Update:
Le gliflozine nella terapia dello scompenso cardiaco del paziente con diabete mellito di tipo 2

Fabio Broglio

Università degli Studi di Torino

AOU Città della Salute e della Scienza di Torino

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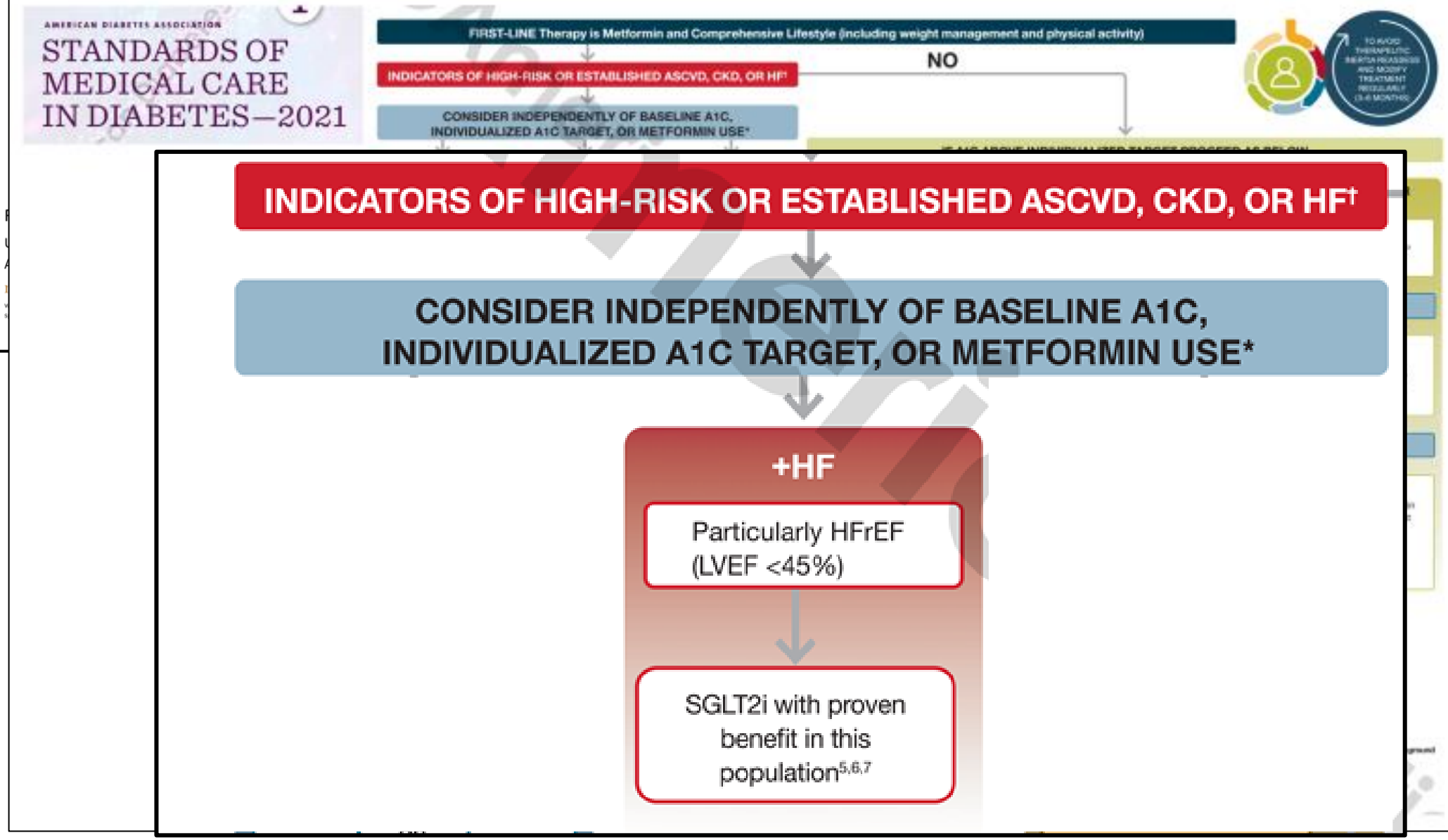
14 ottobre 2023

AMERICAN DIABETES ASSOCIATION

STANDARDS OF MEDICAL CARE IN DIABETES—2021



14 ottobre 2023

Inibitori SGLT2

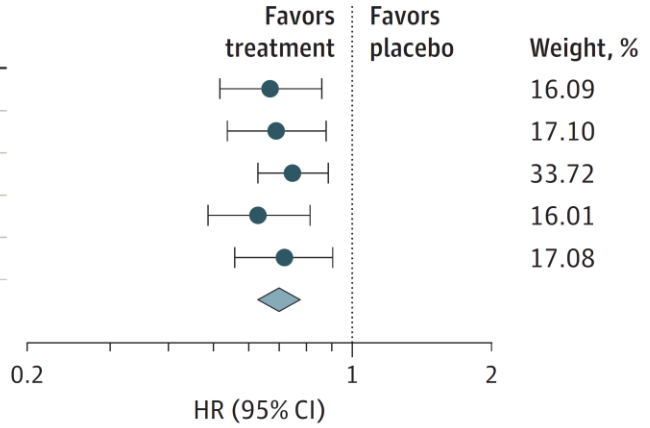
JAMA Cardiology | Original Investigation

Association of SGLT2 Inhibitors With Cardiovascular and Kidney Outcomes in Patients With Type 2 Diabetes
A Meta-analysis

Darren K. McGuire, MD, MHSc; Weichung J. Shih, PhD; Francesco Cosentino, MD, PhD; Bernard Charbonnel, MD; David Z. I. Cherney, MD, PhD; Samuel Dagogo-Jack, MD, DSc; Richard Pratley, MD; Michelle Greenberg, BSc; Shuai Wang, PhD; Susan Huyck, DrPH; Ira Gantz, MD; Steven G. Terra, PharmD; Urszula Masiukiewicz, MD; Christopher P. Cannon, MD

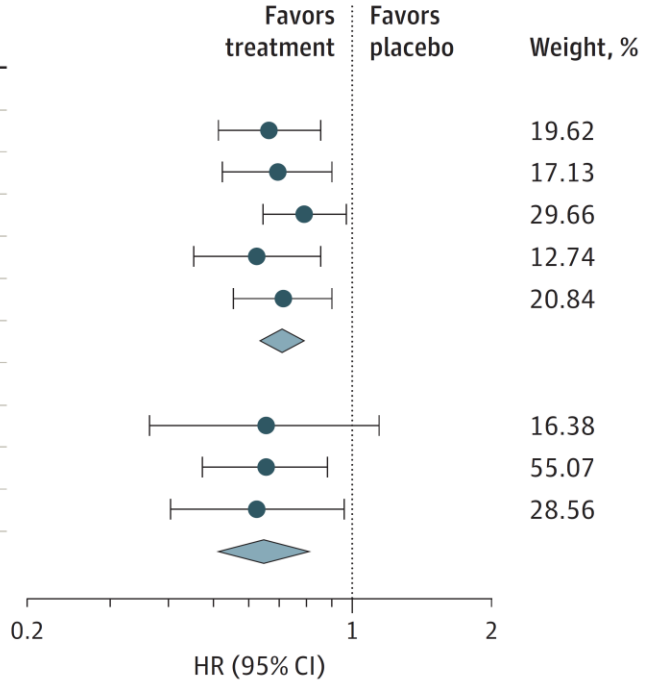
A Overall HHF

	Treatment		Placebo		
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)
EMPA-REG OUTCOME	126/4687	9.4	95/2333	14.5	0.65 (0.50-0.85)
CANVAS program	NA/5795	5.5	NA/4347	8.7	0.67 (0.52-0.87)
DECLARE-TIMI 58	212/8582	6.2	286/8578	8.5	0.73 (0.61-0.88)
CREDENCE	89/2202	15.7	141/2199	25.3	0.61 (0.47-0.80)
VERTIS CV	139/5499	7.3	99/2747	10.5	0.70 (0.54-0.90)
Fixed-effects model (Q = 1.39; *df* = 4; *P* = .85; I^2 = 0.0%)					0.68 (0.61-0.76)



B HHF by ASCVD status

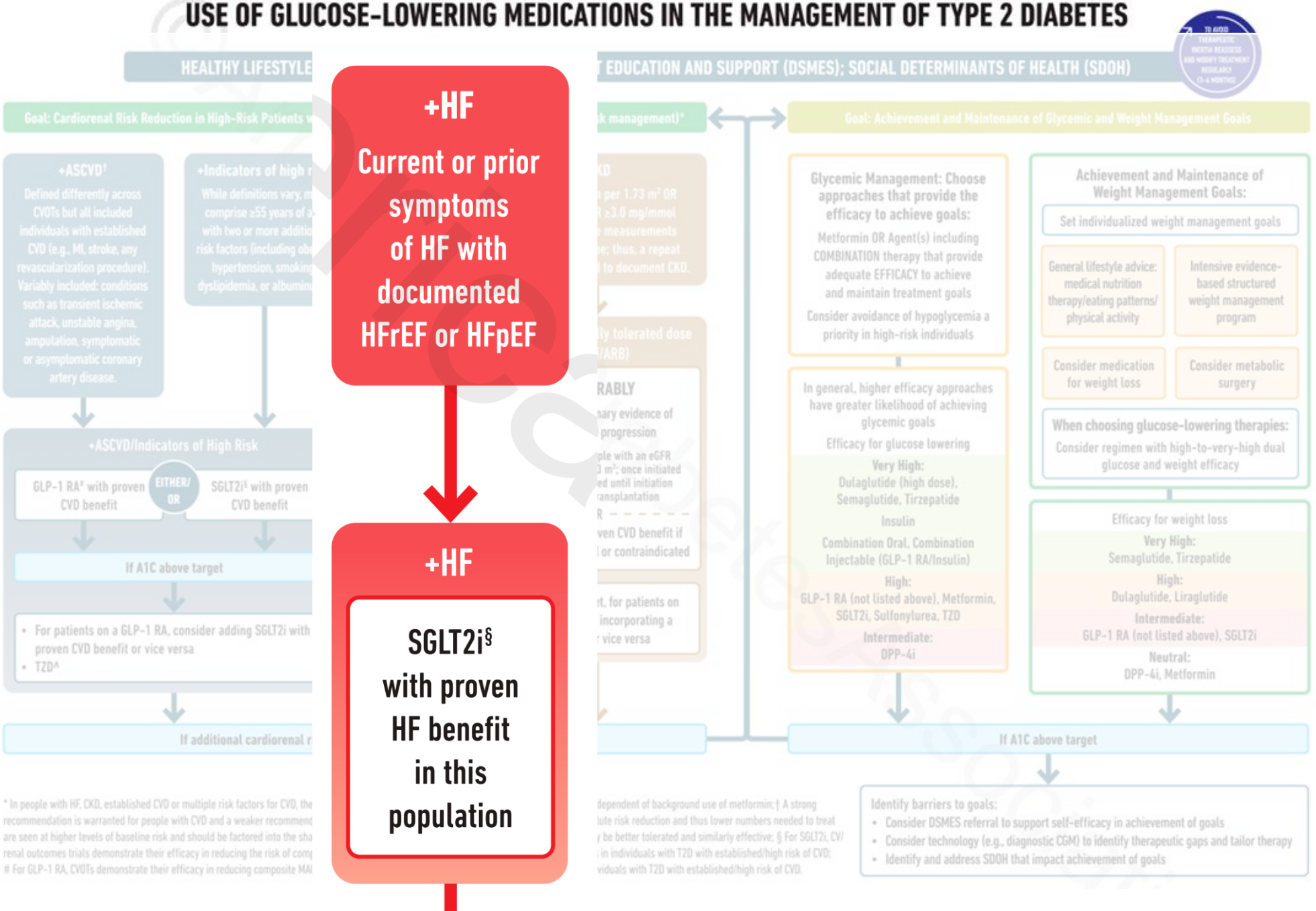
	Treatment		Placebo		
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)
Patients with ASCVD					
EMPA-REG OUTCOME	126/4687	9.4	95/2333	14.5	0.65 (0.50-0.85)
CANVAS program	NA/3756	7.3	NA/2900	11.3	0.68 (0.51-0.90)
DECLARE-TIMI 58	151/3474	11.1	192/3500	14.1	0.78 (0.63-0.97)
CREDENCE	59/1113	20.6	92/1107	33.2	0.61 (0.44-0.85)
VERTIS CV	139/5499	7.3	99/2747	10.5	0.70 (0.54-0.90)
Fixed-effects model (Q = 1.97; *df* = 4; *P* = .74; I^2 = 0.0%)					0.70 (0.62-0.78)
Patients without ASCVD					
CANVAS program	NA/2039	2.6	NA/1447	4.2	0.64 (0.35-1.15)
DECLARE-TIMI 58	61/5108	3.0	94/5078	4.6	0.64 (0.46-0.88)
CREDENCE	30/1089	10.6	49/1092	17.5	0.61 (0.39-0.96)
Fixed-effects model (Q = 0.03; *df* = 2; *P* = .99; I^2 = 0.0%)					0.63 (0.50-0.80)



JAMA Cardiol. 2021;6(2):148-158

Standards of Care in Diabetes—2023

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



Review

SGLT2 Inhibition in Heart Failure with Preserved Ejection Fraction — The New Frontier

Inês Aguiar-Neves[1], Diogo Santos-Ferreira[1,2], Ricardo Fontes-Carvalho[1,2,*]

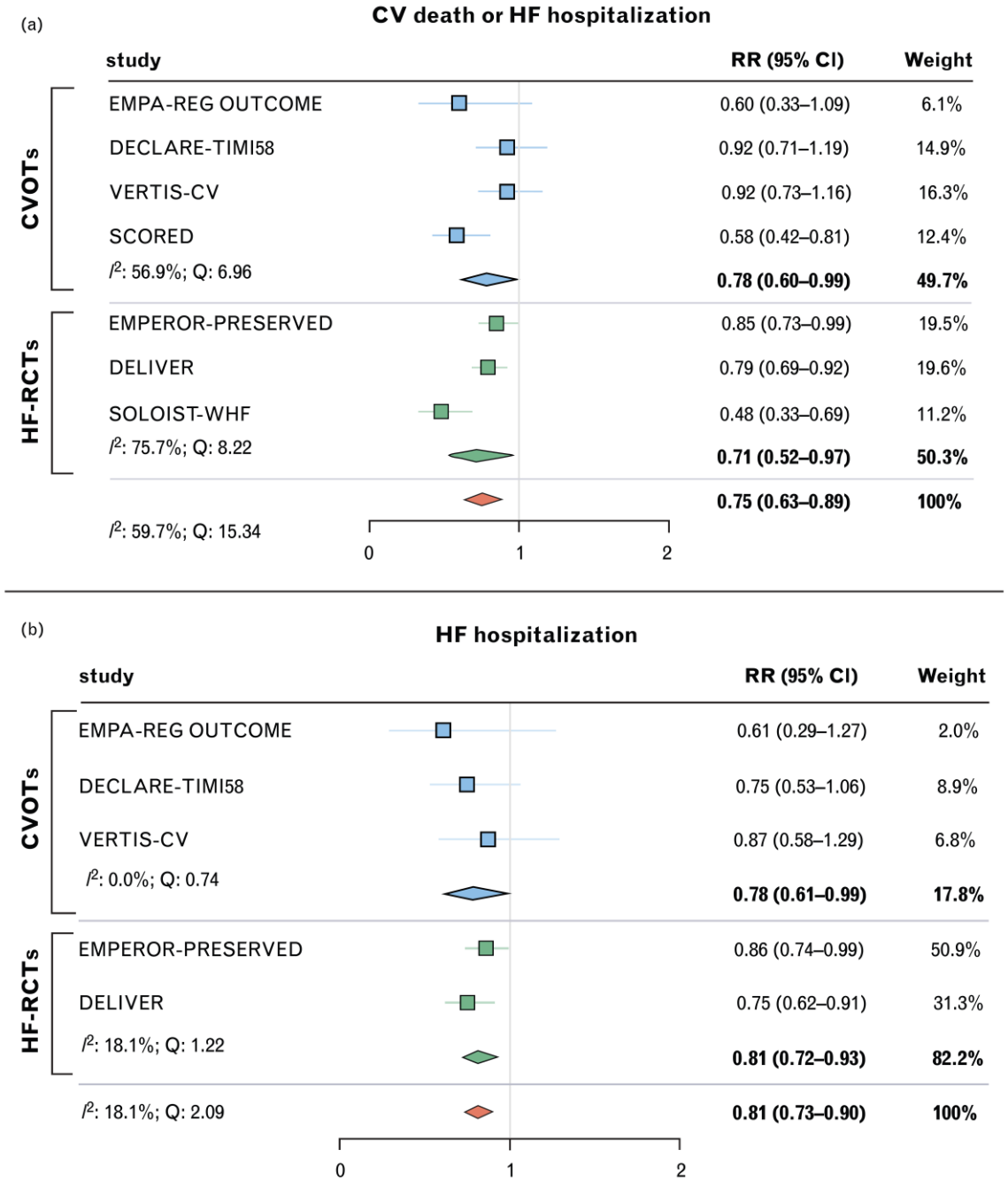
Table 1. Summary of Major Randomized Clinical Trials of SGLT2 Inhibitors in HFpEF.

