

Cardio-kidney –metabolic • syndrome

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- **Disclosures**

- Research funding and consultancy fees :

Bayer AG

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KPB Bioscience

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AstraZeneca

The George Institute for Global Health

Care Dx

Traverse Therapeutics Inc

ProKidney

Boehringer Ingelheim

Goals of presentation



Raising awareness of
the CKM conditions



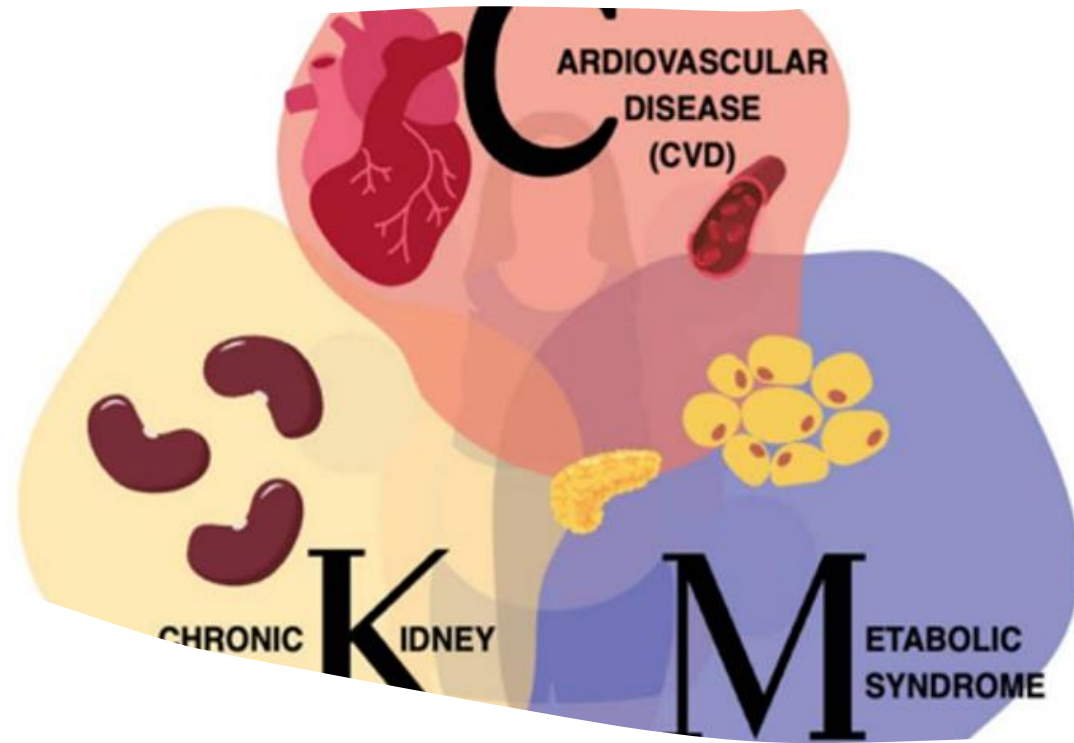
Management of
different stages of CKM
syndrome



Advantages of adopting
concept of CKM
syndrome



Examine the
implementation
barriers and facilitators



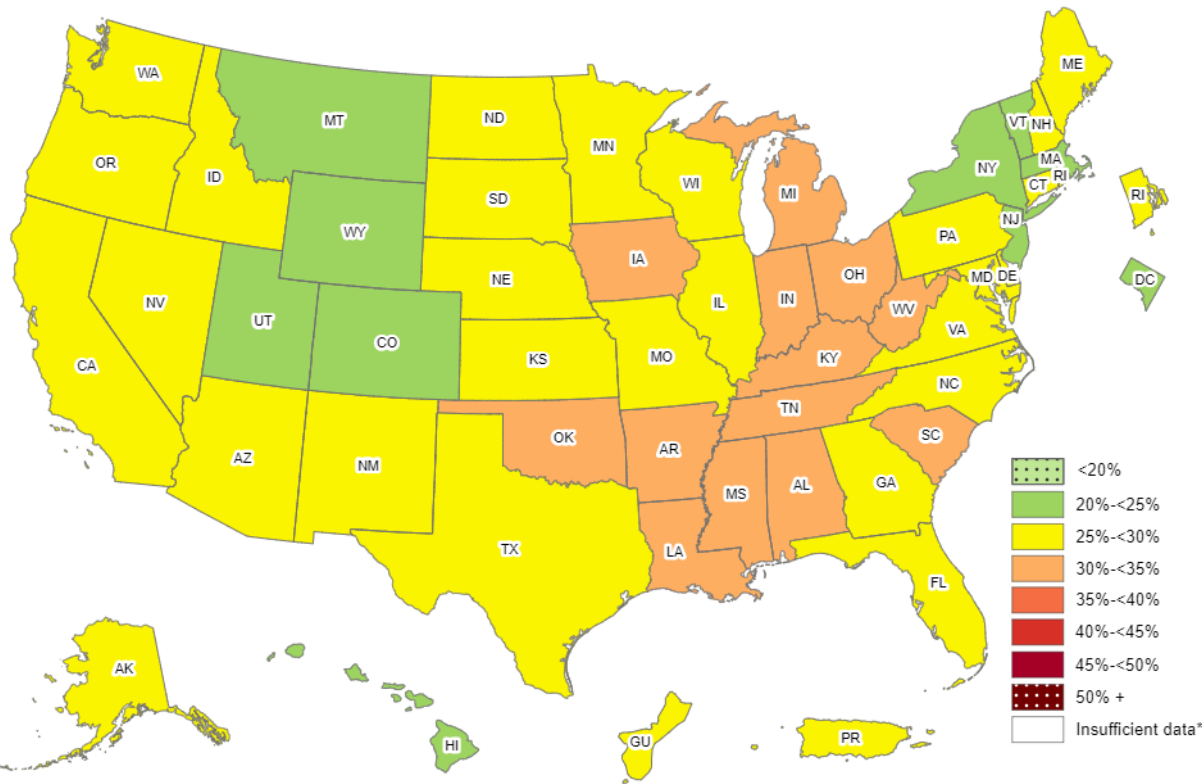
Background

Ranking the top 15 risk factors for premature death from major NCD

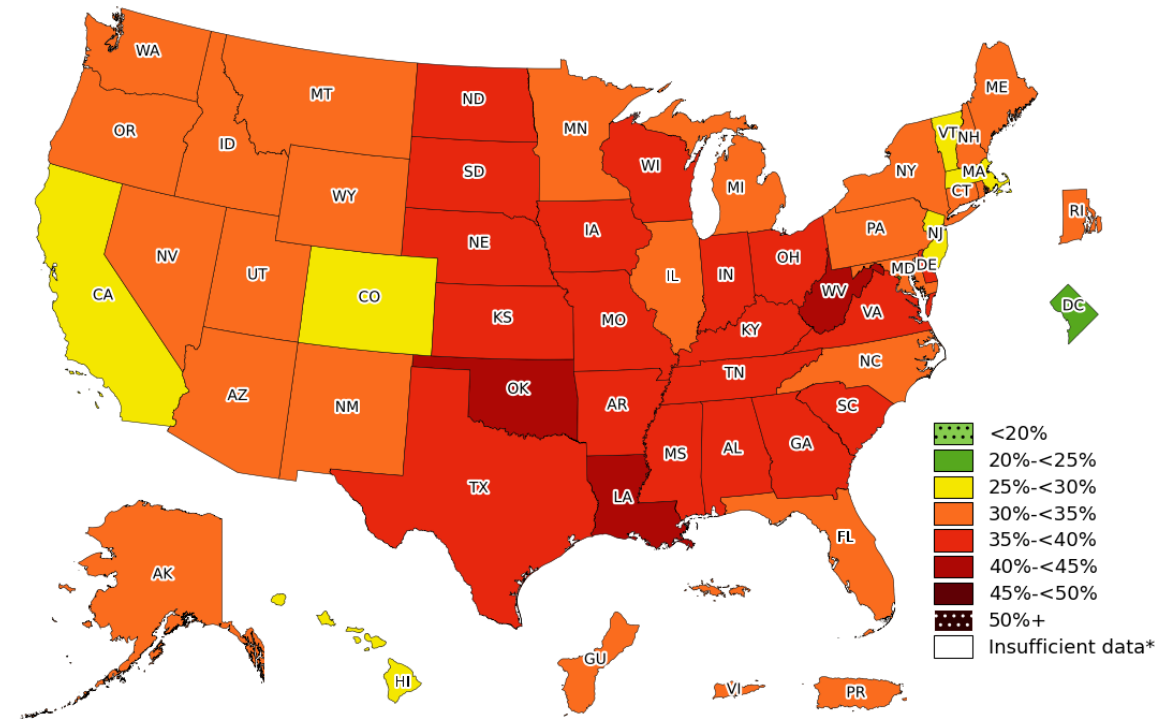
Rank	Cancers	Ischaemic Heart Disease	Stroke	Type 2 Diabetes
1	Tobacco	High systolic blood pressure	High systolic blood pressure	High fasting plasma glucose
2	High alcohol use	High LDL cholesterol	Air pollution	High body-mass index
3	Air pollution	Air pollution	Tobacco	Air pollution
4	High body-mass index	Tobacco	Diet high in sodium	Tobacco
5	Occupational risks	Diet low in whole grains	High LDL cholesterol	Diet high in processed meat
6	High fasting plasma glucose	High body-mass index	Kidney dysfunction	Non-optimal temperature
7	Diet high in red meat	High fasting plasma glucose	Diet low in fruits	Low physical activity
8	Diet low in whole grains	Kidney dysfunction	High fasting plasma glucose	Diet low in whole grains
9	Diet low in milk	Diet low in omega-6 polyunsaturated fatty acids	Non-optimal temperature	Diet low in fruits
10	Diet low in calcium	Diet low in fruits	High alcohol use	Diet high in red meat
11	Diet high in sodium	Diet low in nuts and seeds	High body-mass index	Diet high in sugar-sweetened beverages
12	Drug use	Diet low in seafood omega-3 fatty acids	Diet low in fibre	High alcohol use
13	Diet low in fruits	Diet high in sodium	Diet low in whole grains	Diet low in vegetables
14	Diet low in vegetables	Diet low in fibre	Diet low in vegetables	Diet low in fibre
15	Low physical activity	Non-optimal temperature	Low physical activity	

Self-Reported Obesity Prevalence Among U.S. Adults

2012

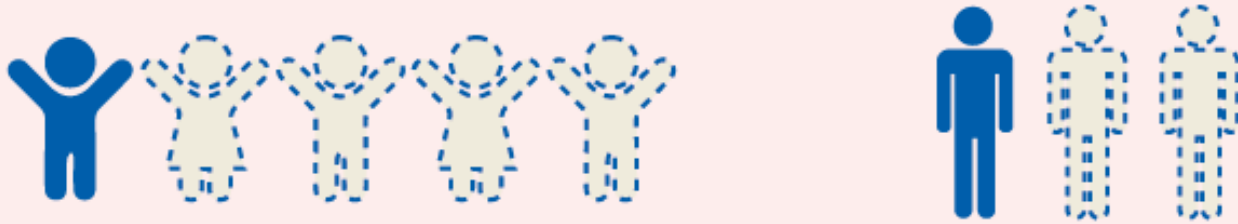


2022

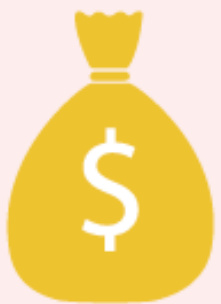


Centers for Disease Control and Prevention (CDC). Adult Obesity Prevalence Maps. Available at:
<https://www.cdc.gov/obesity/data/prevalence-maps.html#overall>

Obesity in the US is Common, Serious & Costly



About **1 in 5 children** and more than **1 in 3 adults** struggle with obesity.



The United States spends
\$147 BILLION
annually on obesity-related
health care.

