Il continuum cardio-nefro-metabolico: il nuovo paradigma della terapia del diabete tipo 2?

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4 luglio 2026

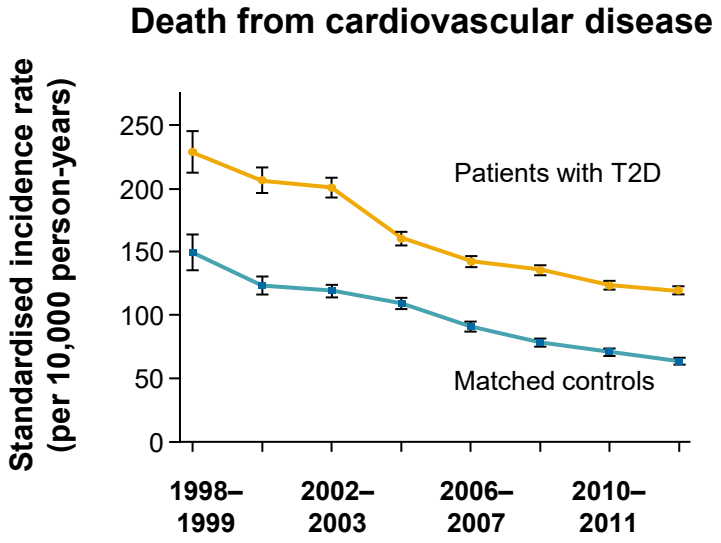
Conflitto di Interessi

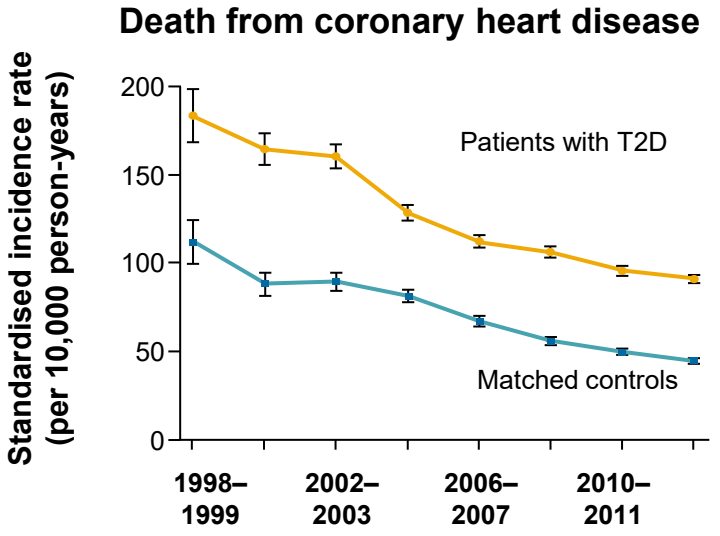
Il dott. Salvatore A. De Cosmo dichiara di aver ricevuto negli ultimi due anni compensi per letture o partecipazione ad Advisory Board dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

Eli Lilly, Boheringer, Astra-Zeneca, MSD, Sanofi, Novo-Nordisk, Daiichi Sankyo, Bayer, Guidotti, Amgen, Abbott.

Deaths due to CV disease are high in patients with T2D and the rate of decline is slowing

Using records from the Swedish National Diabetes Register, the study examined data from 457,473 patients with T2D and matched controls (mean follow-up: 6.5 years)

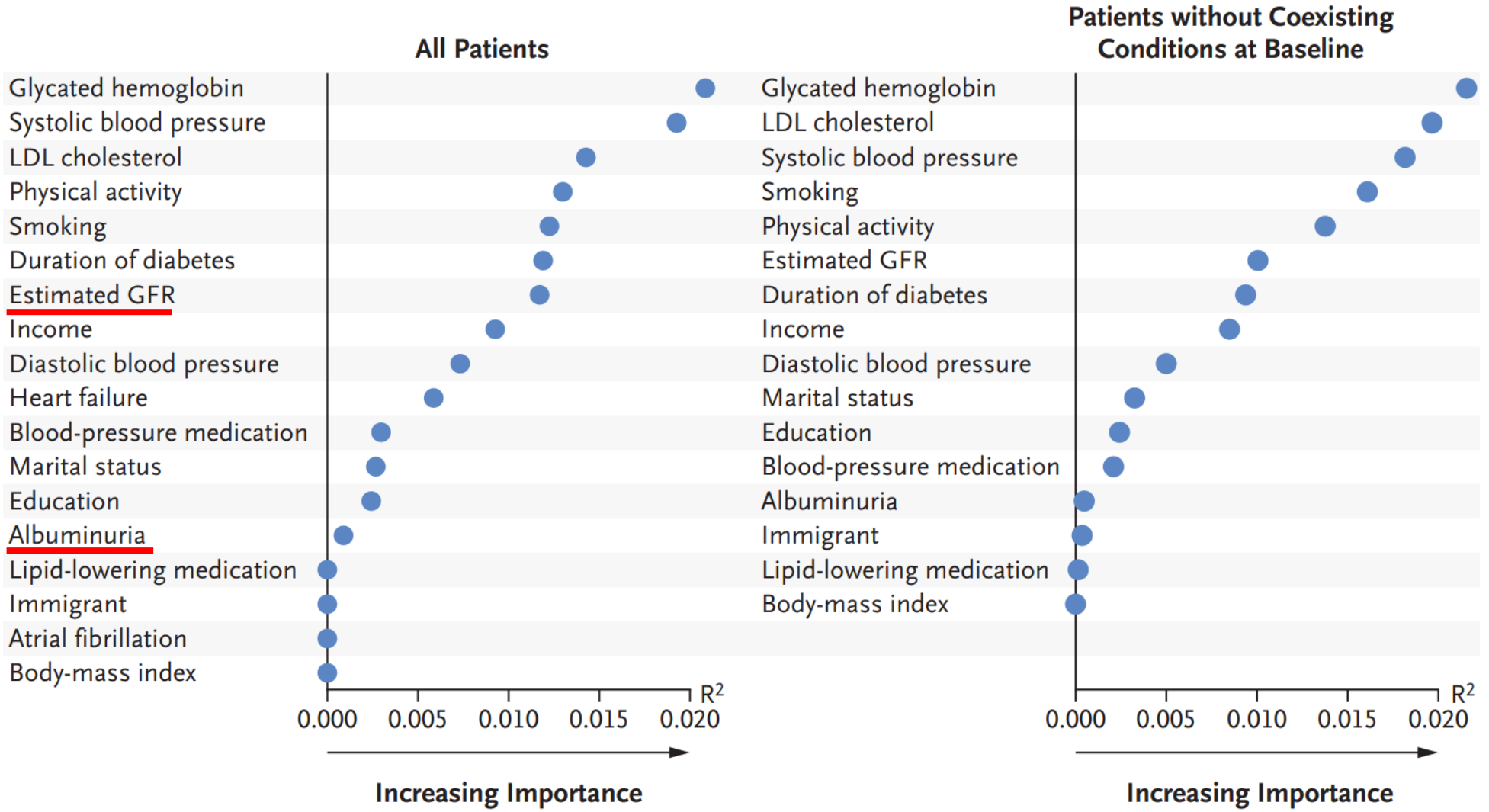




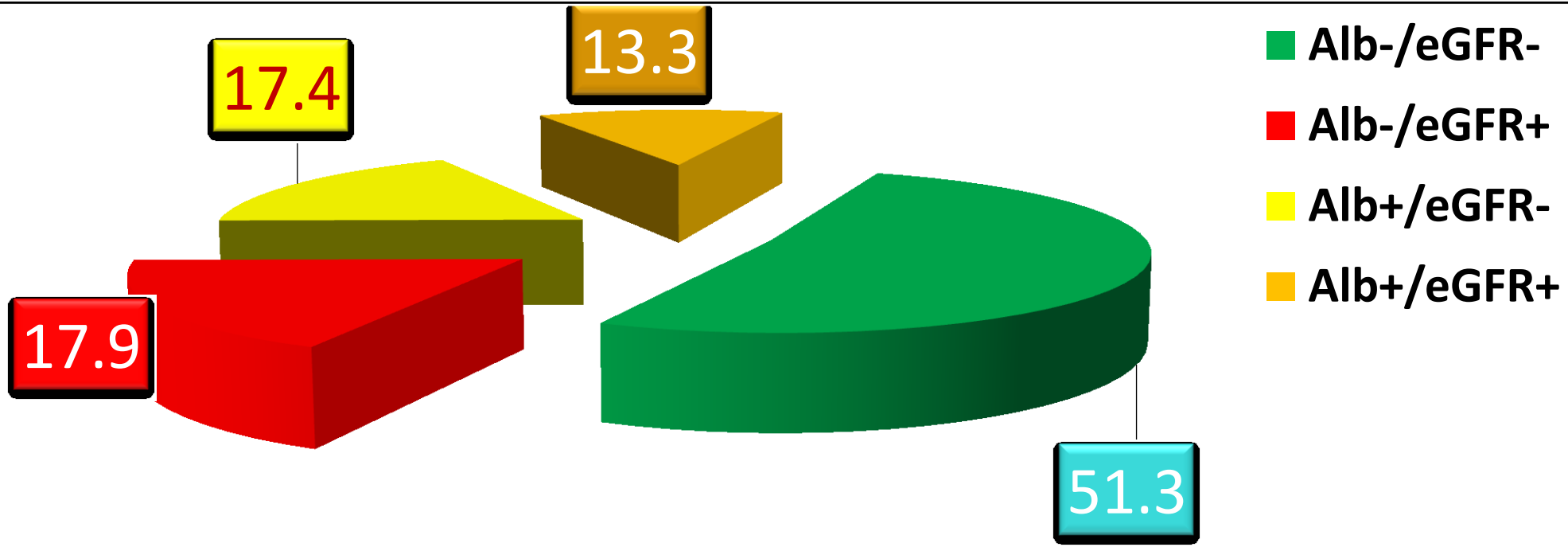
CV, cardiovascular; T2D, type 2 diabetes.

Rawshani A, et al. *N Engl J Med.* 2017;376:1407-1418.

B Acute Myocardial Infarction



Renal phenotypes in n=378.914 patients with type 2 diabetes in Italy



De Cosmo S. et al. on behalf of AMD-Annals, CKJ 2026

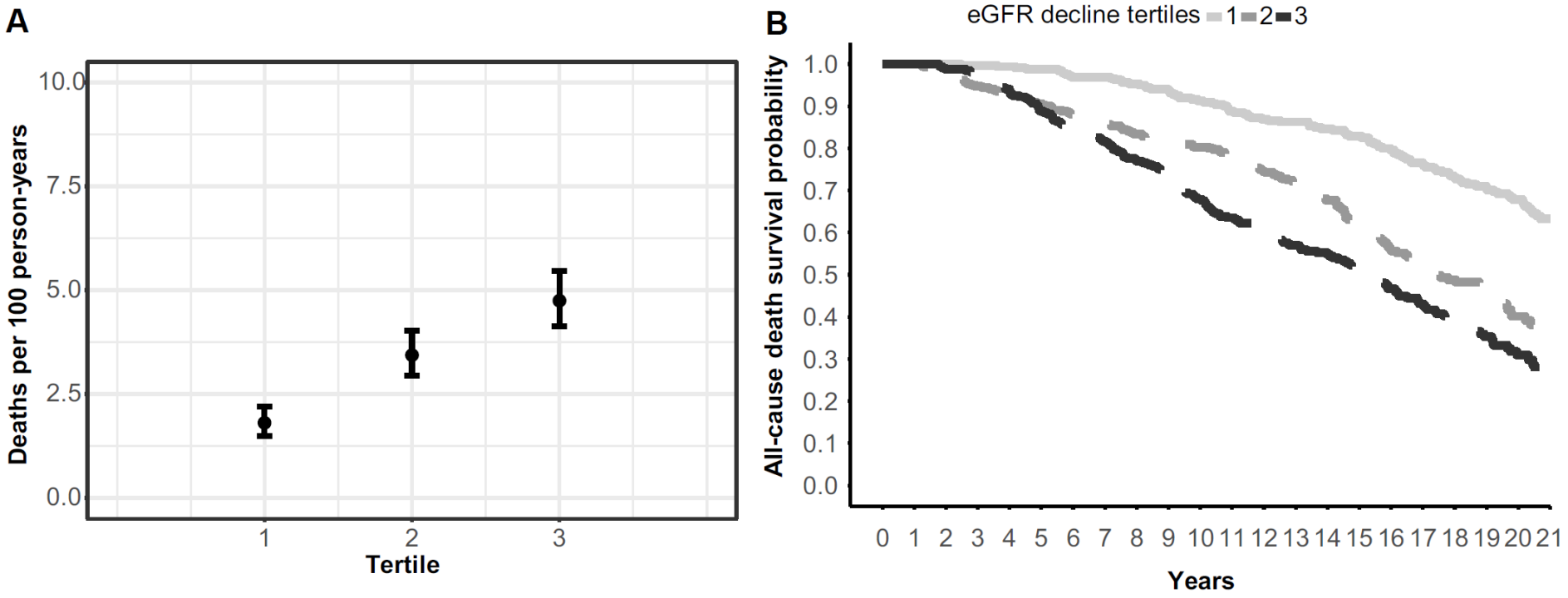


Figure 1. Mortality by tertiles of eGFR decline. (A) Incidence rate of mortality per tertile. The incidence rate is given ×100 person-years after adjustment for age and sex. (B) Kaplan–Meier survival curve: tertile 3 in black, tertile 2 in dark grey, and tertile 1 in light grey.

