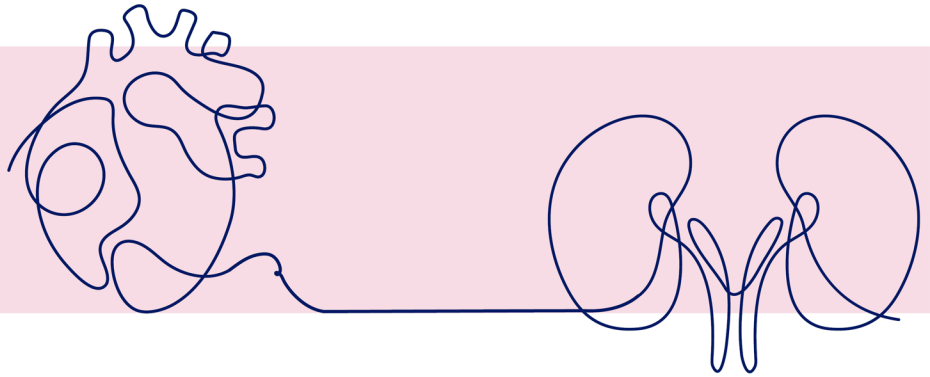
Diagnosi precoce e trattamento efficace della patologia
CARDIONEFRO METABOLICA
DALLA teoria ALLA pratica
Roma
Starhotels Metropole
12 • 13 dicembre 2025

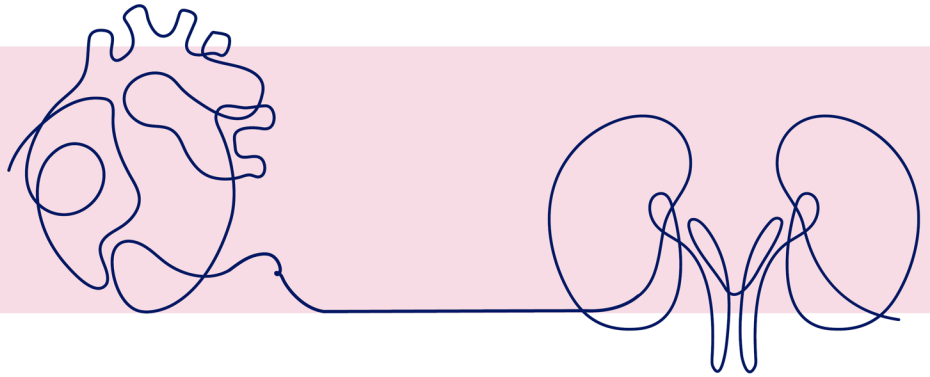


Prevenzione e terapia dello scompenso cardiometabolico: SGLT2i, GLP-1 RA o entrambi?

Martina Vitale

UOSD Endocrinologia e Diabetologia

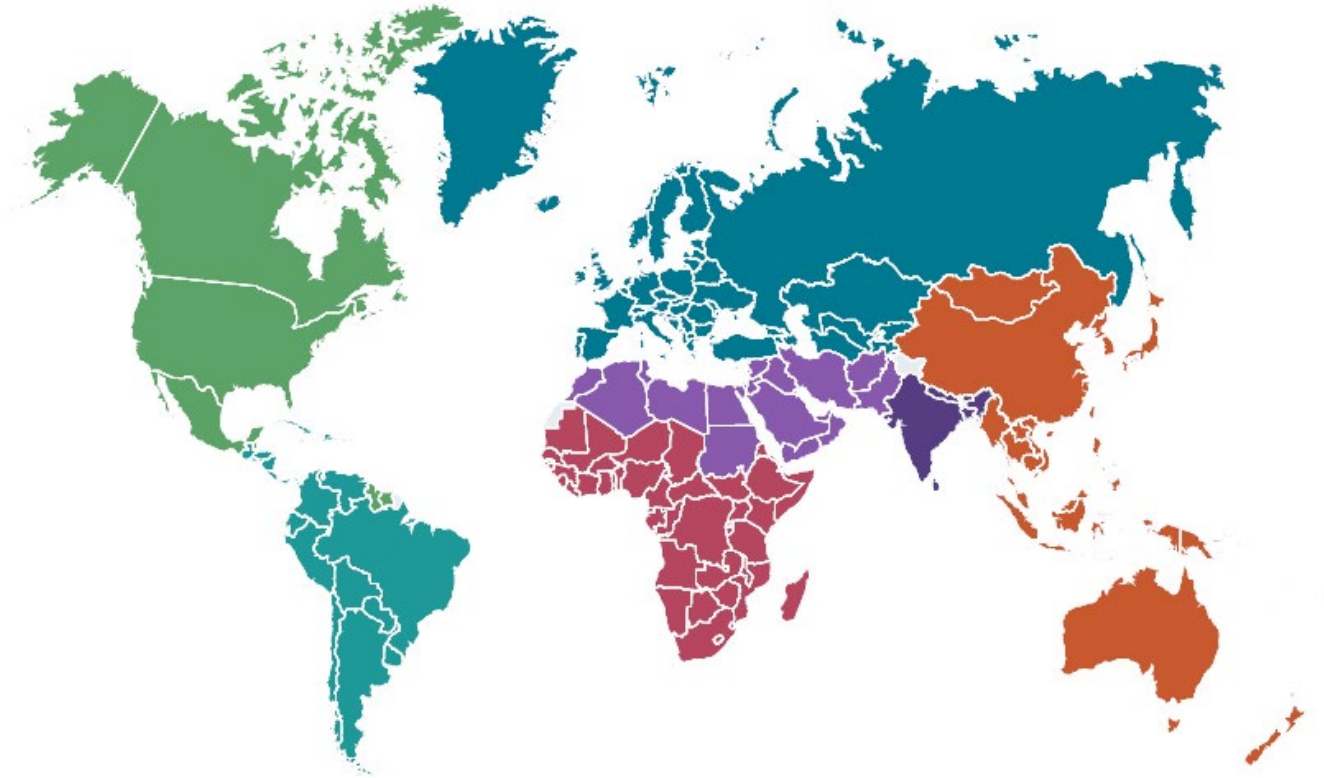
Azienda Ospedaliero-Universitaria Sant'Andrea
Roma



AGENDA

- Introduzione e linee guida
- SGLT2i e GLP-1 RA: meccanismi cardio-metabolici
- SGLT2i e GLP-1 RA: effetti delle due classi
- SGLT2i e GLP-1 RA: uso combinato

Map 1 Number of people with diabetes worldwide and per IDF Region, in 2024–2050 (20–79 years)



World

2050	852.5 Million	45% increase
2024	588.7 Million	

Africa (AFR)

2050	59.5 Million	142% increase
2024	24.6 Million	

Europe (EUR)

2050	72.4 Million	10% increase
2024	65.6 Million	

Middle-East and North Africa (MENA)

2050	162.6 Million	92% increase
2024	84.7 Million	

North America and Caribbean (NAC)

2050	68.1 Million	21% increase
2024	56.2 Million	

South and Central America (SACA)

2050	51.5 Million	45% increase
2024	35.4 Million	

South-East Asia (SEA)

2050	184.5 Million	73% increase
2024	106.9 Million	

Western Pacific (WP)

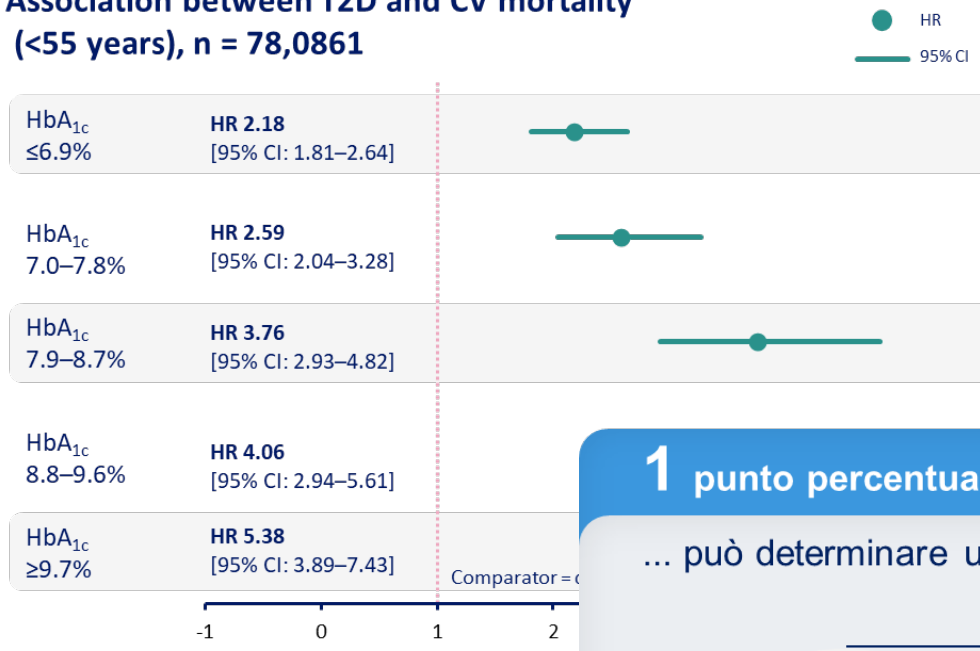
2050	253.8 Million	18% increase
2024	215.4 Million	

589 million people worldwide have diabetes

Findings from these studies indicate that, compared to those without diabetes, people with T2D face:

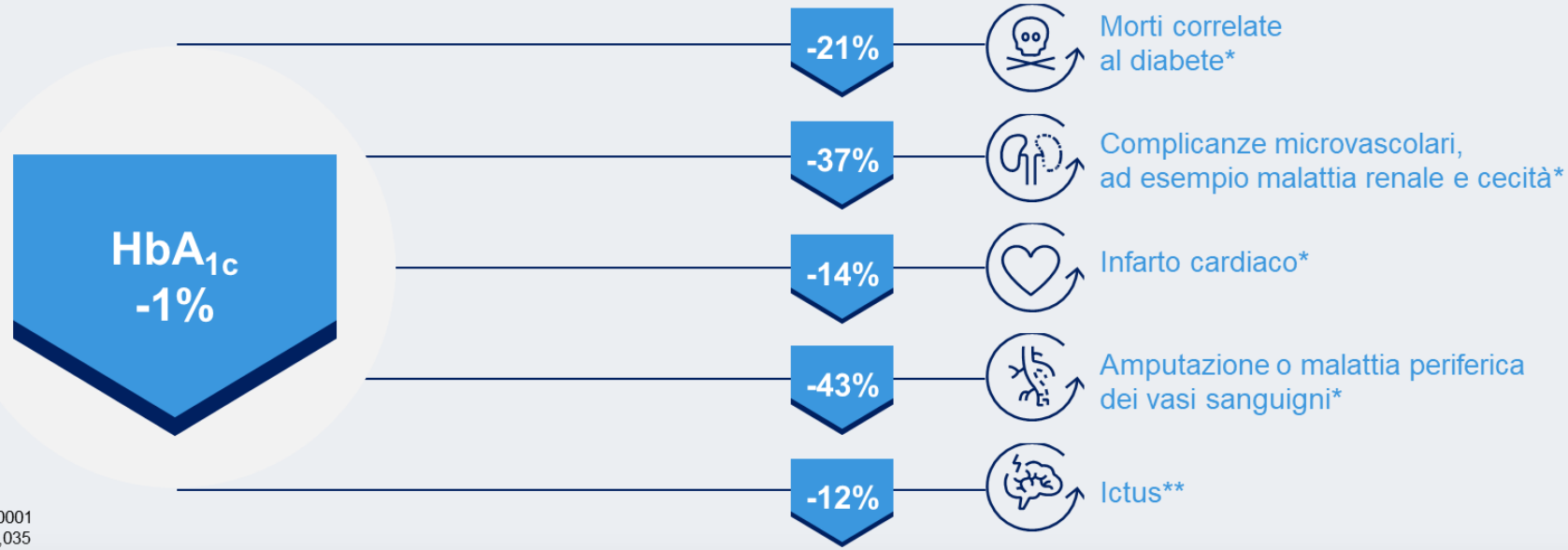
- **60% higher risk** of developing any form of CVD
- **54% higher risk** of stroke
- **73% higher risk** of myocardial infarction (heart attack)
- **84% higher risk** of heart failure

Association between T2D and CV mortality (<55 years), n = 78,0861



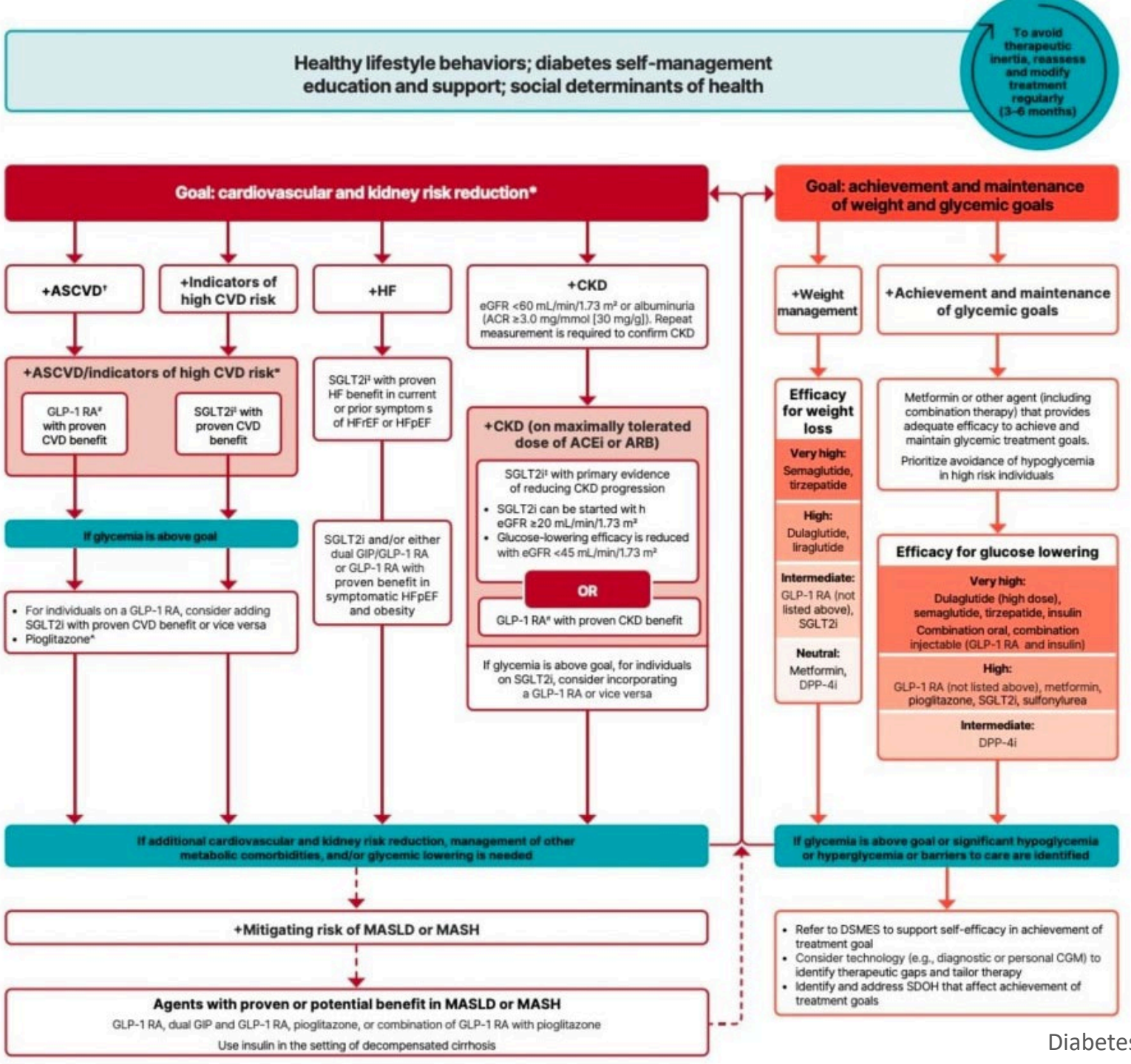
1 punto percentuale in meno di HbA_{1c} (1%)...

... può determinare una riduzione delle complicanze micro- e macro-vascolari:



*p<0,0001
**p=0,035

Tancredi M et al. N Engl J Med 2015;373:1720-32.
Stratton IM et al. BMJ. 2000 Aug 12;321(7258):405-12.



