Terapie ipoglicemizzanti innovative e personalizzazione della terapia ipoglicemizzante: SGLT2 inibitori, GLP1 RA, metformina e fenotipi clinici

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Dichiarazione dei conflitti d'interesse

Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni ho avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

- **Advisory Board Membership and Consultancy**: Boehringer Ingelheim, Eli-Lilly, Mundipharma Pharmaceutica, Novo Nordisk, Astra-Zeneca, Sanofi-Aventis, Roche Diabetes Care.

- **Lectures**: Astra Zeneca, Boehringer Ingelheim, Eli-Lilly, Novo Nordisk, Sanofi-Aventis, Mundipharma Pharmaceutica, Abbott, MSD, Neopharmed Gentili, Menarini, Essex Italia, Ascensia Diabetes.

STADIAZIONE del DIABETE

1. **Durata** (neodiagnosi?)
2. Modalità di **esordio** (diagnosi fatta in corso di OGTT in paziente asintomatico? Esordio con iperglicemia importante?)
3. Compenso glicemico (**Hba1c**)
4. **Riserva pancreatica**
5. **Complicanze** micro e macrovascolari associate
6. Tipo di **trattamento ipoglicemizzante** (Monoterapia o multiterapia? ipoglicemizzante orale o insulina?

STADIAZIONE CLINICA del PAZIENTE

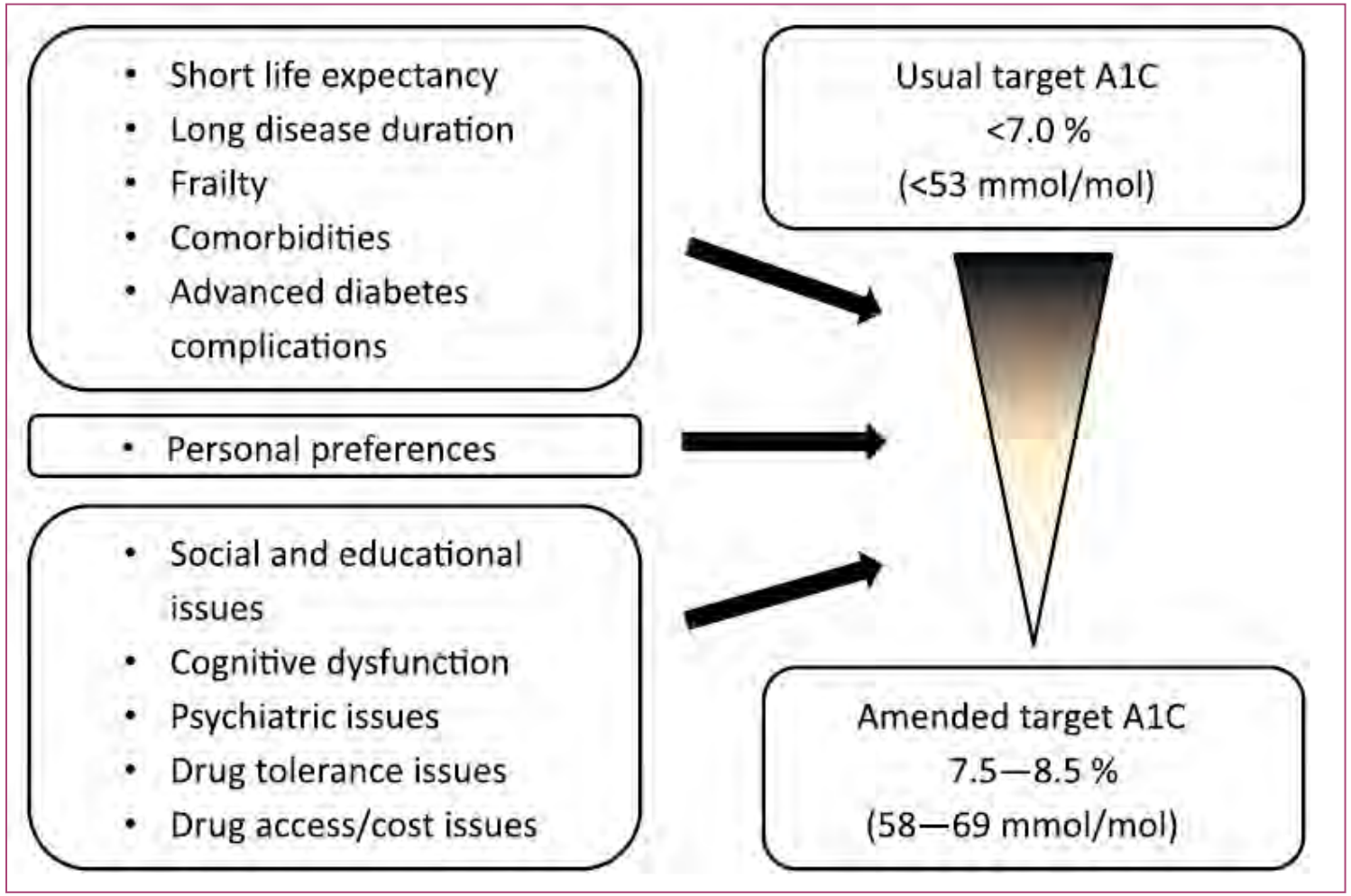
1. Obesità associata (**diabesità**)?
2. Altre **patologie associate**?
   - -Ipertensione arteriosa
   - -Dislipidemia
   - -Cardiopatia ischemica
   - -Malattie cerebrovascolari
   - -Insufficienza renale
   - -Neoplasie
3. **Compliance**
4. **Aspettativa di vita**
5. **Terapia farmacologica** (interazioni farmacologiche?

L'approccio internistico-metabolico deve integrare tutti i diversi aspetti del paziente e individuare un trattamento personalizzato cha abbia come obiettivo la cura della malattia diabetica nella sua complessità piuttosto che la glicemia

Personalized Management of Hyperglycemia in Type 2 Diabetes

Reflections from a *Diabetes Care* Editors' Expert Forum

Itamar Raz, MD[1]
Matthew C. Riddle, MD[2]
Julio Rosenstock, MD[3]
John B. Buse, MD, PHD[4]
Silvio E. Inzucchi, MD[5]
Philip D. Home, DM, DPHIL[6]
Stefano Del Prato, MD[7]
Ele Ferrannini, MD[8]
Juliana C.N. Chan, MD[9]
Lawrence A. Leiter, MD[10]
Derek LeRoith, MD, PHD[11]
Ralph DeFronzo, MD[12]
William T. Cefalu, MD[13]



Linea guida pubblicata nel Sistema Nazionale Linee Guida

Roma, 26 luglio 2021

1.1 Si raccomanda un target di HbA1c tra 49 mmol/mol (6.6%) e 58 mmol/mol (7.5%) in pazienti con diabete di tipo 2 trattati con farmaci associati ad ipoglicemia.

1.2.1. Si raccomanda un target di HbA1c inferiore 53 mmol/mol (7%) in pazienti con diabete di tipo 2 trattati con farmaci non associati ad ipoglicemia.

Forza della raccomandazione: forte. Qualità delle prove: bassa.

1.2.2. Si suggerisce un target di HbA1c inferiore o uguale a 48 mmol/mol (6.5%) in pazienti con diabete di tipo 2 trattati con farmaci non associati ad ipoglicemia.

Forza della raccomandazione: debole. Qualità delle prove: molto bassa.

Considerazioni su sottogruppi di pazienti

- **Non sono disponibili dati** di efficacia e sicurezza **nei soggetti ultrasettantacinquenni** con diabete.
- I **benefici osservati** con l'intensificazione del controllo glicemico **si iniziano ad evidenziare dopo 2 anni di trattamento**.
- Tali considerazioni **porterebbero a raccomandare valori di HbA1c più elevati in soggetti di età avanzata e/o con aspettativa di vita limitata**.

Individualized Glycemic Goals for Older Adults Are a Moving Target

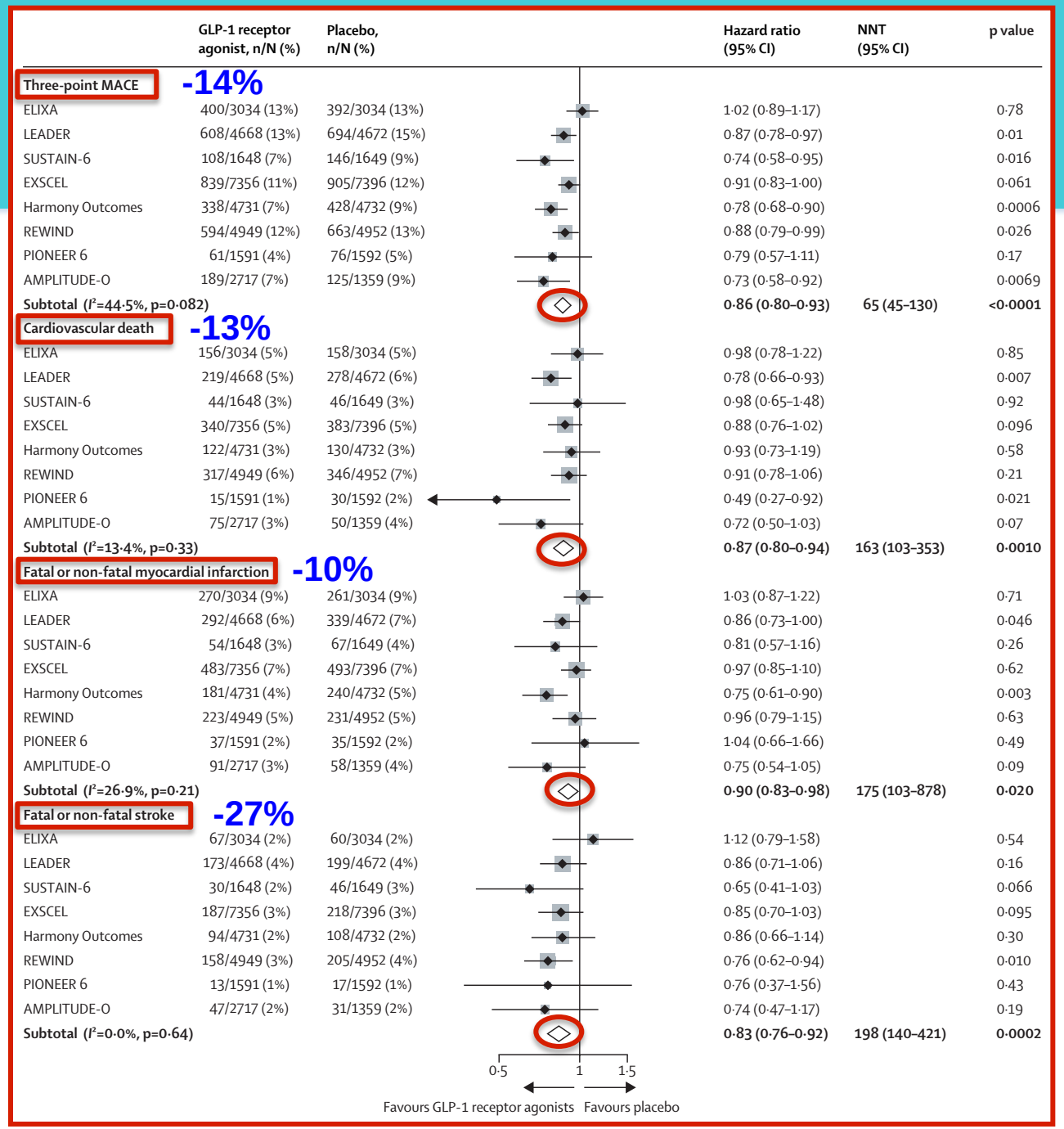
Scott J. Pilla,[1,2,3] Zhinous Shahidzadeh Yazdi,[4] and Simeon I. Taylor[4]

Diabetes Care 2022;45:1029–1031 | https://doi.org/10.2337/dci22-0004

- So long as it can be achieved **safely, a therapeutic target HbA1c <7.0% will provide the best protection** from complications of diabetes.

- Patients with life expectancy of less than 3–5 years are unlikely to benefit from tight glycemic control, although prognosis may be difficult to determine. **Deintensification of drugs with high risk of hypoglycemia** (i.e., insulins and insulin secretagogues) should be strongly considered in patients with limited life expectancy.

