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Cardiometabolic Health Congress

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Foundations of Cardiometabolic Health Certification Course

Certified Cardiometabolic Health Professional (CCHP)

Heart of the Matter: Team-based Care to Improve Quality and Outcomes in Cardiometabolic Disease

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Disclosures

- Research Grants:
  - AstraZeneca, Boehringer Ingelheim

- Clinical Trial Leadership/Consultant:
  - Alnylam, Applied Therapeutics, AstraZeneca, Amgen, Bayer, Boehringer-Ingelheim, Esperion, Janssen, Eli Lilly, Merck (Diabetes and Cardiovascular), Novo Nordisk, Pharmacosmos, Vifor Pharma

  - **Off-label use of medications may be discussed**

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Complex Cardiometabolic Patient Case & Considerations

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Patient Case

50-year-old female presenting for routine follow-up

Type 2 diabetes for 10 years

Sleep apnea

Known ASCVD

- NSTEMI in 2014
- Diagnosed with multi-vessel CAD
- Underwent CABG post-MI
- No current symptoms of angina, but has dyspnea on exertion

ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; CABG, coronary artery bypass graft; MI, myocardial infarction; NSTEMI, non-ST segment elevation MI.

Medications

- ASA 81 mg daily
- Carvedilol 12.5 mg twice daily
- Losartan 100 mg daily
- Atorvastatin 40 mg daily
- Metformin 1000 mg twice daily
- Insulin glargine 15 units at night
  short-acting insulin 12-15 units with each meal

ASA, acetylsalicyclic acid.

Physical Exam

BP: 145/85 mmHg HR: 72 bpm	Wt: 91 kg (200 lbs)	BMI: 37 kg/m^2
Clear lung fields	Normal heart sounds	1+ ankle edema

BP, blood pressure; HR, heart rate; Wt, weight; BMI, body mass index.

Laboratory Data and Imaging

- HbA_{1c} 11.4%
- Total cholesterol 195 mg/dL
  - 330 mg/dL off statin
- LDL 135 mg/dL
  - 235 mg/dL off statins
- Triglycerides 200 mg/dL
- Serum creatinine 1.3 mg/dL, eGFR 50 mL/min/1.73 m^2
- AST 60 U/L, ALT 70 U/L
- NTproBNP 300 pg/mL
- Echocardiogram: LVEF of 60% with apical hypokinesis, enlarged left atrium and moderate diastolic dysfunction

ALT, alanine aminotransferase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated haemoglobin; LDL, low-density lipoprotein;
LVEF, left ventricular ejection fraction; U/L, units per liter.

What are the care priorities?

A: Prevent recurrent ASCVD events

B: Prevent HF hospitalization

C: Prevent progression of kidney disease

D: Lower LDL-c, Blood Pressure and HbA1c

E: All of the above

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Cardiometabolic Disease: Goals of Care & Evolving Evidence

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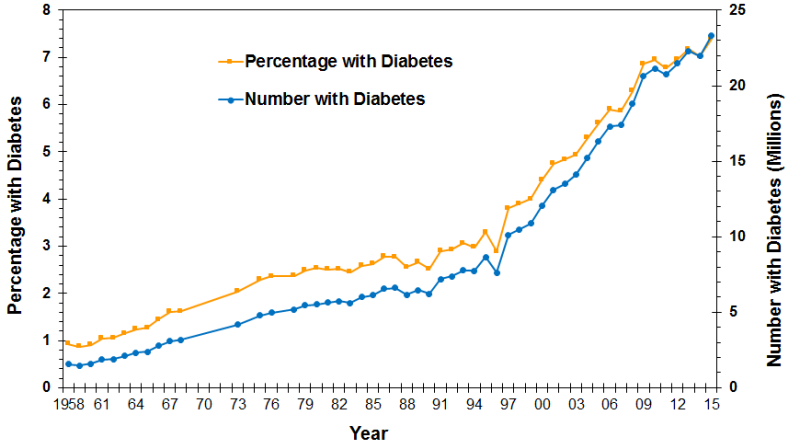
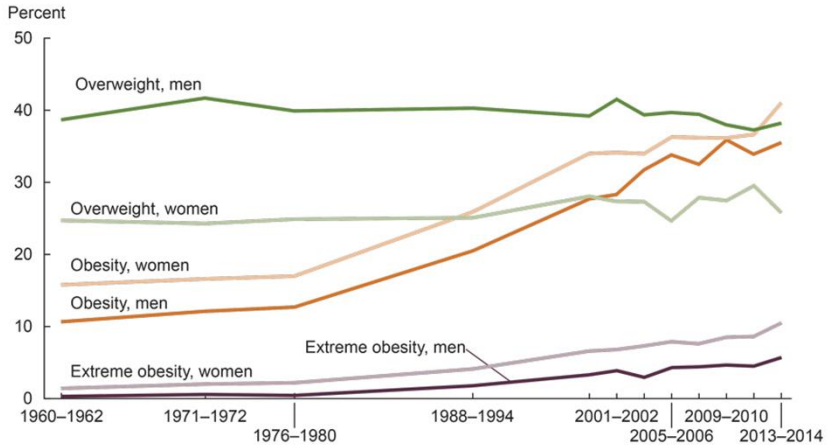
Diabetes and Obesity Trends

Diabetes in US: 1958-2015[1]



CDC's Division of Diabetes Translation. United States Diabetes Surveillance System available at http://www.cdc.gov/diabetes/data

Obesity in US: 1960-2015[2]



NOTES: Age-adjusted by the direct method to the year 2000 U.S. Census Bureau estimates using age groups 20–39, 40–59, and 60–74. Overweight is body mass index (BMI) of 25 kg/m^2 or greater but less than 30 kg/m^2; obesity is BMI greater than or equal to 30; and extreme obesity is BMI greater than or equal to 40. Pregnant females were excluded from the analysis.
SOURCES: NCHS, National Health Examination Survey and National Health and Nutrition Examination Surveys.

1, CDC Division of Diabetes Translation; http://www.cdc.gov/diabetes data - accessed 260319
2. https://www.niddk.nih.gov/health-information/health-statistics/overweight-obesity

