Diabetes and Cardiovascular diseases
Cardiologists view point

M.Vojdanparast
MD. Interventional Cardiologist

Case Presentation

Patient Information

- Age: 60 years
- Gender: Male
- Medical history: Hypertension and Pre-Diabetes
- Medications: Valsartan 160 mg once daily, aspirin 81 mg once daily

Presenting Complaint

The patient presented to the emergency department with chest pain and shortness of breath. He was diagnosed with acute coronary syndrome (ACS) based on his symptoms and electrocardiogram findings.

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Case Presentation

LAB Tests

- Chol: 167mg/dl
- TG: 199mg/dl
- LDL: 95mg/dl
- HDL: 42mg/dl

- Hb: 14.5mg/dl
- Crt : 1.7mg/dl (weight: 81Kg) —— CrCl: 52.9mL/min

- FBS: 139mg/dl
- HbA1c: 7.6

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Epidemiological Studies

Patients with T2D have **twice the risk** of CV disease compared with the general population

Globally, approximately **1/3 of patients** with T2D have CV disease

CV disease can occur **10–15 years earlier** in patients with diabetes compared with those without diabetes[1]

Approximately **50%** of people with T2D still **die from CV disease**

2.5 times more deaths than cancer*

The Emerging Risk Factors Collaboration. *JAMA* 2015;314:52

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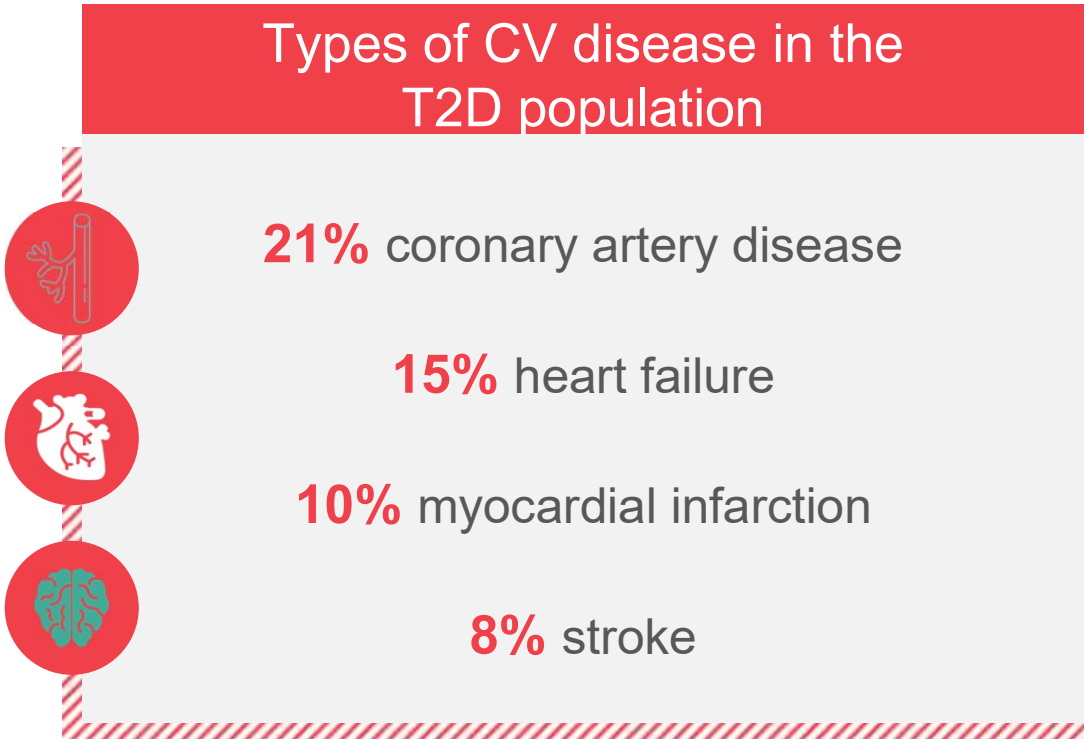
Epidemiological Studies



Analysis of 57 studies with 4,549,481 patients with T2DCV, cardiovascular; T2D, type 2 diabetes
1-Einarson TR *et al. Cardiovasc Diabetol* 2018;17:83

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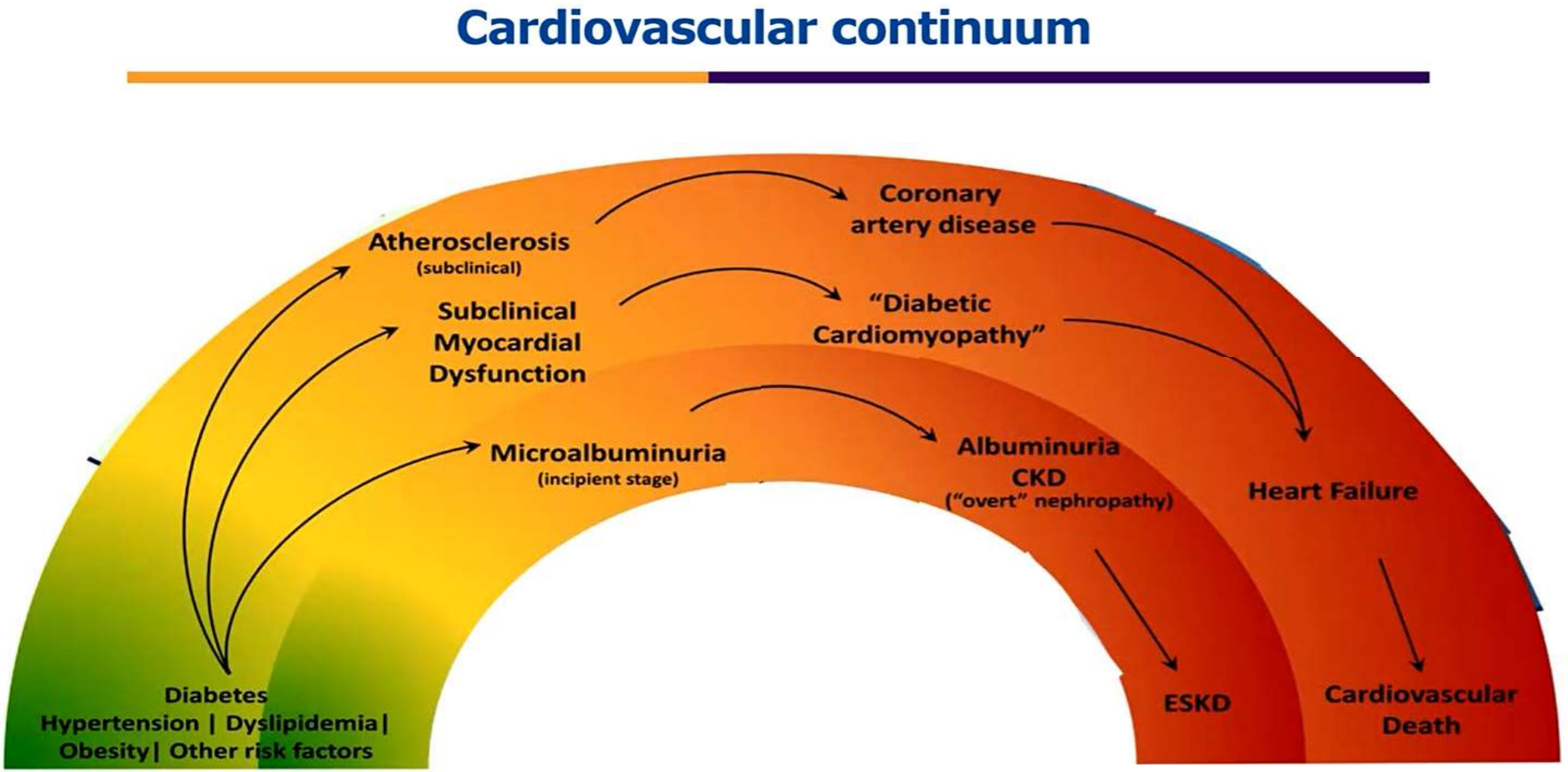
Epidemiological Studies



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Case Presentation

What is the best Anti-diabetic medication for this patient?

