4TH GCC ORGAN TRANSPLANTATION & NEPHROLOGY CONGRESS

DKD
New insights new targets

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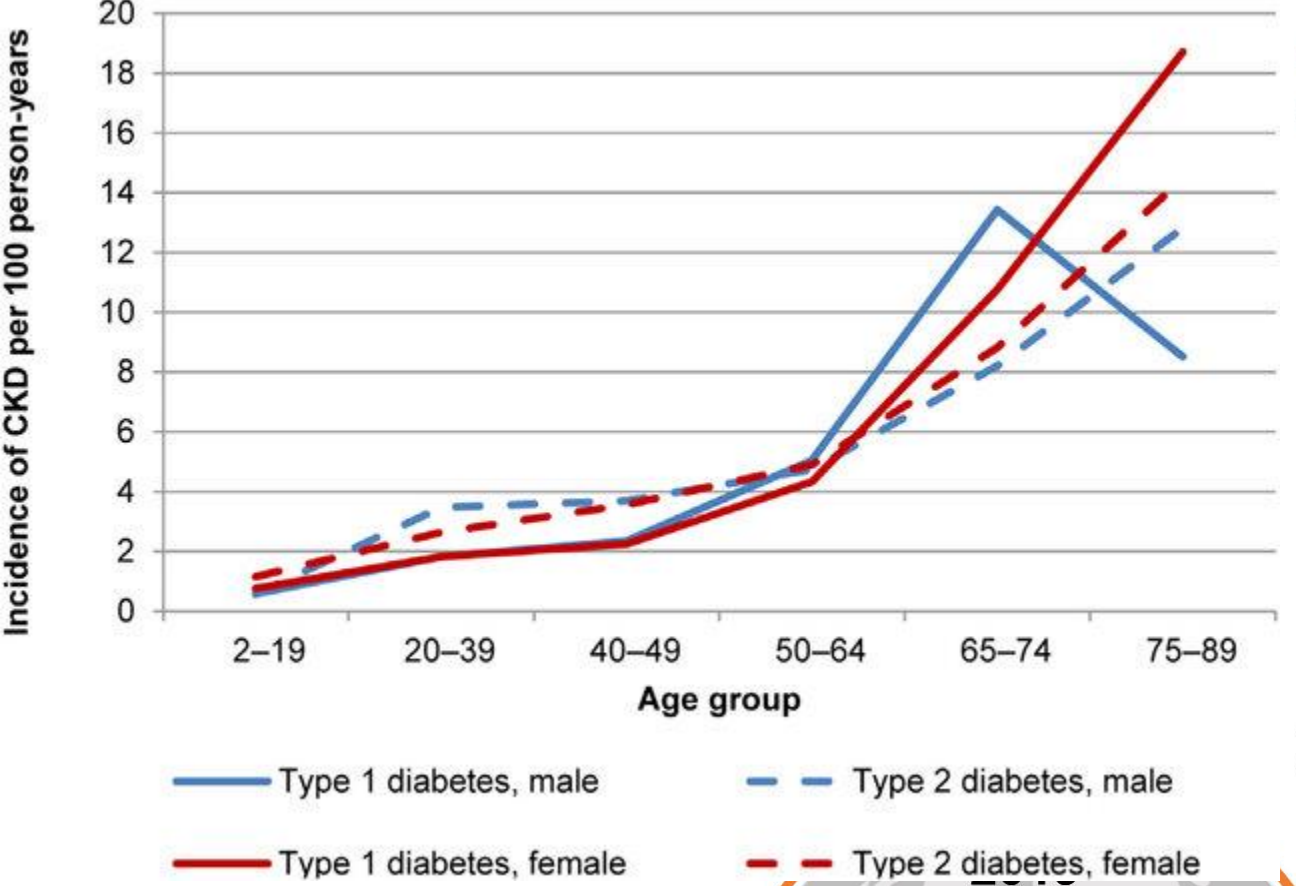


Compared with healthy individuals, having CKD and diabetes can shorten life expectancy by 16 years*

*At age 30 compared to patients without diabetes or CKD. Study population consisted of 543,412 adults who participated in a self-paying comprehensive health surveillance programme between 1994 and 2008. CKD, chronic kidney disease; Early CKD, CKD stages 1–3; T2D, type 2 diabetes

Wen CP et al. Kidney Int 2017; 92:388–396

463 MILLION adults with diabetes

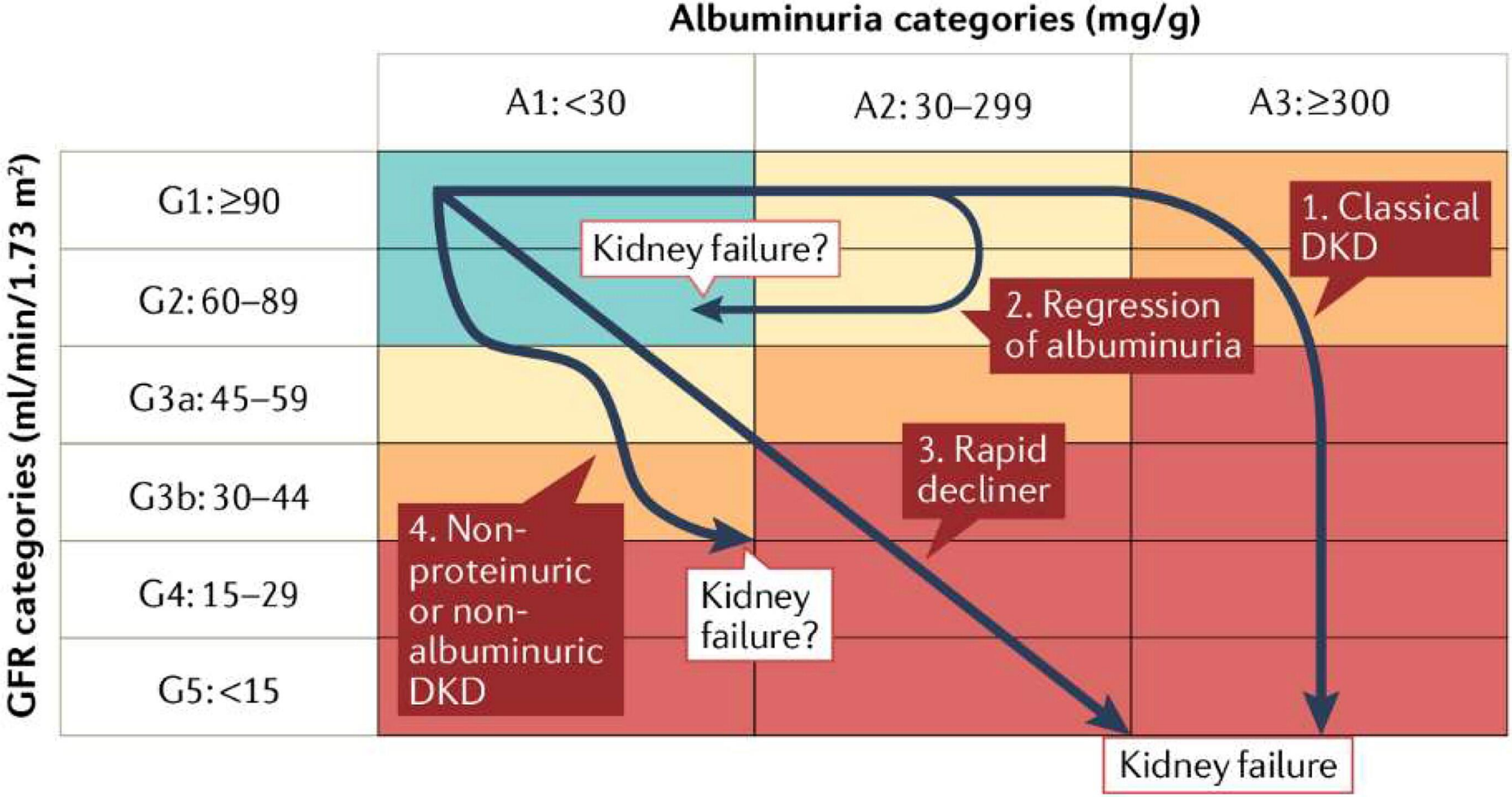
9.3% of global population

2019

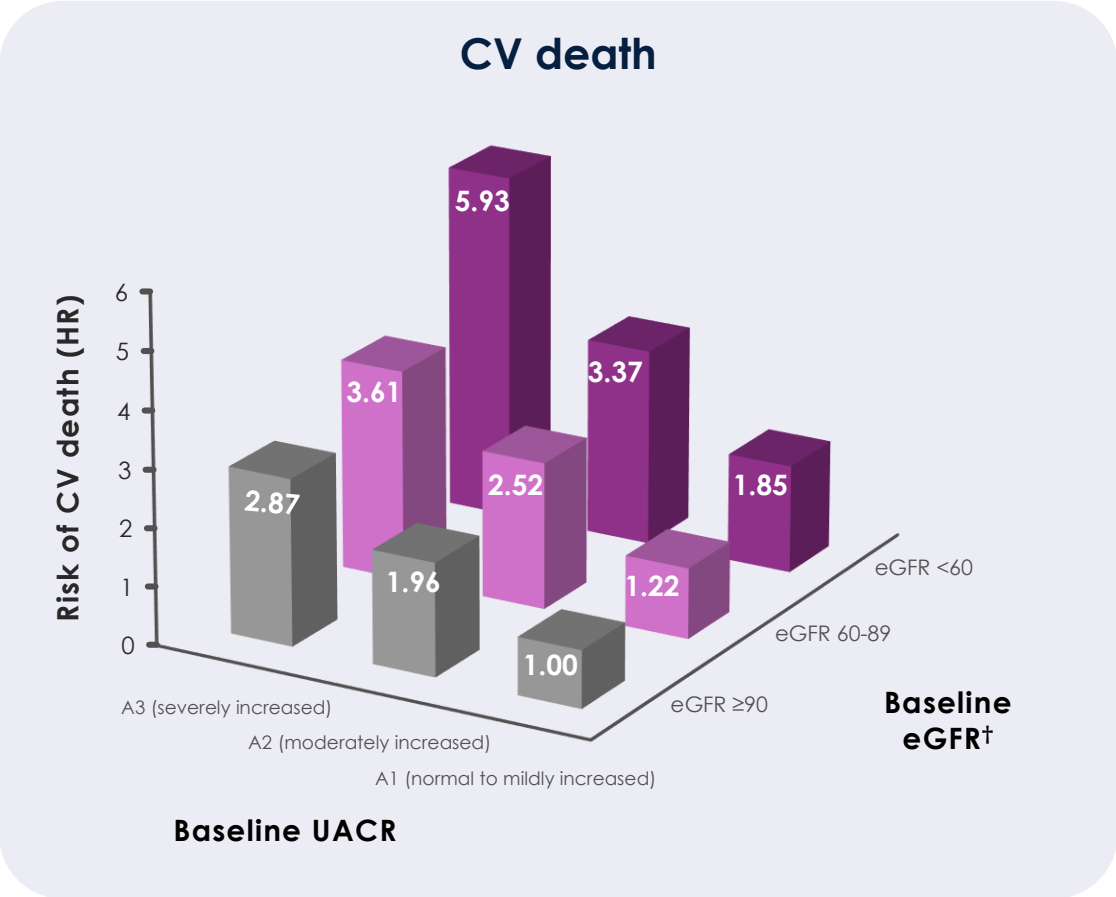
416.7 MILLION adults with T2D

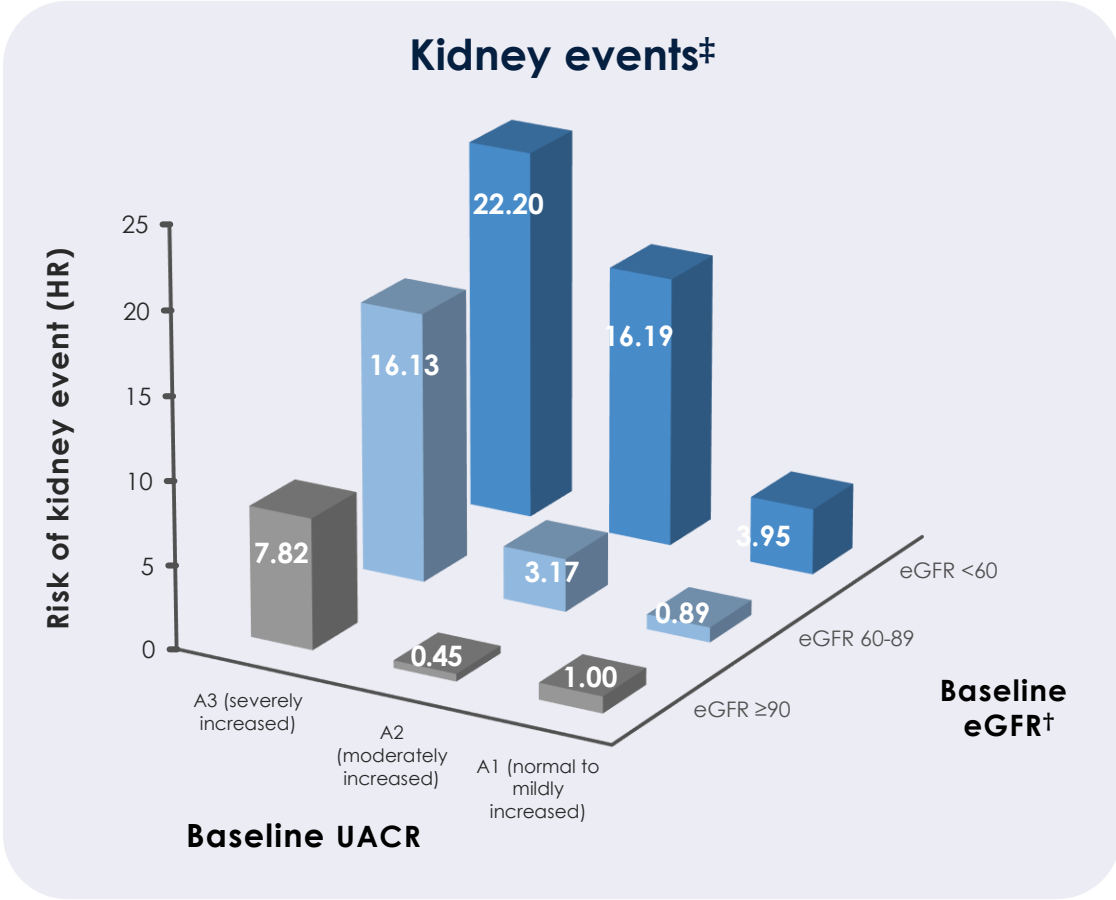
An estimated 160 MILLION adults were living with CKD in T2D in 2019

1. International Diabetes Federation 2019.


Albuminuria categories (mg/g)
A1: <30
A2: 30–299
A3: ≥300
GFR categories (ml/min/1.73 m²)
G1: ≥90
G2: 60–89
G3a: 45–59
G3b: 30–44
G4: 15–29
G5: <15
Kidney failure?
1. Classical DKD
2. Regression of albuminuria
3. Rapid decliner
4. Non-proteinuric or non-albuminuric DKD
Kidney failure?
Kidney failure

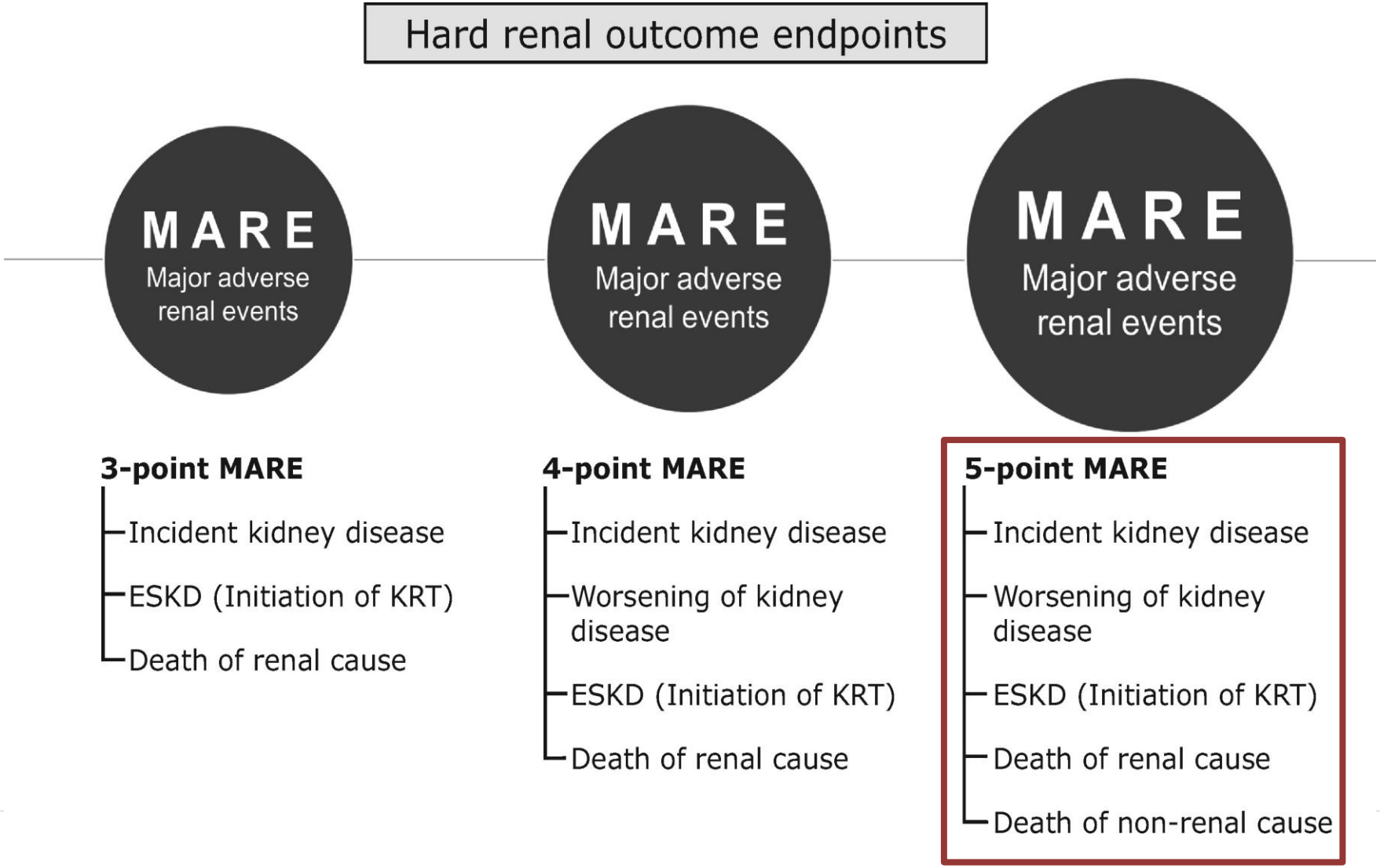
increased risk of CV death and kidney events*





*Average time to follow-up for risk assessment was 4.3 years; †eGFR in mL/min/1.73 m^2; ‡A kidney event was defined as death as a result of kidney disease, requirement for dialysis or transplantation, or doubling of serum creatinine to >2.26 mg/dL. HR, hazard ratio. Figure used with permission of The American Society of Nephrology, from "Albuminuria and Kidney Function Independently Predict Cardiovascular and Renal Outcomes in Diabetes", Ninomiya T, et al, on behalf of the ADVANCE Collaborative Group, Journal of the American Society of Nephrology, vol 20, pages 1813-1821, copyright 2009; permission conveyed through Copyright Clearance Center, Inc.
Ninomiya T *et al. J Am Soc Nephrol* 2009;20:1813

Hard renal outcome endpoints Definition of MARE. Incident kidney disease is defined as new onset of kidney.

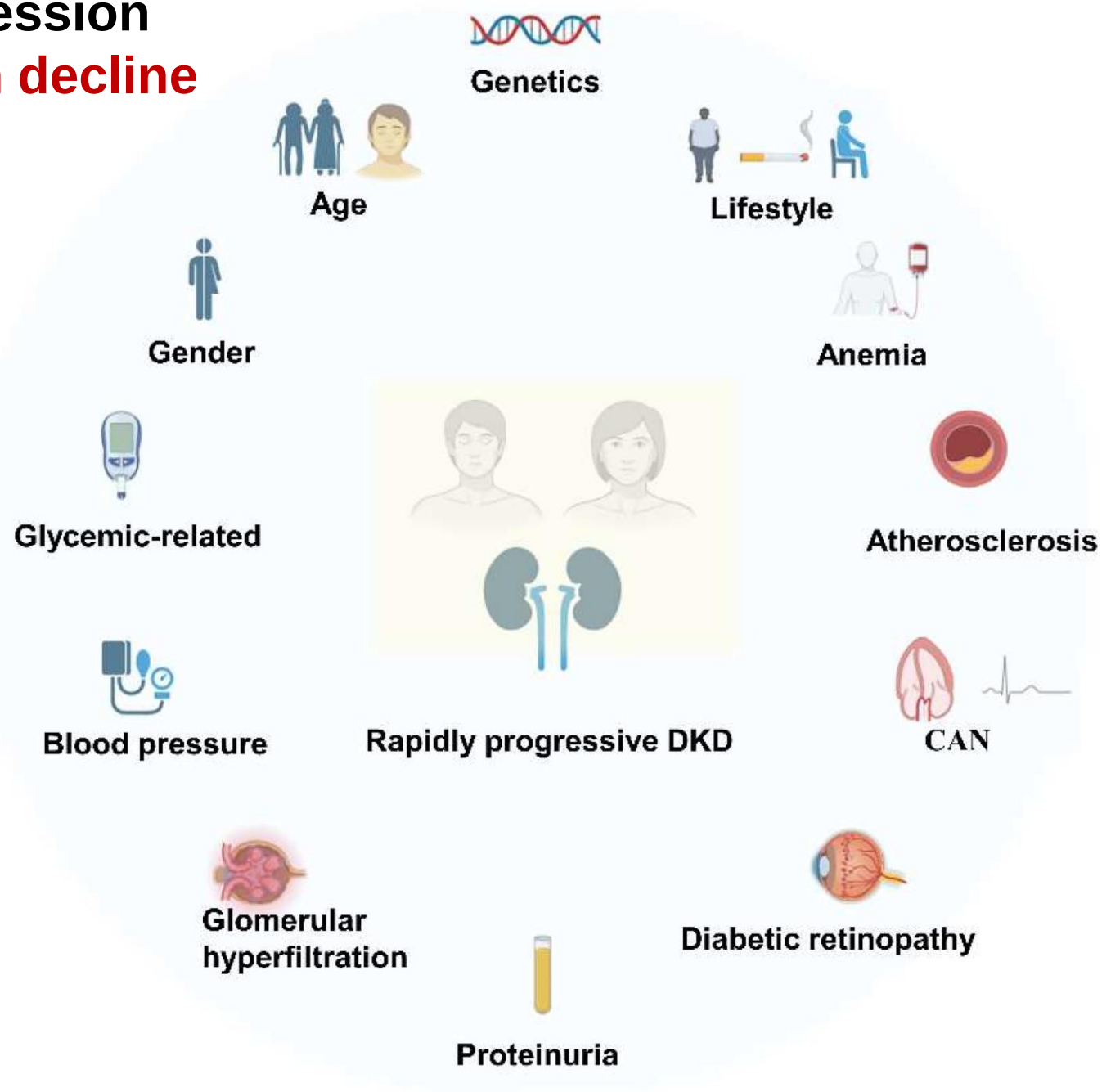


Nephrol Dial Transplant, Volume 36, Issue 3, March 2021, Pages 491–497, https://doi.org/10.1093/ndt/gfz212

Chronic Kidney Disease and Progression

Risk factors for rapid kidney function decline in diabetes patients

The strength of association	Risk factors
Very likely	Genetics, **poor glycemic control**, intensive blood pressure control, **hypertension**, lifestyle
Probable	Older age, rapid glycemic decline, CAN, anemia
Possible	Early-onset type 2 diabetes, atherosclerosis, diabetic retinopathy, proteinuria
Controversial	Gender



Jixin Xing et al., Renal Failure Volume 46, 2024

KDIGO DKD update 2022

Glycemic control is based on insulin for type 1 diabetes and a combination of metformin and SGLT2 inhibitors (SGLT2i) for type 2 diabetes. Metformin may be given when eGFR ≥30 ml/min per 1.73 m^2 and SGLT2i should be used when eGFR is ≥20 ml/min per 1.73 m^2. SGLT2i are recommended for patients with type 2 diabetes and chronic kidney disease (CKD). Renin–angiotensin system (RAS) inhibition is recommended for patients with albuminuria and hypertension. Aspirin generally should be used lifelong for secondary prevention among those with established cardiovascular disease and may be considered for

Chapter 1: Comprehensive care in patients with diabetes and CKD

1.1 Comprehensive diabetes and CKD management

Practice Point 1.1.1: Patients with diabetes and chronic kidney disease (CKD) should be treated with a comprehensive strategy to reduce risks of kidney disease progression and cardiovascular disease (Figures 1 and 2).