Increases Risk for:

- Type 2 diabetes
- Heart disease
- Fatty liver disease
- Respiratory problems
- Osteoarthritis

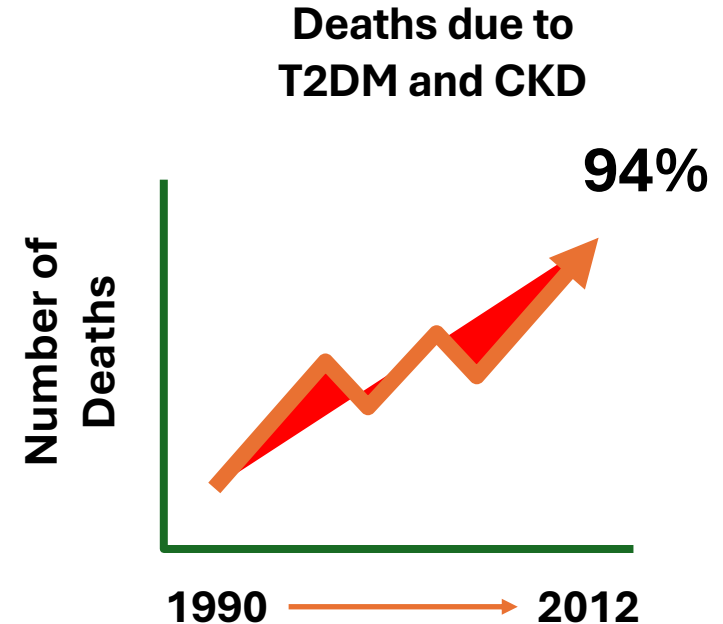
Growing Problem of T2DM and CKD

~ 590
MILLION

1 in 9 adults
(20-79 years)
are living with
diabetes

30 to 40%

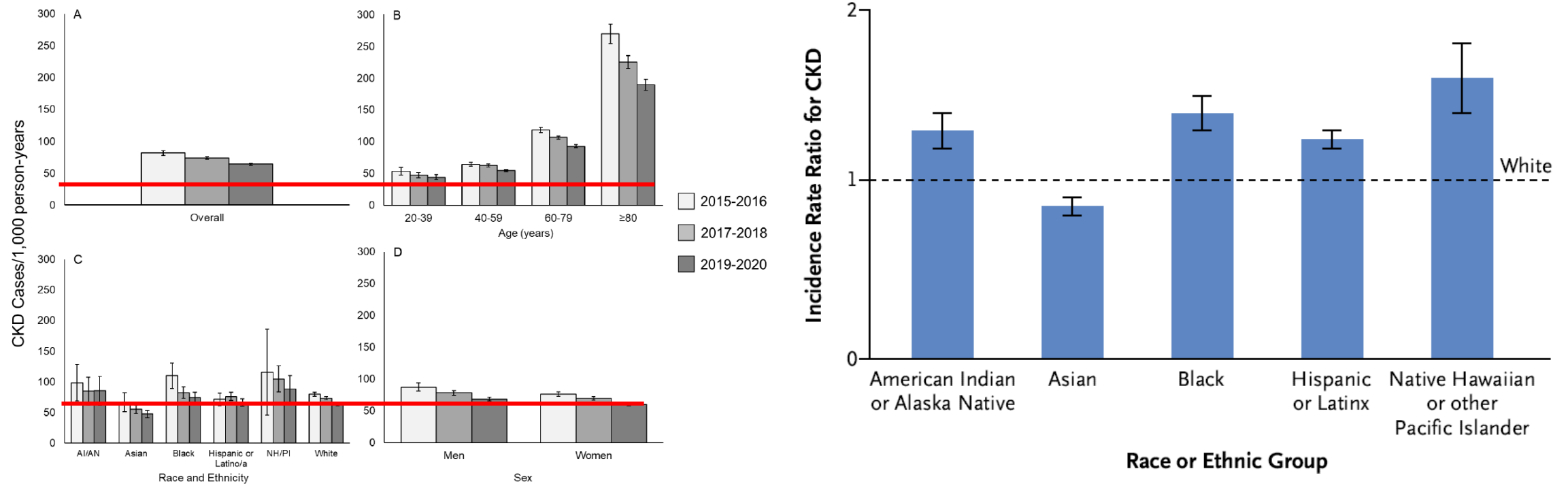
CKD cases in 1990: 378 m - in 2023 :788 million
14 % of global population



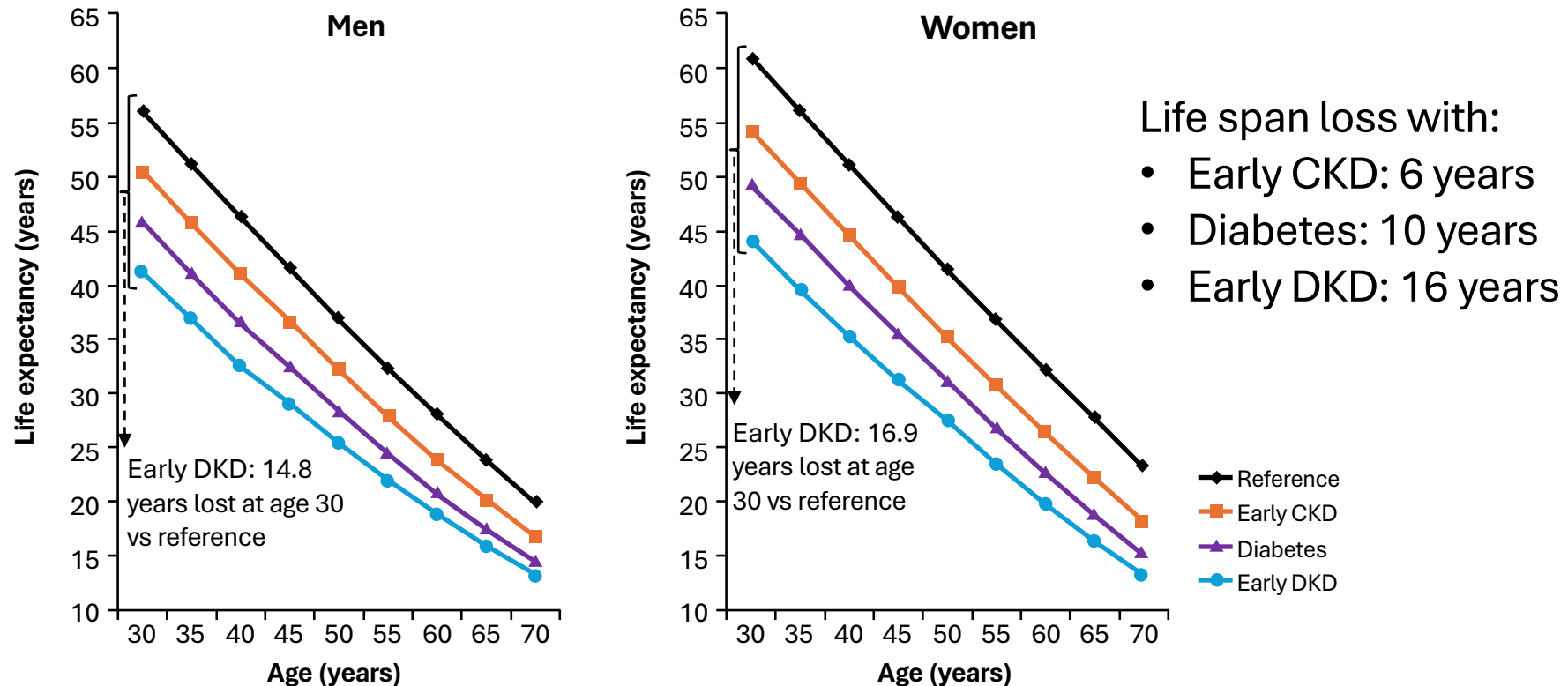
CKD Onset in Diabetes: Who and When?

CURE-CKD 2015-2020 (N=654,459)

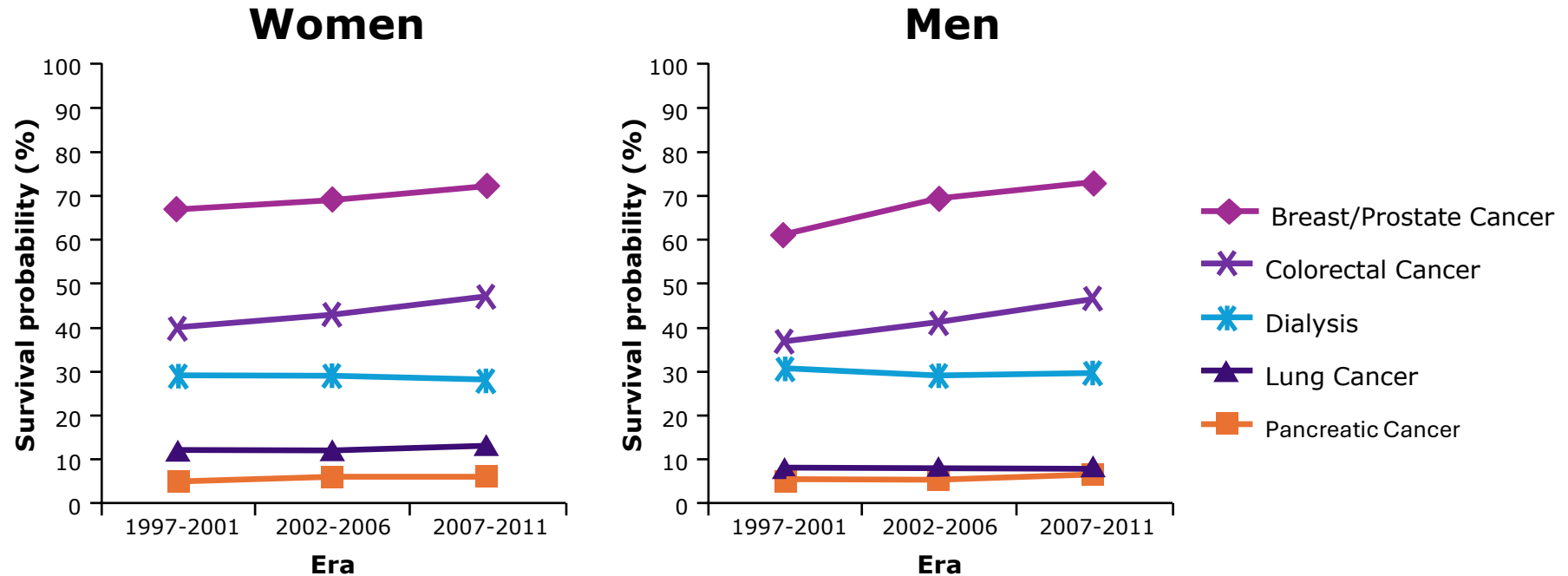
CKD Incidence in Diabetes by Demography



Diabetic Kidney Disease Shortens Life Span by 16 Years



Dialysis Survival Compared to Common Cancers



Unadjusted 10-year survival for all-cause mortality in Canada
N = 33,500 incident maintenance dialysis patients; 532,452 incident cancer patients

COVID-19 Is Not The Only Pandemic Of 21st Century ...

- **Obesity related cardiovascular deaths:**

- ➡ 1.95 million

- **Hyperglycemia attributed deaths :**

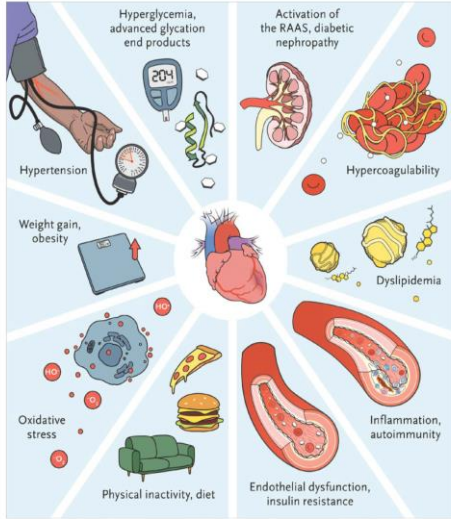
- ➡ 2.3 million cardiovascular

- ➡ 5.4 million all-cause

- **CKD attributed deaths :**

- ➡ 1.87million cardiovascular deaths

- ➡ 3.47 million all-cause deaths



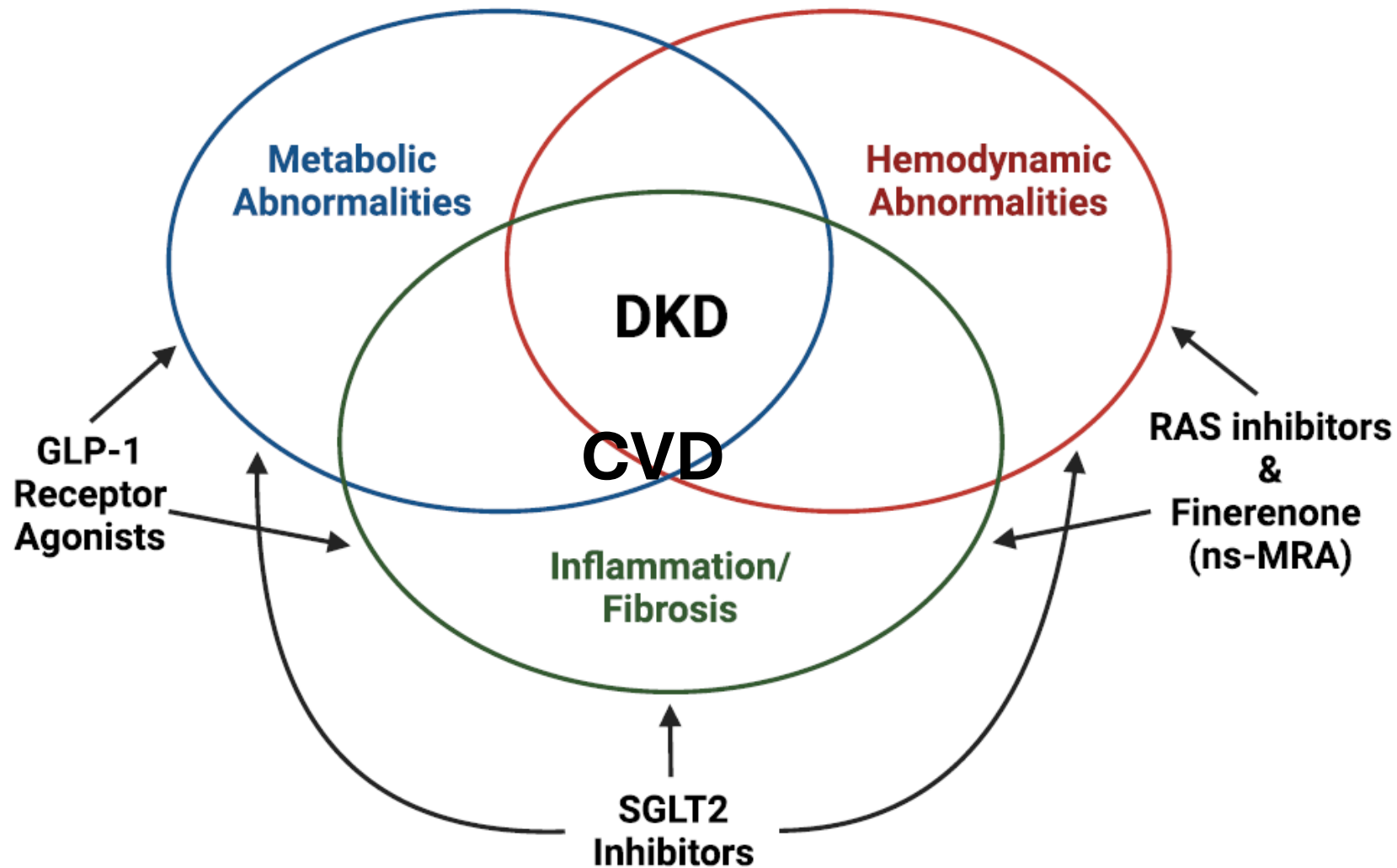
- ❑ A total number of adults (25 + years) is overweight and obese (~ 213 million)
- ❑ 30-53 % new cases of diabetes are linked to obesity
- ❑ 12% of US population and ~ 30 of 65+ have diabetes
- ❑ 1 in 3 adults with diabetes, and 1 in 5 adults with HTN have CKD
- ❑ 60 % of adults with diabetes have a chance to die from heart attack
- ❑ 90 % of US adults meet criteria for CKM

Zhu R, Wang R, He J, et al. JAMA Netw Open. 2024;7(11):e2445309;

Dai MX, et al. The Lancet. 2024;404(10469):2278-2298. ; Natalie A er al. JAHA 2021;10:e018799. <https://doi.org/10.1161/JAHA.120.018799>;

<https://gis.cdc.gov/grasp/diabetes/diabetesatlas-statsreport.html>; <https://www.cdc.gov/nccdphp/index.html>

Arrival of new therapies address metabolic, heart and kidney conditions





American
Heart
Association.



