Hennepin Healthcare

Improving ADRD outcomes by preventing or treating comorbidities:

Chronic Kidney Disease

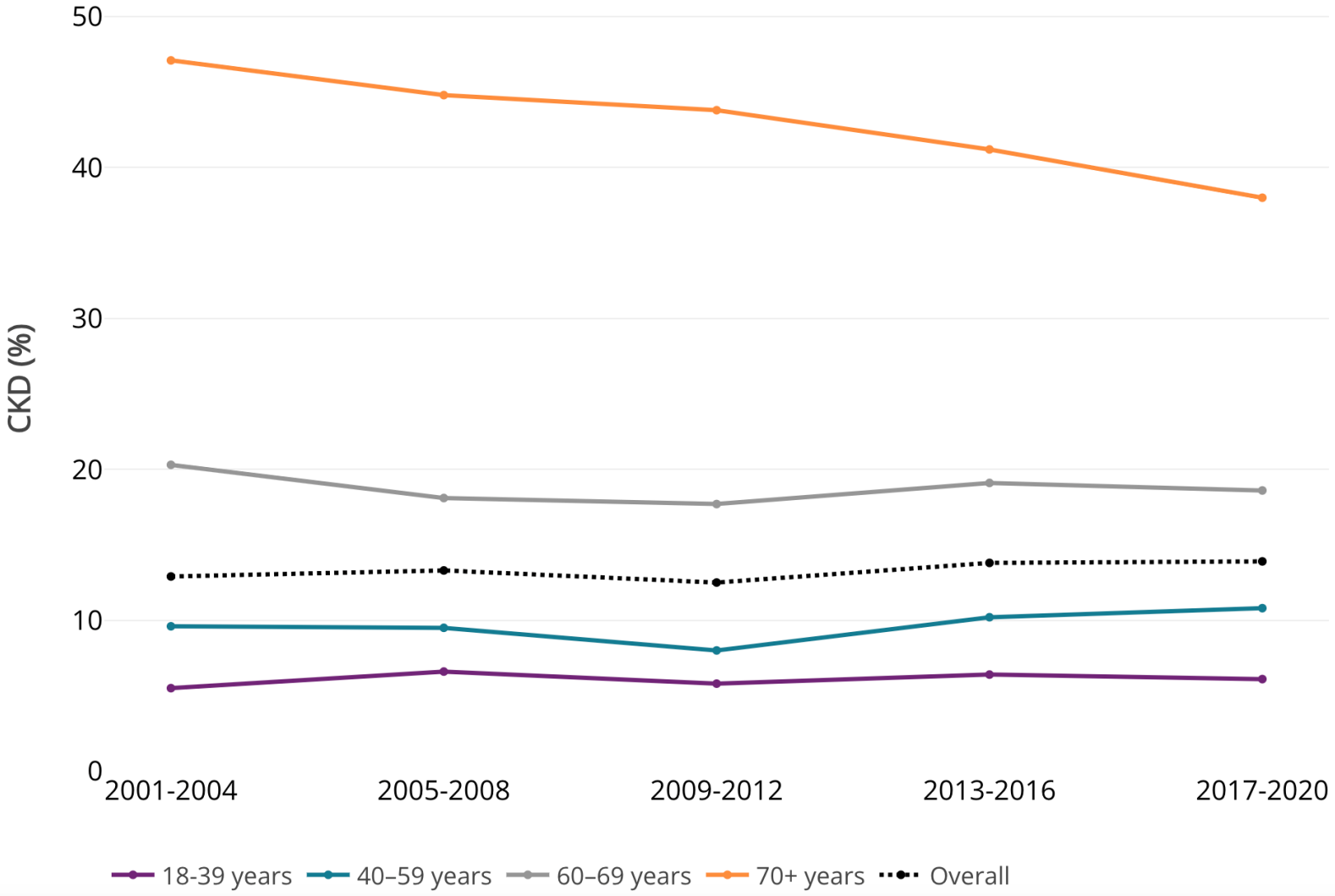
Kerry Sheets, MD, MS

Geriatric Medicine

Disclosures

- Current Funding:
  - Minnesota Center for Learning Health Systems Sciences, University of Minnesota Medical School and School of Public Health (funded by AHRQ)
  - NIA
  - ADACC
  - Minnesota Partnership for Biotechnology and Medical Genomics
- Other financial relationships: None
- Conflicts of interest: None

Chronic Kidney Disease (CKD) is common



(CDC Kidney Disease Surveillance System)