Among 105,163 (57.7% M) subjects with newly diagnosed T2D, 13,587 (12.9 %) subjects showed a rapid

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Original Article

Prevalence and clinical determin with newly diagnosed type 2 di

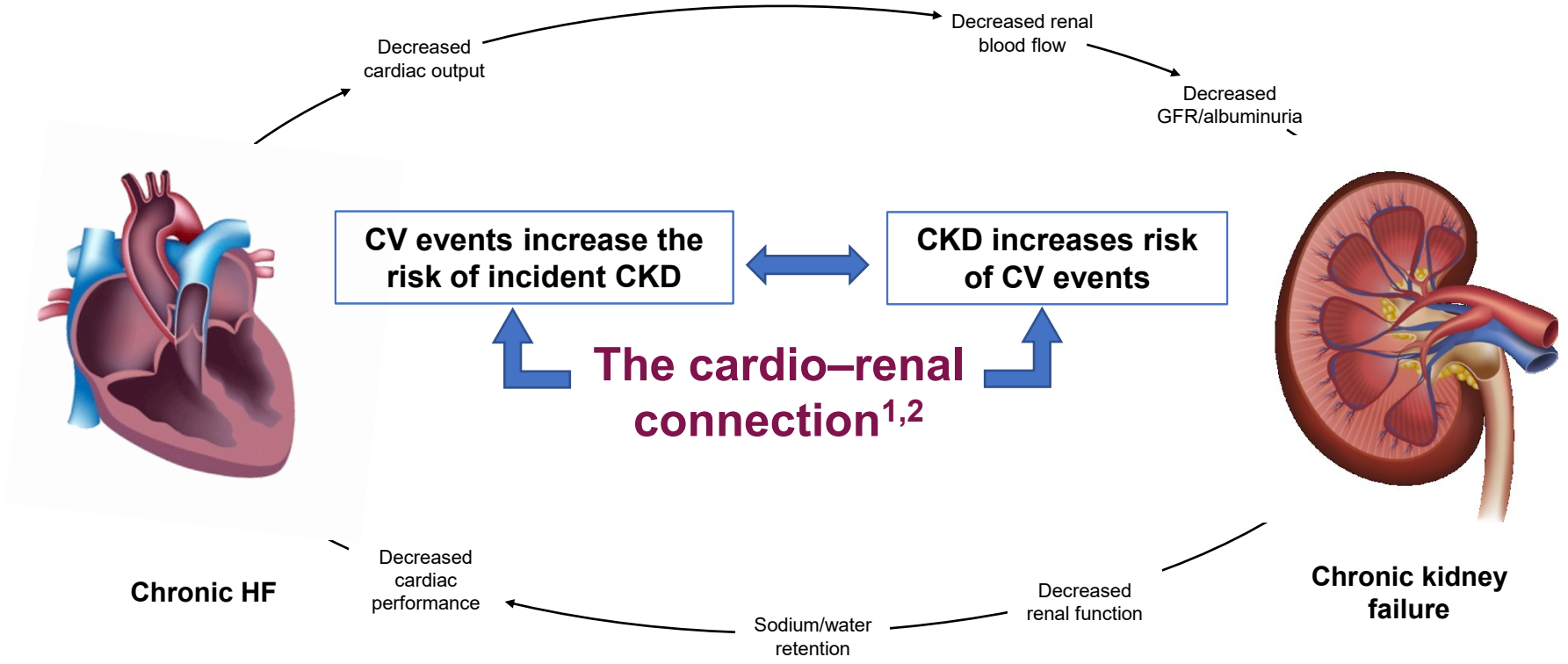
Giuseppina Tiziana Russo [a,1,*], Annalisa Maria Chiara Rossi [b], Pamela Piscitelli [c], Alberto Rocca [f], Valeria Manicardi [g], Gra Antonio Nicolucci [b], Salvatore De Cosmo

Table 2
List of variables related to fast eGFR decline.

Effect	OR	95 % CI
eGFR 30–59 vs. 60–89 mL/min/1.73 m^2	0.41	0.39–0.44
eGFR 90–119 vs. 60–89 mL/min/1.73 m^2	1.37	1.31–1.43
eGFR ≥120 vs. 60–89 mL/min/1.73 m^2	3.26	2.86–3.71
Male vs. Female	0.89	0.86–0.93
Age 55–64 vs. <55 years	1.30	1.23–1.38
Age 65–74 vs. <55 years	1.59	1.50–1.69
Age ≥75 vs. <55 years	2.34	2.19–2.51
BMI 27–29 vs. <27	0.99	0.93–1.05
BMI 30–34 vs. <27	1.07	1.01–1.13
BMI ≥35 vs. <27	1.18	1.11–1.26
HbA1c 7.0–8.0 vs. <7.0 %	1.04	0.99–1.09
HbA1c 8.1–9.0 vs. <7.0 %	1.09	1.02–1.17
HbA1c >9.0 vs. <7.0 %	1.12	1.05–1.19
Smoking status Yes vs. No	1.05	0.98–1.12
Albuminuria Yes vs. No	1.40	1.33–1.48
Retinopathy Yes vs. No	1.53	1.42–1.66
Previous CVE Yes vs. No	1.32	1.17–1.49
Lipid-lowering drugs/statins Yes vs. No	0.98	0.94–1.02
Antihypertensive medication Yes vs. No	1.22	1.17–1.28
Insulin Yes vs. No	1.50	1.43–1.57
Metformin Yes vs. No	1.02	0.97–1.07
Sulphonylureas Yes vs. No	1.18	1.11–1.26
DPP4i Yes vs. No	1.29	1.20–1.39
Glinides Yes vs. No	1.24	1.10–1.40
Glitazones Yes vs. No	0.95	0.81–1.10
GLP1-RAs Yes vs. No	1.18	1.06–1.32
SGLT-2i Yes vs. No	1.04	0.95–1.14
Acarbose Yes vs. No	1.25	1.05–1.47
RAAS inhibitors Yes vs. No	0.97	0.91–1.04



Esiste una stretta e specifica interconnessionefra fisiopatologia cardiaca e renale



1. Damman K, et al. J Am Coll Cardiol 2014;63:853–871;
2. Metra M, et al. Eur Heart J 2012;33:2135–2143; 3. Sarnak MJ, et al. J Am Coll Cardiol 2019;73:1823–1838

La malattia cardiorenale è la più frequente comorbidità nel DMT2

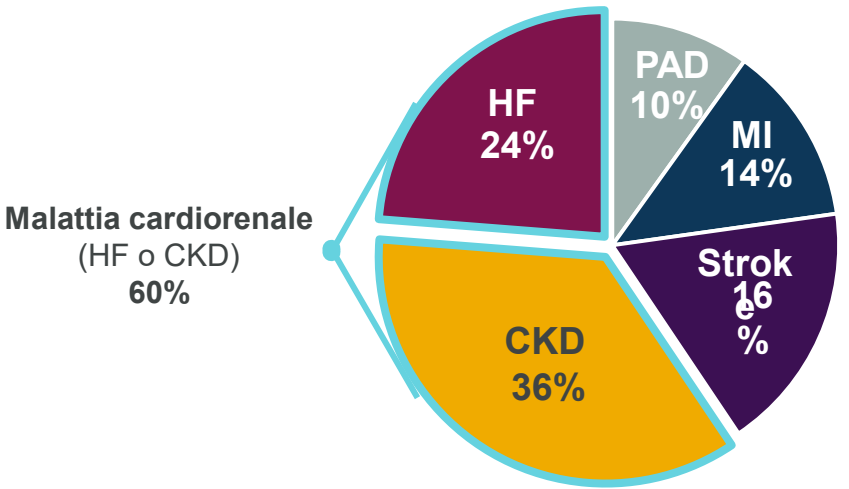
Analisi retrospettiva di dati da >1.1 milioni di pazienti con DMT2

Inizialmente, la maggioranza (66%) dei pazienti erano CVRD-free

Follow-up medio: 4.5 anni

137,081 pazienti (18% della popolazione totale di pazienti CVRD-free) hanno manifestato una CVRD

Prima comorbidità identificata in pazienti CVRD-free con DMT2



Comparata con pazienti senza comorbidità con DMT2, **la malattia cardiorenale è associate ad un aumentato rischio di mortalità** rispetto a Stroke, PAD e MI

DMT2 e malattia cardiorenale sono interconnessi

CKD = chronic kidney disease; CV = cardiovascolare; CVRD = cardiovascular or renal disease; HF = heart failure; MI = myocardial infarction; PAD = peripheral artery disease; DMT2 = diabete mellito di tipo 2.

Birkeland KI et al. *Diabetes Obes Metab.* 2020;22:1607-1618.

Diagnosis of CKD in T2D involves eGFR and UACR screening

CKD is defined as abnormalities in kidney structure or function, present for >3 months, which have implications on health[1]

Early detection of kidney failure facilitates the appropriate diagnosis and treatment of CKD[2]

The clinical diagnosis of CKD in a patient with diabetes is based on:[1–4]

The presence of albuminuria*
(UACR ≥30 mg/g)

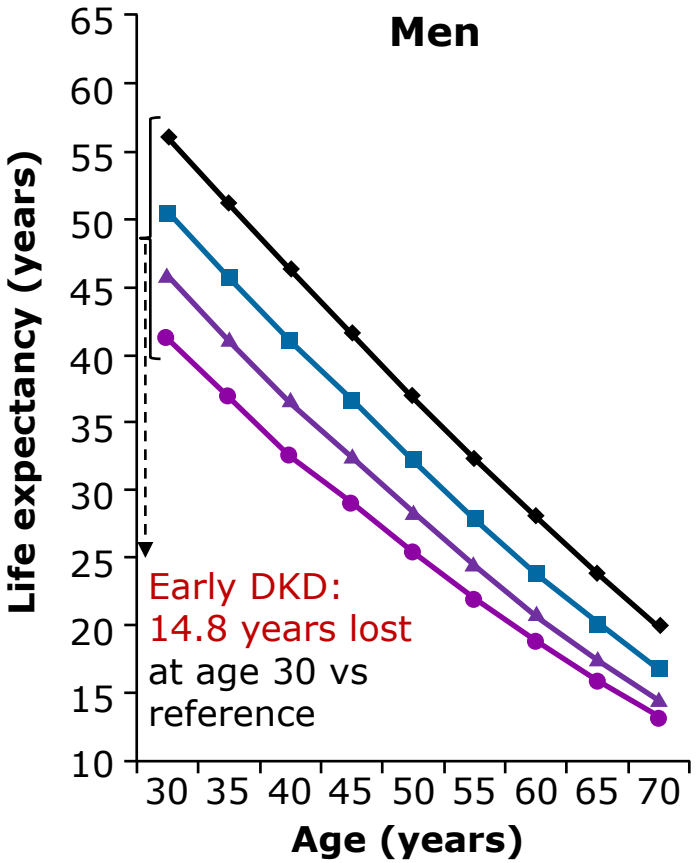
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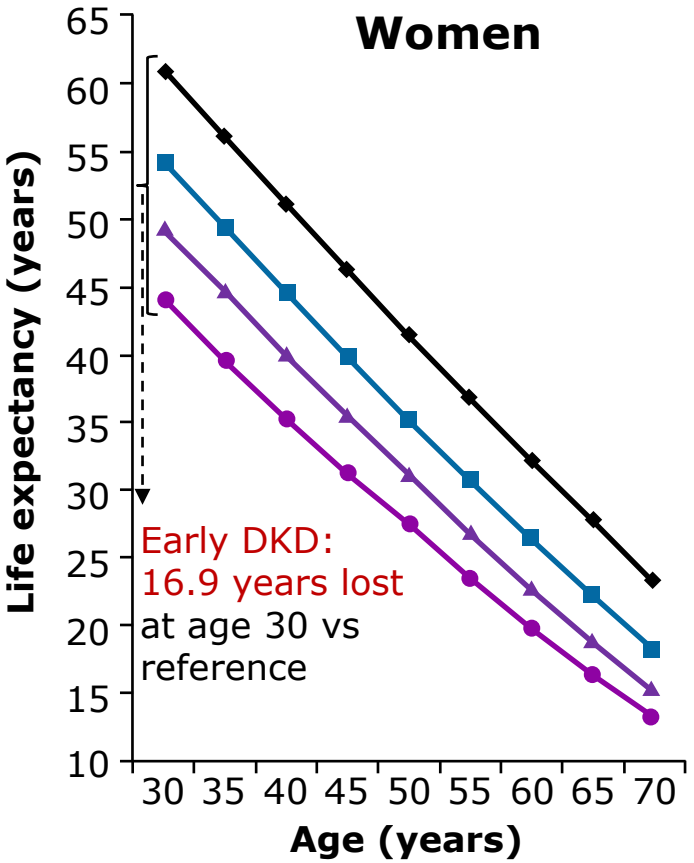
Reduced kidney function
(eGFR <60 ml/min/1.73 m^2)

in the absence of signs or symptoms of other primary causes of kidney damage

1. Kidney Disease Improving Global Outcomes. *Kidney Int Suppl* 2013;3:1–163; 2. Levey AS, *et al. JAMA* 2015;313:837–846 3. National Kidney Foundation. *Am J Kidney Dis* 2007;49(Suppl 2):S1–S180; 4. American Diabetes Association. *Diabetes Care* 2022;45(Suppl 1):S175–S184