- Insulins should be reserved for patients with late-stage T2D with insulin-dependent physiology due to advanced b-cell failure. When insulin is prescribed, **it may be appropriate to relax HbA1c targets (e.g., HbA1c <8.0% rather than <7.0%).**



Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomised trials

Naveed Sattar, Matthew M Y Lee*, Søren L Kristensen*, Kelley R H Branch, Stefano Del Prato, Nardev S Khurmi, Carolyn S P Lam, Renato D Lopes, John J V McMurray, Richard E Pratley, Julio Rosenstock, Hertzel C Gerstein*

Lancet Diabetes Endocrinol 2021 9: 653–62

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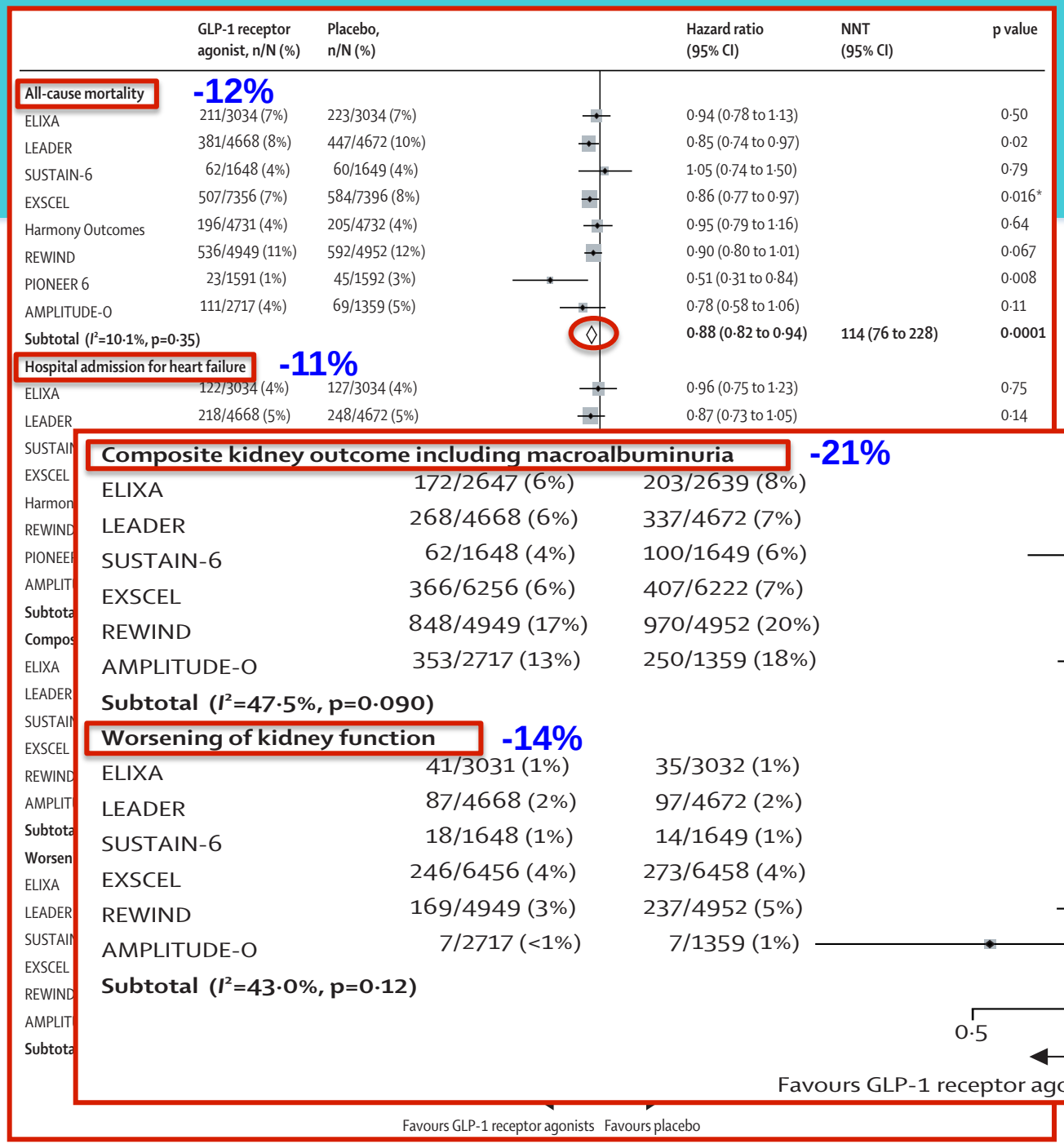

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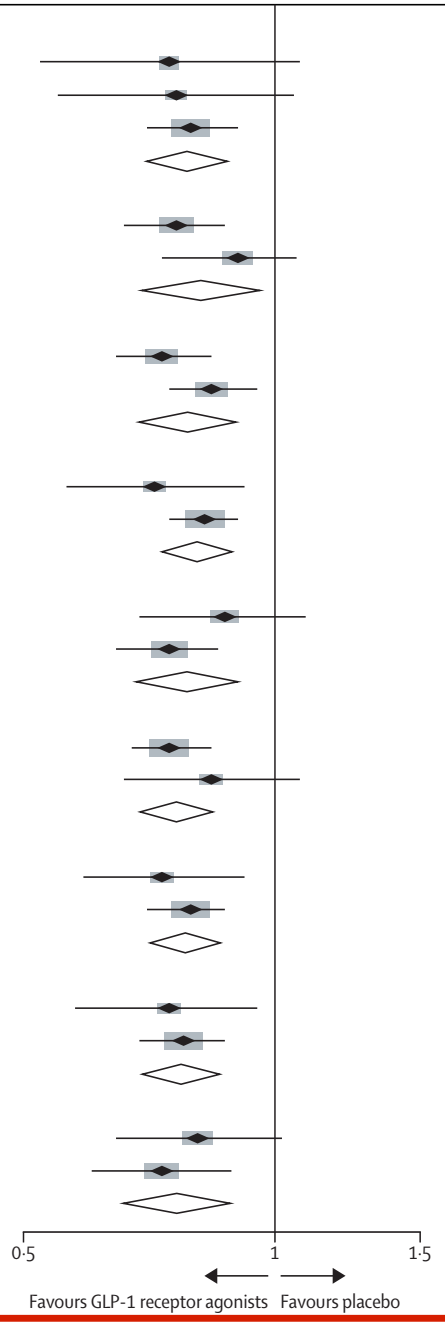
	GLP-1 receptor agonist, n/N (%)	Placebo, n/N (%)	Hazard ratio (95% CI)	$p_{interaction}$
MACE incidence rate in placebo group*				
Higher	927/10 482 (9%)	945/9125 (10%)	0·84 (0·68–1·04)	0·94
Intermediate	947/9004 (11%)	1051/9045 (12%)	0·85 (0·70–1·03)	
Lower	1263/11 208 (11%)	1433/11 216 (13%)	0·87 (0·81–0·94)	
Subtotal (I^2=0·0%, p=0·94)			0·86 (0·81–0·92)	
Established cardiovascular disease				
Yes	2608/23 673 (11%)	2877/22 432 (13%)	0·85 (0·78–0·92)	0·18
No	492/6725 (7%)	521/6684 (8%)	0·94 (0·83–1·06)	
Subtotal (I^2=44·1%, p=0·181)			0·88 (0·80–0·97)	
Baseline HbA_{1c}†				
High	1777/16 361 (11%)	1955/15 237 (13%)	0·83 (0·77–0·90)	0·14
Low	1357/14 270 (10%)	1477/14 081 (10%)	0·90 (0·84–0·97)	
Subtotal (I^2=55·3%, p=0·14)			0·87 (0·80–0·94)	
Median duration of follow-up‡				
<3 years	1096/13 721 (8%)	1167/12 366 (9%)	0·82 (0·71–0·95)	0·30
≥3 years	2041/16 973 (12%)	2262/17 020 (13%)	0·89 (0·84–0·94)	
Subtotal (I^2=5·5%, p=0·30)			0·88 (0·83–0·93)	
Drug dosing				
Daily	1069/9293 (12%)	1162/9298 (12%)	0·92 (0·80–1·05)	0·26
Weekly	2068/21 401 (10%)	2267/20 088 (11%)	0·84 (0·77–0·91)	
Subtotal (I^2=19·9%, p=0·26)			0·86 (0·80–0·94)	
Human GLP-1 homology				
Yes	1709/17 587 (10%)	2007/17 597 (11%)	0·84 (0·79–0·90)	0·39
No	1428/13 107 (11%)	1422/11 789 (12%)	0·90 (0·78–1·04)	
Subtotal (I^2=0·0%, p=0·392)			0·85 (0·80–0·90)	
BMI, kg/m²§				
<30	1341/13 076 (10%)	1476/12 606 (12%)	0·83 (0·73–0·95)	0·53
≥30	1781/17 506 (10%)	1944/16 668 (12%)	0·87 (0·81–0·92)	
Subtotal (I^2=0·0%, p=0·53)			0·86 (0·81–0·91)	
Age, years¶				
<65	1335/15 476 (9%)	1403/14 621 (10%)	0·84 (0·72–0·97)	0·78
≥65	1808/15 218 (12%)	2033/14 765 (14%)	0·86 (0·80–0·92)	
Subtotal (I^2=0·0%, p=0·78)			0·86 (0·80–0·91)	
Baseline eGFR, mL/min per 1·73 m²				
<60	850/6204 (14%)	909/5856 (16%)	0·88 (0·77–1·01)	0·52
≥60	1686/19 507 (9%)	1854/18 531 (10%)	0·83 (0·74–0·93)	
Subtotal (I^2=0·0%, p=0·518)			0·85 (0·78–0·93)	



JAMA Cardiology | Original Investigation

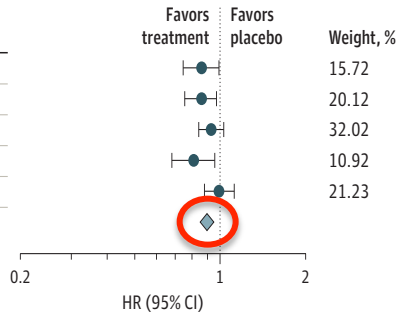
Association of SGLT2 Inhibitors With Cardiovascular and Kidney Outcomes in Patients With Type 2 Diabetes

A Meta-analysis

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

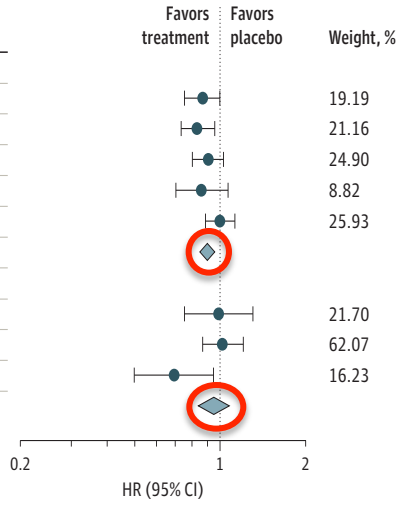
A Overall MACEs

	Treatment		Placebo		
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)
EMPA-REG OUTCOME	490/4687	37.4	282/2333	43.9	0.86 (0.74-0.99)
CANVAS program	NA/5795	26.9	NA/4347	31.5	0.86 (0.75-0.97)
DECLARE-TIMI 58	756/8582	22.6	803/8578	24.2	0.93 (0.84-1.03)
CREDENCE	217/2202	38.7	269/2199	48.7	0.80 (0.67-0.95)
VERTIS CV	735/5499	40.0	368/2747	40.3	0.99 (0.88-1.12)
Fixed-effects model (Q = 5.22; *df* = 4; *P* = .27; I^2 = 23.4%)					0.90 (0.85-0.95)



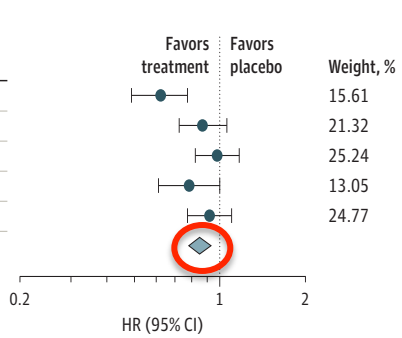
B MACEs by ASCVD status

	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	490/4687	37.4	282/2333	43.9	0.86 (0.74-0.99)
CANVAS program	NA/3756	34.1	NA/2900	41.3	0.82 (0.72-0.95)
DECLARE-TIMI 58	483/3474	36.8	537/3500	41.0	0.90 (0.79-1.02)
CREDENCE	155/1113	55.6	178/1107	65.0	0.85 (0.69-1.06)
VERTIS CV	735/5499	40.0	368/2747	40.3	0.99 (0.88-1.12)
Fixed-effects model (Q = 4.53; *df* = 4; *P* = .34; I^2 = 11.8%)					0.89 (0.84-0.95)
Patients without ASCVD					
CANVAS program	NA/2039	15.8	NA/1447	15.5	0.98 (0.74-1.30)
DECLARE-TIMI 58	273/5108	13.4	266/5078	13.3	1.01 (0.86-1.20)
CREDENCE	62/1089	22.0	91/1092	32.7	0.68 (0.49-0.94)
Fixed-effects model (Q = 4.59; *df* = 2; *P* = .10; I^2 = 56.5%)					0.94 (0.83-1.07)



