New AHA Cardiovascular-Kidney-Metabolic (CKM) Staging Solves All Our Staging Problems and Should Be Applied Universally: The Nephrology Perspective

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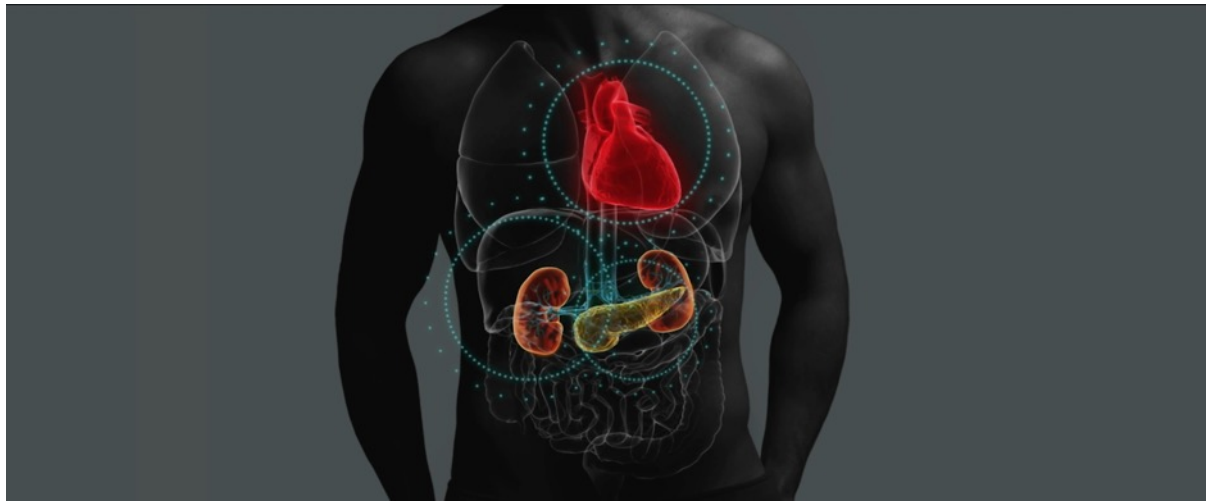


Disclosure and Perspectives

- Clinician
- Administrator
- Researcher
    - International collaborations
    - Clinical Trials : participation, execution, development and review
    - Steering Committees, Data Safety Monitoring Boards
    - Guideline methodology and development
    - CKD and CVD
    - Health systems research
    - Patient oriented research paradigms

Overview

- Perspectives
  - People living with kidney diseases
  - Nephrologists

- The purpose of staging systems
- Differentiating between Classification, Staging and Risk Prediction

- What problem are we solving?
- Towards Integrative frameworks

People with kidney disease(s) ….

Are Complicated

- Physiology
  Pathophysiology

- Drug reactions and interactions
  Differential drug binding

Have Complex interactions

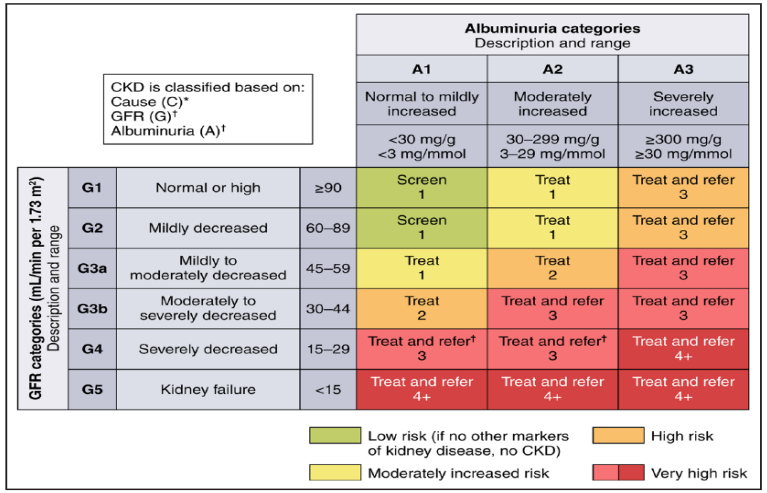
- See multiple specialists
- Take many medications
- Are anxious, depressed and overwhelmed
- Watch their numbers on the lab tests

Are Afraid of needing to start dialysis and…..

Nephrologists are …

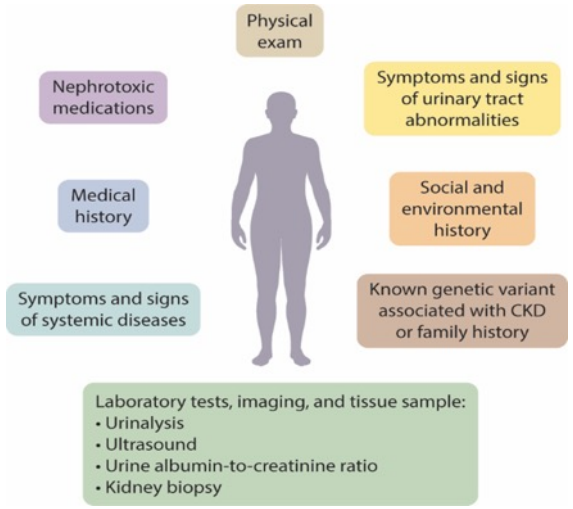
- Diverse group of specialists, interested in complex physiology
- Often Risk averse and conservative
- Worried about side effects of medications and understanding disease processes
- Accustomed to having lots of numbers
- Not accustomed to having a lot of trial data to inform decisions

Nephrologists have spent a long time …



CKD is classified based on: Cause (C)* GFR (G)† Albuminuria (A)†				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (mL/min per 1.73 m²) Description and range	G1	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3
	G4	Severely decreased	15–29	Treat and refer† 3	Treat and refer† 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Low risk (if no other markers of kidney disease, no CKD)
Moderately increased risk
High risk
Very high risk



- Developing and validating eGFR equations
- Developing and validating a staging system for CKD
- Emphasizing need for establishing cause of CKD
- Developing and validating risk prediction equations for different outcomes

The history and intention of 'staging'

- 1929 World Health Organization
  - introduced concept of describing disease by stage or extent
  - First applied to cancer
    - Cancer of cervix

- Purpose of Staging:
  - Common language to help medical professionals communicate information re: disease to others.
  - Diseases can be acute or chronic
    - Cancer, AID, CVD, RA...(CKD)

Staging Systems

- Essential tools in clinical medicine to provide valuable information for patient management and research

- Used across medicine to
  - measure disease severity,
  - estimate patient prognosis
  - determine eligibility for clinical trials and guide clinical care.

- Provide a model
  - natural history of a disease, and
  - framework to validate new biomarkers and test new interventions.

- Require ongoing efforts to standardize terminology contribute to better communication and understanding across the medical community

Definitions of Staging

- Shorthand method for describing disease.

- A coded format
  - e.g. numerical system with increasing values meaning more involvement or severity
  - Can facilitate electronic analysis of cases with similar characteristics.

- A short definition :
  - grouping of cases into broad categories based on extent of disease
- Extent of disease
  - detailed description of how far the (tumor) disease has spread from organ or site of origin (the primary site).
- Extent of disease is an anatomic categorization using descriptors to group individual cases in relation to the human body.

