XXVI Riunione Scientifica Regionale SID-AMD

Il Diabete: una malattia complicata?

Cagliari 29-30 Novembre 2024

Diagnosi precoce, precoce terapia mirata, «agguantare» la memoria metabolica

Dott. Paolo Giuseppe Michele Bianco

SC Diabetologia – ASL Nuoro

Ospedale Cesare Zonchello

Il sottoscritto dottor Bianco Paolo Giuseppe Michele dichiara di

NON aver ricevuto finanziamenti da parte di aziende

farmaceutiche e/o diagnostiche negli ultimi due anni.

Planning

Recent changes in management of Type 2 Diabetes

Early treatment with agents with cardiovascular and kidney benefit

Role of glycometabolic control

Management of Hyperglycemia in Type 2 Diabetes, 2018.
A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

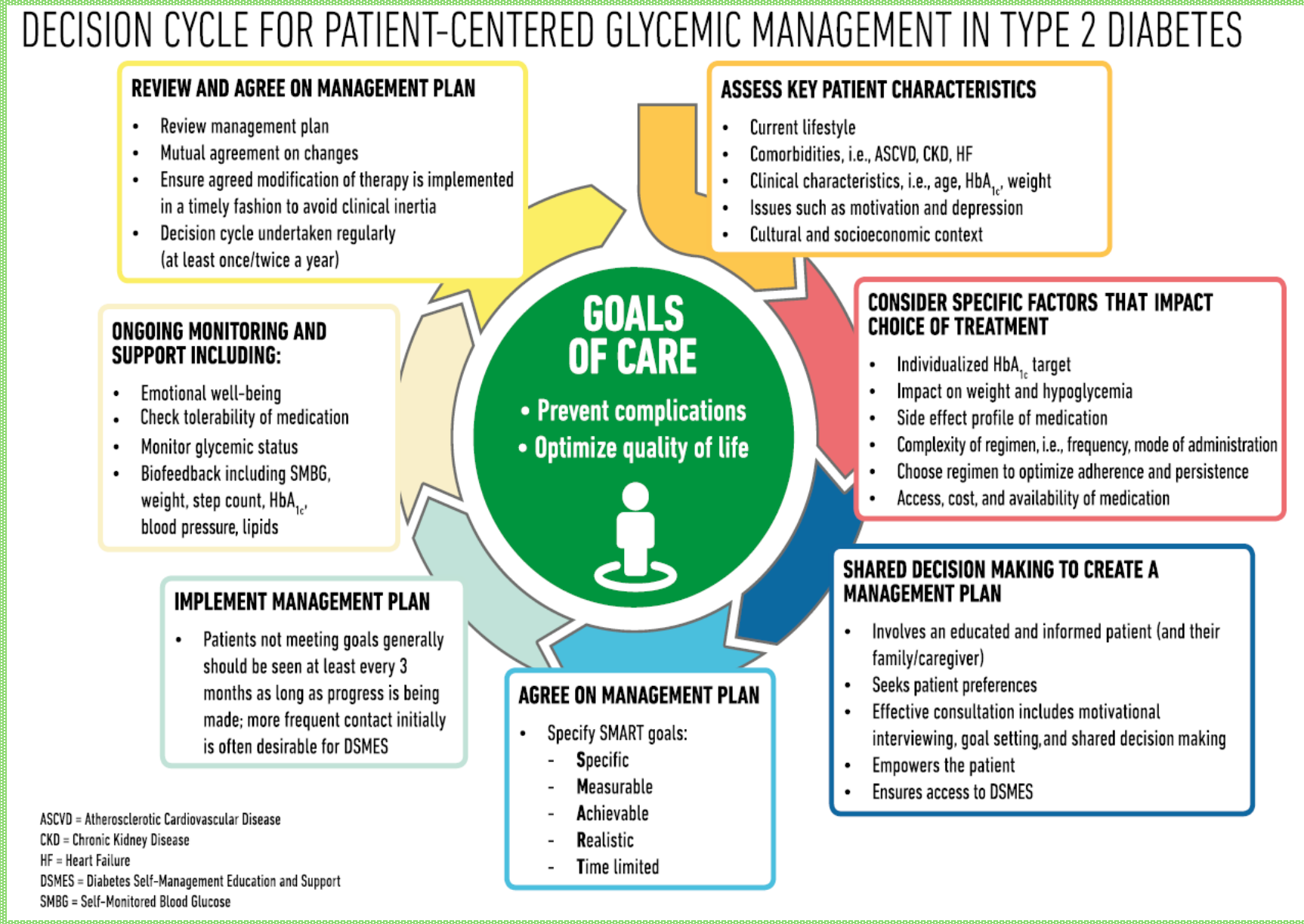
Diabetes Care 2018;41:2669–2701 | https://doi.org/10.2337/dci18-0033

Diabetes Care 2018

Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Diabetes Care 2018;41:2669–2701 | https://doi.org/10.2337/dci18-0033

DECISION CYCLE FOR PATIENT-CENTERED GLYCEMIC MANAGEMENT IN TYPE 2 DIABETES



ASCVD = Atherosclerotic Cardiovascular Disease
CKD = Chronic Kidney Disease
HF = Heart Failure
DSMES = Diabetes Self-Management Education and Support
SMBG = Self-Monitored Blood Glucose

Diabetes Care 2018

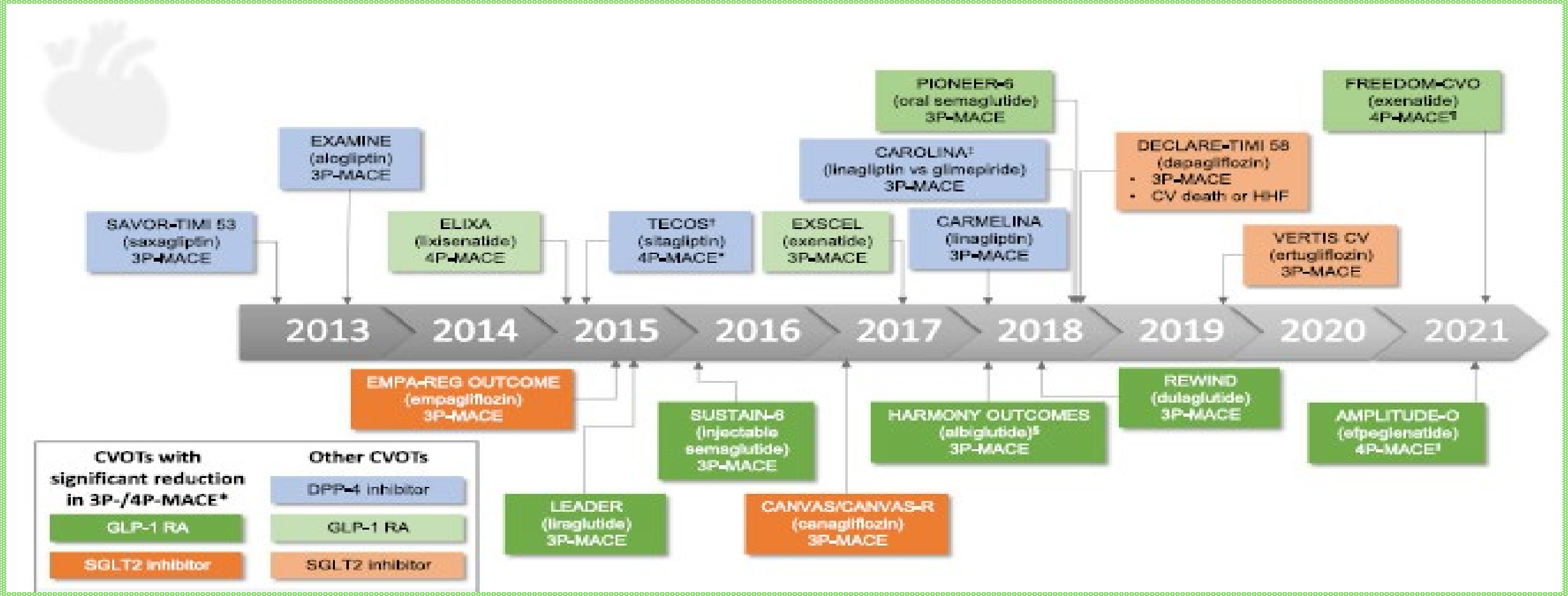
Davies et al. Cardiovascular Diabetology (2022) 21:144
https://doi.org/10.1186/s12933-022-01575-9

Cardiovascular Diabetology

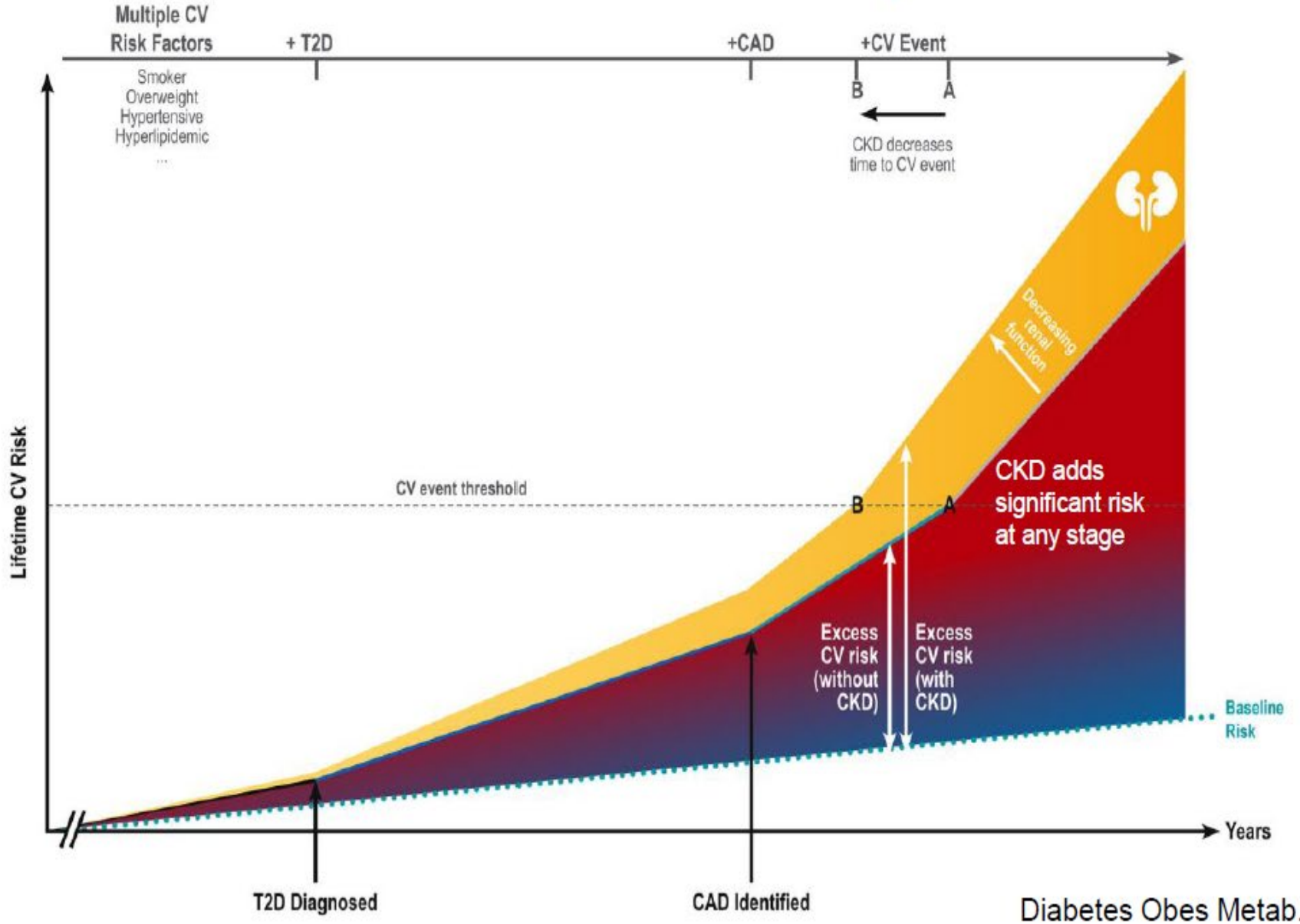
REVIEW Open Access

Cardiovascular outcomes trials: a paradigm shift in the current management of type 2 diabetes

Melanie J. Davies[1,2,3], Heinz Drexel[4], François R. Jornayvaz[5], Zoltan Pataky[5], Petar M. Seferović[6,7*] and Christoph Wanner[8]



The cardiovascular risk continuum in patients with TDM2



Diabetes Obes Metab. 2024;26:1567–1581

Diabetes, Metabolic Syndrome and Obesity

Dovepress

open access to scientific and medical research

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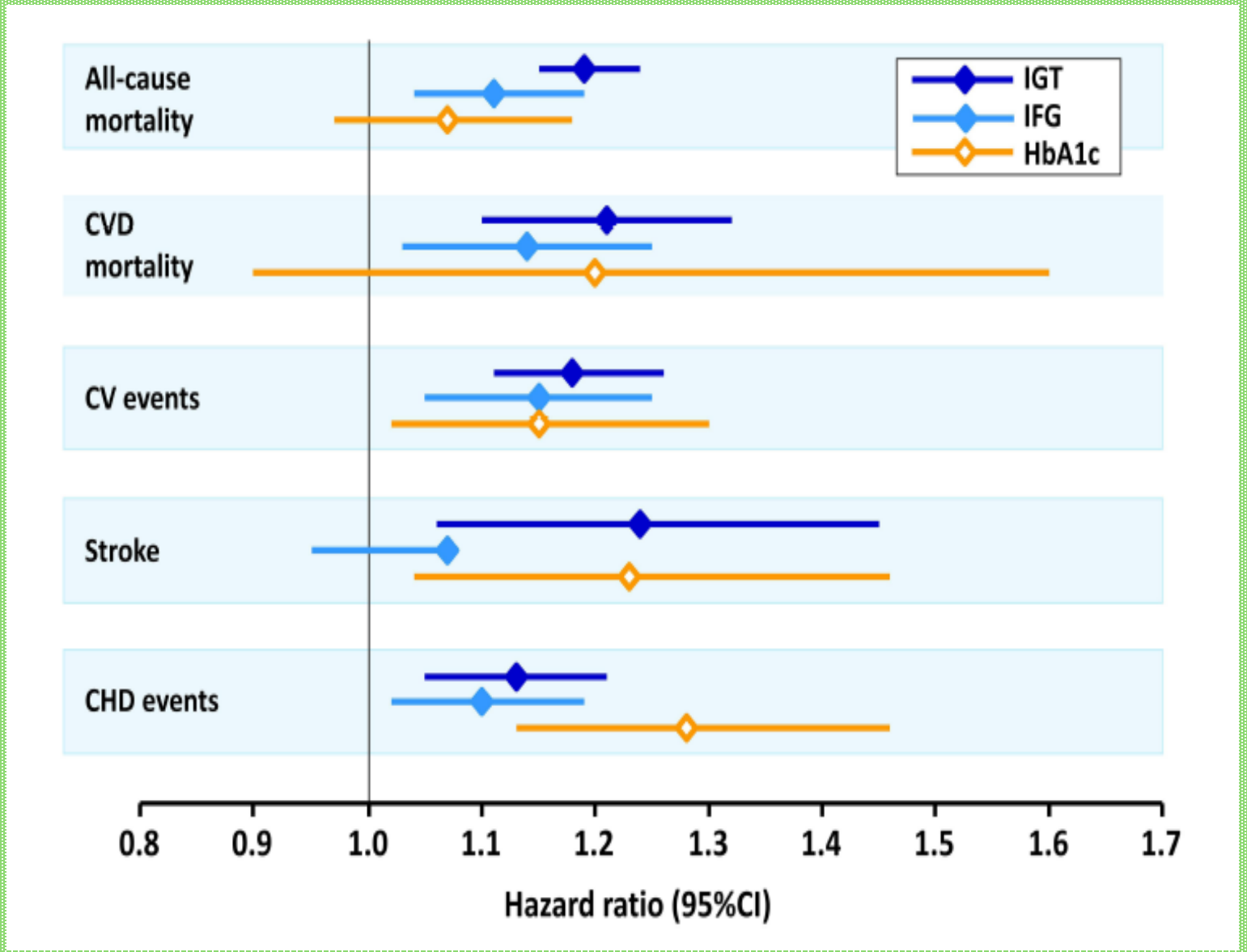
REVIEW