Diabetic Kidney Disease (DKD) Shortens Life Span by 16 Years





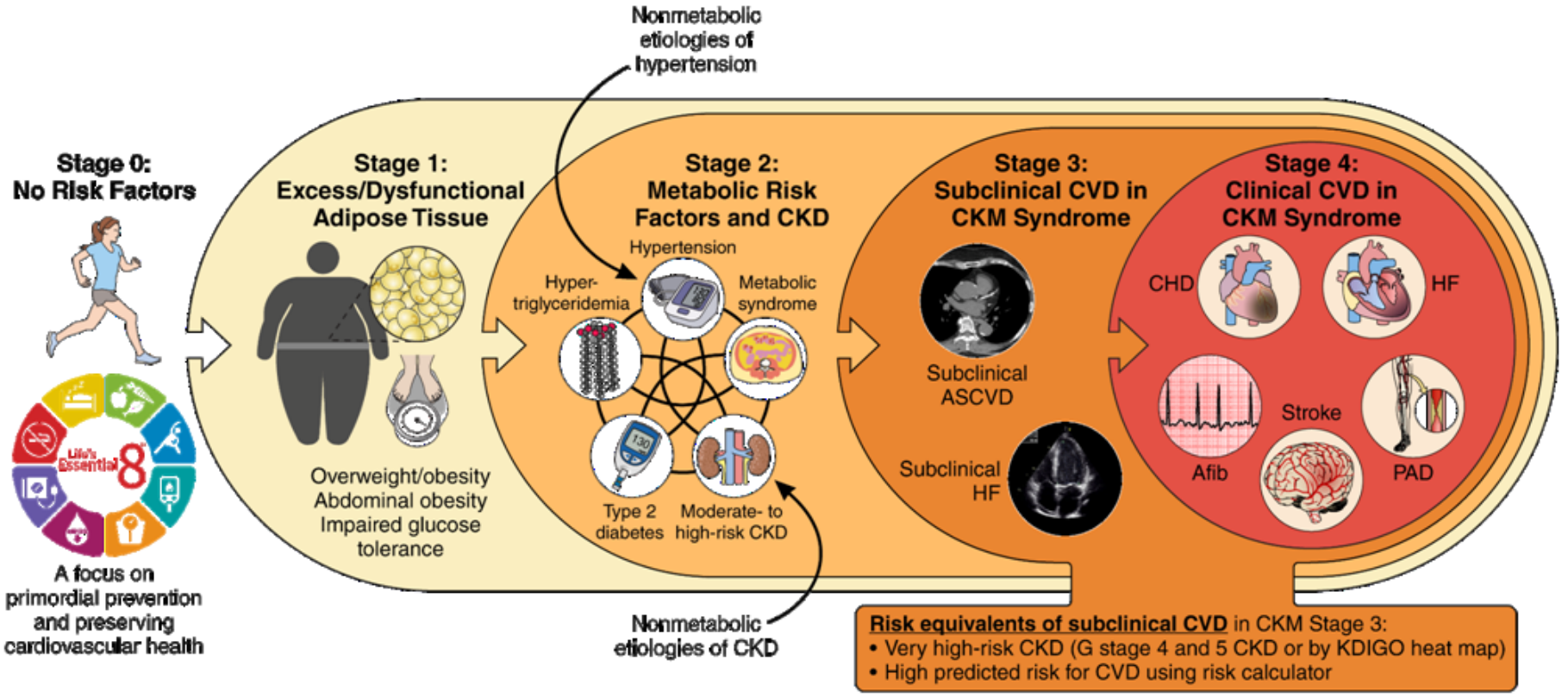
Life span loss with:

- Early CKD: 6 years
- Diabetes: 10 years
- Early DKD: 16 years

Reference
Early CKD
Diabetes
Early DKD

Wen CP, Kidney Int 2017

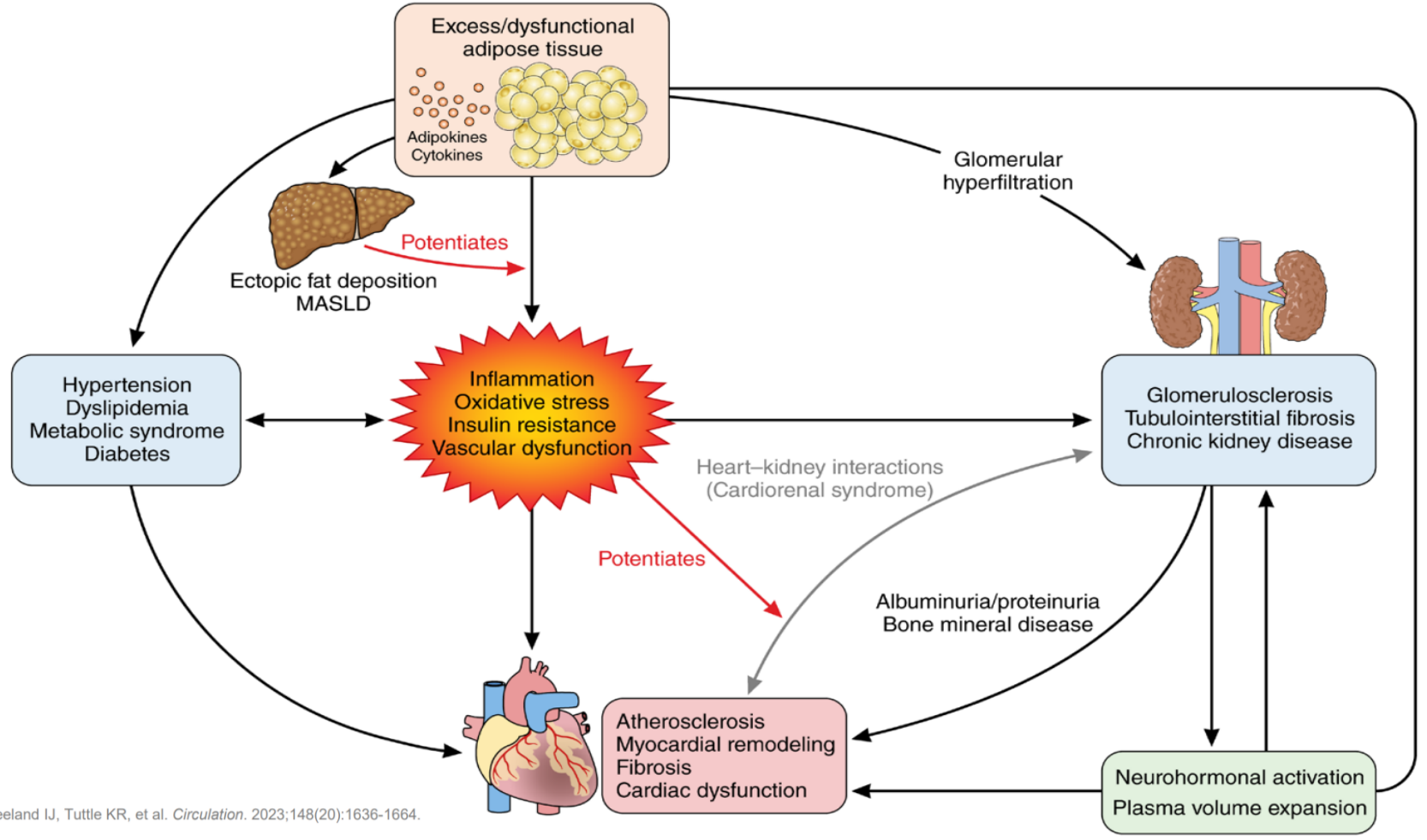
Stages of Cardiovascular-Kidney-Metabolic Syndrome



Abbreviations: Afib indicates atrial fibrillation; ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; CKD, chronic kidney disease: CKM, cardiovascular-kidney-metabolic; CVD, cardiovascular disease; HF, heart failure; KDIGO, Kidney Disease Improving Global Outcomes; and PAD, peripheral artery disease.

