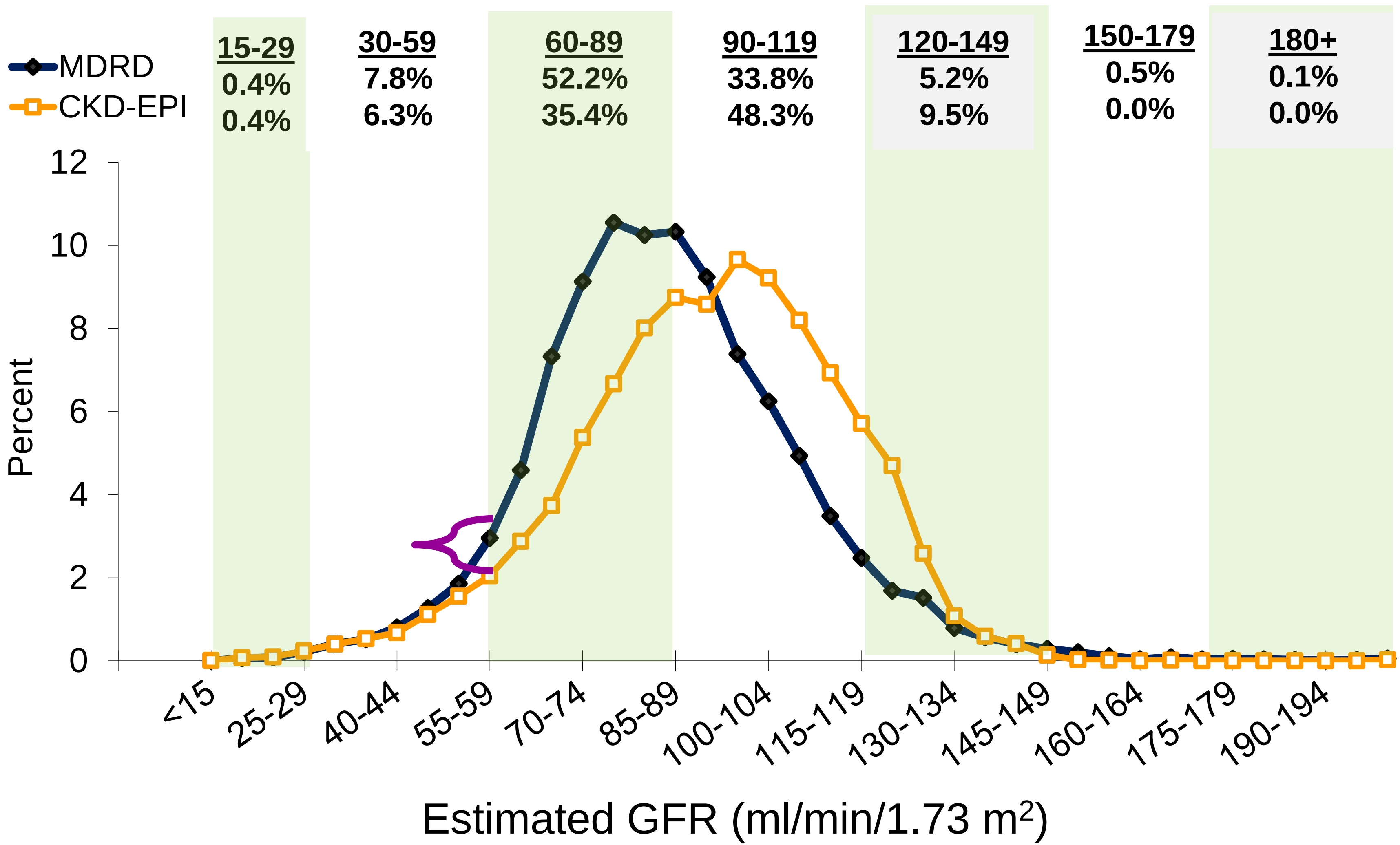
Δ	All	60-89
MDRD	5.5	11.9
CKD-EPI	2.5	4.2
% Δ	***50%***	***59%***

precision

Levey et al ***Ann Int Med*** **2009; 150: 604 612**

Slide courtesy of Lesley A Stevens, MD, MS

Comparison of distribution of estimated GFR for MDRD Study and CKD-EPI equations (NHANES 1999-2004)



Values are plotted at the midpoint.

