

**Day 1**  
**KidneyGenAfrica Workshop**

**Session 2**  
**Measuring kidney function and understanding definitions of  
CKD**

***June Fabian***

**The use of biomarkers to assess kidney function**

***Robert Kalyesubula***

**Introducing the KDIGO CKD Guidelines 2024: Definitions of CKD and their  
relationship to morbidity and mortality, and risk prediction**



# How do we measure kidney function?

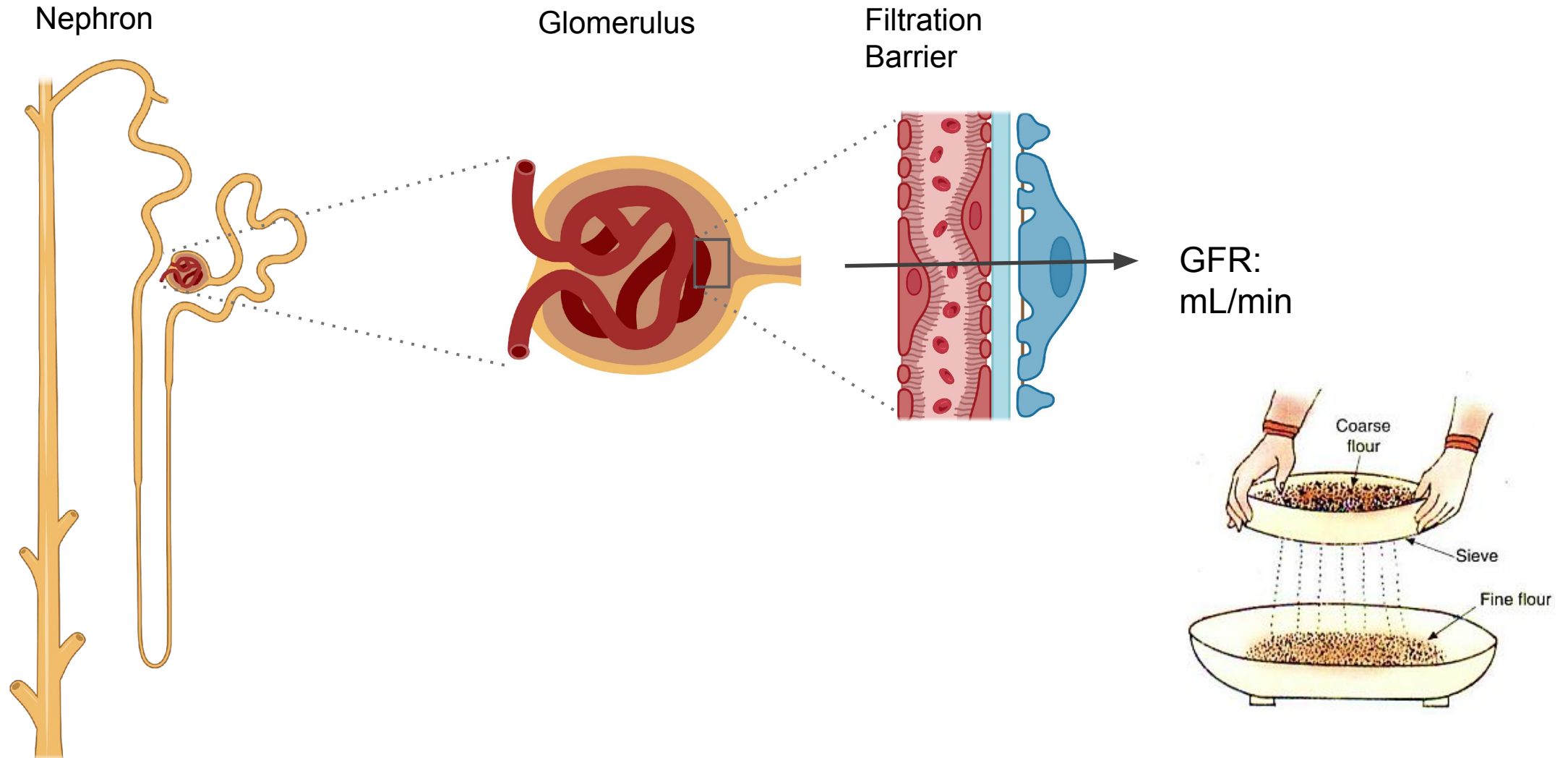
## Glomerular Filtration

### Biomarkers

- Exogenous biomarkers
  - Iohexol
- Endogenous biomarkers
  - Creatinine
  - Cystatin C
- Measured GFR
- Estimated GFR



