Cardiovascular-Kidney-Metabolic Syndrome

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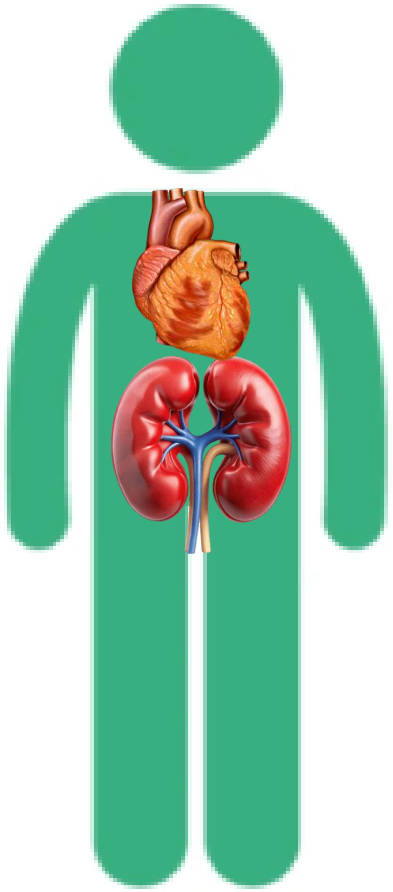
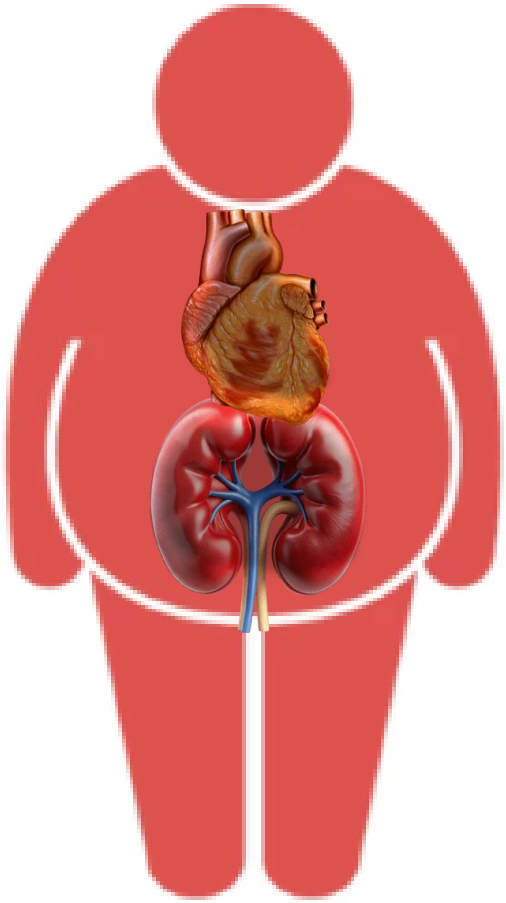
Καθηγητής καρδιολογίας Δ.Π.Θ. Αλεξανδρούπολη

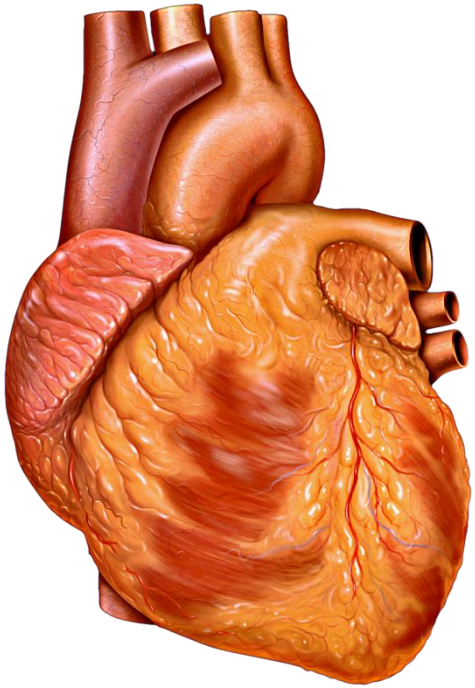




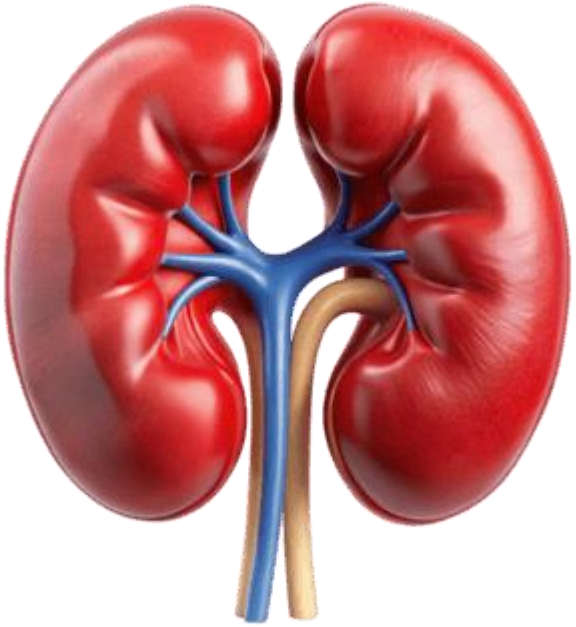
Case.	*Kidney.*	*Pleura.*	*Lung.*	*Pericardium.*	*Heart.*	*Cavity of Abdomen.*	*Peritone m*
34 Mr. R——, æt. 33, *epileptic, & died comatose*	soft, granulated	effusion	emphysema, and œdema	slight effusion	flabby, but hypertrophic in left ventricle; one aortal valve diseased	.....	thickened
5 Mr. G——, *died epileptic*	hard, small, granulated	effusion of serum	emphysema	.....	large, particularly left ventricle; semilunar valves slightly diseased	.....	.....
36. Maria Hill, *died quite suddenly*	soft, large, white	.....	healthy, slight œdema	.....	hypertrophy general, right auricle distended	.....	.....
37. Hugh Maclean, *died of peritonitis*	hard, large, white	healthy	healthy	healthy	large and muscular, valves healthy	inflammatory effusion	inflamed
38. A German, *died suddenly*	hard, scabrous	effusion, old adhesion	healthy	.....	healthy	.....	.....
39. Mary Thomas, æt. 23	hard, granulated	effusion	healthy compressed	slight effusion	healthy	great effusion, mesentery œdematous, some glands enlarged	a few old adhesions on the liver
40. —— Beckwith,	hard, scabrous	.....	emphysema, œdema, trachea, unhealthy	.....	healthy	healthy	a few old adhesions
41. —— ——,	hard, scabrous, lobulated	slight effusion	solid, from œdema and congestion	.....	hypertrophy of left ventricle, valves healthy	mesenteric glands enlarged	.....

Bright R. Cases and observations illustrative of renal disease accompanied by the secretion of albuminous urine. *Guys Hospital Reports. 1836:*338–400.

