Advancing Kidney Health
Through Optimal Medication Management

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Evaluation of Kidney Function

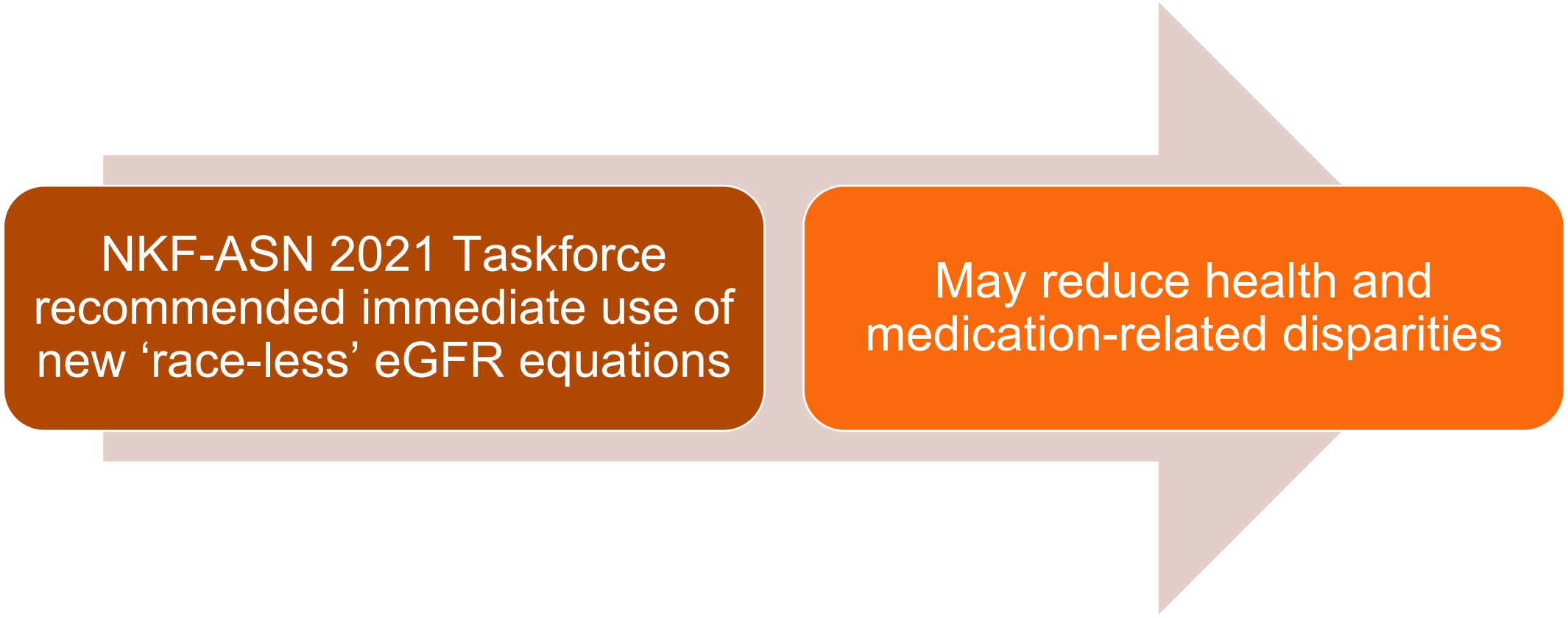
Part 1: Use of “Race-Agnostic” eGFR

Why Does it Matter?

- African Americans are about 3.4x more likely to develop kidney failure
- eGFR equations with a race factor *systematically overestimate* mGFR in African Americans
- mGFR is the gold standard!

eGFR = estimated glomerular filtration rate
mGFR = measure glomerular filtration rate

The Solution



Delgado C et al. JASN 2021;32(12):2994-3015

Estimated Glomerular Filtration Fate (eGFR)

GFR is measured (mGFR) using **exogenous** markers such as iothalamate or iohexol

GFR is estimated (eGFR) using **endogenous** markers; typically, serum creatinine and/or cystatin C

