



**Phòng ngừa sớm biến chứng tim - thận
cho bệnh nhân ĐTĐ típ 2
Vai trò của Dapagliflozin**

**TS. BS Phan Hữu Hên
Khoa Nội tiết – BV Chợ Rẫy**

Tình huống lâm sàng

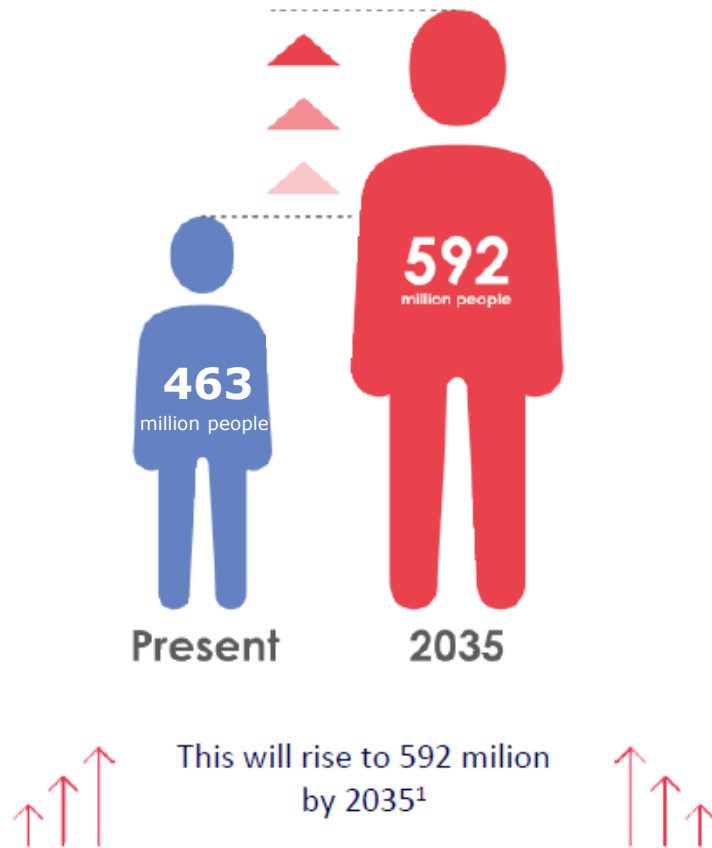
- Bệnh nhân nam 65 tuổi, phát hiện đái tháo đường type 2 hơn 15 năm
 - Nhồi máu cơ tim đã đặt stent mạch vành 5 năm
 - BMI 25
 - ĐH đói 110 mg/dL; HbA1c 7,0%; LDL 80mg/dL; Triglycerid 200 mg/dL
 - Chức năng gan thận bình thường, tỷ số A/C niệu 250 mg/g creatinin

❖ **Câu hỏi: Toa đã và đang dùng 3 tháng nay, có hợp lý ?**

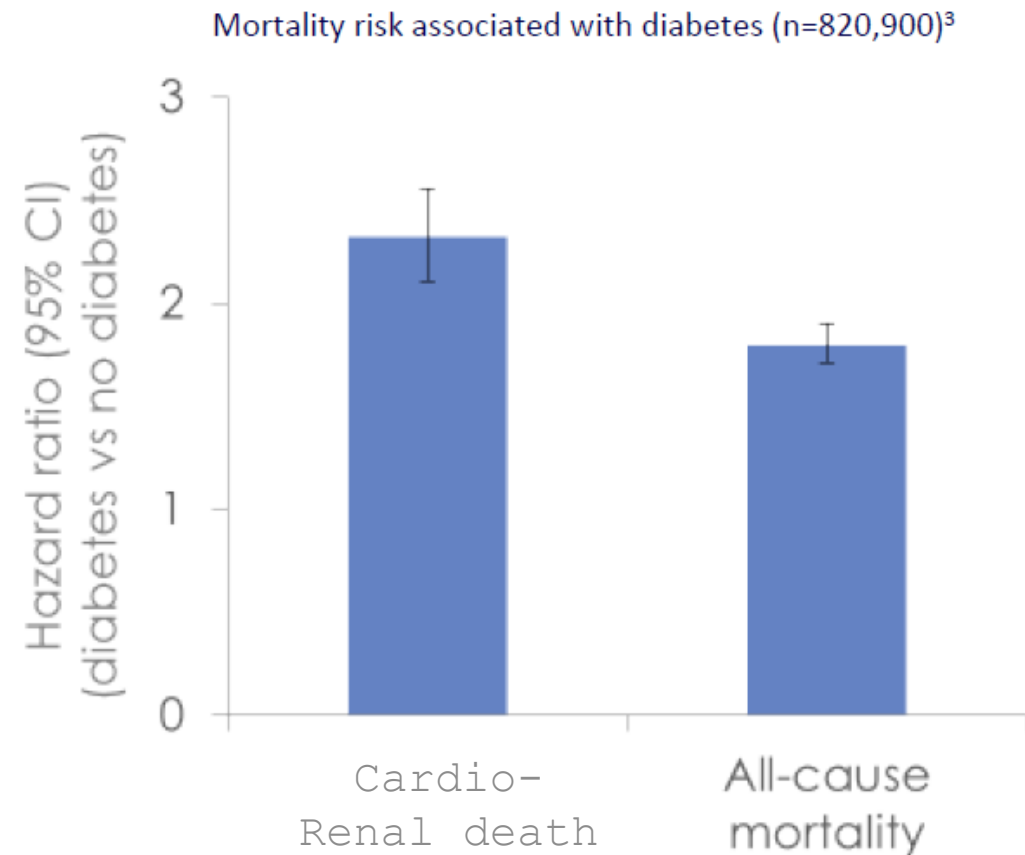
- Gliclazide 60mg 1 viên**
- Trajenta/Metformin 2,5/1000 mg: 1 viên x 2**
- Telmisartan 80mg 1 viên
- Simvastatin 40mg 1 viên
- Clopidogrel 75mg 1 viên

Đái tháo đường: “Đại dịch” trên toàn cầu chưa bao giờ dừng lại

Hiện thế giới có **463** triệu người
Đái tháo đường type 2



68% BN Đái tháo đường type 2 tử vong
do bệnh lý tim mạch-thận



RESEARCH ARTICLE

Prevalence and Clinical Profile of Undiagnosed Diabetes Mellitus: Data from a Tertiary Hospital

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Medicine and
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Abstract: Background: The prevalence of diabetes mellitus in Vietnam is relatively low compared to other Asian countries, but it is accelerating with the economic and cultural transition. This study aimed to estimate the current prevalence and clinical profile of undiagnosed diabetes mellitus in a tertiary hospital in the south of Vietnam.

Methods: A cross-sectional investigation was conducted to recruit 1,250 participants, who were at least 18 years old and randomly sampled from Cho Ray Hospital, Ho Chi Minh City, Vietnam. Fasting blood glucose was measured for each individual. The American Diabetes Association criteria were used to diagnose diabetes. Demographic data and other clinical data including age, sex, residence, educational status, body mass index, blood pressure, and lipid profile were recorded. The prevalence of undiagnosed diabetes mellitus was 7.5% in the population studied. The prevalence of hypertension, overweight, obesity, and dyslipidaemia was 20.5%, 22.5%, 22.2%, and 36.2%, respectively. The prevalence of undiagnosed diabetes mellitus is increasing far more than expected. The prevalence of undiagnosed diabetes mellitus with multiple comorbidities, including over-

Table 2. Prevalence of diabetes and comorbidities

Identified disease	N (%)
Diabetes	94/1250 (7.5)
Hypertension	256/1250 (20.5)
Overweight	281/1250 (22.5)
Obesity	277/1250 (22.2)
Dyslipidaemia	453/1250 (36.2)

**Bác sĩ điều trị bệnh đái tháo đường típ 2
thường quan tâm biến chứng gì?**

Biến chứng mạn tính phổ biến ở bệnh nhân ĐTĐ típ 2

Diabetes cardiovascular risk

Coronary heart disease

Prevalence: 14–21%^{5,16}

Most frequently reported form of CVD and most lethal one.⁵
Risk of death from CHD is higher in women than in men (HR, 95% CI: 1.81 [1.27–2.59] versus 1.48[1.10–1.99]).⁵

Heart failure

Prevalence: 19–26%²⁰

Second most common initial manifestation of CVD in T2DM.¹⁶
Risk of HF is up to 2-fold in men and 5-fold in women.²⁰