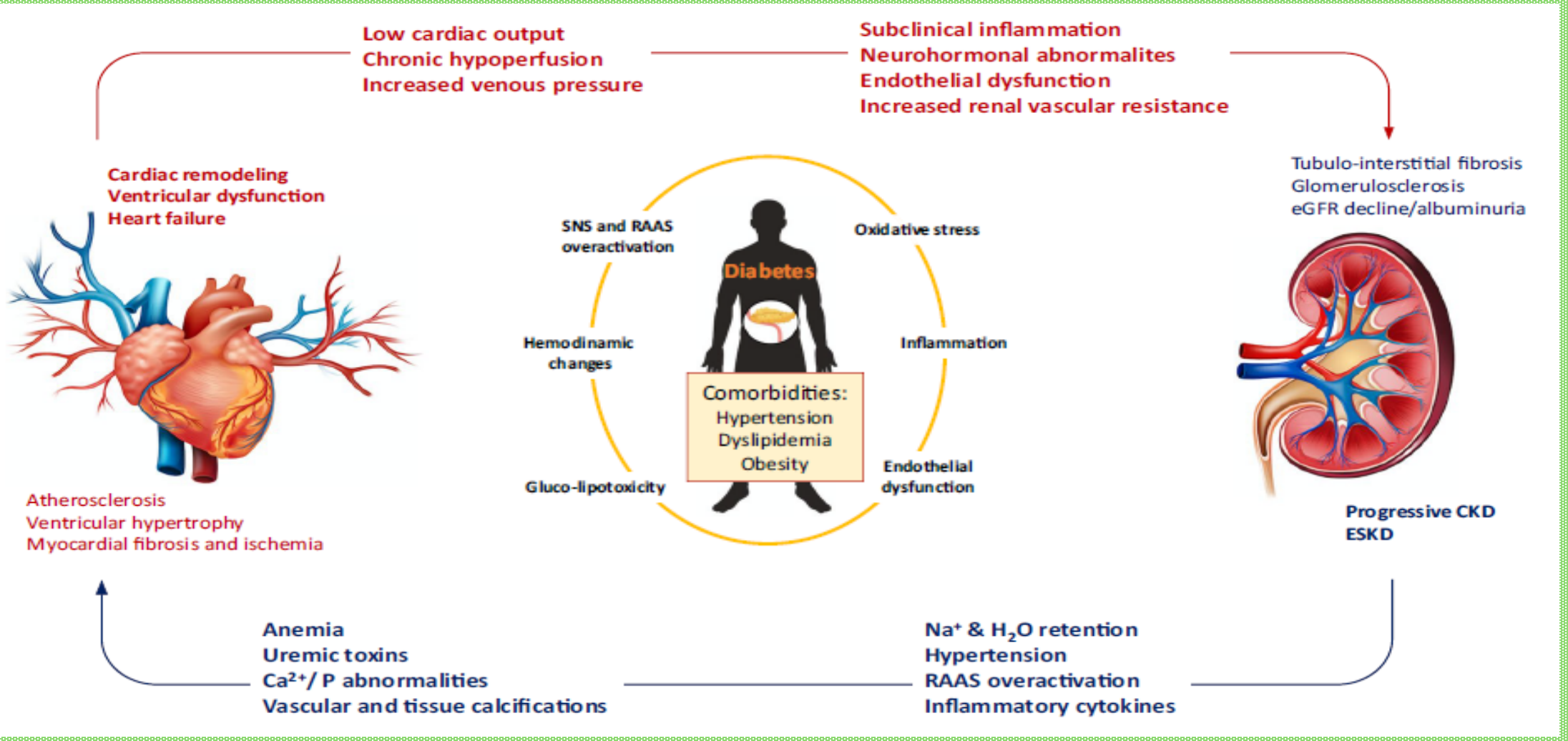
Addressing the Continuum of Dysglycaemia and Vascular Complications in Prediabetes and Type 2 Diabetes: Need for Early and Intensive Treatment

Nadia Ghannam[1], Saleh Alahmed[2], Raed Aldahash[3], Naji Aljohani[4], Afaf Alshammary[5], Ashraf Amir[6], Abdullah Kamal[7], Said Khader[8], Mohammed Salah[9], Hani Shalabi[10,11], Ahmed Abdallah[12], Ahmed Elboghdady[12]



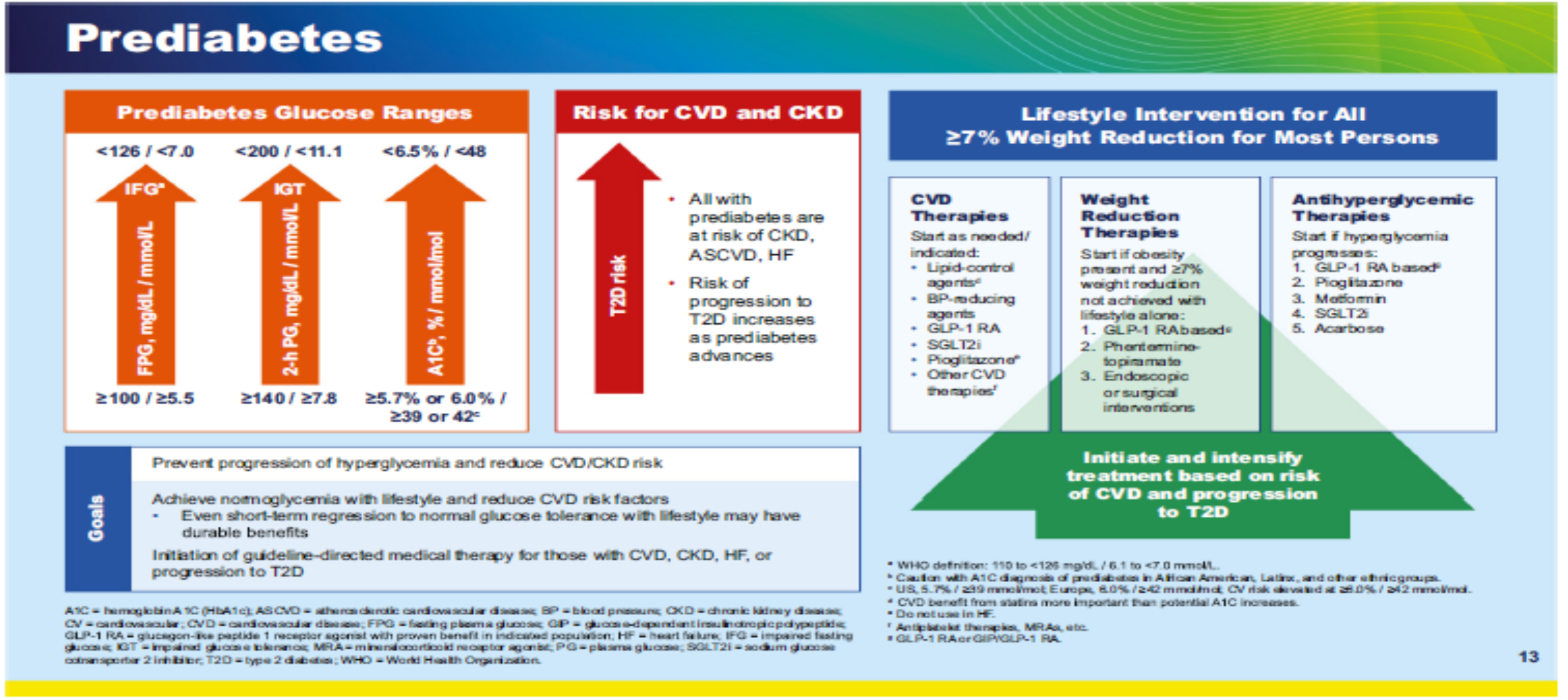
Diabetes, Metabolic Syndrome and Obesity 2023:16

Cardio-renal interplay in the contest of T2D



Cardiovascular Diabetology 2023; 22:195

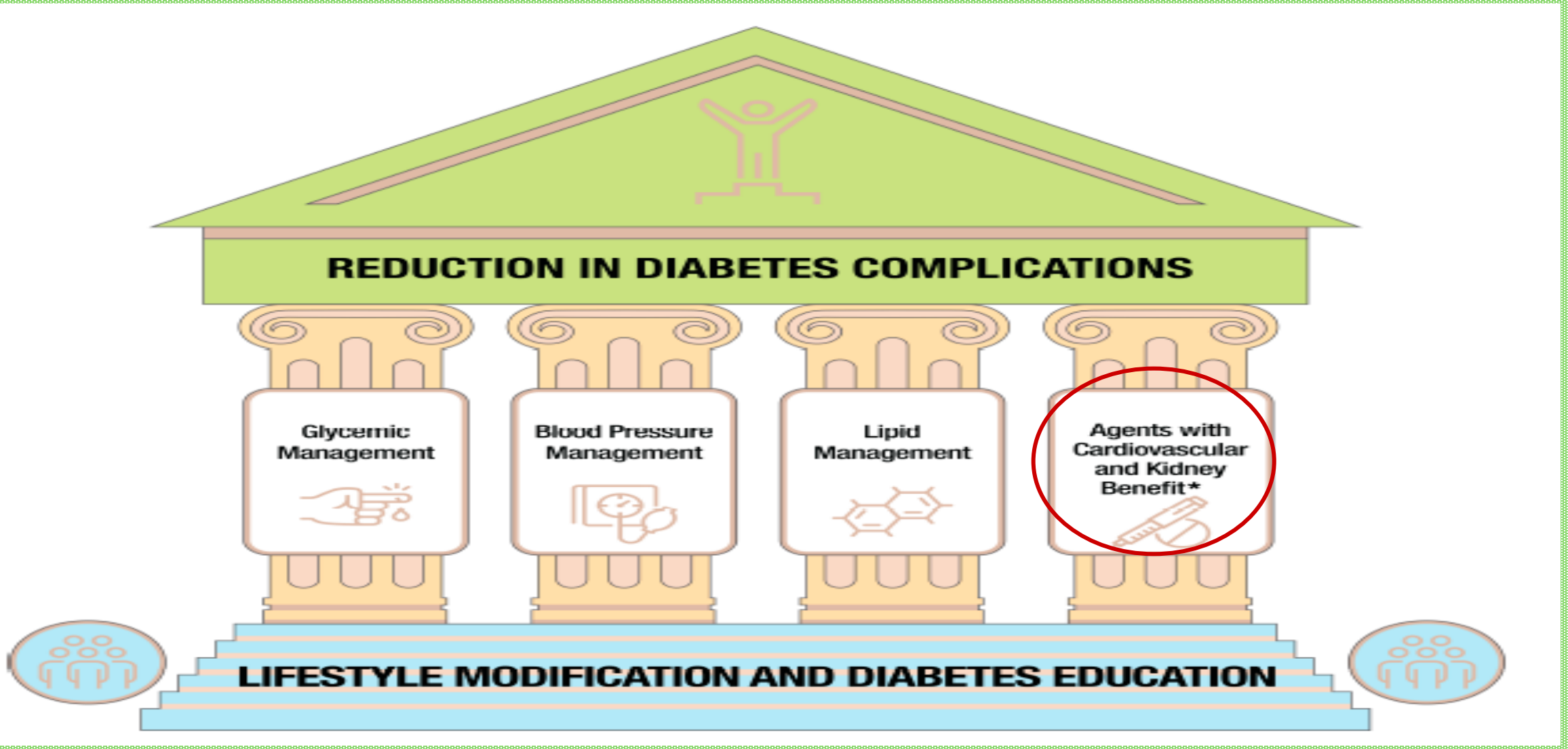
DCRM 2.0: Multispecialty pratice recommendations for the management of diabetes, cardiorenal and metabolic diseases



Y. Handelsman et al Metabolism 2024, 159: 155931

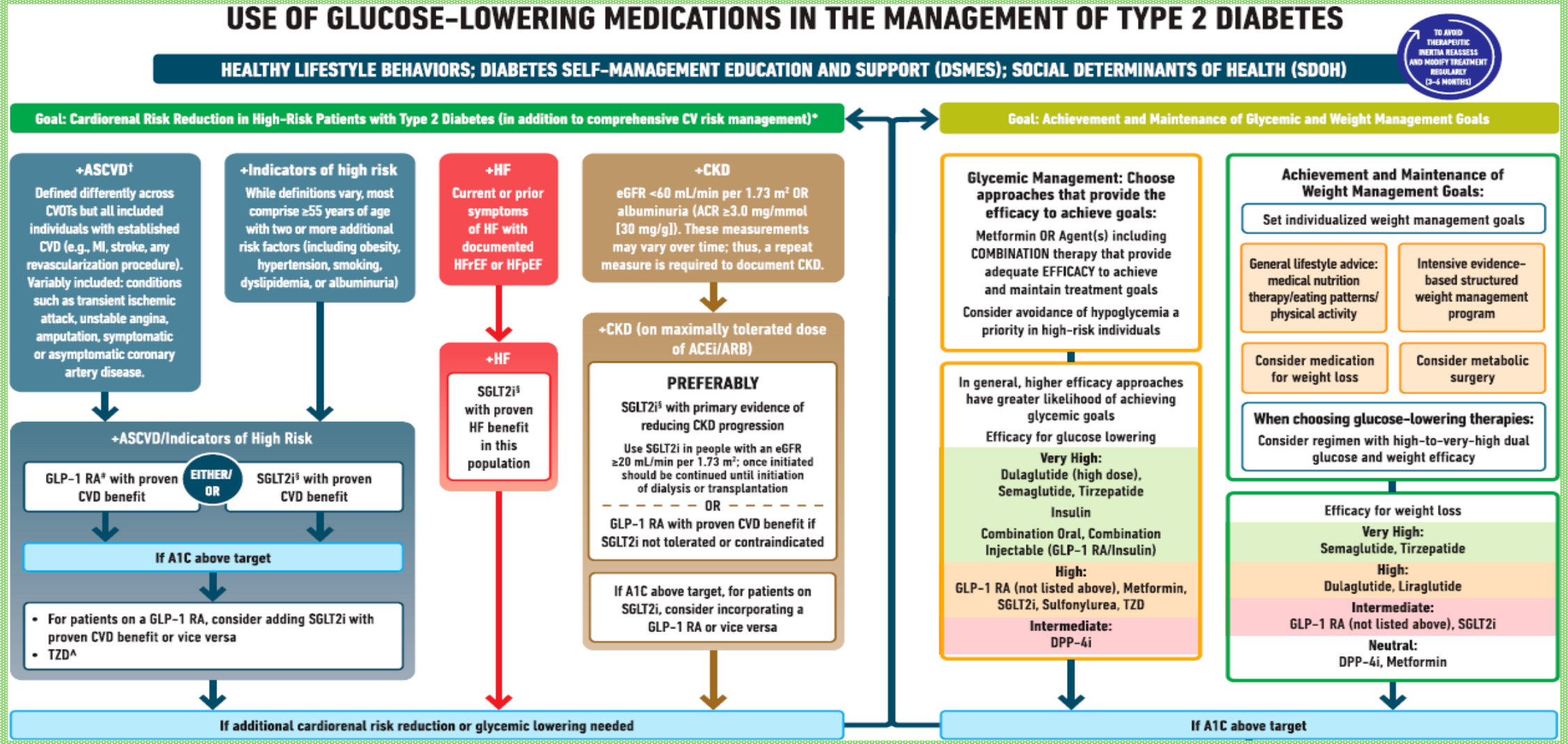
10. Cardiovascular Disease and Risk Management: *Standards of Medical Care in Diabetes—2022*

Diabetes Care 2022;45(Suppl. 1):S144–S175 | https://doi.org/10.2337/dc22-S010



9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes—2023*

Diabetes Care 2023;46(Suppl. 1):S140–S157 | https://doi.org/10.2337/dc23-S009

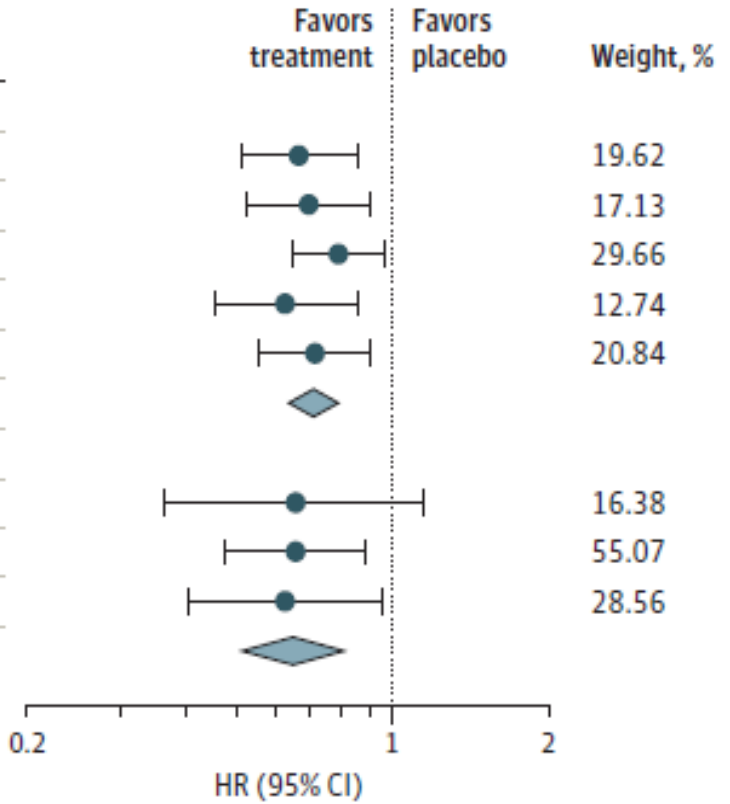


Diabetes Care 2023

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

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)