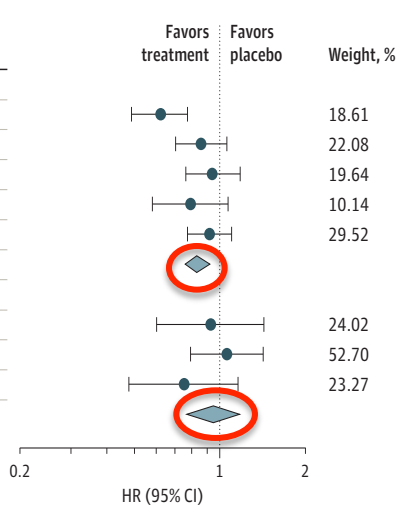
A Overall CV death

	Treatment		Placebo		
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)
EMPA-REG OUTCOME	172/4687	12.4	137/2333	20.2	0.62 (0.49-0.77)
CANVAS program	NA/5795	11.6	NA/4347	12.8	0.87 (0.72-1.06)
DECLARE-TIMI 58	245/8582	7.0	249/8578	7.1	0.98 (0.82-1.17)
CREDENCE	110/2202	19.0	140/2199	24.4	0.78 (0.61-1.00)
VERTIS CV	341/5499	17.6	184/2747	19.0	0.92 (0.77-1.10)
Fixed-effects model (Q = 11.22; *df* = 4; *P* = .02; I^2 = 64.3%)					0.85 (0.78-0.93)



B CV death 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	172/4687	12.4	137/2333	20.2	0.62 (0.49-0.77)
CANVAS program	NA/3756	14.8	NA/2900	16.8	0.86 (0.70-1.06)
DECLARE-TIMI 58	153/3474	10.9	163/3500	11.6	0.94 (0.76-1.18)
CREDENCE	75/1113	25.7	93/1107	32.4	0.79 (0.58-1.07)
VERTIS CV	341/5499	17.6	184/2747	19.0	0.92 (0.77-1.10)
Fixed-effects model (Q = 9.10; *df* = 4; *P* = .06; I^2 = 56.1%)					0.83 (0.76-0.92)
Patients without ASCVD					
CANVAS program	NA/2039	6.5	NA/1447	6.2	0.93 (0.60-1.43)
DECLARE-TIMI 58	92/5108	4.4	86/5078	4.1	1.06 (0.79-1.42)
CREDENCE	35/1089	12.2	47/1092	16.4	0.75 (0.48-1.16)
Fixed-effects model (Q = 1.65; *df* = 2; *P* = .44; I^2 = 0.0%)					0.95 (0.77-1.17)



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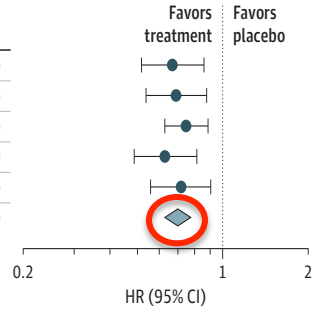
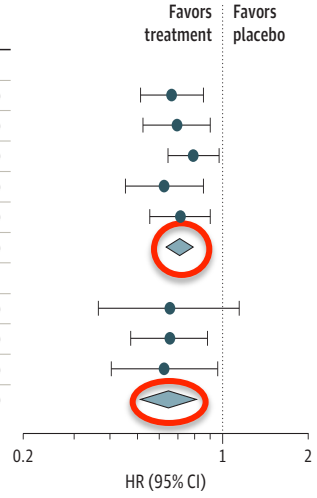
A Overall HHF

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment	Favors placebo	Weight, %
EMPA-REG OUTCOME	126/4687	9.4	95/2333	14.5	0.65 (0.50-0.85)			16.09
CANVAS program	NA/5795	5.5	NA/4347	8.7	0.67 (0.52-0.87)			17.10
DECLARE-TIMI 58	212/8582	6.2	286/8578	8.5	0.73 (0.61-0.88)			33.72
CREDENCE	89/2202	15.7	141/2199	25.3	0.61 (0.47-0.80)			16.01
VERTIS CV	139/5499	7.3	99/2747	10.5	0.70 (0.54-0.90)			17.08
Fixed-effects model (Q = 1.39; *df* = 4; *P* = .85; I^2 = 0.0%)					0.68 (0.61-0.76)			



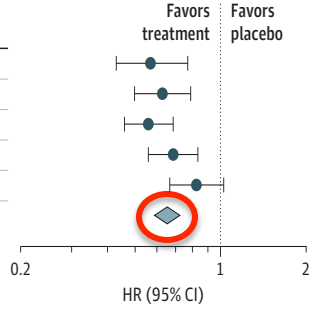
B HHF by ASCVD status

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment	Favors placebo	Weight, %
Patients with ASCVD								
EMPA-REG OUTCOME	126/4687	9.4	95/2333	14.5	0.65 (0.50-0.85)			19.62
CANVAS program	NA/3756	7.3	NA/2900	11.3	0.68 (0.51-0.90)			17.13
DECLARE-TIMI 58	151/3474	11.1	192/3500	14.1	0.78 (0.63-0.97)			29.66
CREDENCE	59/1113	20.6	92/1107	33.2	0.61 (0.44-0.85)			12.74
VERTIS CV	139/5499	7.3	99/2747	10.5	0.70 (0.54-0.90)			20.84
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)			16.38
DECLARE-TIMI 58	61/5108	3.0	94/5078	4.6	0.64 (0.46-0.88)			55.07
CREDENCE	30/1089	10.6	49/1092	17.5	0.61 (0.39-0.96)			28.56
Fixed-effects model (Q = 0.03; *df* = 2; *P* = .99; I^2 = 0.0%)					0.63 (0.50-0.80)			



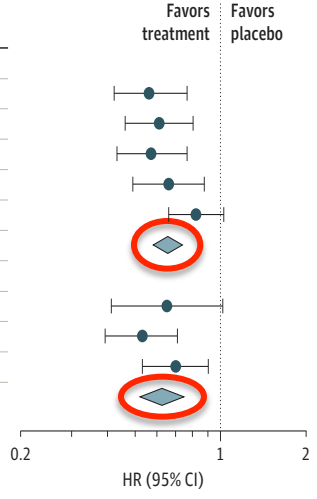
A Overall kidney outcomes

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment	Favors placebo	Weight, %
EMPA-REG OUTCOME	81/4645	6.3	71/2323	11.5	0.54 (0.40-0.75)			11.51
CANVAS program	NA/5795	5.5	NA/4347	9.0	0.60 (0.47-0.77)			18.66
DECLARE-TIMI 58	127/8582	3.7	238/8578	7.0	0.53 (0.43-0.66)			24.77
CREDENCE	153/2202	27.0	224/2199	40.4	0.66 (0.53-0.81)			25.28
VERTIS CV	175/5499	9.3	108/2747	11.5	0.81 (0.64-1.03)			19.79
Fixed-effects model (Q = 7.96; *df* = 4; *P* = .09; I^2 = 49.7%)					0.62 (0.56-0.70)			



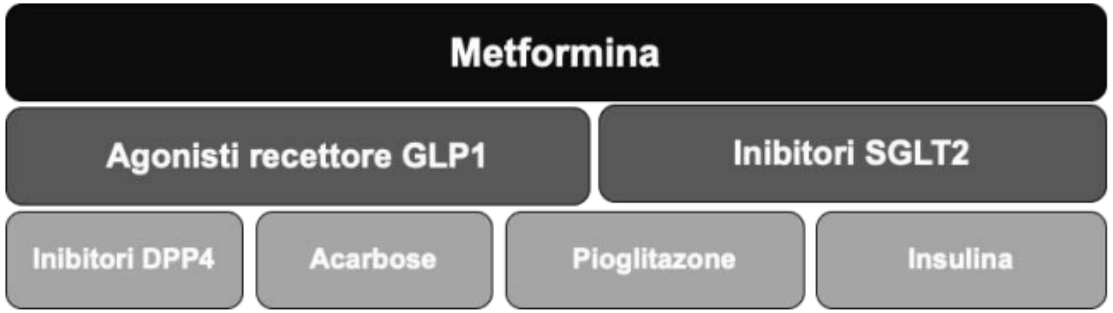
B Kidney outcomes by ASCVD status

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment	Favors placebo	Weight, %
Patients with ASCVD								
EMPA-REG OUTCOME	81/4645	6.3	71/2323	11.5	0.54 (0.40-0.75)			16.67
CANVAS program	NA/3756	6.4	NA/2900	10.5	0.59 (0.44-0.79)			19.23
DECLARE-TIMI 58	65/3474	4.7	118/3500	8.6	0.55 (0.41-0.75)			18.06
CREDENCE	69/1113	24.1	102/1107	36.5	0.64 (0.47-0.87)			17.37
VERTIS CV	175/5499	9.3	108/2747	11.5	0.81 (0.64-1.03)			28.66
Fixed-effects model (Q = 6.09; *df* = 4; *P* = .19; I^2 = 34.4%)					0.64 (0.56-0.72)			
Patients without ASCVD								
CANVAS program	NA/2039	4.1	NA/1447	6.6	0.63 (0.39-1.02)			15.72
DECLARE-TIMI 58	62/5108	3.0	120/5078	5.9	0.51 (0.37-0.69)			37.41
CREDENCE	84/1089	29.9	122/1092	44.3	0.68 (0.51-0.89)			46.87
Fixed-effects model (Q = 1.86; *df* = 2; *P* = .40; I^2 = 0.0%)					0.60 (0.50-0.73)			



Linea Guida SID – AMD 2021
La terapia del diabete mellito di tipo 2

Pazienti con diabete di tipo 2 senza pregressi eventi cardiovascolari



Pazienti con diabete di tipo 2 con pregressi eventi cardiovascolari

Pazienti con diabete di tipo 2 con scompenso cardiaco

9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Medical Care in Diabetes—2022*

Diabetes Care 2022;45(Suppl. 1):S125–S143 | https://doi.org/10.2337/dc22-S009

PHARMACOLOGIC TREATMENT OF HYPERGLYCEMIA IN ADULTS WITH TYPE 2 DIABETES

FIRST-LINE THERAPY depends on comorbidities, patient-centered treatment factors, including cost and access considerations, and management needs and generally includes metformin and comprehensive lifestyle modification^

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

ASCVD/INDICATORS OF HIGH RISK, HF, CKD†

RECOMMEND INDEPENDENTLY OF BASELINE A1C, INDIVIDUALIZED A1C TARGET, OR METFORMIN USE‡

+ASCVD/INDICATORS OF HIGH RISK*

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

IF A1C ABOVE TARGET

- For patients on a GLP-1 RA, consider incorporating SGLT2i with proven CVD benefit and vice versa[1]
- TZD[2]

+HF*

SGLT2i with proven benefit in this population[1]

+CKD**

CKD and albuminuria (e.g., ≥200 mg/g creatinine)

CKD without albuminuria (e.g., eGFR <60 mL/min/1.73 m²)

PREFERABLY

SGLT2i with primary evidence of reducing CKD progression

OR

SGLT2i with evidence of reducing CKD progression in CVOTs

OR

GLP-1 RA with proven CVD benefit[1] if SGLT2i not tolerated or contraindicated

For patients with CKD (e.g., eGFR <60 mL/min/1.73 m²) without albuminuria, recommend the following to decrease cardiovascular risk

EITHER/ OR

- GLP-1 RA with proven CVD benefit[1]
- SGLT2i with proven CVD benefit[1]

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA and vice versa

If A1C remains above target, consider treatment intensification based on comorbidities, patient-centered treatment factors, and management needs

Diabetes Care 2022;45(Suppl. 1):S125–S143 | https://doi.org/10.2337/dc22-S009

9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Medical Care in Diabetes—2022*

