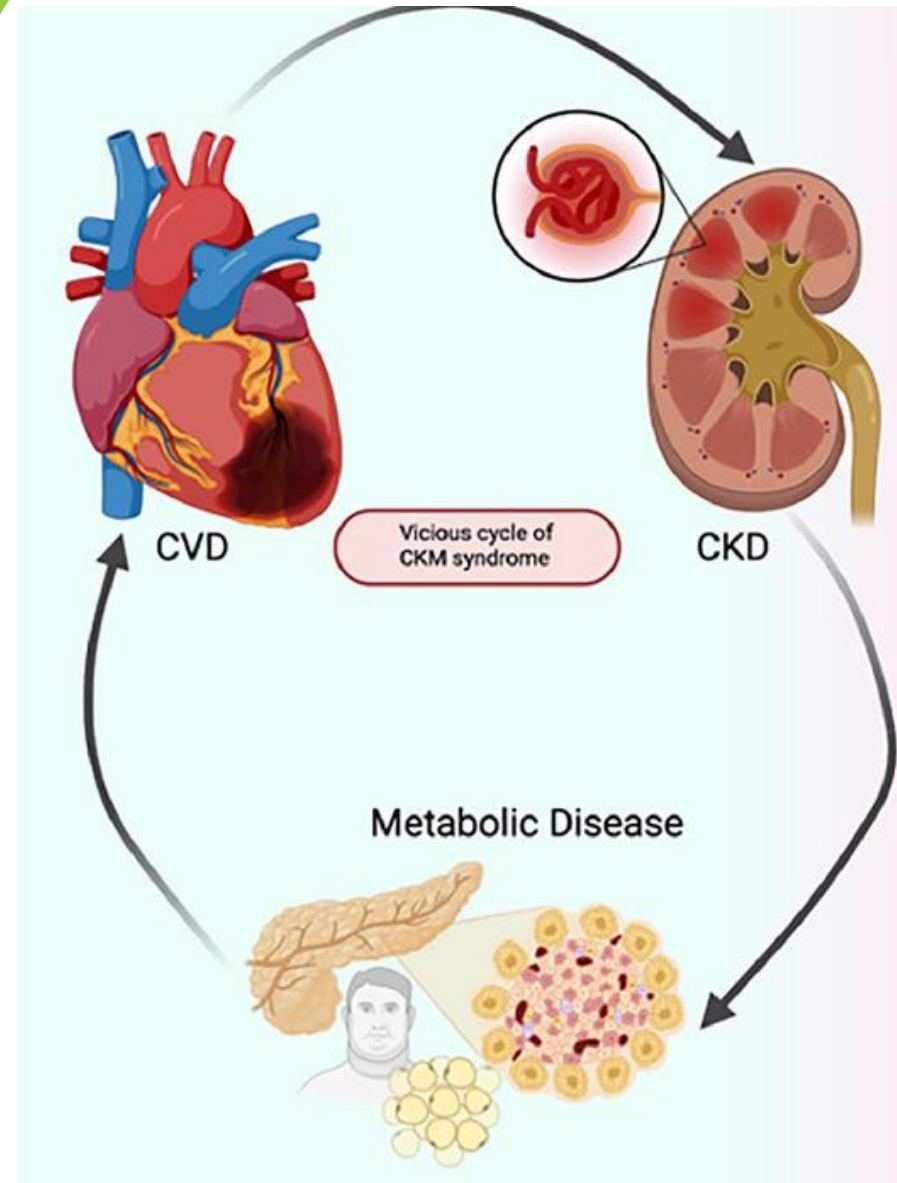


Cardiovascular-Kidney-Metabolic Syndrome:

An Introduction

ERIC L. MARTIN MD, FACC, FASE, FASNC, FSCCT, FSCMR, FASPC
Medical Director
ADVANCED CV IMAGING
PREVENTIVE CARDIOLOGY
SPORTS CARDIOLOGY

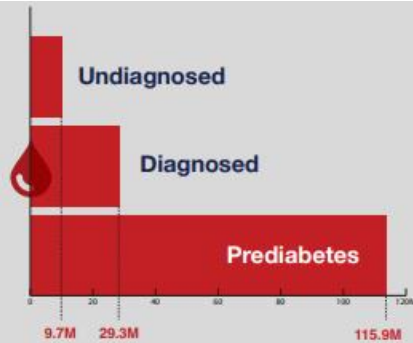


DISCLOSURE

- Principal Investigator- COORDINATE Trial
- Speaker Bureau- Boehringer-Ingelheim
- Speaker Bureau- Astra Zeneca

Heart Disease & Stroke Statistics 2024 Update

The American Heart Association (AHA) **2024 Statistical Update** is a major source for monitoring cardiovascular health, risk factors, and disease in the US and global population. It is published annually in *Circulation* and can be accessed for free at AHAjournals.org/StatUpdate



9.7 million
adults have undiagnosed diabetes

29.3 million
adults have diagnosed diabetes

115.9 million
adults have prediabetes
(based on 2017-2020 data)

25.5%
of US adults have high
LDL-C (≥ 130 mg/dL)
(based on 2017-2020 data)



3.72 million
deaths globally were
attributed to high
LDL-C in 2021

 **224.0**
per 100,000
The age-adjusted US death rate attributable
to CVD *(based on 2021 data)*

 **237.9**
per 100,000
The age-adjusted global death rate attributable
to CVD *(based on 2021 data)*

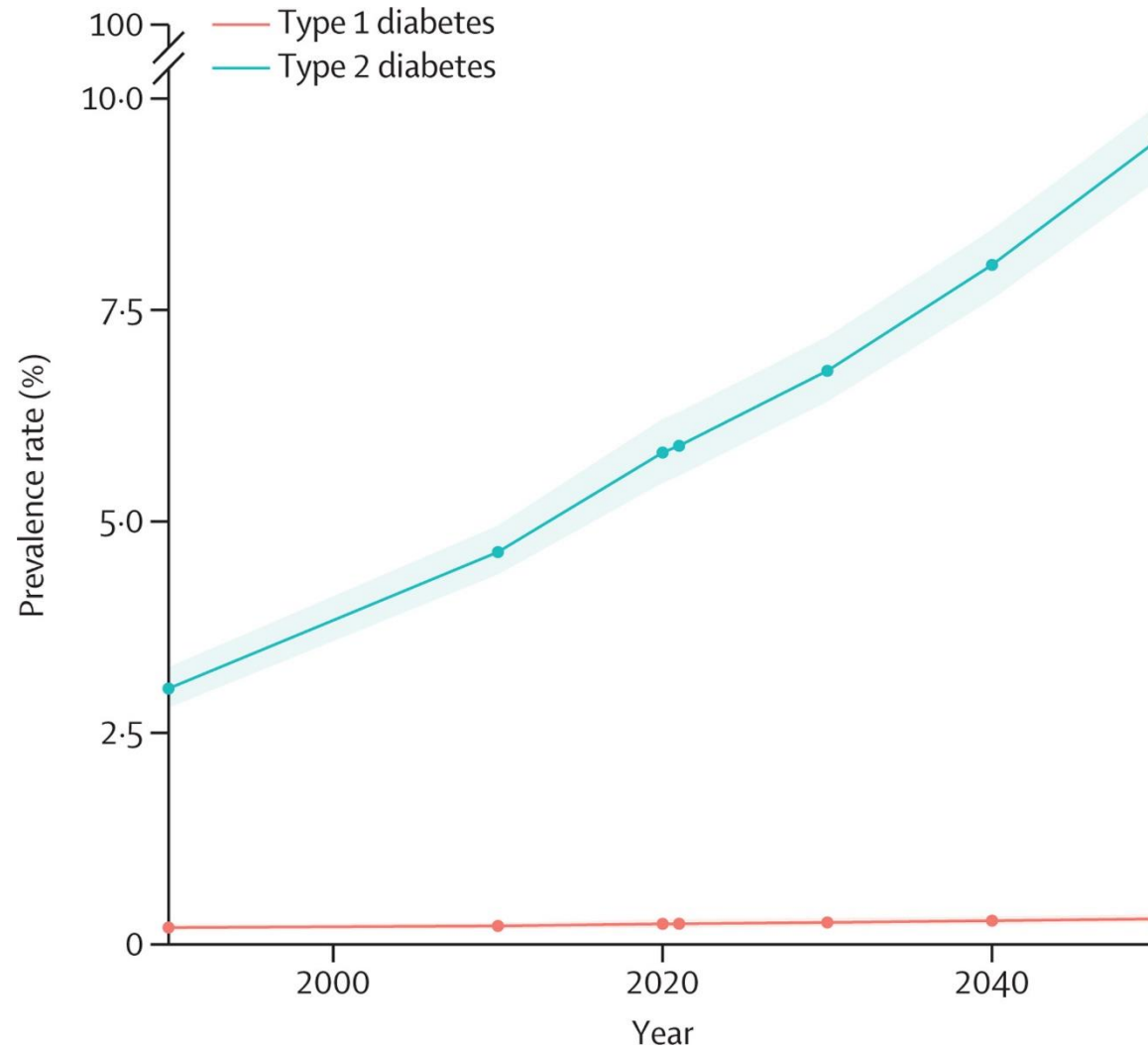


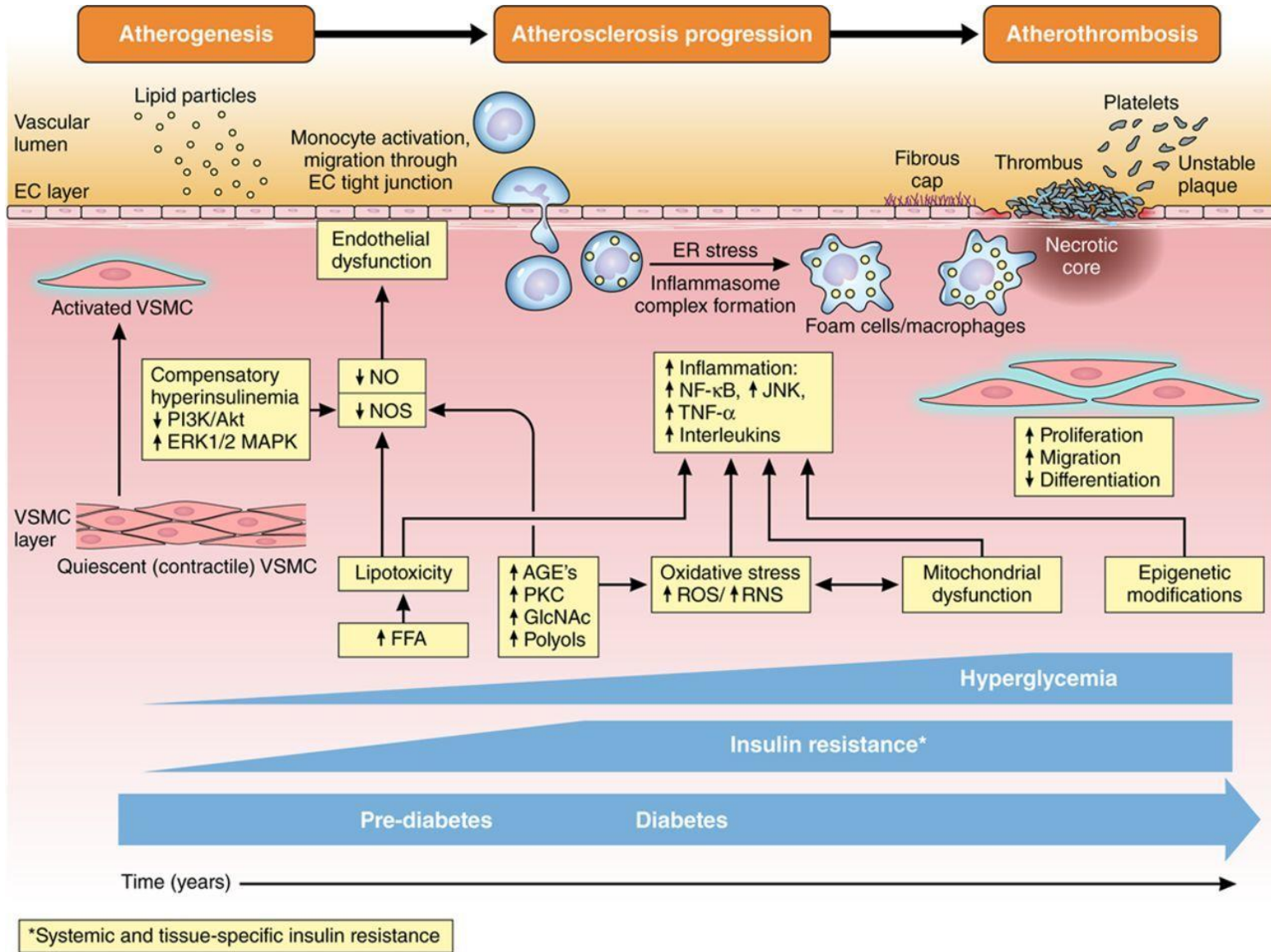
On average, someone in the US
dies of CVD every
34 seconds
2552 US deaths from CVD
each day *(based on 2021 data)*



On average, someone in the US
dies of a stroke every
**3 minutes and
14 seconds**
446 US deaths from stroke
each day *(based on 2021 data)*

