

AGING KIDNEY IN HIV DISEASE

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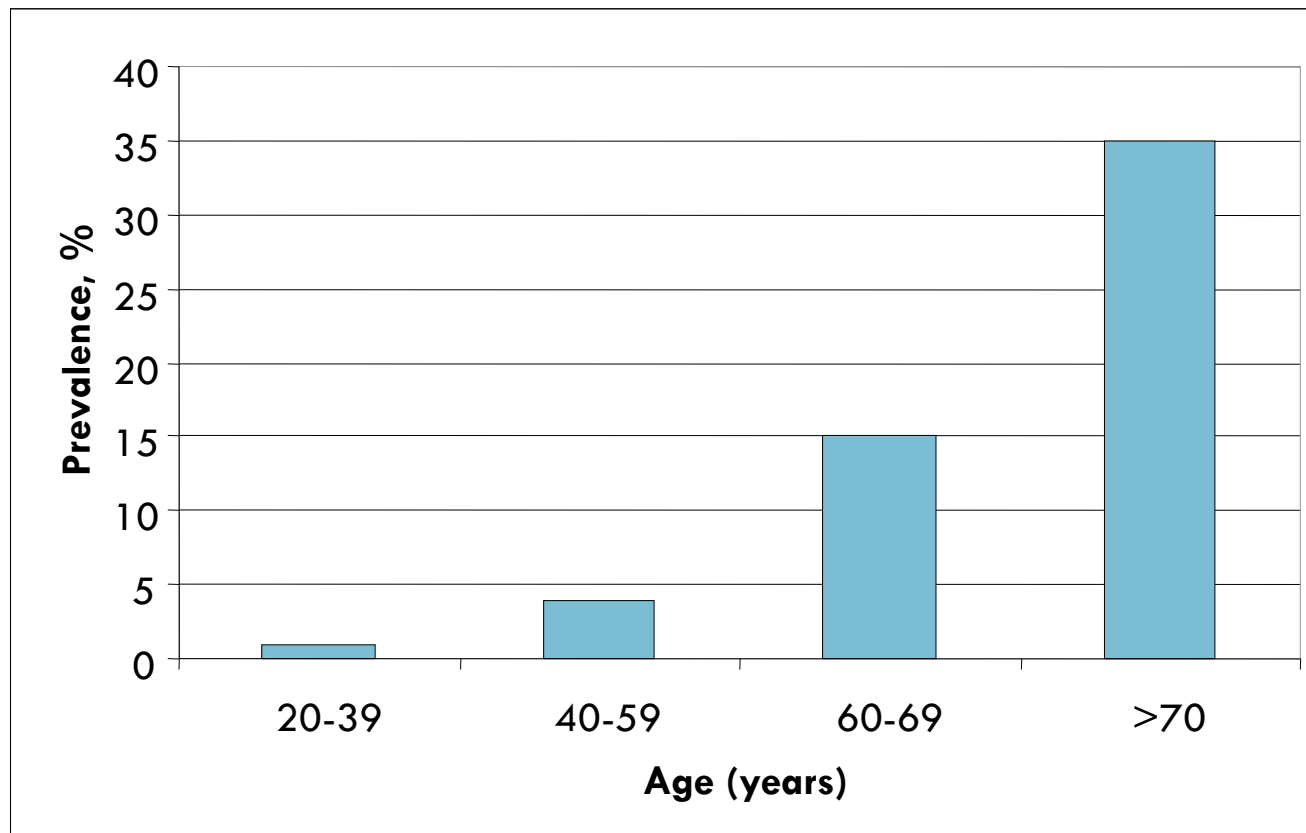
Kidney, Aging and HIV



- In general population, kidney disease disproportionately affects the elderly.
- Evidence that this process is accelerated in HIV:
 - ▣ 10-fold risk of ESRD compared with age-matched controls
 - ▣ 5-fold risk of proteinuria, an important sign of kidney injury
- However, the standard test of kidney function, creatinine, is derived from muscle mass; creatinine is slow to detect in CKD in elderly and HIV
- We need new methods to detect early kidney injury and reduced kidney function in HIV patients