- **Metformin**
- **SGLT2i**
- **GLP-1RA**
- **Gliclazide**

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Case Presentation

This patient is a new case of DM2
What is your CVD estimation risk in the future?

- Low
- Intermediated
- High
- Very High

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Case Discussion

08.Jun.2023

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CVD Risk Estimation

CV risk categories in patient with DM

Intermediate	Young patients (T1DM aged <35 years or T2DM aged <50 years) with DM duration <10 years, without other risk factors
High risk	Patients with DM duration >=10 years without target organ damage any other additional risk factor
Very High risk	Established CVD Target organ damage >=3 major risk factors early onset T1DM (>20 years)

→ **End Organ Damage**

Proteinuria
eGFR <30 mL/min
Left ventricular hypertrophy
Retinopathy

Primary Prevention In Patients without DM

2019 ESC

Low risk	Moderate risk	High Risk	Very High Risk
1. SCORE : <=1%	1. DM1(35yo)/DM2(<50yo) • (Duration < 10yr without RF) 2. SCORE : 1-5%	1. Marked RF: T.Chol>310mg/dl LDL > 190 mg/dl BP > 180/90 2. DM 1.1-2RF 2.More then 10yr 3. CKD (GFR:30 - 59) 4. FH 5. SCORE: 5-10%	1. ASCVD 2. DM EOD >=3RF More than 20yr 3. CKD (GFR < 30) 4. FH + another RF 5. SCORE >= 10%

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Primary Prevention In Patients without DM

2018 AHA

Low
<5%

LifeStyle

Borderline
5-7.5%

LifeStyle

Enhancing Factors

Intermediate
7.5-20%

Intermediate
7.5-20%

Moderate Intensity

LDL lowering 30-50%

Atorvastatin 10 mg (20 mg)

Rosuvastatin (5 mg) 10 mg

Simvastatin 20–40 mg

High
>20%

High Intensity

LDL lowering > 50%

Atorvastatin (40 mg‡) 80 mg

Rosuvastatin 20 mg (40 mg)

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Case Discussion

This patient is a new case of DM2
What is your CVD estimation risk in the future?