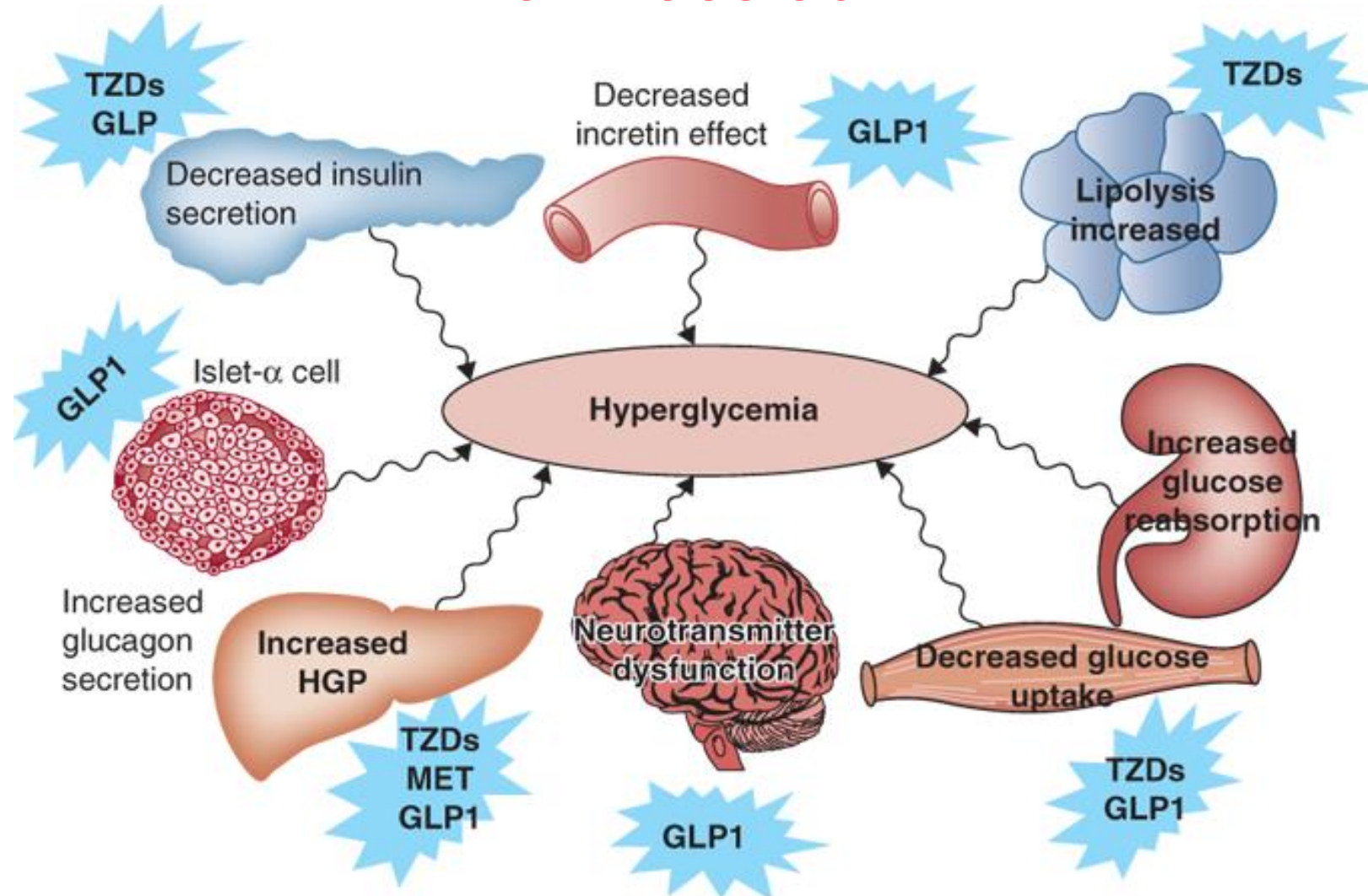
Global age-standardised prevalence of type 1 and type 2 diabetes from 1990 through 2050





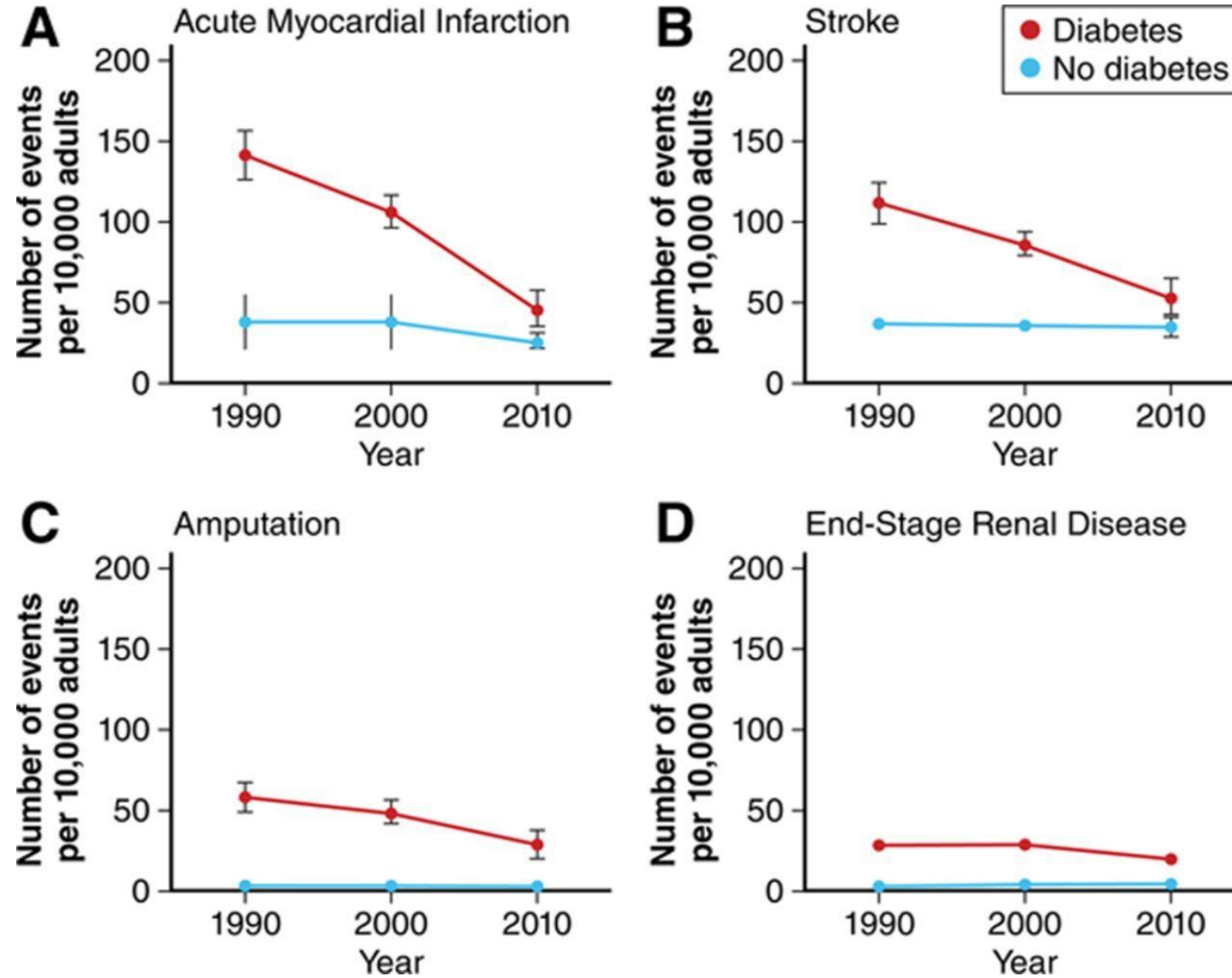
Cecilia C. Low Wang. Circulation. Clinical Update: Cardiovascular Disease in Diabetes Mellitus, Volume: 133, Issue: 24, Pages: 2459-2502, DOI: (10.1161/CIRCULATIONAHA.116.022194)

THE OMINOUS OCTET



Source: Valentin Fuster, Robert A. Harrington, Jagat Narula, Zubin J. Eapen: Hurst's The Heart, Fourteenth Edition: www.accessmedicine.com Copyright © McGraw-Hill Education. All rights reserved.

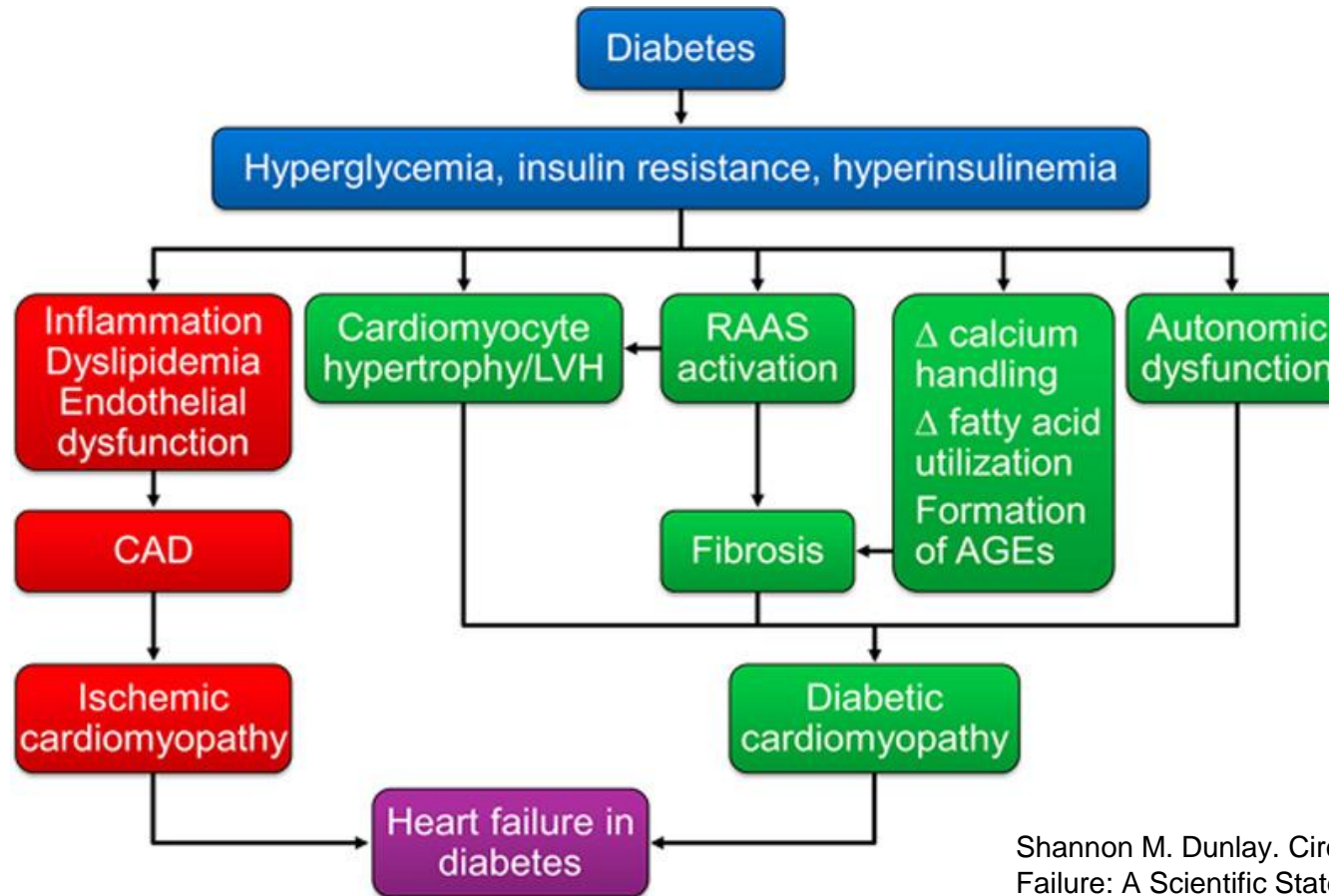
Age-standardized rates of selected Vascular Diseases in individuals with or without Diabetes Mellitus



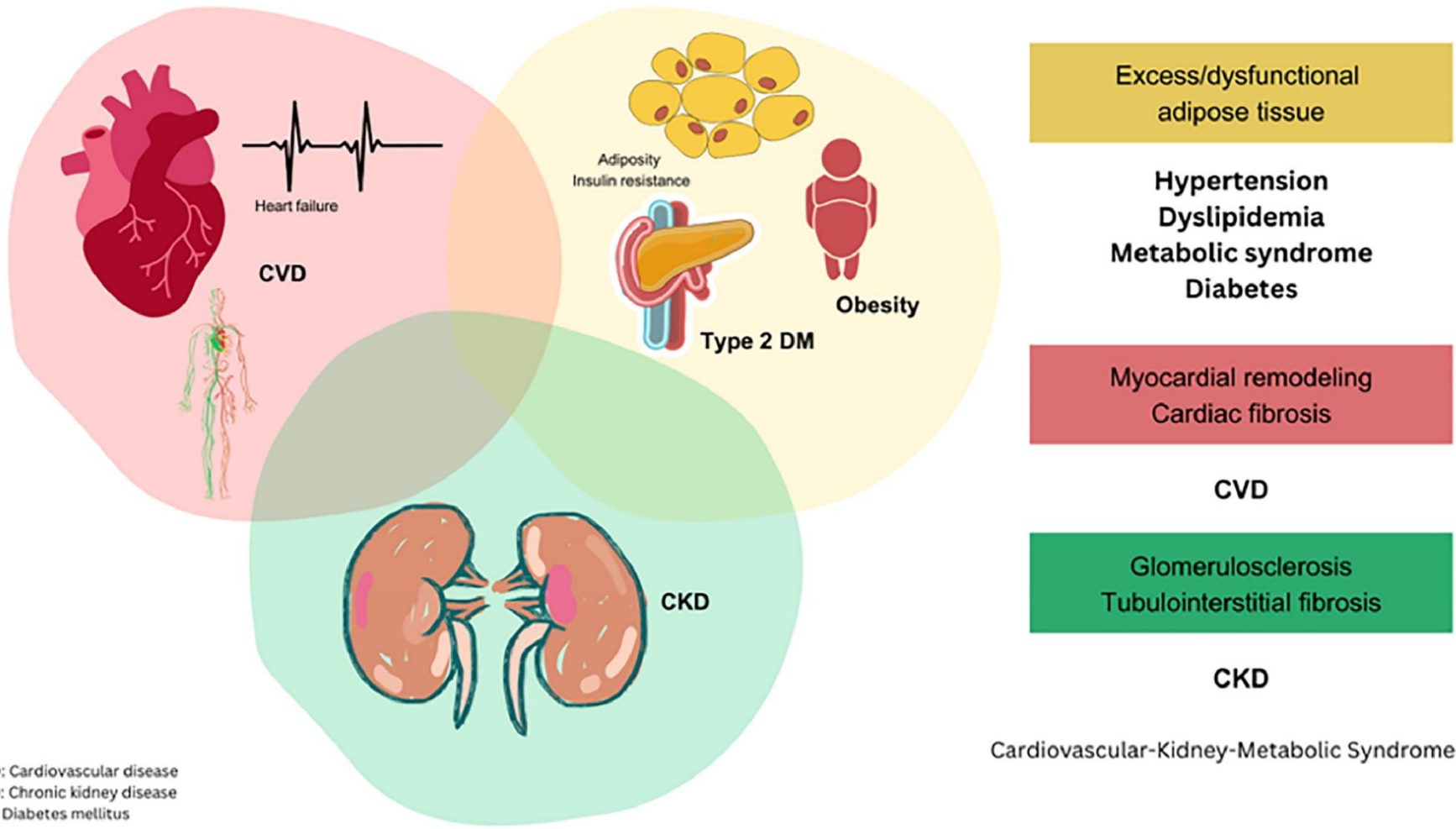
Cecilia C. Low Wang. Circulation. Clinical Update: Cardiovascular Disease in Diabetes Mellitus, Volume: 133, Issue: 24, Pages: 2459-2502, DOI: (10.1161/CIRCULATIONAHA.116.022194)



Pathophysiology of Heart Failure in Diabetes Mellitus



Shannon M. Dunlay. *Circulation*. Type 2 Diabetes Mellitus and Heart Failure: A Scientific Statement From the American Heart Association and the Heart Failure Society of America: This statement does not represent an update of the 2017 ACC/AHA/HFSA heart failure guideline update, Volume: 140, Issue: 7, Pages: e294-e324, DOI: (10.1161/CIR.0000000000000691)