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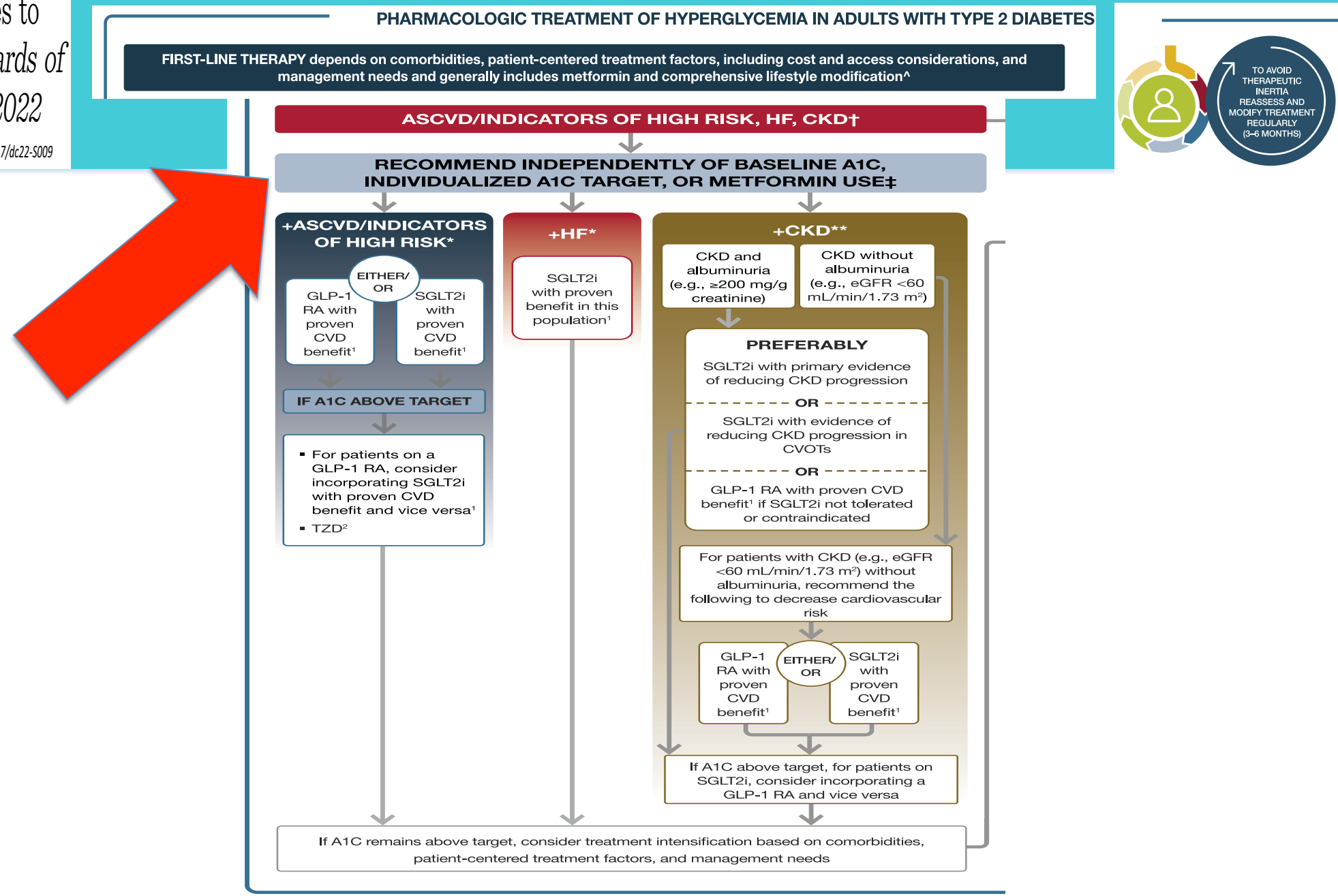
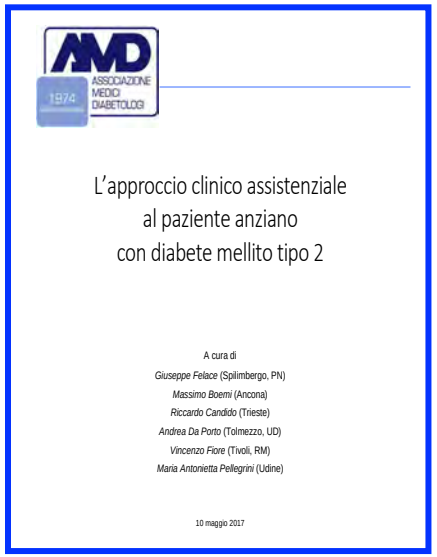


Diabetes Care 2022;45(Suppl. 1):S125–S143 | https://doi.org/10.2337/dc22-S00

Terapia non insulinica nel DM tipo 2 Anziano



L'approccio clinico assistenziale
al paziente anziano
con diabete mellito tipo 2

A cura di

Giuseppe Felace (Spilimbergo, PN)
Massimo Boemi (Ancona)
Riccardo Candido (Trieste)
Andrea Da Porto (Tolmezzo, UD)
Vincenzo Fiore (Tivoli, RM)
Maria Antonietta Pellegrini (Udine)

10 maggio 2017

BOX 4. Metformina e/o DPP4 inibitori sono i farmaci da considerare di prima linea (salvo controindicazioni) nel trattamento del paziente diabetico anziano.

VANTAGGI DEI DPP4-Inibitori

- Sono tutti farmaci somministrabili per os
- Non provocano ipoglicemia
- Sono neutri sul peso corporeo
- Somministrati, con opportune riduzioni di dosaggio e senza effetti avversi, nell'IRC, e persino in pazienti emodializzati
- Sono farmaci che possono vantare il maggior numero di studi di intervento effettuati specificamente su pazienti diabetici di età ≥ 65 e perfino 75 anni
- Sicuri quando usati in pazienti ad elevato rischio CV

Efficacy and Safety of Dapagliflozin According to Frailty in Heart Failure With Reduced Ejection Fraction

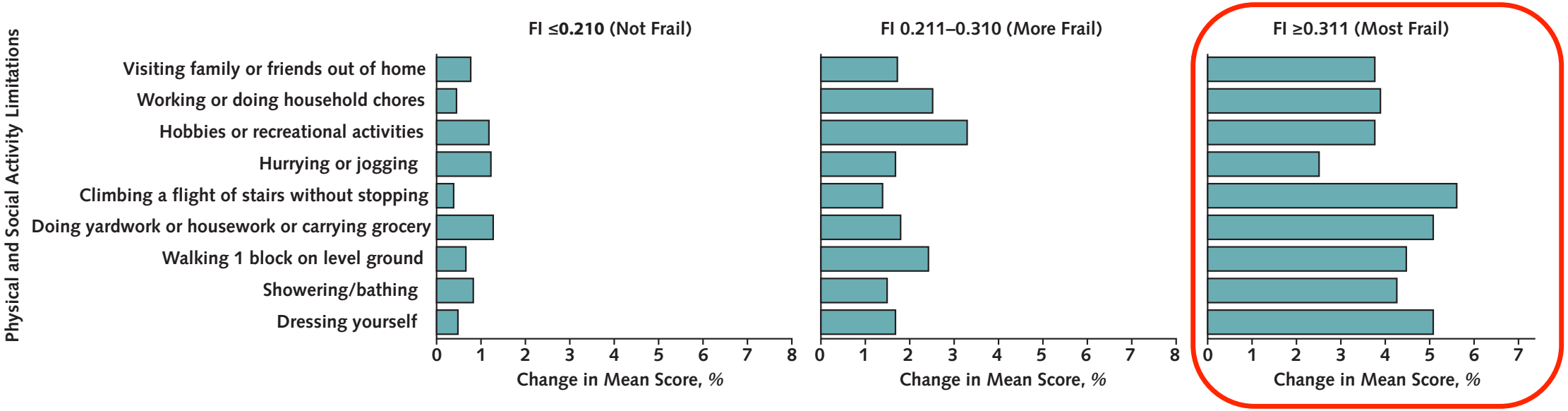
A Post Hoc Analysis of the DAPA-HF Trial

Butt JH et Al. Ann Intern Med 175, 820-830 (2022).

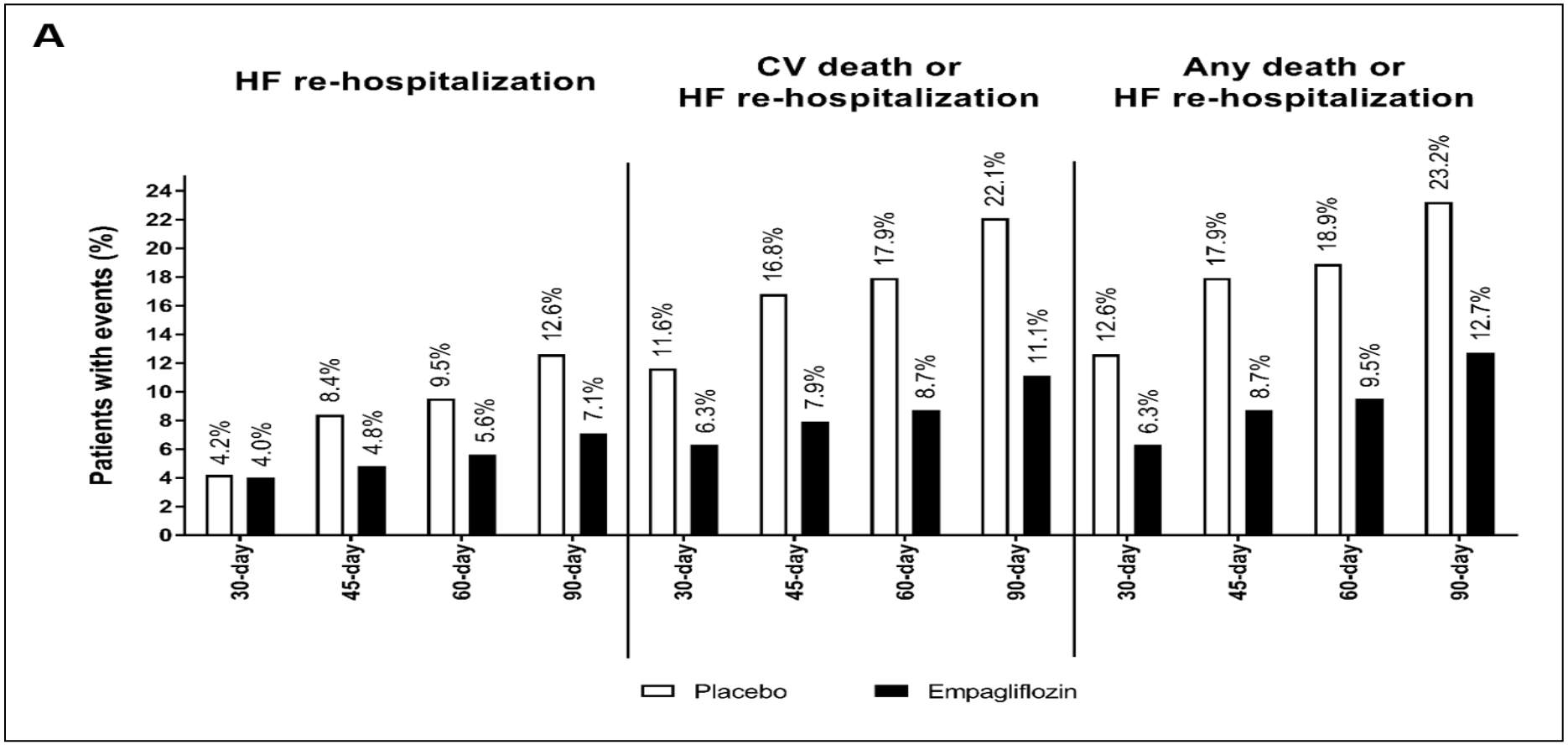
Dapagliflozin substantially reduced the risk for worsening HF events, cardiovascular death, and all-cause death, and improved symptoms, physical function, and quality of life, **regardless of frailty class.**

The absolute reductions in clinical events and improvements in health status were generally larger in the most frail patients.

Figure 2. Mean change in individual physical and social activity items from baseline to 8 months with dapagliflozin versus placebo according to FI.



Across all time points empagliflozin reduced the risk of HF re-hospitalization or death outcomes versus placebo

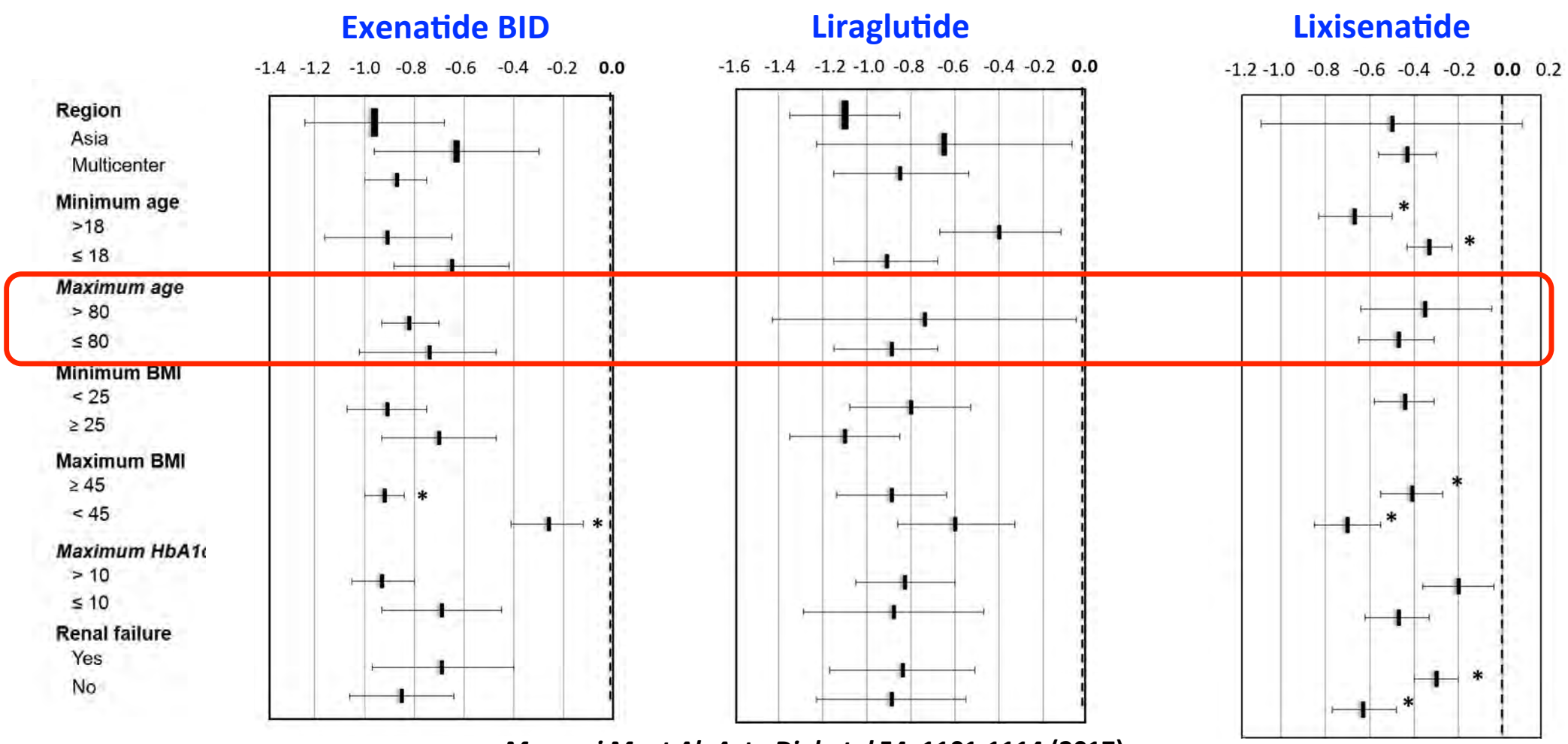


Frequency of HF re-hospitalization (second events), separate or combined with CV death or any death by time window following admission date of first HHF. A total of n=221 patients with index HHF were evaluated (126 receiving either dose of empagliflozin, and 95 receiving placebo). CV, cardiovascular; HF, heart failure; HHF, hospitalization for heart failure.