Figure 1. Kidney-heart risk factor management

Glycemic control

Blood pressure

Lifestyle modification

Other

Volume 109, Issue 8
August 2024

< Previous Next >

JOURNAL ARTICLE

Poor Glycemic Control Is Associated With More Rapid Kidney Function Decline After the Onset of Diabetic Kidney Disease

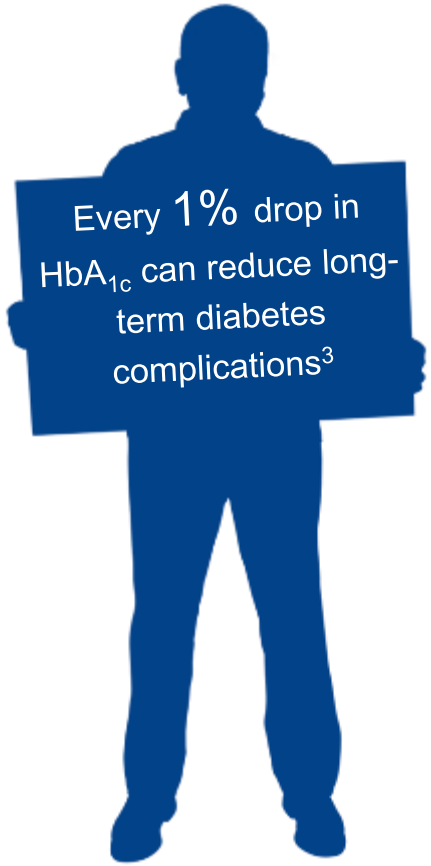
Conclusion

In both type 1 and type 2 diabetes, **poor glycemic control is associated with a more rapid rate of glomerular filtration rate decline after DKD onset,** especially in persons with severe albuminuria.

8, August 2024, Pages 2124–2135,
https://doi.org/10.1210/clinem/dgae044
Published: 23 January 2024 **Article history** ▾

UKPDS 1977-1997
The importance of glycaemic control

Optimal glycaemic control early in the course of diabetes may protect against, or delay, long-term complications of type 2 diabetes (beneficial legacy effect)[1,2]



- ↓ 12% Stroke
- ↓ 19% Cataract extraction
- ↓ 16% Heart failure
- ↓ 14% Myocardial infarction
- ↓ 43% Lower extremity amputation or fatal peripheral vascular disease
- ↓ 37% Microvascular complications

1. Khunti et al. Diabetes Care. 2013;(36):3411–3417.
2. Holman et al. N Engl J Med. 2008;359(15):1577–1589.
3. Stratton et al.. BMJ. 2000;321(7258):405–412.

44 years UKPDS follow up
EASD 2022

Participant Disposition

		Median Follow-up		
		10.0y	*16.9y*	*17.4y*
Aggregate Endpoint		**1997**	**2007**	**2021**
Any diabetes-related endpoint	*RRR:*	12%	9%	10%
	P:	0.029	0.040	0.016
Myocardial infarction	*RRR:*	16%	15%	15%
	P:	0.052	0.014	0.0074
Microvascular disease	*RRR:*	25%	24%	26%
	P:	0.0099	0.001	<0.0001
All-cause mortality	*RRR:*	6%	13%	11%
	P:	0.44	0.007	0.0093

RRR = Relative Risk Reduction, P = Log Rank

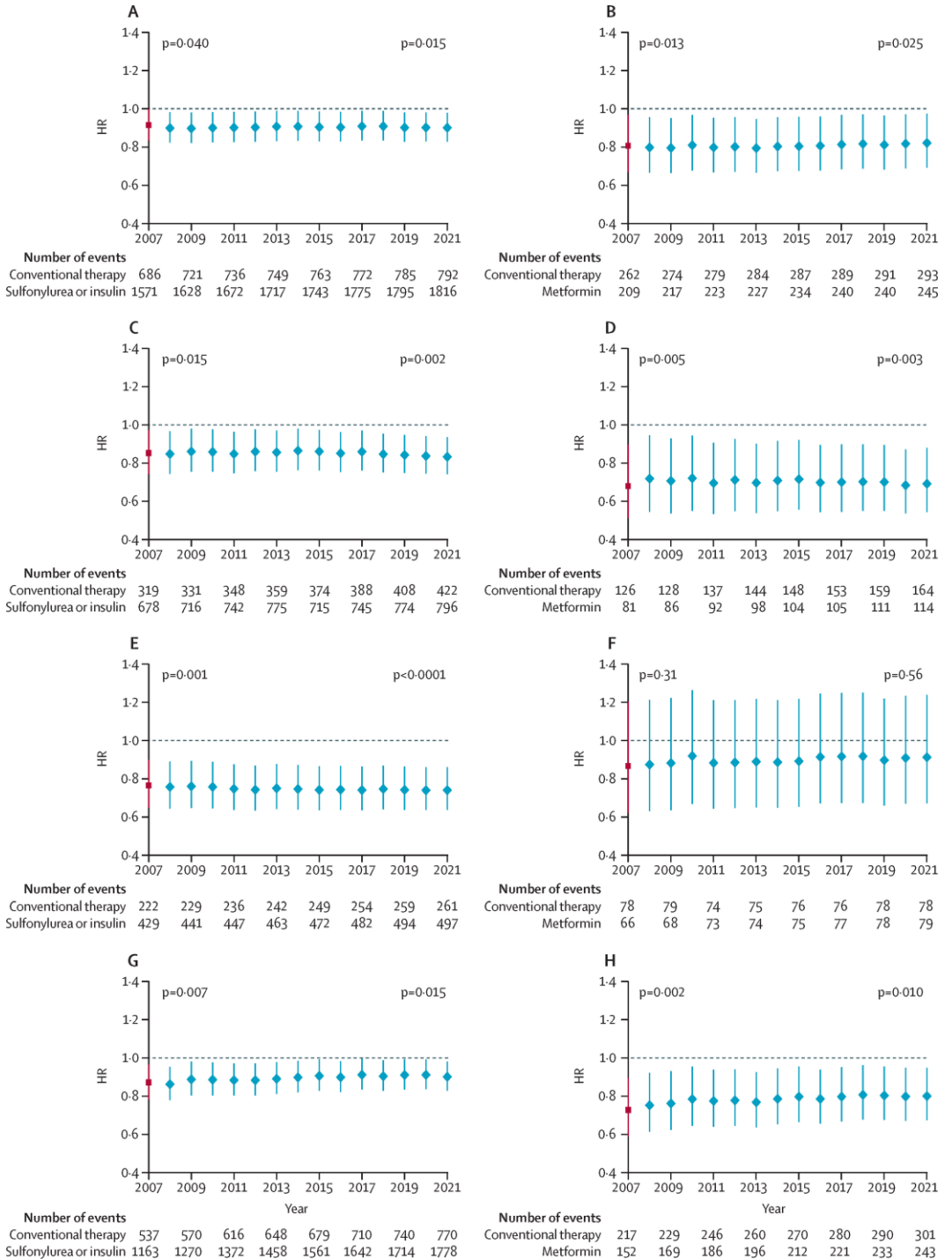
https://easd-elearning.org/44-years-of-the-ukpds/

THE LANCET

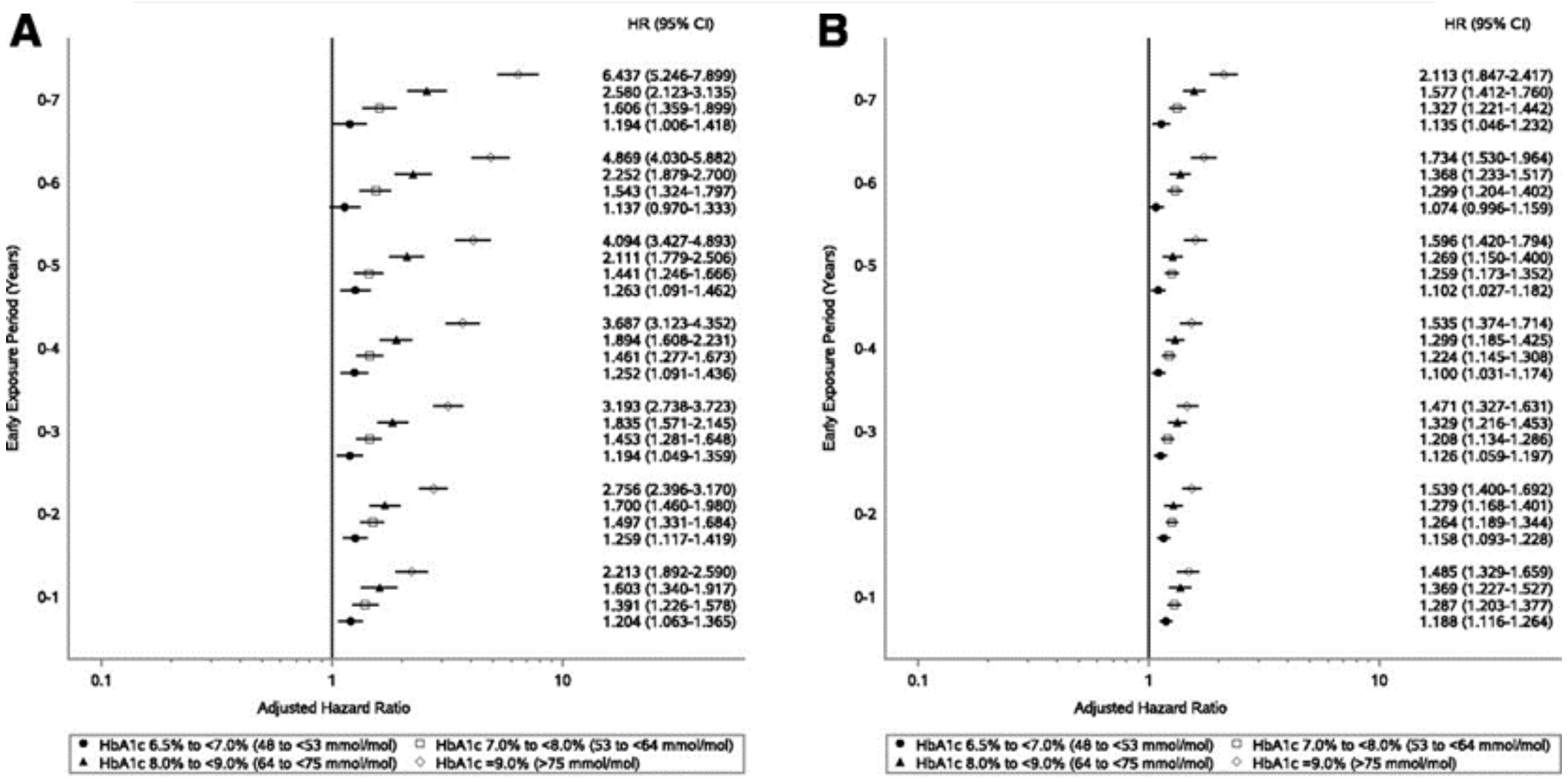
ARTICLES · Volume 404, Issue 10448, P145-155, July 13, 2024 · *Open Access* Download Full Issue

Post-trial monitoring of a randomised controlled trial of intensive glycaemic control in type 2 diabetes extended from 10 years to 24 years (UKPDS 91)

HRs for four prespecified aggregate clinical outcomes
HRs for the UK Prospective Diabetes Study participants who had
any diabetes-related endpoint (A–B),
myocardial infarction (C–D),
microvascular disease (E–F), or
who died from any cause (G–H)



From: **The Legacy Effect in Type 2 Diabetes: Impact of Early Glycemic Control on Future Complications (The Diabetes & Aging Study)**



Diabetes Care. 2018;42(3):416-426. doi:10.2337/dc17-1144

Good health and function, low treatment risks and burdens

Most adults

Healthy older adults

Older adults with complex/ intermediate health

Older adults with very complex/ poor health

Any adults with limited life

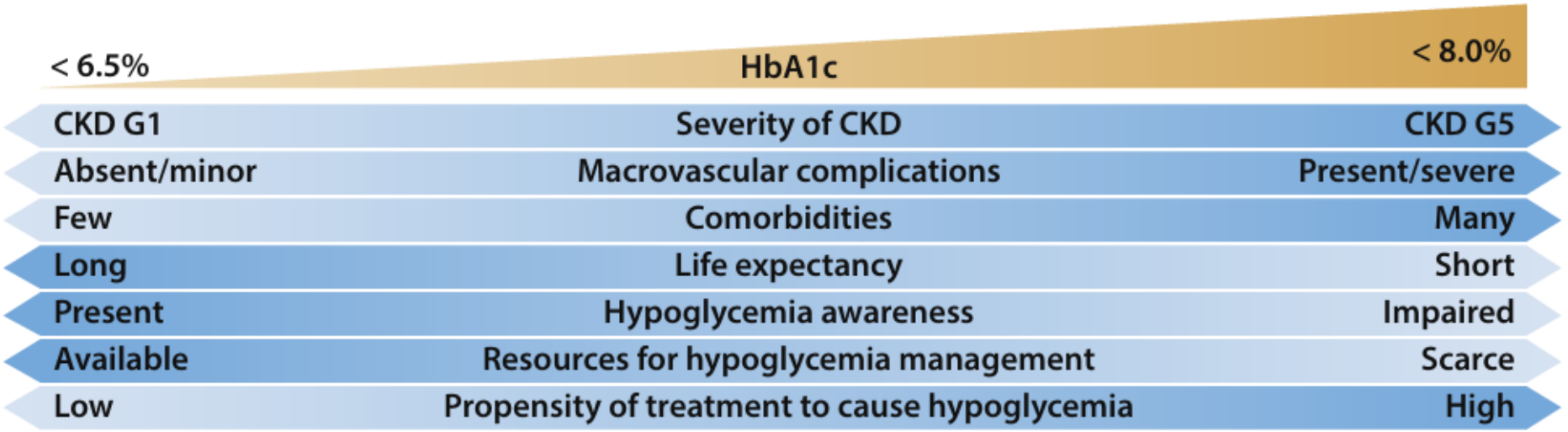
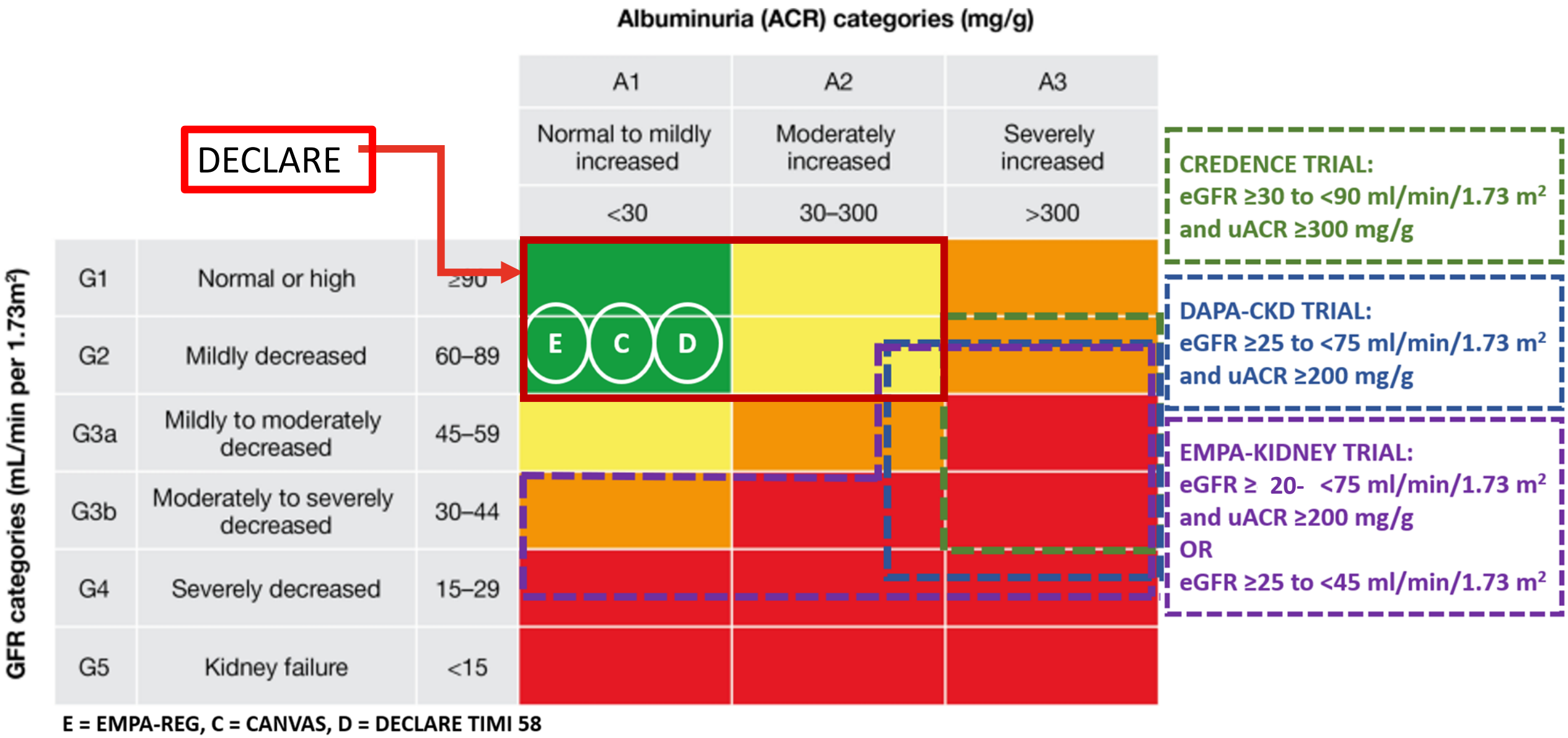


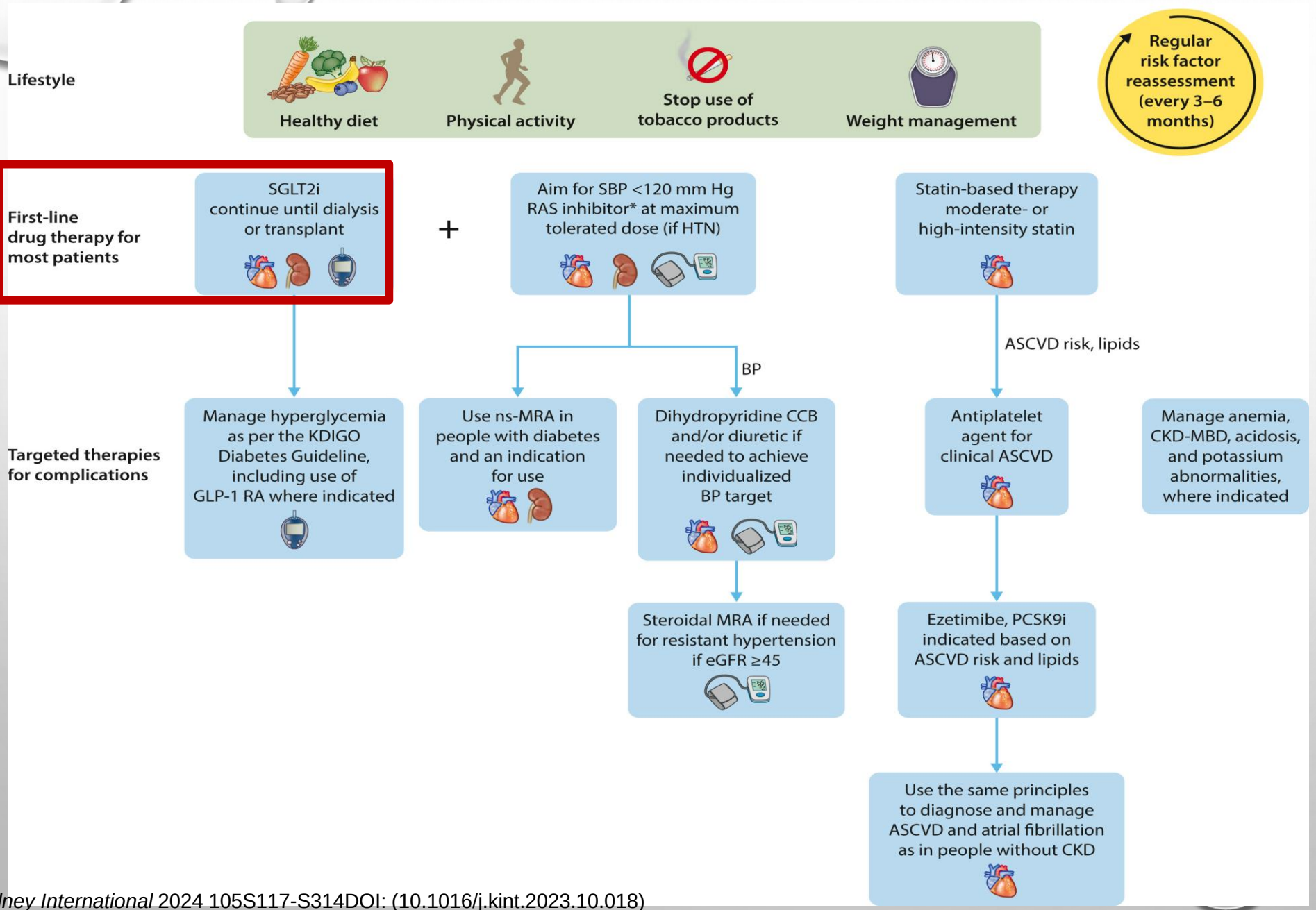
Figure 3 | Factors guiding decisions on individual glycated hemoglobin (HbA1c) targets. CKD, chronic kidney disease; G1, estimated glomerular filtration rate (eGFR) >90 ml/min per 1.73 m^2; G5, eGFR <15 ml/min per 1.73 m^2.

Pharmacotherapy with cardiovascular, kidney, weight, or other benefits	Pharmacotherapy without nonglycemic benefits
No cardiovascular complications	Established cardiovascular complications
Few or minor comorbidities	Severe, life-limiting comorbidities



E = EMPA-REG, C = CANVAS, D = DECLARE TIMI 58

MANAGEMENT- CKD



2024

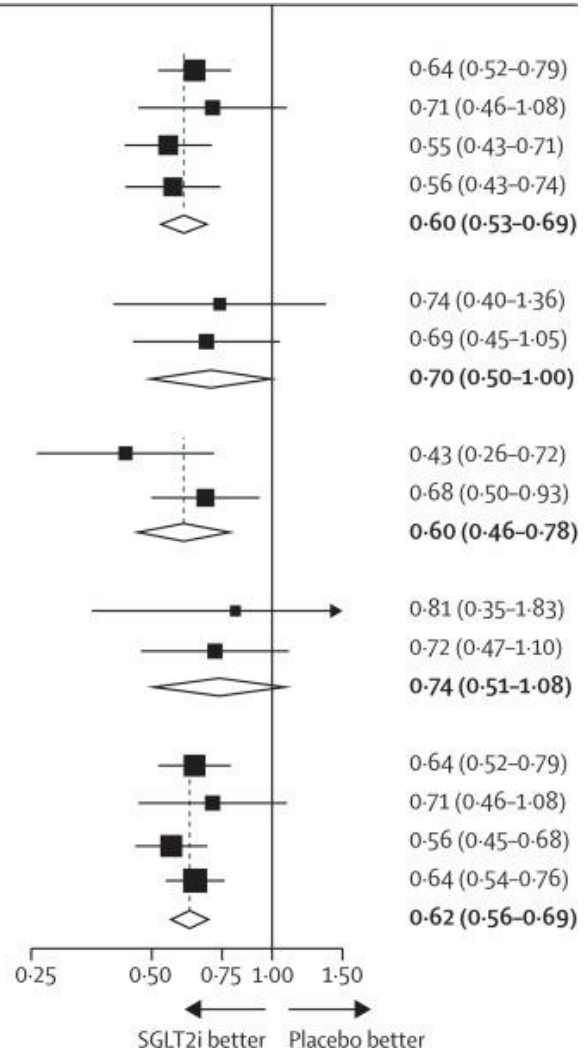
ACE, angiotensin-converting enzyme inhibitor; ACR, albumin-creatinine ratio; ARB, angiotensin II receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CCB, calcium channel blocker; CGM, continuous glucose monitoring; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; MRA, mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; SGLT2, sodium-glucose cotransporter-2; T2D, Type 2 diabetes; TG, triglycerides

Kidney International 2024 105S117-S314DOI: (10.1016/j.kint.2023.10.018)

Effect of sodium glucose co-transporter-2 inhibition on kidney disease progression by presumed primary kidney

	Mean baseline eGFR, mL/min per 1·73m²	Events/participants		Event rate per 1000 patient-years		RR (95% CI)
		SGLT2i	Placebo	SGLT2i	Placebo	
Diabetic kidney disease or nephropathy*						
CREDENCE	56	153/2202	230/2199	27	41	0·64 (0·52–0·79)
SCORED	44	37/5292	52/5292	5	7	0·71 (0·46–1·08)
DAPA–CKD	43	93/1271	157/1239	36	64	0·55 (0·43–0·71)
EMPA–KIDNEY	36	85/1032	133/1025	42	67	0·56 (0·43–0·74)
Subtotal	**46**	**368/9797**	**572/9755**	..	..	**0·60 (0·53–0·69)**
Ischaemic and hypertensive kidney disease						
DAPA–CKD	43	18/324	26/363	28	37	0·74 (0·40–1·36)
EMPA–KIDNEY	35	37/706	52/739	27	37	0·69 (0·45–1·05)
Subtotal	**38**	**55/1030**	**78/1102**	..	..	**0·70 (0·50–1·00)**
Glomerular disease						
DAPA–CKD	43	21/343	46/352	33	70	0·43 (0·26–0·72)
EMPA–KIDNEY	42	69/853	95/816	44	64	0·68 (0·50–0·93)
Subtotal	**42**	**90/1196**	**141/1168**	..	..	**0·60 (0·46–0·78)**
Other kidney disease or unknown						
DAPA–CKD	43	10/214	14/198	25	37	0·81 (0·35–1·83)
EMPA–KIDNEY	36	36/713	52/725	26	36	0·72 (0·47–1·10)
Subtotal	**38**	**46/927**	**66/923**	..	..	**0·74 (0·51–1·08)**
Any diagnosis						
CREDENCE	56	153/2202	230/2199	27	41	0·64 (0·52–0·79)
SCORED	44	37/5292	52/5292	5	7	0·71 (0·46–1·08)
DAPA–CKD	43	142/2152	243/2152	33	58	0·56 (0·45–0·68)
EMPA–KIDNEY	37	227/3304	332/3305	36	52	0·64 (0·54–0·76)
Total	**44**	**559/12 950**	**857/12 948**	..	..	**0·62 (0·56–0·69)**