Diabetes Care 2026;49(Suppl. 1):S183–S215

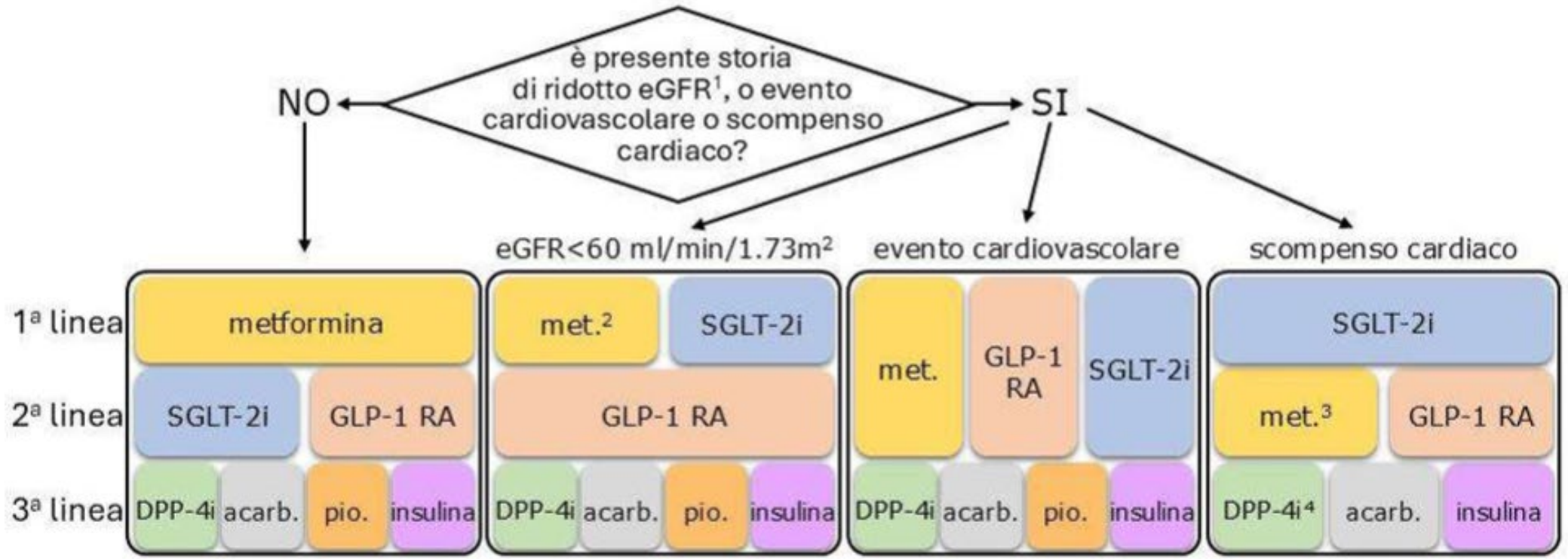
9.7 In adults with type 2 diabetes and established or high risk of atherosclerotic cardiovascular disease, the treatment plan should include medications with demonstrated benefits to reduce cardiovascular events (e.g., glucagon-like peptide 1 receptor agonist [GLP-1 RA] and/or sodium–glucose cotransporter 2 [SGLT2] inhibitor) for glycemic management and comprehensive cardiovascular risk reduction (irrespective of A1C) (**Fig. 9.4** and **Table 9.2**). **A**

10.40b In people with type 2 diabetes and established ASCVD or multiple ASCVD risk factors, or CKD, an SGLT2 inhibitor with demonstrated cardiovascular benefit is recommended to reduce the risk of cardiovascular events. **A**

10.40c In people with type 2 diabetes and established ASCVD or multiple risk factors for ASCVD, or CKD, a GLP-1 RA with demonstrated cardiovascular benefit is recommended to reduce the risk of cardiovascular events. **A**

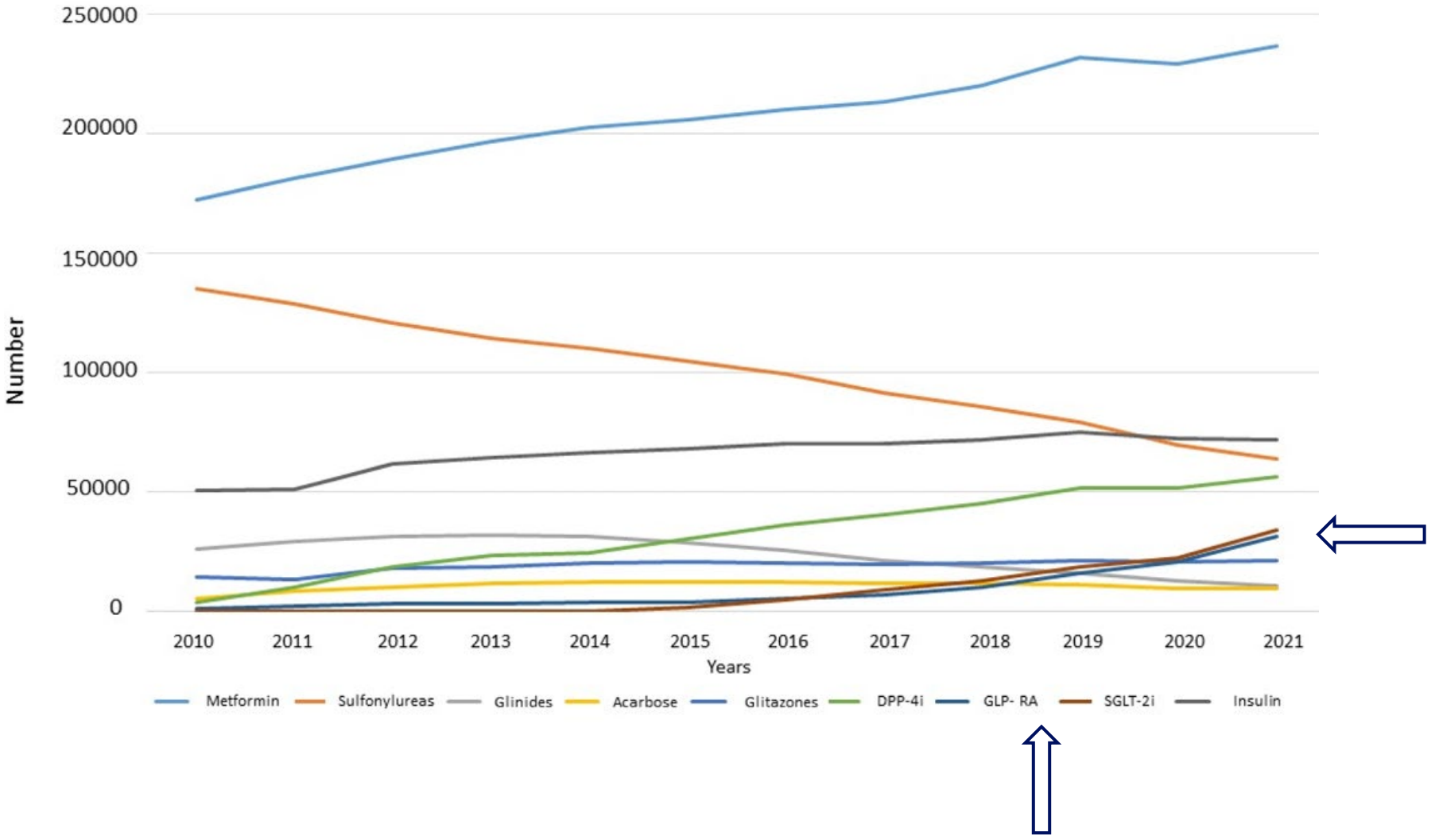
10.40d In people with type 2 diabetes and established ASCVD or multiple risk factors for ASCVD, combined therapy with an SGLT2 inhibitor with demonstrated cardiovascular benefit and a GLP-1 RA with demonstrated cardiovascular benefit may be considered for additive reduction of the risk of adverse cardiovascular and kidney events. **B**

Diabetes Care 2026;49(Suppl. 1):S183–S215



Linee Guida SID-AMD ottobre 2025

Trends of glucose-lowering drugs in older adults

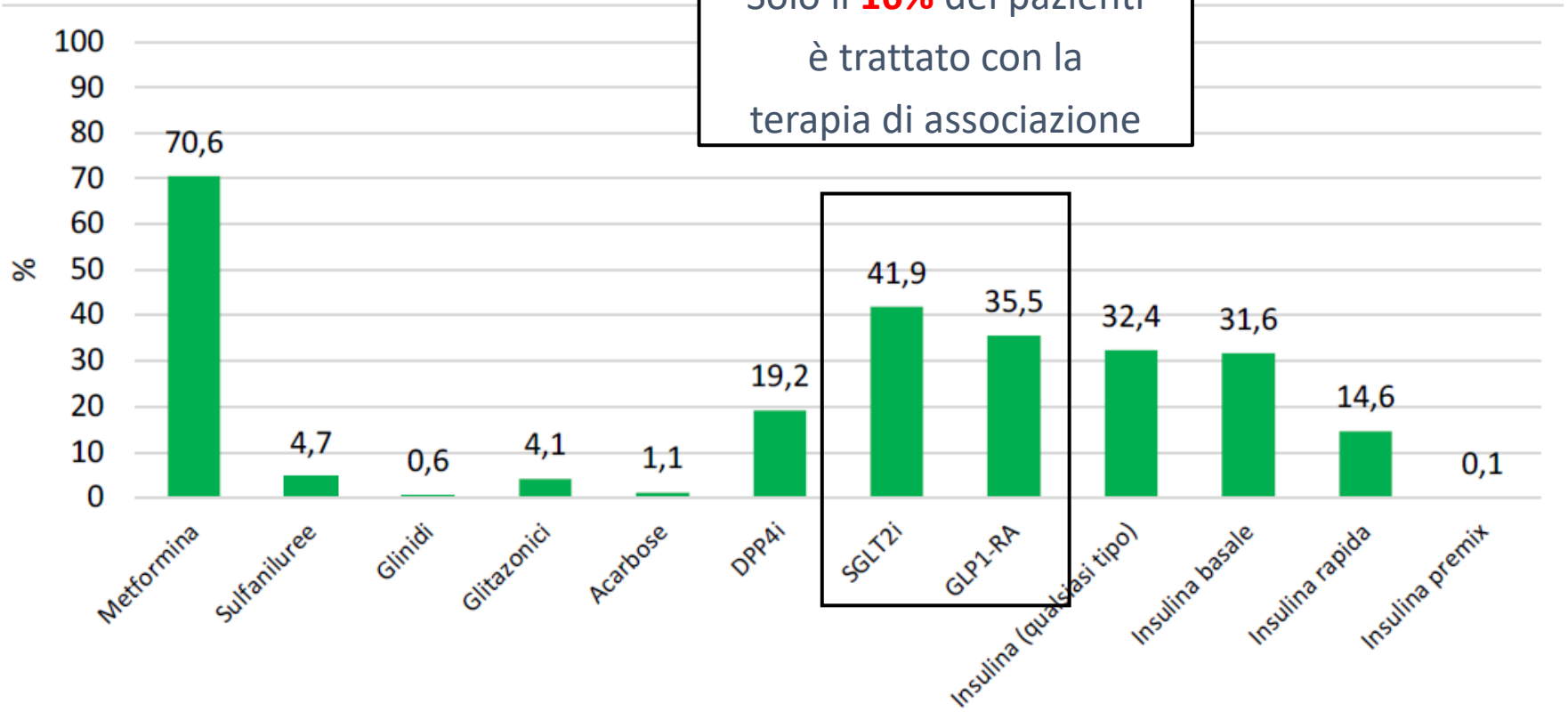


Foresta A, Succurro E et al, Diabetes Res Clin Pract. 2023 Aug:202:110742.

Uso dei farmaci (%)

Farmaci per il diabete (%)

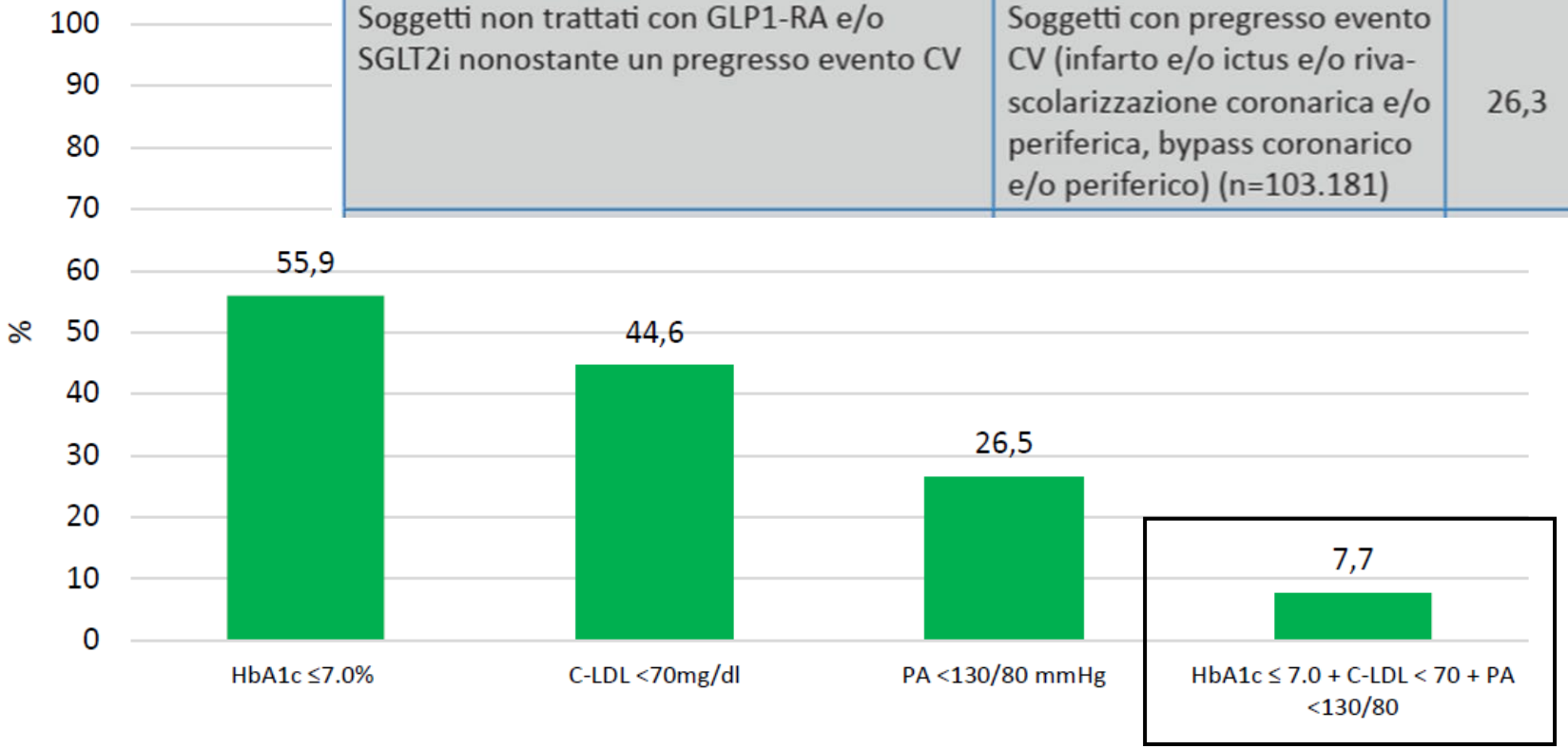
Solo il **16%** dei pazienti
è trattato con la
terapia di associazione

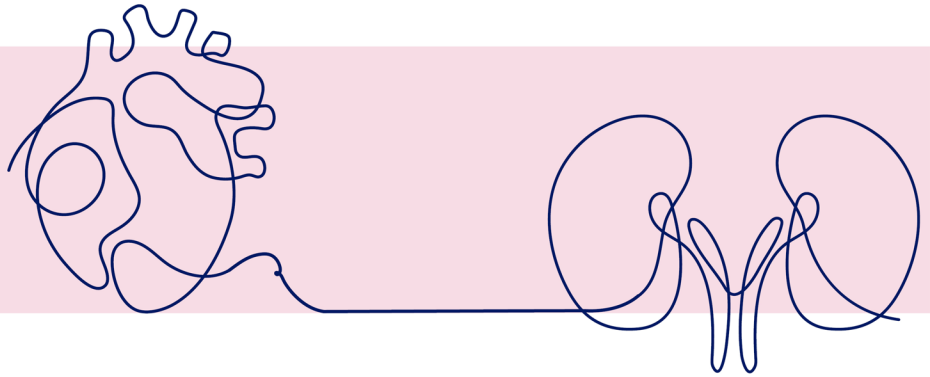


DM2 - Indicatori di esito intermedio

Soggetti con esito in

Indicatore	Denominatore	%	Gold standard (25° o 75° *percentile*)
Soggetti non trattati con GLP1-RA e/o SGLT2i nonostante un pregresso evento CV	Soggetti con pregresso evento CV (infarto e/o ictus e/o riva-scolarizzazione coronarica e/o periferica, bypass coronarico e/o periferico) (n=103.181)	26,3	20,0





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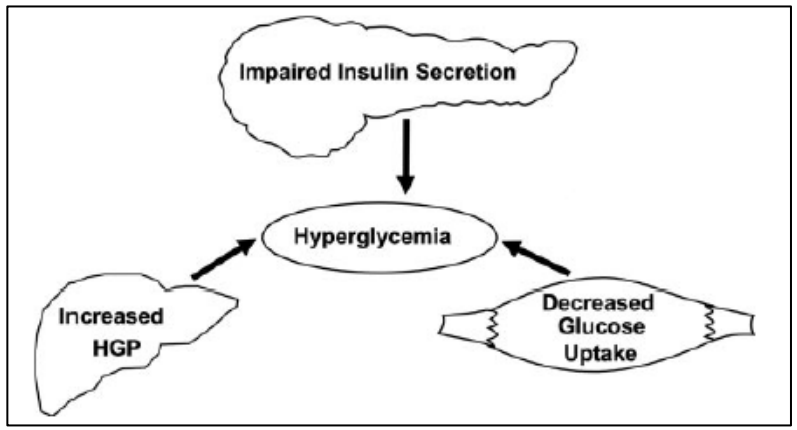
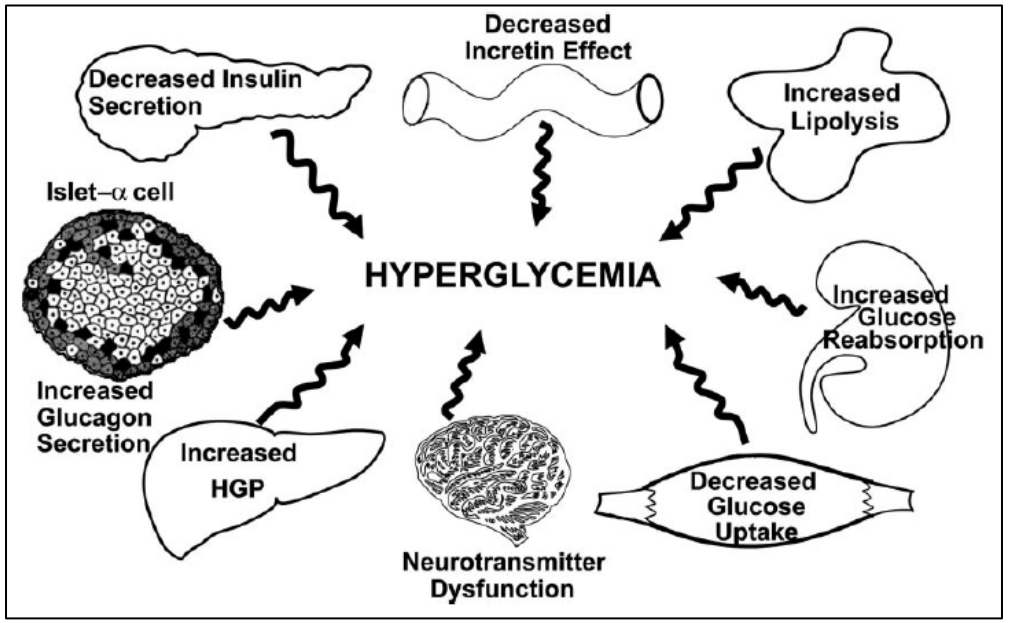
From the Triumvirate to the Ominous Octet: A New Paradigm for the Treatment of Type 2 Diabetes Mellitus