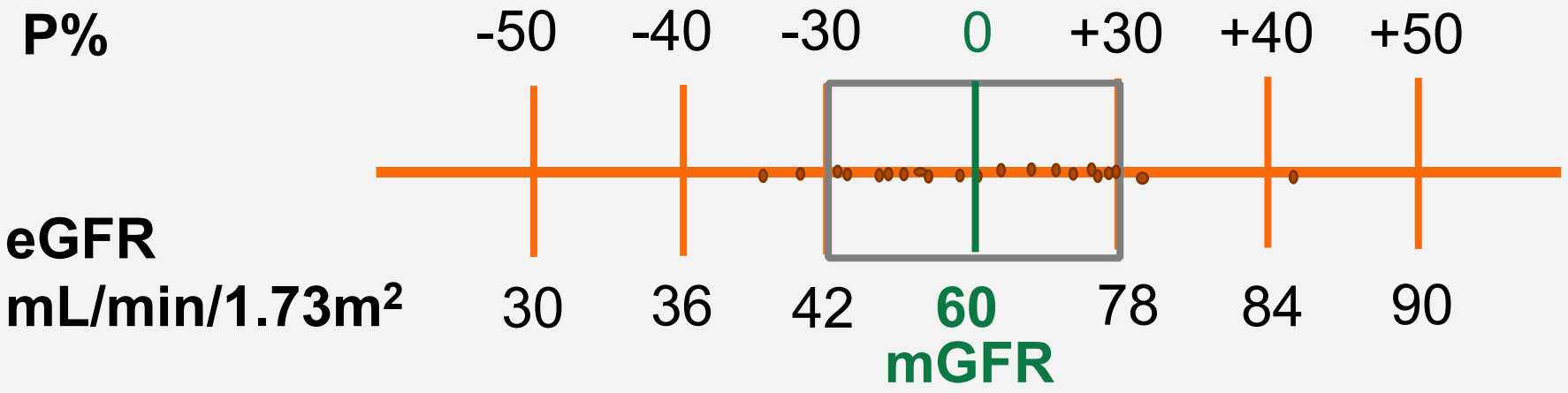
eGFR equations are derived using regression techniques in which sCr and/or cystatin C and various patient factors are included to better predict mGFR

Case

- HPI: referred for initiation of SGLT-2i to reduce risk of CKD progression
- PMH: 45 y/o old male with type 2 diabetes and CKD, self-IDs as African American
- PE: Height: 68 inches, weight: 220 lbs
- Labs: sCr: 2.21 mg/dL, cystatin C (cys): 2.87 mg/L
  - Note: sCr level similar to value obtained 4 months ago
- Meds: metformin 500 mg ER orally twice daily, cholecalciferol 1000 IU orally daily, losartan 100 mg orally in am

Accuracy Measure (p30)

p30 is the percent of people in a dataset whose eGFR values are within ±30% of mGFR



CKD-EPIcr (2009) eqn with Black factor

Percent of eGFR values outside P30 range

- 15% Black (85% accuracy)
- 10.5% Non-Black (89.5% accuracy)

Porrini E et al. Nature Reviews Nephrology 2019;15:177.
Inker LA et al. NEJM 2021;385:1737-49.

Facts on Race and eGFR

AAs have higher sCr, than non-AAs

For each 10% ↑ in African ancestry, sCr ↑'s 1% in AAs & 0.9% in Hispanics

Accuracy measured by p30: % of *individual* values inside the P30 range

Bias: difference between mGFR and eGFR, reported as a *population mean*

MDRD and CKD-EPIcr (2009) *overestimates mGFR in AAs/Blacks*, but not in non-AAs/non-Blacks

Both self-ID'ed race and practitioner-ID'ed race used to determine race/ethnicity; Problematic!!

eGFR equation performance improves with use of biomarker combination (sCr and Cystatin C)

Udler S et al. JASN 2015;26:1682, Delgado C et al. JASN 2021;32(12):2994-3015, Inker LA et al. NEJM 2021;385:1737-49

Biomarker Comparison

Attributes	Serum Creatinine	Serum Cystatin C
Source	endogenous	endogenous
Impacts kidney elimination?	GFR and TS	GFR
Non-GFR impacts	Muscle mass, diet, creatine supplements, ancestry, drugs affecting TS	obesity, smoking, inflammation, ↑↓ thyroid or glucocorticoid levels