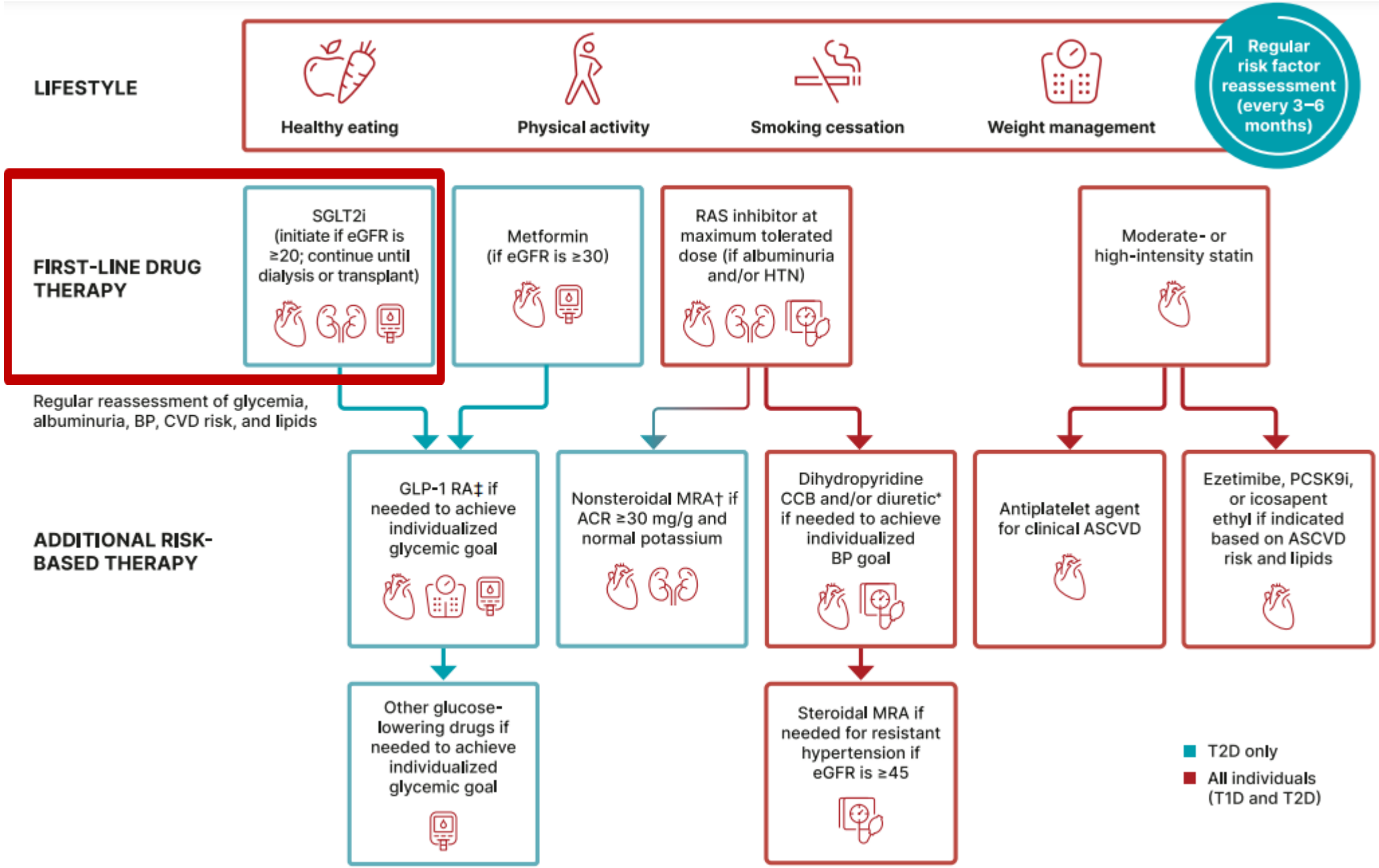
Heterogeneity across groups of primary kidney disease: p=0·67
Trend across trials sorted by eGFR for any diagnosis: p=0·88



www.thelancet.com Published online November 6, 2022

American Diabetes Association

2025



			Primary outcome		Kidney outcomes		
Drug	**Trial**	**Kidney-related eligibility criteria**	**Primary outcome**	**Effect on primary outcome**	**Effect on albuminuria or albuminuria-containing composite outcome**	**Effect on GFR loss[a]**	**Adverse effects**
SGLT2 inhibitors							
Empagliflozin	EMPA-REG OUTCOME	eGFR ≥30 ml/min per 1.73 m^2	MACE	↓	↓↓	↓↓	Genital mycotic infections, DKA
Canagliflozin	CANVAS trials	eGFR ≥30 ml/min per 1.73 m^2	MACE	↓	↓↓	↓↓	Genital mycotic infections, DKA, amputation
	CREDENCE	ACR >300 mg/g [30 mg/mmol] and eGFR 30–90 ml/min per 1.73 m^2	Progression of CKD[b]	↓↓	↓↓	↓↓	Genital mycotic infections, DKA
Dapagliflozin	DECLARE-TIMI 58	CrCl ≥60 ml/min	Dual primary outcomes: MACE and the composite of hospitalization for heart failure or CV death[c]	↔/↓	↓	↓↓	Genital mycotic infections, DKA
GLP-1 receptor agonists							
Lixisenatide	ELIXA	eGFR ≥30 ml/min per 1.73 m^2	MACE	↔	↓	↔	None notable
Liraglutide	LEADER	eGFR ≥15 ml/min per 1.73 m^2	MACE	↓	↓	↔	GI
Semaglutide[d]	SUSTAIN-6	Patients treated with dialysis excluded	MACE	↓	↓↓	NA	GI
	PIONEER 6	eGFR ≥30 ml/min per 1.73 m^2	MACE	↔	NA	NA	GI
Exenatide	EXSCEL	eGFR ≥30 ml/min per 1.73 m^2	MACE	↔	↔	↔	None notable
Albiglutide	HARMONY	eGFR ≥30 ml/min per 1.73 m^2	MACE	↓	↔	NA	Injection site reactions
Dulaglutide	REWIND	eGFR ≥15 ml/min per 1.73 m^2	MACE	↓	↓	↓	GI
DPP-4 inhibitors							
Saxagliptin	SAVOR-TIMI 53	eGFR ≥15 ml/min per 1.73 m^2	MACE	↔	↓	↔	HF; any hypoglycemic event (minor and major) also more common
Alogliptin	EXAMINE	Patients treated with dialysis excluded	MACE	↔	NA	NA	None notable
Sitagliptin	TECOS	eGFR ≥30 ml/min per 1.73 m^2	MACE	↔	NA	NA	None notable
Linagliptin	CARMELINA	eGFR ≥15 ml/min per 1.73 m^2	Progression of CKD[b]	↔	↓	↔	None notable

| Overview of select large, placebo-controlled clinical outcome trials assessing the benefits and harms of sodium–glucose cotransporter-2 (SGLT2) inhibitors, glucagon-

The long-term effects of dapagliflozin in chronic kidney disease: a time-to-event analysis

To extrapolate the outcome-based clinical benefits of treatment with dapagliflozin in patients with chronic kidney disease

Methods

Combine patient-level data from clinical trials of dapagliflozin treatment

Higher-risk	Lower-risk
DAPA-CKD trial	DECLARE-TIMI 58 trial
Whole trial population	CKD subpopulation
CKD 2–4	Early CKD
Elevated albuminuria	Low albuminuria

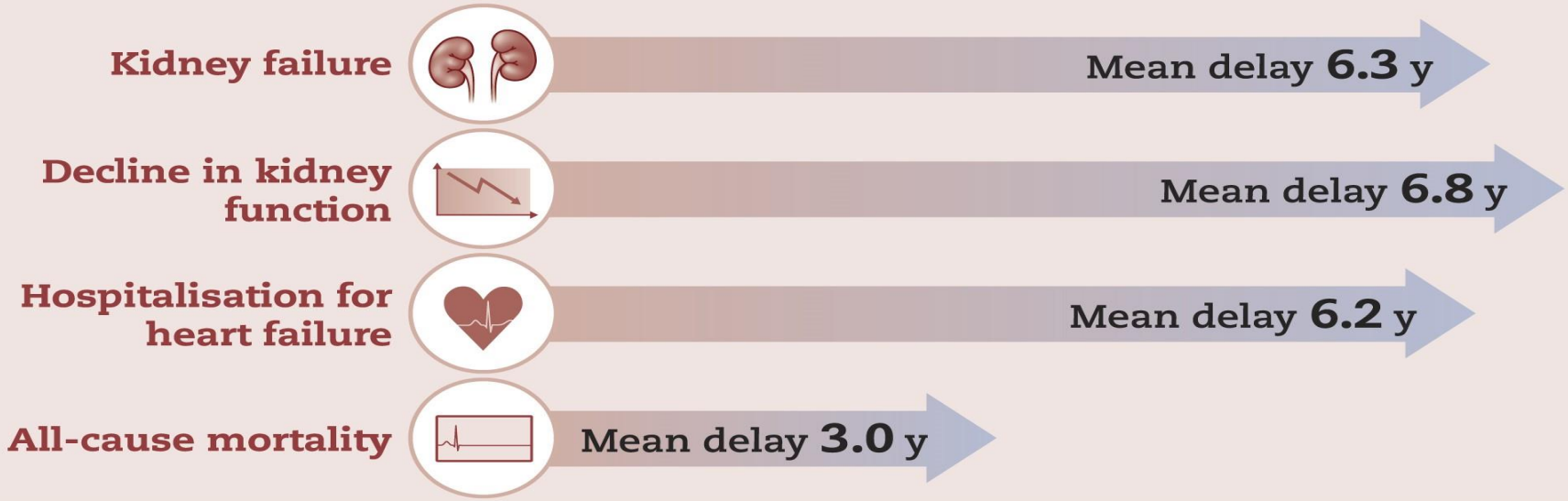
Pooled population with CKD

↓

Calculate mean time to event for clinical endpoints extrapolated across patient lifetime

Results

Treatment of a pooled (mixed higher and lower CKD risk) population with dapagliflozin over a lifetime time horizon was estimated **to delay the onset of adverse clinical events**

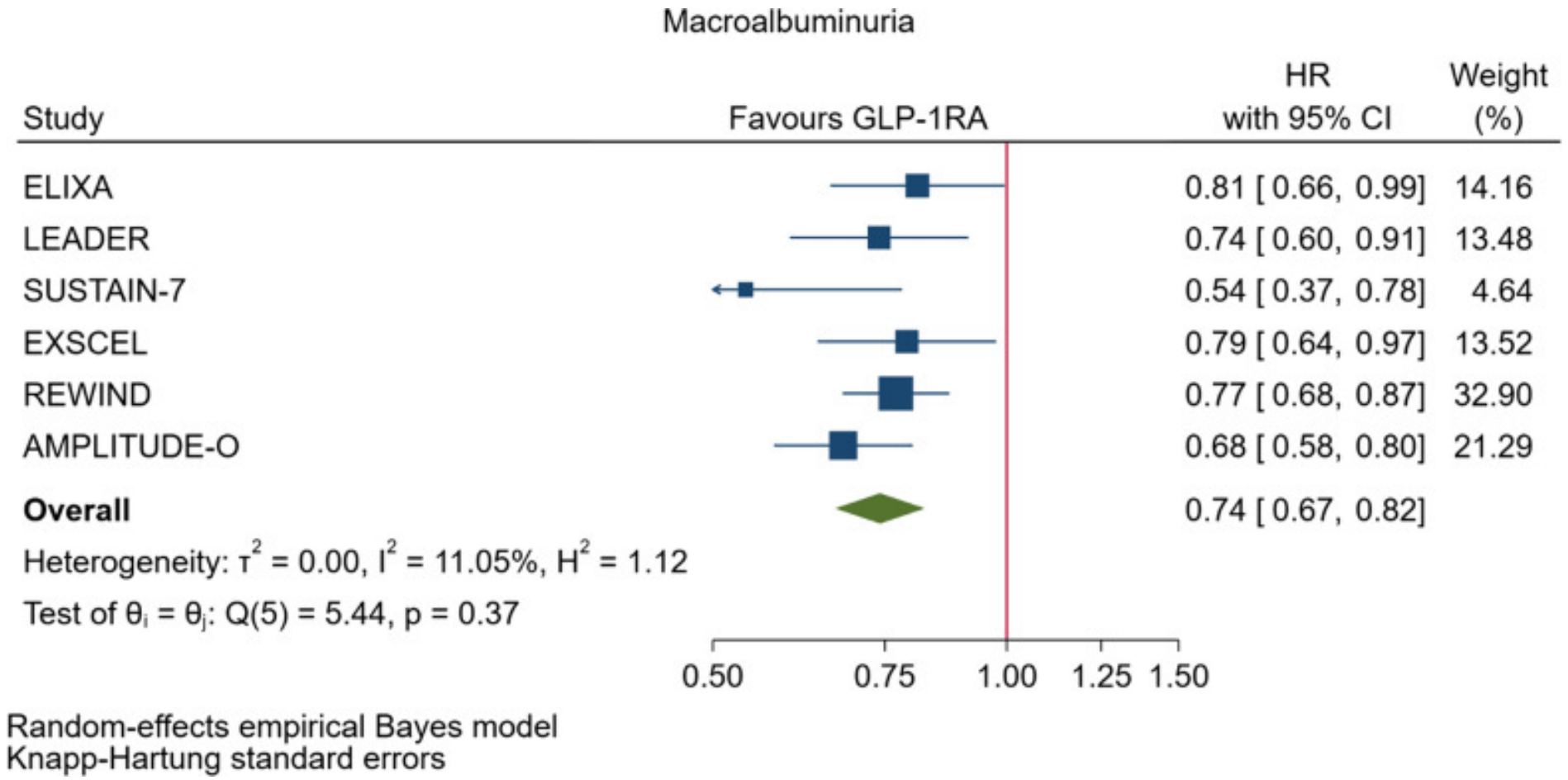


McEwan, P. *et al.*
NDT (2024)
@NDTSocial

Treatment with dapagliflozin over a lifetime time horizon may considerably delay the time to major adverse cardio-renal outcomes and improve life expectancy

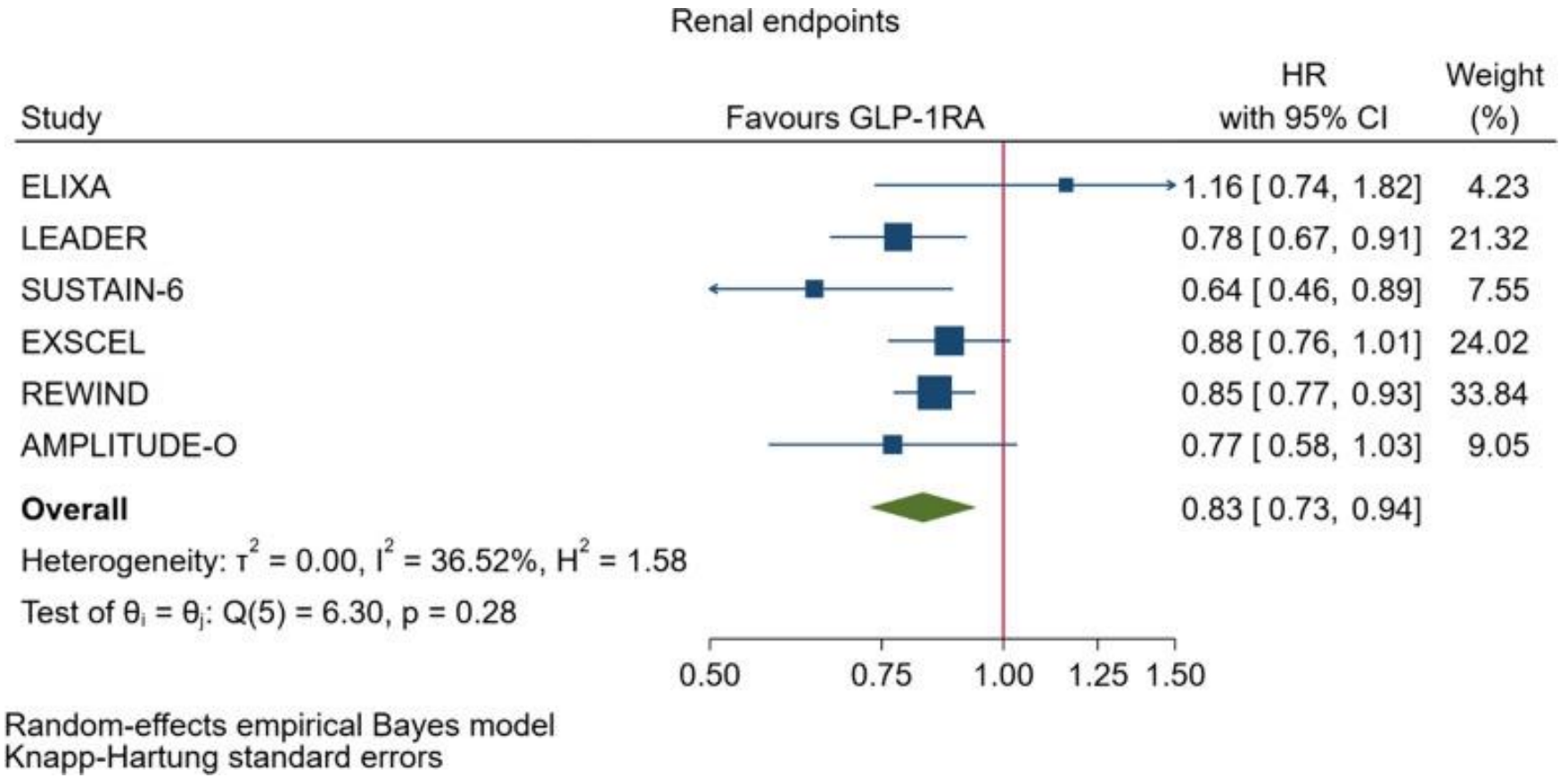
Nephrol Dial Transplant, Volume 39, Issue 12, **December 2024,** Pages 2040–2047,
https://doi.org/10.1093/ndt/gfae106

GLP1
Macroalbuminuria



Daira et al., Cardiovasc Diabetol. 2021

GLP1
Renal Endpoints



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| Overview of select large, placebo-controlled clinical outcome trials assessing the benefits and harms of sodium–glucose cotransporter-2 (SGLT2) inhibitors, glucagon-

The NEW ENGLAND JOURNAL of MEDICINE

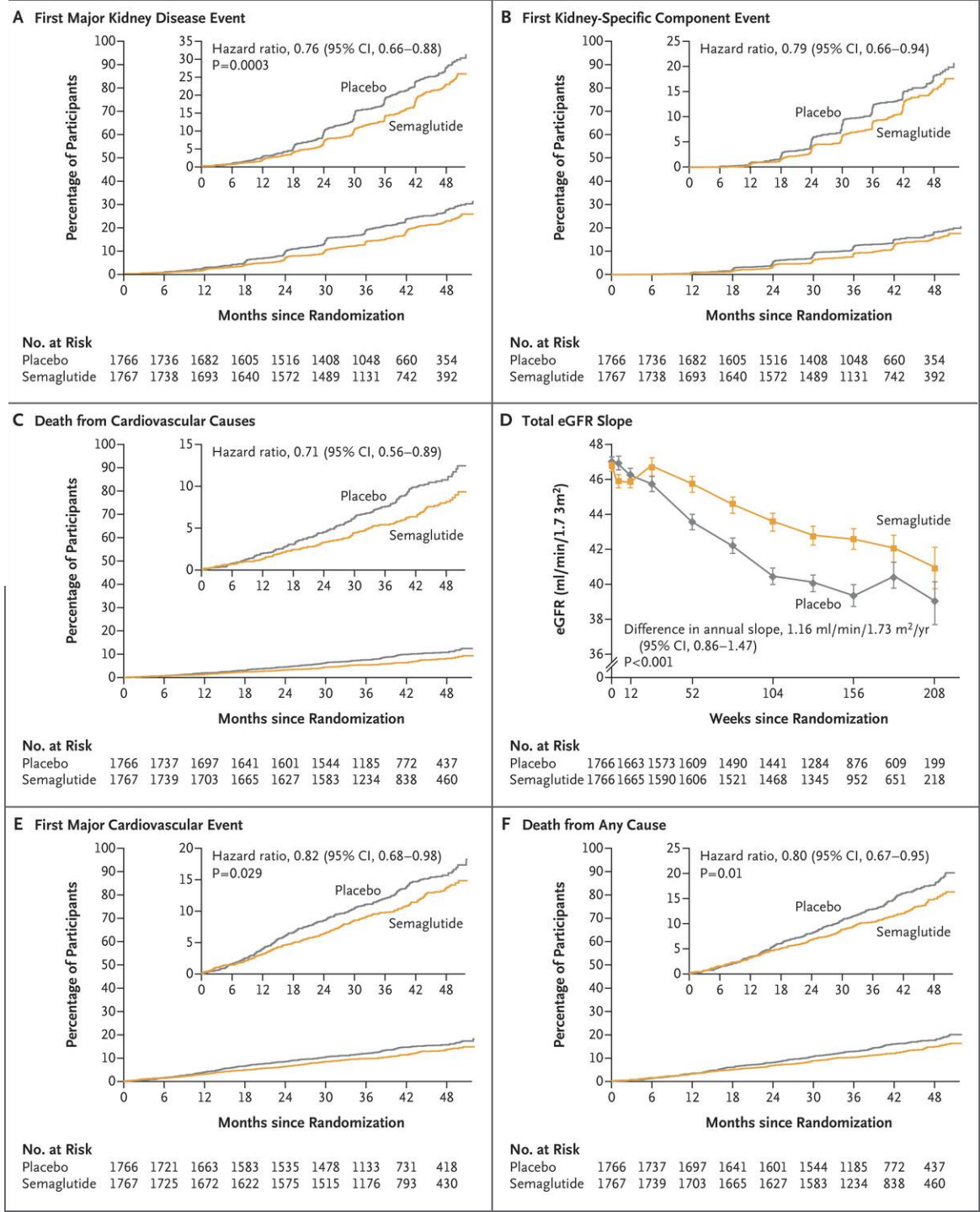
ESTABLISHED IN 1812 JULY 11, 2024 VOL. 391 NO. 2

Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes

Vlado Perkovic, M.B., B.S., Ph.D., Katherine R. Tuttle, M.D., Peter Rossing, M.D., D.M.Sc., Kenneth W. Mahaffey, M.D., Johannes F.E. Mann, M.D., George Bakris, M.D., Florian M.M. Baeres, M.D., Thomas Idorn, M.D., Ph.D., Heidrun Bosch-Traberg, M.D., Nanna Leonora Lausvig, M.Sc., and Richard Pratley, M.D., for the FLOW Trial Committees and Investigators*

ABSTRACT

- CONCLUSIONS
- Semaglutide reduced the risk of clinically important kidney outcomes and death from cardiovascular causes in patients with type 2 diabetes and chronic kidney disease. (Funded by Novo Nordisk; FLOW ClinicalTrials.gov number, NCT03819153.)



Semaglutide for CKD in Patients with Type 2 Diabetes: "FLOW"ing with the Semaglu"TIDE"

#NephJC

METHODS

International, double-blind, placebo-controlled
28 countries

Type 2 DM and CKD:
GFR 50-75 ml/min + ACR 300-5000 mg/g
or
GFR 25-<50 ml/min + ACR 100-5000 mg/g

Median follow-up, 3.4 years

	Major kidney disease events	Death from any causes	Adverse event leading to discontinuation
Placebo n = 1766	7.5 events per 100 patient-years	279(15.8%)	211(11.9%)
	HR 0.76 (95% CI, 0.66-0.88)	HR 0.80 (95% CI, 0.67-0.95)	
Semaglutide n = 1767	5.8 events per 100 patient-years	227(12.8%)	233(13.2%)

Major kidney disease events- kidney failure, ≥50% reduction in GFR, death from CV or kidney-related causes

HR= Hazard ratio

Reference: Perkovic,V et al. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. NEJM, May 2024.