Classification vs Staging

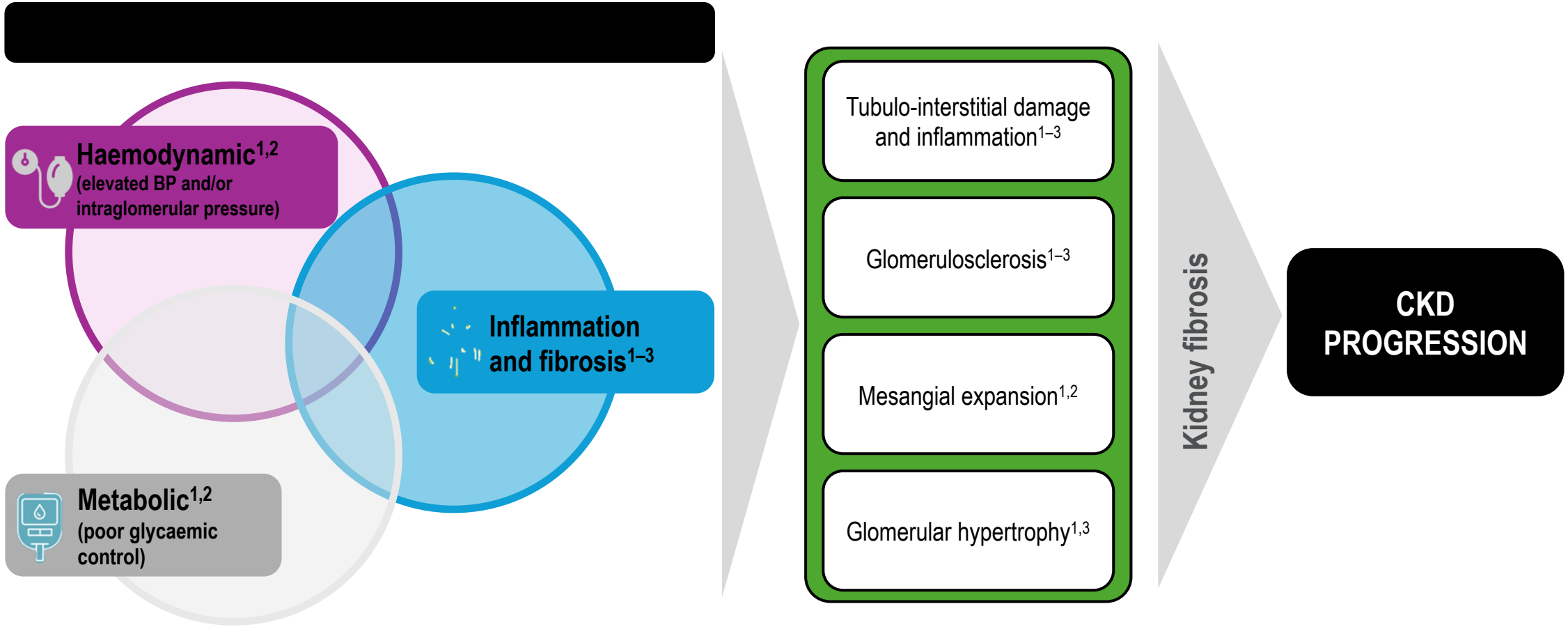
- Classification
  - is the process of grouping cases based on specific criteria.
  - is an orderly arrangement showing relationships among groups.
  - does not necessarily imply a prognosis.
- Relationships b/n staging, extent of disease and classification:
  - extent of disease is a type of classification (based on human anatomy) and pertains to an individual case.
  - Staging is coded shorthand or a notation describing disease in more general terms
- By staging, characteristics about a case (precise extent of disease information) can be grouped into categories.
- Staging translates extent of disease classification about individual conditions into groups that can be studied or evaluated for prognostic significance.

Key Characteristics of Useful Clinical Staging systems

1. **Clinical Relevance**:
   Staging systems should be clinically relevant, providing information that directly impacts patient management and treatment decisions. Guide therapeutic strategies tailored to individual patients.
2. **Customizability**:
   A good staging system allows customization based on specific disease types, patient populations, and other relevant factors. Flexibility ensures applicability across diverse scenarios.
3. **Comprehensive Medical Summary**:
   Staging systems should offer a comprehensive summary of disease status, including relevant clinical features, prognostic indicators, and treatment implications. This aids in informed decision-making.
4. **Incorporation of Pathologic Information**:
   While clinical staging provides an initial assessment, combining it with pathologic data (such as histopathology or molecular markers) enhances accuracy. Pathologic staging improves precision and is crucial for modern clinical trials.
5. **Periodic Revision**:
   Staging systems should evolve based on new clinical and pathological data, improved understanding of biology, and other factors affecting prognosis
6. **Ease of Navigation and Interpretation**:
   Staging systems should be straightforward and easy to use. Clinicians, researchers, and patients should find them accessible and intuitive.

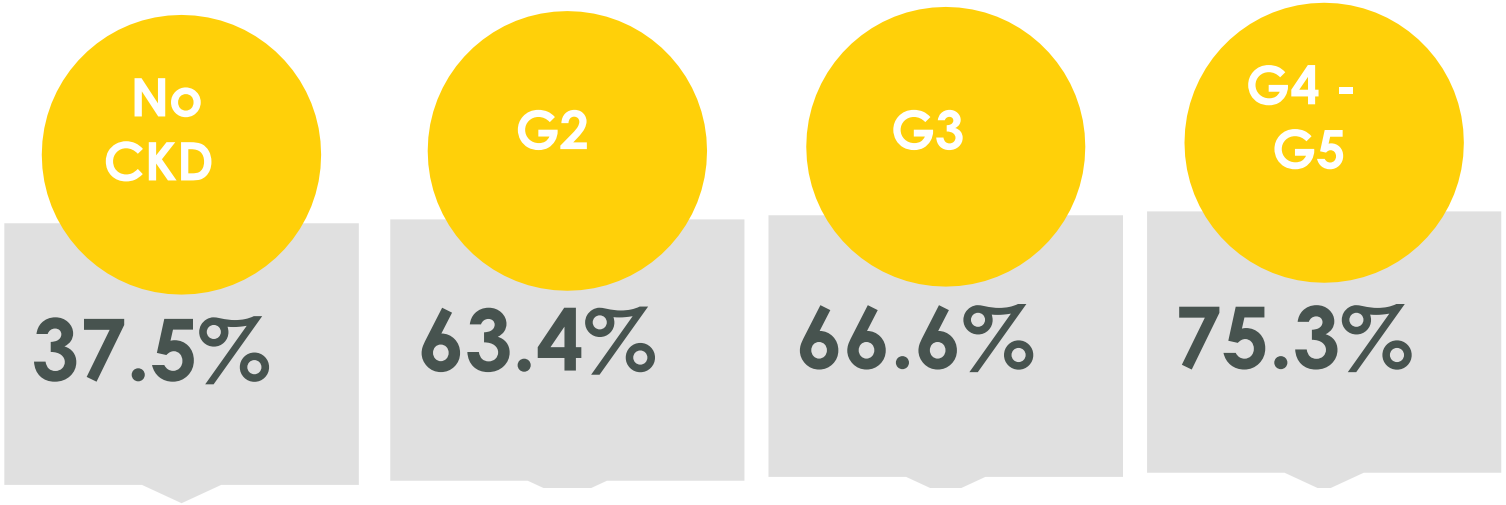
What we know about CVD and CKD….., and how does the CKM Staging system help us?

CKD progression is driven by the combined effects of metabolic, haemodynamic and inflammatory and fibrotic factors (which similarly impact cardiovascular disease)



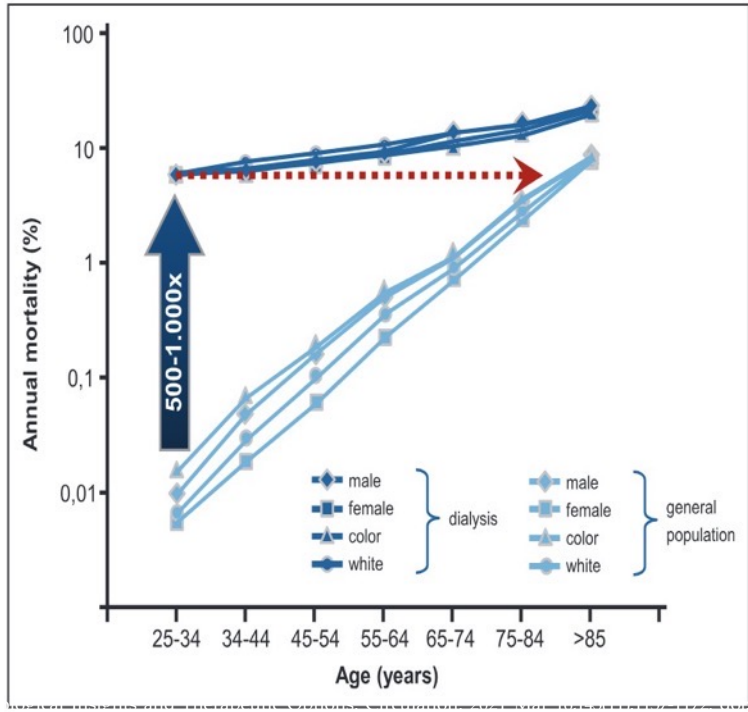
1. Alicic RZ, *et al. Clin J Am Soc Nephrol* 2017;12:2032–2045; 2. Mora-Fernández C, *et al. J Physiol* 2014;18:3997; 3. Bauersachs J, *et al. Hypertension* 2015;65:257–263

CVD is prevalent in people with CKD with high mortality



CVD mortality risk across CKD categories

GFR categories (ml/min/1.73 m²)		Albuminuria categories (mg/g)			
		A1		A2	A3
		<10 mg/g	10-29 mg/g	30–299 mg/g	≥300 mg/g
G1	≥105	0.93 (0.74–1.16)	1.33 (1.04–1.72)	2.46 (1.88–3.23)	2.69 (1.36–5.32)
	90–104	1 (reference)	1.63 (1.20–2.19)	1.82 (1.36–2.45)	4.77 (3.16–7.22)
G2	75–89	1.03 (0.85–1.24)	1.48 (1.23–1.78)	1.73 (1.29–2.32)	4.01 (2.62–6.14)
	60–74	1.09 (0.92–1.29)	1.58 (1.31–1.91)	2.18 (1.58–3.02)	4.23 (2.95–6.06)
G3a	45–59	1.52 (1.18–1.97)	2.38 (1.91–2.96)	3.13 (2.32–4.22)	4.97 (3.70–6.66)
G3b	30–44	2.40 (1.80–3.21)	3.07 (1.73–5.44)	4.12 (2.84–5.98)	6.10 (4.08–9.10)
G4	15–29	13.51 (4.89–37.35)	7.99 (1.95–32.81)	5.60 (3.66–8.57)	9.49 (4.97–18.10)
G5	<15				