Ralph A. DeFronzo

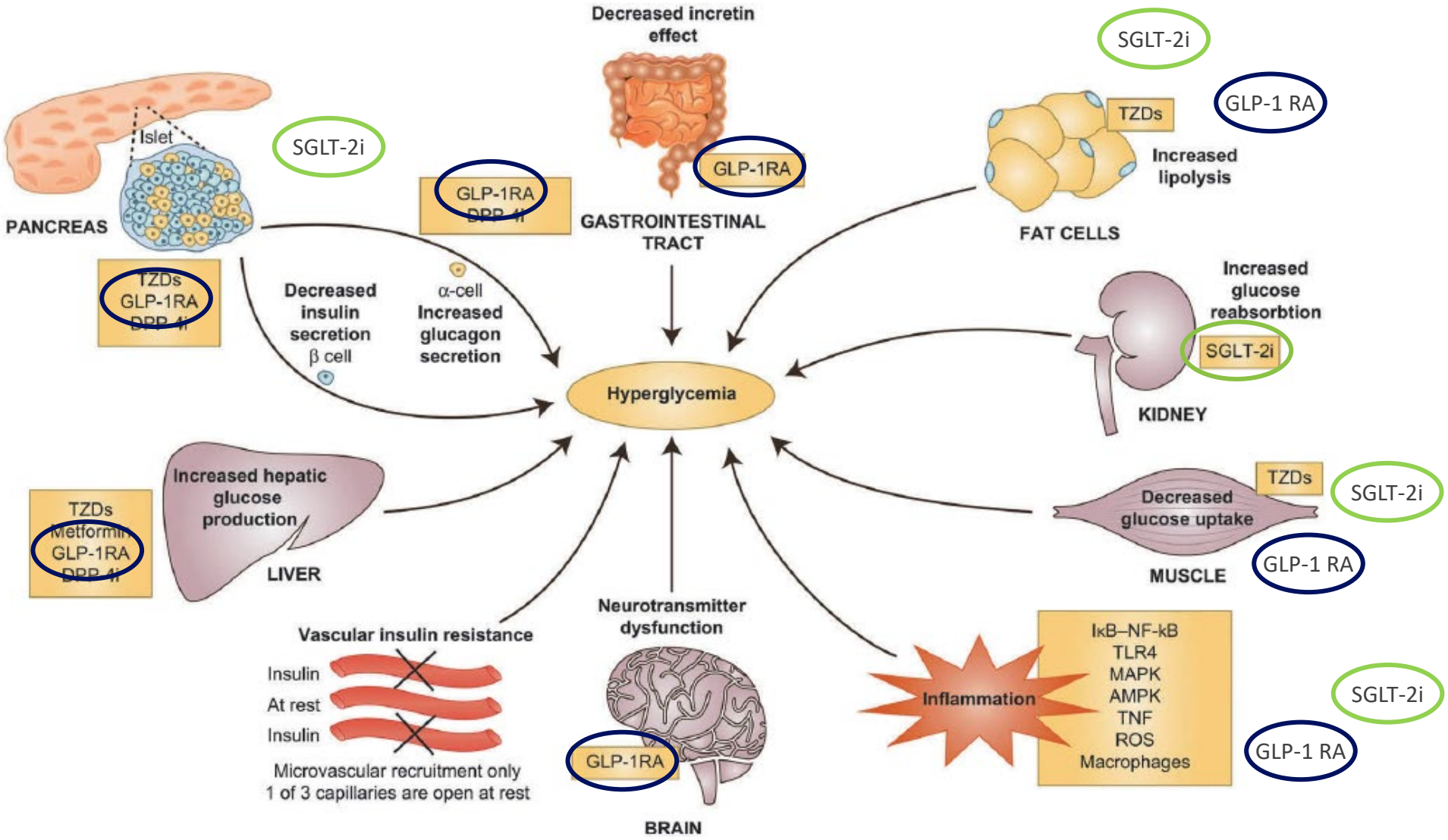




DeFronzo RA Diabetes. 2009 Apr;58(4):773-95.

Combination therapy with GLP-1 receptor agonist and SGLT2 inhibitor

Ralph A. DeFronzo MD



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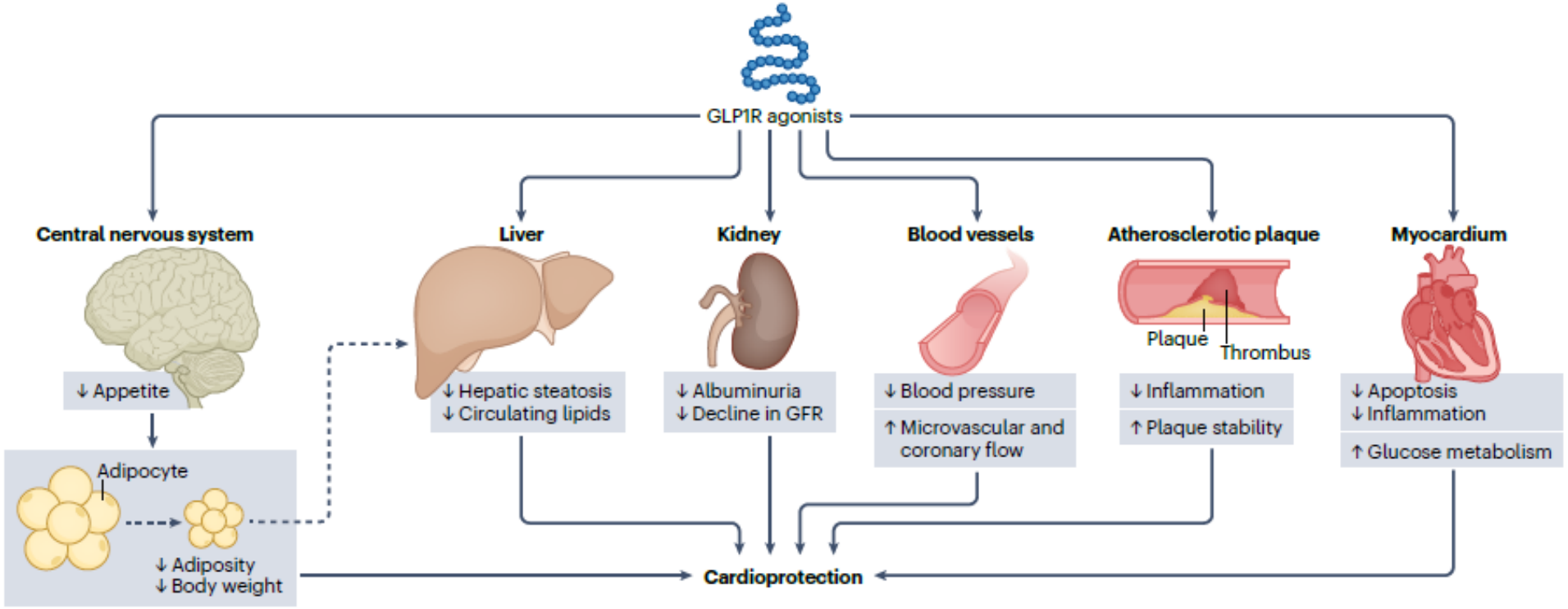
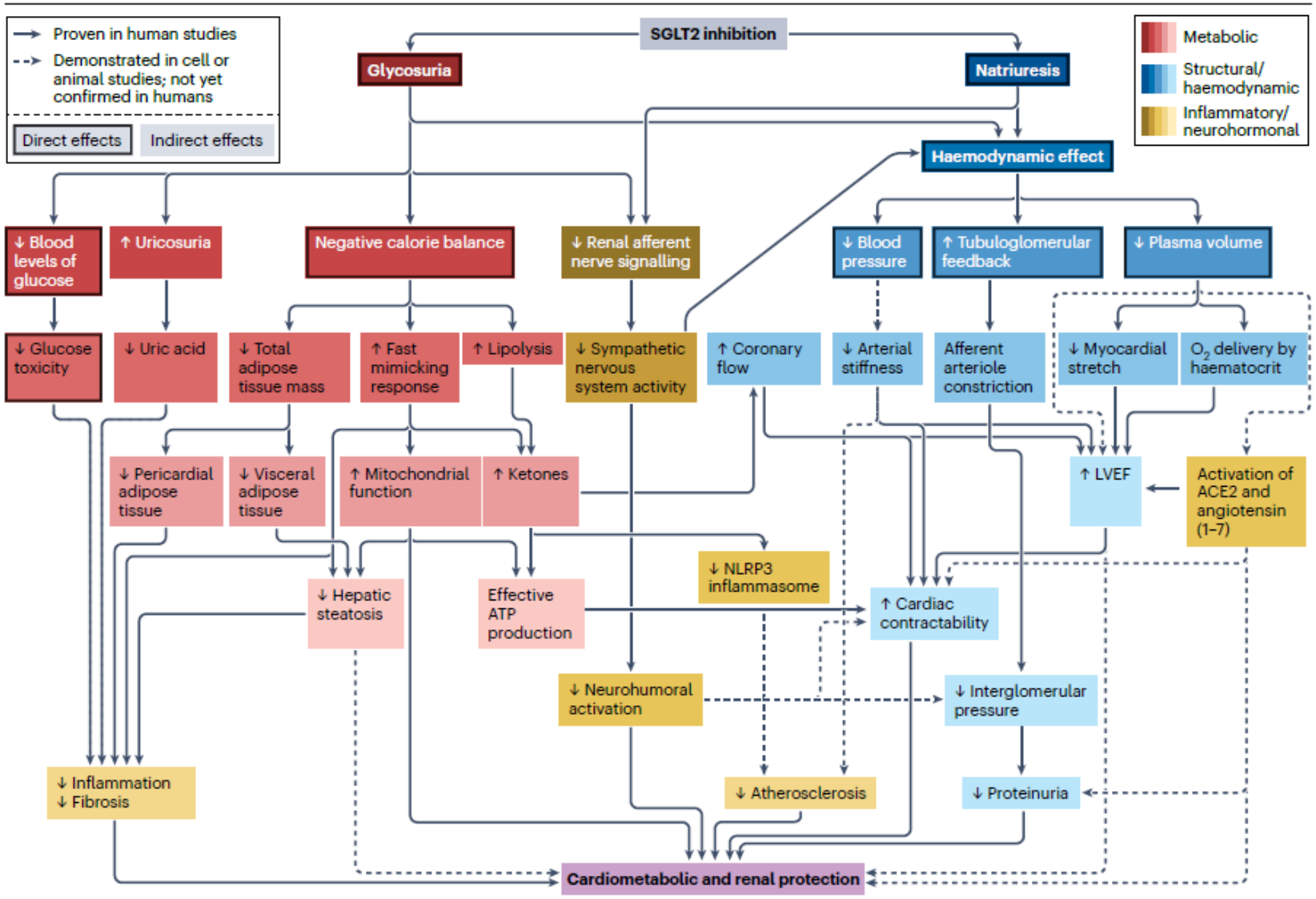
Glucagon-like peptide 1 receptor agonists: cardiovascular benefits and mechanisms of action

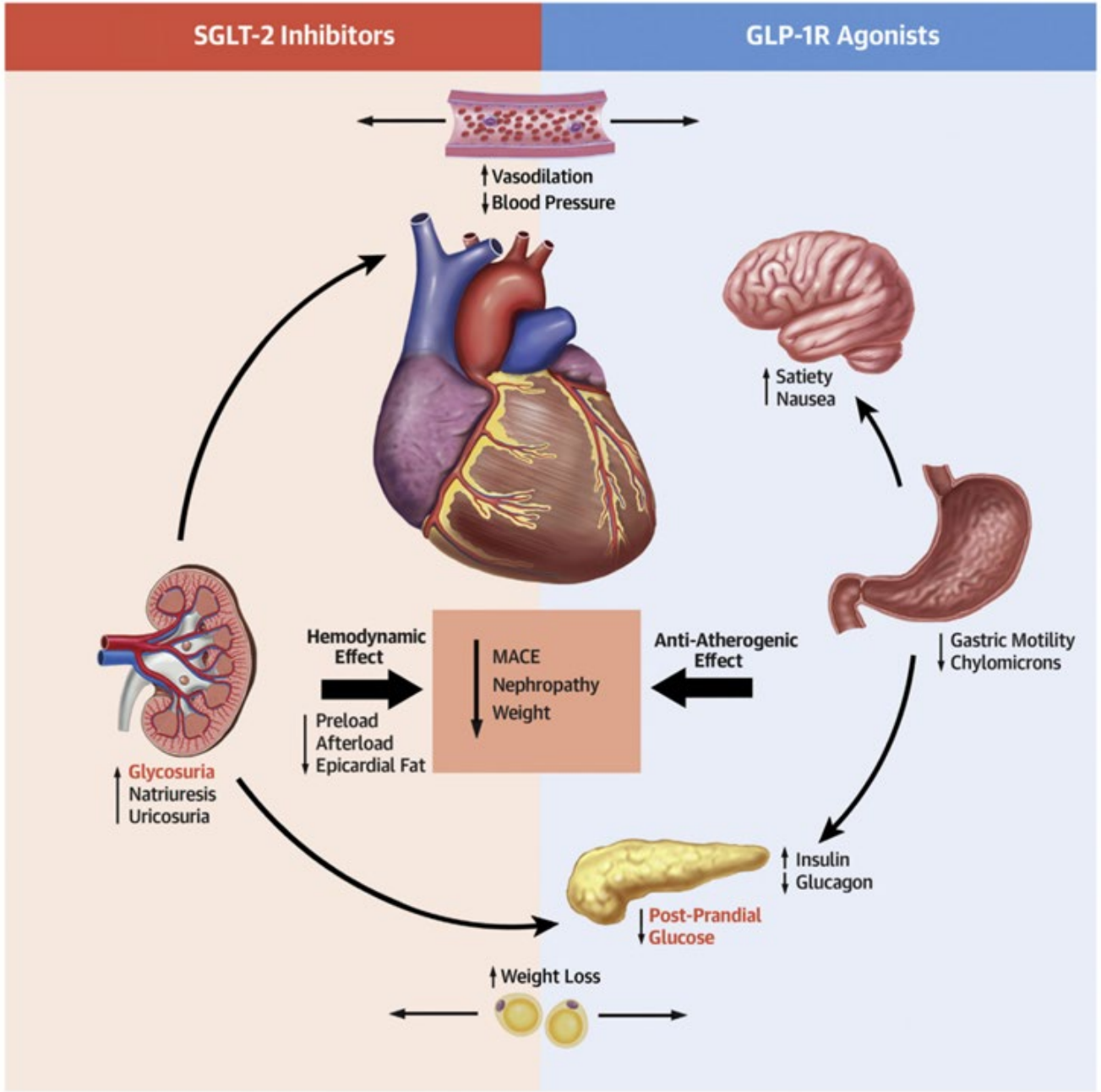


Ussher JR et al. Nat Rev Cardiol. 2023 Jul;20(7):463-474.

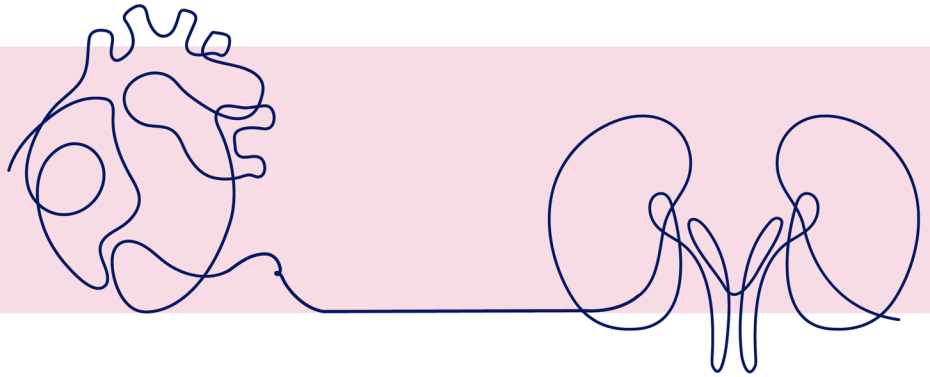
Cardiometabolic and renal benefits of sodium–glucose cotransporter 2 inhibitors



Lee JH et al. Nat Rev Endocrinol. 2025 Dec;21(12):783-798.



Wilcox T et al. J Am Coll Cardiol. 2020 Apr 28;75(16):1956-1974.