Acute or chronic dysfunction



Acute or chronic dysfunction

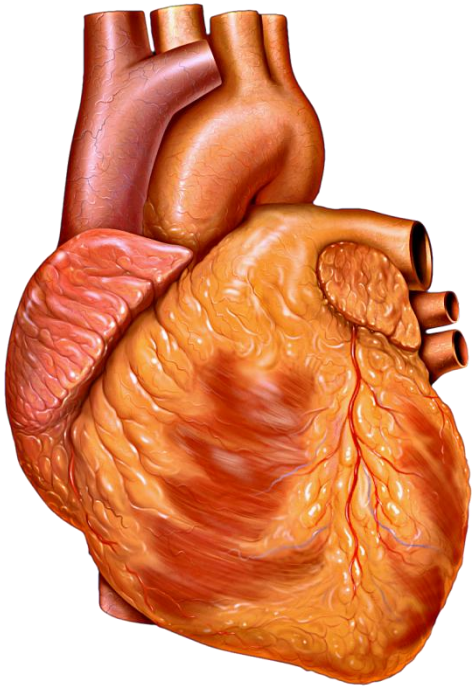


Acute or chronic dysfunction

Acute or chronic dysfunction

Treatment of dysfunction

Worsens function

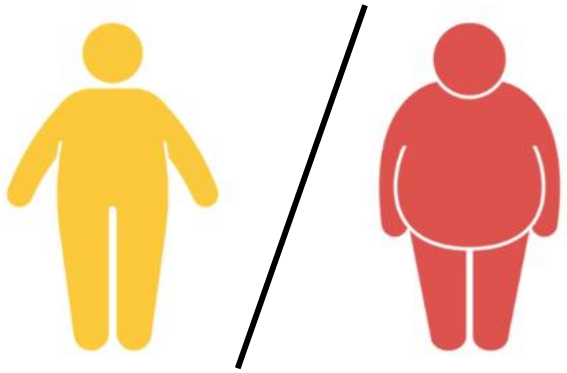


Worsens function

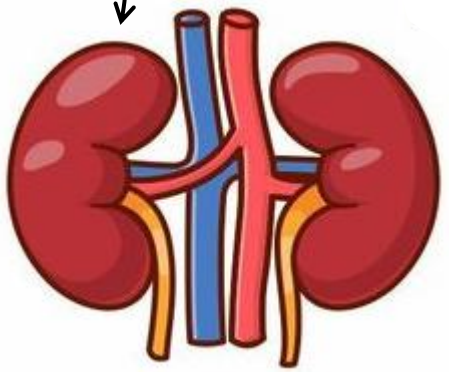
Treatment of dysfunction

Cardiovascular-Kidney-Metabolic Syndrome - CKMS

RISK ENHANCING FACTORS

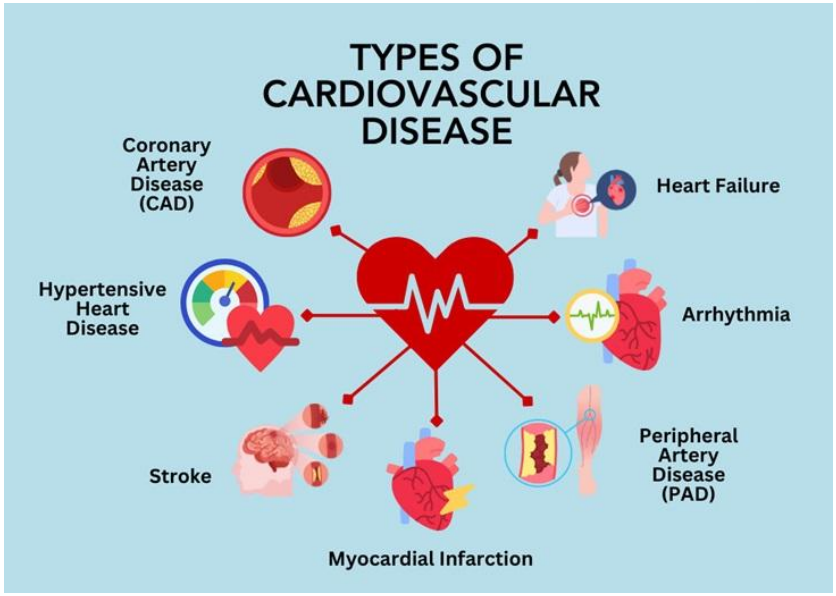


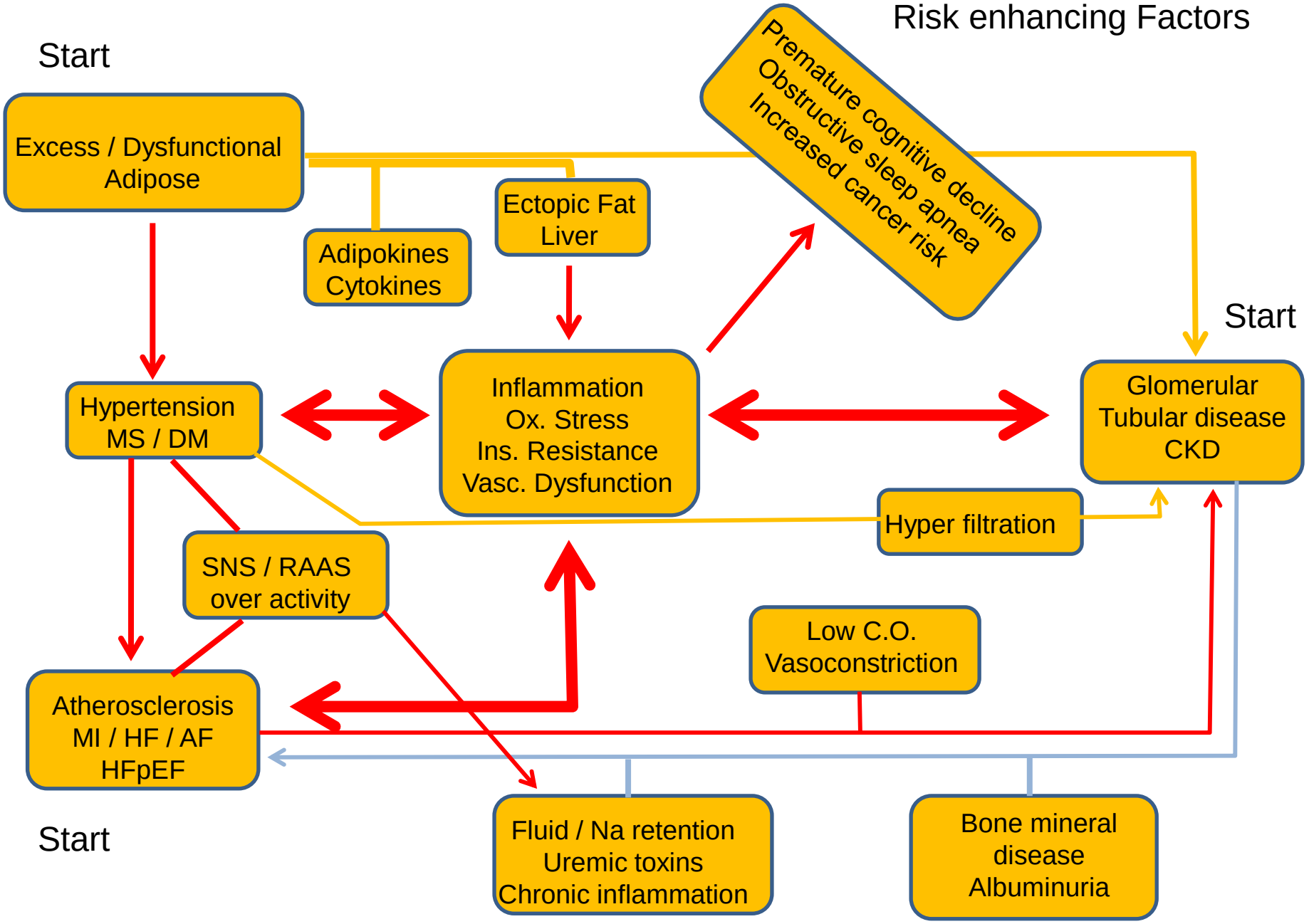
RISK ENHANCING FACTORS

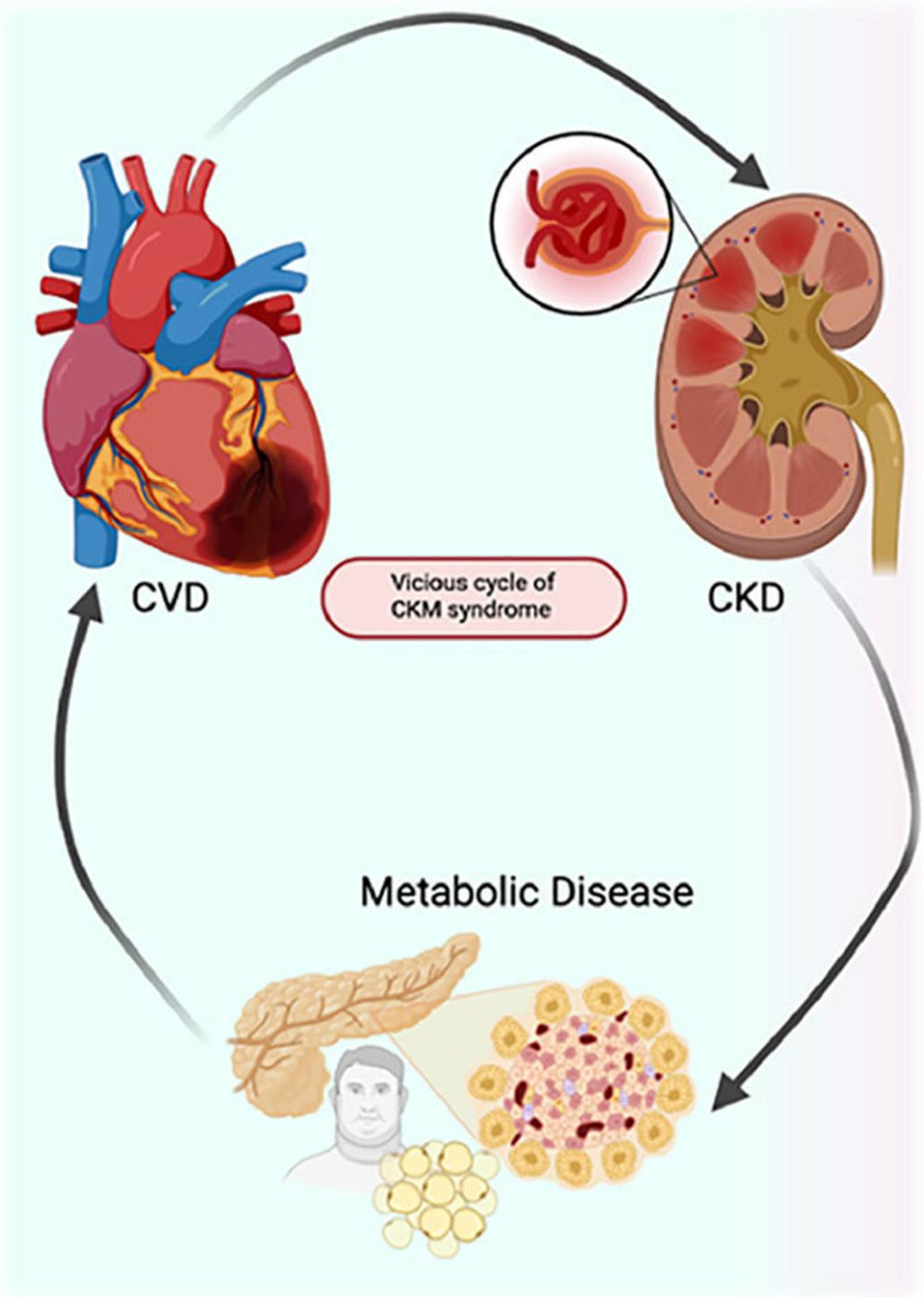


RISK ENHANCING FACTORS

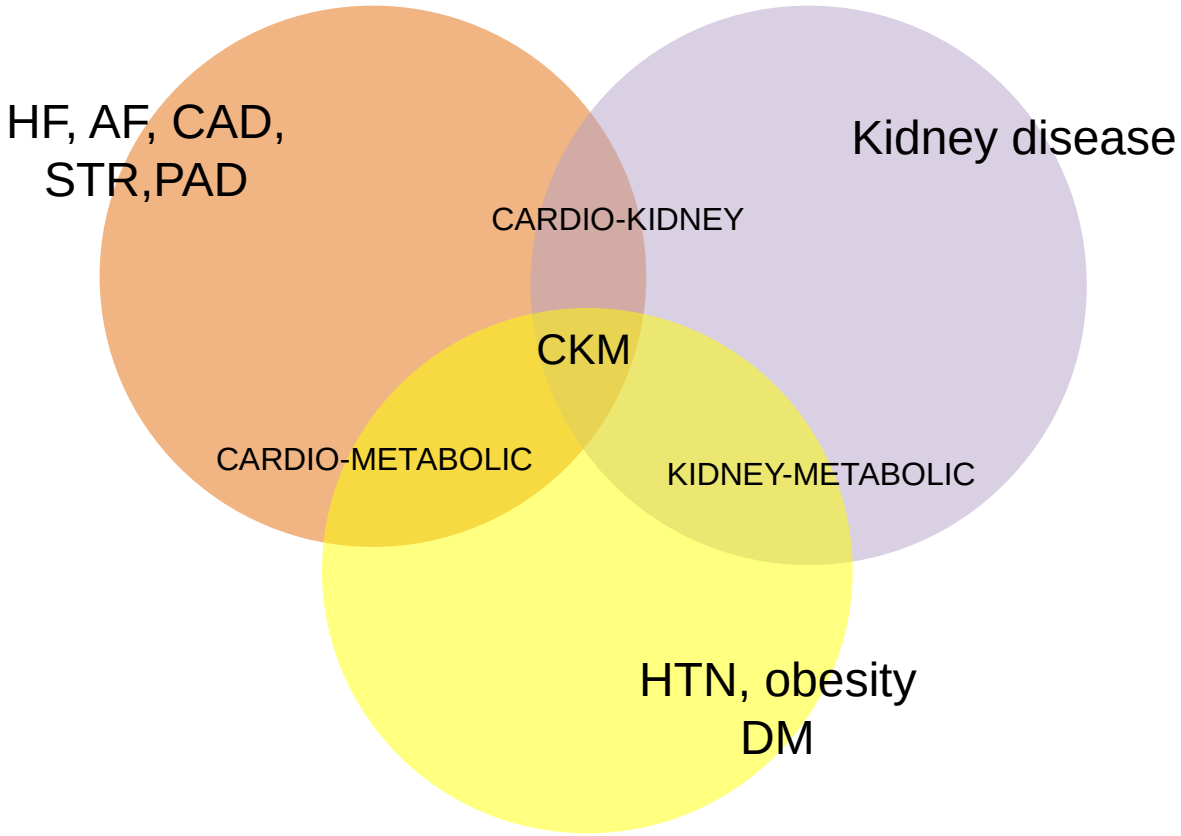
RISK ENHANCING FACTORS




Risk enhancing Factors
Start
Excess / Dysfunctional Adipose
Premature cognitive decline
Obstructive sleep apnea
Increased cancer risk
Adipokines
Cytokines
Ectopic Fat
Liver
Start
Hypertension
MS / DM
Inflammation
Ox. Stress
Ins. Resistance
Vasc. Dysfunction
Glomerular
Tubular disease
CKD
Hyper filtration