Savarese G *et al*. *Circulation* 2019;139:1458

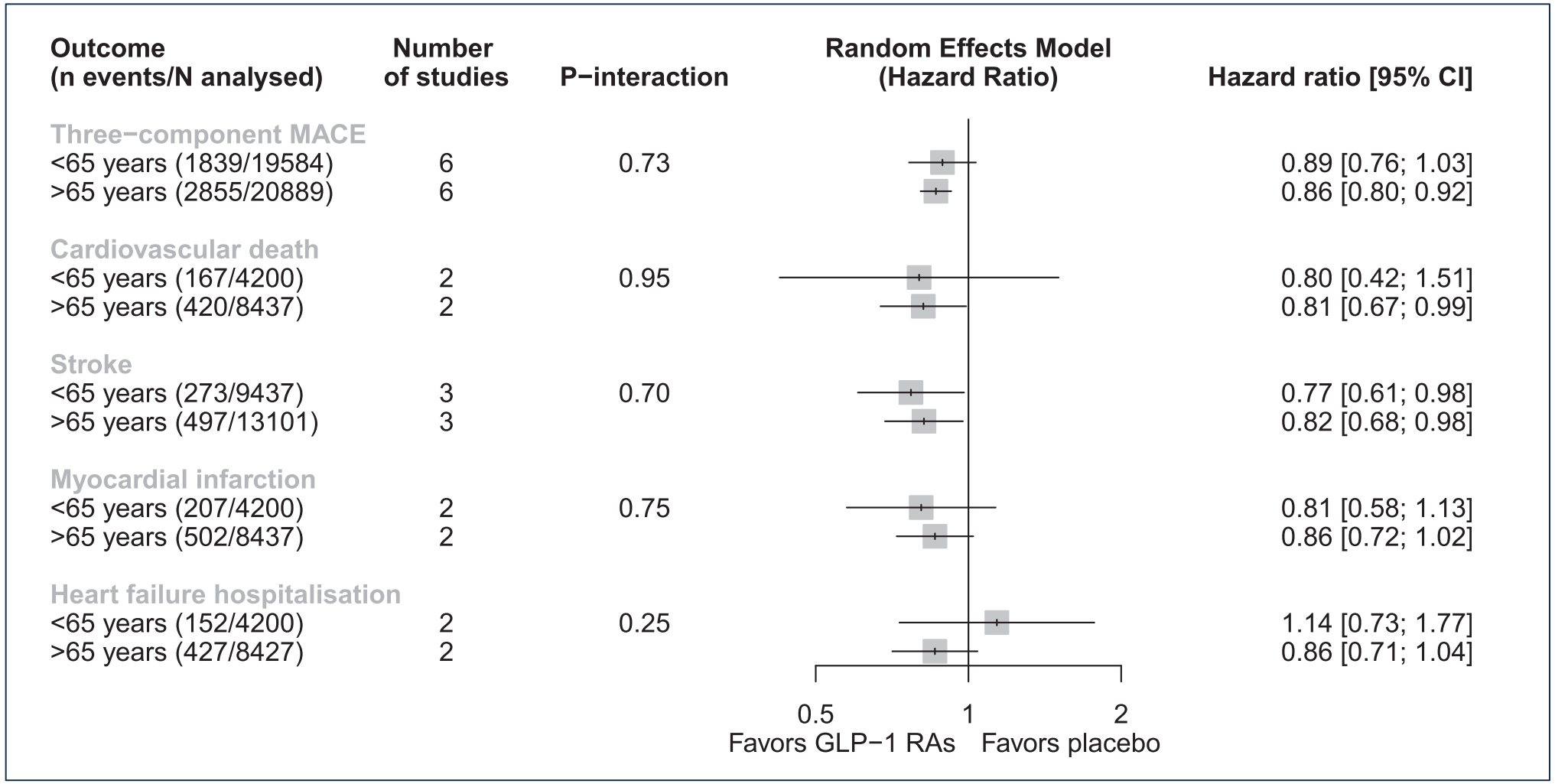
Predictors of response to glucagon-like peptide-1 receptor agonists: a meta-analysis and systematic review of randomized controlled trials

Effect of GLP-1 RA on HbA1c at 24 weeks

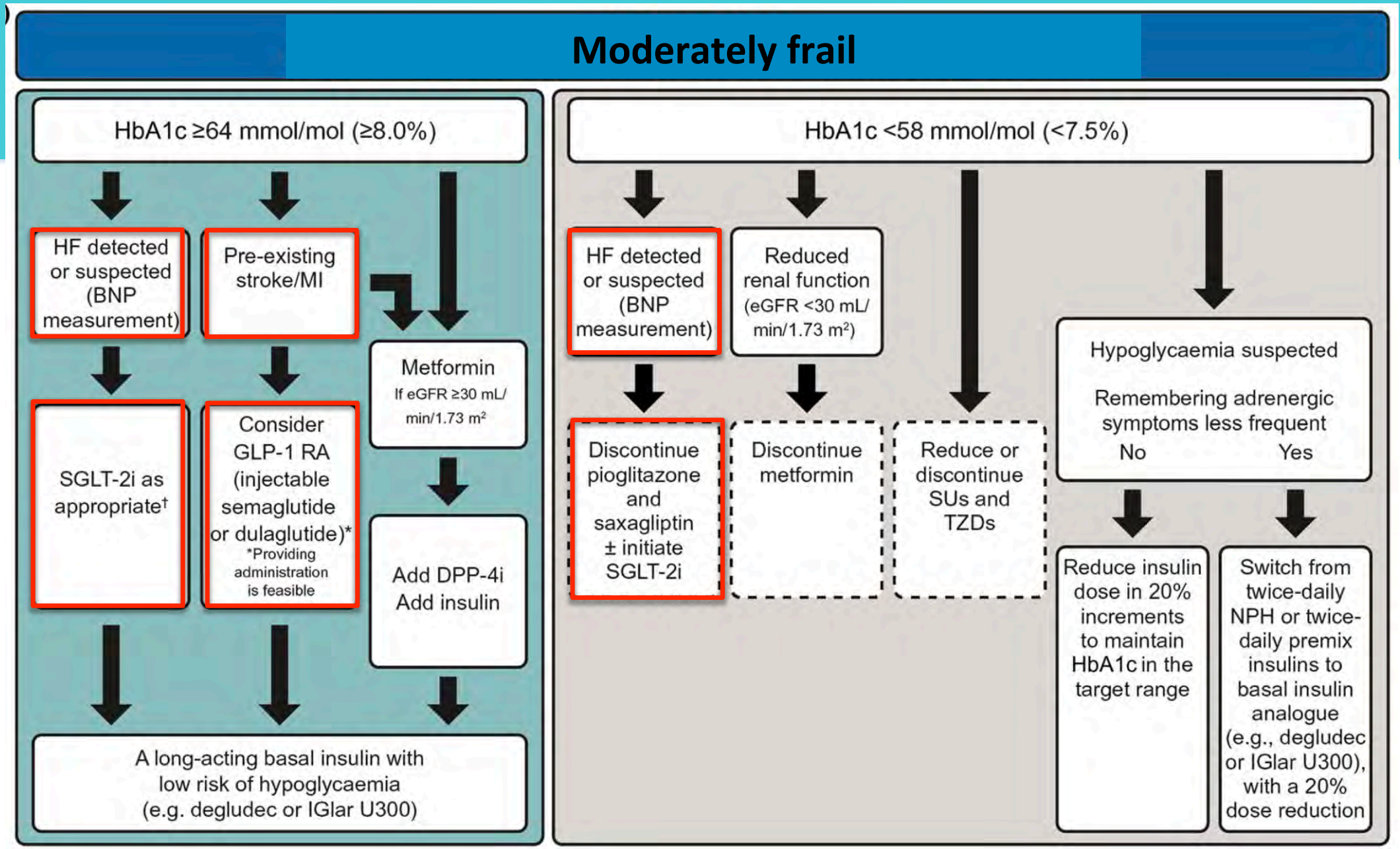


Monami M. et Al. Acta Diabetol 54, 1101-1114 (2017).

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



Karagiannis T et Al. Diabetes Res Clin Pract 174, 108737 (2021)



Diabetes Ther 12, 1227-1247 (2021).

Individualized Glycemic Goals for Older Adults Are a Moving Target

Scott J. Pilla,[1,2,3] Zhinous Shahidzadeh Yazdi,[4] and Simeon I. Taylor[4]

Diabetes Care 2022;45:1029–1031 | https://doi.org/10.2337/dci22-0004

Some coexisting medical conditions (e.g., major adverse cardiovascular disease, congestive heart failure, or diabetic kidney disease) represent indications for using an SGLT2 inhibitor or a GLP-1 receptor agonist, regardless of HbA1c

NOTA 100

Nel paziente **senza malattia renale cronica**, **senza malattia cardiovascolare** e **non ad alto rischio per malattia cardiovascolare**, non sono attualmente disponibili evidenze sufficienti a raccomandare l'utilizzo di una specifica classe di farmaci rispetto alle altre oggetto della Nota. In tali pazienti la **scelta terapeutica** deve tenere conto di diversi fattori quali le **caratteristiche individuali del soggetto**, il **profilo di tollerabilità del farmaco**, **l'entità di riduzione di HbA1c** che si intende raggiungere o **l'effetto sul peso corporeo**.

REVIEW

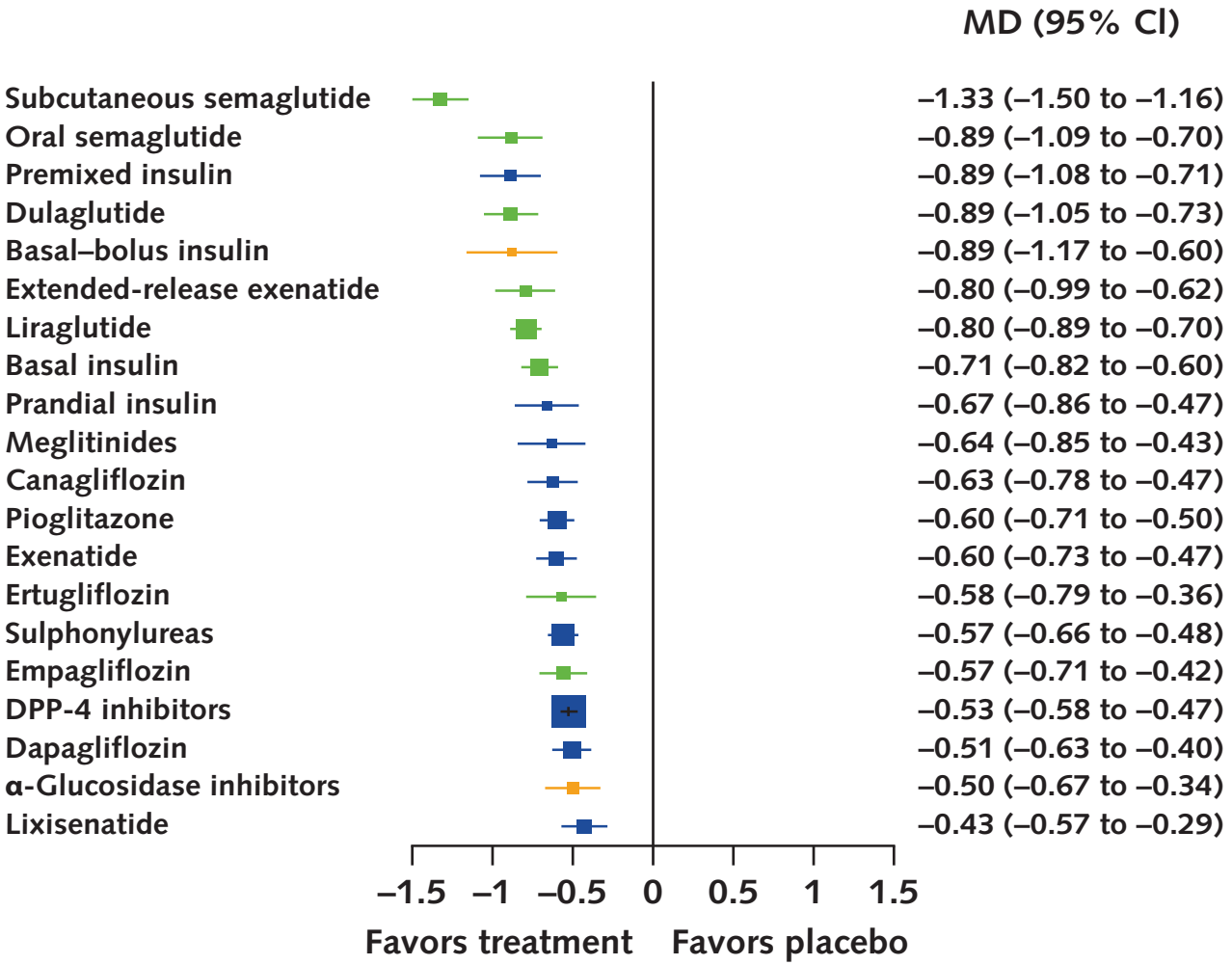
Annals of Internal Medicine

Comparative Effectiveness of Glucose-Lowering Drugs for Type 2 Diabetes

A Systematic Review and Network Meta-analysis

Ann Intern Med. 2020;173:278-286

Change in Hemoglobin A1c Level in Patients Receiving Metformin-Based Background Therapy