AMERICAN
COLLEGE of
CARDIOLOGY®

2026 AHA/ACC/ADA/ASN Guideline for the Prevention, Detection, Evaluation, and Management of Cardiovascular-Kidney-Metabolic Syndrome

A Report of the American College of Cardiology/American Heart Association Joint
Committee on Clinical Practice Guidelines

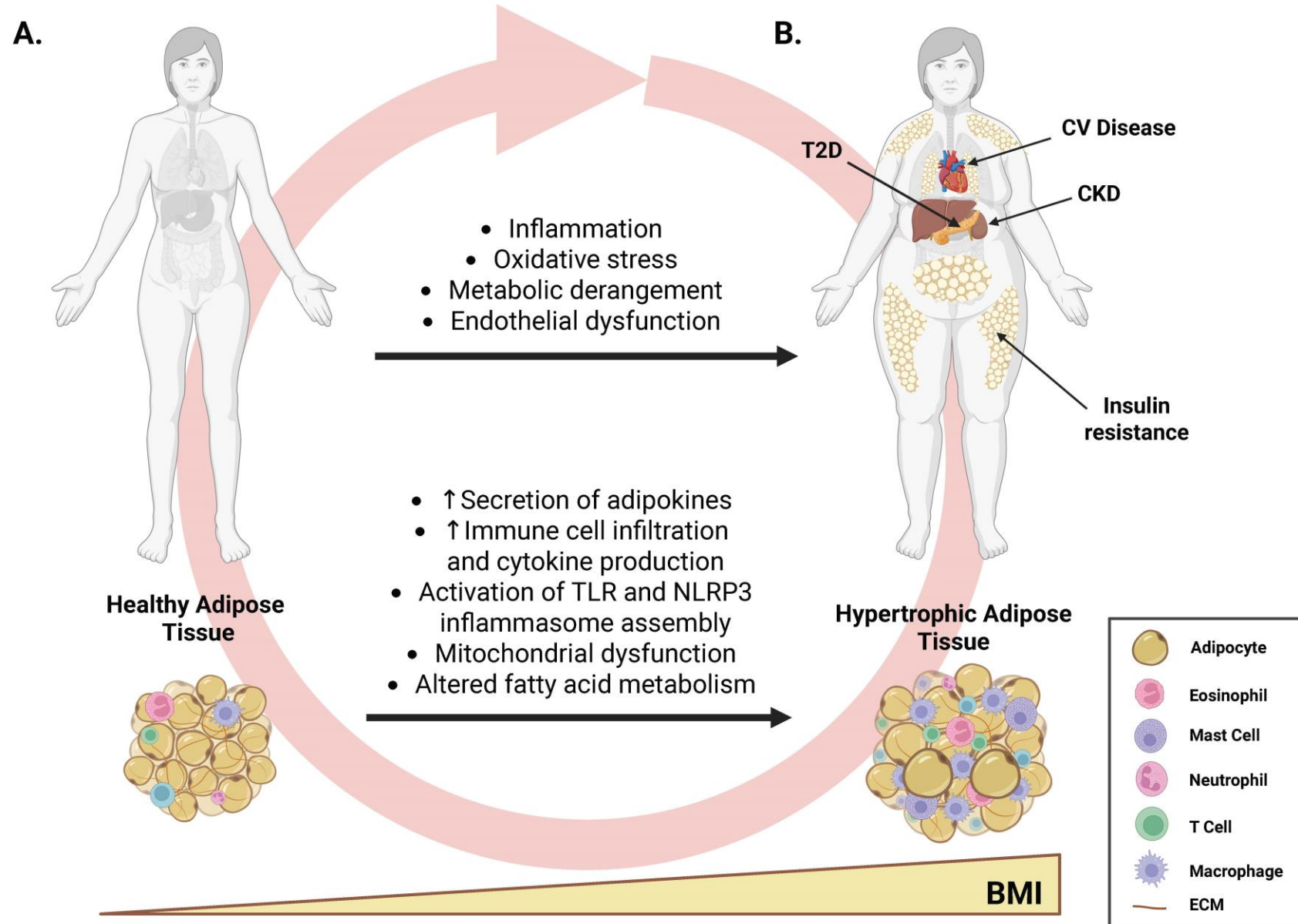
*Developed in Collaboration With and Endorsed by the **American Diabetes Association**, the **Obesity Association**, a division of the American Diabetes Association, and the **American Society of Nephrology***

CKM Syndrome Definition

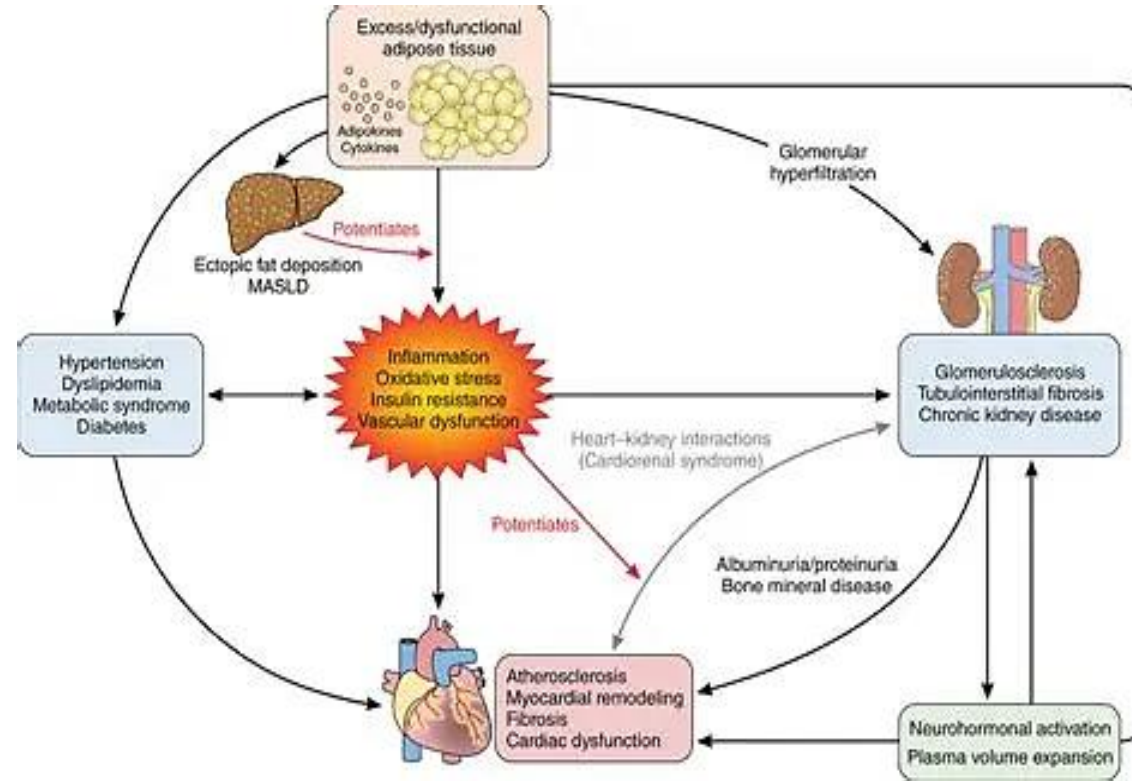
Definition	CKM syndrome is a systemic disorder characterized by pathophysiological interactions among metabolic risk factors, CKD, and the cardiovascular system, leading to multiorgan dysfunction and a high rate of adverse cardiovascular outcomes. CKM syndrome includes both individuals at risk for CVD due to the presence of metabolic risk factors, CKD, or both, and individuals with existing CKD or CVD that is potentially related to or complicates metabolic risk factors. The increased likelihood of CKM syndrome and its adverse outcomes is further influenced by unfavorable conditions for lifestyle and self-care resulting from policies, economics, and the environment.
Simplified Definition	CKM syndrome is a health disorder due to connections among heart disease, kidney disease, diabetes, and obesity, leading to poor health outcomes.

CKD indicates chronic kidney disease; CKM, cardiovascular-kidney-metabolic; and CVD, cardiovascular disease.