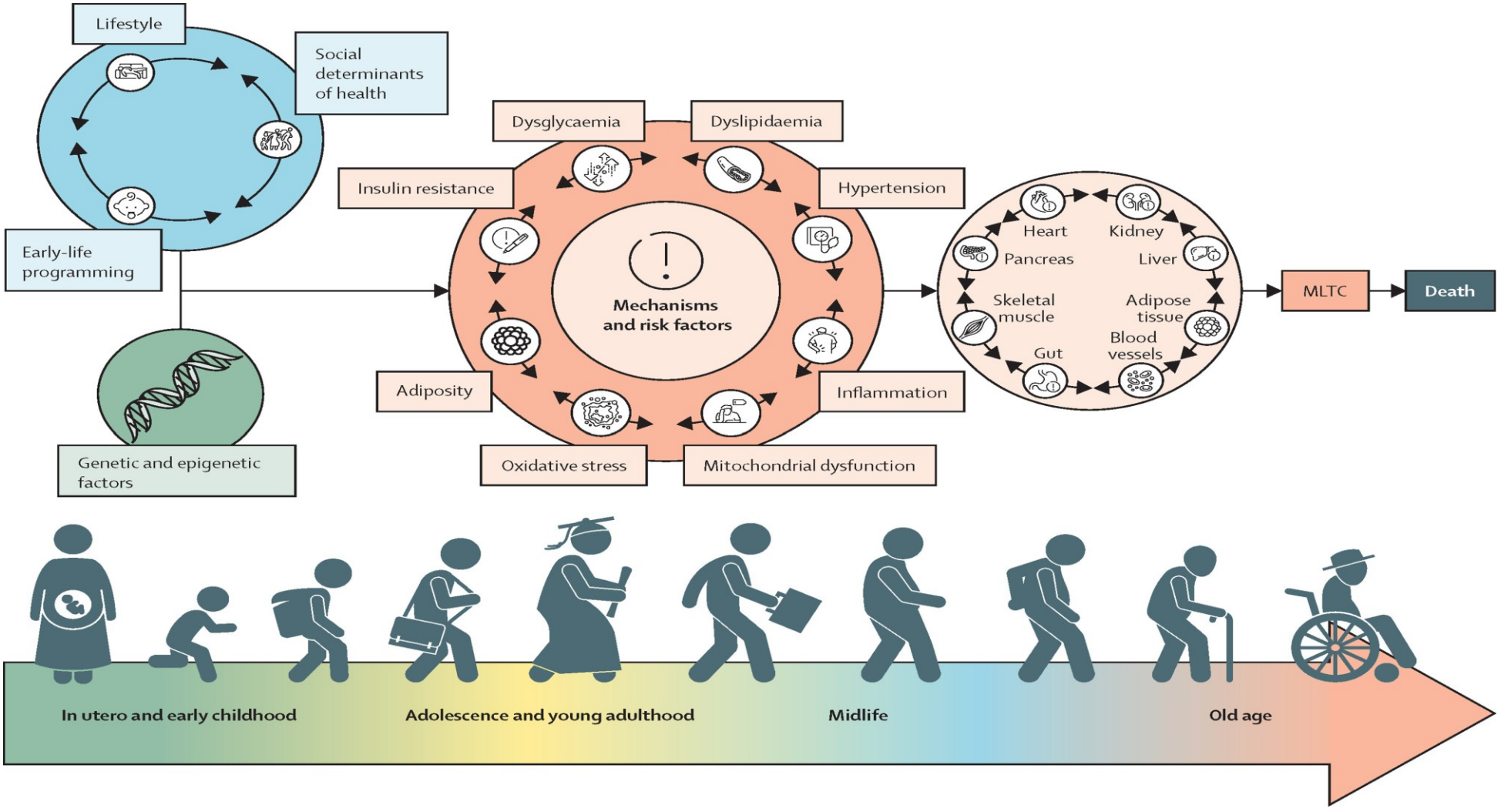
Ndumele, CE et al, *Circulation* 2023

CKM Syndrome: Multisystem Consequence



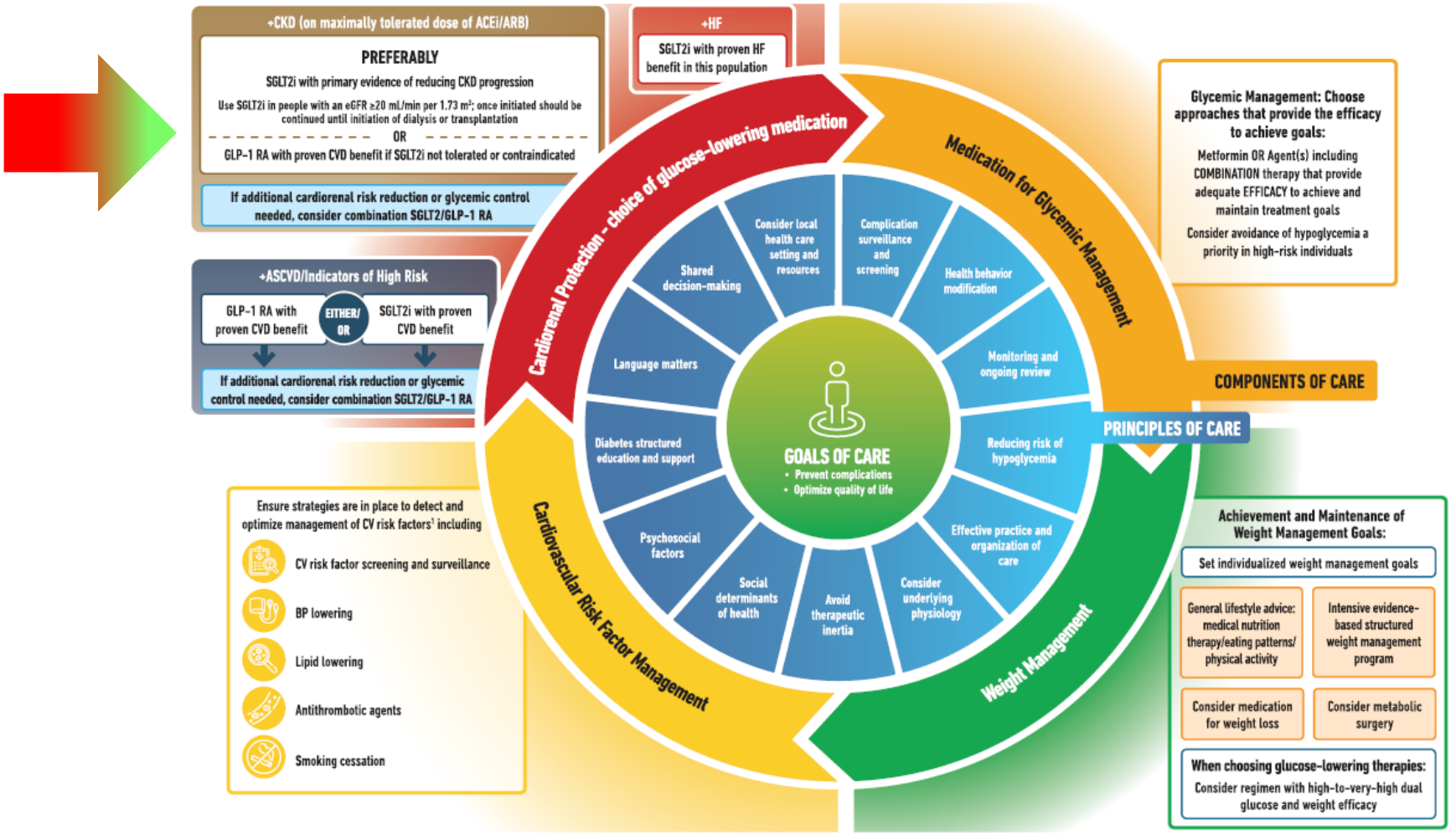
Ndumele CE, Neeland IJ, Tuttle KR, et al. *Circulation*. 2023;148(20):1636-1664.

Biological and mechanistic pathways of cardiometabolic multiple long-term conditions



Lancet 2026; 407: 2655–67

HOLISTIC PERSON–CENTERED APPROACH TO T2DM MANAGEMENT



Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA)and the European Association for the Study of Diabetes (EASD) Diabetes Care 2022;45(11):2753–2786 | https://doi.org/10.2337/dci22-0034





HEALTHY LIFESTYLE BEHAVIOURS | **DIABETES SELF-MANAGEMENT EDUCATION** | **ADDRESS SOCIAL DETERMINANTS OF HEALTH (SDOH)**

To avoid therapeutic inertia, reassess and modify treatment regularly (e.g. 3–6 months)

American Diabetes Association. | EASD European Association for the Study of Diabetes

GOAL: PREVENT LONGITUDINAL COMPLICATIONS ASSOCIATED WITH T2D

Incorporate SGLT2i or/and GLP-1-based therapy§ early to modify disease and complication risk*

PERSONALISE APPROACH

Achieve and maintain glycaemic goals

Treatment plan that provides adequate EFFICACY to achieve and maintain glycaemic treatment goals, including combination therapy

Efficacy for glucose lowering

- **Very high:** tirzepatide, semaglutide (sq), dulaglutide (high dose), insulin, combination therapy
- **High:** GLP-1RA (not listed above), metformin, pioglitazone, SGLT2i, sulfonylurea
- **Intermediate:** DPP-4i, alpha glucosidase inhibitors

If glycaemia is above goal or significant hypoglycaemia, consider technology (e.g., CGM) to identify therapeutic gaps and tailor therapy

Weight management

Achieve and maintain weight management goals:

Set individualised weight management goals

- General lifestyle behaviour advice
- Intensive evidence-based structured weight management programme
- Consider medication for weight loss
- Consider metabolic surgery

When choosing glucose-lowering therapies: Consider treatment plan with dual glucose and weight efficacy

Efficacy for weight loss in T2D

- **Highest:** Tirzepatide
- **Very high:** Semagutide
- **High:** Dulaglutide, liraglutide
- **Intermediate:** GLP-1 RA (not listed above), SGLT2i
- **Neutral:** Metformin, DPP-4i

+ASCVD

+ASCVD/indicators of high CVD risk

GLP-1-based therapies§ with proven CVD benefit and/or SGLT2i with proven CVD benefit‡

- For individuals on GLP-1-based therapy§, consider adding SGLT2i with proven CVD benefit or vice versa based on indication
- Pioglitazone

+CKD†

+CKD

SGLT2i with primary evidence of reducing CKD progression and/or GLP-1-based therapy§ with proven CKD benefit‡

For individuals on SGLT2i, consider incorporating an GLP-1-based therapy§ or vice versa based on indication

+HF

+HFrEF or HFpEF

SGLT2i with proven HF benefit

+HFpEF and obesity

SGLT2i and/or GLP-1-based therapy§‡

+MASLD or MASH

Agents with proven or potential benefit in MASLD or MASH

- GLP-1-based therapy§ and/or pioglitazone
- SGLT2i

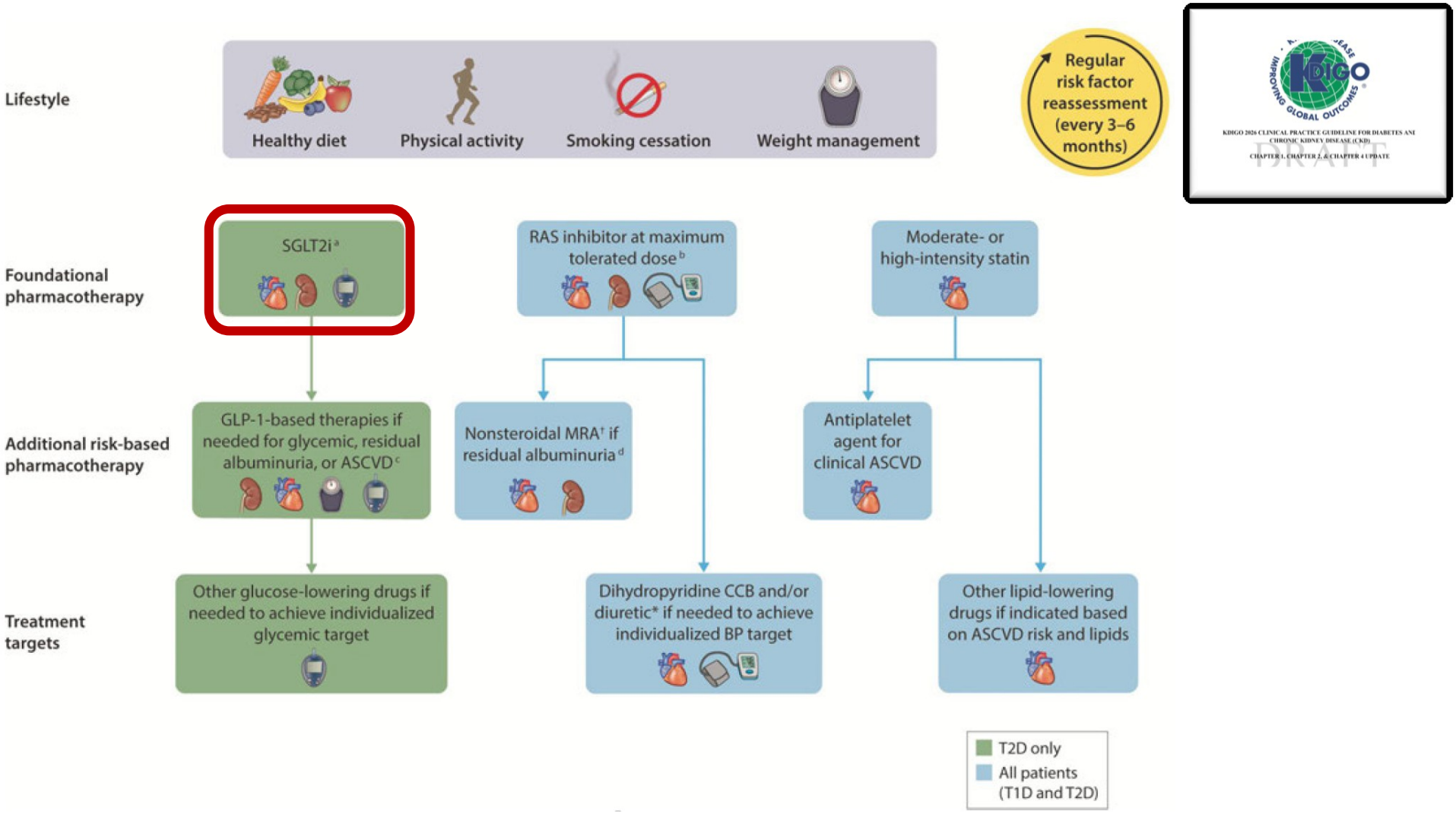
Use insulin in the setting of decompensated cirrhosis

Iterative review of glycaemic, weight, and cardio-kidney care goals, addressing identified barriers

Reconsider DSMES to support self-efficacy and continue to address SDOH and other factors that impact on achievement of goals

DRAFT

Holistic approach for improving outcomes in people with diabetes and CKD



SGLT2i: The largest updated meta-analysis

Impact of diabetes on the effects of sodium glucose co-transporter-2 inhibitors on kidney outcomes: collaborative meta-analysis of large placebo-controlled trials

Diabetes Mellitus type 2

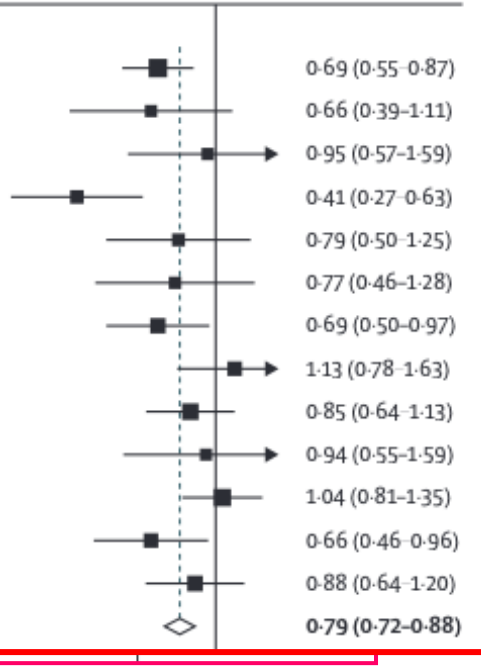
The Nuffield Department of Population Health Renal Studies Group and the SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium**

Cardiovascular death or hospitalisation for heart failure*

		Mean baseline eGFR, mL/min per 1·73m²	Events/partici… SGLT2 inhibito…
Diabetes			
High atherosclerotic cardiovascular risk trials	80		1490/24563
Stable heart failure trials†	61		923/5046
Chronic kidney disease trials	45		643/10474
Subtotal: diabetes	**67**		**3056/40691**
SCORED			
DAPA–CKD			
EMPA–KIDNEY			
Subtotal: diabetes			