Drug name	Trial name	Study population	Primary outcome	Main results
Sotagliflozin	SOLOIST-WHF	1222 patients (20% with LVEF >50%) Age ≥18 years Recent HHF T2DM	Composite of total number of CV deaths and HF exacerbations (HHF or urgent visit)	HR for composite outcome: 0.67 (95% CI 0.52–0.85) HR for CV death: 0.84 (95% CI 0.58–1.22) HR for WHF: 0.64 (95% CI 0.49–0.83)
Empagliflozin	EMPEROR-Preserved	5988 patients Age ≥18 years NYHA II–IV LVEF >40%	Composite of CV death or HHF	HR for composite outcome: 0.79 (95% CI 0.69–0.90) HR for CV death: 0.91 (95% CI 0.76–1.09) HR for HHF: 0.71 (95% CI 0.60–0.83)
	EMPERIAL-Preserved	315 patients Age ≥18 years LVEF >40%	6MWD change after 12 weeks	Change in 6MWD: 4.0m (95% CI −5.0–13.0)
Dapagliflozin	DELIVER	6263 patients Age ≥40 years NYHA II–IV LVEF >40% (including prior LVEF ≤40%)	Composite of CV death or HF exacerbations (HHF or urgent visit)	HR for composite outcome: 0.82 (95% CI 0.73–0.92) HR for CV death: 0.88 (95% CI 0.74–1.05) HR for WHF: 0.79 (95% CI 0.69–0.91)
	PRESERVED-HF	324 patients Age ≥18 years NYHA II–IV LVEF ≥45%	Change in KCCQ Clinical Summary Score after 12 weeks	Change in KCCQ: 5.8 points (95% CI 2.3–9.2)
Canagliflozin	CANONICAL	82 patients Age ≥65 years LVEF ≥50% T2DM	Change in body weight and plasma BNP levels after 24 weeks	Reduction in body weight with canagliflozin (p = 0.019) No significant change in BNP levels
	CHIEF-HF	476 patients (276 with HFpEF) Age ≥18 years History of HF (LVEF ≥40% for HFpEF group)	Change in KCCQ Total Symptom Score after 24 weeks	Change in KCCQ: 4.3 points (95% CI 0.8–7.8) Change in KCCQ (HFpEF group): 4.5 points (95% CI −0.3–9.4)
Ertugliflozin	VERTIS-CV	8246 patients (1007 patients with LVEF >45%) Age ≥40 years T2DM	Composite of CV death, non-fatal MI or non-fatal stroke	HR for composite outcome: 0.97 (95% CI 0.85–1.11) HR for first HHF: (LVEF >45%): 0.86 (95% CI 0.58–1.29)
Luseogliflozin	MUSCAT-HF (luseogliflozin vs. voglibose)	190 patients Age ≥20 years LVEF >45% T2DM	Change in plasma BNP levels after 12 weeks	Change in ratio of BNP levels: 0.93 (95% CI, 0.78–1.10)
Ipragliflozin	EXCEED	68 patients Age ≥20 years LVEF ≥50% T2DM	Change in E/e' and e' after 24 weeks	Change in E/e': –0.04 (95% CI –1.3–1.2) Change in e': 0.3 cm/s (95% CI –0.9–0.3)

Efficacy of SGLT2-inhibitors across different definitions of heart failure with preserved ejection fraction

Vincenzo De Marzo[a], Gianluigi Savarese[b], Italo Porto[a,c], Marco Metra[d,e] and Pietro Ameri[a,c]

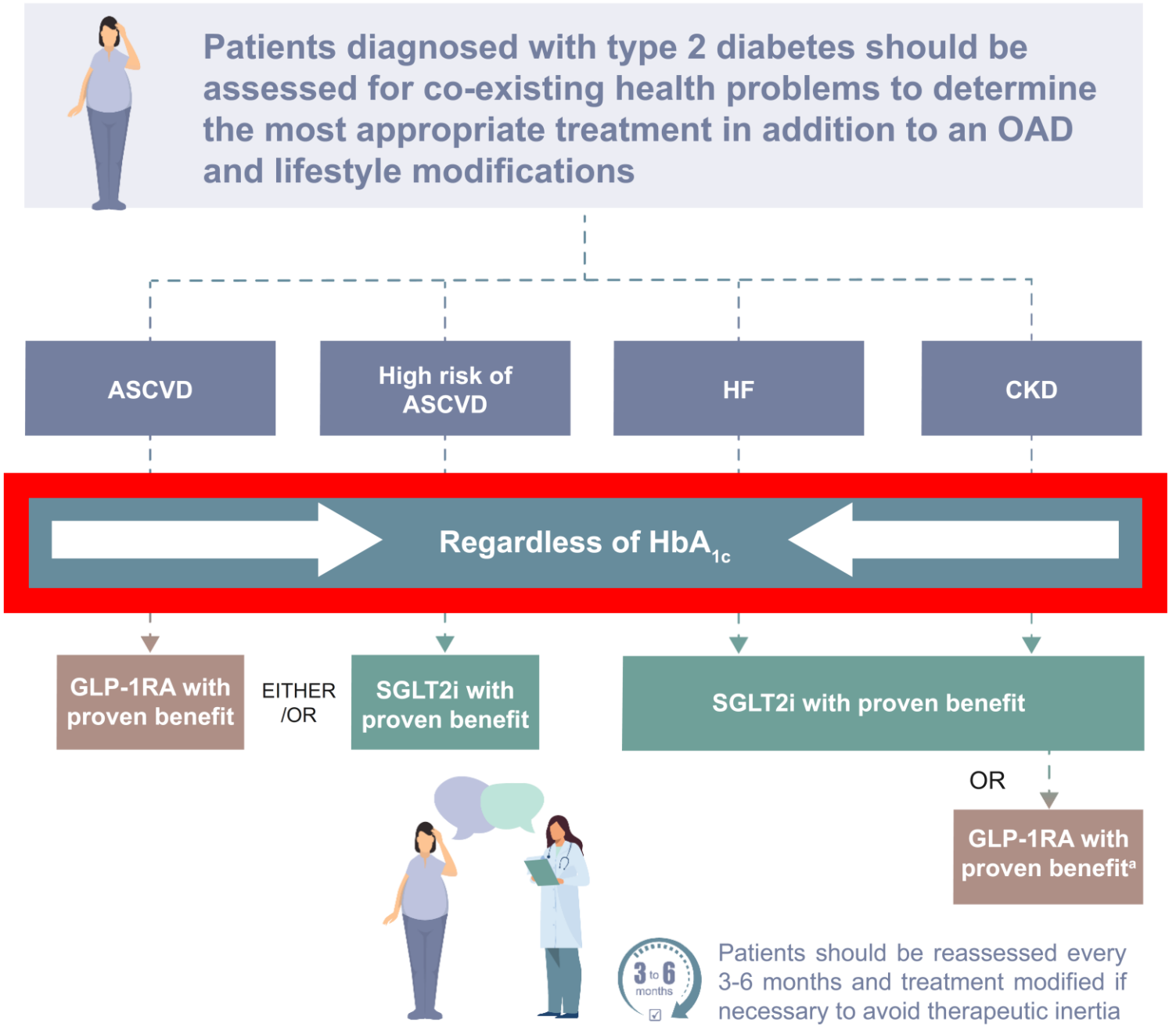
J Cardiovasc Med 2023, 24:537–543



Type 2 diabetes and cardiovascular disease: risk reduction and early intervention

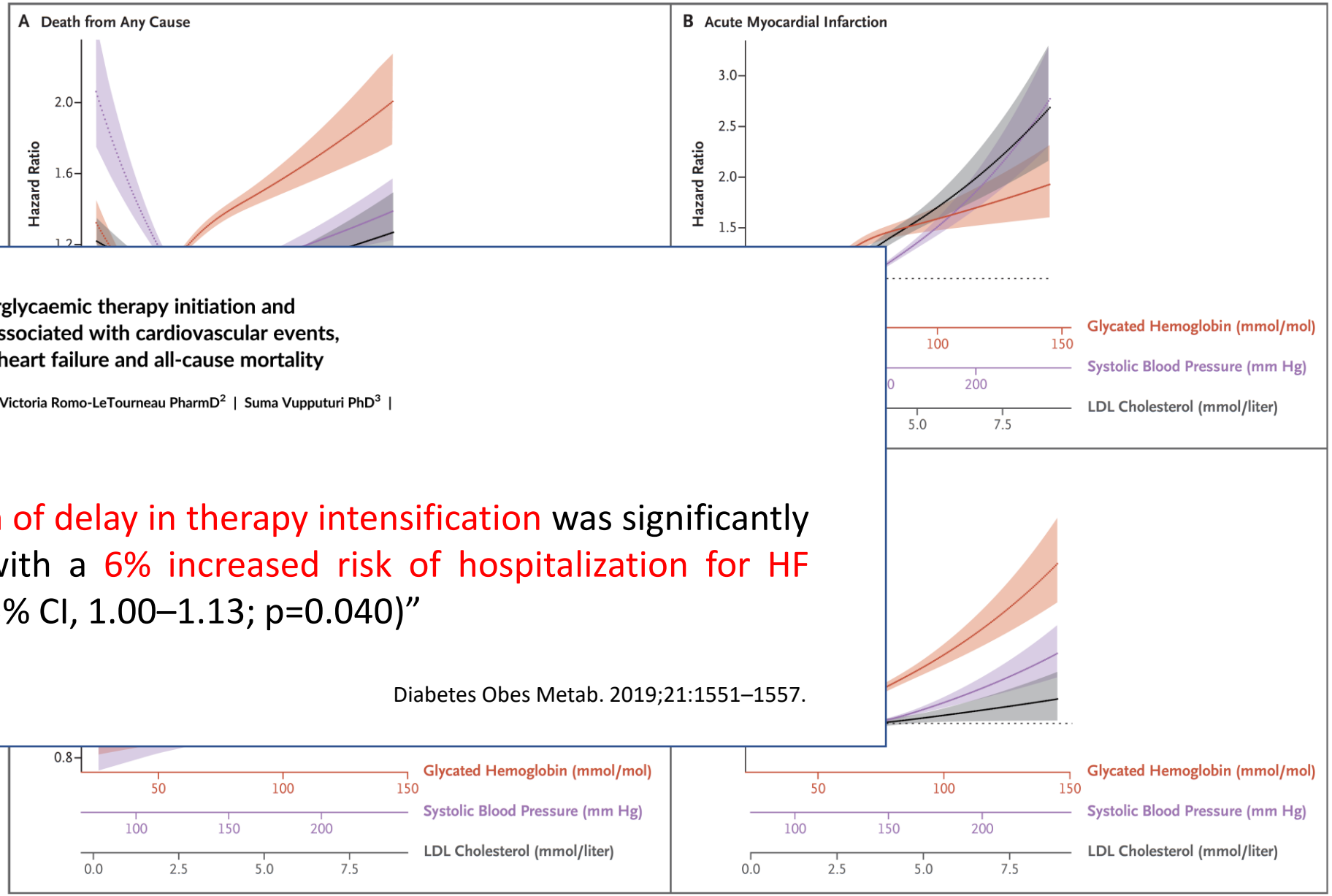
Debbie Hinnen [a], Davida Kruger [b] and Melissa Magwire [c]

Postgraduate Medicine, 135:1, 2-12,



Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Aidin Rawshani, M.D., Araz Rawshani, M.D., Ph.D., Stefan Franzén, Ph.D., Naveed Sattar, M.D., Ph.D., Björn Eliasson, M.D., Ph.D., Ann-Marie Svensson, Ph.D., Björn Zethelius, M.D., Ph.D., Mervete Miftaraj, M.Sc., Darren K. McGuire, M.D., M.H.Sc., Annika Rosengren, M.D., Ph.D., and Soffia Gudbjörnsdottir, M.D., Ph.D.



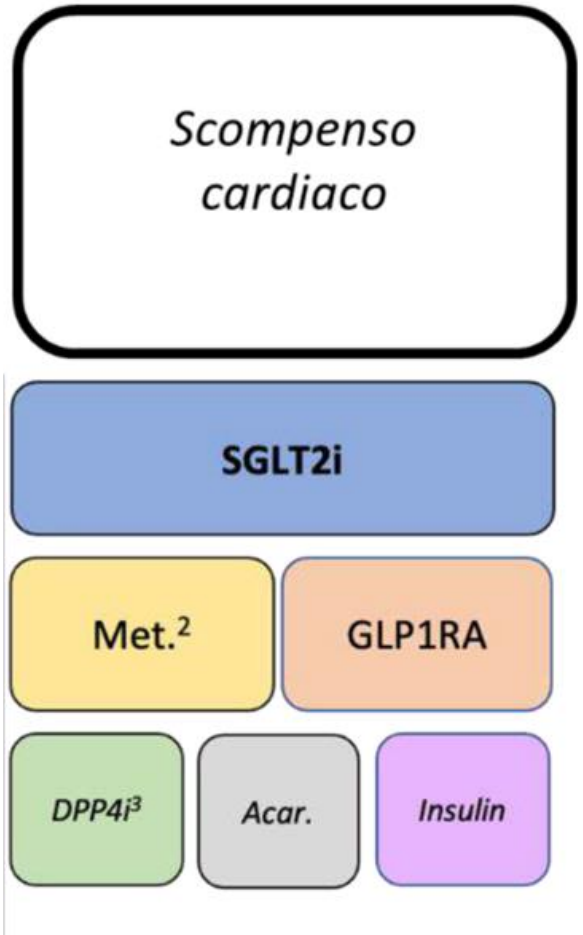
Delays in anti-hyperglycaemic therapy initiation and intensification are associated with cardiovascular events, hospitalizations for heart failure and all-cause mortality

Gregory A. Nichols PhD[1] | Victoria Romo-LeTourneau PharmD[2] | Suma Vupputuri PhD[3] | Sheila M. Thomas PharmD[2]

"Each month of delay in therapy intensification was significantly associated with a 6% increased risk of hospitalization for HF (HR, 1.06; 95% CI, 1.00–1.13; p=0.040)"

Diabetes Obes Metab. 2019;21:1551–1557.

N Engl J Med 2018;379:633-44.