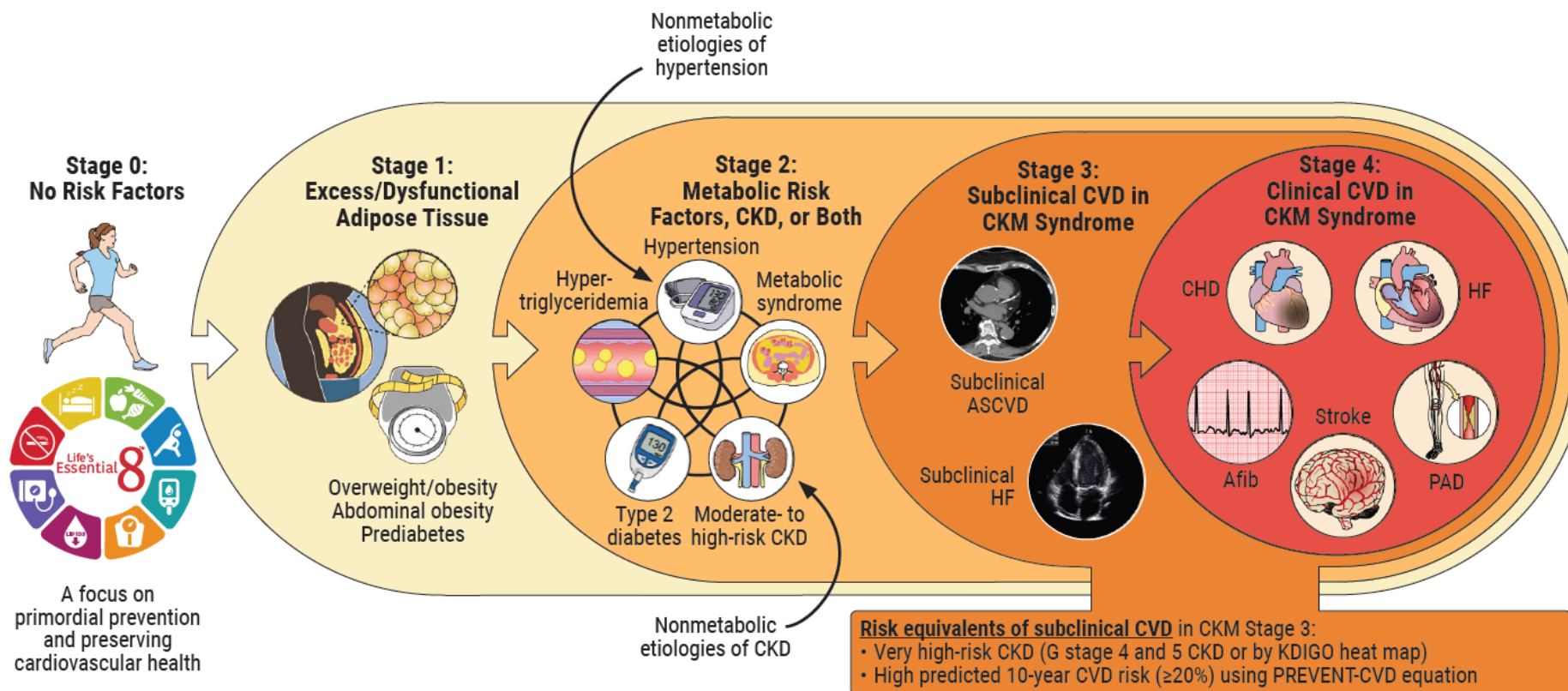
Abnormalities associated with obesity

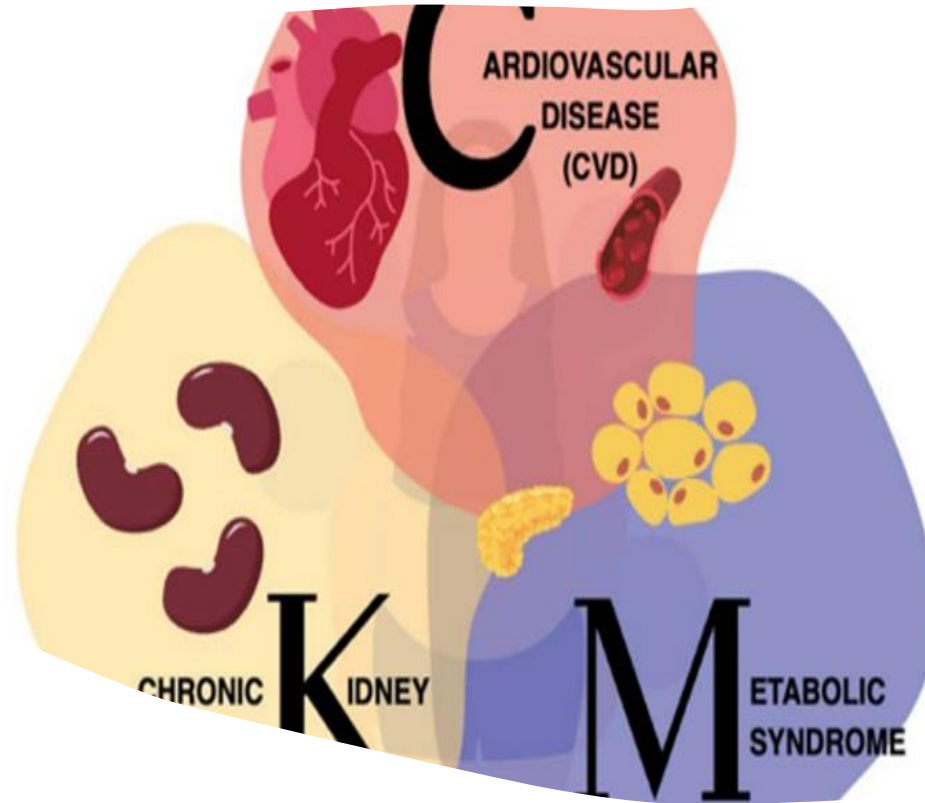


CKM syndrome pathophysiology



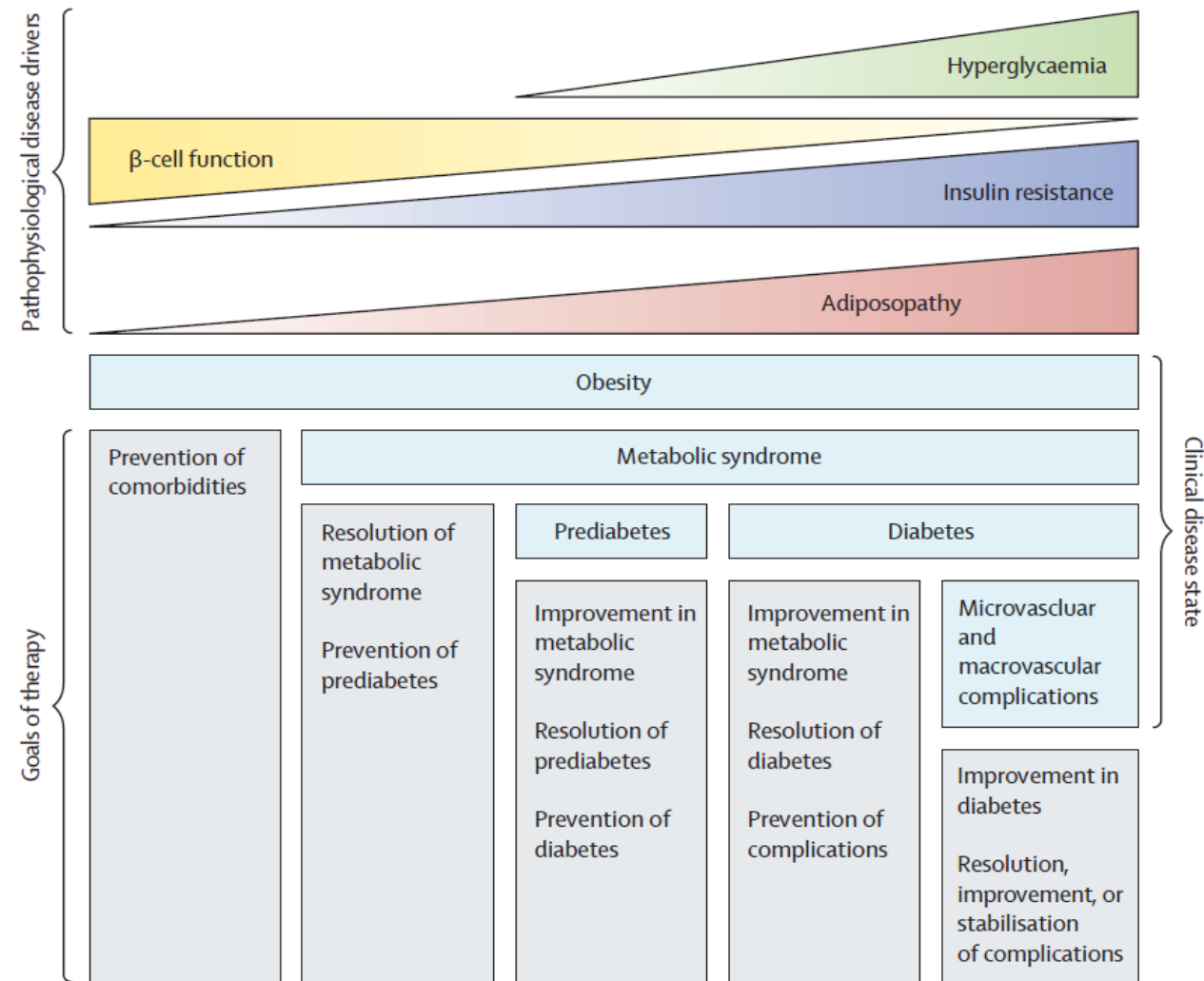
Stages of CKM Syndrome





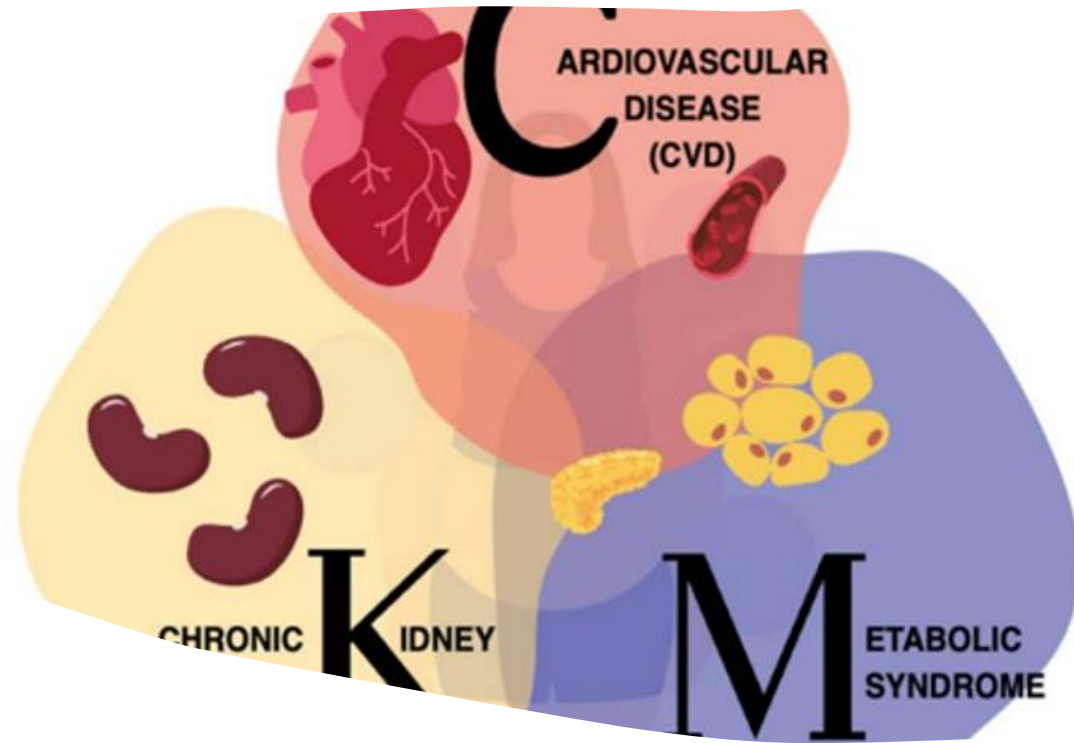
The reasons to adopt the "New syndrome"?

CKM offers framework for a comprehensive strategy for addressing the disease continuum



More reasons ...

- CKM highlights the importance of adopting lifestyle modifications.
- The CKM framework takes a holistic approach to the patient, considering overall health instead of isolated organ systems.
- Internists take ownership of treatment of obesity, diabetes, hypertension, dyslipidemia, and stable cardiovascular disease.
- It offers a chance to improve CKD detection through the combined use of AUCR and eGFR.



Diagnosis, Risk Assessment and Management

CKD Identification, Monitoring, and Actions by Risk Categories

- Risks:
- CKD progression
 - Kidney failure
 - CVD events

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 m ²) 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

Inclusion of PREVENT CVD Risk Equation in EHR

- Developed by the AHA in 2023, the Predicting Risk of Cardiovascular Disease EVENTS (PREVENT) equations estimate 10-year and 30-year risk for total cardiovascular disease (CVD), including atherosclerotic CVD (ASCVD) and heart failure (HF).
- It is the first risk tool to combine cardiovascular, kidney, and metabolic health measures to guide primary prevention-focused treatment decisions.

PREVENT™ Online Calculator

Welcome to the American Heart Association Predicting Risk of cardiovascular disease EVENTS (PREVENT™). This app should be used for primary prevention patients (those without atherosclerotic cardiovascular disease or heart failure) only.

The screenshot shows the PREVENT™ Online Calculator form. It includes fields for Sex (Male/Female), Age (30-79 years), Total Cholesterol (130-320 mg/dL), HDL Cholesterol (20-100 mg/dL), SBP (90-200 mmHg), BMI (18.5-39.9), eGFR (15-140), Diabetes (No/Yes), Current Smoking (No/Yes), Anti-hypertensive medication (No/Yes), Lipid-lowering medication (No/Yes), UACR (No/Yes), and HbA1c (No/Yes). Each field has a red information icon (i). Four orange arrows point to the BMI, eGFR, UACR, and HbA1c fields. Below the optional predictors, a note states: "The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available, please click on yes and enter the value".

Sex ☒ Male ☐ Female

Age years *i*

Total Cholesterol mg/dL *i*

HDL Cholesterol mg/dL *i*

SBP mmHg *i*

BMI *i*

eGFR *i*

Diabetes ☒ No ☐ Yes *i*

Current Smoking ☒ No ☐ Yes *i*

Anti-hypertensive medication ☒ No ☐ Yes *i*

Lipid-lowering medication ☒ No ☐ Yes *i*

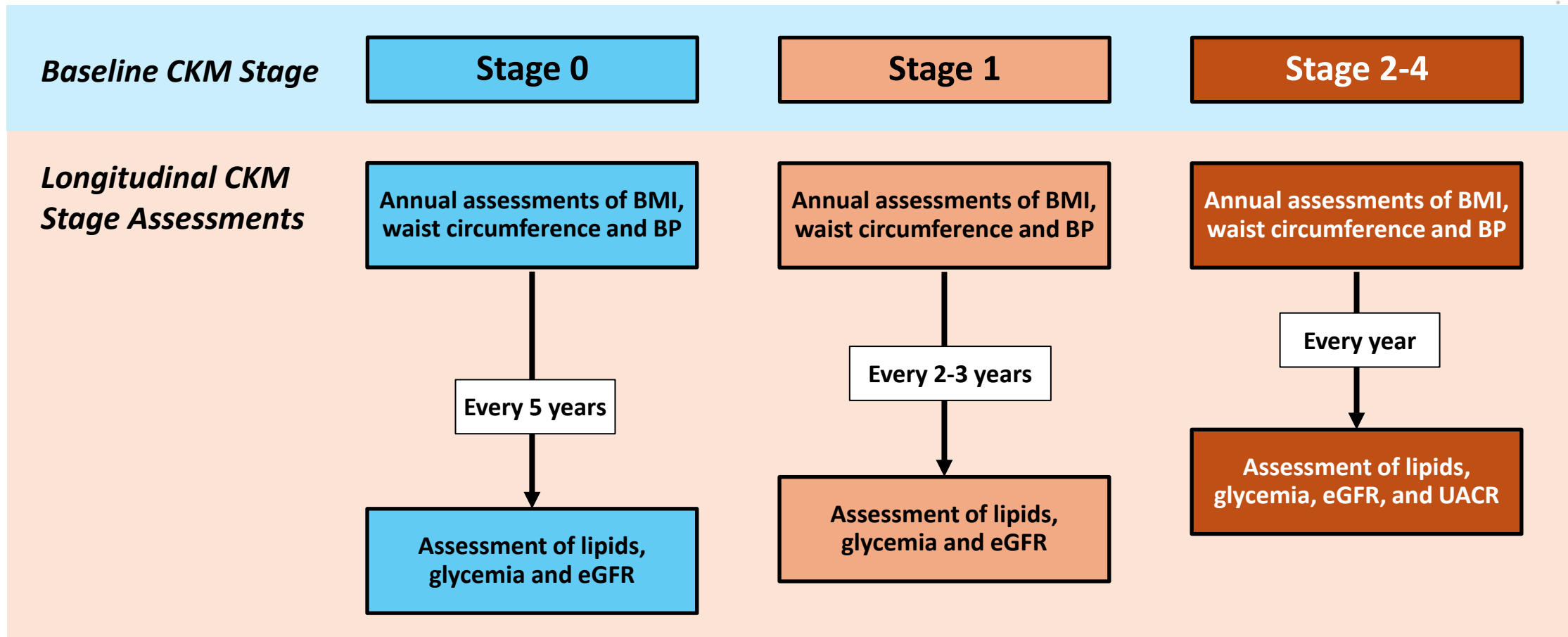
The following three predictors are optional for further personalization of risk assessment. When they are clinically indicated or available, please click on yes and enter the value