McGuire et al. Jama Cardiol 2021

RESEARCH ARTICLE

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]*

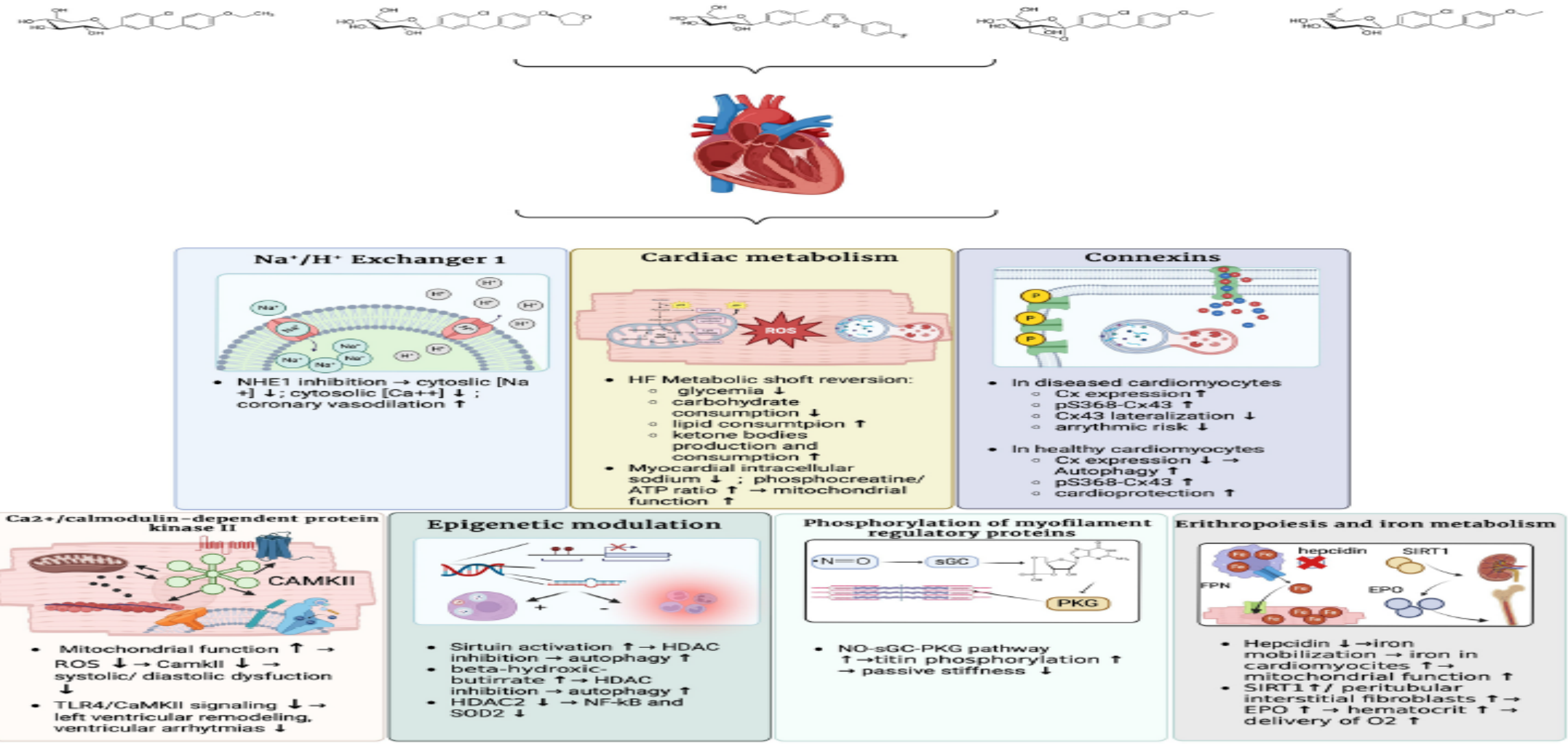
1 Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China, 2 Heart & Vascular Institute, The Chinese University of Hong Kong, Hong Kong, China, 3 Li Ka Shing Institute of Health Sciences, The Chinese University of Hong Kong, Hong Kong, China

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)	

Plos ONE 2022

Molecular targets, signaling pathways and cardiac effects of SGLT2i

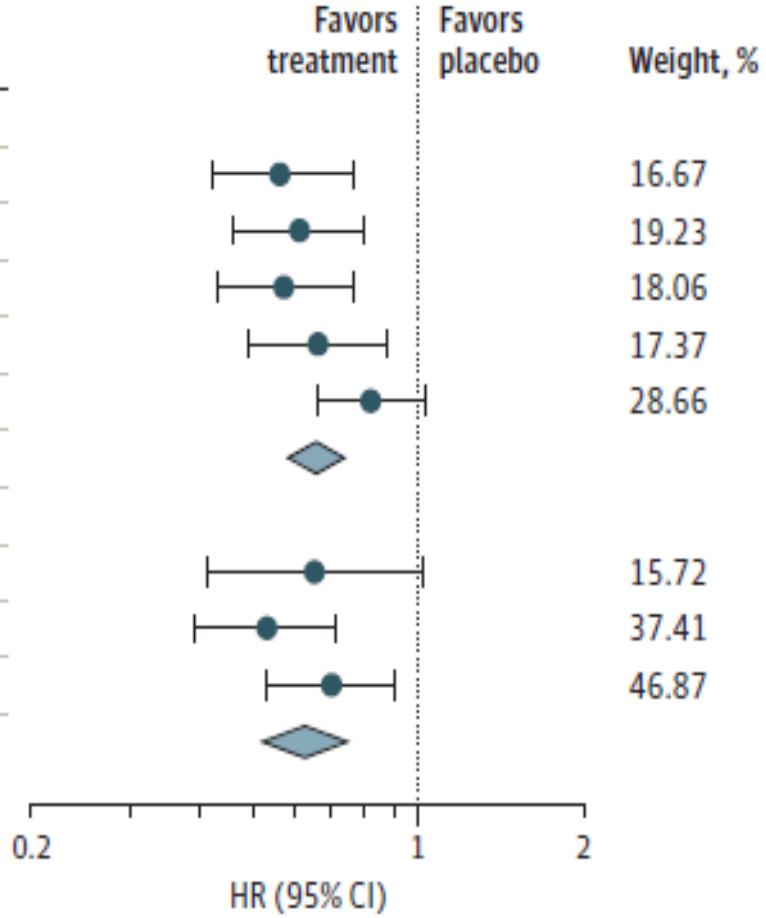


Biomedicine and Pharmacotherapy 2024

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

B Kidney outcomes by ASCVD status

	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)			
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)			



McGuire et al. Jama Cardiol 2021

Kidney outcome trials for sodium-glucose cotransporter-2 inhibitors

	CREDENCE	DAPA-CKD	EMPA-KIDNEY
Drug	Canagliflozin 100 mg once daily	Dapagliflozin 10 mg once daily	Empagliflozin 10 mg once daily
Total of participants	4401	4304	6609
% with CVD	50	37.4	27
eGFR criteria for enrollment (ml/min per 1.73 m²)	30–90	25–75	≥20–<45 or ≥45–<90
Mean eGFR at enrollment (ml/min per 1.73 m²)	56	43	37.5
% with eGFR <60	59	88	No information [<45: 5185 (78%); ≥45: 1424 (22%)]
ACR	Criteria: ACR >300–5000 mg/g [>30–500 mg/mmol] Median ACR 927 mg/g [92.7 mg/mmol]	ACR 200–5000 mg/g [20–500 mg/mmol] ACR Median DAPA: 965 mg/g [96.5 mg/mmol]; Placebo: 934 mg/g [93.4 mg/mmol]	eGFR ≥45–<90: ACR ≥200 mg/g [≥20 mg/mmol] (or PCR ≥300 mg/g [≥30 mg/mmol]) No ACR criteria for eGFR ≥40–<45 Median ACR 412 mg/g [41.2 mg/mmol]
Follow-up (yr)	2.6	2.4	Expected ≥3
Primary outcome(s)	Composite of kidney failure, doubling of SCr, or death from kidney or CV causes	First occurrence of a ≥50% decline in eGFR, the onset of kidney failure, or death from kidney or CV causes	First occurrence of a composite of kidney disease progression (kidney failure, sustained decline in eGFR to <10 ml/min/1.73 m², sustained decline in eGFR ≥40%, or renal death) or CV death
CV outcome results	CV death, MI, stroke: HR: 0.80; 95% CI: 0.67–0.95; hospitalization for HF: HR: 0.61; 95% CI: 0.47–0.80	Secondary composite of CV death or hospitalization for HF: HR: 0.71; 95% CI: 0.55-0.92	Not reported
Kidney outcome	Composite of kidney failure, doubling SCr, or death from kidney or CV causes	First occurrence of a ≥50% decline in eGFR, the onset of kidney failure, or death from kidney or CV causes	First occurrence of kidney failure, sustained decline in eGFR to <10 ml/min/1.73 m², sustained decline in eGFR ≥40%, or renal death
Kidney outcome results	Primary kidney: HR: 0.70; 95% CI: 0.59–0.82	Primary outcome: HR: 0.61; 95% CI: 0.51– 0.72	[Trial stopped early due to positive results]

KDIGO 2022

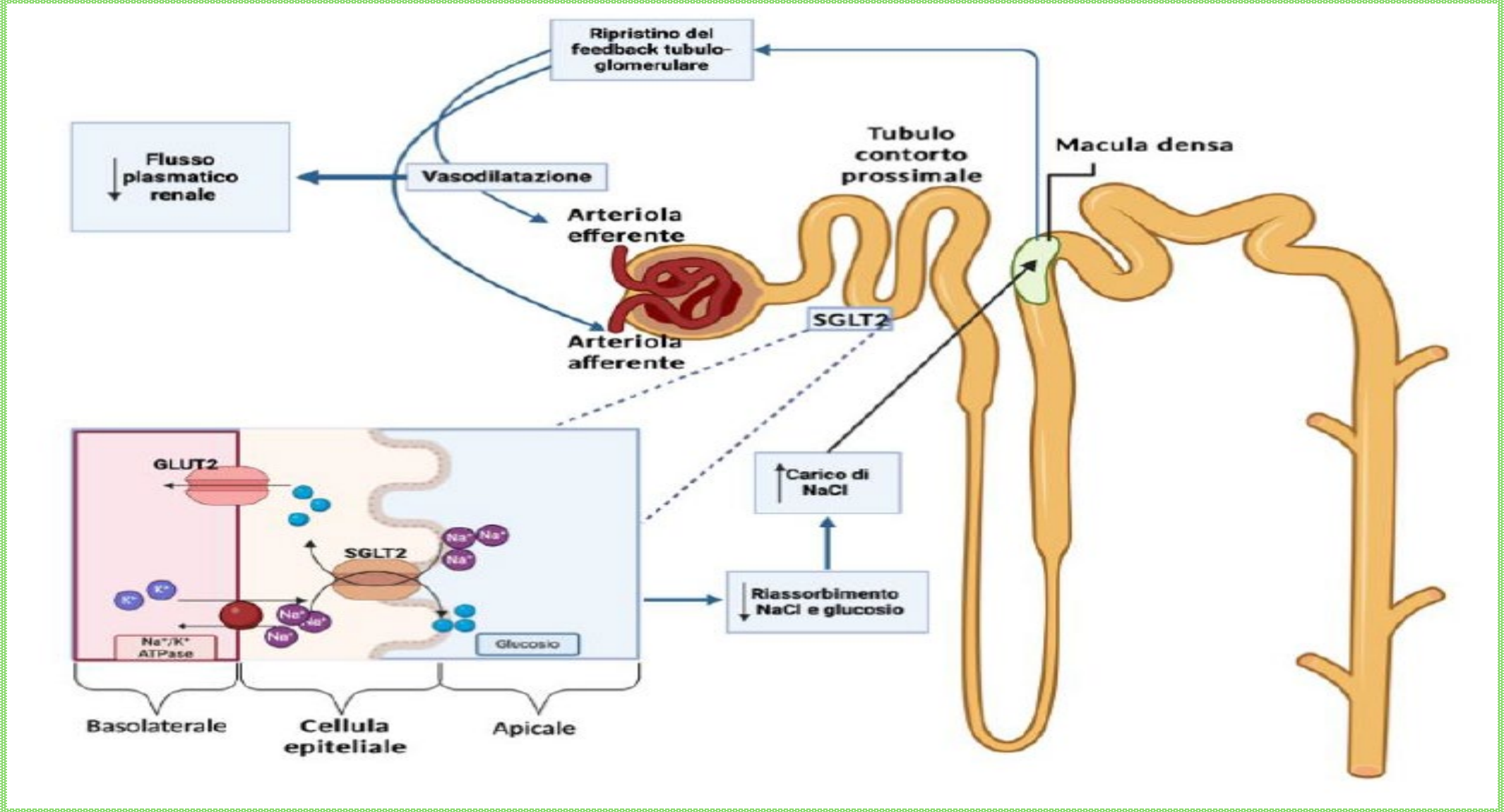
Long-term benefits of dapagliflozin on renal outcomes of type 2 diabetes under routine care: a comparative effectiveness study on propensity score matched cohorts at low renal risk

Gian Paolo Fadini,[a,b,f,*] Enrico Longato,[c,f] Mario Luca Morieri,[a] Stefano Del Prato,[d] Angelo Avogaro,[a] and Anna Solini,[e]
DARWIN-Renal Study Investigators

	Before PSM			After PSM		
	Dapagliflozin	Comparators	SMD	Dapagliflozin	Comparators	SMD
Number	7588	27,717		6200	6200	
Demographics						
Sex male, n (%)	4575 (60.3)	16,796 (60.6)	<0.01	3808 (61.4)	3789 (61.1)	<0.01
Age, years	60.9 (9.0)	63.6 (8.8)	0.30	61.0 (9.0)	61.3 (9.6)	0.03
Diabetes duration, years	11.6 (8.4)	10.6 (7.9)	0.12	10.6 (7.9)	10.4 (8.3)	0.02
Complications						
Chronic kidney disease, n (%)	1535 (20.2)	7750 (28.0)	0.18	1219 (19.7)	1246 (20.1)	0.01
EGFR <60 ml/min/1.73 m^2, n (%)	416 (5.5)	4651 (16.8)	0.33	394 (6.4)	389 (6.3)	<0.01
UACR >30 mg/g, n (%)	1229 (16.2)	4182 (15.1)	0.03	952 (15.4)	928 (15.0)	0.01
Diabetic retinopathy, n (%)	1399 (18.4)	3723 (13.4)	0.14	927 (15.0)	919 (14.8)	<0.01
Diabetic macular edema, n (%)	200 (2.6)	507 (1.8)	0.06	127 (2.0)	140 (2.3)	0.01
Stroke/TIA, n (%)	106 (1.4)	439 (1.6)	0.02	79 (1.3)	84 (1.4)	<0.01
Carotid atherosclerosis, n (%)	1397 (18.4)	5886 (21.2)	0.07	1090 (17.6)	1127 (18.2)	0.02
Ischemic heart disease, n (%)	800 (10.5)	3009 (10.9)	0.01	594 (9.6)	582 (9.4)	<0.01
Left ventricular hypertrophy, n (%)	581 (7.7)	2214 (8.0)	0.01	461 (7.4)	460 (7.4)	<0.01
Heart failure, n (%)	234 (3.1)	693 (2.5)	0.04	179 (2.9)	171 (2.8)	<0.01
Any site revascularization, n (%)	527 (6.9)	2130 (7.7)	0.03	387 (6.2)	387 (6.2)	<0.01
Microvascular complications, n (%)	2824 (37.2)	11,116 (40.1)	0.06	2119 (34.2)	2093 (33.8)	<0.01
Macrovascular complications, n (%)	2376 (31.3)	9383 (33.9)	0.05	1847 (29.8)	1826 (29.5)	<0.01
Established CVD, n (%)	975 (12.8)	3776 (13.6)	0.02	725 (11.7)	720 (11.6)	<0.01

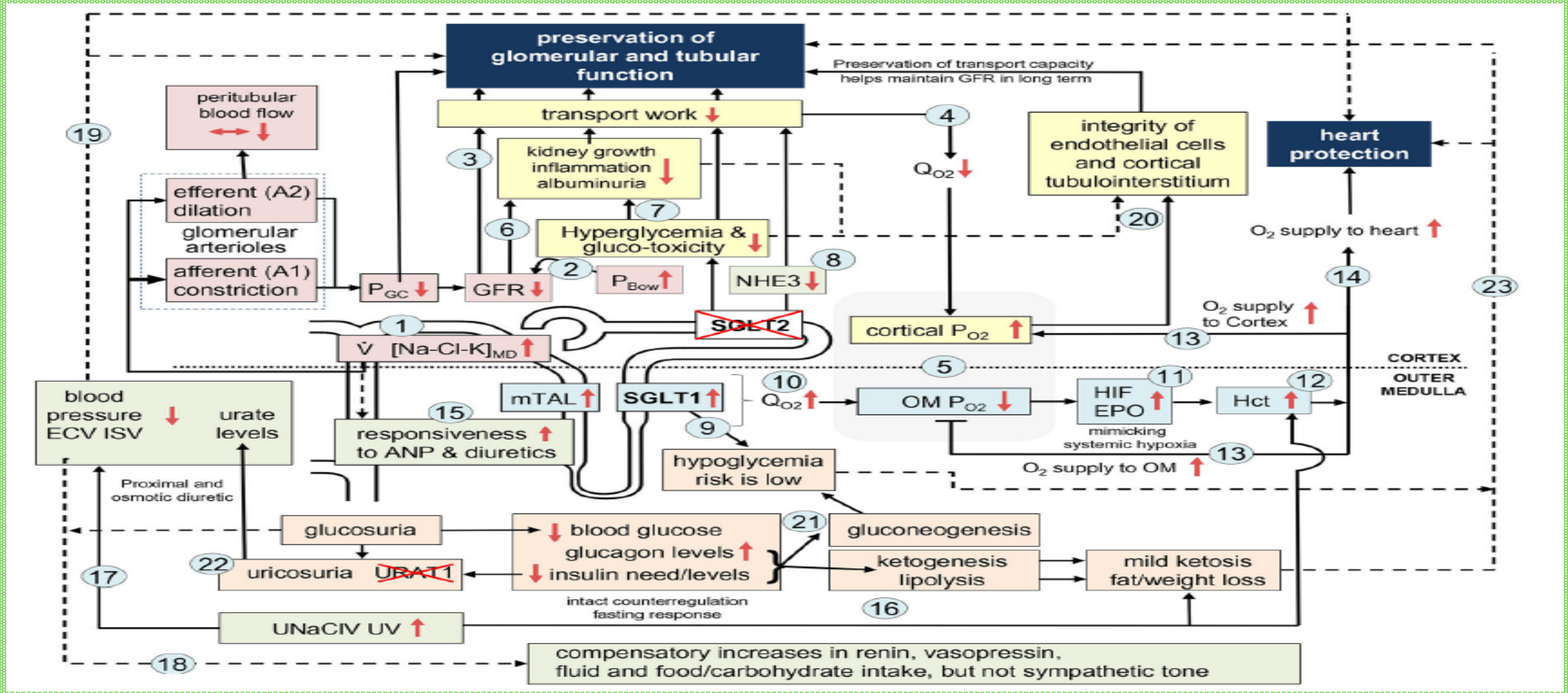
The Lancet Regional Health – Europe 2024

