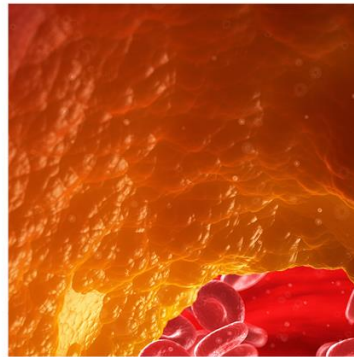
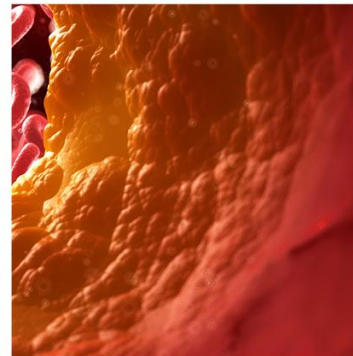
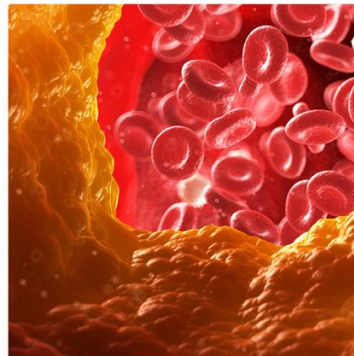


The 2019 EMEA Cardiometabolic Workshop



Saturday,
16 November 2019

Baku, Azerbaijan



Case presentation

Professor Paolo Pozzilli

The subject is a 56 year-old man, diagnosed in 2014 with type 2 diabetes mellitus, who has been taking metformin since diagnosis.

He was hospitalized in 2016 for acute myocardial infarction, which was followed by double percutaneous coronary angioplasty. Three months later, restenosis was treated with an **aorto-coronary bypass**

- His cardiac conditions are currently stable (NYHA II heart failure), but for the last few months he has had poor glucose control as a consequence of his lifestyle choices

NYHA Class	Level of Clinical Impairment
I 	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
II 	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
III 	Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
IV 	Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

Medical history (as at 10.03.2019)

- **Therapy:**

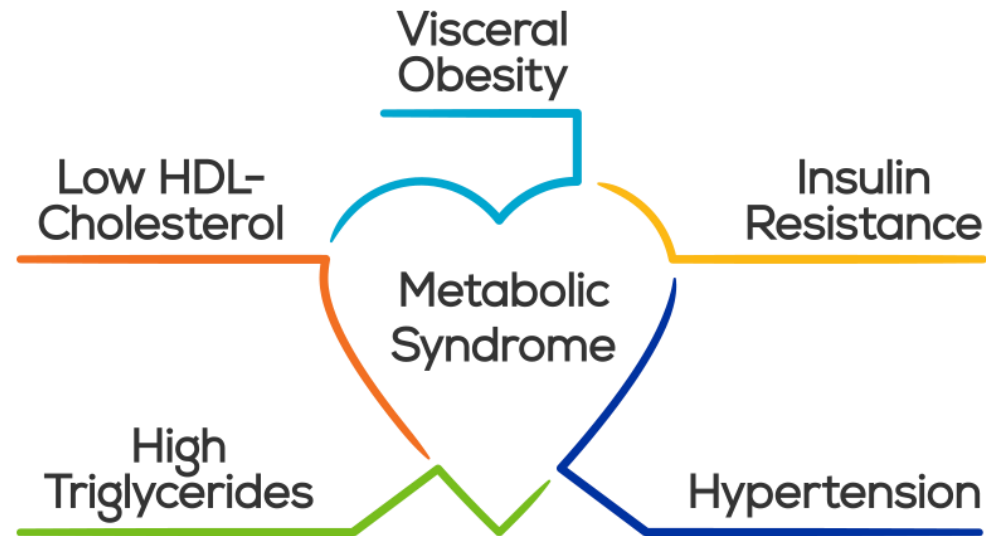
Long-acting metformin 1000 mg: 1 qt
Olmesartan 20 mg: 1 tb qt
Simvastatin 20 mg: 1 tb qt
Cardioaspirin 100 mg: 1 tb qt
Furosemide 25 mg: 1 tb bid

- **Physical examination:**

CV 102 cm
Weight 98 Kg
Height 176 cm
BMI 31.6 Kg/m²
BP 140/85 mmHg

- **Family history:**

Mother with type 2 diabetes
Father with ictus cerebri



- **Other information:**

Smokes 15 cigarettes/day
Eats a diet rich in carbohydrates
Undertakes no regular physical activity
Allergic to amoxicillin
Irritable bowel syndrome

Laboratory tests (27.02.2019)

