Diabetes and Hypertension Project ECHO* Clinic

*ECHO: Extension of Community Healthcare Outcomes

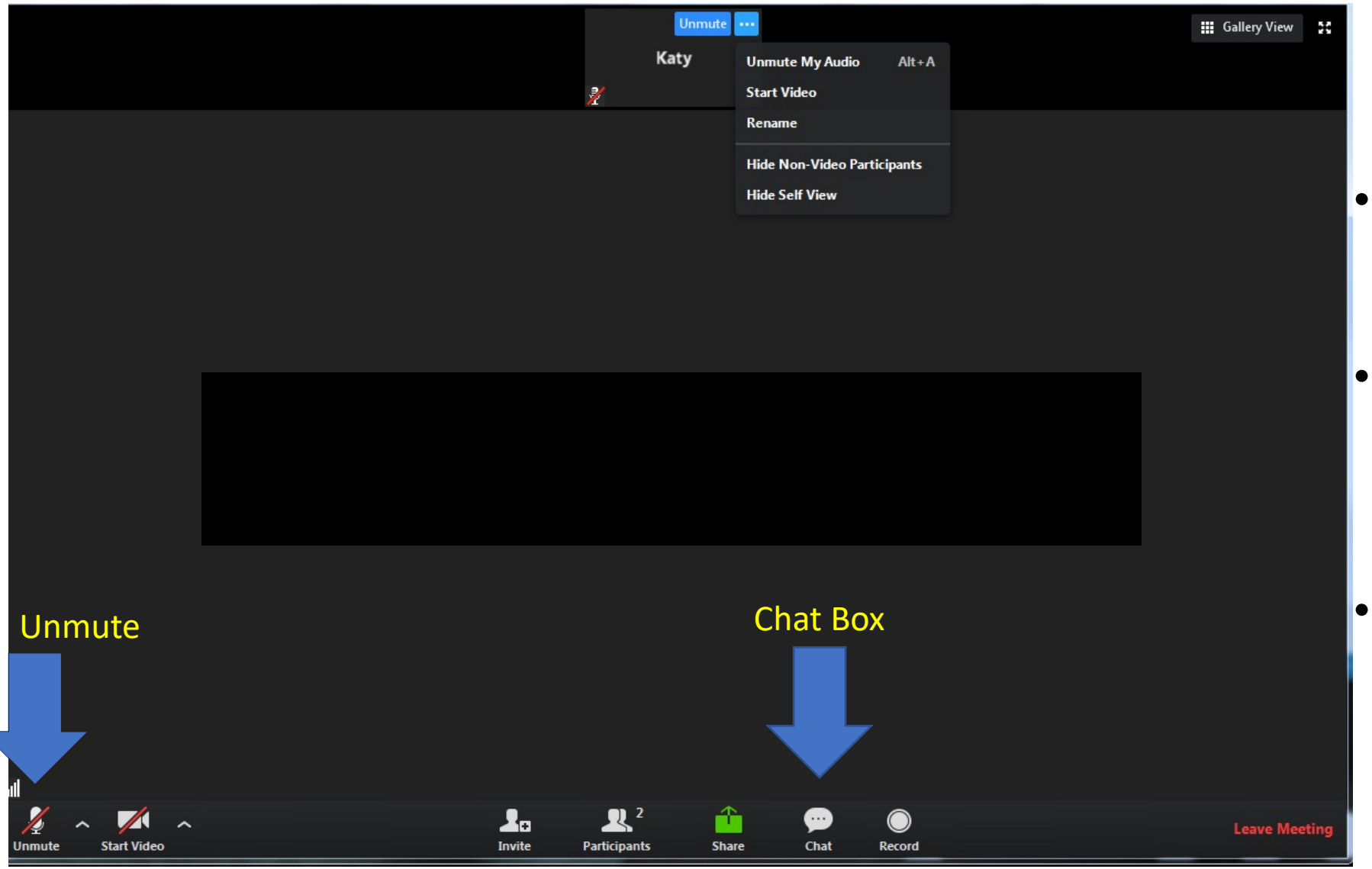
Jan. 13, 2022

Before we begin:

- Rename your Zoom screen with your name and organization
- Claim CE: text 25390-25389 to 804-625-4041
  - Go to **vcuhealth.org/echodmhtn** for instructions on creating your account

The Diabetes and Hypertension ECHO is made possible by funding through CDC Cooperative Agreement NU58DP006620-InnoVAte.

Zoom Reminders



- You are all on mute. Please unmute to talk.
- If joining by telephone audio only, press *6 to mute and unmute.
- Use the chat function to speak with our team or ask questions.

Helpful Reminders

- Please feel free to eat your lunch or step away briefly if needed
- We are recording and can share sessions upon request
  - Each session's slides are available on www.vcuhealth.org/echodmhtn
- Please **do not share any protected health information** in your discussion or the chat box
- Project ECHO operates on the "All Teach, All Learn" model
  - Feel free to ask questions in the chat or unmute to ask questions at designated times
  - We're all here to learn from each other and value each person's input and expertise!