Low	Intermediated	High	Very High

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Management of IHD

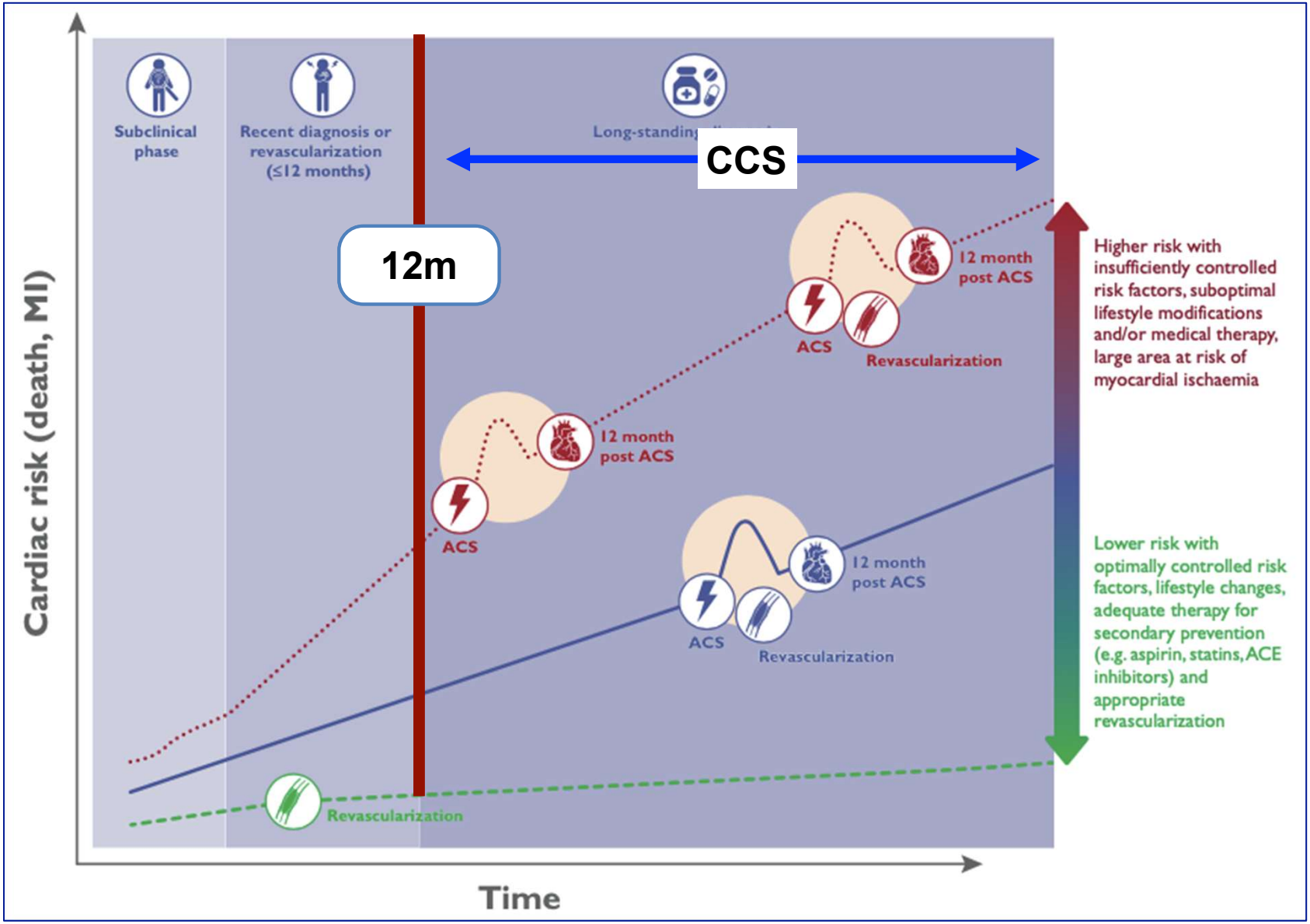
Anti-ischemic drugs

- B Blockers
- CCBs
- Nitrates
- Ranolazine
- Nicorandil

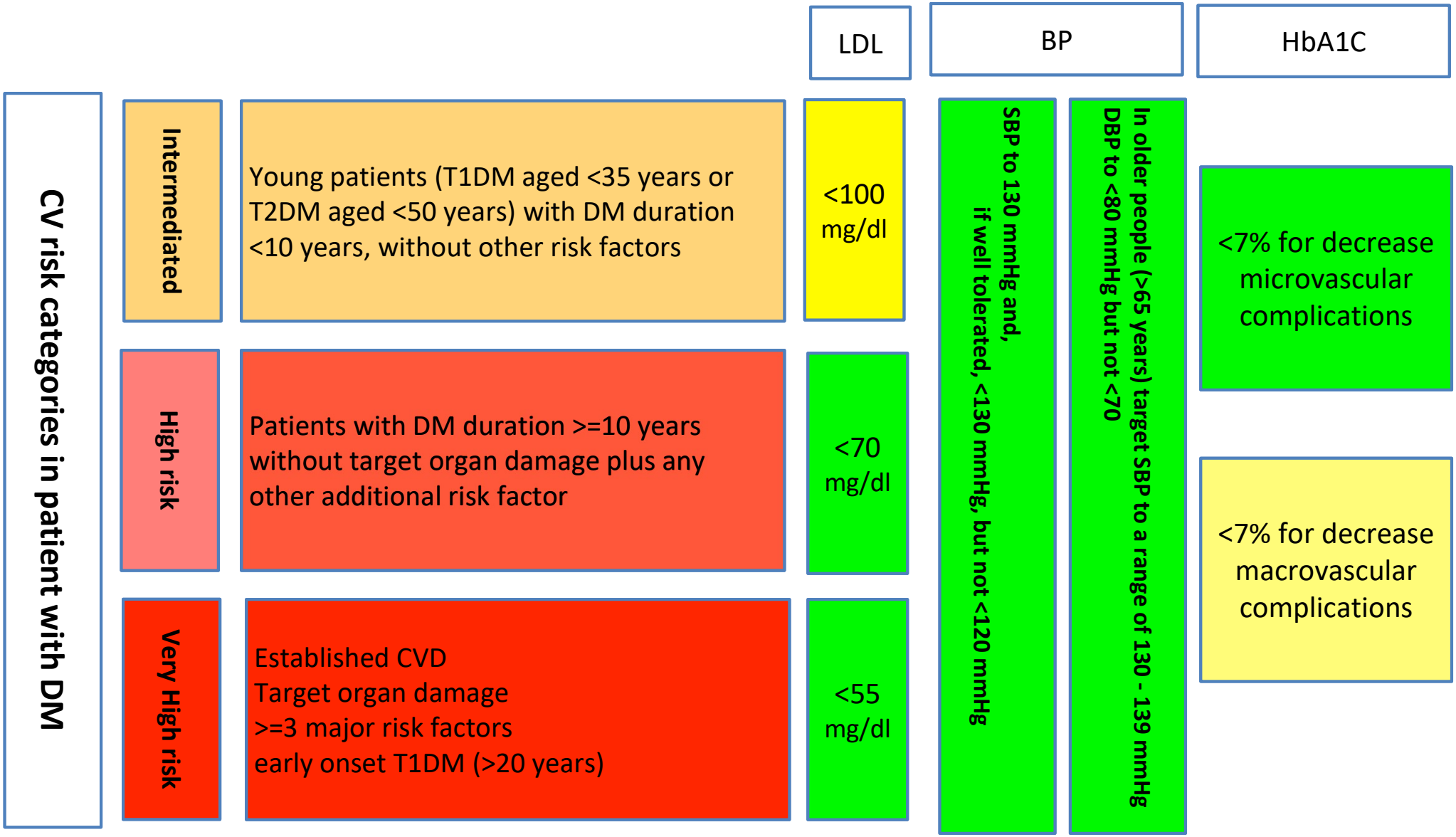
Event prevention

- Antithrombotic
  - Antiplatelets
  - Anticoagulants
    - Af Rhythm
    - Sinus
- Statin therapy
- Risk Factors
  - DM

Transition from ACS to CCS



CVD Risk management



2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases

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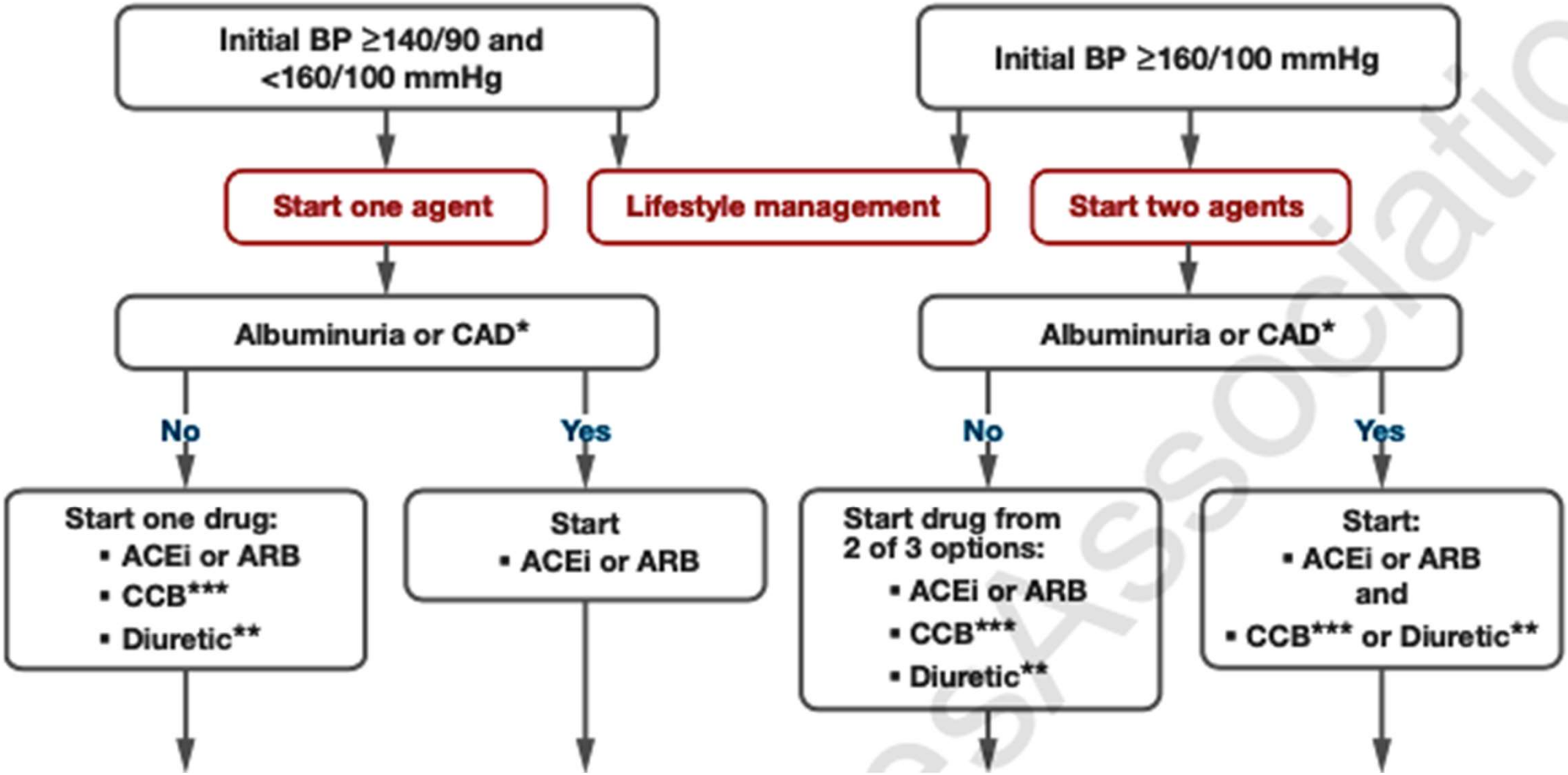
CVD Risk management