Goals of Care in Cardiometabolic Disease

Prolong life

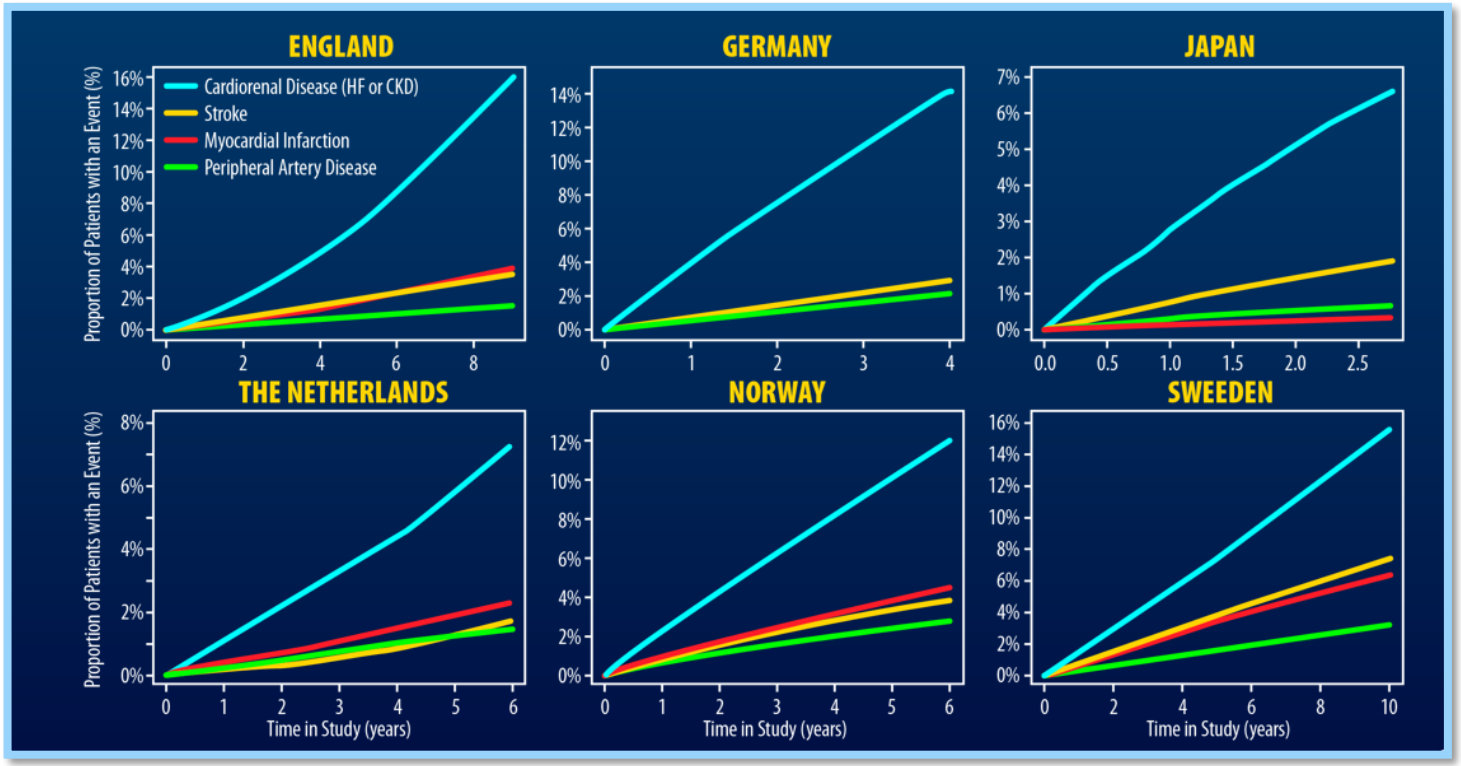
Keep patients out of the hospital/ED

Improve the quality of life

- Best accomplished by preventing morbid complications
- Cardiovascular disease and DKD are the two most common and morbid complications of T2D

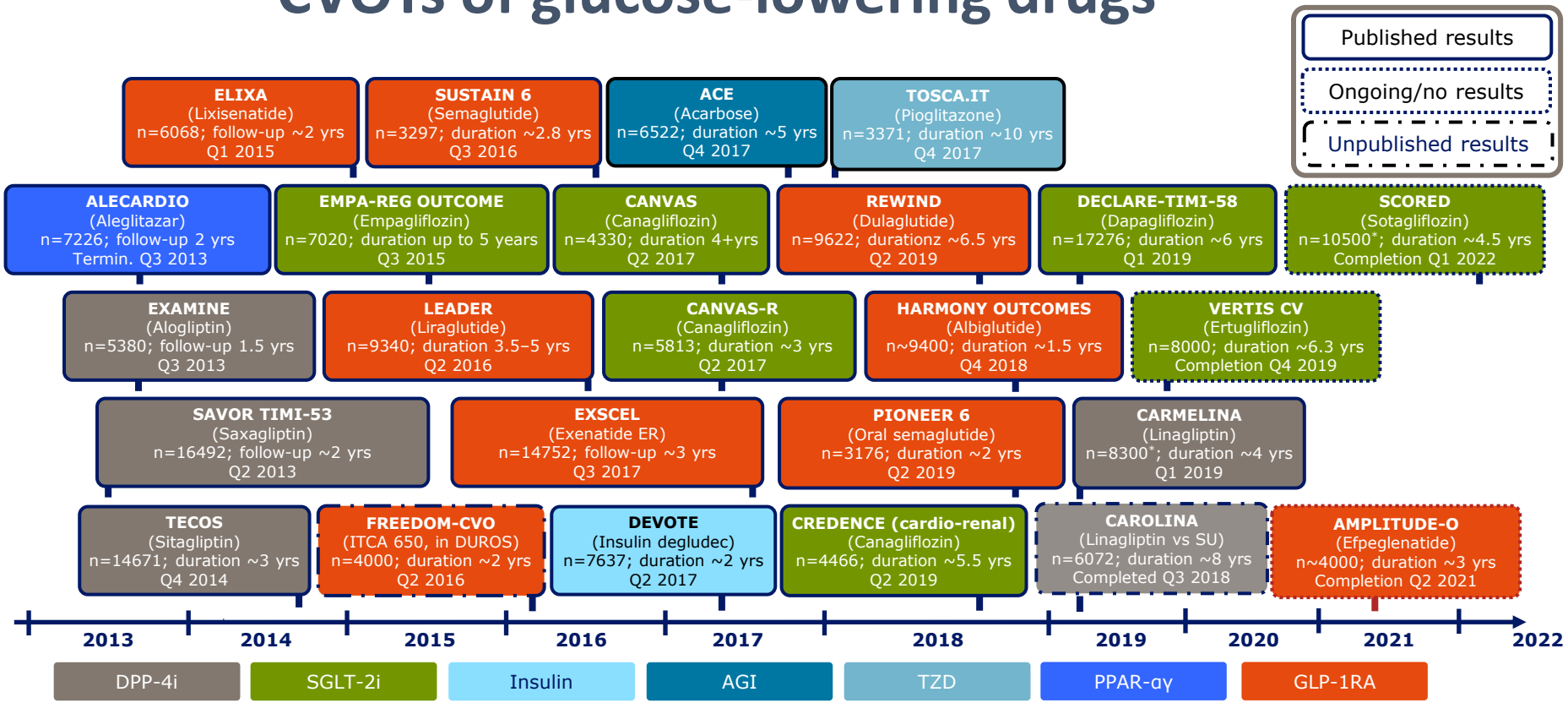
DKD, diabetic kidney disease; T2D, type 2 diabetes.

Cardiovascular Manifestation During Follow-up in Initially CV- and Renal Disease Free T2DM Patients



Birkeland et al. In Press. doi: 10.1111/dom.14074

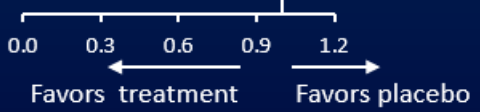
CVOTs of glucose-lowering drugs



*Estimated enrolment. AGI, alpha-glucosidase inhibitor; CV, cardiovascular; CVOT, cardiovascular outcomes trial; DPP-4i, dipeptidyl peptidase-4 inhibitor; ER, extended release; GLP-1RA, glucagon-like peptide-1 receptor agonist; ITCA 650, continuous subcutaneous delivery of exenatide; PPAR-αγ, peroxisome proliferator-activated receptors-α and γ; QW, once weekly; SGLT-2i, sodium-glucose cotransporter-2 inhibitor; SU, sulphonylurea; TZD, thiazolidinedione. ClinicalTrials.gov. Accessed July 11, 2019.

Time to first HHF

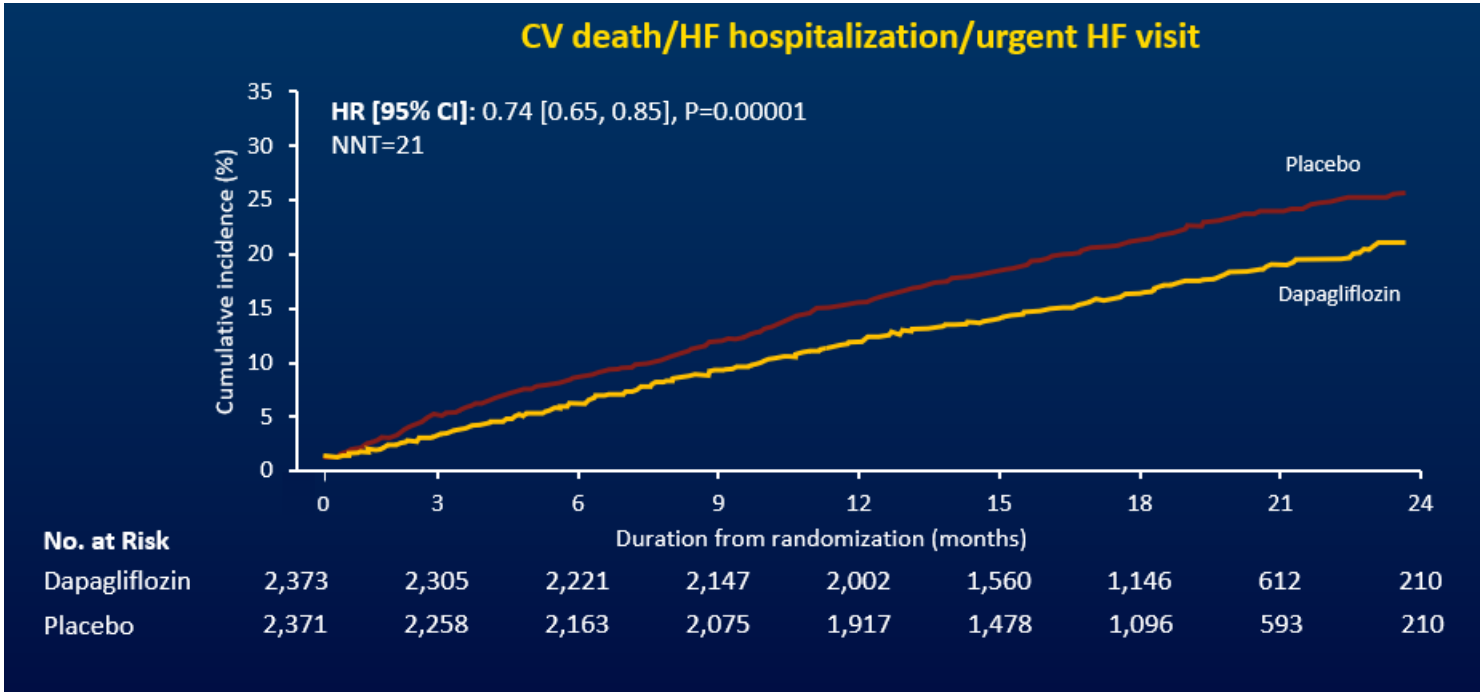
Trial name	Treatment Rate/1000 patient-years	Placebo Rate/1000 patient-years	HR (95% CI)
EMPA-REG OUTCOME	9.4	14.5	0.65 (0.50–0.85)
CANVAS Program	5.5	8.7	0.67 (0.52–0.87)
DECLARE-TIMI 58	6.2	8.5	0.73 (0.61–0.88)
CREDENCE*	15.7	25.3	0.61 (0.47–0.80)
VERTIS CV	7.3	10.5	0.70 (0.54–0.90)
Pooled estimate (Q statistic P=0.85; I^2=0.0%)			**0.68 (0.61–0.76)**