HbA1c: 8.6%; total cholesterol: 212 mg/dl; HDL: 34 mg/dl;
 triglycerides: 198 mg/dl; LDLc: 139 mg/dl; creatinine: 0.98 mg/dl; GFR: 86 ml/min; Na⁺: 143 mEq/L; K⁺: 4.2 mEq/L; urine test: **glucose 200 mg/dl**

Daily glucose profile

BB	AB	BL	AL	BD	AD
188	192				
174		167			212
	156		178	147	
169		171	194		183

BB/AB: before/after breakfast

BL/AL: before/after lunch

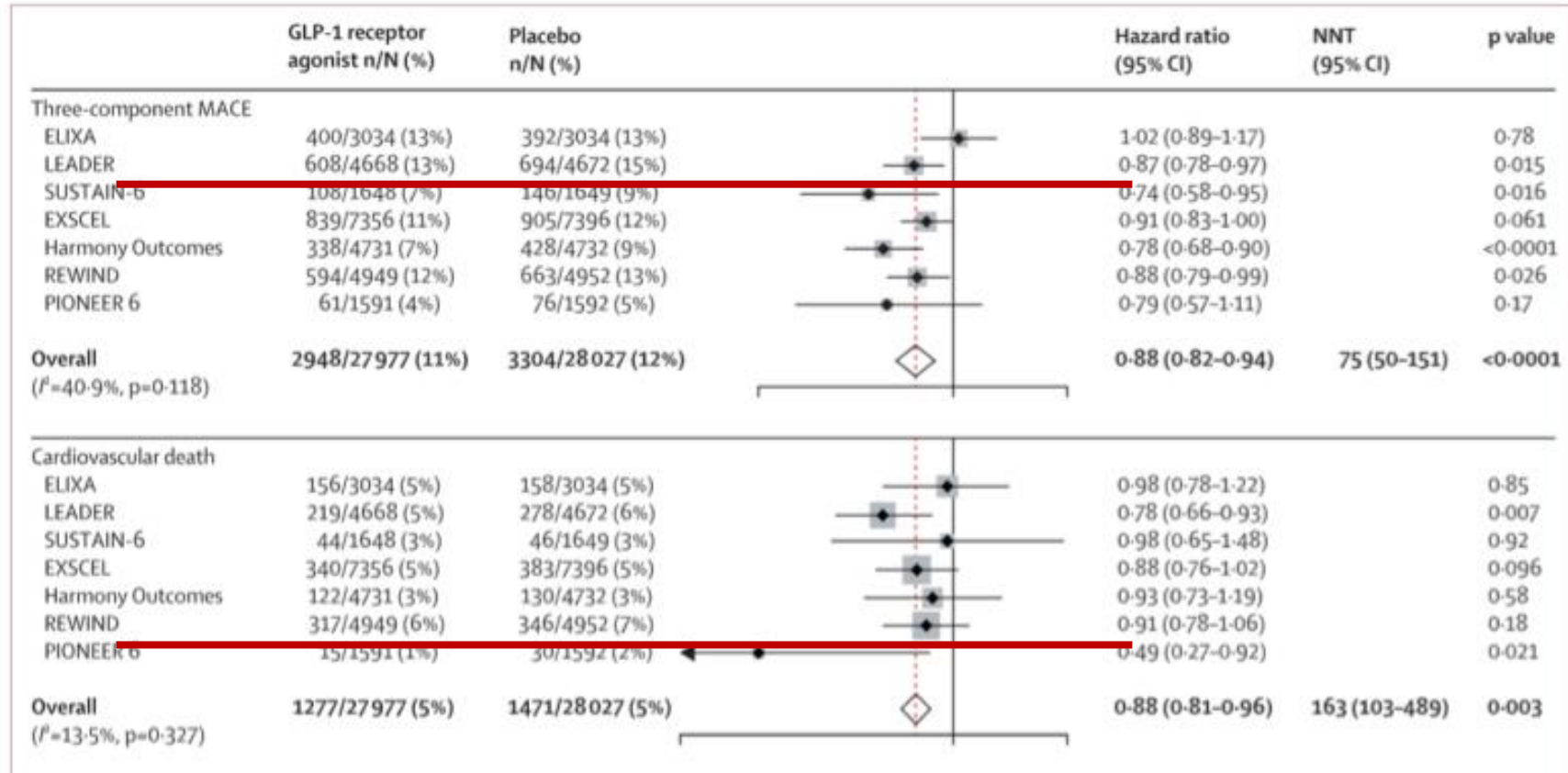
BD/AD: before/after dinner



What therapy would be best?