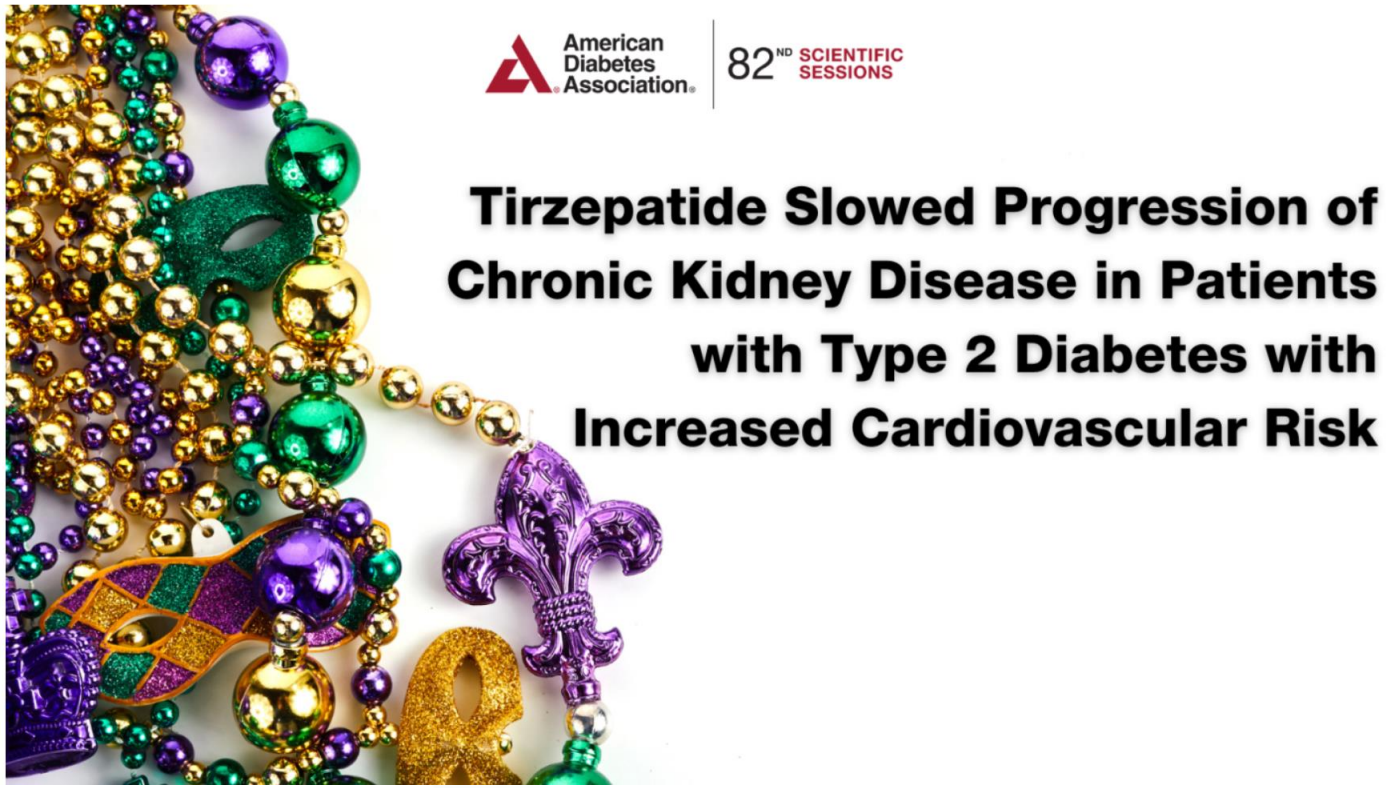
VA by Anjana Gopal 𝕏@anjanagopal9

Conclusion: Semaglutide reduced the risk of clinically important kidney outcomes and death from cardiovascular causes in patients with type 2 diabetes and chronic kidney disease.

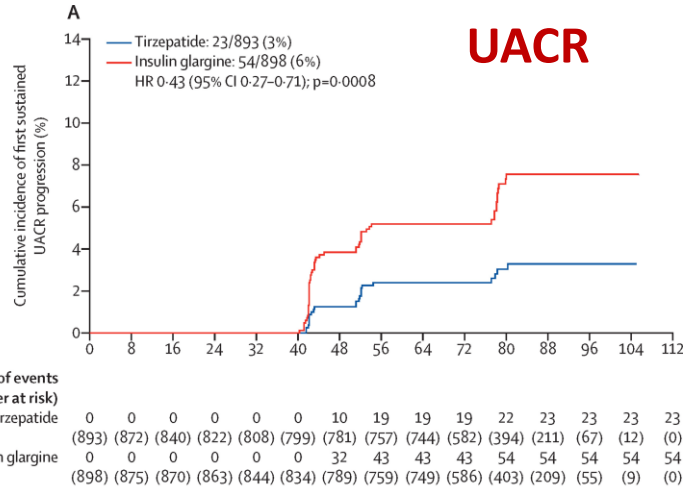
Press release

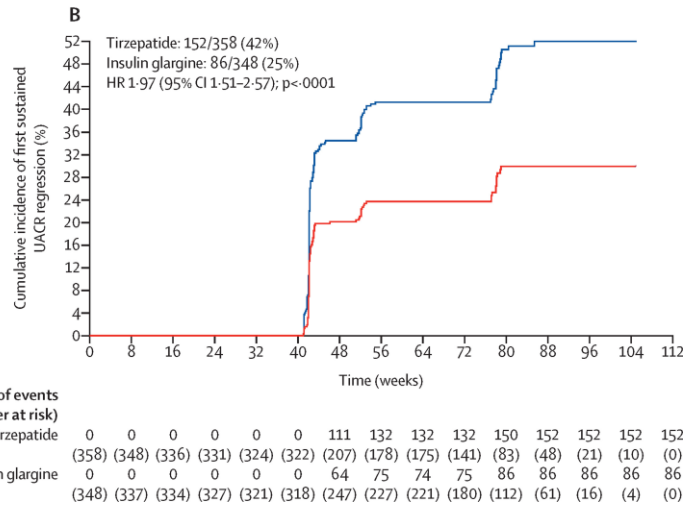
Tirzepatide Slowed Progression of Chronic Kidney Disease in Patients with Type 2 Diabetes with Increased Cardiovascular Risk

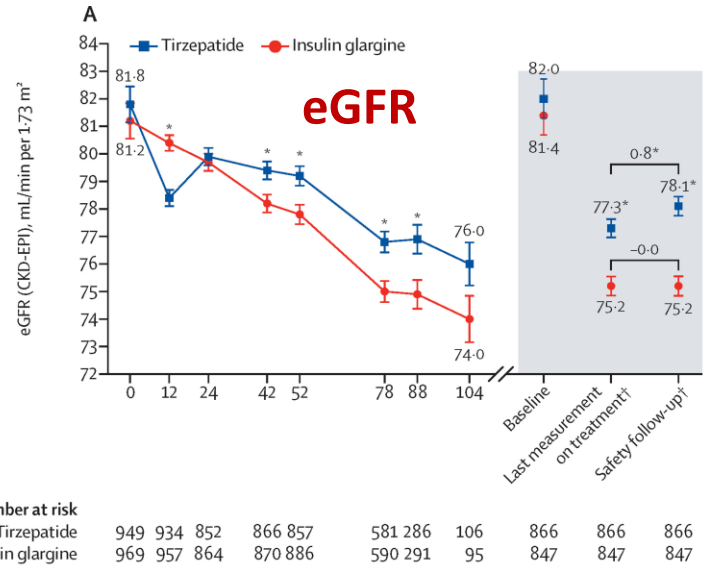
June 03, 2022 | New Orleans, Louisiana

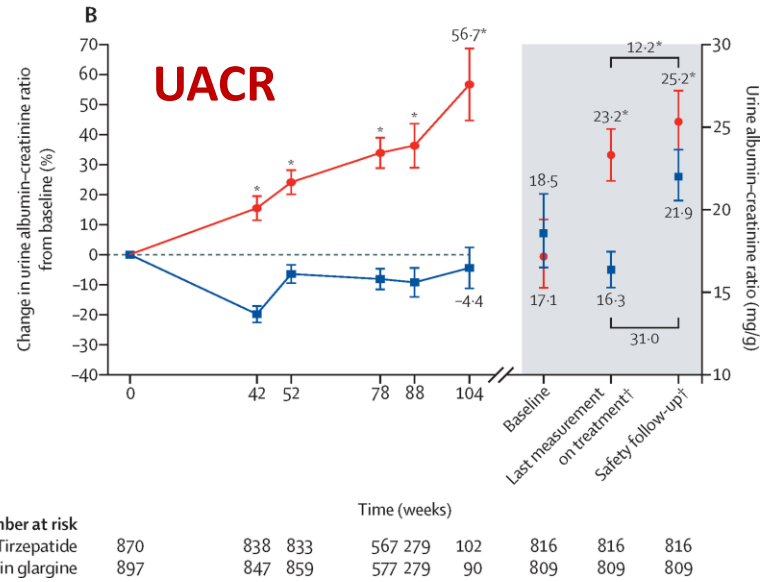


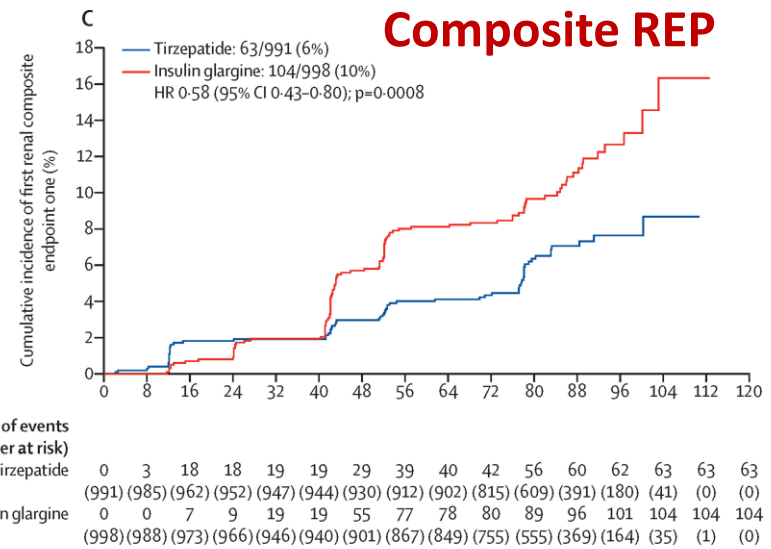
Effects of tirzepatide versus insulin glargine on kidney outcomes in type 2 diabetes in the SURPASS-4 trial: post-hoc analysis of an open-label, randomised, phase 3 trial

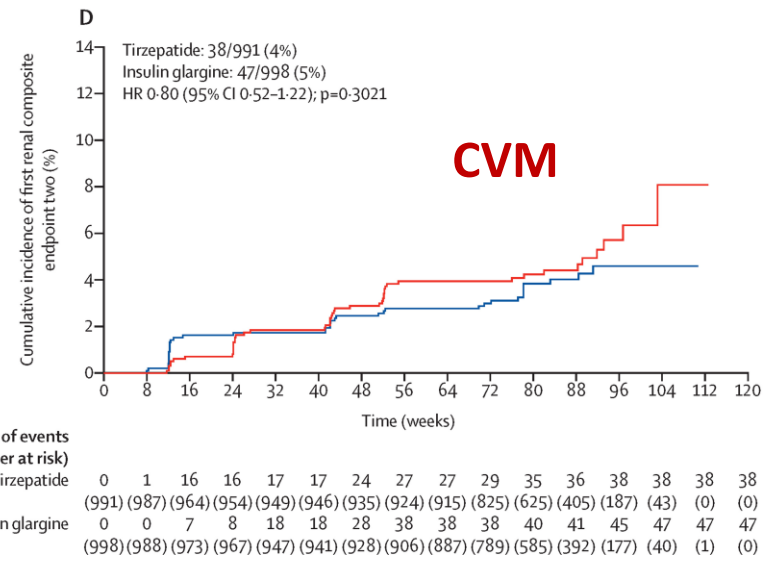










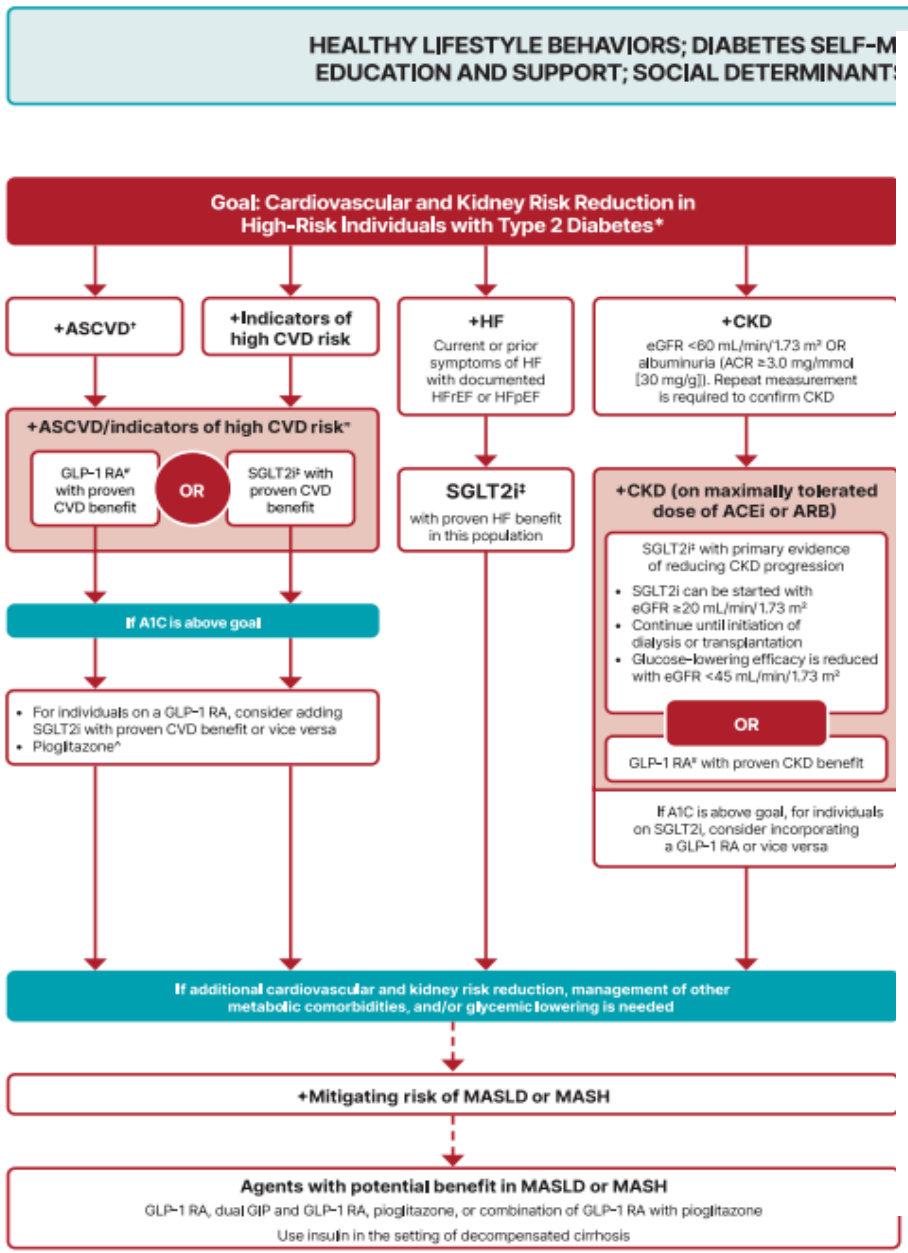


THE LANCET
Diabetes & Endocrinology
September 21, 2022

American Diabetes Association

2025

Use of Glucose-Lowering Medications in the Manage



+CKD
eGFR <60 mL/min/1.73 m² OR
+CKD (on maximally tolerated dose of ACEi or ARB)
SGLT2i‡ with primary evidence of reducing CKD progression
• SGLT2i can be started with eGFR ≥20 mL/min/1.73 m²
• Continue until initiation of dialysis or transplantation
• Glucose-lowering efficacy is reduced with eGFR <45 mL/min/1.73 m²
OR
GLP-1 RA# with proven CKD benefit
If A1C is above goal, for individuals on SGLT2i, consider incorporating a GLP-1 RA or vice versa
on SGLT2i, consider incorporating a GLP-1 RA or vice versa

American Diabetes Association.

2025

Efficacy for weight loss

Very high:
Semaglutide, tirzepatide

High:
Dulaglutide, liraglutide

Intermediate:
GLP-1 RA (not listed above), SGLT2i

Neutral:
Metformin, DPP-4i

Metformin or other agent (including combination therapy) that provides adequate EFFICACY to achieve and maintain glycemic treatment goals

Prioritize avoidance of hypoglycemia in high-risk individuals

Efficacy for glucose lowering

Very high:
Dulaglutide (high dose), semaglutide, tirzepatide, insulin

Combination oral, combination injectable (GLP-1 RA and insulin)

High:
GLP-1 RA (not listed above), metformin, pioglitazone, SGLT2i, sulfonylurea

Intermediate:
DPP-4i

Goal: Achievement and Maintenance of Weight and Glycemic Goals

+Weight management

Efficacy for weight loss

Very high: Semaglutide, tirzepatide

High: Dulaglutide, liraglutide

Intermediate: GLP-1 RA (not listed above), SGLT2i

Neutral: Metformin, DPP-4i

+Achievement and maintenance of glycemic goals

Metformin or other agent (including combination therapy) that provides adequate EFFICACY to achieve and maintain glycemic treatment goals

Prioritize avoidance of hypoglycemia in high-risk individuals

Efficacy for glucose lowering

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Combination oral, combination injectable (GLP-1 RA and insulin)

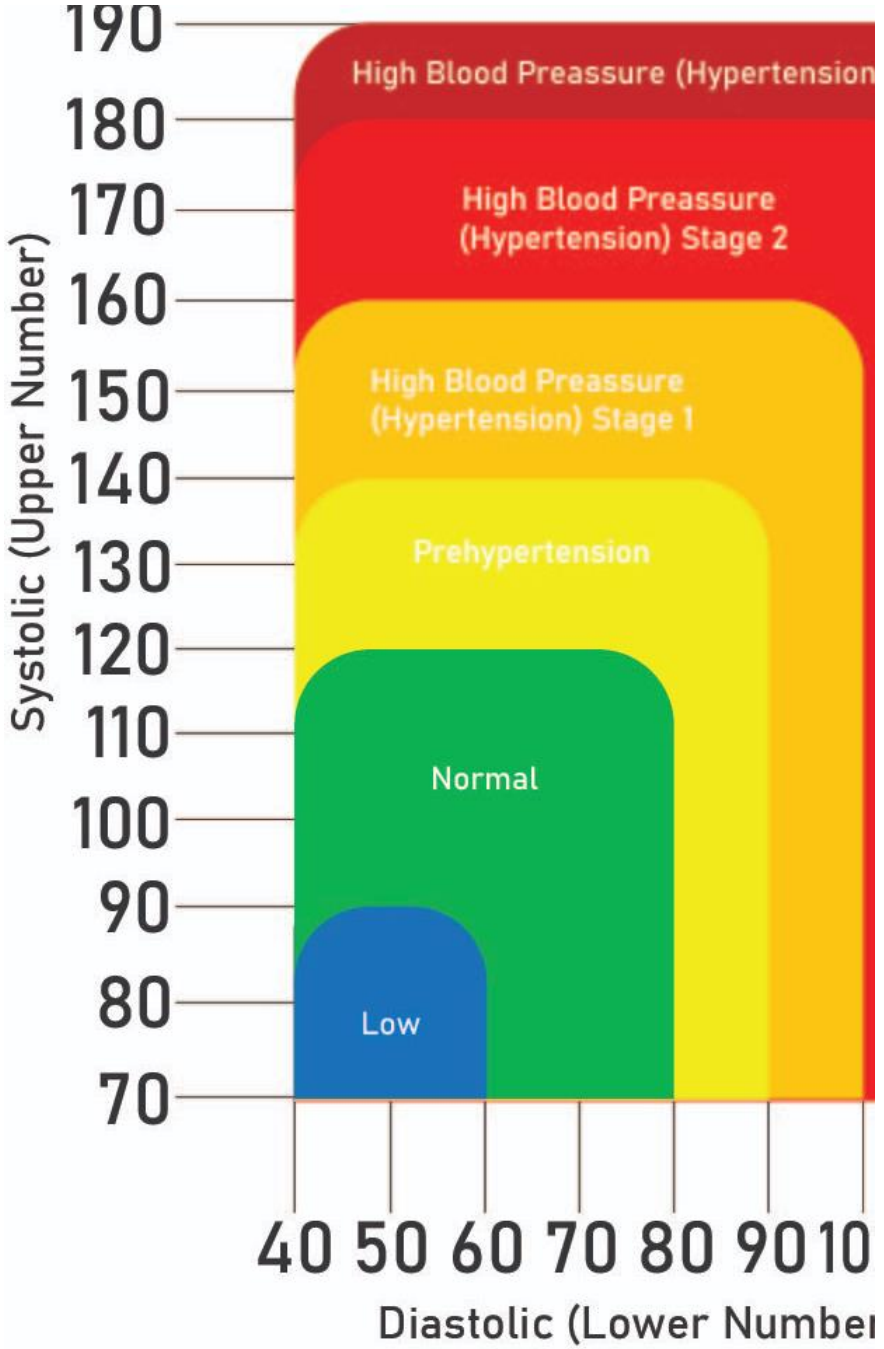
High: GLP-1 RA (not listed above), metformin, pioglitazone, SGLT2i, sulfonylurea

Intermediate: DPP-4i

If A1C is above goal or significant hypoglycemia or hyperglycemia or barriers to care are identified

- Refer to DSMES to support self-efficacy in achievement of treatment goals
- Consider technology (e.g., diagnostic or personal CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of treatment goals

BLOOD PRESSURE



Diabetes Spectr. 2001;14(4):235-240. doi:10.2337/diaspect.14.4.235

UKPDS

	Number of events		
	Intensive	*Conventional*	**NNT*
Glucose control	41	46	20 (95% CI 10–500)
Blood pressure control	51	67	6 (3–10)

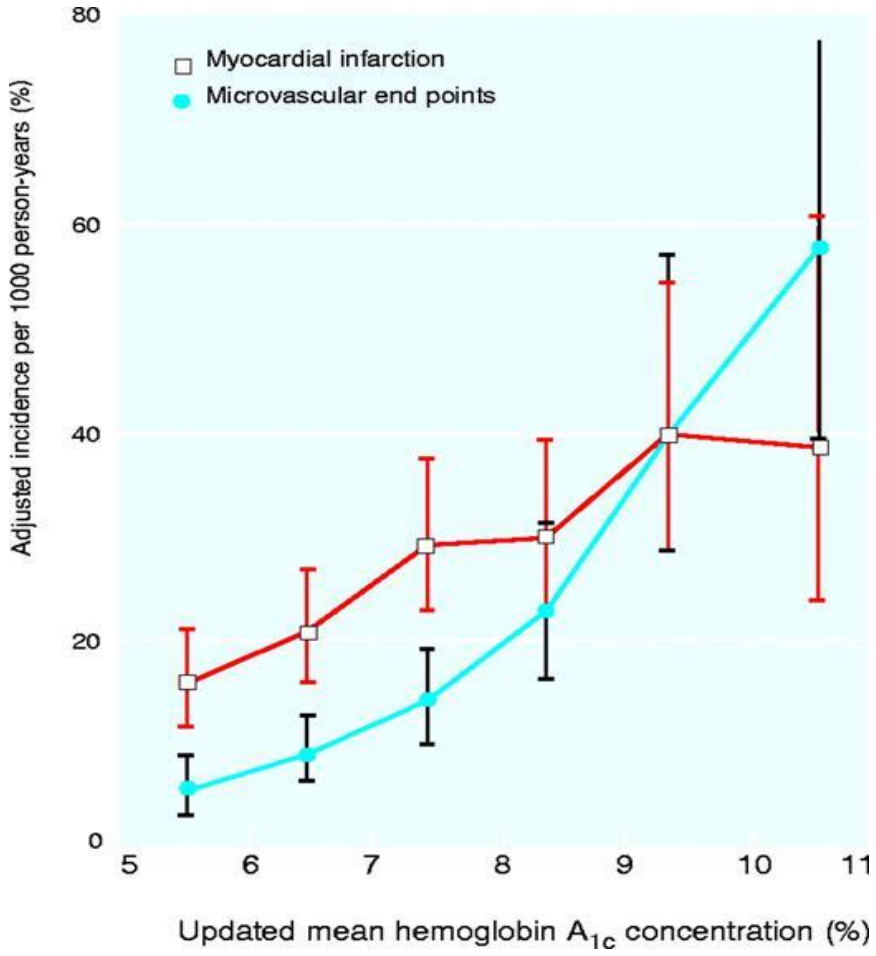
*number needed to treat for 10 years to prevent 1 event.

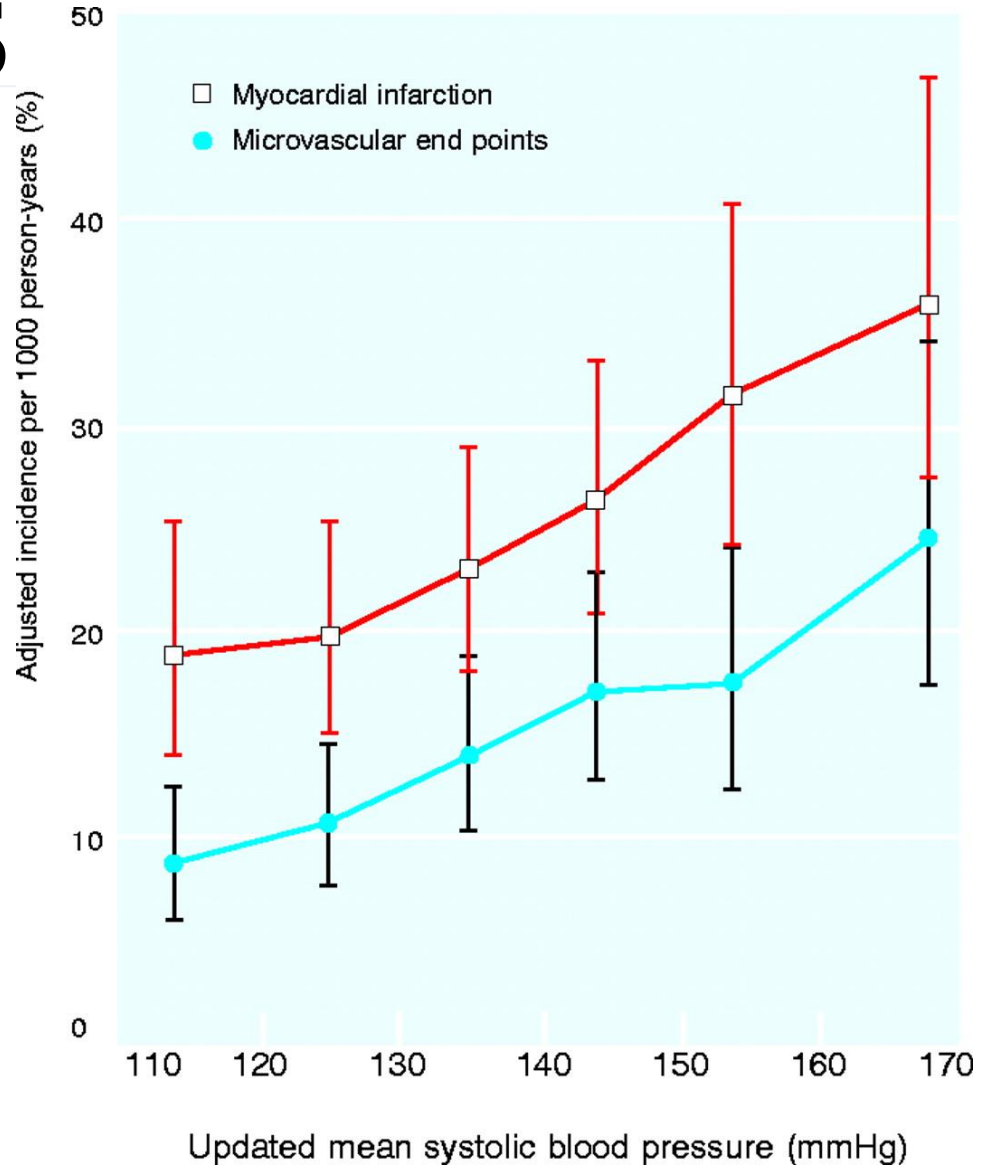
American Diabetes Association®

From: Blood Pressure and the U.K. Prospective Diabetes Study

UKPDS

Diabetes Spectr. 2001;14(4):235-240. doi:10.2337/diaspect.14.4.235





Adjusted incidence of myocardial infarction per 1,000 person-years (%) by systolic blood pressure. Reprinted with permission from Ref. 17.

