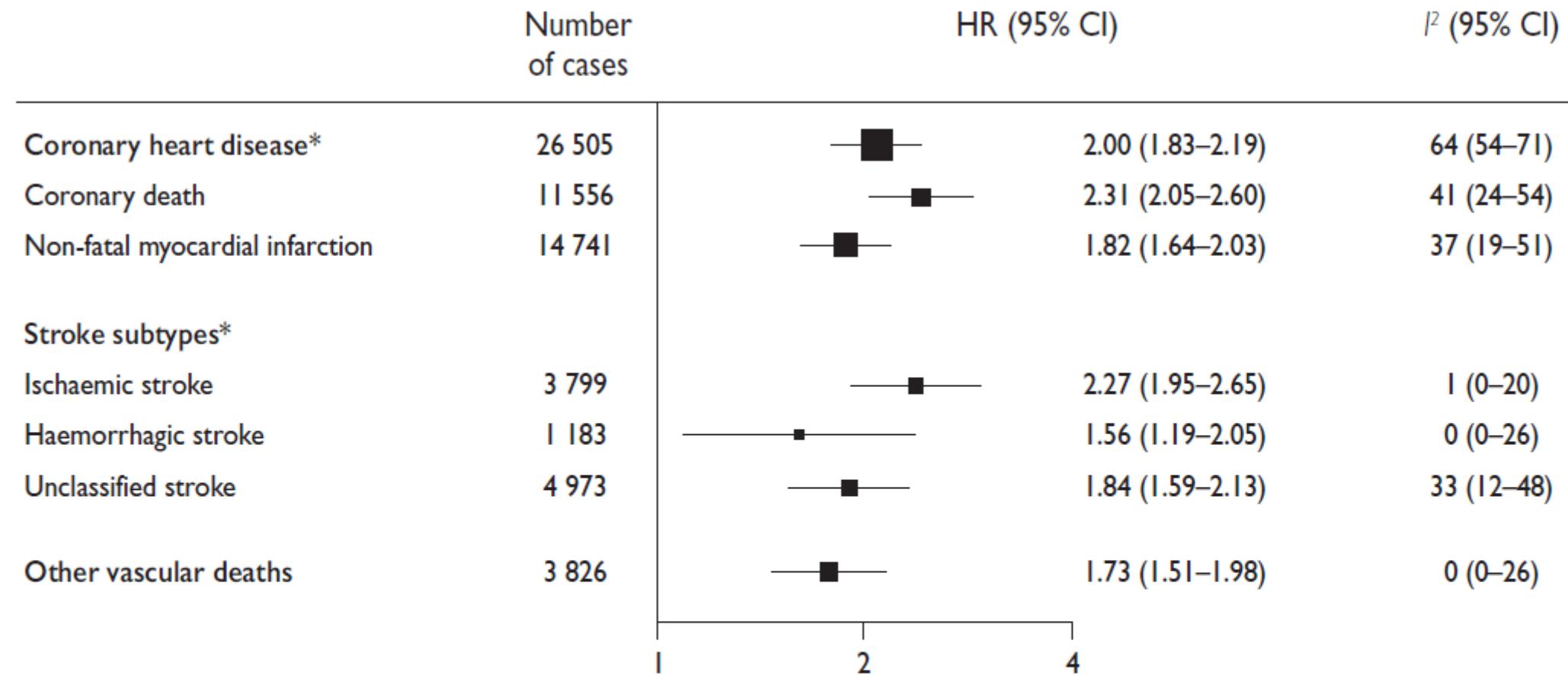




# Bénéfices des anti diabétiques au niveau cardio-vasculaire en 2023

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Cardiologie  
Hôpital de la Citadelle.



**Figure 1** Hazard ratios for vascular outcomes in people with vs. without diabetes mellitus at baseline, based on analyses of 530 083 patients. Reproduced with permission.<sup>23</sup> Hazard ratios were adjusted for age, smoking status, body mass index, and systolic blood pressure, and—where appropriate—stratified by sex and trial arm. The 208 coronary heart disease outcomes that contributed to the grand total could not contribute to the subtotals of coronary death or non-fatal myocardial infarction because there were <11 cases of these coronary disease subtypes in some studies. CI = confidence interval; HR = hazard ratio. \*Includes fatal and non-fatal events.

Class and Drug	Decrease in Glycated Hemoglobin Level	Mechanism	Selected Adverse Effects	Benefits and Considerations
<b>Sulfonylureas</b> Glyburide Glipizide Glimepiride	Up to 2.0%	Stimulate pancreas to release insulin over hours, activating sulfonylurea receptors on beta cells	Hypoglycemia Weight gain	High rate of secondary failure Low cost
<b>Biguanide</b> Metformin	Up to 2.0%	Inhibits hepatic glucose production through multiple mechanisms; also increases insulin-mediated glucose uptake in muscle, increases intestinal glucose uptake, and alters gut microbiota	Nausea, diarrhea, abdominal pain Vitamin B <sub>12</sub> deficiency Rare lactic acidosis (i.e., in severe chronic kidney disease, liver failure, hypoxic states)	Often considered first-line therapy Weight neutral (or potential weight loss) Low risk of hypoglycemia Low cost
<b>α-Glucosidase inhibitors</b> Acarbose Miglitol	Up to 1.0%	Inhibit intestinal α-glucosidase, slowing digestion and absorption of carbohydrates	Flatulence, diarrhea, abdominal pain Contraindicated with cirrhosis, chronic intestinal disease, inflammatory bowel disease	Weight neutral Low risk of hypoglycemia Taken before meals Low cost
<b>Meglitinides</b> Repaglinide Nateglinide	Up to 2.0%	Short-acting secretagogues that stimulate pancreas to release insulin, activating sulfonylurea receptors on beta cells	Hypoglycemia (less than with sulfonylureas) Weight gain	Taken before meals Low cost
<b>Thiazolidinediones</b> Pioglitazone Rosiglitazone	Up to 1.5%	Decrease insulin resistance in muscle, liver, and adipocytes, which results in increased insulin-dependent glucose disposal through activation of peroxisome proliferator–receptor gamma	Weight gain, edema Can cause or exacerbate heart failure in some patients Contraindicated in heart failure, NYHA class III or IV Fractures, macular edema, liver failure Warnings regarding bladder cancer (pioglitazone) or myocardial infarction (rosiglitazone)	Low risk of hypoglycemia Durability Increase in HDL cholesterol level Low cost
<b>DPP-4 inhibitors</b> Sitagliptin Saxagliptin Linagliptin Alogliptin	Up to 1.0%	Inhibit the enzyme that breaks down incretins, leading to increase in glucose-dependent pancreatic insulin release, decrease in glucagon release	Nausea, diarrhea Upper respiratory symptoms Possible pancreatitis† Rare severe joint pains Warning regarding heart failure (saxagliptin, alogliptin)	Weight neutral Low risk of hypoglycemia High cost

## GLP-1RAs

**ViCTOZA®**  
liraglutide injection 1.2 mg | 1.8 mg

**OZEMPIC®**  
semaglutide injection

**trulicity**  
dulaglutide (rDNAorigin) injection

**RYBELSUS®**  
semaglutide tablets

## SGLT2i

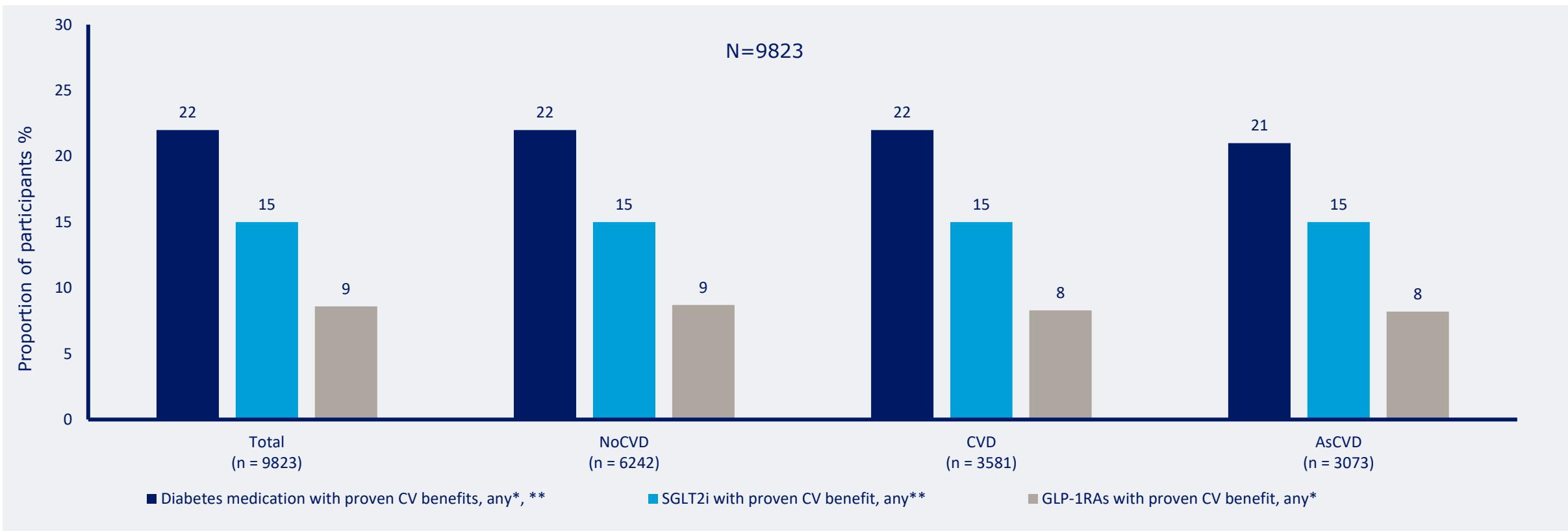
**Jardiance®**  
(empagliflozin) tablets  
10 mg/25 mg

**forxiga.**  
(dapagliflozin)

**InVOKANA®**  
canagliflozin tablets

**Steglatro™**  
(ertugliflozin)  
5 mg, 15 mg tablets

# Only 2 in 10 patients of the CAPTURE study population received a diabetes medication with proven CV benefit in line with international guidelines<sup>1</sup>



\*Liraglutide, Semaglutide, Dulaglutide   \*\*Empagliflozin, Canagliflozin, Dapagliflozin.

AsCVD, atherosclerotic cardiovascular disease; CV, cardiovascular, CVD, cardiovascular disease; GLP-1RA, glucagon-like peptide-1 receptor agonist; SGLT-2, sodium-glucose co-transporter-2.

<sup>1</sup>ADA Diabetes Care 2020;43(Suppl 1):S98–110

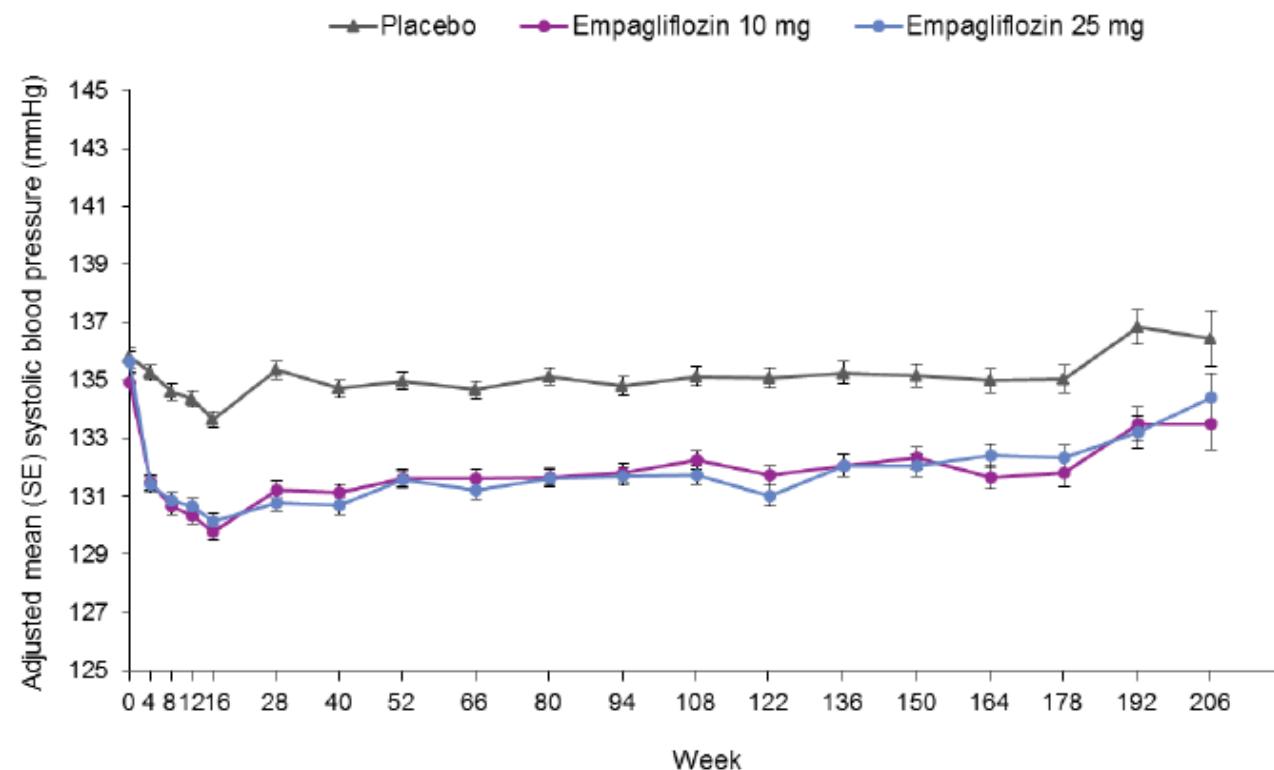
Mosenzon O, Alguwaihes A, Arenas Leon J.L., et al. CAPTURE: a cross-sectional study of the contemporary (2019) prevalence of cardiovascular disease in adults with type 2 diabetes across 13 countries. Abstract 158. Presented at the 56th Annual Meeting of the European Association of the Study of Diabetes, Macrovascular complications and beyond, 10:15 CEST on 24 September 2020.