Chronic Kidney Disease (CKD) Stages

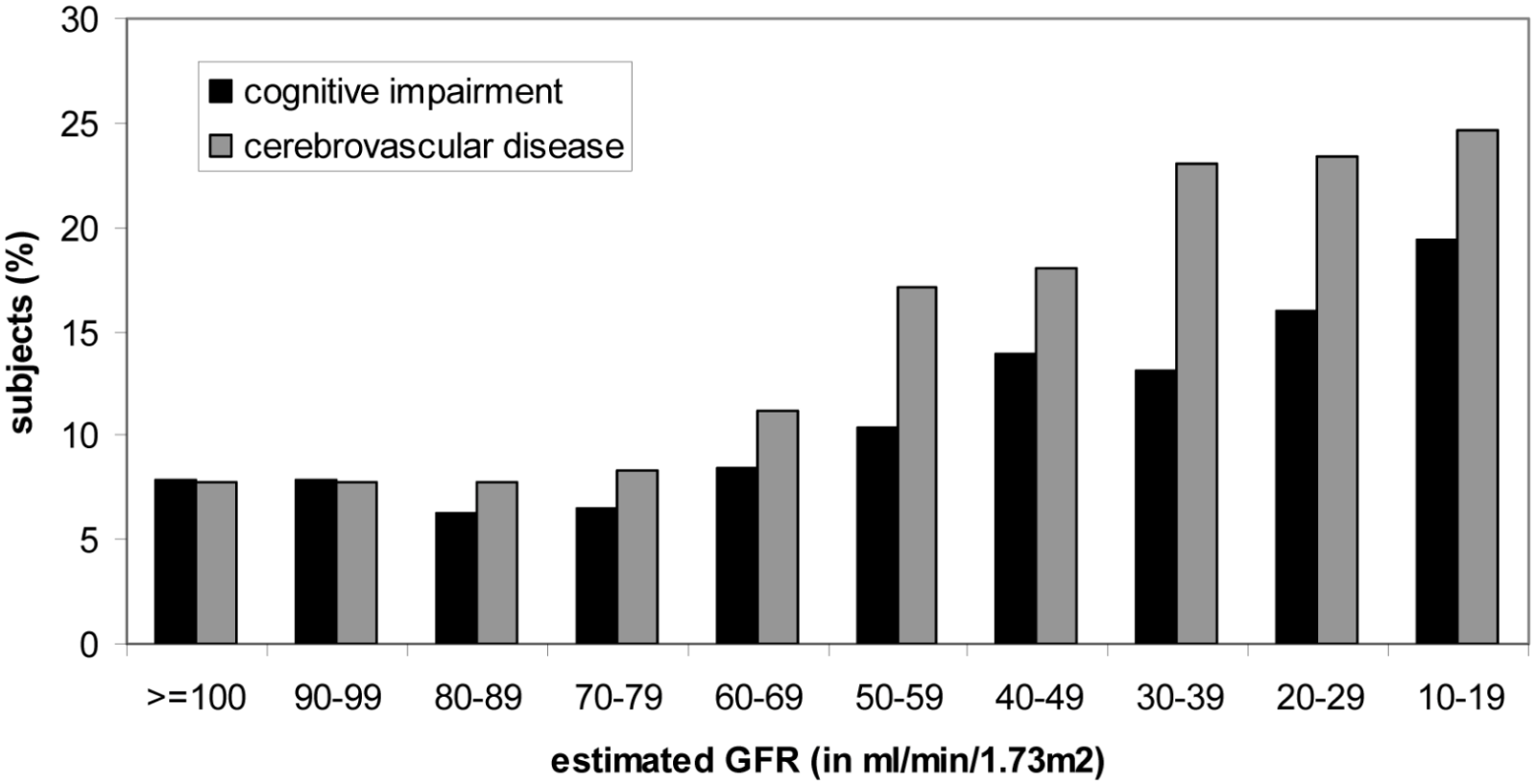
- Abnormalities in kidney structure or function present for > 3 months
- Classified by cause, GFR category, and albuminuria
- Most common causes: Diabetes and hypertension

KDIGO: Prognosis of CKD by GFR and albuminuria categories

GFR categories (ml/min/1.73 m²) Description and range			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
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			

(KDIGO CKD work group *Kidney Inter* 2024;105(4S))

Reduced eGFR is a risk factor for CI



(Fig 3 in Kurella-Tamura et al. *Am J Kidney Dis* 2008;52(5))

Albumineria is also a risk factor for CI

Chronic kidney disease biomarkers, cognitive impairment and incident dementia in an older healthy cohort

Kidney360

Methods

Longitudinal Cohort
ASPREE trial population

eGFR
Creatinine CKD-EPI mL/min/1.73m2

Albuminuria
albumin-to-creatinine ratio UACR mg/mmol (mg/g)

Cognitive Tests

No prior Cardiovascular Disease, Dementia or physical disability

Baseline

Population
n= 18,131

Median

74 *Years*

74 *ml/min/1.73m2* *IQR (63 to 84)*

0.8 *mg/mmol* *IQR (0.5-1.5)*

7.1 *mg/g* *IQR (4.4-13.3)*

Follow-up of 4.7 years

Baseline eGFR

cross-sectional analysis

Not associated with
- Performance on any cognitive tests
- NO incident CIND* or dementia