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CVD Risk management

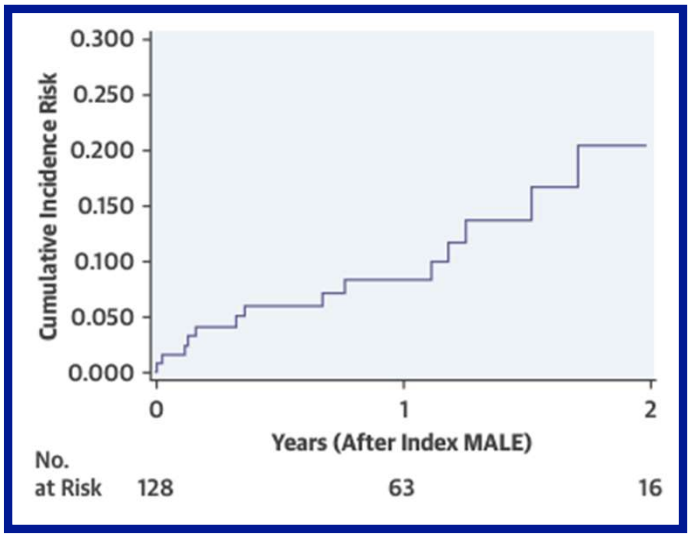
Recommendations for Resting ABI for Diagnosing PAD		
COR	LOE	Recommendations
I	B-NR	In patients with history or physical examination findings suggestive of PAD (Table 4), the resting ABI wa dia
IIa	B-NR	In p with sug res

Table 3. Patients at Increased Risk of PAD

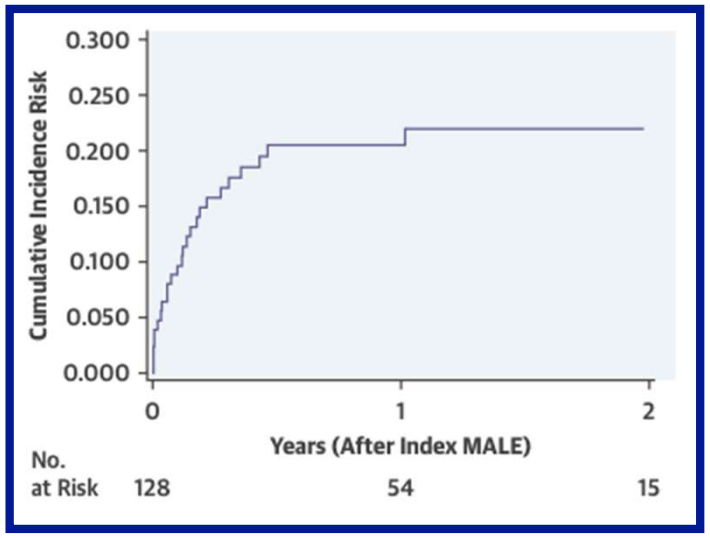
Age ≥65 y
Age 50–64 y, with risk factors for atherosclerosis (eg, diabetes mellitus, history of smoking, hyperlipidemia, hypertension) or family history of PAD[52]
Age <50 y, with diabetes mellitus and 1 additional risk factor for atherosclerosis
Individuals with known atherosclerotic disease in another vascular bed (eg, coronary, carotid, subclavian, renal, mesenteric artery stenosis, or AAA)

Major Adverse Limb Events and Mortality in Patients With Peripheral Artery Disease (The COMPASS Trial)

Death

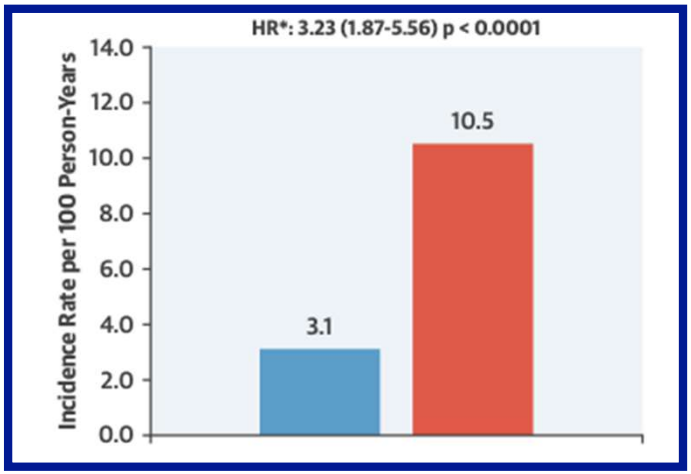


Amputation

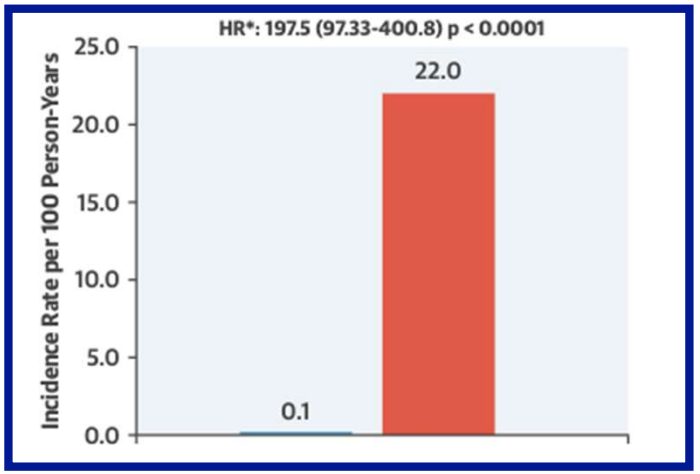


Death & Amputation after MALE

Death



Amputation



Death & Amputation
Pre- MALE
Post- MALE

Fox, K.A.A. et al. J Am Coll Cardiol. 2019;73(18):2243–50.