*CREDENCE is a renal outcomes trial and not a cardiovascular outcomes trial

CI, confidence interval; CV, cardiovascular; HR, hazard ratio CI, confidence interval; HHF, hospitalization for heart failure; HR, hazard ratio

DAPA-HF: Primary composite outcome



CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; NNT, number needed to treat

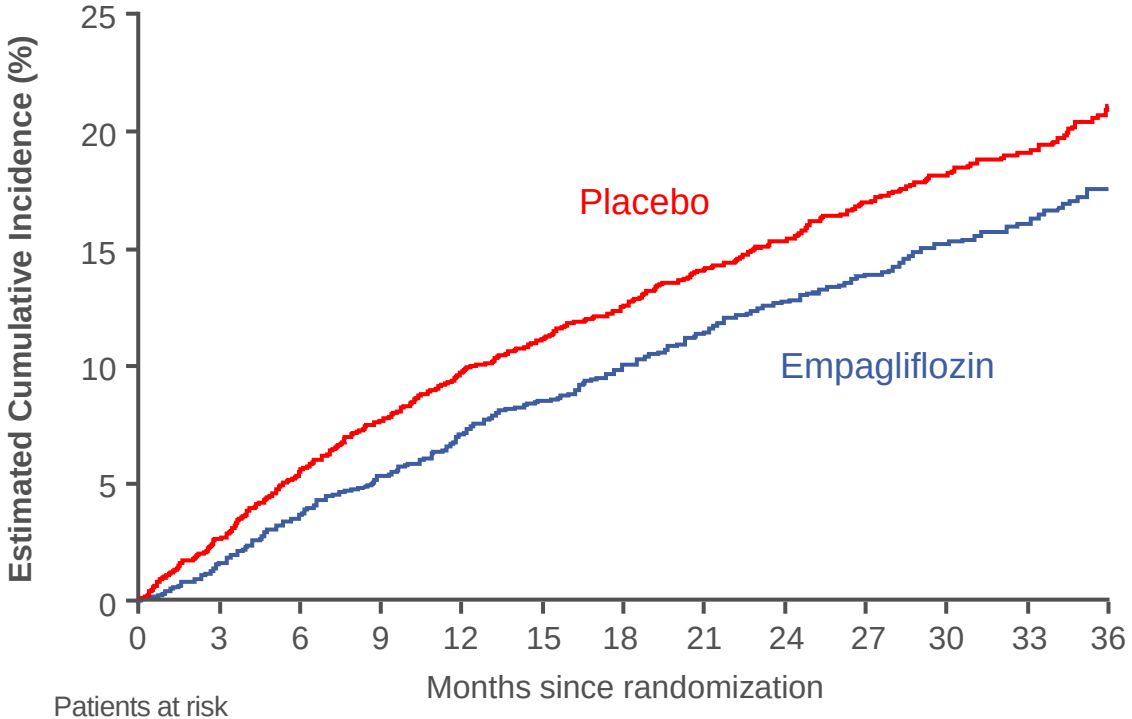
McMurray JJV et al. N Engl J Med. 2019;381:1995-2008

The Five Pillars of HFrEF Therapy 2020

The "Five Alive"

ACEi/ARB | Neprilysin inhibitor | Beta Blockers | MRA | SGLT2 inhibitor

Primary Endpoint – Composite of Cardiovascular Death or Heart Failure Hospitalization