UACR ☒ No ☐ Yes *i*

HbA1c ☒ No ☐ Yes *i*

(<https://professional.heart.org/en/guidelines-and-statements/prevent-calculator>)

Longitudinal Assessments for Adults According to Baseline CKM Syndrome Stage

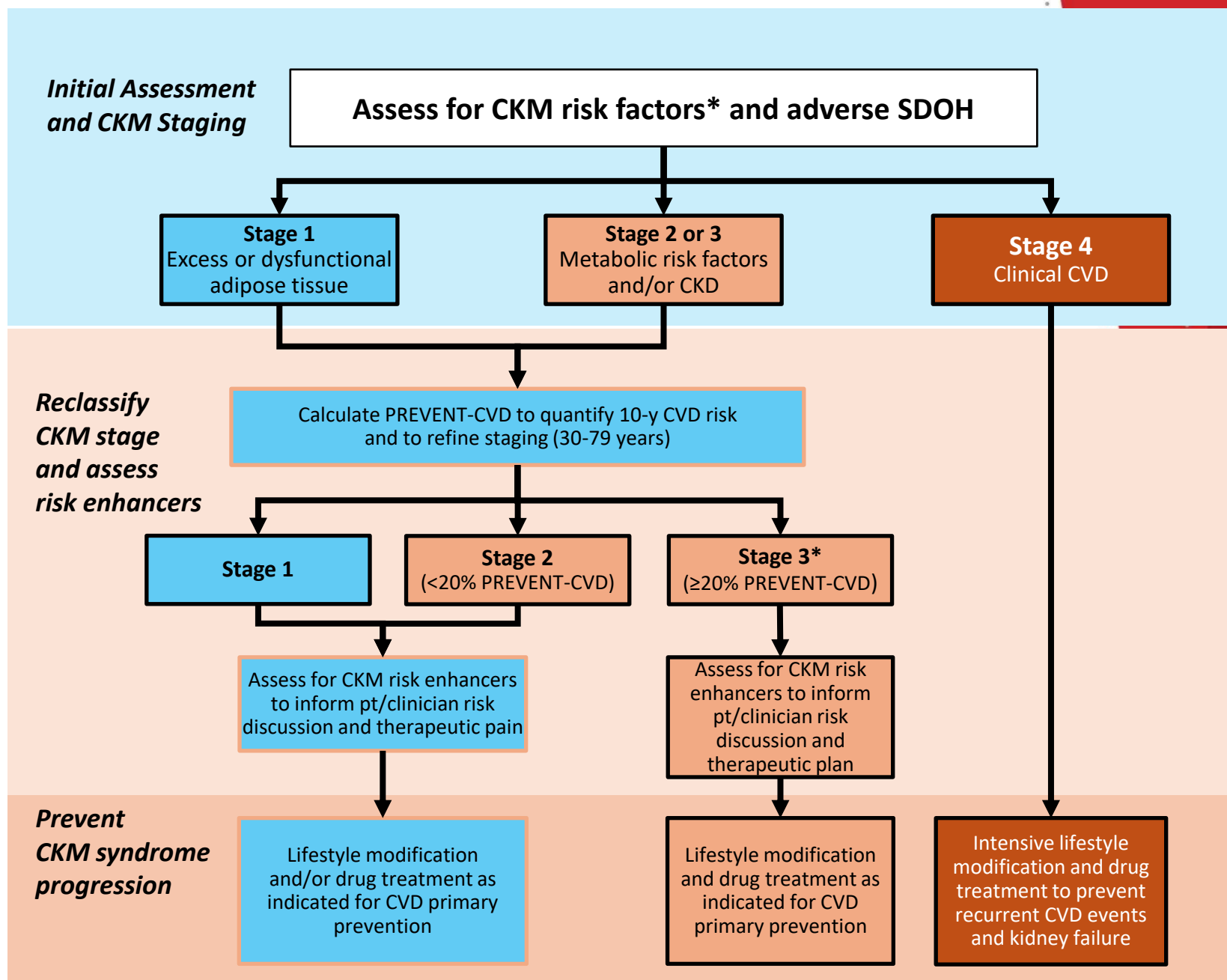


Abbreviations: BMI indicates body mass index; BP, blood pressure; CKM, cardiovascular kidney metabolic; eGFR, estimated glomerular filtration rate; and UACR, urine albumin-to-creatinine ratio.

Ndumele, C.E., et al. 2026 AHA/ACC/ADA/ASN Guideline for the Prevention, Detection, Evaluation, and Management of CKM Syndrome. *Circulation*.

Conceptual Approach to CKM Risk Assessment and Refinement

Abbreviations: CKM indicates cardiovascular kidney metabolic; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; pt, patient; and SDOH, social determinants of health.



Overview of Management Principles for CKM Syndrome Stages 1 to 3 for Patients With Obesity, Type 2 Diabetes, or CKD

Abbreviations: CHW indicates community health worker; CKD, chronic kidney disease; CKM, cardiovascular kidney metabolic; CV, cardiovascular; CVD, cardiovascular disease; DM, diabetes; GLP-1, glucagon-like peptide-1; RASi; renin-angiotensin system inhibitors; SDOH, social determinants of health; SGLT2i ; sodium-glucose cotransporter-2 inhibitors; and T2D, type 2 diabetes.

Apply the Principles of CKM Management

- Promote cardiovascular health using Life's Essential 8 Framework
- When confluent CKM conditions present (T2D, CKD, substantial subclinical CVD), facilitate interdisciplinary care, including CKM coordination point person
- Address adverse SDOH using CHW/social workers and leveraging community resources
- Manage blood pressure and lipids as per current guidelines



Manage CKM Syndrome Guided by Patient Risk Profile



For Patients With Obesity

- Non-judgmental weight loss counseling
- Lifestyle modification and behavioral interventions to support $\geq 5\text{--}10\%$ weight loss and reduce risk for CKM syndrome progression
- If not reaching weight loss goals, consider GLP-1 based therapy or metabolic and bariatric surgery to reduce weight and risk for CKM syndrome progression



For Patients With T2D

- Lifestyle modification and weight management to improve glycemic control
- Collective risk factor control with lifestyle change and targeted pharmacotherapy
- If increased CVD risk (PREVENT-CVD 10 y risk $\geq 7.5\%$ or age >50 y with other risk factors), initiate GLP-1 based agent or SGLT2i to reduce CVD events and CVD mortality
- If HbA1c $0.5\text{--}1\%$ above glycemic goal, co-utilize metformin with SGLT2i or GLP-1 based agent

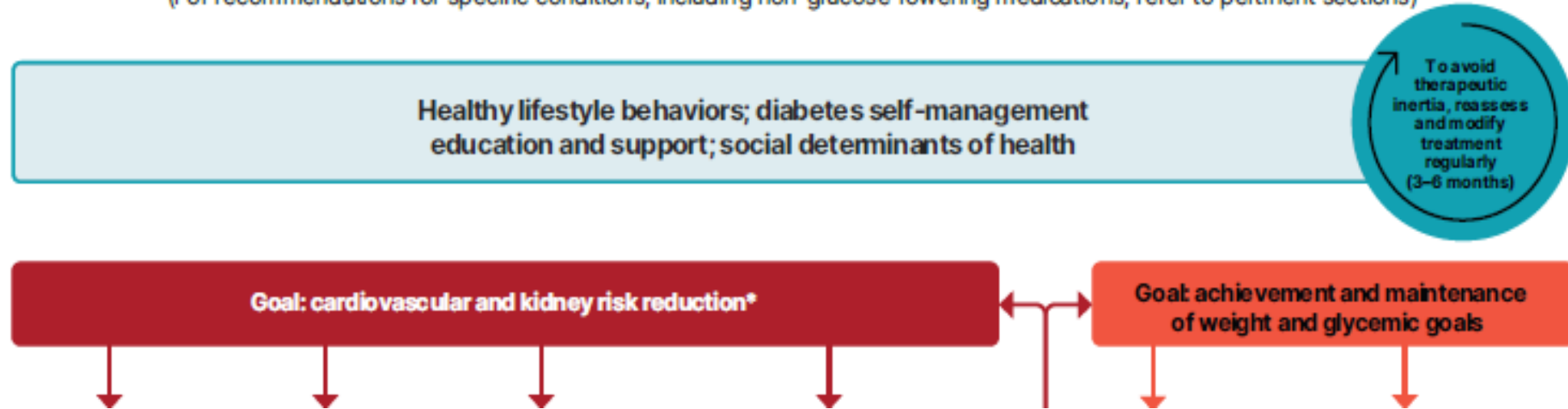


For Patients With CKD

- In patients with T2D or albuminuria, use RASi and SGLT2i as 1st line therapies to improve cardiovascular and kidney outcomes
- In patients with T2D and persistent albuminuria despite 1st line therapies, consider addition of a GLP-1 based therapy or finerenone to improve cardiovascular and kidney outcomes

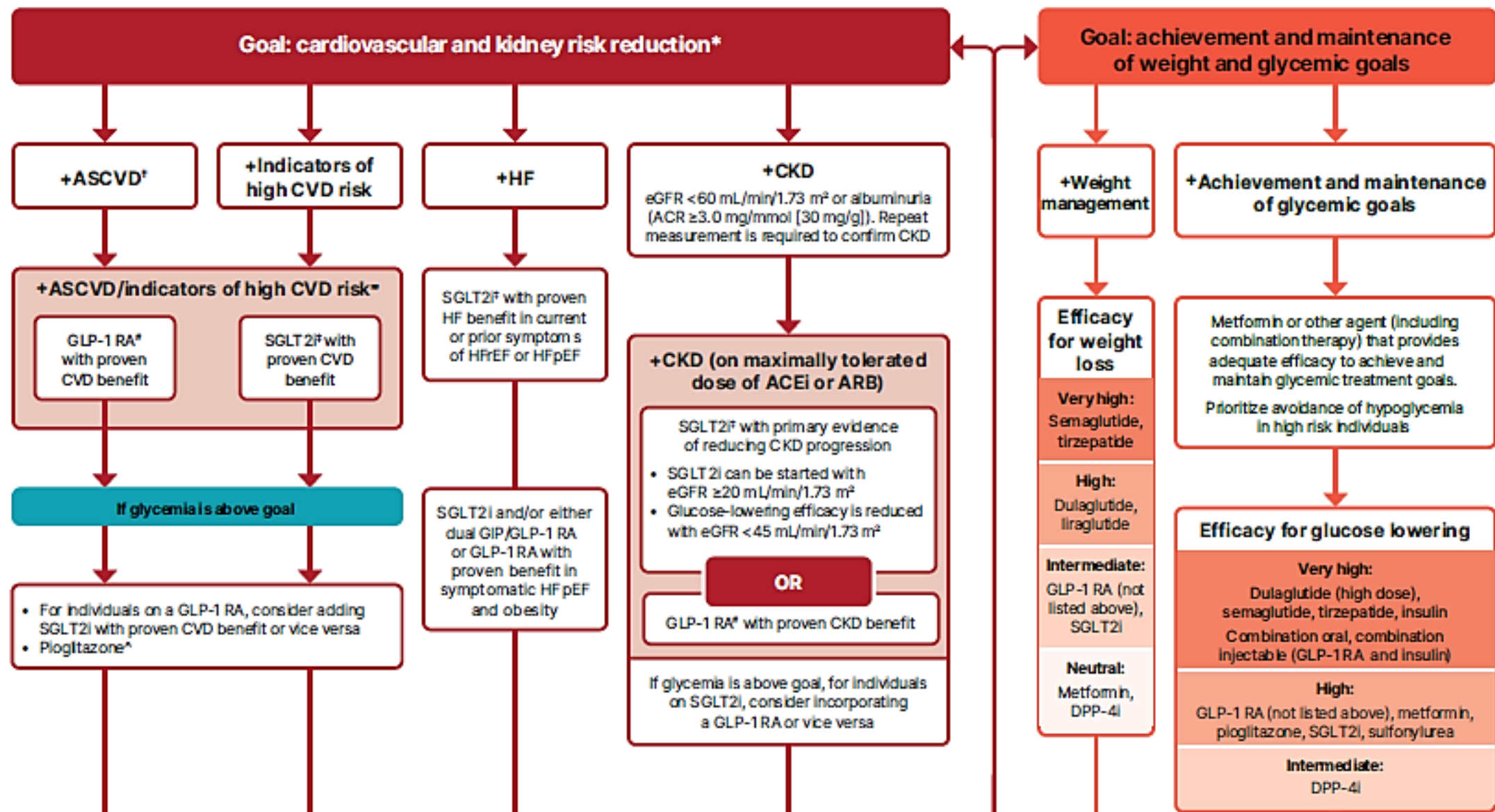
Use of glucose-lowering medications in the management of type 2 diabetes

(For recommendations for specific conditions, including non-glucose-lowering medications, refer to pertinent sections)