VCU Health Diabetes & Hypertension ECHO Clinics

VCU Hub Team	
Principal Investigator	Dave Dixon, PharmD
Administrative Medical Director ECHO Hub	Vimal Mishra, MD, MMCi
Clinical Experts	Niraj Kothari, MD Trang Le, MD
Project Coordinator/IT Support	Madeleine Wagner

- One-hour ECHO clinics on 2nd Thursdays
- Every ECHO clinic includes a didactic presentation followed by case discussions
- Website: www.vcuhealth.org/echodmhtn
  - Directions for claiming CE can be found here
  - You have up to six days after our session to claim CE by texting **25390-25389** to **804-625-4041**

Disclosures

Trang Le, M.D., has no financial conflicts of interest to disclose.

Niraj Kothari, M.D., has no financial conflicts of interest to disclose.

There is no commercial or in-kind support for this activity.

Clinical Assessment of Kidney Function

Learning objectives

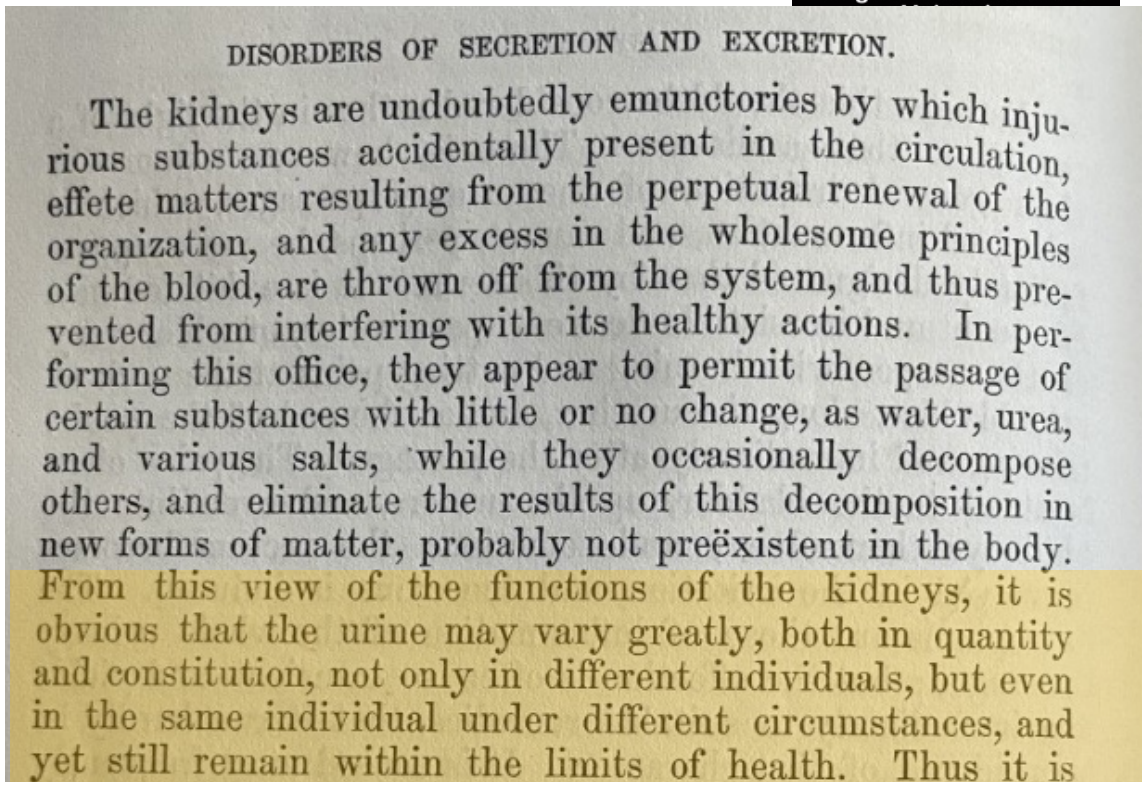
- Understand the importance of steady-state measurements in estimation of kidney function
- Recall physiologic conditions that may alter GFR
- Recall benefits and disadvantages of equations for estimating kidney function (Cockcroft-Gault, MDRD, old CKD-EPI, 2021 CKD-EPI)

Why should you care?

- Most EMRs will calculate “kidney function” for us
- We need to understand the underlying principles to interpret the results correctly
- What if labs are changing? What if we amputate a leg? Medications?
- As with many other topics in medicine, some of this has been well understood for a long time, other aspects have not been understood or have been applied in a harmful way

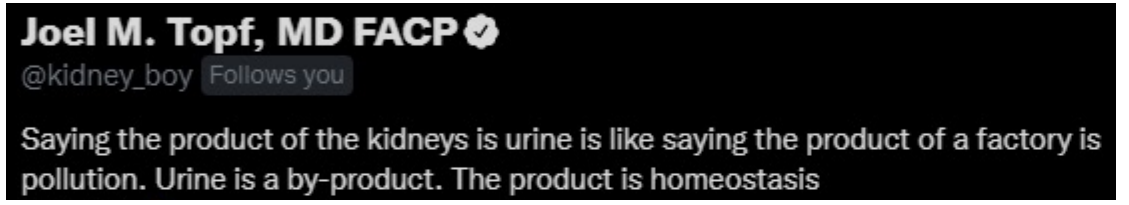
How can we figure out what the kidneys are doing?

- Urine output?
- Symptoms?
- Lab work?
  - But which labs?
    - What are we looking for?
      - Functional nephron mass/excretory capacity
      - Need patient to be in steady state



DISORDERS OF SECRETION AND EXCRETION.