SNS / RAAS
over activity
Low C.O.
Vasoconstriction
Atherosclerosis
MI / HF / AF
HFpEF
Start
Fluid / Na retention
Uremic toxins
Chronic inflammation
Bone mineral
disease
Albuminuria


CVD
Vicious cycle of
CKM syndrome
CKD
Metabolic Disease

CKM phenotypes




CRP
Risk-enhancing factors for
CKM syndrome

Stages of CKMS

Stage 0: **No** CKM risk factors

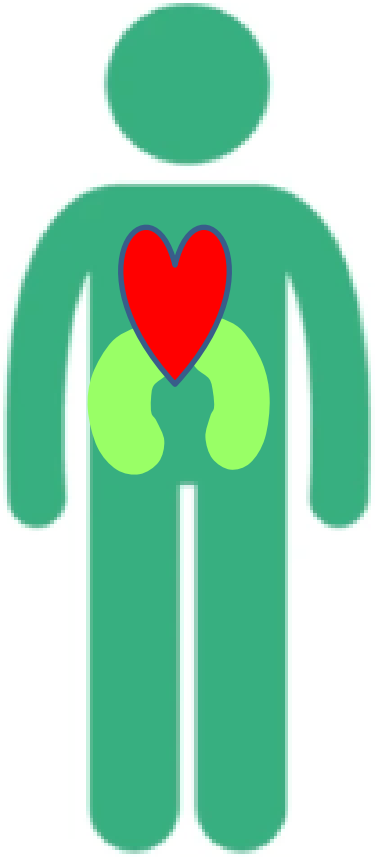
Stage 1: excess or dysfunctional **adiposity**

Stage 2: **metabolic** risk factors

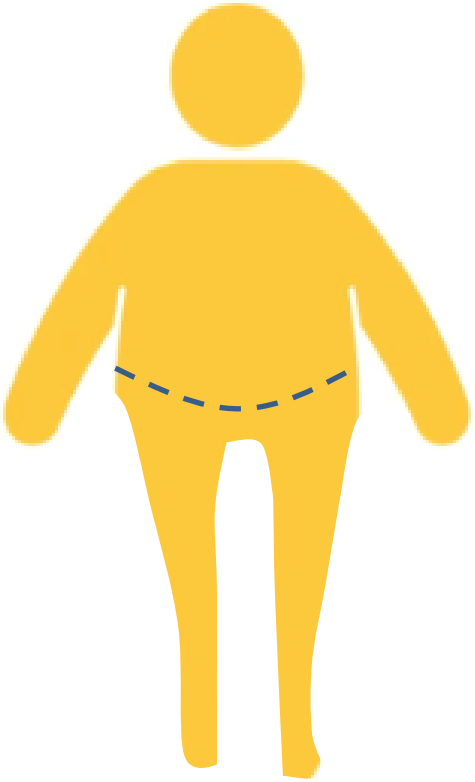
Stage 3: **subclinical** CVD or risk equivalents or very high-risk CKD

Stage 4: **clinical** CVD in CKM syndrome – end stage CKD

Stage 0: No CKM risk factors



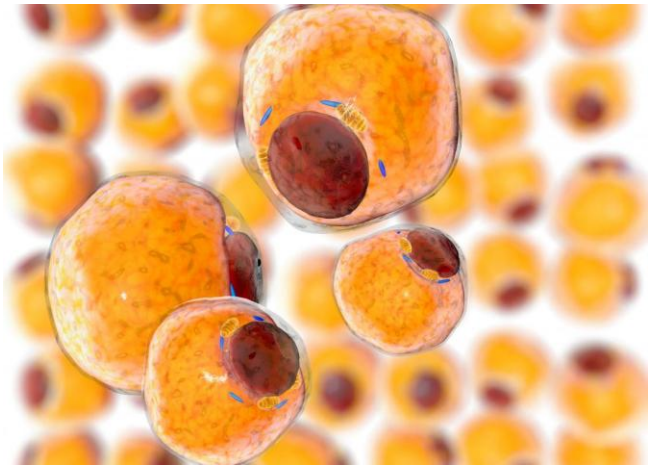
Stage 1: Excess or dysfunctional **adiposity**

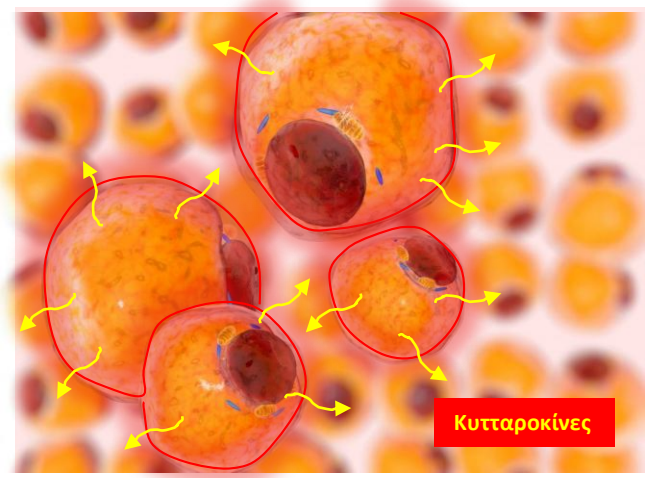


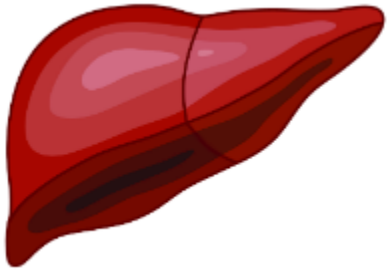
Over weight / obesity
Abdominal obesity
BMI ≥25 kg/m2
Waist circumference ≥88 (W)/102 (M)