Different relative risks for **various** CVD outcomes by eGFR and uACR

Heatmaps evaluated by age, eGFRcr-cys

10 outcomes, 6 cardiovascular, 2 kidney specific, 2 general
27.5 million people,
699 K with Cystatin and creatinine

Relative risks much more similar by age when using eGFRcr-cys

G3A associated with significant risk in every outcome (both optimal ACR <10; and high normal ACR 10-29)

Grams et al JAMA Oct 2023

Age <65	ACR, mg/g				ACR, mg/g			
eGFRcr-cys	<10	10–29	30–299	300+	<10	10–29	30–299	300+
	All-cause mortality				Myocardial infarction			
105+	0.99	1.2	1.5	2.4	0.93	1.0	1.1	2.6
90–104	ref	1.3	1.5	2.5	ref	1.2	1.3	1.9
60–89	1.2	1.6	2.0	2.9	1.3	1.4	1.6	2.1
45–59	2.1	2.7	2.9	4.5	1.8	2.6	3.1	3.5
30–44	2.7	3.8	4.2	5.6	1.9	2.3	3.0	3.9
<30	5.2	4.0	7.1	8.6	4.1	3.6	4.7	5.8
	Cardiovascular mortality				Stroke			
105+	0.95	1.4	1.7	4	0.96	1.2	1.6	2.7
90–104	ref	1.6	1.8	3.5	ref	1.2	1.5	2.2
60–89	1.3	1.7	2.3	3.9	1.2	1.4	1.7	2.6
45–59	2.5	4.0	4.6	6.0	1.9	2.0	2.5	3.8
30–44	3.1	6.6	5.3	7.1	2.6	3.7	3.5	3.5
<30	6.0	5.5	9.4	12	2.6	2.9	5.1	5.1
	Kidney failure replacement therapy				Heart failure			
105+	0.57	0.77	2.3	12	0.86	1.1	1.7	3.4
90–104	ref	1.4	3.9	11	ref	1.3	1.5	3.0
60–89	1.9	3.7	8.3	33	1.2	1.7	2.1	3.6
45–59	7.0	16	28	100	1.7	3.3	3.4	5.3
30–44	22	34	109	210	3.5	4.3	6.8	5.7
<30	335	267	419	625	7.5	6.3	9.7	8.9
	Acute kidney injury				Atrial fibrillation			
105+	0.75	1.0	1.4	3.4	0.93	1.0	1.3	1.9
90–104	ref	1.2	1.8	2.6	ref	1.2	1.4	2.3
60–89	1.6	2.7	2.9	5.8	1.1	1.3	1.5	1.8
45–59	4.2	6.0	5.6	7.6	1.5	2.0	2.1	2.6
30–44	5.7	9.4	9.8	9.4	1.8	2.4	3.0	2.8
<30	15	14	14	13	3.7	2.9	4.3	5.4
	Hospitalization				Peripheral artery disease			
105+	1.0	1.1	1.1	1.5	0.93	1.9	1.5	2.6
90–104	ref	1.1	1.2	1.3	ref	1.8	2.1	3.9
60–89	1.1	1.2	1.3	1.6	1.2	2.1	2.2	5.4
45–59	1.3	1.7	1.5	2.0	3.2	7.3	3.4	8.4
30–44	1.5	1.8	1.6	2.1	6.5	9.1	6.6	13
<30	2.1	2.4	2.4	3.5	1.4	7.6	18	16

Age 65+	ACR, mg/g				ACR, mg/g			
eGFRcr-cys	<10	10–29	30–299	300+	<10	10–29	30–299	300+
	All-cause mortality				Myocardial infarction			
105+	1.2	1.4	1.9	3.5	0.97	1.4	2.0	19
90–104	ref	1.2	1.4	2.0	ref	1.2	1.1	1.9
60–89	1.2	1.5	1.8	2.3	1.1	1.4	1.5	1.9
45–59	1.6	2.0	2.4	2.9	1.6	1.9	2.3	3.4
30–44	2.0	2.4	3.2	4.1	2.1	2.6	3.1	3.8
<30	3.4	4.1	5.1	6.5	4.9	3.0	5.1	5.0
	Cardiovascular mortality				Stroke			
105+	1.1	1.5	2.0	12	1.2	1.3	1.5	3.3
90–104	ref	1.4	1.4	3.4	ref	1.3	1.3	2.8
60–89	1.2	1.7	2.2	3.1	1.1	1.4	1.8	2.5
45–59	1.7	2.4	3.0	4.3	1.5	1.7	2.0	2.3
30–44	2.4	3.1	4.5	5.8	1.5	2.0	2.1	2.3
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	Kidney failure replacement therapy				Heart failure			
105+	2.0	1.0	2.1		0.99	1.5	1.7	7.0
90–104	ref	1.9	4.7	10	ref	1.3	1.5	2.2
60–89	1.4	2.6	6.2	19	1.2	1.5	2.0	3.2
45–59	3.7	7.9	16	42	1.6	2.0	2.9	4.1
30–44	14	14	46	137	2.3	2.9	3.5	6.1
<30	87	364	241	406	4.4	4.1	5.5	7.2
	Acute kidney injury				Atrial fibrillation			
105+	0.91	1.1	1.3	1.9	0.95	1.1	1.0	3.7
90–104	ref	1.3	1.4	3.9	ref	1.2	1.3	2.4
60–89	1.5	2.1	2.7	4.7	1.1	1.2	1.5	2.0
45–59	3.6	4.3	5.1	7.3	1.2	1.4	1.7	1.9
30–44	5.7	5.9	7.2	9.8	1.5	1.8	2.0	2.2
<30	10	11	11	22	1.8	1.8	2.2	3.2
	Hospitalization				Peripheral artery disease			
105+	1.0	1.1	1.2	2.2	1.1	2.3	2.9	4.9
90–104	ref	1.1	1.3	1.4	ref	1.3	2.0	4.8
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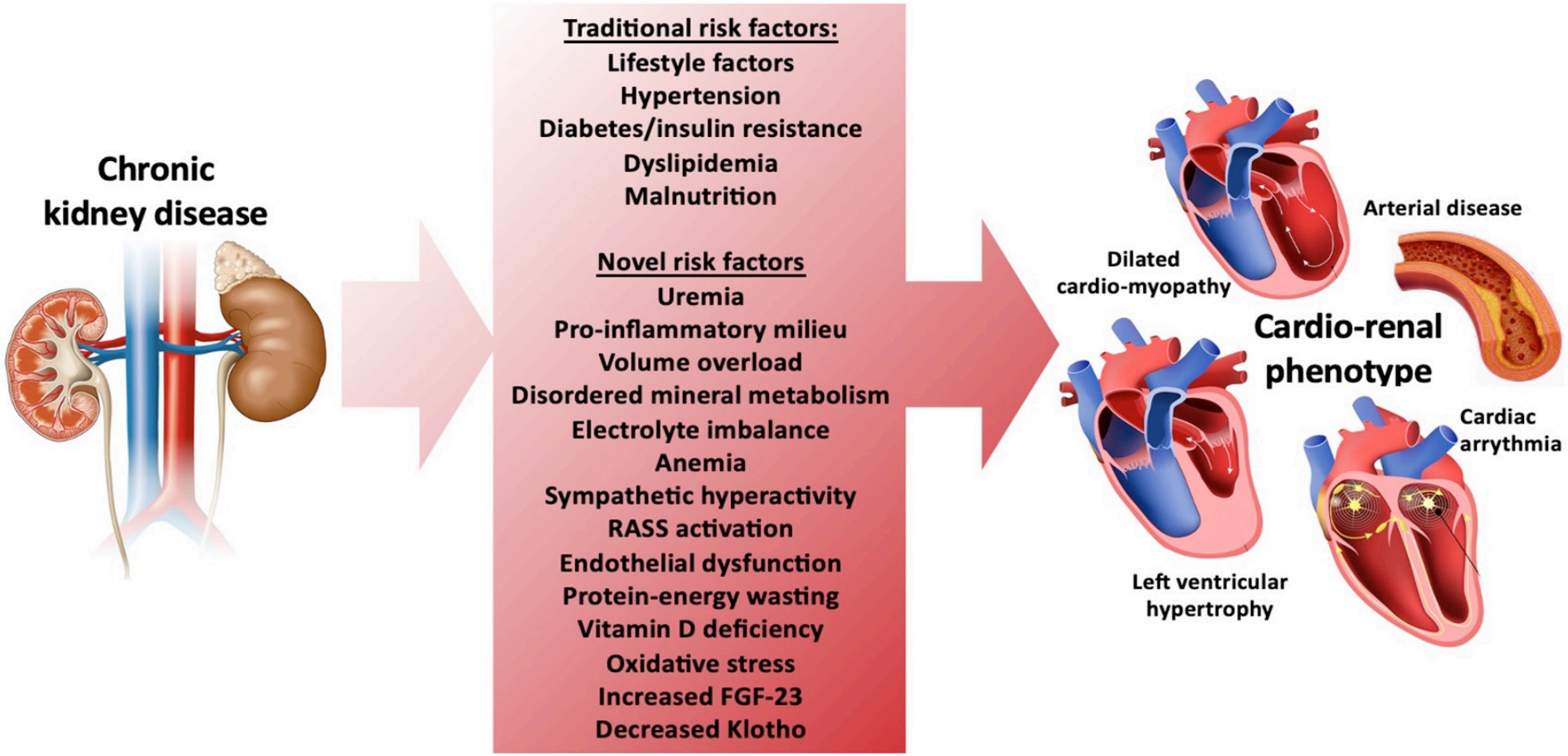
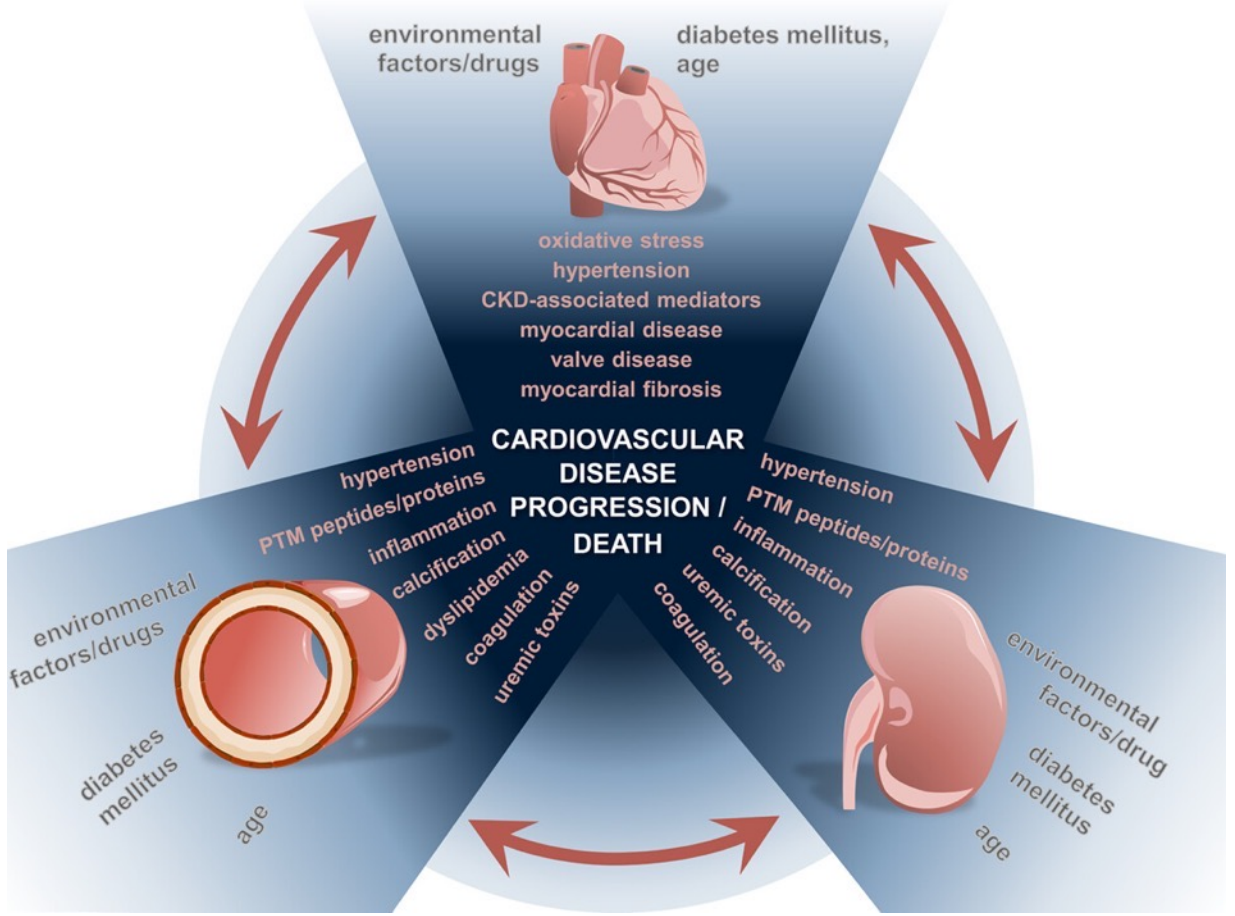
45–59	1.2	1.2	1.4	1.6	2.0	2.8	3.1	3.1
30–44	1.5	1.4	1.6	2.0	3.5	2.8	3.8	5.9
<30	1.9	1.9	2.0	2.6	8.4	4.1	5.9	10