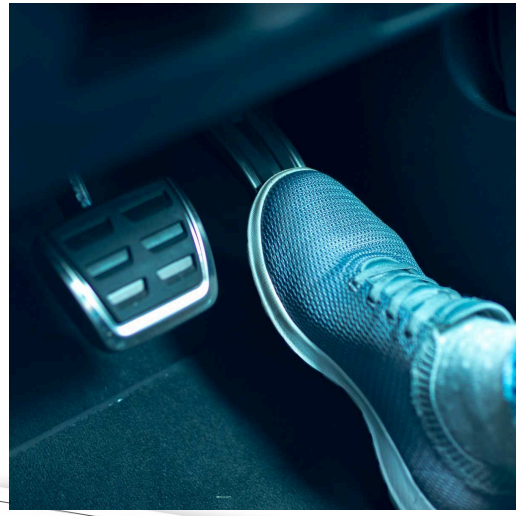
The kidneys are undoubtedly emunctories by which injurious substances accidentally present in the circulation, effete matters resulting from the perpetual renewal of the organization, and any excess in the wholesome principles of the blood, are thrown off from the system, and thus prevented from interfering with its healthy actions. In performing this office, they appear to permit the passage of certain substances with little or no change, as water, urea, and various salts, while they occasionally decompose others, and eliminate the results of this decomposition in new forms of matter, probably not preëxistent in the body. From this view of the functions of the kidneys, it is obvious that the urine may vary greatly, both in quantity and constitution, not only in different individuals, but even in the same individual under different circumstances, and yet still remain within the limits of health. Thus it is



Thompson R. (1879)

Why do we need the patient to be in steady state?

- Creatinine is NOT the same as GFR. It is affected by GFR.
  - Lower GFR will lead to rising creatinine concentrations, and vice versa
- Gas pedal vs. speed::GFR vs. creatinine
  - increased speed (lower creatinine) needs increased pressure on gas pedal (higher GFR)
  - an external observer only notes the creatinine/speed



Creatinine clearance

- More commonly used for drug dosing
- Can be directly measured (with 24 hour urine collection) or estimated (with serum creatinine level)
- Slightly overestimates GFR in normal patients
- Overestimates GFR in patients with impaired kidney function
  - Increased serum Cr levels -> increased tubular secretion of Cr – proportion of urinary Cr from tubular secretion (as opposed to Cr filtered through glomerulus) increases with lower GFR

Glomerular filtration rate (GFR)

- Used to estimate functioning nephron mass and excretory capacity
- Decreased GFR is used to define the progressive stages of kidney disease and acute kidney injury
- Transplant
  - Accrue time on list once GFR < 20mL/min/1.73m^2
  - Donation qualification

Physiologic alterations in GFR

- **Diurnal Variation**: highest values in the afternoon and lowest values in the middle of the night.
- **Exercise** transiently lowers filtration rate
- GFR increases during **pregnancy**
- GFR increases with over **hydration** and decreases with water restriction. These are usually small changes except in pathologic conditions.
- GFR changes with **age**. Newborns have a GFR<50% that at age 1 year. Over age 1, GFR in children is the same as young adults and is constant until the fourth decade. After the fourth decade it begins to gradually decline with advancing age.

Ripley B (2020)

“Normal” Range of GFR

Varies with age, gender and body size

Males:

Age 20-30 approximately 110mL/min/1.73m^2
Age 70-80 approximately 65mL/min/1.73m^2

Females:

Age 20-30 approximately 100mL/min/1.73m^2
Age 70-80 approximately 50mL/min/1.73m^2

Ripley B (2020)

Why do we have this 1.73m^2 everywhere?

STUDIES OF UREA EXCRETION. III.

THE INFLUENCE OF BODY SIZE ON UREA OUTPUT

BY JOHN F. McINTOSH, EGGERT MÖLLER, AND DONALD D. VAN SLYKE

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

(Received for publication August 21, 1928)