Azione degli SGLT2i sull'emodinamica glomerulare



Giornale Italiano di Nefrologia 2024

Potential kidney-protective effects of SGLT2 inhibition



Annu Rev Physiol. 2021

The legacy effect of hyperglycemia and early use of SGLT-2 inhibitors: a cohort study with newly-diagnosed people with type 2 diabetes

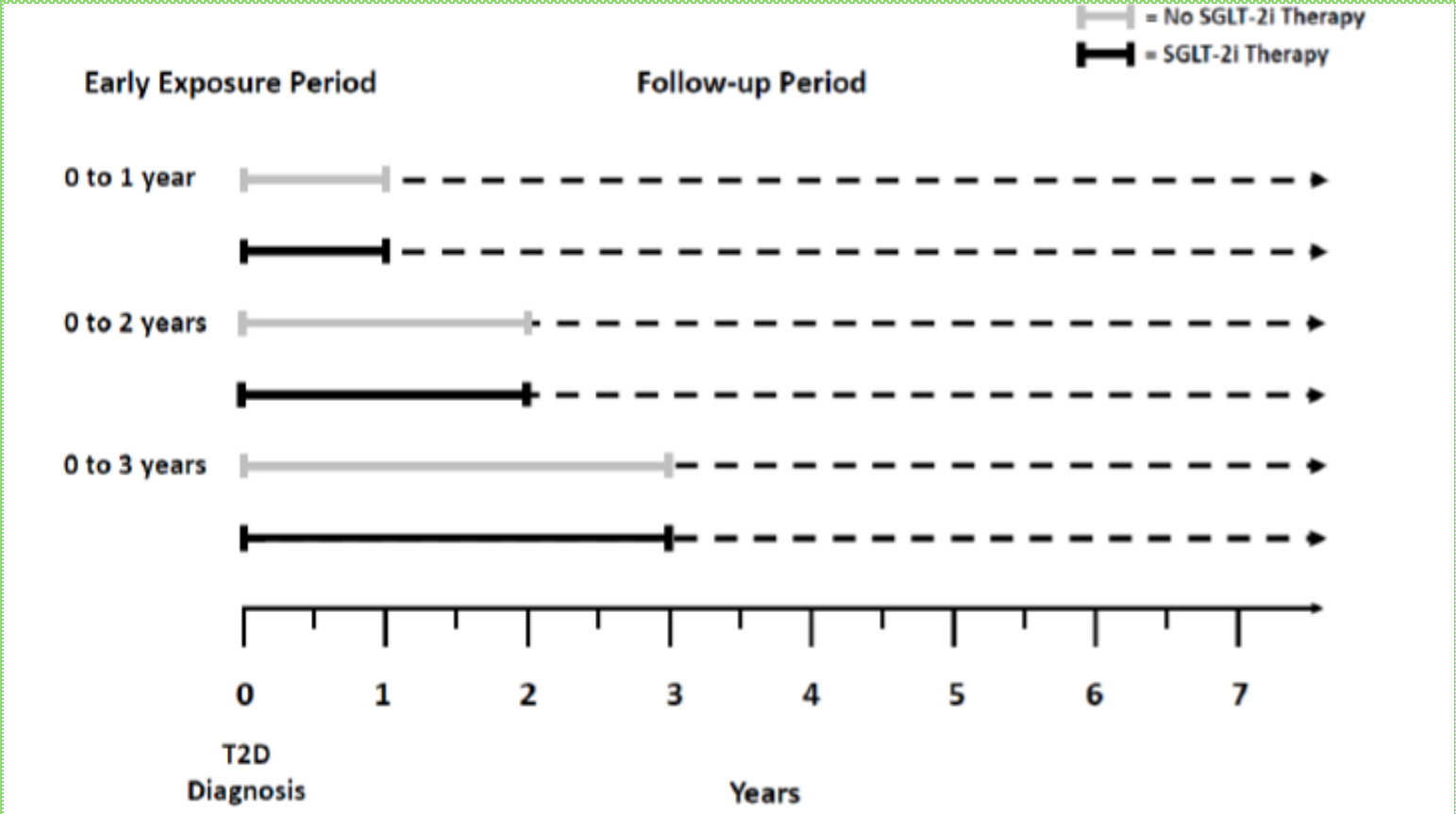
Antonio Ceriello,[a,*] Giuseppe Lucisano,[b] Francesco Prattichizzo,[a,**] Rosalba La Grotta,[a] Chiara Frigé,[a] Salvatore De Cosmo,[c] Paolo Di Bartolo,[d] Graziano Di Cianni,[e] Paola Fioretto,[f] Carlo Bruno Giorda,[g] Roberto Pontremoli,[h] Giuseppina Russo,[i] Francesca Viazzi,[h] and Antonio Nicolucci,[b] AMD Annals study group,[j]

Various degrees of glycemic control

<7.0%

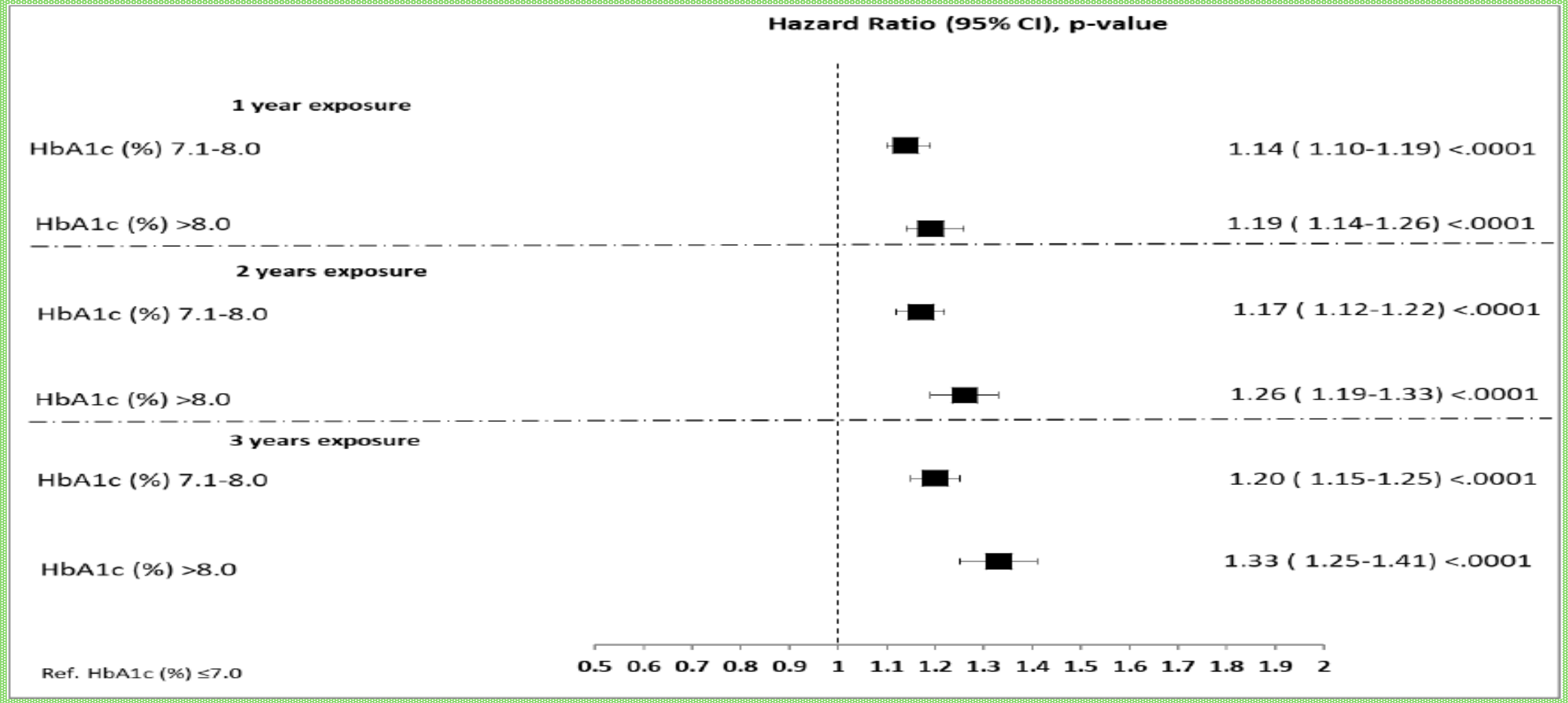
7.1%-8.0%

>8.0%



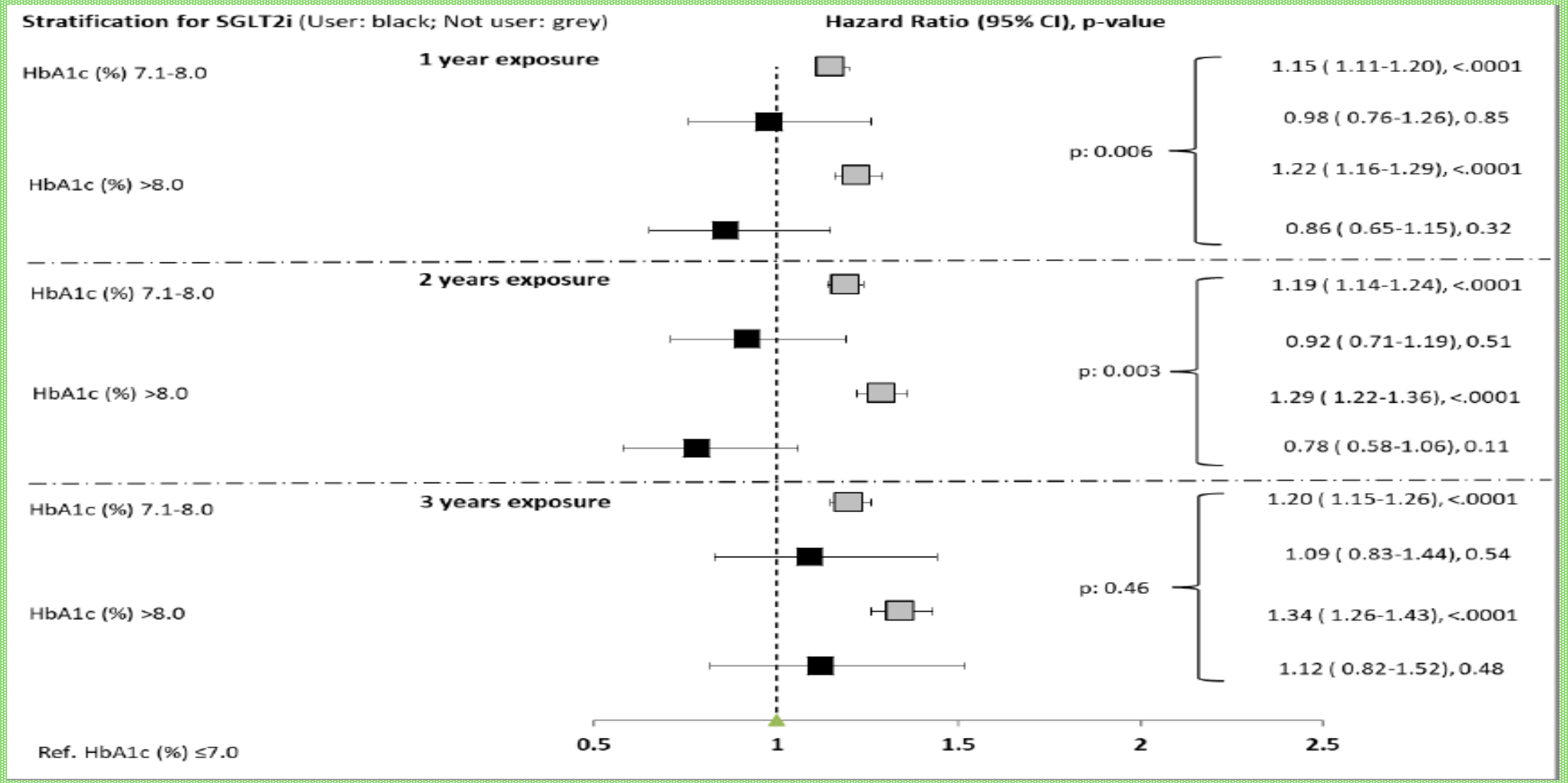
The Lancet Regional Health – Europe 2023

Poor, early glycemic control and the subsequent risk of cardiovasculare disease



Ceriello et al. The Lancet Regional Health – Europe 2023

Early introduction of SGLT2i attenuate metabolic memory

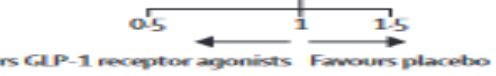


Ceriello et al. The Lancet Regional Health – Europe 2023

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

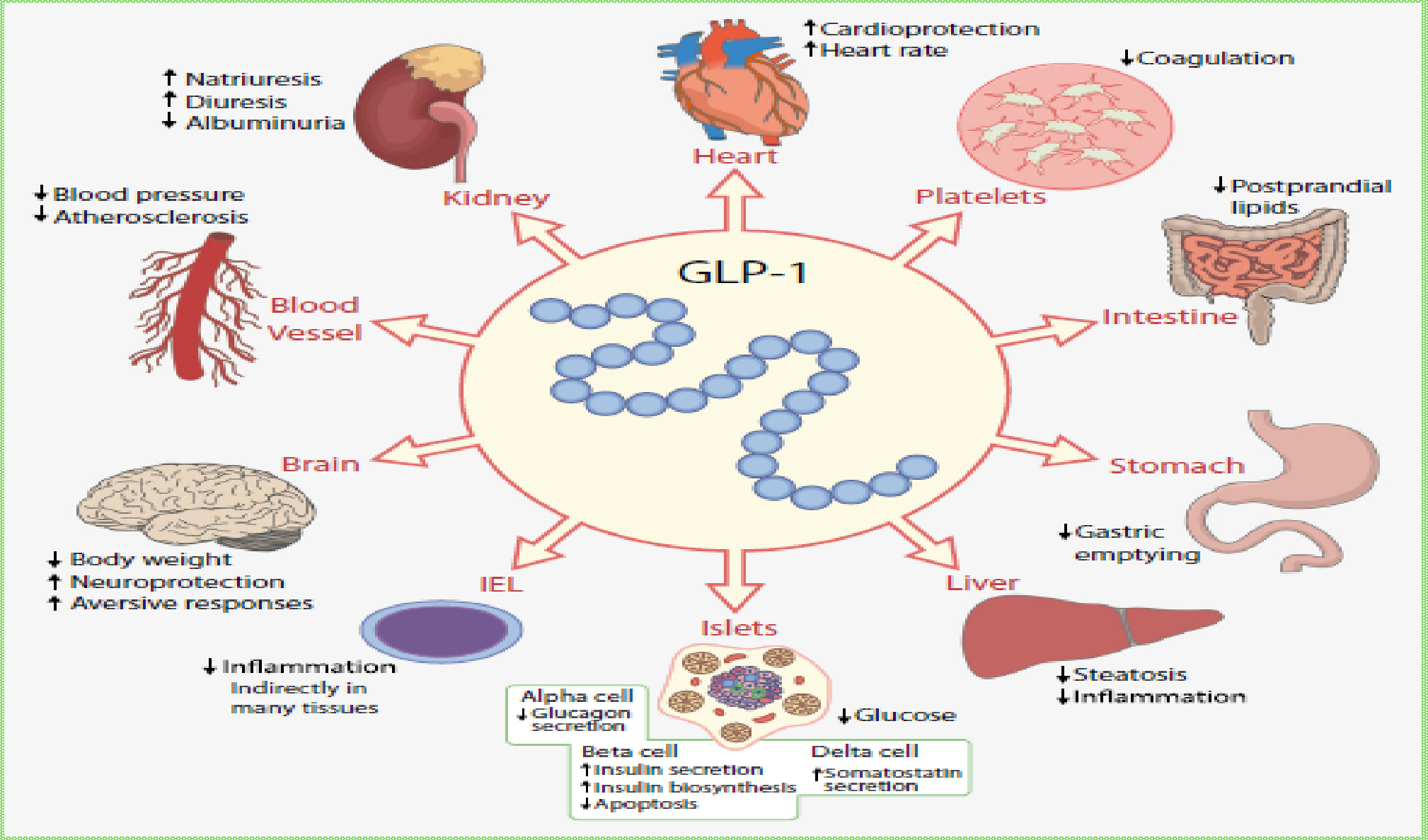
Naveed Sattar, Matthew M Y Lee*, Søren L Kristensen*, Kelley R H Branch, Stefano Del Prato, Nardev S Khurmi, Carolyn S P Lam, Renato D Lopes, John J V McMurray, Richard E Pratley, Julio Rosenstock, Hertzel C Gerstein*