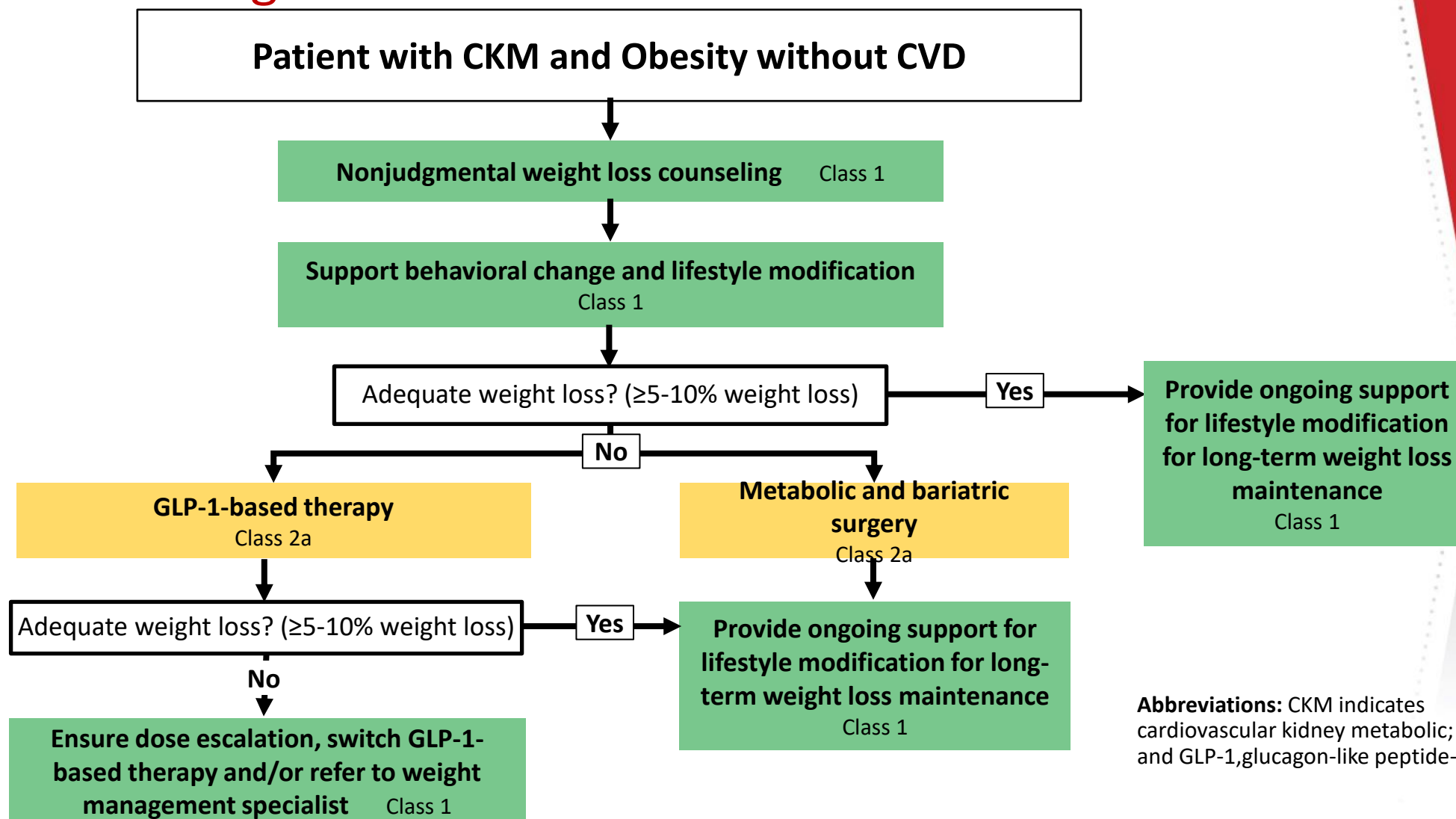


Key Concepts:

- At diagnosis:
 - Emphasize healthy lifestyle, provide DSMES, & consider impact of SDOH
- **Treatment addresses two key goals:**
 - **Cardiovascular and Kidney Risk Reduction in at-risk individuals**
 - **Achieve & Maintain Weight and Glycemic Goals**



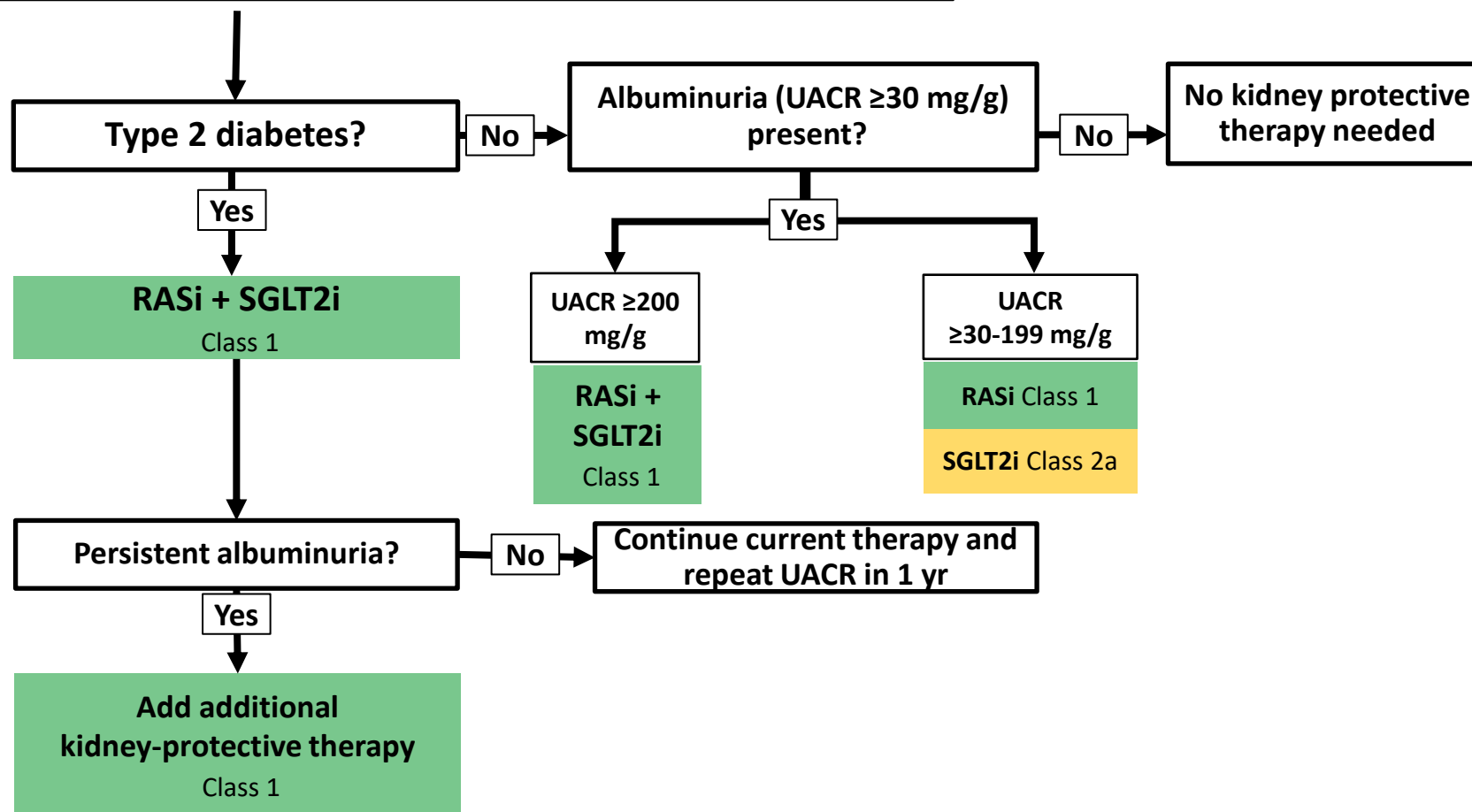
Management of Obesity in CKM Syndrome Stages 1-3



Abbreviations: CKM indicates cardiovascular kidney metabolic; and GLP-1, glucagon-like peptide-1.

Management of CKD in CKM Syndrome Stage 2-3

CKM syndrome with CKD (eGFR <60 and/or UACR ≥30 mg/g) without CVD



SGLT-2 Inhibitors: Pros & Cons

Pros:

- Intermediate to high efficacy for blood glucose control , used for organ protection
- Modest weight loss
- Modest decrease in BP
- Oral administration
- Low hypoglycemia risk (monotherapy or combination with metformin)
- Unique MOA (pairs well with all other med classes in combination)
- Organ protection :
 - ASCVD benefits
 - First line therapy for reduce and preserved HF
 - First line therapy for CKD

Potential Cons:

- Cost
- Genitourinary infections (primarily genital mycotic)
- Volume depletion/hypotension
- Rare/Serious Safety Concerns: eDKA, pyelonephritis/urosepsis, Fournier's gangrene

Consideration

Monitoring and/or risk mitigation strategies

Volume depletion/hypovolemia

- Proactive dose reduction of diuretics in patients at high risk for hypovolemia

Euglycemic diabetic ketoacidosis (eDKA)

- Educate about signs/symptoms to facilitate early recognition
- Monitor blood or urine ketones in high-risk patients
- Institute a sick day protocol (hold SGLT2 inhibitor, test for ketones, maintain fluid intake and carbohydrate coverage, use supplemental insulin)
- Maintain at least low-dose insulin in insulin-requiring individuals

Genital mycotic infections

- Counsel on genital hygiene (e.g., regular bathing and wearing clean undergarments)

Serum creatinine elevation (“GFR dip”)

- Expected 3-5 ml/min/1.73m² dip (up to 30% acceptable)
- If dip exceeds 30%, address hypotension or volume depletion and consider nephrology referral

Hypoglycemia

- Adjust background glucose-lowering agents (e.g., insulin and/or sulfonylureas) as appropriate

GLP-1 and GLP-1/GIP receptor agonists : Pros & Cons

- High and very high glucose lowering
- Low hypoglycemia risk
- Intermediate and high weight loss
- Mild blood pressure lowering
- Approved for adults with established or at high risk for ASCVD
- In adults with T2D and metabolic dysfunction–associated steatotic liver disease (MASLD), and overweight or obesity, consider using a GLP-1 RA with demonstrated benefits in metabolic dysfunction–associated steatohepatitis (MASH) or a dual GIP and GLP-1 RA with potential benefits in MAS
- Nausea , vomiting
- Volume depletion
- Cost