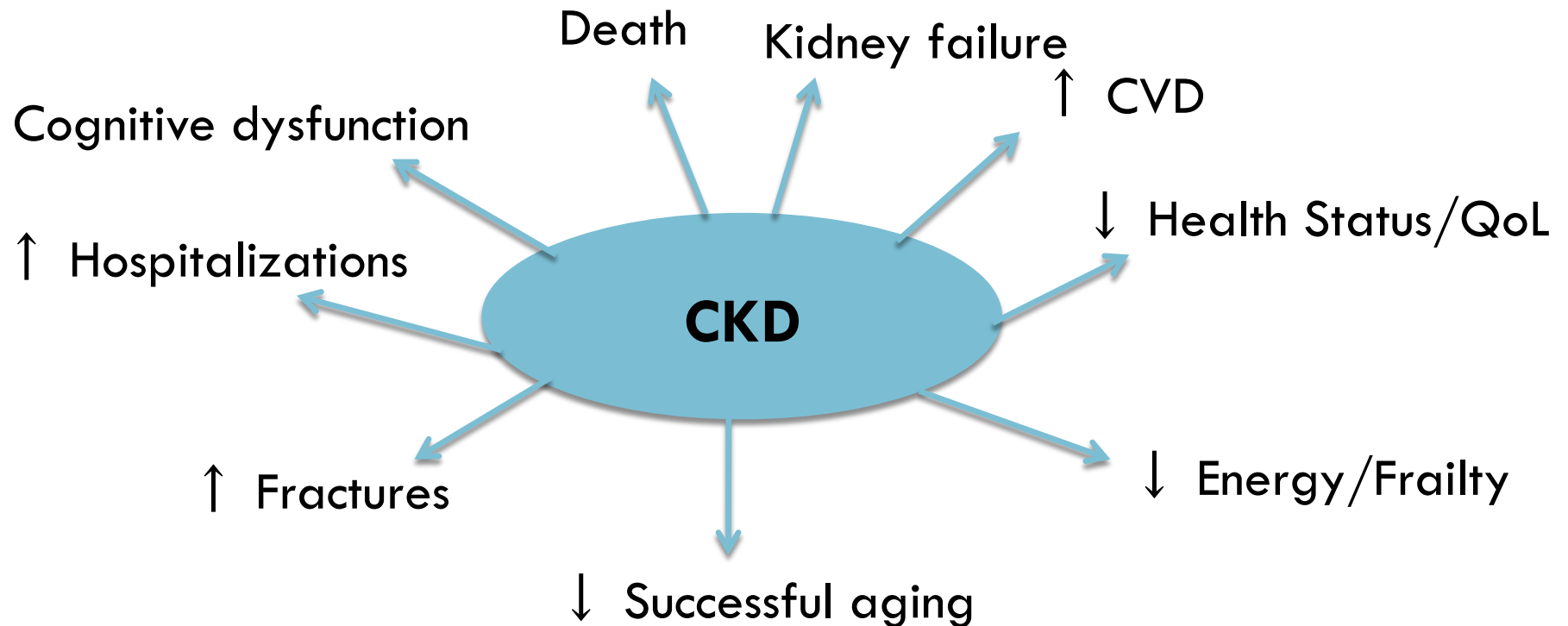
Age and CKD in General Population

NHANES 1999-2004



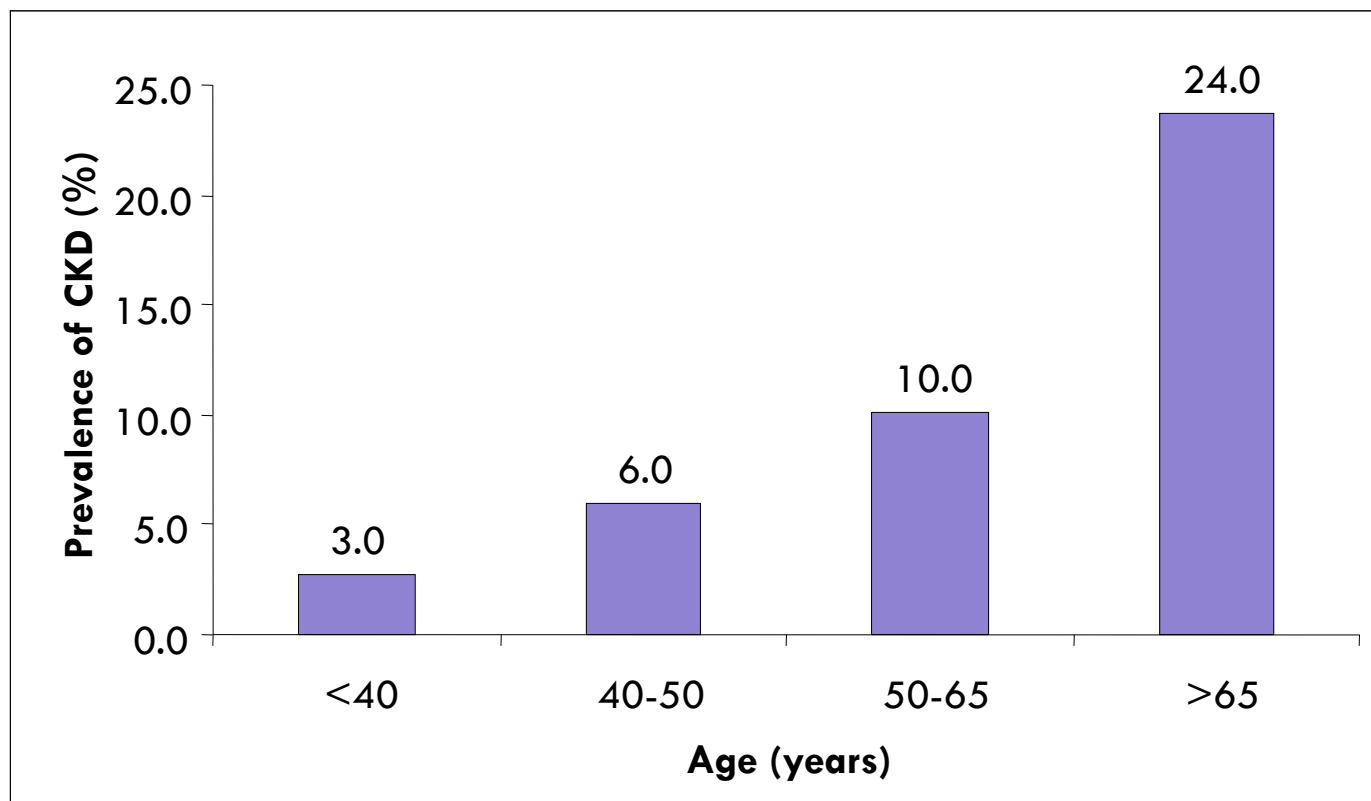
Coresh J et al. JAMA 2007

CKD and Complications in General Population



Age and CKD in the HIV Population

VA Registry



CKD and Cardiovascular Disease in VA Registry (N= 17,264)

7%- eGFR < 60

31%- proteinuria

Risk of Adverse Cardiovascular Outcomes (HR; 95% CI)				
	Normal N=11,420	Proteinuria N=4,650	eGFR < 60 N=395	Both N=799
Cardiovascular Disease N= 833 events				
Multivariate Adjusted*	1.0 (ref)	1.35 (1.15 - 1.59)	1.61 (1.19 - 2.18)	2.62 (2.13 - 3.20)
Heart Failure N= 377 events				
Multivariate Adjusted*	1.0 (ref)	2.54 (1.94 - 3.33)	3.86 (2.45 - 6.06)	8.63 (6.50 - 11.47)

Multivariable-adjusted models control for age, sex, race, and time-updated hypertension, diabetes mellitus, chronic obstructive lung disease, dyslipidemia, smoking, CD4 count, HIV viral load, ART. "Normal" defined as albuminuria level 0 mg/dL with an eGFR 60 mL/min per 1.73 m². "Both conditions" defined as an eGFR 60 mL/min per 1.73 m² with an albuminuria level 30 mg/dL.