# Measuring kidney function using GFR



# Criteria for biomarkers as measures of GFR

## ***Renal handling***

- Freely filtered by the glomerulus
- No active secretion or reabsorption by the tubules
- Not metabolized by the kidney

## ***Systemic handling***

- Produced at a constant rate
- Not eliminated by non-renal routes
- No external metabolism

## ***Measurement***

- Stable in blood and urine
- Easy to measure accurately and reproducibly
- Low analytical variability - standardized assays across labs

## ***Portable across populations***

## ***non-GFR determinants***



# Examples of biomarkers used for GFR – Creatinine

*Where does creatinine come from?*

*What is the renal handling of creatinine?*

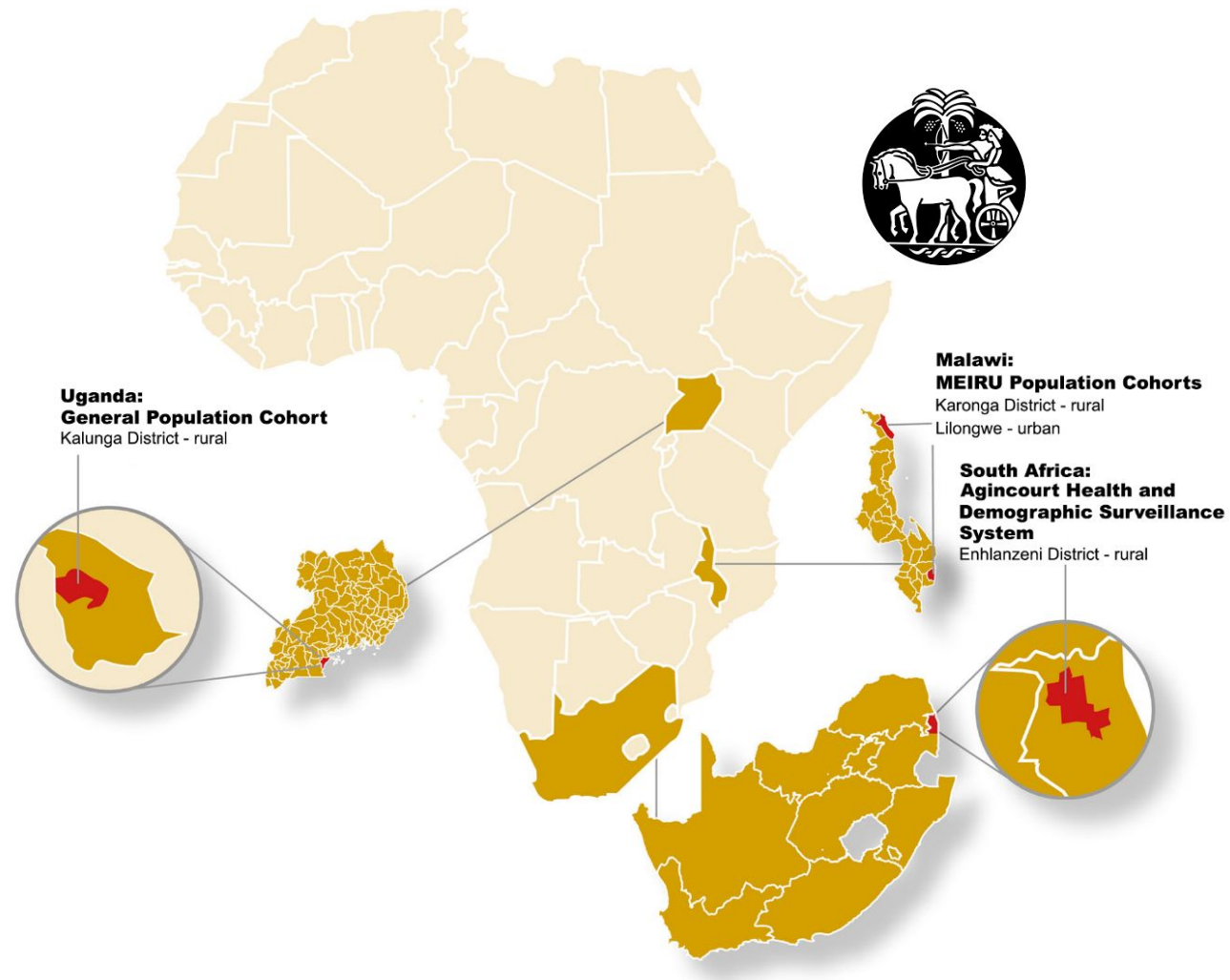
*What is the systemic handling of creatinine?*