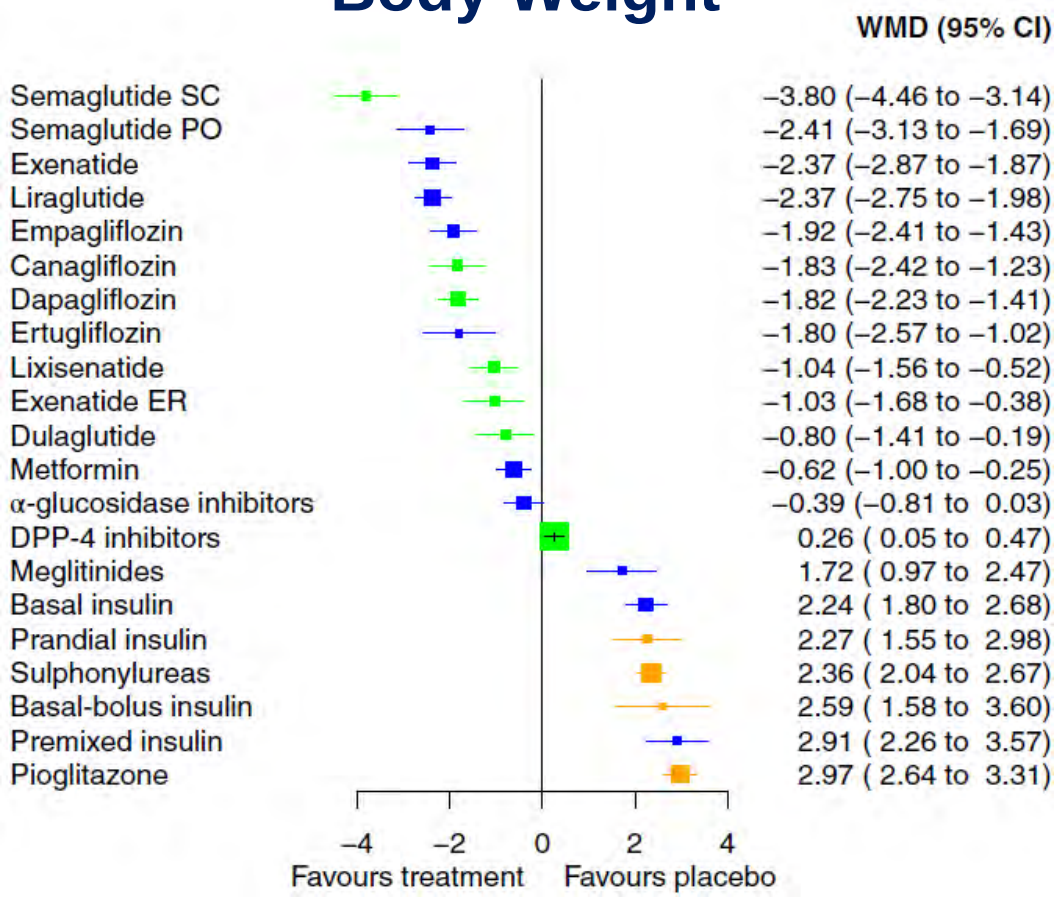
Annals of Internal Medicine

Comparative Effectiveness of Glucose-Lowering Drugs for Type 2 Diabetes

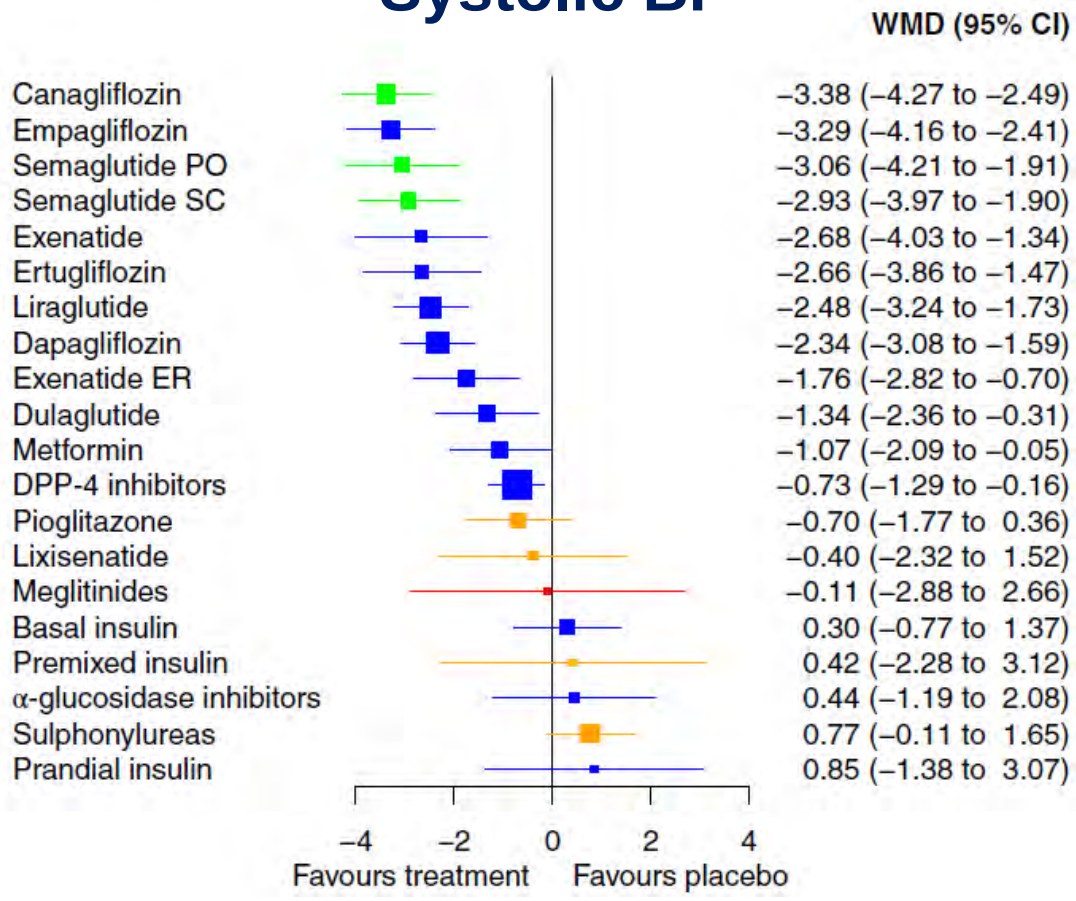
A Systematic Review and Network Meta-analysis

Ann Intern Med. 2020;173:278-286

Body Weight



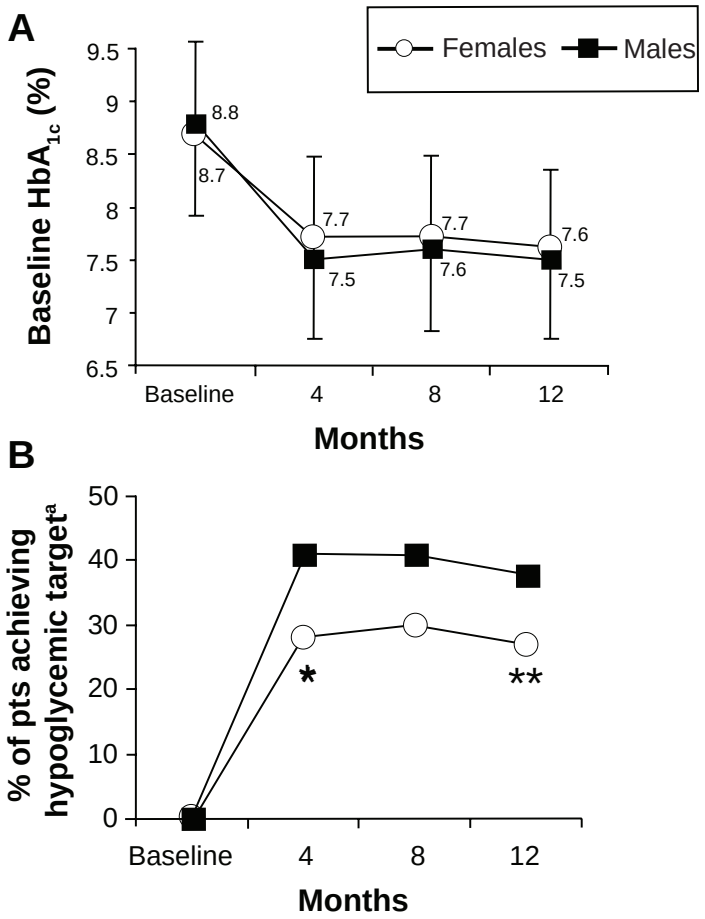
Systolic BP



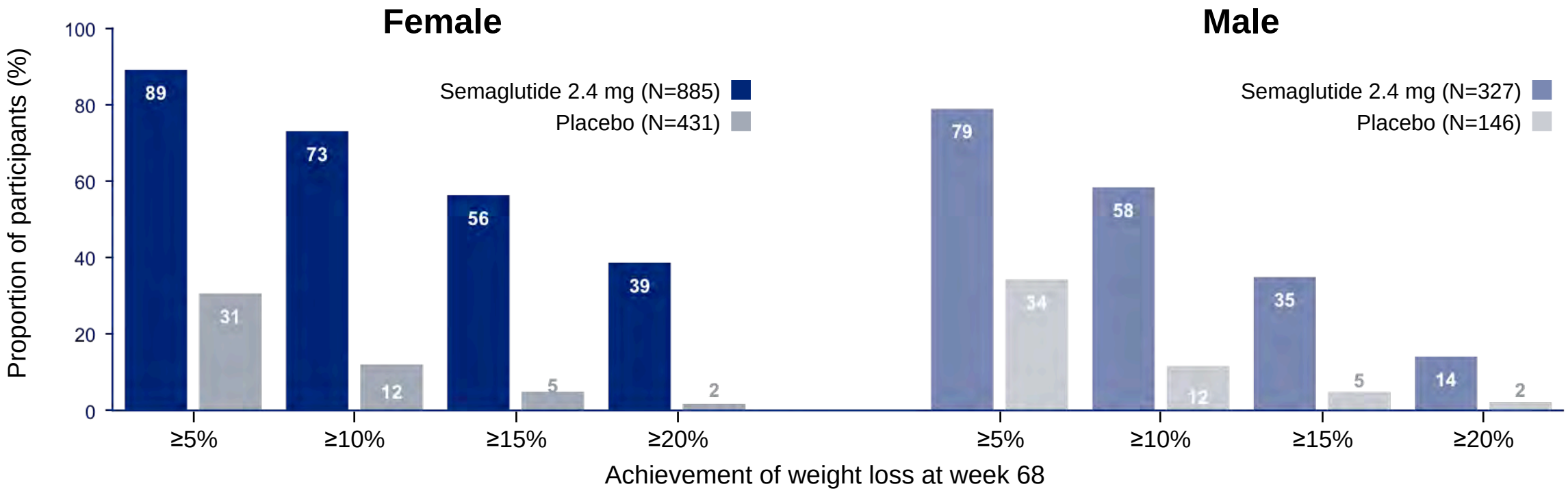
Tsapas A et al., Comparative efficacy of glucose-lowering medications on body weight and blood pressure in patients with type 2 diabetes: A systematic review and network meta-analysis; Diabetes Obes Metab 2021; 1-9.

Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy
Dovepress
open access to scientific and medical research
Open Access Full Text Article
ORIGINAL RESEARCH

Gender difference in response predictors after 1-year exenatide therapy twice daily in type 2 diabetic patients: a real world experience



Proportion of participants achieving different categories of weight loss at week 68 by sex



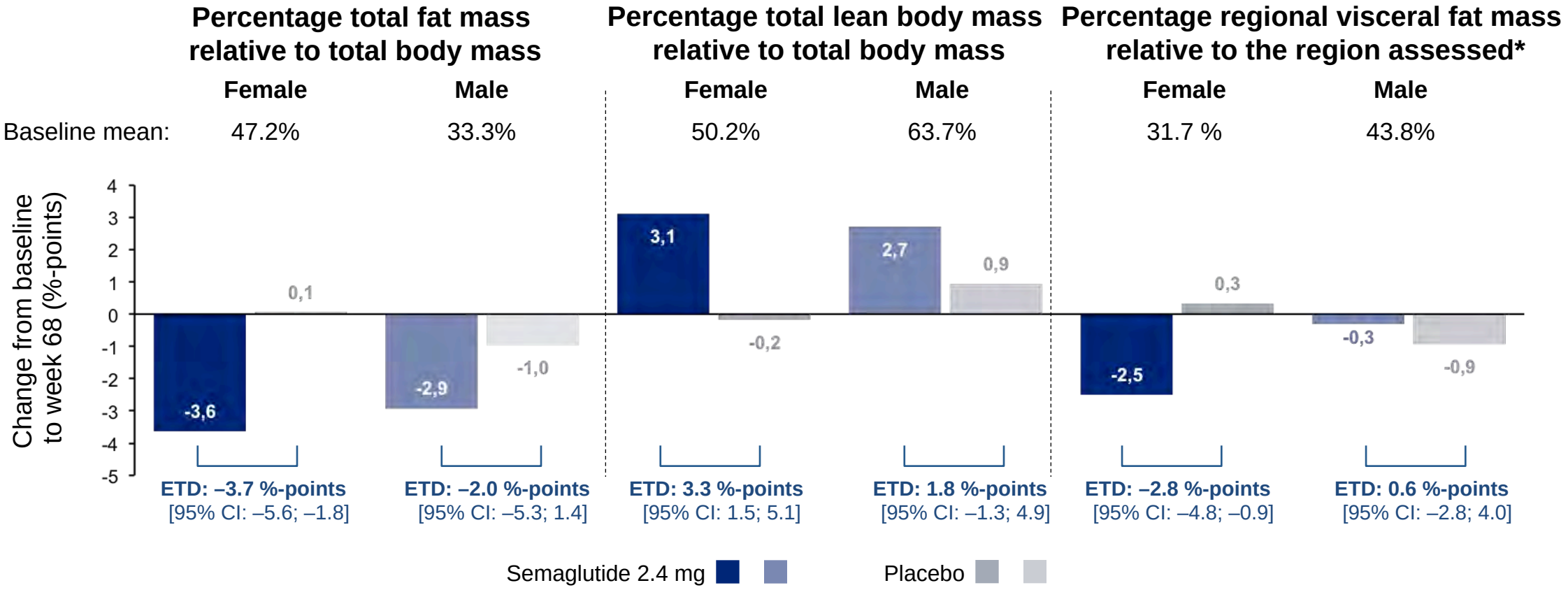
More semaglutide-treated females achieved weight loss of ≥5%, ≥10%, ≥15% and ≥20% than males

Similar proportions of females and males receiving placebo achieved each weight loss category

Batterham RL et al. presented at the America College of Obstetrician and Gynecologist Annual Meeting- April 30-May 2 ,2021

Relative change in body composition (%-points) from baseline to week 68 by sex (DEXA subgroup)

Changes relative to total body mass



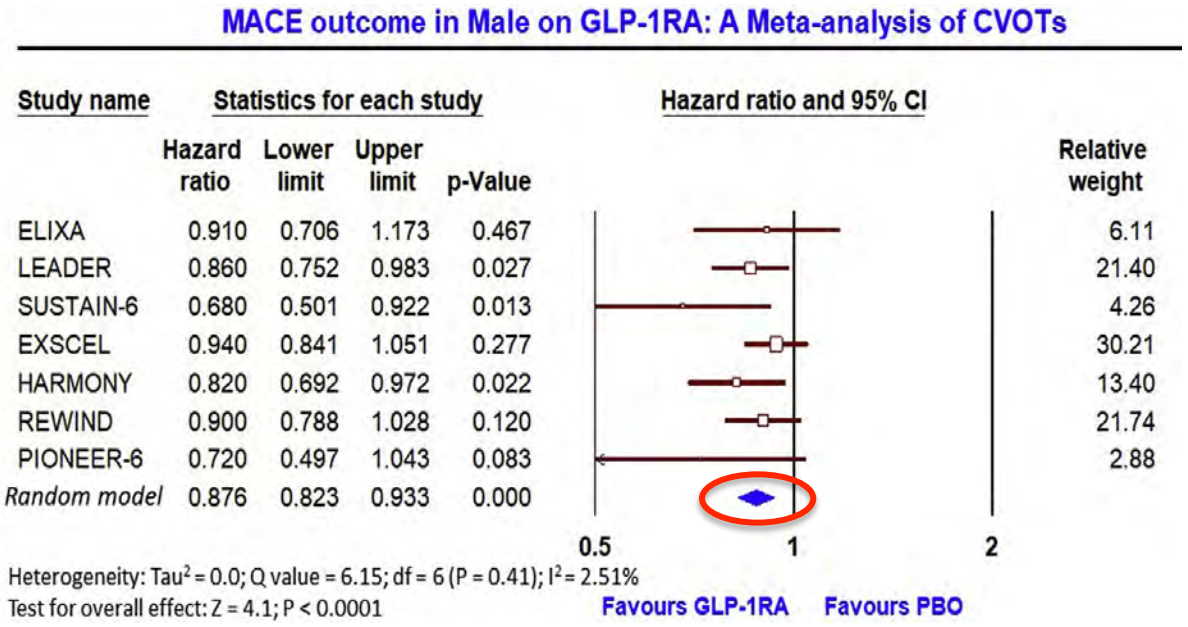
*Visceral fat mass was calculated in the L4 region (males or females), android region (males only), or in the gynoid region (females only), depending on the methodology of the scanner available at participating study sites. Treatment policy estimand data. CI, confidence interval; DEXA, dual energy X-ray absorptiometry; ETD, estimated treatment difference

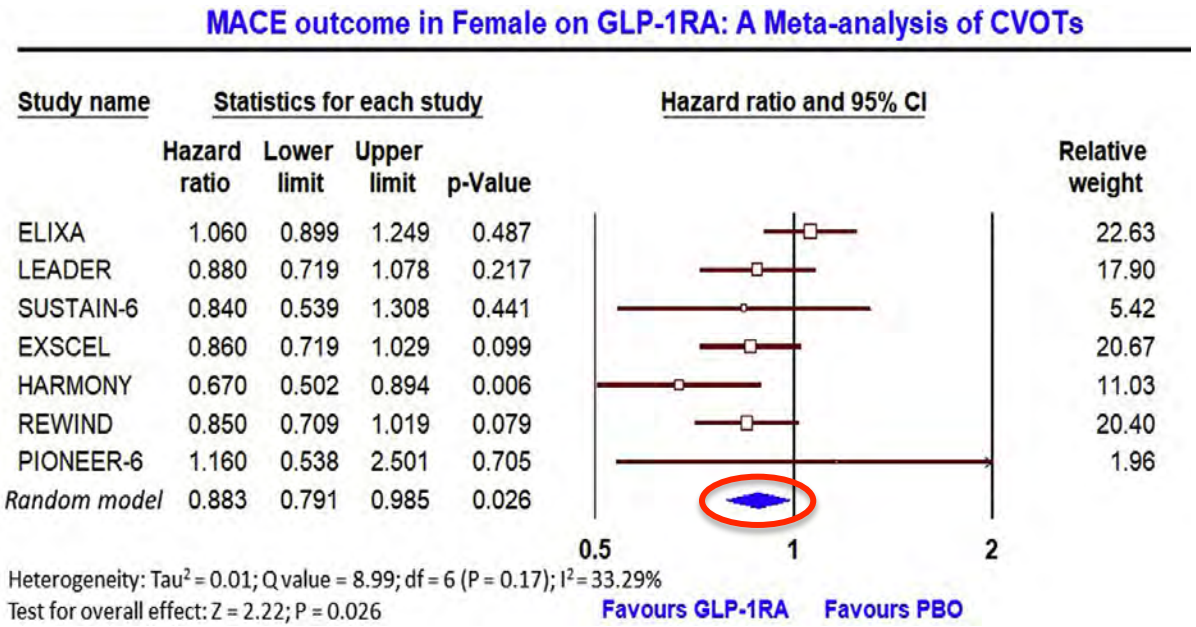
Batterham RL et al. presented at the America College of Obstetrician and Gynecologist Annual Meeting- April 30-May 2 ,2021

Gender difference in cardiovascular outcomes with SGLT-2 inhibitors and GLP-1 receptor agonist in type 2 diabetes: A systematic review and meta-analysis of cardio-vascular outcome trials

Awadhesh Kumar Singh*, Ritu Singh

Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14 (2020) 181–187





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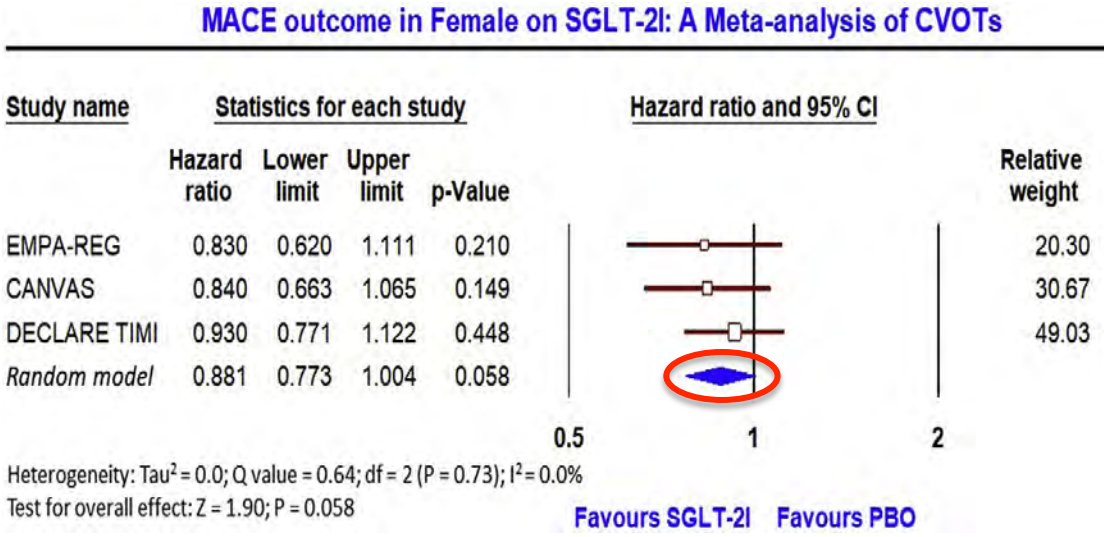

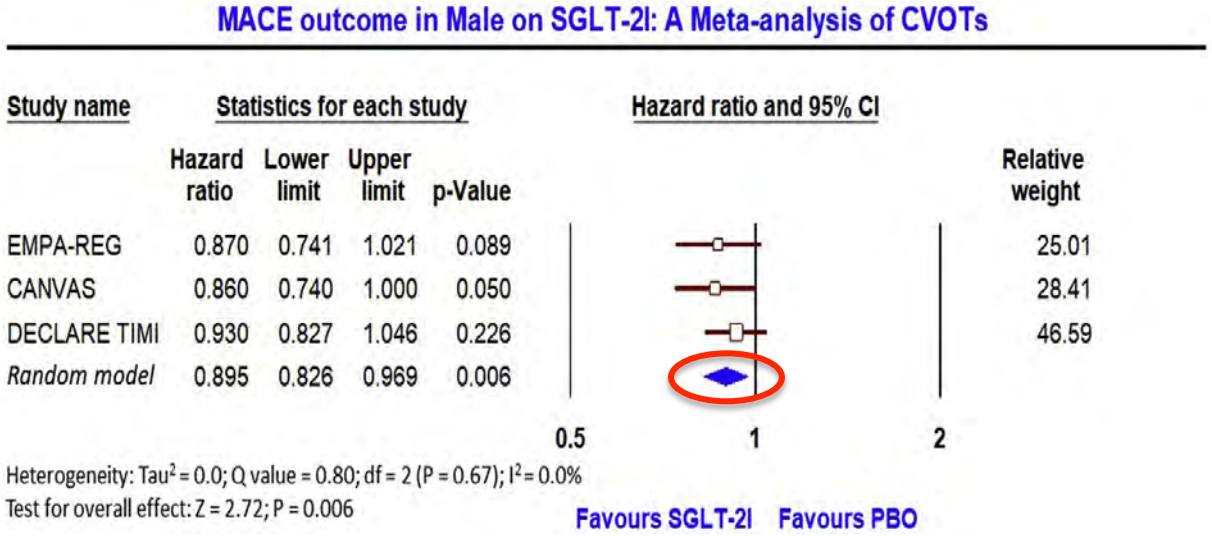

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Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14 (2020) 181–187