Peripheral artery disease

Prevalence: 16–29%^{15,16}

Most common initial manifestation of CVD in T2DM.¹⁶
Prevalence is 1.8-fold higher in women compared to men.¹⁶

Stroke

Prevalence: 8–12%^{2,10}

Second more frequent cause of death in patients with T2DM after CHD¹⁰
Prevalence is similar in men and women.²¹



Retinopathy

Prevalence: 34%²⁹

Most common microvascular complication of diabetes;²⁹
responsible of 2.6% of all cases of blindness worldwide.²⁹
Prevalence rates are higher in T1DM compared to T2DM (77.3 vs. 25.2%).³¹

Neuropathy

Cardiac autonomic neuropathy

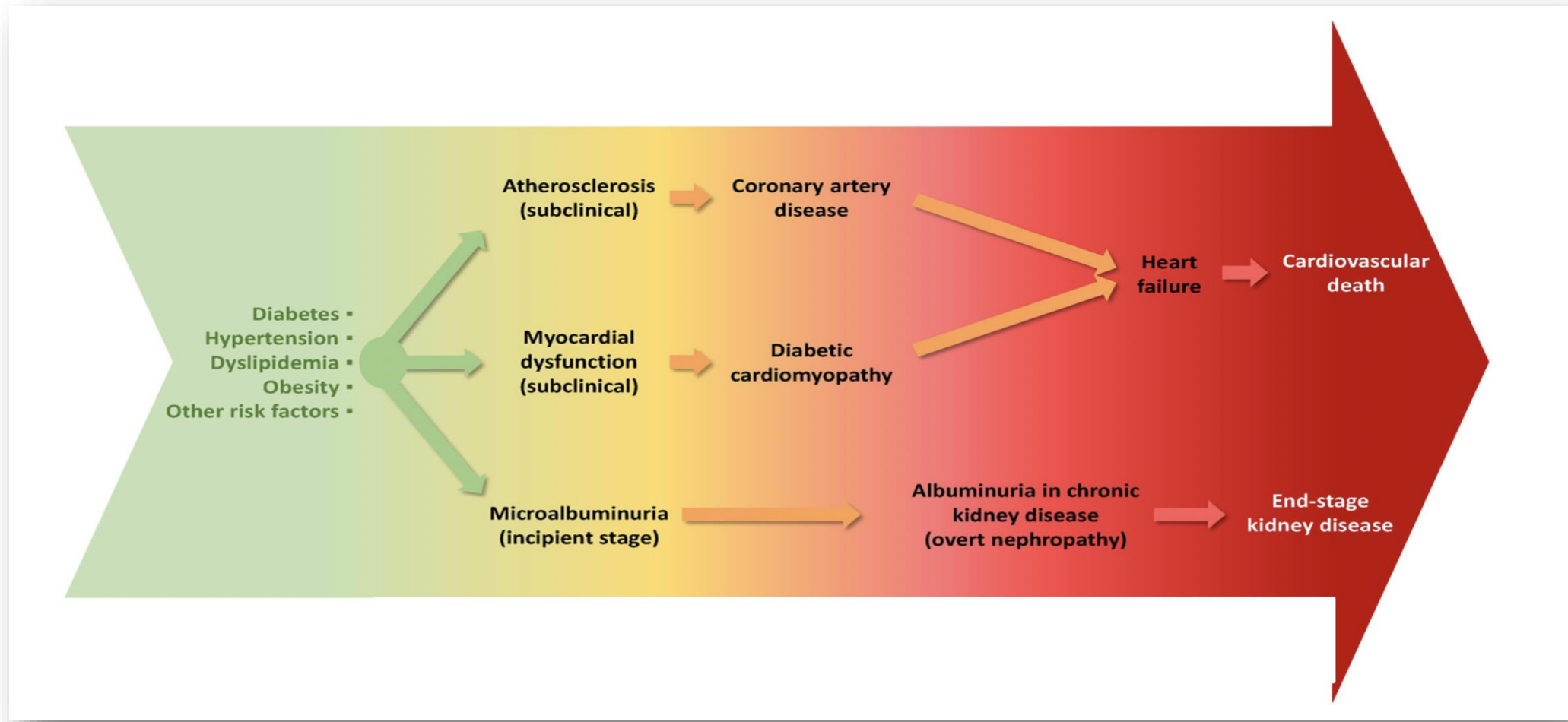
Prevalence: 31–73% in people with T2DM³²
No difference in prevalence between men and women.³²

Nephropathy

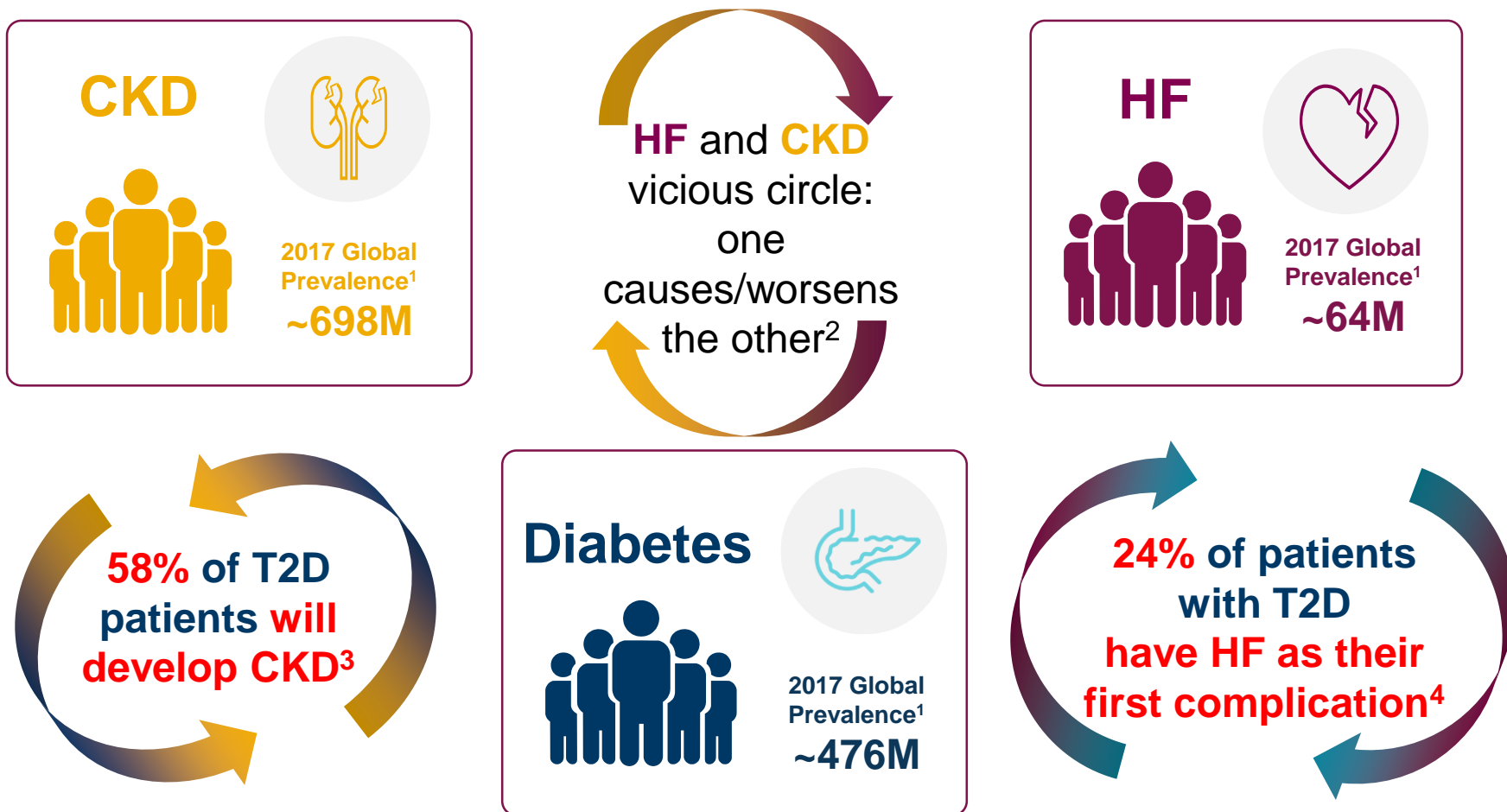
Prevalence: 29–61%²⁸

Leading cause of end stage renal disease in the adult population worldwide.²
Female sex is a risk factor for nephropathy in T2DM.²⁸