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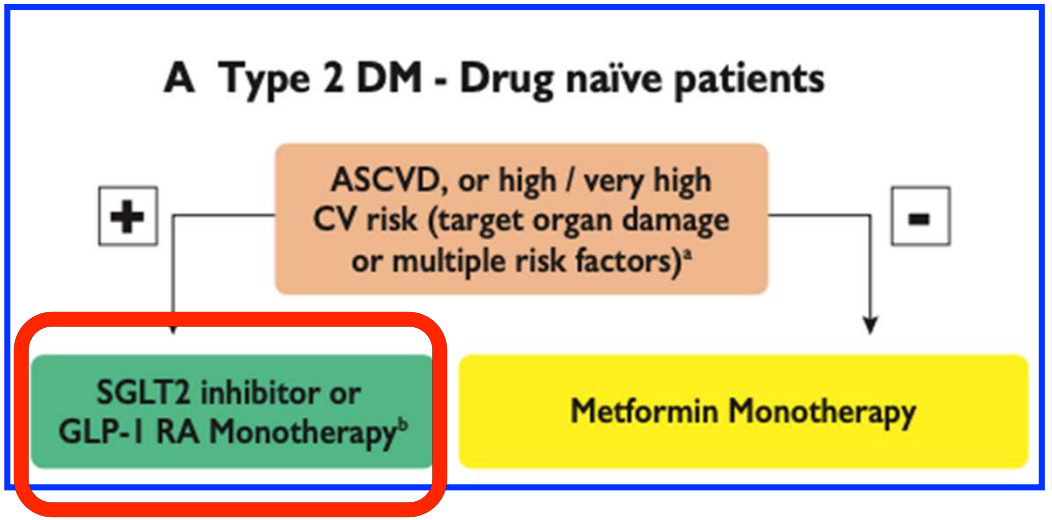
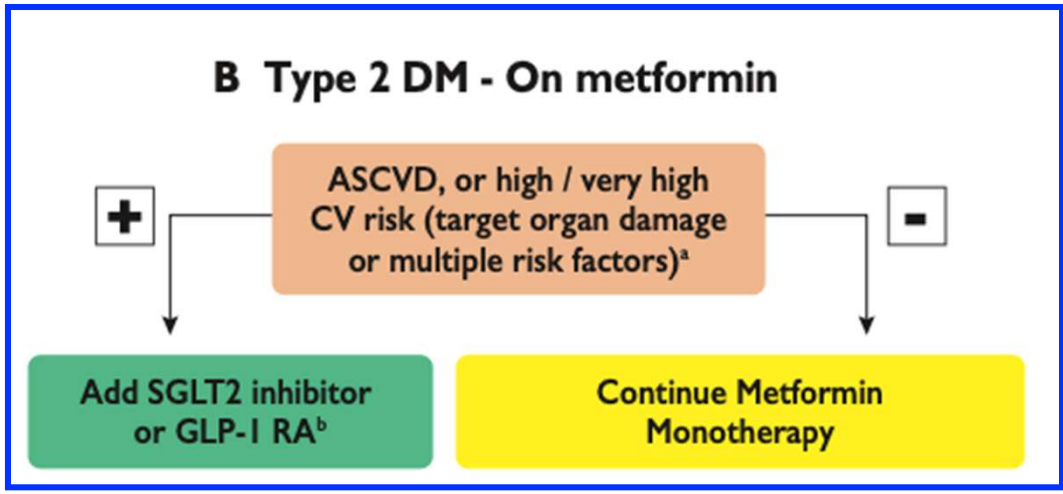
What is the Best Choice?

2019 ESC

DM >=10 years
Single risk factor

Established CVD
Target organ damage
>=3 major RF
early onset T1DM (>20 years)





2020 ADA

First Line: Metformin

ASCVD or High risk

+ASCVD/Indicators of High Risk

- Established ASCVD
- Indicators of high ASCVD risk (age ≥55 years with coronary, carotid, or lower-extremity artery stenosis >50%, or LVH)

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

+HF

Particularly HFrEF (LVEF <45%)

SGLT2i with proven benefit in this population[5,6,7]

+CKD

\+ DKD and Albuminuria[8] −

PREFERABLY

SGLT2i with primary evidence of reducing CKD progression

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1,7]

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EMPA-REG OUTCOME

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

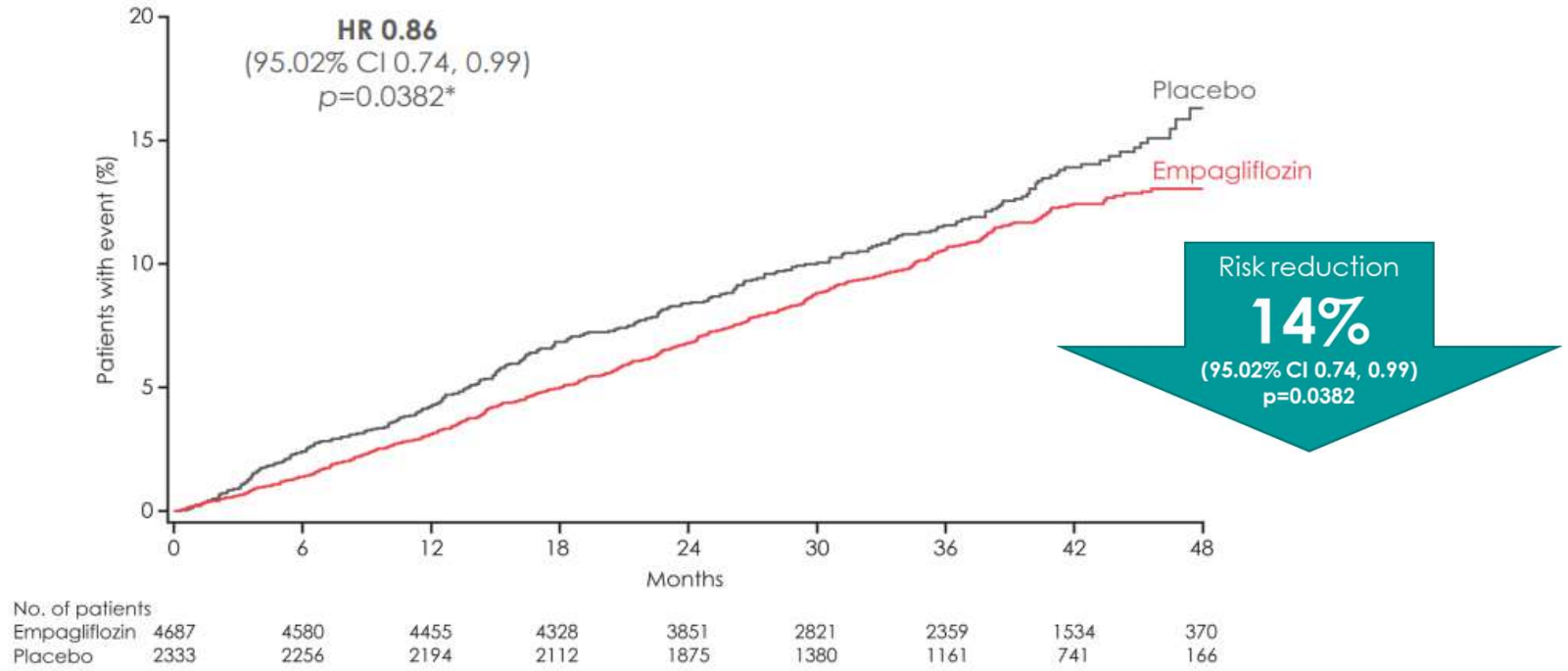
Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D., Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H., Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D., and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine. 2015; 26;373(22):2117-28.

EMPA-REG OUTCOME

Primary Outcome: 3-point MACE (CV death, Nonfatal MI, Nonfatal stroke)[1]



Cumulative incidence function. MACE, Major Adverse Cardiovascular Event; HR, hazard ratio.
* Two-sided tests for superiority were conducted (statistical significance was indicated if p≤0.0498)

Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine. 2015; 26;373(22):2117-28.