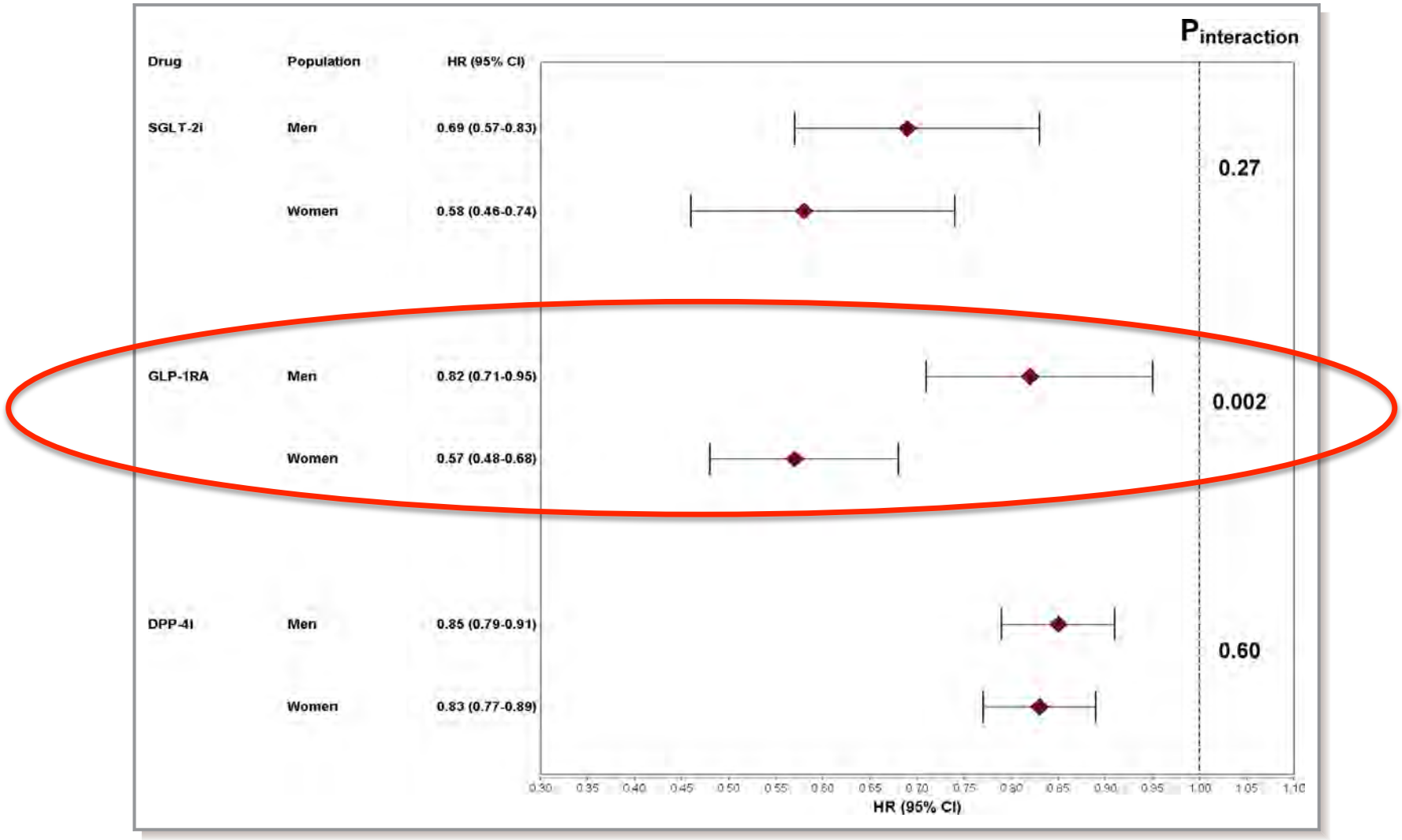
Conclusions:

- GLP-1RAs confers a similar reduction in MACE, irrespective of the gender.
- Whether these results are related to inadequate statistical power (underrepresentation of women) in CVOT, or it reflects a true gender difference, still remains to be established.
- **Whether this could be related to a relative larger weight loss due to the reduced fat mass with GLP- 1RAs compared to SGLT-2Is, remains to be established.**

Sex Differences in Cardiovascular Effectiveness of Newer Glucose-Lowering Drugs Added to Metformin in Type 2 Diabetes Mellitus

Valeria Raparelli, MD, PhD; Malik Elharram, MD; Cristiano S. Moura, PhD; Michal Abrahamowicz, PhD; Sasha Bernatsky, MD, PhD; Hassan Behlouli, PhD; Louise Pilote MD, MPH, PhD

J Am Heart Assoc. 2020;9:e012940



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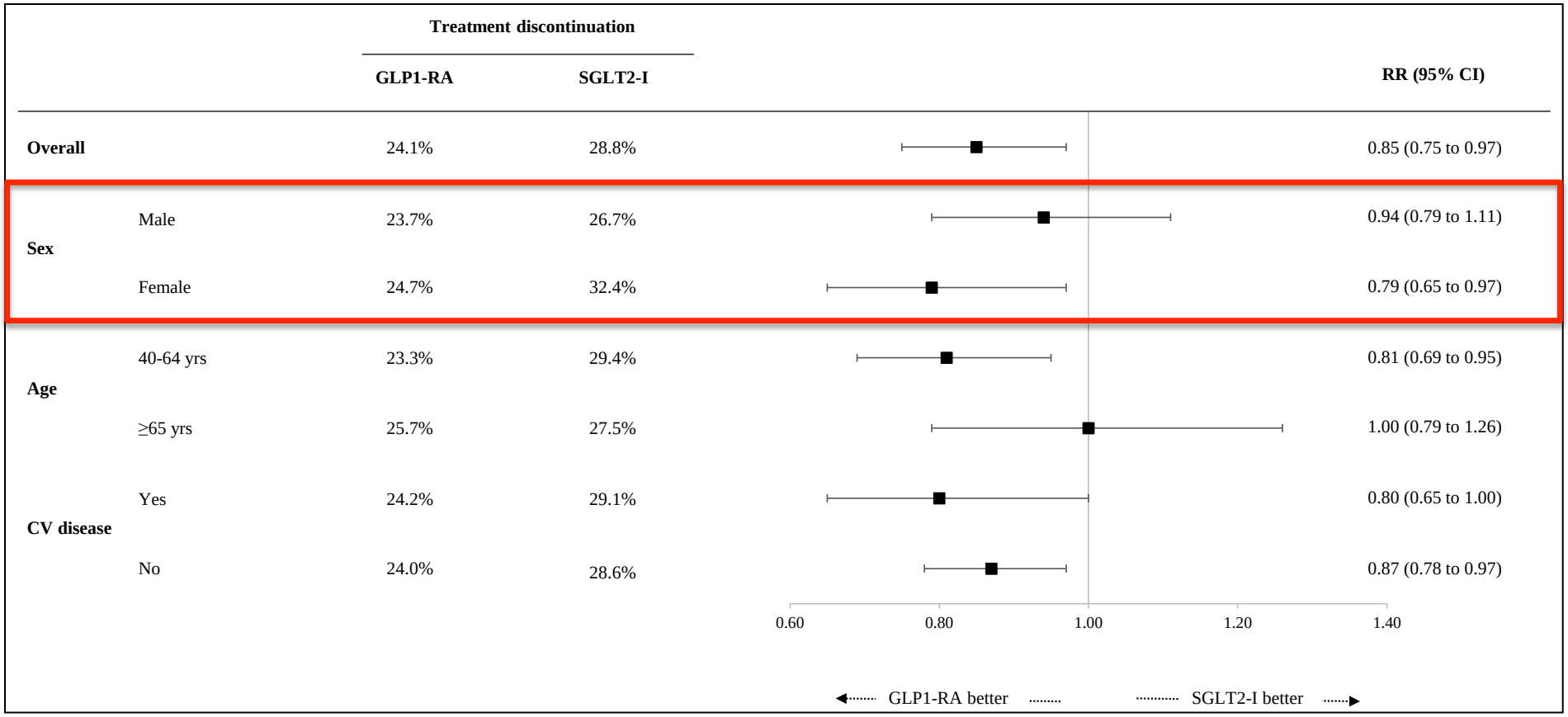
J Am Heart Assoc. 2020;9:e012940

- Our findings are certainly **hypothesis-generating** and, at the moment, we can **only speculate on the reasons** underlying the greater effect of GLP-1RA in women.
- A study reported that the **function of the receptor for glucagon-like peptide can be modified by sex hormones**, while some authors proposed the hypothesis that **GLP-1 receptor stimulation may have the potential to reduce platelet aggregation**, resulting in the lower cardiovascular risk **especially in women who have higher baseline platelet activation than men**.

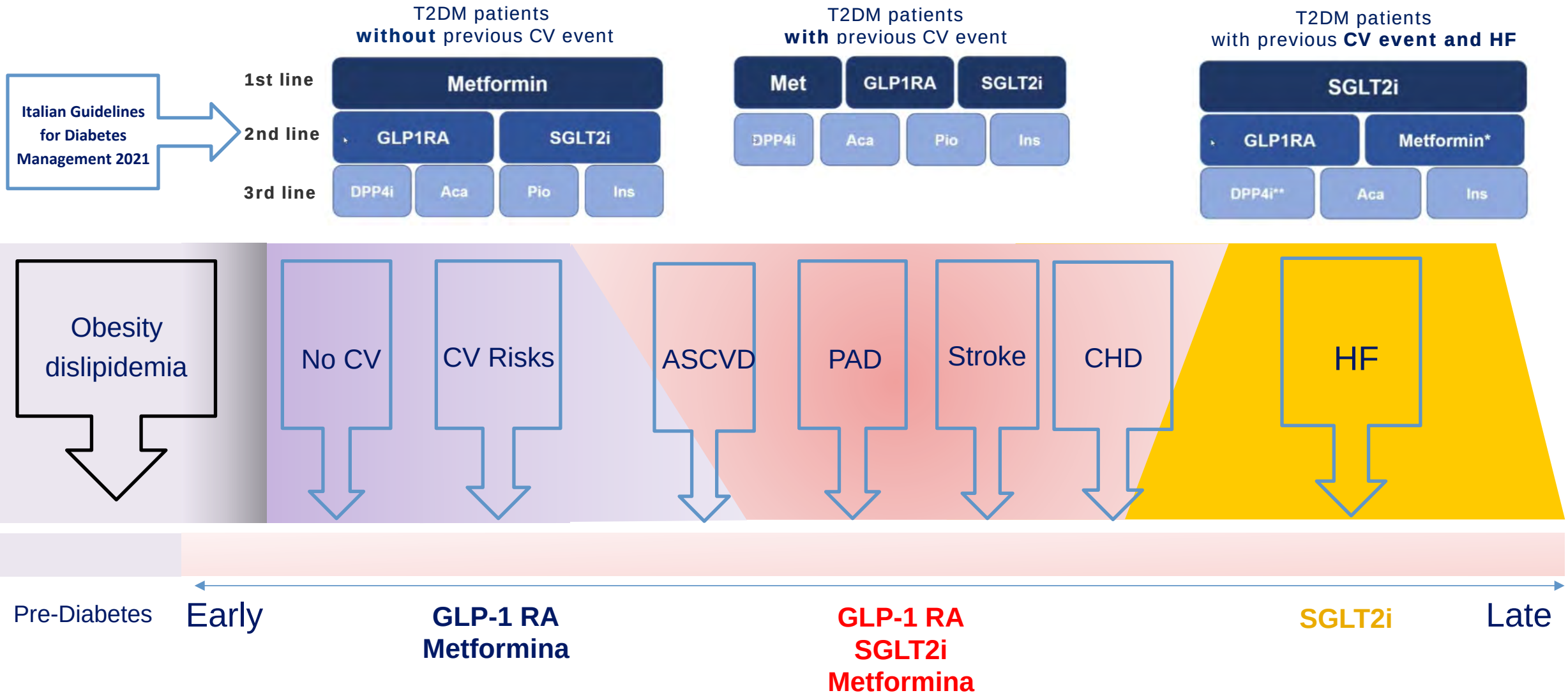
Comparing medication persistence among patients with type 2 diabetes using sodium-glucose cotransporter 2 inhibitors or glucagon-like peptide-1 receptor agonists in real-world setting

Federico Rea [a,b,1], Stefano Ciardullo [c,d,1], Laura Savaré [a,b,*], Gianluca Perseghin [c,d,2], Giovanni Corrao [a,b,2]

Diab Res Clin Pract 180 (2021) 109035



NUOVO PARADIGMA NELLA CURA DEL DIABETE



ADA 2022 Standard of Medical Care: il treat to care e l'importanza di trattare subito