•. 2023
•. 2023
•. 2023

Current status of rapid decline in renal function owing to diabetes mellitus and its associated factors.

Setting & Participants	Exposure & Outcomes	Results
Japan NDB (national database)	Current clinical practice recommendations	Incidence of 141.50 cases (95% CI 141.07, 141.92) per 1,000 PY
29,396,195 individuals underwent specific health	SBP: 6 categories HbA1c: 5 categories Urine protein: 5 categories Hemoglobin: 4 categories	With diabetes mellitus SBP: Adjusted OR (95%CI)

Overall, 20.83% of patients with DM had a rapid decline in renal function within the observation period. **A rapid decline in renal function was associated with high systolic blood pressure**, poor or strict DM control, increased urinary protein excretion, and decreased blood hemoglobin levels.

Conclusion: The rapid decline in renal function for approximately 1 year was associated with classical risks based on big real-world data in the national database of medical insurance in Japan.

Makoto Fujii et al., Hypertens Res, 2023

Time-centered Approach to Understanding Risk Factors for the Progression of Chronic Kidney Disease

CJASN
Clinical Journal of American Society of Nephrology

Methods

3682 participants from Chronic Renal Insufficiency Cohort Study

GFR 20 to 70 ml/min/1.73 m²
Age 58 ± 11 years
Black 42%
DM 48%

Median Time Spent in CKD Stages	Stage 3a	Stage 3b	Stage 4	Stage 5
	7.9 Years	5 Years	4.2 Years	0.8 Years

Poorly controlled DM	1.8	Years less in CKD stage 3a
	1.4	Years less in CKD stage 3b
	0.1	Years less in CKD stage 5

Systolic BP ≥140 mmHg	6.1	Years less in CKD stage 3a
	3.3	Years less in CKD stage 3b
	0.2	Years less in CKD stage 5

Conclusions There are marked variations in the time spent in the different stages of CKD based on risk factors of interest and stage of disease.

Elaine Ku, Kirsten L. Johansen, and Charles E. McCulloch. Time-centered Approach to Understanding Risk Factors for the Progression of Chronic Kidney Disease. CJASN doi: 10.2215/CJN.10360917.

Elaine Ku et al. CJASN 2018;13:693-701

CJASN

Recom

Recommendations	Class[a]	Level[b]
In patients with diabetic or non-diabetic moderate-to-severe CKD and confirmed BP ≥130/80 mmHg, lifestyle optimization and BP-lowering medication are recommended to reduce CVD risk, provided such treatment is well tolerated.[275,766]	I	A
In adults with moderate-to-severe CKD who are receiving BP-lowering drugs and who have eGFR >30 mL/min/1.73 m^2, it is recommended to target systolic BP to 120–129 mmHg, if tolerated. Individualized BP targets are recommended for those with lower eGFR or renal transplantation.[274,779]	I	A
In hypertensive patients with CKD and eGFR >20 mL/min/1.73 m^2, SGLT2 inhibitors are recommended to improve outcomes in the context of their modest BP-lowering properties.[776,777]	I	A
ACE inhibitors or ARBs are more effective at reducing albuminuria than other BP-lowering agents and should be considered as part of the treatment strategy for patients with hypertension and microalbuminuria or proteinuria.[780–782]	IIa	B

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CKD, chronic kidney disease, eGFR, estimated glomerular filtration rate; SGLT2, sodium–glucose co-transporter 2.
[a]Class of recommendation.
[b]Level of evidence.

ESC 2023

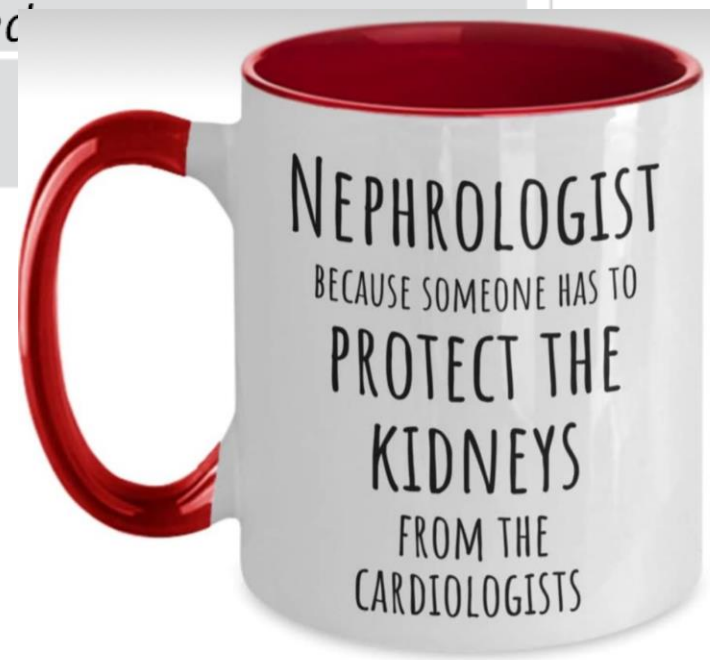
Age gr

18–69

≥70 ye

DBP tr
target

mHg)		
KD	+ CAD	+ Stroke/TIA
–130	120–130	120–130
ble if tolerated		
0 mmHg if tolerated		
ble if tolerate		
ed patients		



Blood Pressure control

2021 HTN Guidelines

Chapter 3: Blood pressure management in patients with CKD, with or without diabetes, not receiving dialysis	
• **Recommendation 3.1.1**	We suggest that adults with high BP and CKD be treated with a target systolic blood pressure (SBP) of <120 mm Hg, when tolerated, using standardized office BP measurement *(2B)*.

Chapter 4: Blood pressure management in kidney transplant recipients (CKD G1T–G5T)	
• **Practice Point 4.1**	Treat adult kidney transplant recipients with high BP to a target BP of <130 mm Hg systolic and <80 mm Hg diastolic using standardized office BP measurement (see

Blood Pressure control

2024 CKD Guidelines

Chapter 3: Blood pressure management in patients with CKD, with or without diabetes, not receiving dialysis	
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#NephJC

Shahin Mohammed, @shahsonride.bsky.social

	BPROAD	ACCORD	SPRINT	ESPRIT
N=	12821	4733	9261	11255
Age	>50	40-79 with CVD or 55-79 with subclinical CVD	>55	>50
Diabetes	100%	100%	Excluded	38.7%
Chronic Kidney Disease Exclusion Criteria	Excluded if eGFR <30 or creatinine >2 mg/dl	Excluded creatinine >1.5 mg/dl	Excluded if eGFR <20	Excluded eGFR < 45
	Exclude if • Proteinuria > 1 g/day • GN	Exclude if • Proteinuria > 1 g/day • Organ transplant	Exclude if • Proteinuria > 1 g/day • GN likely/needing IS • Organ transplant	Exclude if • Proteinuria ≥ 2+ in last 6 months • GN likely/needing IS • Organ transplant
Country	China	USA, Canada	USA	China
Mean Age	63.8	62.2	67.9	64.6
BP method	Automated (Omron)	Automated (Omron)	Automated (Omron) Mainly unattended	Automated (Omron)

#NephJC

Shahin Mohammed, @shahsonride.bsky.social

	BPROAD	ACCORD	SPRINT	ESPRIT
Median follow-up	4.2 years	4.7 years	3.26 years	3.4 years
Mean achieved Systolic BP (SBP)	121.6 vs 133.2	119.3 vs 133.5	121.4 vs 136.2	119.1 vs 134.8
Mean achieved SBP difference	-11.6 at 1 year	-14.2 at 1 year	-14.8 at 1 year	-15.7
Composite CV Outcomes	IR 1.65 vs 2.09 HR 0.79 (0.69-0.90)	1.87 vs 2.89% /year HR 0.88 (0.73- 1.06)	1.65 vs 2.19% /year HR 0.75 (0.64-0.89)	7.4 vs 8.8% HR 0.88 (0.78-0.99)
All Cause Mortality	IR 0.69 vs 0.73 HR 0.95 (0.77-1.17)	1.28 vs 1.19 % /year HR 1.07 (0.85-1.35)	1.03 vs 1.4% /year HR 0.73 (0.60-0.90)	2.8 vs 3.6% HR 0.79 (0.64-0.97)
Stroke	IR 1.19 vs 1.5 HR 0.79 (0.67-0.92)	0.32 vs 0.53% /year HR 0.59 (0.39-0.89)	0.41 vs 0.47% /year HR 0.89 (0.63-1.25)	4.7 vs 5.4% HR 0.86 (0.73-1.02)
Heart Failure	IR 0.13 vs .19 HR 0.66 (0.41-1.04)	0.73 vs 0.78% /year HR 0.94 (0.70-1.26)	0.41 vs 0.67% /year HR 0.62 (0.45-0.84)	1 vs 1.4% HR 0.73 (0.52-1.03)
CV Death	IR 0.24 vs 0.32 HR 0.76 (0.55-1.06)	0.52 vs 0.49% /year HR 1.06 (0.74-1.52)	0.25 vs 0.43% /year HR 0.57 (0.38-0.85)	1.1 vs 1.7% HR 0.61 (0.44-0.84)

Between Sept 17, 2019, and July 13, 2020, **11 255 participants (4359 with diabetes and 3022 with previous stroke)** were assigned to intensive treatment (n=5624) or standard treatment (n=5631).

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ARTICLES | VOLUME 404, ISSUE 10449, P245-255, JULY 20, 2024

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Lowering systolic blood pressure to less than 120 mm Hg versus less than 140 mm Hg in patients with high cardiovascular risk with and without diabetes or previous stroke: an open-label, blinded-outcome, randomised trial

Jiamin Liu, MD * • Yan Li, MD * • Jinzhuo Ge, BM * • Xiaofang Yan, MD * • Haibo Zhang, MD • Prof Xin Zheng, PhD • et al. Show all authors • Show footnotes

Published: June 27, 2024 • DOI: https://doi.org/10.1016/S0140-6736(24)01028-6 • Check for updates

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ARTICLES | VOLUME 404, ISSUE 10449, P245-255, JULY 20, 2024

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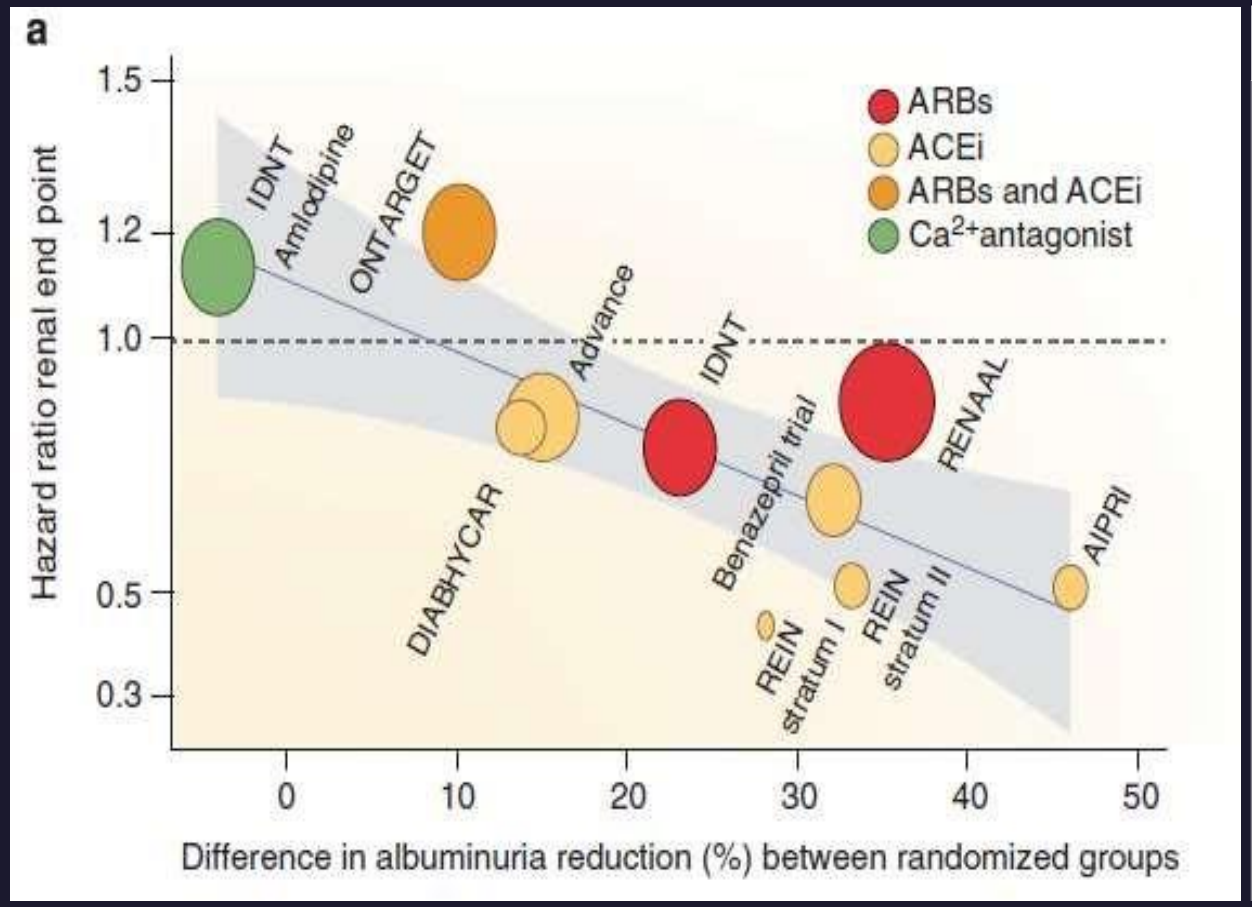
Lowering systolic blood pressure to less than 120 mm Hg versus less than 140 mm Hg in patients with high cardiovascular risk with and without diabetes or previous stroke: an open-label, blinded-outcome, randomised trial

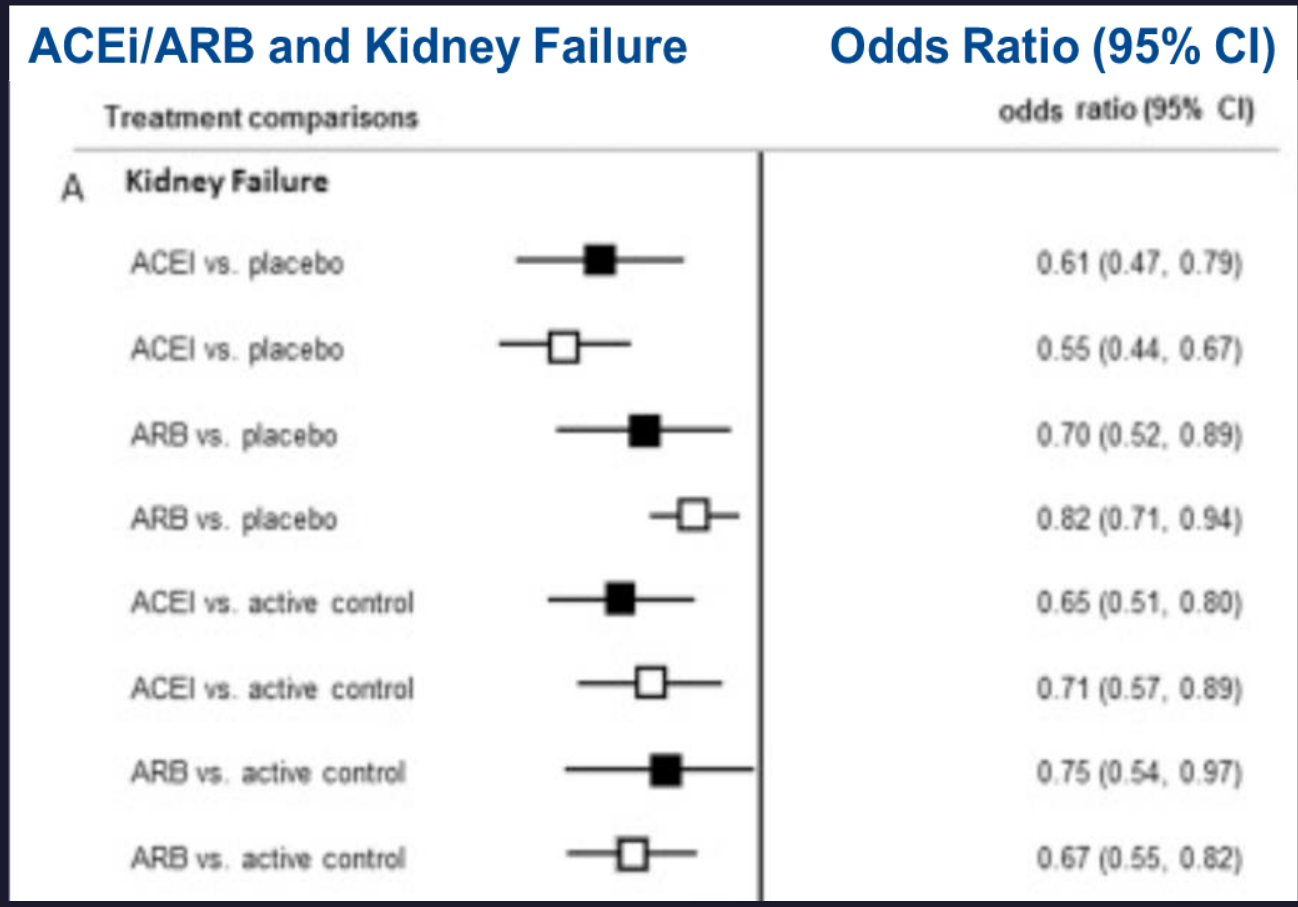
Interpretation

For hypertensive patients at high cardiovascular risk, regardless of the status of diabetes or history of stroke, the treatment strategy of **targeting systolic blood pressure of less than 120 mm Hg**, as compared with that of less than 140 mm Hg, **prevents major vascular events, with minor excess risk**.

RAAS in RCTs

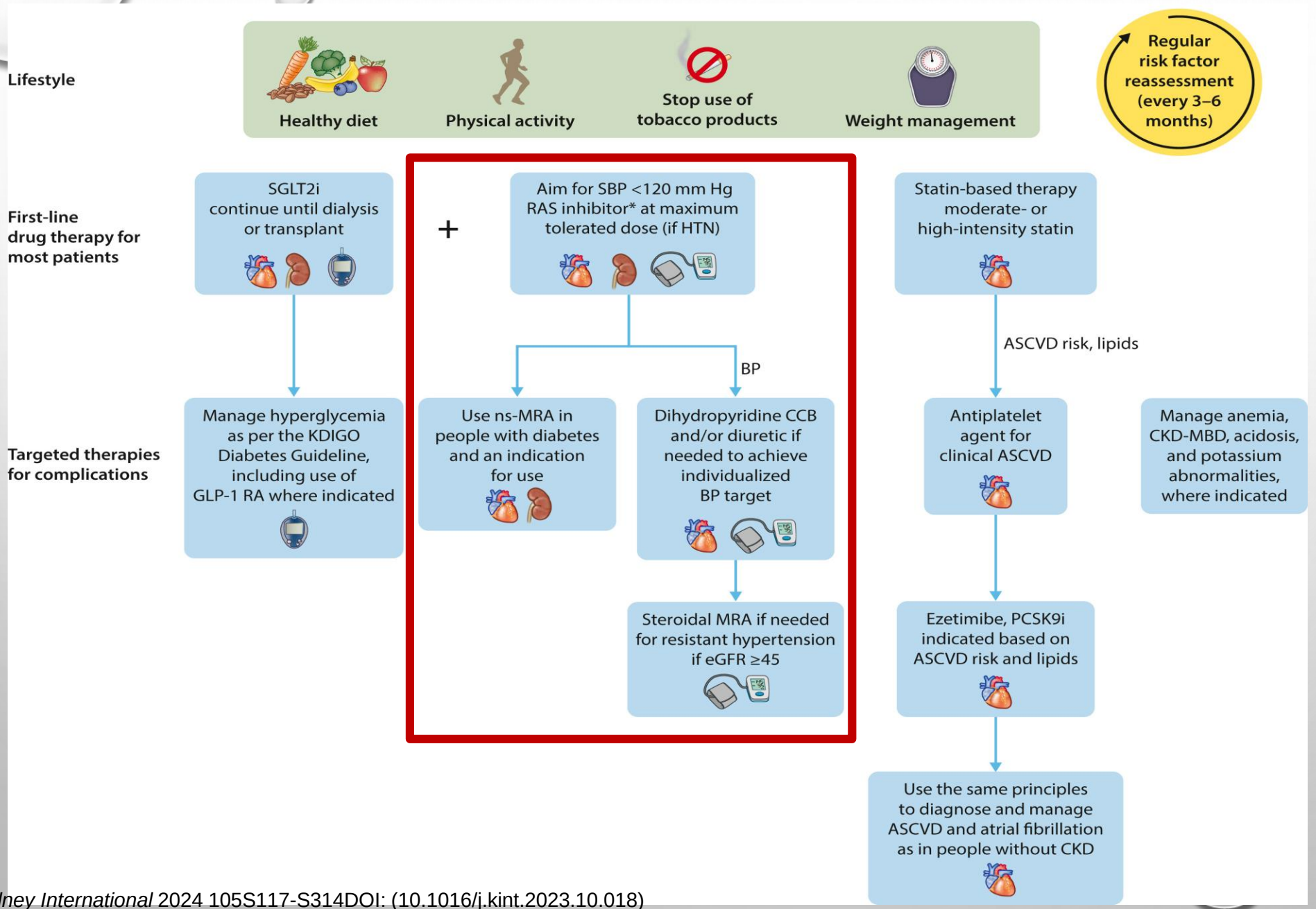
ALBUMINURIA REDUCTION





Kidney International (2014) 86, 40–49; doi:10.1038/ki.2013.490

MANAGEMENT- CKD



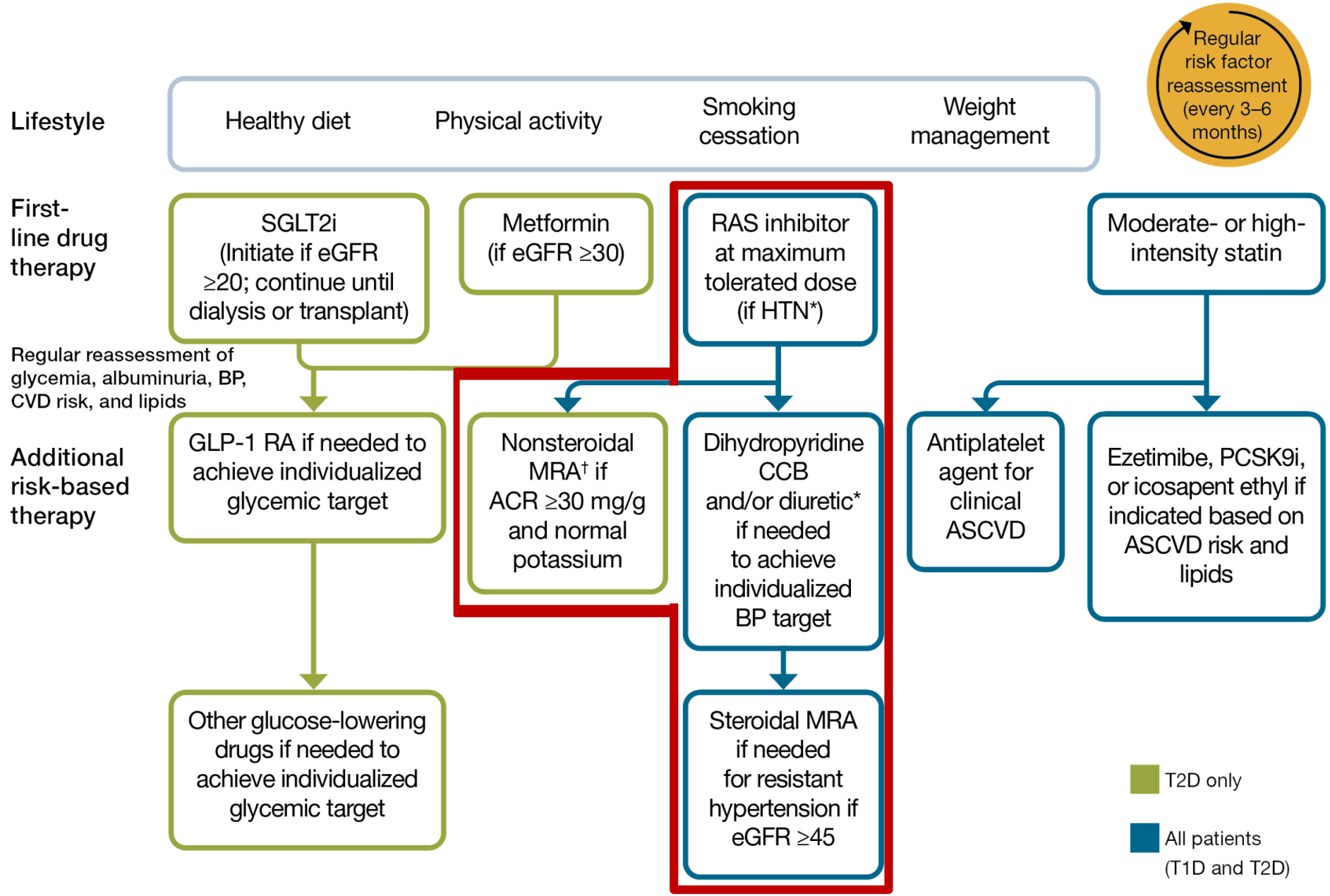
KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES — KDIGO