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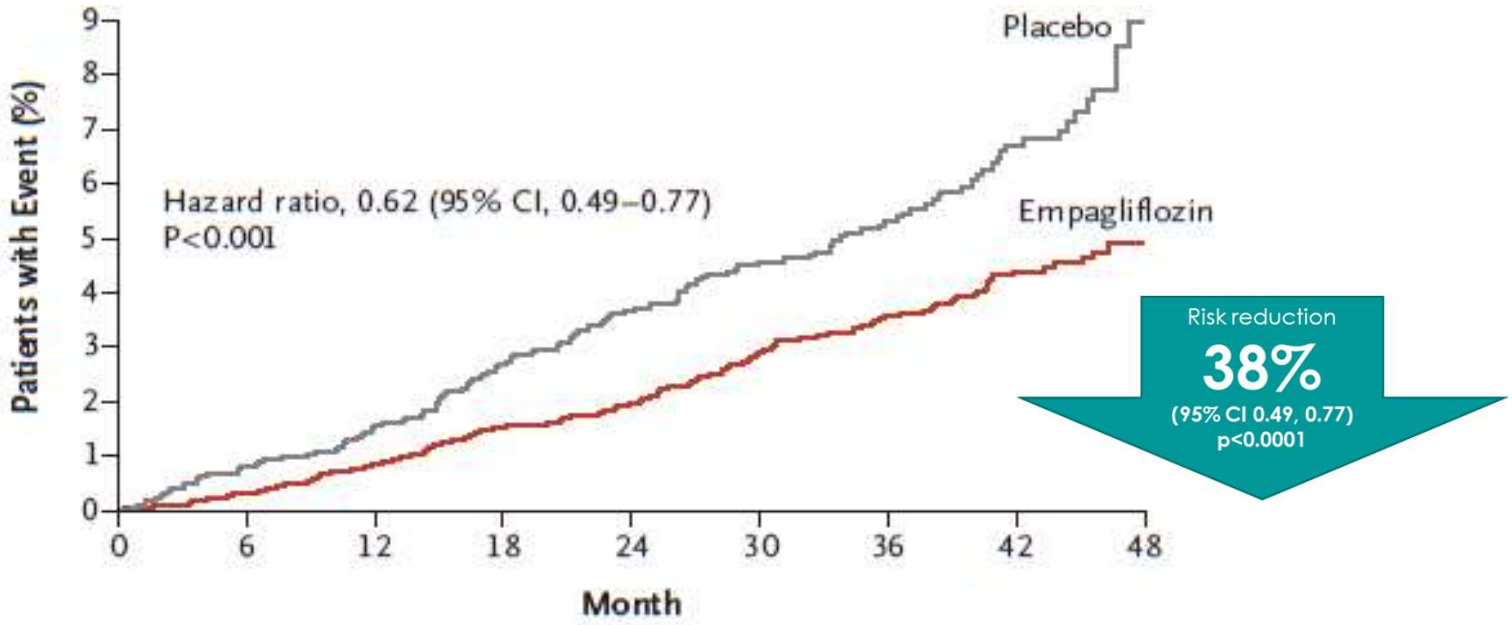
EMPA-REG OUTCOME

Primary Outcome: 3-point MACE (CV death, Nonfatal MI, Nonfatal stroke)[1]



No. at Risk									
Empagliflozin	4687	4651	4608	4556	4128	3079	2617	1722	414
Placebo	2333	2303	2280	2243	2012	1503	1281	825	177

Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine. 2015; 26;373(22):2117-28.

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EMPA-REG OUTCOME

Empagliflozin in addition to standard of care reduced CV risk and improved overall survival in adults with T2D at high CV risk[1]

14%	38%	32%	35%
			
↓ 3P-MACE	↓ CV death	↓ All-cause mortality	↓ Heart failure hospitalizations

Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New England Journal of Medicine. 2015; 26;373(22):2117-28.

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NEW

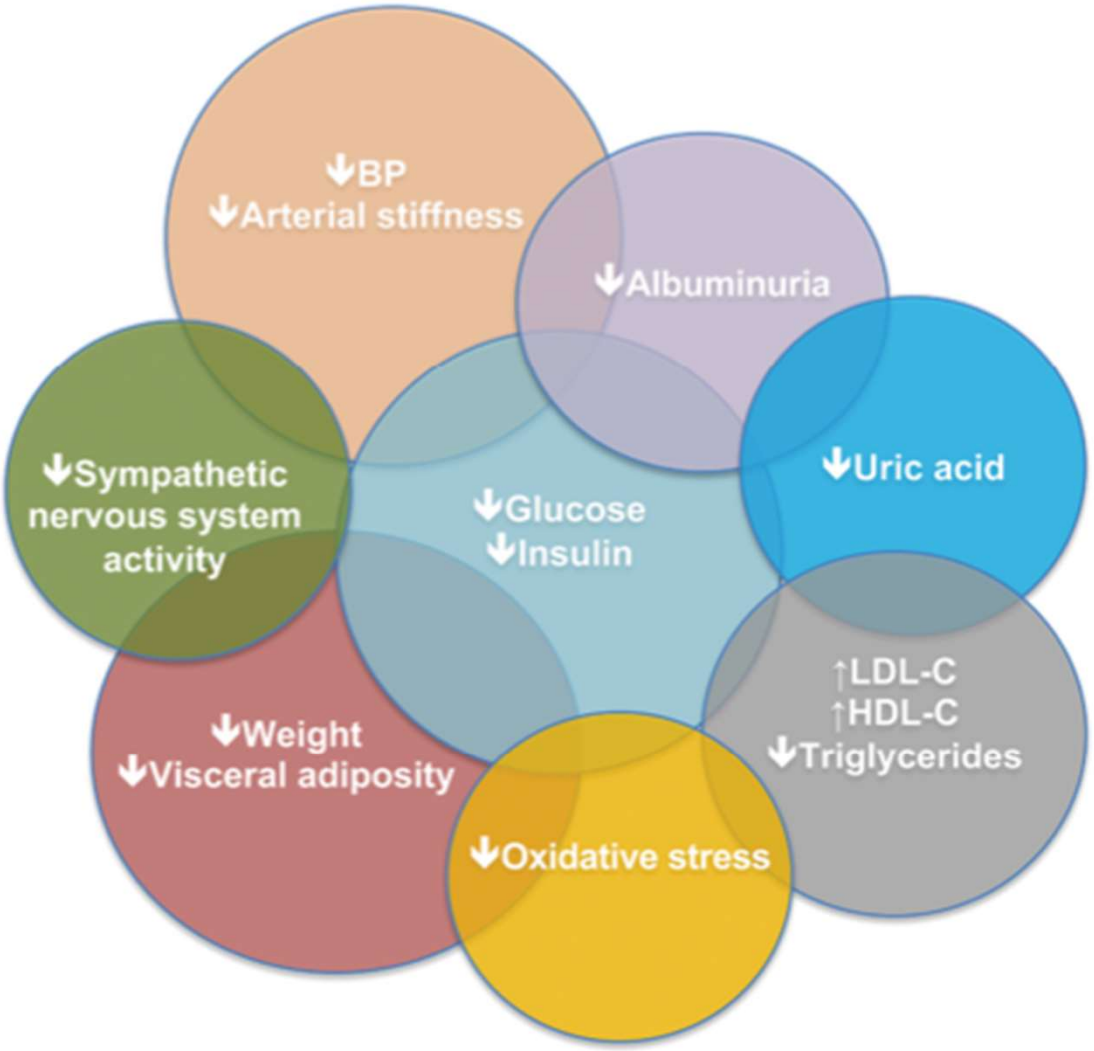
Recommendations for glucose-lowering treatment