Đái tháo đường típ 2 và biến chứng tim - thận



Vòng xoắn bệnh lý Tim – Thận – Chuyển hóa



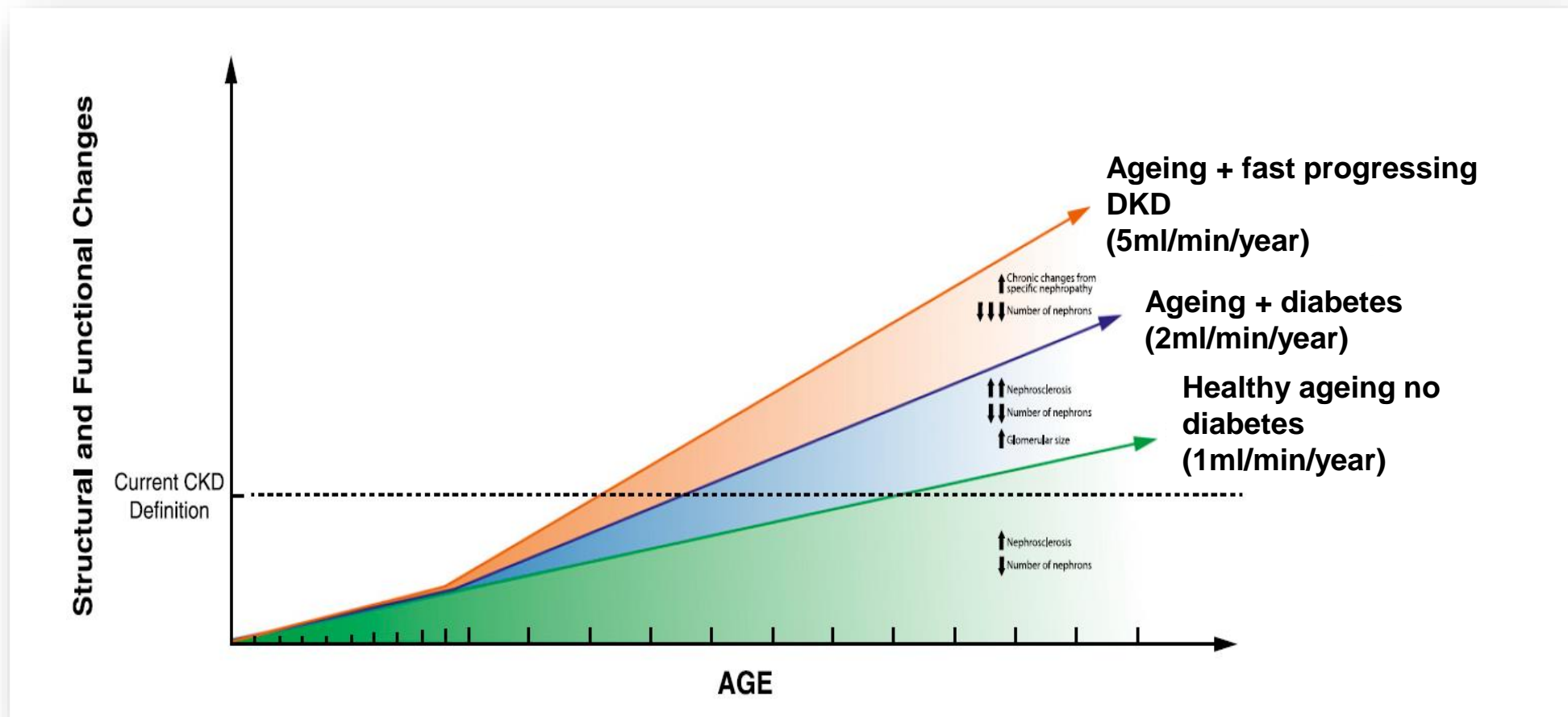
- CKD = bệnh thận mạn; HF = Suy tim; T2D = Đái tháo đường týp 2
- 1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet*. 2018;392:1789-1858; 2. Ronco C et al. *J Am Coll Cardiol*. 2008;52:1527-1539; 3. Parving HH et al. *Kidney Int*. 2006;69:2057-2063; 4. Birkeland KI et al. *Diabetes Obes Metab*. 2020;22:1607-1618.

ESC 2023: Yếu tố nguy cơ và phân loại suy tim trên bệnh nhân ĐTDĐ cấp 2

Table 9 Heart failure phenotypes according to ejection fraction distribution⁴⁴⁵

HF phenotype	HFpEF	HFmrEF	HFrEF
Criterion 1	Symptoms and/or signs ^a	Symptoms and/or signs ^a	Symptoms and/or signs ^a
Criterion 2	LVEF $\geq 50\%$	LVEF 41–49%	LVEF $\leq 40\%$
Criterion 3	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction or raised filling pressures, including raised natriuretic peptides	None	None

Thay đổi chức năng thận trên bệnh nhân đái tháo đường



Khuyến cáo điều trị ĐTĐ thay đổi theo thời gian

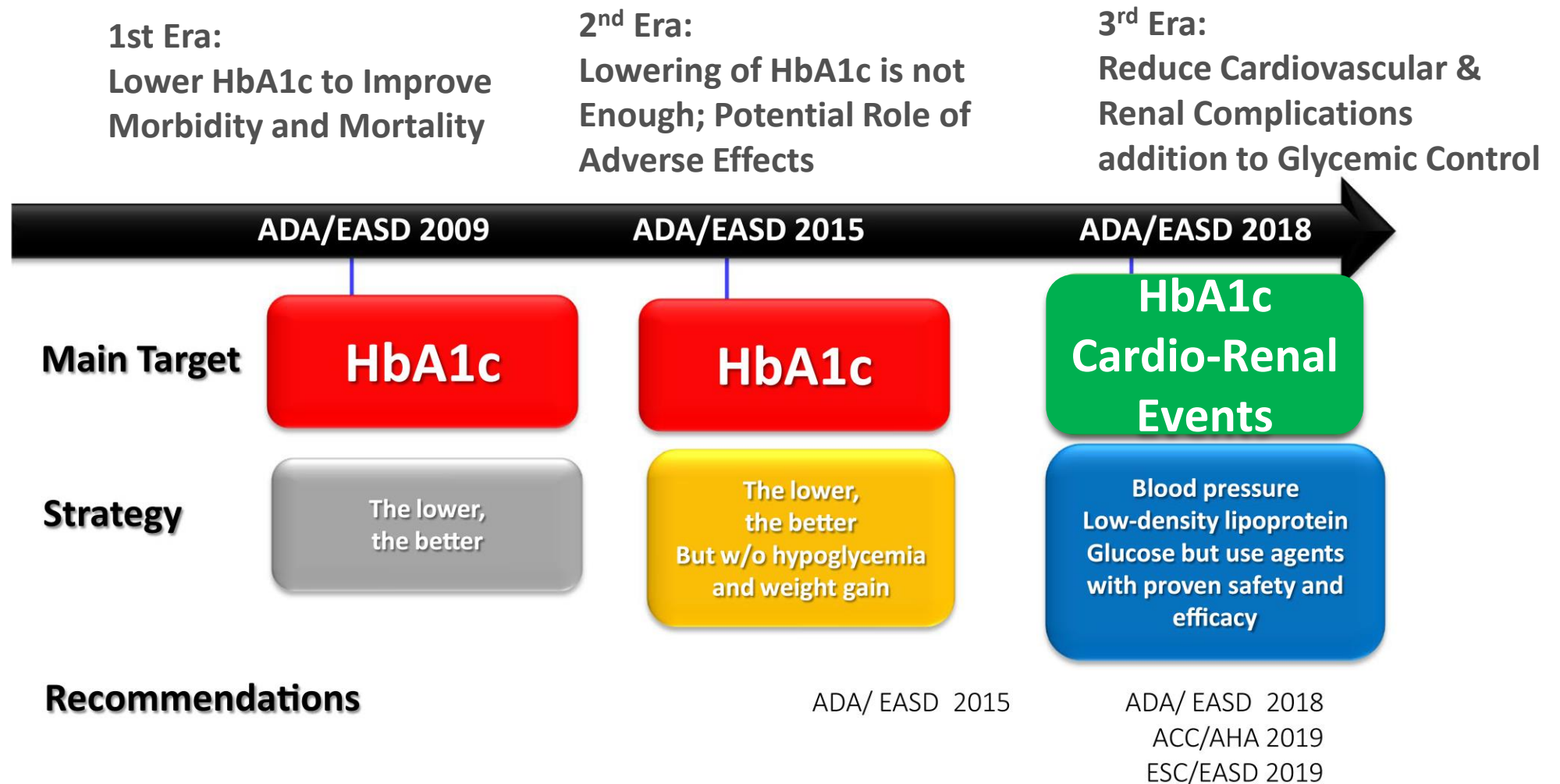


Fig. 1 Evolution of the treatment recommendations in type 2 diabetes management. *ADA* American Diabetes Association, *EASD* European Association for the Study of Diabetes, *AHA* American Heart Association, *ESC* European Society for Cardiology