Baseline Albuminuria UACR **If ≥ 3 mg/mmol 26.6 mg/g**

Associated with

Incident CIND*
HR 1.19
1.07-1.33

Dementia
HR 1.32
1.06-1.66

**CIND: Cognitive Impairment No Dementia*

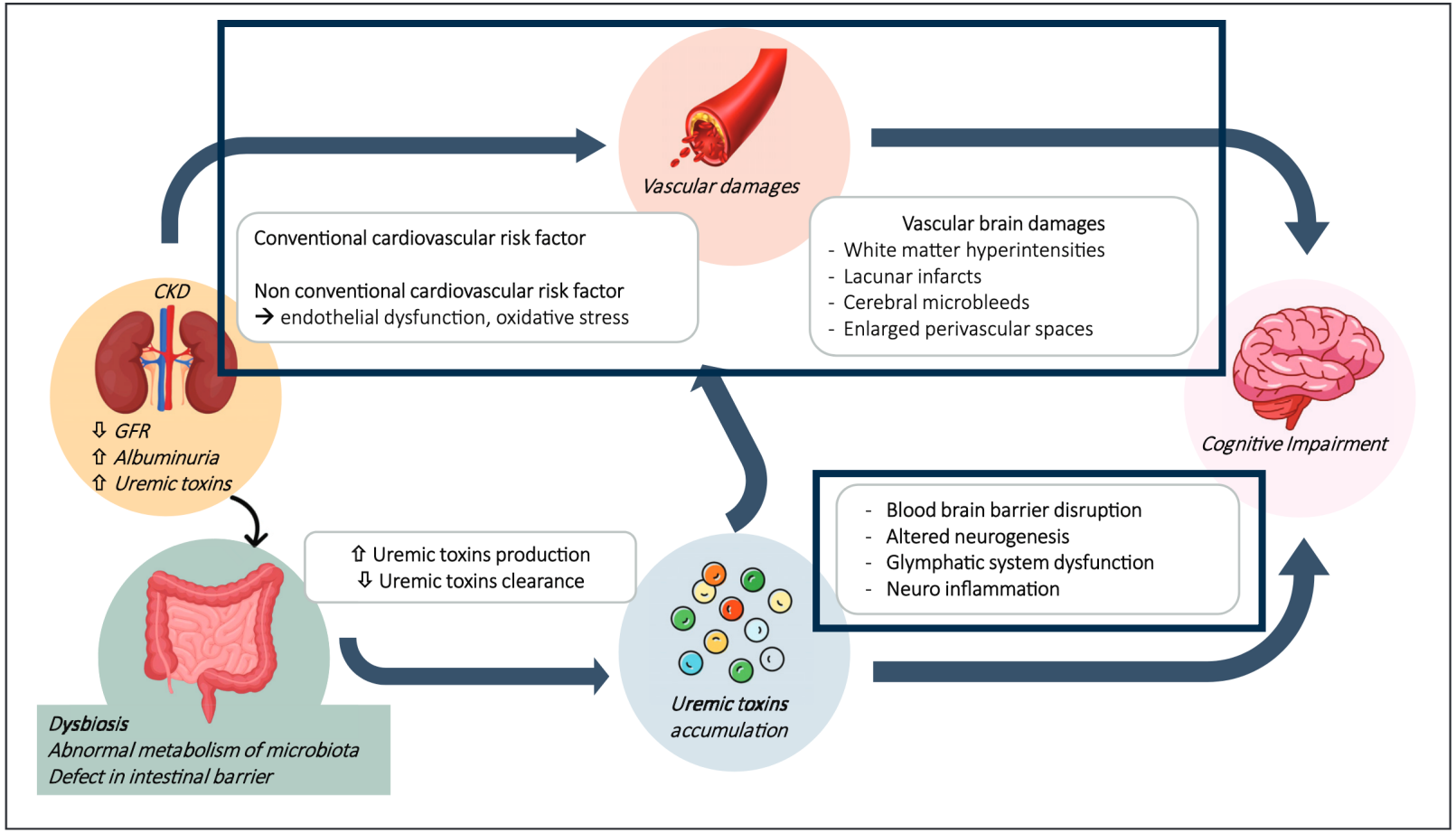
Conclusions: Mild albuminuria was associated with worse baseline cognitive function, cognitive decline, and increased risk for incident CIND and dementia. Screening global cognitive tests for older persons with UACR ≥ 3 mg/mmol could identify those at elevated risk of cognitive decline and dementia.

disease biomarkers, cognitive impairment and incident dementia in an older healthy cohort. *Kidney360.* DOI: 10.34067/KID.0005672021