Scompenso cardiaco
SGLT2i
Met.2
GLP1RA
DPP4i3
Acar.
Insulin

The effect of DPP-4 inhibitors, GLP-1 receptor agonists and SGLT-2 inhibitors on cardiorenal outcomes: a network meta-analysis of 23 CVOTs

Dario Giugliano[1*], Miriam Longo[1,2], Simona Signoriello[3], Maria Ida Maiorino[1,2], Bruno Solerte[4], Paolo Chiodini[3] and Katherine Esposito[1,2]

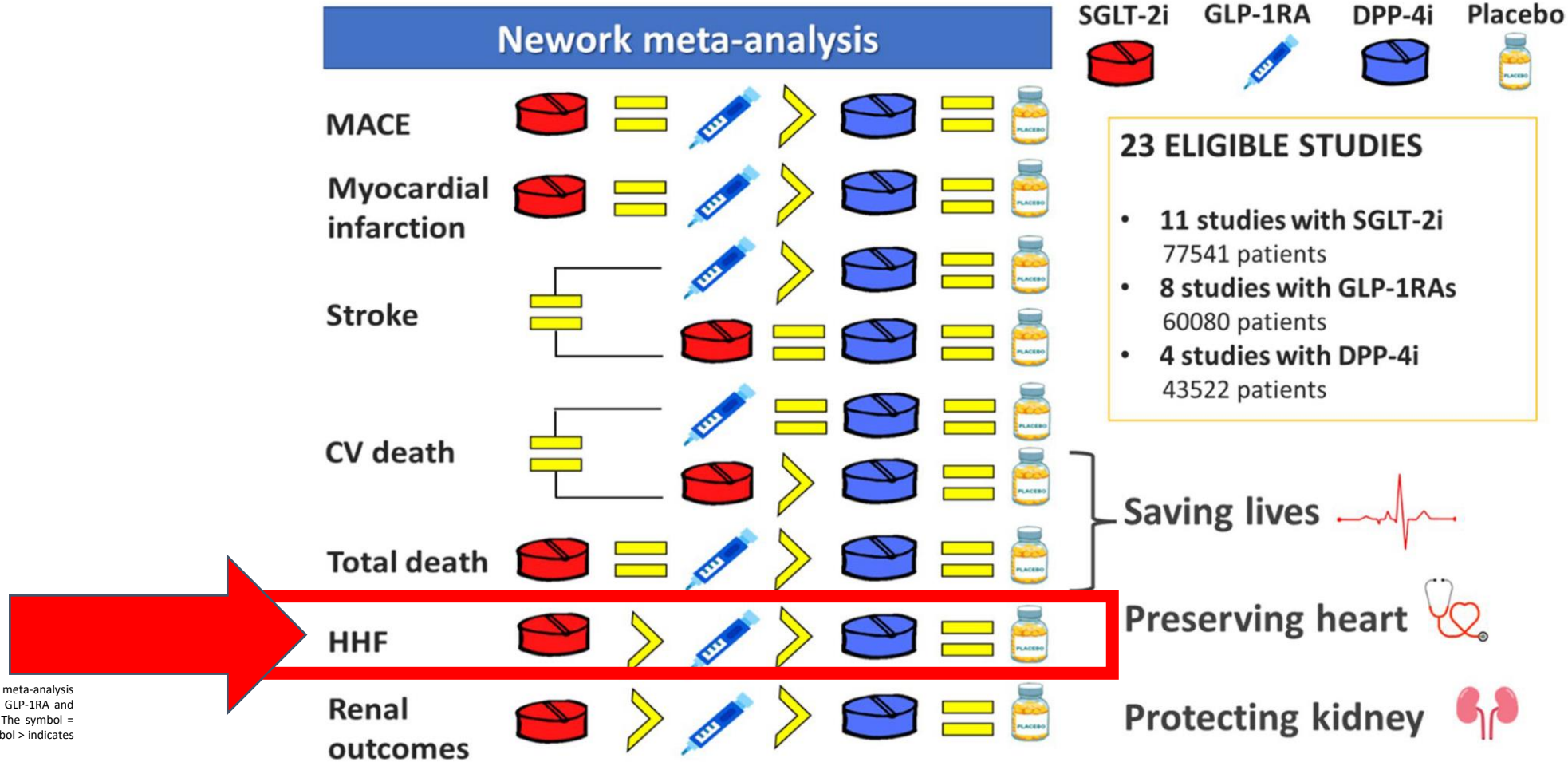
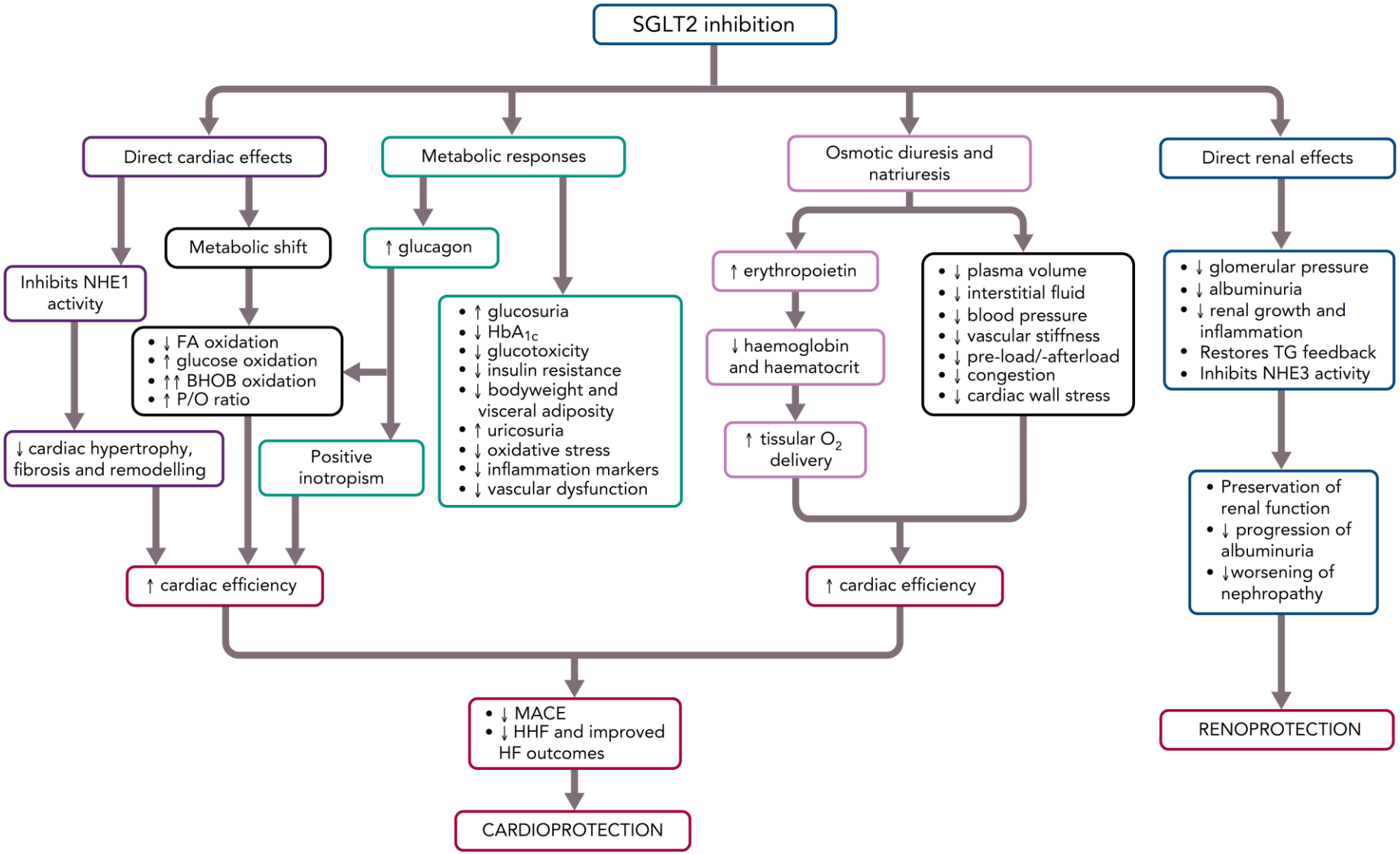


Fig. 4 Summary "at glance" of the network meta-analysis comparing the effects of SGLT-2 inhibitors, GLP-1RA and DPP-4 inhibitors on cardiorenal outcomes. The symbol = indicates non significantly different; the symbol > indicates significantly different

Potential Mechanisms Involved in the Cardioprotective and Renoprotective Effects of Sodium–glucose Cotransporter 2 Inhibitors



Time to cardiovascular benefits of empagliflozin: a *post hoc* observation from the EMPA-REG OUTCOME trial

Subodh Verma[1]*, Lawrence A. Leiter[2], Bernard Zinman[3], Abhinav Sharma[4], Michaela Mattheus[5], David Fitchett[6], Jyothis George[7†], Anne Pernille Ofstad[8], Mikhail N. Kosiborod[9], Christoph Wanner[10] and Silvio E. Inzucchi[11]

cardiovascular death

hospitalization for heart failure

hospitalization for HF/CV death

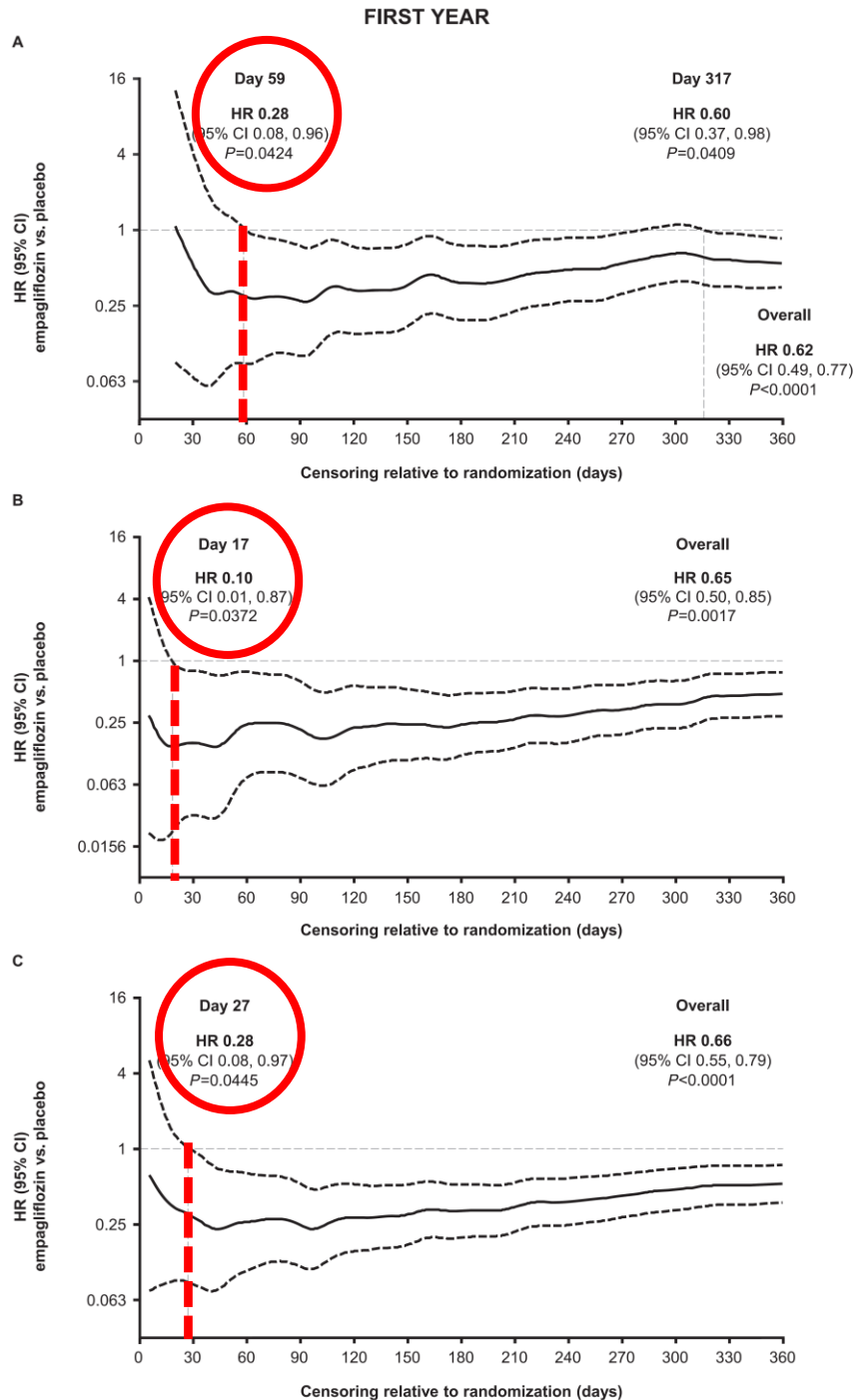


Figure 1 Smoothed curves for successive hazard ratios (HRs; 95% confidence intervals [CI]) for empagliflozin vs. placebo for (A) cardiovascular death, (B) hospitalization for heart failure, and (C) hospitalization for heart failure/cardiovascular death (excluding fatal stroke) with a vertical line demonstrating the day the benefits reach statistical significance. HRs and 95% CIs are shown in relation to time point of censoring—treated set. Overall results apply to the complete study duration.

ESC Heart Failure 2021; 8: 2603–2607

Empagliflozin Reduced Mortality and Hospitalization for Heart Failure Across the Spectrum of Cardiovascular Risk in the EMPA-REG OUTCOME Trial

David Fitchett, MD
Silvio E. Inzucchi, MD
Christopher P. Cannon, MD
Darren K. McGuire, MD, MHSc
Benjamin M. Scirica, MD
Odd Erik Johansen, MD, PhD
Steven Sambevski, MD
Stefan Kaspers, MD
Egon Pfarr, MS
Jyothis T. George, MBBS, PhD
Bernard Zinman, MD

	Empagliflozin			Placebo					Randomized group by subgroup interaction
	n/N	*%*	*Rate/1000 patient-years*	*n/N*	*%*	*Rate/1000 patient-years*	HR (95% CI)	HR (95% CI)	
CV death									
All patients	172/4687	3.7	12.4	137/2333	5.9	20.2	0.62 (0.49, 0.77)		
Estimated CV risk at baseline									*P*=0.9492
Lowest	9/564	1.6	5.2	6/275	2.2	7.2	0.72 (0.25, 2.01)		
Intermediate	45/1869	2.4	8.2	37/961	3.9	13.0	0.63 (0.41, 0.97)		
High	57/1446	3.9	13.4	46/667	6.9	24.0	0.56 (0.38, 0.83)		
Highest	61/805	7.6	26.3	48/428	11.2	40.2	0.65 (0.44, 0.95)		
All-cause mortality									
All patients	269/4687	5.7	19.4	194/2333	8.3	28.6	0.68 (0.57, 0.82)		
Estimated CV risk at baseline									*P*=0.8446
Lowest	12/564	2.1	6.9	11/275	4.0	13.2	0.52 (0.23, 1.19)		
Intermediate	71/1869	3.8	12.9	51/961	5.3	17.9	0.71 (0.50, 1.02)		
High	95/1446	6.6	22.4	59/667	8.8	30.7	0.73 (0.53, 1.01)		
Highest	91/805	11.3	39.2	73/428	17.1	61.1	0.64 (0.47, 0.87)		

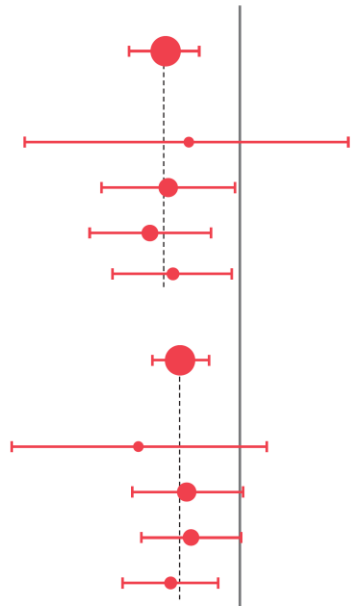
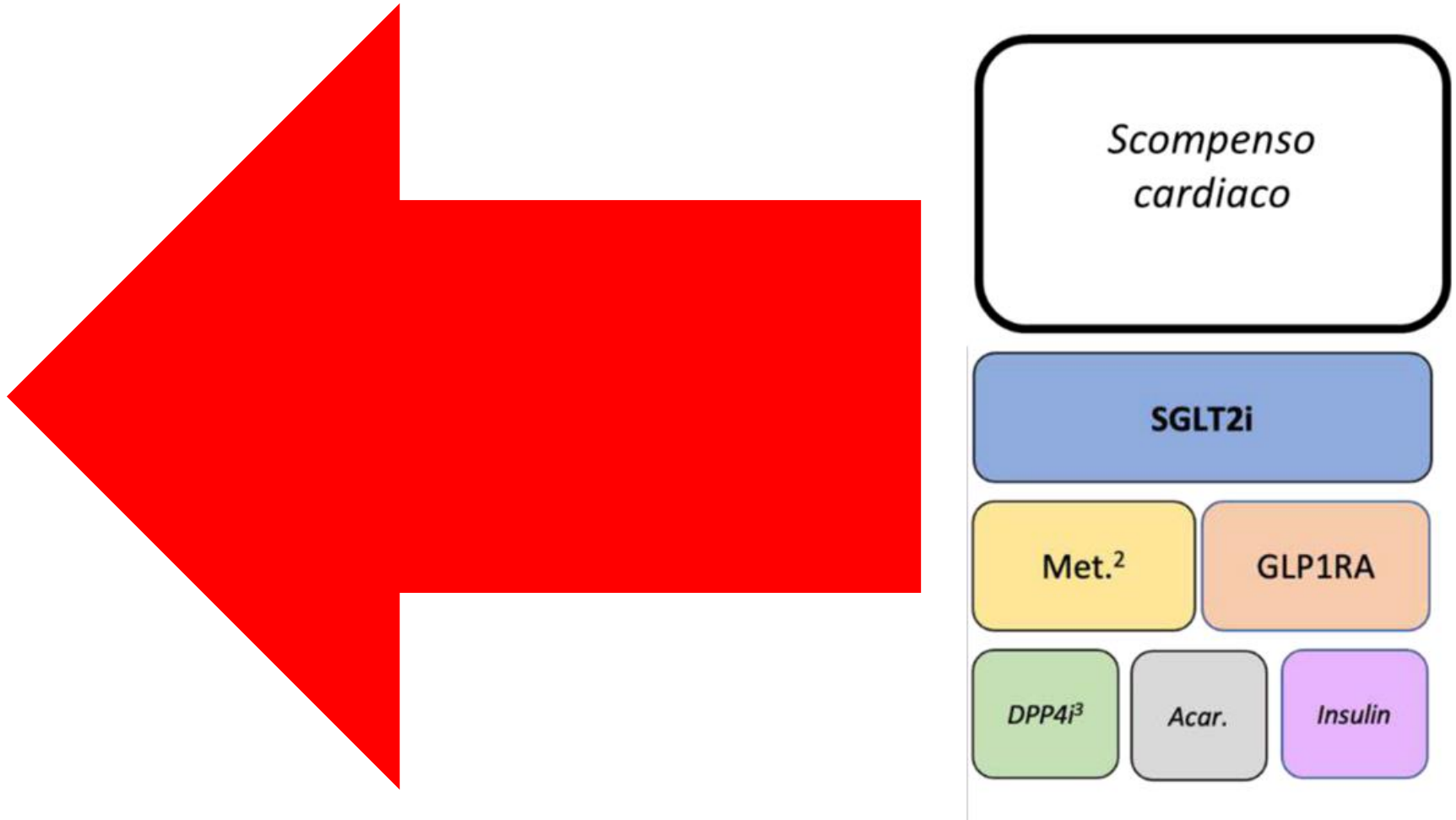


Figure 6. Cardiovascular (CV) outcomes and mortality with empagliflozin versus placebo by estimated CV risk according to 10-point TIMI Risk Score for Secondary Prevention at baseline: low, ≤2 points; intermediate, 3 points; high, 4 points; and highest, ≥5 points. Cox proportional hazards regression analyses in patients who received study drug. HR indicates hazard ratio; and MACE, major adverse cardiovascular events.