# Bénéfices au niveau cardio-vasculaire des SGLT2i et GLP1a

- Prévention sur les autres facteurs de risque CV ( HTA, dyslipidémie)
- Prévention athérosclérose
- Prévention des évènements cardio-vasculaires
- Prévention et traitement de l'insuffisance cardiaque
- Prévention FA

HTA

## C. Systolic blood pressure



Placebo	2322	2235	2203	2161	2133	2073	2024	1974	1771	1492	1274	1126	981	735	450	171
Empagliflozin 10 mg	2322	2250	2235	2193	2174	2125	2095	2072	1853	1556	1327	1189	1034	790	518	199
Empagliflozin 25 mg	2323	2247	2221	2197	2169	2129	2102	2066	1878	1571	1351	1212	1070	842	528	216

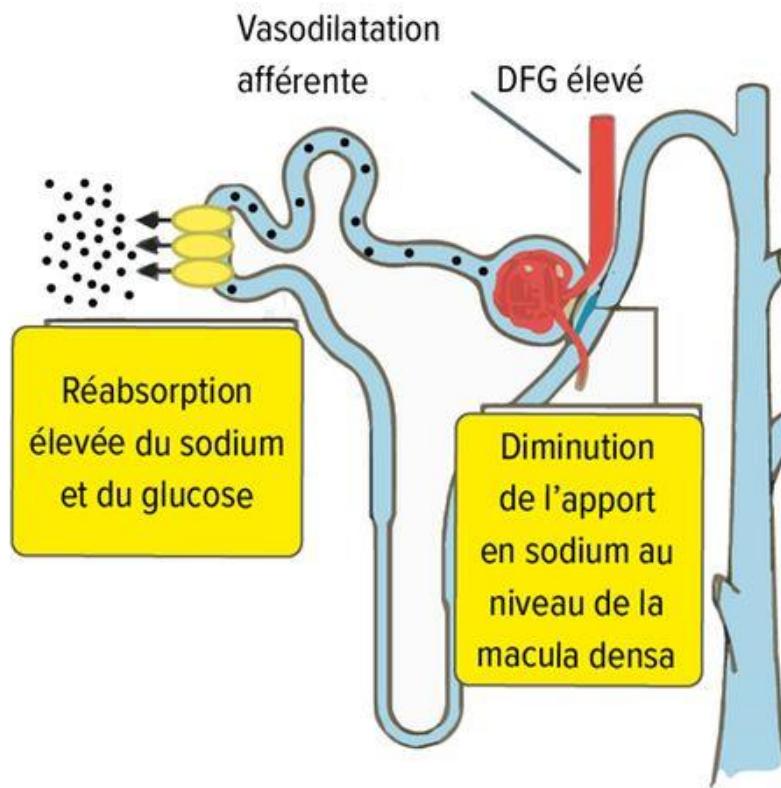
## SGLT2i et HTA

↓ poids et activité sympathique

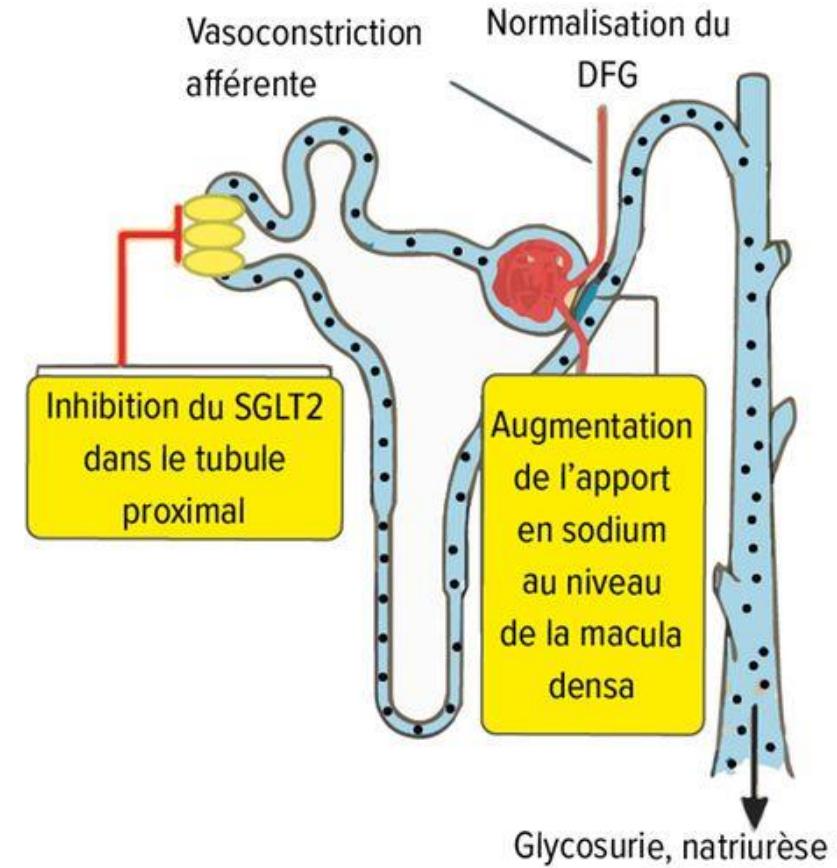
Effet natriurétique et glycosurie, diurèse osmotique

Effet sur la rigidité artérielle et fonction endothéliale?

### Hyperfiltration en cas de néphropathie diabétique



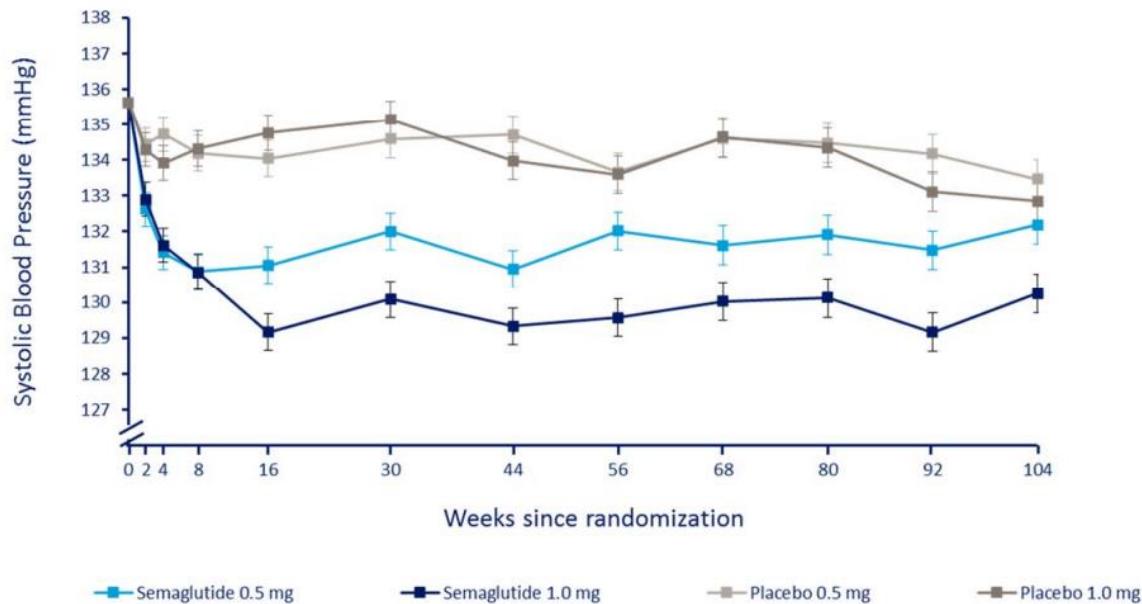
### Effet des inhibiteurs du SGLT2



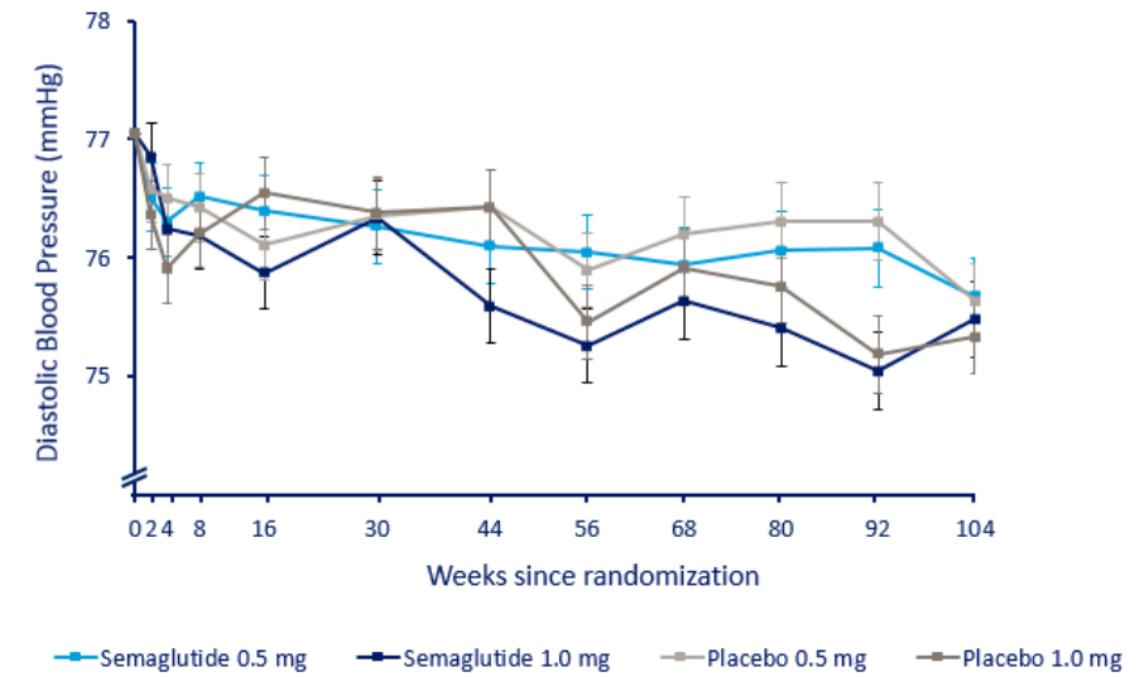
Supplement to: Marso SP, Bain SC, Consoli A, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med 2016;375:1834-44. DOI: 10.1056/NEJMoa1607141

**Figure S6.** Changes in Mean Systolic (Panel A) and Diastolic (Panel B) Blood Pressure Over Time

**A. Systolic blood pressure**



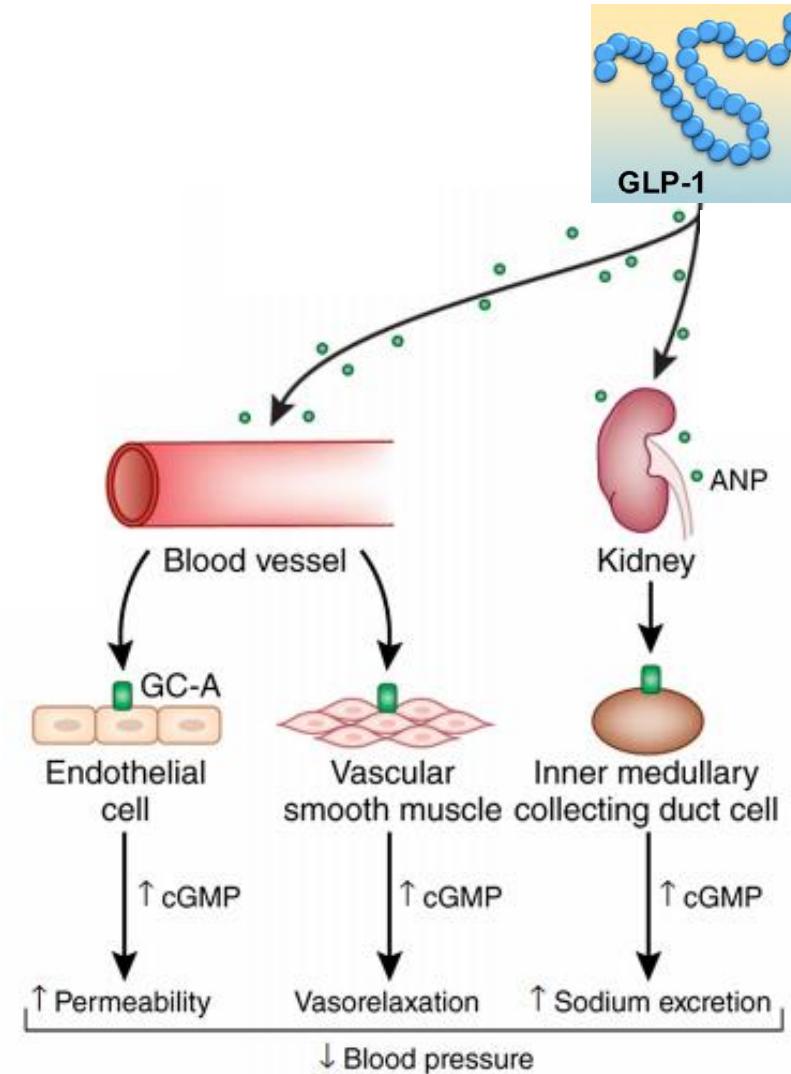
**B. Diastolic blood pressure**



HTA SUSTAIN 6

# How do GLP-1 RA reduce systolic blood pressure?

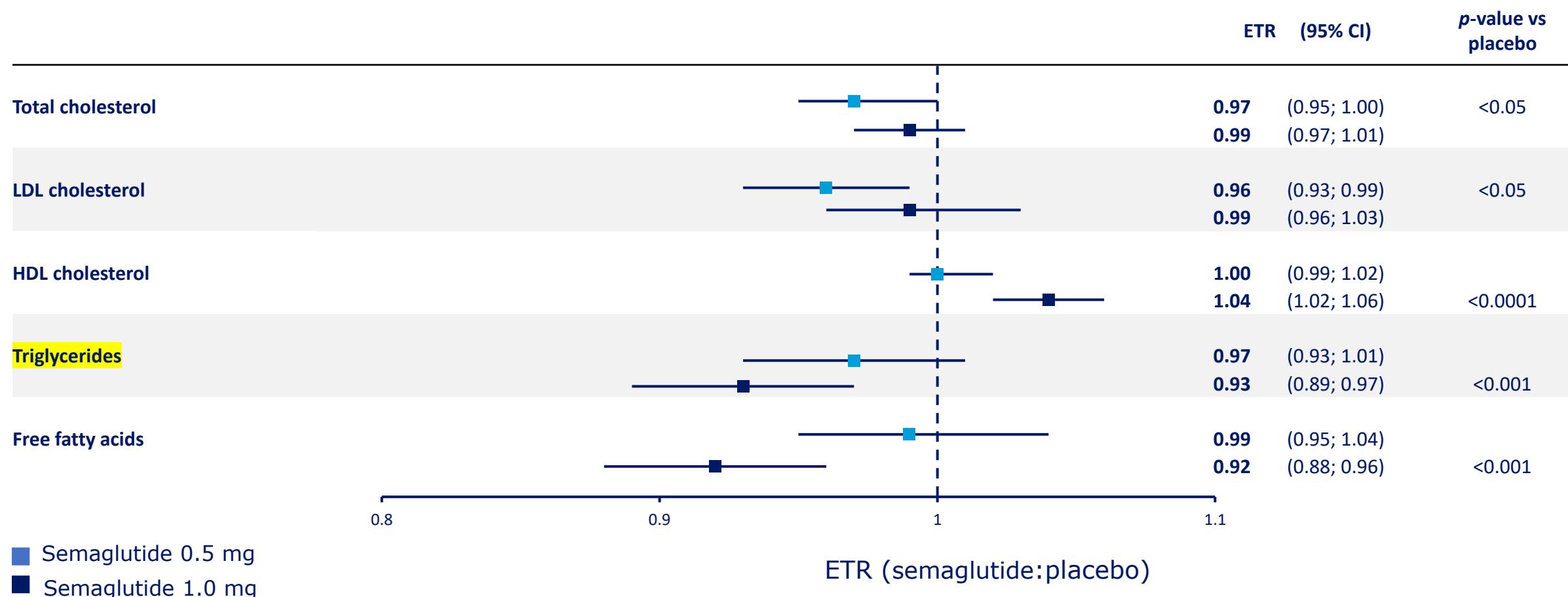
- Weight loss
- Diuresis and natriuresis
- Vascular relaxation/vasodilation
- Potential effects on RAAS
- CNS/neural mechanisms?