Visual Abstract by Verner Venegas

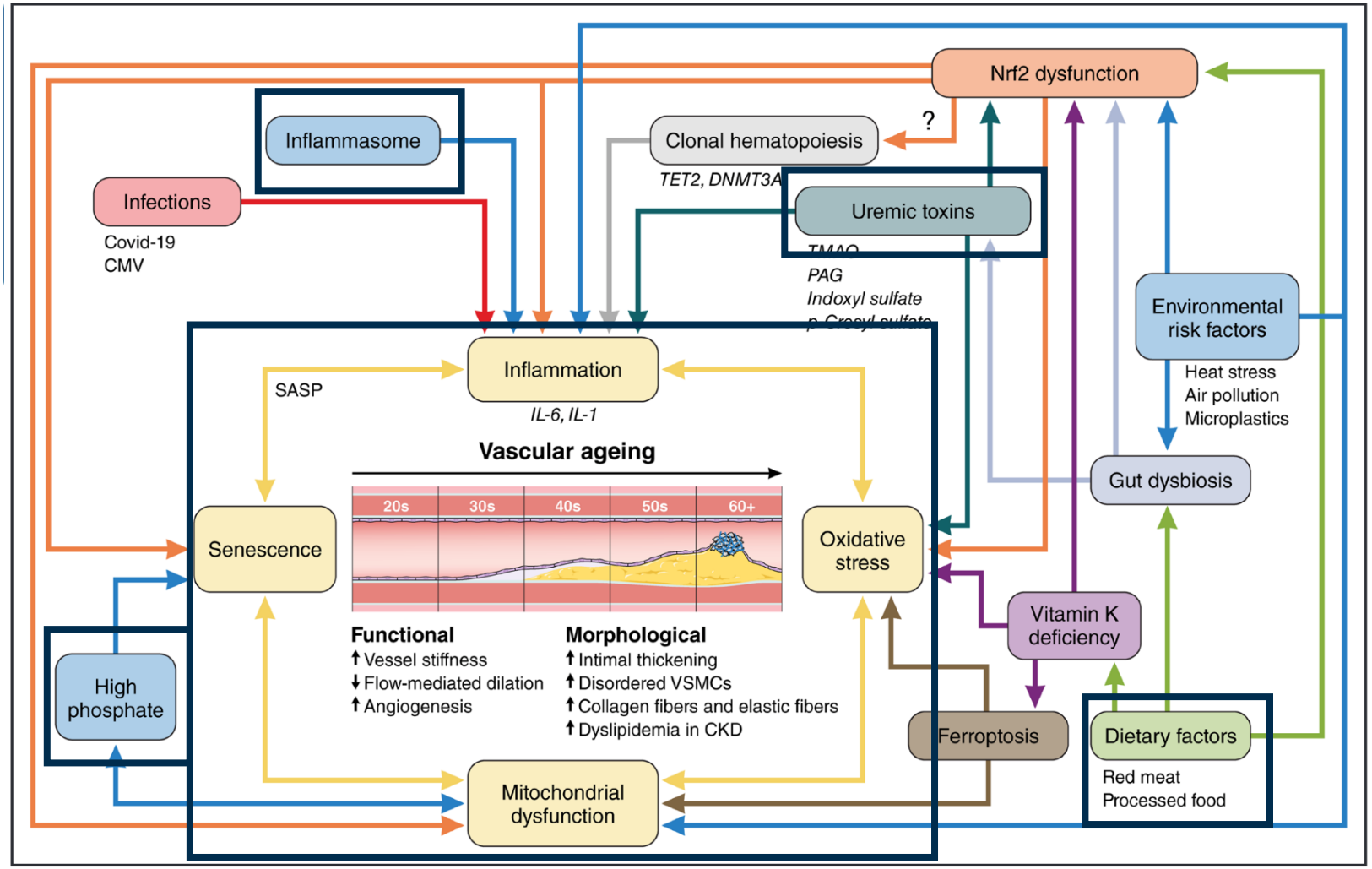
HennepinHealthcare

Mechanisms of CI in CKD



(Fig 1 in Pepin et al. *Curr Opin Nehprol Hypertens* 2024;33(6))

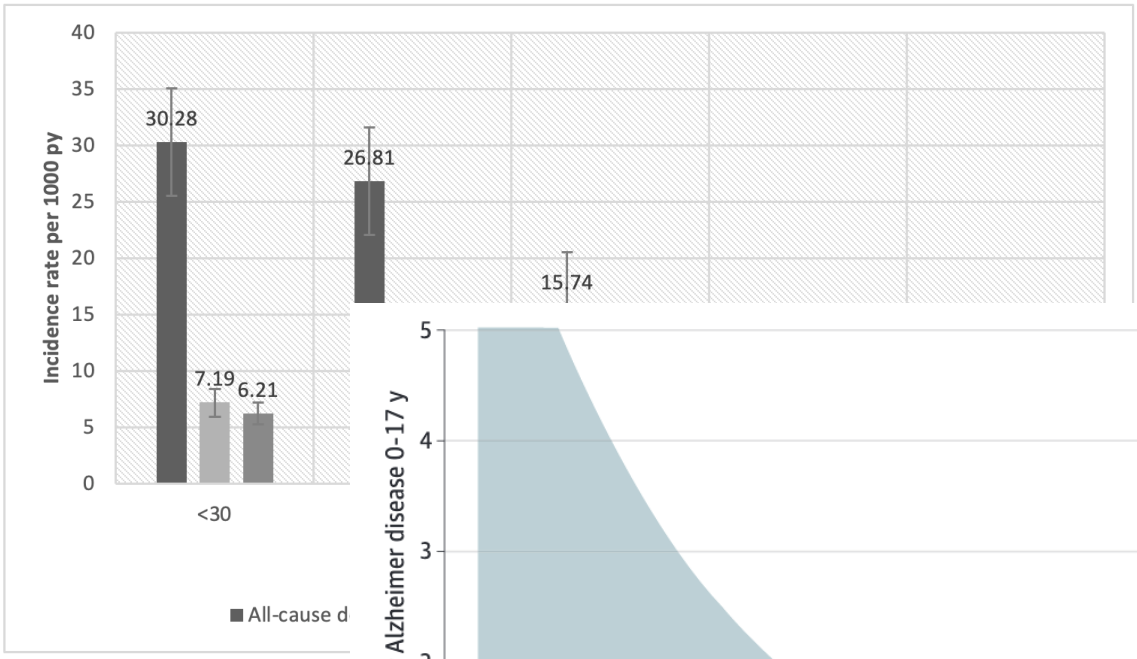
CKD as a model of accelerated vascular aging and CI