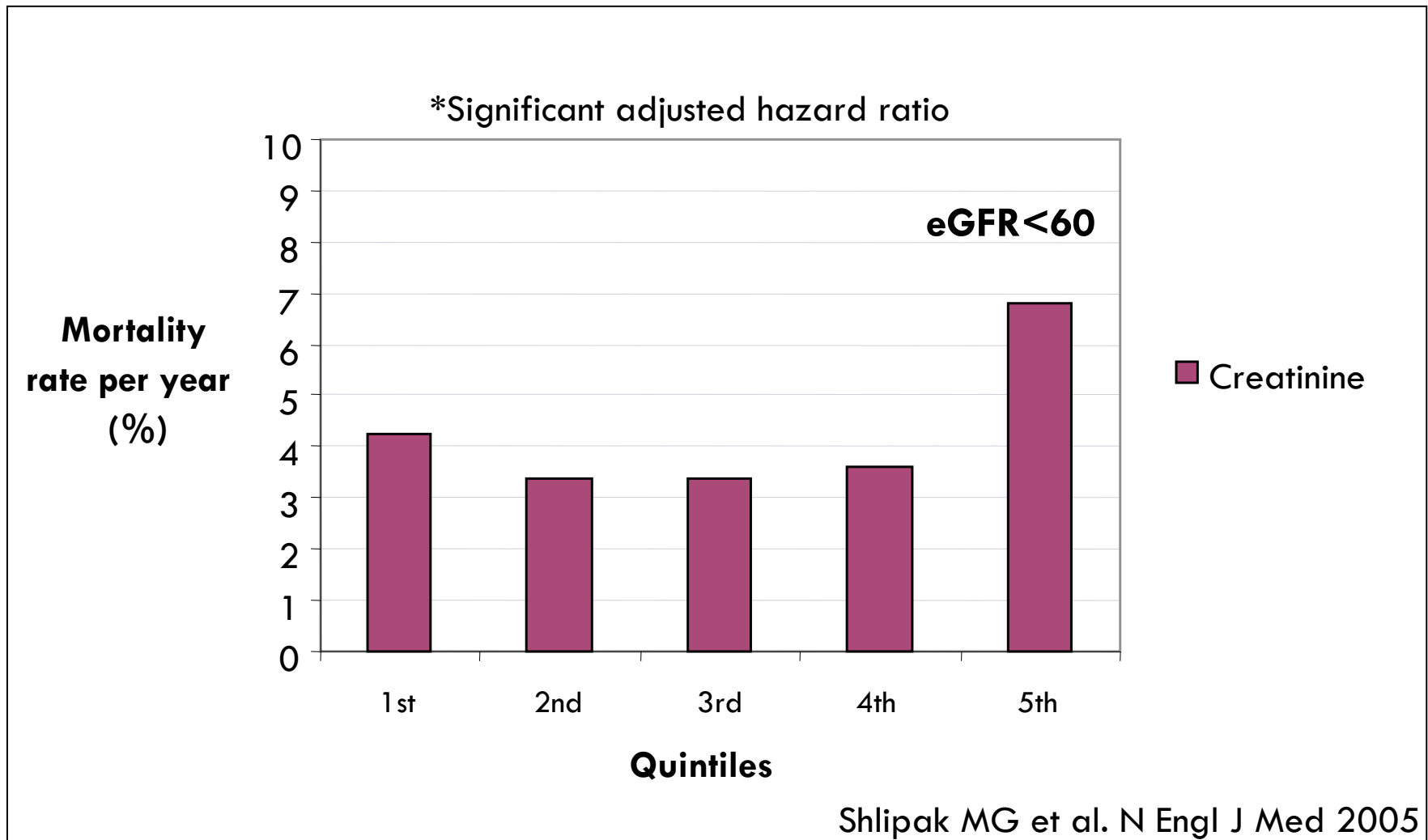
Choi AJ et al. Circulation 2010

Cystatin C

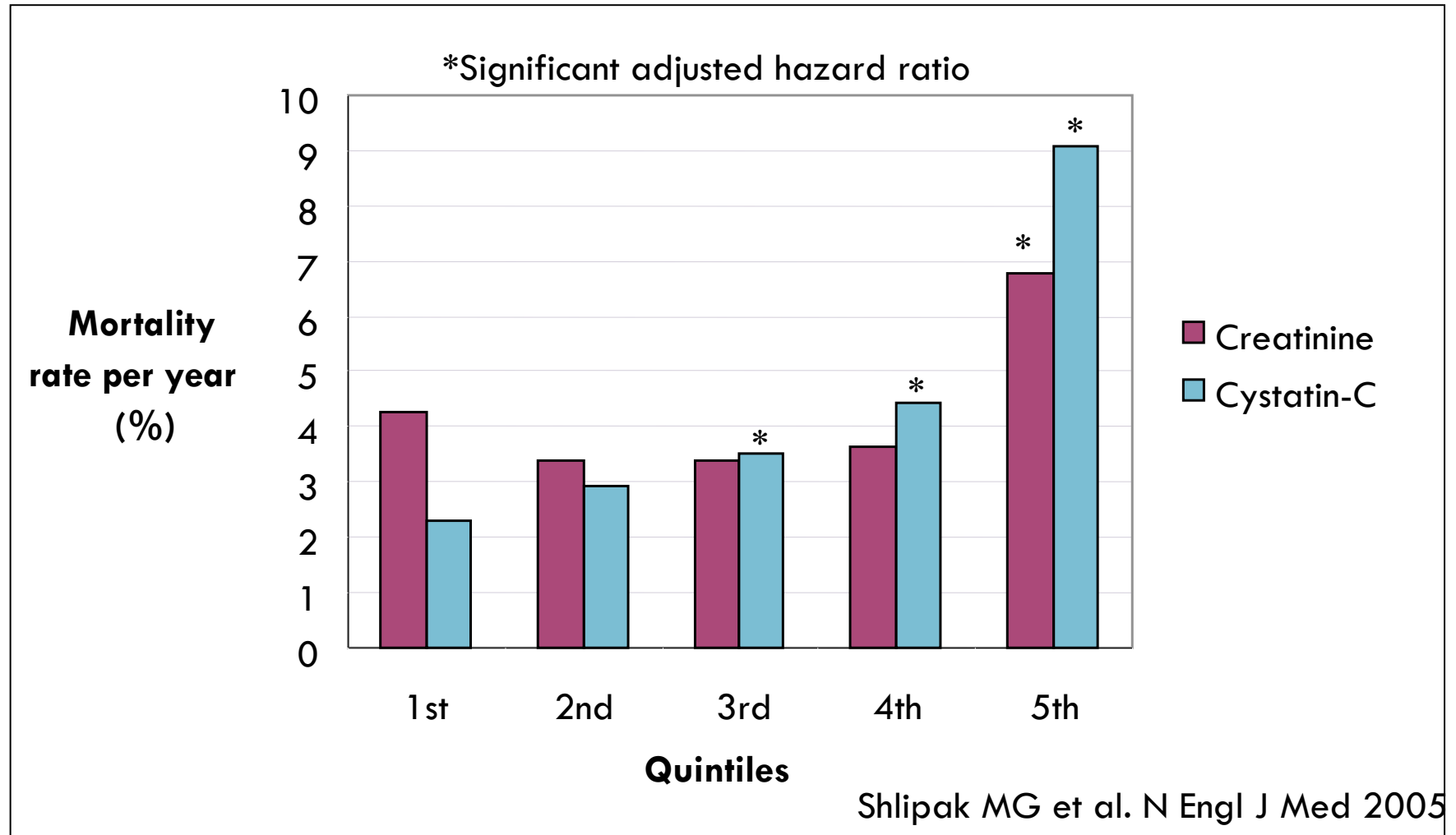


- Cystatin C is an alternate test of kidney function
- Unlike creatinine, not related to muscle mass so has advantages in elderly and HIV population
- FDA approved, widely available, but rarely used clinically
- To understand prevalence and outcomes of kidney disease in elderly and HIV, we need to add cystatin C