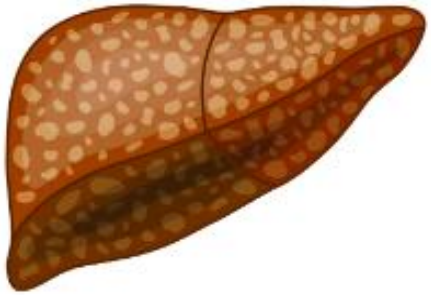
Fasting blood glucose ≥100–124 mg/dL or
HbA1c between 5.7% and 6.4%

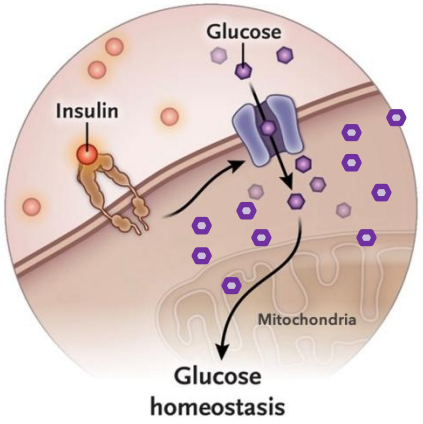
Stage 1: Excess or dysfunctional **adiposity**

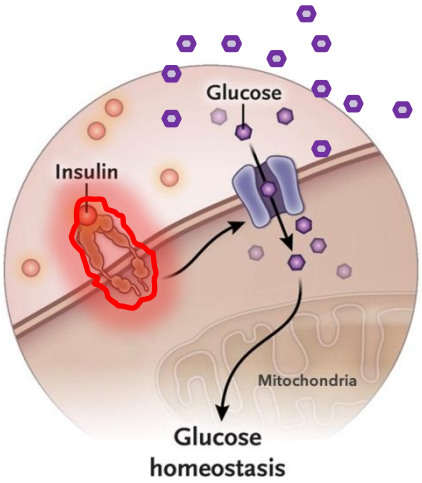












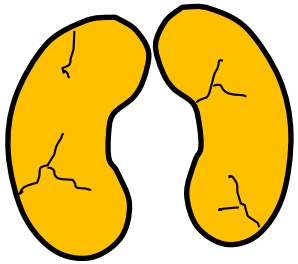
Stage 2: **Metabolic** risk factors

Hypertriglyceridemia
Low HDL

Diabetes

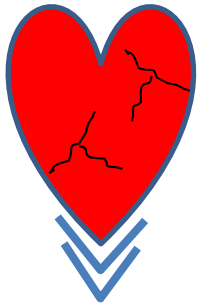
Hypertension

Inflammation
Hypercoagulability
Endothelial dysfunction



CKD

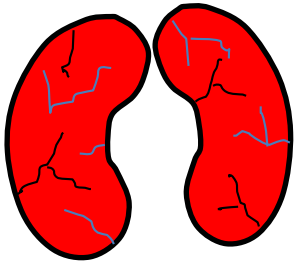
Stage 3: **subclinical** CVD in CKM syndrome or high predicted CVD risk or very high-risk CKD



Echo/biomarkers

NT-proBNP ≥125 pg/mL
hs-troponin T ≥14 ng/L

very high-risk CVD

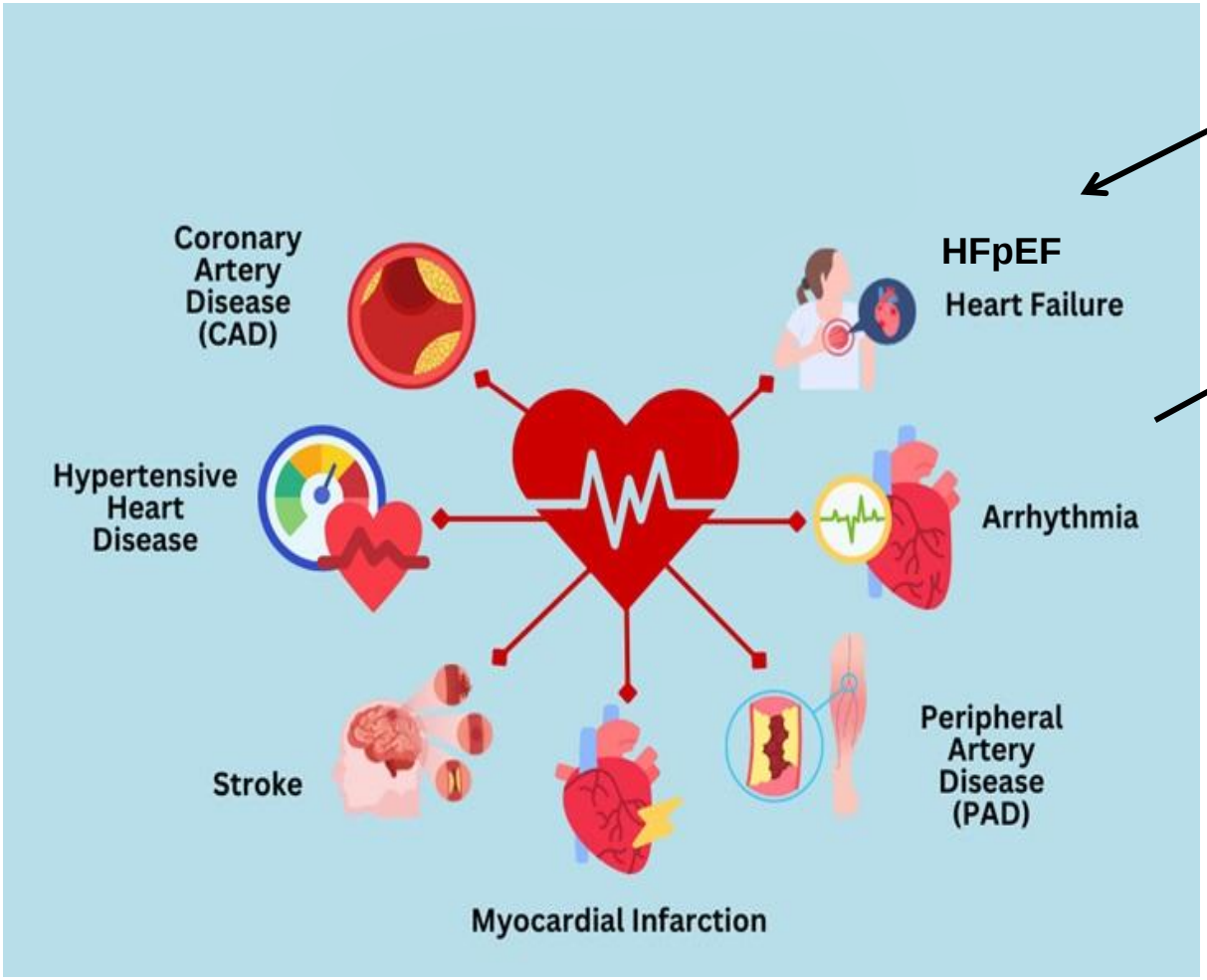


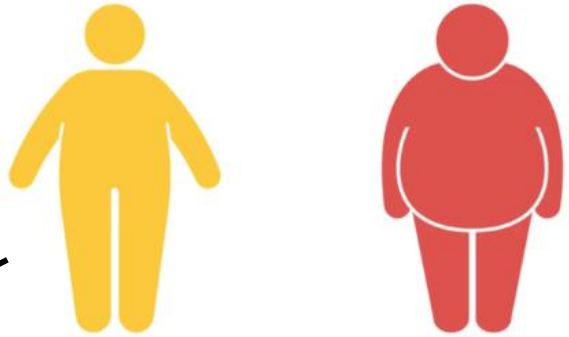
very high-risk CKD

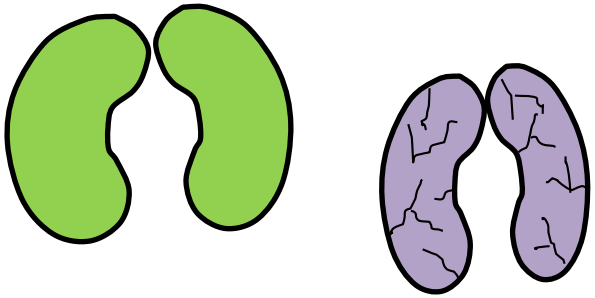
G4 or G5 CKD or
Very high risk (KDIGO)

Individuals with metabolic risk factors

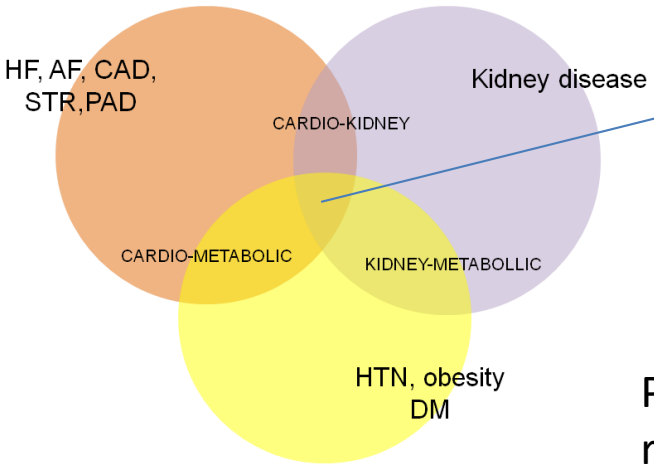
Stage 4: **Clinical** CVD in CKM syndrome