…ey injury

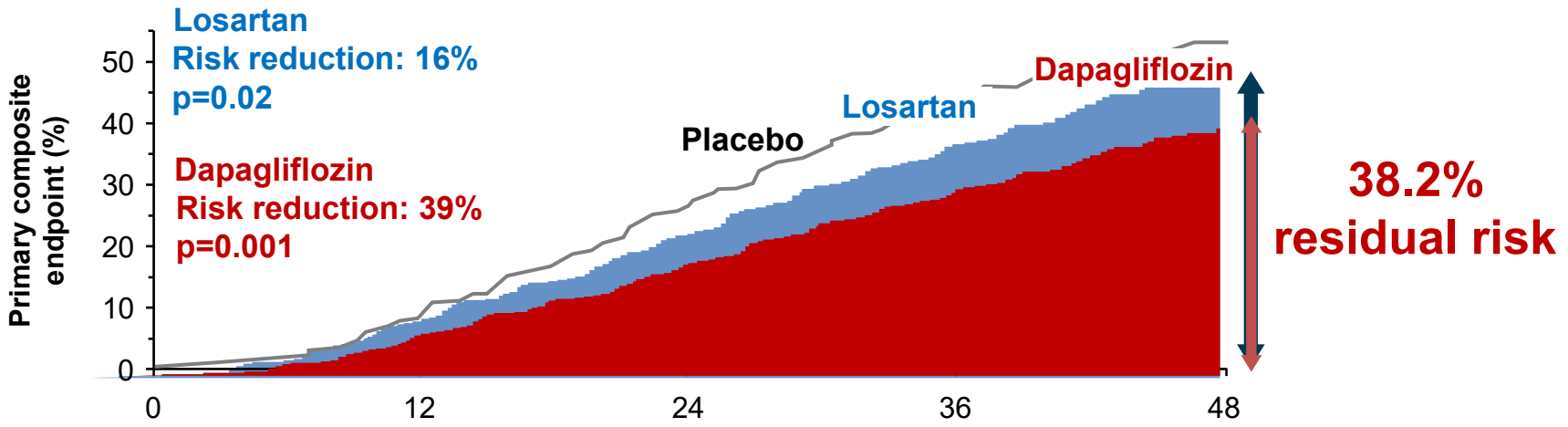
		…cipants SGLT2 inhibitor	…cipants Placebo	Event rate per 1000 patient years SGLT2 inhibitor	Event rate per 1000 patient years Placebo	RR (95% CI)
Diabetes						
DECLARE–TIMI 58	85	325/8574	175/8569	3·5	4·9	0·69 (0·55–0·87)
CANVAS Program	77	30/5790	28/4344	1·6	2·5	0·66 (0·39–1·11)
VERTIS CV	76	42/5493	22/2745	2·5	2·7	0·95 (0·57–1·59)
EMPA–REG OUTCOME	74	45/4687	37/2333	2·5	6·2	0·41 (0·27–0·63)
DAPA–HF	63	31/1073	39/1063	19	24	0·79 (0·50–1·25)
EMPEROR–REDUCED	61	26/927	33/929	21	27	0·77 (0·46–1·28)
EMPEROR–PRESERVED	60	60/1466	84/1472	20	28	0·69 (0·50–0·97)
DELIVER	60	59/1578	52/1572	17	15	1·13 (0·78–1·63)
CREDENCE	56	86/2200	98/2197	17	20	0·85 (0·64–1·13)
SOLOIST–WHF	51	25/605	27/611	55	59	0·94 (0·55–1·59)
SCORED	44	116/5291	111/5286	16	16	1·04 (0·81–1·35)
DAPA–CKD	44	48/1455	69/1451	15	22	0·66 (0·46–0·96)
EMPA–KIDNEY	36	73/1525	81/1515	24	27	0·88 (0·64–1·20)
Subtotal: diabetes	**67**	**66/40664**	**856/34087**	..	..	**0·79 (0·72–0·88)**



Lancet, November 6, 2022

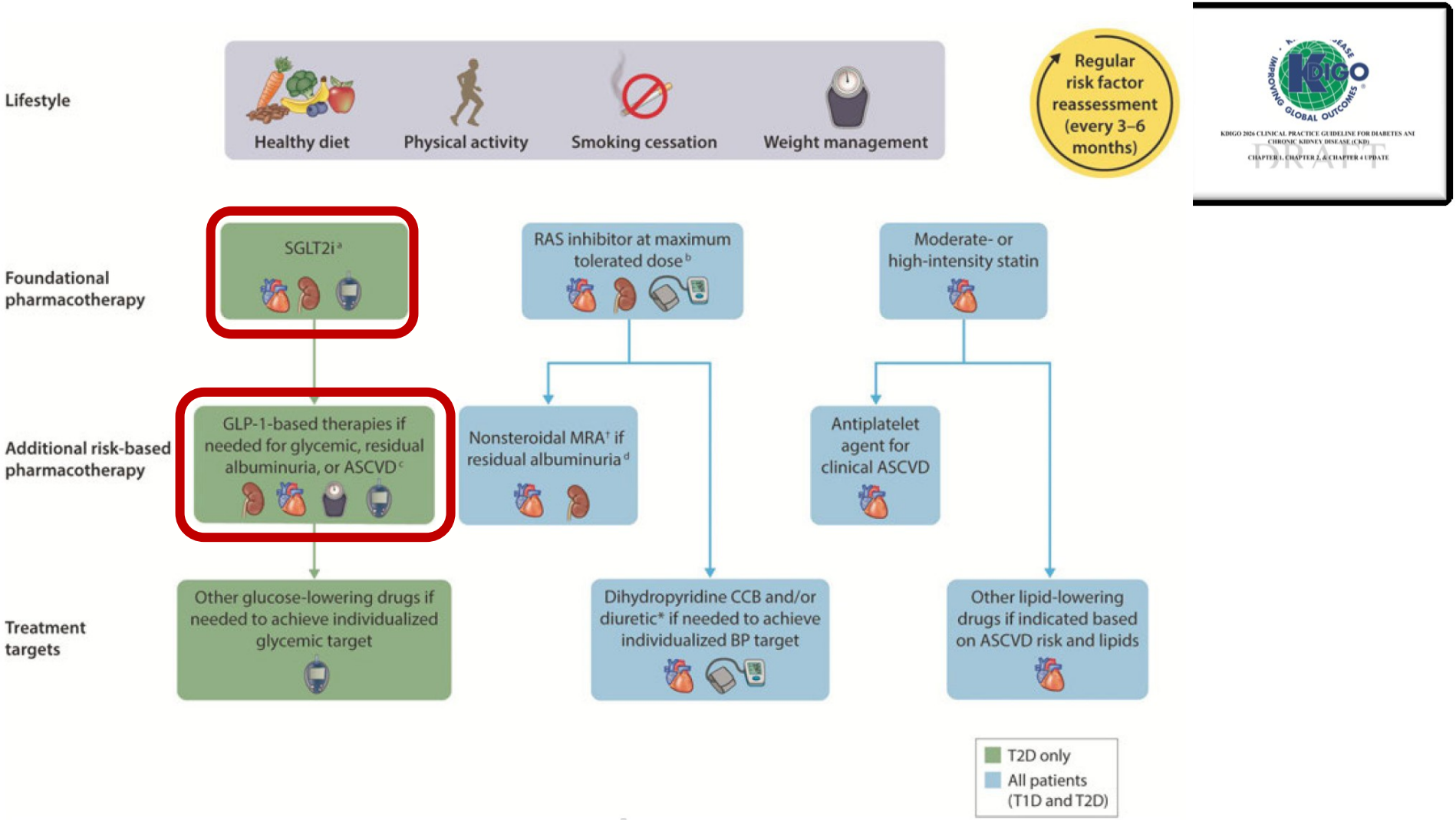
RENAAL and DAPA-CKD

Risk of 2xsCr, ESKD, or death in patients with T2D and overt nephropathy



Brenner BM, et al. N Engl J Med 2001; Heerspink HJL et al. N Engl J Med. 2020

Holistic approach for improving outcomes in people with diabetes and CKD



Primary kidney endpoint

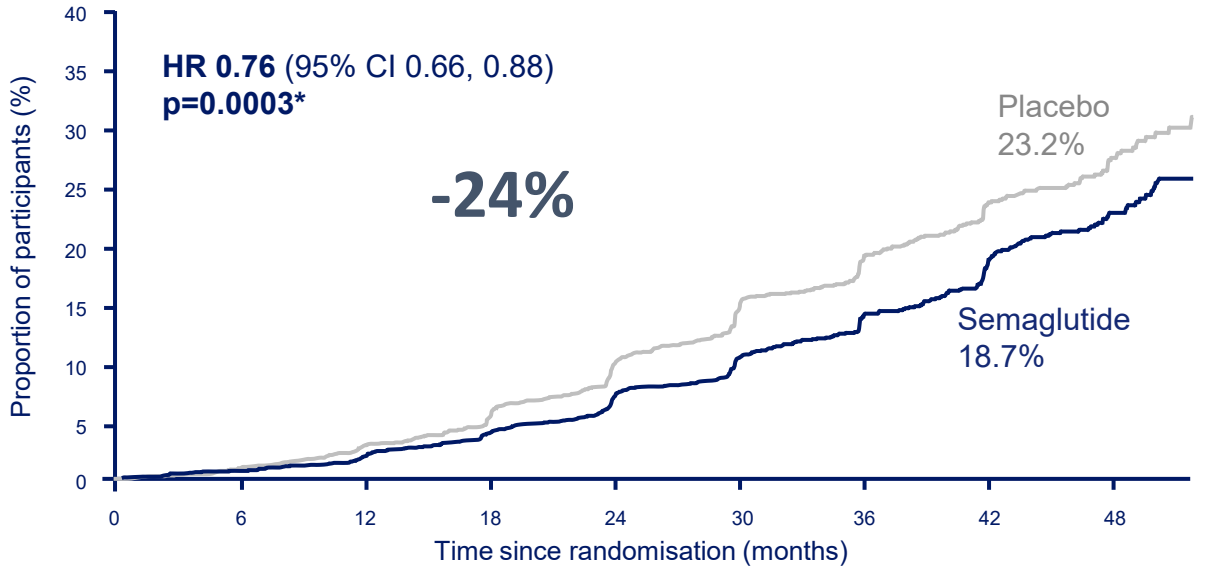
FLOW
semaglutide | renal outcomes trial

Semaglutide demonstrated a 24% risk reduction of a composite outcome, incl. kidney disease progression, CV and kidney death in people with CKD and T2D

Time to first occurrence of a composite endpoint consisting of:

- Onset of persistent ≥50% reduction in eGFR compared with baseline
- Onset of persistent eGFR <15 mL/min/1.73 m^2
- Initiation of chronic renal replacement therapy (dialysis or kidney transplantation)
- Renal death
- CV death

First composite kidney event: Primary outcome



Semaglutide	1,767	1,738	1,693	1,640	1,572	1,489	1,131	742	392
Placebo	1,766	1,736	1,682	1,605	1,516	1,408	1,048	660	354

*Full analysis set. Data from the in-trial period. * Superiority if p value <0.0322*
Numbers shown in the lower panels represent the number of participants at risk. CI, confidence interval; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HR, hazard ratio. Perkovic V, et al. N Engl J Med. 2024: DOI: 10.1056/NEJMoa2403347

Nephrol Dial Transplant, 2026, **41**, 681–691
https://doi.org/10.1093/ndt/gfaf193
Advance access publication date: 22 September 2025

The effect of GLP-1 receptor agonists on renal outcomes: a systematic review and meta-analysis

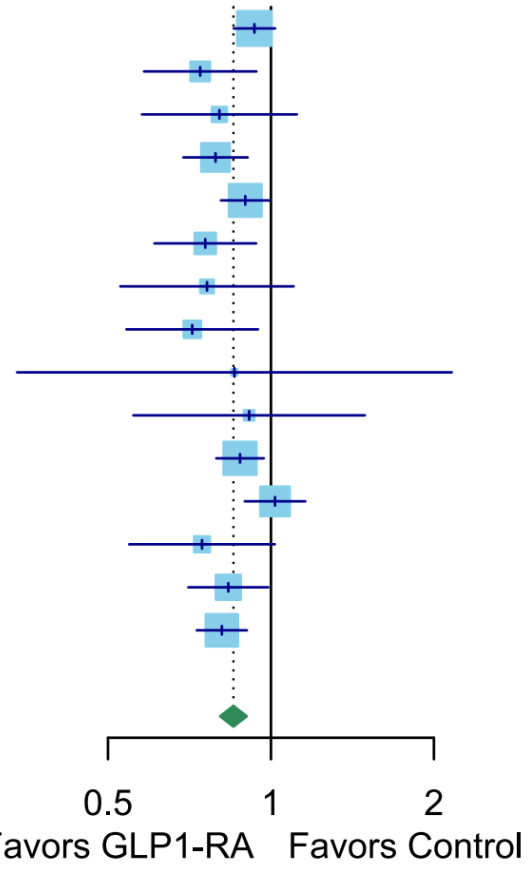
Takaya Sasaki[1,2], Samantha My-Linh Giang[3,4], Jiajia Wu[5], Takashi Yokoo[2], Martin Gallagher[1], Rinaldo Bellomo[6] and Amanda Ying Wang[1,4,7]

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[4]Concord Clinical School, Faculty of Medicine, University of Sydney, Sydney, NSW, Australia
[5]Department of Nephrology, Sir Run Run Shaw Hospital, Zhejiang University, Hangzhou, China
[6]Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), School of Public Health and Preventative Medicine, Monash University, Melbourne, Australia
[7]The Faculty of Medicine and Health Sciences, Macquarie University, Sydney, NSW, Australia
Correspondence to: Amanda Ying Wang; E-mail: awang@georgeinstitute.org.au