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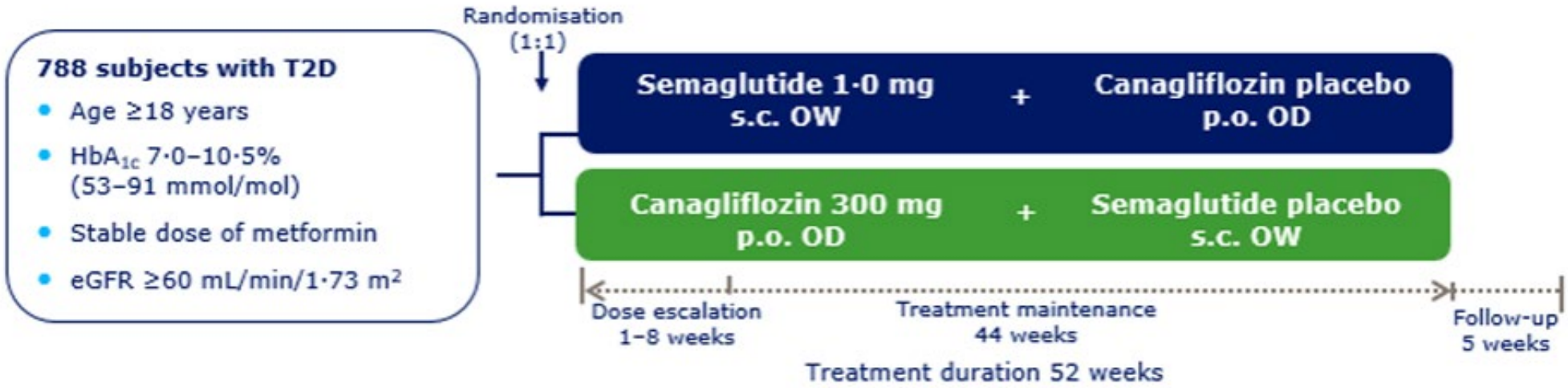
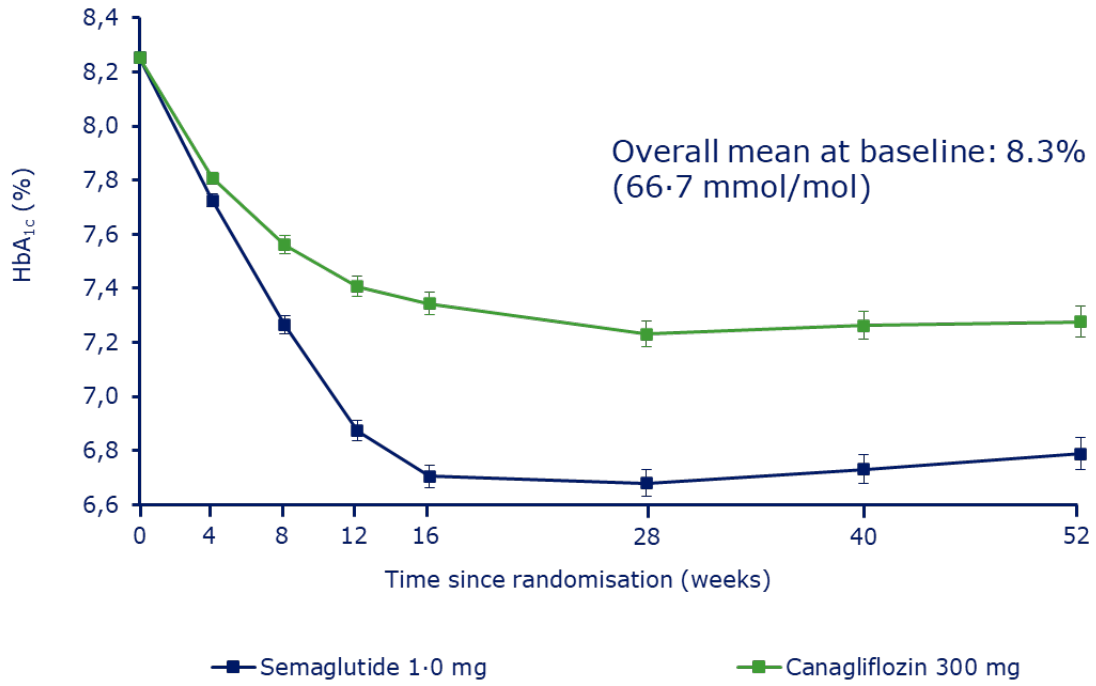
Efficacy and safety of once-weekly semaglutide versus daily canagliflozin as add-on to metformin in patients with type 2 diabetes (SUSTAIN 8)

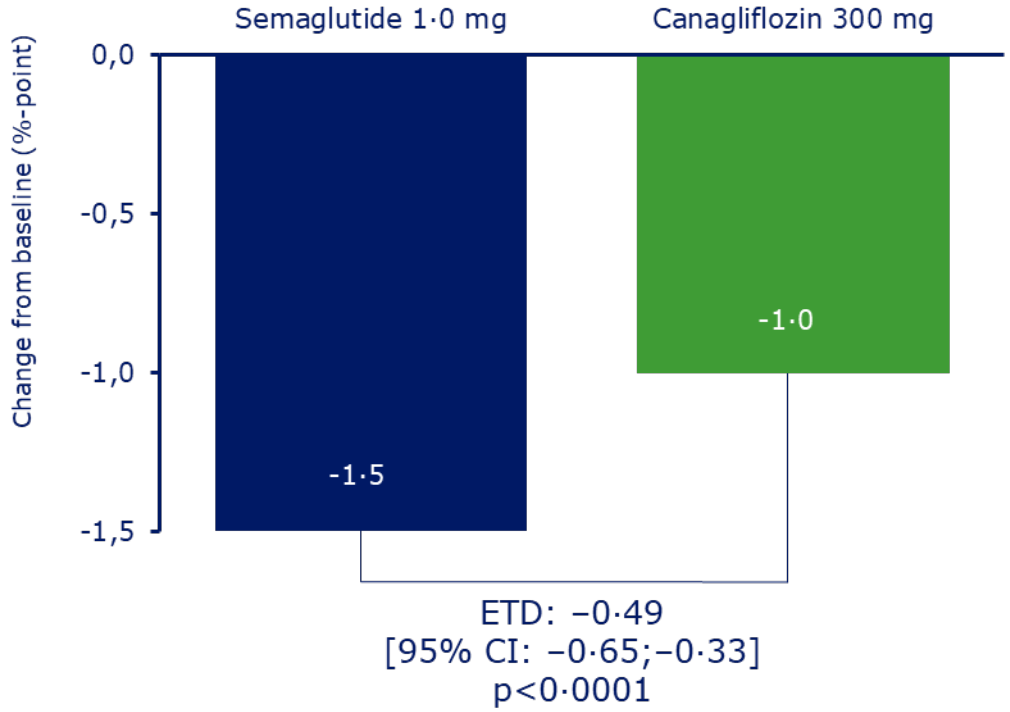


Lingvay I et al. Lancet Diabetes Endocrinol 2019; 7: 834–44

Efficacy and safety of once-weekly semaglutide versus daily canagliflozin as add-on to metformin in patients with type 2 diabetes (SUSTAIN 8)

HbA1c – primary endpoint





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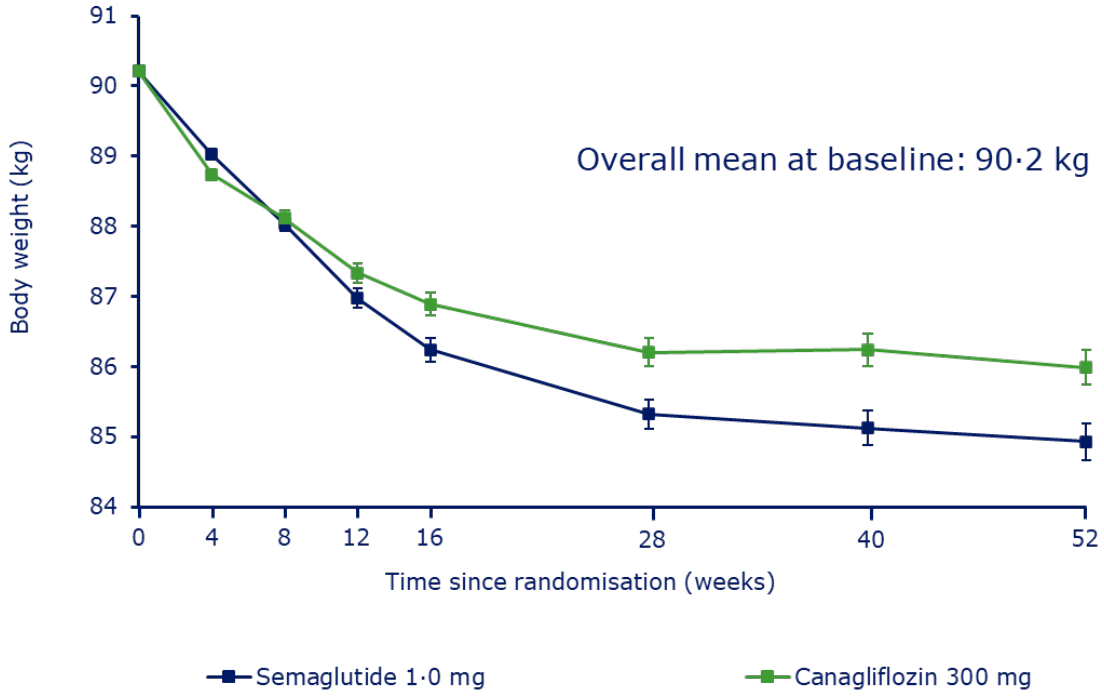
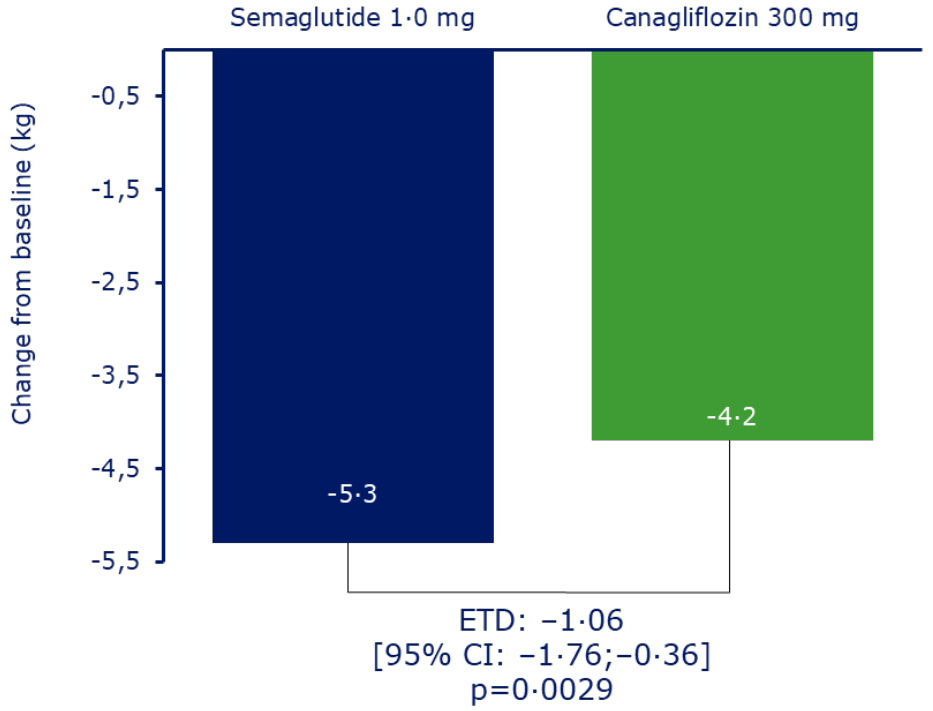
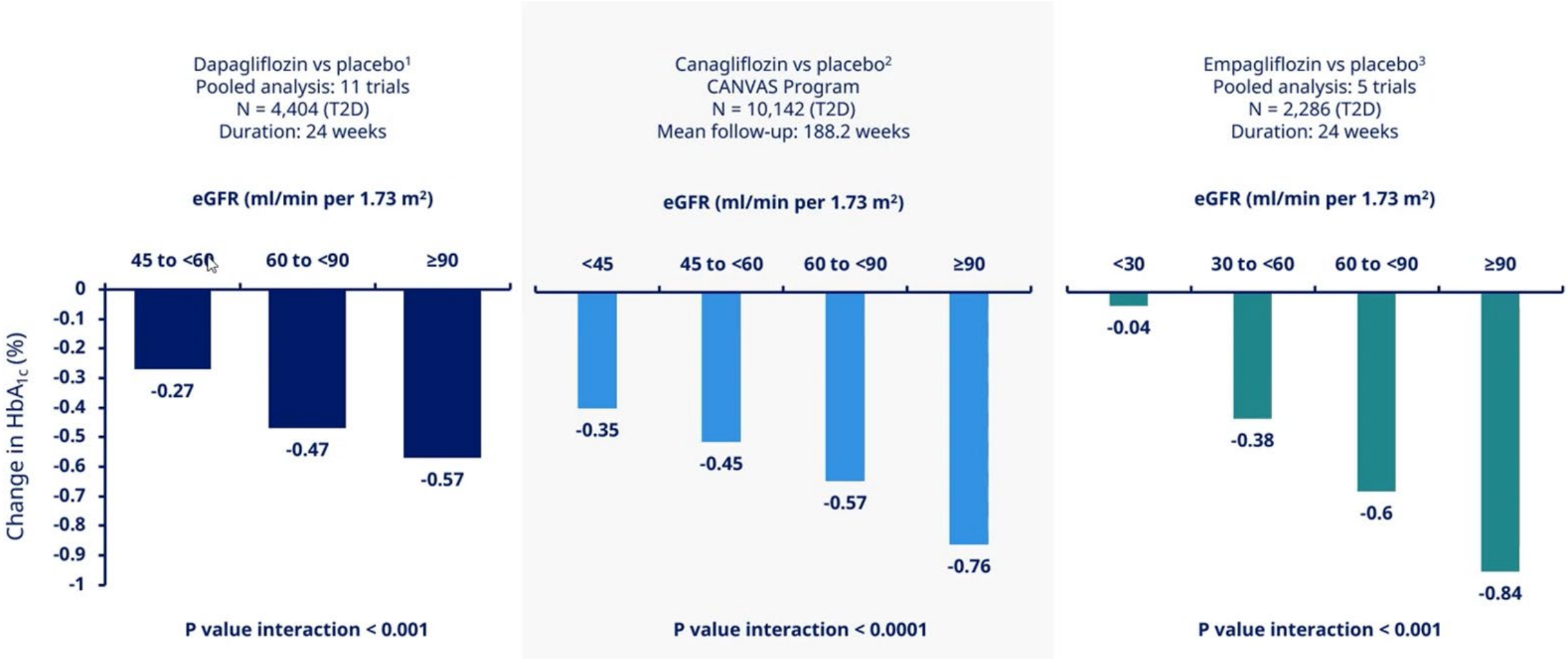
Body Weight





Lingvay I et al. Lancet Diabetes Endocrinol 2019; 7: 834–44

The glycemic efficacy of SGLT2i decreases as renal function declines



1. Petrykiv S. et al. Clin J Am Soc Nephrol. 2017;12(5):751-759; 2. Neuen BL et al. Circulation. 2018;138(15):1537-1550; 3. Cherney DZI et al. Kidney Int. 2018;93(1):231-244

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

A Overall HHF

	Treatment		Placebo			Favors treatment	Favors placebo	Weight, %
	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)			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/					
VERTIS CV	139/5499	7.3	99/2					
Fixed-effects model (Q = 1.39; *df* = 4; *P* = .85; I^2 = 0.0%)								

A Overall CV death

	Treatment		Placebo			Favors treatment	Favors placebo	Weight, %
	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)			15.61
CANVAS program	NA/5795	11.6	NA/4347	12.8	0.87 (0.72-1.06)			21.32
DECLARE-TIMI 58	245/8582	7.0	249/8578	7.1	0.98 (0.82-1.17)			25.24
CREDENCE	110/2202	19.0	140/2199	24.4	0.78 (0.61-1.00)			13.05
VERTIS CV	341/5499	17.6	184/2747	19.0	0.92 (0.77-1.10)			24.77
Fixed-effects model (Q = 11.22; *df* = 4; *P* = .02; I^2 = 64.3%)					0.85 (0.78-0.93)			

0.2 1 2

HR (95% CI)

A Overall MACEs

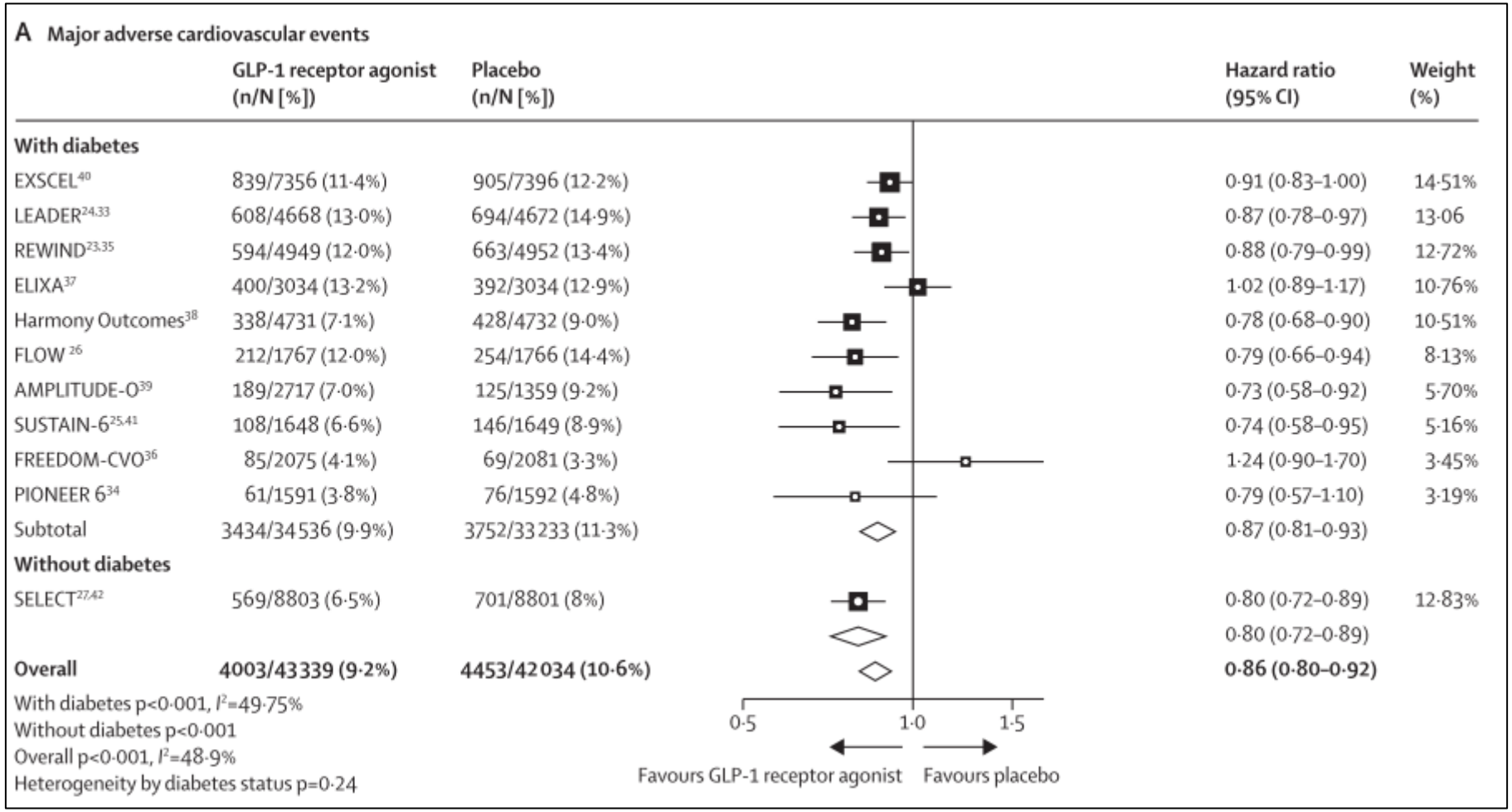
	Treatment		Plac			
	No./total No.	Rate/1000 patient-years	No./			
EMPA-REG OUTCOME	490/4687	37.4	282/			
CANVAS program	NA/5795	26.9	NA/			
DECLARE-TIMI 58	756/8582	22.6	803/8578	24.2	0.93 (0.84-1.03)	32.02
CREDENCE	217/2202	38.7	269/2199	48.7	0.80 (0.67-0.95)	10.92
VERTIS CV	735/5499	40.0	368/2747	40.3	0.99 (0.88-1.12)	21.23
Fixed-effects model (Q = 5.22; *df* = 4; *P* = .27; I^2 = 23.4%)					0.90 (0.85-0.95)	