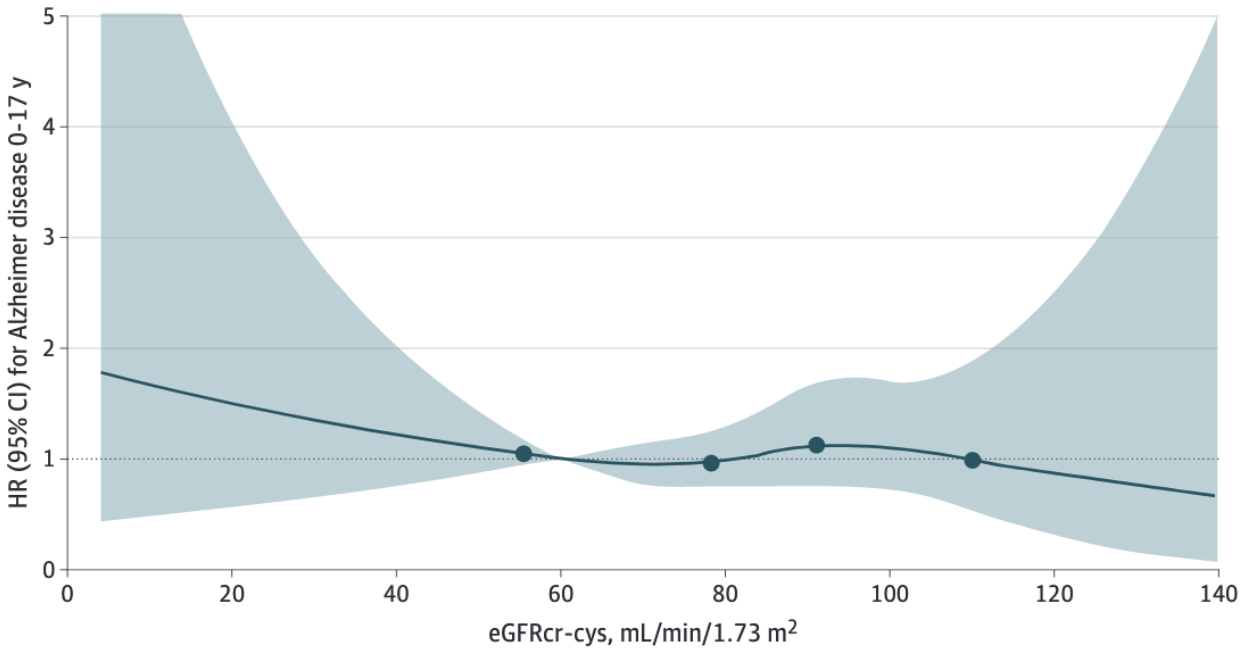


HennepinHealthcare

(Fig 6 in Hobson et al. *Circulation Research* 2023;132))