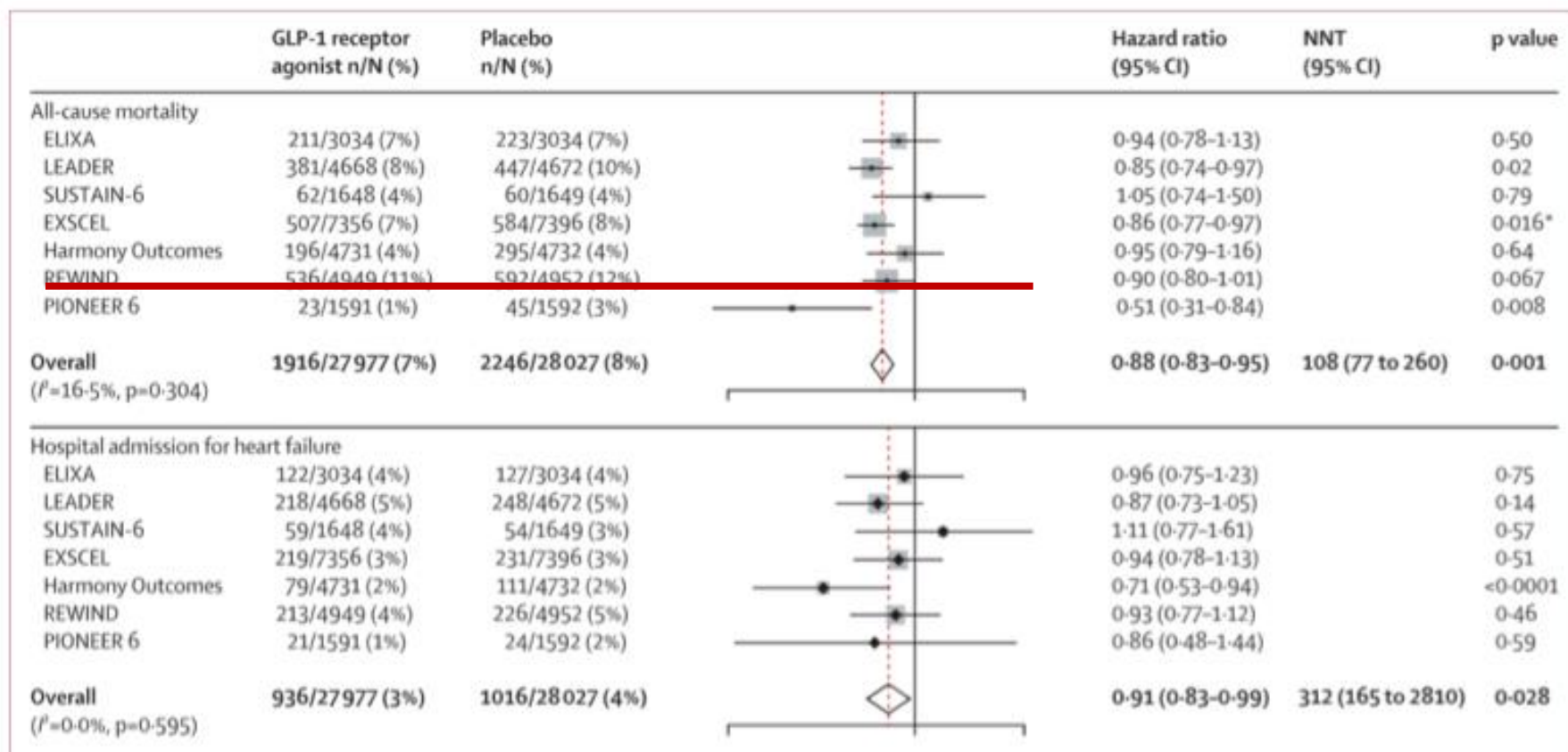


Focus on GLP-1 receptor agonists



Kristensen KL, et al. Lancet Diabetes Endocrinol 2019;7:776–785.

Focus on GLP-1 receptor agonists



Kristensen KL, et al. Lancet Diabetes Endocrinol 2019;7:776–785.