Circulation. 2019;139:1384–1395.

Linea Guida della Società Italiana di Diabetologia (SID) e dell'Associazione dei Medici Diabetologi (AMD)

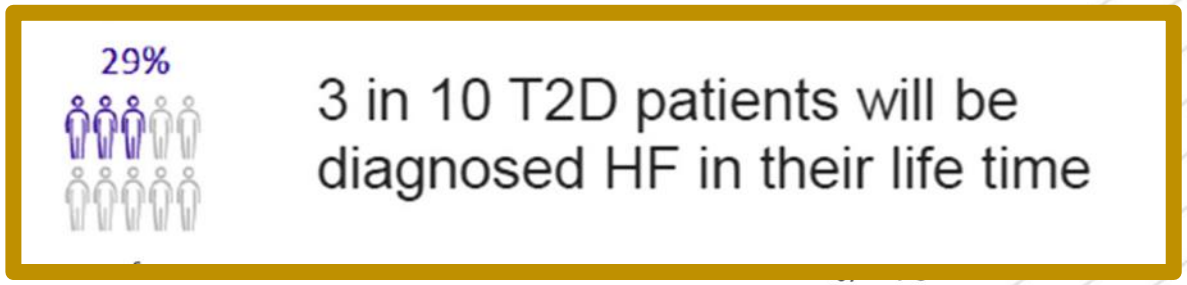
La terapia del diabete mellito di tipo 2



[1]*Se la metformina non è controindicata per ridotto eGFR.*
[2]*Se la metformina non è controindicata per ridotta funzione cardiaca.*
[3]*Eccetto saxagliptin che non è indicato in caso di scompenso cardiaco.*
La raccomandazione sui pazienti con eGFR< 60ml/min è debole per carenza di studi clinici effettuati su questa popolazione
Si raccomanda la deprescrizione di sulfanilurre e glinidi

Lifetime risk of cardiovascular-renal disease in type 2 diabetes: a population-based study in 473,399 individuals

Ruiqi Zhang[1,2], Jil Billy Mamza[2], Tamsin Morris[2], George Godfrey[2], Folkert W. Asselbergs[3,4,5], Spiros Denaxas[3,6], Harry Hemingway[3,6] and Amitava Banerjee[3,6,7,8*]



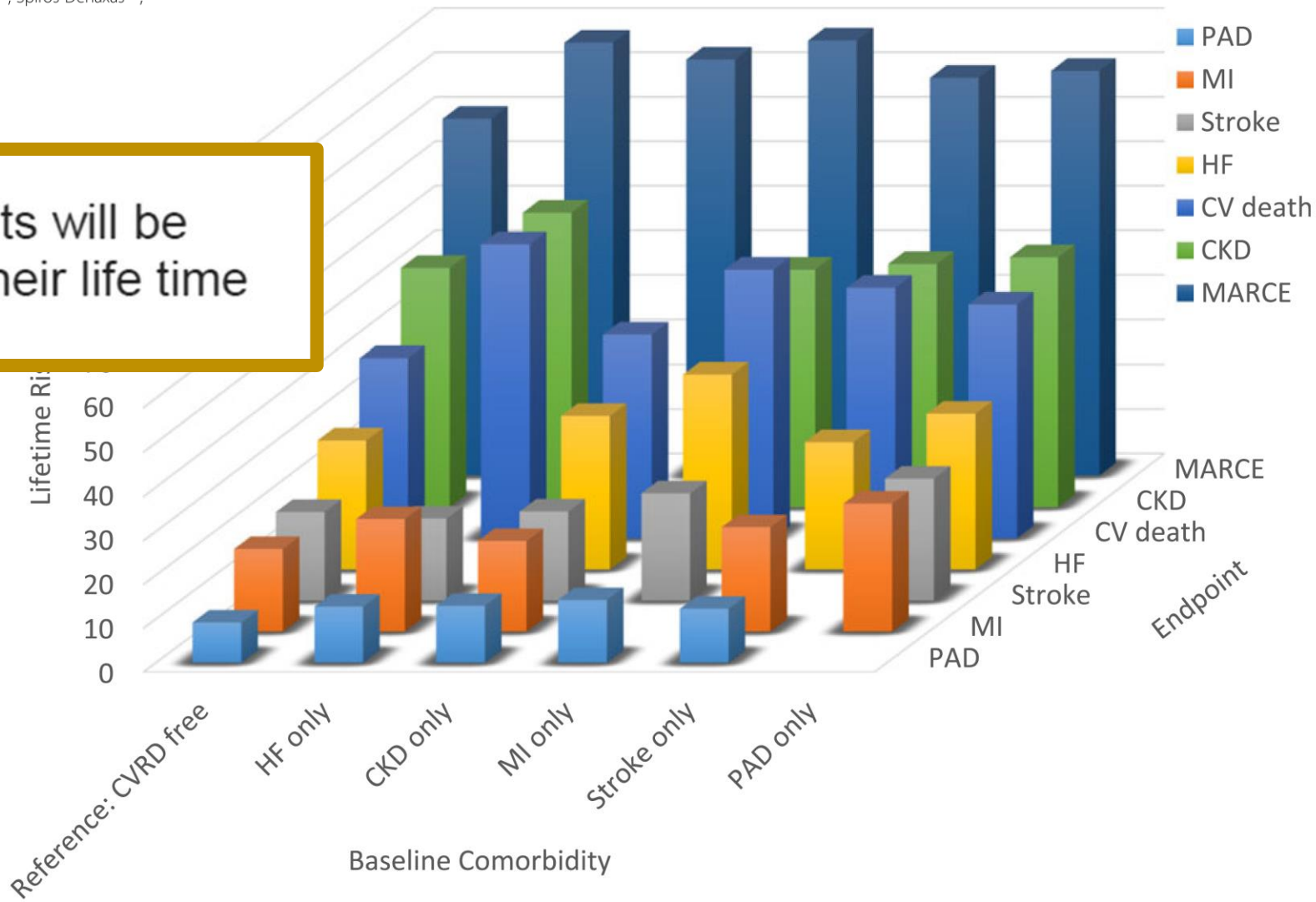


Fig. 3 Lifetime risk of individual and composite major adverse renal and cardiovascular events. Abbreviations: cardiovascular and renal diseases, CVRD; heart failure, HF; chronic kidney disease, CKD; myocardial infarction, MI; peripheral artery disease, PAD

Zhang et al. BMC Medicine (2022) 20:63

Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Aidin Rawshani, M.D., Araz Rawshani, M.D., Ph.D., Stefan Franzén, Ph.D., Naveed Sattar, M.D., Ph.D., Björn Eliasson, M.D., Ph.D., Ann-Marie Svensson, Ph.D., Björn Zethelius, M.D., Ph.D., Mervete Miftaraj, M.Sc., Darren K. McGuire, M.D., M.H.Sc., Annika Rosengren, M.D., Ph.D., and Soffia Gudbjörnsdottir, M.D., Ph.D.

5 risk factors: elevated HbA1c, elevated LDL, albuminuria, smoking, and elevated blood pressure

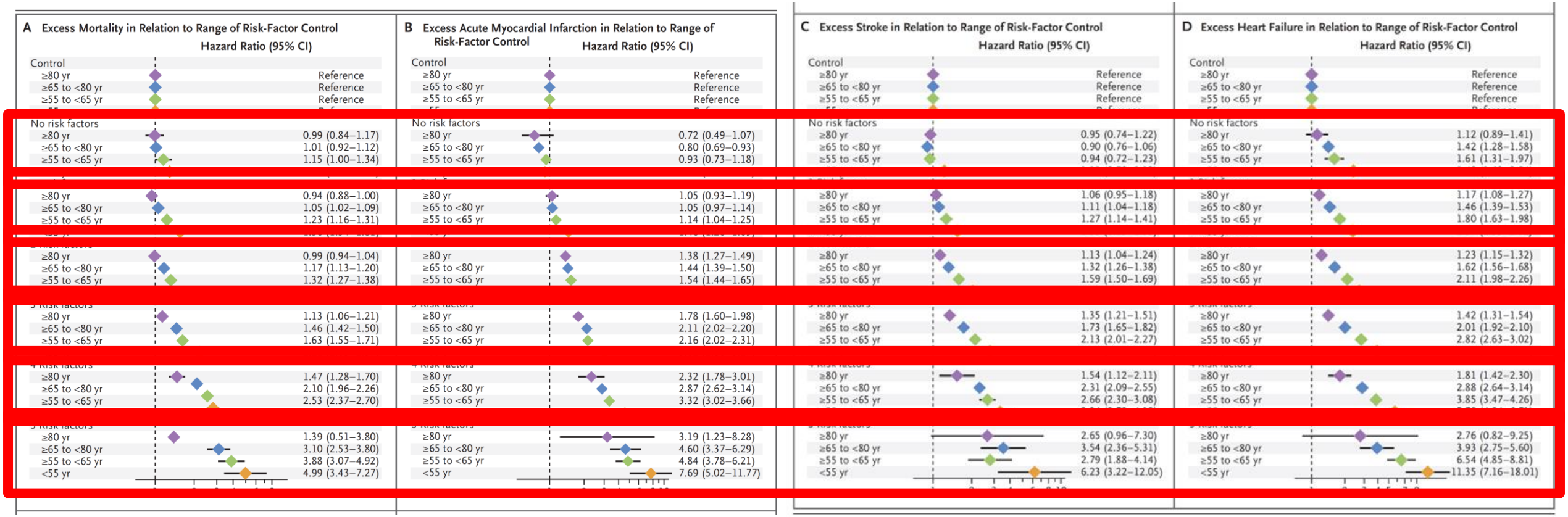


Figure 1 (facing page). Adjusted Hazard Ratios for Outcomes, According to Age Category and Number of Risk-Factor Variables outside Target Ranges, among Patients with Type 2 Diabetes, as ompared with Matched Controls. Hazard ratios show the excess risk of each outcome among patients with type 2 diabetes, as compared with matched controls from the general population, according to age categories and to the number of riskfactor variables (scale, none to five) that were outside target ranges currently recommended in guidelines. The analysis included patients ith type 2 diabetes and controls matched for age, sex, and county in Sweden. We constructed a Cox hazards model for each ge category, and these models were adjusted for the covariable category"; this covariable denotes the number of risk-factor variables that were within target ranges. These Cox model analyses were performed on five imputed data sets for each age ategory, and hazard ratios were pooled from all the data sets with the use of Rubin's rule.

N Engl J Med 2018;379:633-44.

Impact of early initiation of sodium-glucose cotransporter 2 inhibitor on cardiovascular outcomes in people with diabetes and known or at risk of atherosclerotic cardiovascular disease: Propensity score matched analysis

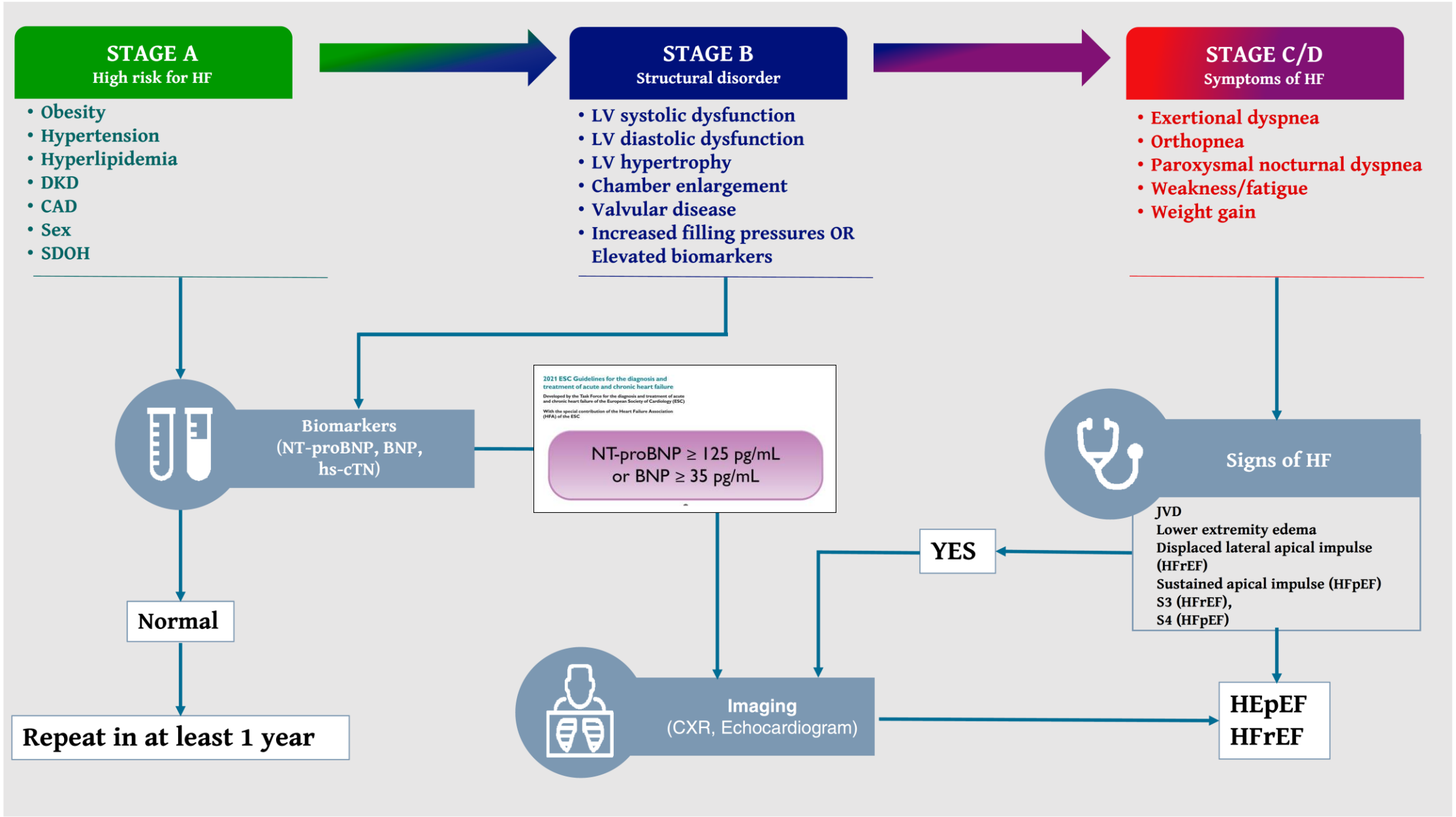
Wen Sun[1,2], Alice P. S. Kong[1,3], Bryan P. Yan[1,2]*

Table 2. MACE with Dx-to-Rx time ≤12 months versus >12 months in subgroups stratified by presence or absence of known ASCVD or risk factors.