Consideration

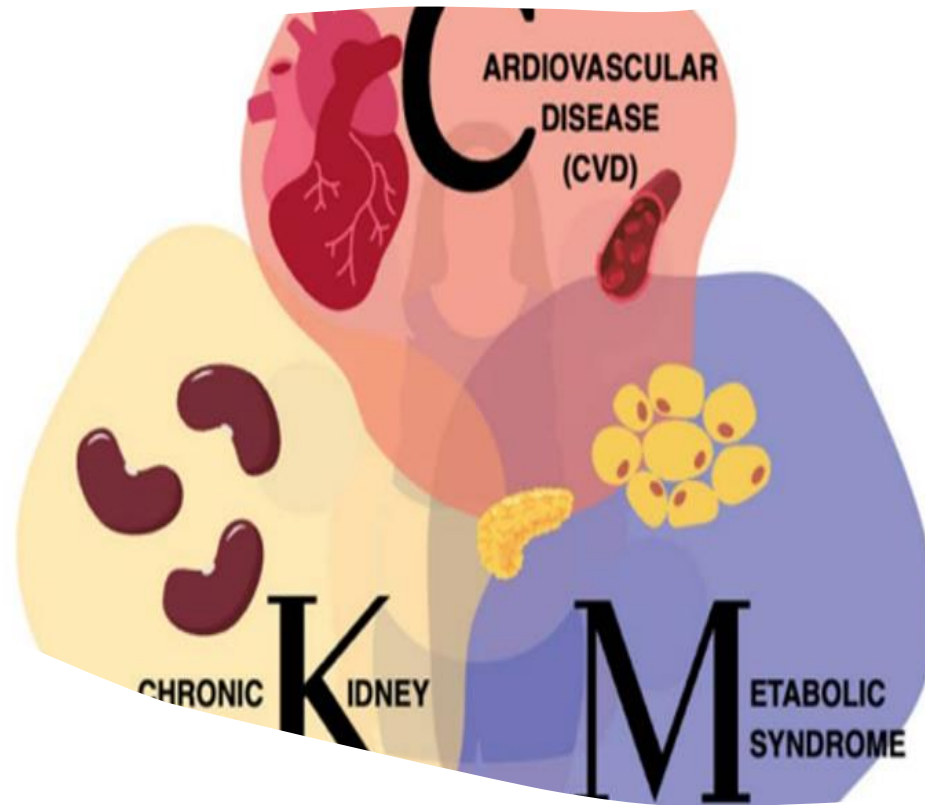
Nausea/vomiting/diarrhea

Hypoglycemia

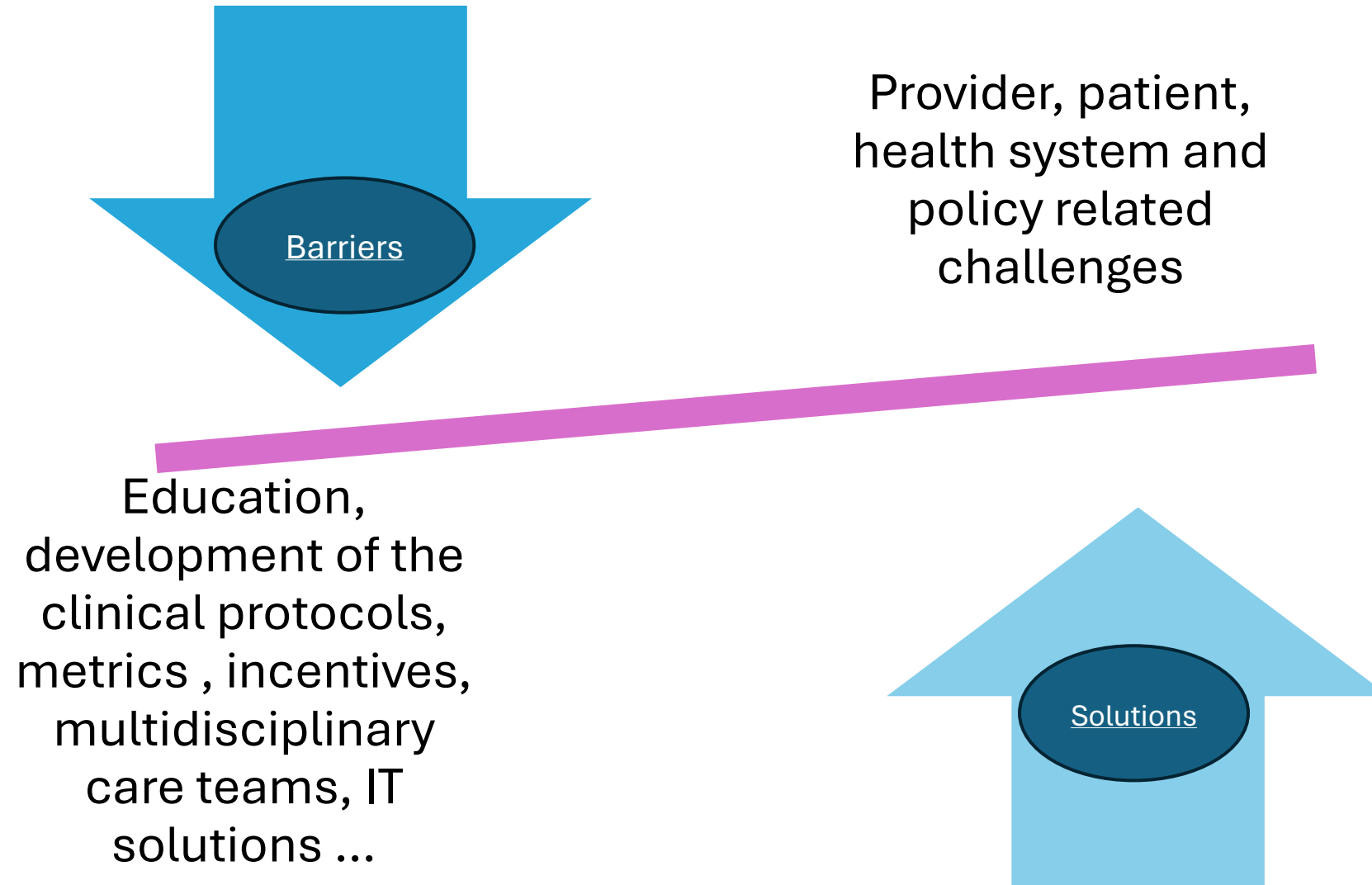
Volume depletion/hypovolemia

Monitoring and/or risk mitigation strategies

- Start at lowest recommended dose and titrate slowly
- Educate on potential GI intolerance and importance of communicating severe symptoms to care team
- Adjust background glucose-lowering agents (e.g., insulin and/or sulfonylureas) as appropriate
- Exercise caution in individuals experiencing severe nausea/vomiting at risk of acute volume depletion

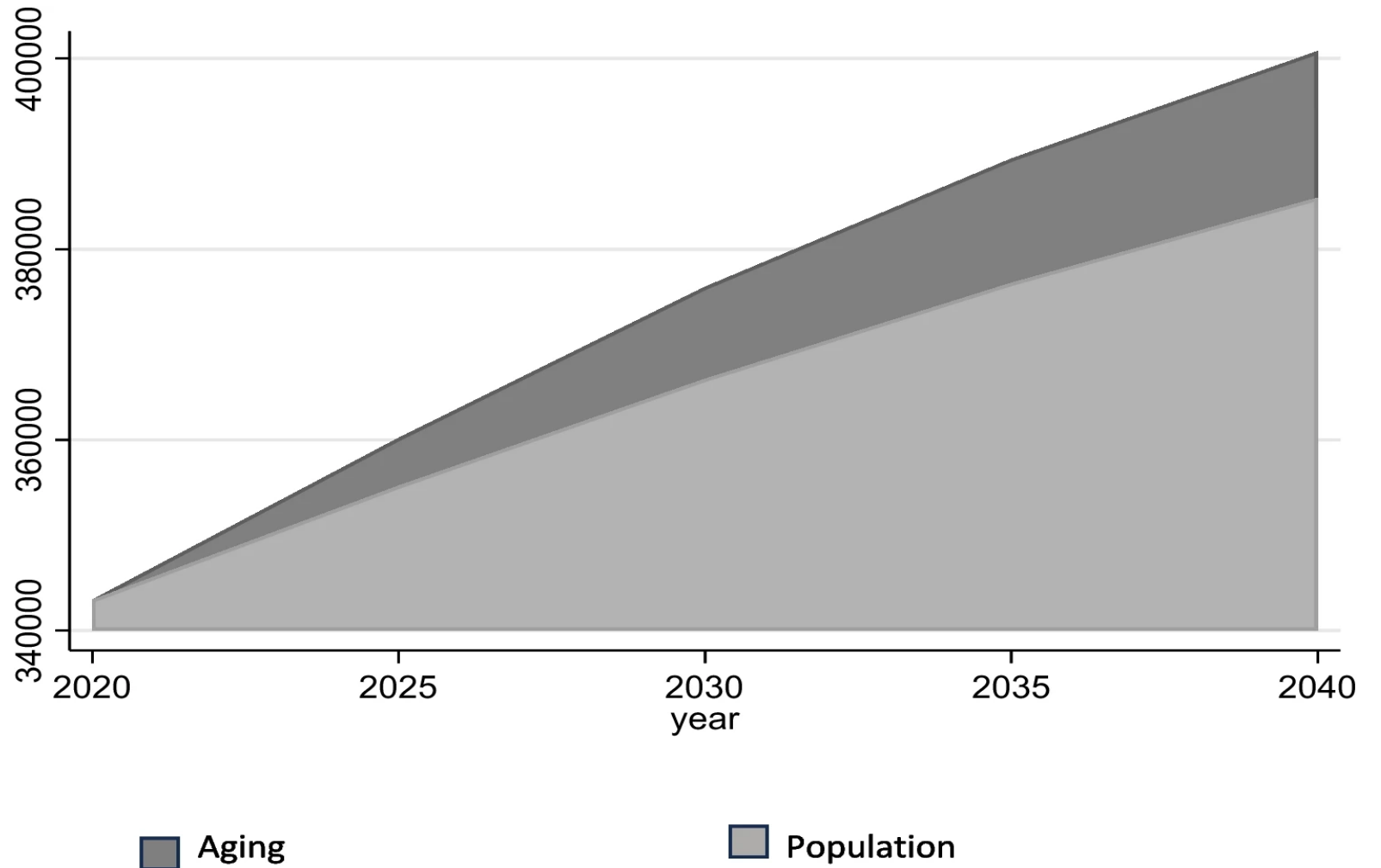


Implementation



US Primary Care Workforce Growth: Projected needs

Y axis = no. of
primary care
clinicians
needed, X axis =
year.



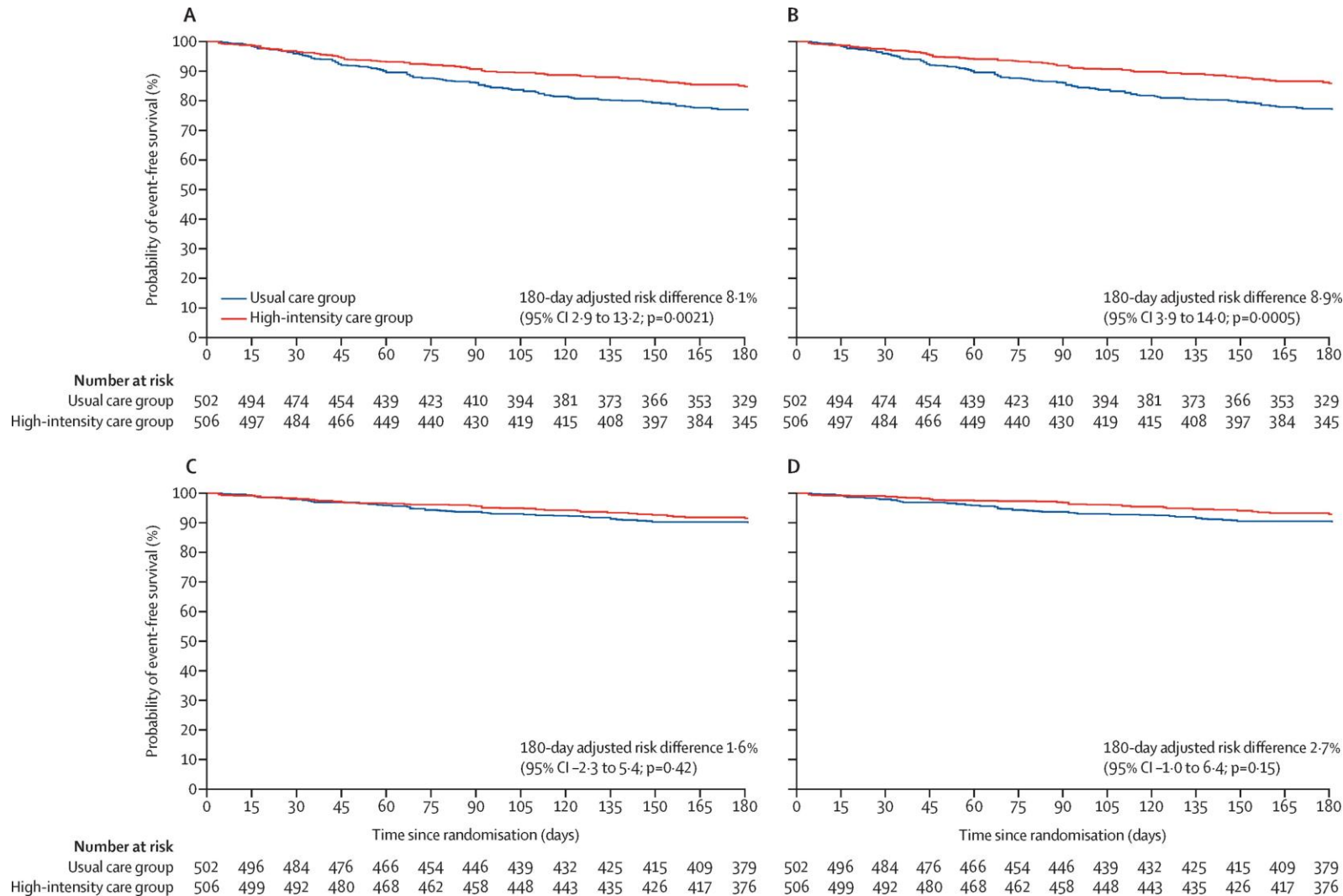
Inpatient and outpatient implementation barriers

- Key gaps in the screening approaches and recommendations
- Lack of harmonized professional society recommendations
- Lack of standardized discharge planning
- Absence of Inpatient to Outpatient transitioning (bridging) protocols
- Limited information on initiation, cadence and titration of GDMT
- Lack of monitoring protocols
- Limited information on risk reduction interventions (e.g. start SGLT2 inhibitor ahead of nsMRAs)

Patient Related Barriers

- Limited access to new treatments and healthcare
- Transportation issues
- Time constraints
- Language barriers
- Communication gaps, information sharing, feedback interventions
- High burden of health care cost
- Limited health literacy including technical health literacy

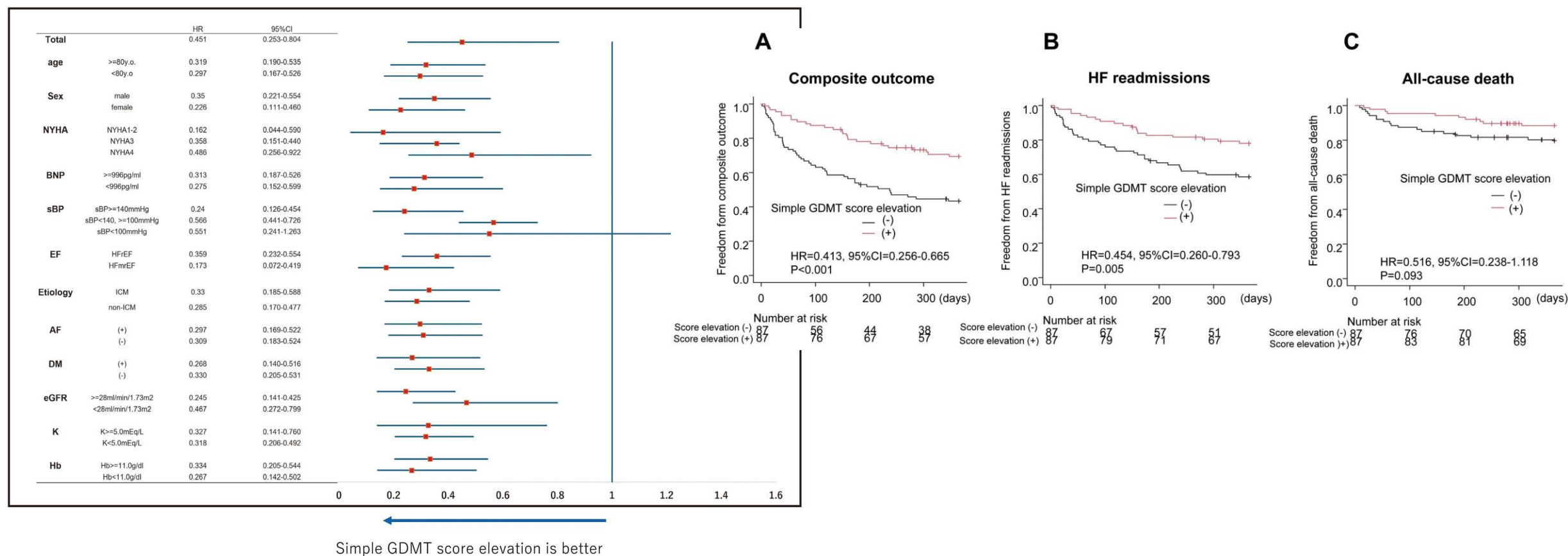
STRONG-HF trial



Primary outcome : 180-day heart failure readmissions or all-cause death

Secondary endpoints: change in quality of life (EQ-5D) , 180-day all –cause death, and 90-days HR readmission or all-case death