Focus on SGLT-2 inhibitors

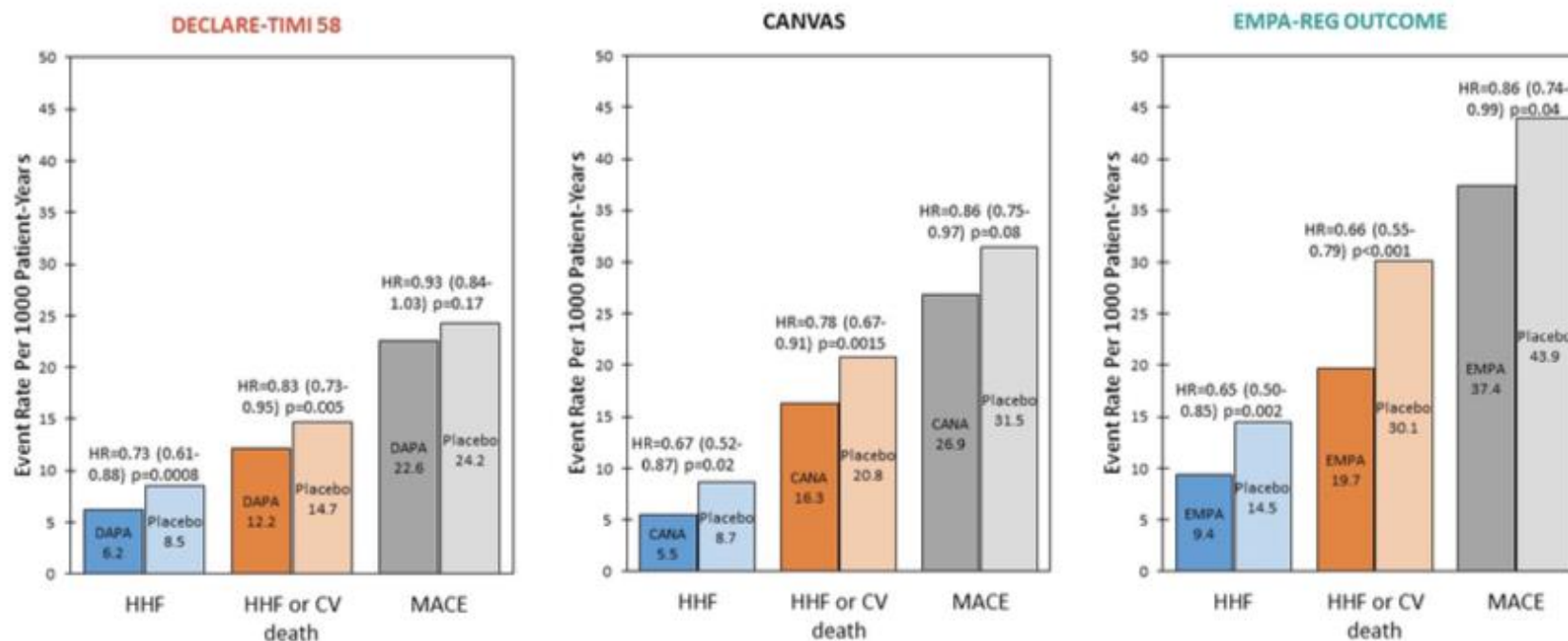


Figure 1. Heart failure hospitalization (HHF), HHF and cardiovascular (CV) death, and major adverse cardiovascular event (MACE) event rates per 1000 patients in the Dapagliflozin Effect on Cardiovascular Events (DECLARE-TIMI 58), Canagliflozin Cardiovascular Assessment Study (CANVAS), and Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME) trials. Statistical outcomes displayed as hazard ratio (HR) (95% confidence interval) p-value. DAPA=dapagliflozin, CANA = canagliflozin, EMPA = empagliflozin.