# Lipides

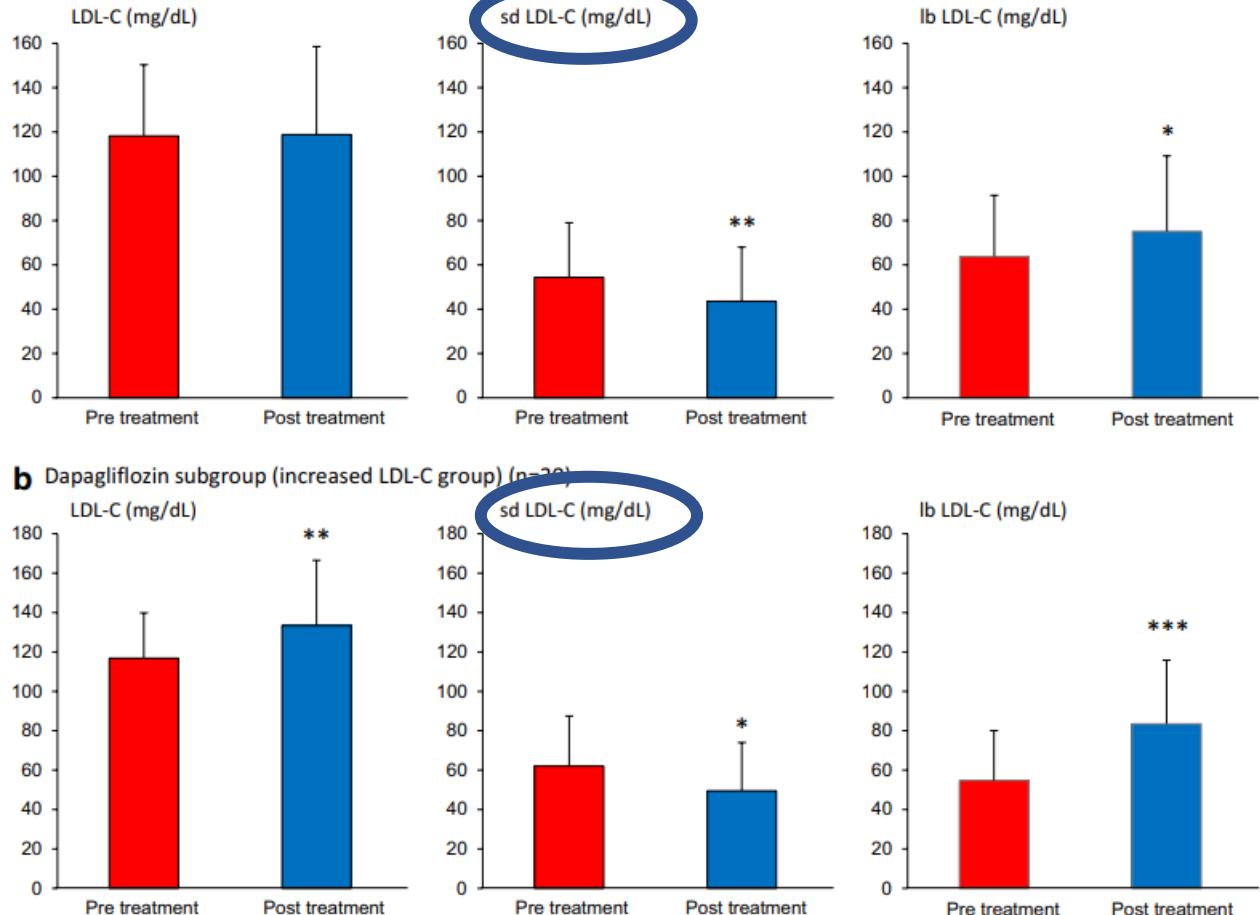
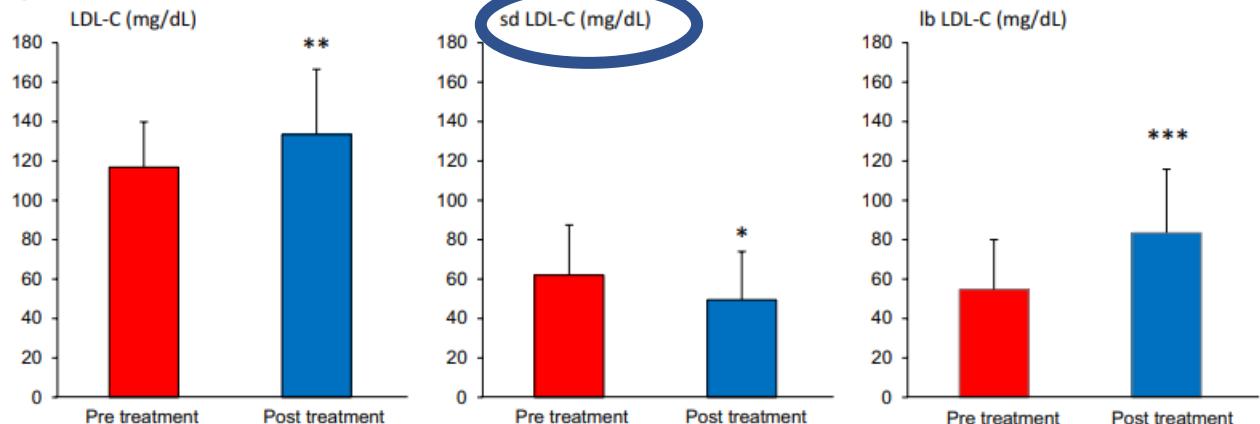
# Effect of semaglutide on lipids

## SUSTAIN 6 – Ratio to baseline

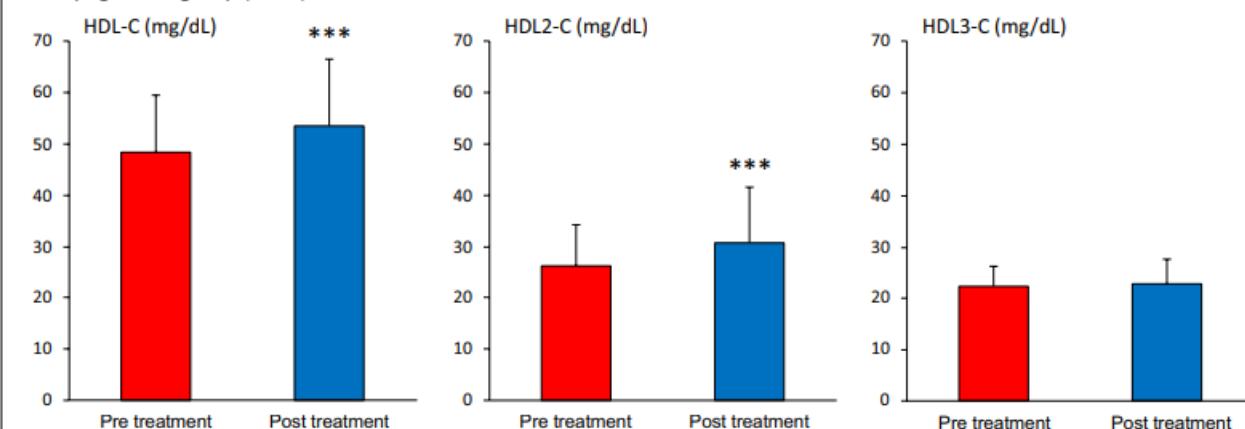


Data are ETRs to baseline, and treatment ratios with CI, based on in-trial data for scheduled visits for the full analysis set. Each parameter was analysed by a mixed model for repeated measures with treatment group (semaglutide 0.5 and 1.0 mg and corresponding placebo doses) and stratification (9 levels) as fixed factors and the corresponding baseline value of the parameter as a covariate, all nested within visit. Lipid parameters were analysed on log-scale. CI, confidence interval; ETR, estimated treatment ratio; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol

Marsø SP et al. *N Engl J Med* 2016; 375:1834–1844.

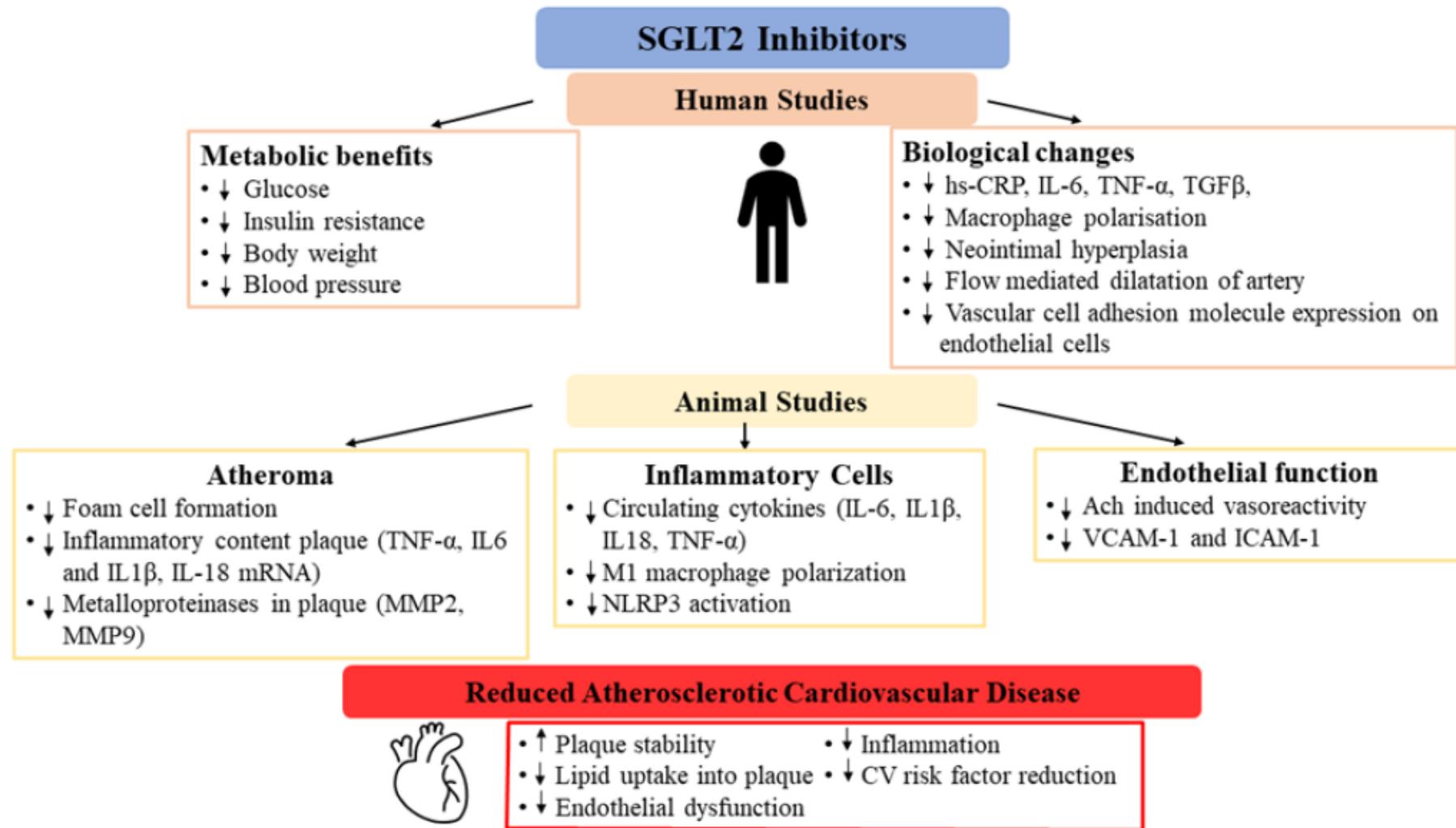
**a Dapagliflozin group (n=40)****b Dapagliflozin subgroup (increased LDL-C group) (n=20)****Dapagliflozin (n = 40)**

	Pre treatment	Post treatment	% change	p value <sup>a</sup>
Total-C (mg/dL)	193.5 ± 36.6	198.4 ± 45.9	2.5	0.863
TG (mg/dL)	152.6 ± 63.7	133.7 ± 75.8	-12.4	0.145
HDL-C (mg/dL)	48.4 ± 11.1	53.5 ± 13.0	10.5	<0.001*
LDL-C (mg/dL)	118.2 ± 32.1	118.8 ± 39.7	0.5	0.875
Non HDL-C (mg/dL)	145.1 ± 36.0	144.9 ± 43.9	-0.1	0.947

**a Dapagliflozin group (n=40)**

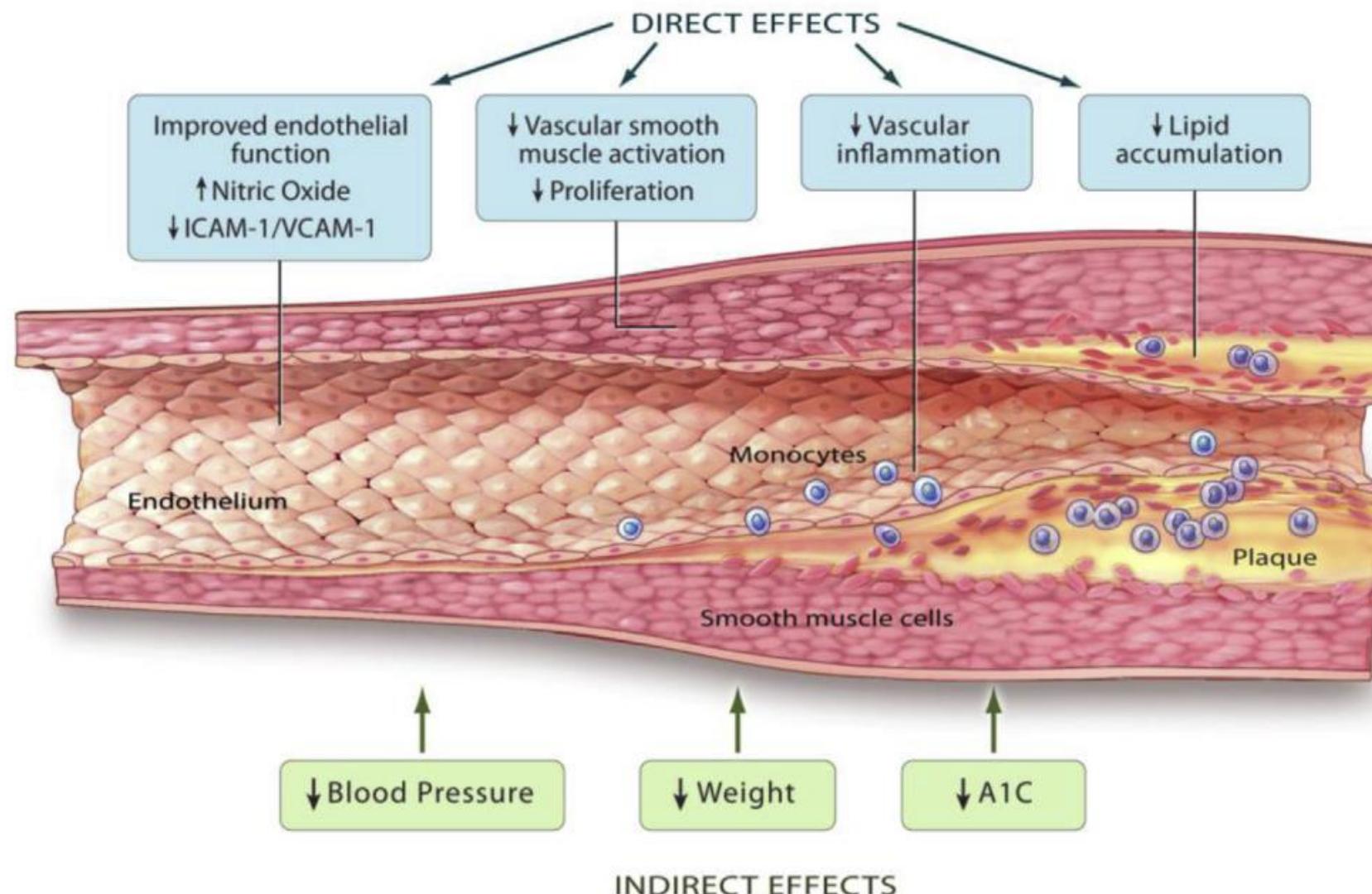
**Fig. 1** Effects of dapagliflozin on LDL-C and its subspecies. Data are expressed as mean ± standard deviation. LDL-C and its subspecies values in the dapagliflozin group (**a**) or subgroup whose LDL-C was increased by dapagliflozin treatment (**b**) were compared between before and after the treatment. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  (pre vs. post treatment values). LDL-C low-density lipoprotein-cholesterol, sd LDL-C small dense LDL-cholesterol, lb LDL-C large buoyant LDL-cholesterol

# Prévention athérosclérose



**Figure 1.** Mechanisms of action of SGLT2 inhibitors in atherosclerotic cardiovascular disease; Ach—acetylcholine; hs-CRP—high sensitivity C reactive protein; ICAM—intercellular adhesion molecule; IL—interleukin; NLRP3—NLR family pyrin domain containing 3; CV—cardiovascular, VCAM—vascular cell adhesion molecule; TNF—tumour necrosis factor; TGF—transforming growth factor.