*How is creatinine measured?*

*Is it portable across populations?*

*What are the non-GFR determinants of creatinine?*

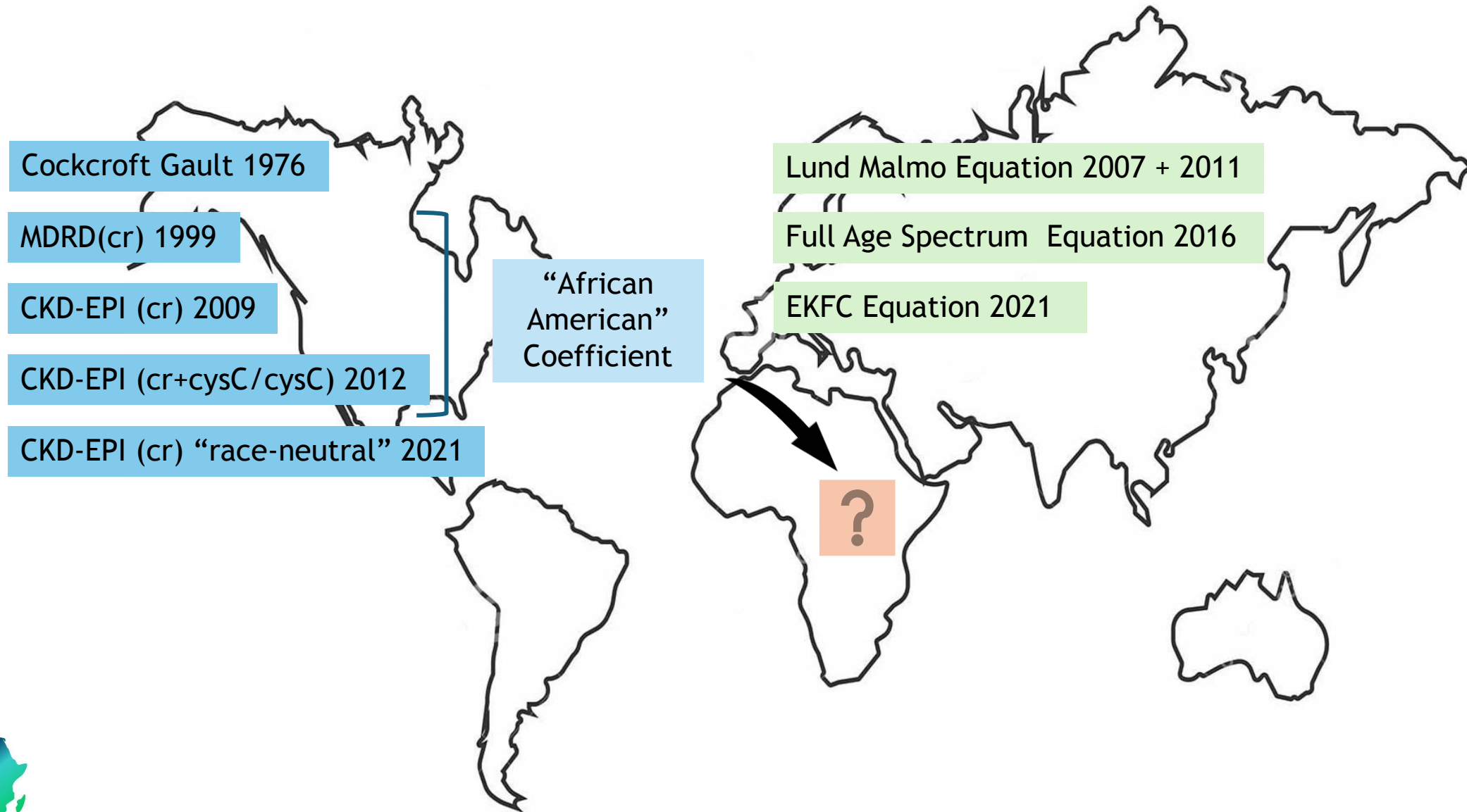




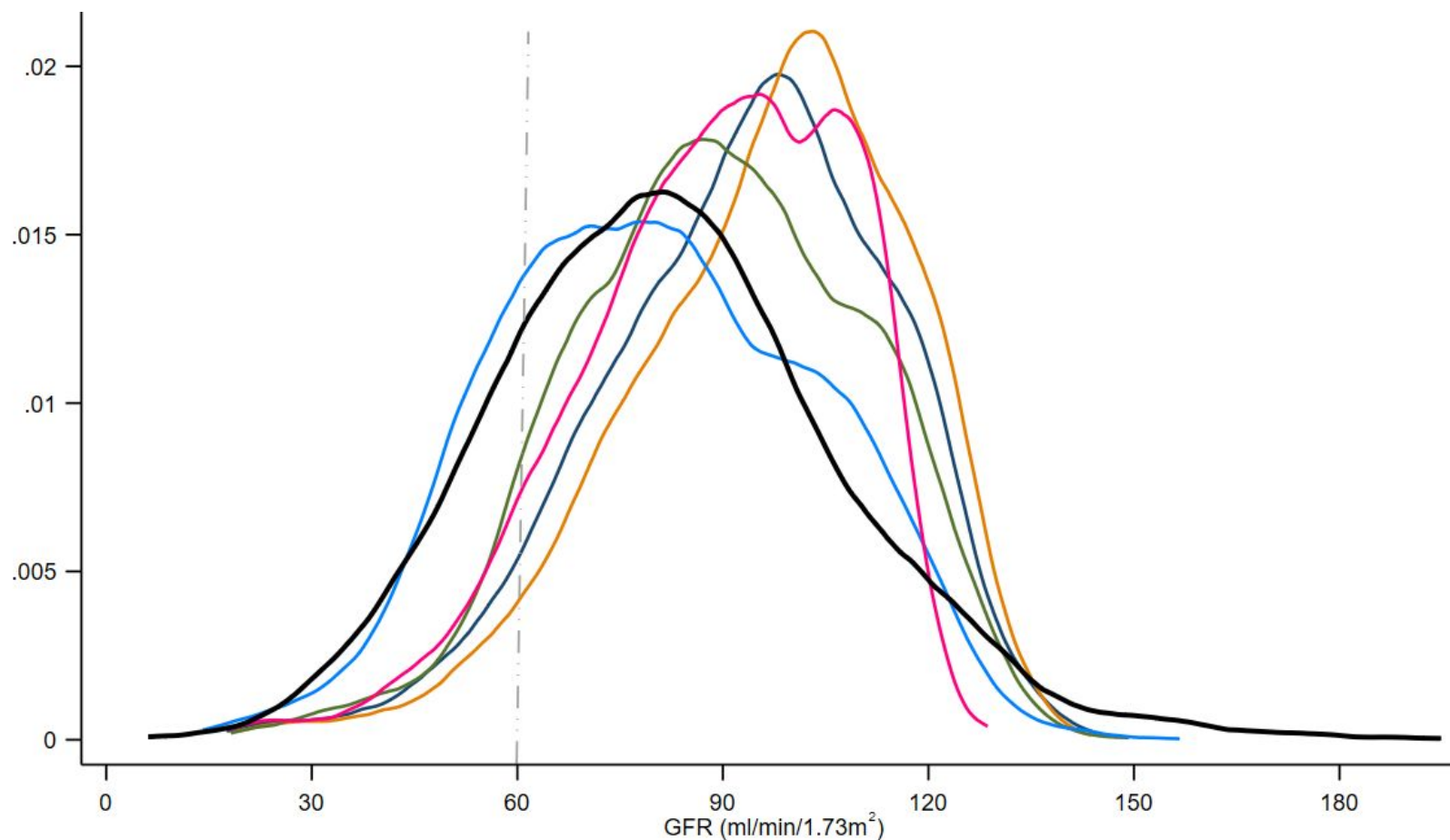
Kalyesubula, R., et al. (2020). "How to estimate glomerular filtration rate in sub-Saharan Africa: design and methods of the African Research into Kidney Diseases (ARK) study." BMC nephrology **21**(1): 1-12.