Recommendations	Class	Level
SGLT2 inhibitors		
Empagliflozin, canagliflozin, or dapagliflozin are recommended in patients with T2DM and CVD or at very high/high CV risk to reduce CV events.	I	A
Empagliflozin is recommended in patients with T2DM and CVD to reduce the risk of death.	I	B

Recommendations for glucose-lowering treatment

Recommendations	Class	Level
GLP1-RAs		
Liraglutide, semaglutide or dulaglutide are recommended in patients with T2DM and CVD or at very high/high CV risk to reduce CV events.	I	A
Liraglutide is recommended in patients with T2DM and CVD or at very high/high CV risk to reduce the risk of death.	I	B

SGLT2 inhibitors modulate several CV risk factors, but direct mechanism of cardioprotection unknown



Circulation. 2022;145:DOI: 10.1161/CIR.0000000000001040

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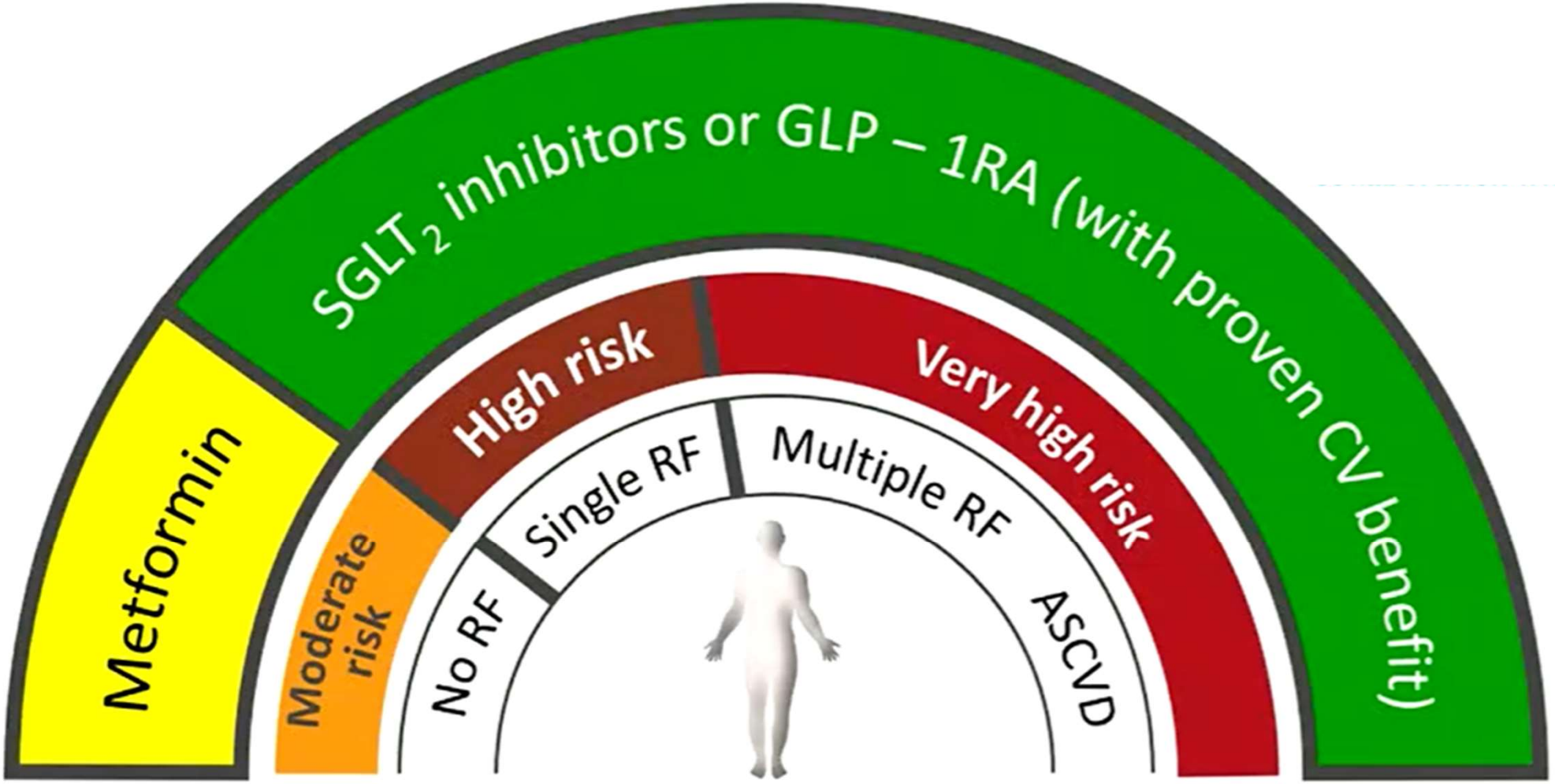
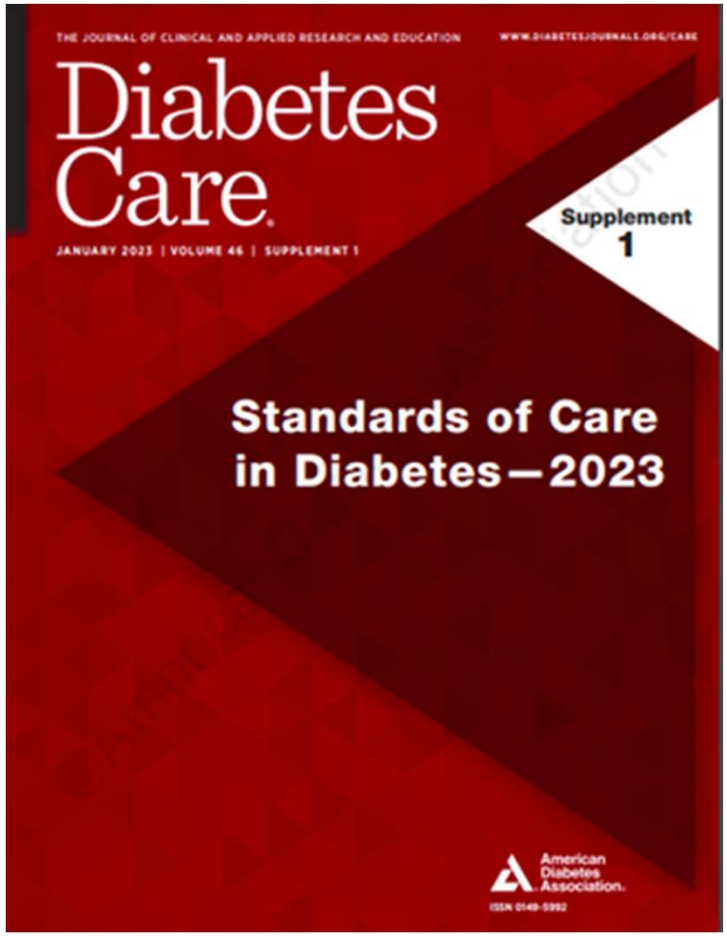
Cardiologists



Pharmacologic Approaches to Glycemic Treatment



USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

Goal: Cardiorenal Risk Reduction in High-Risk Patients with Type 2 Diabetes (in addition to comprehensive CV risk management)*

+ASCVD†

Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, any revascularization procedure). Variably included: conditions such as transient ischemic

+Indicators of high risk

While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria)

+HF

Current or prior symptoms of HF with documented HFrEF or HFpEF

+CKD

eGFR <60 mL/min per 1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). These measurements may vary over time; thus, a repeat measure is required to document CKD.