	Dx-to-Rx time ≤12 months			Dx-to-Rx time >12 months			Hazard ratio (95%CI)	P for interaction
MACE	**n/N**	**%**	**Rate/1000 person-years**	**n/N**	**%**	**Rate/1000 person-years**		
All patients	**30/1685**	**1.8**	**6.0**	**71/1685**	**4.2**	**14.2**	**0.27 (0.17–0.42)**	
Neither ASCVD nor CV risk factor	1/317	0.3	1.1	1/280	0.4	1.3	0.52 (0.03–8.27)	0.001
CV Risk factor only	4/932	0.4	1.4	14/864	1.6	5.3	0.11(0.03–0.42)	
ASCVD	25/436	5.7	20.1	56/541	10.4	35.4	0.49(0.30–0.80)	

Heart Failure: An Underappreciated Complication of Diabetes. A Consensus Report of the American Diabetes Association

Rodica Pop-Busui,[1] James L. Januzzi,[2] Dennis Bruemmer,[3] Sonia Butalia,[4] Jennifer B. Green,[5] William B. Horton,[6] Colette Knight,[7] Moshe Levi,[8] Neda Rasouli,[9] and Caroline R. Richardson[10]



Diabetes Care 2022;45:1670–1690

Figure 1—Stepwise approach for screening and diagnosis across HF stages. CXR, chest X-ray; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; hs-cTN, high-sensitivity cardiac troponin; JVD, jugular vein distension; LV, left ventricle

Incidence of atrial fibrillation, ischaemic heart disease and heart failure in patients with diabetes

Amy Groenewegen[1*], Victor W. Zwartkruis[2], Betül Cekic[1], Rudolf. A. de Boer[2], Michiel Rienstra[2], Arno W. Hoes[3], Frans H. Rutten[1] and Monika Hollander[1]

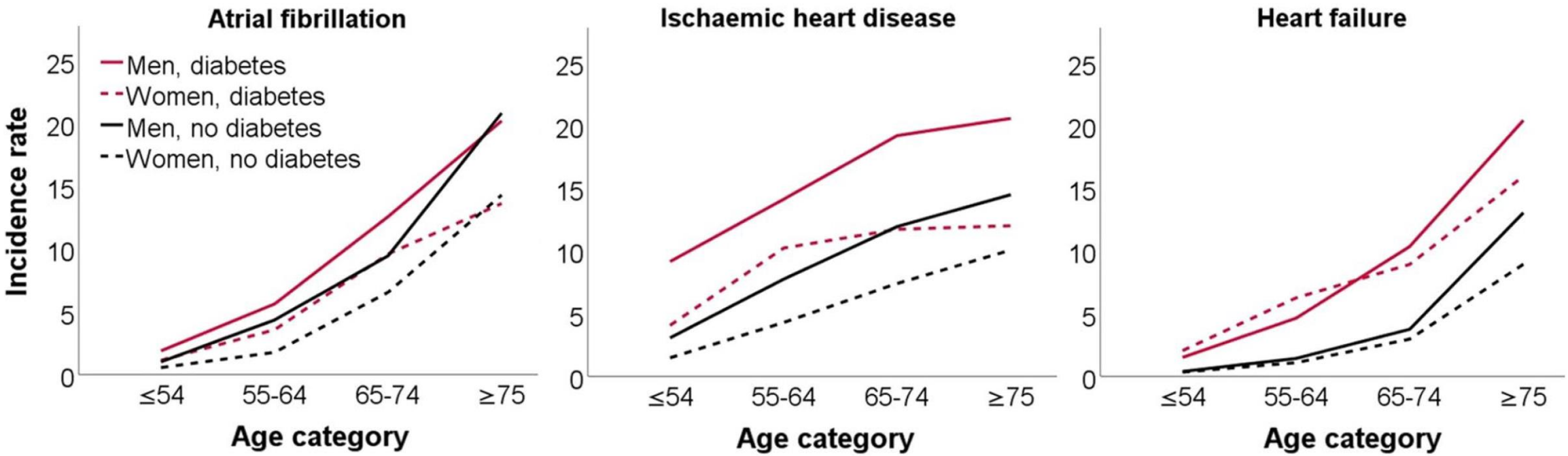
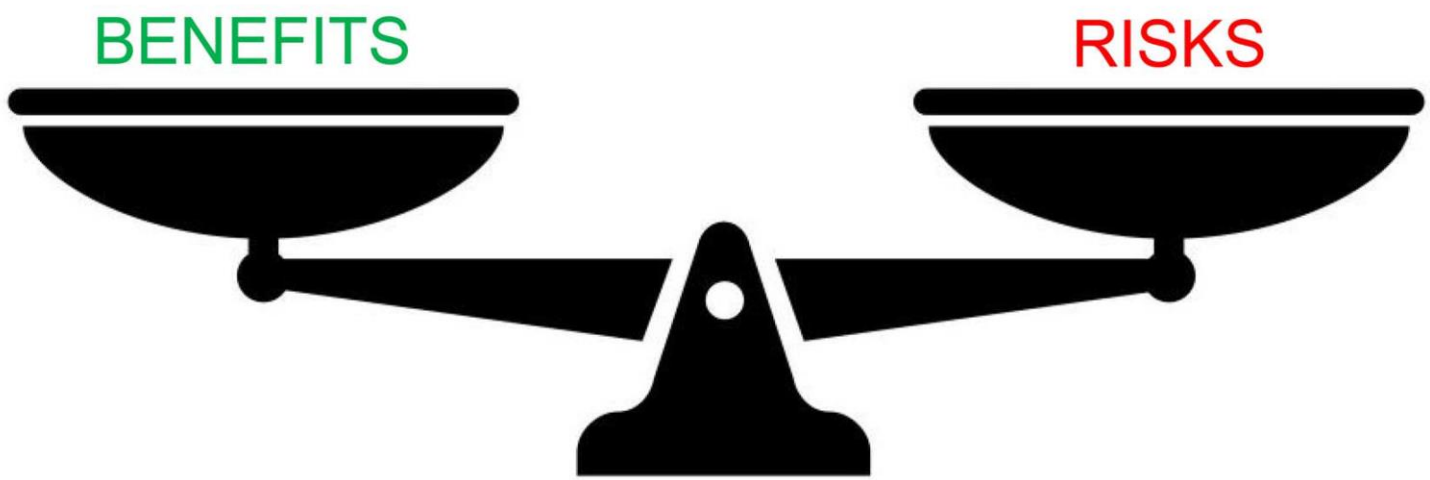


Fig. 3 Incidence of cardiovascular diseases per 1000 person-years, for patients with and without diabetes, per age category

The role of sodium-glucose co-transporter-2 inhibitors in frail older adults with or without type 2 diabetes mellitus

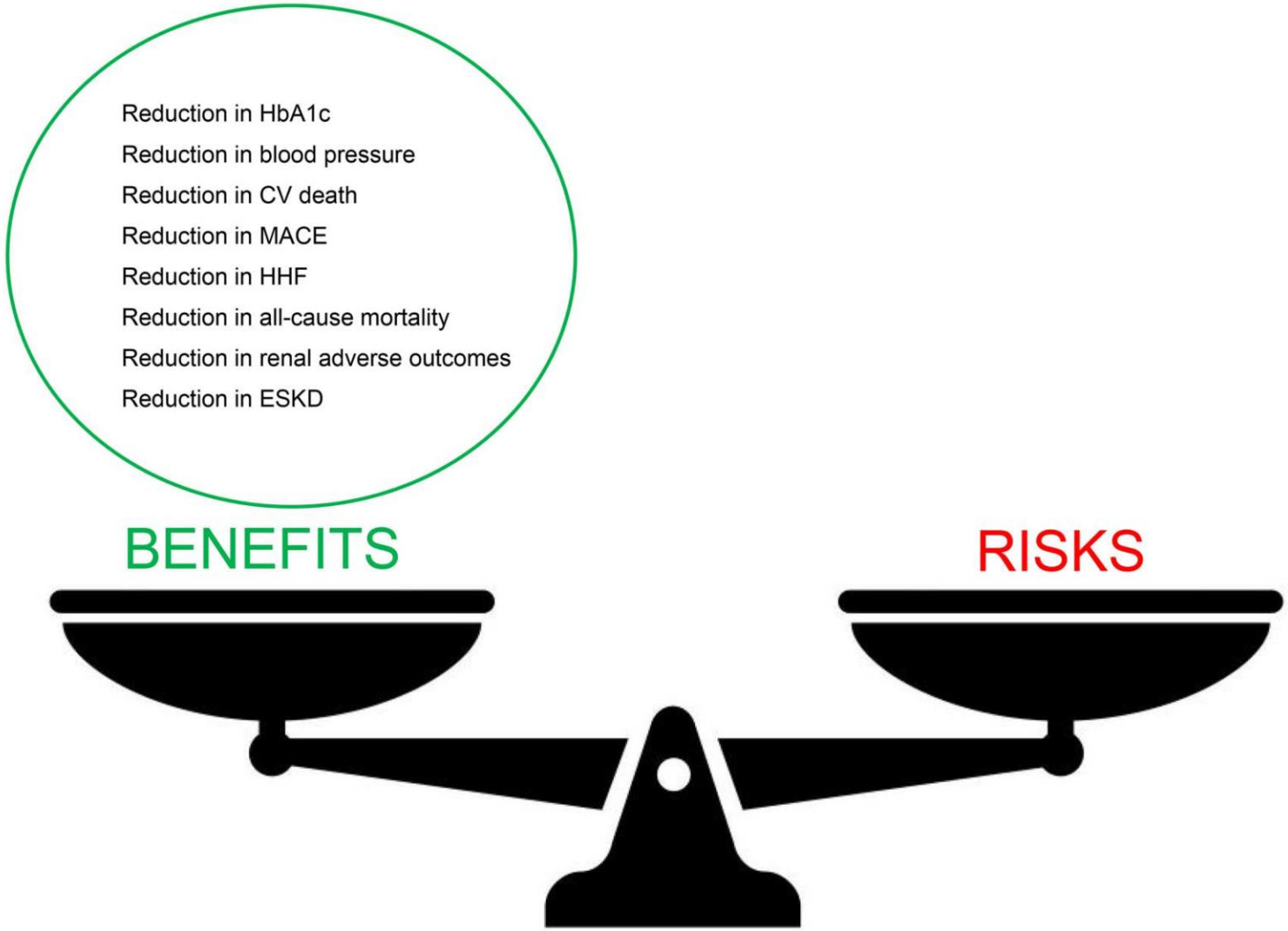
Marc Evans[1], Angharad R. Morgan[2], Sarah Davies[3], Hannah Beba[4], William David Strain[5,6]



Age and Ageing 2022; 51: 1–8

The role of sodium-glucose co-transporter-2 inhibitors in frail older adults with or without type 2 diabetes mellitus

Marc Evans[1], Angharad R. Morgan[2], Sarah Davies[3], Hannah Beba[4], William David Strain[5,6]



Age and Ageing 2022; 51: 1–8

Independent effects of 15 commonly prescribed drugs on all-cause mortality among US elderly patients with type 2 diabetes mellitus

Seo H Baik, Clement J McDonald

Table 3 Marginal HRs of all-cause mortality for each drug

Rx use	(A) Full cohort n=360 437 HR (95% CI)	(B) Full cohort+IPSW n=360 437 HR (95% CI)	(C) DM Rx incident cohort n=143 693 HR (95% CI)	(D) Non-DM Rx incident cohort n=44 375 HR (95% CI)
Metformin	1.05 (1.02 to 1.08)*	0.92 (0.90 to 0.94)†	0.91 (0.86 to 0.96)*	1.10 (1.01 to 1.20)
Insulin	1.55 (1.51 to 1.59)†	1.40 (1.36 to 1.43)†	1.35 (1.26 to 1.45)†	1.43 (1.31 to 1.57)
Sulfonylurea	1.16 (1.13 to 1.20)†	1.06 (1.03 to 1.09)†	1.16 (1.08 to 1.24)†	1.28 (1.16 to 1.41)
Thiazolidinedione	1.03 (0.99 to 1.08)	0.96 (0.92 to 1.00)*	1.01 (0.85 to 1.20)	1.06 (0.89 to 1.27)
GLP-1 agonist	0.75 (0.70 to 0.80)†	0.78 (0.73 to 0.84)†	0.66 (0.49 to 0.88)*	0.66 (0.47 to 0.93)
DPP-4 inhibitor	0.94 (0.91 to 0.98)*	0.97 (0.94 to 1.00)	0.87 (0.78 to 0.97)*	0.81 (0.70 to 0.93)
SGLT2 inhibitor	0.73 (0.64 to 0.84)†	0.80 (0.70 to 0.91)*	0.41 (0.24 to 0.70)*	0.32 (0.16 to 0.65)
Other glucose-lowering Rx	0.97 (0.90 to 1.04)	0.95 (0.89 to 1.02)	0.99 (0.77 to 1.29)	1.05 (0.79 to 1.40)
All antihypertensive	0.97 (0.96 to 0.98)†	0.91 (0.90 to 0.92)†	0.92 (0.90 to 0.93)	0.84 (0.81 to 0.87)†
Diuretic—thiazide/thiazide-like	0.89 (0.87 to 0.92)†	0.83 (0.81 to 0.85)†	0.88 (0.84 to 0.93)	0.80 (0.72 to 0.89)†
Beta-blocker	1.07 (1.04 to 1.11)†	0.87 (0.85 to 0.90)†	0.99 (0.94 to 1.04)	0.93 (0.86 to 1.01)
DHP CCB	0.99 (0.96 to 1.02)	0.95 (0.92 to 0.97)†	0.95 (0.91 to 1.00)	0.85 (0.77 to 0.94)*
Non-DHP CCB	1.05 (1.02 to 1.09)*	1.30 (1.26 to 1.33)†	0.96 (0.90 to 1.03)	0.94 (0.83 to 1.07)
ACE inhibitor	0.98 (0.96 to 1.01)	0.84 (0.82 to 0.86)†	0.94 (0.89 to 0.98)	0.84 (0.77 to 0.92)†
ARB	0.86 (0.84 to 0.89)†	0.77 (0.75 to 0.80)†	0.80 (0.76 to 0.85)	0.71 (0.62 to 0.80)†
Statin	0.83 (0.80 to 0.85)†	0.65 (0.64 to 0.67)†	0.70 (0.67 to 0.74)	0.61 (0.56 to 0.66)†

BMJ Open Diab Res Care 2020;8:e000940

Efficacy, renal safety and tolerability of sodium-glucose cotransporter 2 inhibitors (SGLT2i) in elderly patients with type 2 diabetes: A real-world experience

Andrea Tumminia, Marco Graziano, Federica Vinciguerra, Andrea Lomonaco, Lucia Frittita*

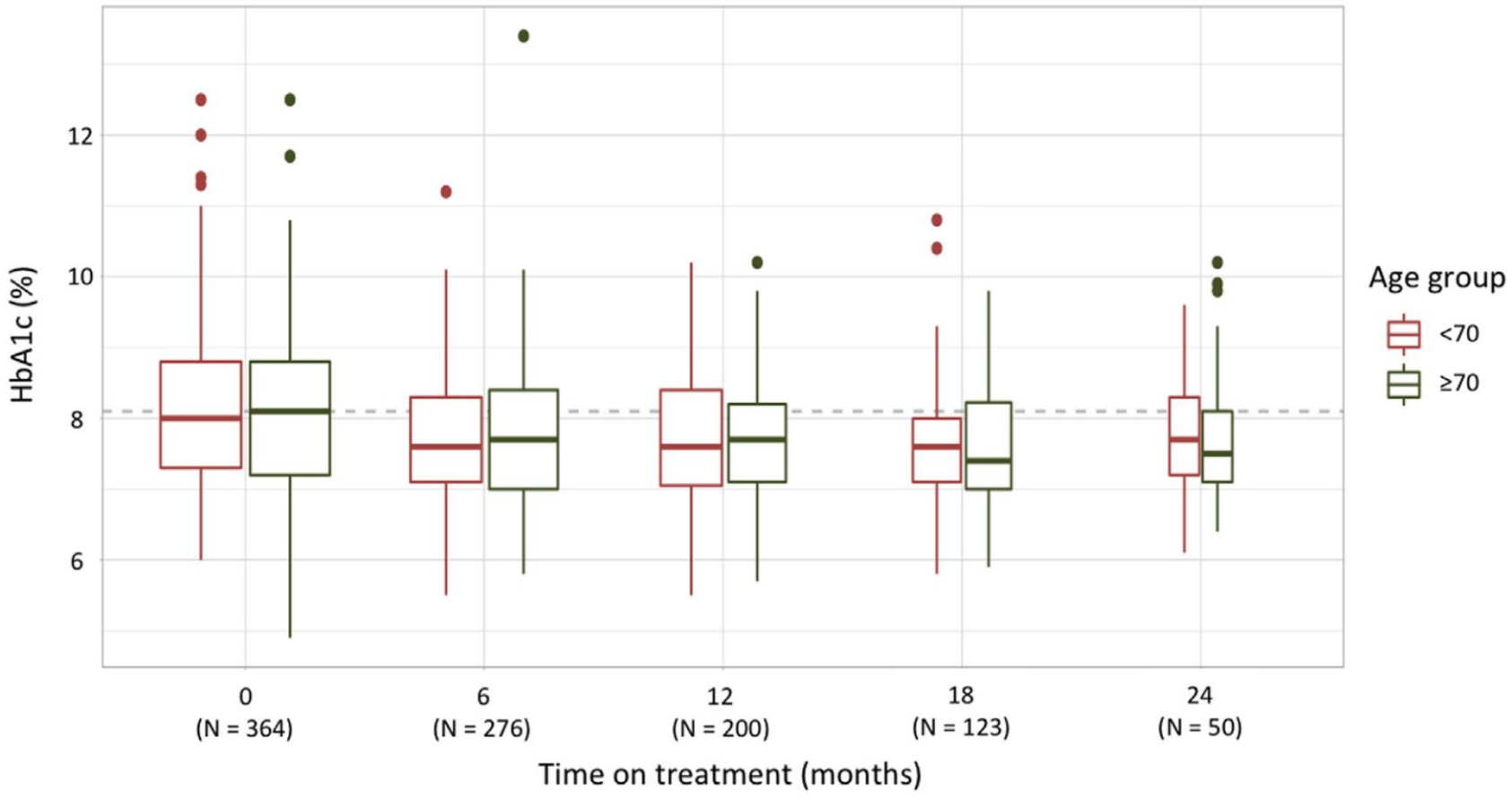


Fig. 1. Longitudinal distributions and trends of HbA1c levels during 24-months follow-up, by age class.Each box width is consistent with the number of observations at the corresponding timepoint. A horizontal dashed line represents the median HbA1c at baseline.