Slide courtesy of Lesley A Stevens, MD, MS

Levey et al *Ann Int Med* 2009; 150: 604 612

All GFR equations (incl. MDRD & CKD-EPI)

- Some imprecision and several limitations
  - Use of serum creatinine and its limitations
- All need to be used in **steady state**
  - Don’t use in AKI
- **Not recommended for use** in patients
  - under the age of 18,
  - with extremes in body size or muscle mass,
  - with severe alterations in dietary intake (vegetarians, using creatine supplements),
  - in very elderly (>85 years),
  - in pregnant patients.

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

Which one is the best ?

Annals of Internal Medicine

Ann Intern Med. 2012;156:785-795.

REVIEW

Estimating Equations for Glomerular Filtration Rate in the Era of Creatinine Standardization

A Systematic Review

Amy Earley, BS; Dana Miskulin, MD, MS; Edmund J. Lamb, PhD; Andrew S. Levey, MD; and Katrin Uhlig, MD, MS

Neither the CKD-EPI nor the MDRD Study equation is optimal for all populations and GFR ranges. Using a single equation for reporting requires a tradeoff to optimize performance at either higher or lower GFR ranges. *A general practice and public health perspective favors the CKD-EPI equation.*

CKD-EPI Equation

KDIGO 2012 *clinical practice guideline for the evaluation and management of chronic kidney disease recommends* ***to use CKD-EPI equation for GFR estimation.***

Serum Cystatin C and GFR Equations

- A 122 amino acid with molecular weight (13-kDa) cysteine protease inhibitor
  - Produced by all nucleated cells
- Freely filtered by the renal glomerulus
- No tubular secretion
- Reabsorbed and completely catabolized by tubular cells, not excreted

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

Cystatin C.....drawbacks

- Cystatin C generation rate and serum levels have been influenced by **age, sex, cell turnover rate, steroid use, body mass index, inflammation, and diabetes**
- There is an **extrarenal elimination** of cystatin C at low levels of GFR
- Cystatin C measurements are **not standardized** yet and still evolving

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

Cystatin C.....drawbacks

- Other studies have suggested that **inflammation, adiposity, thyroid diseases, certain malignancies, smoking, and use of glucocorticoids** may increase cystatin C levels.

Inker LA, Levey AS. National Kidney Foundation's Primer on Kidney Diseases , Elsevier Saunders, 2014.