# Which eGFR equation?



# Performance of eGFR equations compared to iohexol mGFR



— CKD-EPI (creatinine) 2009 (AS)	— CKD-EPI (creatinine) 2021
— CKD-EPI (creatinine-cystatin C) 2021	— CKD-EPI cystatin C 2012
— EKFC (creatinine)	— Iohexol measured GFR





## Misclassification by GFR stage: eGFR compared to measured-GFR

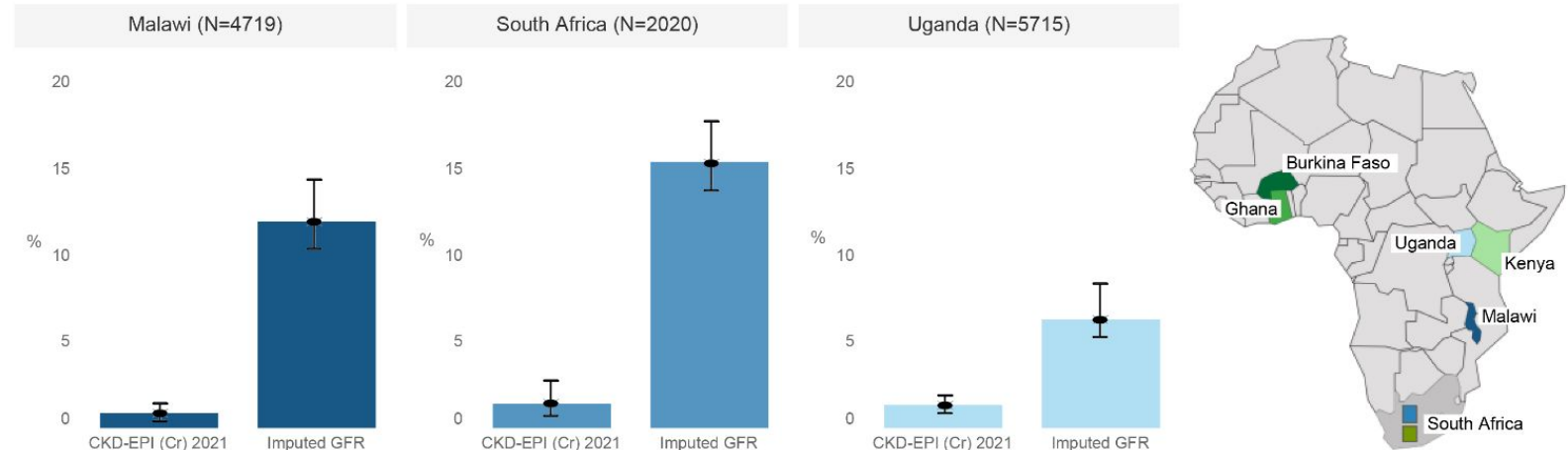
GFR staging	Iohexol GFR	Cockcroft Gault	MDRD	Lund-Malmö (rev)	FAS (Cr)	ARK (Cr)	CKD-EPI (Cr)	CKD-EPI (Cr+cysC)	CKD-EPI (cysC)
G1 +G2 (GFR≥60)	2077/2578 (80.6)	2314/2578 (89.8)	2340/2578 (90.8)	2344/2578 (90.9)	2376/2578 (92.2)	592/651 (90.9%)	2408/2578 (93.4)	2183/2433 (89.7)	1924 /2433 (79.1)
G3-5 (GFR<60)	501/2578 (19.4)	264/2578 (10.2)	238/2578 (9.2)	234 /2578 (9.1)	202/2578 (7.8)	59/651 (9.1)	170/2578 (6.6)	250/2433 (10.3)	509/2433 (20.9)

Data represented as number(%); KDIGO CKD staging by GFR (ml/min/1.73m<sup>2</sup>): G1 ≥90; G2 60-89; G3a 45-59; G3b 30-44; G4 15-29; G5 <15; CKD-EPI (creatinine; creatinine + cystatin C) and MDRD equations exclude African-American coefficients