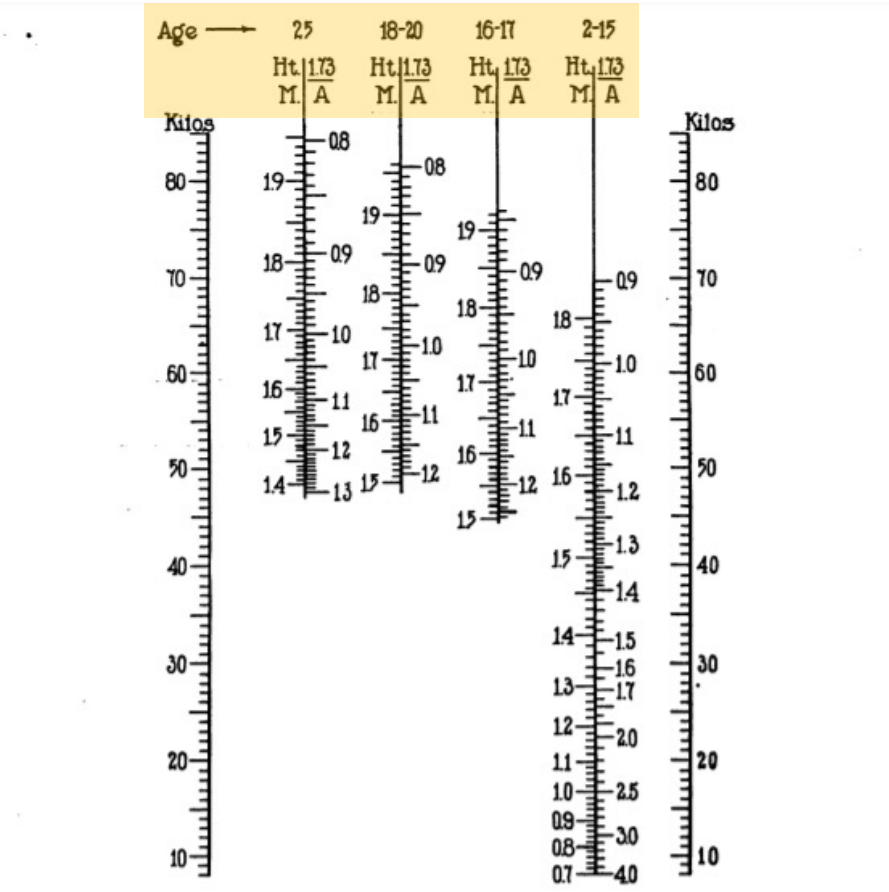


FIG. 1. CHART FOR ESTIMATING VALUES OF THE CORRECTION FACTORS, $\frac{1.73}{A}$, FROM HEIGHT AND AGE, AND FOR COMPARING OBSERVED WEIGHTS WITH WEIGHTS NORMAL FOR THE SUBJECTS EXAMINED

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^2) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

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

2012 KDOQI

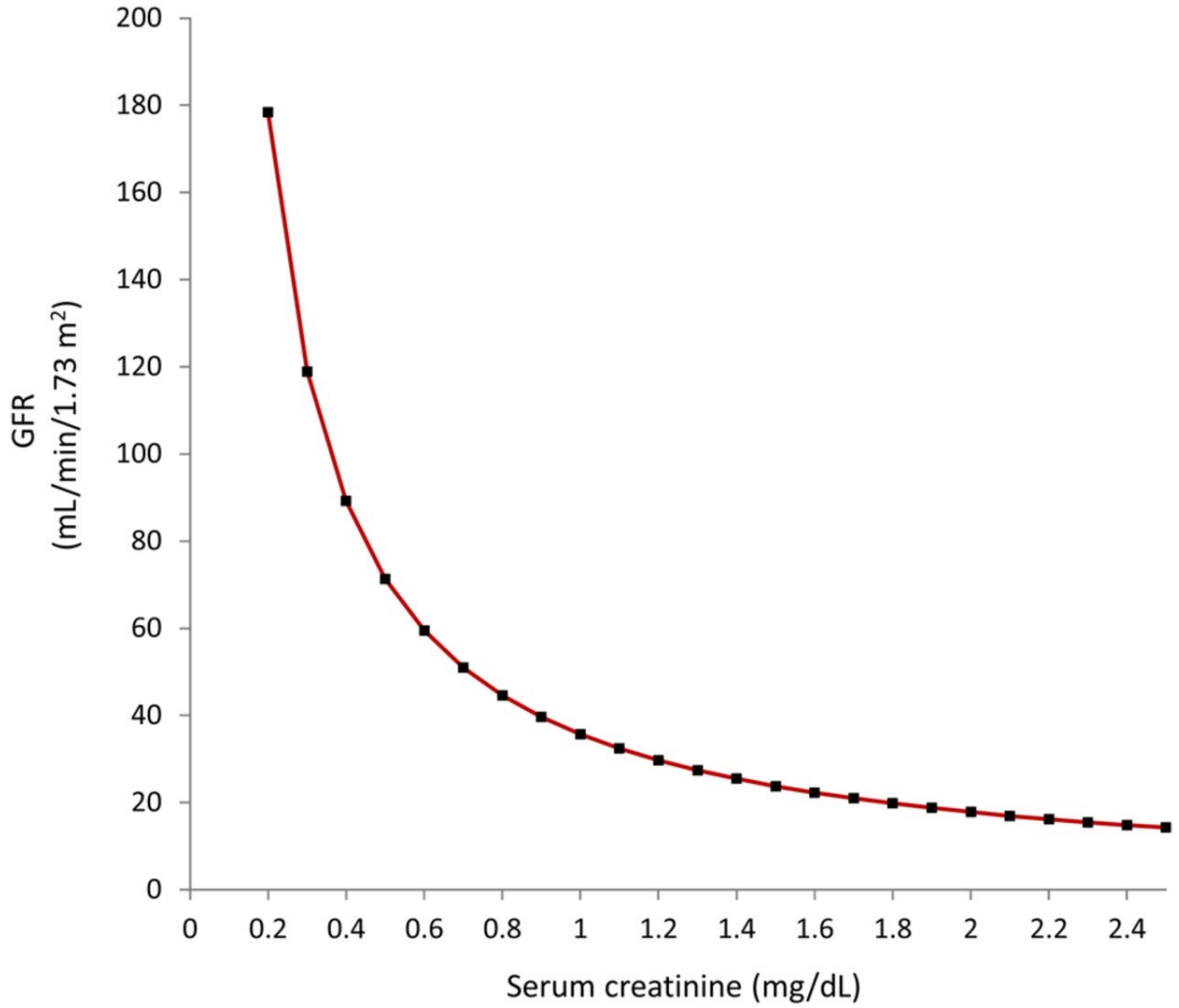
How can we estimate GFR?