# Mechanisms whereby GLP-1 analogues modify the risk of cardiovascular outcomes



# Prévention des évènements cardio-vasculaires

# Prévention des évènements cardio-vasculaires

GLP1a

9340 pts D2 ( $\text{HbA1c} \geq 7\%$ )

### Haut risque CV:

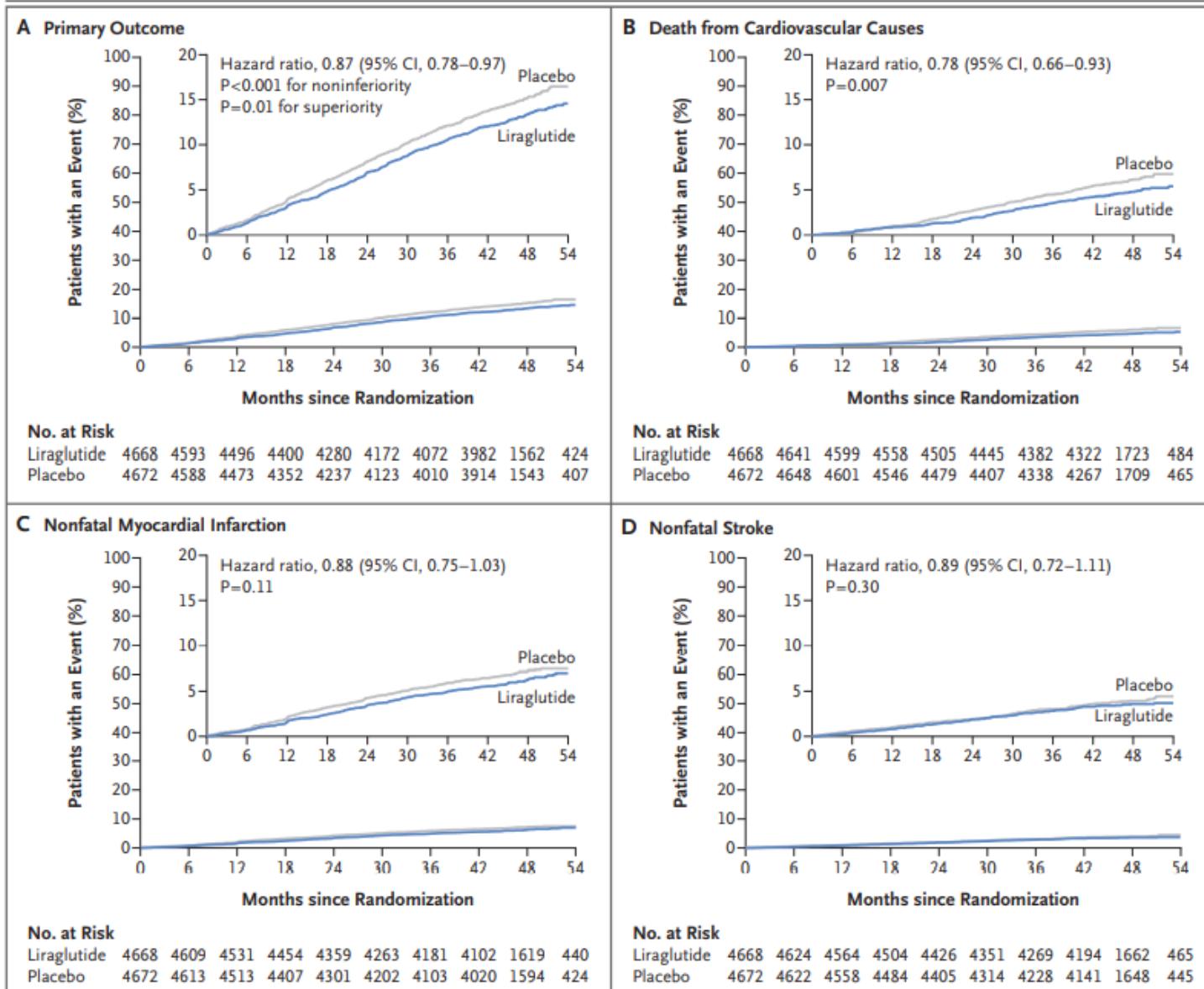
50 ans et une maladie CV (CAD, PAD, CVD, HF, IRC  $\geq 3$ )

60 ans et  $\geq 1$  FRCV  
(microalbuminurie, HTA,  
hypertrophie VG, dysfonction  
systolique ou diastolique VG, IPS < 9)

FUP med 3,8 ans

Primary Outcome: mortalité  
CV, MI, Stroke

81% ont une maladie CV



3297 pts diabète type 2 ( $\text{HbA1c} \geq 7\%$ )

Haut risque CV:

72% ont une maladie CV

*50 ans et une maladie CV (CAD, PAD, CVD, HF, IRC  $\geq 3$ )*

*60 ans et  $\geq 1$  FRCV*

Fup médian 2,1 ans

Semaglutide 0,5mg ou 1mg vs placebo

Primary Outcome: mortalité CV, MI, stroke

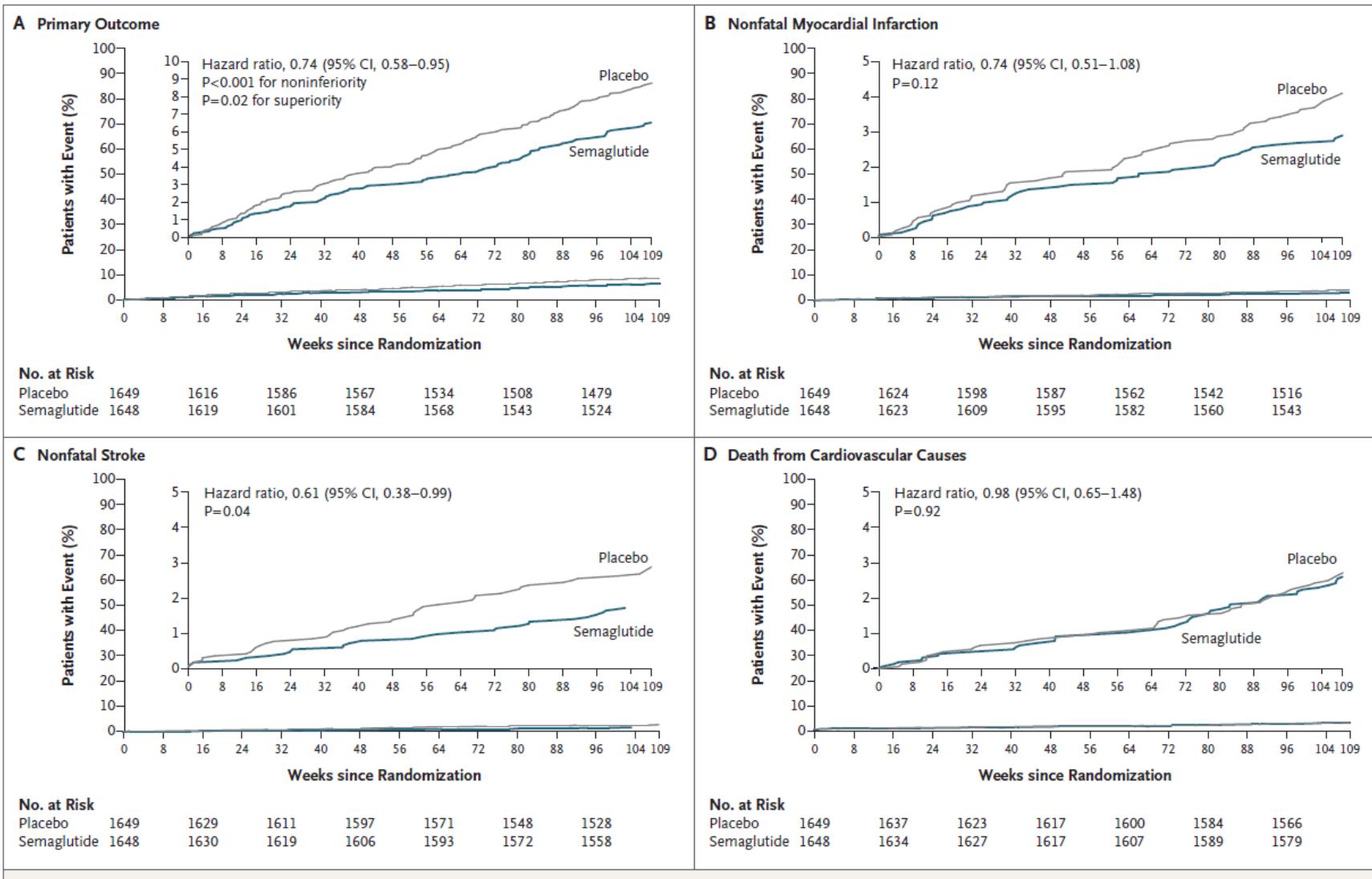


Figure 1. Cardiovascular Outcomes.

## REWIND

### Dulaglutide

9901 pts Diabète II, 66 ans HbA<sub>1c</sub>

7,2

Haut risque CV,

- 50 ans avec maladie cvasculaire
- 55 ans maladie cvasculaire ou HVG, ou GFR < 60ml ou albuminuria
- 60 ans et au moins 2 FRCV tabac, dyslipidémie, HTA, obésité abdo

**31% ont une maladie CV**

Dulaglutide 1,5mg sc OW vs placebo

Fup med 5,4 ans

Primary Outcome: mortalité CV, MI, stroke

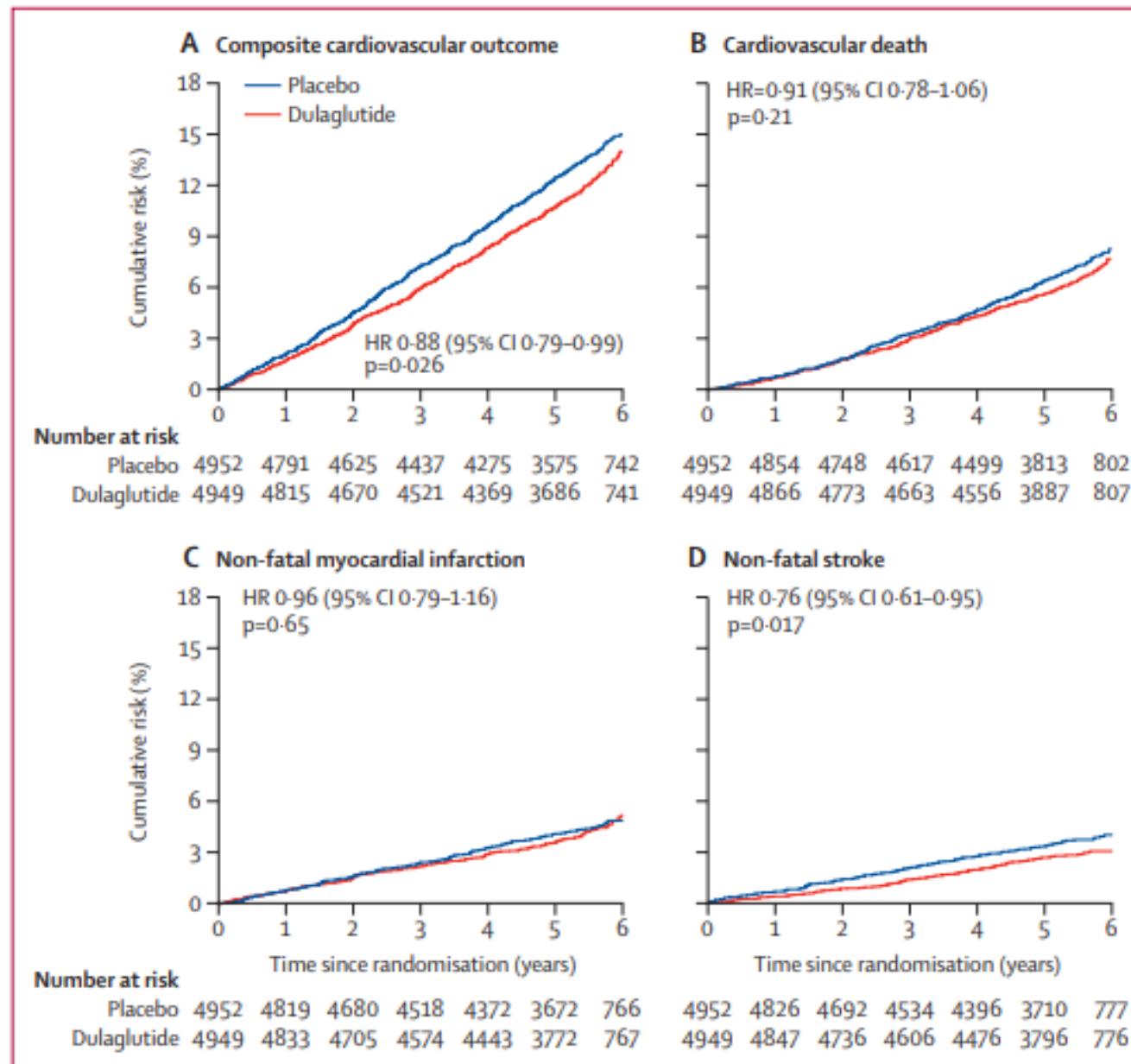


Figure 2: Cumulative incidence of cardiovascular outcomes  
HR=hazard ratio. HbA<sub>1c</sub>=glycated haemoglobin A<sub>1c</sub>.