Complex physiology of Cardiac and Vascular diseases in CKD



Complex interactions of CVD and CKD over the life course of an individual



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https://doi.org/10.1161/CIRCULATIONAHA.120.050686

Complex physiology may explain differences in rates of **different CVD conditions** in CKD

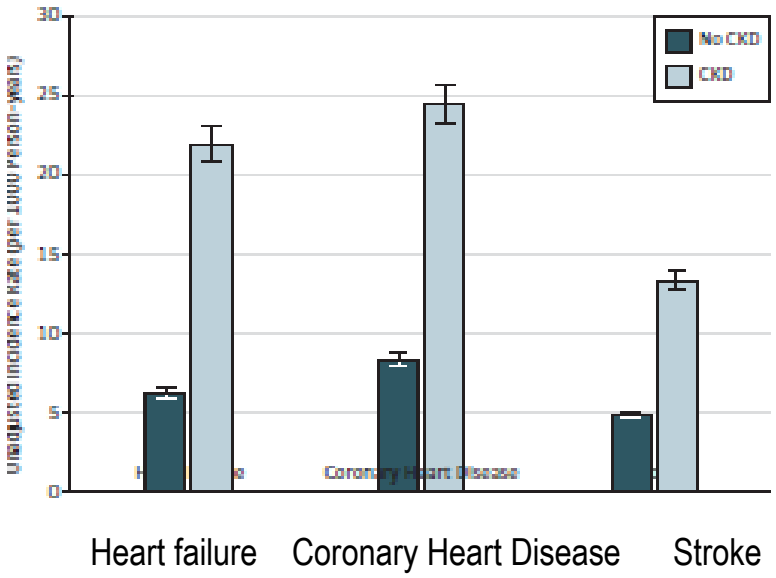
JAMA Cardiology | Brief Report

Absolute Rates of Heart Failure, Coronary Heart Disease, and Stroke in Chronic Kidney Disease

An Analysis of 3 Community-Based Cohort Studies

Nisha Bansal, MD, MAS; Ronit Katz, DPhil; Cassianne Robinson-Cohen, PhD; Michelle C. Odden, PhD; Lorien Dalrymple, MD; Michael G. Shlipak, MD; Mark J. Sarnak, MD; David S. Siscovick, MD; Leila Zelnick, PhD; Bruce M. Psaty, MD, PhD; Bryan Kestenbaum, MD; Adolfo Correa, MD, PhD; Maryam Afkarian, MD, PhD; Bessie Young, MD; Ian H. de Boer, MD

Figure 1. Unadjusted Incidence Rates and Risk Differences (per 1000 Person-years) of Heart Failure, Coronary Heart Disease, and Stroke Among Those With vs Without Chronic Kidney Disease (CKD)



Key Points

Question How do the absolute rates and risk differences of incident heart failure, coronary heart disease, and stroke differ in participants with and without chronic kidney disease?

Findings This analysis of 3 community-based cohort studies found that the adjusted risk differences comparing participants with vs without chronic kidney disease (per 1000 person-years) were highest for heart failure and coronary heart disease (and lower for stroke).

Meaning Chronic kidney disease is associated with an excess risk of heart failure that was similar in magnitude to coronary heart disease and greater than stroke.

Circulation

IN DEPTH

Cardiovascular Disease in Chronic Kidney Disease

Pathophysiological Insights and Therapeutic Options

Joachim Jankowski, PhD
Jürgen Floege, MD
Danilo Fliser, MD
Michael Böhm, MD
Nikolaus Marx, MD

Traditional and non-traditional risk factors well articulated

BUT Relative contribution of each to **atherosclerotic disease vs heart failure** less well articulated

Table. Traditional and Nontraditional Risk Factors for CVD in CKD

Risk factors for CVD in CKD	Specific aspects/treatment options compared with the non-CKD population	Ref.
Traditional		
Hypertension	Optimal target blood pressure has not yet been established	41
Dyslipidemia	Characteristic lipid pattern of hypertriglyceridemia and HDL cholesterol levels	42
Smoking	—	
Hyperglycemia	Intensive glucose control beneficial to avoid microvascular complications	43
Nontraditional		
Vascular calcifications	Treatment of electrolyte imbalances with magnesium	44, 45
	Vitamin K administration might be beneficial	46
Inflammation	Inhibition of proinflammatory effector molecule interleukin-1ß (IL-1ß) with canakinumab after myocardial infarction	47
Increased proteinuria	RAS blockade	48

CKD indicates chronic kidney disease; CVD, cardiovascular disease; HDL, high-density lipoprotein; and RAS, renin-angiotensin system.