- Direct measurement with exogenous markers: most accurate, most cumbersome
- Endogenous markers:
  - Creatinine
  - BUN (blood urea nitrogen)
  - Cystatin C

Creatinine

- Easy (included on basic metabolic panel), widely available, inexpensive
- Varies up to 10% day to day
- Not especially sensitive—GFR must decrease substantially prior to a noticeable change in creatinine
- Medications (i.e. cimetidine, trimethoprim) can cause increased levels (by decreasing creatinine secretion but not GFR)
- Production is influenced by liver function and muscle mass

Estimated glomerular filtration rate (GFR) for a hypothetical 2-year-old child, height 86.4 cm



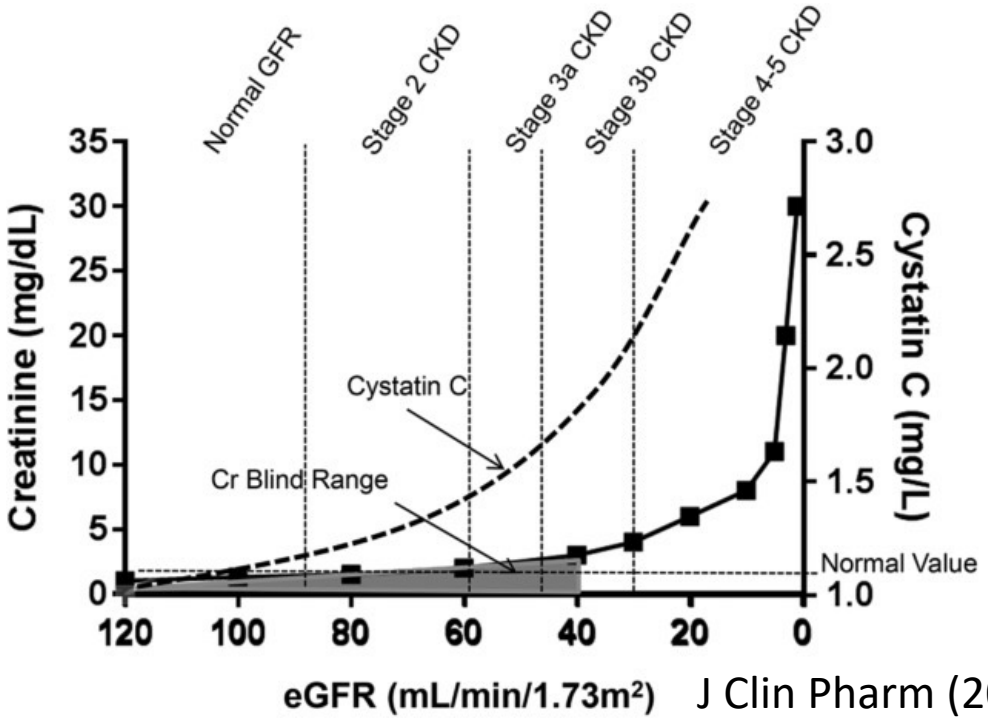
Swetha Pasala, and J Bryan Carmody Arch Dis Child Educ Pract Ed 2017;102:37-43

Blood urea nitrogen (BUN)

- Easy (included in basic metabolic panel), widely available, inexpensive
- Production is not constant – affected by protein intake, GI hemorrhage, infection, corticosteroid therapy
- Not validated to estimate GFR