Cystatin C and Outcomes

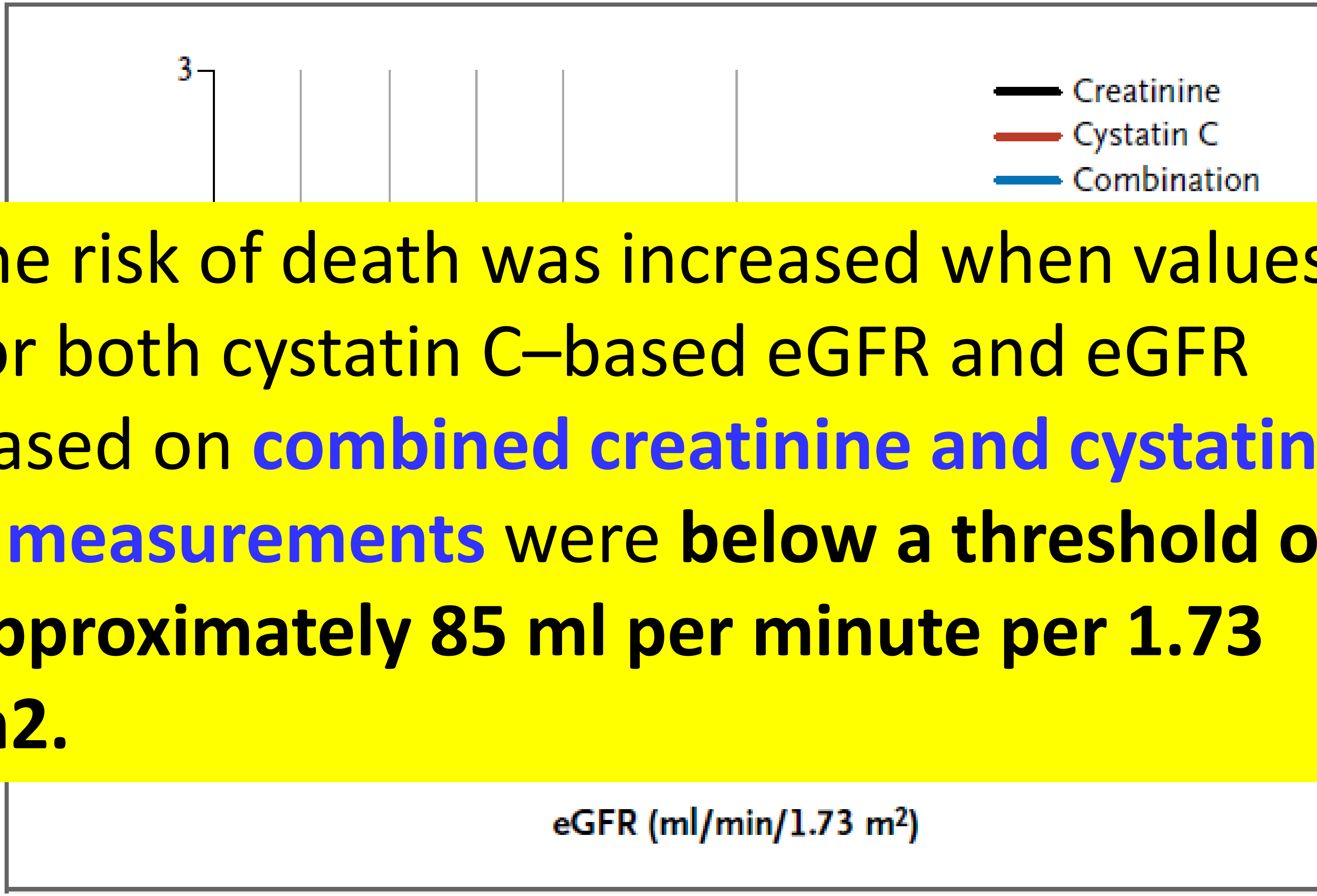
- Higher levels of cystatin C are a better predictor of the risk of cardiovascular disease and total mortality.

Inker LA, Levey AS. National Kidney foundation's Primer on Kidney Diseases , Elsevier Saunders, 2014.

Cystatin C use in GFR equations

- Cystatin C itself or equations based on cystatin C alone are not more accurate than creatinine-based estimating equations, rather, it is the **combination of the two markers** that results in the most accurate estimate in populations with and without CKD.

Inker LA, Levey AS. National Kidney foundation's Primer on Kidney Diseases , Elsevier Saunders, 2014.



the risk of death was increased when values for both cystatin C–based eGFR and eGFR based on **combined creatinine and cystatin C measurements** were **below a threshold of approximately 85 ml per minute per 1.73 m2.**

Formulas again....

CKD-EPI Cystatin C equation:

$$\text{GFR (ml/min/1.73 m}^2\text{)} = 133 \times \min(\text{SCysC}/0.8, 1)^{-0.499} \times \max(\text{SCysC}/0.8, 1)^{-1.328} \times 0.996\text{Age} \; [\times 0.932 \text{ if female}],$$

where SCysC is serum cystatin C (in mg/l), min indicates the minimum of SCysC/0.8 or 1, and max indicates the maximum of SCysC/0.8 or 1.