0.2 1 2

HR (95% CI)

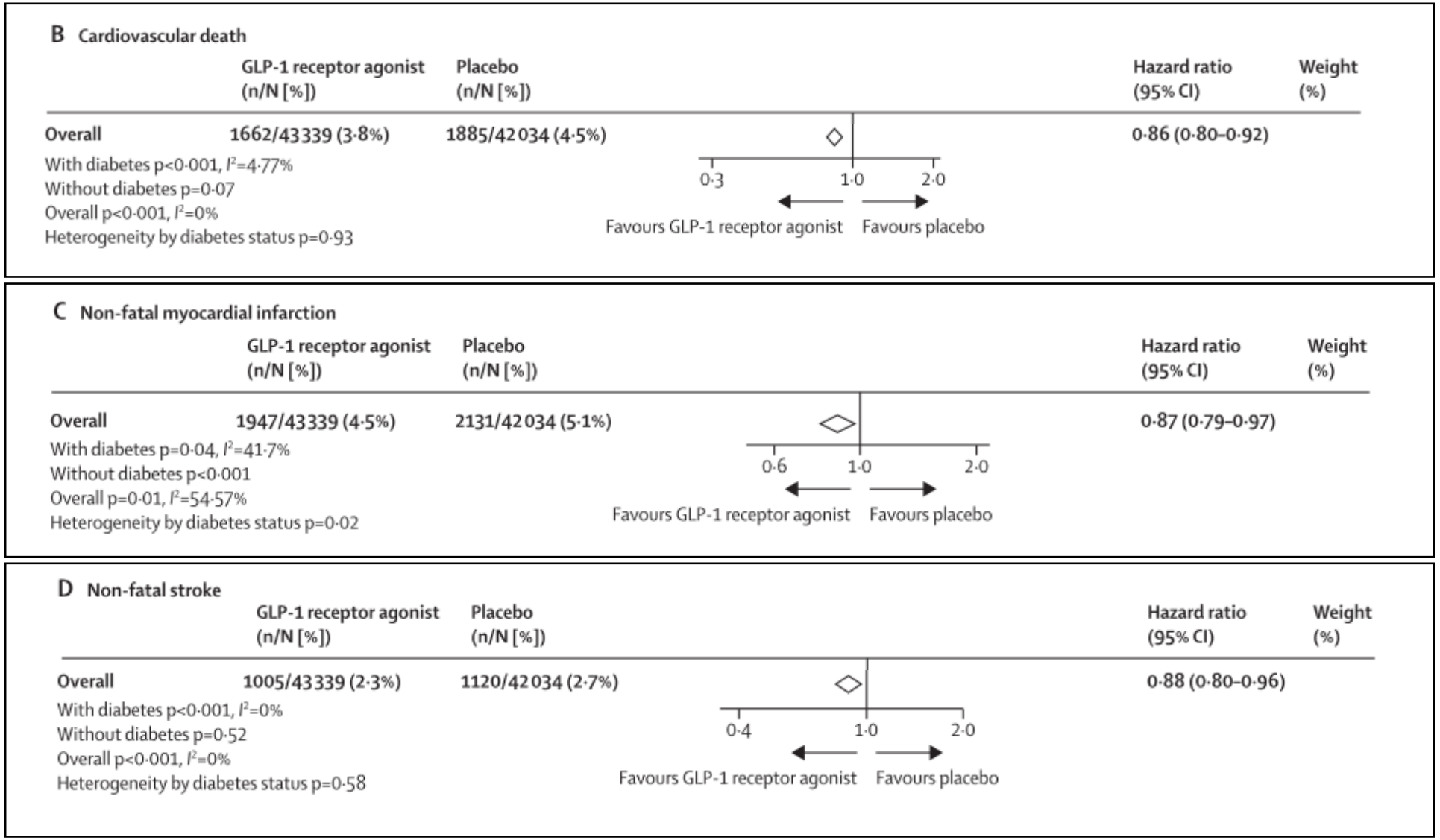
McGuire DK et al. JAMA Cardiol. 2021 Feb 1;6(2):148-158

Effects of GLP-1 receptor agonists on kidney and cardiovascular disease outcomes: a meta-analysis of randomised controlled trials



Badve SV et al. Lancet Diabetes Endocrinol. 2025; 13: 15–28

Effects of GLP-1 receptor agonists on kidney and cardiovascular disease outcomes: a meta-analysis of randomised controlled trials



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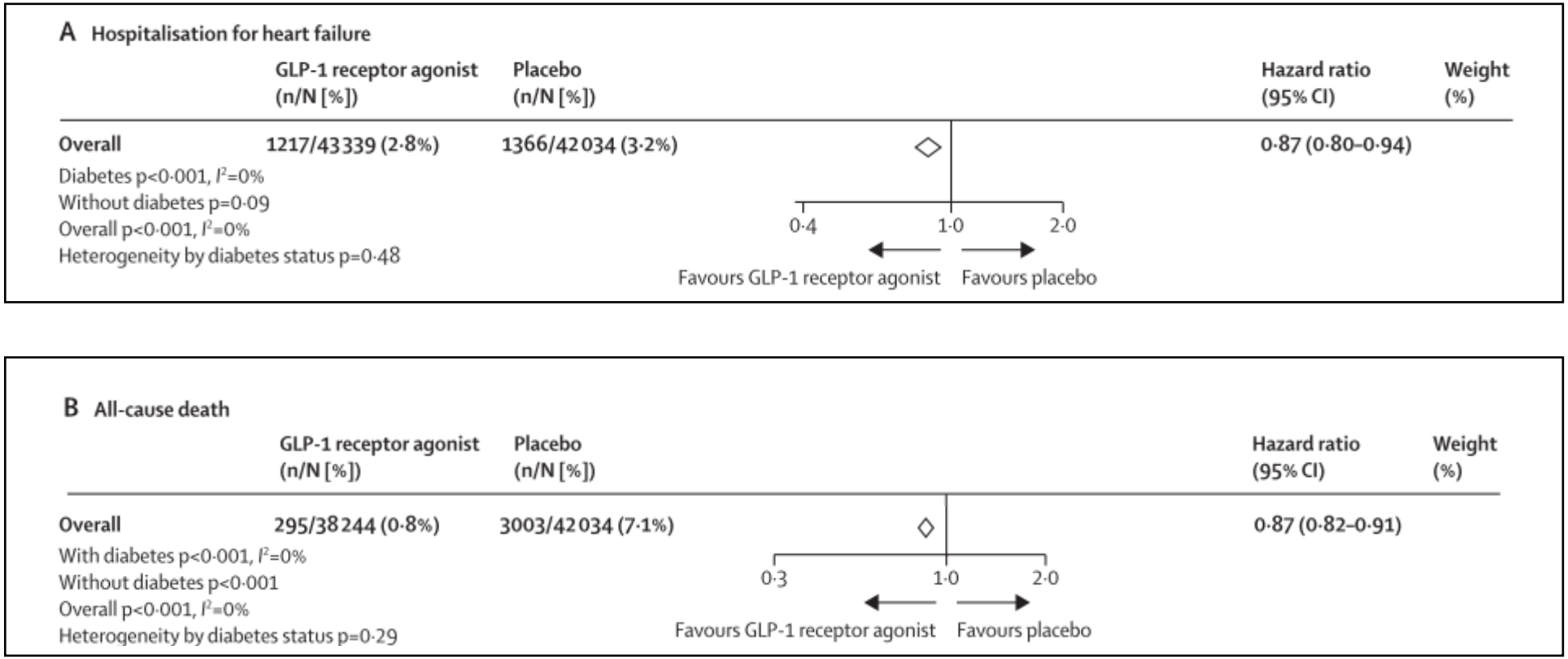
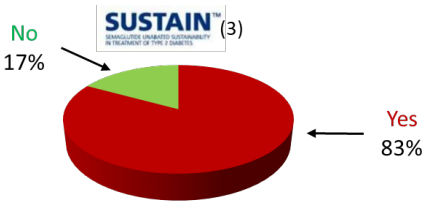
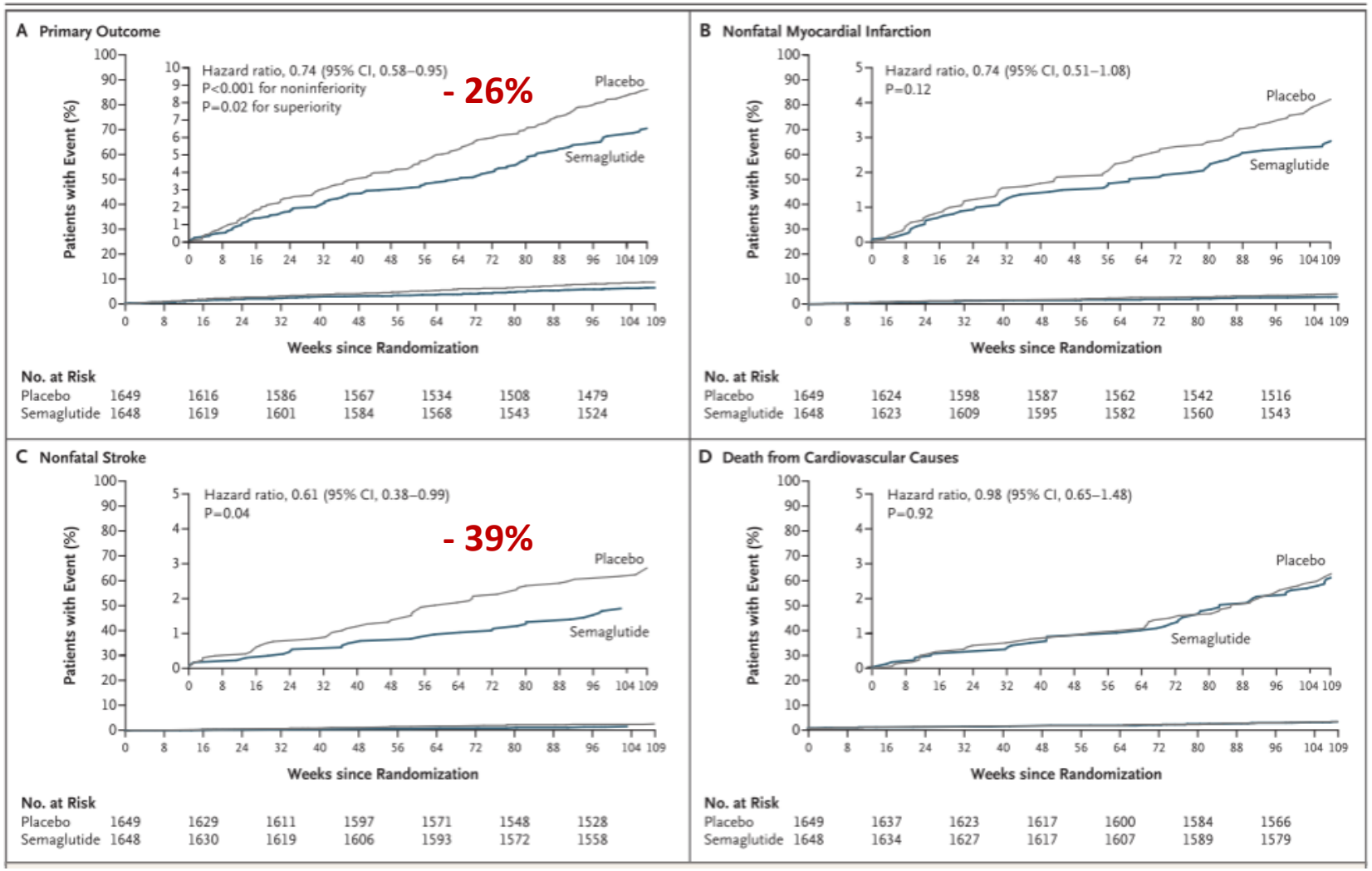


Badve SV et al. Lancet Diabetes Endocrinol. 2025; 13: 15–28

Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes the SUSTAIN-6 trial

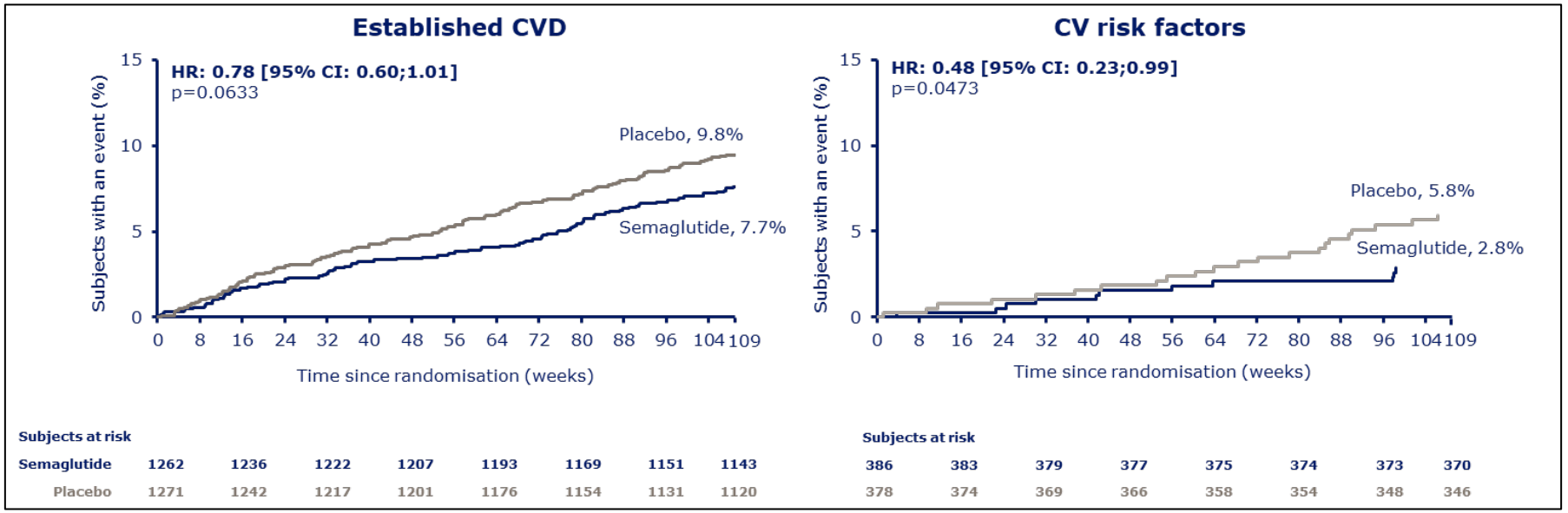




Marso SP et al. N Engl J Med. 2016;375;1834–1844

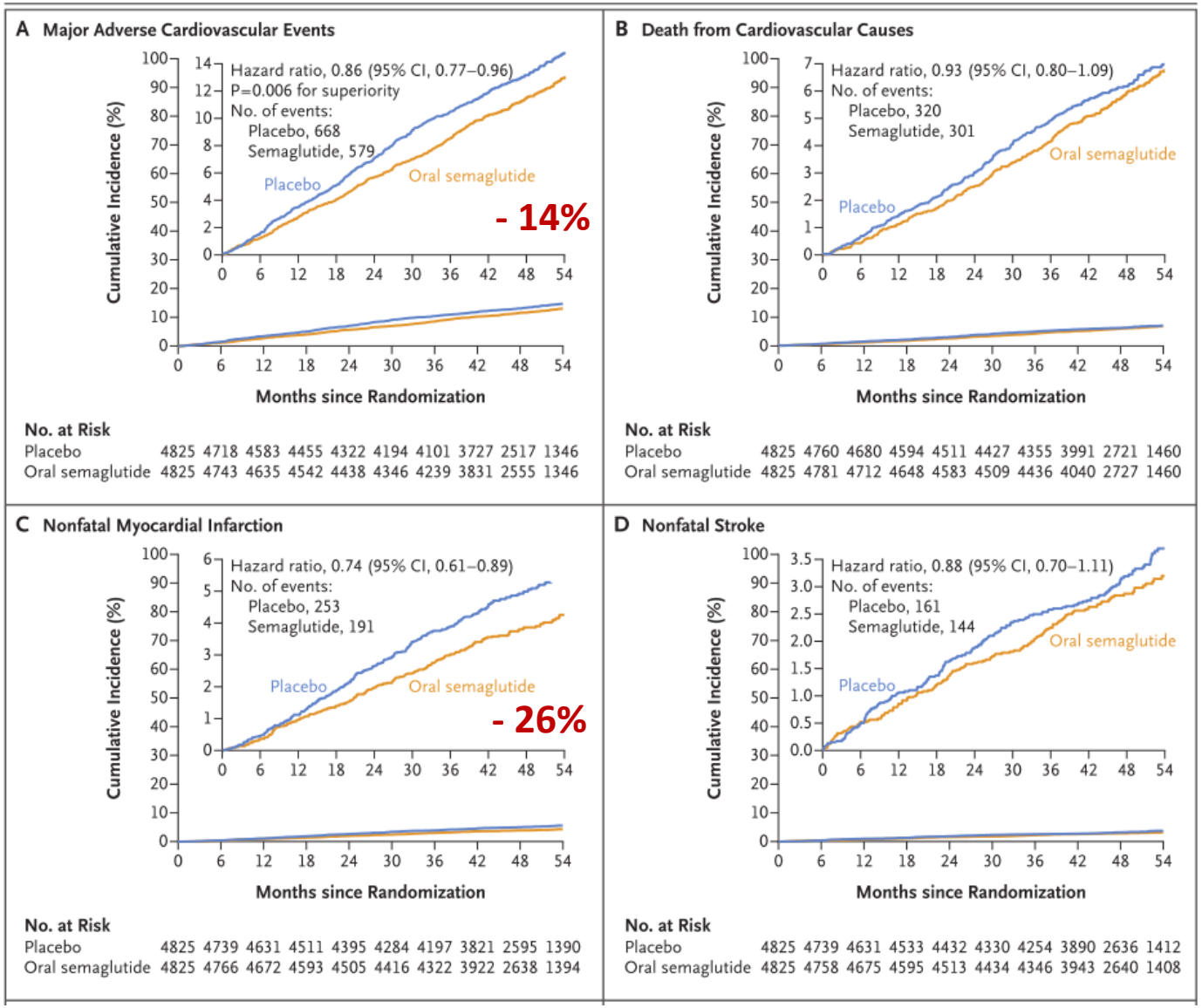
Cardiovascular risk reduction with semaglutide: a post hoc analysis of gender, age, and baseline CV risk profile in the SUSTAIN 6 trial

Event/subgroup	Events (subjects) semaglutide / placebo	HR	[95% CI]	Interaction p-value
MACE				
All subjects	108 (1648) / 146 (1649)	0.74	[0.58;0.95]	
Gender				
Male	73 (1013) / 103 (989)	0.68	[0.50;0.92]	0.45
Female	35 (635) / 43 (660)	0.84	[0.54;1.31]	
Age, years				
≤65	57 (950) / 76 (929)	0.72	[0.51;1.02]	0.92
>65	51 (698) / 70 (720)	0.74	[0.52;1.06]	
CV risk				
Prior MI/stroke	66 (673) / 88 (694)	0.76	[0.55;1.05]	0.75
No prior MI/stroke	42 (975) / 58 (955)	0.70	[0.47;1.04]	
Established CVD	97 (1262) / 124 (1271)	0.78	[0.60;1.01]	0.22
CV risk factors	11 (386) / 22 (378)	0.48	[0.23;0.99]	



Leiter LA et al. Cardiovasc Diabetol. 2019 Jun 6;18(1):73.