Focus on SGLT-2 inhibitors

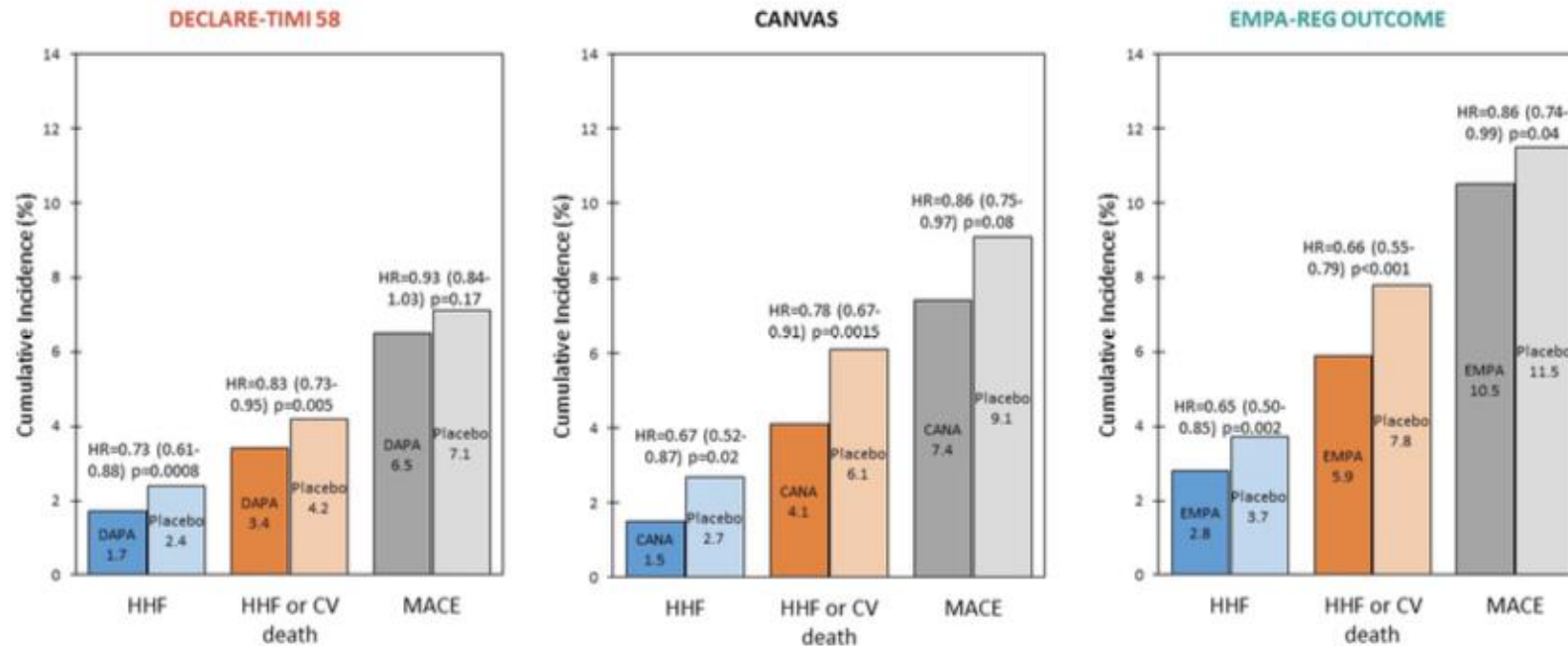


Figure 2. Heart failure hospitalization (HHF), HHF and cardiovascular (CV) death, and major adverse cardiovascular event (MACE) cumulative incidence percentages at 3 years in the Dapagliflozin Effect on Cardiovascular Events (DECLARE-TIMI 58), Canagliflozin Cardiovascular Assessment Study (CANVAS), and Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME) trials. Statistical outcomes displayed as hazard ratio (HR) (95% confidence interval) p-value. DAPA = dapagliflozin, CANA = canagliflozin, EMPA = empagliflozin.