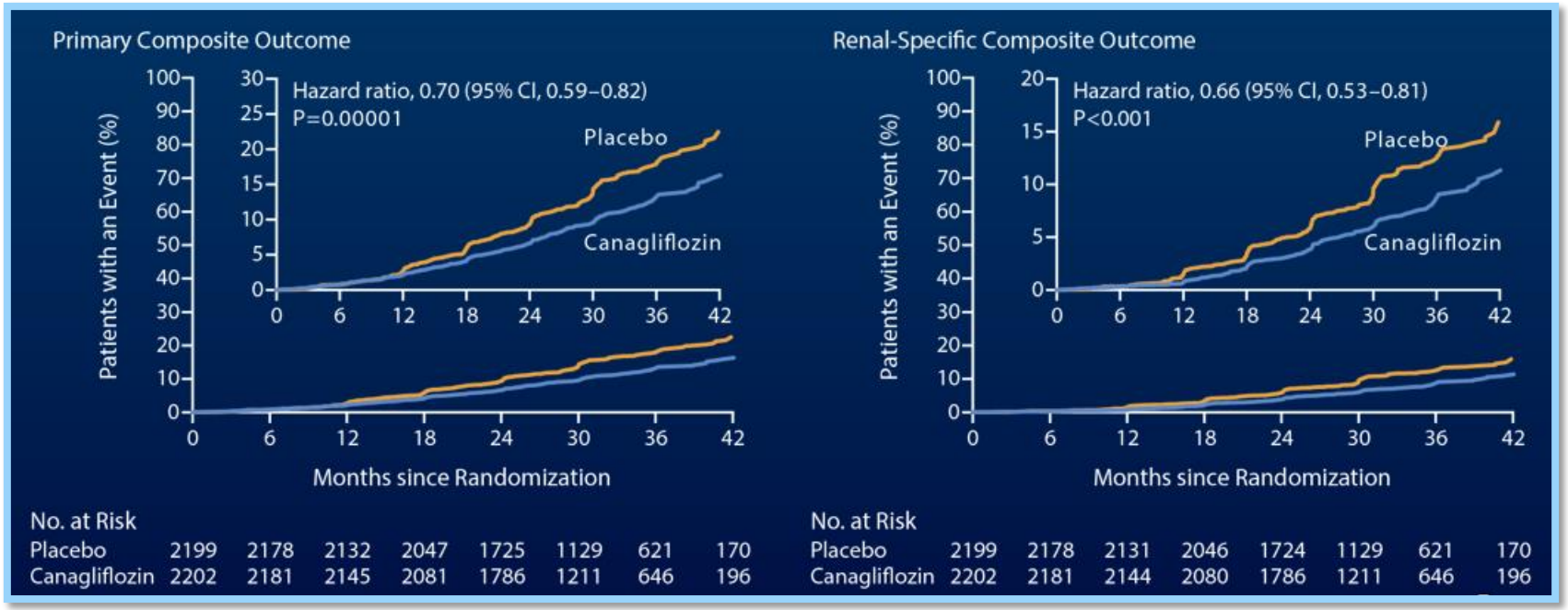


HR 0.79
(95% CI 0.69, 0.90)
P = 0.0003

Placebo:
511 patients with event
Rate: 8.7 per 100 patient-years

Empagliflozin:
415 patients with event
Rate: 6.9 per 100 patient-years

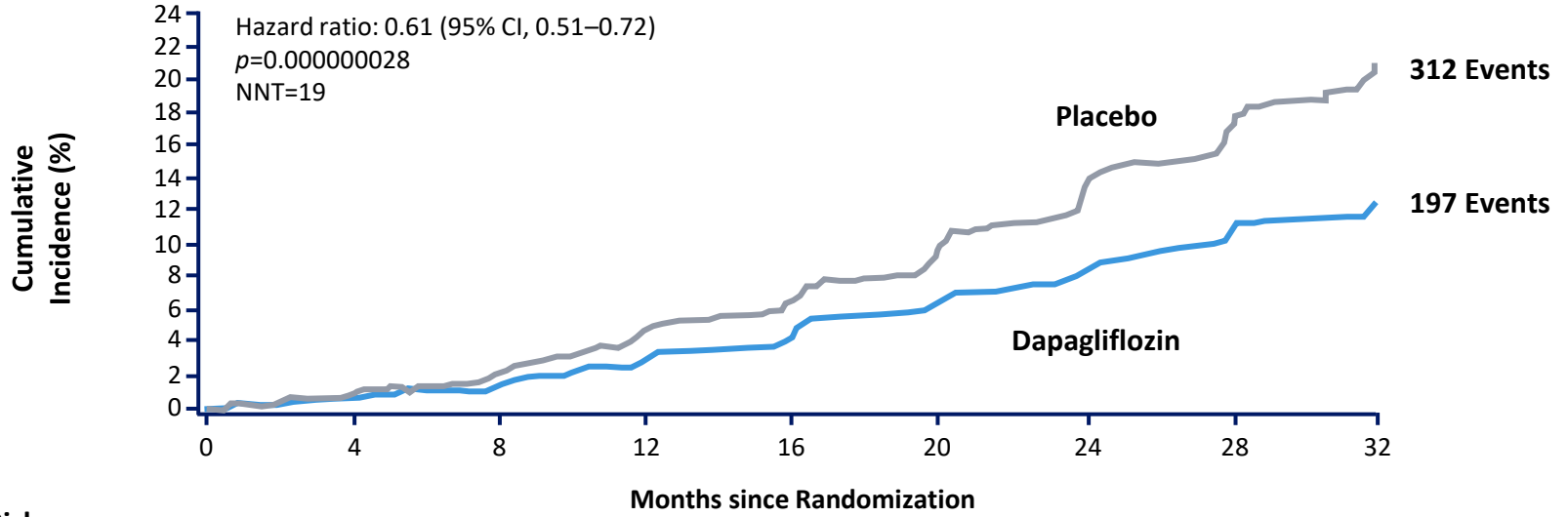
Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy



V. Perkovic et al. April 14, 2019 NEJM.com DOI: 10.1056/NEJMoa1811744

Primary Outcome: Composite Cardiorenal Outcomes

Sustained ≥50% eGFR decline, ESKD*, renal or CV death



No. at Risk

Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309
Placebo	2152	1993	1936	1858	1791	1664	1232	774	270

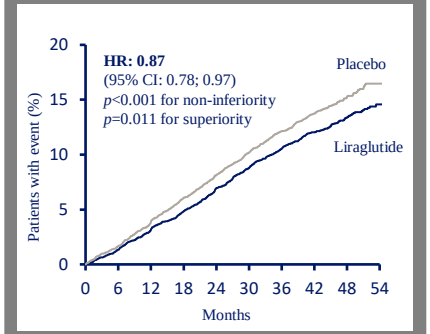
*need for chronic dialysis (≥28 days) and renal transplantation or eGFR <15 mL/min/1.73 m2 (≥28 days)
CV, cardiovascular; CI, confidence interval; eGFR, estimated glomerular filtration ratel ESKD, end stage kidney disease

Heerspink H et al. Data presented at ESC 2020

CVOTs showing a CV benefit: GLP-1RAs

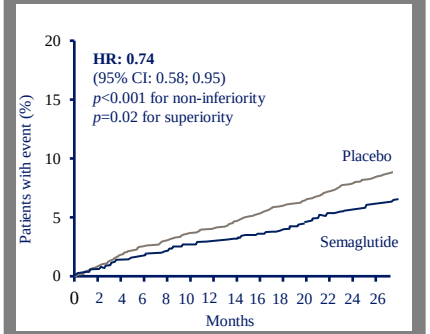
LEADER[1]

- Liraglutide superior to placebo for time to 3-point MACE in T2D with established CVD, chronic renal failure or aged ≥60 years with CV risk



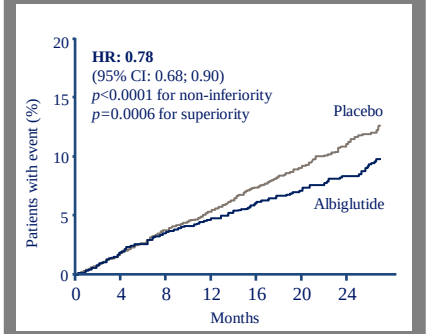
SUSTAIN 6[2]

- Semaglutide superior to placebo for time to 3-point MACE in T2D with established CVD, chronic renal failure or aged ≥60 years with CV risk



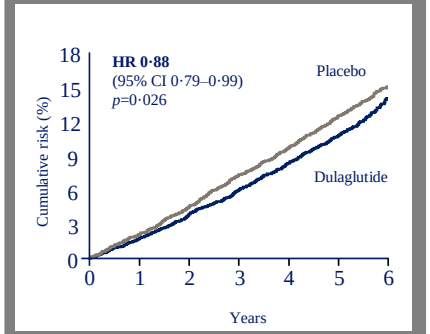
HARMONY[3]

- Albiglutide superior to placebo for time to 3-point MACE in T2D with established CVD, aged ≥40 years old



REWIND[4]

- Dulaglutide is superior to placebo for time to 3-point MACE in T2D with low CV risk population



***Not pre-specified. CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; CVOT, cardiovascular outcomes trial; GLP-1RA, glucagon-like peptide 1 receptor agonist; HR, hazard ratio; MACE, major adverse cardiovascular events; T2D, type 2 diabetes.**

1. Marso SP et al. *N Engl J Med* 2016;375:311–322; 2. Marso SP et al. *N Engl J Med* 2016;375:1834–1844; 3. Hernandez AF et al. *Lancet* 2018;392:1519–1529; 4. Gerstein HC et al. *Lancet* 2019; S0140-6736:31149-31153.

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Changing Guidelines and Evolving Treatment Landscapes