3183 pts diabète II  
Semaglutide cible 14mg  
OD vs placebo

50 ans et une maladie CV  
(CAD, PAD, CVD, HF, IRC)  
≥3) 84% des pts

60 ans et ≥1FRCV

Fup median 15,9 mois

Primary Outcome:  
mortalité CV, MI, stroke

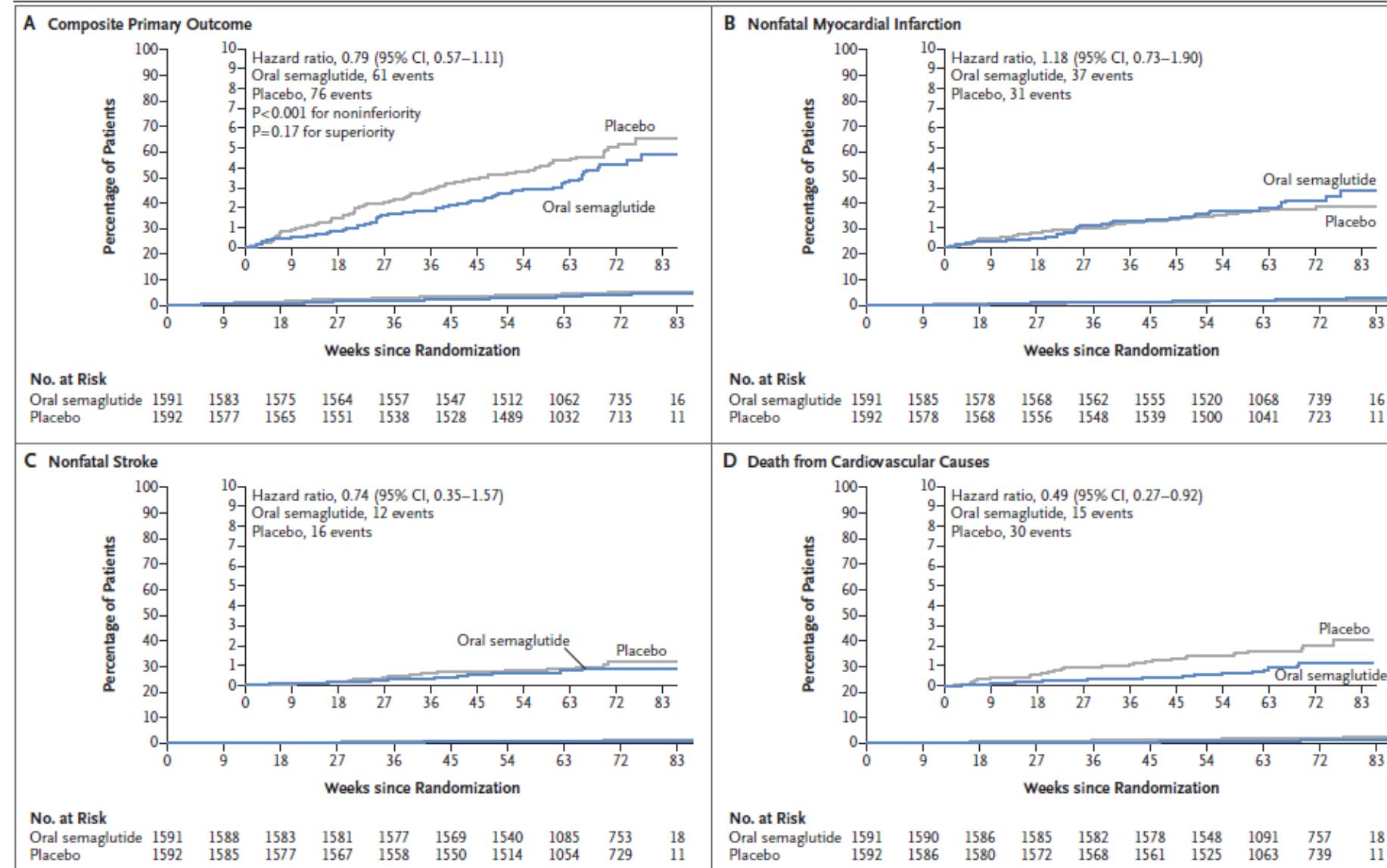
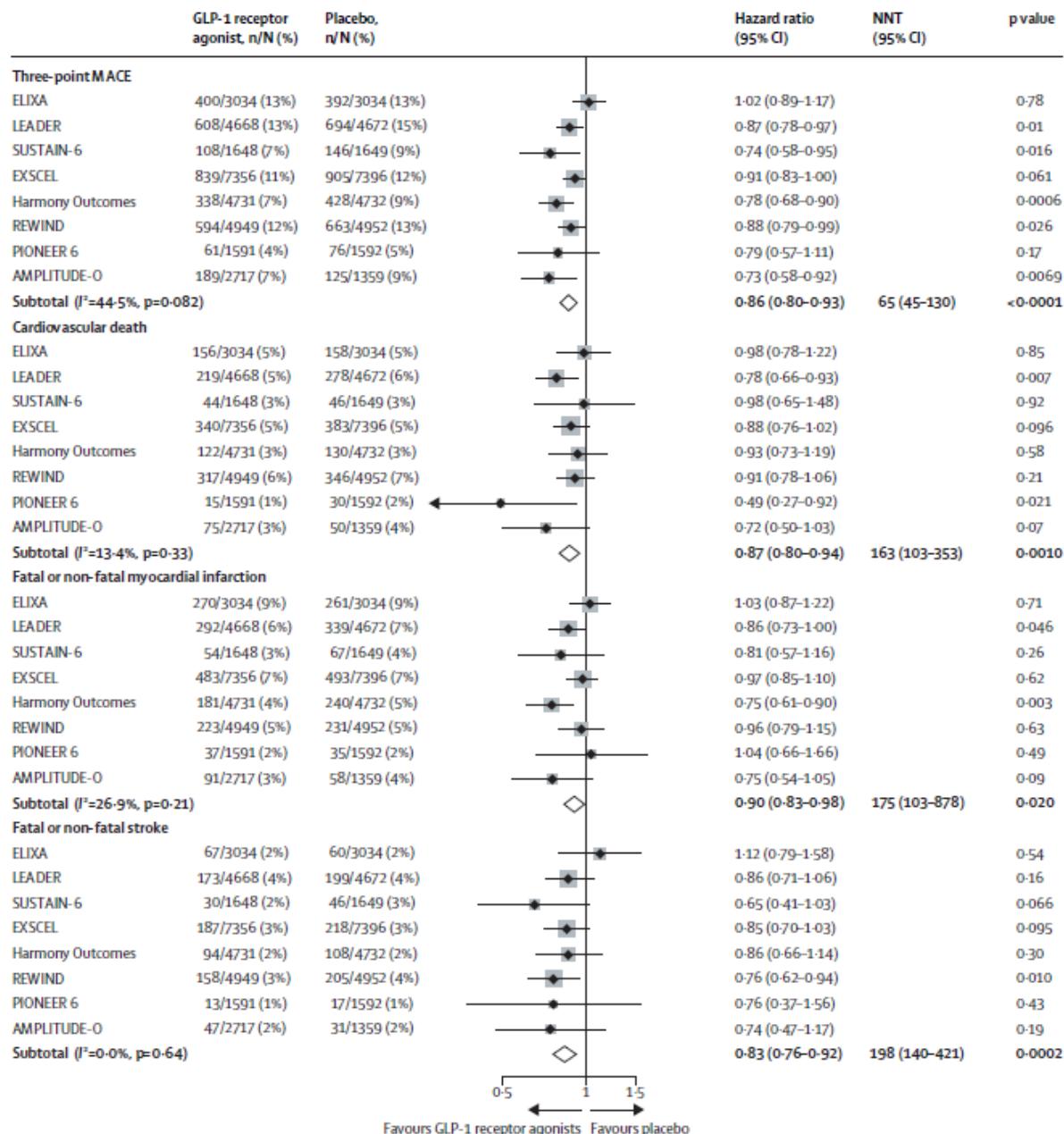


Figure 1. Cardiovascular Outcomes.

# Meta-analysis of GLP-1RA CVOTs



	ELIXA (n=6068)	LEADER (n=9340)	SUSTAIN-6 (n=3297)	EXSCEL (n=14 752)	Harmony Outcomes (n=9463)	REWIND (n=9901)	PIONEER 6 (n=3183)	AMPLITUDE-O (n=4076)
Drug	Lixisenatide	Liraglutide	Semaglutide	Exenatide	Albiglutide	Dulaglutide	Semaglutide	Efpeglenatide
Structural basis	Exendin-4	Human GLP-1	Human GLP-1	Exendin-4	Human GLP-1	Human GLP-1	Human GLP-1	Exendin-4

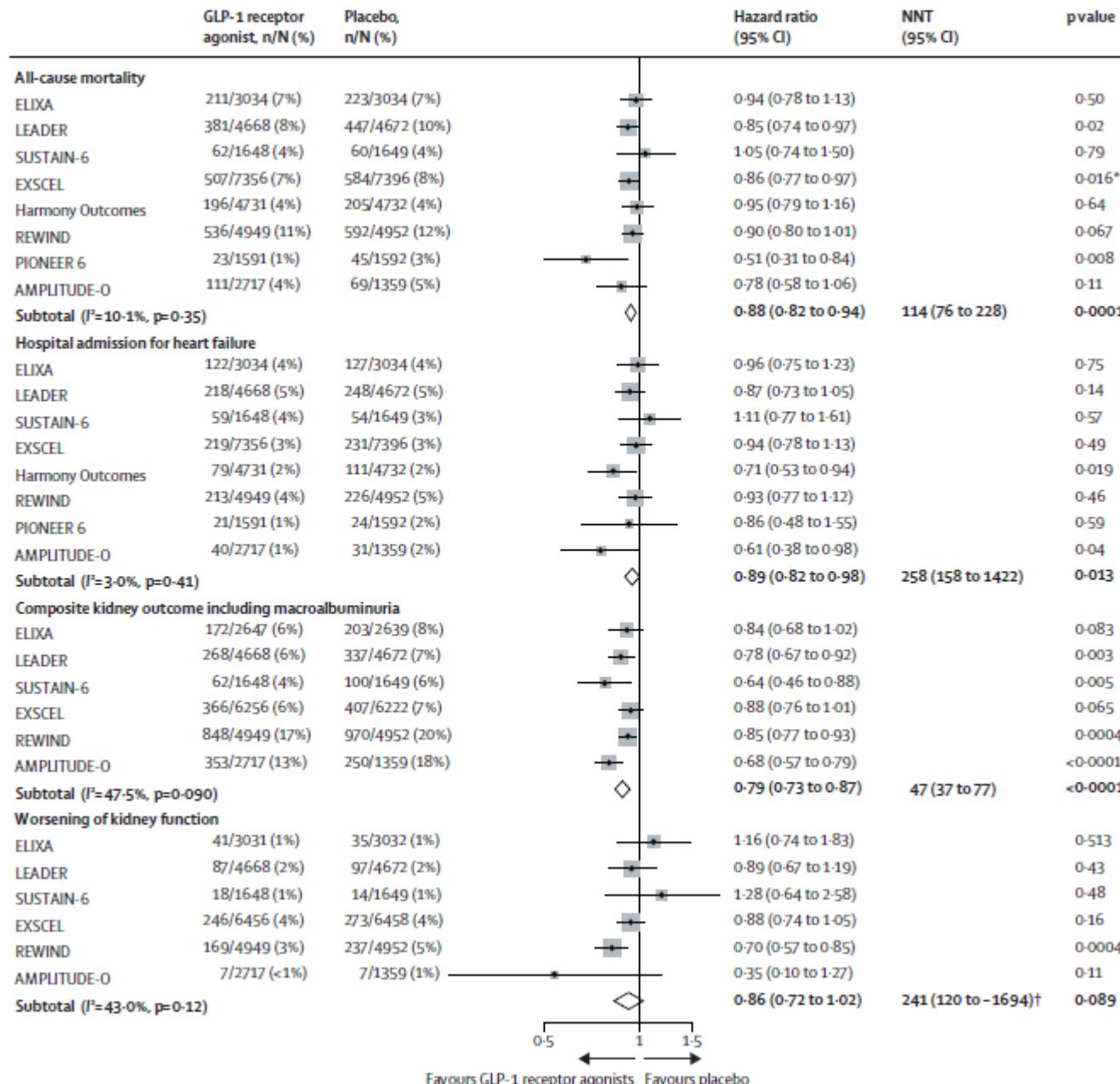
**MACE -14% (p<0.0001)**

**CV Death -13% (p=0.0010)**

**MI -10% (p=0.020)**

**Stroke -17% (p=0.0002)**

# Meta-analysis of GLP-1RA CVOTs



**All-cause mortality -12% (p=0.0001)**

**hospital admission for heart failure  
-11% (p=0.013)**

**kidney outcomes -21% (p<0.0001)**

Sattar N et al. Lancet Diabetes Endocrinol 2021 9: 653-62

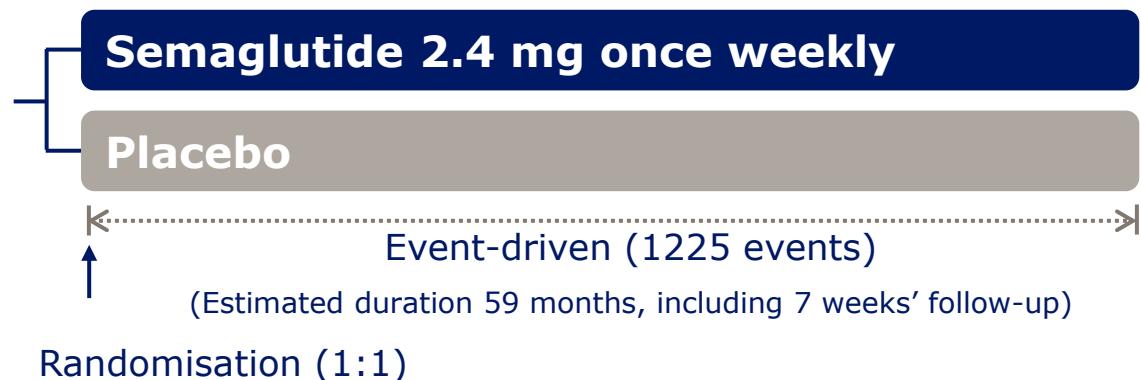
Composite kidney outcome consisting of development of macroalbuminuria, doubling of serum creatinine, or at least 40% decline in estimated glomerular filtration rate (eGFR), kidney replacement therapy, or death due to kidney disease

# SELECT

## SEMAGLUTIDE 2.4 MG OW

### 17,500 patients

- Male or female age  $\geq 45$  years
- BMI  $\geq 27 \text{ kg/m}^2$
- Established CVD:
  - MI  $\geq 60$  days ago
  - Stroke  $\geq 60$  days ago
  - Symptomatic PAD
- NYHA IV excluded
- Screening HbA<sub>1c</sub>  $< 6.5\%$



### Trial objective

To demonstrate that s.c. semaglutide 2.4 mg once weekly lowers the risk of MACE versus placebo both added to standard of care, in subjects with established CVD and overweight or obesity

### Primary endpoint

- Time from randomisation to first occurrence of MACE (nonfatal MI, nonfatal stroke, CV death)

### Confirmatory secondary endpoints

- Time from randomisation to (first) occurrence of CV death or all-cause death

### Trial information

- Superiority trial
- 90% power based on an assumed true risk reduction of 17% with semaglutide
- Assumed combined event rate: 2.0%
- Mean follow-up  $\approx 3$  years and 8 months