2023 ADA: Pharmacologic treatment of hyperglycemia in adults with T2D

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). Variability included: conditions such as transient ischaemic attack, unstable angina, amputation, symptomatic or asymptomatic aortic stenosis

+Indicators of high risk

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

+ ASCVD/Indicators of high risk

GLP-1 RA#
with proven
CVD benefit

Either/
OR

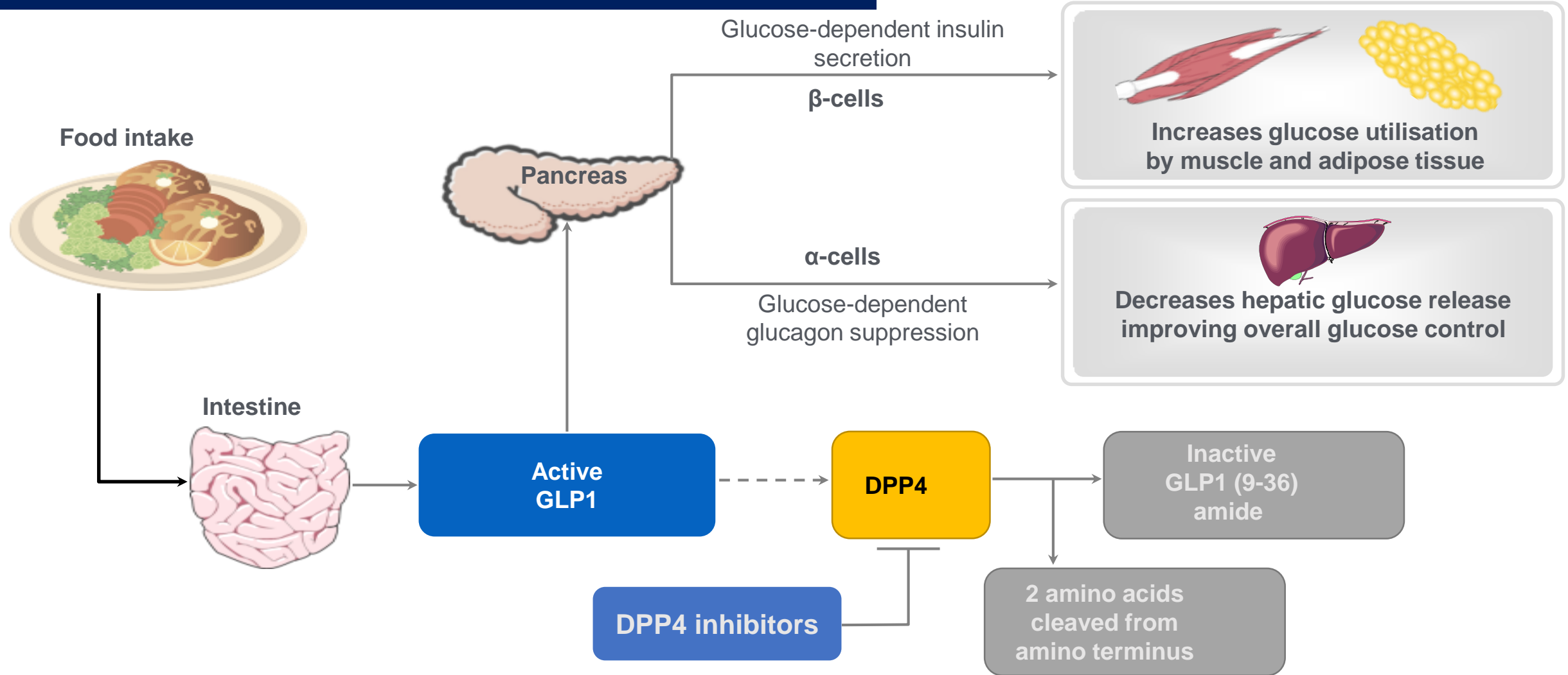
SGLT-2i§
with proven
CVD benefit

If HbA_{1c} above target

- For patients on a GLP-1 RA, consider adding SGLT-2i with proven CVD benefit and vice versa
- TZD^

If additional cardiorenal risk reduction or glycemic lowering needed

GLP1 - RA: Mechanism of action



Adapted from Drucker. Expert Opin Invest Drugs 2003;12:87–100 and Ahrén Curr Diab Rep. 2003;3:365–372.

ADA 2023: Lợi ích tim mạch của GLP1 RA có hiệu quả nhóm ?

GLP-1 RAs

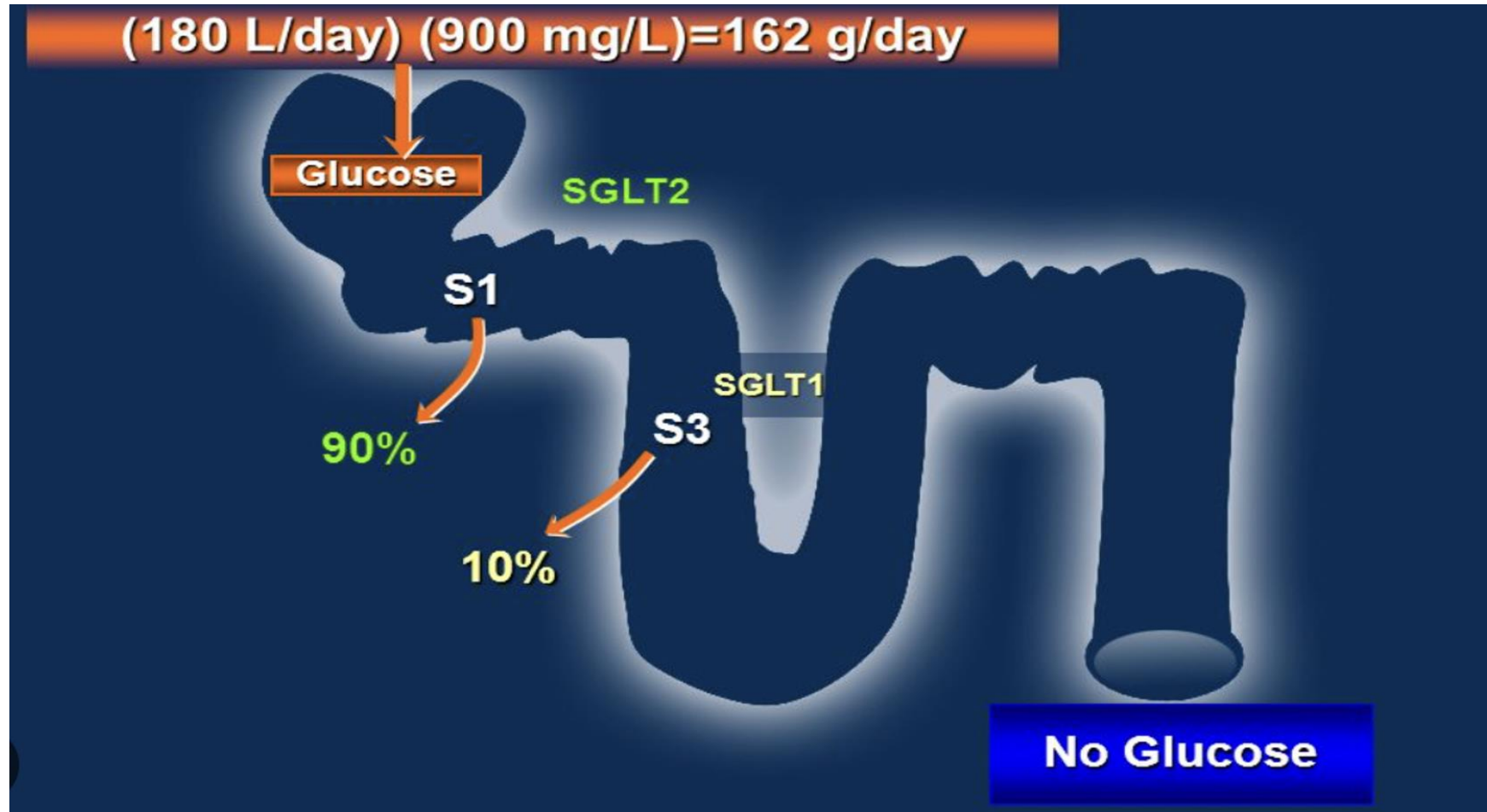
- Exenatide (extended release)
- Exenatide
- Dulaglutide
- Semaglutide