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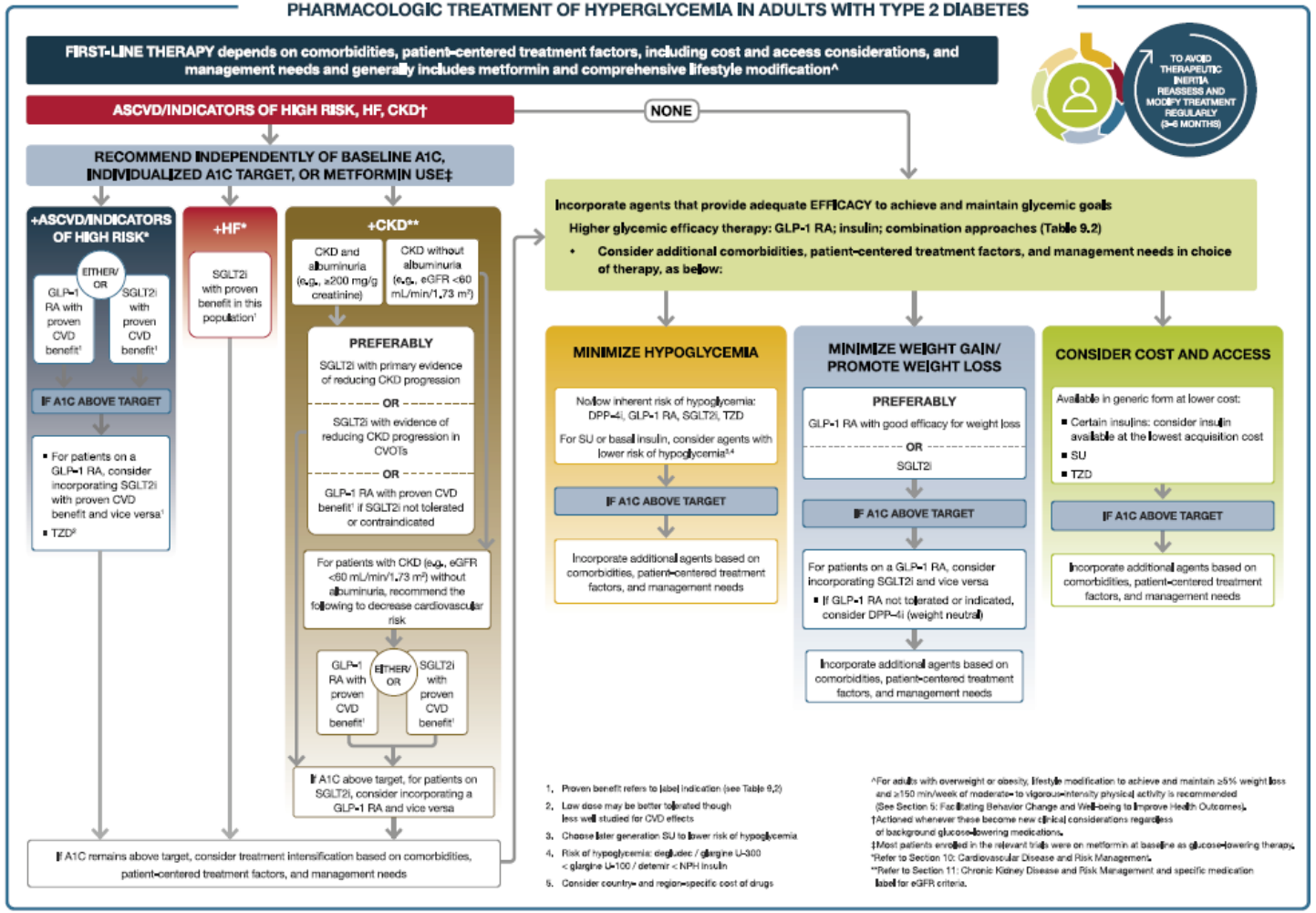
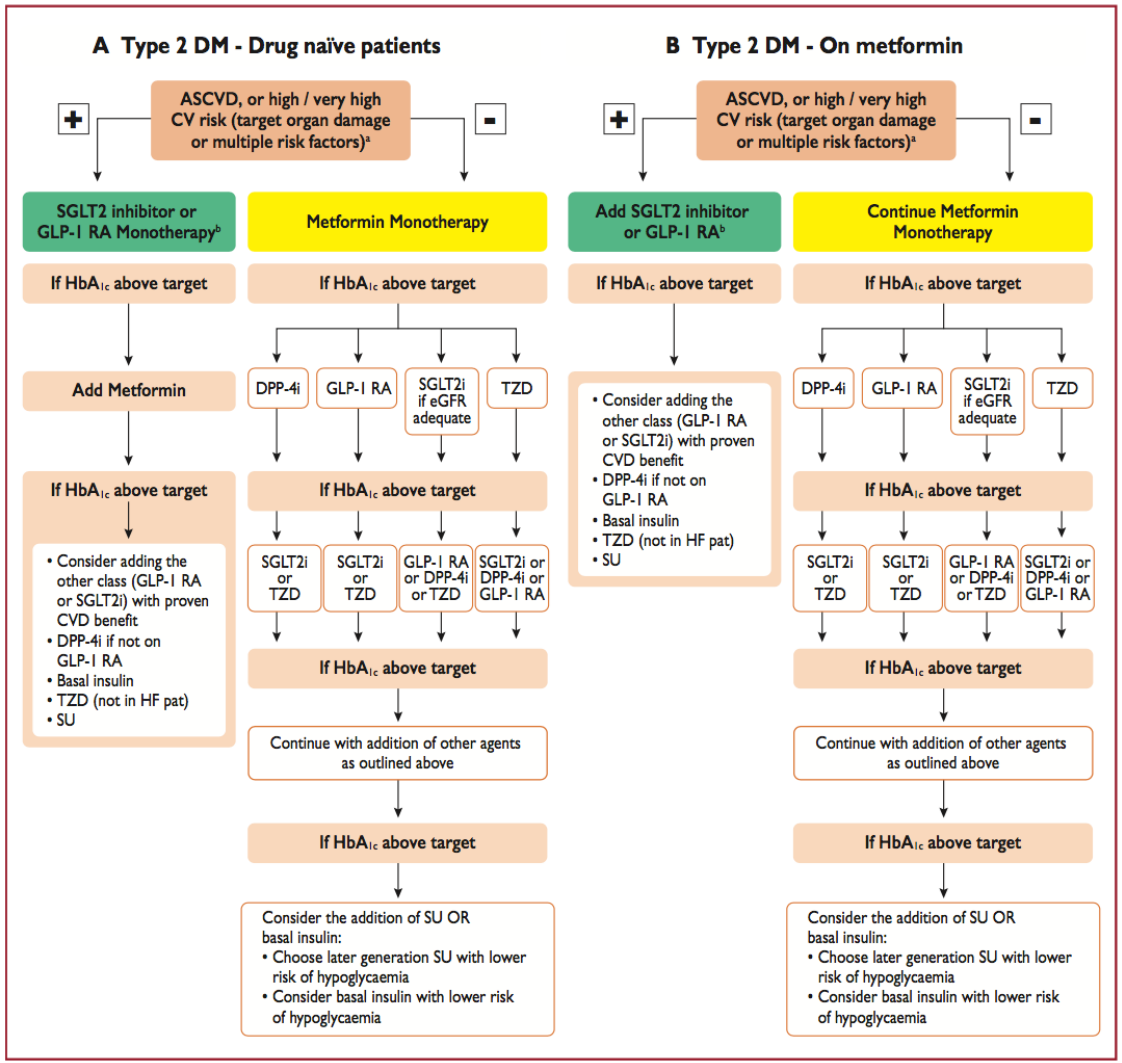


Glucose-lowering Medication in Type 2 Diabetes: 2022 ADA Professional Practice Committee (PPC) adaptation of Davies et al. and Buse et al.

Pharmacologic Approaches to Glycemic Management: ***Standards of Medical Care in Diabetes - 2022. Diabetes Care*** **2022**

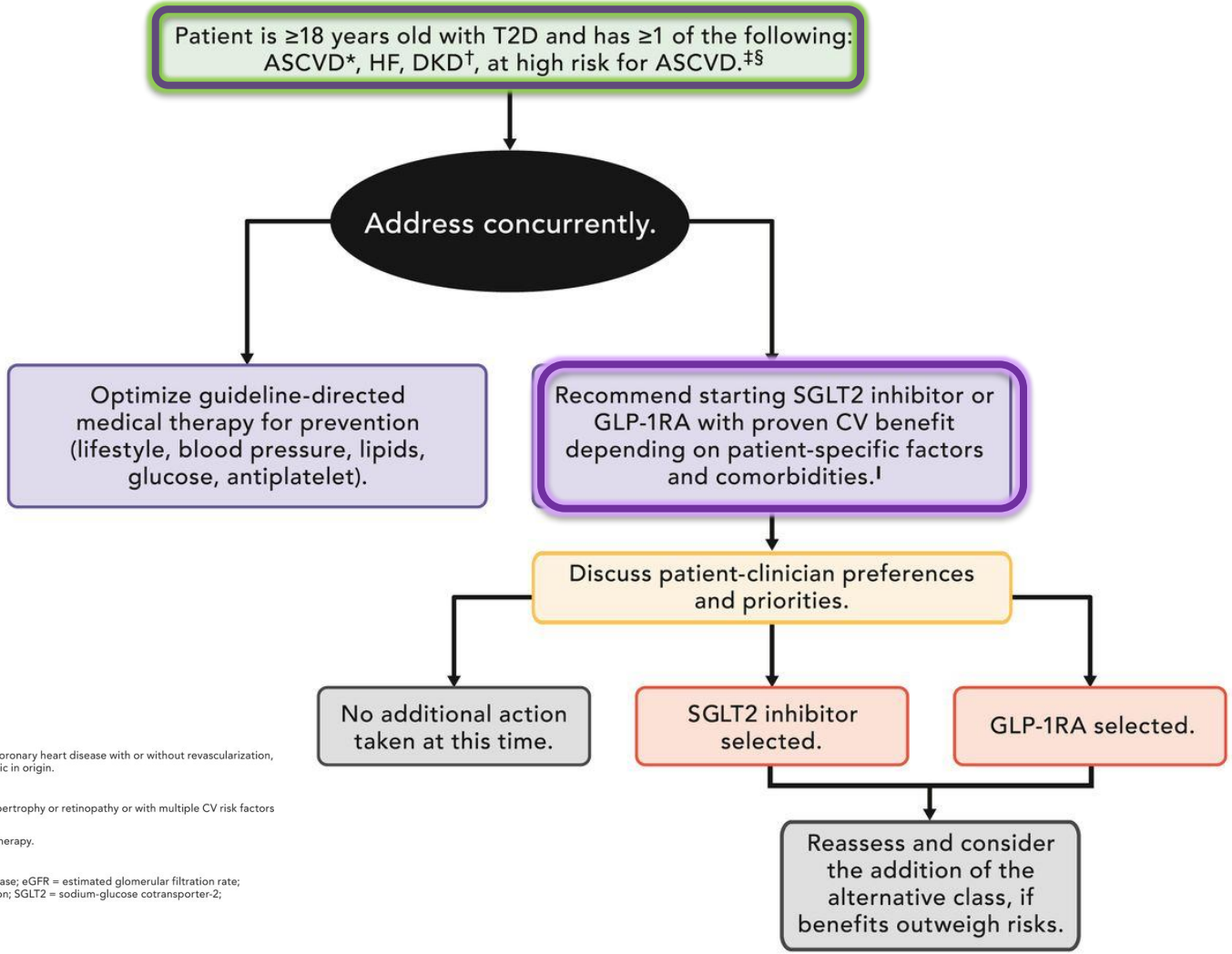
2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD

The Task Force for diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD)



Cosentino, Francesco, et al. *European heart journal* (2019).