CKD-EPI Creatinine-Cystatin C equation:

$$\text{GFR (ml/min/1.73 m}^2\text{)} = 135 \times \min(\text{SCr}/\kappa, 1)^{\alpha} \times \max(\text{SCr}/\kappa, 1)^{-0.601} \times \min(\text{SCysC}/0.8, 1)^{-0.375} \times \max(\text{SCysC}/0.8, 1)^{-0.711} \times 0.995^{\text{Age}} \; [\times 0.969 \text{ if female}] \; [\times 1.08 \text{ if black}],$$

where SCr is serum creatinine (in mg/dl), SCysC is serum cystatin C (in mg/l), κ is 0.7 for females and 0.9 for males, α is –0.248 for females and –0.207 for males, min(SCr/κ, 1) indicates the minimum of SCr/κ or 1,and max(SCr/κ, 1) indicates the maximum of SCr/κ or 1; min(SCysC/0.8, 1) indicates the minimum of SCysC/0.8 or 1 and max(SCysC/0.8, 1) indicates the maximum of SCysC/0.8 or 1.

Cystatin C

KDIGO 2012 *clinical practice guideline for the evaluation and management of chronic kidney disease has recommended to* ***measure cystatin C to confirm CKD in adults if eGFR based on serum creatinine was between 45 and 59 ml/min/1.73 m2*** *without any markers of kidney damage.*

To tie or conclude....

Creatinine versus Cystatin C

Variable	Creatinine	Cystatin C
	Molecular Properties	
Weight	113 Da	13,300 Da
Structure	Amino acid derivative	Nonglycosylated basic protein
	Physiologic Determinants of Serum Level	
Generation	Varies according to muscle mass and dietary protein; lower in elderly persons, women, and whites	Made by all nucleated cells; thought to be mostly constant; increases in hyperthyroid states and with steroid use; lower in elderly persons and women
Handling by the kidney	Filtered, secreted, and excreted in urine	Filtered, reabsorbed, and catabolized
Extrarenal elimination	Yes; increases at reduced GFR	Preliminary evidence of increases at reduced GFR
	Use in GFR Estimating Equations	
Demographic and clinical variables as surrogates for physiologic determinants	Age, sex, and race; related to muscle mass	Age and sex
Factors associated with inaccurate estimates	Nonsteady state; GFR > 60 mL/min/1.73 m^2; conditions associated with alterations in muscle mass, drugs that inhibit tubular secretion, interferents with serum assays	Nonsteady state; GFR > 60 mL/min/1.73 m^2; conditions associated with alterations in thyroid or steroid hormones, possibly obesity
	Assay	
Method	Colorimetric and enzymatic	Immunoassays
Assay precision	Very good except at low range	Precision varies across assays
Clinical laboratory practice	Multiple assays; widely used; widely standardized	Not on most autoanalyzers; becoming standardized
Standardized reference materials	SRM 967	ERM-DA471/IFCC
Reference assay	IDMS	PENIA, PETIA, enzyme-amplified single radial immunodiffusion

Andrew S. Levey, et al. Am J Kidney Dis. 63(5):820-834.

Formulas, formulas, formulas...

Endogenous Filtration Marker; Notation	Group; Year	Development Population: Characteristics	Development Population: GFR Measurement Method	Development Population: Endogenous Filtration Marker Assay	Equation	Advantages
Creatinine; $eGFR_{cr}$	MDRD Study; 1999	N = 1,628 with CKD, mean mGFR = 40	Urinary clearance of iothalamate	Nonstandardized	6-variable MDRD Study equation and 4-variable MDRD Study equation	4-variable recommended by 2002 NKF-KDOQI[6]; useful for reporting eGFR < 60
	MDRD Study; 2006	Same as above	Same as above	Standardized	IDMS-traceable 4-variable MDRD Study equation	Re-expressed for use with standardized assays
	CKD-EPI; 2009	*Diverse population, N = 8,254; mean mGFR = 68*	*Urinary clearance of iothalamate*	*Standardized*	*2009 CKD-EPI creatinine equation*[a]	*Lesser bias at eGFR > 60; recommended by 2012 KDIGO*[8]*; useful for reporting eGFR throughout the range*
Cystatin C; $eGFR_{cys}$	CKD-EPI; 2008	N = 2,980 with CKD; mean mGFR = 48	Urinary clearance of iothalamate	Nonstandardized	2008 CKD-EPI cystatin C equation	$eGFR_{cys}$ as accurate as $eGFR_{cr}$
	CKD-EPI; 2011	Same as above	Same as above	Standardized	2011 CKD-EPI cystatin C equation	Re-expressed for use with standardized assays
	CKD-EPI; 2012	*Diverse population, N = 5,352; mean mGFR = 68*	*Urinary clearance of iothalamate*	*Standardized*	*2012 CKD-EPI cystatin C equation*[a]	*Lesser bias at eGFR > 60; as accurate as* $eGFR_{cr}$ *without requiring specification of race and may be more accurate if muscle mass is decreased*
Creatinine and Cystatin C; $eGFR_{cr\text{-}cys}$	CKD-EPI; 2008	N = 2,980 with CKD, mean mGFR = 48	Urinary clearance of iothalamate	Standardized creatinine; nonstandardized cystatin C	2008 CKD-EPI creatinine–cystatin C equation	$eGFR_{cr\text{-}cys}$ more precise than $eGFR_{cr}$ or $eGFR_{cys}$
	CKD-EPI; 2011	Same as above	Same as above	Standardized creatinine and cystatin C	2011 CKD-EPI creatinine–cystatin C equation	Re-expressed for use with standardized assays
	CKD-EPI; 2012	*Diverse population, N = 5,352; mean mGFR = 68*	*Urinary clearance of iothalamate*	*Standardized creatinine and cystatin C*	*2012 CKD-EPI creatinine–cystatin C equation*[a]	*Recommended by 2012 KDIGO*[8] *as a confirmatory test*