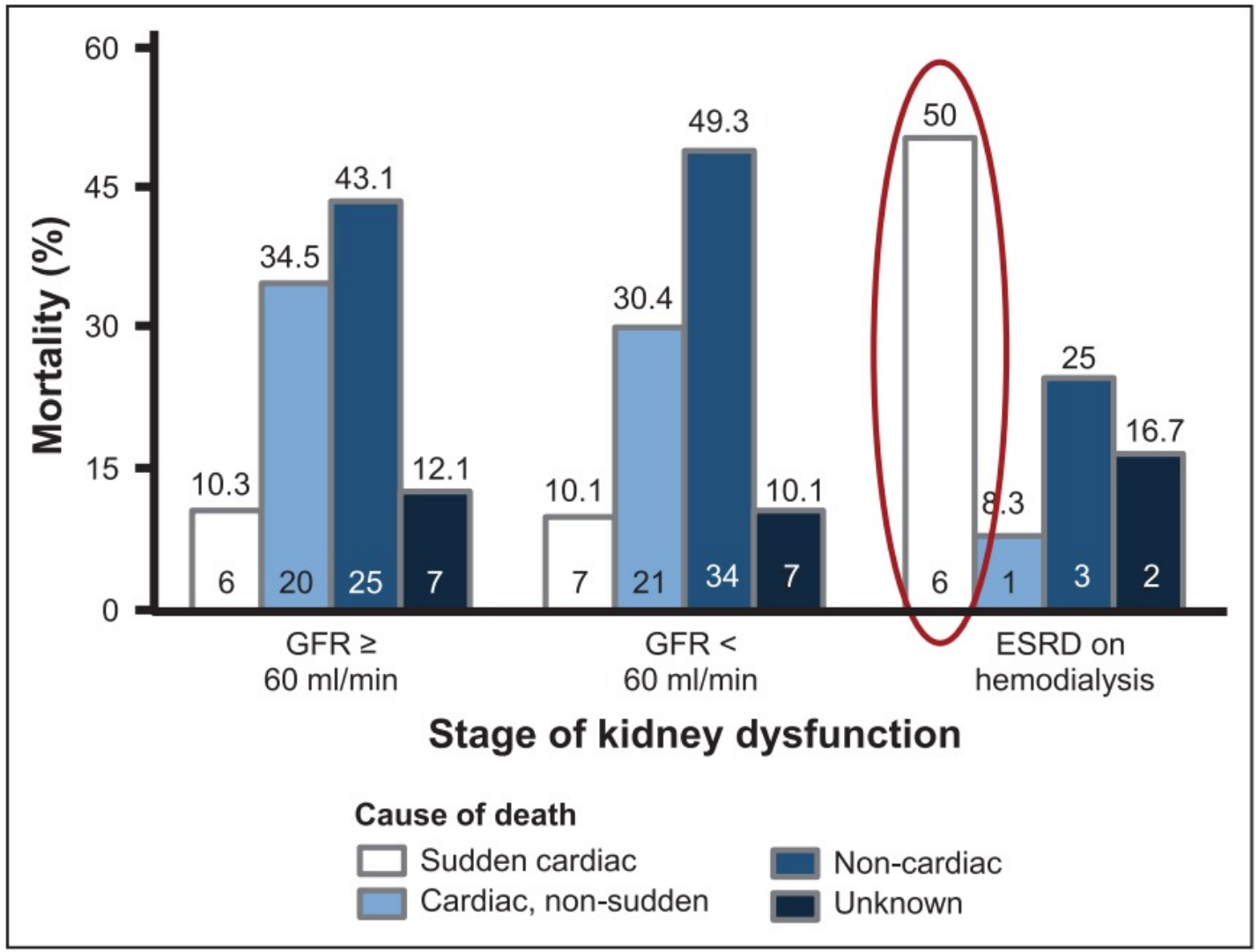


Figure 7. Cause-specific mortality according to varying levels of kidney dysfunction. For the 3 categories of kidney dysfunction, cause-specific mortality is depicted. Sudden cardiac death was the major cause of death in patients with end-stage renal disease (ESRD) on dialysis (50.0% vs 10.1% [glomerular filtration rate {GFR} <60 mL/min] vs 10.3% [GFR ≥60 mL/min], χ^2 P=0.010). Number at the top of each bar is the mortality rate; number within the bar is the n per group. The unknown category was reserved for those patients whose cause of death could not be determined. Adapted from Cheema et al.[115]

Disproportional incidence of Sudden cardiac death on HD may be due to combination of electrolyte disturbances leading to dysrhythmia +/- fibrosis +/- Atherosclerotic disease

Highlights

- Chronic kidney disease is associated with an increase in atherosclerotic burden from early stages.
- Progression of chronic kidney disease is associated with progression of atherosclerosis.
- Specific risk factors related with chronic kidney disease are involved in the accelerated atherosclerosis observed in these patients.
- Subclinical atherosclerotic detection by arterial ultrasound could improve cardiovascular risk prediction in chronic kidney disease patients.

Attempts at understanding contributions to atherosclerotic processes and events

Table 2. Association of Biochemical and Vascular Ultrasound Parameters With Outcomes in CKD G3-G5D Patients

	Plaque Progression	IMT Progression	Cardiovascular Events
Full cohort	Lower FGF2		Atheromatous plaque
	rs495392 Klotho polymorphism		Higher CKD G category
	Lower TWEAK		Lower 25(OH)D
G3	Atheromatous plaque at baseline	Higher phosphate	Atheromatous plaque
	Higher phosphate		Higher potassium
	Lower 25(OH)D		Lower 25(OH)D
G4	Atheromatous plaque at baseline	Lower 25(OH)D	Atheromatous plaque
	Higher ferritin	PTH over recommended level	Higher potassium
			Lower 25(OH)D
G5	Lower 25(OH)D	Higher phosphate	Atheromatous plaque
	Higher ferritin	PTH outside the recommended level	Higher phosphate
	Higher uric acid		

Novel factors found in the NEFRONA study (Observatorio Nacional de Atherosclerosis en NEFrologia) being independently associated with progression of subclinical atherosclerosis and cardiovascular events in CKD patients.[173,186,237,243,276,294] CKD indicates chronic kidney disease; FGF, fibroblast growth factor; IMT, intima-media thickness; PTH, parathyroid hormone; and TWEAK, TNF-related weak inducer of apoptosis.

Arterioscler Thromb Vasc Biol. 2019;39:1938–1966. DOI: 10.1161/ATVBAHA.119.312705

New paradigms and models for risk prediction

Changes in care Pattern

Wide spread use of antiHTN

Integrating new models

Incorporating new risk predictors

Development and Validation of the American Heart Association Predicting Risk of Cardiovascular Disease EVENTs (PREVENT) Equations

Sadiya S. Khan, Kunihiro Matsushita, Yingying Sang, Shoshana H. Ballew, Morgan E. Grams, Aditya Surapaneni, Michael J. Blaha, April P. Carson, Alexander R. Chang, Elizabeth Ciemins, Alan S. Go, … **See all authors**
and for the Chronic Kidney Disease Prognosis Consortium and the American Heart Association Cardiovascular-Kidney-Metabolic Science Advisory Group

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AHA SCIENTIFIC STATEMENT

Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement From the American Heart Association

Sadiya S. Khan, MD, MSc, FAHA, Chair; Josef Coresh, MD, PhD, FAHA, Vice Chair; Michael J. Pencina, PhD;

Circulation

AHA SCIENTIFIC STATEMENT

A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association

Chiadi E. Ndumele, MD, PhD, FAHA, Chair; Ian J. Neeland, MD, FAHA; Katherine R. Tuttle, MD; Sheryl L. Chow, PharmD, FAHA, Vice Chair; Roy O. Mathew, MD; Sadiya S. Khan, MD, MSc, FAHA; Josef Coresh, MD, PhD; Carissa M. Baker-Smith, MD, MPH, FAHA; Mercedes R. Carnethon, PhD, FAHA; Jean-Pierre Després, PhD, FAHA; Jennifer E. Ho, MD, FAHA; Joshua J. Joseph, MD, MPH, FAHA; Walter N. Kernan, MD; Amit Khera, MD, MSc, FAHA; Mikhail N. Kosiborod, MD; Carolyn L. Lekavich, PhD; Eldrin F. Lewis, MD, MPH, FAHA; Kevin B. Lo, MD; Bige Ozkan, MD, ScM; Latha P. Palaniappan, MD, MS, FAHA; Sonali S. Patel, MD, PhD; Michael J. Pencina, PhD; Tiffany M. Powell-Wiley, MD, MPH, FAHA; Laurence S. Sperling, MD, FAHA; Salim S. Virani, MD, PhD, FAHA; Jackson T. Wright, MD, PhD; Radhika Rajgopal Singh, PhD, FAHA; Mitchell S.V. Elkind MD, MS, FAHA; Janani Rangaswami, MD, FAHA, Vice Chair; on behalf of the American Heart Association