2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes



* ASCVD is defined as a history of an acute coronary syndrome or MI, stable or unstable angina, coronary heart disease with or without revascularization, other arterial revascularization, stroke, or peripheral artery disease assumed to be atherosclerotic in origin.

† DKD is a clinical diagnosis marked by reduced eGFR , the presence of albuminuria, or both.

‡ Patients at high risk for ASCVD include those with end organ damage such as left ventricular hypertrophy or retinopathy or with multiple CV risk factors (e.g., age, hypertension, smoking, dyslipidemia, obesity).

§ Most patients enrolled in the relevant trials were on metformin at baseline as glucose-lowering therapy.

ǁ This may include the addition of a GLP-1RA in the appropriate patient (see Section 5.3.3).

ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; DKD = diabetic kidney disease; eGFR = estimated glomerular filtration rate; GLP-1RA = glucagon-like peptide-1 receptor agonist; HF = heart failure; MI = myocardial infarction; SGLT2 = sodium-glucose cotransporter-2; T2D = type 2 diabetes

Das, Sandeep R., et al. *Journal of the American College of Cardiology* 76.9 (2020): 1117-1145.

2020 KDIGO Treatment Algorithm for Patients with T2D and CKD

Lifestyle therapy

Physical activity
Nutrition
Weight loss

First-line therapy
eGFR ≥30 mL/min/1.73m^2

Metformin
eGFR <45: reduce dose
eGFR <30 or dialysis: DC

SGLT-2i
eGFR <30: do not initiate
Dialysis: DC

Additional drug therapy as needed for glycemic control

GLP-1 RA
(preferred)

DPP-4i **Insulin**

SU **TZD**

AG-i

- Guided by patient preferences, comorbidities, eGFR and cost
- Includes patients with eGFR<30 mLmin/1.73m^2 or treated with dialysis

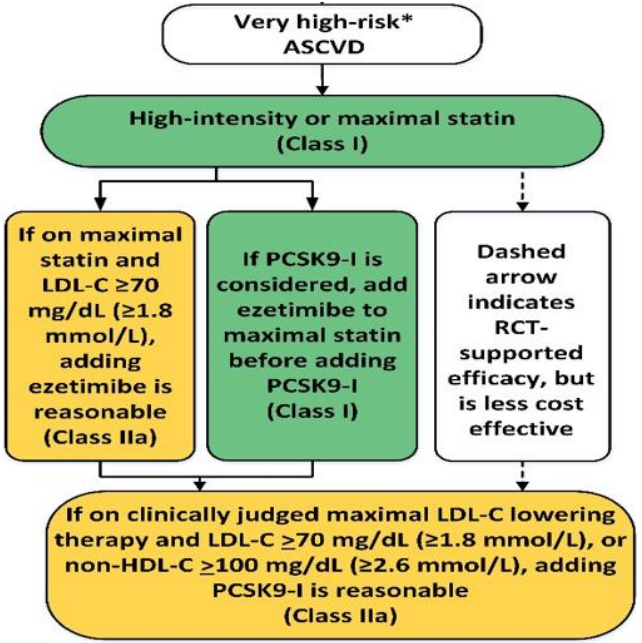
- AG-i = alpha-glucosidase inhibitor; CKD = chronic kidney disease; D/C = discontinue; DPP-4i = dipeptidyl peptidase-4 inhibitor; eGFR = estimated glomerular filtration rate; GLP-1 RA = glucagon-like peptide-1 receptor agonist; SGLT2-i = sodium-glucose cotransporter 2 inhibitor; SU = sulfonylurea; T2D = type 2 diabetes; TZD = thiazolidinedione.

de Boer IH et al. *Kidney Int.* 2020;98:839-848.

Lipid Lowering 2018 AHA/ACC Multi-society Guideline Recommendations for Very High-Risk ASCVD Patients

Very high risk ASCVD is defined as a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions

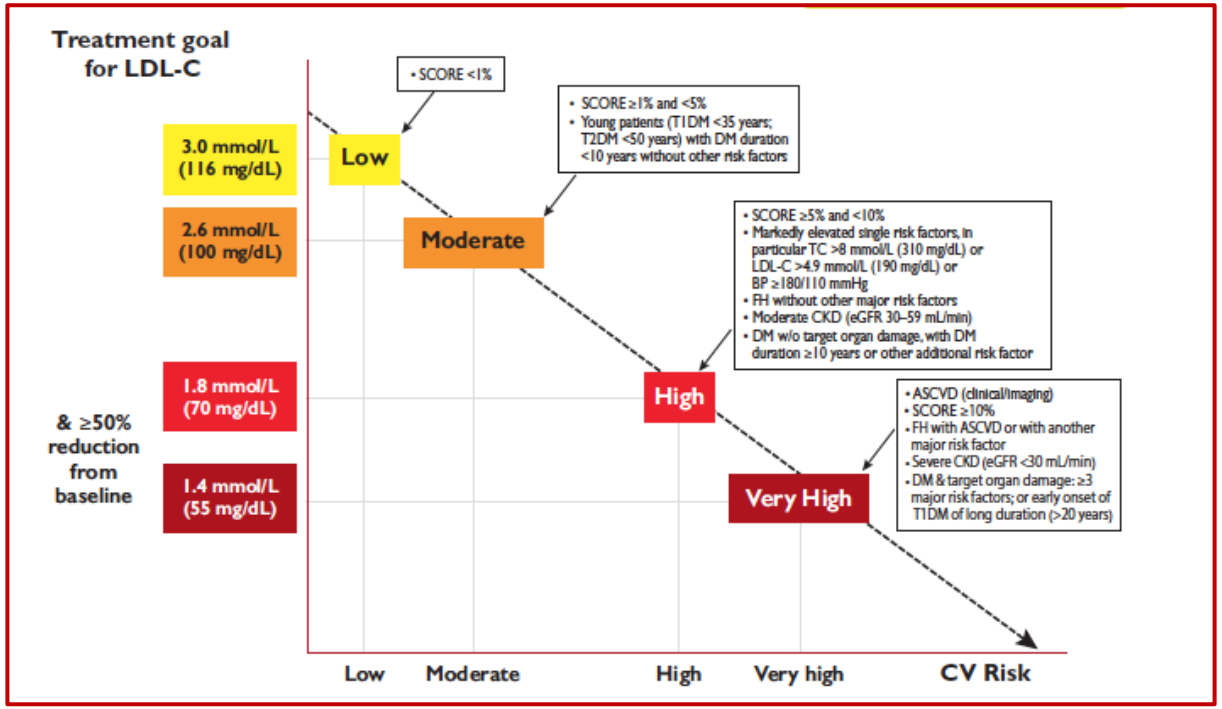
Clinical Factors for Very High-Risk ASCVD	
ASCVD events	• Recent ACS (within past 12 months) • History of myocardial infarction (other than recent ACS event listed above) • History of ischemic stroke • Symptomatic PAD*
High-risk conditions	• Age ≥ 65 years • HeFH • Prior coronary artery bypass surgery or percutaneous coronary intervention • Diabetes mellitus • Hypertension • CKD (eGFR 15-59 mL/min/1.73 m^2) • Currently smoking • Persistently elevated LDL-C ≥ 100 mg/dL despite maximally tolerated statin and ezetimibe therapies • History of congestive heart failure



ACC = American College of Cardiology; AHA = American Heart Association; ASCVD = atherosclerotic cardiovascular disease; LDL-C = low-density lipoprotein cholesterol; non-HDL-C = high-density lipoprotein cholesterol; PCSK9i = proprotein convertase subtilisin/kexin type 9 inhibitor; RCT = randomized controlled trial.