Andrew S. Levey, et al. Am J Kidney Dis. 63(5):820-834.

Comparison of Formulas

Study Reference	Characteristics (Validation Population)	GFR Measurement Method (Validation Population)	Endogenous Filtration Marker Assays (Validation Population)	Equation	Bias[a] (mL/min/1.73 m^2)	P_{30} (%)
Stevens et al[27] (*JASN*, 2007)	Diverse population, N = 5,504; mean mGFR = 68	Urinary clearance of iothalamate	Standardized	eClCr by Cockcroft-Gault 1976[28,b]	11.4	69
				$eGFR_{cr}$ by 2006 MDRD Study	5.8[c]	83[c]
Levey et al[12] (*Annals*, 2009)	Diverse population; N = 3,771; mean mGFR = 68	Urinary clearance of iothalamate or EDTA, plasma clearance of iohexol	Standardized	$eGFR_{cr}$ by 2006 MDRD Study[b]	5.5	80.6
				$eGFR_{cr}$ by 2009 CKD-EPI	2.5[c]	84.1[c]
Inker et al[15] (*NEJM*, 2012)	Diverse population; N = 1,119; mean mGFR = 70	Urinary clearance of EDTA, plasma clearance of iohexol	Standardized	$eGFR_{cr}$ by 2009 CKD-EPI[b]	3.7	87.2
				$eGFR_{cys}$ by 2012 CKD-EPI	3.4	85.9
				$eGFR_{cr\text{-}cys}$ by 2012 CKD-EPI	3.9	91.5[c]
				Average of $eGFR_{cr}$ and $eGFR_{cys}$ by 2012 CKD-EPI	3.5	91.8[c]

Andrew S. Levey, et al. Am J Kidney Dis. 63(5):820-834.

Newer Equations, Markers and Methods

- **Berlin Initiative Study (BIS)** equations for elderly based on standardized creatinine (BIS1) and cystatin C (BIS2) methodology

Ann Intern Med 2012;157:471–481.

- **Beta trace protein** (BTP, also known as prostaglandin D2 synthase)
- **Symmetric dimethylarginine** (SDMA)
- Dynamic contrast-enhanced **magnetic resonance imaging**

What about the opponents ?

There are three kinds of people in the world, the wills, the won'ts and the can'ts. The first accomplish everything; the second oppose everything; the third fail in everything...