- Liraglutide
- Lixisenatide

Cardiovascular Outcomes Trials

There are now multiple large randomized controlled trials reporting statistically significant reductions in cardiovascular events in patients with type 2 diabetes treated with an SGLT2 inhibitor (empagliflozin, canagliflozin, dapagliflozin) or GLP-1 RA (liraglutide, semaglutide, dulaglutide); see Section 10 “Cardiovas-

Cơ chế SGLT2i



Dapagliflozin trong bảo vệ cơ quan đích cho BN Tim mạch – thận- chuyển hóa

DECLARE TIMI 58¹



7% CKD

10% HF

Type 2 Diabetes

Chronic
Kidney
Disease

Heart
Failure

68% T2D

DAPA-CKD²

11% HF

45% T2D

DAPA-HF^{3,4}

41% CKD

Renal composite outcome

HR (95%CI)

↓ 47% DECLARE

↓ 29% DAPA-HF

↓ 44% DAPA-CKD

CV death & hHF

HR (95%CI)

↓ 17% DECLARE

↓ 25% DAPA-HF

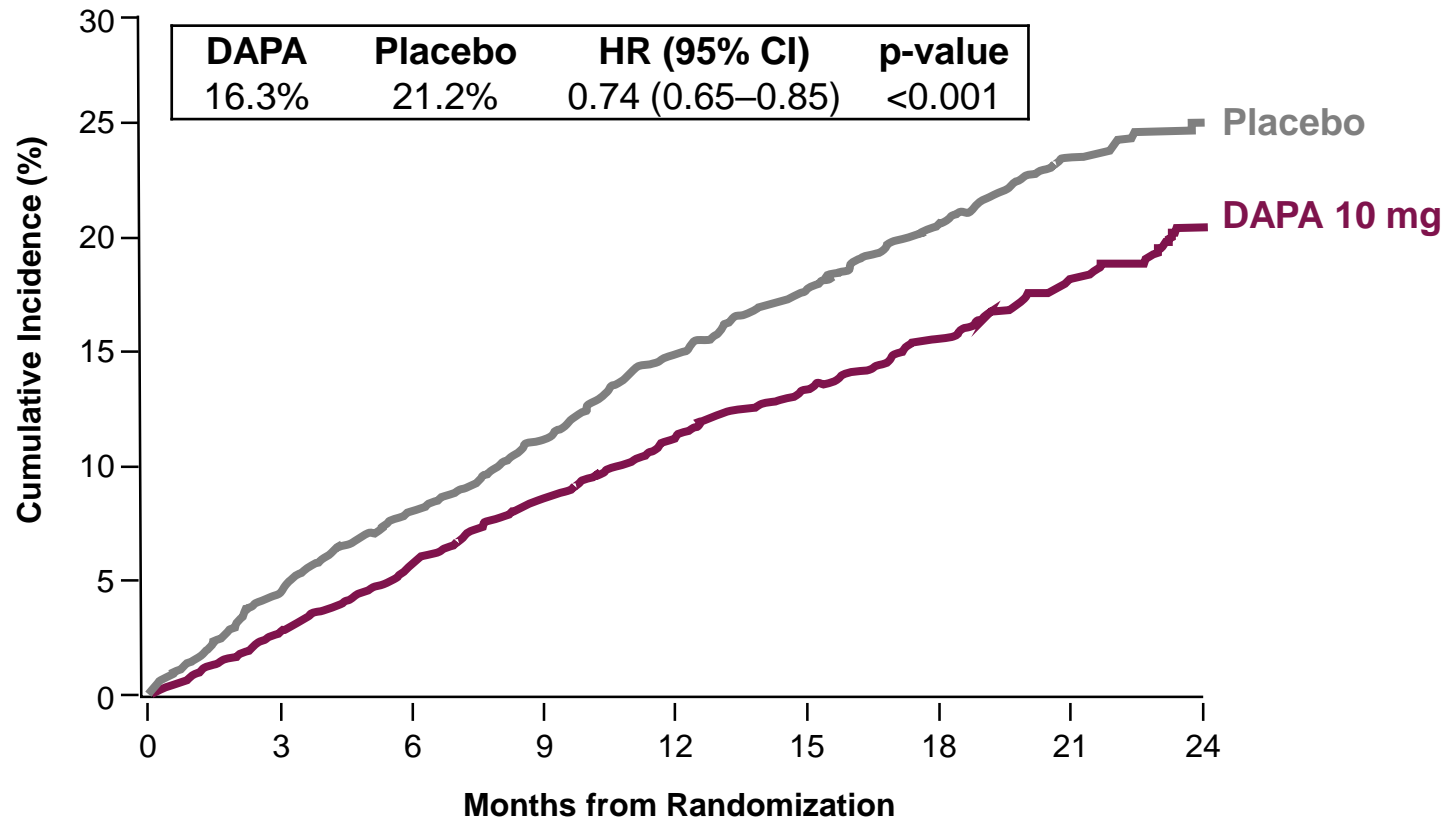
↓ 29% DAPA-CKD

Vui lòng tham khảo thông tin kê toa Dapagliflozin tại Việt Nam

1. Wiviott SD et al. *N Engl J Med*, 2019;380:347-357; 2. Heerspink HJL. Et al. *N Engl J Med* 2020; 383: 1436-1446;

3. McMurray JJV et al. *N Engl J Med* 2019;381;1995-2008; 4. Petrie et al. *JAMA* 2020;323; 1353-1386

Dapagliflozin giảm nguy cơ tử vong do tim mạch hoặc biến cố suy tim sớm từ ngày thứ 28



**26%
RRR**

4.9% ARR

NNT=21

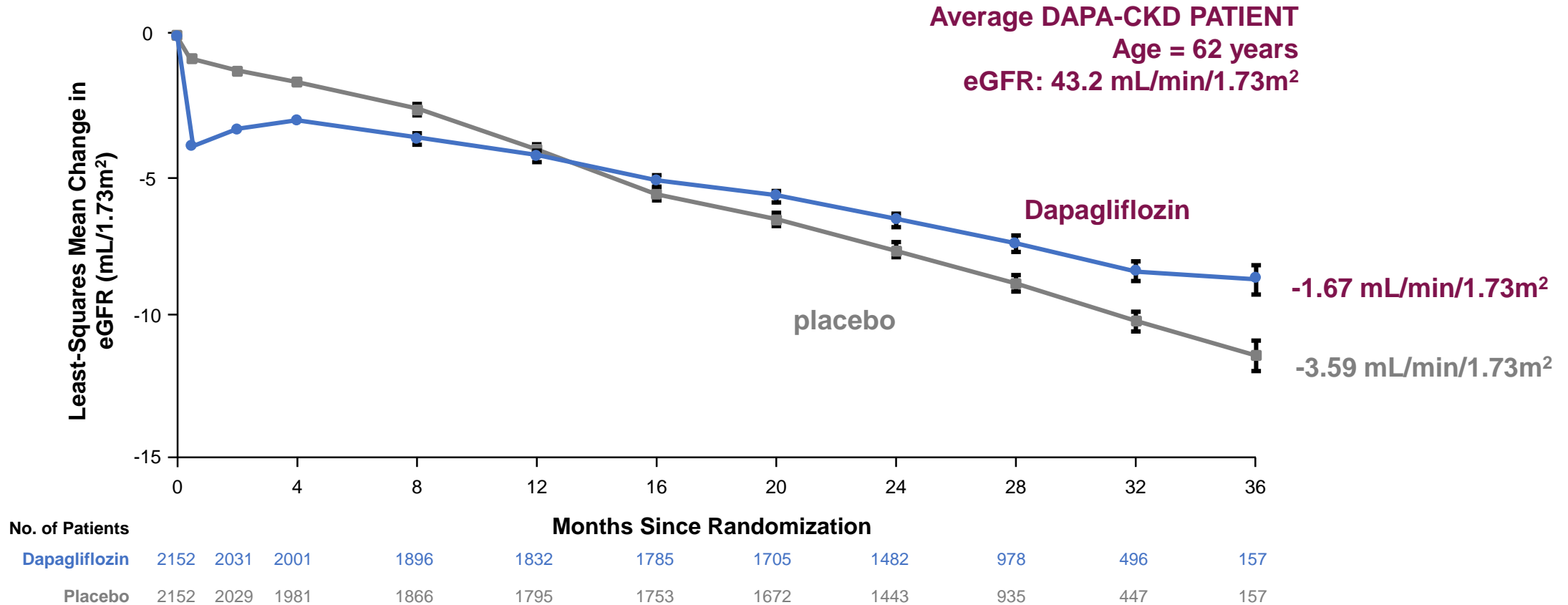
Number at Risk

DAPA 10 mg	2373	2305	2221	2147	2002	1560	1146	612	210
Placebo	2371	2258	2163	2075	1917	1478	1096	593	210

^aWorsening HF includes hHF or urgent HF visit.