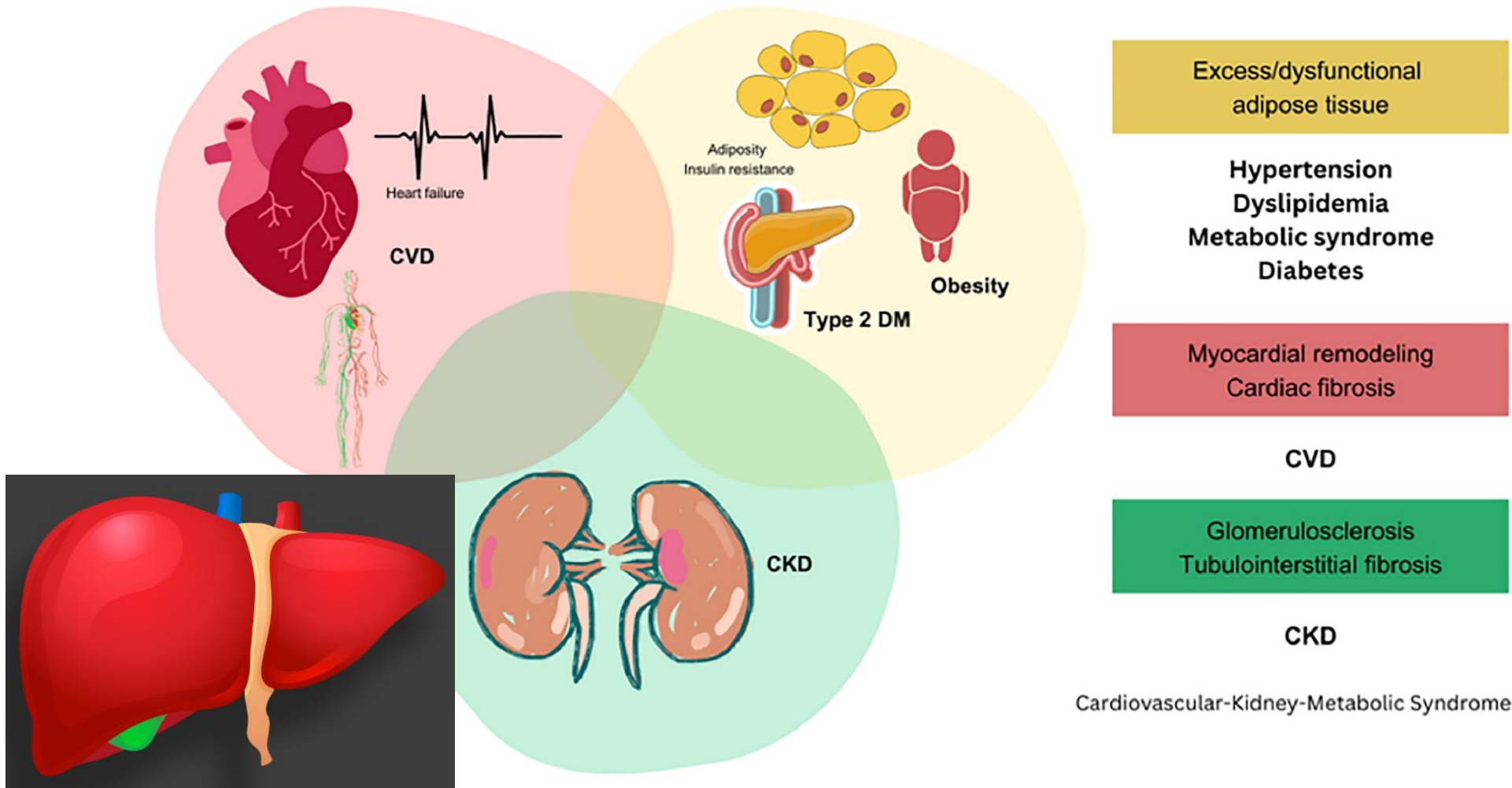
Cardiovascular-Kidney-Metabolic (CKM) syndrome: A state-of-the-art review
Sebastian, Sneha Annie, MD, Current Problems in Cardiology, Volume 49, Issue 2, 102344

Circulation

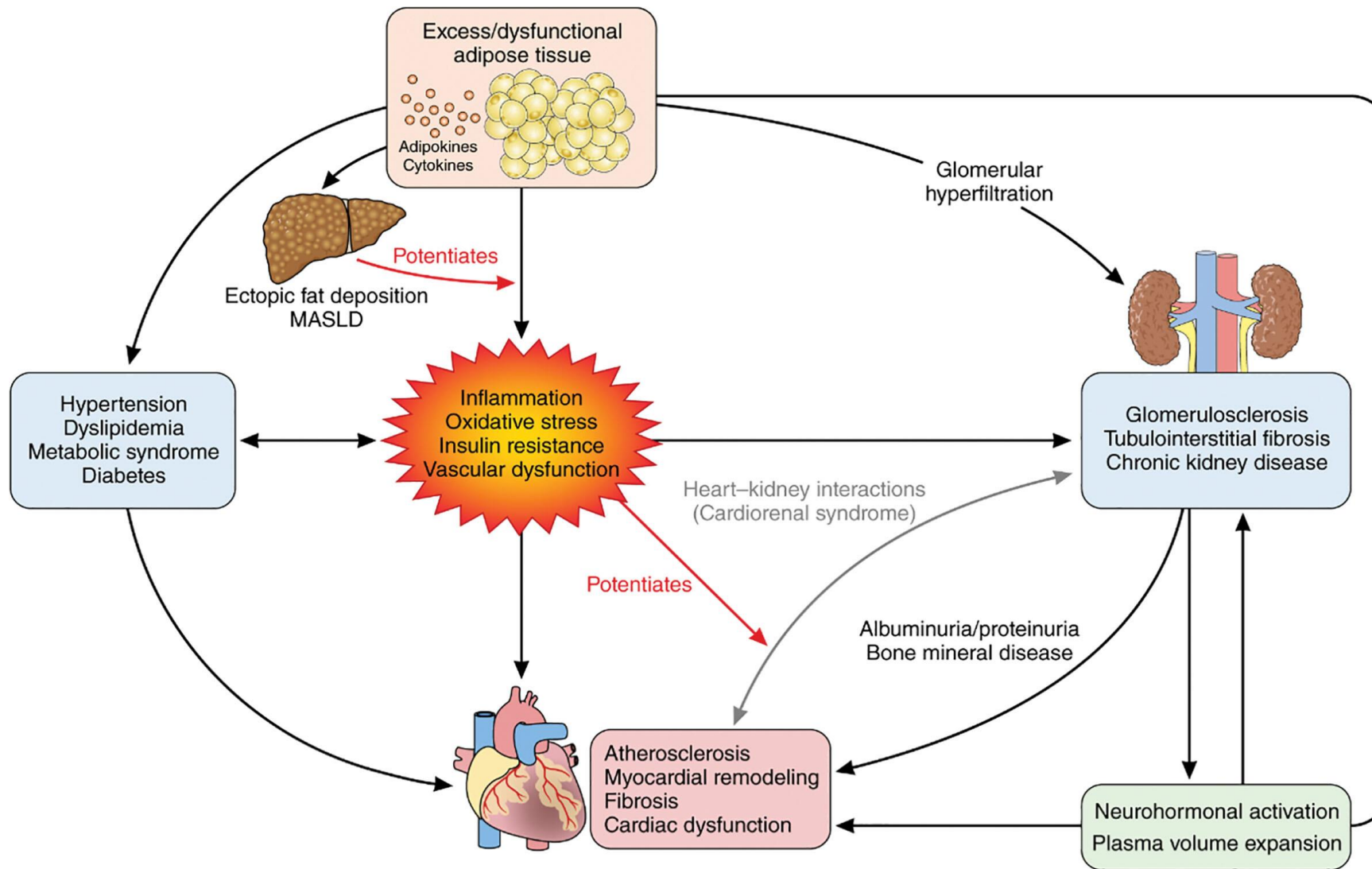
A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association

Chiadi E. Ndumele, Ian J. Neeland, Katherine R. Tuttle, Sheryl L. Chow, Roy O. Mathew, Sadiya S. Khan, Josef Coresh, Carissa M. Baker-Smith, Mercedes R. Carnethon, Jean-Pierre Després, Jennifer E. Ho, Joshua J. Joseph, ... [See all authors](#) 

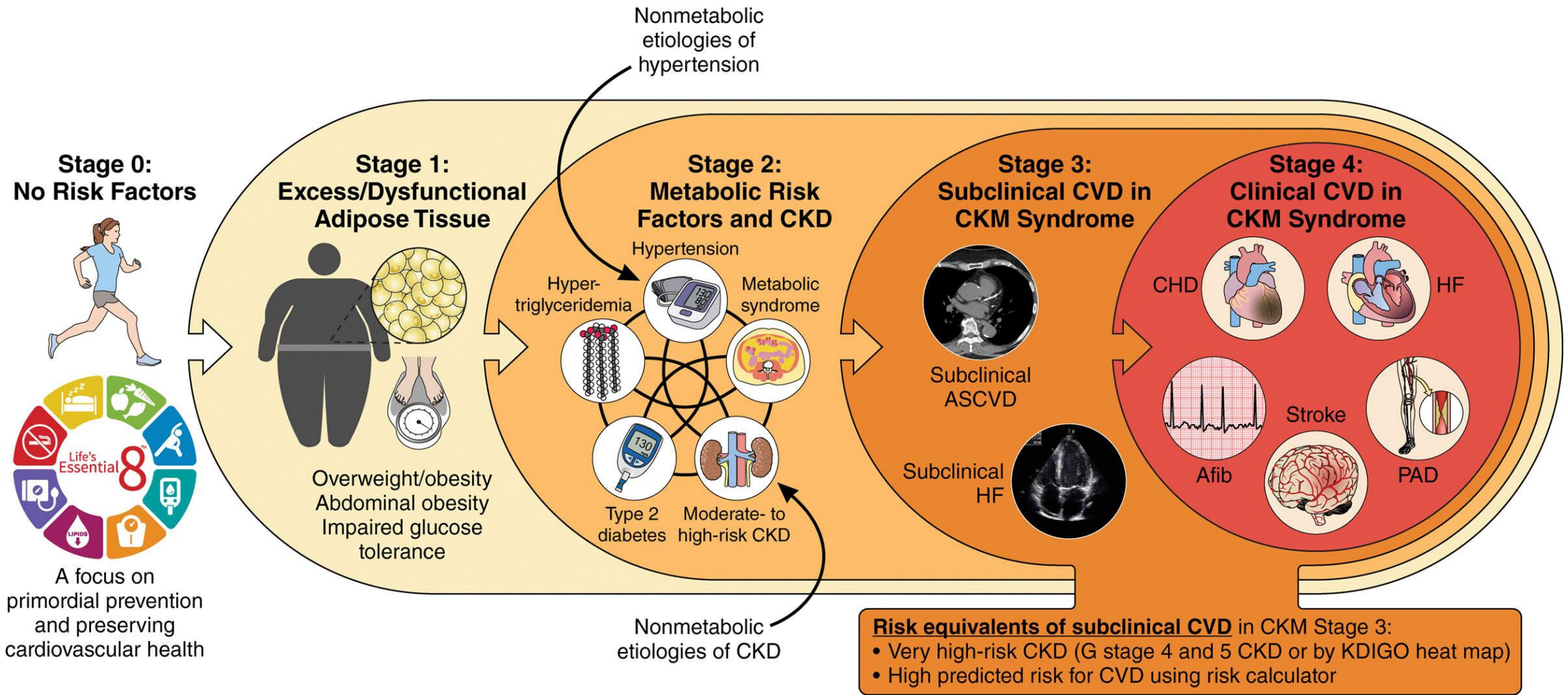
Originally published 9 Oct 2023 | <https://doi.org/10.1161/CIR.0000000000001186> | Circulation. 2023;148:1636–1664



Cardiovascular-Kidney-Metabolic (CKM) syndrome: A state-of-the-art review
 Sebastian, Sneha Annie, MD, Current Problems in Cardiology, Volume 49, Issue 2, 102344



Chiadi E. Ndumele. Circulation. 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, Volume: 148, Issue: 20, Pages: 1636-1664, DOI: (10.1161/CIR.0000000000001186)



Chiadi E. Ndumele. Circulation. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association, Volume: 148, Issue: 20, Pages: 1606-1635, DOI: (10.1161/CIR.0000000000001184)

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.

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.

Sex Male Female

Age years ⓘ

Total Cholesterol mg/dL ⓘ

HDL Cholesterol mg/dL ⓘ

SBP mmHg ⓘ

BMI ⓘ

eGFR ⓘ

Diabetes No Yes ⓘ

Current Smoking No Yes ⓘ

Anti-hypertensive medication No Yes ⓘ

Lipid-lowering medication No Yes ⓘ

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 ⓘ

HbA1C No Yes ⓘ

Zip Code (for estimating social deprivation index [SDI]) No Yes ⓘ

Risk of CVD Risk of ASCVD Risk of Heart Failure

Table 2. Risk-Enhancing Factors for CKM Syndrome*

Chronic inflammatory conditions (eg, psoriasis, RA, lupus, HIV/AIDS)
High-risk demographic groups (eg, South Asian ancestry, lower socioeconomic status)
High burden of adverse SDOH
Mental health disorders (eg, depression and anxiety)
Sleep disorders (eg, obstructive sleep apnea)
Sex-specific risk enhancers (beyond gestational diabetes consideration in stage 1)
History of premature menopause (age <40 y)
History of adverse pregnancy outcomes (eg, hypertensive disorders of pregnancy, preterm birth, small for gestational age)
Polycystic ovarian syndrome
Erectile dysfunction
Elevated high-sensitivity C-reactive protein (≥ 2.0 mg/L if measured)
Family history of kidney failure; family history of diabetes

Table 3. Screening Approaches for CKM Syndrome

Period	Screening approach
Early life (<21 y)	<p>Screening for overweight and obesity using sex- and age-specific CDC growth charts: annually</p> <p>Blood pressure assessment (stronger evidence/recommendation for those with CKM factors): starting at age 3 y, annually for children with no risk factors; at every health encounter for children with overweight/obesity, diabetes, kidney disease, or structural heart disease</p> <p>Mental and behavioral health, SDOH screening for all children</p> <p>Fasting lipid panel recommended: once between 9 and 11 y of age and then again between 17 and 21 y of age</p> <p>Screening is advised beginning at 2 y of age if a family history is suggestive of either early CVD or significant primary hypercholesterolemia.</p> <p>Additionally check FPG/OGTT/HbA1c, ALT: starting at 9-11 y of age</p> <p>If normal, may repeat every 2–3 y for all children with obesity</p> <p>If normal, may repeat every 2–3 y for children with overweight if additional risk factors present (family history of obesity-related diseases, elevated blood pressure or lipid levels, tobacco use)</p>

Adulthood
(≥21 y)

Screening for social determinants of health (see [Table 4](#))

Measurement of BMI and waist circumference: annually

Screening for MetS components (elevated blood pressure, elevated triglycerides, low HDL cholesterol, and hyperglycemia)