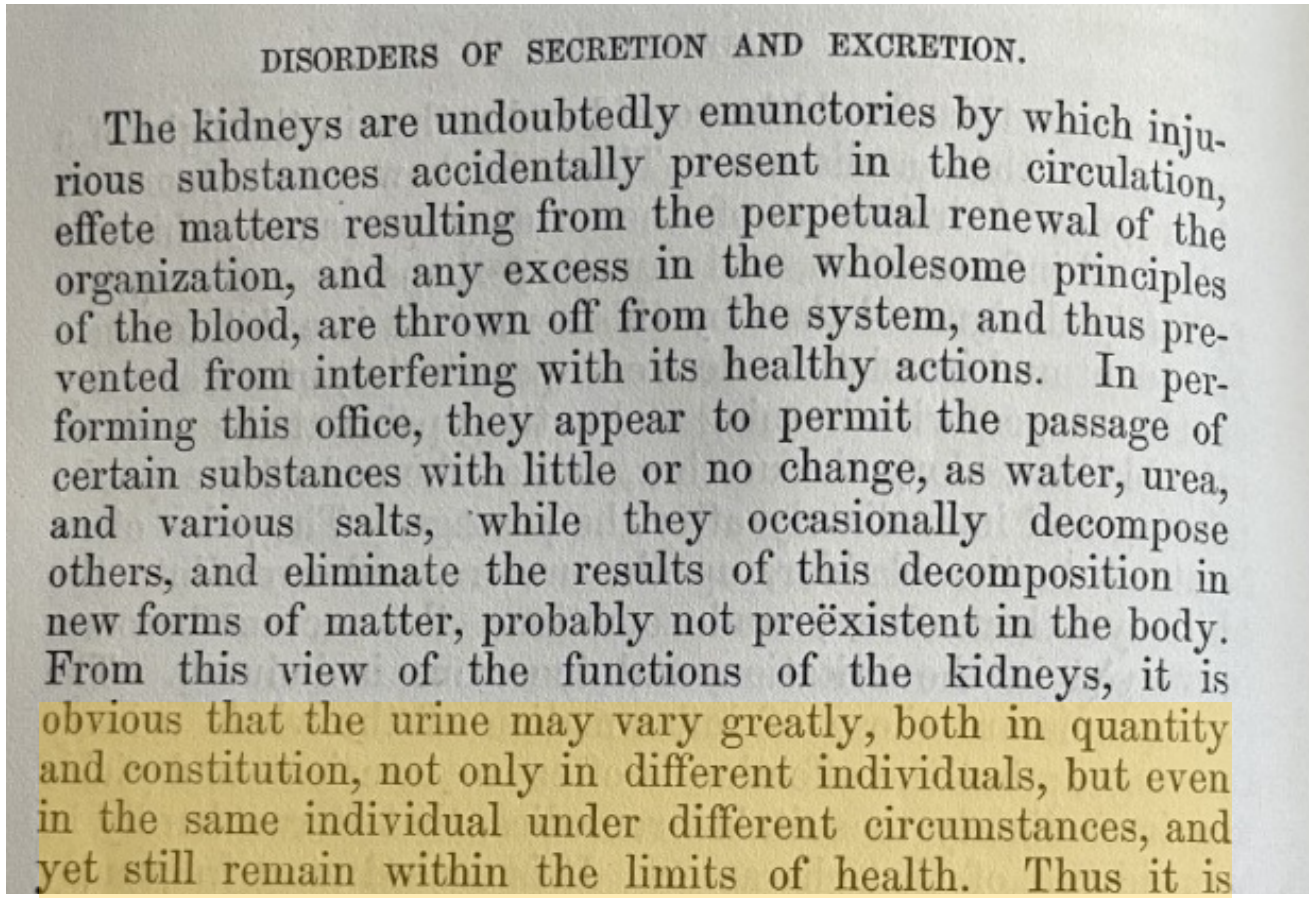
Cystatin C

- Produced at a constant rate by all nucleated cells
- Less dependent than creatinine on muscle mass/diet
- May be more sensitive to GFR changes than creatinine
- More expensive than creatinine testing
- Affected by cardiovascular disease
- May be affected by steroid use



J Clin Pharm (2018)

We need to change how we practice



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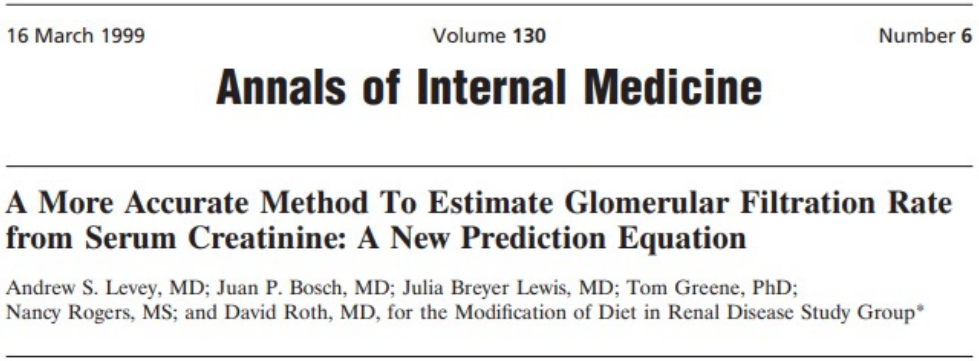
Treatment.—In idiopathic suppression, it is highly important to begin with treatment early in the case, when there may be good hope of saving the patient. Blood should be drawn by cups or leeches from the small of the back. At the

Thompson R. (1879)

eGFR estimation: MDRD (1999)

- 1628 adult patients had GFR estimated by iothalamate clearance
  - 88% Caucasian, 60% male subjects
  - Mean age 51 yo
  - Non diabetic kidney disease
  - Mean GFR 40mL/min/1.73m^2



16 March 1999 Volume 130 Number 6

Annals of Internal Medicine

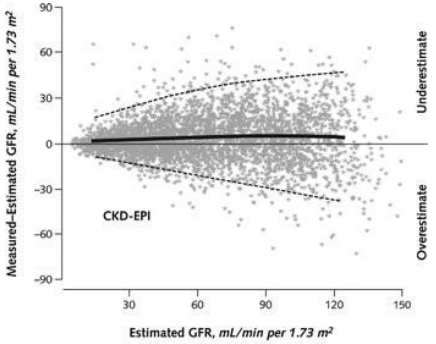
A More Accurate Method To Estimate Glomerular Filtration Rate from Serum Creatinine: A New Prediction Equation

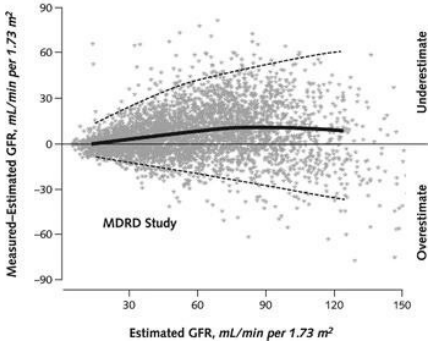
Andrew S. Levey, MD; Juan P. Bosch, MD; Julia Breyer Lewis, MD; Tom Greene, PhD; Nancy Rogers, MS; and David Roth, MD, for the Modification of Diet in Renal Disease Study Group*