Focus on SGLT-2 inhibitors

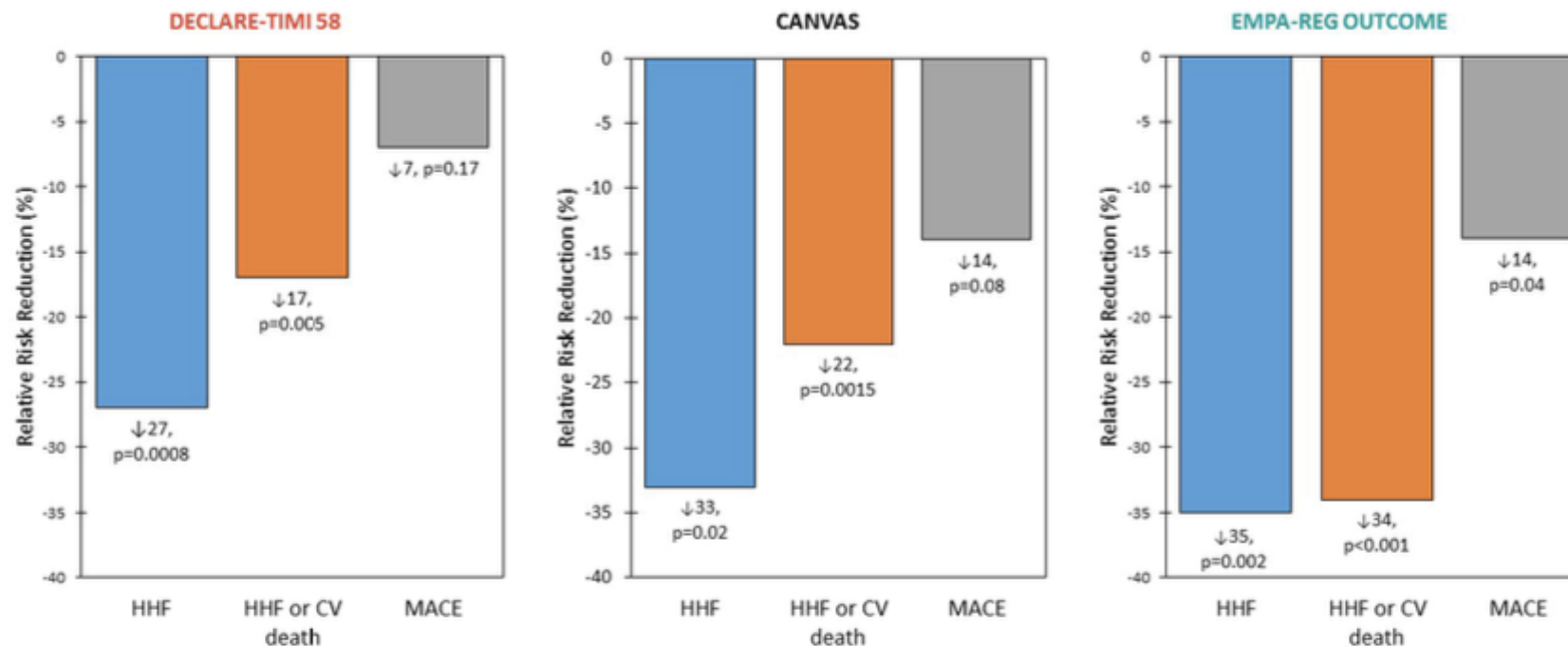
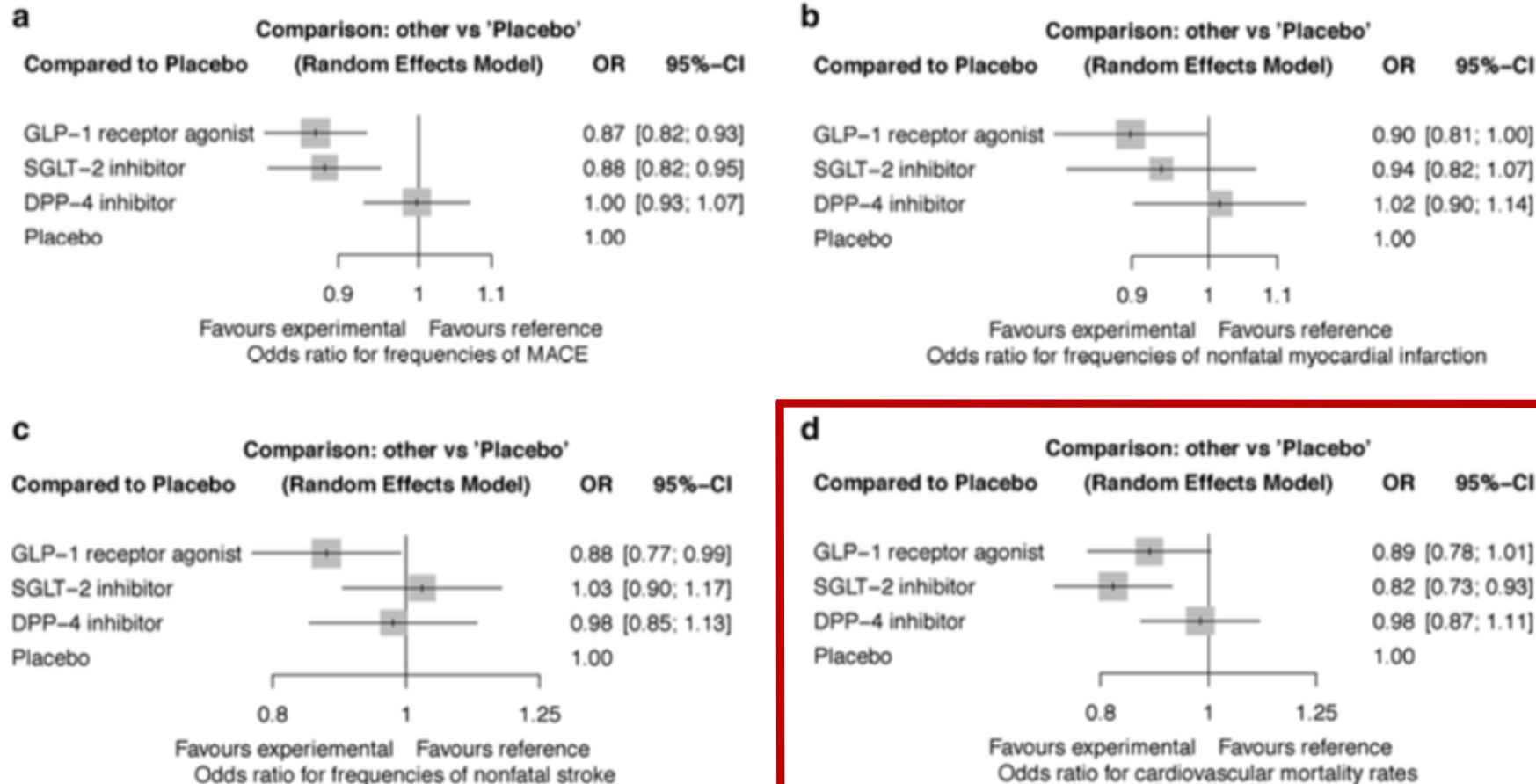