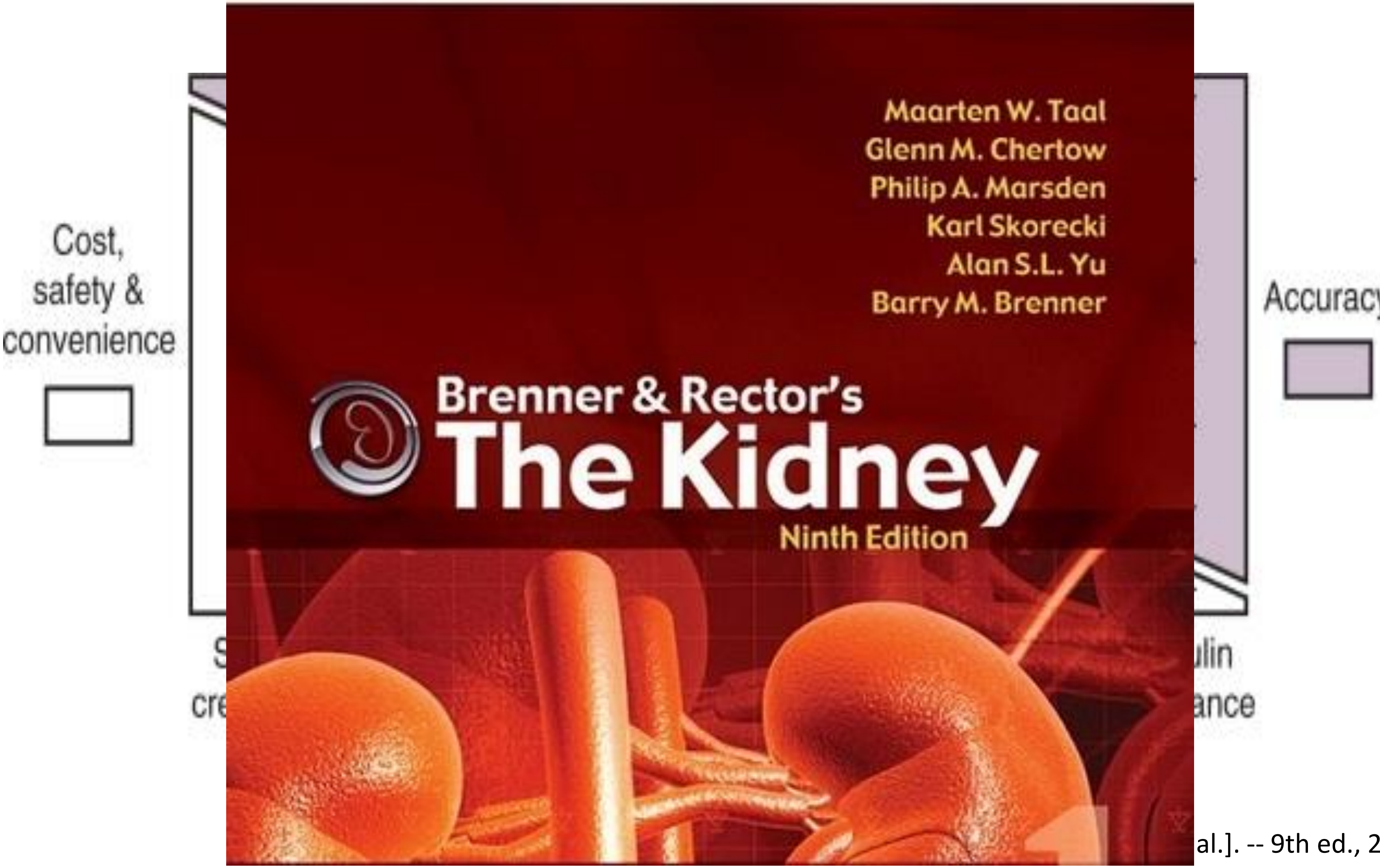
- Unknown

Opponents of GFR formula

- The use of eGFR should be limited to settings **where knowing actual GFR is relevant and eGFR is more informative** about GFR than serum creatinine or cystatin C alone. Such settings include **staging CKD severity by GFR and dosing medications** cleared by glomerular filtration.
- Alternatively, **the diagnosis of CKD, the longitudinal progression of CKD, and prognostic models for CKD** are settings where **serum creatinine and cystatin C can be better applied** and interpreted without eGFR.

Andrew D. Rule and Richard J. Glassock. CJASN ePress. Published on May 23, 2013

What shall we do, then ?