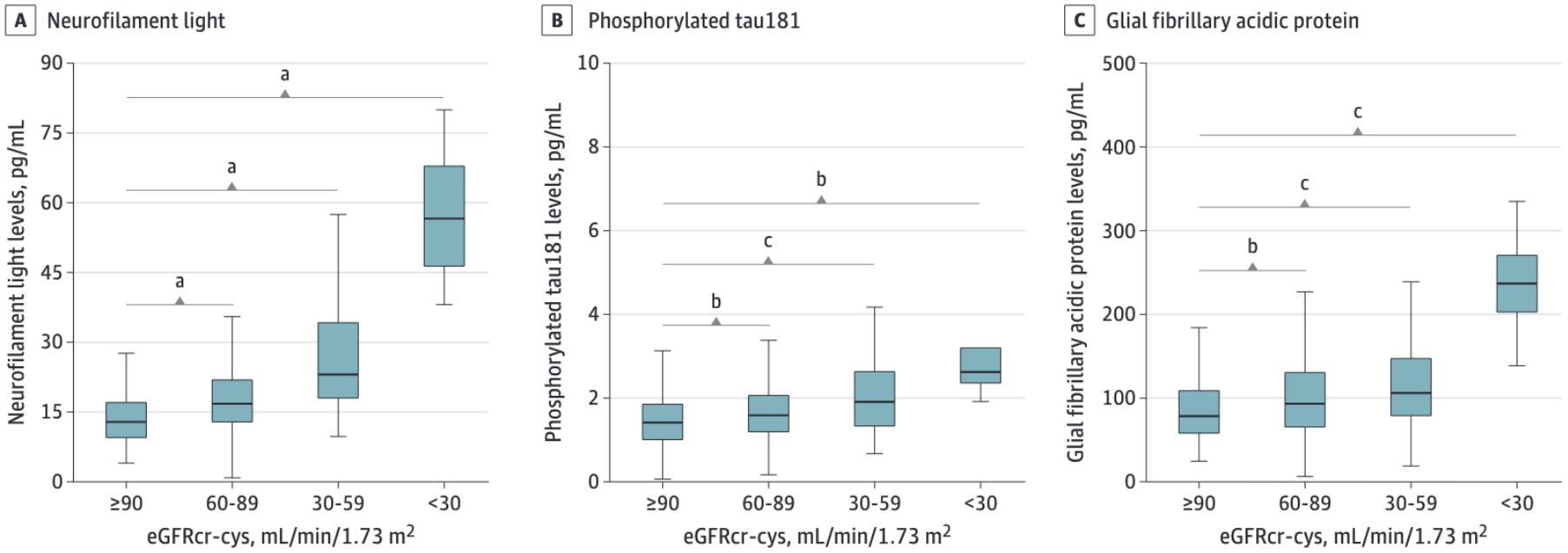
CKD is not clearly associated with AD





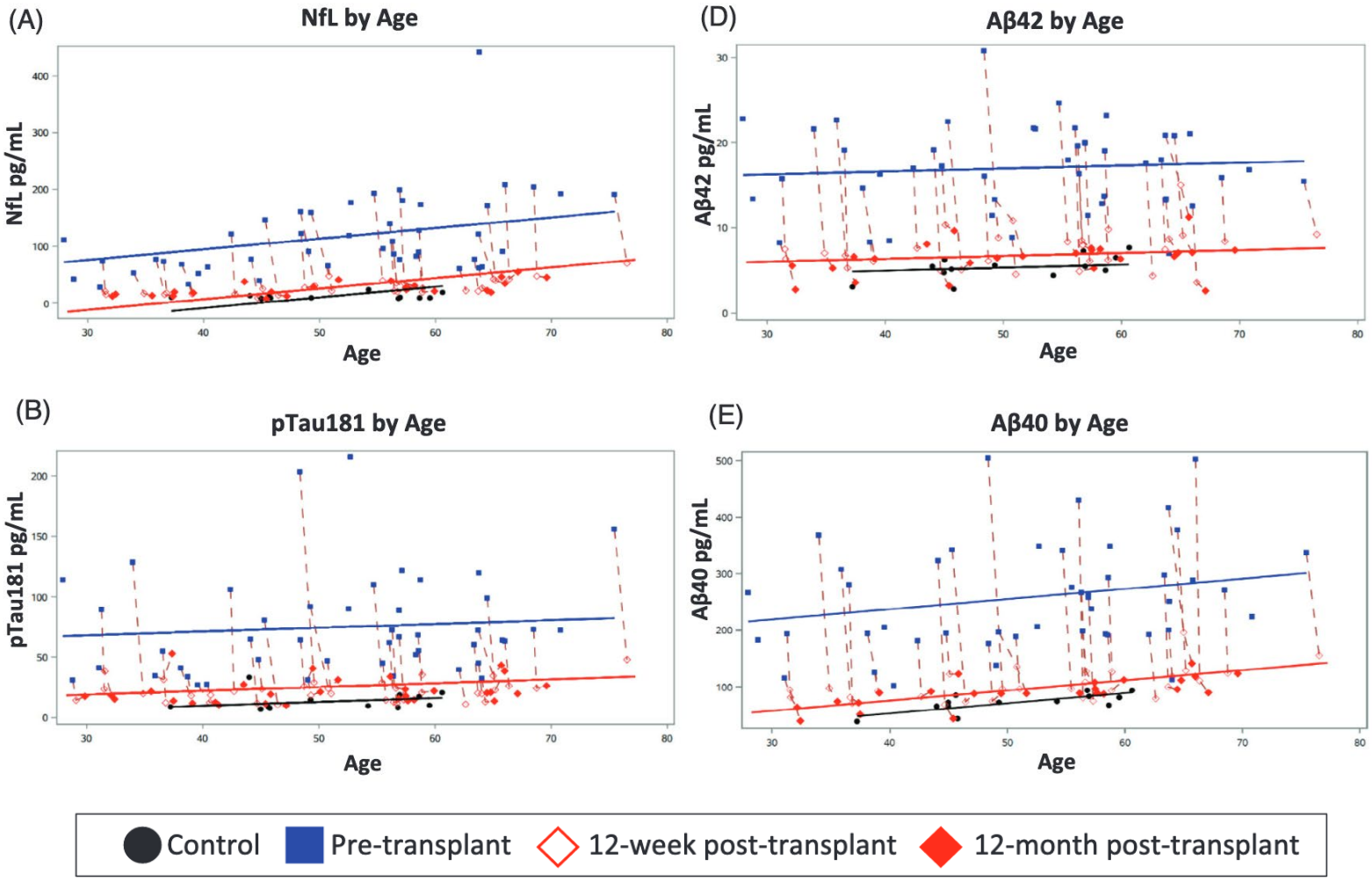
(Supp Fig 2 Xu et al. Neurology 20201;96
Fig 1b in Stocker et al. *JAMA Open* 2023;6(1))

CKD is associated with elevated levels of AD blood-based biomarkers



(Fig 2 in Stocker et al. *JAMA Open* 2023;6(1))