Annually for those with stage 2 CKM

Every 2–3 y for those with stage 1 CKM or history of gestational diabetes

Every 3–5 y for those with stage 0 CKM

Screening for advanced liver fibrosis related to MASLD every 1–2 y for individuals with diabetes, prediabetes, or ≥2 metabolic risk factors using the FIB-4 index

Assessment of UACR along with serum creatinine/cystatin C for accurate KDIGO staging

Annually for those with stage 2 CKM or higher

More frequently for those with higher KDIGO risk

Coronary artery calcium screening reasonable in those with intermediate 10-y ASCVD risk to guide intensification of preventive therapies

Subclinical HF screening with echocardiogram and/or cardiac biomarkers likely based on age/comorbidities/risk score but not yet defined

TARGETS FOR CARDIOMETABOLIC DRUGS

- **SGLT co-transporters** (*SGLT1i*, *SGLT2i*)

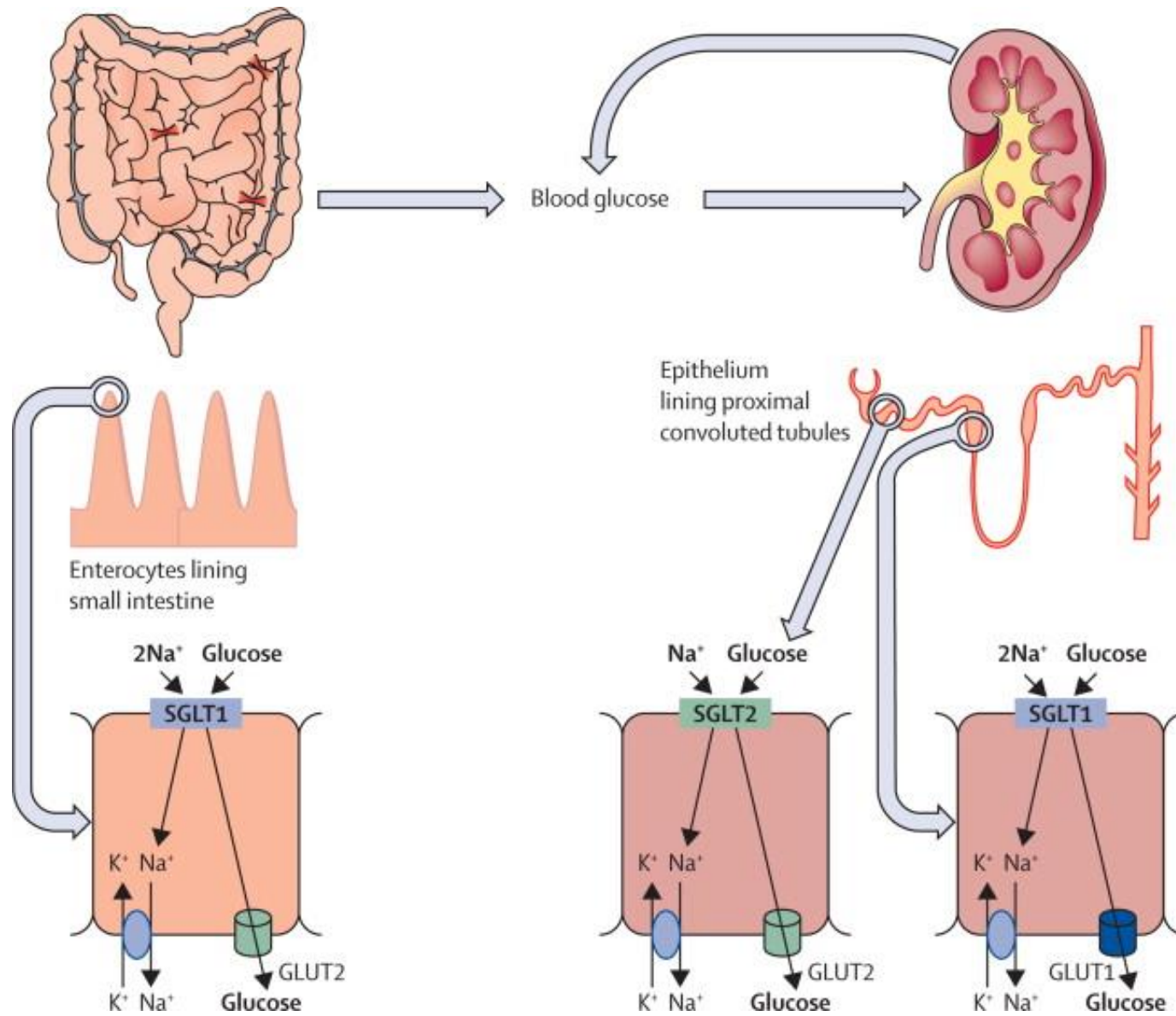
Phlorizin Analogues with Proven CV Benefits

Dapaglifozin

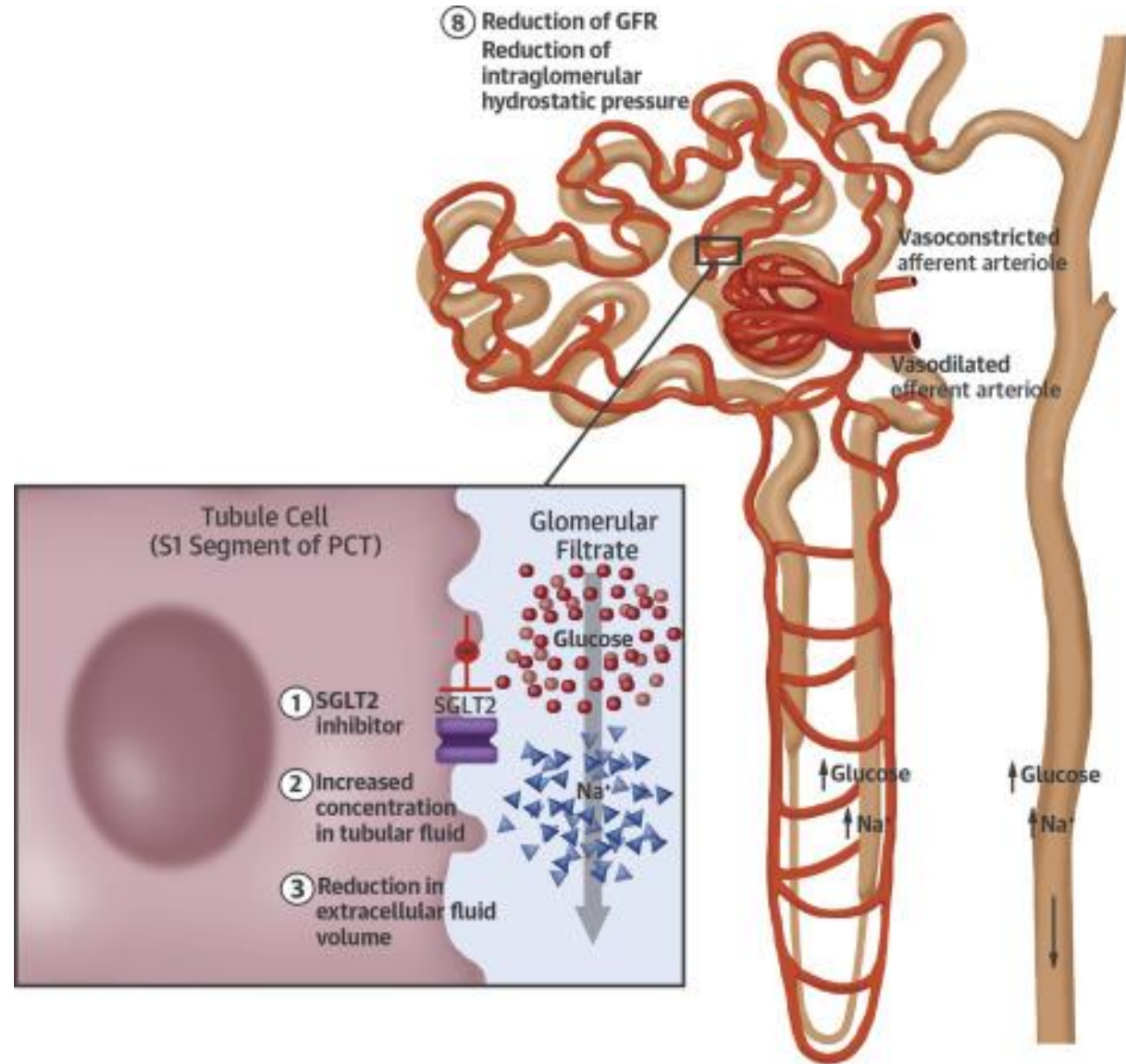
Canaglifozin

Empaglifozin

Sotaglifozin

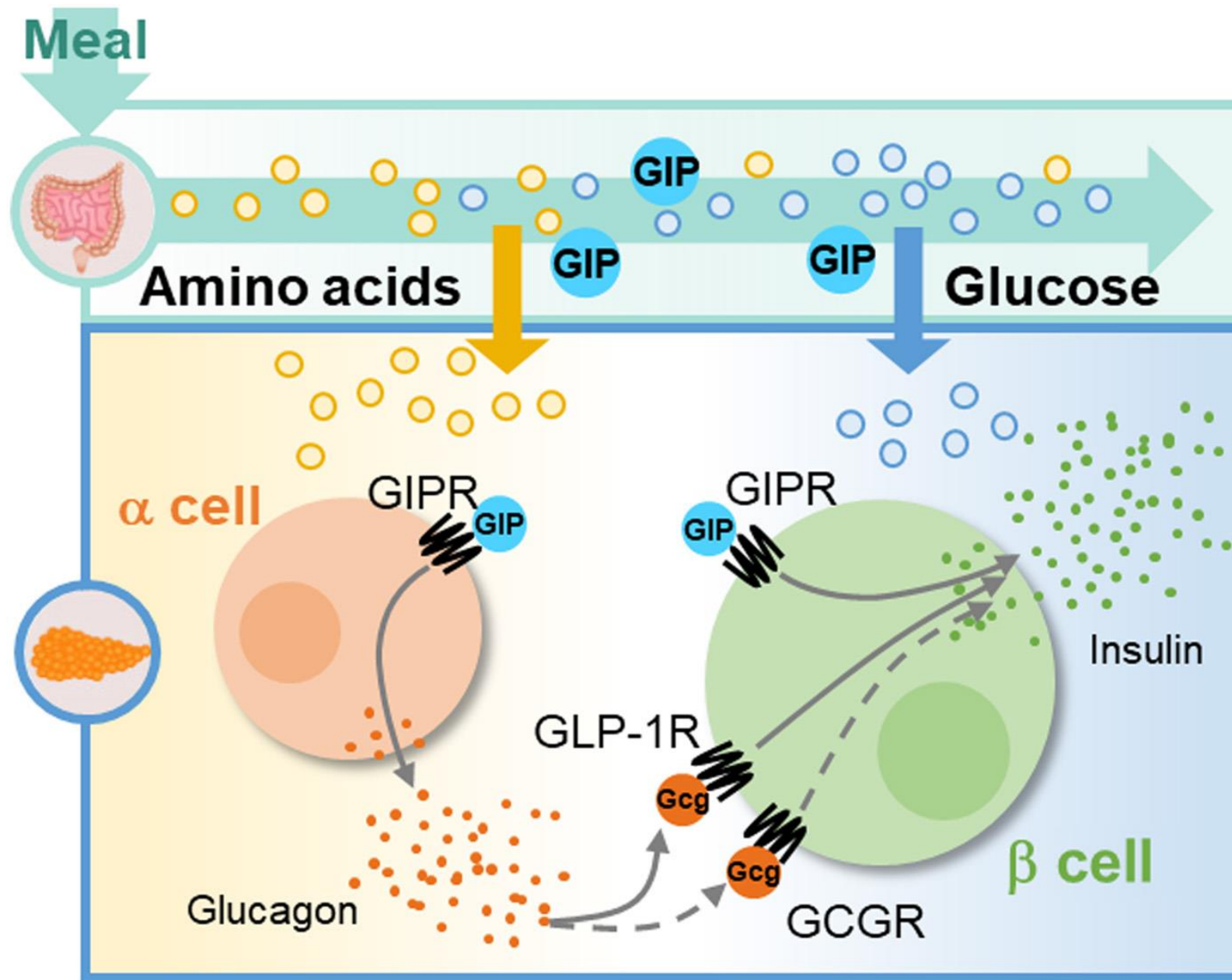


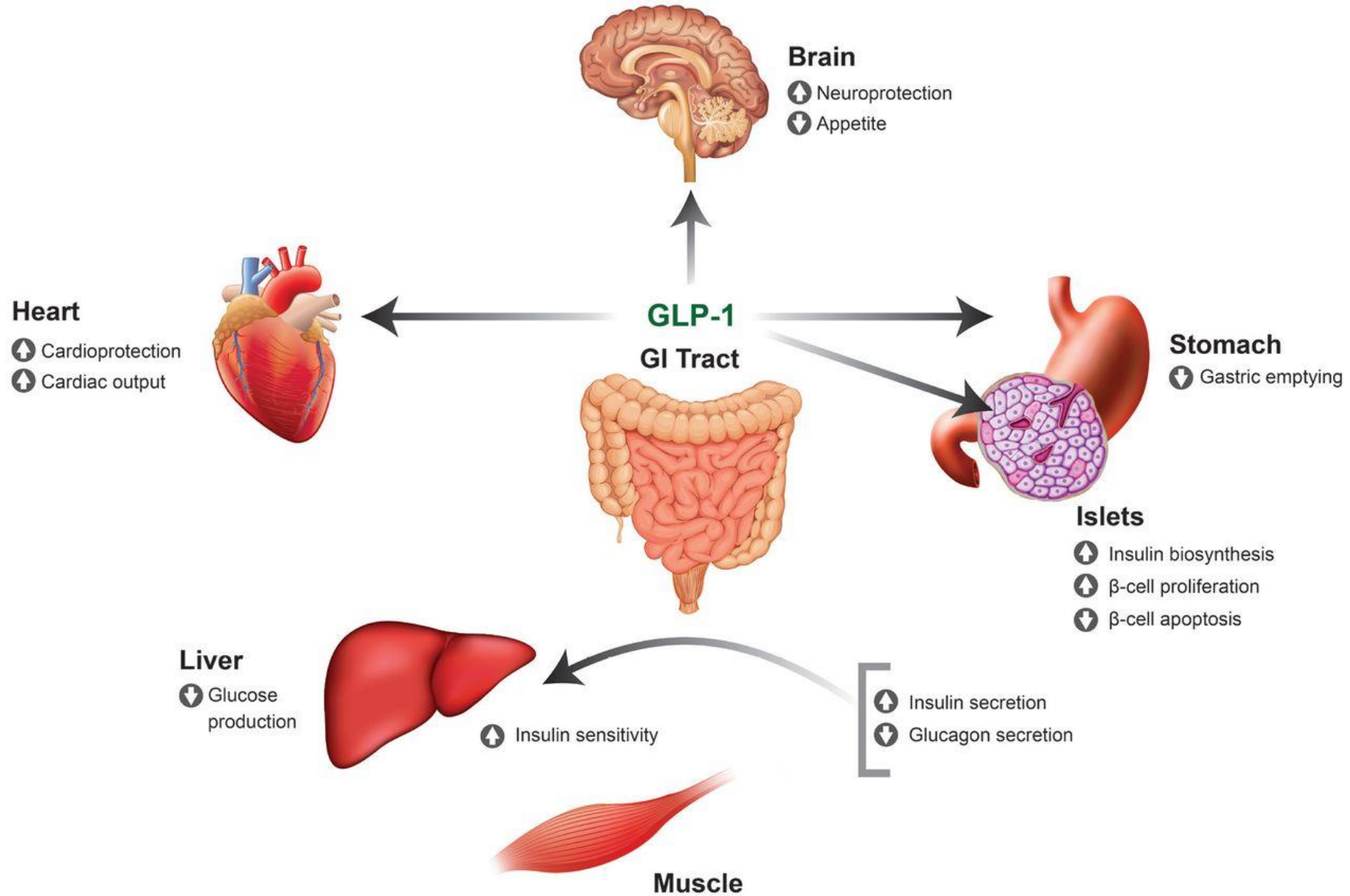
CHANGES AFTER SGLT2 INHIBITION



TARGETS FOR CARDIOMETABOLIC DRUGS

- **SGLT co-transporters** (*SGLT1i, SGLT2i*)
- **Incretins** (*GIP-RA, GLP1RA*)