GLP-1 receptor agonists and SGLT2 inhibitors for older people with type 2 diabetes: A systematic review and meta-analysis

Thomas Karagiannis [a,*], *Apostolos Tsapas* [a,b,c], *Eleni Athanasiadou* [a], *Ioannis Avgerinos* [a], *Aris Liakos* [a], *David R. Matthews* [c,d], *Eleni Bekiari* [a,b]

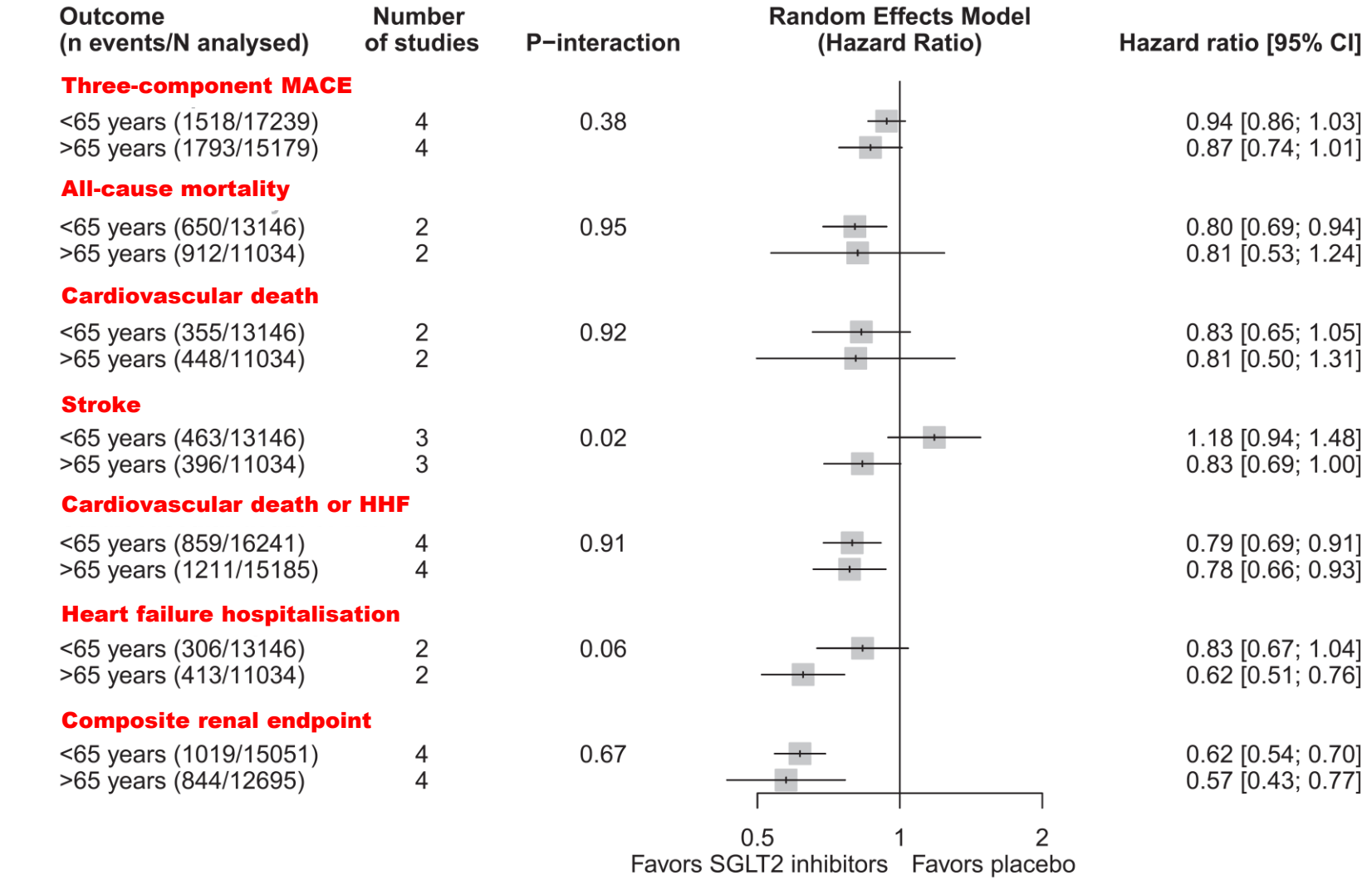


Fig. 2 – Meta-analysis results versus placebo in subgroups of patients <65 years and 65 years for trials with SGLT2 inhibitors. The effect estimate for the overall populationwas in favor of GLT2 nhibitors for three-component MACE, all-cause mortality, cardiovascular death, stroke, cardiovascular death or HHF, heart failure hospitalization, and the composite renal endpoint. Number f events (n) and patients analyzed (N) include data both for SGLT2 inhibitor and placebo arms. CI, confidence interval; HHF, hospitalization for heart failure; MACE, major adverse cardiovascular vents; SGLT2, sodium-glucose cotransporter 2.

Clinical benefits of empagliflozin in very old patients with type 2 diabetes hospitalized for acute heart failure

Luis M. Pérez-Belmonte MD, PhD[1,2,3,4] | Jaime Sanz-Cánovas MD[1] | Mercedes Millán-Gómez MD, PhD[4] | Julio Osuna-Sánchez MD[3,5] | Almudena López-Sampalo MD[1] | Michele Ricci MD[1] | Manuel Jiménez-Navarro MD, PhD[6] | Maria D. López-Carmona MD, PhD[1] | María Rosa Bernal-López PhD[1,7] | Miguel A. Barbancho MD, PhD[3] | José P. Lara MD, PhD[3] | Ricardo Gómez-Huelgas MD, PhD[1,6]

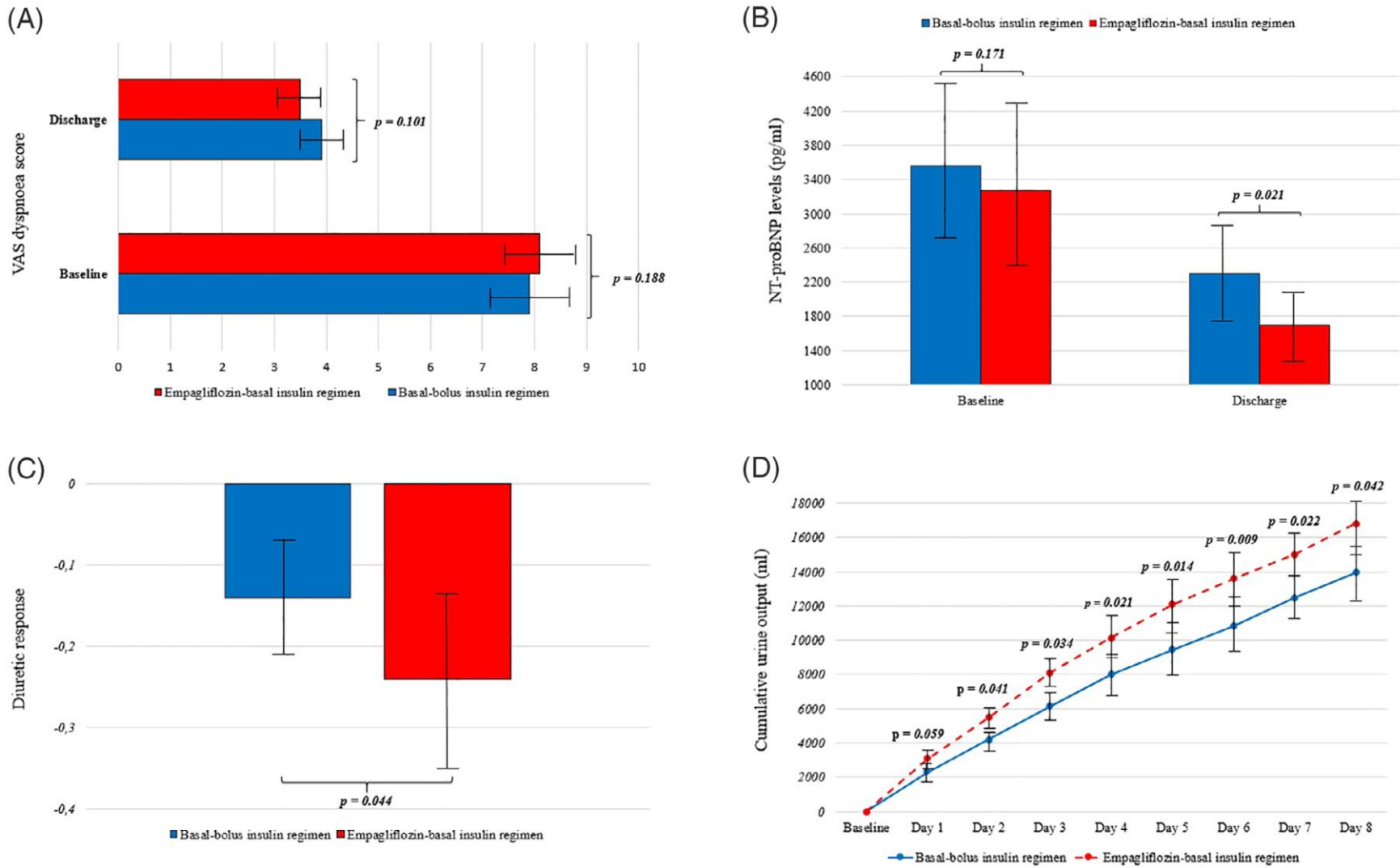
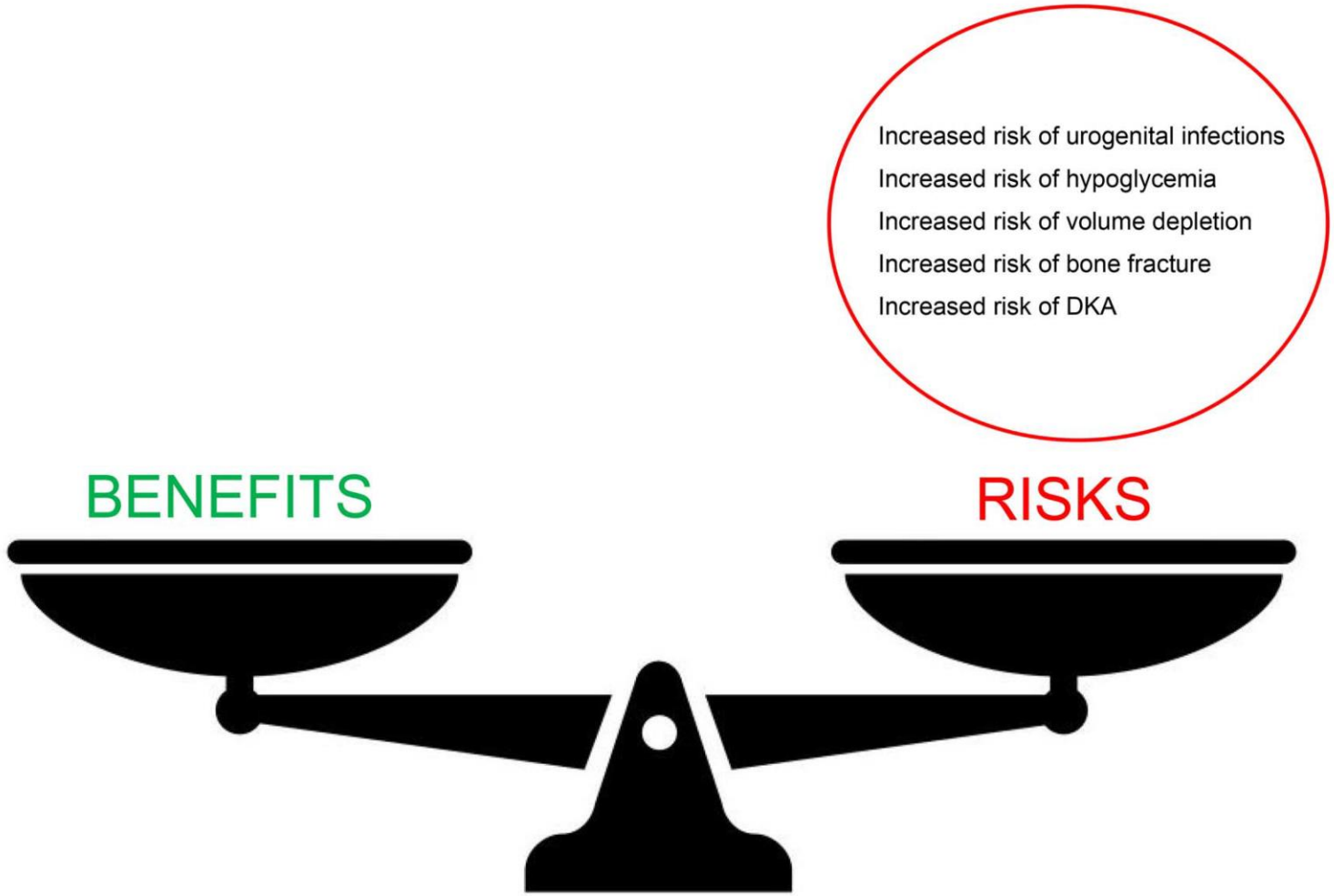


FIGURE 1 Visual analogue scale dyspnea score (A), N-terminal pro-brain natriuretic peptide (NT-proBNP) levels (B), diuretic response (C), and cumulative urine output (D), according to the ntihyperglycemic regimen. Differences between regimens in regard to visual analogue scale dyspnea score (A) and NT-proBNP levels (B) from baseline (at admission) to discharge, diuretic esponse (C) (defined as body weight loss (kilograms) per 40 mg furosemide or equivalent) at discharge, and cumulative urine output (D) during hospitalization are shown. Variables are shown s means ± standard deviation. Values were considered to be statistically significant when $p < 0.05$. NTproBNP, N-terminal pro-brain natriuretic peptide; VAS, visual analogue scale

J Am Geriatr Soc. 2022;70:862–871

The role of sodium-glucose co-transporter-2 inhibitors in frail older adults with or without type 2 diabetes mellitus

Marc Evans[1], Angharad R. Morgan[2], Sarah Davies[3], Hannah Beba[4], William David Strain[5,6]