2024

ACE, angiotensin-converting enzyme inhibitor; ACR, albumin-creatinine ratio; ARB, angiotensin II receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CCB, calcium channel blocker; CGM, continuous glucose monitoring; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; MRA, mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; SGLT2, sodium-glucose cotransporter-2; T2D, Type 2 diabetes; TG, triglycerides

Kidney International 2024 105S117-S314DOI: (10.1016/j.kint.2023.10.018)

Holistic Approach to Improving Outcomes in People With Diabetes and CKD



American Diabetes Association

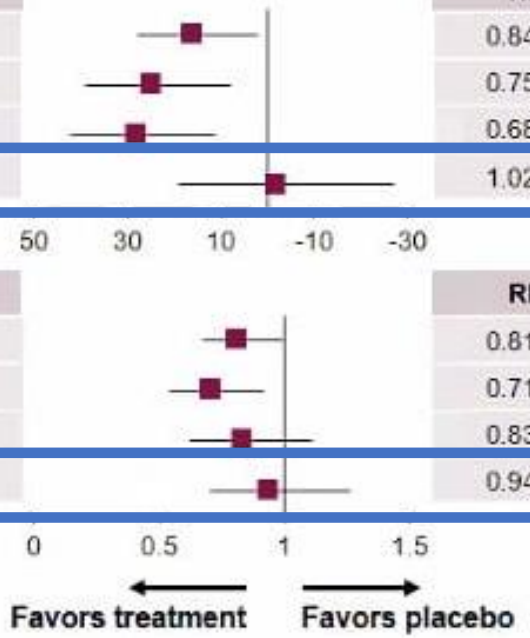
2025

American Diabetes Association Primary Care Advisory Group. 11. Chronic kidney disease and risk management: *Standards of Care in Diabetes—2024* abridged for primary care professionals. Clin Diabetes 2024;42:212–213 (doi: 10.2337/cd24-a011)

RAASi do not reduce risk of death for CKD patients

Effect of losartan and irbesartan, compared to placebo, on the risk of renal composite[1,2]

Renal outcome	Treatment group Number (%)	Treatment group Events per 100 P-Y	Placebo group Number (%)	Placebo group Events per 100 P-Y	Risk value	*P* value
RENAAL[1]					**HR (95% CI)**	
Primary composite end point	327 (43.5)	15.9	359 (47.1)	18.1	0.84 (0.72, 0.98)	0.02
dSCr	162 (21.6)	7.9	198 (26.0)	10.0	0.75 (0.61, 0.92)	0.006
ESRD	147 (19.6)	6.8	194 (25.5)	9.1	0.68 (0.58, 0.89)	0.002
All-cause mortality	158 (21.0)	6.8	155 (20.3)	6.6	1.02 (0.81, 1.27)	0.88
IDNT[2]					**RR (95% CI)**	
Primary composite end point	189 (32.6)	–	222 (39.0)	–	0.81 (0.67–0.99)	0.03
dSCr	98 (16.9)	–	135 (23.7)	–	0.71 (0.54–0.92)	0.009
ESRD	82 (14.2)	–	101 (17.8)	–	0.83 (0.62–1.11)	0.19
All-cause mortality	87 (15.0)	–	93 (16.3)	–	0.94 (0.70–1.27)	0.69



- 1. Brer

What is the role of initiation of ACEi or ARB in advanced chronic kidney disease?

#NephJC

Systematic review and meta-analysis

Ovid Medline & CKD EPI Clinical Trials Consortium

1739 participants from 18 trials

Mean eGFR 22.2 ml/min/1.73 m^2

Objective

To compare use of ACEi/ARB Vs. placebo or other antihypertensives in patients with Stage 4 CKD with rates of KFRT and death

Findings

624 (35.9%) developed KFRT

133 (7.6%) died during a median follow-up of 34 months

KFRT- Kidney failure with renal replacement therapy

Outcomes

ACEi/ARB treatment initiation led to lower risk for KFRT HR 0.66 (95% CI, 0.55 to 0.79)

No risk reduction for risk of death
HR 0.86
(95 % CI 0.58-1.28)

Conclusion: Initiation of ACEi or ARB therapy protects against KFRT, but not death, in people with advanced CKD

Reference: Ku E et al Ann Intern Med. 2024 Jul;177(7):953-963. doi: 10.7326/M23-3236

VA by Nikhil Elenjickal MD, DNB @DrNikhilJ1

AJKD NATIONAL KIDNEY FOUNDATION

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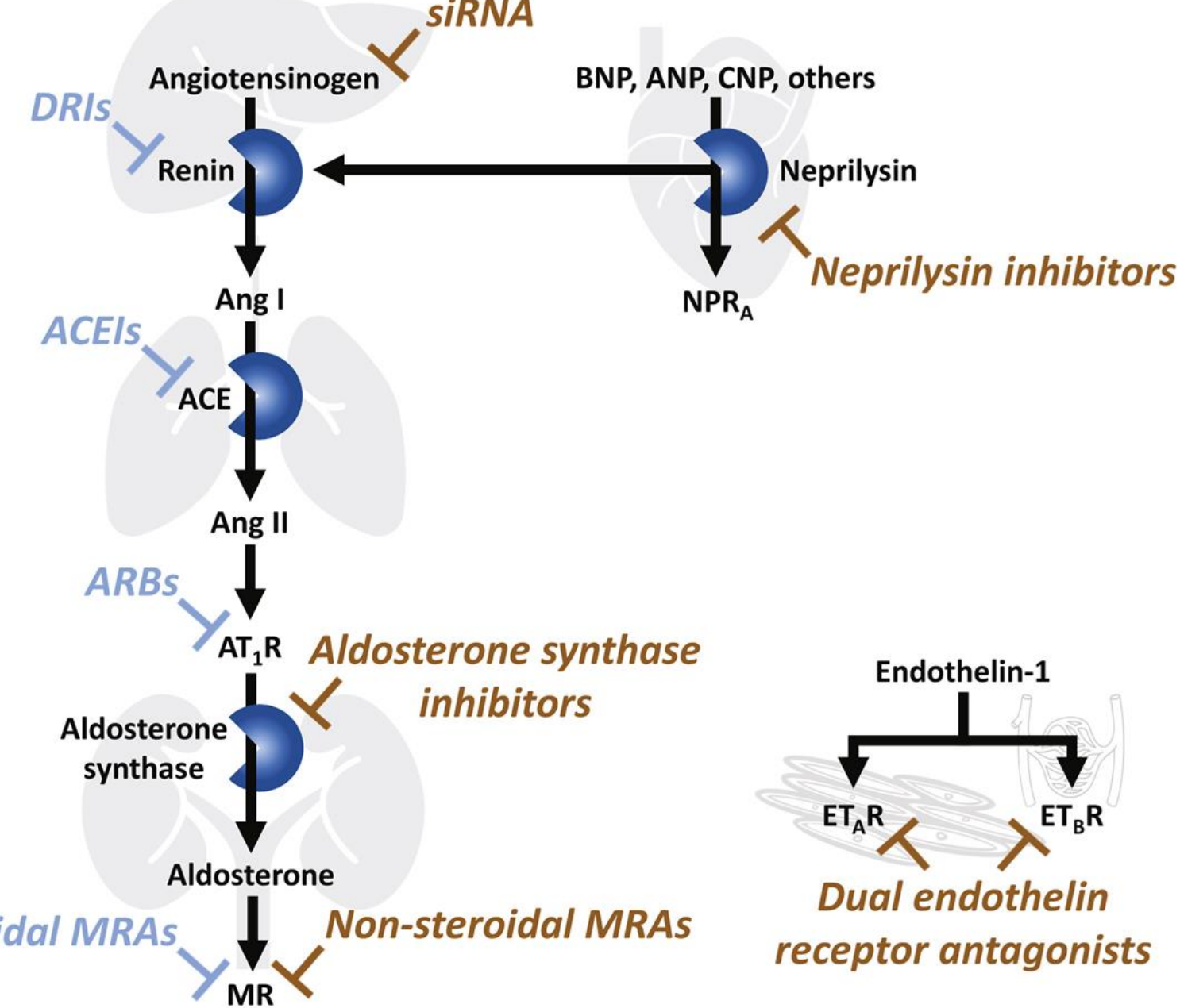
IN THE LITERATURE · Volume 83, Issue 3, P411-414, March 2024 Download Full Issue

Entering a New Era of Antihypertensive Therapy

Jordana B. Cohen [1,2,3] · Adam P. Bress [4]

Affiliations & Notes Article Info



Mechanistic targets of several existing (light blue) and nov
antihypertensive classes currently under investigation. Ab
angiotensin-converting enzyme inhibitor; Ang, angiotensi
receptor blocker; ANP, A-type natriuretic peptide; AT1R, a
receptor; BNP, B-type natriuretic peptide; CNP, C-type nat
direct renin inhibitor; ETAR, endothelin type A receptor; E
B receptor; MR, mineralocorticoid receptor; MRA, mineralocorticoid receptor antagonist; NPRA, natriuretic peptide receptor A.

Jordana B. Cohen, Adam P. Bress, AJKD 2024

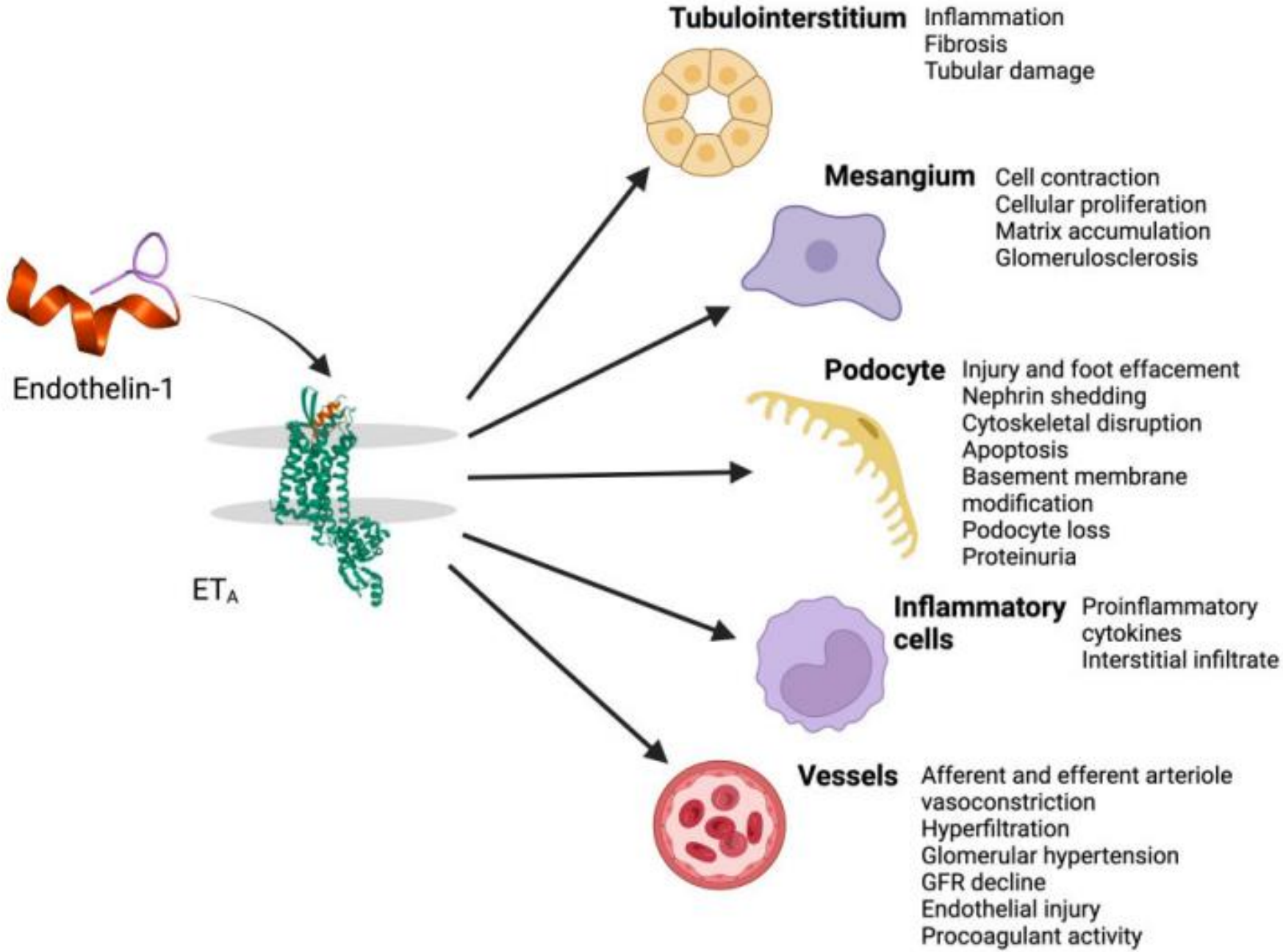
Clinical Kidney Journal, 2024, vol. 17, no. 4, sfae072

https:/doi.org/10.1093/ckj/sfae072
Advance Access Publication Date: 19 March 2024
CKJ Review

CKJ REVIEW

Endothelin receptor antagonists in diabetic and non-diabetic chronic kidney disease

Vanja Ivković[1,2] and Annette Bruchfeld[3,4]



Endothelin-1 actions in the kidney contributing to the development of CKD.

SONAR

Atrasentan gives a weak signal for improving diabetic nephropathy

N = 5117

Type 2 DM, 18-85 years

eGFR: 25 -75 ml/min

UACR: 300 – 5000 mg/dl

Max. RAAS blockade

N = 5117

All atrasentan 0.75mg

IF

> 30 %

No fluid overload

Non-responders (N = 2469) excluded from primary analysis

N = 2648

Responders 52%

N = 1323
Placebo

N = 1325
Atrasentan 0.75mg

ESRD, 2x sCr	CV death, AMI, stroke	Heart failure hospitalization
8%	13%	2%
p = 0.004	p = 0.049	p = 0.20
6%	11%	3%

Median follow-up = 2.2 years

Interpretation: Atrasentan reduced the risk of renal events in selected patients with diabetic nephropathy at high risk for developing ESRD.

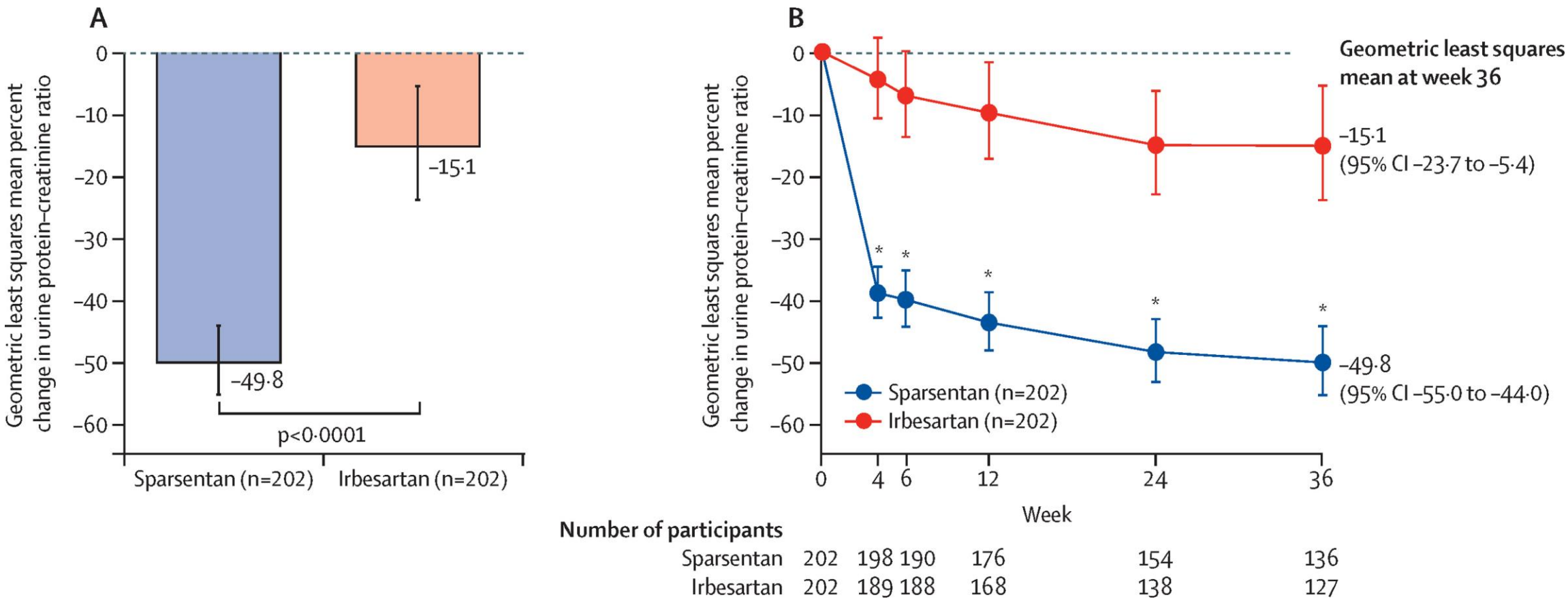
Heerspink H, Parving H-H, Andress D, Bakris G, Correa-Rotter R, Hou F-F, et al. Atrasentan and renal events in patients with type 2 diabetes and chronic kidney disease (SONAR): a double-blind, randomised, placebo-controlled trial. Lancet 2019

@NephroGuy

SPARSANTAN

- SPARSANTAN: an Endothelin Receptor Antagonist and Angiotensin 2 Receptor Blocker.

UACR


A
Geometric least squares mean percent change in urine protein–creatinine ratio
0
−10
−20
−30
−40
−50
−60
−49·8
−15·1
p<0·0001
Sparsentan (n=202)
Irbesartan (n=202)
B
Geometric least squares mean percent change in urine protein–creatinine ratio
Geometric least squares mean at week 36
−15·1
(95% CI −23·7 to −5·4)
−49·8
(95% CI −55·0 to −44·0)
Sparsentan (n=202)
Irbesartan (n=202)
0
4
6
12
24
36
Week
Number of participants
Sparsentan 202 198 190 176 154 136
Irbesartan 202 189 188 168 138 127

Is Zibotentan Safe and Efficacious in Retarding Chronic Kidney Disease Progression? (ZENITH-CKD)

#NephJC

- 18 countries
- Randomized, Double blinded
- Age ≥ 18 to ≤ 90 (Median age 62.8 years)
- eGFR ≥ 20 ml/min
- UACR 150-5000 mg/g (Median – 565 mg/g)
- April 2021 – Jan 2023
- Stable dose of ACEi or ARBs for 4 weeks

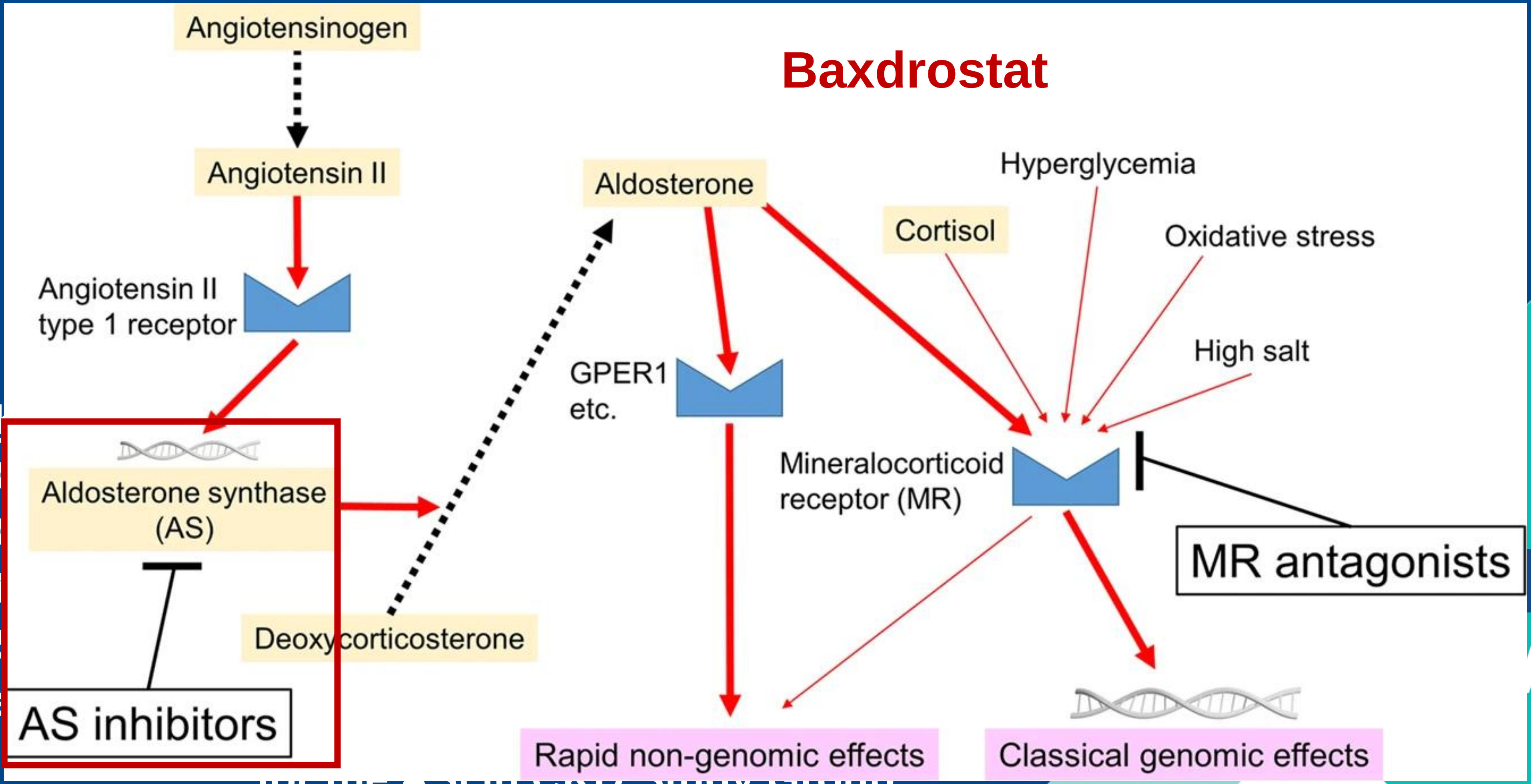
Randomized into three groups 2:1:2	All were on Dapagliflozin 10 mg		
	Zibotentan 1.5 mg	Zibotentan 0.25 mg	Placebo
Number of patients	179	91	177
% Mean change in UACR (baseline to 12 weeks)	-52.5% (-59 to -44.9) (P<0.0001)	-47.7% (-55.7 to -38.2) (P=0.0022)	-28.3% (-37.8 to -17.4) (ref)
Fluid retention events	18%	9%	8%

Conclusion: Zibotentan reduced albuminuria with an acceptable tolerability and safety profile in chronic kidney disease patients already receiving currently recommended therapy