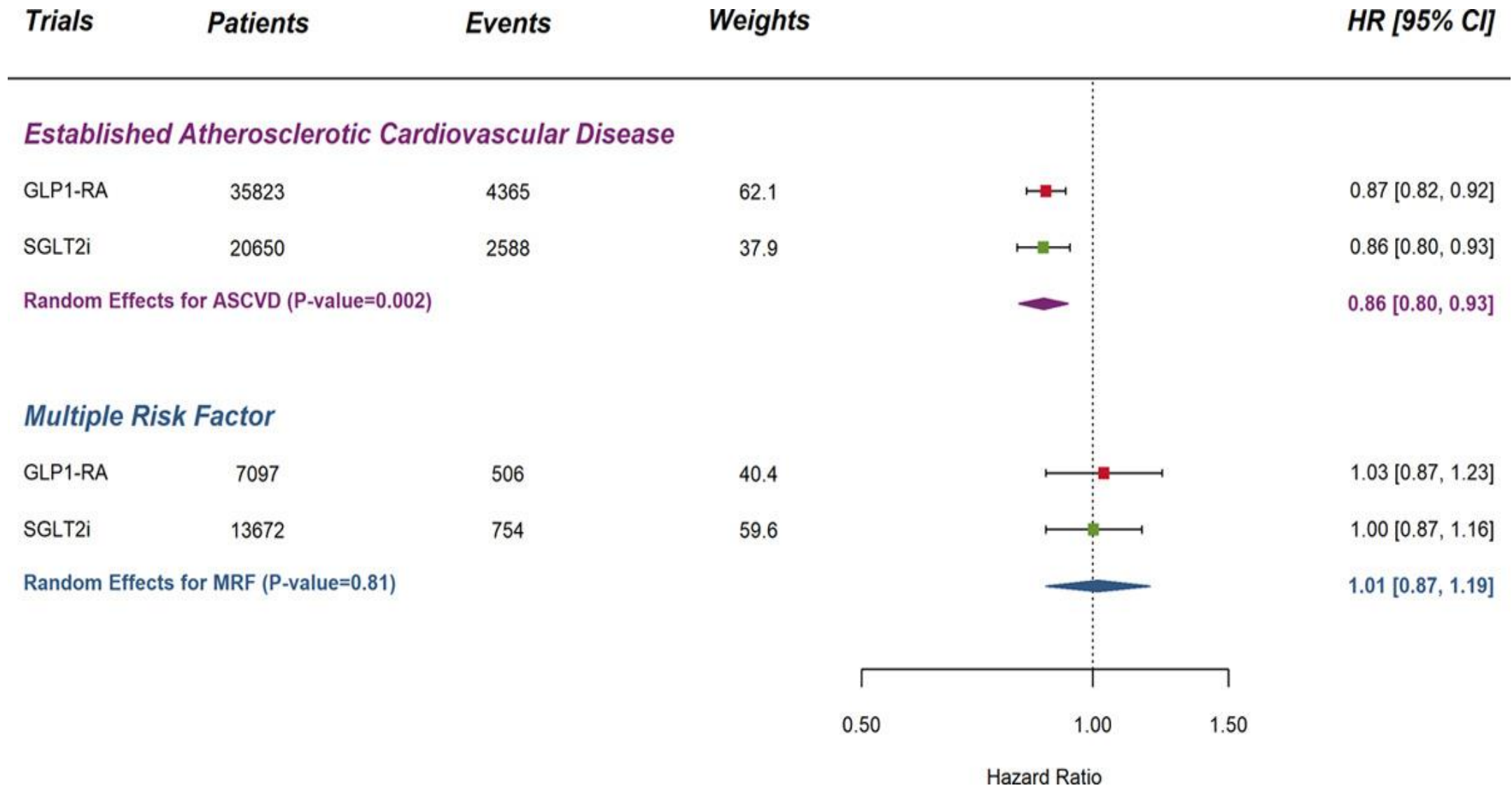
Incretin Analogues with Proven CV Benefits

Liraglutide

Semaglutide

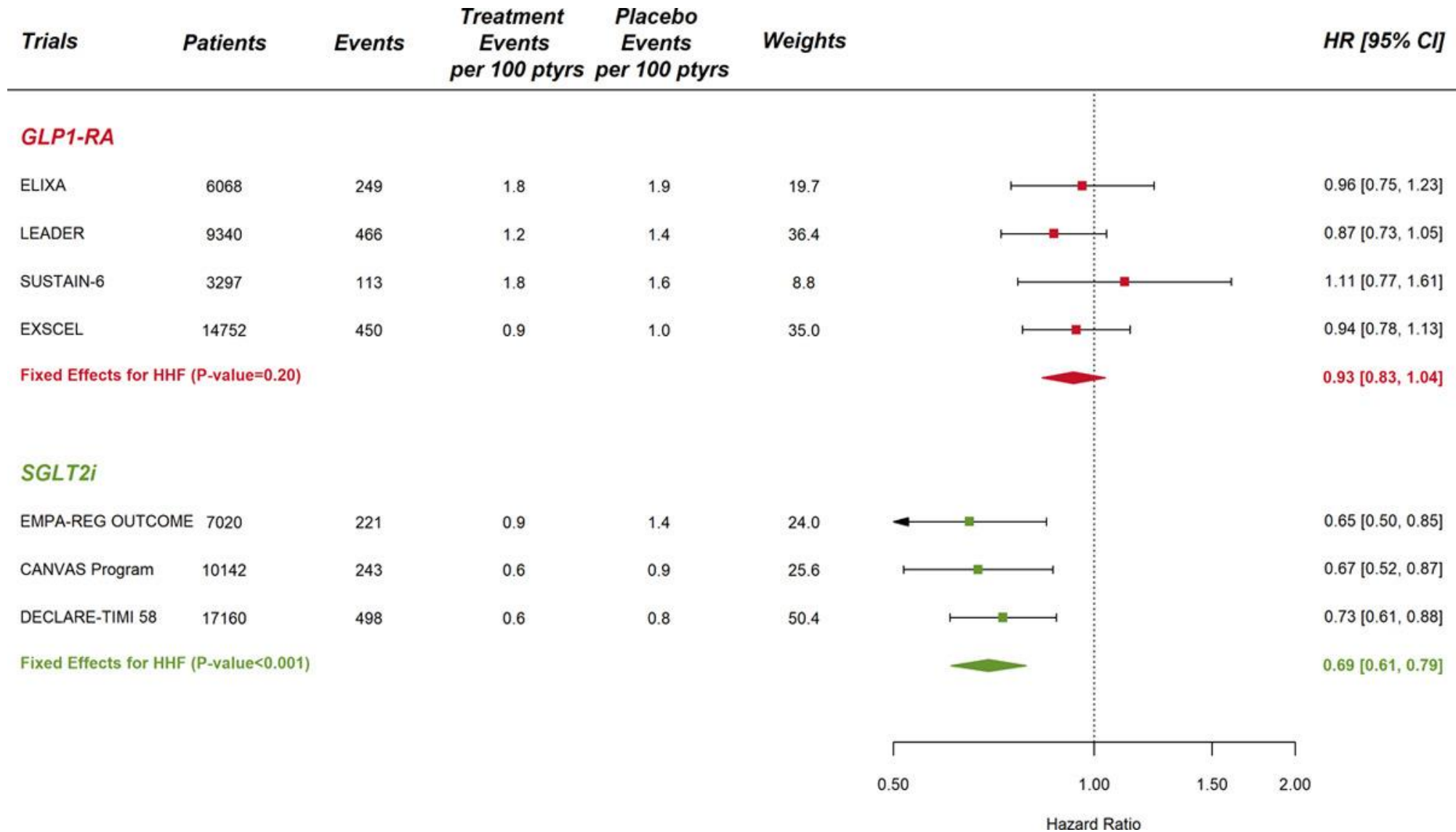
Dulaglutide

MI, STROKE AND CV DEATH



Thomas A. Zelniker. Circulation. Comparison of the Effects of Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus, Volume: 139, Issue: 17, Pages: 2022-2031, DOI: (10.1161/CIRCULATIONAHA.118.038868)

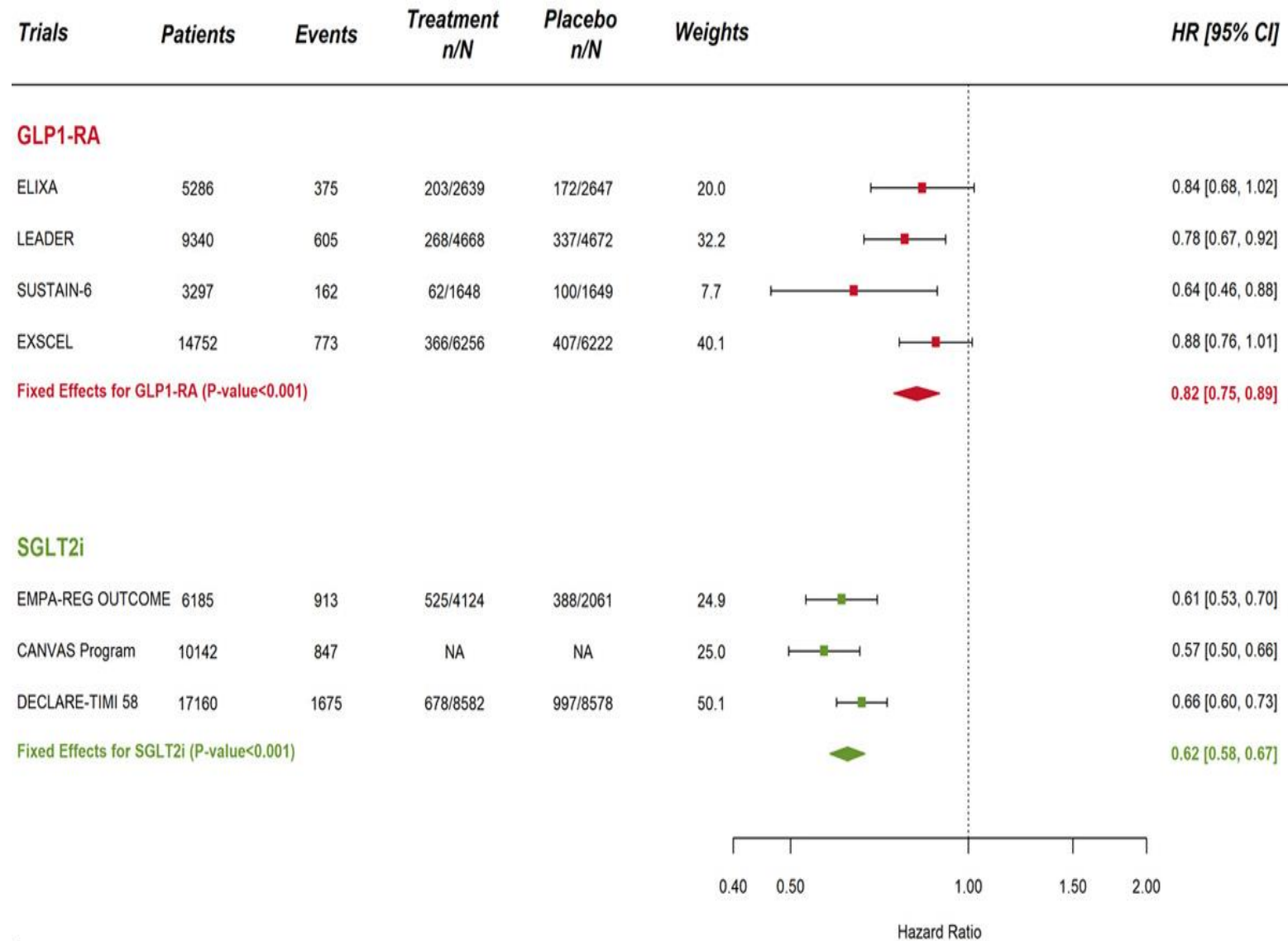
HOSPITALIZATION FOR HEART FAILURE



Thomas A. Zelniker. Circulation. Comparison of the Effects of Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus, Volume: 139, Issue: 17, Pages: 2022-2031, DOI: (10.1161/CIRCULATIONAHA.118.038868)