Biomarker Comparison

Attributes	Serum Creatinine	Serum Cystatin C
Widely available?	Yes	No, <10% of labs
Cost	$	$$ to $$$
Other considerations	Assay interferences	Not included on autoanalyzers

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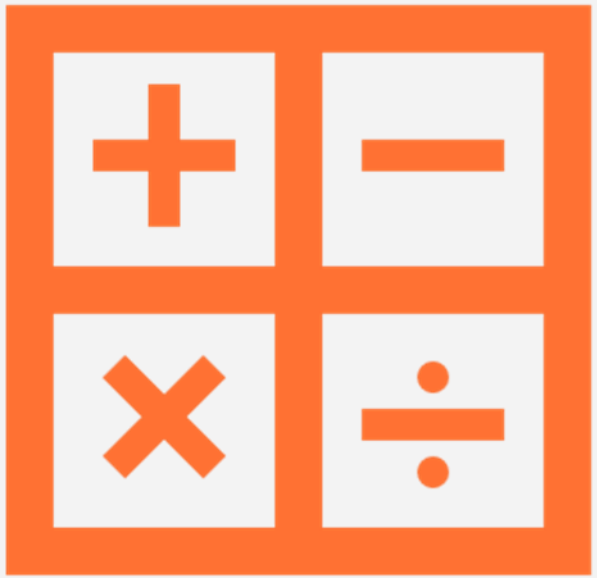
Use eGFR adjusted for Body Surface Area for Drug-related Decision-making

The Problem	• Many practitioners use standardized values ($mL/min1.73m^2$) when determining drug doses
The issue	• Kidney drug clearance is proportional to individual's mGFR (mL/min), not standardized values ($mL/min/1.73m^2$)
What to do?	• Convert to $eGFR_{BSAadj}$ value by multiplying standardized eGFR results by patient's BSA and dividing by 1.73
When?	• in overweight or underweight

Titan S. Am J Kidney Dis 2020;76(3):446-9.
Bouquegneau A. Br J Clin Pharmacol 2015;81(2):349-61.

Concepts to Application



- Calculate standardized eGFR and $eGFR_{BSAadj}$ values for our patient
- NKF eGFR calculator (link will be on next slide)
- Enter
  - sCr and cystatin C results
  - Indicated age and gender
  - Choose ‘yes’ for standardized assay
  - Choose ‘No’ for standardized eGFR values
  - Choose ‘Yes’ for $eGFR_{BSAadj}$ (enter height and weight)

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eGFR calculator: https://www.kidney.org/professionals/kdoqi/gfr_calculator

Note: CKD-EPIcr and CKD-EPIcr-cys (indexed and non-indexed)

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Choosing a race-agnostic eGFR equation for drug-related decision-making

Use 2021 CKD-EPIcr

- for most decisions
- if cystatin C is not available
- If patient has non-GFR factors that affect cystatin C levels

Use 2021 CKD-EPIcr-cys

- If CKD-EPIcr results are close to critical decision-making cut-points
  - e.g. SGLT-2i should not be initiated if eGFR <20
- if cystatin C levels are inexpensive

Consider 2012 CKD-EPIcys (2012)

- If patient has non-GFR factors that affect sCr levels

Consider mGFR or mCrCL

- with drugs with high toxicity potential (e.g. chemotherapy) in patients where eGFR has been show to be very inaccurate (age or weight extremes, muscle wasting, etc.)

How can we do our best for this patient?

Know his healthcare and medication-related goals

Improve his health literacy

- Kidney numbers: eGFR and UACR

His 2021 CKD-EPIcr $eGFR_{BSAadj}$ was 45 mL/min (much higher than eGFR of 30 or 20), so no need to confirm with 2021 CKD-EPIcr-cys $eGFR_{BSAadj}$

- Metformin can be continued
- SGLT-2i can be initiated to reduce risk of CKD progression

Shared decision-making is key!

Summary

New ‘race-agnostic’ eGFR equations may reduce some disparities in CKD

No eGFR equation is very accurate in individual patients

There are limitations to our current biomarkers used in calculating eGFR

Use $eGFR_{BSAadj}$ in overweight and underweight for drug-related decision-making

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Thank you!