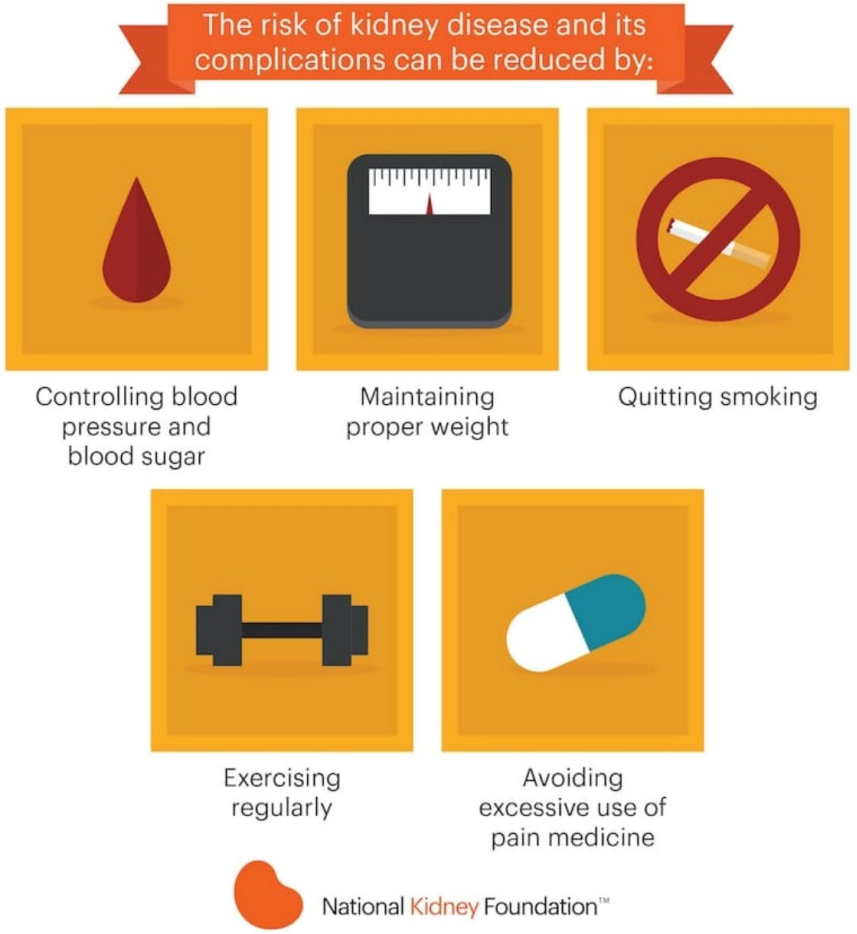
Levels of AD biomarkers decrease after kidney transplant



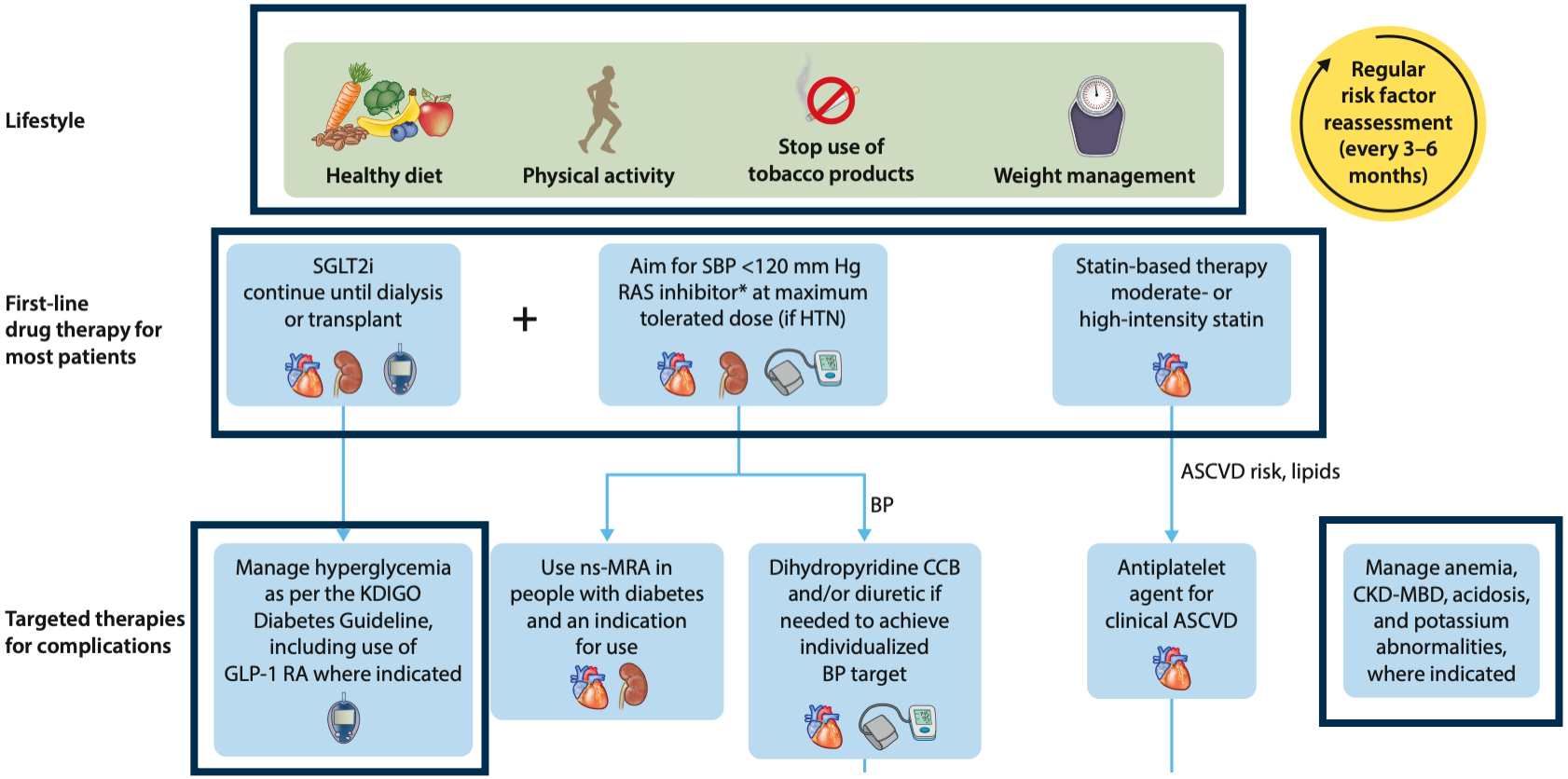
(Fig 1 in Blankenship et al. *Alzheimer's Dement* 2024;e12614)