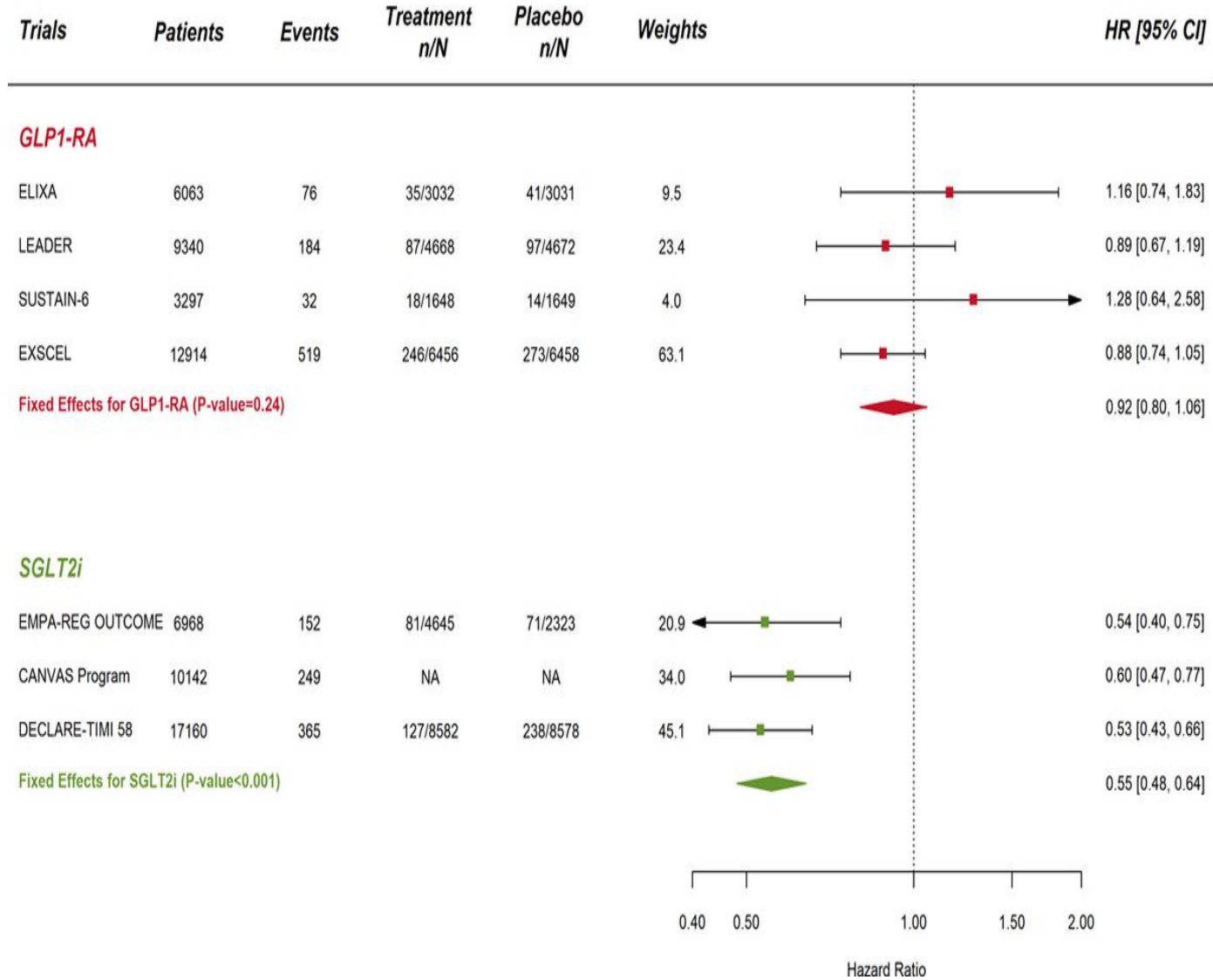


BROAD RENAL OUTCOMES



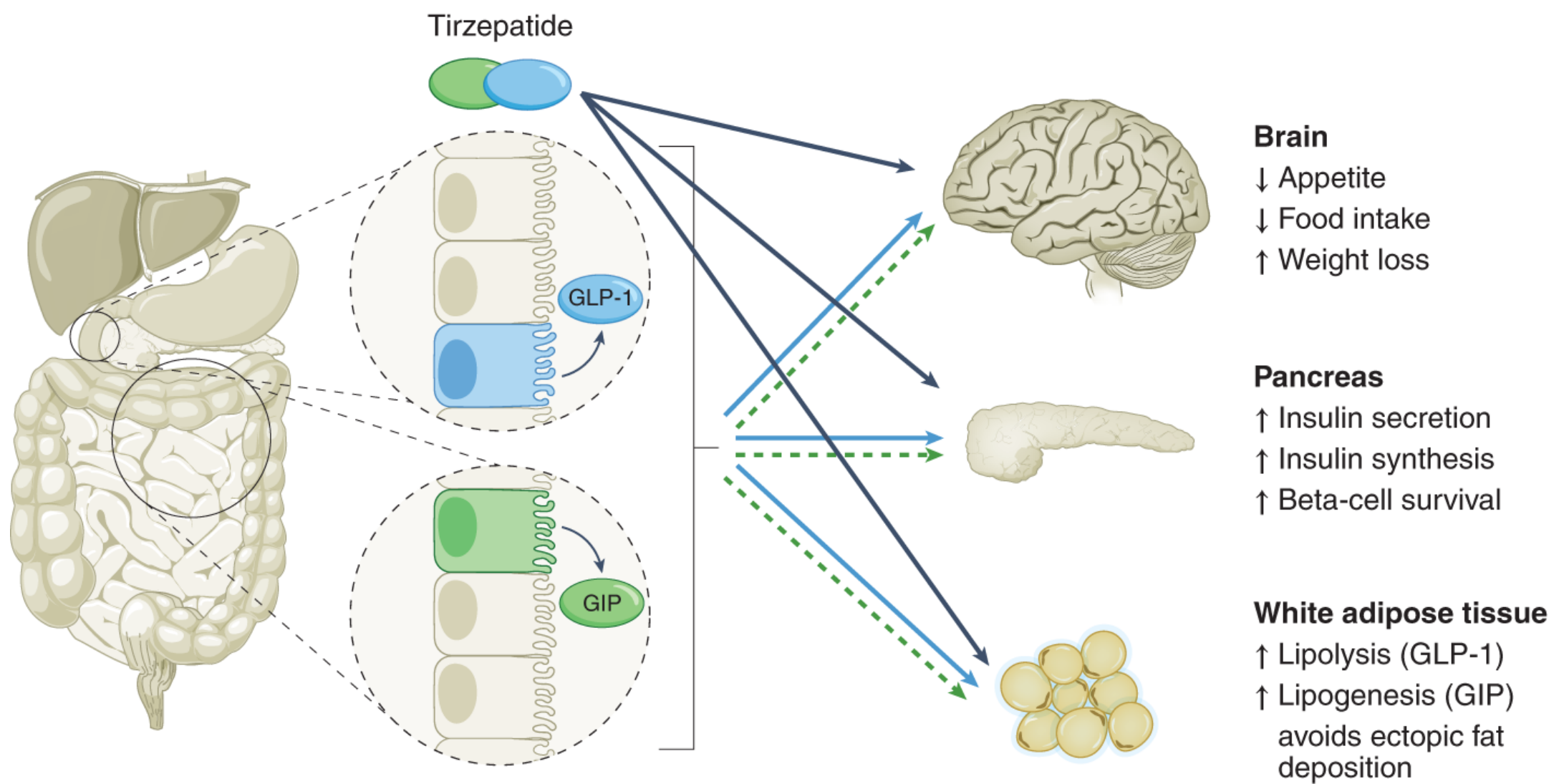
Thomas A. Zelniker. Circulation. Comparison of the Effects of Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus, Volume: 139, Issue: 17, Pages: 2022-2031, DOI: (10.1161/CIRCULATIONAHA.118.038868)

RENAL OUTCOME EXCLUDING MACROALBUMINURIA



Thomas A. Zelniker. Circulation. Comparison of the Effects of Glucagon-Like Peptide Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors for Prevention of Major Adverse Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus, Volume: 139, Issue: 17, Pages: 2022-2031, DOI: (10.1161/CIRCULATIONAHA.118.038868)





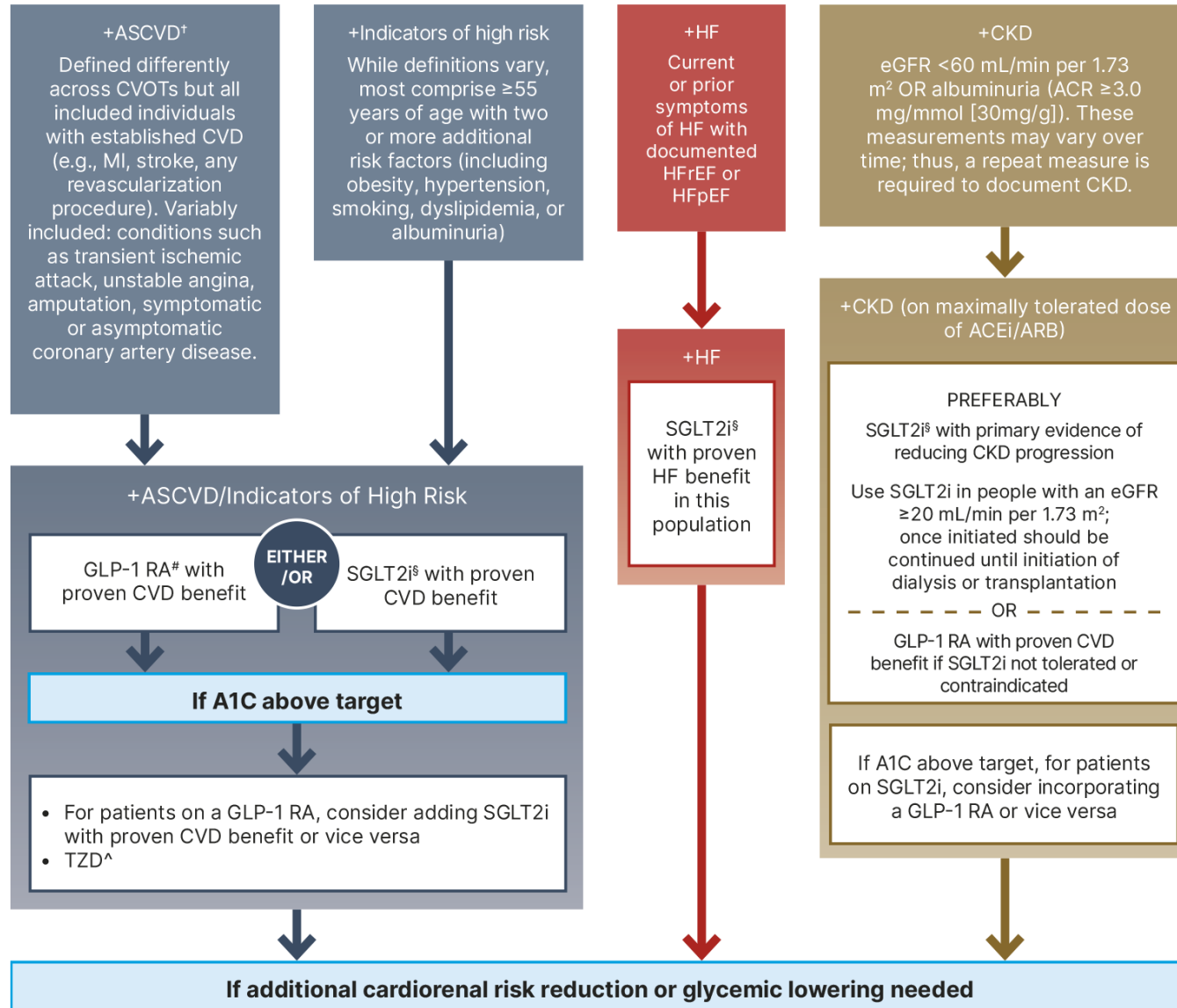
SURPASS-CVOT

Trial population:

People with type 2 diabetes, confirmed atherosclerotic cardiovascular disease, and overweight

October 2024

ADA 2024 Standards of Care in Diabetes



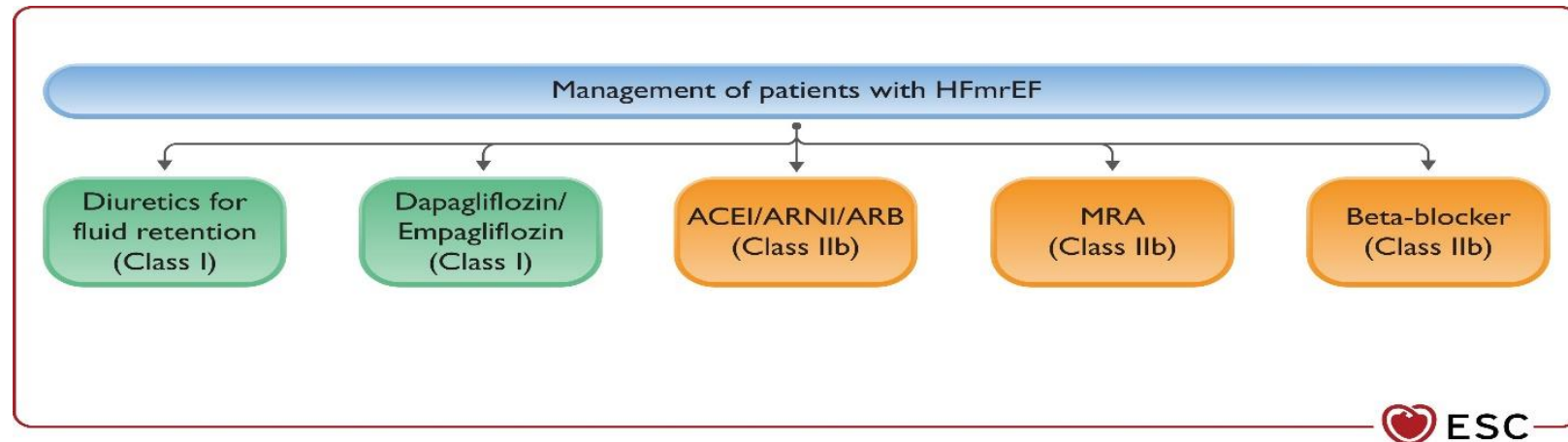
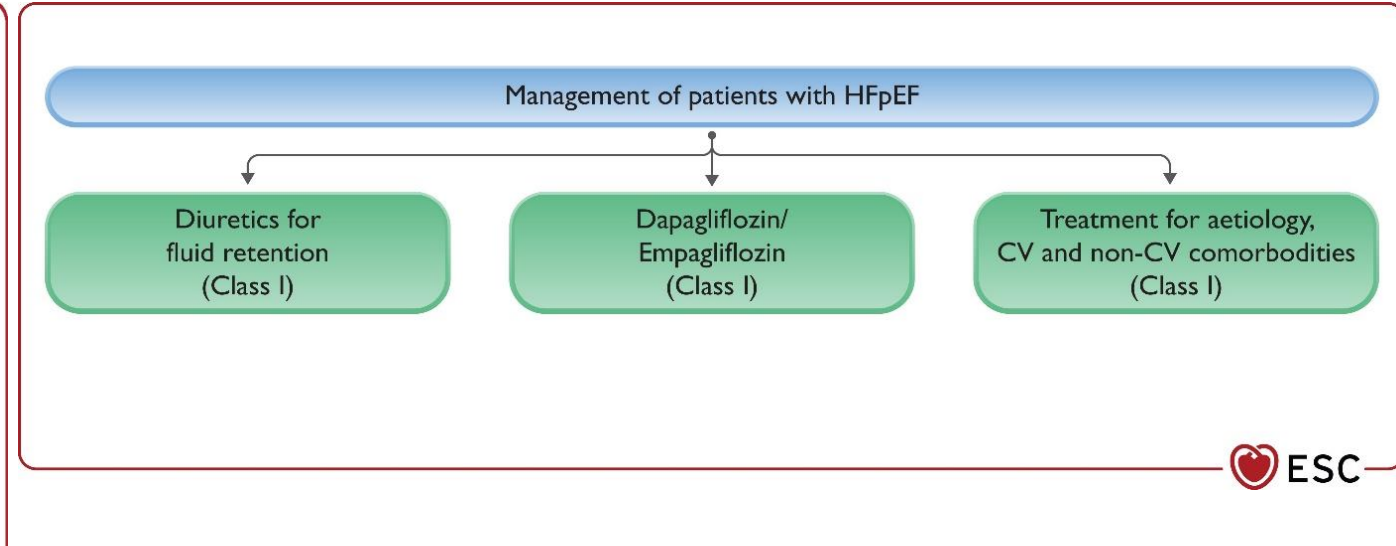
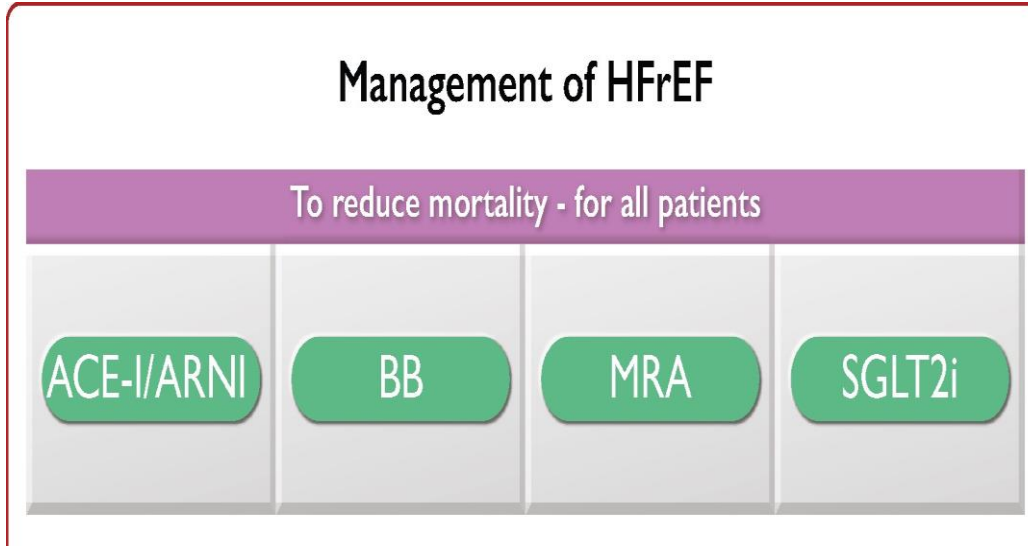
2022 AHA/ACC/HFSA GUIDELINE FOR MANAGEMENT OF HEART FAILURE