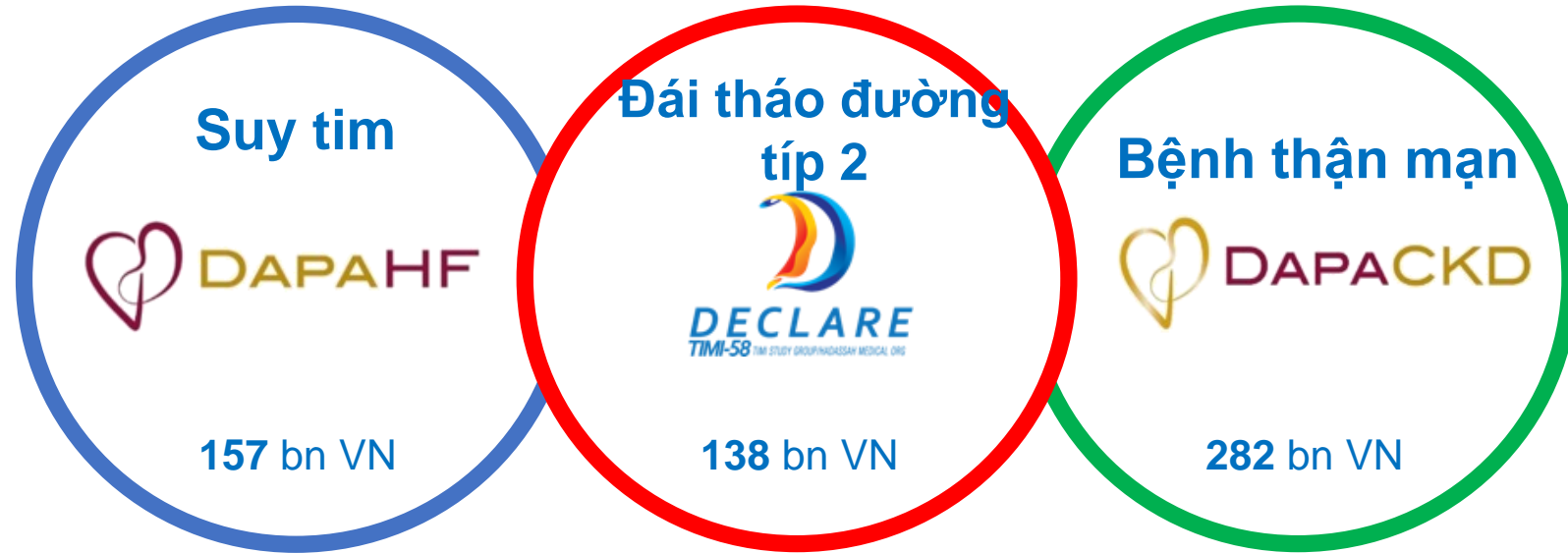
1. McMurray JJV et al. *N Engl J Med.* 2019;381:1995-2008; 2. Sabatine MS et al. Presented at: AHA Scientific Sessions; November 16-18, 2019; Philadelphia, PA.

Dapagliflozin cải thiện làm chậm mức giảm eGFR



- BL = baseline; DAPA= dapagliflozin; eGFR = estimated glomerular filtration rate; PBO = placebo.
- Heerspink HJL et al. Online ahead of print. *N Engl J Med.* 2020.

Dapagliflozin được BHYT Việt Nam phê duyệt cho 3 chỉ định



**Bảo hiểm y tế thanh toán
cả 3 chỉ định**



**Liều đơn giản
10mg, ngày 1 lần**



eGFR \geq 25 ml/phút
Tiếp tục đến khi chạy thận,
thay thế thận

Tình huống lâm sàng

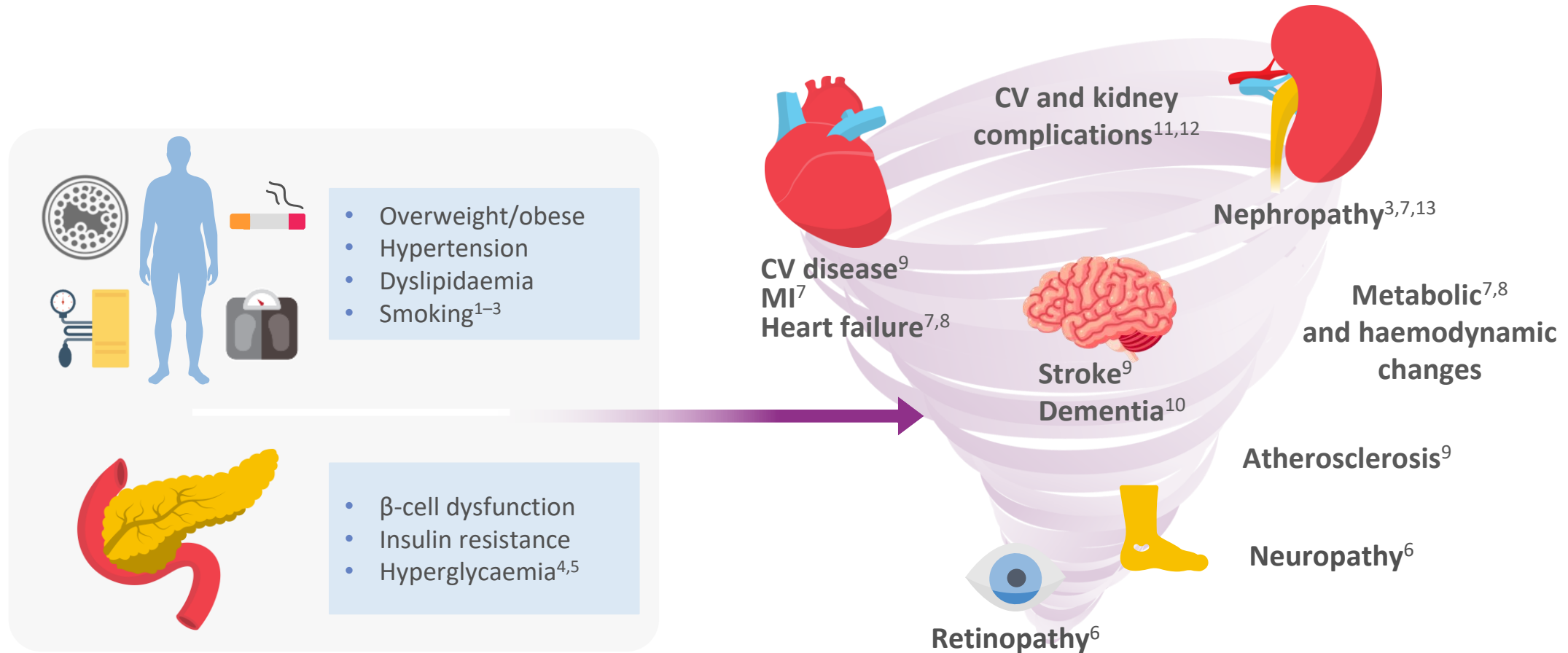
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**Bác sĩ lâm sàng bị “ấn tượng” bởi biến cố tim mạch, suy tim, bệnh thận mạn
– trì hoãn sử dụng thuốc SGLT2i/GLP1 RA?**

Bệnh nhân ĐTĐ giai đoạn sớm tăng nguy cơ mắc các biến chứng do các rối loạn chuyển hóa¹⁻¹⁰



Leading hypotheses shown; additional factors may contribute to progression of complications

1. Leon BM & Maddox TM. *World J Diabetes* 2015;6:1246; 2. Sposito AC et al. *Cardiovasc Diabetol* 2018;17:157; 3. Cade WT. *Phys Ther* 2008;88:1322; 4. Marwick TH et al. *J Am Coll Cardiol* 2018;71:339; 5. DeFronzo RA et al. *Diabetes* 2009;58:773; 6. Fowler MJ. *Clinical Diabetes* 2011;29:116; 7. Song MK et al. *J Diabetes Res* 2014;2014:e313718; 8. Bugger H & Abel ED. *Diabetologia* 2014;57:660; 9. Galicia-Garcia U et al. *Int J Mol Sci* 2020;21:6275; 10. Hayden MR et al. *Cardiorenal Med* 2013;3:265; 11. Ronco C et al. *J Am Coll Cardiol* 2008;52:1527; 12. McCullough PA et al. *Contrib Nephrol* 2013;182:82; 13. Chen Y et al. *Kidney Dis* 2020;6:225

ESC 2023: Kiểm soát nguy cơ tim mạch ở BN ĐTĐ típ 2

Multifactorial approach in patients with diabetes—Section 5.7

Identifying and treating risk factors and comorbidities early is recommended.