- $GFR = 186\ x\ Scr^{-1.154}\ x\ age^{-0.203}\ x\ 1.212\ (if\ Black)\ x\ 0.742\ (if\ female)$
- Reasonably accurate in CKD patients
- Less accurate in patients with higher GFR > 60mL/min/1.73m^2

eGFR estimation: CKD-EPI (2009)

- 8254 patients had GFR estimated by iothalamate clearance
  - 63% Caucasian, 57% male subjects
  - Mean age 47yo
  - Mean GFR 68mL/min/1.73m2
- $GFR = 141\ x \min\left(\frac{Scr}{\kappa}, 1\right)^{\alpha}\ x \max\left(\frac{Scr}{\kappa}, 1\right)^{-1.209}\ x\ 0.993^{Age}$ x 1.018 (if female)x 1.159 (if Black)
- κ = 0.7 if female, 0.9 if male
- α = -0.329 if female, -0.411 if male
- Designed to provide more accurate estimates at higher GFR
- As accurate as MDRD at lower GFR
- CKD-EPI equations also exist using cysC and composite Cr-cysC





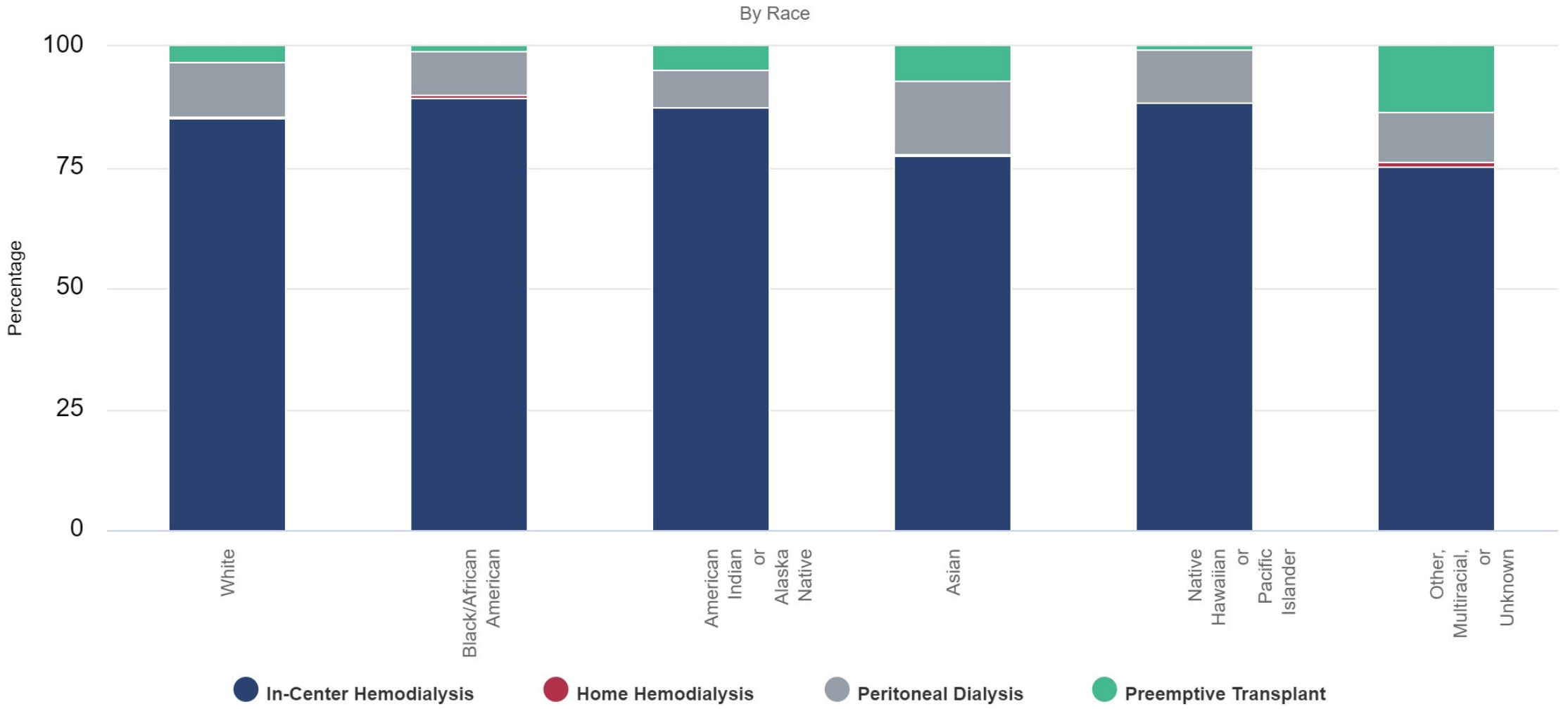
ARTICLE | Annals of Internal Medicine

A New Equation to Estimate Glomerular Filtration Rate

Andrew S. Levey, MD; Lesley A. Stevens, MD, MS; Christopher H. Schmid, PhD; Yaping (Lucy) Zhang, MS; Alejandro F. Castro III, MPH; Harold I. Feldman, MD, MSCE; John W. Kusek, PhD; Paul Eggers, PhD; Frederick Van Lente, PhD; Tom Greene, PhD; and Josef Coresh, MD, PhD, MHS, for the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration)*

Not all ESKD treatments are created equal

Figure 1.10 Distribution of modality among incident ESRD patients, by age, race, ethnicity, sex, and primary cause of ESRD, 2018



Data Source: 2020 United States Renal Data System Annual Data Report

Why eliminate race as a variable?