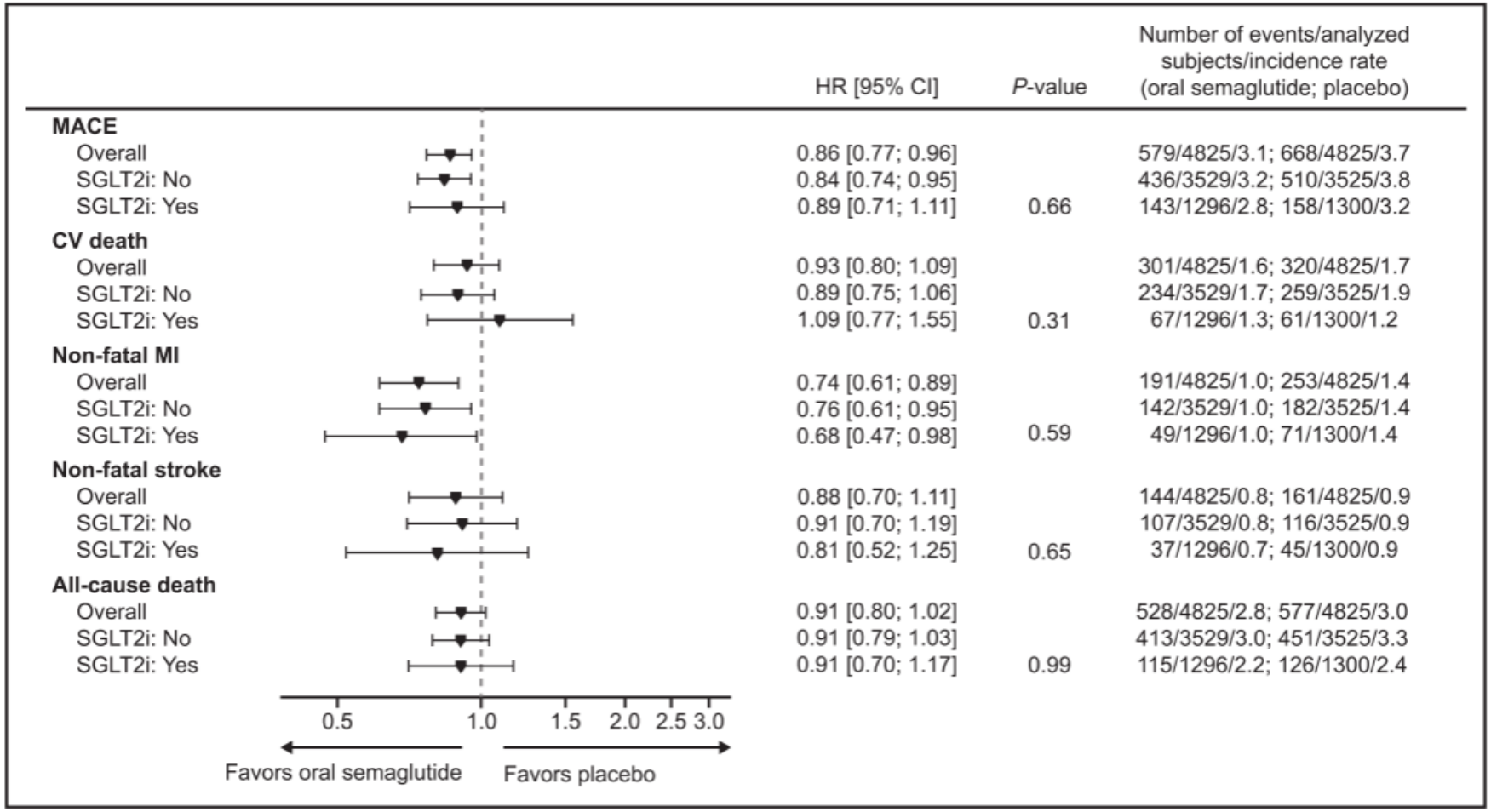
Oral Semaglutide and Cardiovascular Outcomes in High-Risk Type 2 Diabetes
The SOUL trial



McGuire DK et al. N Engl J Med. 2025 May 29;392(20):2001-2012.

Oral Semaglutide and Cardiovascular Outcomes According to SGLT2i Use: Prespecified Analyses of the SOUL Randomized Trial

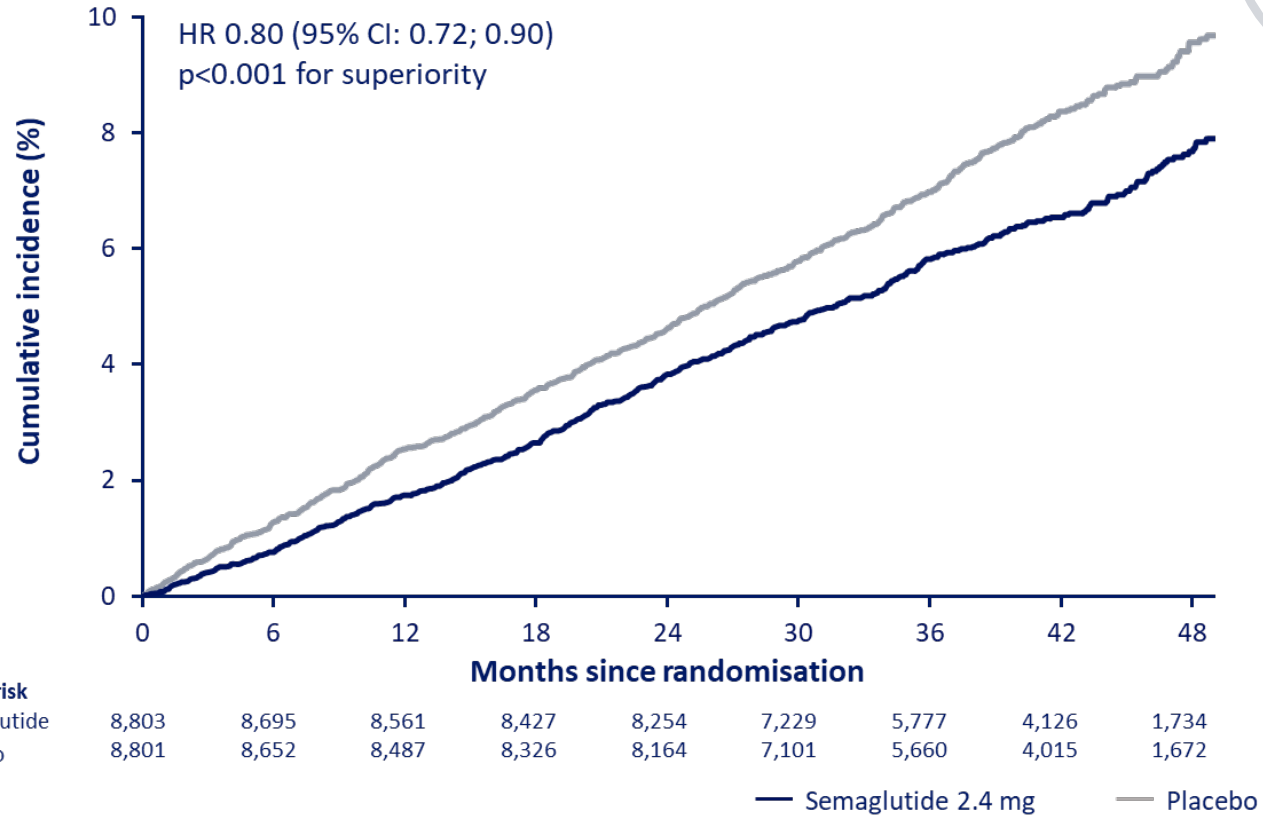
26.9% participants were receiving SGLT2i at baseline.
During the trial, SGLT2i use was **44.9%** of participants randomized to oral semaglutide and **52.8%** of participants randomized to placebo.



Marx N et al. Circulation. 2025 Jun 10;151(23):1639-1650.

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes
The SELECT trial

Composite of death from cardiovascular causes, nonfatal myocardial infarction, or non-fatal stroke



20%
reduction in risk of MACE

Semaglutide 2.4 mg significantly reduced the risk of MACE by 20% compared with placebo in people with obesity and established CVD, without T2D

All three components (death from CV causes, non-fatal MI and non-fatal stroke) contributed to MACE risk reduction

Mean follow-up time was 39.8 months

18%
reduction in risk of HF

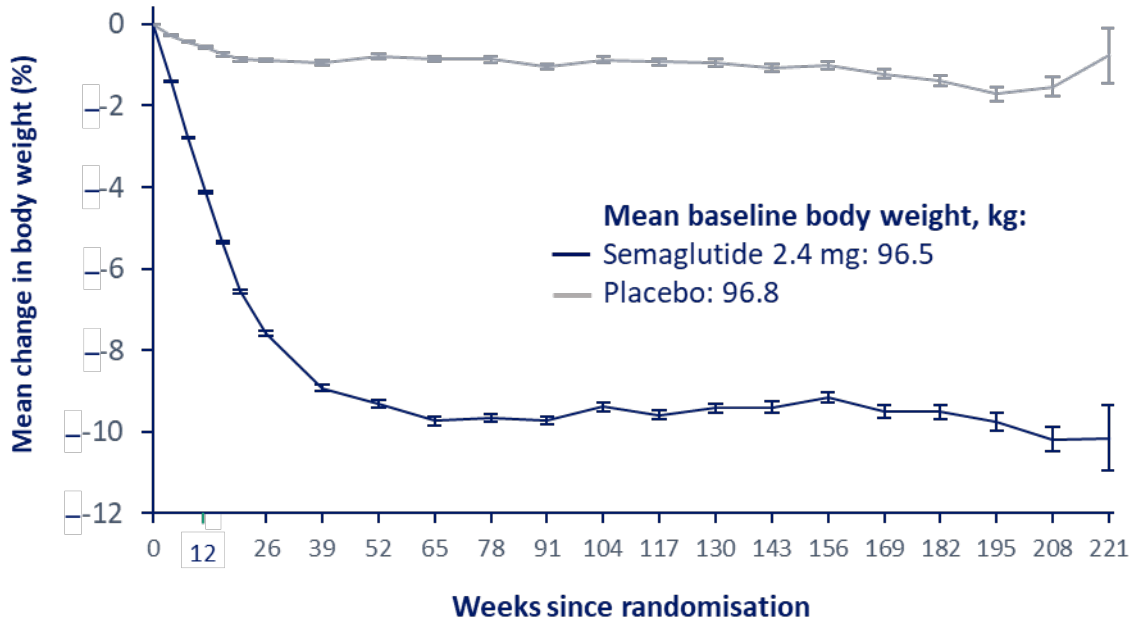
19%
reduction in risk of death

Lincoff AM et al. N Engl J Med 2023;389:2221-32.

Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes
The SELECT trial

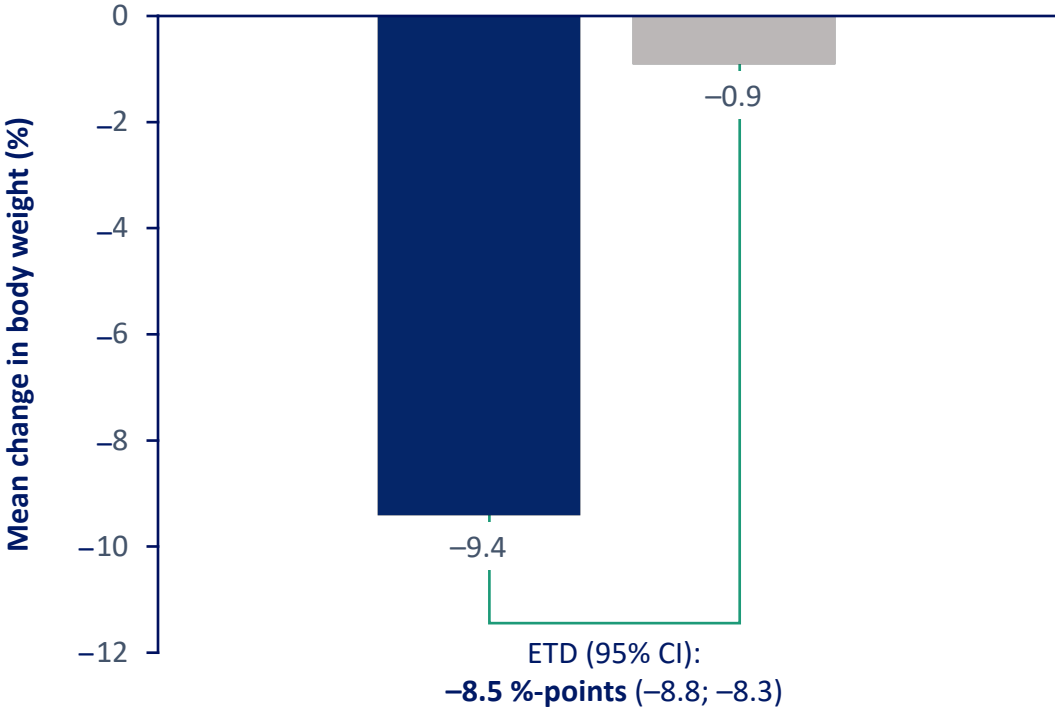
Change in body weight

Observed change from baseline over time

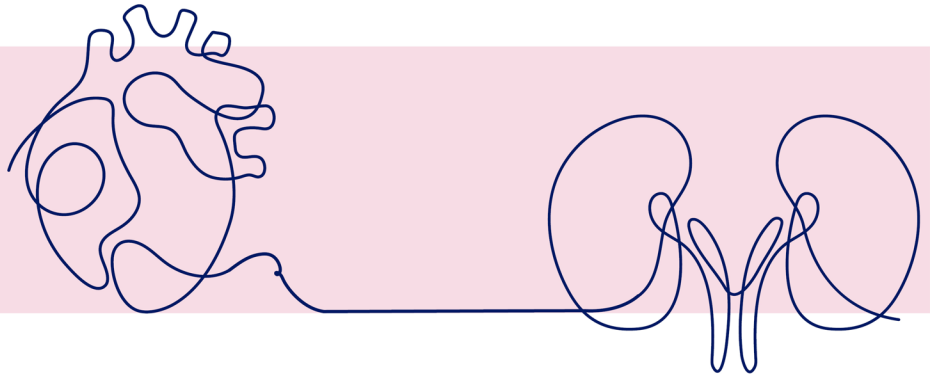


No. of participants																		
Semaglutide	8,803	7,647	7,493	6,690	7,290	6,447	7,282	6,460	7,474	5,991	5,898	4,686	5,085	3,650	2,954	1,737	921	157
Placebo	8,801	7,715	7,516	6,704	7,269	6,340	7,272	6,392	7,378	5,871	5,879	4,583	5,014	3,560	2,890	1,698	898	152

Estimated change from baseline to week 104



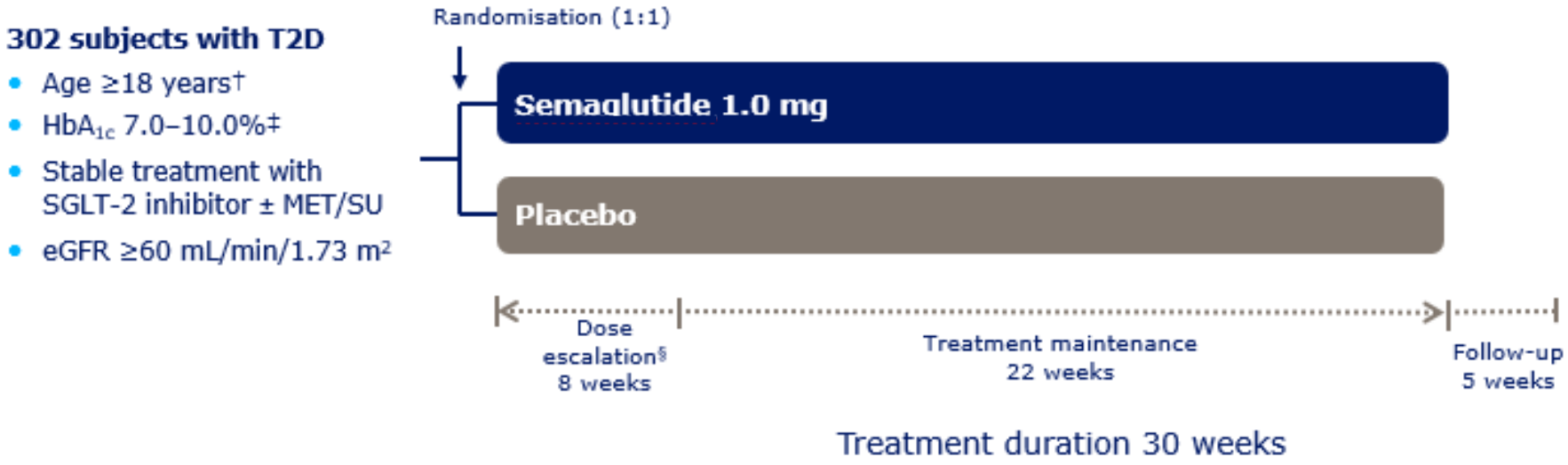
Lincoff AM et al. N Engl J Med 2023;389:2221-32.