Figure 3. Heart failure hospitalization (HHF), HHF and cardiovascular (CV) death, and major adverse cardiovascular event (MACE) relative risk (RR) reduction percentages in the Dapagliflozin Effect on Cardiovascular Events (DECLARE-TIMI 58), Canagliflozin Cardiovascular Assessment Study (CANVAS), and Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME) trials. Statistical outcomes displayed as RR reduction percentage, p-value. RR reduction percentages were calculated from hazard ratios.

SGLT-2 inhibitors vs GLP-1 receptor agonists



SGLT-2 inhibitors vs GLP-1 receptor agonists

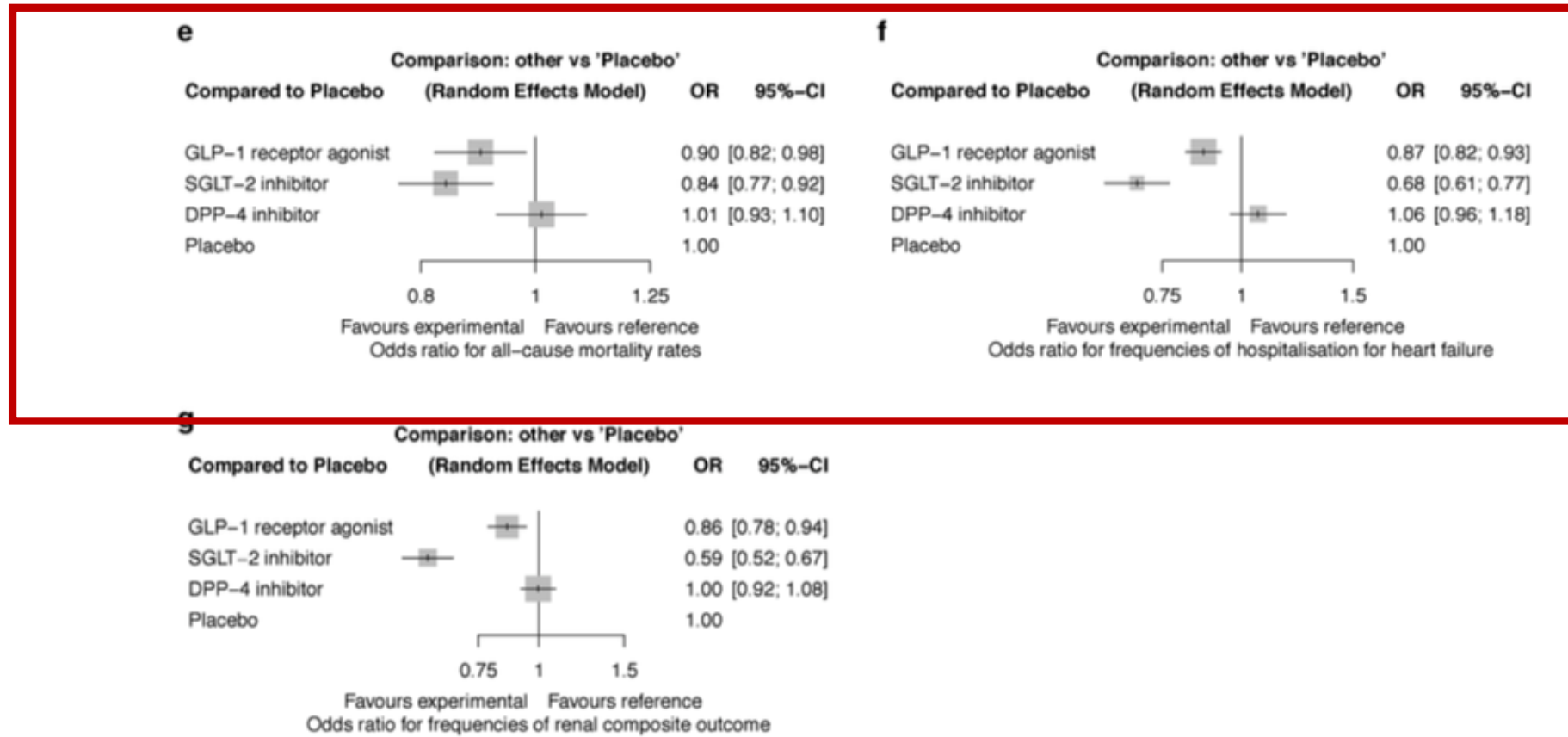
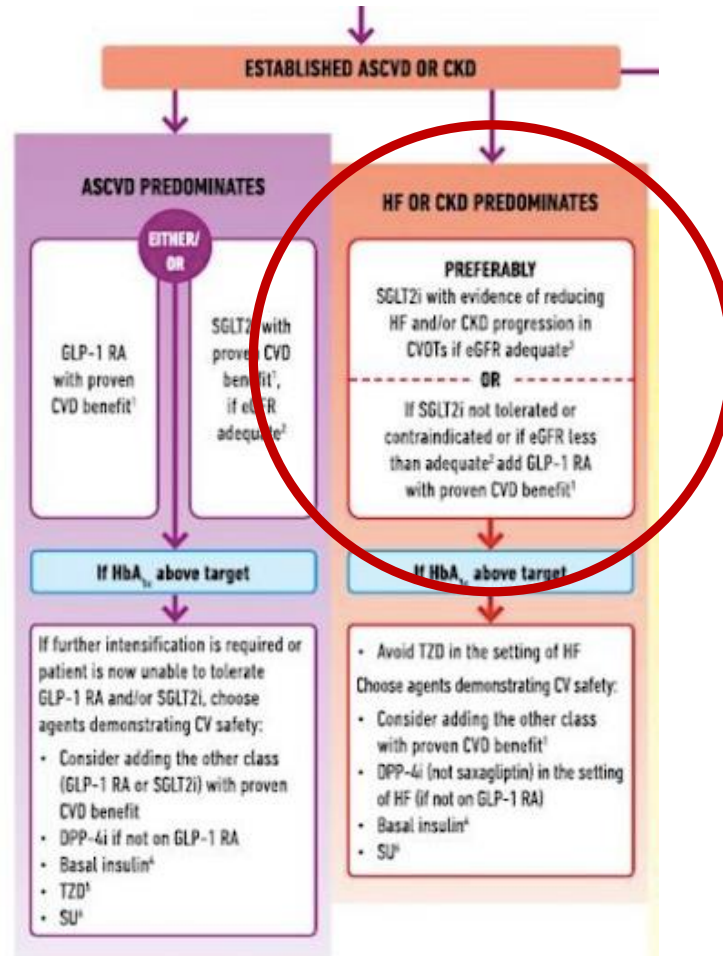