CKD stage 4a / 4b



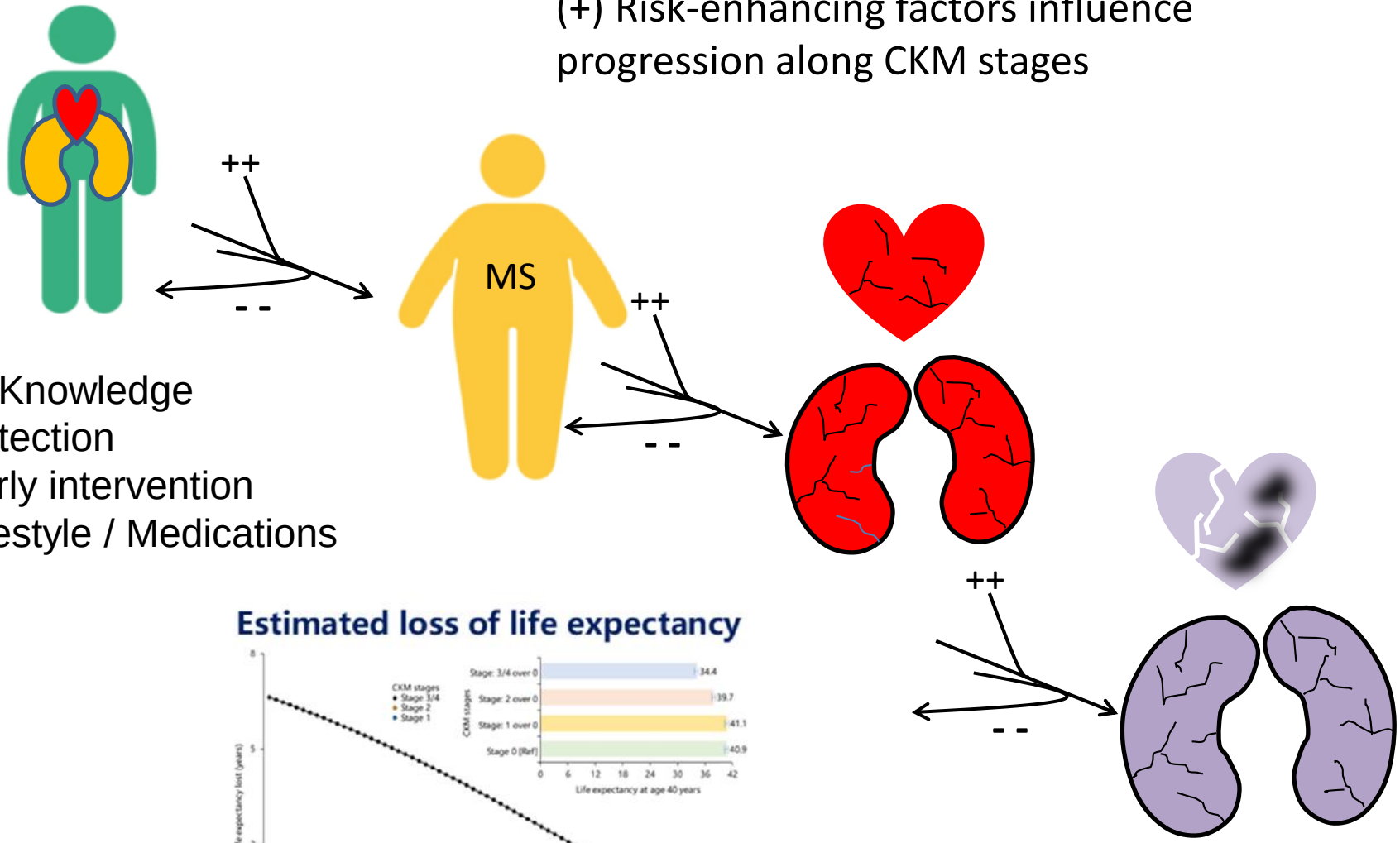
HF / ischemic heart disease/AF + CKD (4b)

Particularly high risk for recurrent CVD events and mortality

Unique treatment challenges

Imperative interdisciplinary care

(+) Risk-enhancing factors influence progression along CKM stages



(-) Knowledge
Detection
Early intervention
Lifestyle / Medications

6.81-year reduction in LE for participants in CKM stage 3/4 compared to stage 0

Screening for CKM risk factors

Life time

Frequency and intensity
according to the CKM stage

Early life (<21 y)

Screening for

- Overweight and **obesity**: annually
- High **blood pressure**: 3y, annually
- Mental and behavioral health, **SDOH** screening for all children
- Fasting **lipid** panel recommended: 9 - 11y → 17-21y (FH..?)
- **FPG/OGTT/HbA1c, ALT**: 9-11y → (repeat in obese children)

Adulthood (≥21 y)

Screening for (frequency according to stage)

Obesity: annually

MetS components (every 1, 3. 5y according to CKM stage)

Liver fibrosis related to MASLD

KDIGO staging (UACR/ serum creatinine/cystatin C (frequency according to stage)

Subclinical HF / CVD / CAC…

Social determinants of health

SDOH, social determinants of health

- Personal characteristics: **race**, ethnicity
- **Economic** stability
- Parental **unemployment**
- **Food** insufficiency, **housing** instability
- Child's **education** needs
- Child's health **insurance**
- **Neighborhood** environment
- Difficulty paying **bills**
- Parental **education**
- Partner **violence** in household
- **Alcohol** / **substance** use in household
- Parental **depression**

The American Heart Association PREVENT™ Online Calculator

About the PREVENT Equations | Online Calculator

10-year and 30-year risk for total CVD

CVD | ASCVD | Heart Failure

Sex*
Male Female

Age (years)*
30-79

SBP (mmHg)*
90-200

Total Cholesterol (mg/dL)*
130-320

HDL Cholesterol (mg/dL)*
20-100

eGFR (mL/min/1.73m²)*
15-140

BMI (kg/m²)*
18.5-39.9

Diabetes
Any history of diabetes.
No Yes

Current Smoking
Any cigarette use within the last 30 days
No Yes

Lipid-lowering medication
Current use of statin medication to lower cholesterol
No Yes

Anti-hypertensive medication
Current use of any medication for hypertension
No Yes

The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available,

If available or indicated, select "Yes" and enter the value.

UACR (mg/g)
UACR is clinically indicated for individuals with chronic kidney disease, diabetes, or hypertension
No Yes

HbA1C
HbA1c is clinically indicated for individuals with diabetes, prediabetes, overweight, or obesity, or those with history of gestational diabetes
No Yes

Zip Code
valid 5-digit zip code is needed to estimate social deprivation index [SDI]
No Yes

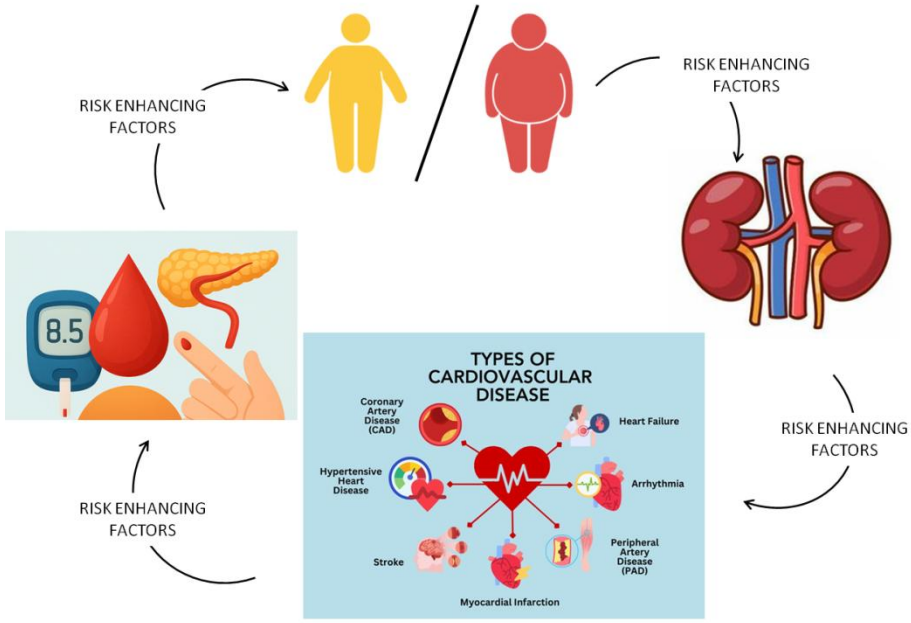
Calculate Reset

Development and Validation of the AHA PREVENT Equations Circulation. 2023

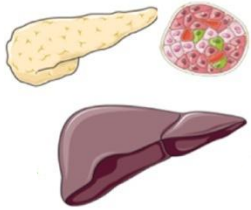
Cardiovascular-Kidney-Metabolic Syndrome – CKMS therapies:

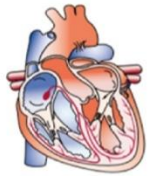
Disease → Pathophysiology → Treatment

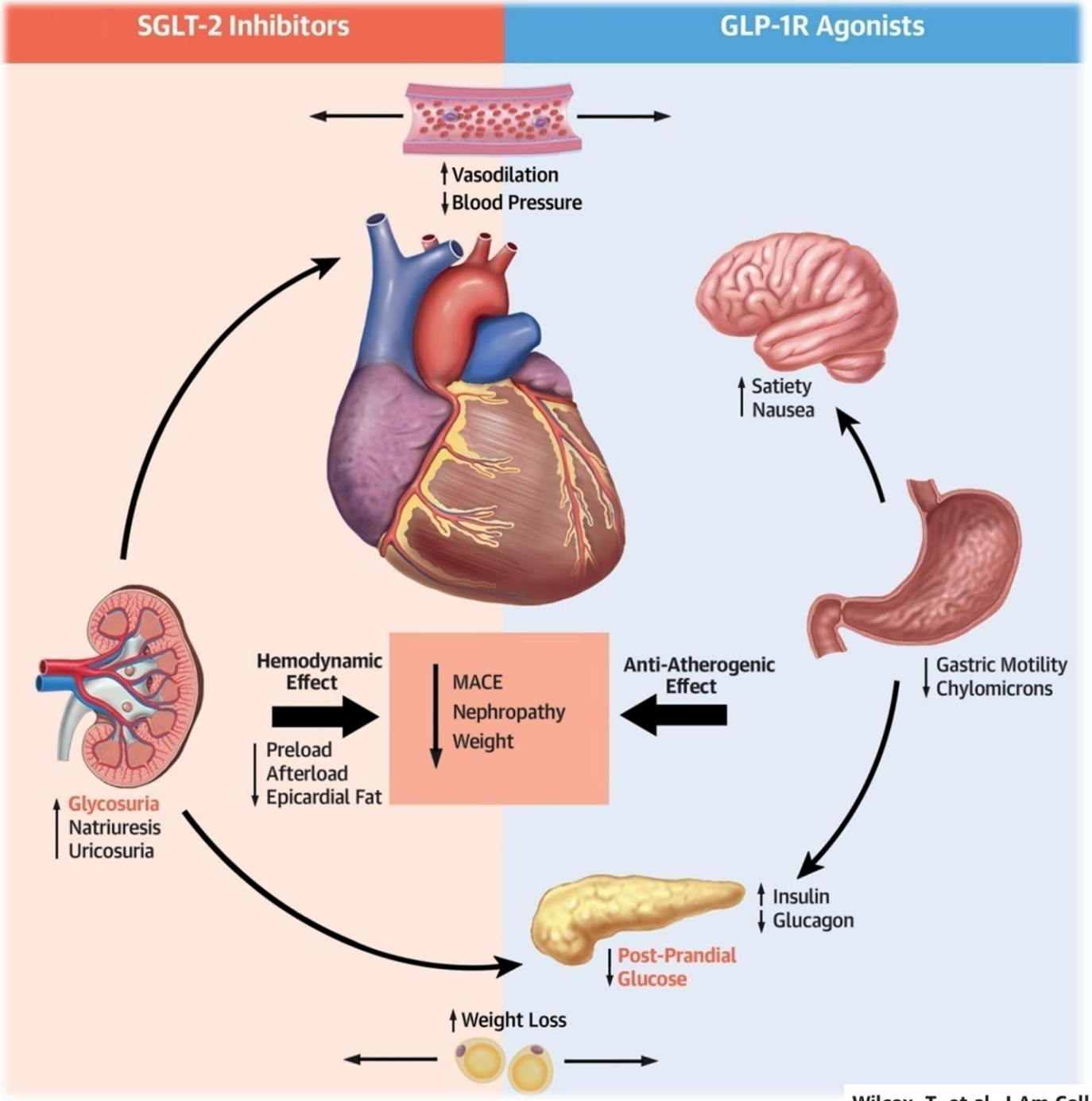
Beneficial metabolic effects
CVD protection
Nephroprotection
Mortality