Grundy SM et al. J Am College Cardiol. 2019;73:e285- e350.

ESC Prevention Guidelines 2019



Mach F et al. Eur Heart J (2019) online

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The Need for Comprehensive Care for Cardiometabolic Patients

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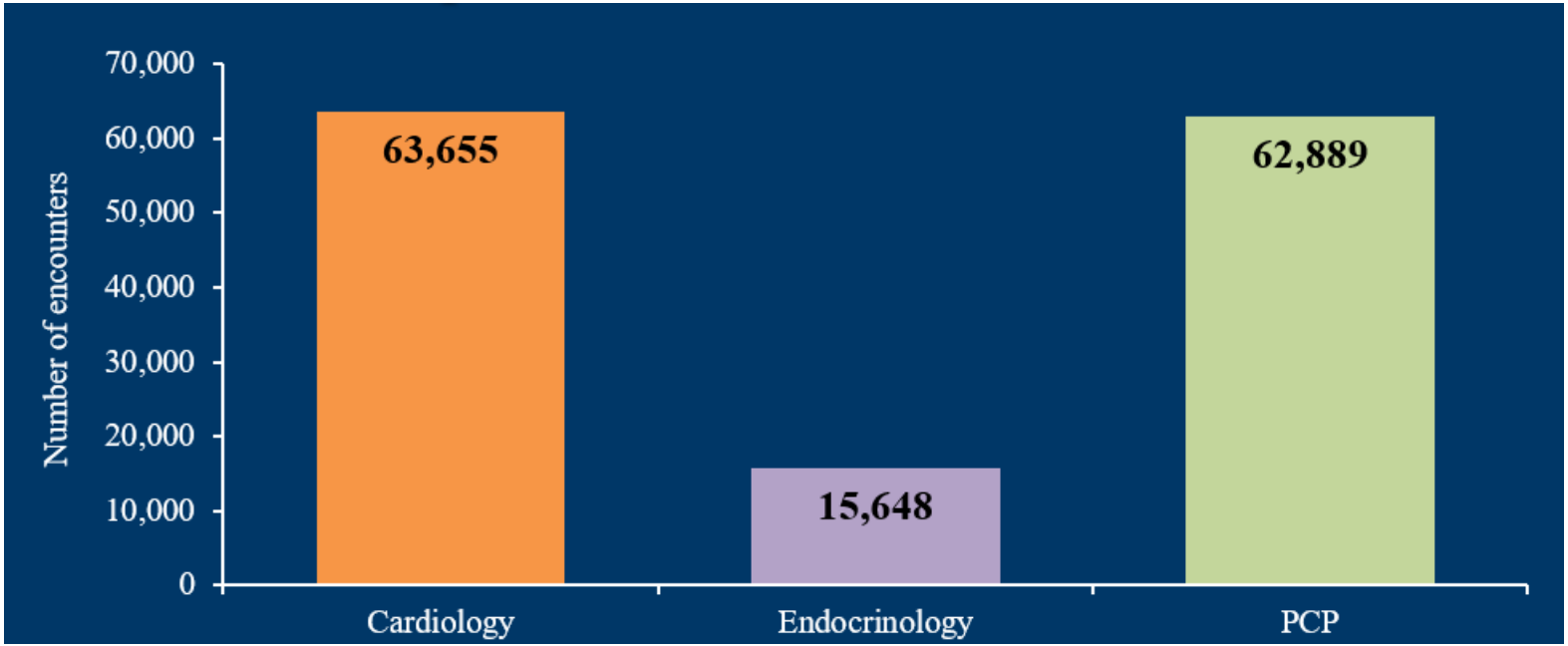
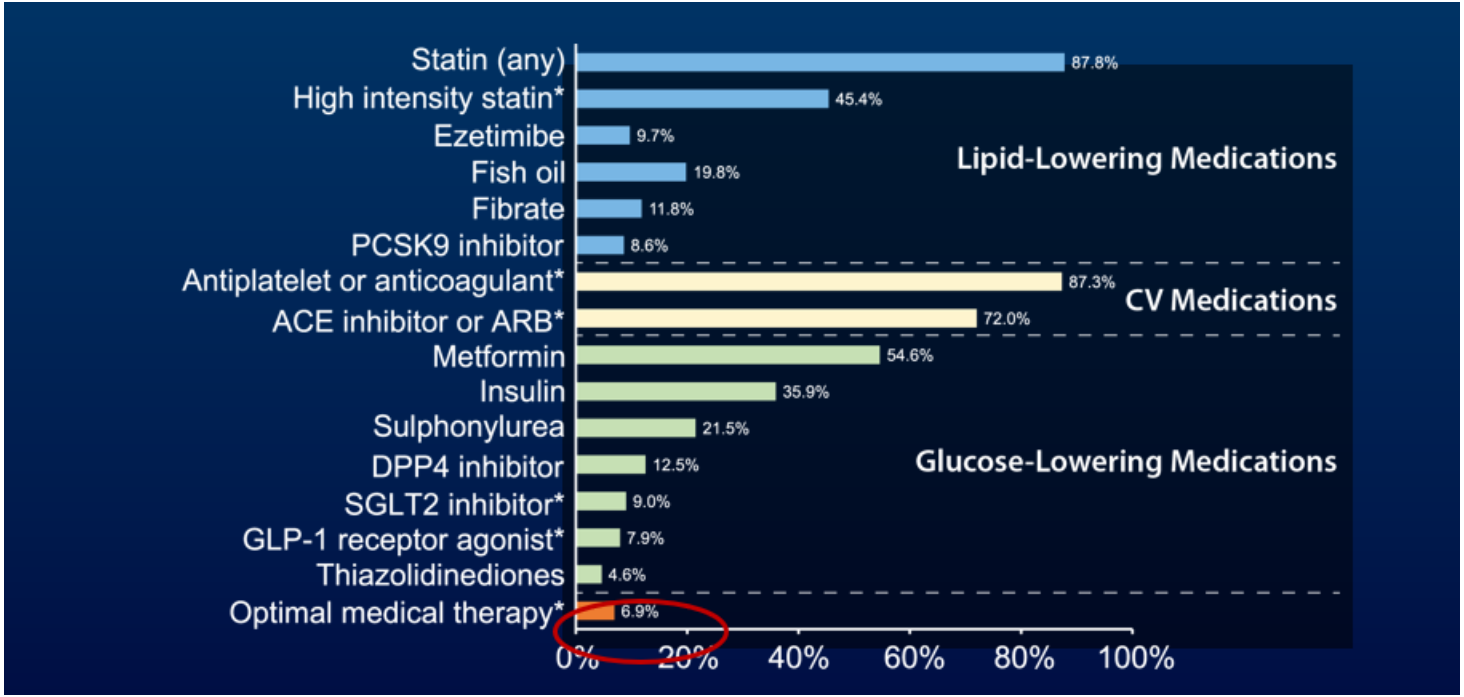
Number of outpatient encounters by specialty in patients with T2D and CVD



CV, cardiovascular; PCP, primary care practitioner; T2D, type 2 diabetes.

Gunawan et al. *Cardiovascular Endocrinology & Metabolism* 2020;9:56.

Use of Cardioprotective and Anti-Diabetic Agents in Patients with T2D and ASCVD – 120 US Centers



SV Arnold et al. Circulation. 2019;140:618-620.