Guideline Directed Medical Therapy Across Heart Failure Stages

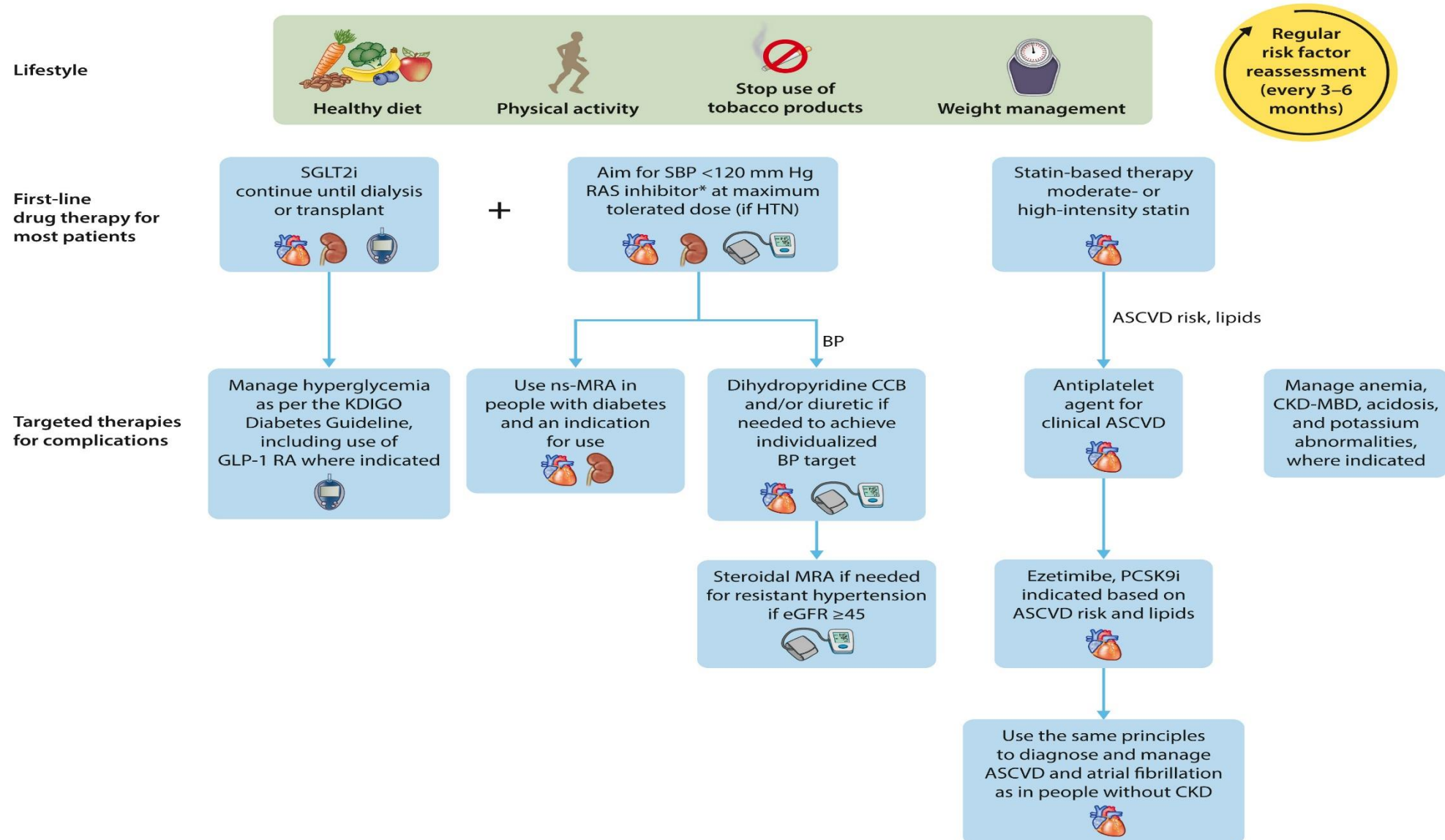
Use this tool to reference guideline directed medical therapy (GDMT) across the four ACC/AHA stages of Heart Failure (HF) as outlined in the 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure. See the guideline for specific patient population criteria.

GDMT of major medication classes	Stage A	Stage B	Stage C & D		
	At-Risk for Heart Failure	Pre-Heart Failure	Stage C: Symptomatic Heart Failure & Stage D: Advanced Heart Failure		
			HFrEF LVEF ≤40%	HFmrEF LVEF 41-49%	HFpEF LVEF ≥50%
	SGLT2i in pts with DM (1)	SGLT2i in pts with DM (1)	ARNi in NYHA II-III; ACEi or ARB in NYHA II-IV (1)	Diuretics, as needed (1)	Diuretics, as needed (1)
		ACEi (1)	Beta blocker (1)	SGLT2i (2a)	SGLT2i (2a)
		ARB if ACEi intolerant (1)	MRA (1)	ACEi, ARB, ARNi (2b)	ARNi (2b)
		Beta blocker (1)	SGLT2i (1)	MRA (2b)	MRA (2b)
			Diuretics, as needed (1)	Beta blocker (2b)	ARB (2b)
			Hydral-nitrates for NYHA III-IV, in African American pts (1)		