(A) MACE

Study	GLP1-RA Events	GLP1-RA Total	Control Events	Control Total	RR	[95% CI]	Weight
EXCEL	839	7356	905	7396	0.93	[0.85; 1.02]	13.9%
SUSTAIN6	108	1648	146	1649	0.74	[0.58; 0.94]	4.4%
PIONEER6	61	1591	76	1592	0.80	[0.58; 1.12]	2.6%
HARMONY	338	4731	428	4732	0.79	[0.69; 0.91]	9.4%
REWIND	594	4949	663	4952	0.90	[0.81; 0.99]	12.4%
AMPLITUDE-O	189	2717	125	1359	0.76	[0.61; 0.94]	5.2%
SURPASS4	47	995	62	1000	0.76	[0.53; 1.10]	2.1%
STEP1	107	1306	75	655	0.72	[0.54; 0.95]	3.4%
STEP2	12	807	7	403	0.86	[0.34; 2.16]	0.4%
STEP3	40	407	22	204	0.91	[0.56; 1.49]	1.2%
LEADER	608	4668	694	4672	0.88	[0.79; 0.97]	12.6%
ELIXA	406	3034	399	3034	1.02	[0.89; 1.16]	10.1%
GRADE	48	1262	193	3785	0.75	[0.55; 1.02]	2.9%
FLOW	212	1767	254	1766	0.83	[0.70; 0.99]	7.3%
SELECT	569	8803	701	8801	0.81	[0.73; 0.90]	12.1%
Random effects model		**46041**		**46000**	**0.85**	**[0.81; 0.90]**	**100.0%**

Heterogeneity: I^2 = 27%, τ^2 = 0.0039, p = 0.16



Kidney Composite Outcome

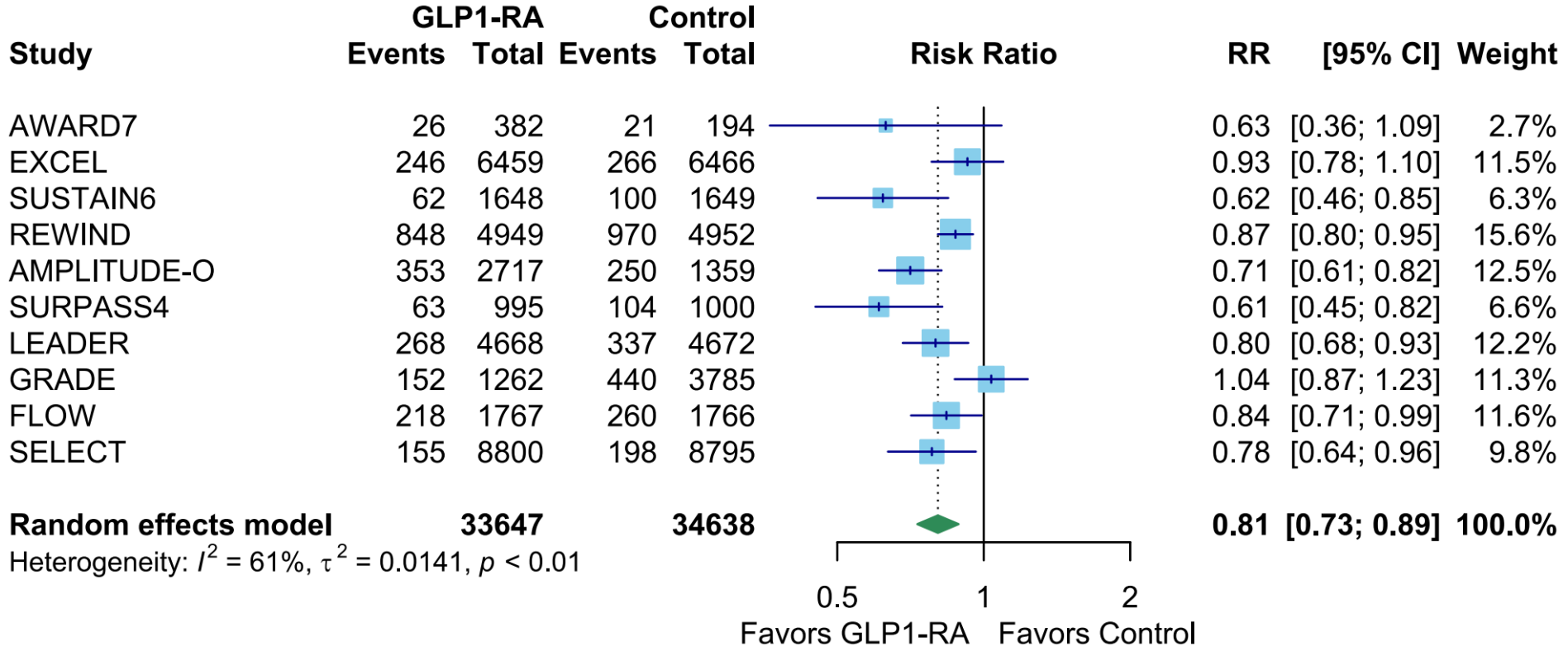
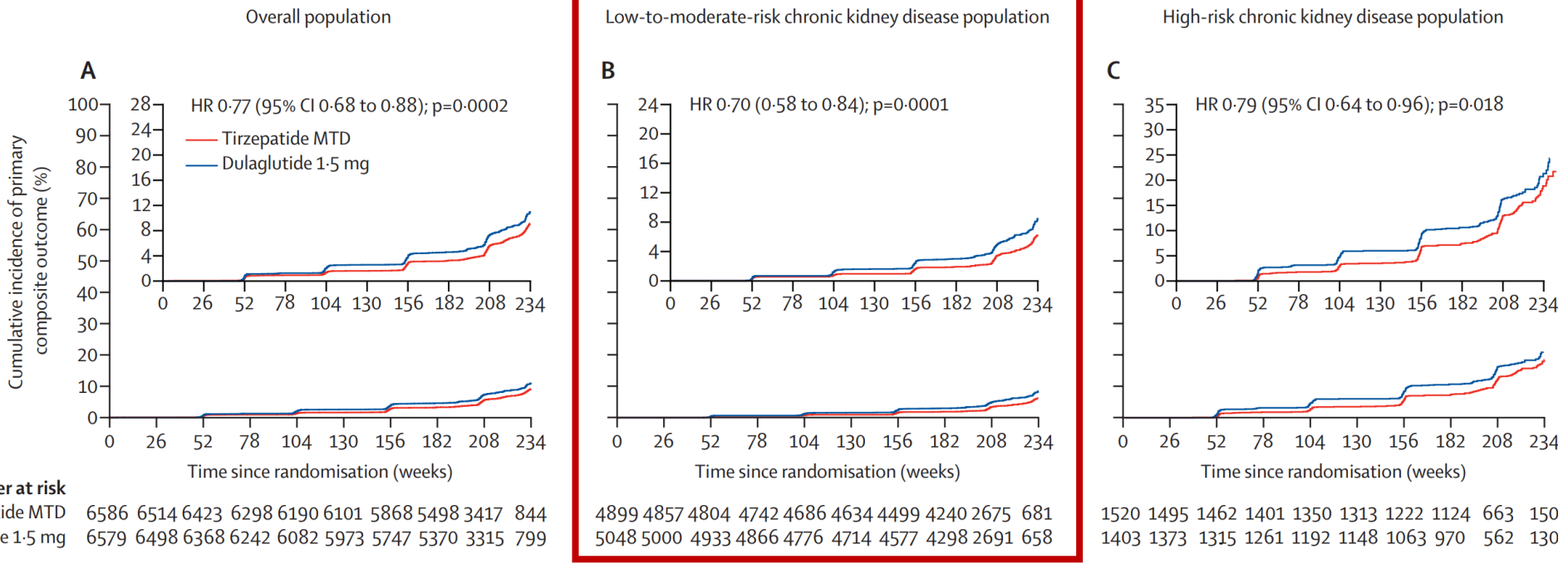


Figure 2: The effect of GLP1-RAs on kidney composite outcomes. Kidney composite outcomes are defined as combined renal outcomes including kidney dysfunction as defined in each individual study.

A comparison of the effects of tirzepatide and dulaglutide on major kidney events in people with type 2 diabetes: pre-specified exploratory analyses of the SURPASS-CVOT trial

Sophia Zoungas, David D'Alessio, Imre Pavo, Deepak L Bhatt, John B Buse, Stefano Del Prato, Steven E Kahn, A Michael Lincoff, Darren K McGuire, Michael A Nauck, Steven E Nissen, Naveed Sattar, Bernard Zinman, Antonio Ceriello, Lars Stechemesser, Ann Verhaegen, Jonathan C Broder, Rory Wolfe, Debra Miller, Hiroshi Nishiyama, Xiaomei Wang, Govinda Weerakkody, Russell J Wiese, Stephen J Nicholls

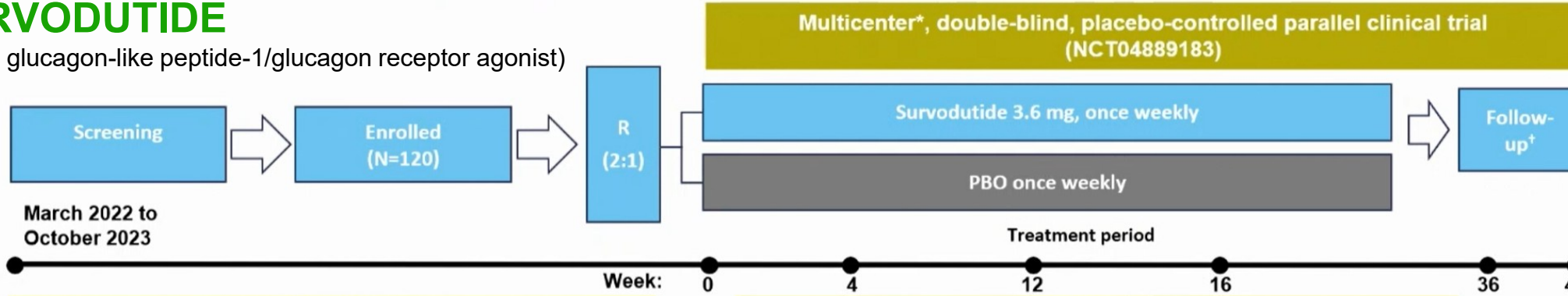


Lancet Diabetes Endocrinol 2026

ARTIST: Investigator Initiated Randomized Placebo Controlled Trial in Participants with CKD (NCT07206290)

SURVODUTIDE

(a dual glucagon-like peptide-1/glucagon receptor agonist)



Population

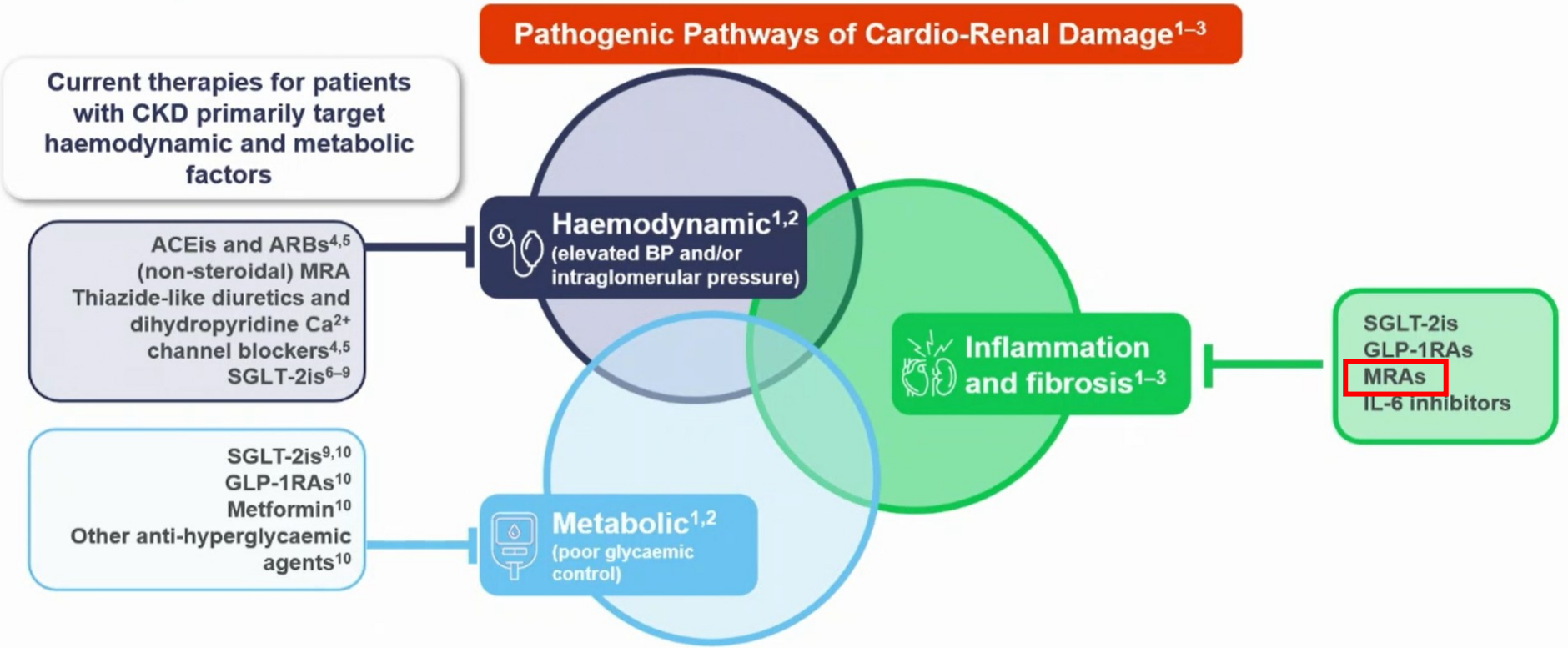
Inclusion criteria	Exclusion criteria
• Age (18–75 years) • BMI ≥ 23 kg/m² • CKD • UACR >30 and ≤3500 mg/g • eGFR ≥20 and <90 mL/min/1.73m² • Stable dose of ACEi or ARB for ≥4 weeks prior to randomization • If using SGLT2i or MRA, stable dose for ≥8 weeks	• T1DM • ADPKD, lupus nephritis, or ANCA-associated vasculitis • Elevated lipase (>3* ULN) • History of Pancreatitis • Calcitonin levels >100 pg/mL • Systolic BP ≥ 180mmHg • Hba1c >10.5%