Acknowledging the complexity of interactions

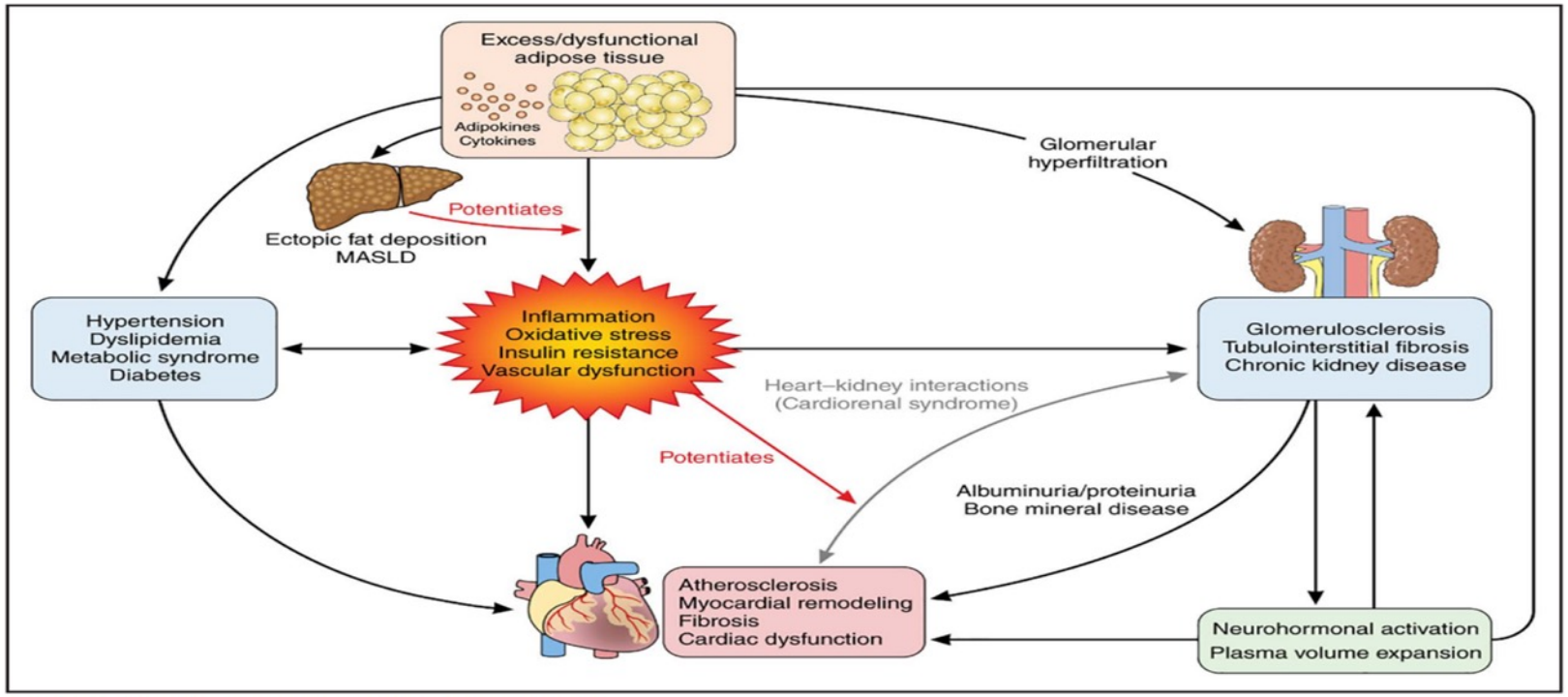
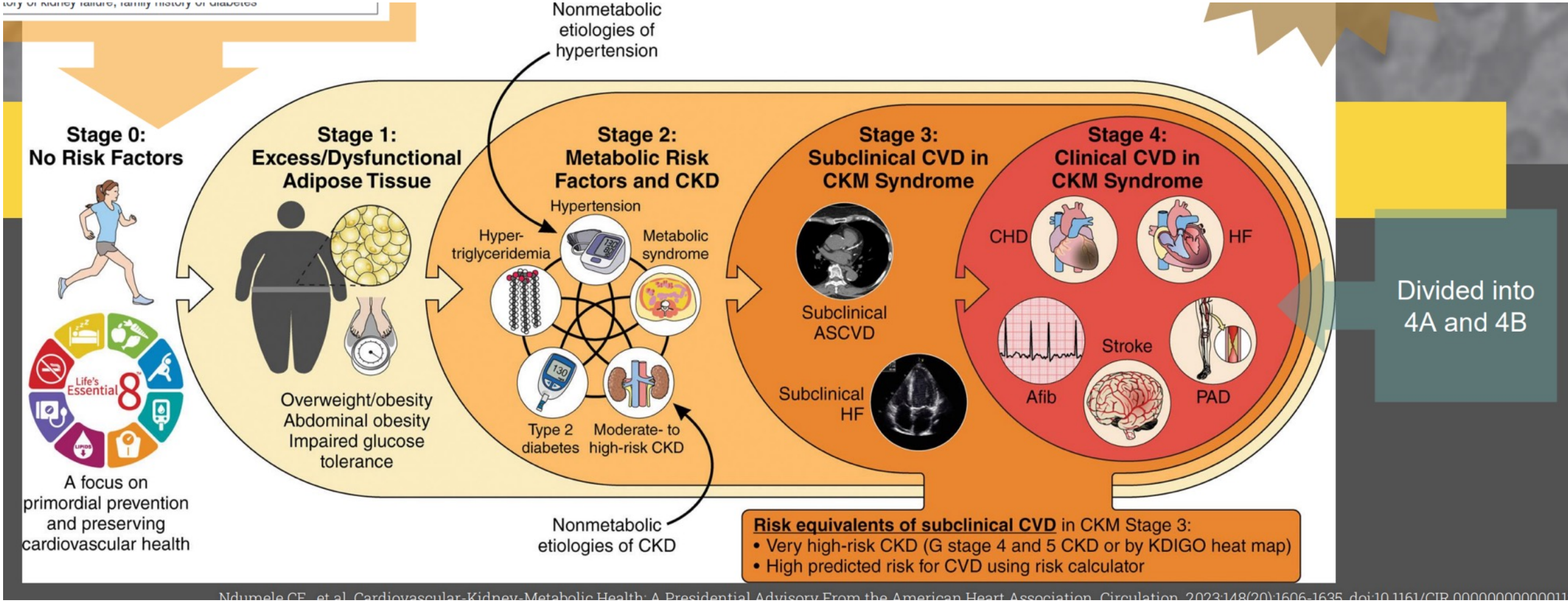


Figure 1. Conceptual diagram for CKM syndrome.
The image displays the pathophysiology underlying cardiovascular-kidney-metabolic (CKM) syndrome. CKM syndrome most commonly originates from excess adipose tissue, dysfunctional adipose tissue, or both. Multiple pathological processes related to dysfunctional adipose tissue result in insulin resistance and eventual hyperglycemia. Inflammation, oxidative stress, insulin resistance, and vascular dysfunction are highlighted as central processes leading to the development of metabolic risk factors, to the progression of kidney disease, to the potentiation of heart-kidney interactions, and to the development of cardiovascular diseases. Metabolic risk factors and chronic kidney disease further predispose to cardiovascular diseases through multiple direct and indirect pathways. MASLD indicates metabolic dysfunction–associated steatotic liver disease.

‘Stages’ of CKM : Describing processes and syndromes (in linear manner)



Ndumele CE, et al. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. Circulation. 2023;148(20):1606-1635. doi:10.1161/CIR.0000000000001

CKM Health Stages

- Describe characteristics of different risks
- Uses multiple types of information
  - Imaging
  - History
  - Laboratory data (specialized and common)
  - Risks and risk equivalents
  - Events
  - And/ or
- ? Clinical utility of the staging system

Table 3. Definitions of CKM Health Stages

CKM health stages	Definition
Stage 0: No CKM health risk factors	Individuals without overweight/obesity, metabolic risk factors (hypertension, hypertriglyceridemia, MetS, diabetes), CKD, or subclinical/clinical CVD
Stage 1: Excess and/or dysfunctional adiposity	Individuals with overweight/obesity, abdominal obesity, or dysfunctional adipose tissue, without the presence of other metabolic risk factors or CKD BMI ≥25 kg/m² (or ≥23 kg/m² if Asian ancestry) Waist circumference ≥88/102 cm in women/men (or if Asian ancestry, ≥80/90 cm in women/men) and/or Fasting blood glucose ≥100–124 mg/dL or HbA1c between 5.7% and 6.4%*
Stage 2: Metabolic risk factors and CKD	Individuals with metabolic risk factors (hypertriglyceridemia (≥135 mg/dL), hypertension, MetS†, diabetes) or CKD
Stage 3: Subclinical CVD in CKM	Subclinical ASCVD or subclinical HF among individuals with excess/dysfunctional adiposity, other metabolic risk factors, or CKD Subclinical ASCVD to be principally diagnosed by coronary artery calcification (subclinical atherosclerosis by coronary catheterization/CT angiography also meets criteria) Subclinical HF diagnosed by elevated cardiac biomarkers (NT-proBNP ≥125 pg/mL, high-sensitivity troponin T ≥14 ng/L for women and ≥22 ng/L for men, high-sensitivity troponin I ≥10 ng/L for women and ≥12 ng/L for men) or by echocardiographic parameters, with combination indicating highest HF risk. Risk equivalents of subclinical CVD Very high-risk CKD (G4 or G5 CKD or very high risk per KDIGO classification) High predicted 10-y CVD risk
Stage 4: Clinical CVD in CKM	Clinical CVD (coronary heart disease, heart failure, stroke, peripheral artery disease, AFib) among individuals with excess/dysfunctional adiposity, other metabolic risk factors, or CKD Stage 4a: no kidney failure Stage 4b: kidney failure present

New AHA Cardiovascular-Kidney-Metabolic (CKM) Staging **Solves All Our Staging Problems** and Should Be Applied Universally

- What problem are we trying to solve ?
- Do we have a staging problem ?