Improving ADRD outcomes by preventing CKD

- Encourage healthy behaviors
- Diagnose and treat diabetes and hypertension

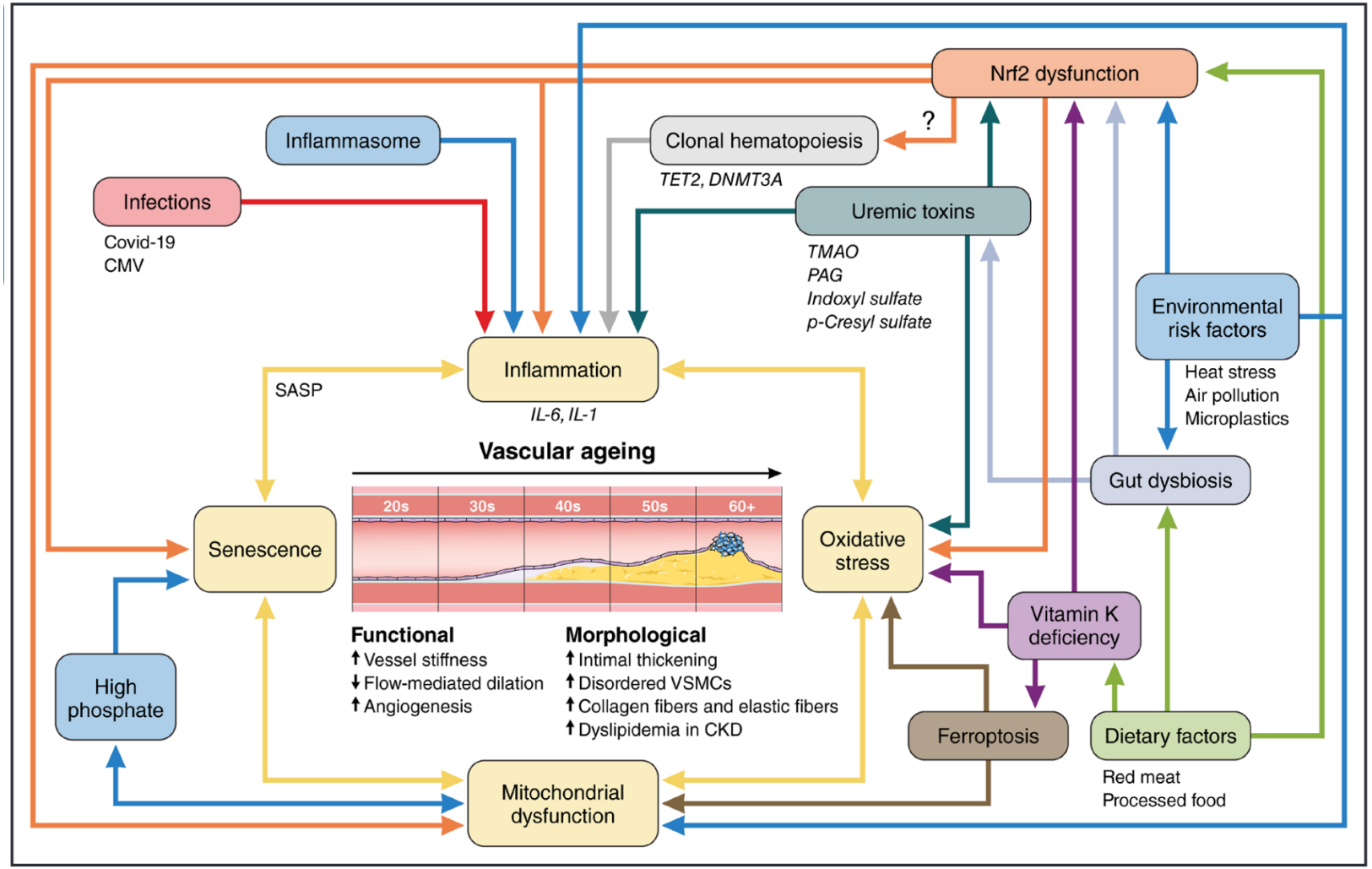


Improving ADRD outcomes by treating CKD



(Fig 18 in KDIGO 2024 Clinical Practice Guideline *Kidney Intern*;105 (45))

Goal = reduce accelerated vascular aging



HennepinHealthcare

(Fig 6 in Hobson et al. *Circulation Research* 2023;132))

Hennepin Healthcare

Thank You!

Acknowledgements:
ADACC
Dr. Anne Murray