I

A

Multidisciplinary behavioural approaches that combine the knowledge and skills of different caregivers are recommended.

I

C

Principles of motivational interviewing should be considered to induce behavioural changes.

IIa

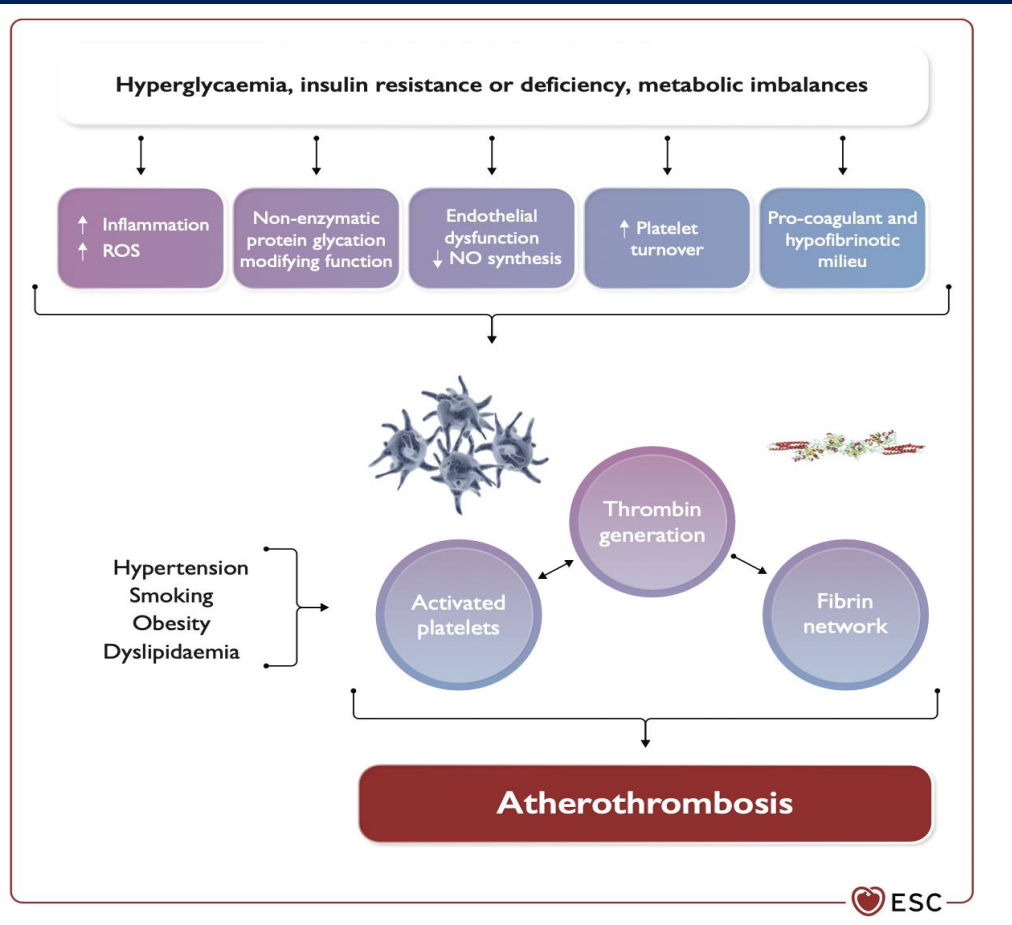
C

Telehealth may be considered to improve risk profile.

IIb

B

ESC 2023: Kiểm soát nguy cơ tim mạch ở BN ĐTĐ típ 2



Weight reduction in patients with diabetes—Section 5.1.1

It is recommended that individuals living with overweight or obesity aim to reduce weight and increase physical exercise to improve metabolic control and overall CVD risk profile.

Glucose-lowering medications with effects on weight loss (e.g. GLP-1 RAs) should be considered in patients with overweight or obesity to reduce weight.

Bariatric surgery should be considered for high and very high risk patients with BMI ≥ 35 kg/m² (\geq Class II) when repetitive and structured efforts of lifestyle changes combined with weight-reducing medications do not result in maintained weight loss.

I

A

IIa

B

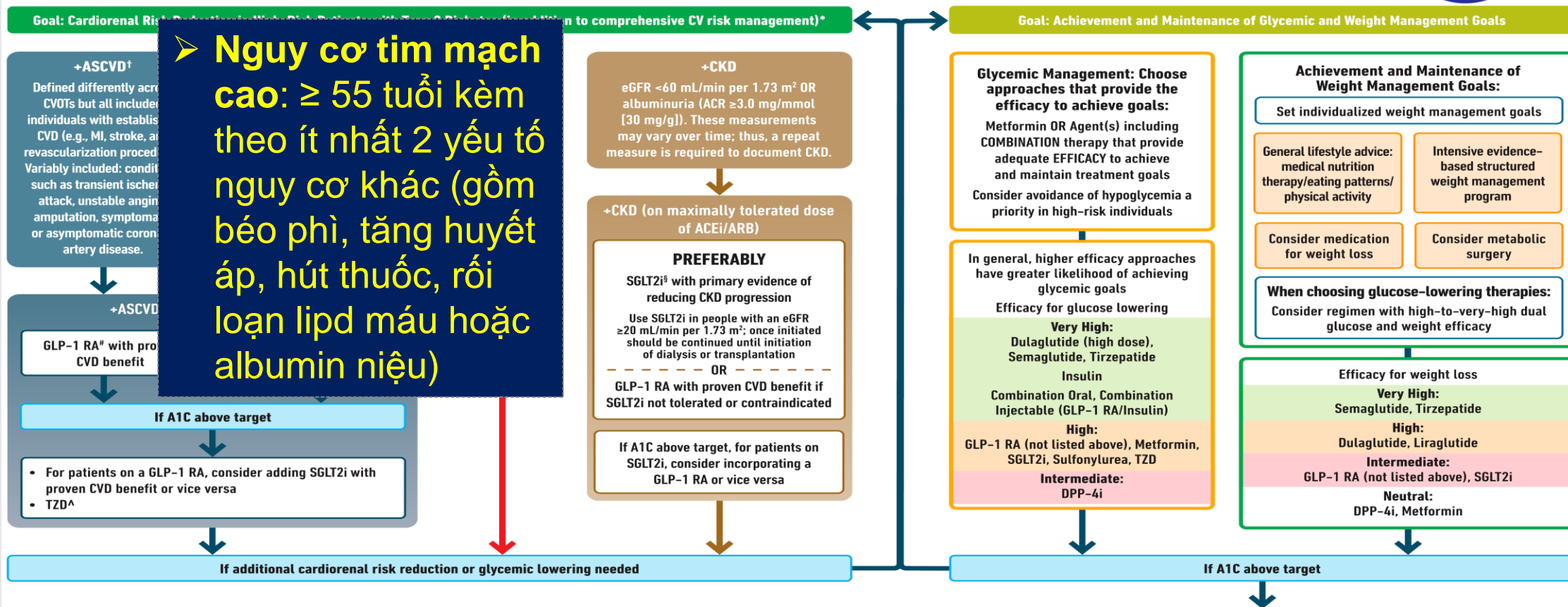
IIa

B

ADA 2023: Lựa chọn thuốc theo mục tiêu điều trị

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

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



➤ **Nguy cơ tim mạch cao: ≥ 55 tuổi kèm theo ít nhất 2 yếu tố nguy cơ khác (gồm béo phì, tăng huyết áp, hút thuốc, rối loạn lipid máu hoặc albumin niệu)**

* In people with HF, CKD, established CVD or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin;† A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HFrEF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