- Does the proposed CKM staging foster awareness of complex physiology and identify gaps in knowledge ?

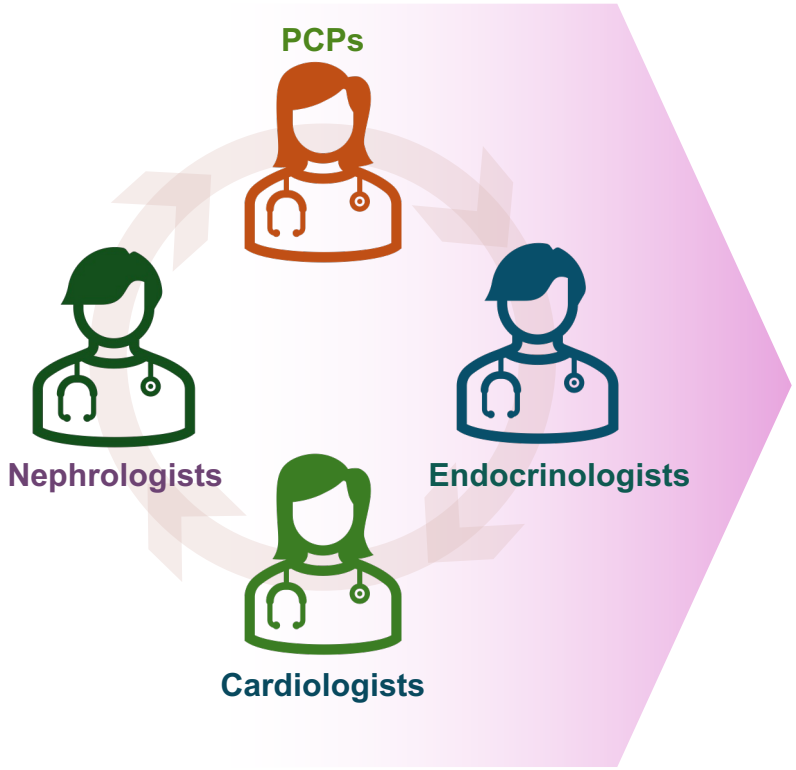
- Does the proposed CKD staging foster integration of strategies for identification and care, and enrolment into clinical studies?

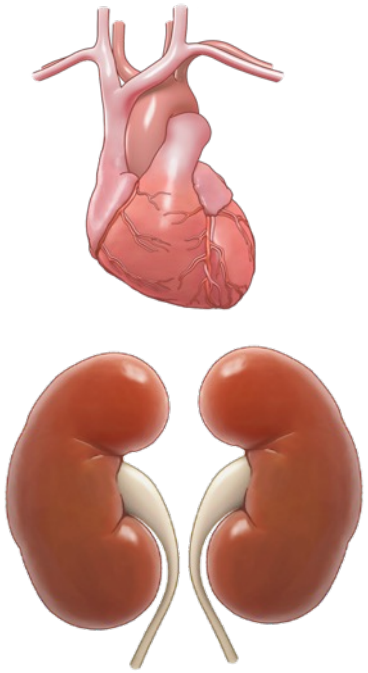
What we do not know…..

- Relative importance of different risk factors / biomarkers
  - in different kidney diseases and by CKD stage
- Relative importance of constellations of risk factors/ biomarkers within different people with different phenotypes
- Best value for therapeutic options at different time points
  - Stages of disease vs disease(s)

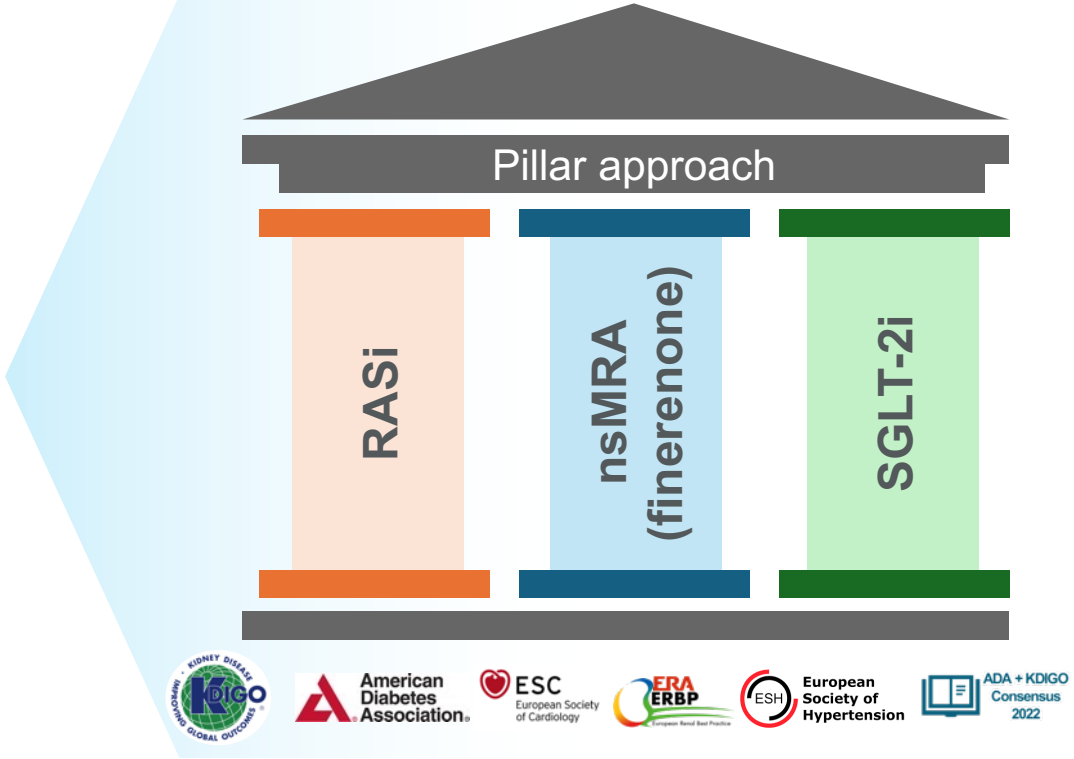
Our common goal is to prevent CV and kidney outcomes through identifying triggers for early intervention

Approaches are multidisciplinary…





…multifactorial and guideline recommended[1–7]



ADA, American Diabetes Association; ERA, European Renal Association; ERBP, European Renal Best Practice; ESC, European Society of Cardiology; ESH, European Society of Hypertension; KDIGO, Kidney Disease Improving Global Outcomes; nsMRA, nonsteroidal mineralocorticoid receptor antagonist; PCP, primary care physician;
RASi, renin–angiotensin system inhibitor; SGLT-2i, sodium-glucose co-transporter-2 inhibitor

1. Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2022;102:S1–S128; 2. American Diabetes Association. *Diabetes Care* 2023;46 (Suppl 1):S191–S202; 3. de Boer IH, *et al. Diabetes Care* 2022;45:3075–3090; 4. Sarafidis PA, *et al. Clin Kidney J* 2023: doi: 10.1093/ckj/sfad139; 5. Mancia G, *et al. J Hypertens* 2023: doi: 10.1097/HJH.0000000000003480; 6. Marx N, *et al. Eur Heart J* 2023; doi: 10.1093/eurheartj/ehad192; 7. Blazek O, *et al. Am Heart J Plus* 2022;19:100187