	GLP-1 receptor agonist, n/N (%)	Placebo, n/N (%)	Hazard ratio (95% CI)	NNT (95% CI)	p value
Three-point MACE					
ELIXA	400/3034 (13%)	392/3034 (13%)	1·02 (0·89–1·17)		0·78
LEADER	608/4668 (13%)	694/4672 (15%)	0·87 (0·78–0·97)		0·01
SUSTAIN-6	108/1648 (7%)	146/1649 (9%)	0·74 (0·58–0·95)		0·016
EXSCEL	839/7356 (11%)	905/7396 (12%)	0·91 (0·83–1·00)		0·061
Harmony Outcomes	338/4731 (7%)	428/4732 (9%)	0·78 (0·68–0·90)		0·0006
REWIND	594/4949 (12%)	663/4952 (13%)	0·88 (0·79–0·99)		0·026
PIONEER 6	61/1591 (4%)	76/1592 (5%)	0·79 (0·57–1·11)		0·17
AMPLITUDE-O	189/2717 (7%)	125/1359 (9%)	0·73 (0·58–0·92)		0·0069
Subtotal (I^2=44·5%, p=0·082)			**0·86 (0·80–0·93)**	**65 (45–130)**	**<0·0001**
Cardiovascular death					
ELIXA	156/3034 (5%)	158/3034 (5%)	0·98 (0·78–1·22)		0·85
LEADER	219/4668 (5%)	278/4672 (6%)	0·78 (0·66–0·93)		0·007
SUSTAIN-6	44/1648 (3%)	46/1649 (3%)	0·98 (0·65–1·48)		0·92
EXSCEL	340/7356 (5%)	383/7396 (5%)	0·88 (0·76–1·02)		0·096
Harmony Outcomes	122/4731 (3%)	130/4732 (3%)	0·93 (0·73–1·19)		0·58
REWIND	317/4949 (6%)	346/4952 (7%)	0·91 (0·78–1·06)		0·21
PIONEER 6	15/1591 (1%)	30/1592 (2%)	0·49 (0·27–0·92)		0·021
AMPLITUDE-O	75/2717 (3%)	50/1359 (4%)	0·72 (0·50–1·03)		0·07
Subtotal (I^2=13·4%, p=0·33)			**0·87 (0·80–0·94)**	**163 (103–353)**	**0·0010**
Fatal or non-fatal myocardial infarction					
ELIXA	270/3034 (9%)	261/3034 (9%)	1·03 (0·87–1·22)		0·71
LEADER	292/4668 (6%)	339/4672 (7%)	0·86 (0·73–1·00)		0·046
SUSTAIN-6	54/1648 (3%)	67/1649 (4%)	0·81 (0·57–1·16)		0·26
EXSCEL	483/7356 (7%)	493/7396 (7%)	0·97 (0·85–1·10)		0·62
Harmony Outcomes	181/4731 (4%)	240/4732 (5%)	0·75 (0·61–0·90)		0·003
REWIND	223/4949 (5%)	231/4952 (5%)	0·96 (0·79–1·15)		0·63
PIONEER 6	37/1591 (2%)	35/1592 (2%)	1·04 (0·66–1·66)		0·49
AMPLITUDE-O	91/2717 (3%)	58/1359 (4%)	0·75 (0·54–1·05)		0·09
Subtotal (I^2=26·9%, p=0·21)			**0·90 (0·83–0·98)**	**175 (103–878)**	**0·020**
Fatal or non-fatal stroke					
ELIXA	67/3034 (2%)	60/3034 (2%)	1·12 (0·79–1·58)		0·54
LEADER	173/4668 (4%)	199/4672 (4%)	0·86 (0·71–1·06)		0·16
SUSTAIN-6	30/1648 (2%)	46/1649 (3%)	0·65 (0·41–1·03)		0·066
EXSCEL	187/7356 (3%)	218/7396 (3%)	0·85 (0·70–1·03)		0·095
Harmony Outcomes	94/4731 (2%)	108/4732 (2%)	0·86 (0·66–1·14)		0·30
REWIND	158/4949 (3%)	205/4952 (4%)	0·76 (0·62–0·94)		0·010
PIONEER 6	13/1591 (1%)	17/1592 (1%)	0·76 (0·37–1·56)		0·43
AMPLITUDE-O	47/2717 (2%)	31/1359 (2%)	0·74 (0·47–1·17)		0·19
Subtotal (I^2=0·0%, p=0·64)			**0·83 (0·76–0·92)**	**198 (140–421)**	**0·0002**



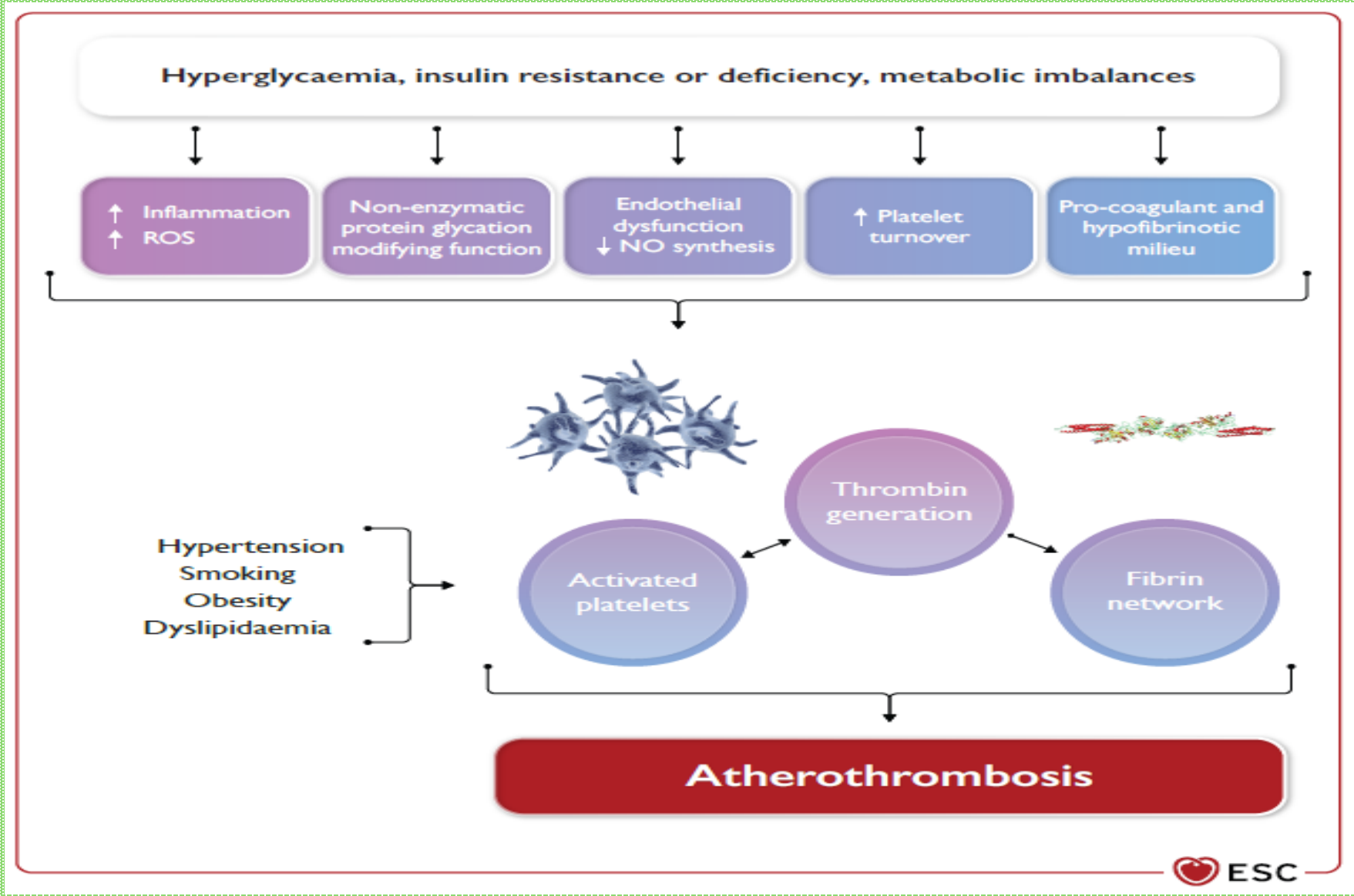
Lancet Diabetes Endocrinol 2021

Pleiotropic Effects of GLP-1



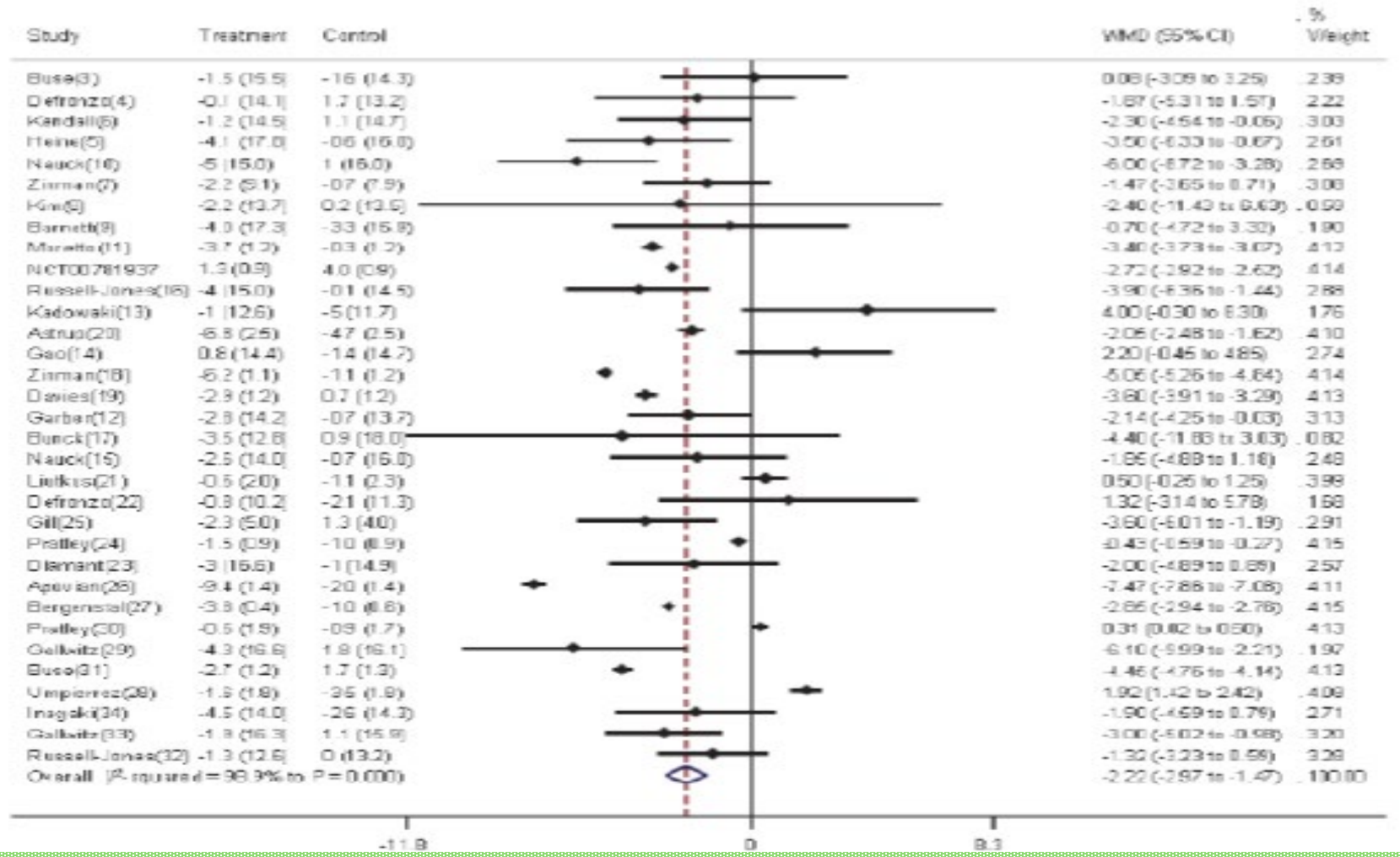
Drucker D., Holst J., NEJM 2023

Mechanisms contributing to altered platelet activation and atherothrombosis in patients with diabetes



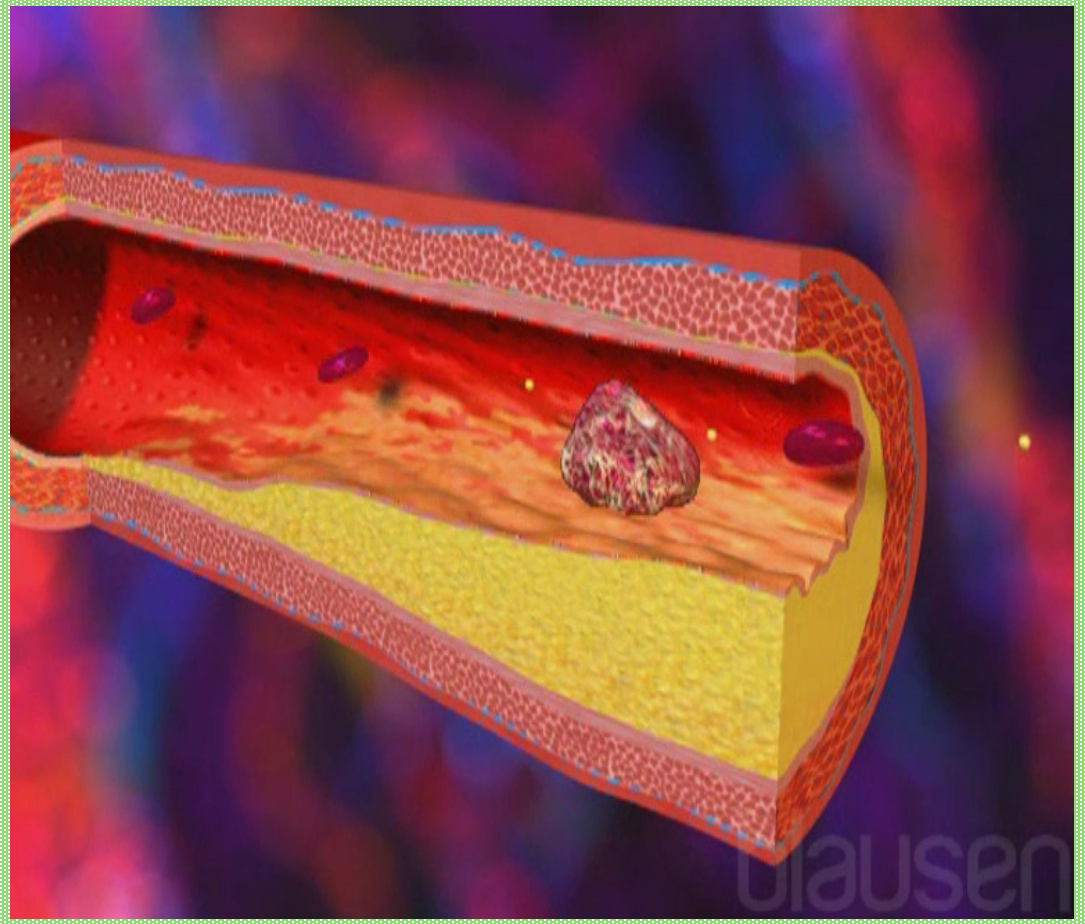
2023 ESC Guidelines – Eur Heart Journal

Meta-analysis of change in systolic blood pressure in RCTs after at least 12 weeks of treatment with GLP-1 RA



Katout et al. Am J Hypertens 2014

Molecular mechanism of anti-AS by GLP-1RAs



Inhibition of the endotelial cells expression of inflammatory factors and adhesion molecules

Induction of NO synthesis in endothelial cells

Protection of mitochondrial function and inhibition of oxidative stress in endothelial cells