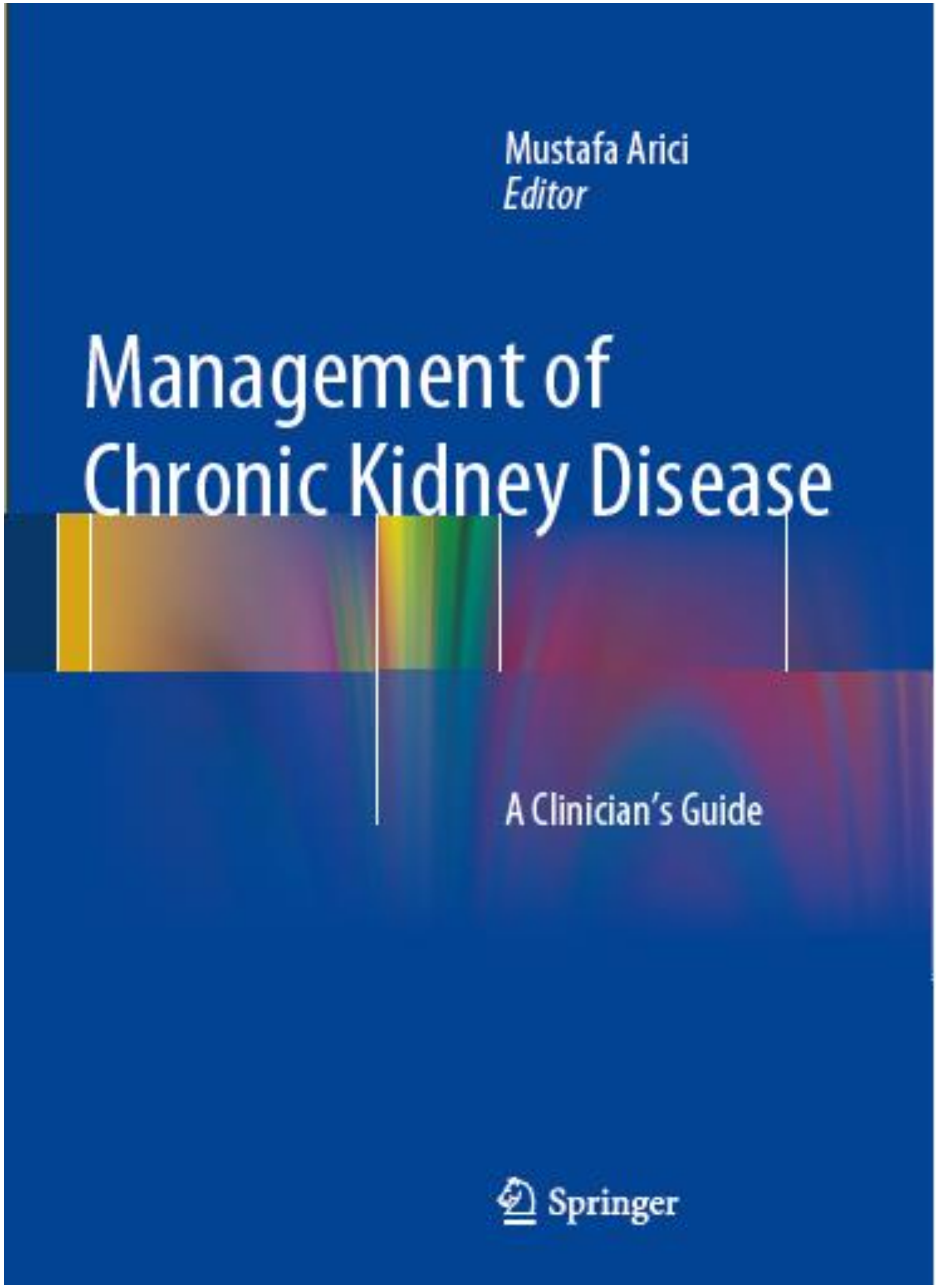
al.]. -- 9th ed., 2012

Guidelines

Arici M. Management of Chronic Kidney Disease, Springer, 2014.

What shall we do, then ?

It is not the numbers who diagnoses or treats a patient….but a skilled physician.



Thank you very much for your attention !

http://www.springer.com/medicine/nephrology/book/978-3-642-54636-5