If additional cardiorenal risk reduction or glycemic lowering needed

+ASCVD/Indicators of High Risk

GLP-1 RA‡ with proven CVD benefit **EITHER/OR** SGLT2i§ with proven CVD benefit

If A1C above target

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit or vice versa
- TZD^

with proven HF benefit in this population

SGLT2i§ with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation

OR

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiorenal risk reduction or glycemic lowering needed

Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

Glycemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Consider avoidance of hypoglycemia a

If A1C above target

have greater likelihood of achieving glycemic goals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide

Insulin

Combination Oral, Combination Injectable (GLP-1 RA/Insulin)

High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD

Intermediate:
DPP-4i

Achievement and Maintenance of Weight Management Goals:

Set individualized weight management goals

General lifestyle advice: medical nutrition therapy/eating patterns/ physical activity

Intensive evidence-based structured weight management program

When choosing glucose-lowering therapies:

Consider regimen with high-to-very-high dual glucose and weight efficacy

Efficacy for weight loss

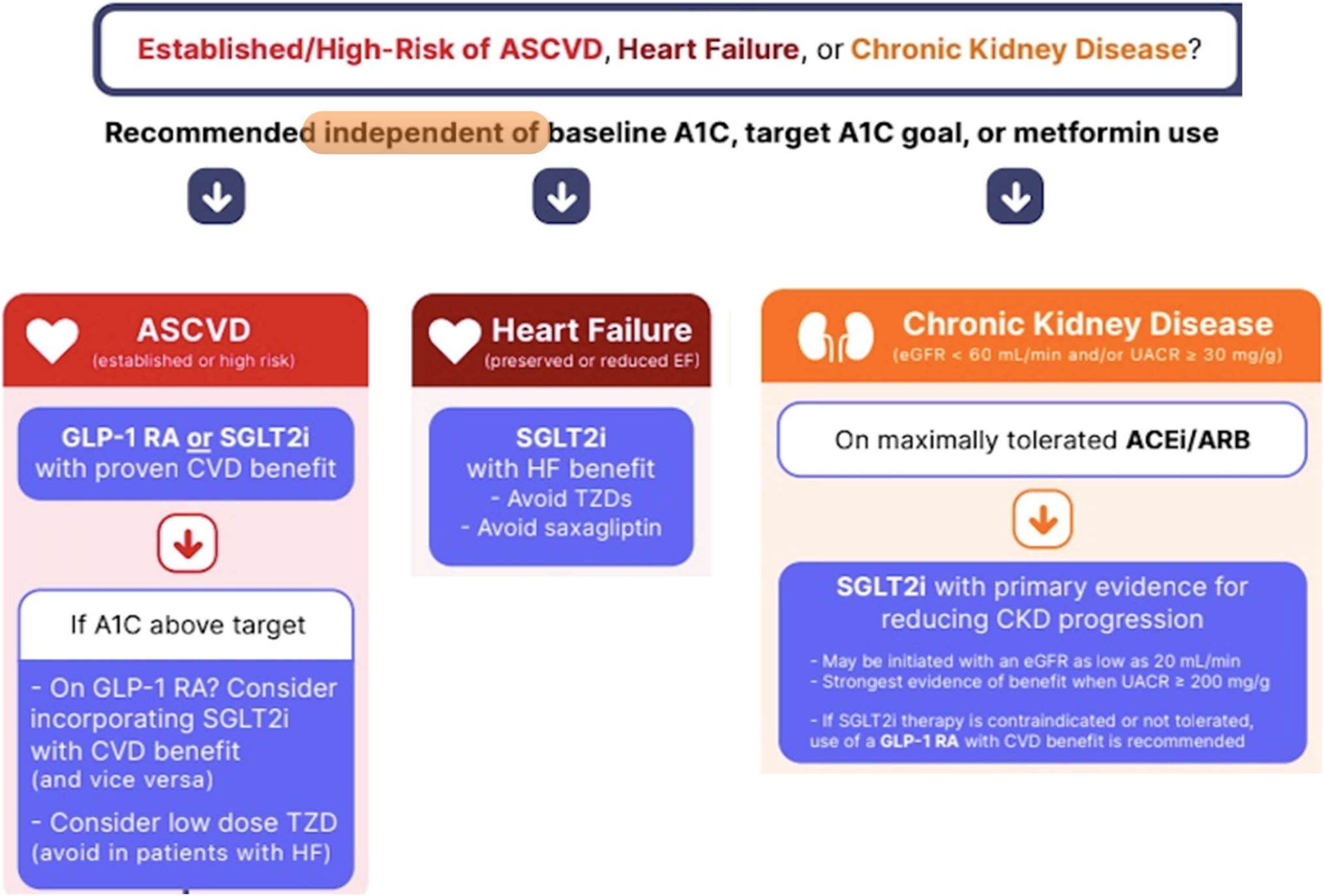
Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1 RA (not listed above), SGLT2i

Neutral:
DPP-4i, Metformin

If A1C above target



08.Jun.2023

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Case Presentation

What is the best Anti-diabetic medication for this patient?

- Metformin
- SGLT2i
- GLP-1RA
- Gliclazide

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SGLT2i

GLP-1RA

CLASS	ASCVD	+CKD (on maximally tolerated dose of ACEi/ARB)
SGLT2is	**FDA approved CVD benefit:** • canagliflozin • empagliflozin **Neutral:** • dapagliflozin • ertugliflozin	**PREFERABLY** SGLT2i[f] with primary evidence of reducing CKD progression Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m^2; once initiated should be continued until initiation of dialysis or transplantation OR GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated
GLP-1 RAs & GLP-1/GIP RAs GLP-1/GIP RA tirzepatide is under investigation for CV	**FDA approved CVD benefit:** • dulaglutide • liraglutide • semaglutide (SUBQ) **Neutral:** • exenatide ER • lixisenatide • semaglutide (oral)	If A1C above target, for patients on

• lixisenatide
• semaglutide (oral)

Case Presentation

60yrs old Male + DM + HTN + ACS

— LDL: 95mg/dl

— Crt: 1.7mg/dl (weight: 81Kg) —— CrCl: 52.9mL/min

— HbA1c: 7.6

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Monotherapy

HbA1c

Combination Therapy

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Diabetes