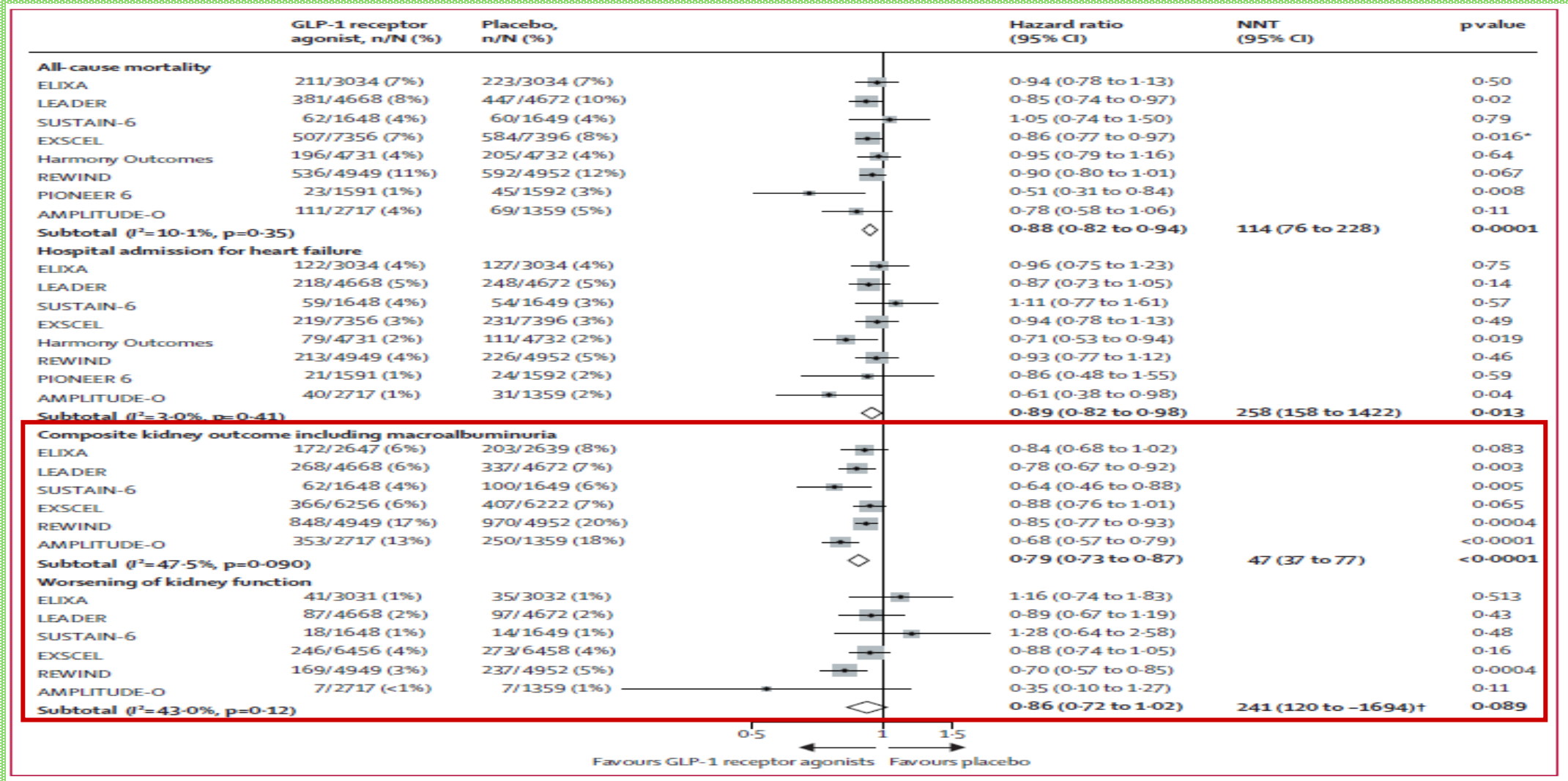
Reduction of macrophage inflammation and foam cell formation

Improvement of VSMC disfunction

Frontiers in Pharmacology 2024

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

KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

Recommendation 1.3.1: We recommend treating patients with type 2 diabetes (T2D), CKD, and an eGFR ≥20 ml/min per 1.73 m^2 with an SGLT2i *(1A)*.

Practice Point 1.3.1: The recommendation for SGLT2i is for kidney and cardiovascular protection and SGLT2i have been shown to have safety and benefit in CKD patients, even for those without T2D. Thus, if patients are already being treated with other glucose-lowering agents, an SGLT2i can be added to the current treatment regimen (Figure 6).

Practice Point 1.3.2: The choice of an SGLT2i should prioritize agents with documented kidney or cardiovascular benefits and take eGFR into account.

Practice Point 1.3.3: It is reasonable to withhold SGLT2i during times of prolonged fasting, surgery, or critical medical illness (when patients may be at greater risk for ketosis).

Practice Point 1.3.4: If a patient is at risk for hypovolemia, consider decreasing thiazide or loop diuretic dosages before commencement of SGLT2i treatment, advise patients about symptoms of volume depletion and low blood pressure, and follow up on volume status after drug initiation.

Practice Point 1.3.5: A reversible decrease in the eGFR with commencement of SGLT2i treatment may occur and is generally not an indication to discontinue therapy.

Practice Point 1.3.6: Once an SGLT2i is initiated, it is reasonable to continue an SGLT2i even if the eGFR falls below 20 ml/min per 1.73 m^2, unless it is not tolerated or kidney replacement therapy is initiated.

Practice Point 1.3.7: SGLT2i have not been adequately studied in kidney transplant recipients, who may benefit from SGLT2i treatment, but are immunosuppressed and potentially at increased risk for infections; therefore, the recommendation to use SGLT2i does not apply to kidney transplant recipients (see Recommendation 1.3.1).

Kidney International 2022

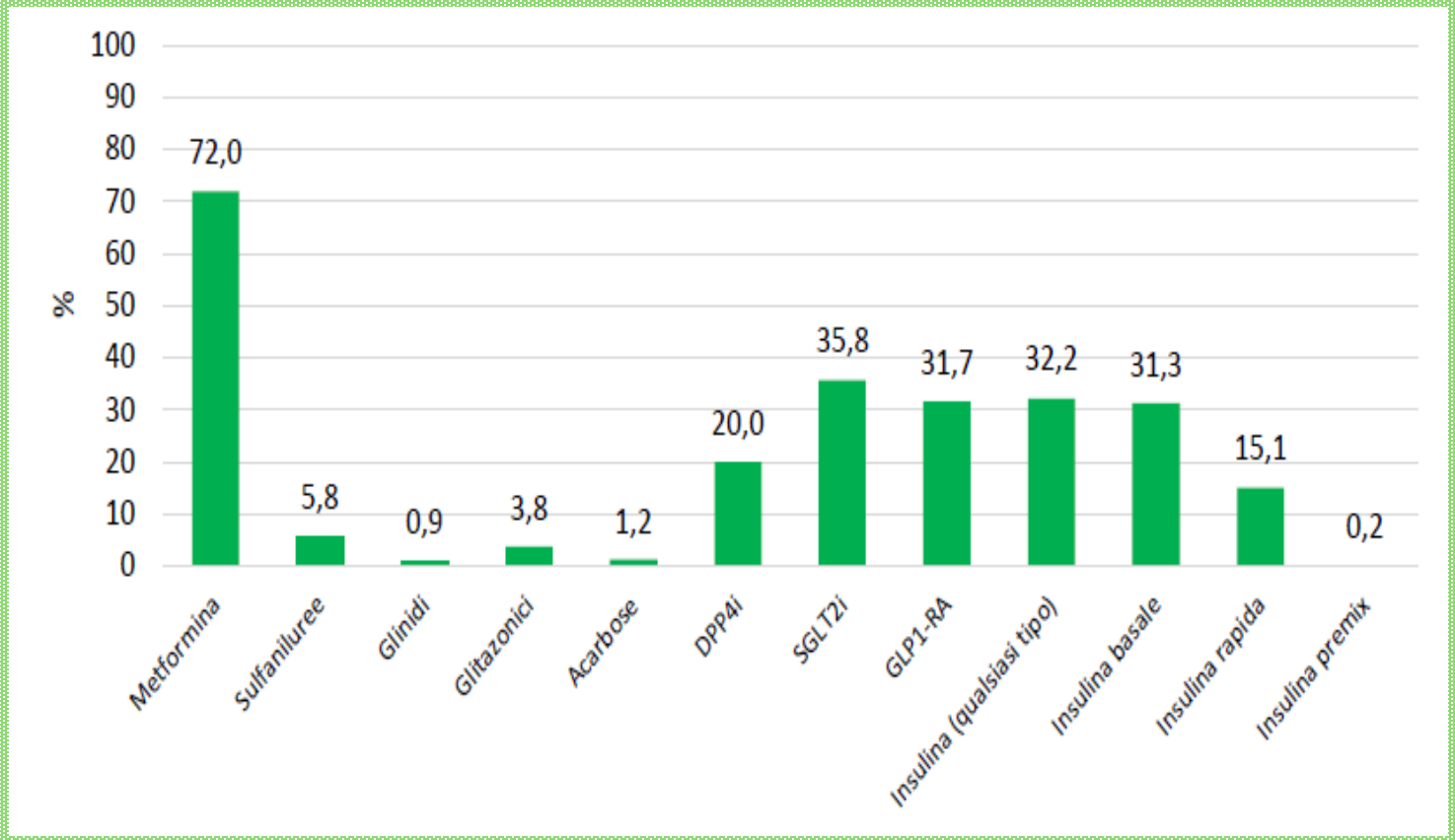
ESC European Society of Cardiology
European Heart Journal (2023) **00**, 1–98
https://doi.org/10.1093/eurheartj/ehad192

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

Recommendations	Class[a]	Level[b]
CCS patients with type 2 diabetes		
SGLT2 inhibitors with proven CV benefit[c] are recommended in patients with T2DM and CCS to reduce CV events, independent of baseline or target HbA1c and independent of concomitant glucose-lowering medication.[86,688,695,697,700]	I	A
GLP-1 receptor agonists with proven CV benefit[d] are recommended in patients with T2DM and CCS to reduce CV events, independent of baseline or target HbA1c and independent of concomitant glucose-lowering medication.[710,711]	I	A
CCS patients without type 2 diabetes		
The GLP-1 receptor agonist semaglutide should be considered in overweight (BMI > 27 kg/m^2) or obese CCS patients without diabetes to reduce CV mortality, MI, or stroke.[465]	IIa	B

ANNALI AMD 2024

Indicatori di intensità/appropriatezza del trattamento farmacologico



ANNALI AMD 2024

Indicatori di appropriatezza del trattamento farmacologico

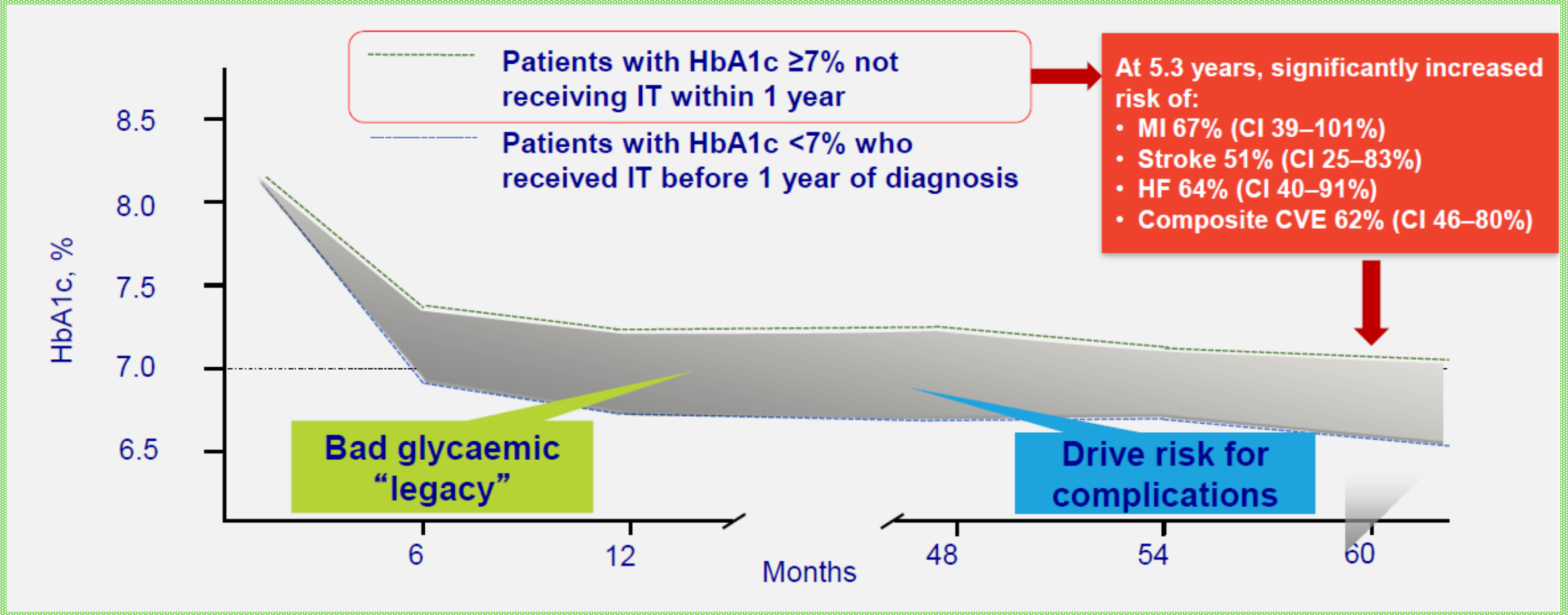
Indicatore	Denominatore	%	Gold standard (25° *percentile*)
Soggetti non trattati con SGLT2i e/o GLP1 RA nonostante la presenza di albuminuria	Soggetti con micro/macroalbuminuria (n=119.406)	39,1	31,0
Soggetti non trattati con SGLT2i nonostante la presenza di eGFR<60 ml/min	Soggetti con eGFR<60 ml/min (n=163.921)	62,5	56,0
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 rivascolarizzazione coronarica e/o periferica, bypass coronarico e/o periferico (n=85.108)	31,9	23,5
Soggetti non trattati con SGLT2i nonostante la presenza di scompenso cardiaco	Soggetti con scompenso cardiaco (n=18.336)	38,6	27,9