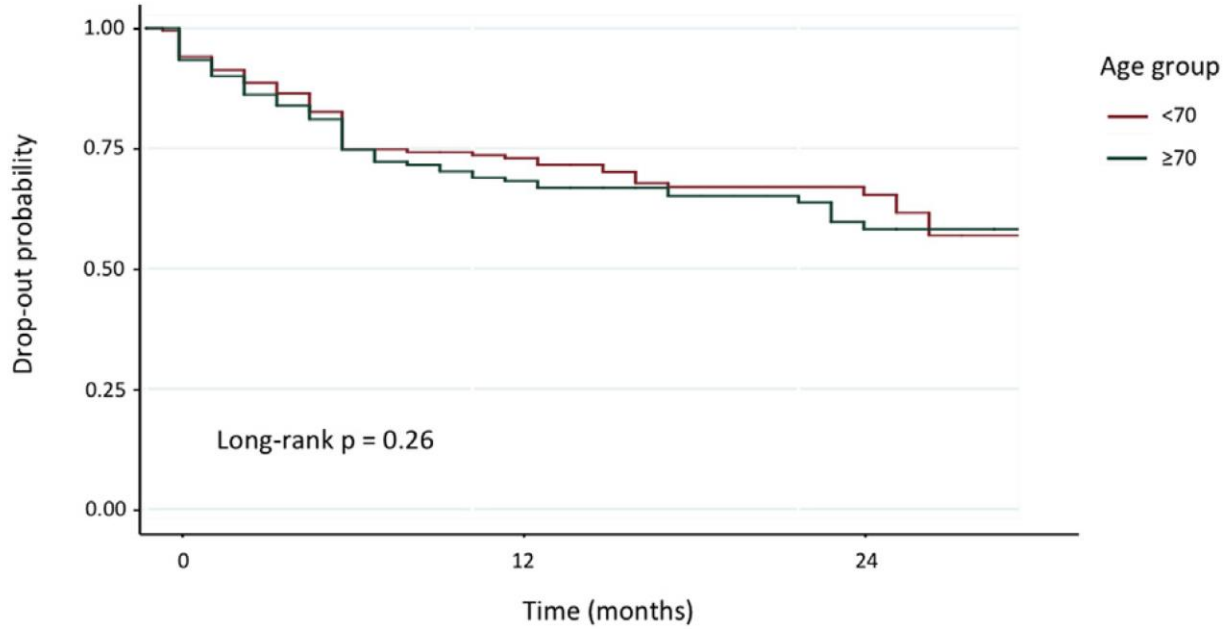


Age and Ageing 2022; 51: 1–8

Efficacy, renal safety and tolerability of sodium-glucose cotransporter 2 inhibitors (SGLT2i) in elderly patients with type 2 diabetes: A real-world experience

Andrea Tumminia, Marco Graziano, Federica Vinciguerra, Andrea Lomonaco, Lucia Frittita*

Discontinuation rate during follow-up



Causes of treatment discontinuation (N, %)	Overall patientsN = 364	65–69 yearsN = 184	≥70 yearsN = 180	P
Overall causes	128 (35.2)	63 (34.2)	65 (36.1)	0.71
Genitourinary tract infections	60 (16.5)	29 (15.8)	31 (17.2)	0.69
Lack of efficacy/poor metabolic control	25 (6.9)	16 (8.7)	9 (5.0)	0.16
Poor patient compliance	32 (8.8)	18 (9.7)	14 (7.8)	0.49
Persistent (≥3 months) eGFR decline (≤45 ml/min)	8 (2.2)	0 (0)	8 (4.4)	NA
Orthostatic hypotension	3 (0.8)	0 (0)	3 (1.7)	NA

P-values <0.05 are statistically significant.
Abbreviations: eGFR, estimated Glomerular Filtration Rate; NA, not applicable.

Primary Care Diabetes 15 (2021) 283–288

Efficacy and safety of sodium-glucose co-transporter 2 inhibitors in the elderly *versus* non-elderly patients with type 2 diabetes mellitus: a meta-analysis

Yao Wang[1)] *, Xian Shao[2)] * and Zewen Liu[3)]

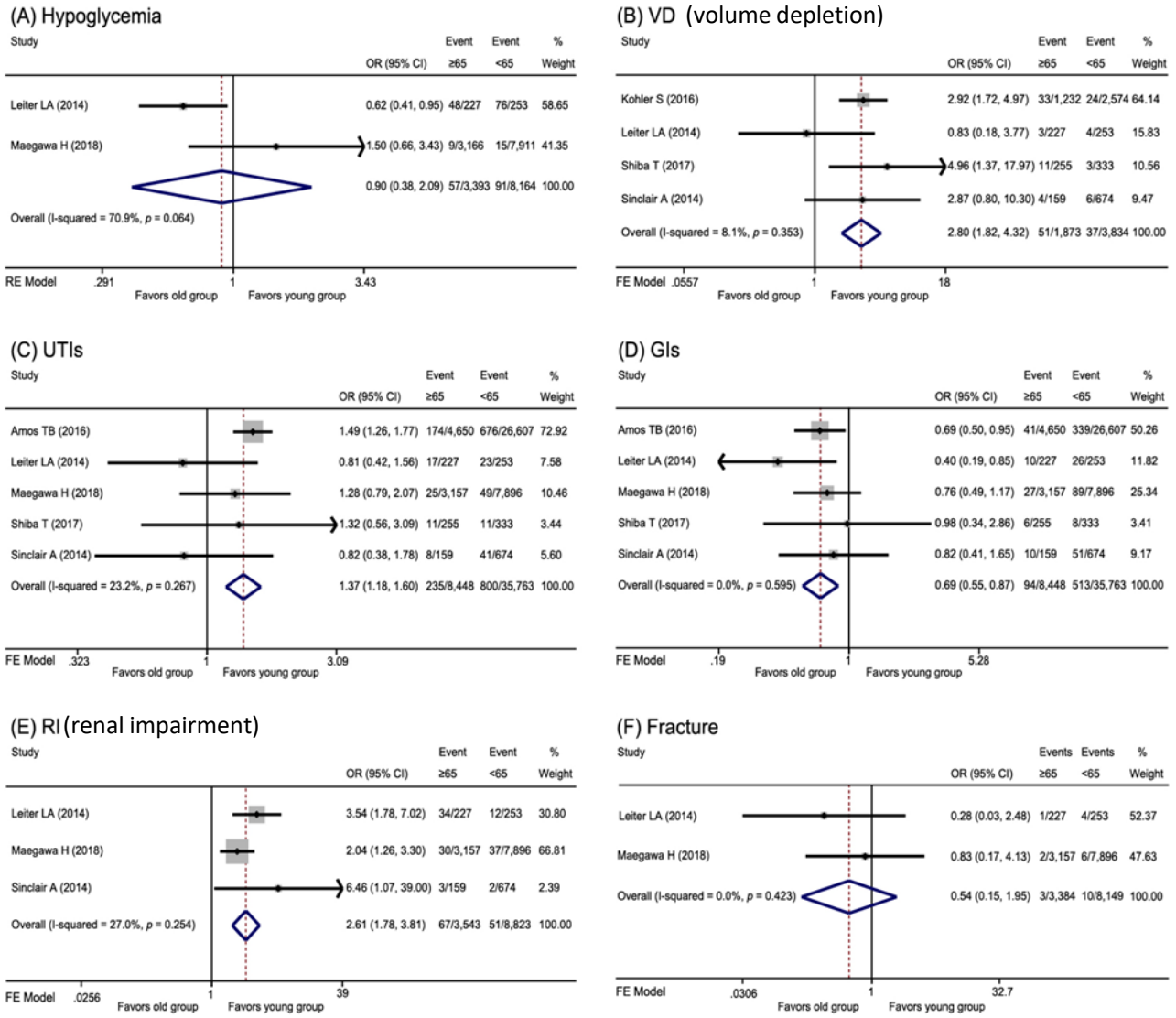


Fig. 4 Forest plot of safety of SLGT2i in two age groups. (A) Hypoglycemia; (B) VD; (C) UTIs; (D) GIs; (E) RI; (F) Fracture.

Endocrine Journal 2022, 69 (6), 669-679

Safety and efficacy of empagliflozin in elderly Japanese patients with type 2 diabetes mellitus: A post hoc analysis of data from the SACRA study

Kenta Okada MD, PhD[1] | Satoshi Hoshide MD, PhD[2] | Mitsutoshi Kato MD, PhD[3] | Hiroshi Kanegae BSc[2] | Shun Ishibashi MD, PhD[1] | Kazuomi Kario MD, PhD[2]

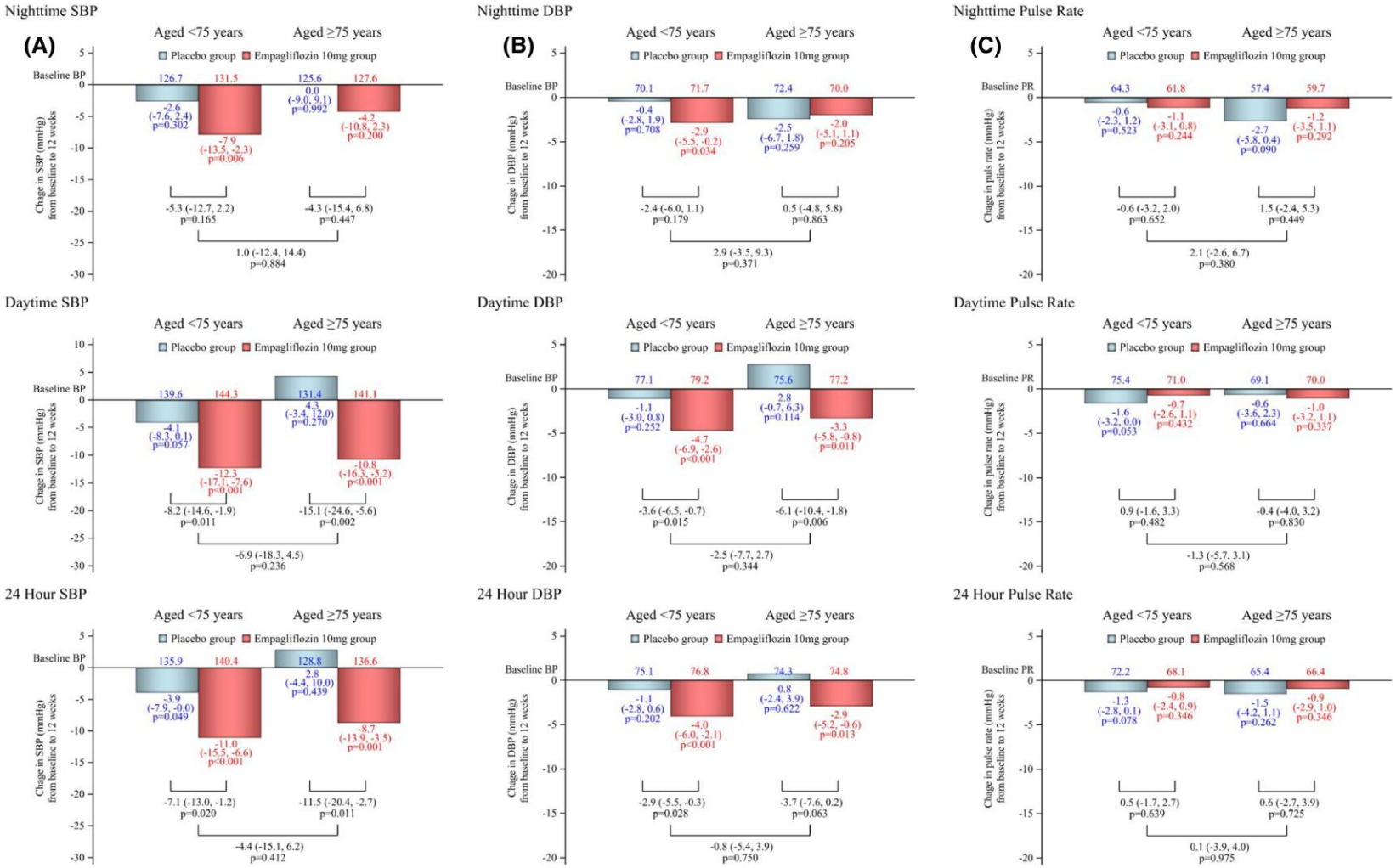


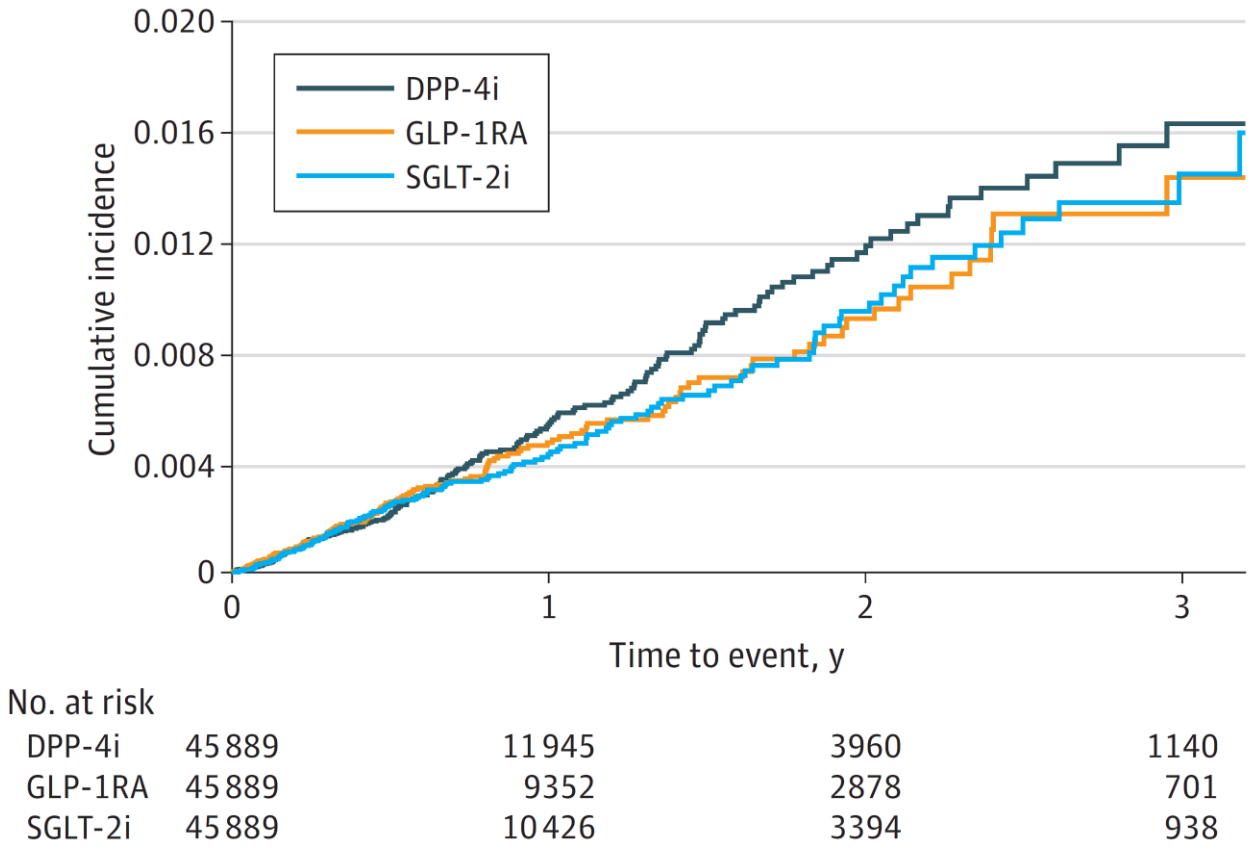
FIGURE1 Changes from baseline in nighttime, daytime, and 24-h systolic (SBP) (A), diastolic (DBP) (B) blood pressure, and pulse rate (C). Bars and values represent the changes (means and 95% CIs) from baseline, which were compared using mixed-effects models with repeated measures, adjusted for age and sex. The p-values quoted are for comparisons of the changes from baseline, and the between-group and between-age group differences

J Clin Hypertens. 2021;23:860–869

Association of Sodium-Glucose Cotransporter–2 Inhibitors With Fracture Risk in Older Adults With Type 2 Diabetes