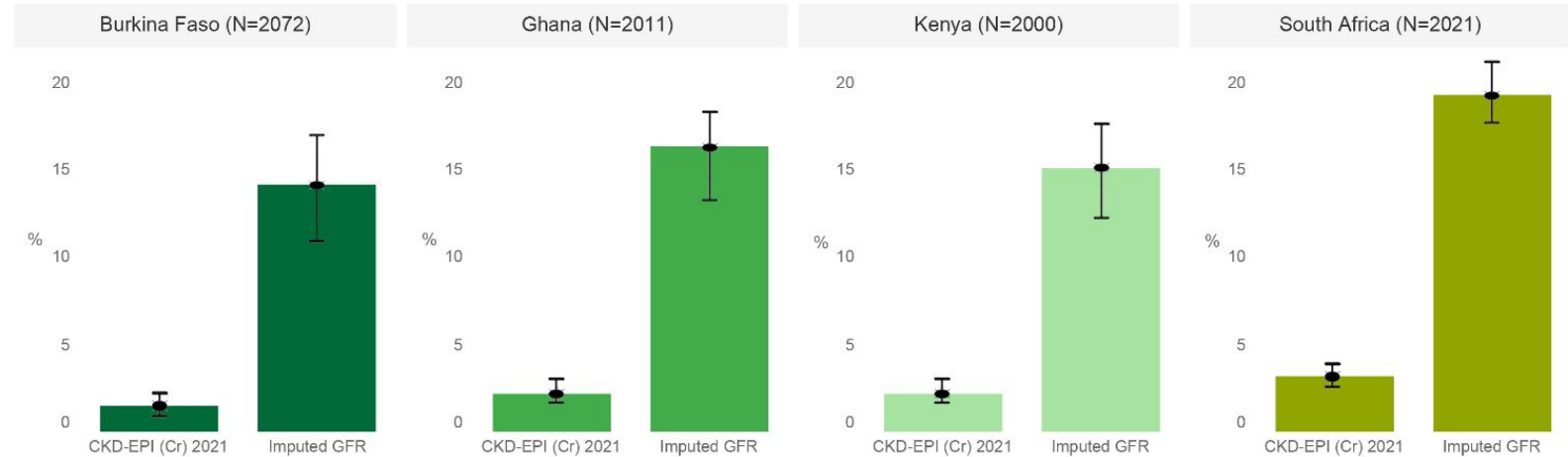


Prevalence of CKD is 3-5 x higher than currently estimated if we use “race-neutral” CKD-EPI (cr) 2021

#### ARK-CKD population prevalence studies



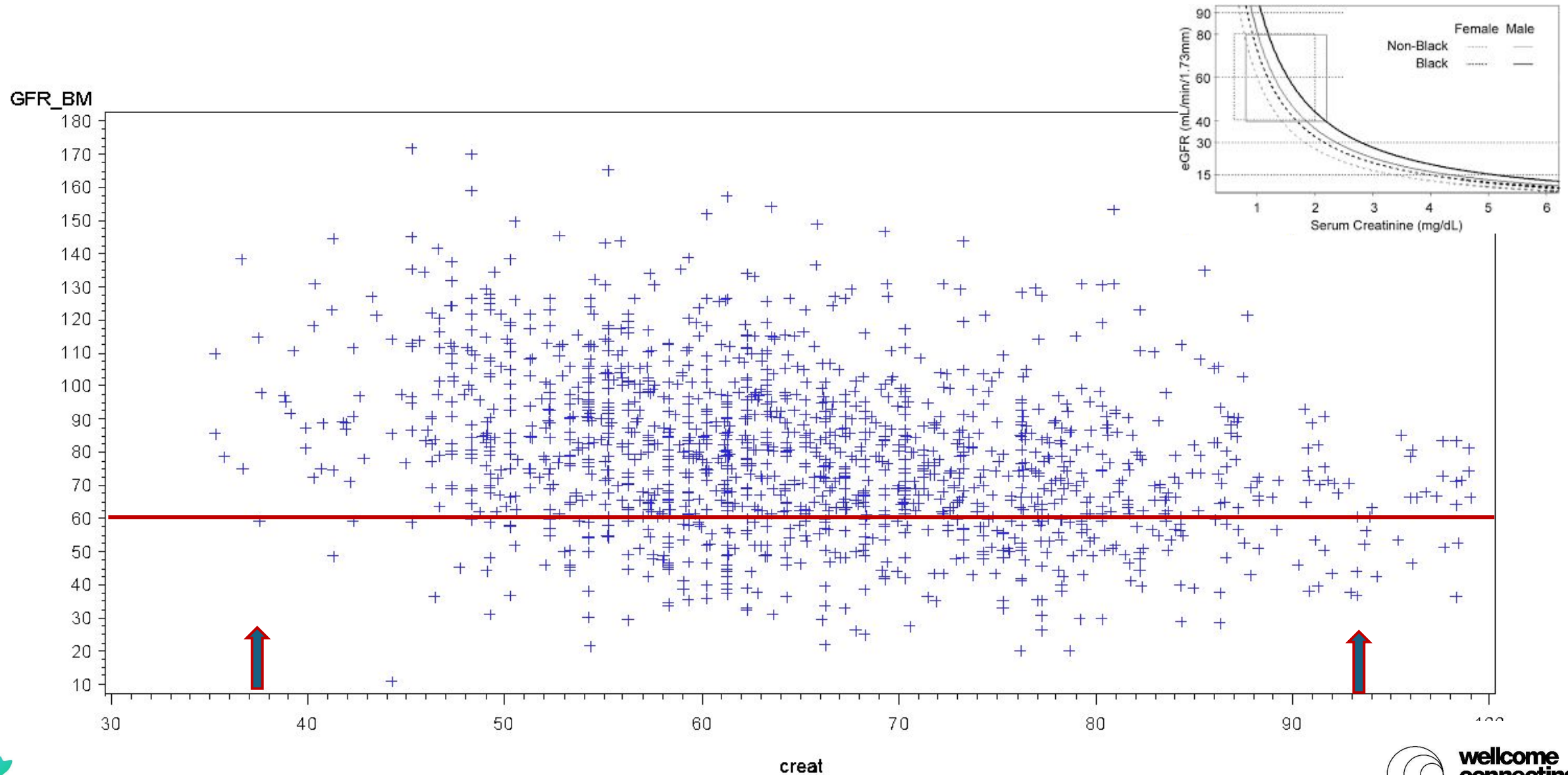
#### AWI-Gen population prevalence studies