Adv Ther (2018) 35:1735–1745
https://doi.org/10.1007/s12325-018-0819-5

REVIEW

Addressing Clinical Inertia in Type 2 Diabetes Mellitus: A Review

Jennifer Okemah · John Peng · Manuel Quiñones



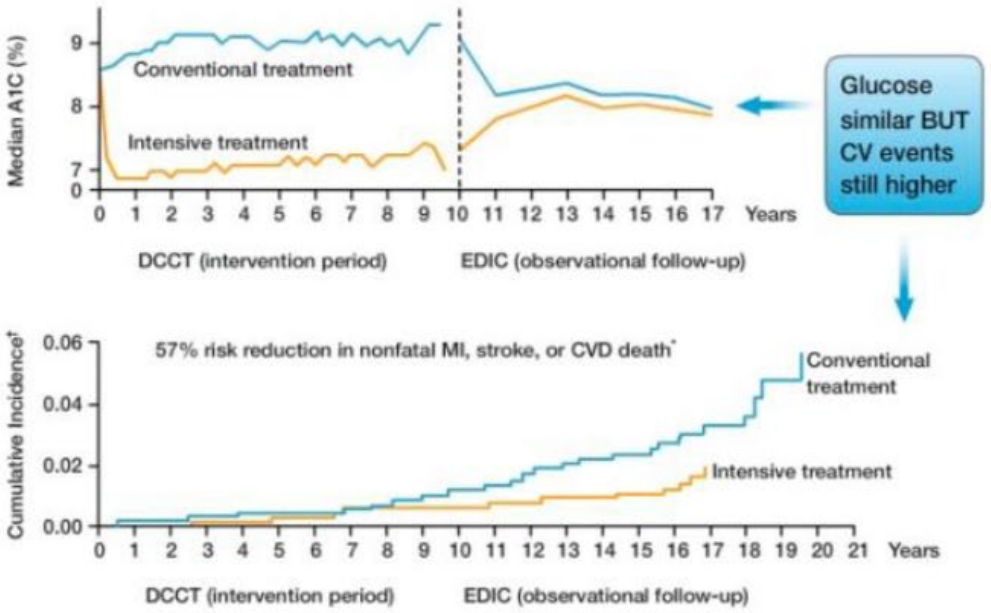
Okhema J. et al. Adv Ther 2018

Discovery of Legacy Effect: role of early intensive glycemic control

Type 1 Diabetes

DCCT/EDIC

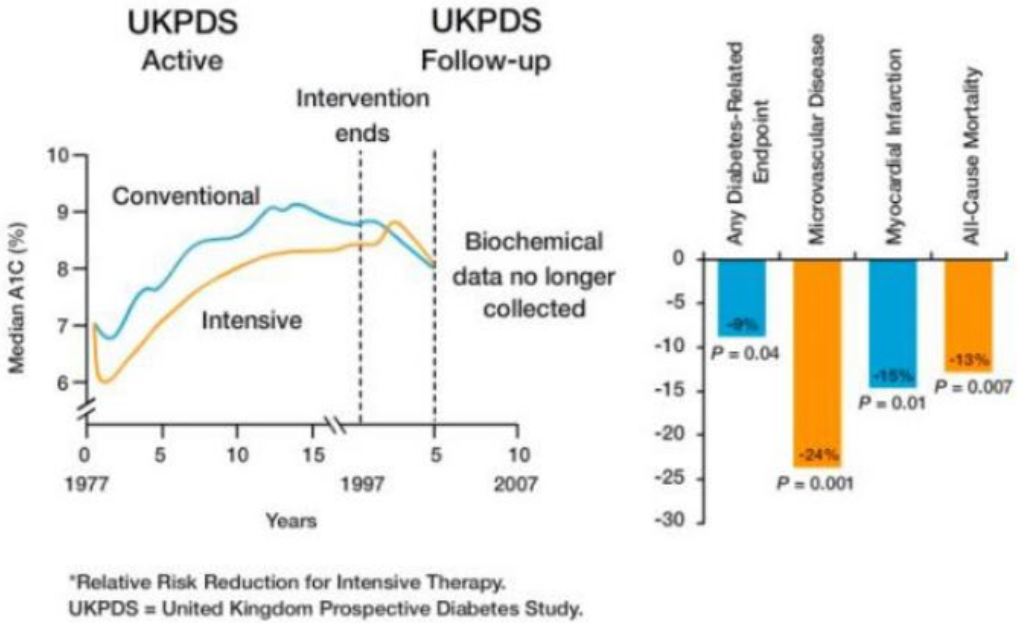
Long-term Follow-up and Legacy Effect



Type 2 Diabetes

UKPDS

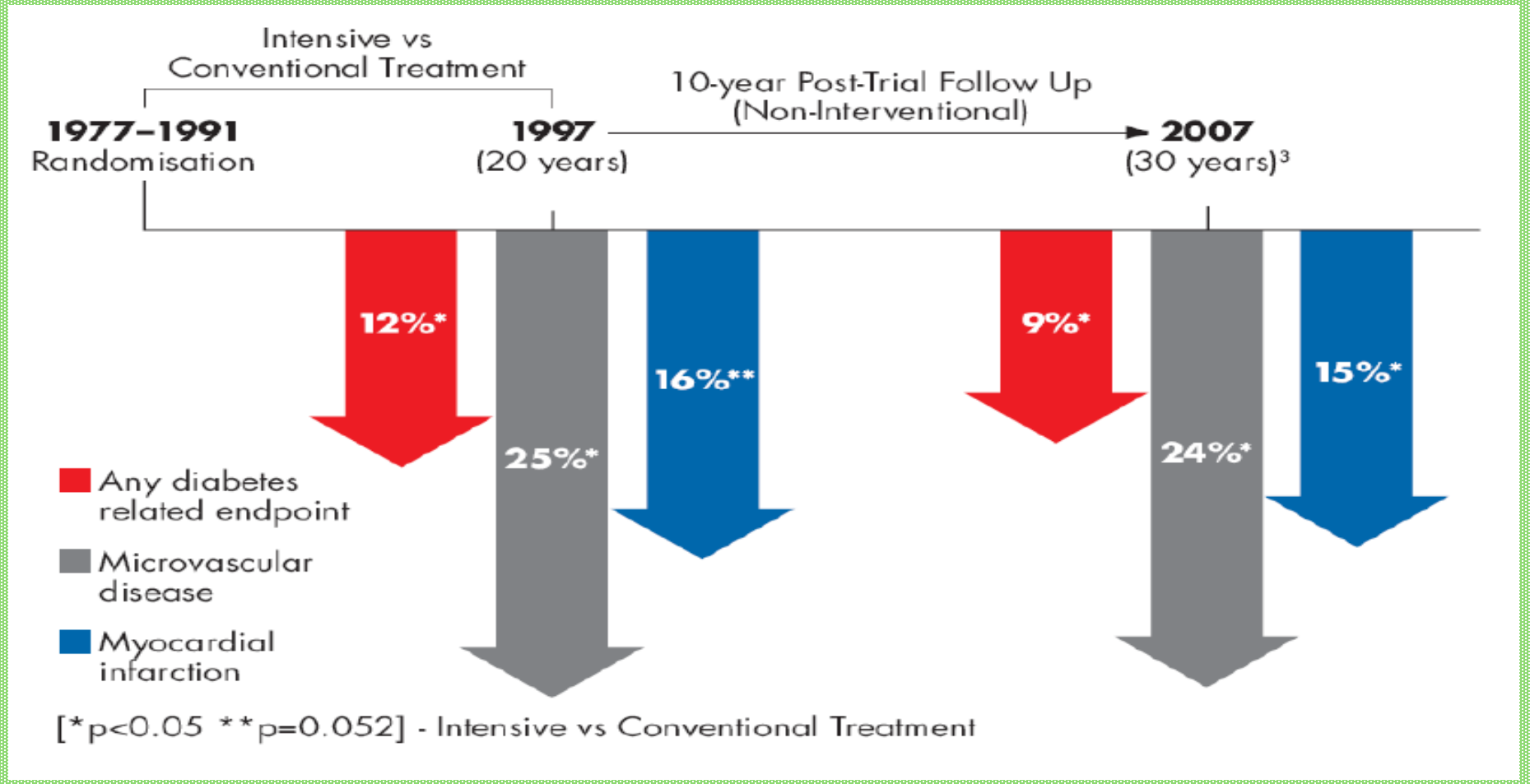
Long-term Follow-up and Legacy Effect



*Relative Risk Reduction for Intensive Therapy.
UKPDS = United Kingdom Prospective Diabetes Study.

Ramachandran et al. J Diabetes Metab 2015

The benefits of early tight control: UKPDS 10-years post trial follow up



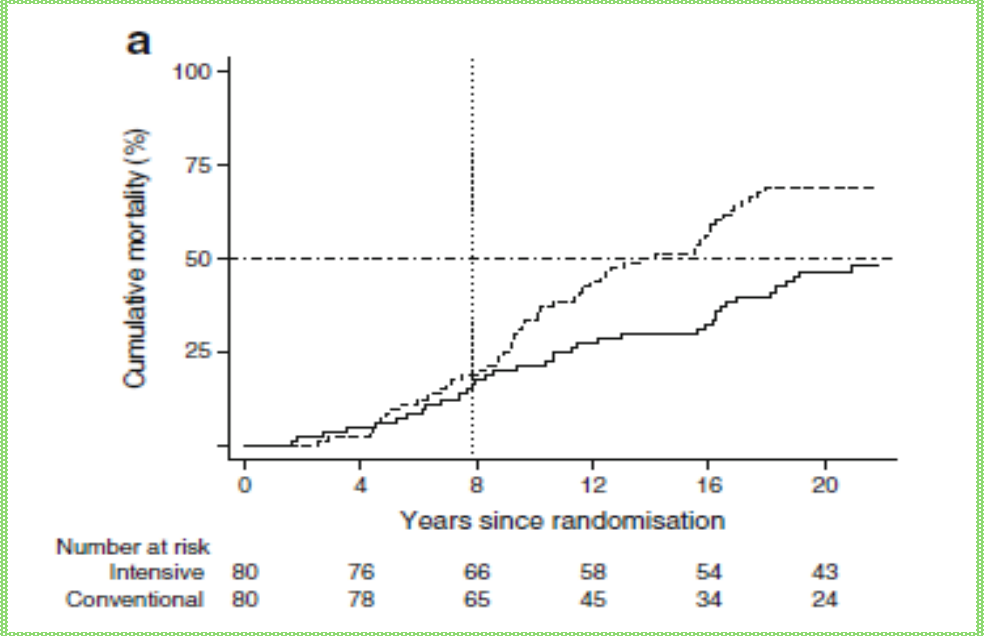
UKPDS Study Group. Lancet 1988
Holman et al. NEJM 2008

Diabetologia (2016) 59:2298–2307
DOI 10.1007/s00125-016-4065-6

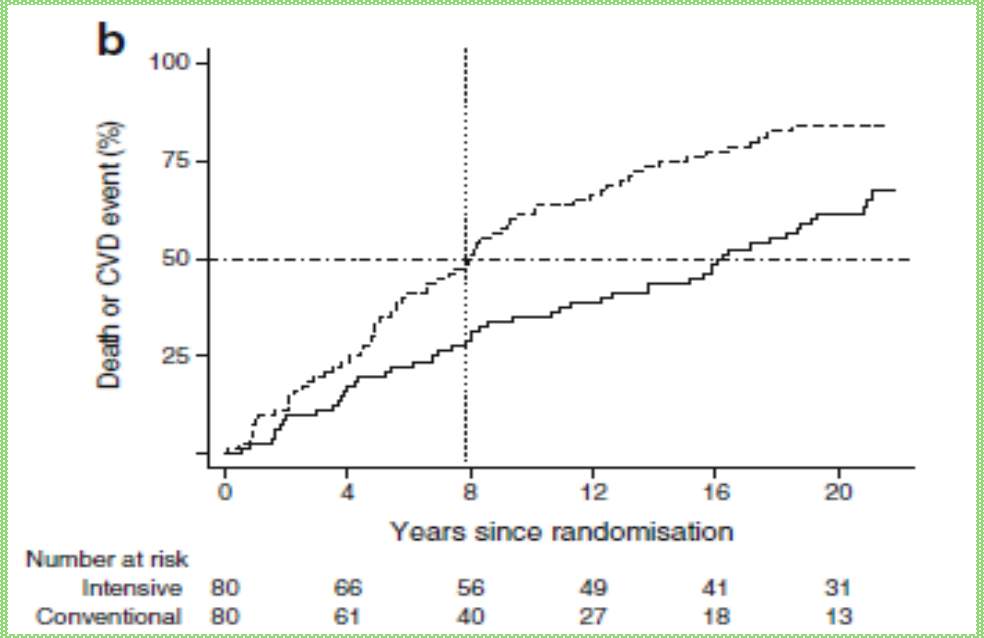
ARTICLE

Years of life gained by multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: 21 years follow-up on the Steno-2 randomised trial

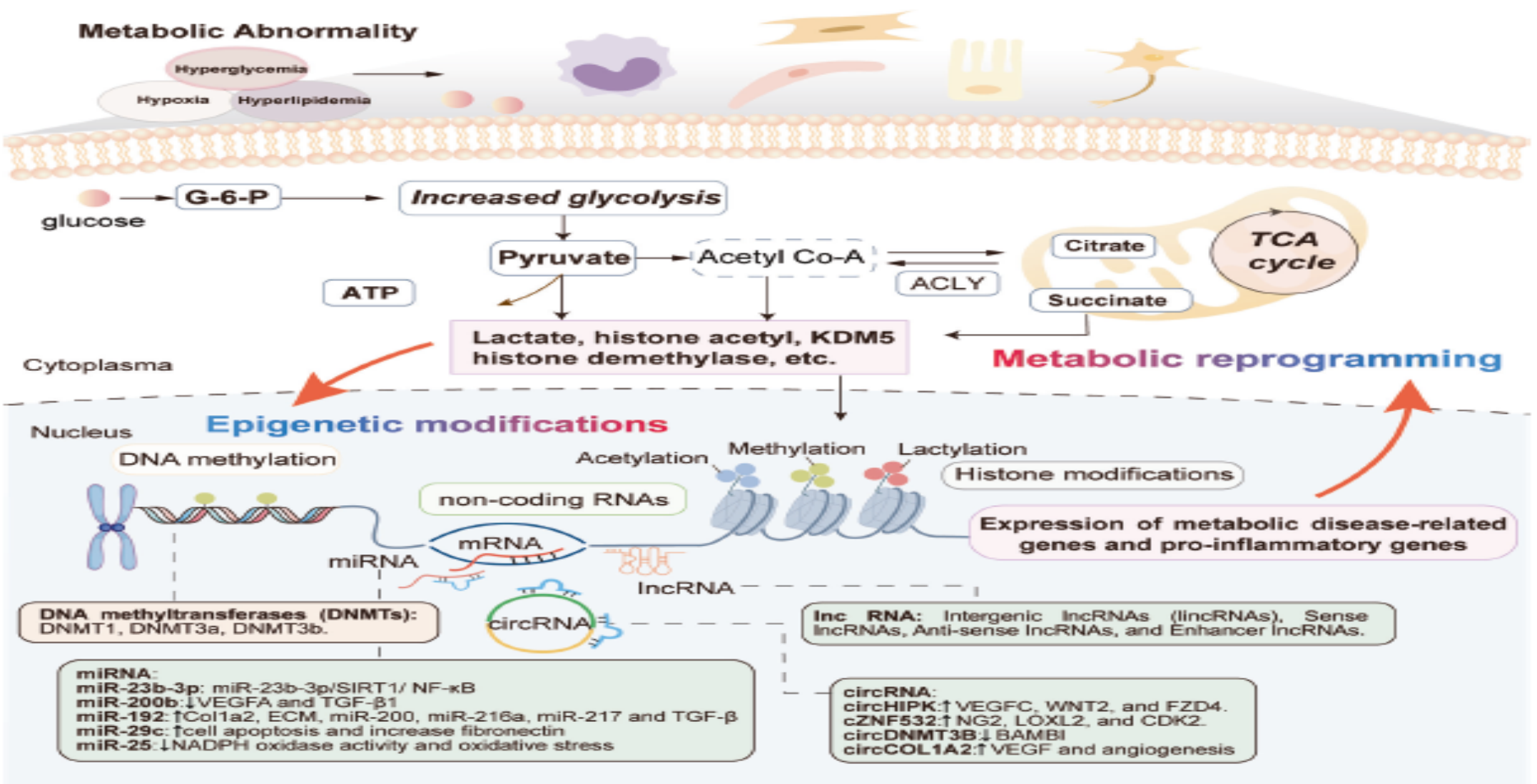
Peter Gæde[1,2] · Jens Oellgaard[1,2,3] · Bendix Carstensen[3] · Peter Rossing[3,4,5] · Henrik Lund-Andersen[3,5,6] · Hans-Henrik Parving[5,7] · Oluf Pedersen[8]



Early and intensified risk factor control in patients with type 2 diabetes with microalbuminuria increase mediane life and is matched by time free from incident cardiovascular disease



Interplay between epigenetic modifications and metabolic reprogramming during metabolic memory



Dong et al. Nature 2024; 9:38

Diabetes. 2024 Oct 17:db240166. doi: 10.2337/db24-0166. Online ahead of print.

When does metabolic memory start? Insights from the AMD Annals Initiative on stringent HbA1c targets

Giuseppina T Russo [1], Antonio Nicolucci [2], Giuseppe Lucisano [2], Maria Chiara Rossi [2], Antonio Ceriello [3], Francesco Prattichizzo [3], Valeria Manicardi [4], Alberto Rocca [5], Paolo Di Bartolo [6], Salvatore De Cosmo [7], Graziano Di Cianni [8], Riccardo Candido [9]