Outcomes

Primary	Secondary	Exploratory	Safety
• Percentage change from baseline in UACR	• Changes in: – mGFR – MRI – Body weight – SBP	• Changes in: – hsCRP – NTproBNP – RBF – Exploratory biomarkers	• Number of: – AEs – AESIs – SAEs

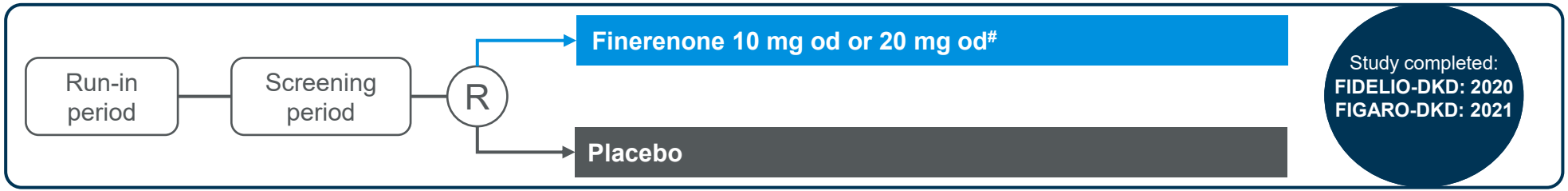
*Conducted in hospitals in the Netherlands, Germany, Spain and Australia. †A follow-up visit was scheduled 4 weeks after the last treatment period to assess off-treatment effects.
ACEi, angiotensin-converting enzyme inhibitor; AE, adverse event; AESI, adverse event of special interest; ANCA, antineutrophil cytoplasmic antibody; ARB, angiotensin II receptor blocker; CKD, chronic kidney disease; DAPA, dapagliflozin; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; mGFR, measured glomerular filtration rate; PBO, placebo; R, randomized; SAE, serious adverse event; SBP, systolic blood pressure, T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus

Metabolic, Hemodynamic and Inflammatory pathways implicated in the pathogenesis of Cardiovascular and Renal Diseases



1. Alicic RZ, et al. Clin J Am Soc Nephrol 2017;12:2032–2045; 2. Mora-Fernández C, et al. J Physiol 2014;18:3997; 3. Bauersachs J, et al. Hypertension 2015;65:257–263; 4. American Diabetes Association. Diabetes Care 2022;45(Suppl 1):S175–S184; 5. American Diabetes Association. Diabetes Care 2022;45(Suppl 1):S144–S174; 6. Kidokoro K, et al. Circulation 2019:140;303–315; 7. Zelniker TA & Braunwald E. J Am Coll Cardiol 2018;72:1845–1855; 8. Heerspink HJ, et al. Circulation 2016;134:752–772; 9. Zelniker TA & Braunwald E. J Am Coll Cardiol 2020;75:422–434; 10. American Diabetes Association. Diabetes Care 2022;45(Suppl 1):S125–S143; 11. Agarwal R, et al. Eur Heart J 2021;42:152–162; 12. Agarwal R, et al. Nephrol Dial Transplant 2022;37:1014–1023

FIDELIO-DKD and FIGARO-DKD are investigating effects of finerenone on kidney and CV outcomes in patients with CKD and T2D



	FIDELIO-DKD[1]	FIGARO-DKD[2]
Clinical efficacy primary endpoint	**Composite endpoint**: time to onset of kidney failure* or decrease of eGFR ≥40% from baseline or death due to kidney disease	**Composite endpoint**: time to CV death, non-fatal MI, non-fatal stroke or hospitalisation for HF
Key secondary endpoints	Same as primary endpoint in **FIGARO-DKD**	Same as primary endpoint in **FIDELIO-DKD**
Enrolled patients	5734 patients with: • ACR 30-300 mg/g and eGFR 25-60 mL/min/1.73 m^2. • ACR 300-5000 and eGFR 25-75 mL/min/1.73 m^2.	7437 patients with: • ACR 30-300 mg/g and eGFR 25-90 mL/min/1.73 m^2. • ACR 300-5000 and eGFR >60 mL/min/1.73 m^2.

1. Bakris GL, *et al. Am J Nephrol* 2019;50:333–344; 2. Ruilope LM, *et al. Am J Nephrol* 2019;50:345–356

FIDELITY Pooled Analysis

FIDELIO-DKD

GFR categories (ml/min per 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
G1	Normal or high	≥90				
G2	Mildly decreased	60–89				10%
G3a	Mildly to moderately decreased	45–59			4%	75%
G3b	Moderately to severely decreased	30–44			6%	
G4	Severely decreased	15–29				
G5	Kidney failure	<15				

+

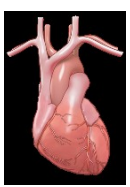
FIGARO-DKD

Persistent albuminuria categories Description and range		
A1	A2	A3
Normal to mildly increased	Moderately increased	Severely increased
<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
		45%
	13%	
	15%	
	13%	

=

FIDELITY
(FIDELIO-DKD + FIGARO-DKD pooled)

Persistent albuminuria categories Description and range		
A1	A2	A3
Normal to mildly increased	Moderately increased	Severely increased
<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol



PRIMARY CV ENDPOINT

Time to CV death, non-fatal MI, non-fatal stroke or hospitalisation for HF



KEY SECONDARY KIDNEY ENDPOINT

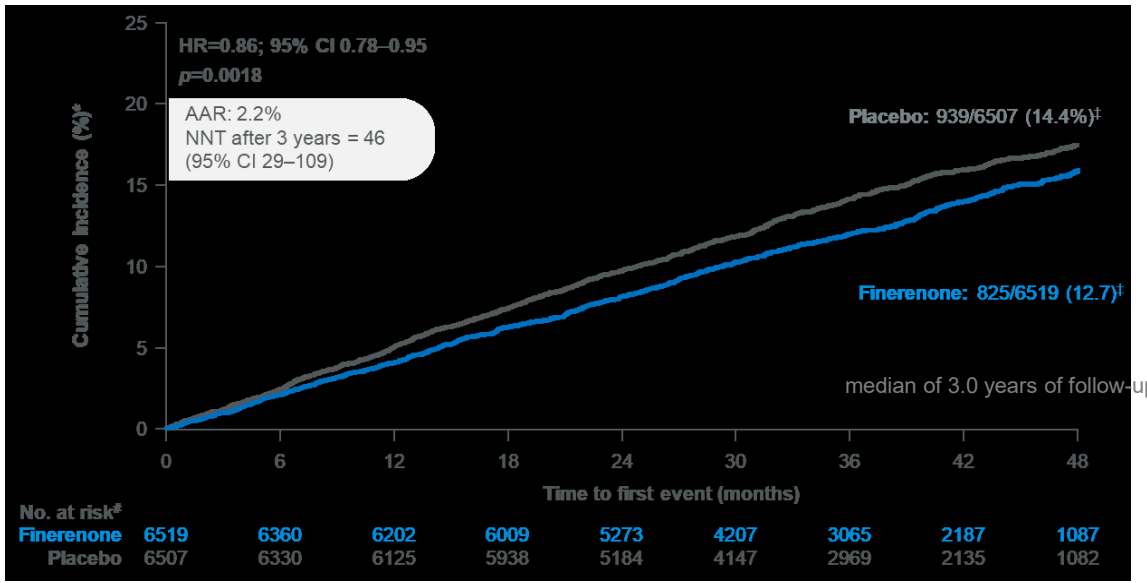
Time to kidney failure (initiation of chronic dialysis for ≥90 days, kidney transplantation or sustained eGFR <15 ml/min/1.73 m²), **sustained ≥57% decrease in eGFR from baseline, or renal death**

30≤UACR<300 mg/g and **25≤eGFR<90** mL/min/1.73m²

300≤UACR≤5000 mg/g and **eGFR≥25** mL/min/1.73m²

1. KDIGO. *Kidney Int* 2020;98:S1–S115; 2. Ruilope LM, *et al. Am J Nephrol* 2019;50:345–356; 3. Bakris GL, *et al. Am J Nephrol* 2019;50:333–344 4. Agarwal R et al. *Eur Heart J* 2021. DOI: 10.1093/eurheartj/ehab777/6433104

Finerenone significantly reduced the risk of the CV composite outcome by 14% and had consistent effects on CV death, MI and hospitalisation for HF



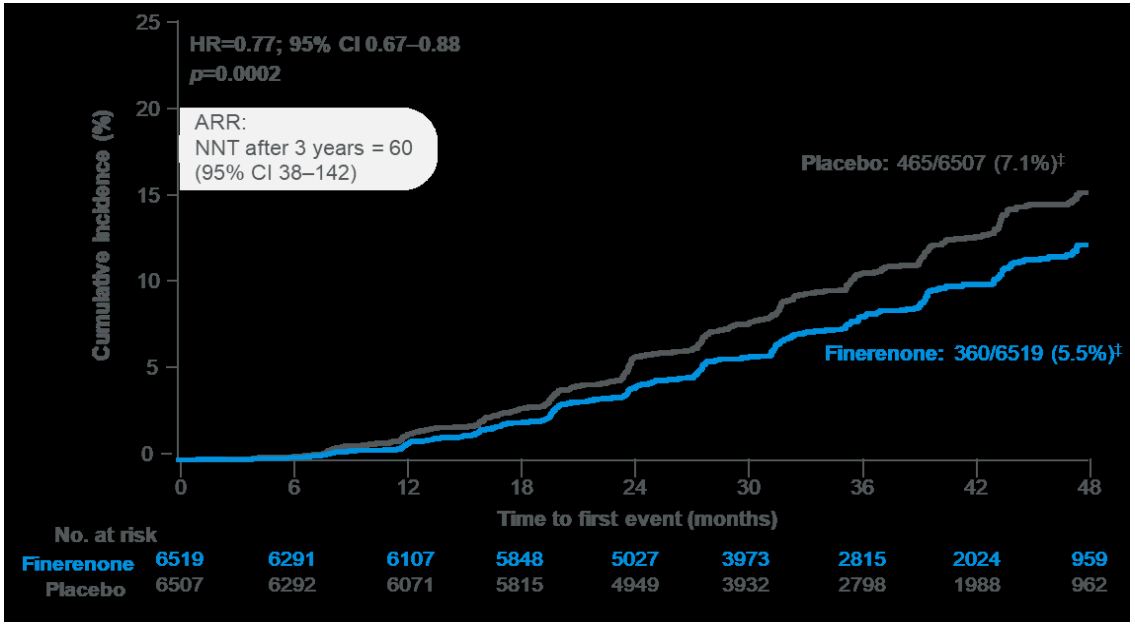
Outcome	Finerenone (n=6519) n (%)	Placebo (n=6507) n (%)	Hazard ratio (95% CI)	p-value
Composite CV outcome§	**825 (12.7)**	**939 (14.4)**	**0.86 (0.78–0.95)**	**0.0018**
CV death	322 (4.9)	364 (5.6)	0.88 (0.76–1.02)	0.0922
Non-fatal MI	173 (2.7)	189 (2.8)	0.91 (0.74–1.12)	0.3601
Non-fatal stroke	198 (3.0)	198 (3.0)	0.99 (0.82–1.21)	0.9460
Hospitalisation for HF	256 (3.9)	325 (5.0)	0.78 (0.66–0.92)	0.0030



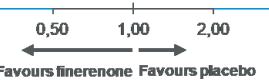
*Cumulative incidence calculated by Aalen-Johansen estimator using deaths due to other causes as competing risk; #at-risk subjects were calculated at start of time point; ‡number of patients with an event over a median of 3.0 years of follow-up; § composite of time to first onset of CV death, non-fatal MI, non-fatal stroke or hospitalisation for HF

Agarwal R et al. Eur Heart J 2021. DOI: 10.1093/eurheartj/ehab777/6433104

Finerenone reduced the risk of the renal composite outcome by 23% and had consistent effects on kidney failure and ≥57% decrease in GFR respect baseline