Fig. 2 Risk of outcomes with different antidiabetic drug classes compared to placebo. **a** MACE (major adverse cardiovascular events). **b** Nonfatal myocardial infarction. **c** Nonfatal stroke. **d** Cardiovascular mortality. **e** All-cause mortality. **f** Hospitalisation for heart failure. **g** Renal composite outcome

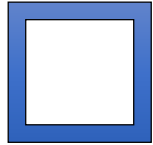
SGLT-2 inhibitors vs GLP-1 receptor agonists



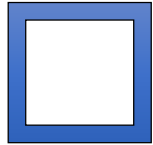
SGLT-2 inhibitors are the first line of treatment in patients with heart failure

Davies MJ, et al. Diabetologia 2018;61:2461–2498.

What therapy to suggest?



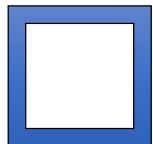
Dapagliflozin 10 mg: 1 tb qt +
long-acting metformin 1000 mg: 1 tb qt



Liraglutide 1.8 mg: 1 inj. qt +
long-acting metformin 1000 mg: 1 tb qt



Empagliflozin 10 mg: 1 tb qt +
long-acting metformin 1000 mg: 1 tb qt



Semaglutide 0.5 mg: 1 inj. weekly + long-
acting metformin 1000 mg: 1 tb qt

Laboratory tests (04.09.2019)

HbA1c: 7.4%; total cholesterol: 178 mg/dl; HDL: 39 mg/dl; triglycerides: 164 mg/dl;
 LDLc: 107; creatinine: 1.14 mg/dl; GFR: 71 ml/min; Na⁺: 145 mEq/L; K⁺: 4 mEq/L; Urine test:
 glucose: 500 mg/dl

CV: 95 cm; weight: 92 Kg; height: 176 cm; **BMI: 29.7 Kg/m²**

Daily glucose profile

BB	AB	BL	AL	BD	AD
132			158	141	
	138	127			163
129			147	130	
	144	129	152		

BB/AB: before/after breakfast

BL/AL: before/after lunch

BD/AD: before/after dinner



Why is a SGLT-2 inhibitor better than a GLP-1 receptor agonist for this patient?

- **Better compliance** (oral vs subcutaneous injection)
- **Gastrointestinal tolerance**
- Major impact on hospitalization and death rates in patients with **heart failure**