Its actually about the care, and the people

Circulation: Cardiovascular Quality and Outcomes

CARDIOVASCULAR PERSPECTIVE

Cardio-Renal-Metabolic Care Models

Toward Achieving Effective Interdisciplinary Care

Janani Rangaswami, MD
Katherine Tuttle, MD
Muthiah Vaduganathan, MD, MPH

2020

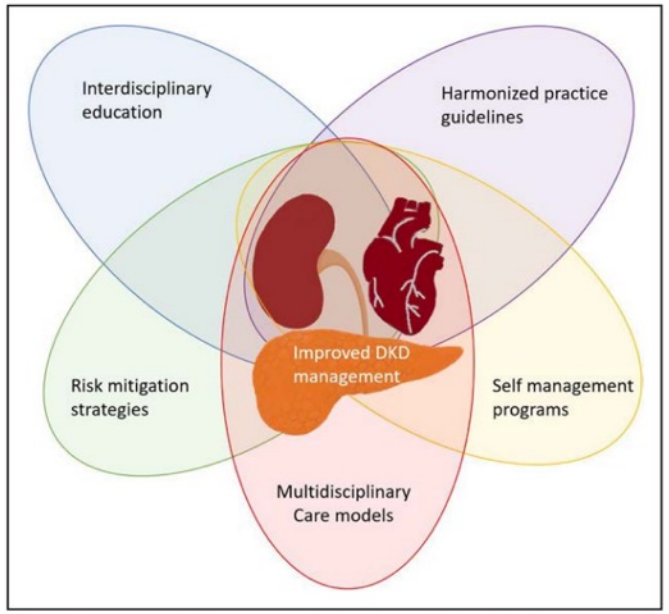


Figure. Components of a successful cardio-renal-metabolic care model at an institutional level.
A successful multidisciplinary model would include physician or advanced

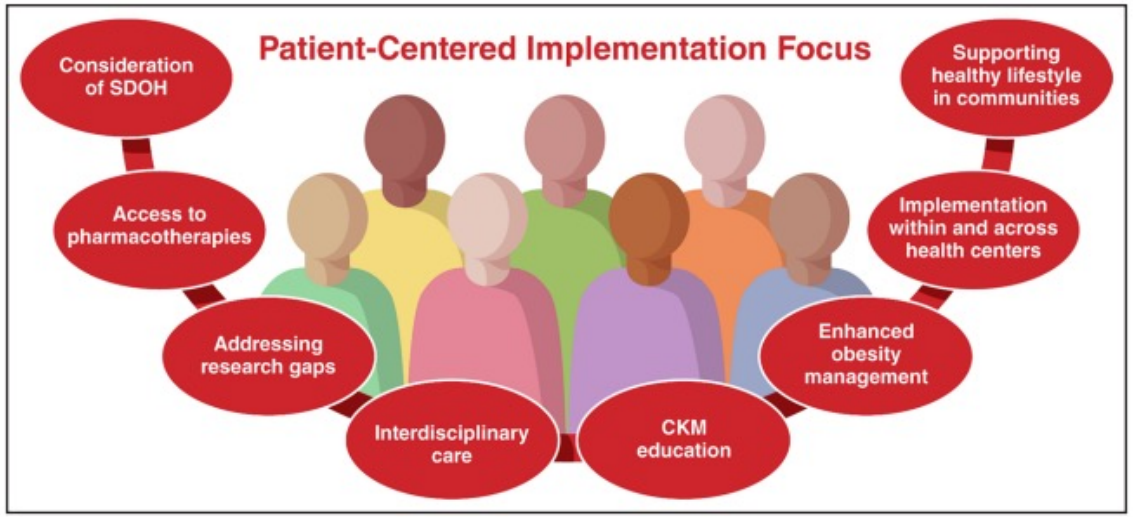
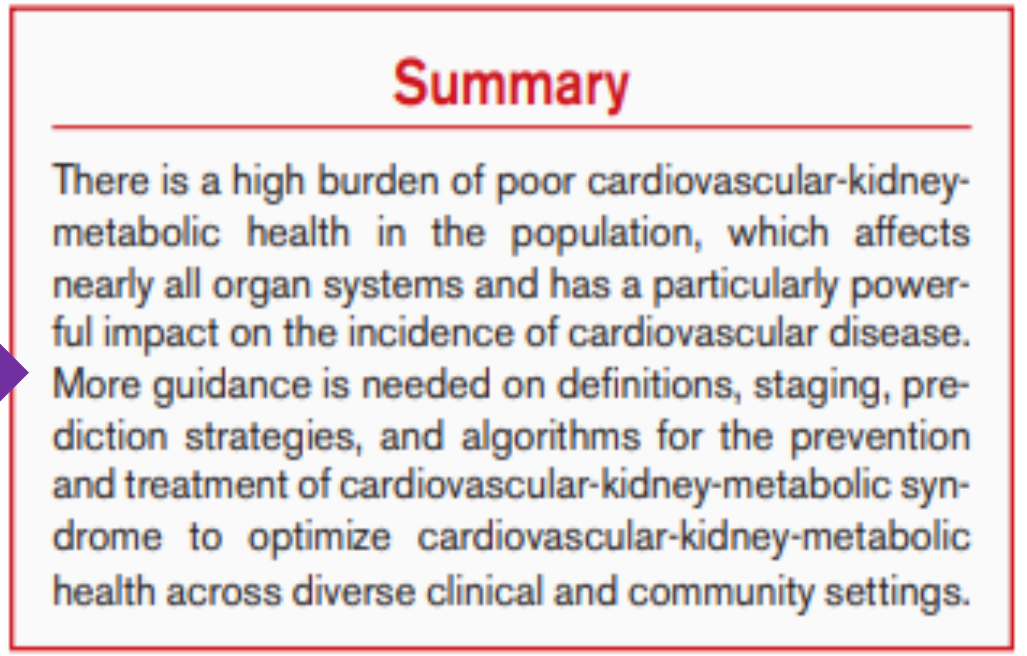


Figure 5. Components of a CKM syndrome call to action.
The components of the call to action for optimizing cardiovascular-kidney-metabolic (CKM) health in the population include (1) systematically considering social determinants of health (SDOH) in the care model for CKM syndrome; (2) enhancing access to pharmacotherapies that positively affect outcomes related to CKM syndrome; (3) addressing research gaps related to CKM syndrome; (4) facilitating interdisciplinary care and reducing care fragmentation; (5) improving the education of health care professionals and the lay community related to CKM syndrome; (6) enhancing management of obesity as the root cause of much of CKM syndrome; (7) implementing CKM syndrome care models within and across health centers; and (8) building multistakeholder partnerships to support healthy lifestyle and the achievement of ideal cardiovascular health across diverse communities.

"New AHA Cardiovascular-Kidney-Metabolic (CKM) Staging **Solves All Our Staging Problems** and Should Be Applied Universally"…

- Not really
- The concept of Cardiovascular Kidney Metabolic syndrome
  - Recognizes the complexity of disease processes currently impacting a lot of people worldwide
  - Offers opportunities for collaboration in research and care paradigms
- The staging system
  - Ignores etiologies of different kidney and CV diseases
  - Is not simple to use for clinicians or researchers yet
  - May inadvertently thwart research and validation efforts
  - Is better as a 'framework' for education and needs to be tested in terms of utility

Actual wording acknowledges this



Summary

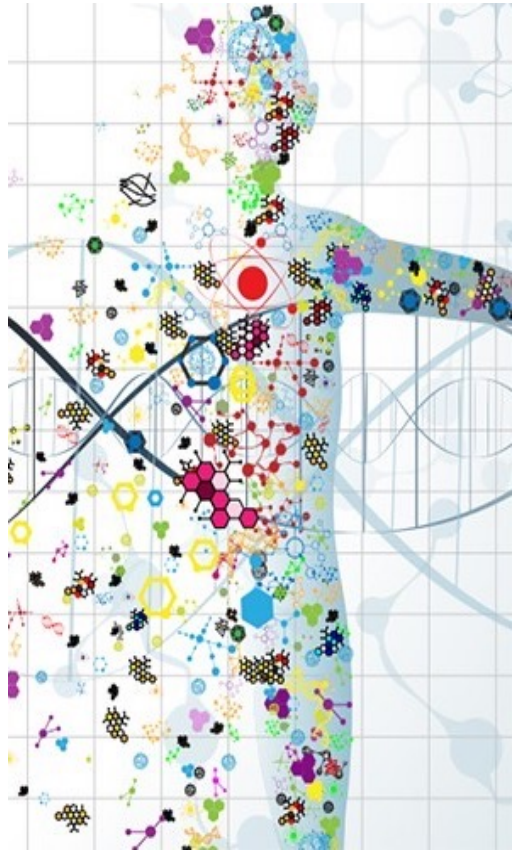
There is a high burden of poor cardiovascular-kidney-metabolic health in the population, which affects nearly all organ systems and has a particularly powerful impact on the incidence of cardiovascular disease. More guidance is needed on definitions, staging, prediction strategies, and algorithms for the prevention and treatment of cardiovascular-kidney-metabolic syndrome to optimize cardiovascular-kidney-metabolic health across diverse clinical and community settings.

Ongoing tensions between Inclusive frameworks and GDMT and Precision Medicine

Timing and individualization

Identifying phenotypes within classification systems

- Lean
- Overweight
- Diabetes
- No Diabetes
- Age/ Sex




One nephrologist’s
perspective...

Thank you and looking forward to the Discussion