Creatinine Quintiles and Mortality Risk

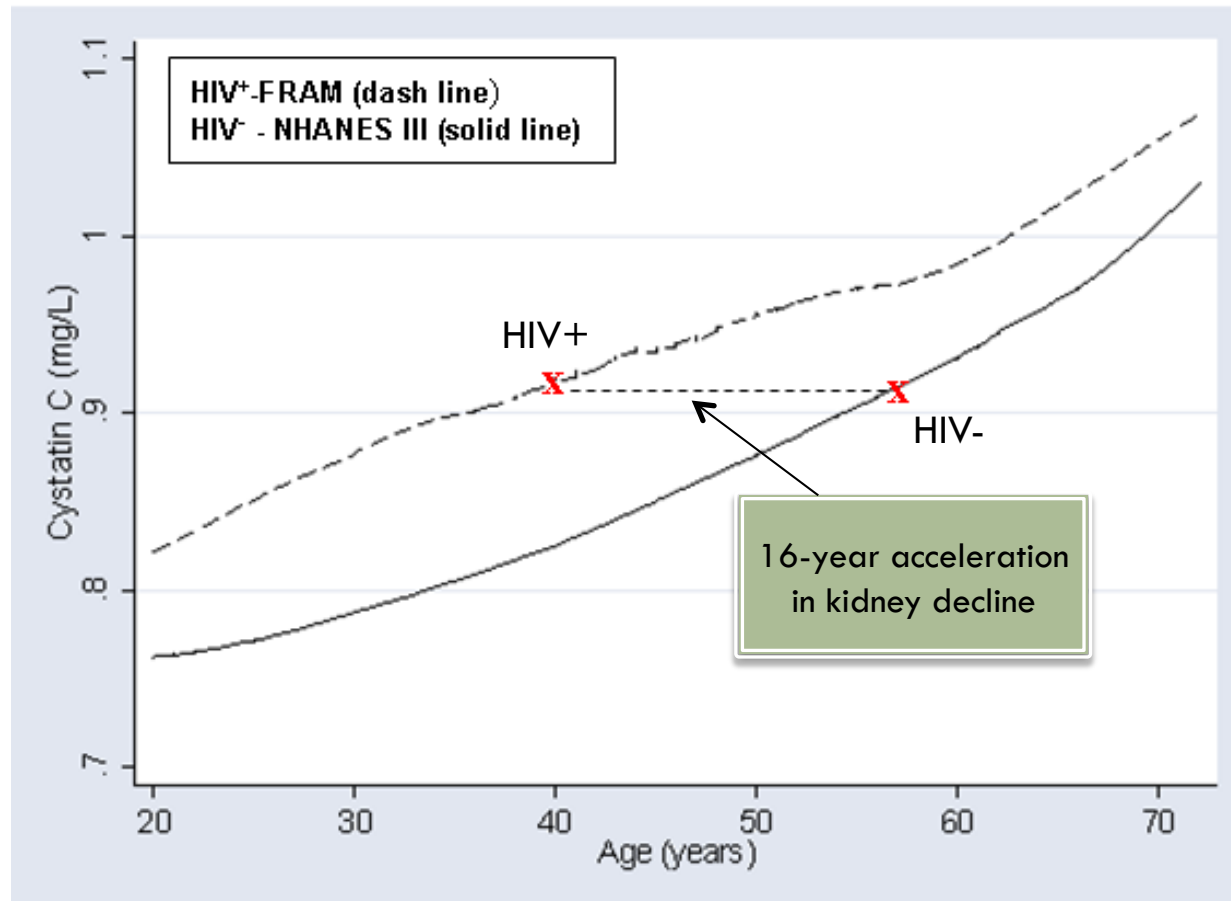


Cystatin C Quintiles and Mortality Risk



Kidney Disease Accelerated in HIV

FRAM, NHANES Comparison of Cystatin C

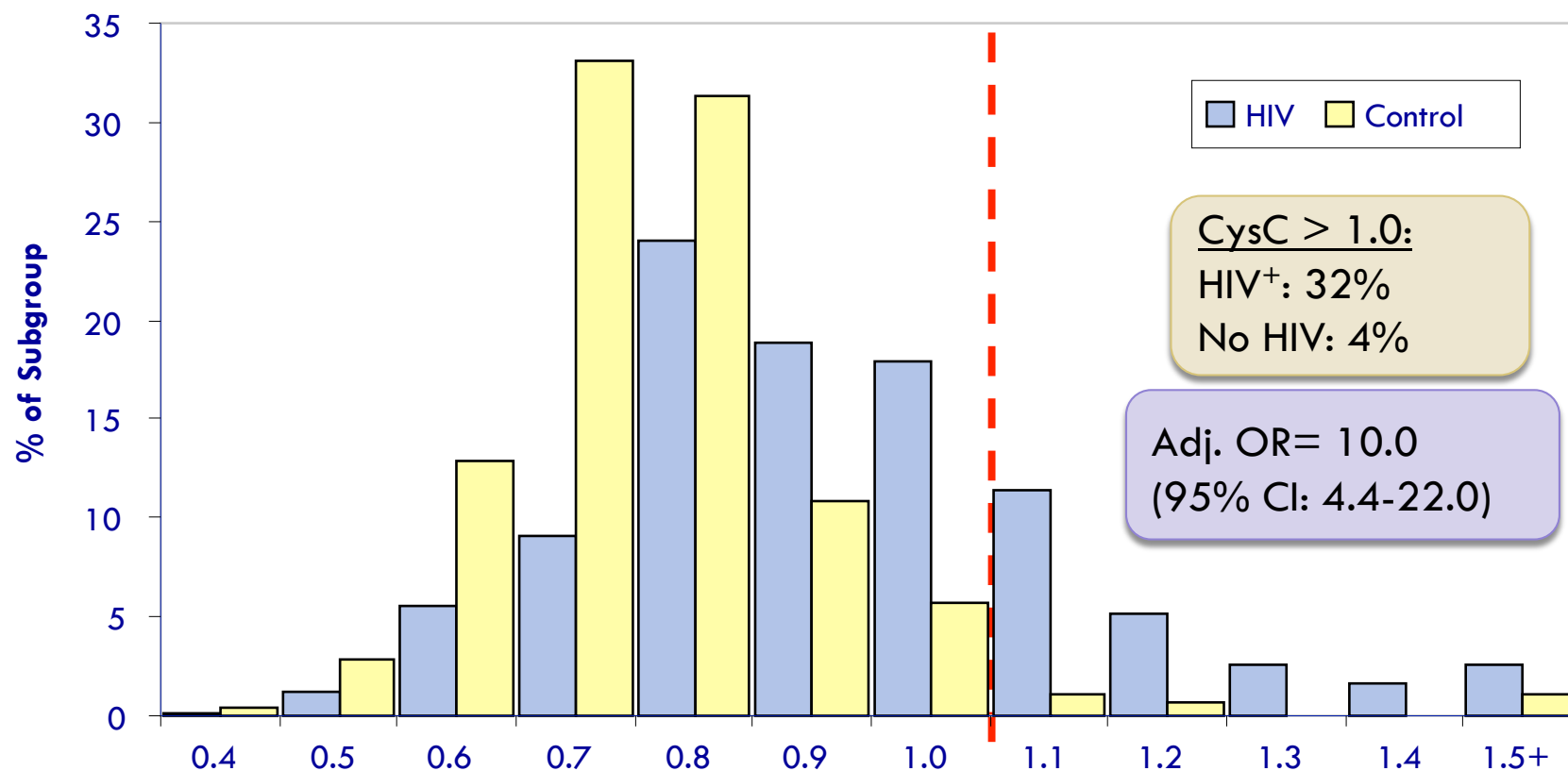


Kidney Function in HIV vs. Controls

FRAM Study

	Mean $\pm$ SD		p-value
	HIV (n = 519)	Control (n = 290)	
Creatinine (mg/L)	0.87 $\pm$ 0.21	0.85 $\pm$ 0.19	0.35
eGFR (ml/min/1.73m ²)	110 $\pm$ 26	106 $\pm$ 23	0.06
Cystatin C (mg/dL)	0.92 $\pm$ 0.22	0.76 $\pm$ 0.15	<0.001

Distribution of Cystatin C in HIV and Control Patients in FRAM



Adjusted for sex, age, ethnicity, tobacco use, hypertension, diabetes; systolic blood pressure, glucose, HDL, LDL, triglyceride, C-reactive protein, and uric acid levels, BMI, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use; albumin-creatinine ratio, proteinuria, current illicit drug use and total lean body mass

What Do These Findings Mean?



- HIV-infected persons have elevated cystatin C, but similar creatinine levels compared with HIV- persons.
- This implies either:
 - a) epidemic of unrecognized kidney disease in HIV
 - b) cystatin C levels biased and not useful in HIV
- To date, only very small GFR studies completed in HIV