- Social construct, not physiologic
- Used as a binary variable “Black or non-Black”
- Small numbers included in modeling

NKF and ASN form joint task force to focus on use of race in eGFR

August 24, 2020, 12:22pm EDT

In August of 2020, the National Kidney Foundation (NKF) and the American Society of Nephrology (ASN) formed a joint task force to focus on the use of race to estimate GFR. For more information, please read the joint NKF-ASN statement on "Establishing a Task Force to Reassess the Inclusion of Race in Diagnosing Kidney Diseases."

eGFR estimation: CKD-EPI (2021)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race

L.A. Inker, N.D. Eneanya, J. Coresh, H. Tighiouart, D. Wang, Y. Sang, D.C. Crews, A. Doria, M.M. Estrella, M. Froissart, M.E. Grams, T. Greene, A. Grubb, V. Gudnason, O.M. Gutiérrez, R. Kalil, A.B. Karger, M. Mauer, G. Navis, R.G. Nelson, E.D. Poggio, R. Rodby, P. Rossing, A.D. Rule, E. Selvin, J.C. Seegmiller, M.G. Shlipak, V.E. Torres, W. Yang, S.H. Ballew, S.J. Couture, N.R. Powe, and A.S. Levey, for the Chronic Kidney Disease Epidemiology Collaboration*

- Re-fitting of CKD-EPI equation to remove race as a variable
- $GFR = 142\ x \min\left(\frac{Scr}{\kappa}, 1\right)^{\alpha} x \max\left(\frac{Scr}{\kappa}, 1\right)^{-1.200} x\ 0.994^{Age}$ x 1.012 (if female)
- κ = 0.7 if female, 0.9 if male
- α = -0.241 if female, -0.302 if male
- CKD-EPI equations also exist using cysC and composite Cr-cysC

Where do we go from here?

- The next step in my view will be to address gender—current equations only accommodate cisgender binary patients
- Kinetic eGFR
- Is GFR itself useful enough?
- Other biomarkers/genetic mutations
  - APOL1
- AI/machine learning

Questions?

Case Study #1

- **66yo male, severe peripheral vascular disease**
- **Consulted for AKI on significant CKD**
- **Creatinine 3.5mg/dL on day of consult**
- **Patient subsequently underwent bilateral above-the-knee amputations**
- **Creatinine level is now 2.0mg/dL on the day after surgery**
- **How would you interpret this result?**
- **What other clues could aid in thinking about relative kidney function?**

Any clarifying questions?

Case Study #2

- 55yo female, presenting to clinic for HTN management
- Feels well but is annoyed because she went to the wrong clinic building at first
- PMH: hypertension, diabetes type 1, chronic kidney disease
- Meds: amlodipine, metoprolol, carvedilol
- BP 160/95, HR 55
- How would you approach this patient?

Case Studies

- Anyone can submit cases: www.vcuhealth.org/echodmhtn
- Receive feedback from participants and content experts
- Earn **$150** for submitting and presenting

Provide Feedback

www.vcuhealth.org/echodmhtn

- Feedback
  - Overall feedback related to session content and flow?
  - Ideas for guest speakers?

Access Your Evaluation

vcuhealth.org/services/telehealth/for-providers/education/diabetes-and-hypertension-project-echo

For Providers

- Education
  - **Diabetes and Hypertension Project ECHO**
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  - VCU Nursing Home ECHO
  - VCU Health Palliative Care ECHO
  - Virginia Opioid Addiction ECHO
  - Virginia Sickle Cell Disease ECHO

Diabetes and Hypertension Project ECHO

Welcome to the Diabetes and Hypertension Extension for Community Health Outcomes or ECHO, a virtual network of multidisciplinary diabetes and hypertension experts. An ECHO model connects professionals with each other in real-time collaborative virtual sessions on Zoom. Participants present de-identified cases to one another, share resources, connect to each other, and grow in their expertise. This ECHO will address practice level issues and solutions related to managing complex patients with difficult to control diabetes and hypertension. Register now for an ECHO Session!

Network, Participate and Present

- Engage in a collaborative community with your peers.
- Listen, learn and discuss informational and case presentations in real-time.
- Take the opportunity to submit your de-identified case study for feedback from a team of specialists for diabetes and hypertension.
- Provide valuable feedback.
- Claim CE credit by texting in attendance.

Benefits

VCU Diabetes & Hypertension Project ECHO Clinics

2nd Thursdays — 12 p.m. to 1 p.m.

Mark Your Calendars — Upcoming Sessions

Feb. 10: Aspirin Use in Diabetic/Hypertensive Patients

March 10: Diabetes in Older Adults

Please register at www.vcuhealth.org/echodmhtn

Thank you for coming!

Text **25390-25389** to **804-625-4041** for CE credit

Reminder: Mute and Unmute to talk
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