# Prévention des évènements cardio-vasculaires

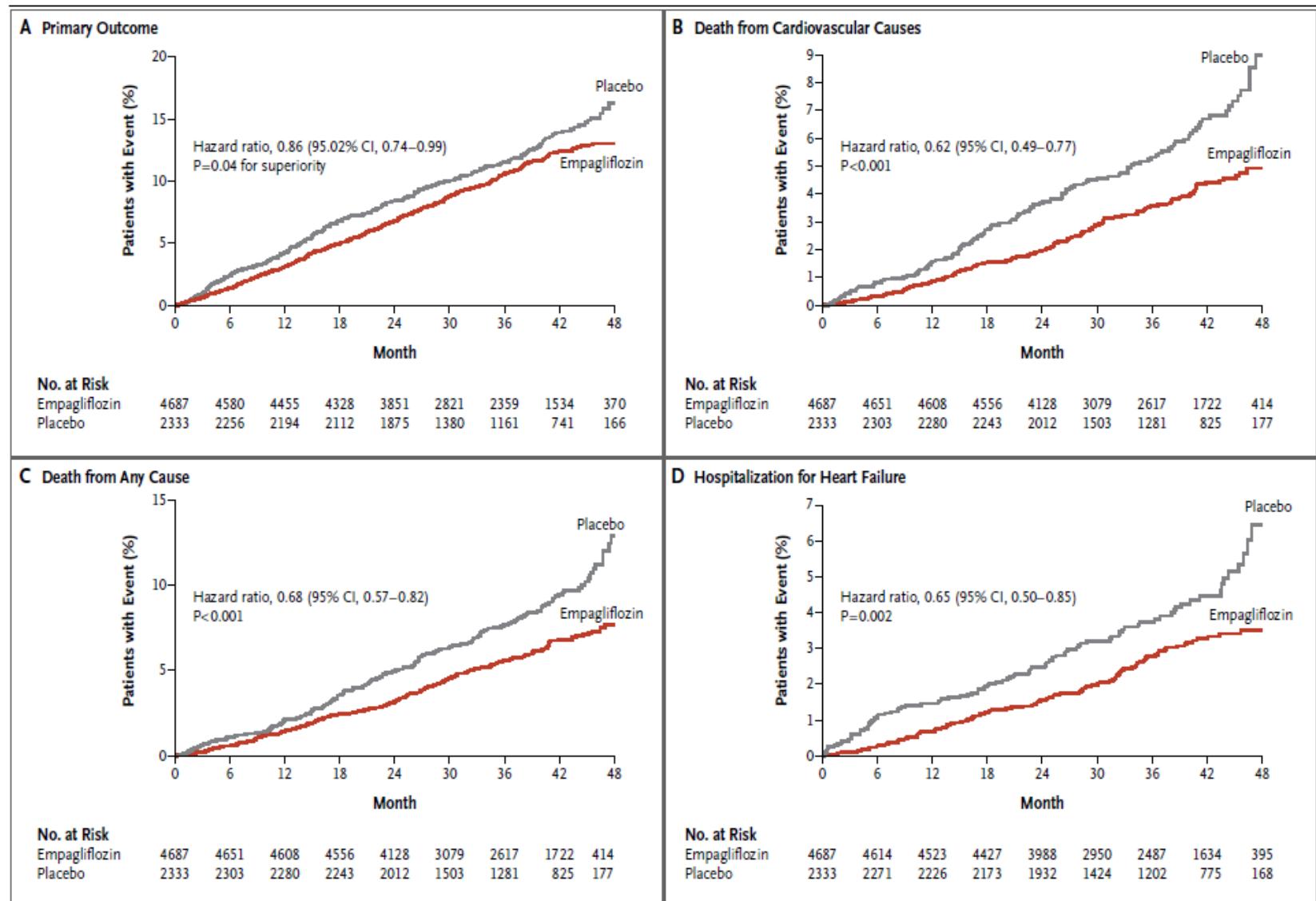
SGLT2i

Aucun effet sur MI ou stroke

7020 Pts Diabète type II  
Empagliflozin 10-25mg-  
placebo  
HbA1c  $\geq 7$

100% maladie CV  
préalable, 75% CAD,  
10% HF

Primary Outcome:  
mortalité CV, MI, stroke

**Figure 1. Cardiovascular Outcomes and Death from Any Cause.**

Shown are the cumulative incidence of the primary outcome (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke) (Panel A), cumulative incidence of death from cardiovascular causes (Panel B), the Kaplan-Meier estimate for death from any cause (Panel C), and the cumulative incidence of hospitalization for heart failure (Panel D) in the pooled empagliflozin group and the placebo group among patients who received at least one dose of a study drug. Hazard ratios are based on Cox regression analyses.

# Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes

DECLARE-TIMI 58 Investigators\*

N ENGL J MED 380;4 NEJM.ORG JANUARY 24, 2019

17160 pts à risque CV (CVD ou multiples FRCV)

63 ans, HbA1c 8,3, BMI 32

10186 sans CVD avérée

40% CVD, 32% CAD, 6% PAD

HF 9,9%

GFR>60ml/min

**Primary Safety Outcome:** MACE (mortalité CV, MI, ischemic stroke)

**Primary Efficacy Outcome:**

1° MACE

2° composite mortalité CV et hospitalisation pour HF

Fup médian 4,2 ans

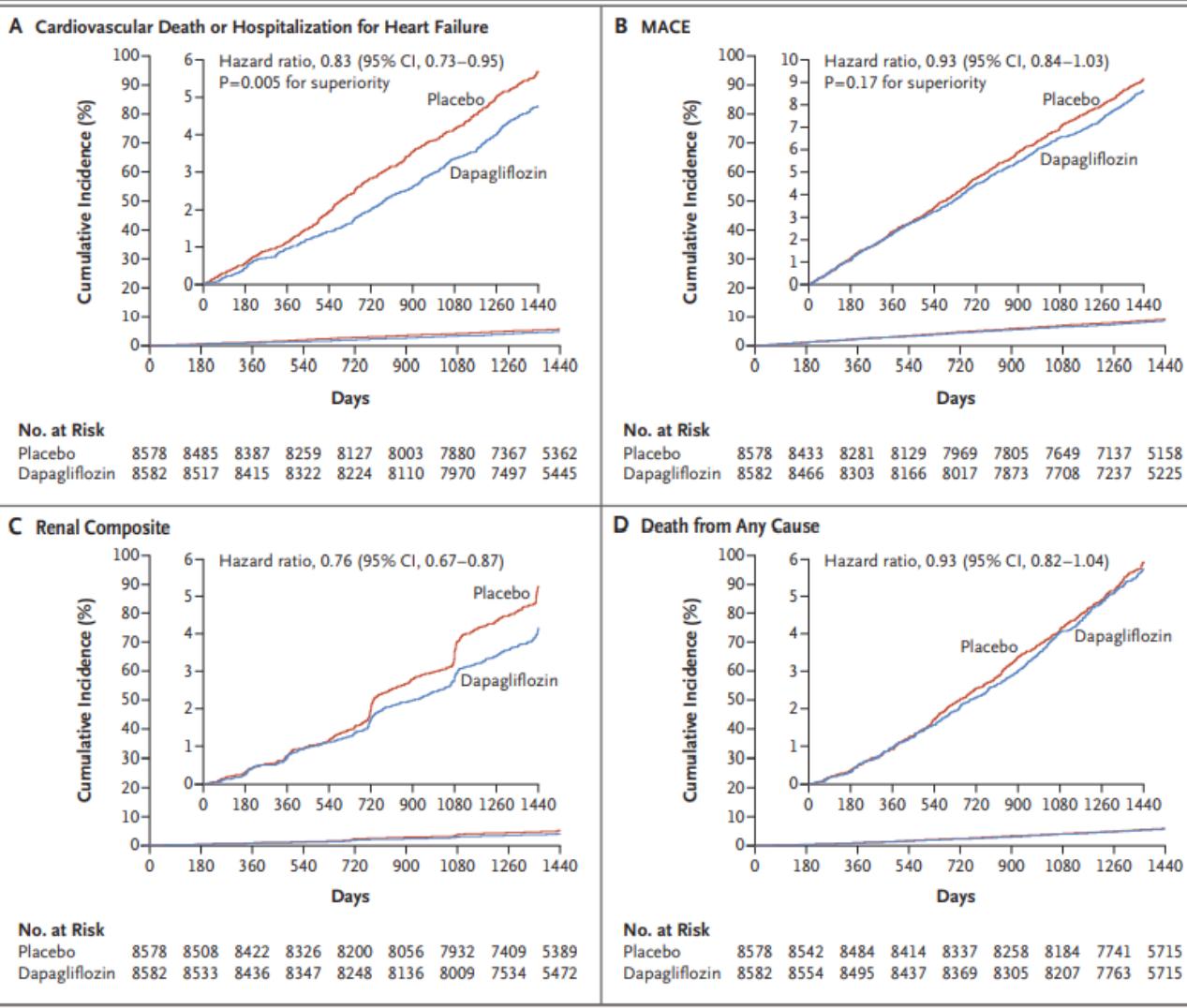


Figure 1. Major Cardiovascular and Renal Outcomes and Death from Any Cause.

Aucun effet stroke et NS pour MI

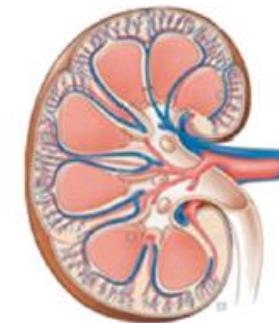
**FIG 2** Résultats cardiovasculaires et rénaux dans les quatre grandes études princeps

Les résultats sont exprimés par les «hazard ratio» avec intervalle de confiance à 95%.

En rose: différence non significative; en vert: différence statistiquement significative versus placebo.

CV: cardiovasculaire; hIC: hospitalisation pour insuffisance cardiaque; MACE: événements CV majeurs; MRC: maladie rénale chronique; MRC (1<sup>o</sup>): critère rénal composite combinant doublement de la créatinine (EMPA-REG OUTCOME, VERTIS CV, CANVAS) ou diminution du débit de filtration glomérulaire ≥ 40% (DECLARE-TIMI 58) avec progression versus l'insuffisance rénale terminale ou le décès d'origine rénale; MRC (2<sup>o</sup>): homogénéisation du critère rénal composite prenant en compte la diminution du débit de filtration glomérulaire ≥ 40% dans les quatre essais.

Rev Med Suisse 2021; 17: 1397-403



Essais cliniques	Critères cardiovasculaires			Critères rénaux	
	MACE	Décès CV	hIC	MRC (1 <sup>o</sup> )	MRC (2 <sup>o</sup> )
EMPA-REG OUTCOME	0,86 (0,74-0,99)	0,62 (0,49-0,77)	0,65 (0,50-0,85)	0,55 (0,41-0,73)	0,55 (0,41-0,73)
CANVAS	0,86 (0,75-0,97)	0,87 (0,72-1,06)	0,67 (0,52-0,87)	0,60 (0,47-0,77)	0,60 (0,47-0,77)
DECLARE-TIMI 58	0,93 (0,84-1,03)	0,98 (0,82-1,17)	0,73 (0,61-0,88)	0,53 (0,43-0,66)	0,53 (0,43-0,66)
VERTIS CV	0,97 (0,85-1,11)	0,92 (0,77-1,11)	0,70 (0,54-0,90)	0,81 (0,63-1,04)	0,66 (0,50-0,88)

Etudes spécifiques insuffisance cardiaque

	EMPEROR-Reduced		DAPA-HF	
	Empagliflozin	Placebo	Dapagliflozin	Placebo
Number of participants	1863	1867	2373	2371
Age, years	67·2 (10·8)	66·5 (11·2)	66·2 (11·0)	66·5 (10·8)
Sex				
Men	1426 (76·5%)	1411 (75·6%)	1809 (76·2%)	1826 (77·0%)
Women	437 (23·5%)	456 (24·4%)	564 (23·8%)	545 (23·0%)
NYHA functional classification				
II	1399 (75·1%)	1401 (75·0%)	1606 (67·7%)	1597 (67·4%)
III	455 (24·4%)	455 (24·4%)	747 (31·5%)	751 (31·7%)
IV	9 (0·5%)	11 (0·6%)	20 (0·8%)	23 (1·0%)
Mean LVEF, %	27·7 (6·0)	27·2 (6·1)	31·2 (6·7)	30·9 (6·9)
NT-pro BNP, pg/mL	1887 (1077–3429)	1926 (1153–3525)	1428 (857–2655)	1446 (857–2641)
Medical history				
Hospitalisation for heart failure*	577 (31·0%)	574 (30·7%)	1124 (47·4%)	1127 (47·5%)
Diabetes†	927 (49·8%)	929 (49·8%)	1075 (45·3%)	1064 (44·9%)
eGFR, mL/min per 1·73 m²‡	61·8 (21·7)	62·2 (21·5)	66·0 (19·6)	65·5 (19·3)
Heart failure medications				
ACE inhibitor	867 (46·5%)	836 (44·8%)	1332 (56·1%)	1329 (56·1%)
ARB	451 (24·2%)	457 (24·5%)	675 (28·4%)	632 (26·7%)
Mineralocorticoid receptor antagonist	1306 (70·1%)	1355 (72·6%)	1696 (71·5%)	1674 (70·6%)
ARNI	340 (18·3%)	387 (20·7%)	250 (10·5%)	258 (10·9%)
Device therapy				
ICD or CRT-D	578 (31·0%)	593 (31·8%)	622 (26·2%)	620 (26·1%)
CRT-D or CRT-P	220 (11·8%)	222 (11·9%)	190 (8·0%)	164 (6·9%)

Data are n (%), mean (SD), or median (IQR). ACE=angiotensin converting enzyme. ARB=angiotensin receptor blocker. ARNI=angiotensin receptor neprilysin inhibitor. CRT-D=cardiac resynchronisation therapy defibrillator. CRT-P=cardiac resynchronisation therapy pacemaker. eGFR=estimated glomerular filtration rate. ICD=implantable cardiac defibrillator. LVEF=left ventricular ejection fraction. NT-pro BNP=N-terminal pro B-type natriuretic peptide. NYHA=New York Heart Association. \*For EMPEROR-Reduced: preceding 12 months. †Determined by a combination of medical history and pre-treatment glycated haemoglobin. ‡Chronic Kidney Disease Epidemiology Collaboration formula.

Table 1: Overview of main characteristics of the two trial populations at baseline

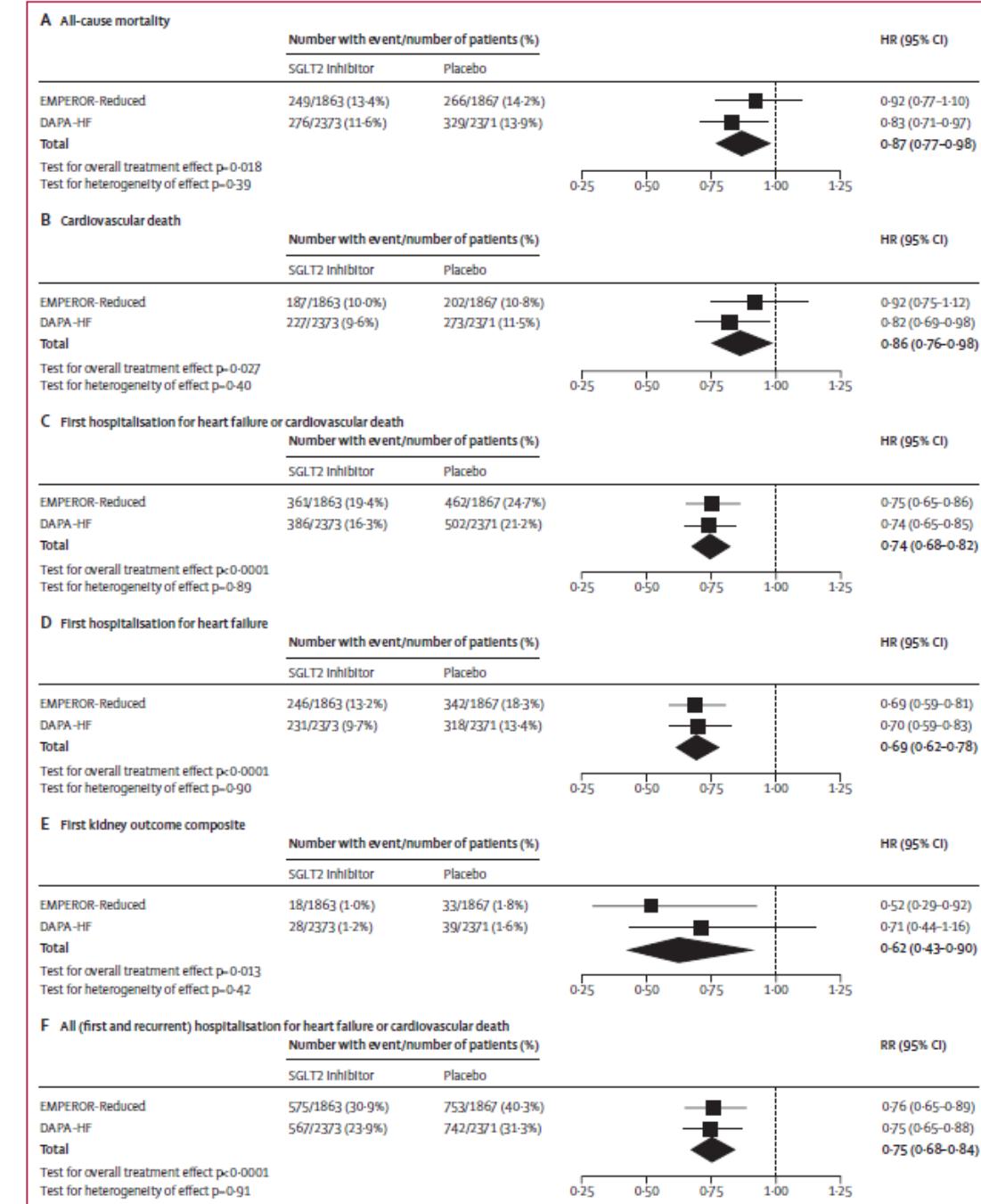


Figure 1: Meta-analysis of EMPEROR-Reduced and DAPA-HF trials

	EMPEROR-Reduced	DAPA-HF		
	Empagliflozin			
Number of participants	1863			
Age, years	67.2 (10.8)			
Sex				
Men	1426 (76.5%)			
Women	437 (23.5%)			
NYHA functional classification				
II	1399 (75.1%)			
III	455 (24.4%)			
IV				
Mean LVEF, %	HFrEF			
NT-pro BNP, pg/mL				
Medical history				
Hospitalisation for heart failure*				
Diabetes†				
eGFR, mL/min				
Heart failure risk score				
ACE inhibitor				
ARB	451 (24.2%)	457 (24.5%)	675 (28.4%)	632 (26.7%)
Mineralocorticoid receptor antagonist	1306 (70.1%)	1355 (72.6%)	1696 (71.5%)	1674 (70.6%)
ARNI	340 (18.3%)	387 (20.7%)	250 (10.5%)	258 (10.9%)
Device therapy				
ICD or CRT-D	578 (31.0%)	593 (31.8%)	622 (26.2%)	620 (26.1%)
CRT-D or CRT-P	220 (11.8%)	222 (11.9%)	190 (8.0%)	164 (6.9%)