Kidney Function and Mortality in HIV Infection

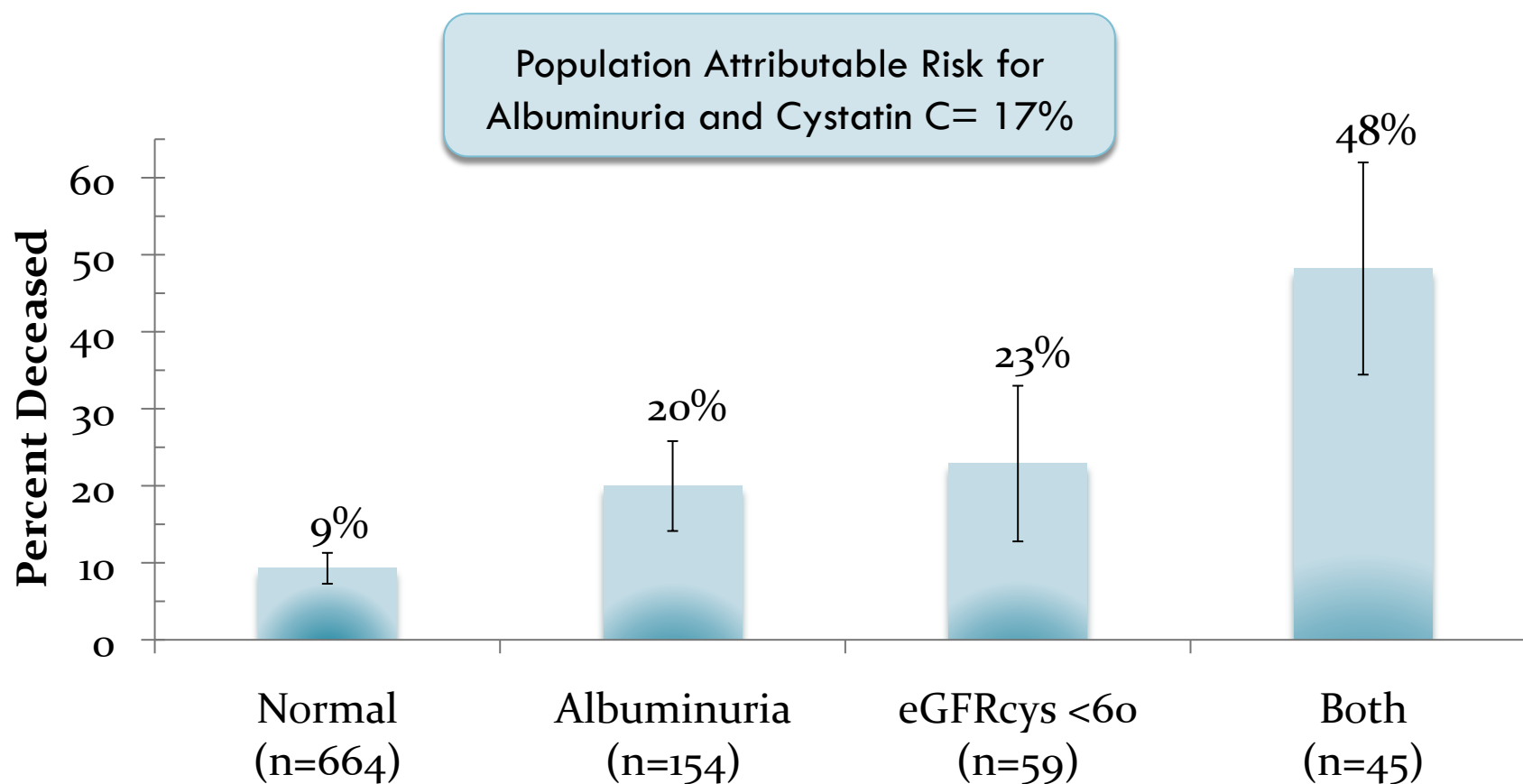


- 5 years of follow-up of FRAM for mortality
- Comparison of cystatin C and creatinine with mortality risk
- Albuminuria and mortality

Creatinine, cystatin C, and Albuminuria with Mortality

	N (%)	Adjusted Odds Ratio
Linear eGFR _{cr} (per 10 ↓)		1.05 (0.95, 1.15)
Linear eGFR _{cys} (per 10 ↓)		1.20 (1.09, 1.32)
CKD (eGFR<60) by Creatinine	46 (5%)	1.40 (0.60, 3.20)
CKD (eGFR<60) by Cystatin C	104 (11%)	2.30 (1.30, 3.80)
Albuminuria	199 (22%)	2.20 (1.30, 3.70)

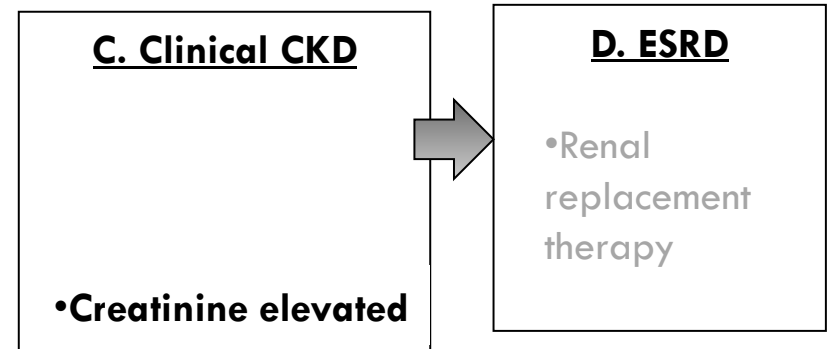
5 Year Mortality Risk by Cystatin C and Albuminuria Categories