AGENDA

- Introduzione e linee guida
- SGLT2i e GLP-1 RA: meccanismi cardio-metabolici
- SGLT2i e GLP-1 RA: effetti delle due classi
- SGLT2i e GLP-1 RA: uso combinato

Semaglutide once-weekly as add-on to SGLT-2 inhibitor therapy in type 2 diabetes (SUSTAIN 9): a randomised, placebo-controlled trial



Primary Endpoint:

Change in HbA1c from baseline to week 30

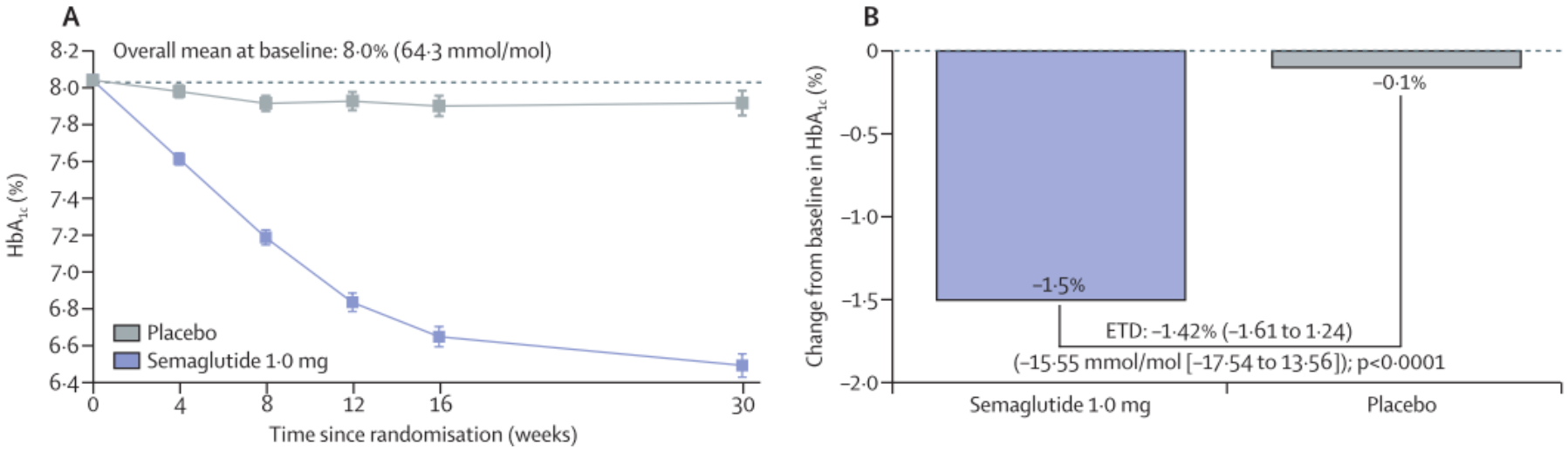
Secondary Endpoints:

- percentage of patients achieving HbA1c <7.0%
- change in bodyweight
- change in FPG
- percentage of patients achieving HbA1c ≤6.5%
- change in seven-point SMBG profile

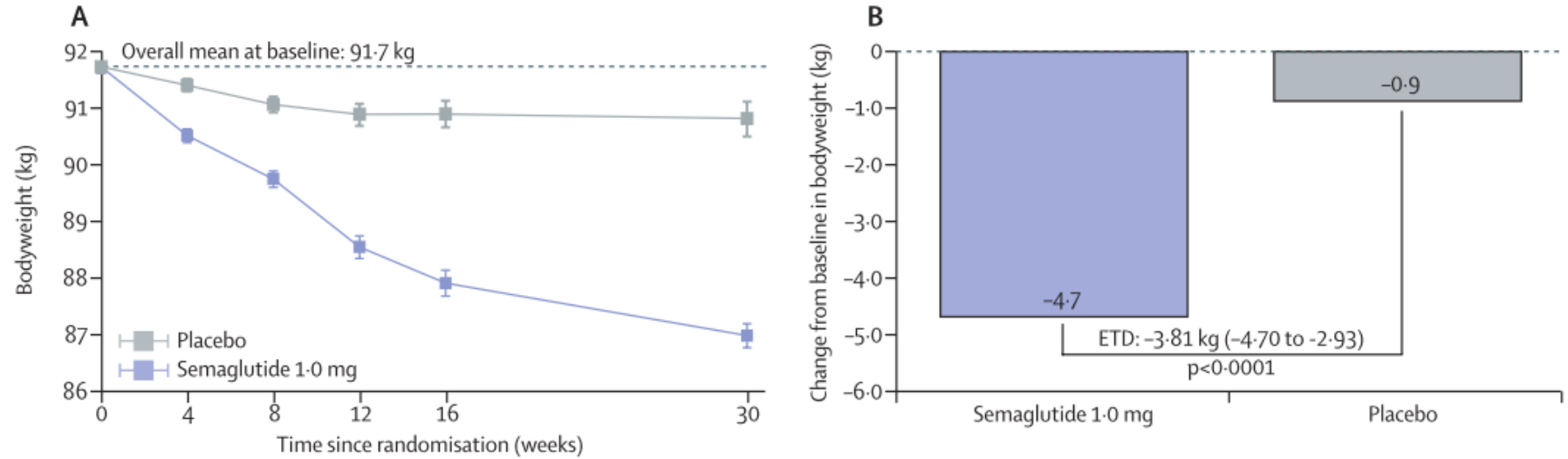
Zinman B G et al. Lancet Diabetes Endocrinol 2019; 7: 356–67

Semaglutide once-weekly as add-on to SGLT-2 inhibitor therapy in type 2 diabetes (SUSTAIN 9): a randomised, placebo-controlled trial

efficacy on
glycaemic control



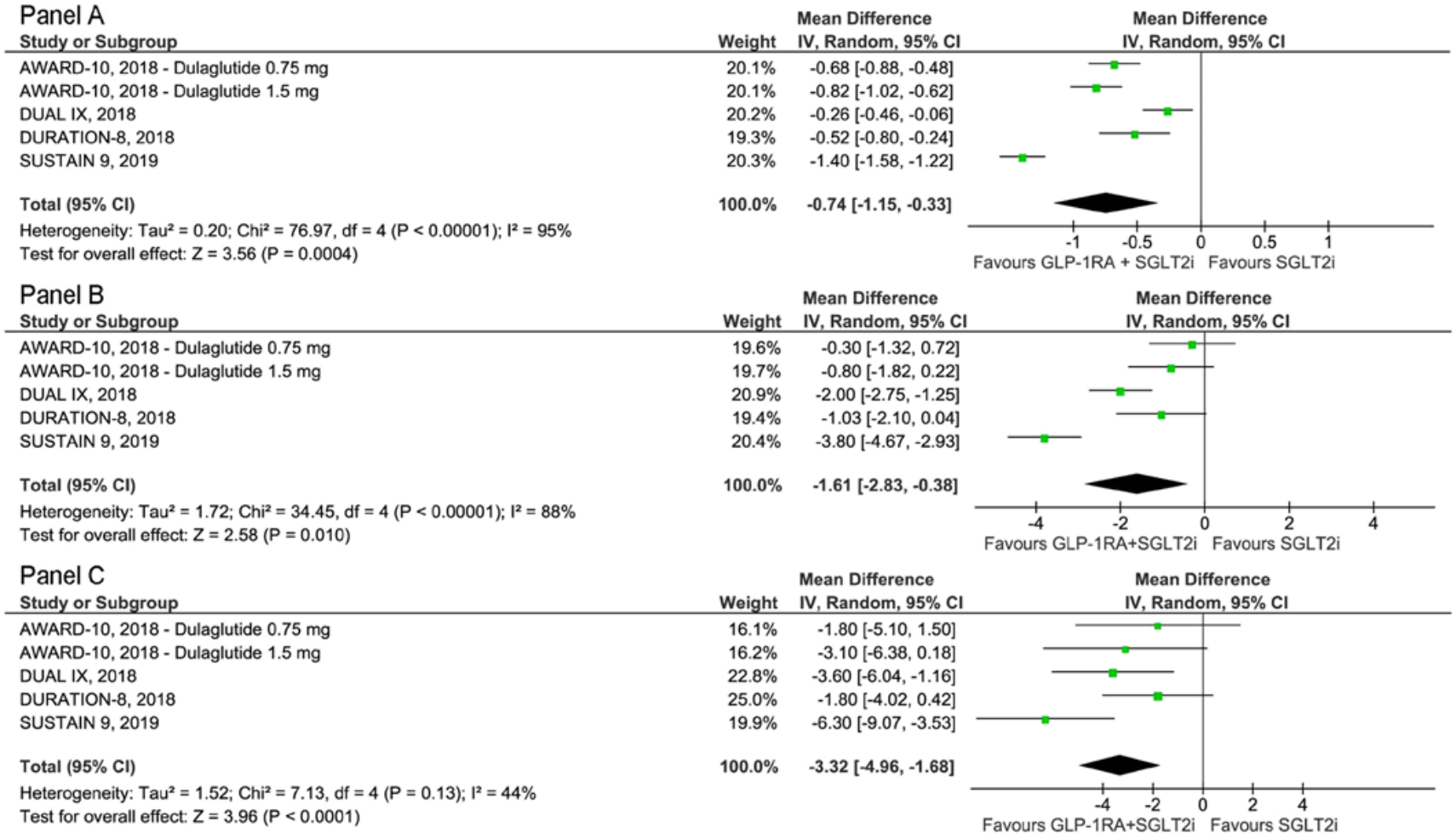
efficacy on
body weight reduction



Zinman B G et al. Lancet Diabetes Endocrinol 2019; 7: 356–67

Efficacy and safety of GLP-1 receptor agonists as add-on to SGLT2 inhibitors in type 2 diabetes mellitus: A meta-analysis

Marco Castellana, Angelo Cignarelli, Francesco Brescia, Sebastio Perrini, Annalisa Natalicchio, Luigi Laviola & Francesco Giorgino*



HbA1c

Body weight

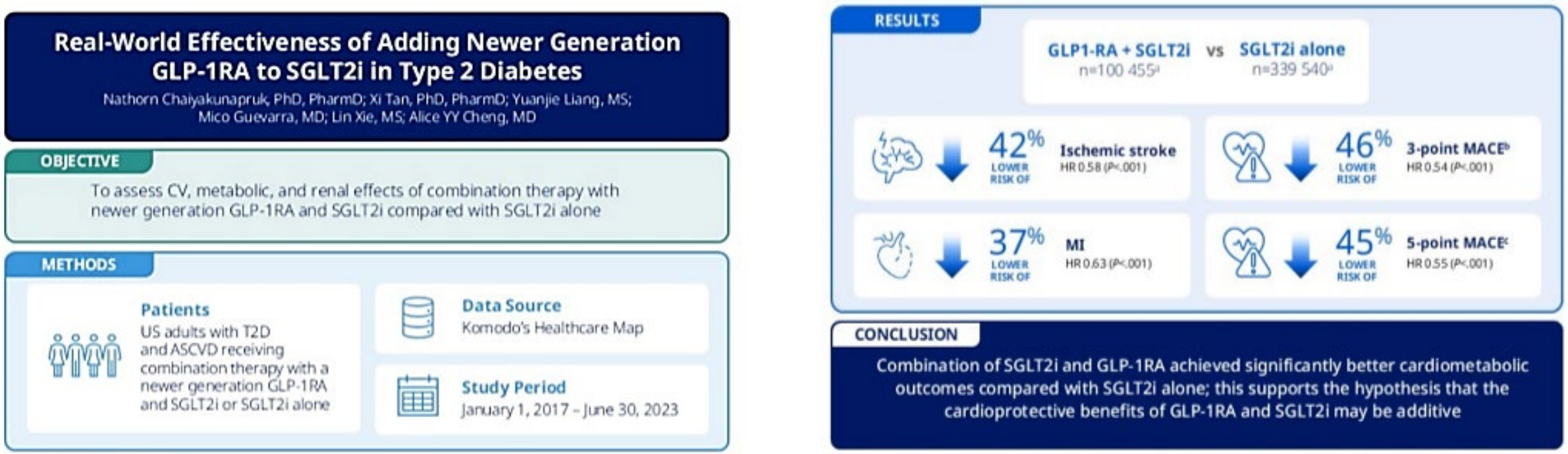
SBP

Castellana M et al. Sci Rep. 2019 Dec 18;9(1):19351.

Additive benefits of GLP-1RA and SGLT2i: real-world analysis

Real-world effectiveness of adding newer generation GLP-1RA to SGLT2i in type 2 diabetes

Nathorn Chaiyakunapruk[1,2], Xi Tan[3], Yuanjie Liang[3], Mico Guevarra[3], Lin Xie[3] and Alice Y. Y. Cheng[4*]

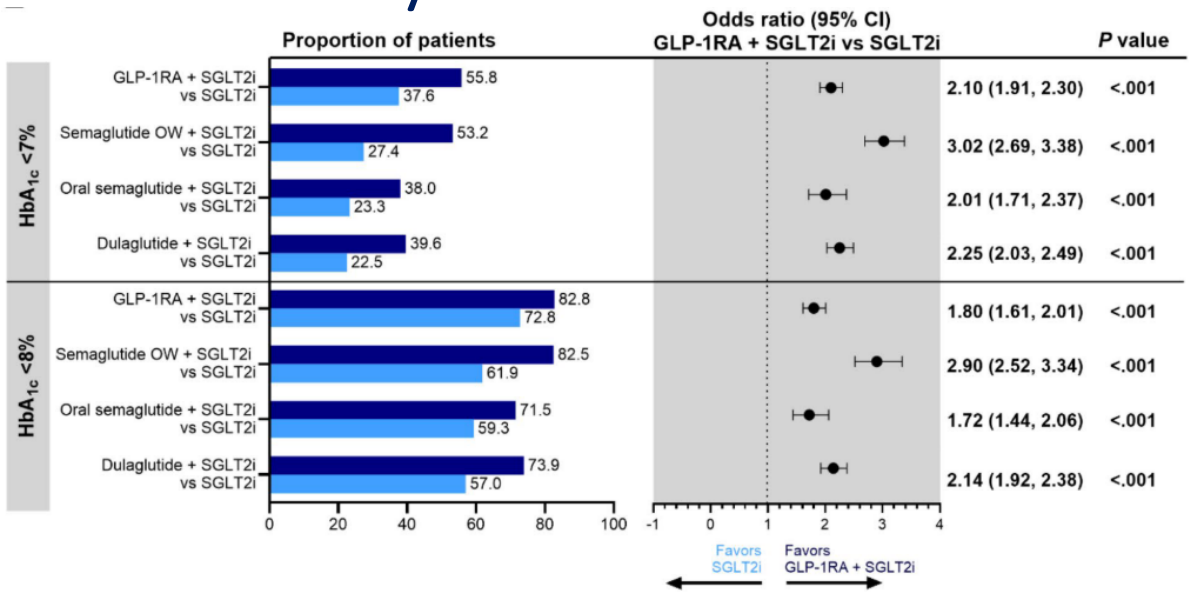


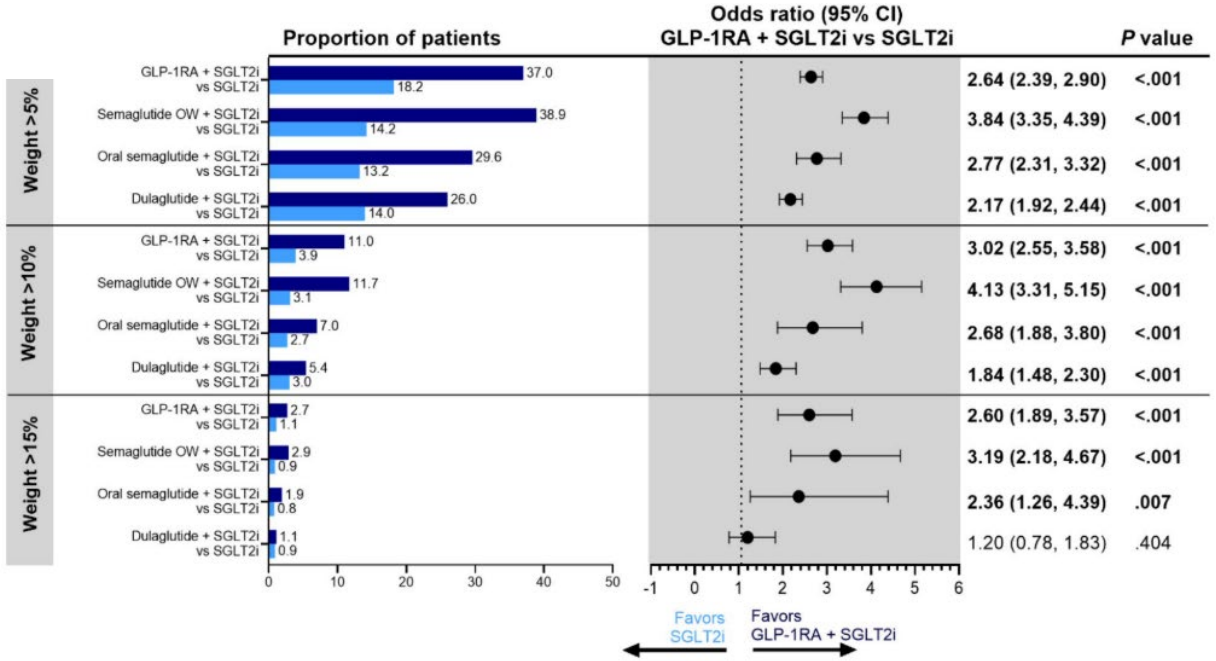
Chaiyakunapruk N et al. Cardiovasc Diabetol. 2025 Apr 24;24(1):177.