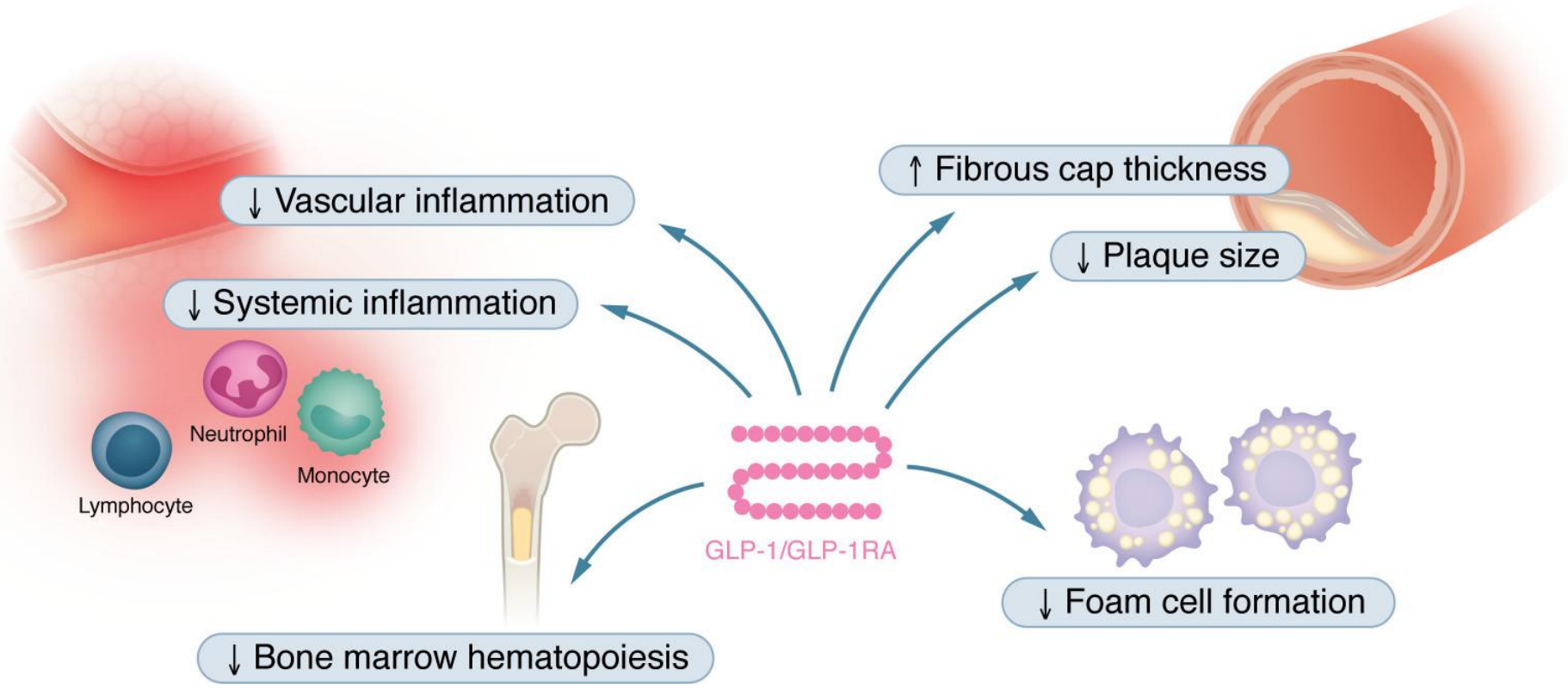
SYNDROME

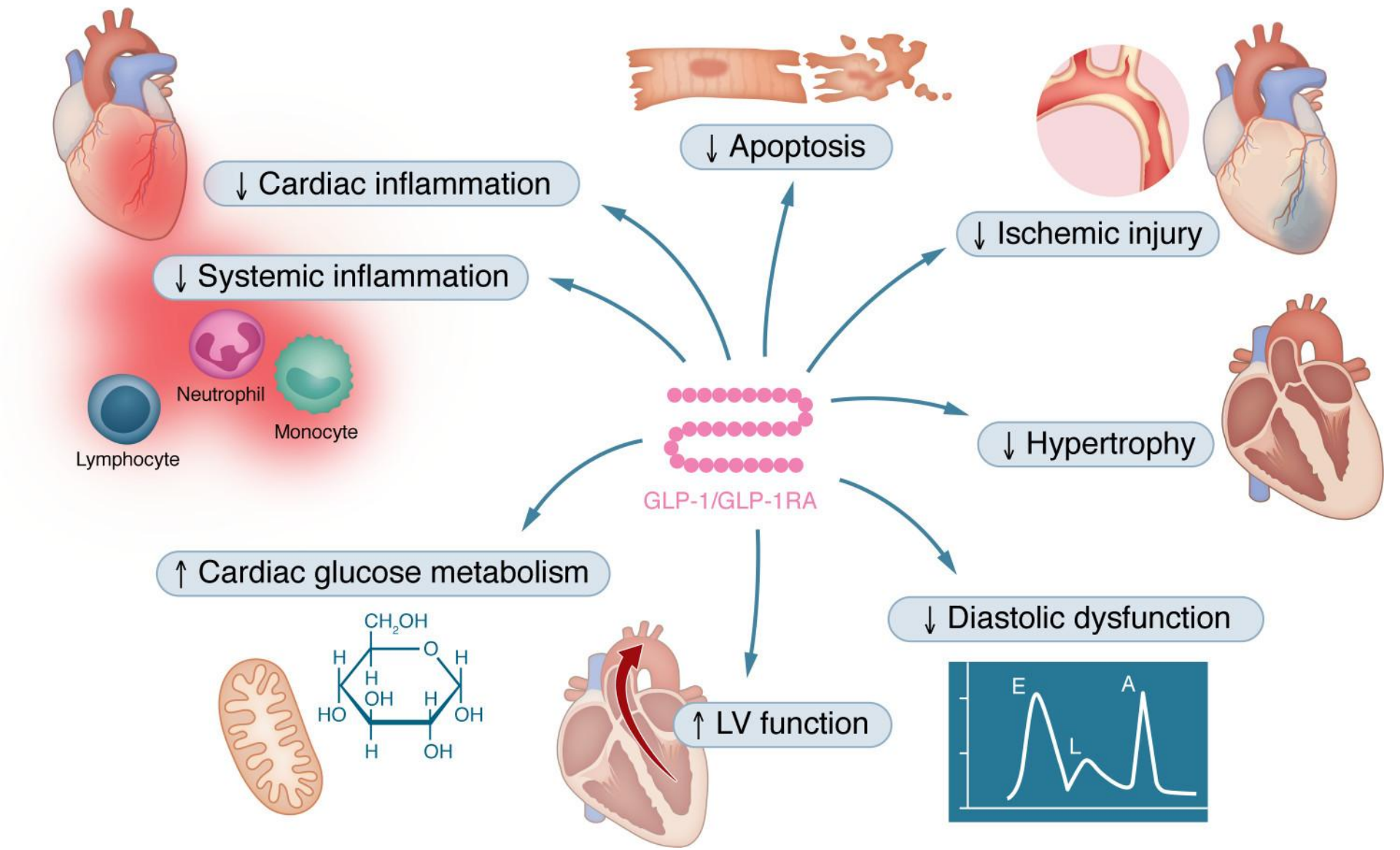




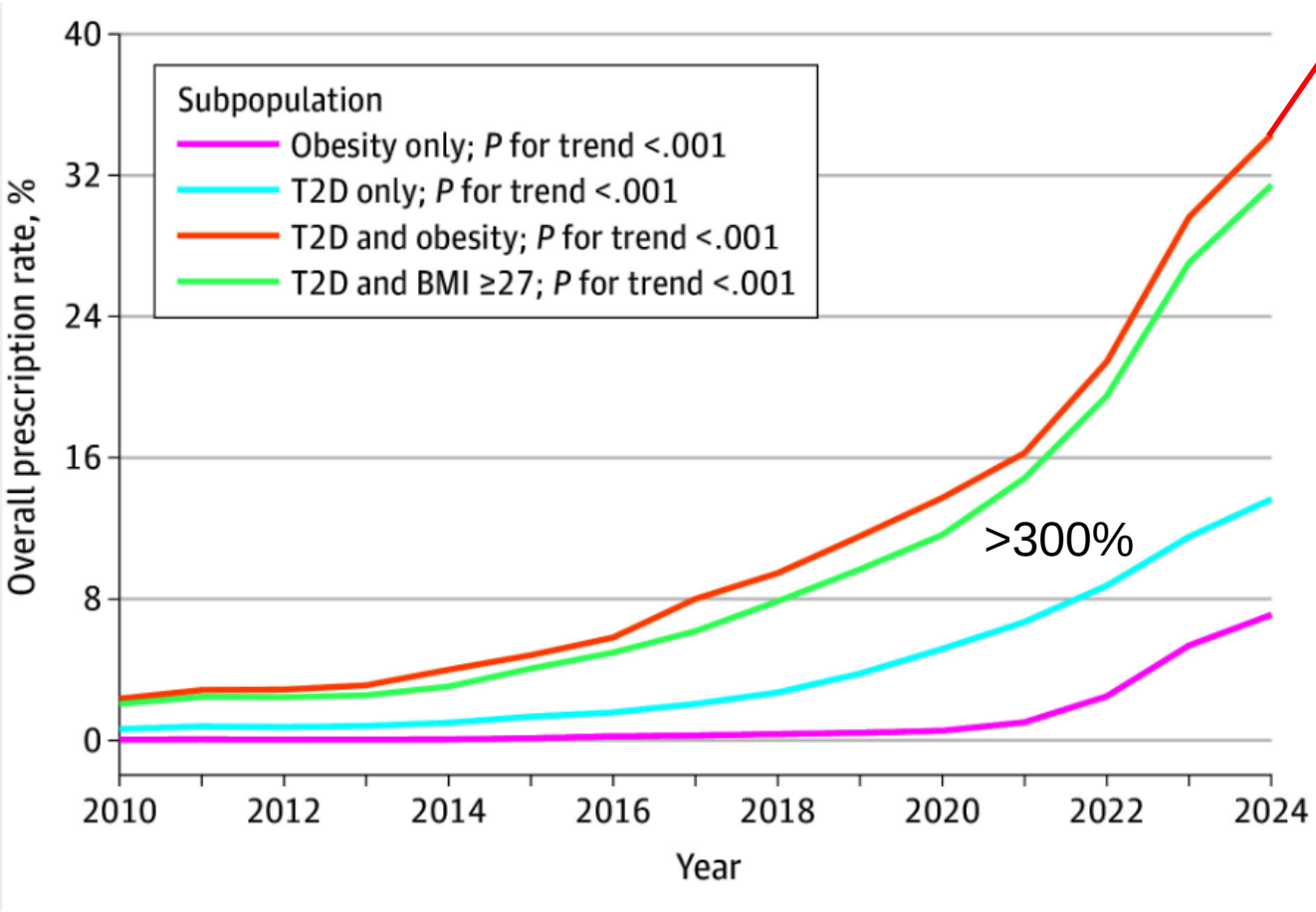


Wilcox, T. et al. J Am Coll Cardiol. 2020;75(16):1956-74.


↓ Vascular inflammation
↓ Systemic inflammation
Neutrophil
Monocyte
Lymphocyte
↑ Fibrous cap thickness
↓ Plaque size
GLP-1/GLP-1RA
↓ Foam cell formation
↓ Bone marrow hematopoiesis

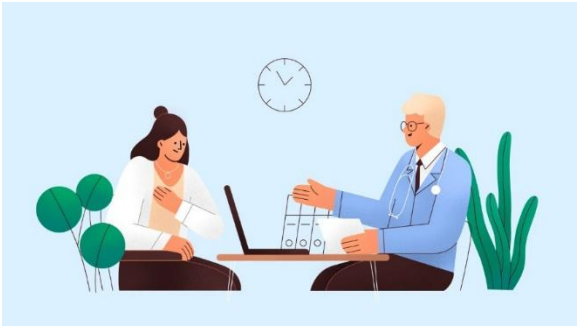

↓ Cardiac inflammation
↓ Apoptosis
↓ Ischemic injury
↓ Systemic inflammation
Neutrophil
Monocyte
Lymphocyte
↓ Hypertrophy
GLP-1/GLP-1RA
↑ Cardiac glucose metabolism
↓ Diastolic dysfunction
↑ LV function
E
A
L

Alzheimer's, depression, alcohol abuse, non-alcoholic fatty liver disease

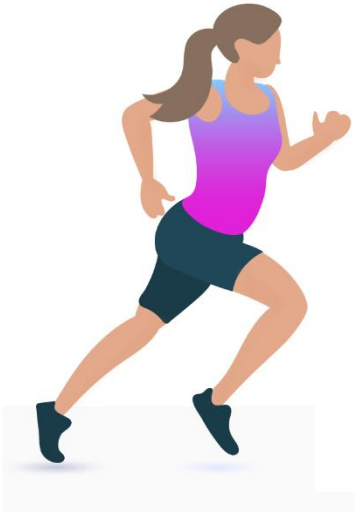


Stage 1

Discuss benefits/methods



Lifestyle intervention



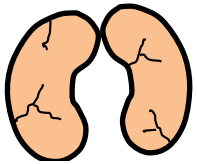
Bariatric surgery

Metformin if IGT appears

Pharmacotherapies

Stage 2

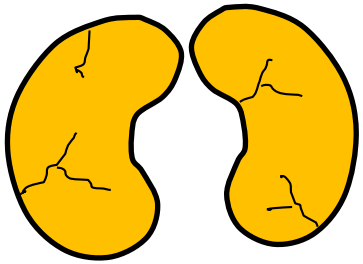
Lifestyle / statins / fibrates / ω3



SGLT2i

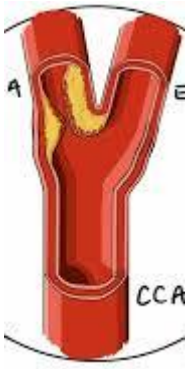
GLP1-RA

ACEI / ARBs



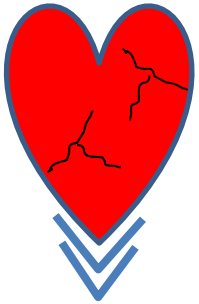
ACEI / ARBs / SGLT2i / FINERINONE (DKD ?)