Data are n (%), mean (SD), or median (IQR). ACE=angiotensin converting enzyme. ARB=angiotensin receptor blocker. ARNI=angiotensin receptor neprilysin inhibitor. CRT-D=cardiac resynchronisation therapy defibrillator. CRT-P=cardiac resynchronisation therapy pacemaker. eGFR=estimated glomerular filtration rate. ICD=implantable cardiac defibrillator. LVEF=left ventricular ejection fraction. NT-pro BNP=N-terminal pro B-type natriuretic peptide. NYHA=New York Heart Association. \*For EMPEROR-Reduced: preceding 12 months. †Determined by a combination of medical history and pre-treatment glycated haemoglobin. ‡Chronic Kidney Disease Epidemiology Collaboration formula.

Table 1: Overview of main characteristics of the two trial populations at baseline



## DAPA-HF

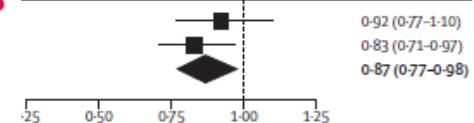
European Heart Journal (2021) 42, 3599–3726  
doi:10.1093/eurheartj/ehab368

### A All-cause mortality

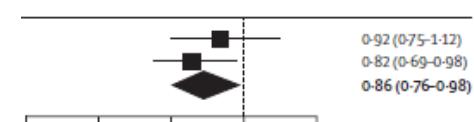
Number with event/number of patients (%)

HR (95% CI)

## ESC GUIDELINES



HR (95% CI)



HR (95% CI)



HR (95% CI)



HR (95% CI)

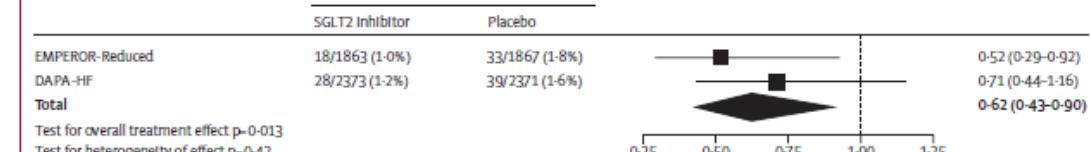
### Total

Test for overall treatment effect p<0.0001  
Test for heterogeneity of effect p=0.90

### E First kidney outcome composite

Number with event/number of patients (%)

HR (95% CI)

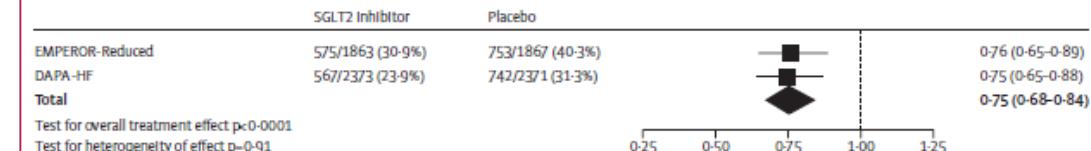


HR (95% CI)

### F All (first and recurrent) hospitalisation for heart failure or cardiovascular death

Number with event/number of patients (%)

RR (95% CI)



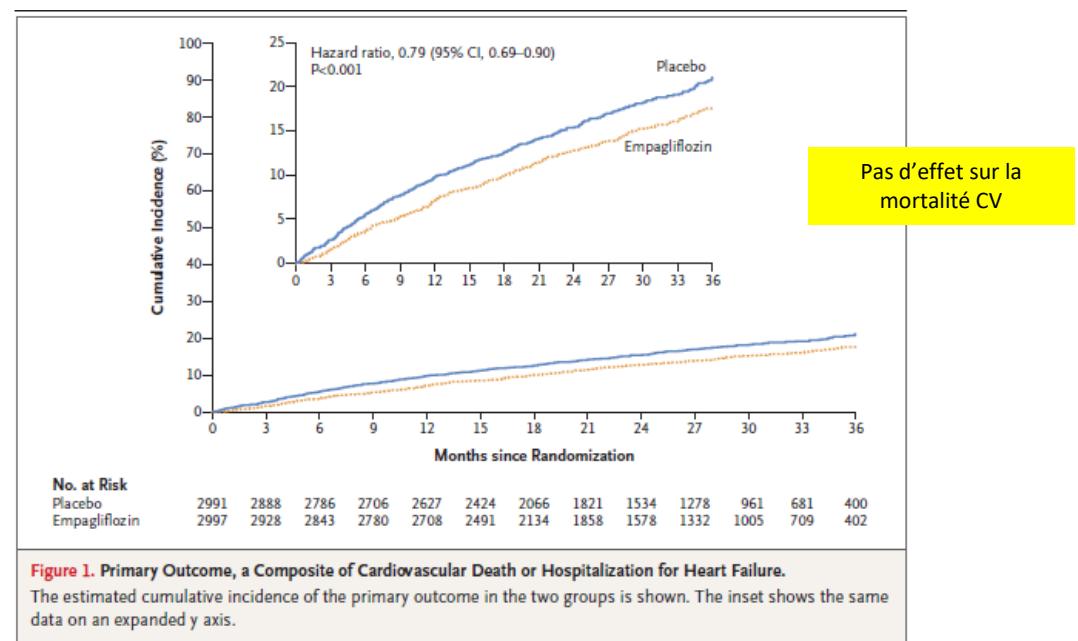
RR (95% CI)

Figure 1: Meta-analysis of EMPEROR-Reduced and DAPA-HF trials

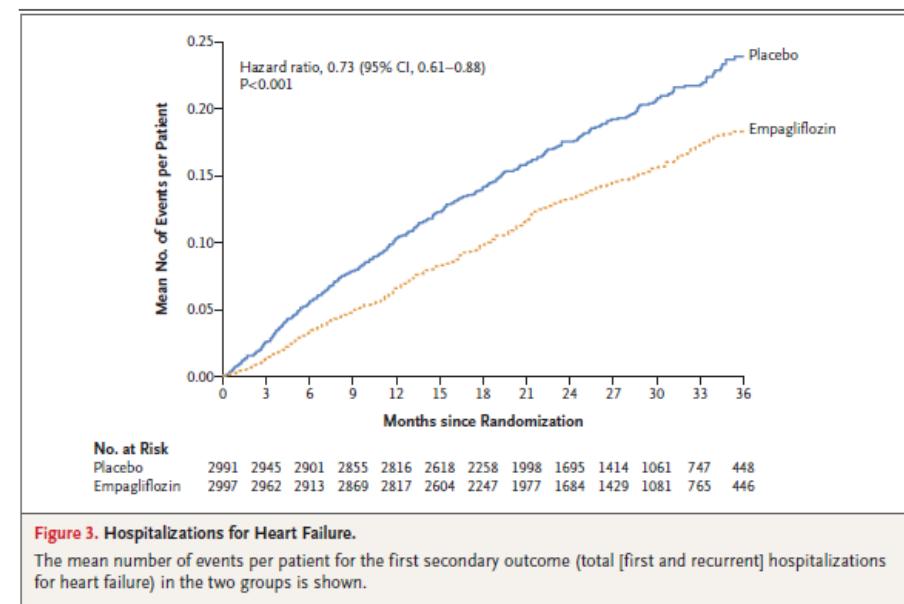
# Empagliflozin in Heart Failure with a Preserved Ejection Fraction

**Table 1.** Characteristics of the Patients at Baseline.\*

Characteristic	Empagliflozin (N=2997)	Placebo (N=2991)
Age — yr	71.8±9.3	71.9±9.6
NYHA functional classification — no. (%)		
Class I	3 (0.1)	1 (<0.1)
Class II	2432 (81.1)	2451 (81.9)
Class III	552 (18.4)	531 (17.8)
Class IV	10 (0.3)	8 (0.3)
Body-mass index‡	29.77±5.8	29.90±5.9
Heart rate — beats per minute	70.4±12.0	70.3±11.80
Systolic blood pressure — mm Hg	131.8±15.6	131.9±15.7
Left ventricular ejection fraction		
Mean left ventricular ejection fraction — %	54.3±8.8	54.3±8.8
Left ventricular ejection fraction >40% to <50% — no. (%)§	995 (33.2)	988 (33.0)
Left ventricular ejection fraction ≥50% to <60% — no. (%)	1028 (34.3)	1030 (34.4)
Left ventricular ejection fraction ≥60% — no. (%)	974 (32.5)	973 (32.5)
Median NT-proBNP (interquartile range) — pg/ml	994 (501–1740)	946 (498–1725)
Heart failure category — no. (%)		
Ischemic	1079 (36.0)	1038 (34.7)
Nonischemic	1917 (64.0)	1953 (65.3)
Cardiovascular history — no. (%)		
Hospitalization for heart failure during previous 12 mo	699 (23.3)	670 (22.4)
Atrial fibrillation	1543 (51.5)	1514 (50.6)
Diabetes mellitus	1466 (48.9)	1472 (49.2)
Hypertension	2721 (90.8)	2703 (90.4)
Mean eGFR — ml/min/1.73 m <sup>2</sup>	60.6±19.8	60.6±19.9
eGFR <60 ml/min/1.73 m <sup>2</sup> — no./total no. (%)	1504/2997 (50.2)	1484/2989 (49.6)



**Figure 1.** Primary Outcome, a Composite of Cardiovascular Death or Hospitalization for Heart Failure.  
The estimated cumulative incidence of the primary outcome in the two groups is shown. The inset shows the same data on an expanded y axis.