Various degrees of glycemic control

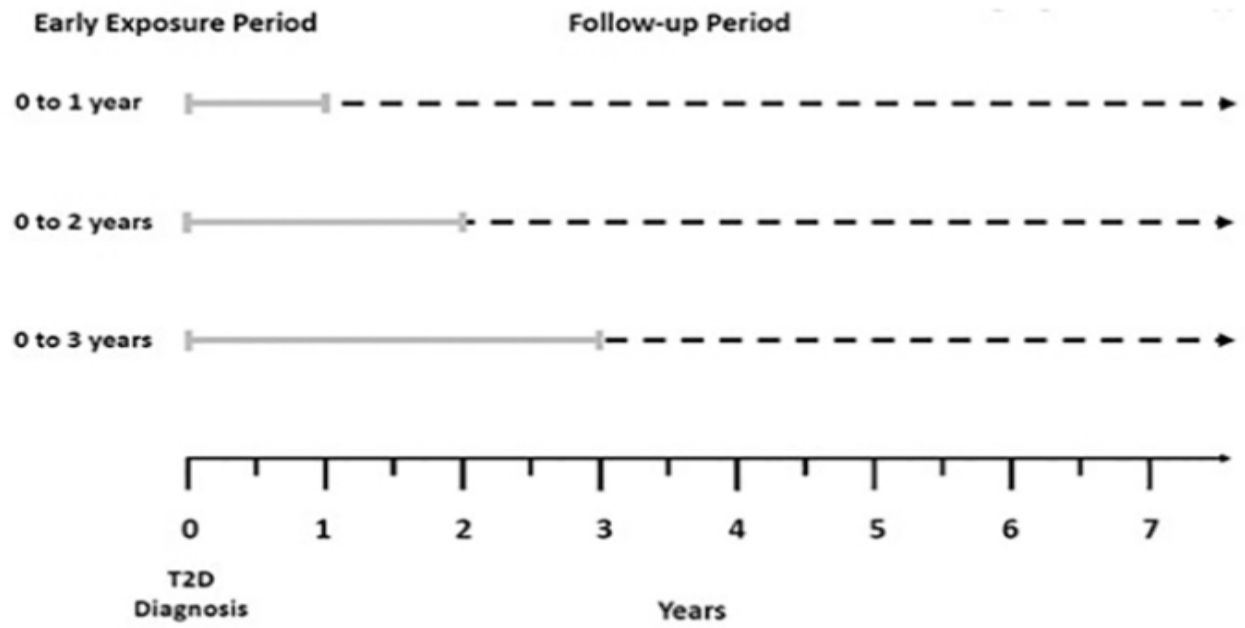
<5.7%

5.7%-6.4%

6.5%-7.0%

7.1%-8.0%

>8.0%



Follow Up 4.6±2.9 years

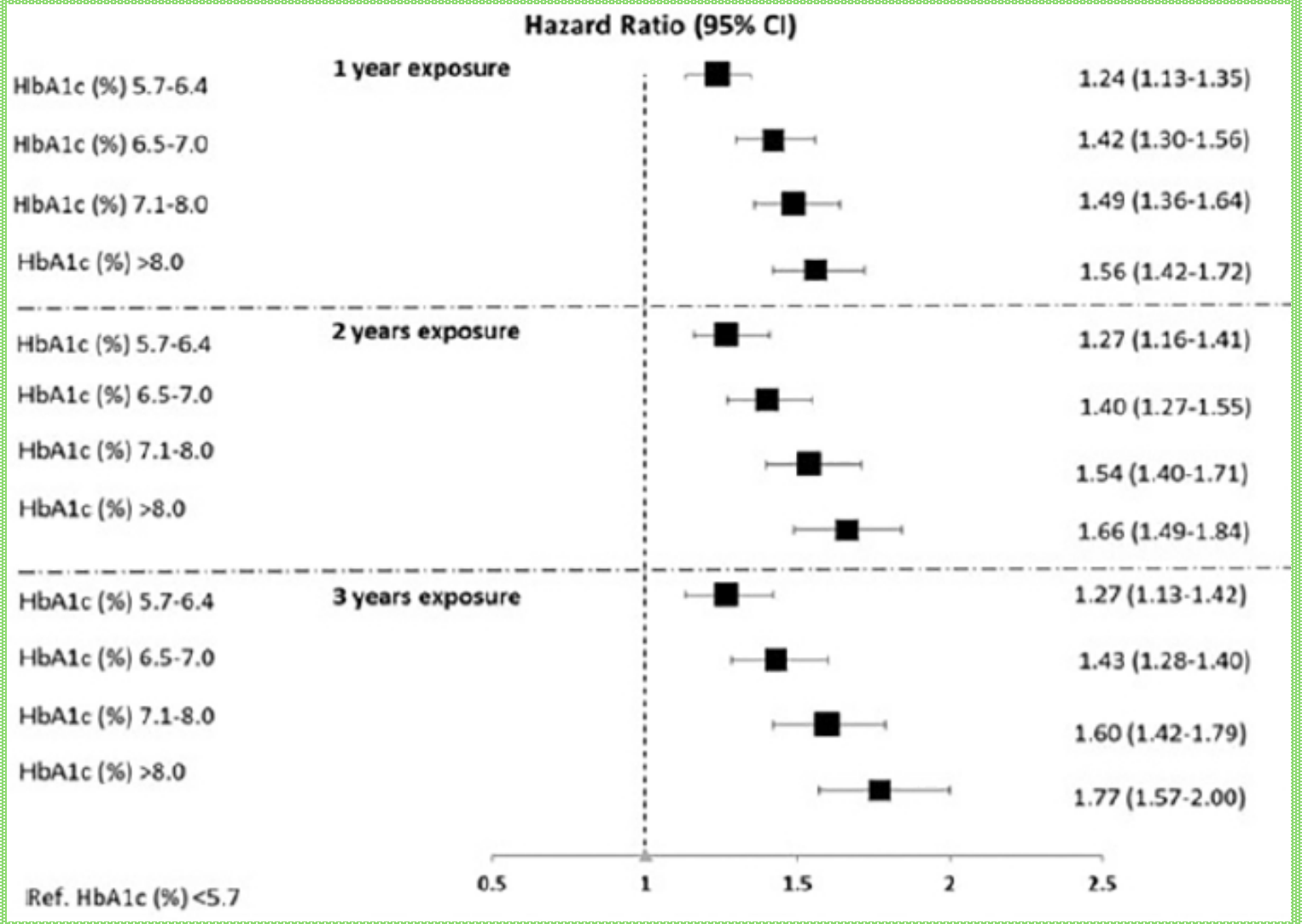
> Diabetes. 2024 Oct 17:db240166. doi: 10.2337/db24-0166. Online ahead of print.

When does metabolic memory start? Insights from the AMD Annals Initiative on stringent HbA1c targets

Giuseppina T Russo [1], Antonio Nicolucci [2], Giuseppe Lucisano [2], Maria Chiara Rossi [2], Antonio Ceriello [3], Francesco Prattichizzo [3], Valeria Manicardi [4], Alberto Rocca [5], Paolo Di Bartolo [6], Salvatore De Cosmo [7], Graziano Di Cianni [8], Riccardo Candido [9]

Early achievement of HbA1c <5,7% is associated with lower incidence of CV events

Compared with mean HbA1c <5,7% during the first year after diagnosis, CVD risk was 24%, 42%, 49% and 56% higher for patients with HbA1c of 5,7%-6,4% or above



Russo et al. Diabetes 2024

> Diabetes. 2024 Oct 17:db240166. doi: 10.2337/db24-0166. Online ahead of print.

When does metabolic memory start? Insights from the AMD Annals Initiative on stringent HbA1c targets

Giuseppina T Russo [1], Antonio Nicolucci [2], Giuseppe Lucisano [2], Maria Chiara Rossi [2], Antonio Ceriello [3], Francesco Prattichizzo [3], Valeria Manicardi [4], Alberto Rocca [5], Paolo Di Bartolo [6], Salvatore De Cosmo [7], Graziano Di Cianni [8], Riccardo Candido [9]

CV risk is a continuum in the clinical hystory of Diabetes

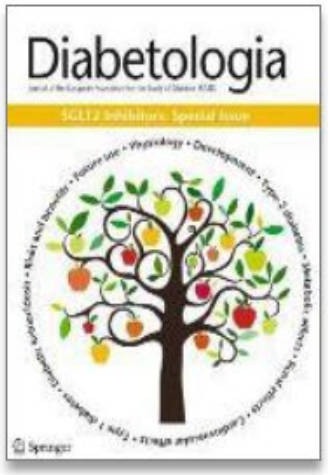
Achieving more ambitious glycemic targets, immediately after diagnosis, may prevent CV risk in patients with type 2 Diabetes

The principle of « the lowest is best» is hard to be proposed in diabetology field because of the risks associated with hypoglycemia

Today many drugs do not cause hypoglycemia, allowing to rethink about proper glucose targets in many patients

TAKE HOME MESSAGES

New evidences support the importance of not reglecting the «treat-to-target» approach in the «treat-to-benefit» era, provided than an optimal metabolic control is achieved with the most appropriated drugs



HOLISTIC PERSON-CENTRED APPROACH TO T2DM MANAGEMENT

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY

SGLT2i with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥ 20 ml/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation

OR

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

If additional cardiorenal risk reduction or glycaemic control needed consider combination SGLT2/GLP-1 RA

+HF

SGLT2i with proven HF benefit in this population

+ASCVD/indicators of High Risk

GLP-1 RA with proven CVD benefit — EITHER/OR — SGLT2i with proven CVD benefit

If additional cardiorenal risk reduction or glycaemic control needed consider combination SGLT2/GLP-1 RA

Glycaemic Management: Choose approaches that provide the efficacy to achieve goals:

Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals

Consider avoidance of hypoglycaemia a priority in high-risk individuals

Cardiorenal Protection – choice of glucose-lowering medication

Medication for Glycaemic Management

Weight Management

Cardiovascular Risk Factor Management

COMPONENTS OF CARE

PRINCIPLES OF CARE

GOALS OF CARE
- Prevent complications
- Optimise quality of life

Consider local healthcare setting and resources

Complication surveillance and screening

Health behaviour modification

Monitoring and ongoing review

Reducing risk of hypoglycaemia

Effective practice and organisation of care

Consider underlying physiology

Avoid therapeutic inertia

Social determinants of health

Psychosocial factors

Diabetes structured education and support

Language matters

Shared decision making

Ensure strategies are in place to detect and optimise management of CV risk factors[1] including

- CV risk factor screening and surveillance
- BP lowering
- Lipid lowering
- Antithrombotic agents
- Smoking cessation

Achievement and Maintenance of Weight Management Goals:

Set individualised weight management goals

General lifestyle advice: medical nutrition therapy/eating patterns/physical activity

Intensive evidence-based structured weight management programme

Consider medication for weight loss

Consider metabolic surgery

When choosing glucose-lowering therapies:

Consider regimen with high-to-very-high dual glucose and weight efficacy

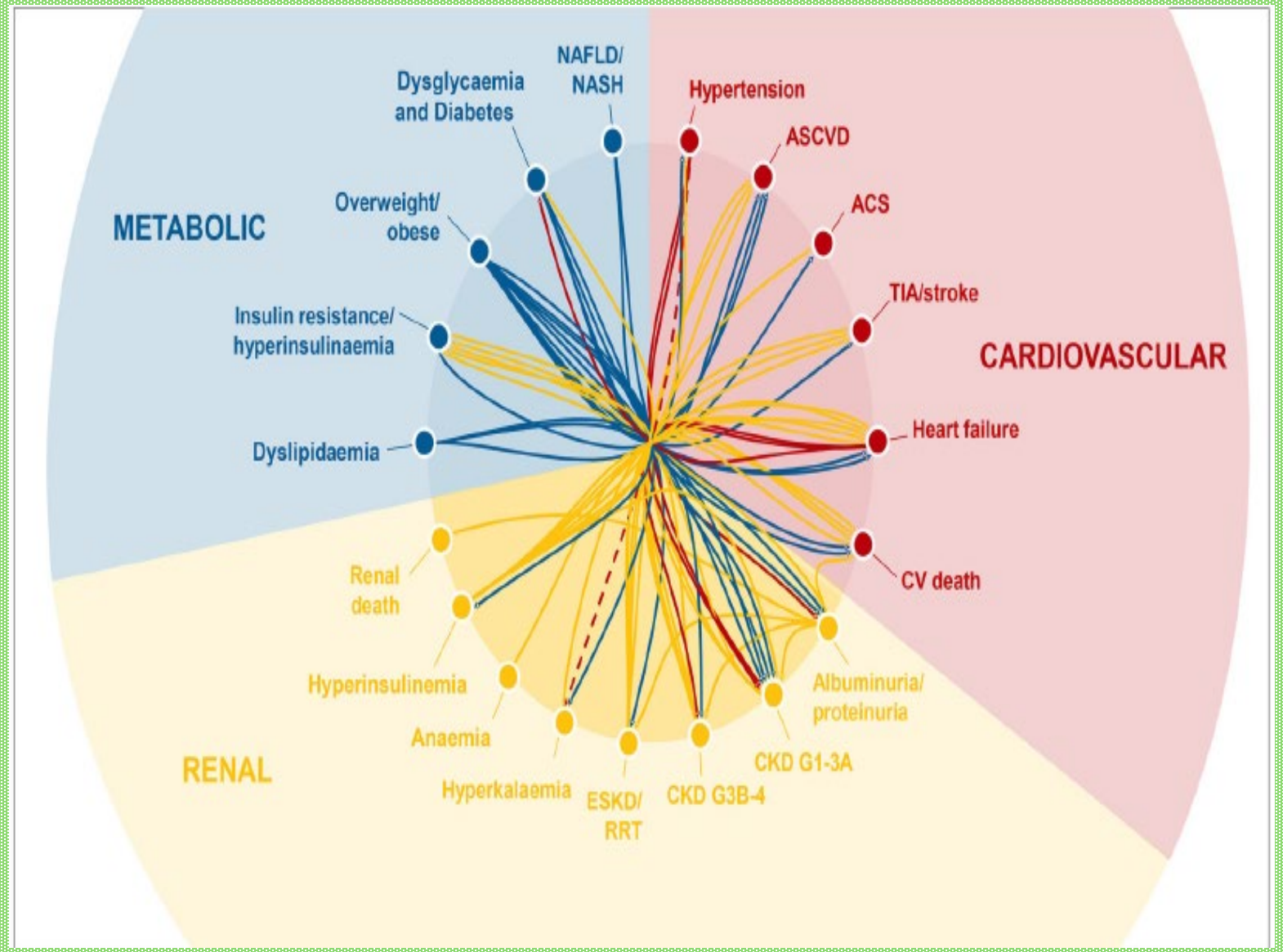
1 = American Diabetes Association Professional Practice Committee. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2022. Diabetes Care. 2022 Jan 1;45(Suppl 1):S144-74.

ACEi, Angiotensin-Converting Enzyme Inhibitor; ARB, Angiotensin Receptor Blockers; ASCVD, Atherosclerotic Cardiovascular Disease; BP, Blood Pressure; CKD, Chronic Kidney Disease; CV, Cardiovascular; eGFR, Estimated Glomerular Filtration Rate; GLP-1 RA, Glucagon-Like Peptide-1 Receptor Agonist; HF, Heart Failure; SGLT2i, Sodium-Glucose Cotransporter-2 Inhibitor; T2D, Type 2 Diabetes.

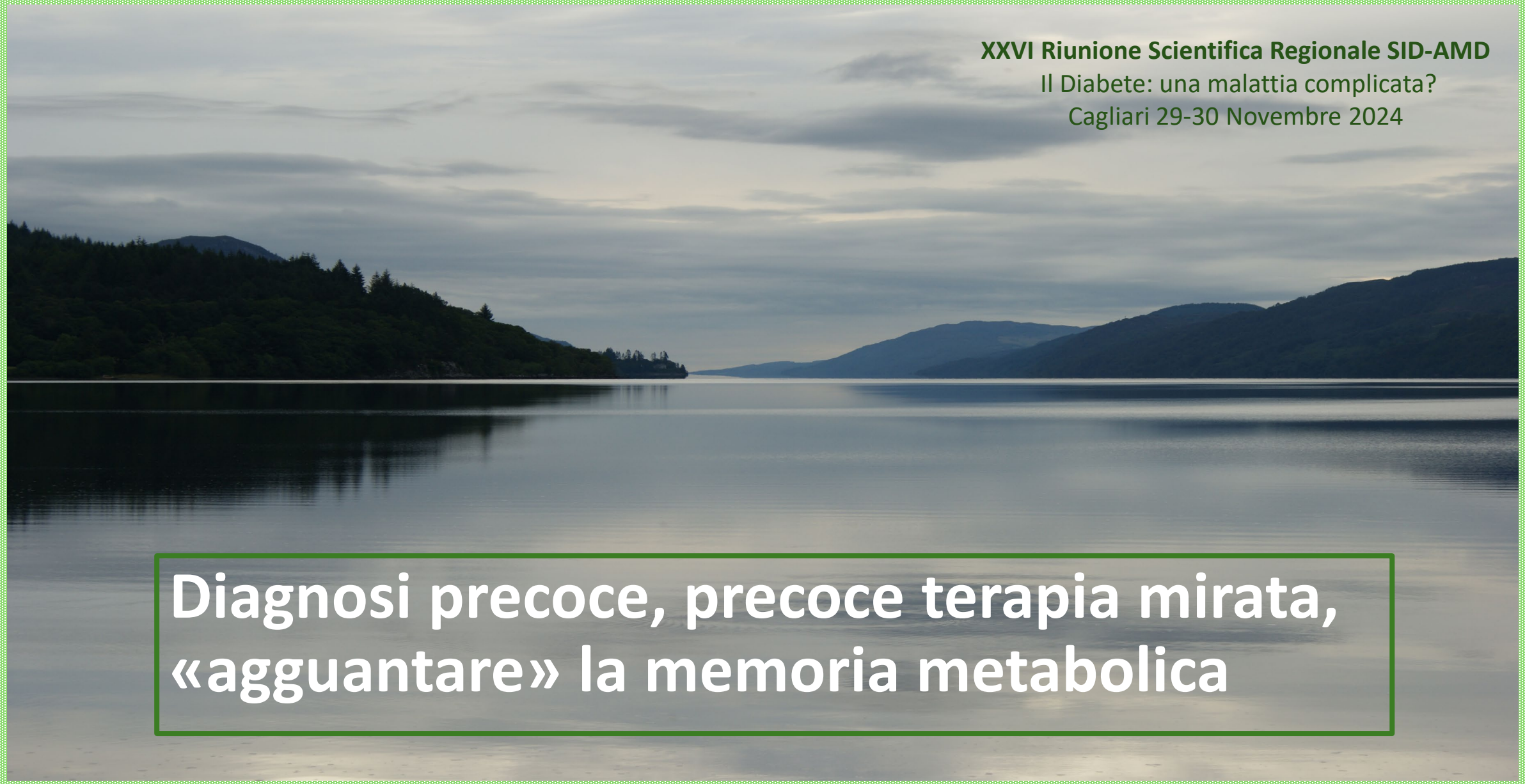
Consensus ADA-EASD 2022

Inter-relationships between cardiovascular, renal and metabolic diseases: Underlying evidence and implications for integrated interdisciplinary care and management

Jiten Vora MD[1] | David Cherney MD[2,3,4,5] | Mikhail N. Kosiborod MD[6,7] | Jonas Spaak MD[8] | Naresh Kanumilli MD[9] | Kamlesh Khunti MD[10] | Carolyn S. P. Lam MBBS[11] | Michael Bachmann MSc[12] | Peter Fenici MD[13,14,15] | on behalf of the CaReMe Global Alliance



Diabetes Obes Metabol. 2024; 26: 1567-1581



XXVI Riunione Scientifica Regionale SID-AMD
Il Diabete: una malattia complicata?
Cagliari 29-30 Novembre 2024

Diagnosi precoce, precoce terapia mirata, «agguantare» la memoria metabolica

GRAZIE PER L'ATTENZIONE