Effective Clinical Care Models Don’t Exist

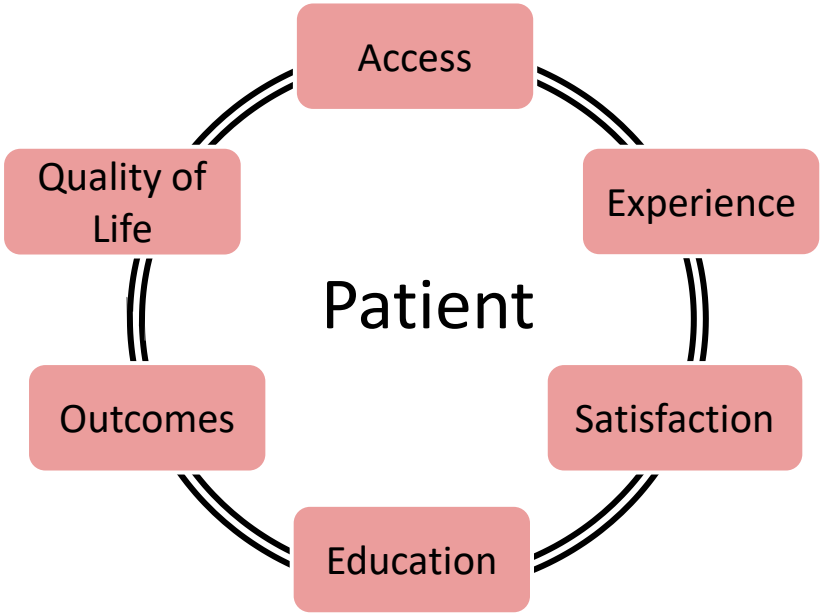
Saint Luke's™

MICHAEL & MARLYS HAVERTY
CARDIO METABOLIC CENTER OF EXCELLENCE

Comprehensive, Collaborative Care

Key Support Staff & Personnel

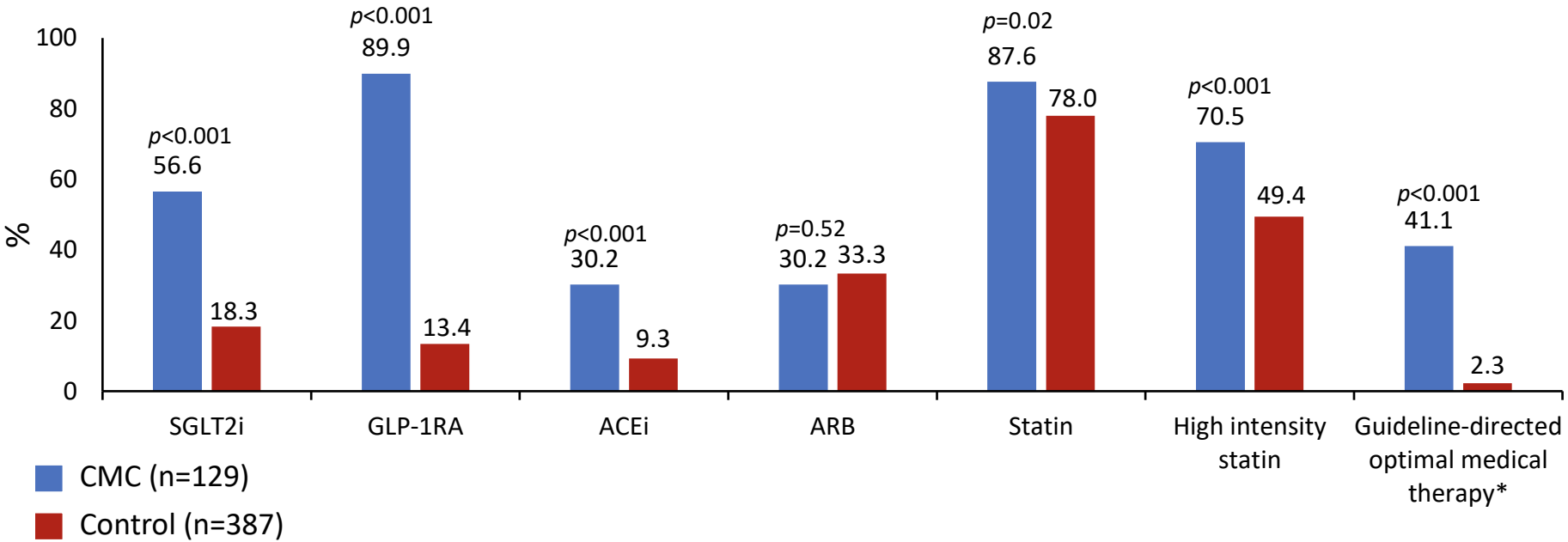
- Driven by preventive cardiology in collaboration with endocrinology and primary care
- Support staff including advance practice providers, nurse navigators and others cross-trained in both cardiovascular disease and T2D
- Key support personnel includes certified diabetes educator, dietician, and pharmacist with plan to include others over time



Comprehensive Treatment Plans

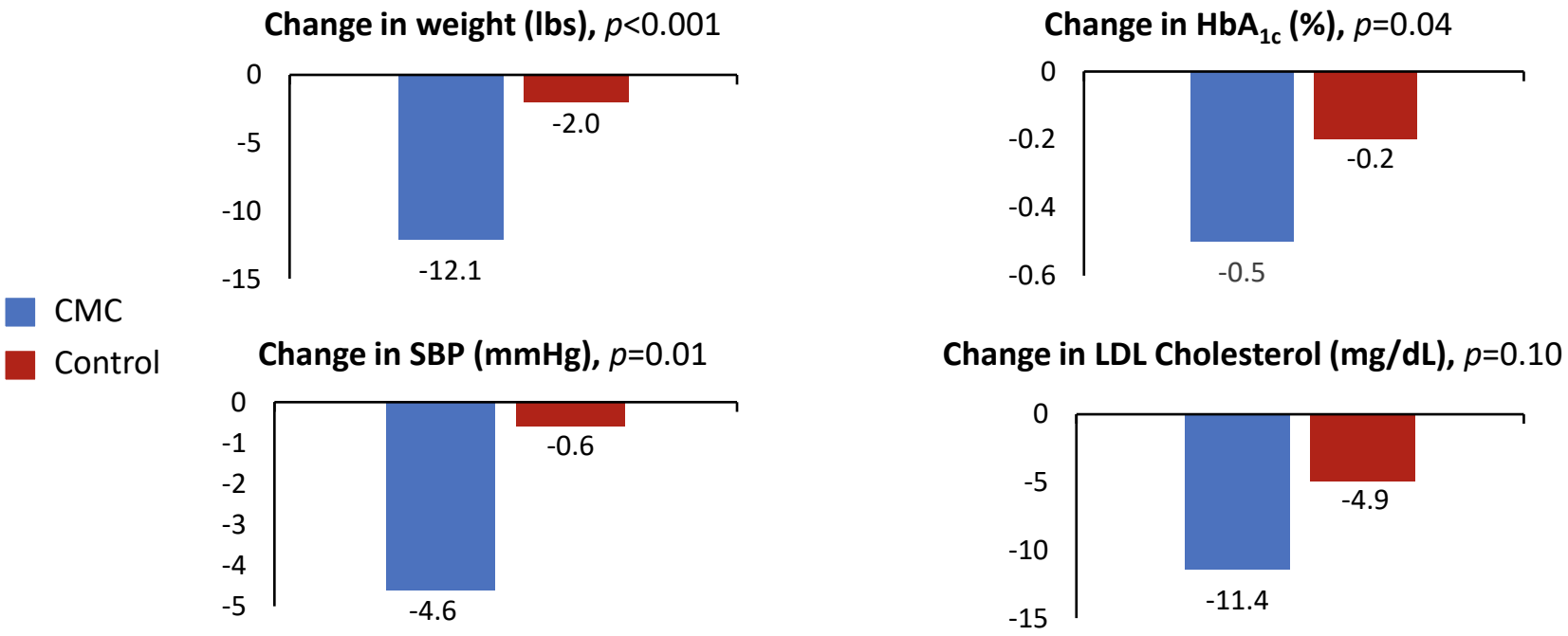
- Both cardiovascular and diabetes-related aspects of care addressed at each visit
- Comprehensive treatment plan developed and tailored to individual patients with chief objective of aggressive secondary risk reduction

Comparison of Guideline-Directed Medical Therapies



ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers; GLP-1RA, glucagon-like peptide-1 receptor agonists; SGLT2i, sodium-glucose cotransporter 2 inhibitor. *Guideline-directed optimal medical therapy = high intensity statin + antiplatelet or anticoagulant + ACEi/ARB + either SGLT2-i or GLP-1RA.

Saint Luke's Haverty Cardiometabolic Center of Excellence Results



LDL, low-density lipoprotein; SBP, systolic blood pressure. Thomas et al. AHA Q4 2020 [abstract].


Cardiometabolic
Center Alliance™
Founded by Saint Luke's Mid America Heart Institute

Take-home Points

- Cardiometabolic disease a huge public health threat
- Rapid growth in the number of efficacious, evidence-based therapies that can transform care and improve outcomes
- Rapid incorporation of data into practice guidelines
- Increasing complexity, fragmentation of care hampers implementation
- Team-based, coordinated care via Cardiometabolic Center approach a real opportunity to improve outcomes – "all hands on deck" approach
- Efforts under way to make this novel care delivery model widely accessible

CV, cardiovascular; CVOT, cardiovascular outcomes trial; GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT2i, sodium glucose co-transporter-2 inhibitor; T2D, type 2 diabetes.