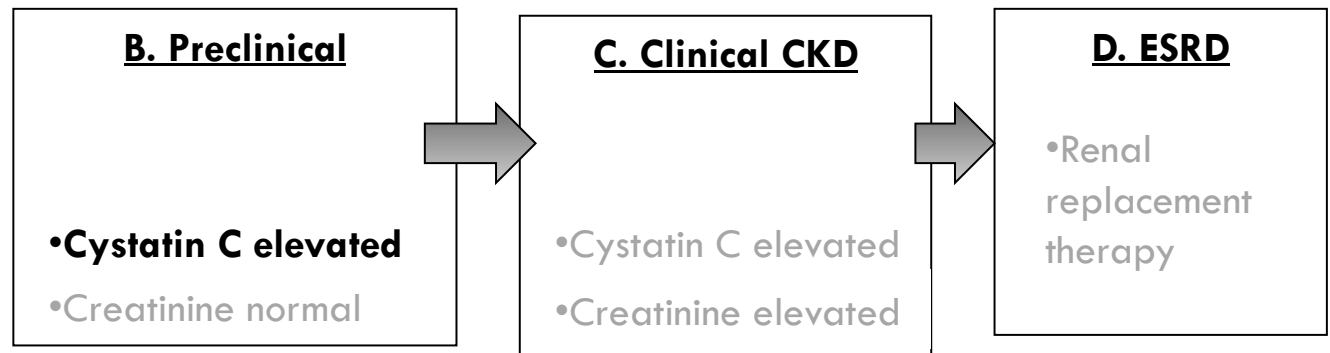


Future Directions in Aging Kidney Research

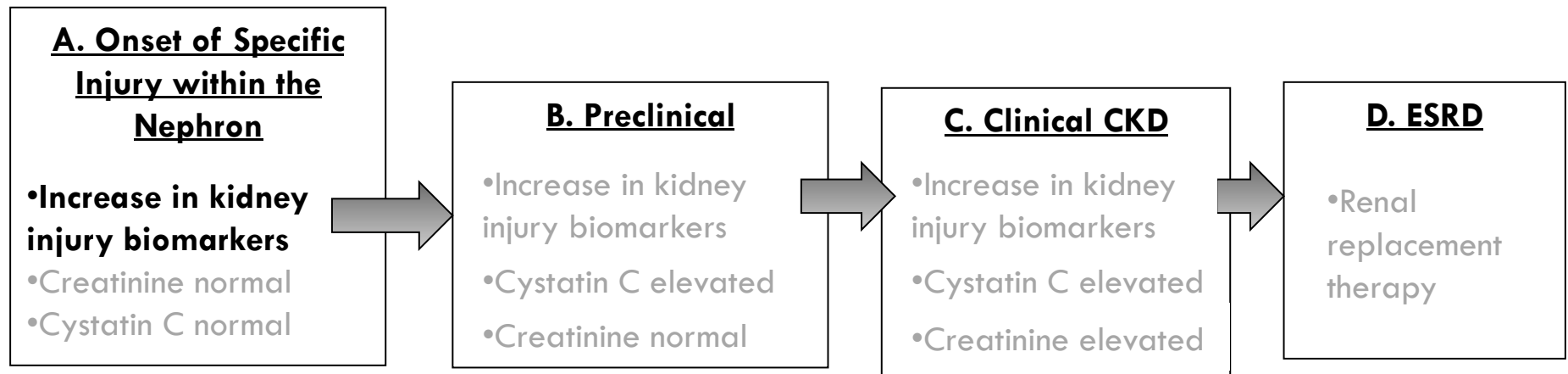
Our Framework/Paradigm



Our Framework/Paradigm



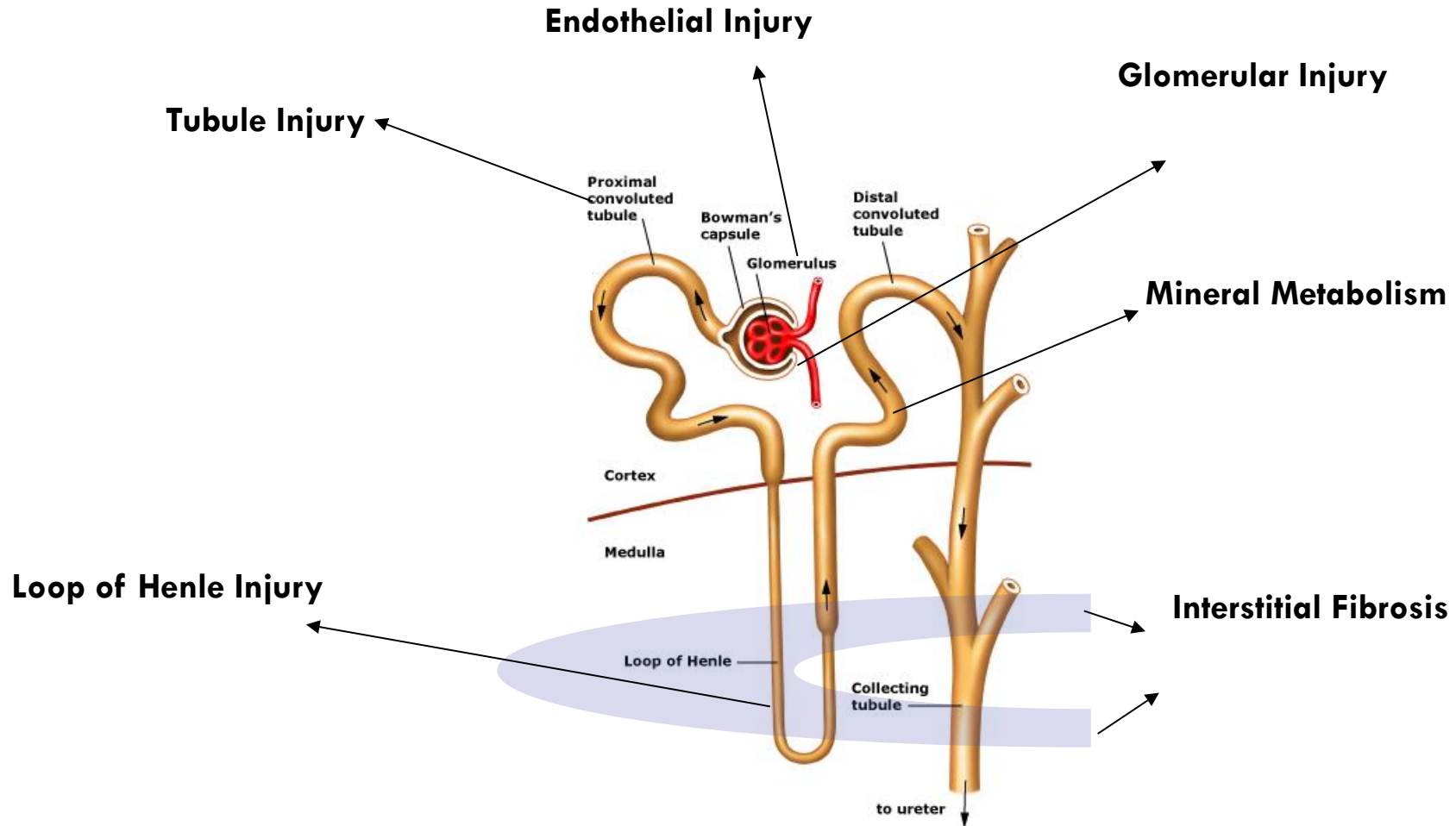
Our Framework/Paradigm



Novel Markers of Kidney Injury

A Non Invasive Kidney Biopsy?