Additive *metabolic* benefits of GLP-1RA and SGLT2i: real-world analysis

Real-world effectiveness of adding newer generation GLP-1RA to SGLT2i in type 2 diabetes

Nathorn Chaiyakunapruk[1,2], Xi Tan[3], Yuanjie Liang[3], Mico Guevarra[3], Lin Xie[3] and Alice Y. Y. Cheng[4*]



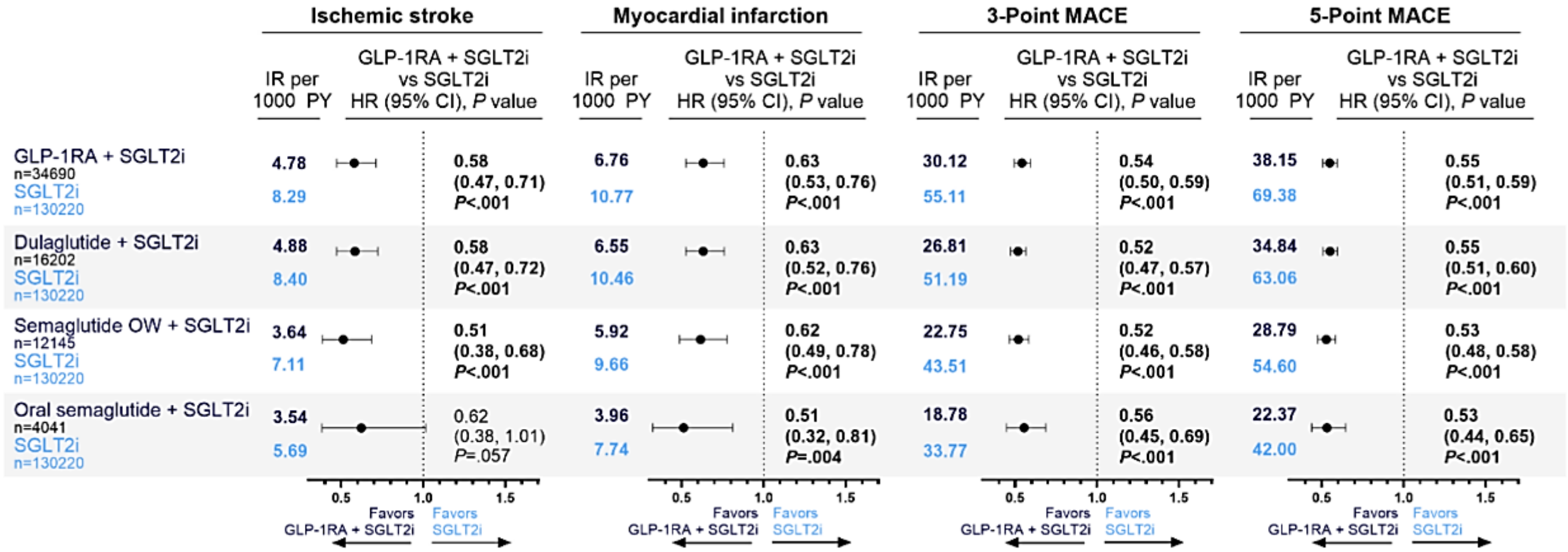


Chaiyakunapruk N et al. Cardiovasc Diabetol. 2025 Apr 24;24(1):177.

Additive *cardioprotective* benefits of GLP-1RA and SGLT2i: real-world analysis

Real-world effectiveness of adding newer generation GLP-1RA to SGLT2i in type 2 diabetes

Nathorn Chaiyakunapruk[1,2], Xi Tan[3], Yuanjie Liang[3], Mico Guevarra[3], Lin Xie[3] and Alice Y. Y. Cheng[4*]



Chaiyakunapruk N et al. Cardiovasc Diabetol. 2025 Apr 24;24(1):177.

Additive *cardioprotective* benefits of GLP-1RA and SGLT2i: real-world analysis

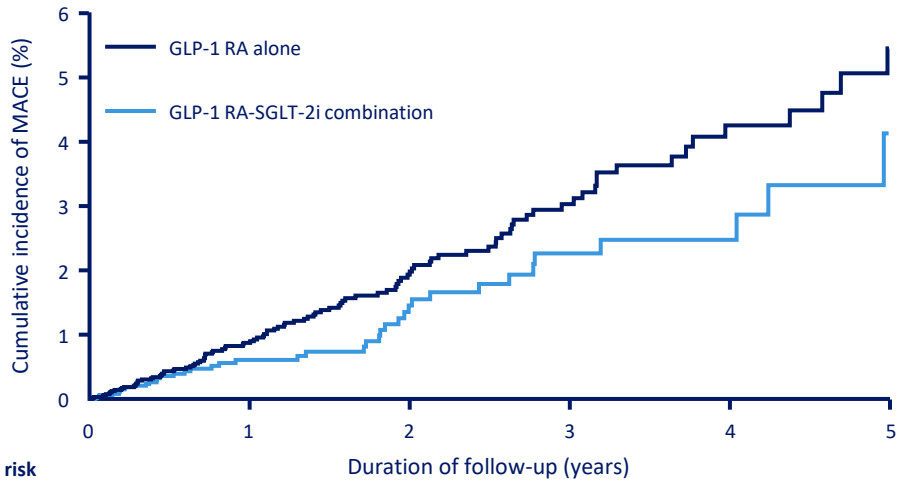
Effect of combination treatment with glucagon-like peptide-1 receptor agonists and sodium-glucose cotransporter-2 inhibitors on incidence of cardiovascular and serious renal events: population based cohort study

Nikita Simms-Williams,[1] Nir Treves,[2] Hui Yin,[1] Sally Lu,[3] Oriana Yu,[3,4] Richeek Pradhan,[5] Christel Renoux,[3,6,7] Samy Suissa,[3,6] Laurent Azoulay[3,6,8]

Hazard ratios for primary and secondary outcomes comparing GLP-1RAs-SGLT-2i combination with GLP-1RA use alone

Exposure	No of patients	Events	Person years	Incidence rate (95% CI)*	Hazard ratio (95% CI)†
Primary outcomes					
MACE:					
GLP-1 RAs	6696	113	10971	10.3 (8.5 to 12.4)	1.00 (reference)
GLP-1 RA-SGLT-2i combination	6696	45	6417	7.0 (5.1 to 9.4)	0.70 (0.49 to 0.99)
Serious renal events:					
GLP-1 RAs	6696	51	10992	4.6 (3.5 to 6.1)	1.00 (reference)
GLP-1 RA-SGLT-2i combination	6696	13	6453	2.0 (1.1 to 3.4)	0.43 (0.23 to 0.80)
Secondary outcomes					
Myocardial infarction:					
GLP-1 RAs	6696	60	10971	5.5 (4.2 to 7.0)	1.00 (reference)
GLP-1 RA-SGLT-2i combination	6696	24	6417	3.7 (2.4 to 5.6)	0.73 (0.45 to 1.17)
Ischaemic stroke:					
GLP-1 RAs	6696	30	10971	2.7 (1.8 to 3.9)	1.00 (reference)
GLP-1 RA-SGLT-2i combination	6696	15	6417	2.3 (1.3 to 3.9)	0.90 (0.48 to 1.67)
Cardiovascular mortality:					
GLP-1 RAs	6696	32	10971	2.9 (2.0 to 4.1)	1.00 (reference)
GLP-1 RA-SGLT-2i combination	6696	7	6417	1.1 (0.4 to 2.3)	0.35 (0.15 to 0.80)
Heart failure:					
GLP-1 RAs	6696	67	10979	6.1 (4.7 to 7.8)	1.00 (reference)
GLP-1 RA-SGLT-2i combination	6696	23	6446	3.6 (2.3 to 5.4)	0.57 (0.35 to 0.91)
All cause mortality:					
GLP-1 RAs	6696	102	11056	9.2 (7.5 to 11.2)	1.00 (reference)
GLP-1 RA-SGLT-2i combination	6696	41	6459	6.4 (4.6 to 8.6)	0.71 (0.49 to 1.02)

Cumulative incidence curves of MACE for GLP-1RA-SGLT-2i combination versus GLP-1 RAs



No at risk

GLP-1 RA alone	6696	3798	1996	1072	532	242
GLP-1 RA-SGLT-2i combination	6696	1986	1000	519	259	114

Simms-Williams N et al. BMJ 2024;385:e078242

Additive *cardioprotective* benefits of GLP-1RA and SGLT2i: real-world analysis

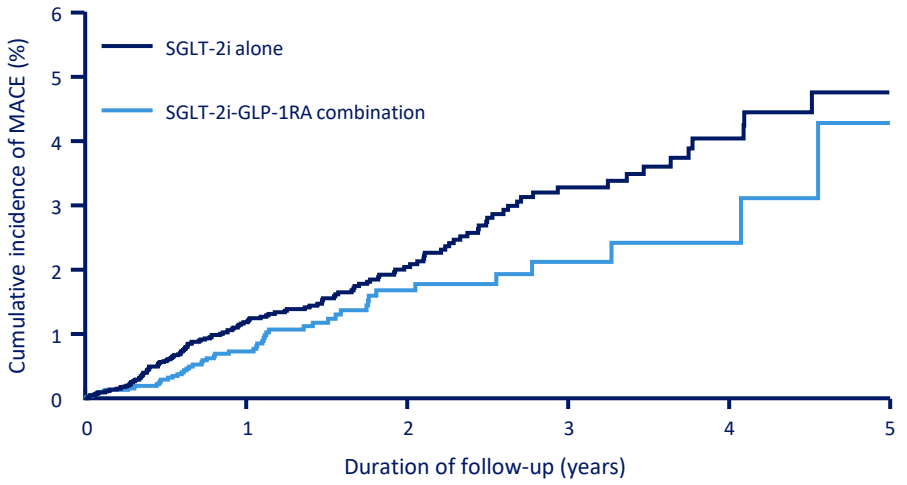
Effect of combination treatment with glucagon-like peptide-1 receptor agonists and sodium-glucose cotransporter-2 inhibitors on incidence of cardiovascular and serious renal events: population based cohort study

Nikita Simms-Williams,[1] Nir Treves,[2] Hui Yin,[1] Sally Lu,[3] Oriana Yu,[3,4] Richeek Pradhan,[5] Christel Renoux,[3,6,7] Samy Suissa,[3,6] Laurent Azoulay[3,6,8]

Hazard ratios for primary and secondary outcomes comparing GLP-1RAs-SGLT-2i combination with SGLT-2i use alone

Exposure	No of patients	Events	Person years	Incidence rate (95% CI)*	Hazard ratio (95% CI)†
Primary outcomes					
MACE:					
SGLT-2i	8942	141	13160	10.7 (9.0 to 12.6)	1.00 (reference)
SGLT-2i-GLP-1 RA combination	8942	55	7250	7.6 (5.7 to 9.9)	0.71 (0.52 to 0.98)
Serious renal events:					
SGLT-2i	8942	26	13243	2.0 (1.3 to 2.9)	1.00 (reference)
SGLT-2i-GLP-1 RA combination	8942	10	7278	1.4 (0.7 to 2.5)	0.67 (0.32 to 1.41)
Secondary outcomes					
Myocardial infarction:					
SGLT-2i	8942	75	13160	5.7 (4.5 to 7.1)	1.00 (reference)
SGLT-2i-GLP-1 RA combination	8942	30	7250	4.1 (2.8 to 5.9)	0.73 (0.48 to 1.12)
Ischaemic stroke:					
SGLT-2i	8942	33	13160	2.5 (1.7 to 3.5)	1.00 (reference)
SGLT-2i-GLP-1 RA combination	8942	15	7250	2.1 (1.2 to 3.4)	0.86 (0.46 to 1.59)
Cardiovascular mortality:					
SGLT-2i	8942	44	13160	3.3 (2.4 to 4.5)	1.00 (reference)
SGLT-2i-GLP-1 RA combination	8942	13	7250	1.8 (1.0 to 3.1)	0.54 (0.29 to 1.01)
Heart failure:					
SGLT-2i	8942	43	13235	3.3 (2.4 to 4.4)	1.00 (reference)
SGLT-2i-GLP-1 RA combination	8942	17	7274	2.3 (1.4 to 3.7)	0.70 (0.40 to 1.23)
All cause mortality:					
SGLT-2i	8942	130	13259	9.8 (8.2 to 11.6)	1.00 (reference)
SGLT-2i-GLP-1 RA combination	8942	50	7284	6.9 (5.1 to 9.1)	0.73 (0.52 to 1.01)

Cumulative incidence curves of MACE for GLP-1RA-SGLT-2i combination versus SGLT-2i



No at risk

SGLT-2 inhibitor alone	8942	4732	2347	1146	514	176
SGLT-2 inhibitor-GLP-1 RA combination	8942	2556	1035	428	157	48

Simms-Williams N et al. BMJ 2024;385:e078242

Diabetologia (2026) 69:36–49
https://doi.org/10.1007/s00125-025-06565-6

ARTICLE

Effectiveness and safety of combining SGLT2 inhibitors and GLP-1 receptor agonists in individuals with type 2 diabetes: a systematic review and meta-analysis of cohort studies

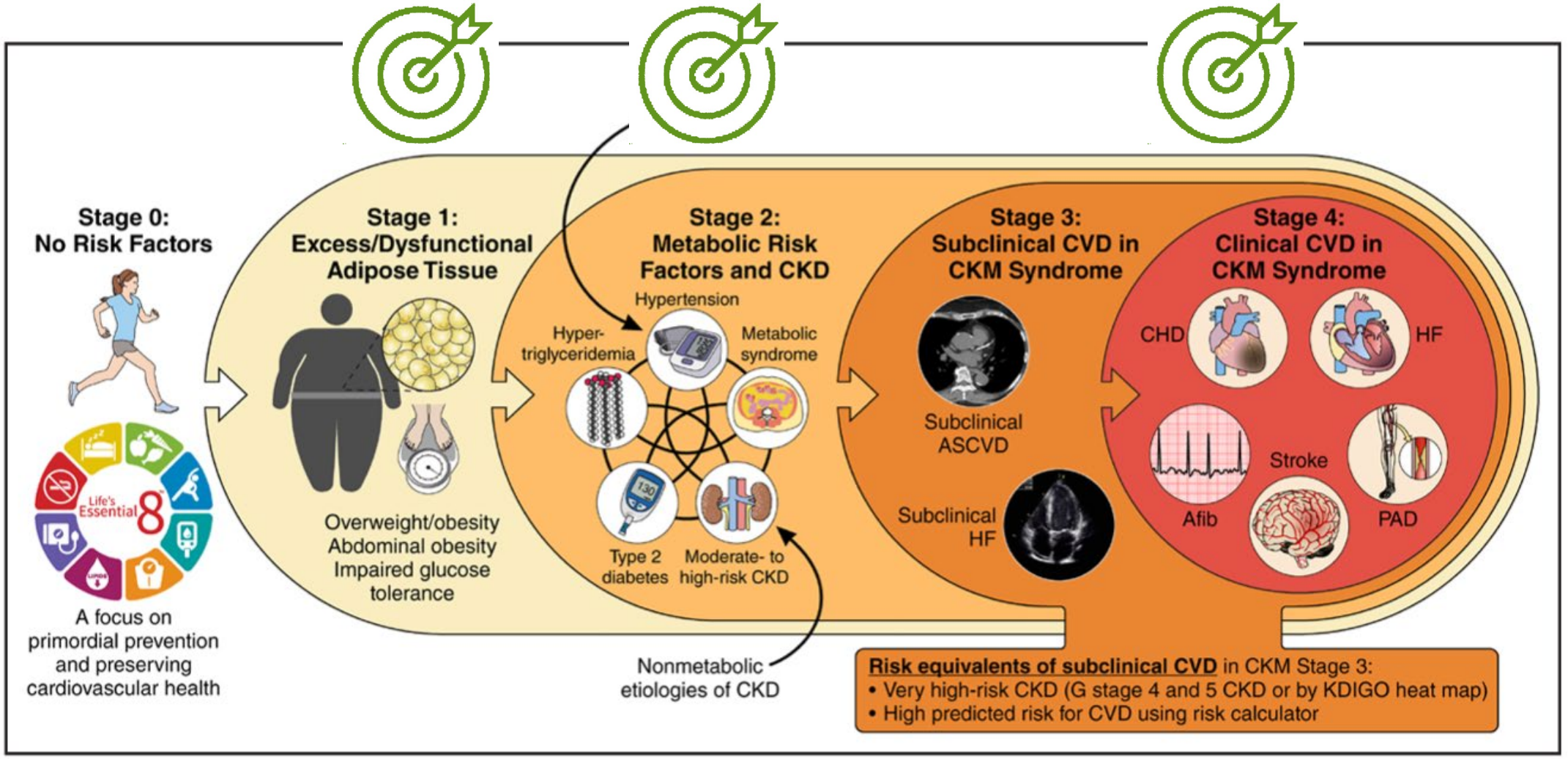
Julia M. T. Colombijn[1,2] · Jan F. de Leijer[3] · Frank L. J. Visseren[3] · Marianne C. Verhaar[1] · Daniël H. van Raalte[4] · Naveed Sattar[5] · Robin W. M. Vernooij[1,2] · Thomas T. van Sloten[3]

Table 2 Summary of findings: Combining a SGLT2 inhibitor and GLP-1 receptor agonist in individuals with type 2 diabetes

Outcome	No. of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects (95% CI)		Certainty (GRADE)
			Monotherapy	Combination therapy	
MACE	364,369 (9)	0.56 (0.43, 0.71)	54 / 1000	30 / 1000 (23, 38)	⨁⨁⨀⨀[a,b]
All-cause mortality	542,989 (10)	0.50 (0.40, 0.63)	38 / 1000	19 / 1000 (1, 24)	⨁⨁⨀⨀[a,b]
Cardiovascular mortality	31,692 (2)	0.26 (0.16, 0.43)	5 / 1000	1 / 1000 (1, 2)	⨁⨁⨀⨀[a,c]
Kidney composite endpoint	299,583 (6)	0.48 (0.32, 0.73)	77 / 1000	35 / 1000 (22, 56)	⨁⨀⨀⨀[a,b,d]
Hospitalisation for heart failure	43,246 (5)	0.67 (0.64, 0.71)	101 / 1000	68 / 1000 (65, 72)	⨁⨁⨁⨀[a]
Myocardial infarction	508,018 (6)	0.62 (0.48, 0.80)	22 / 1000	14 / 1000 (11, 18)	⨁⨁⨀⨀[a,b]
Stroke	509,116 (6)	0.65 (0.49, 0.86)	23 / 1000	15 / 1000 (11, 20)	⨁⨁⨀⨀[a,b]

Conclusions/interpretation Observational studies suggest that combining an SGLT2 inhibitor and a GLP-1 RA in type 2 diabetes may lower the risk of MACE, all-cause and cardiovascular mortality, hospitalisation for heart failure and kidney composite endpoints compared with monotherapy with either drug. Of course, residual confounding cannot be overcome but results support the need for future randomised trials of combined vs monotherapy.

Conclusions
Cardiovascular-Kidney-Metabolic (CKM) syndrome



Ndumele EC et al. Circulation. 2023;148:1606–1635.