Stage 3

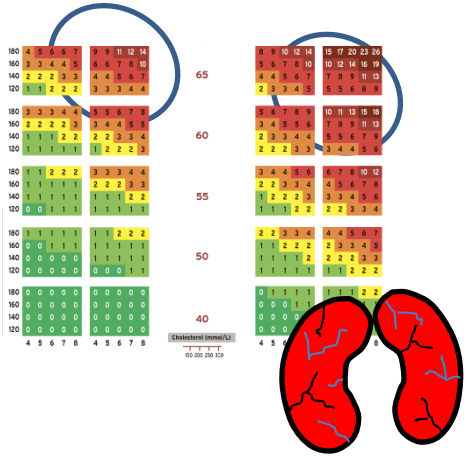


Statins ± aspirin +…

GLP-1RAs in various subgroups of patients with CKM



…SGLT2i delay disease progression, prevent symptomatic HF, and reduce CV mortality



type 2 DM and/or multiple high CKM risk factors
SGLT2i and GLP-1RA combination..
For CVD MACE risk reduction

ACEI / ARBs / SGLT2i / FINERINONE

Secondary CVD prevention and concurrent metabolic factors, CKD, or both

Stage 4:

CVD

IHD: aspirin or $P2Y_{12}$ inhibitors

LIPIDS: high-intensity statins, PCSK9i, bempedoic acid, inclisiran

MS: Fibrates, ω3

CVD CKD

Maximally tolerated ACEi / statins / SGTL2i / long-acting GLP-1RA / Finerenone

HF

β-blockers, ARBs/neprilysin inhibitors, MRAs, SGLT2i (HFr/pEF)

HF CKD

SGLT2i regardless of EF, DM status, and baseline UACR

eGFR > 20 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$ (patients on maintenance dialysis or recipients of kidney transplant allografts → NCT05374291).

GLP-1RA

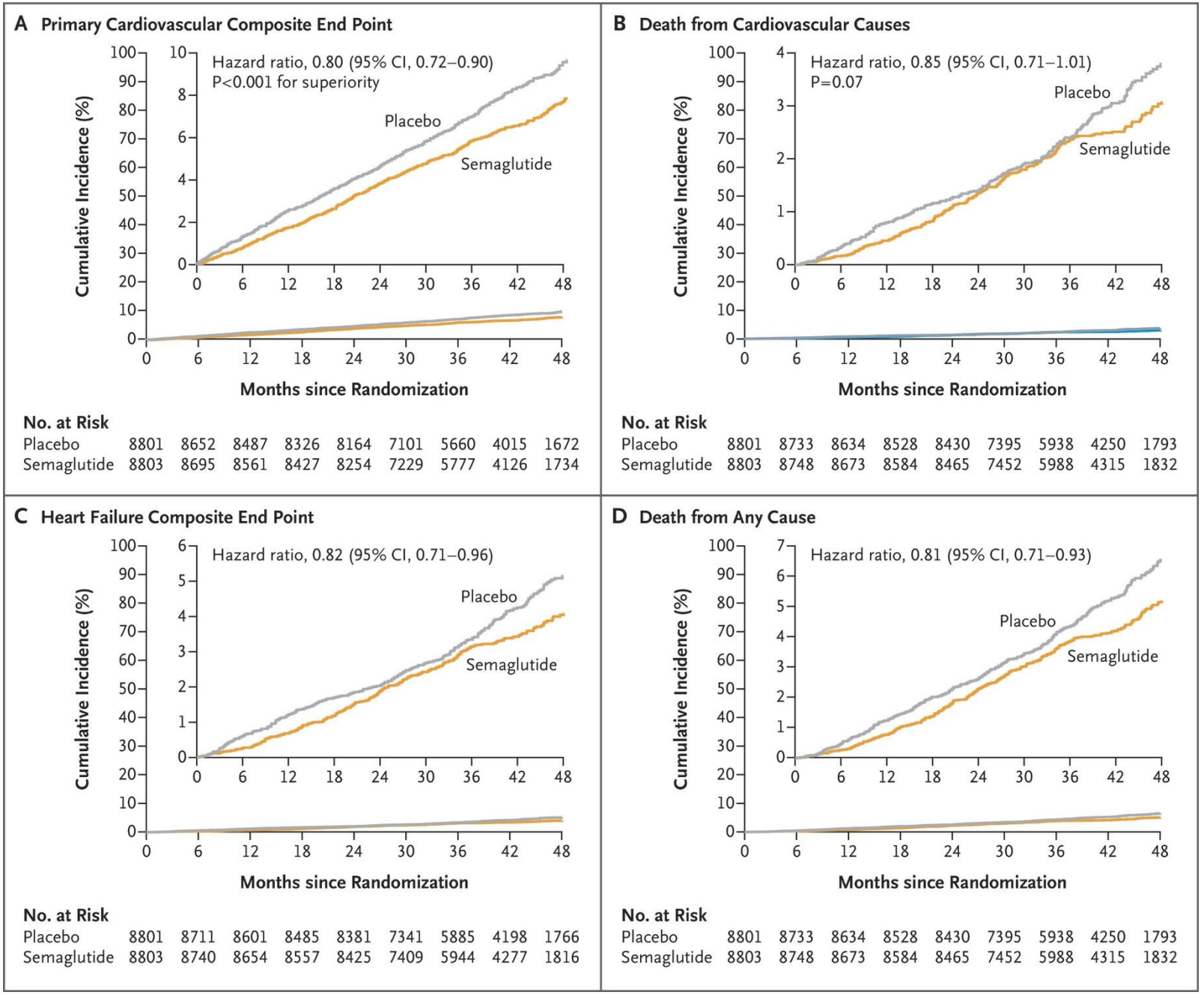
ARNi preferred over ACEi /ARBs

MRAs

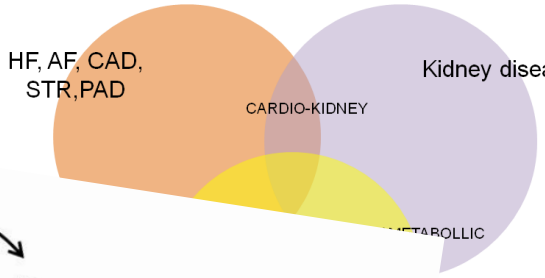
17,000: MI, stroke, PAD, BMI>27, HF (except IV), CKD (except ESKD), no DM

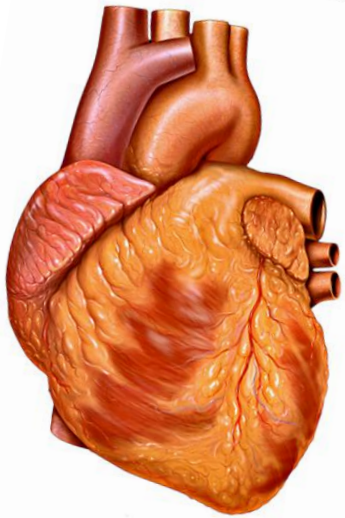
Stage 4:

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. SELECT clinical trial



N Engl J Med 2023;389:2221-2232



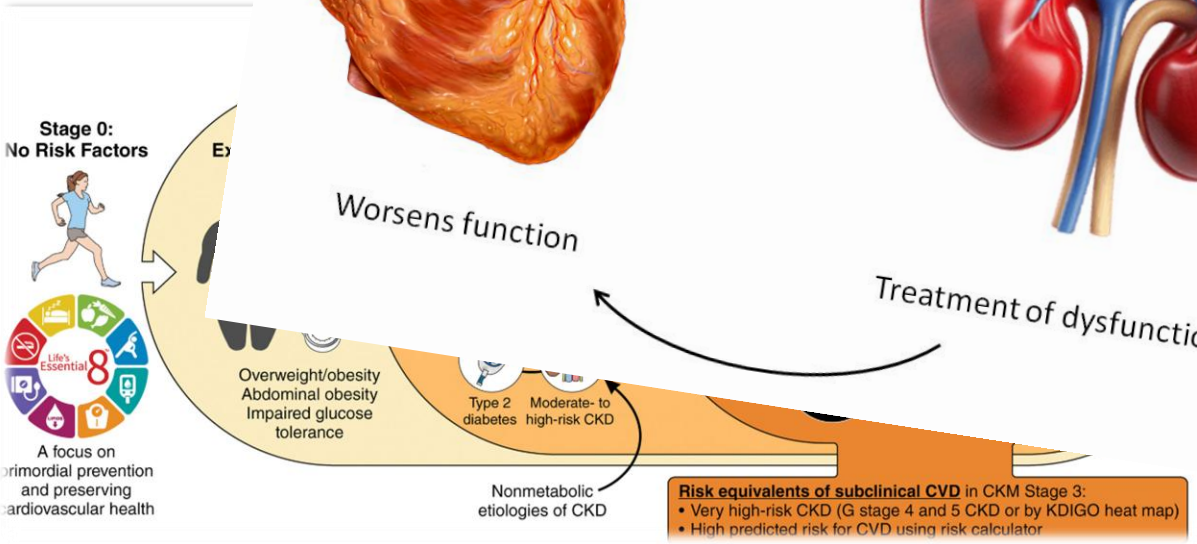


Treatment of dysfunction

Worsens function

Worsens function

Treatment of dysfunction



ity

al characteristics: race, ethnicity

mic stability

tal unemployment

insufficiency, housing instability

's education needs

d's health insurance

ghborhood environment

ficulty paying bills

arental education

- Partner violence in household
- Alcohol / substance use in household
- Parental depression