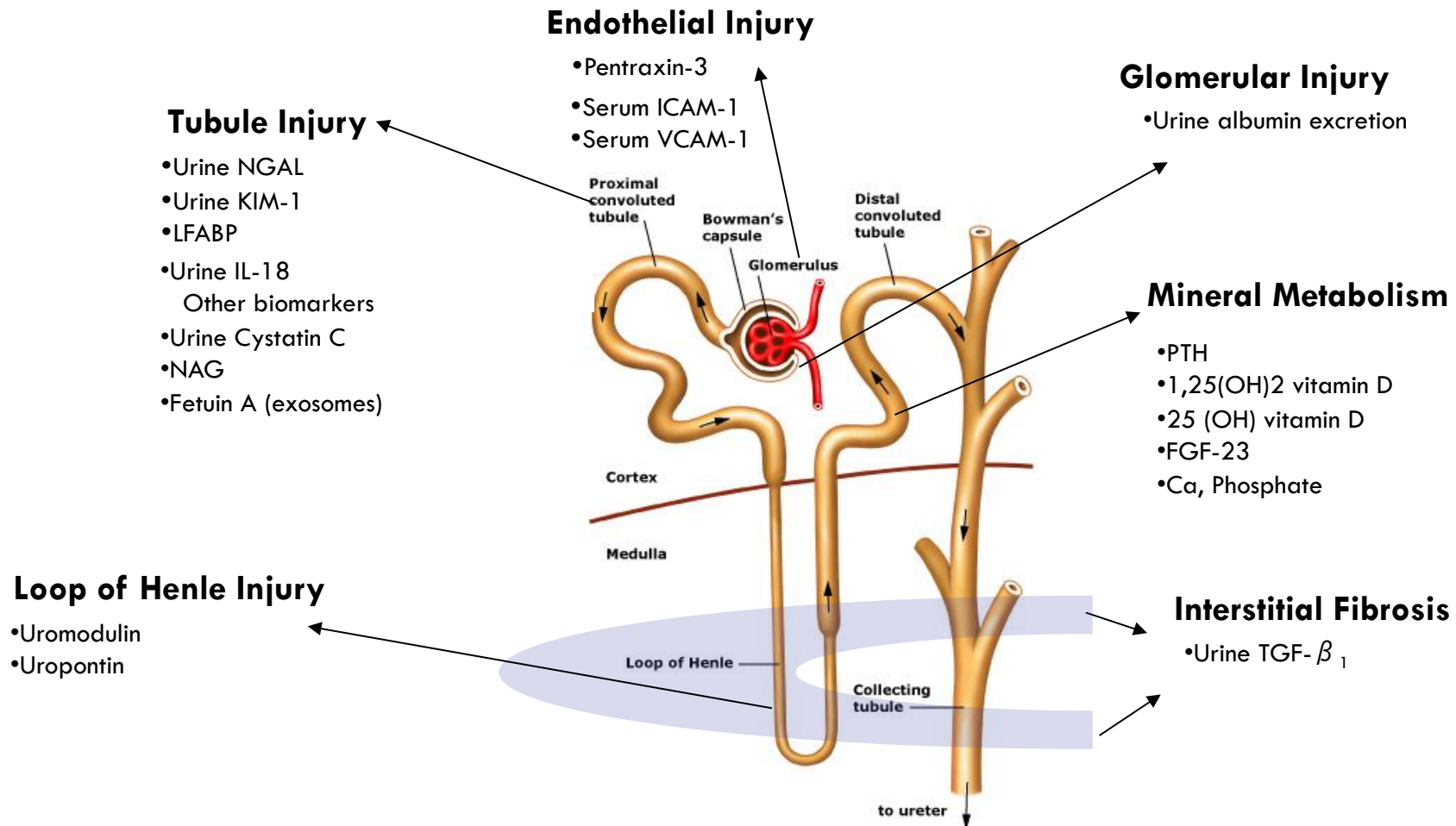
NIA-funded R01: The Aging Kidney in HIV-Infection: Biomarkers for early detection of injury (PI-Shlipak)



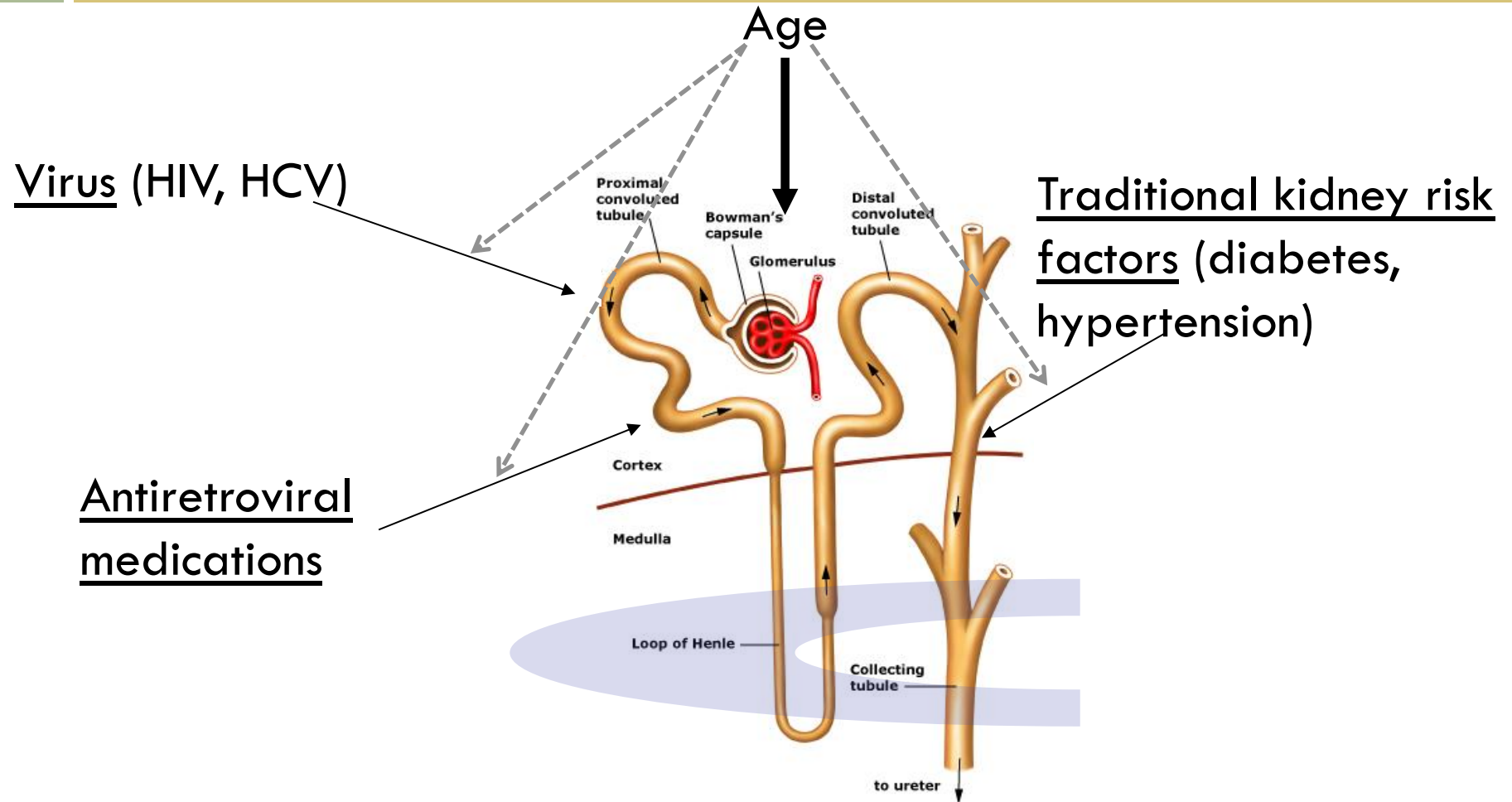
Novel Markers of Kidney Injury

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Determinants of Kidney Injury in HIV



Future Directions for Aging Kidney Research



- Biomarkers for detection of early injury- virus, medications, risk factors
- Clinical strategies for measuring kidney function- creatinine and/or cystatin C
- Risk/benefit trade-off of medications
- Understand health consequences of CKD in HIV population- beyond cardiovascular disease, ESRD, and death

Acknowledgements



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