# DELIVER Trial

6200 pts

Hfpef FEVG >40%

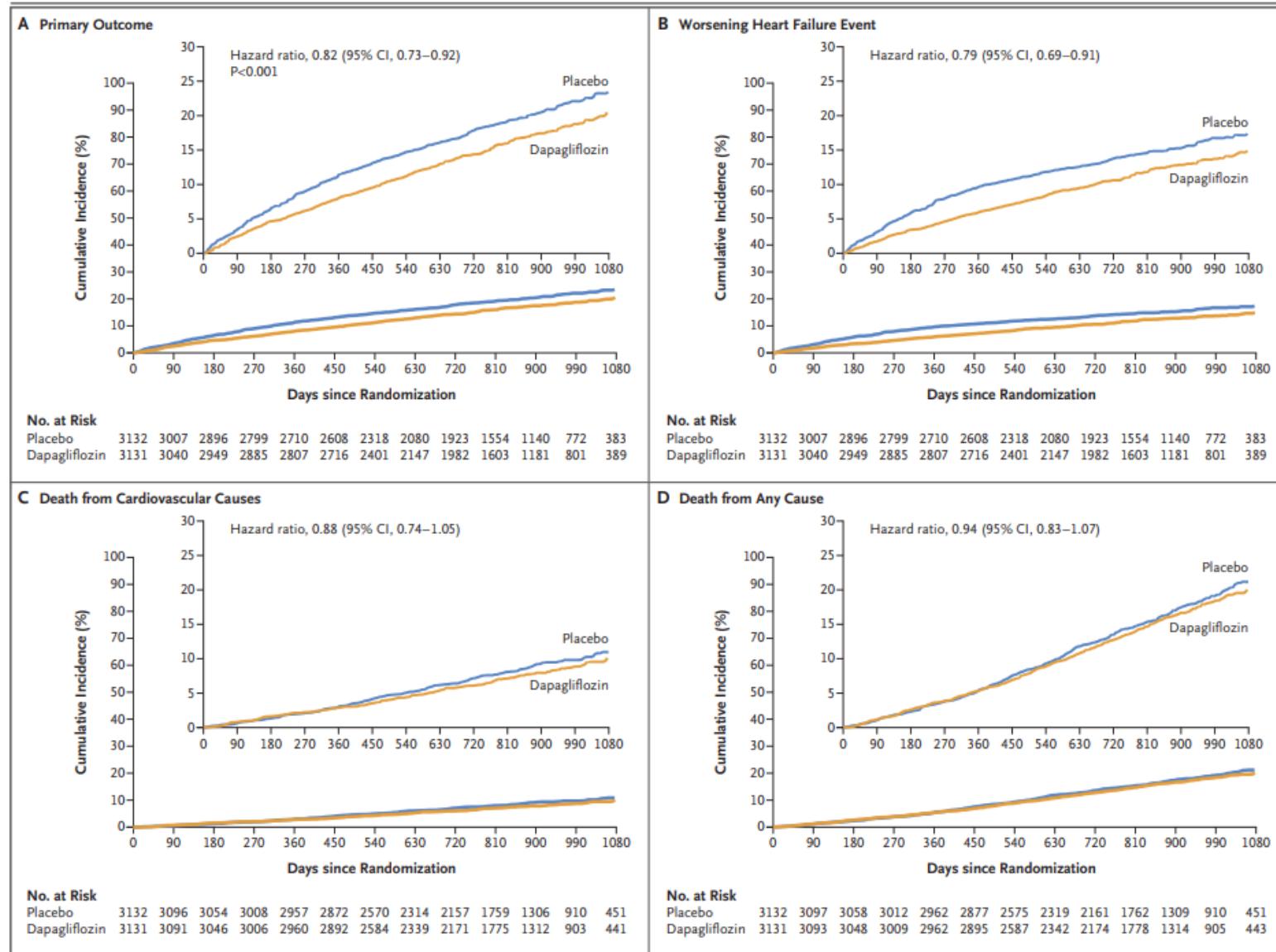
Fup 2,3 ans

Dapa 10mg od vs placebo

Primay Outcome: worsening HF or CV death

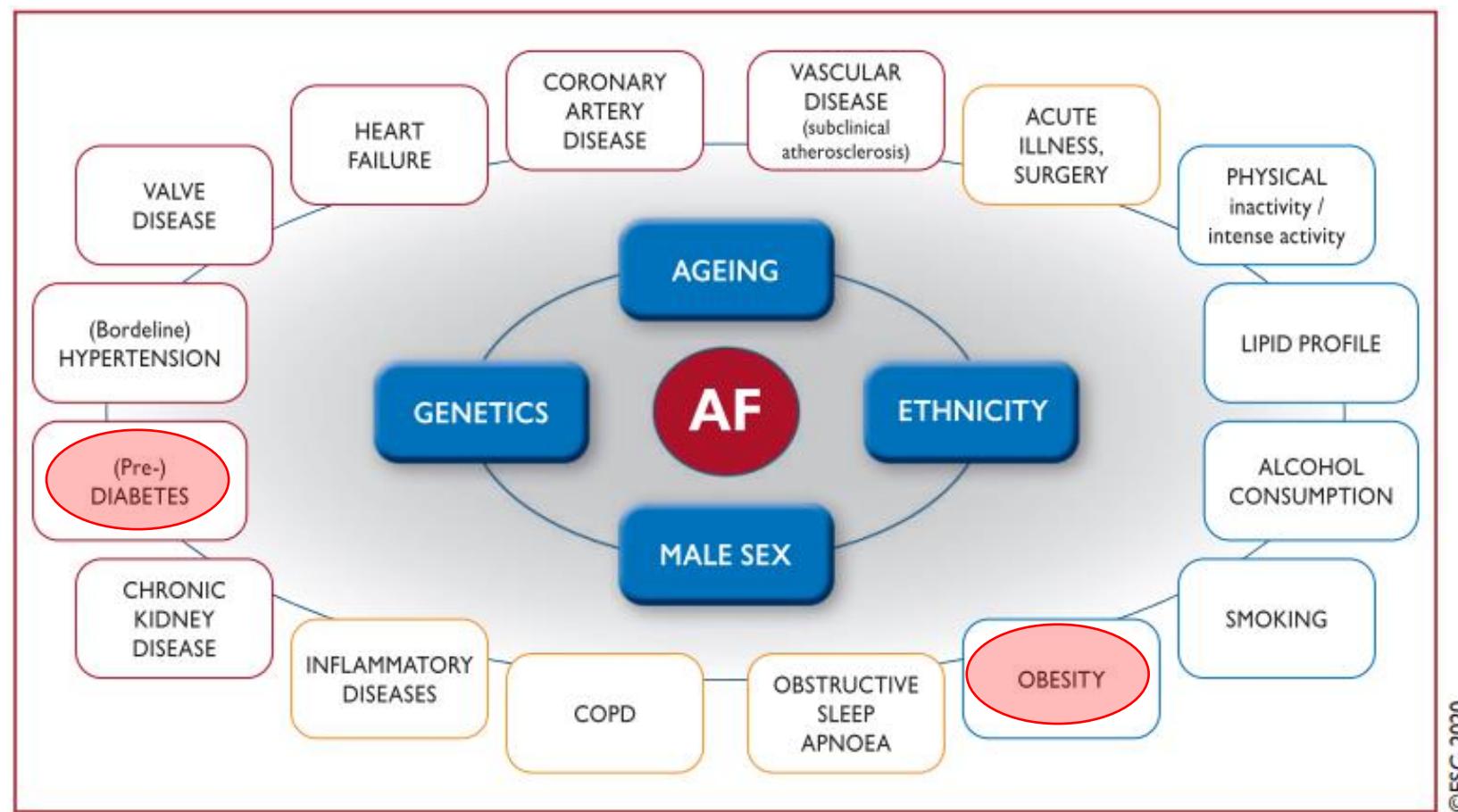
**Table 1.** Characteristics of the Patients at Baseline.\*

Characteristic	Dapagliflozin (N=3131)	Placebo (N=3132)
Age — yr	71.8±9.6	71.5±9.5
Female sex — no. (%)	1364 (43.6)	1383 (44.2)
Race — no. (%)†		
Asian	630 (20.1)	644 (20.6)
Black	81 (2.6)	78 (2.5)
White	2214 (70.7)	2225 (71.0)
Other	206 (6.6)	185 (5.9)
Geographic region — no. (%)		
North America	428 (13.7)	423 (13.5)
Latin America	602 (19.2)	579 (18.5)
Europe or Saudi Arabia	1494 (47.7)	1511 (48.2)
Asia	607 (19.4)	619 (19.8)
NYHA class — no. (%)‡		
II	2314 (73.9)	2399 (76.6)
III	807 (25.8)	724 (23.1)
IV	10 (0.3)	8 (0.3)
Left ventricular ejection fraction		
Mean — %	54.0±8.6	54.3±8.9
Distribution — no. (%)		
≤49%	1067 (34.1)	1049 (33.5)
50–59%	1133 (36.2)	1123 (35.9)
≥60%	931 (29.7)	960 (30.7)
Medical history — no. (%)		
Type 2 diabetes mellitus	1401 (44.7)	1405 (44.9)
Hypertension	2755 (88.0)	2798 (89.3)
Previous left ventricular ejection fraction ≤40%	572 (18.3)	579 (18.5)
Estimated GFR — ml/min/1.73 m²	61±19	61±19



# Diabète et FA

# Risk factors for incident atrial fibrillation



**Figure 3** Summary of risk factors for incident AF<sup>10,22,33,35–72</sup> (Supplementary Table 1 for full list). AF = atrial fibrillation; COPD = chronic obstructive pulmonary disease.

## FA et chirurgie bariatrique

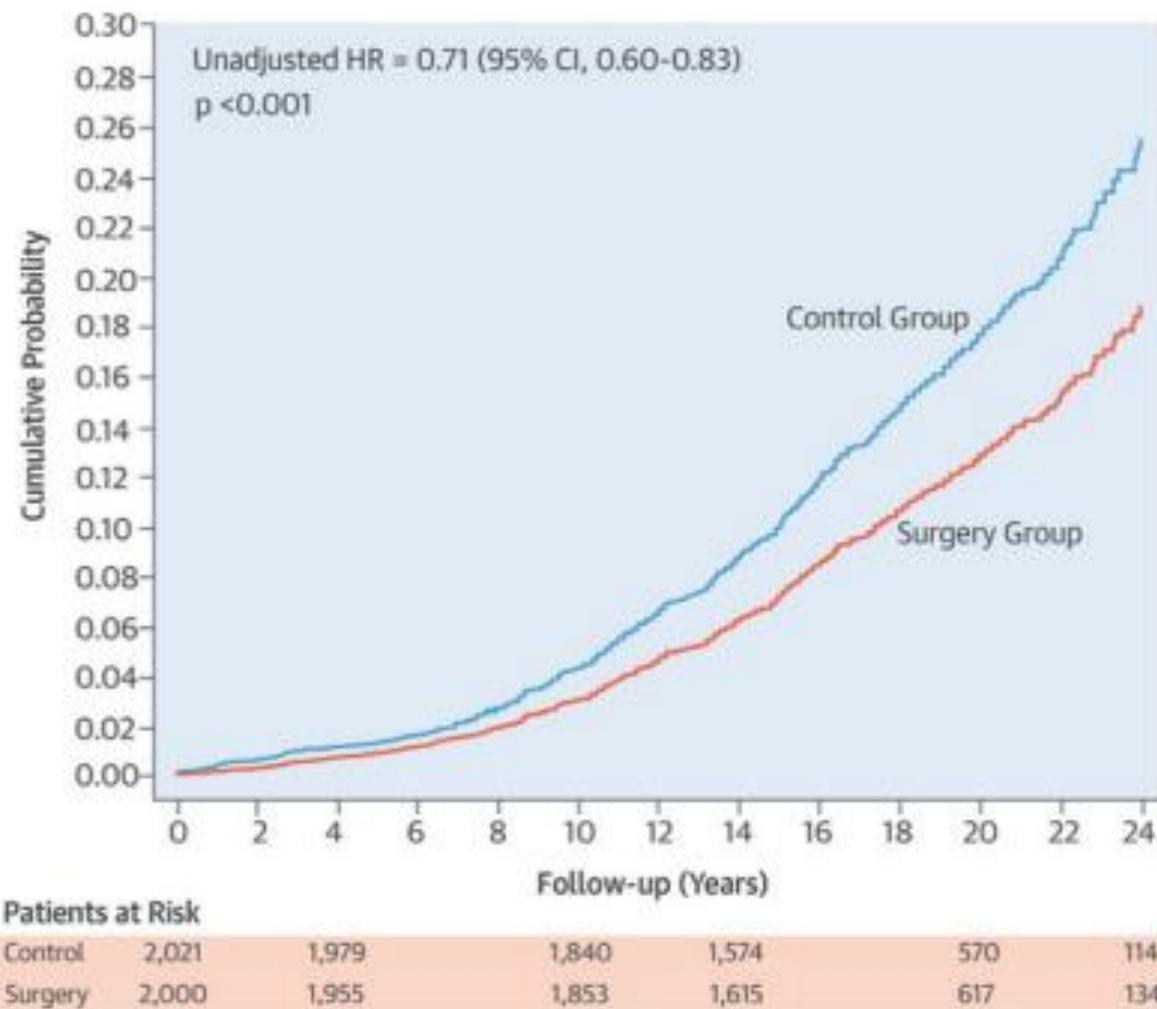


Figure 2. Bariatric surgery reduces AF. Time to recurrence of AF among morbidly obese patients after bariatric surgery compared with control subjects.<sup>23</sup> | Jamaly S, Carlsson L, Peltonen M, Jacobson P, Sjöström L, Karason K. Bariatric surgery and the risk of new-onset atrial fibrillation in Swedish obese subjects. *J Am Coll Cardiol* 2016;68:2497–2504.

# GLP1a et FA patients diabétiques



Heterogeneity:  $\chi^2 = 12.56$ , df = 7 ( $P = 0.08$ );  $I^2 = 44\%$

Test for overall effect:  $Z = 0.79$  ( $P = 0.43$ )

DOI 10.3389/fendo.2022.910256

## 3.2.2 Atrial Flutter

	Events	Total	Events	Total	Weight	Risk Ratio	
						M-H, Fixed, 95% CI	
AMPLITUDE-O 2020-12	7	2718	2	1355	0.3%	1.74 [0.36, 8.39]	
ELIXA 2015-2	3	3031	5	3032	0.6%	0.60 [0.14, 2.51]	
HARMONY 2018-3	6	4717	14	4715	1.6%	0.43 [0.16, 1.11]	
LEADER 2015-12	17	4668	16	4672	1.8%	1.06 [0.54, 2.10]	
PIONEER-6 2018-9	3	1591	1	1591	0.1%	3.00 [0.31, 28.81]	
REWIND 2018-8	15	4943	18	4949	2.0%	0.83 [0.42, 1.65]	
SUSTAIN-6 2016-3	2	1648	5	1649	0.6%	0.40 [0.08, 2.06]	
<b>Subtotal (95% CI)</b>	<b>23316</b>		<b>21963</b>		<b>7.0%</b>	<b>0.82 [0.57, 1.19]</b>	
Total events	53		61				

Heterogeneity:  $\chi^2 = 5.41$ , df = 6 ( $P = 0.49$ );  $I^2 = 0\%$

Test for overall effect:  $Z = 1.03$  ( $P = 0.30$ )



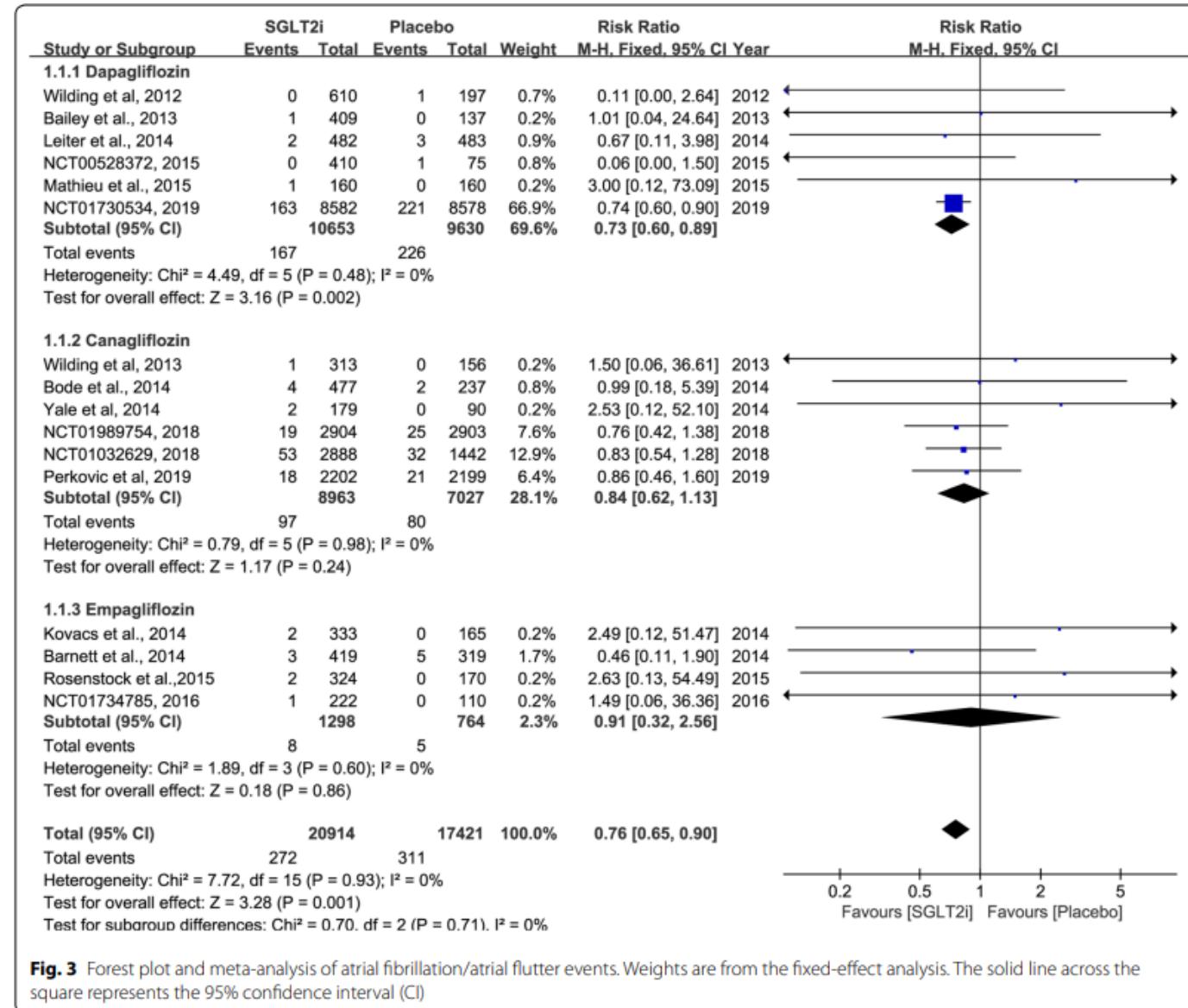
Wei and Wang

Faveur GLP1a

DOI 10.3389/fendo.2022.910256

Frontiers in Endocrinology

# SGLT2i et FA patients diabétiques



# Conclusion

- Les SGLT2i et les GLP1a ont montré une sécurité et un bénéfice sur le plan cardio-vasculaire chez le patient diabétique de type 2.
- Les SGLT2i > si insuffisance cardiaque.
- Les GLP1a > si obésité et haut risque cardio-vasculaire, athérothrombose.
- Utilisation des bons critères de remboursement pour garder la possibilité d'associer SGLT2i et GLP1a.
- Dans le futur, intérêt des GLP1a GIPa? Intérêt des GLP1a haute dose?