2023 FOCUSED UPDATE OF 2021 ESC GUIDELINES

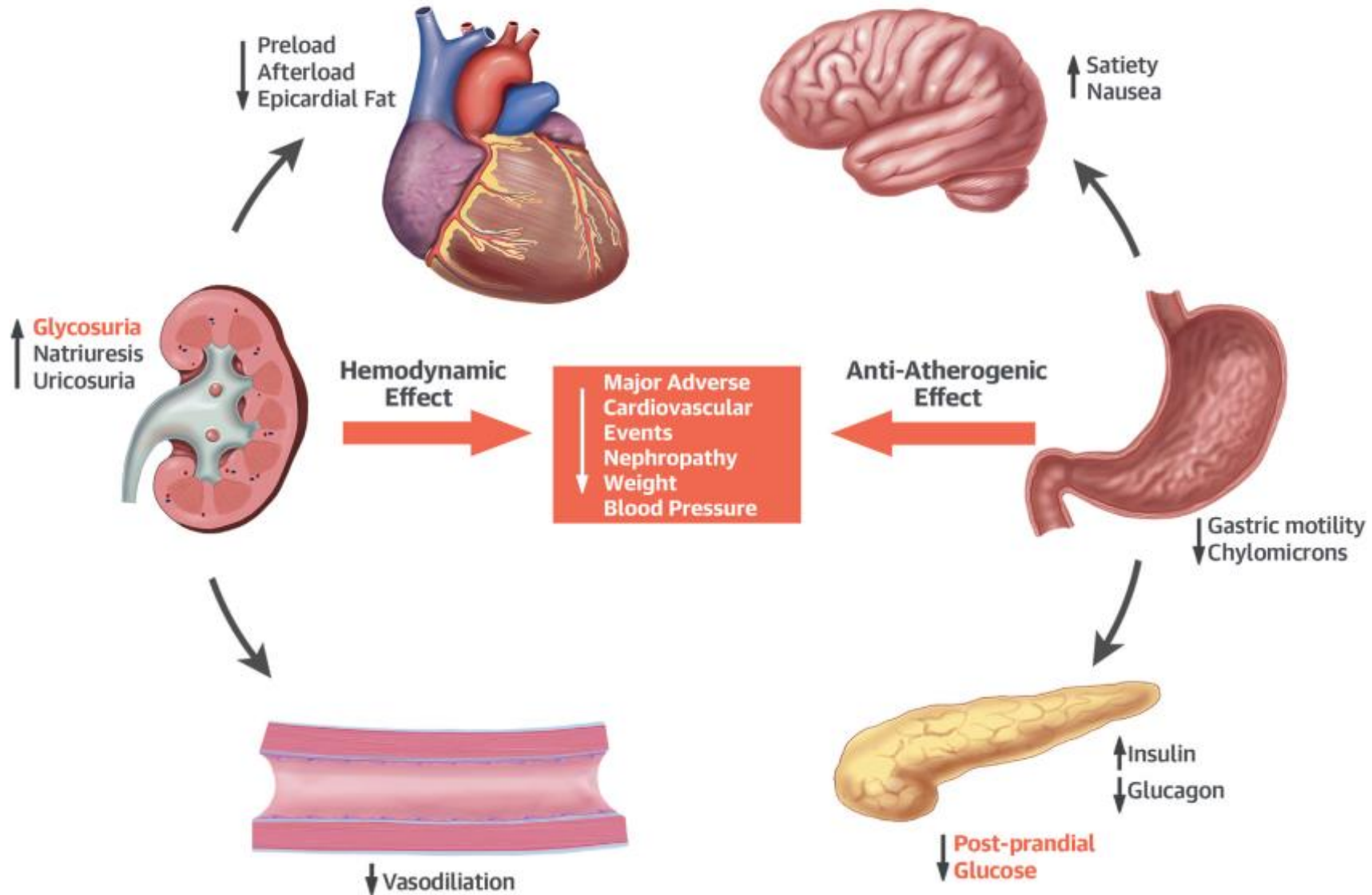


KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

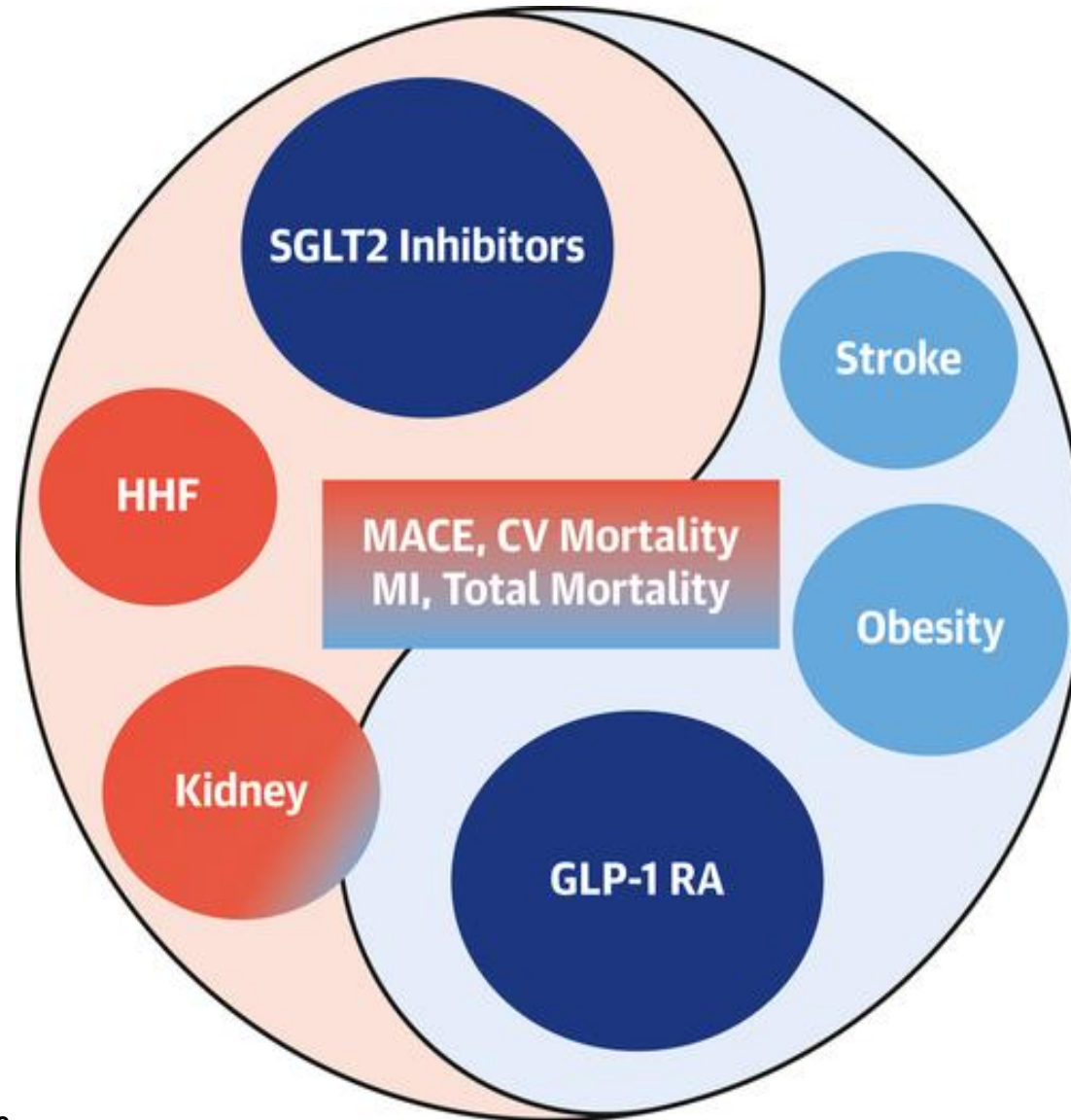


SGLT-2 Inhibitors

GLP-1R Agonists



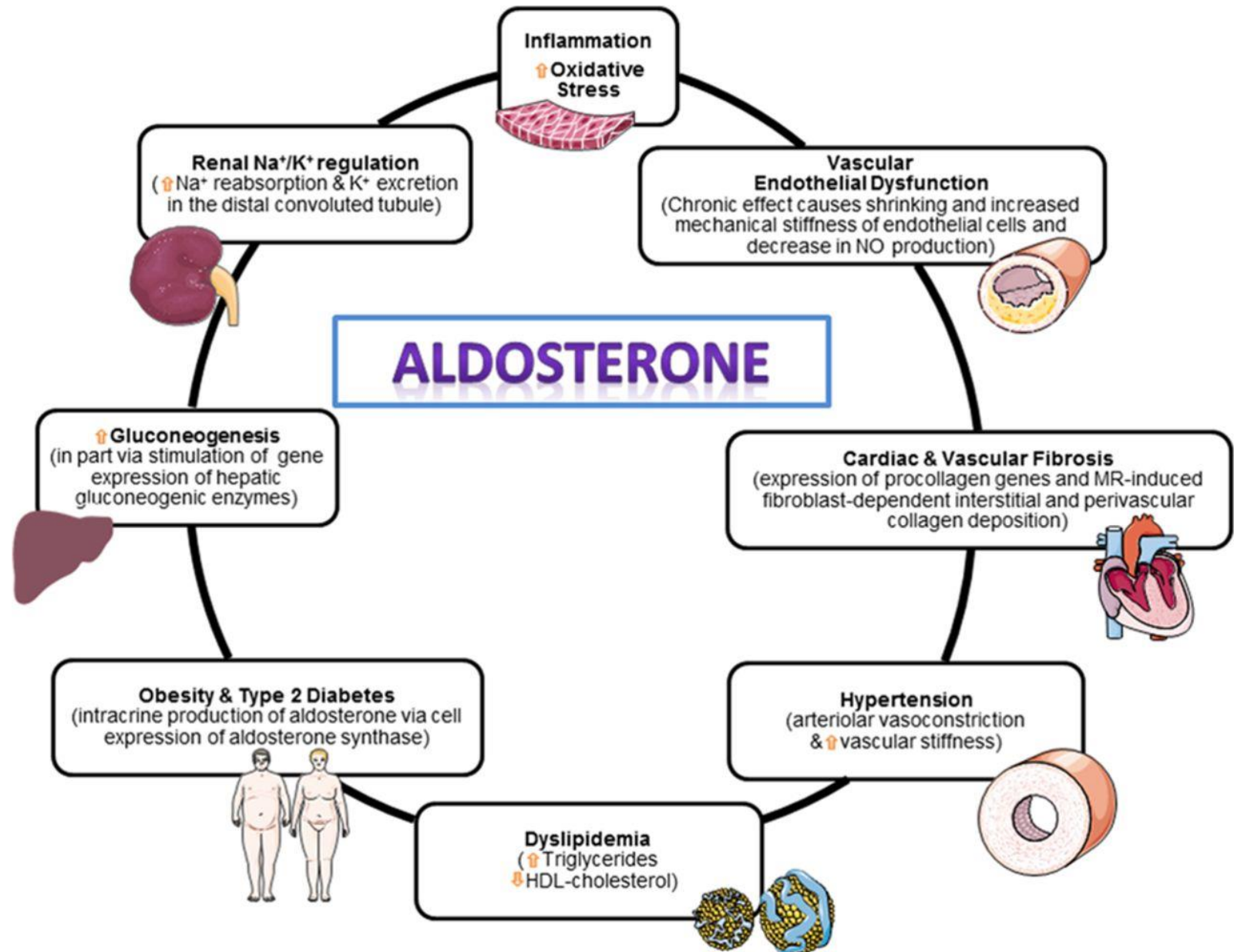
Complementary roles of GLP-1 RA and SGLT2 inhibitors in Cardio-renal Risk Reduction

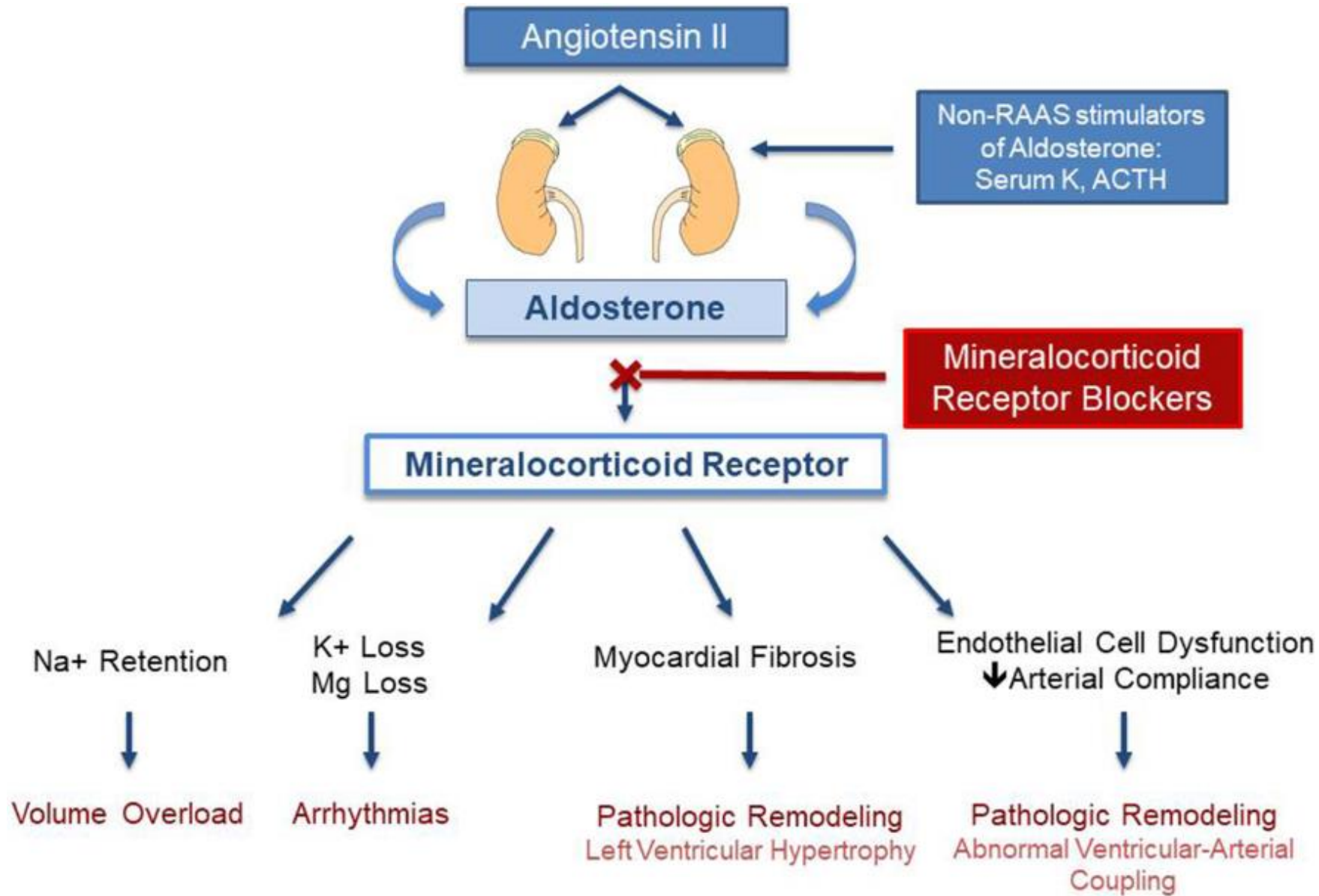


Vanita R. Aroda et al. *J Am Coll Cardiol* 2023; 82:526-528.

TARGETS FOR CARDIOMETABOLIC DRUGS

- **SGLT co-transporters** (*SGLT1i, SGLT2i*)
- **Incretins** (*GIP-RA, GLP1RA*)
- **Aldosterone** (*MRA*)





Mineralocorticoid Receptor Antagonists

	Steroidal MRA		Nonsteroidal MRA
	SPIRONOLACTONE	EPLERENONE	FINERENONE
MR Antagonism	Potent Non-selective	Less potent More selective	Potent Selective
Tissue Distribution	Kidney > Heart	Kidney > Heart	Kidney = Heart
Pharmacokinetics	Prodrug Multiple active metabolites with long half-lives	No active metabolites Half-life = 4-6 hrs	No active metabolites Short half-life
Hyperkalemia	+++	++	+

FIDELITY

Results



Endpoint CV composite

HR (95% CI) 0.86 (0.78 – 0.95) p-value 0.0018 Risk ↓ 14%



Kidney composite

HR (95% CI) 0.77 (0.67 – 0.88) p-value 0.0002 Risk ↓ 23%



HHF

0.78 (0.66 – 0.92) 0.0030 22%













Dialysis

0.80 (0.64 – 0.99) 0.040 20%

Conclusion

Finerenone on top of standard of care reduces the risk of clinically meaningful cardiovascular and kidney outcomes in patients with type 2 diabetes over a broad spectrum of chronic kidney disease

Public health actions to promote healthy lifestyles and tackle obesity

Health education and health promotion	Environmental changes and physical activity promotion
 <p>Food labelling schemes</p>	 <p>School-based programmes</p>
 <p>Menu labelling schemes</p>	 <p>Increase in access to public transport</p>
 <p>Mass media campaigns</p>	 <p>Workplace wellness/ sedentary behaviour programmes</p>
 <p>Prescription of physical activity by healthcare professionals</p>	 <p>Food reformulation</p>
 <p>Mobile apps to promote healthier lifestyle</p>	 <p>Regulation of advertising of unhealthy food to children</p>

Eur Heart J, Volume 44, Issue 39, 14 October 2023, Pages 4141–4156, <https://doi.org/10.1093/eurheartj/ehad445>

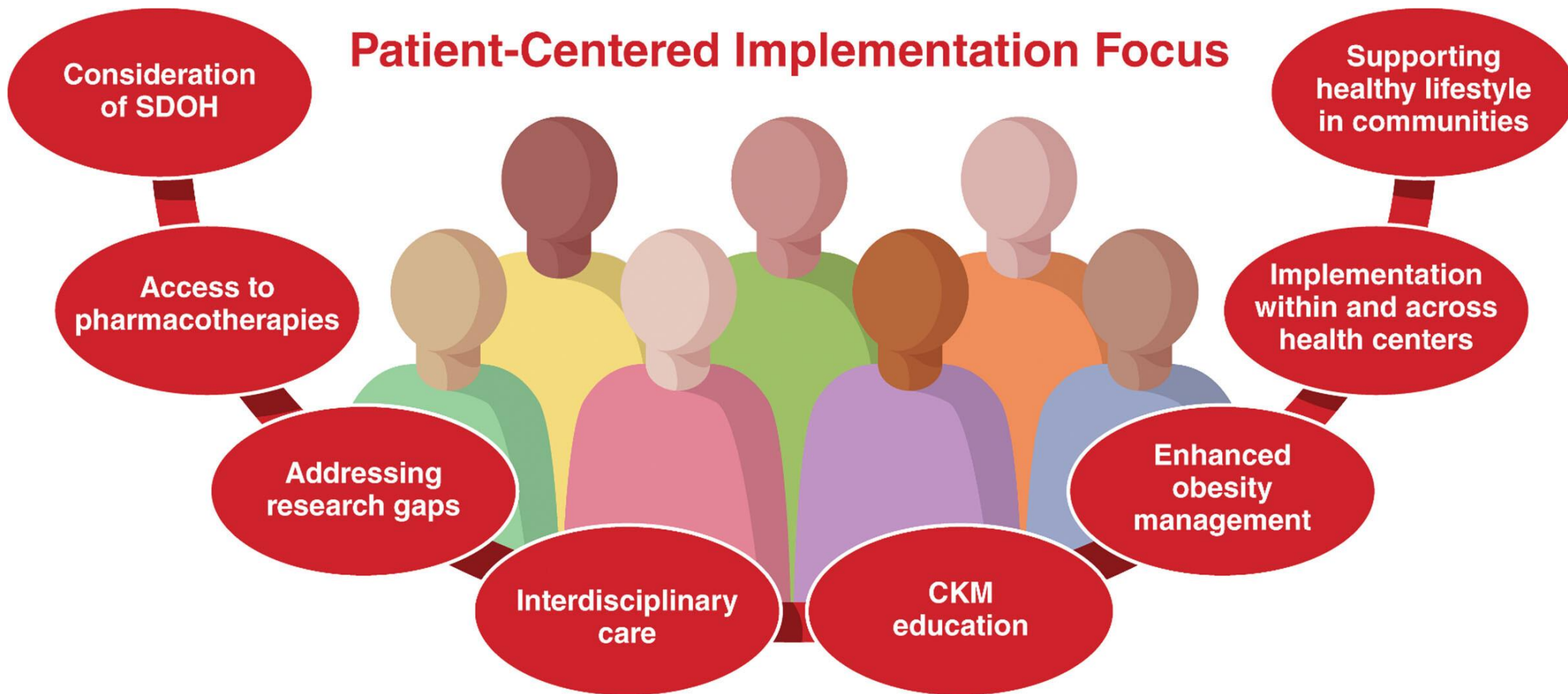
The content of this slide may be subject to copyright: please see the slide notes for details.

Strategies to address the challenges and barriers in the prevention, recognition, and treatment of cardiometabolic comorbidities

- Target lifestyle modification
- Target screening and diagnosis
- Target cross-specialty care
- Target optimal use of current therapies

A CALL TO ACTION!!!

Patient-Centered Implementation Focus



Chiadi E. Ndumele. Circulation. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association, Volume: 148, Issue: 20, Pages: 1606-1635, DOI: (10.1161/CIR.0000000000001184)

Circulation

ON MY MIND

Are We Ready to Bell The Cat?

A Call for Cardiologists to Embrace Glucose-Lowering Therapies Proven to Improve Cardiovascular Outcomes

Michael E. Nassif, MD
Mikhail Kosiborod, MD

**Times change.
We need to change as well.**

- Nelson Mandela

**THANK YOU VERY MUCH FOR
YOUR ATTENTION**

MercyOne IOWA HEART CENTER
PREVENTION AND WELLNESS CLINIC
We aim not only to INFORM but also to TRANSFORM