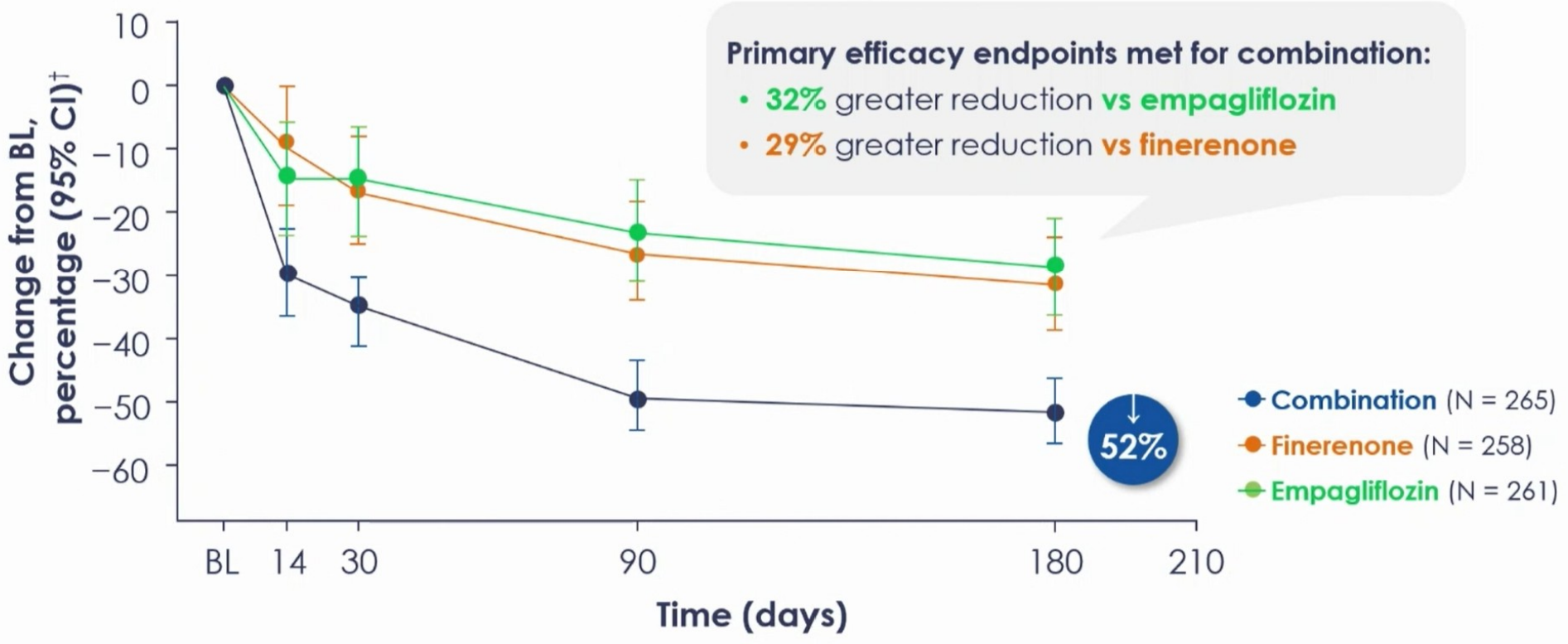
Outcome	Finerenone (n=6519) n (%)	Placebo (n=6507) n (%)	HR (95% CI)	*p*-value
≥57% eGFR kidney composite outcome	**360 (5.5)**	**465 (7.1)**	**0.77 (0.67–0.88)**	**0.0002**
Kidney failure*	254 (3.9)	297 (4.6)	0.84 (0.71–0.99)	0.039
ESKD	151 (2.3)	188 (2.9)	0.80 (0.64–0.99)	0.040¶
Sustained# decrease in eGFR to <15 ml/min/1.73 m^2	195 (3.0)	237 (3.6)	0.81 (0.67–0.98)	0.026¶
Sustained# ≥57% decrease in eGFR from baseline	257 (3.9)	361 (5.5)	0.70 (0.60–0.83)	<0.0001
Renal death‡	2 (<0.1)	4 (<0.1)	0.53 (0.10–2.91)	0.459



*ESKD or sustained decrease in eGFR <15 ml/min/1.73 m^2; #confirmed by two eGFR measurements ≥4 weeks apart; ‡events were classified as renal death if: (1) the patient died; (2) KRT had not been initiated despite being clinically indicated; and (3) there was no other likely cause of death; § number of patients with an event over a median of 3.0 years of follow-up; ¶analyses for *p*-values not prespecified

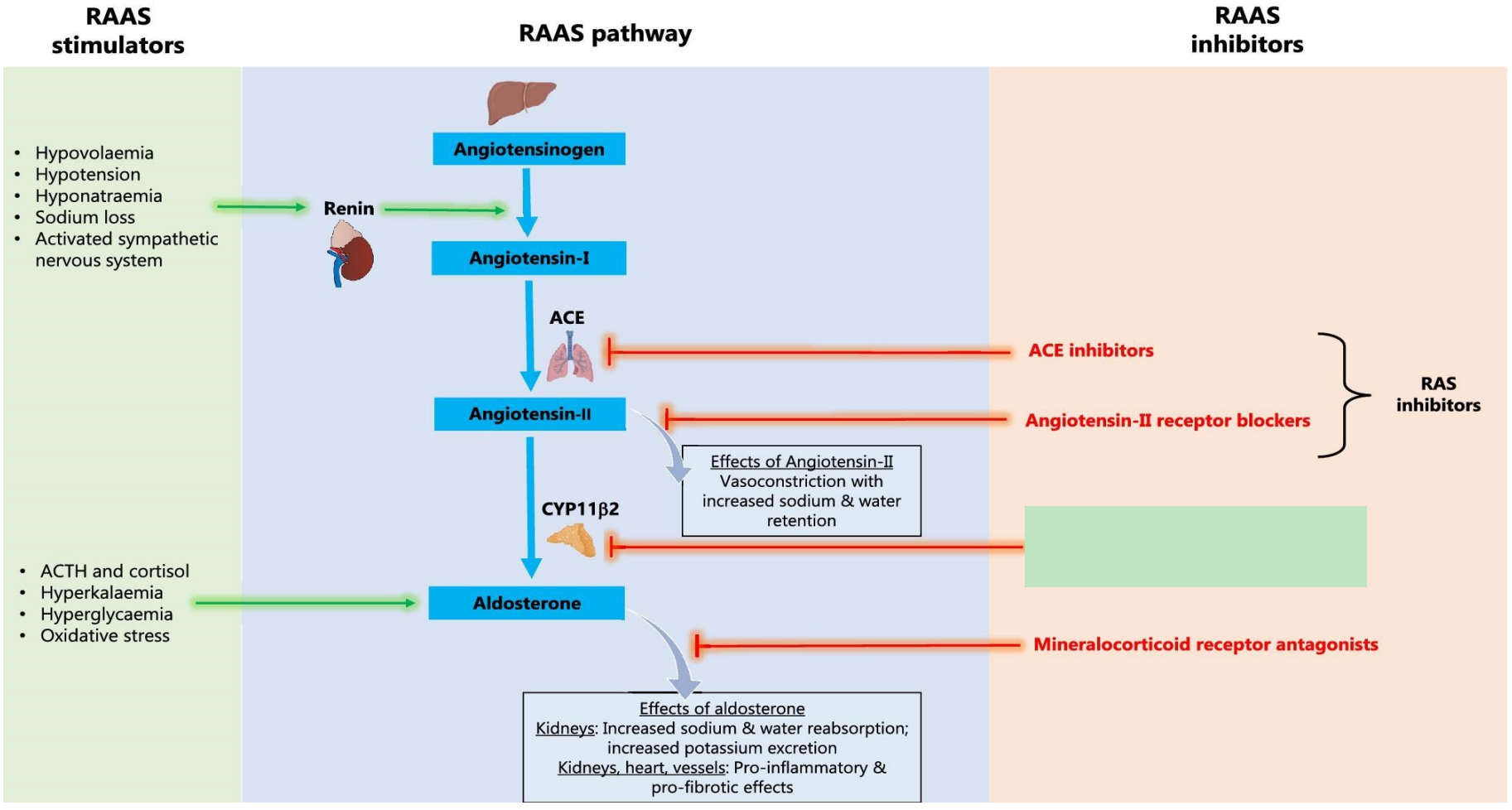
Agarwal R et al. Eur Heart J 2021. DOI: 10.1093/eurheartj/ehab777/6433104

Simultaneous initiation of finerenone and empagliflozin led to early and additive reduction of UACR



Percentage change calculation = (least squares mean ratio to baseline − 1)×100.
BL, baseline; CI, confidence interval; SGLT2i, sodium-glucose cotransporter 2 inhibitor; UACR, urinary albumin-to-creatinine ratio.
Agarwal et al. New Engl J Med 2025

The renin-angiotensin-aldosterone system (RAAS) pathway and mechanisms of inhibition



Nephrol Dial Transplant, Volume 40, Issue 6, June 2025, Pages 1175–1186, https://doi.org/10.1093/ndt/gfae263.

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ORIGINAL ARTICLE

Efficacy and Safety of Baxdrostat in Uncontrolled and Resistant Hypertension

Authors: John M. Flack, M.D., Michel Azizi, M.D., Jenifer M. Brown, M.D., Jamie P. Dwyer, M.D., Jakub Fronczek, M.D., Erika S.W. Jones, M.D., Daniel S. Olsson, M.D., +6 , for the BaxHTN Investigators* Author Info & Affiliations

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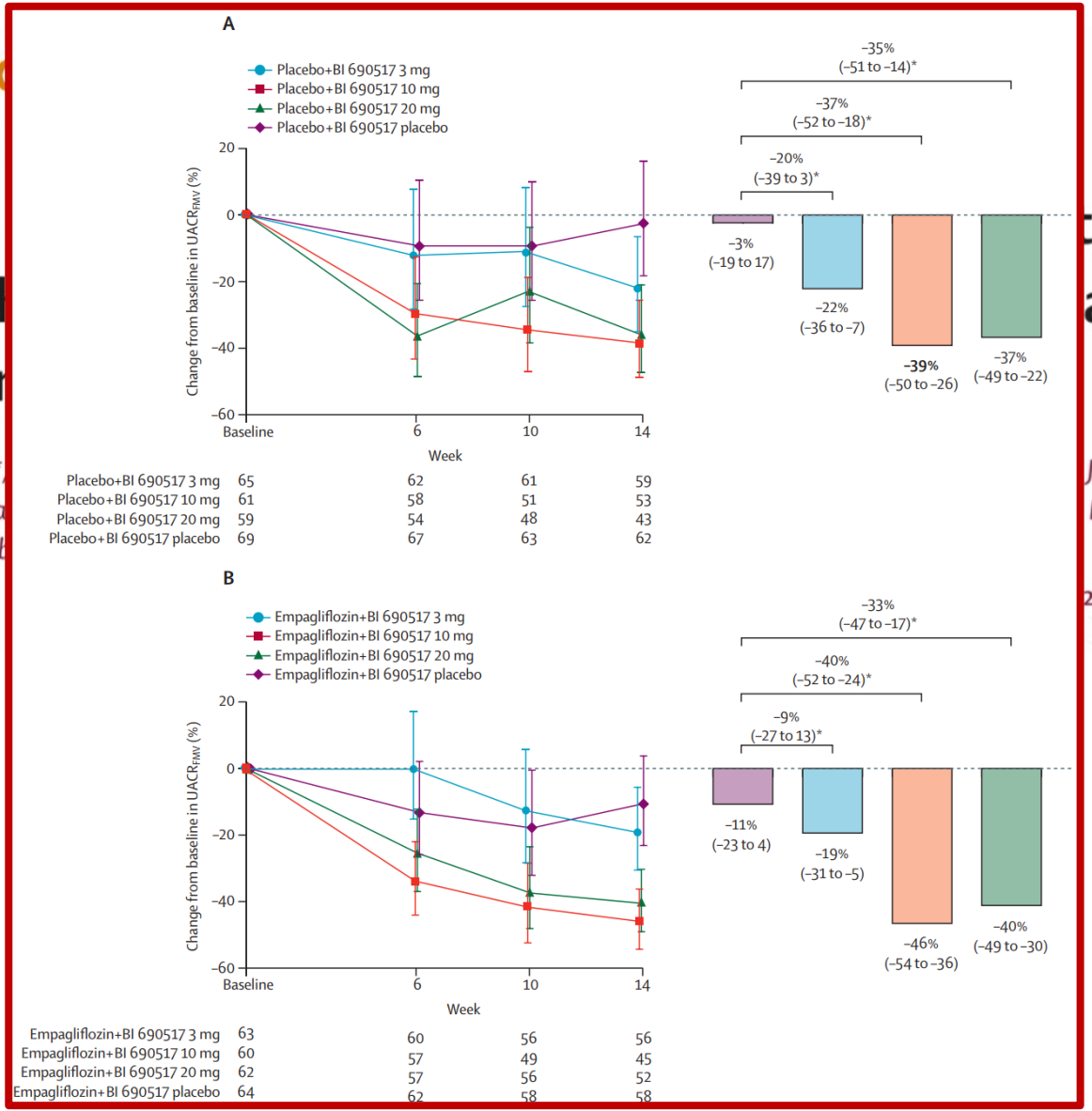
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Grazie per l’attenzione