Optimizing GDMT during Hospitalization Improves Prognosis in HF patients



Success story : Implementation of SGLT2inhibitors in inpatient and outpatient setting

- American Heart Association engagement and advocacy
- Public awareness of cardiovascular disease crucial for prevention and management
- Hospital assessment based on the heart failure readmissions
- Existing metric focusing on adherence of evidence –based interventions

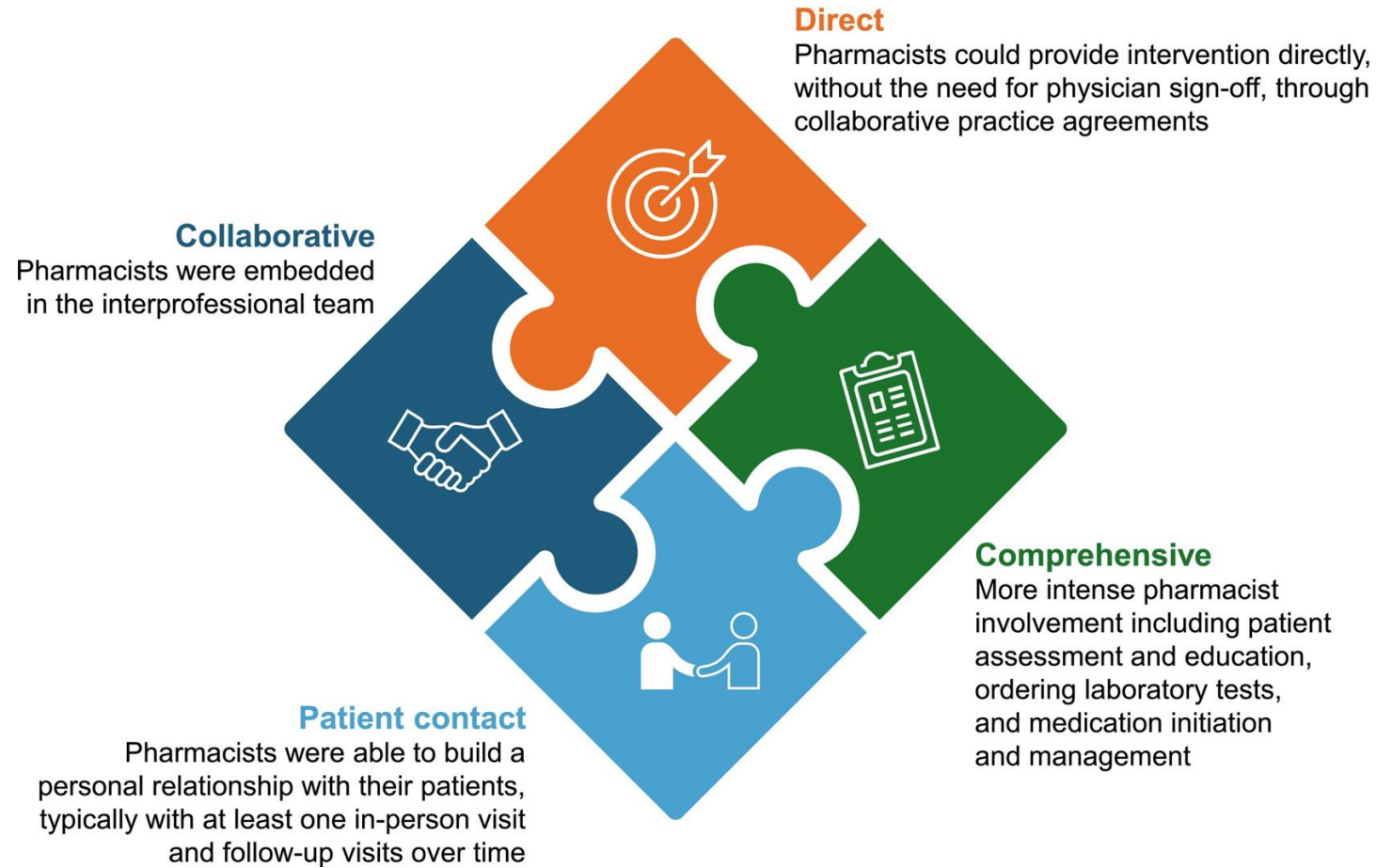
★ SGLT2 inhibitors included in the hospital preference list for one indication: heart failure



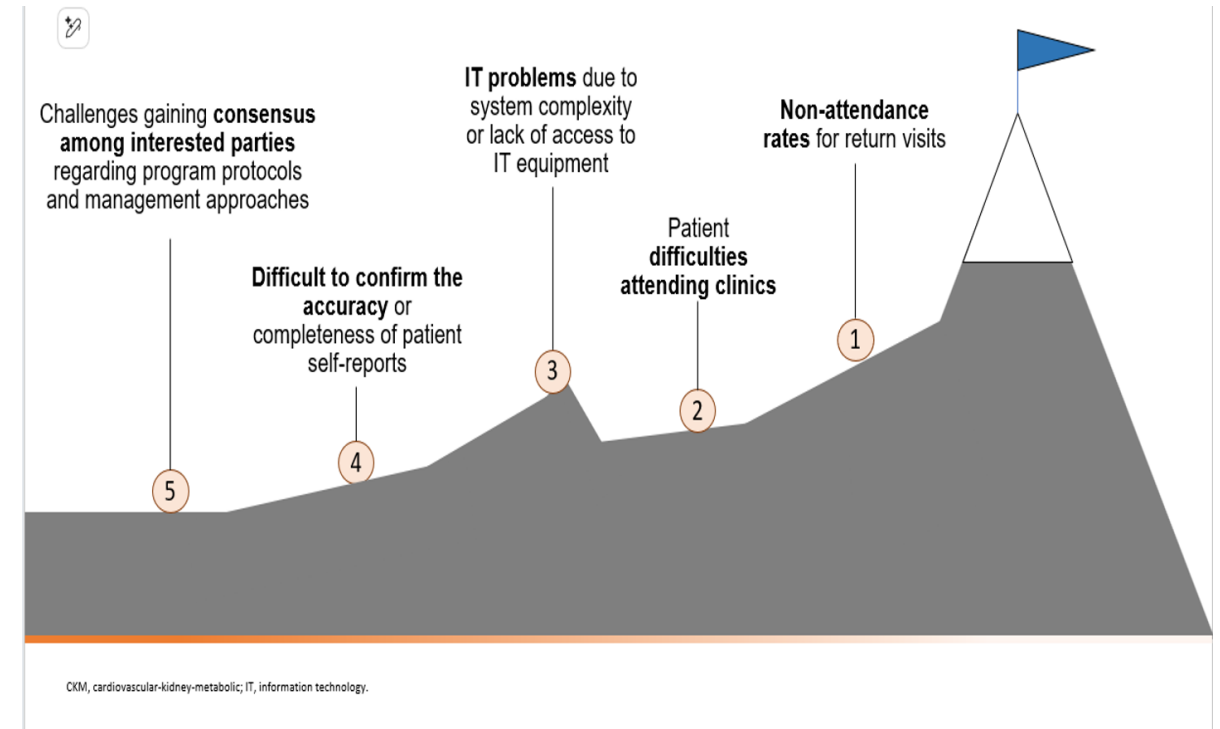
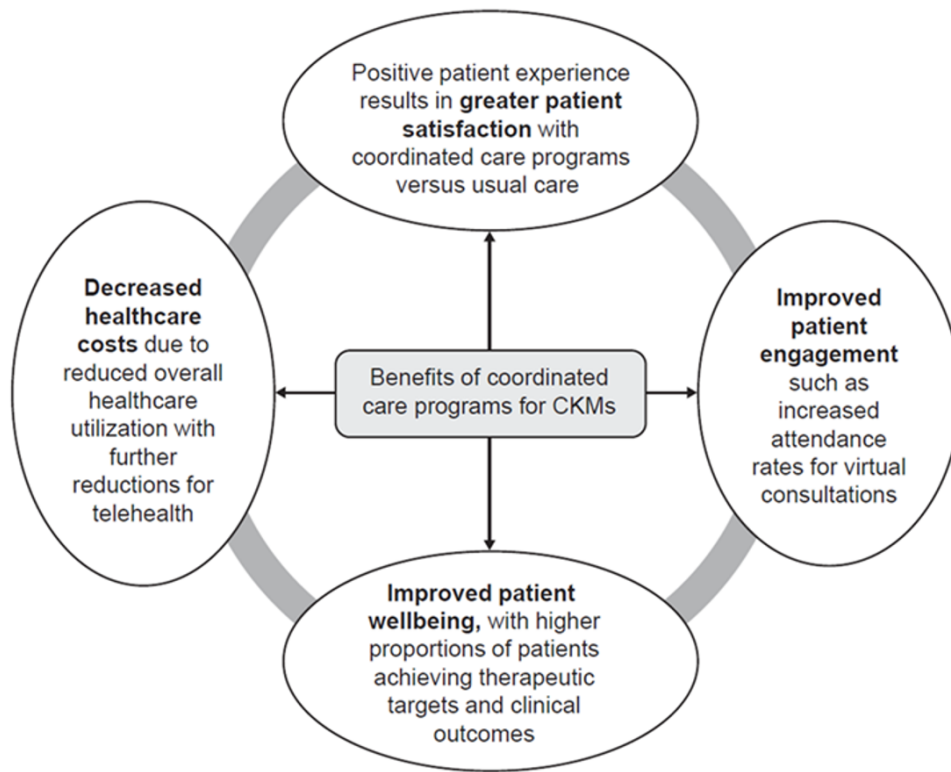
How to implement CKM paradigm in internist practice

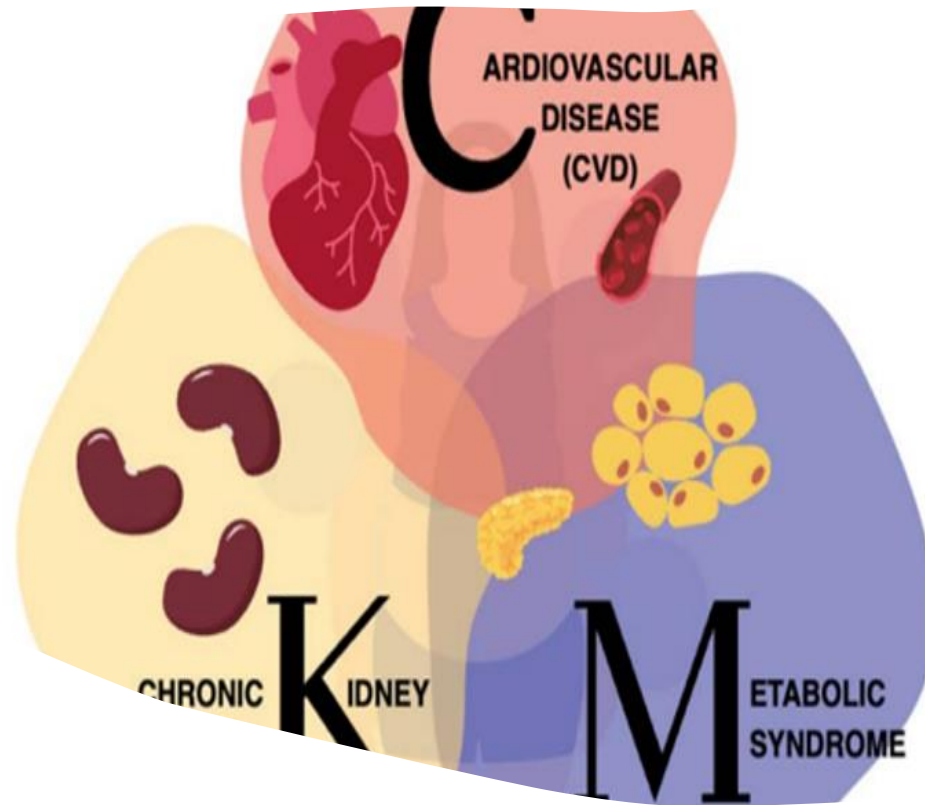
- Greater involvement of professional organizations (American College of Physicians, American Medical Society, Society of Internal Medicine, Society of Hospital Medicine),
- Support from institutions and policy frameworks, focus on value – based care
- Education regarding the concept of CKM syndrome,
- Formation of multidisciplinary teams and panel management,
- Implementation of quality improvement programs,
- Modification of metrics and incentives,
- Creation of clinical protocols,
- Establishing EHR-based algorithms for decision support and panel management.

Multidisciplinary Care Models



Benefits and Challenges implementing CKM coordinated care





Questions ?

SHMC