CKD-EPI (Cr) 2021: CKD-EPI (creatinine) 2021 equation; data presented as percent (95% confidence interval); datasets for South Africa did not overlap; reported prevalence was unadjusted.



# Modelling the ARK equation: relationship between creatinine and GFR



# Why is creatinine a poor biomarker for kidney function in African populations?

Jaffe vs enzymatic method

Low BMI + BSA

Adverse perinatal + early childhood factors (stunting, nephron mass, stature, muscle mass)

Wasting - chronic infection or inflammation (HIV, TB)

Low dietary protein (poverty + food insecurity)

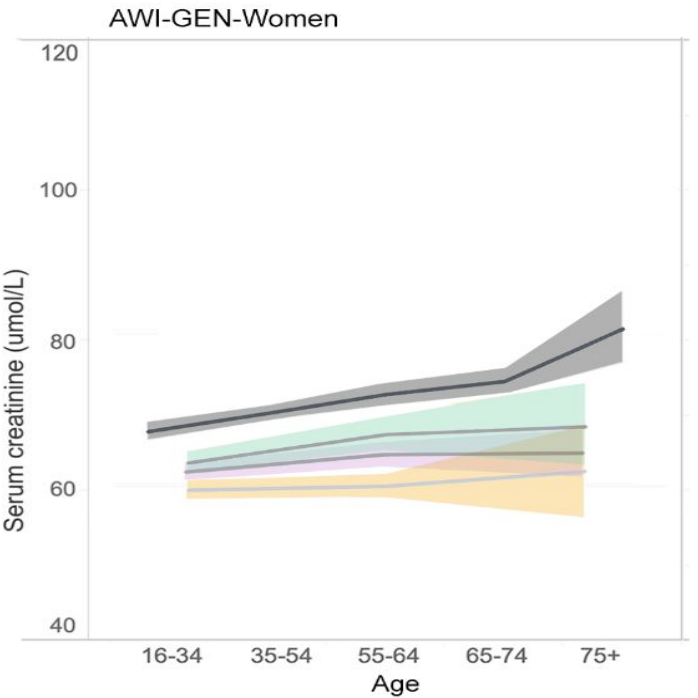
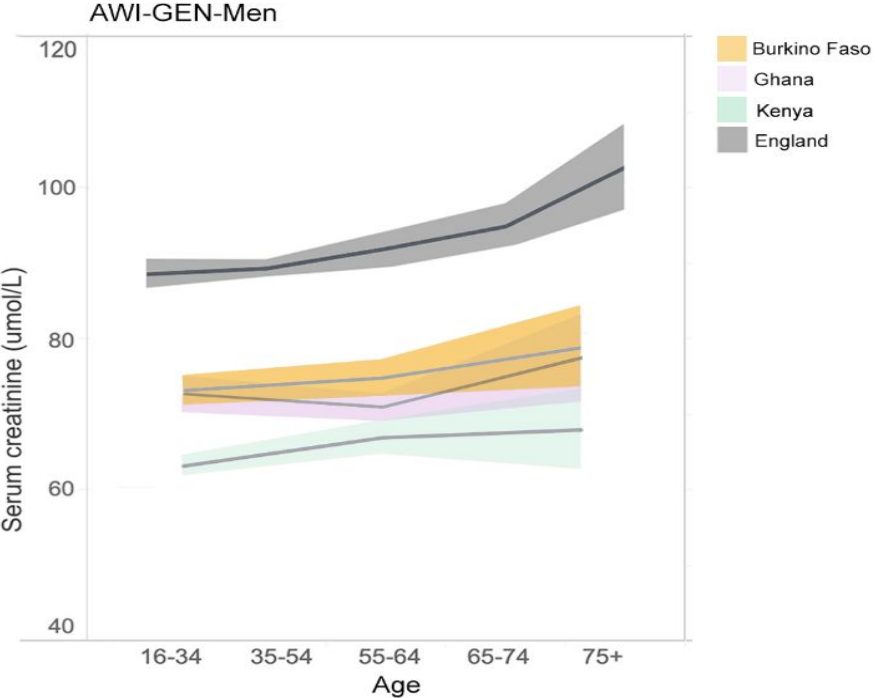
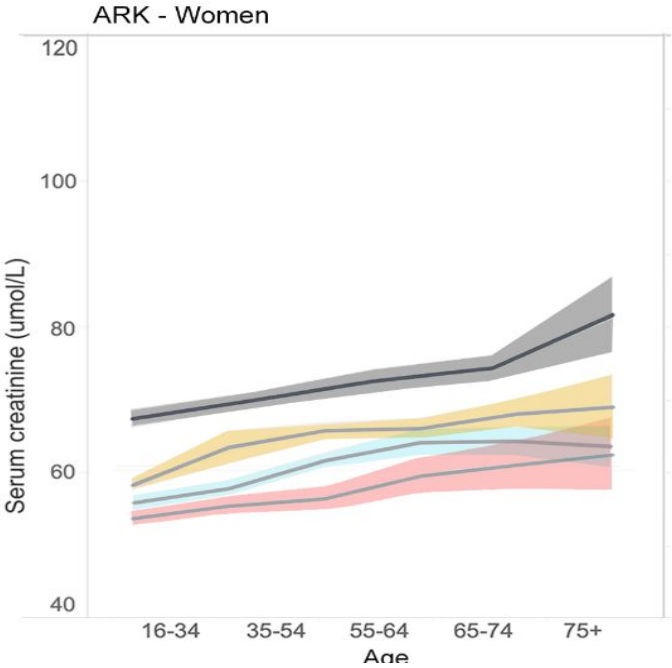
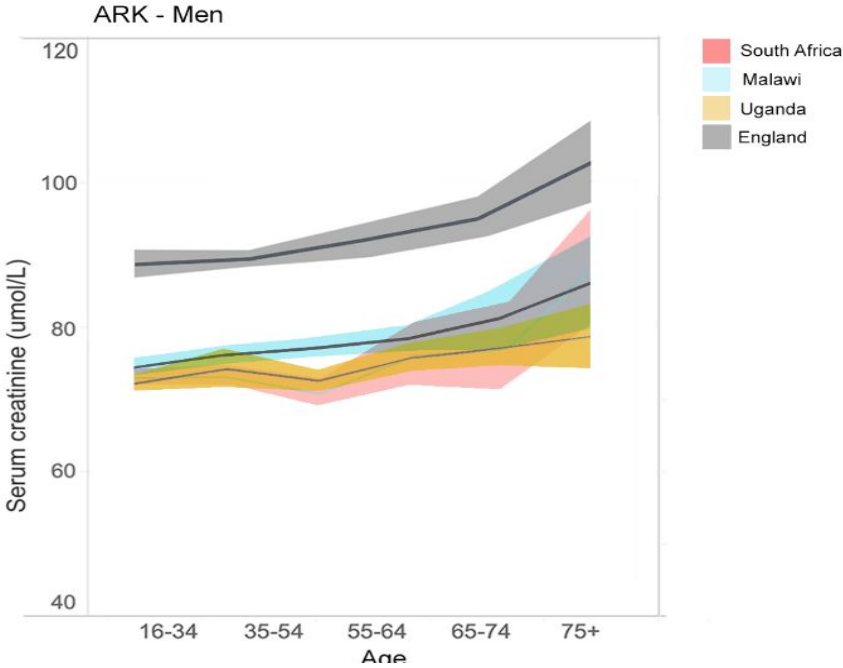
Undiagnosed liver disease

Genetic factors - tubular secretion of creatinine

Impact of ART on tubular secretion of creatinine



Population differences in creatinine



# Let's recap!



# Open the floor Q & A