Heerspink HJL et al, Lancet 2023

VA by
Dr Sabarinath S MD DM FASN
@sabarivenus

Aldosterone synthase inhibition with or without

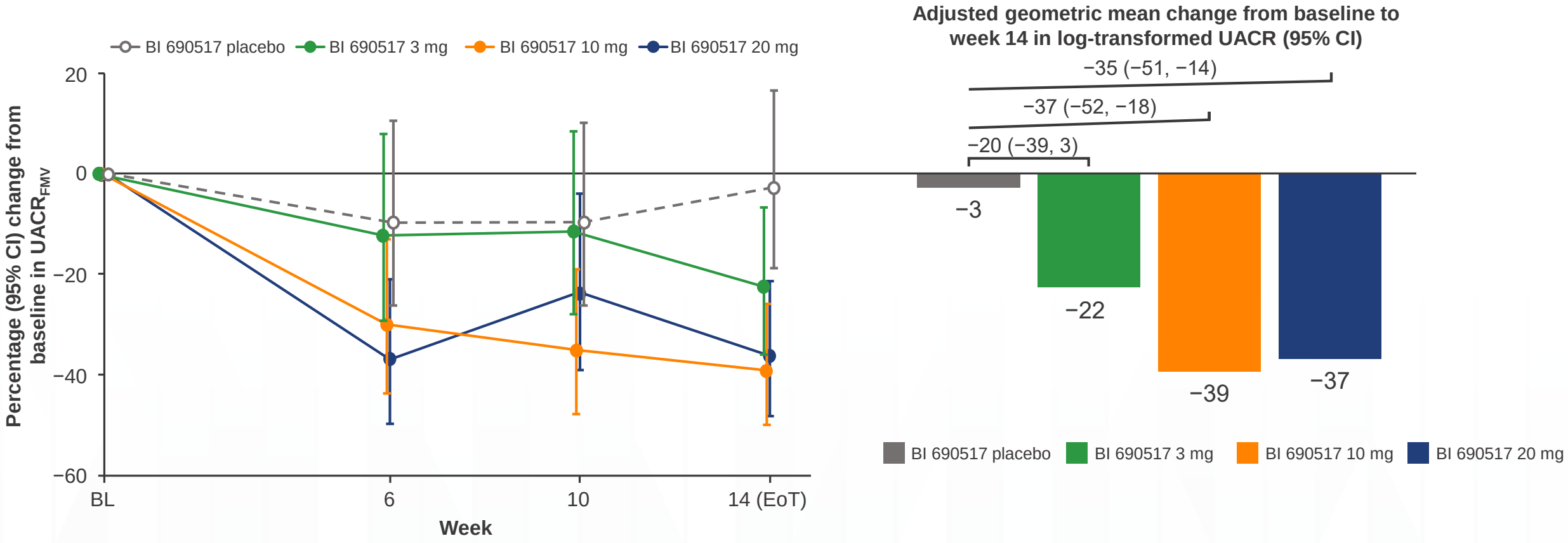


for the ASi in CKD Study Group

KIDNEY WEEK 2023

Primary endpoint: $UACR_{FMV}$ percentage change from baseline to week 14

Patients without empagliflozin in the background

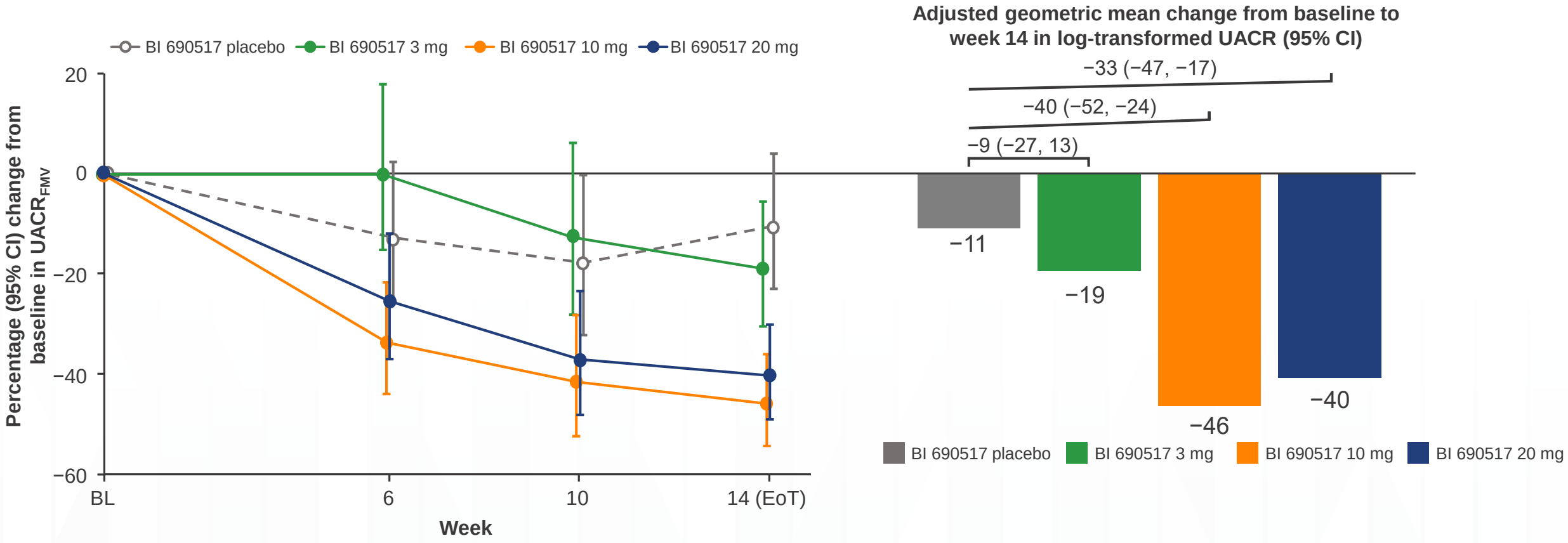


FMV, first morning void

Adjusted effect of log-transformed UACR from baseline to week 14 was estimated using a mixed model for repeated measures (MMRM). The MMRM included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, and randomization stratum as main effects, as well as random effects of patient

Primary endpoint: $UACR_{FMV}$ percentage change from baseline to week 14

Patients with empagliflozin in the background



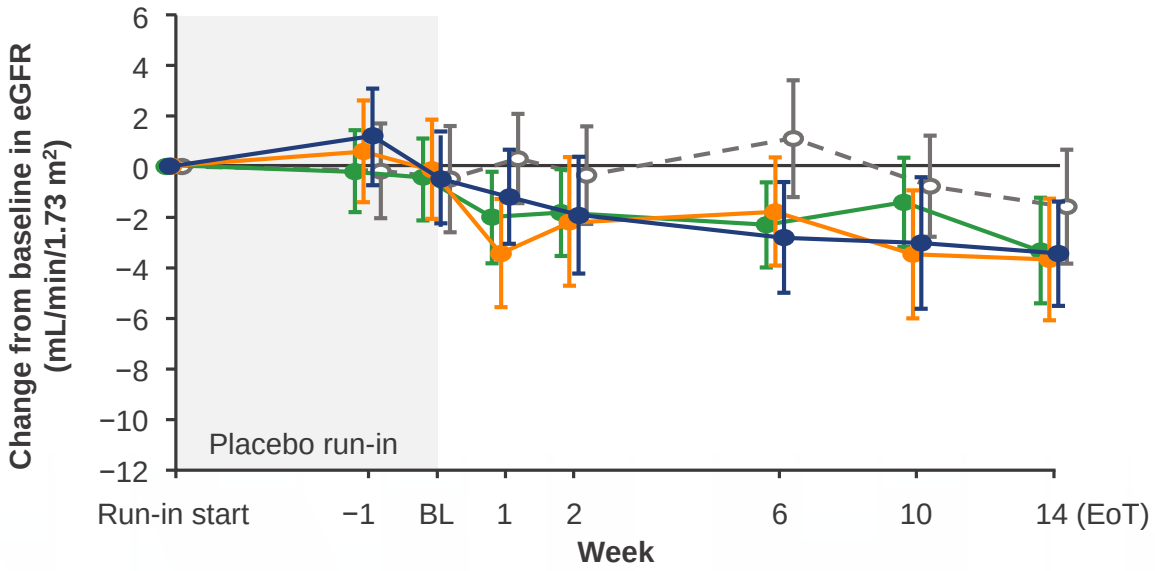
FMV, first morning void

Adjusted effect of log-transformed UACR from baseline to week 14 was estimated using a mixed model for repeated measures (MMRM). The MMRM included the fixed effects of treatment at each visit, baseline (continuous) at each visit, and baseline, visit, treatment, and randomization stratum as main effects, as well as random effects of patient

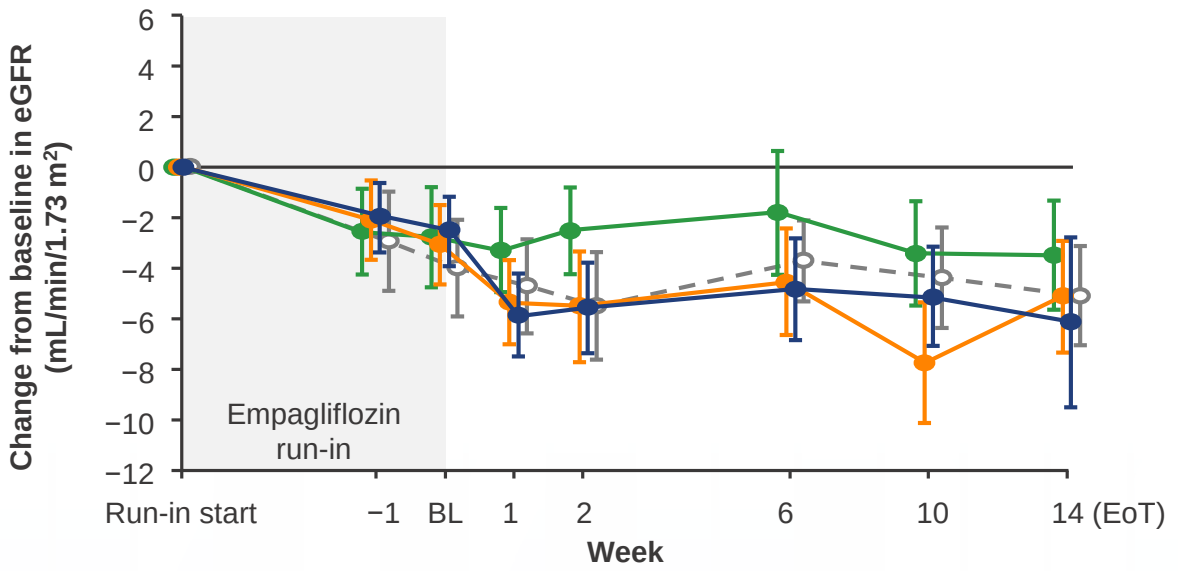
Additional endpoint: Change in eGFR

BI 690517 had similar effects on eGFR irrespective of empagliflozin background treatment

Patients without empagliflozin in the background

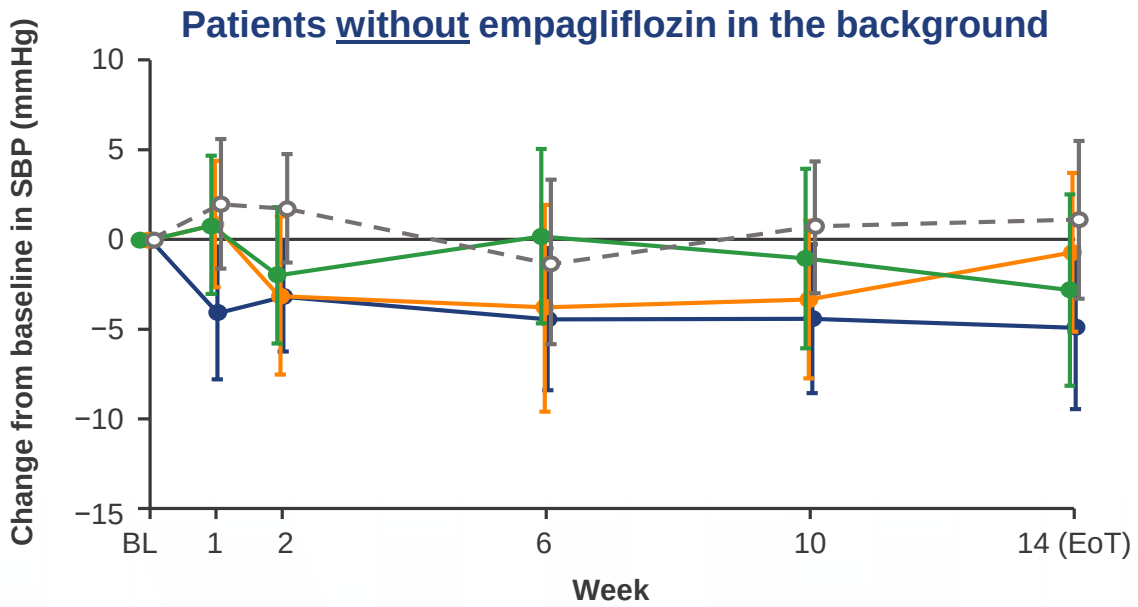


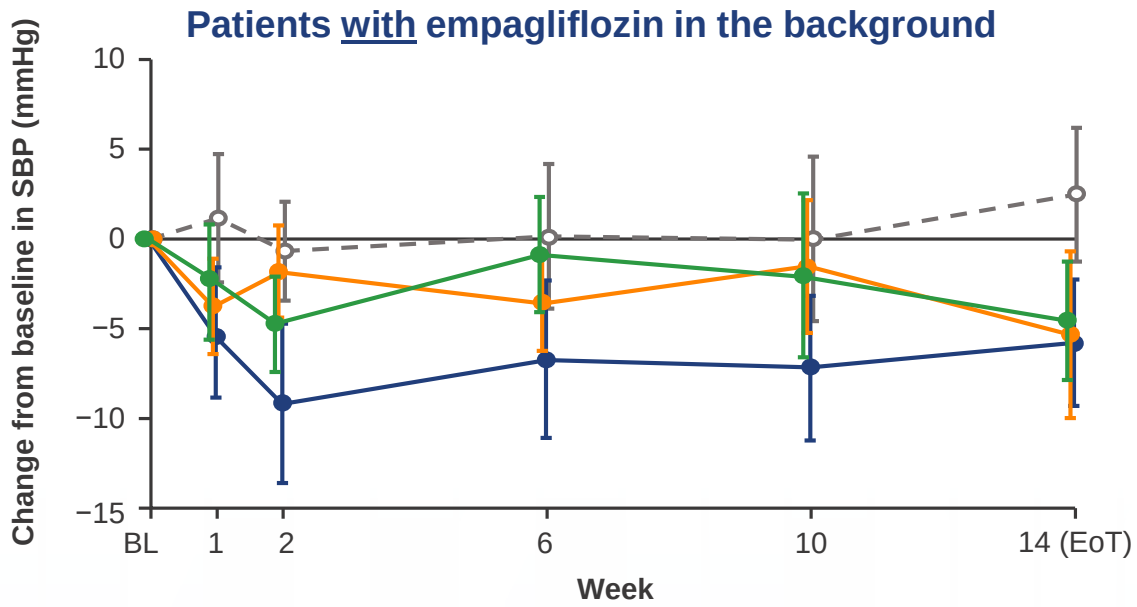
Patients with empagliflozin in the background



Change from baseline to week 14	Mean change (95% CI)	PBO-corrected change (95% CI)	Mean change (95% CI)	PBO-corrected change (95% CI)
BI 690517 placebo	–1.17 (–3.04, 0.70)	Ref	–0.69 (–2.39, 1.01)	Ref
BI 690517 3 mg	–3.51 (–5.67, –1.35)	–2.34 (–5.15, 0.47)	–1.64 (–3.34, 0.06)	–0.95 (–3.33, 1.43)
BI 690517 10 mg	–4.75 (–7.35, –2.16)	–3.59 (–6.68, –0.50)	–3.04 (–5.11, –0.97)	–2.35 (–4.98, 0.28)
BI 690517 20 mg	–4.13 (–6.32, –1.94)	–2.96 (–5.80, –0.11)	–4.40 (–7.56, –1.24)	–3.71 (–7.21, –0.21)

Additional endpoint: Change in systolic blood pressure

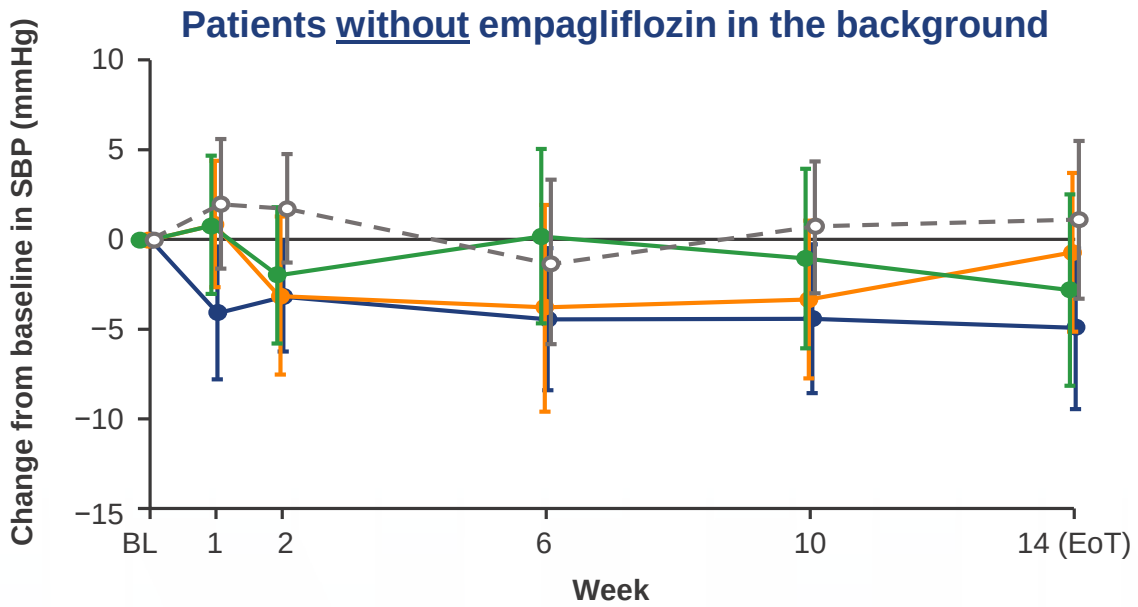


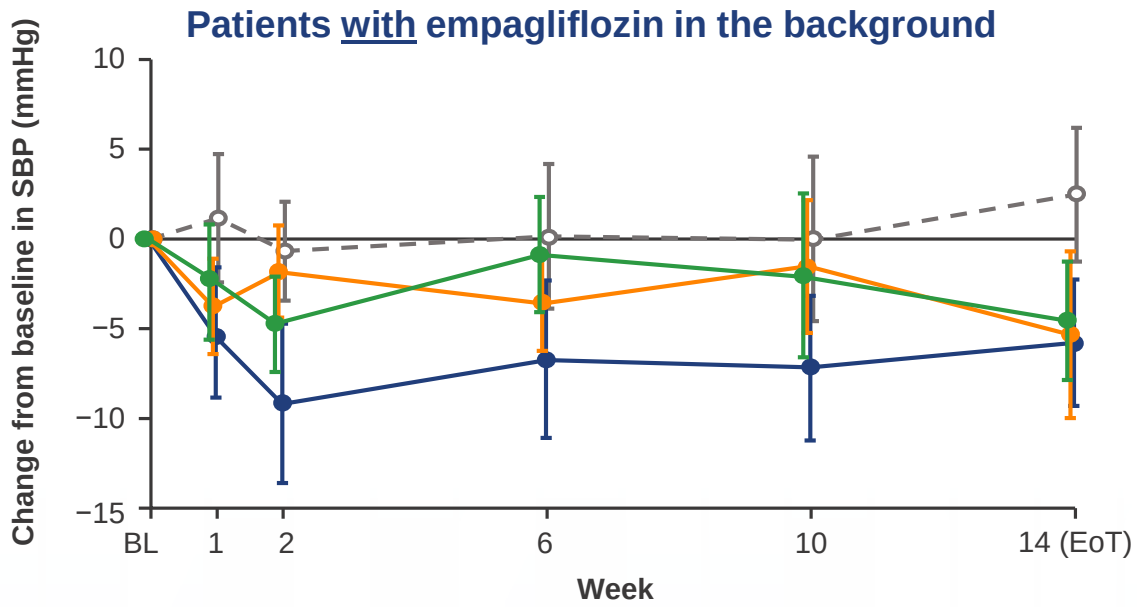


Change from baseline to week 14	Mean change (95% CI)	PBO-corrected change (95% CI)	Mean change (95% CI)	PBO-corrected change (95% CI)
BI 690517 placebo	1.09 (–3.35, 5.53)	Ref	2.47 (–1.30, 6.23)	Ref
BI 690517 3 mg	–2.80 (–8.15, 2.56)	−3.89 (−10.73, 2.95)	–4.56 (–7.94, –1.17)	–7.02 (–12.02, –2.02)
BI 690517 10 mg	–0.72 (–5.18, 3.74)	−1.81 (−8.10, 4.48)	–5.34 (–10.04, –0.64)	–7.81 (–13.69, –1.92)
BI 690517 20 mg	–4.94 (–9.44, –0.43)	−6.03 (−12.44, 0.38)	–5.78 (–9.37, –2.19)	–8.25 (–13.40, –3.09)

Additional endpoint: Change in systolic blood pressure

More pronounced SBP changes were observed with BI 690517 in combination with empagliflozin vs placebo background





Change from baseline to week 14	Mean change (95% CI)	PBO-corrected change (95% CI)	Mean change (95% CI)	PBO-corrected change (95% CI)
BI 690517 placebo	1.09 (–3.35, 5.53)	Ref	2.47 (–1.30, 6.23)	Ref
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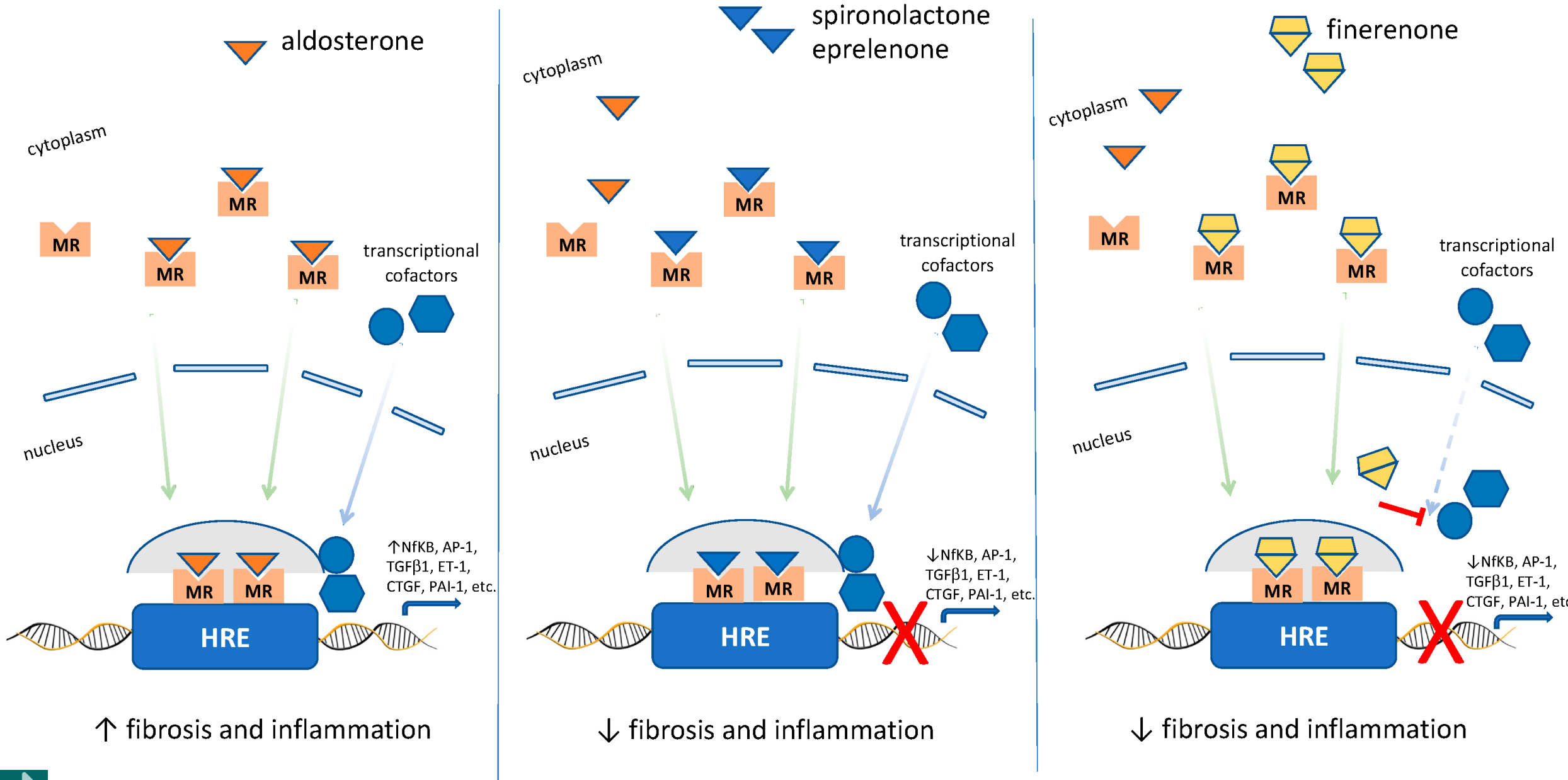
BI 690517 10 mg	–0.72 (–5.18, 3.74)	−1.81 (−8.10, 4.48)	–5.34 (–10.04, –0.64)	–7.81 (–13.69, –1.92)
BI 690517 20 mg	–4.94 (–9.44, –0.43)	−6.03 (−12.44, 0.38)	–5.78 (–9.37, –2.19)	–8.25 (–13.40, –3.09)