Min Zhuo, MD, MPH; Chelsea E. Hawley, PharmD, MPH; Julie M. Paik, MD, MPH, ScD; Lily G. Bessette, BS; Deborah J. Wexler, MD; Dae H. Kim, MD, MPH, ScD; Angela Y. Tong, MS; Seoyoung C. Kim, MD, ScD; Elisabetta Patorno, MD, DrPH

cumulative incidence of fractures

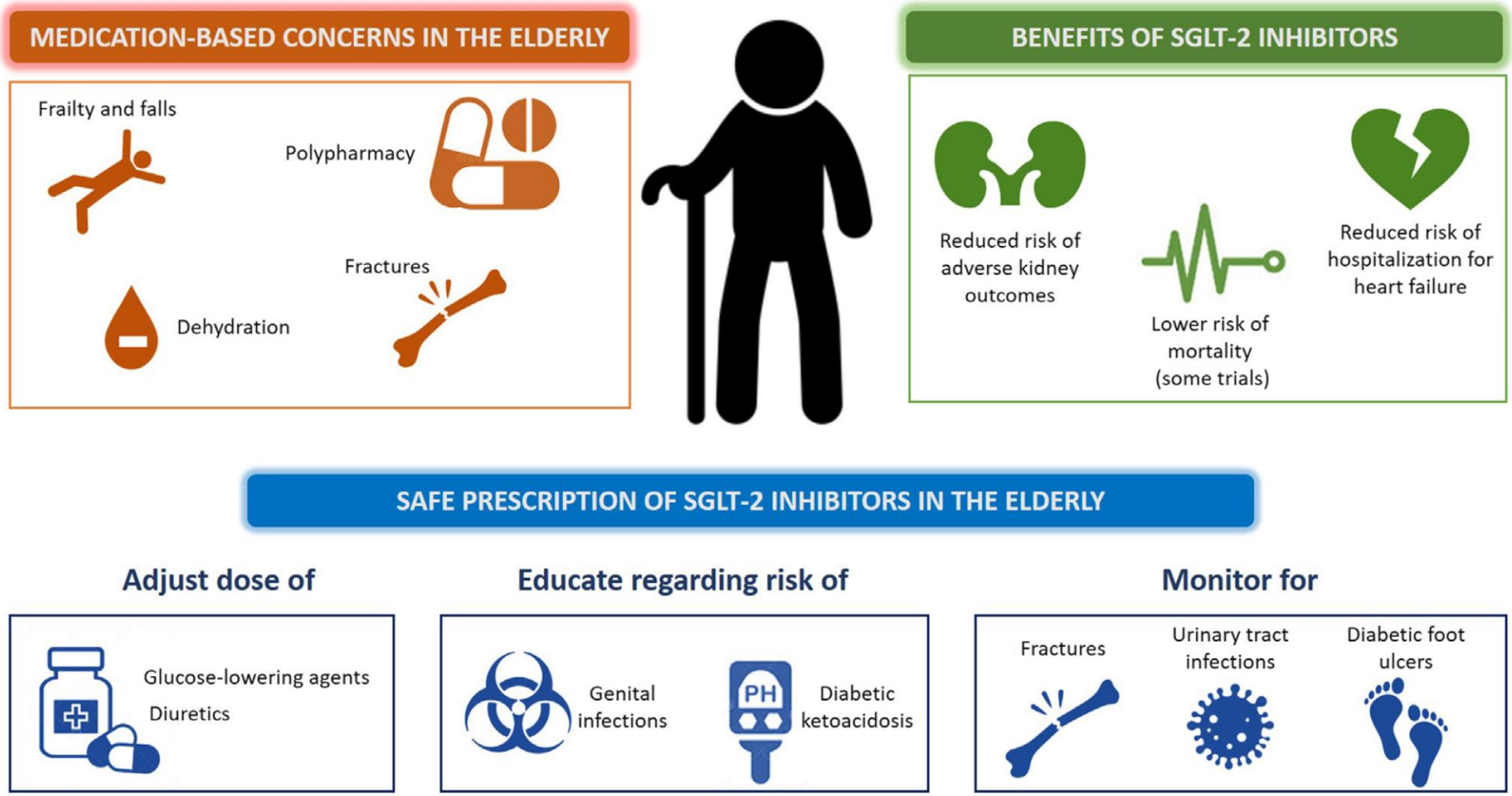


The cumulative incidence of fractures within the 3 groups is shown in this Kaplan-Meier plot.We observed a total of 501 fracture events. There were 158 events in sodium-glucose otransporter–2 inhibitor (SGLT-2i) users (incidence ratio [IR], 4.69 fractures per 1000 person-years) compared with 195 in dipeptidyl peptidase 4 inhibitor (DPP-4i) users (IR, 5.26 fractures per 00 person-years) and 148 in glucagon-like peptide 1 receptor agonist (GLP-1RA) users (IR, 4.71 fractures per 1000 person-years). SGLT-2i use was not with associated fracture compared with PP-4i (hazard ratio, 0.90; 95%CI, 0.73-1.11) or GLP-1RA use (hazard ratio, 1.00; 95%CI, 0.80-1.25).

JAMA Network Open. 2021;4(10):e2130762

SGLT2 Inhibitors and Safety in Older Patients

Rena Pollack, MD[a,b], Avivit Cahn, MD[a,c,*]



Heart Failure Clin 18 (2022) 635–643

Incidence of atrial fibrillation, ischaemic heart disease and heart failure in patients with diabetes

Amy Groenewegen[1*], Victor W. Zwartkruis[2], Betül Cekic[1], Rudolf. A. de Boer[2], Michiel Rienstra[2], Arno W. Hoes[3], Frans H. Rutten[1] and Monika Hollander[1]

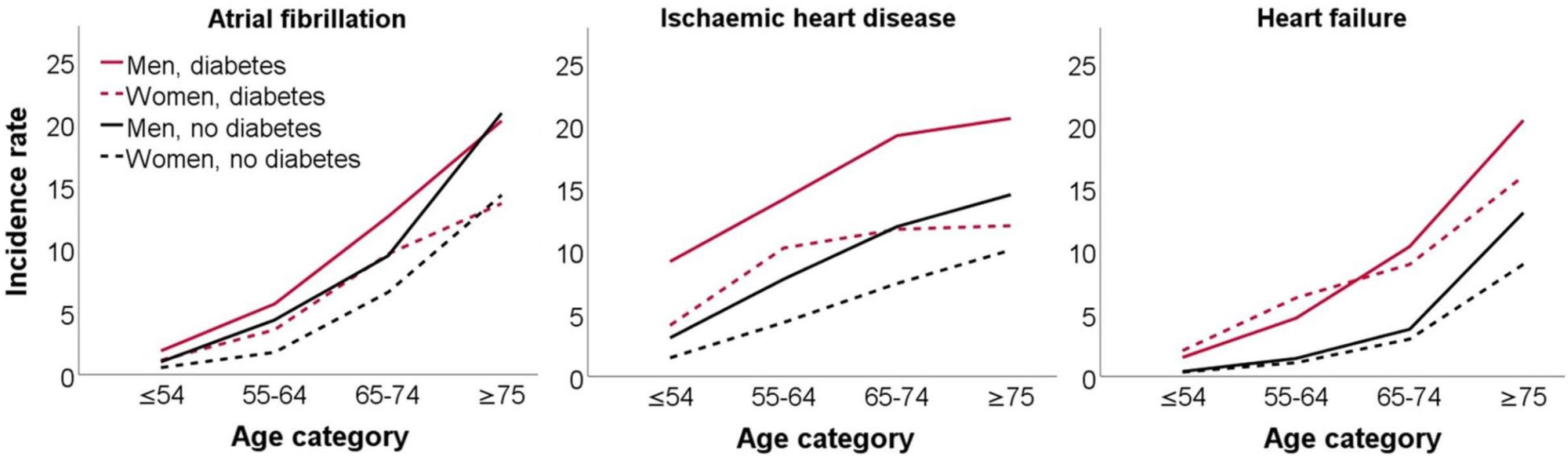


Fig. 3 Incidence of cardiovascular diseases per 1000 person-years, for patients with and without diabetes, per age category

Sodium-Glucose Cotransporter-2 Inhibition Benefits in Cardiorenal Risk in Men and Women

Jacob E. Pruett,[1] Seth T. Lirette,[2] Damian G. Romero,[1,3,4,5] and Licy L. Yanes Cardozo[1,3,4,5,6]

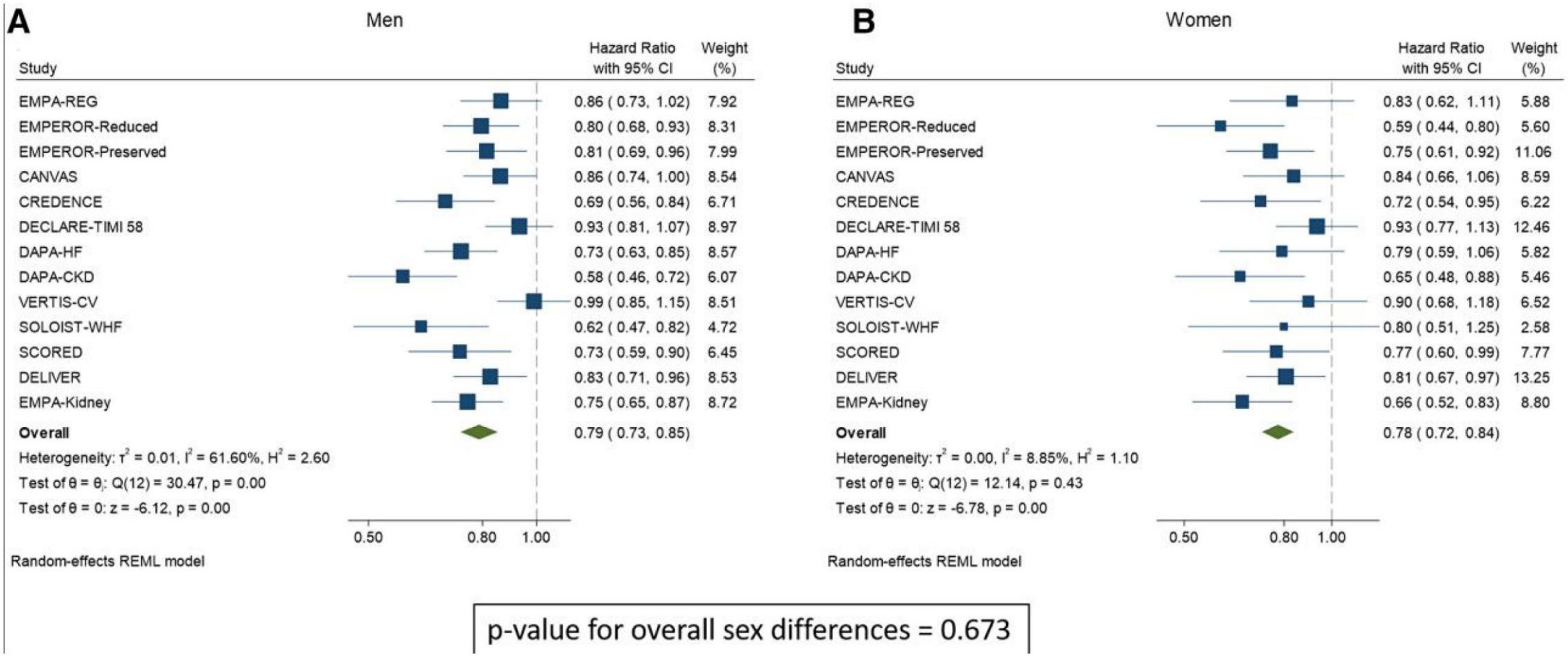


Figure 2.Effect of sodium-glucose cotransporter-2 inhibitors compared to control on the risk for the primary composite cardiorenal endpoint in men (A) and women (B).

Le Monografie degli Annali AMD 2021

Valutazione della Qualità dell'assistenza al diabete in Italia in base al genere

Differenze di Genere nel Diabete di tipo 2

Distribuzione dei pazienti con DM2 per classe di farmaco anti-iperglicemizzante (%)

Trattamento	Donne	Uomini
Metformina	70,0	71,7
Sulfanilurea	14,6	13,5
Glinide	2,8	2,7
Glitazone	3,7	5,1
Acarbose	2,1	1,9
DPPIVi	22,2	21,6
GLP1-RA	10,7	11,1
SGLT2i	9,8	13,8
Insulina	33,8	32,0
Insulina basale	29,0	27,5
Insulina rapida	20,3	18,3

JAMD, http://www.aemmedi.it

Gender disparities in time-to-initiation of cardioprotective glucose-lowering drugs in patients with type 2 diabetes and cardiovascular disease: a Danish nationwide cohort study

Kristian Løkke Funck[1], Lasse Bjerg[1,2], Anders Aasted Isaksen[2], Annelli Sandbæk[1,2] and Erik Lerkevang Grove[3,4*]

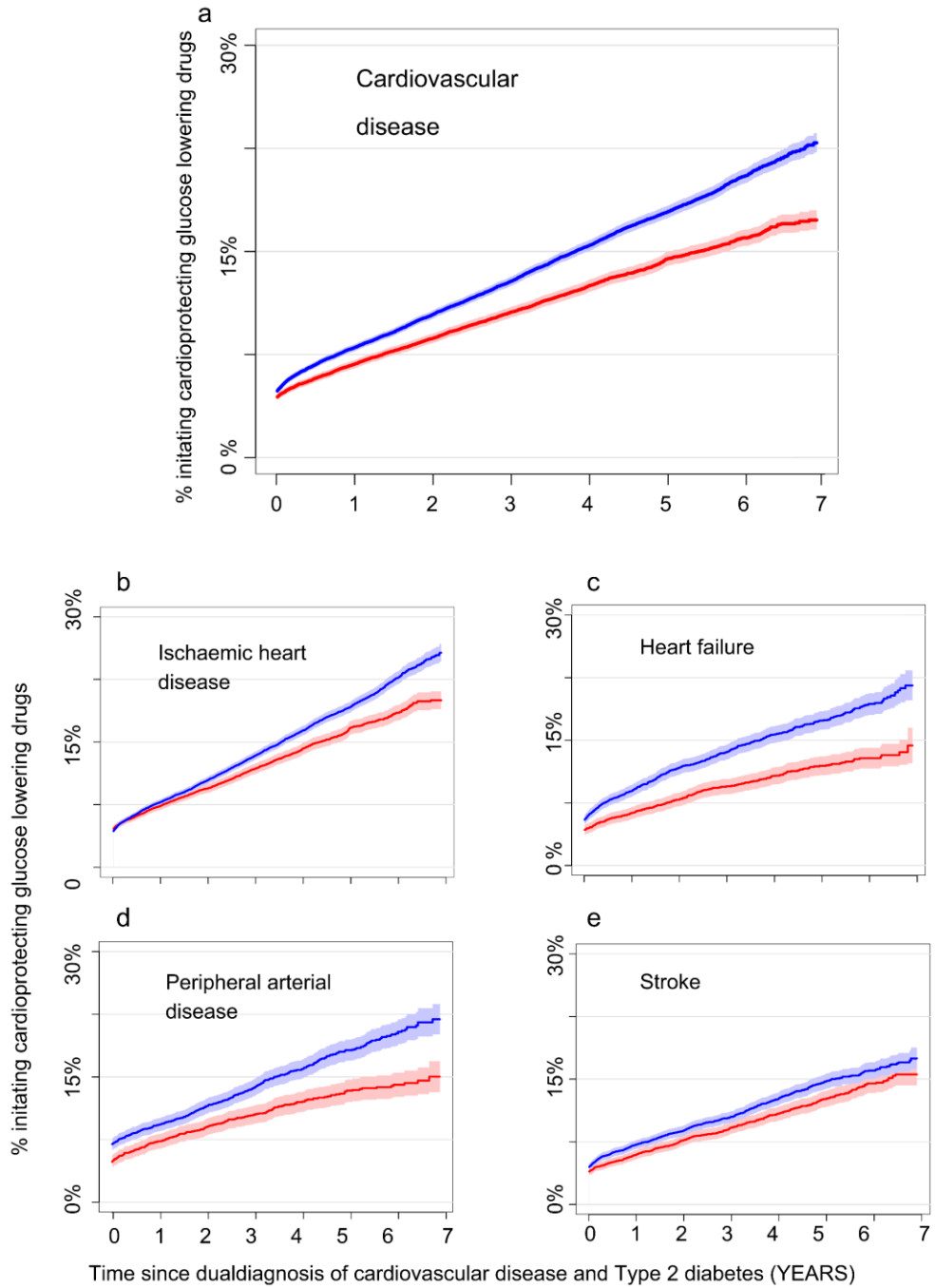


Fig. 1 Time to initiation of cardioprotective glucose-lowering drugs in male and female patients with a first dual diagnosis of type 2 diabetes and cardiovascular disease. A Male and female patients with a new-onset dual diagnosis of type 2 diabetes and any cardiovascular disease. B Male and female patients with new-onset T2DM and schemic heart disease. C Male and female patients with new-onset T2DM and stroke. D Male and female patients with new-onset T2DM and peripheral artery disease. E Male and female atients with new-onset T2DM and heart failure. Prevalent users of cardioprotective GLDs are included in graph at time = 0. Red = women, blue = men. GLP-1RA glucagon-like peptide-1 eceptor agonist; SGLT2 sodium-glucose co-transporter-2

Cardiovascular Diabetology (2022) 21:279

Conclusioni

Lo scompenso cardiaco è una complicanza potenziale frequente, spesso misconosciuta, del diabete mellito.
La maggior parte di farmaci ipoglicemizzanti hanno dati limitati o (se valutati nei CVOT) si sono dimostrati, nella migliore delle ipotesi, neutri in termini di ricovero per scompenso cardiaco o, come in alcuni casi, possono aumentare il rischio di insufficienza cardiaca.

Su tali basi l'opportunità dell'effetto degli SGLT-2 inibitori nella prevenzione e trattamento dello scompendo cardiaco rappresenta oggi un caposaldo della strategia terapeutica della persona con diabete mellito.