Identify barriers to goals:

- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g., diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of goals



Year: 2022

Protective effects of SGLT-2 in
two fac

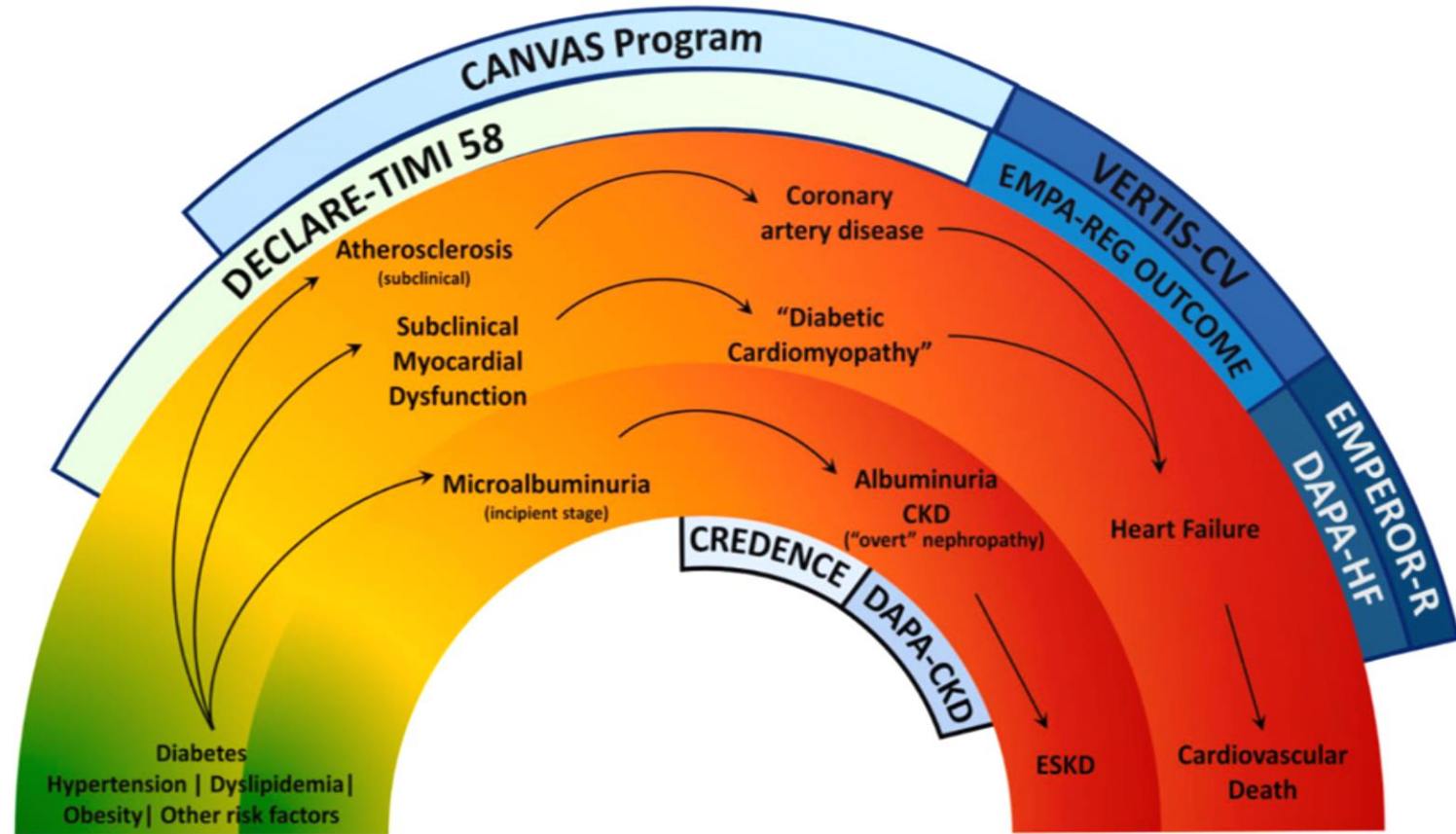


Figure 1 Clinical trials of SGLT2 inhibitors across the cardiorenal continuum.

Similarities and Differences Between SGLT2 Inhibitor CVOTs

	DECLARE-TIMI 58 ^{1,2,3}	CANVAS Program ⁴	EMPA-REG OUTCOME ⁵
Number of patients	17,160	10,142 (CANVAS: 4330; CANVAS-R: 5812)	7020
Key inclusion criteria	<ul style="list-style-type: none"> HbA1c ≥6.5% and <12%^a CrCl^b ≥60 mL/min 	<ul style="list-style-type: none"> HbA1c ≥7% and ≤10.5% eGFR^c >30 mL/min/1.73 m² 	<ul style="list-style-type: none"> HbA1c ≥7% and ≤10% eGFR^c ≥30 mL/min/1.73 m²
Study population	MRF: 59.4%; ECVD: 40.6%	MRF: 34.4%; ECVD: 65.6%	ECVD: >99%
Interventions (randomization ratio)	DAPA 10 mg or PBO (1:1)	CANVAS: CANA 100 mg, CANA 300 mg, or PBO (1:1:1) CANVAS-R: CANA 100 mg with optional increase to 300 mg or PBO (1:1)	EMPA 10 mg, EMPA 25 mg, or PBO (1:1:1)
Number of events	1559 (Actual)	CANVAS: 658; CANVAS-R: 353 (Actual)	772 (Actual)
Median follow-up	4.2 years	2.4 years (CANVAS: 5.7 years; CANVAS-R: 2.1 years)	3.1 years
Primary endpoint	Primary safety endpoint: MACE (composite of CV death, nonfatal MI, or nonfatal ischemic stroke). Primary efficacy endpoints: <ul style="list-style-type: none"> MACE Composite of CV death or hHF 	Pooled MACE (composite of CV death, nonfatal MI, or nonfatal stroke) from CANVAS & CANVAS-R	Pooled MACE (composite of CV death, nonfatal MI, or nonfatal stroke) from 2 doses
Important secondary endpoints	Renal composite endpoint (sustained ≥40% decrease in eGFR to eGFR <60 mL/min/1.73 m ² and/or ESRD and/or renal or CV death), all-cause mortality	All-cause mortality, CV death, albuminuria progression (>30% increase in albuminuria and change in category), composite of CV mortality or hHF	Composite of MACE or hospitalization for UA, silent MI, hHF, microvascular composite, new onset microalbuminuria, new onset macroalbuminuria

^aProportion of patients with HbA1c of 6.5% to <7% capped at ~5%; ^bBased on Cockcroft-Gault equation; ^cBased on Modification of Diet in Renal Disease criteria.

CANA, canagliflozin; CrCl, creatinine clearance; CV, cardiovascular; CVOTs, cardiovascular outcome trials; DAPA, dapagliflozin; ECVD, established atherosclerotic cardiovascular disease; eGFR, estimated glomerular filtration rate; EMPA, empagliflozin; ESRD, end-stage renal disease; HbA1c, glycated hemoglobin; hHF, hospitalization for heart failure; MACE, major adverse cardiovascular event; MI, myocardial infarction; MRF, multiple risk factors for cardiovascular disease; PBO, placebo; SGLT2, sodium-glucose cotransporter 2; UA, unstable angina.

1. Raz I et al. *Diabetes Obes Metab.* 2018;20:1102-1110; 2. Wiviott SD et al. *Am Heart J.* 2018;200:83-89; 3. Wiviott SD et al. Online ahead of print. *New Engl J Med.* 2018; 4. Neal B et al. Article, online protocol, and supplementary appendix. *N Engl J Med.* 2017;377:644-657; 5. Zinman B et al. Article, online protocol, and supplementary appendix. *N Engl J Med.* 2015;373:2117-2128.

KẾT LUẬN

- ❖ Biến chứng TM và bệnh thận mạn là những biến chứng rất nguy hiểm và thường gặp trên ĐTĐ típ 2
- ❖ Tiếp cận điều trị bệnh nhân ĐTĐ típ 2 hiện đã thay đổi: Bên cạnh kiểm soát đường huyết còn đồng thời quản lý sớm các yếu tố nguy cơ và dự phòng biến cố tim mạch-thận.
- ❖ SGLT2i/GLP1 RA được khuyến cáo là phương pháp điều trị ưu tiên ở BN ĐTĐ típ 2 có nguy cơ cao hoặc mắc BTMDXV, suy tim hoặc bệnh thận mạn

Cám ơn sự theo dõi của Quý đồng nghiệp