MRAs



pharmaceutics Jessica Kearney, andLuigi Gnudi et al., 2023

Hypertension

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RESEARCH ARTICLE

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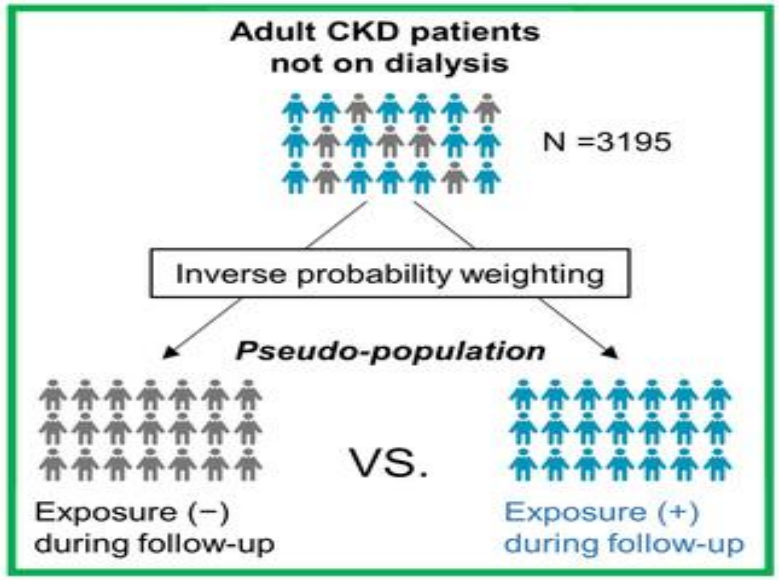
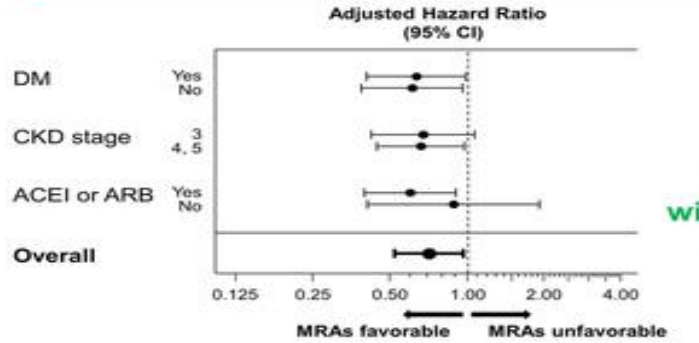
Mineralocorticoid Receptor Antagonist Use and Hard Renal Outcomes in Real-World Patients With Chronic Kidney Disease

Tatsufumi Oka, Yusuke Sakaguchi, Koki Hattori, Yuta Asahina, Sachio Kajimoto, Yohei Doi, Jun-Ya Kaimori and Yoshitaka Isaka

Originally published 14 Jan 2022 | https://doi.org/10.1161/HYPERTENSIONAHA.121.18360 | Hypertension. 2022;79:679–689





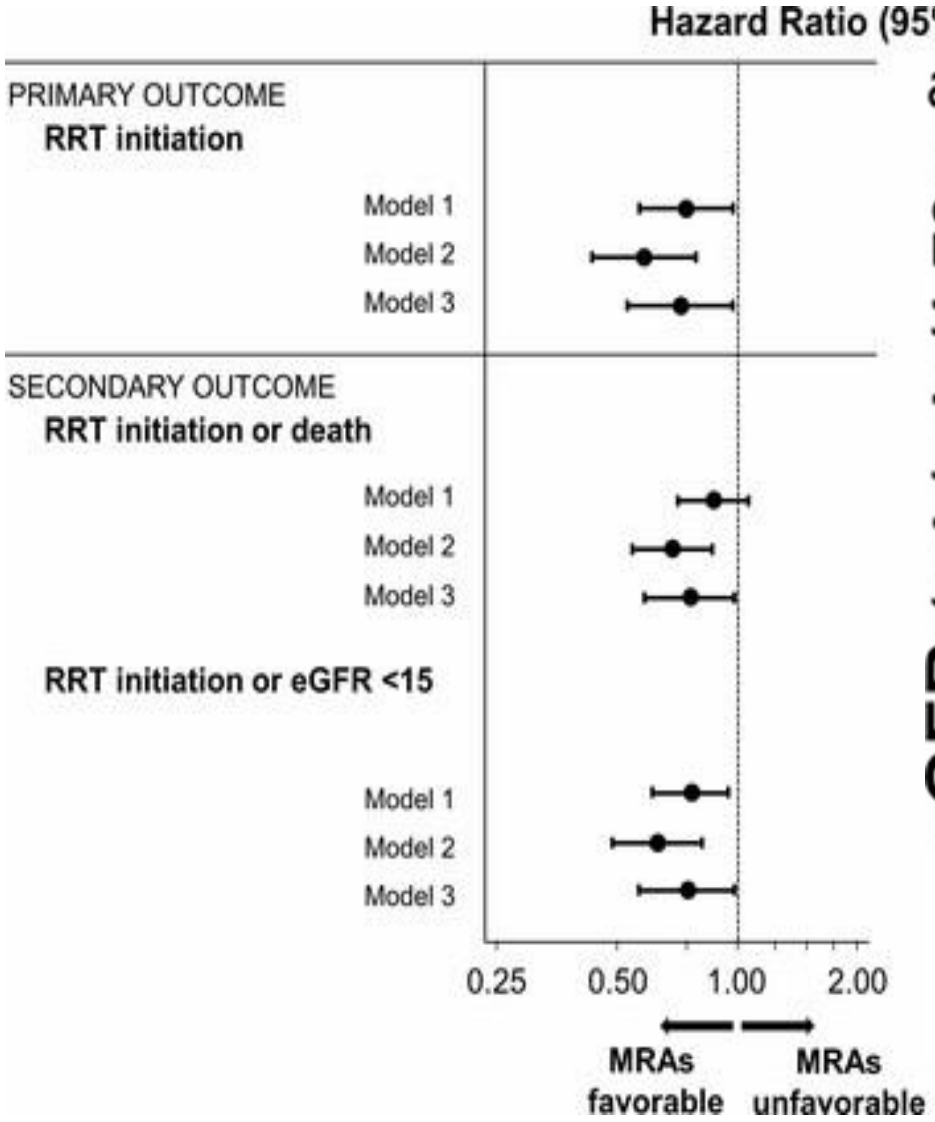
CONCLUSION

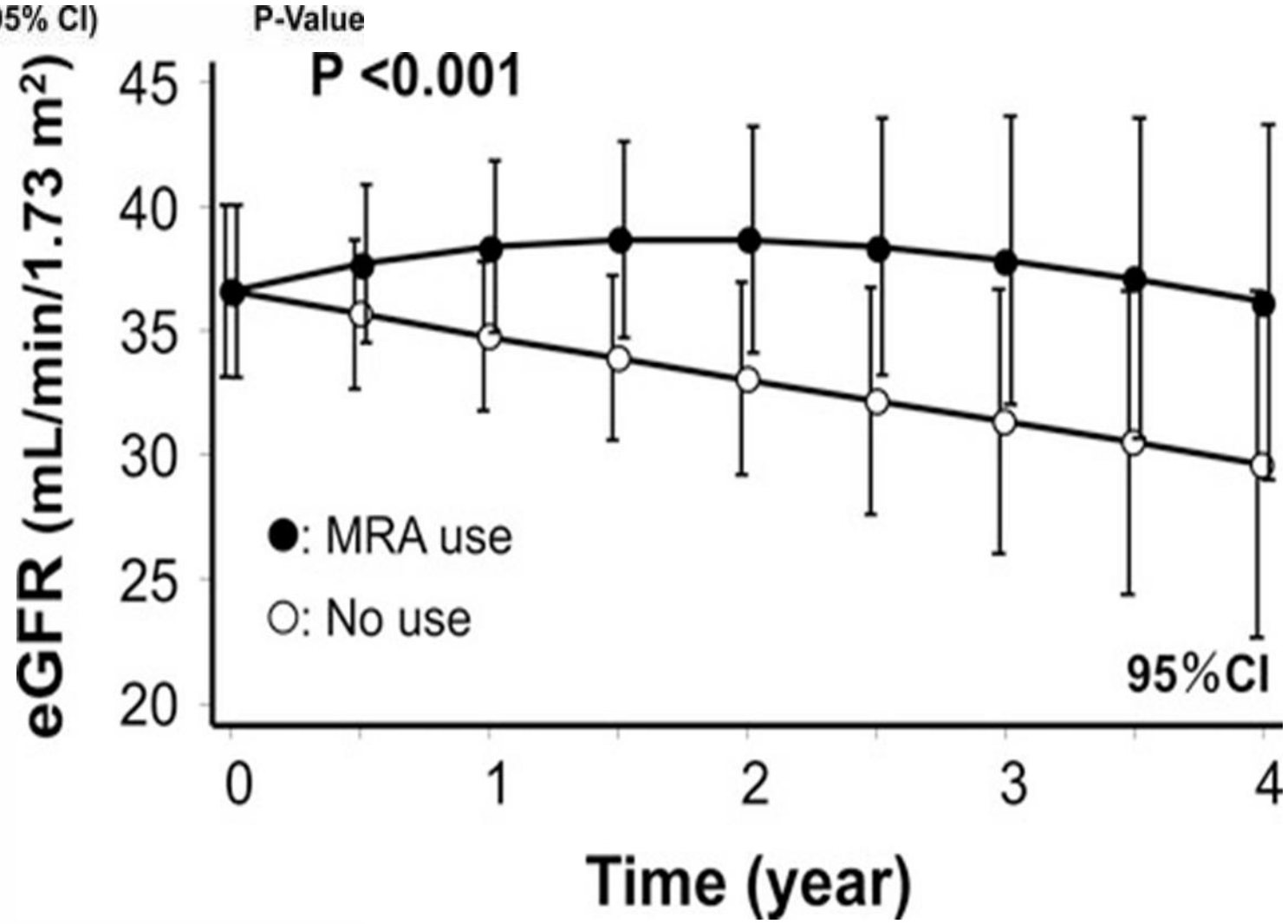
MRA use was associated with a lower rate of RRT initiation In real-world CKD patients.

The main inclusion criteria were estimated glomerular filtration rate ≥10 and <60 mL/min per 1.73 m2 and follow-up ≥90 days.

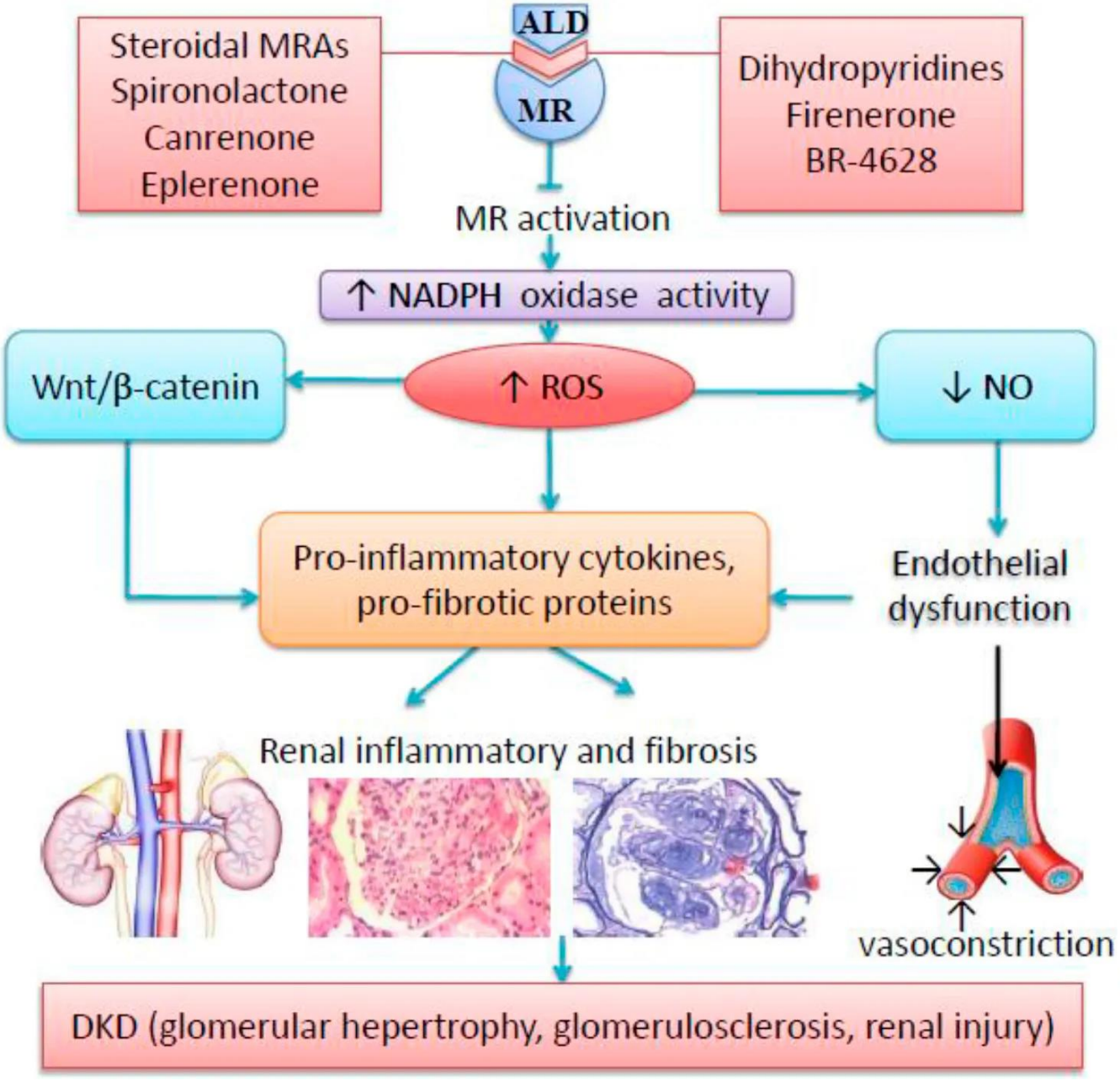
The **primary outcome was RRT initiation**, defined as the initiation of chronic hemodialysis, peritoneal dialysis, or kidney transplantation.
The **secondary outcomes** were the composite of **death from any cause and RRT initiation**

Tatsufumi Oka. Hypertension. 2022





Tatsufumi Oka. Hypertension. Mineralocorticoid Receptor Antagonist Use and Hard Renal Outcomes in Real-World Patients With Chronic Kidney Disease, Volume: 79, Issue: 3, Pages: 679-689, DOI: (10.1161/HYPERTENSIONAHA.121.18360)



metabolism ,2016

nsMRAs

Diabetes with CKD

Finerenone in Predominantly Advanced CKD in Type 2 Diabetes With or Without SGLT-2i Therapy

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Methods

Subgroup Analysis of FIDELIO-DKD

Placebo (with or without SGLT-2i)

vs

Finerenone (with or without SGLT-2i)

FIDELIO-DKD design

Global, multicenter, RCT, double blind, phase III trial (n = 5674)

eGFR 25-75 ml/min/1.73m^2

UACR 30-5000 mg/g

Type 2 diabetes

Finerenone vs Placebo

Findings

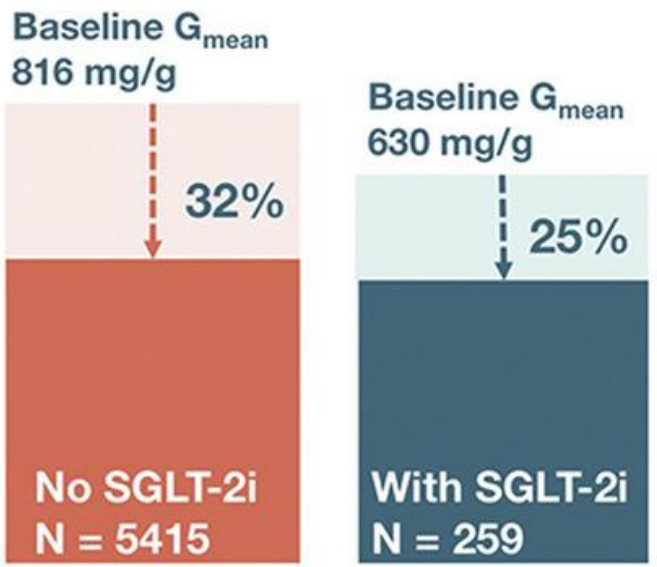
*Compared to those not treated with SGLT-2i

Finerenone with SGLT-2i use characteristics at baseline*

Higher eGFR

Lower UACR

UACR reduction (compared to placebo)



Compared to placebo, the kidney and CV benefits of Finerenone were consistent irrespective of SGLT2i use

Patients on SGLT-2i had fewer hyperkalemia events

SGLT-2i, sodium glucose cotransporter-2 inhibitor; RCT, randomized controlled trial; UACR, urine albumin creatinine ratio; CV, cardiovascular; G_{mean}, geometric mean

KI REPORTS
Kidney International Reports

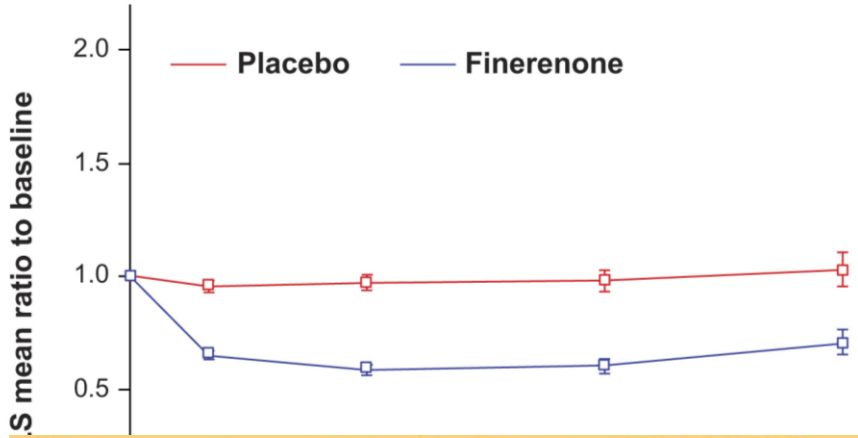
Rossing et al, 2022

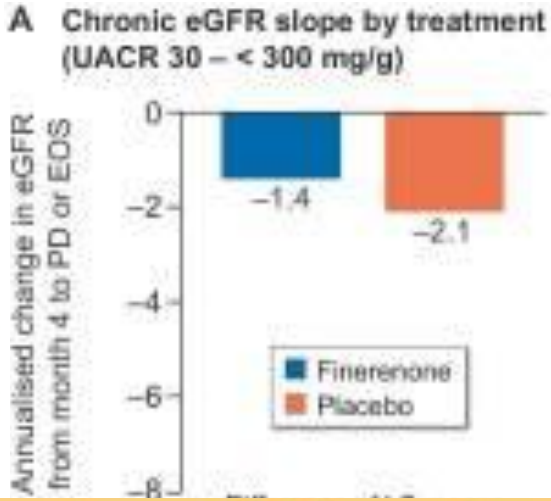
Visual abstract by:
Sophia Ambruso, DO
@Sophia_kidney

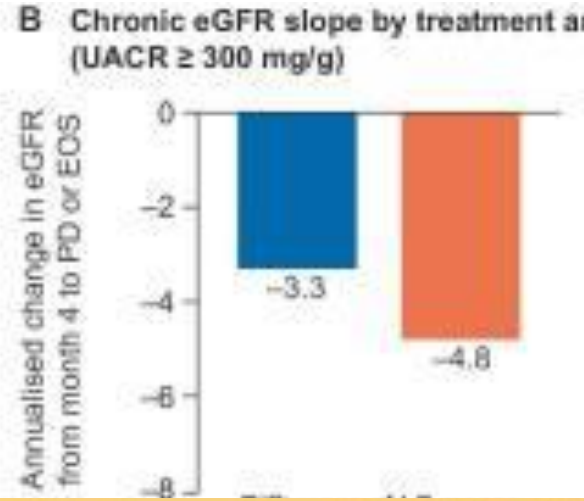
Conclusion UACR improvement was observed with finerenone in patients with CKD and T2D already receiving SGLT-2i at baseline and benefits on kidney and cardiovascular outcomes appear consistent irrespective of SGLT-2i use.

NEPHROLOGY DIALYSIS TRANSPLANTATION
ERA
OXFORD UNIVERSITY PRESS

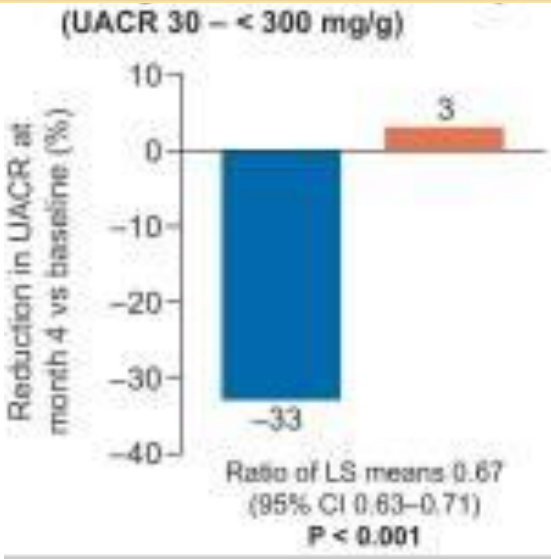
Nephrol Dial Transplant. 2023 Feb

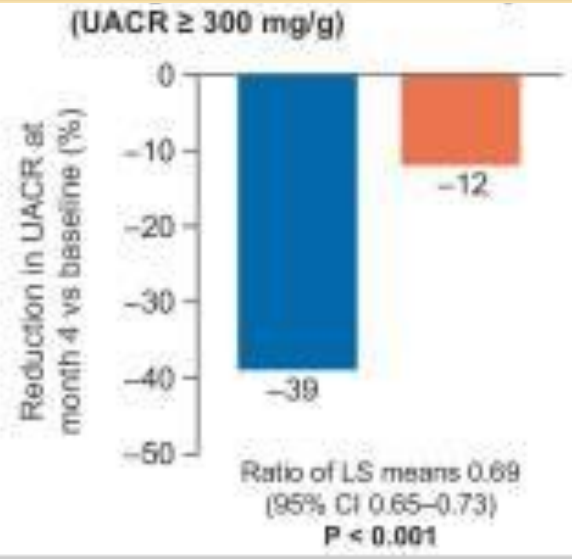






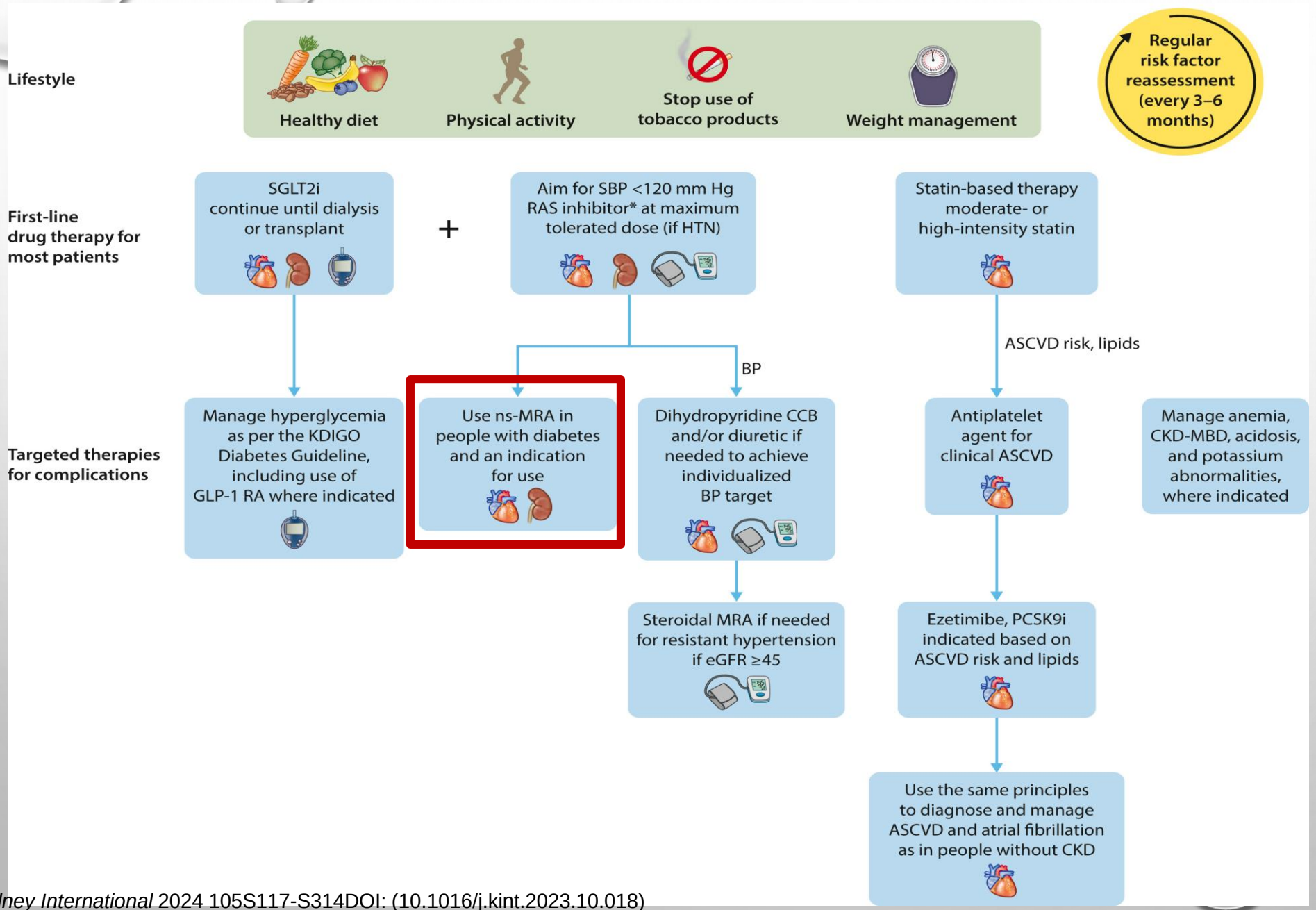
Finerenone protects against CV events and kidney disease progression in patients with T2D and early- or late-stage CKD.





Nephrol Dial Transplant. 2023 Feb; 38(2): 372–383.Published online 2022 Apr 22. doi: 10.1093/ndt/gfac157

MANAGEMENT- CKD



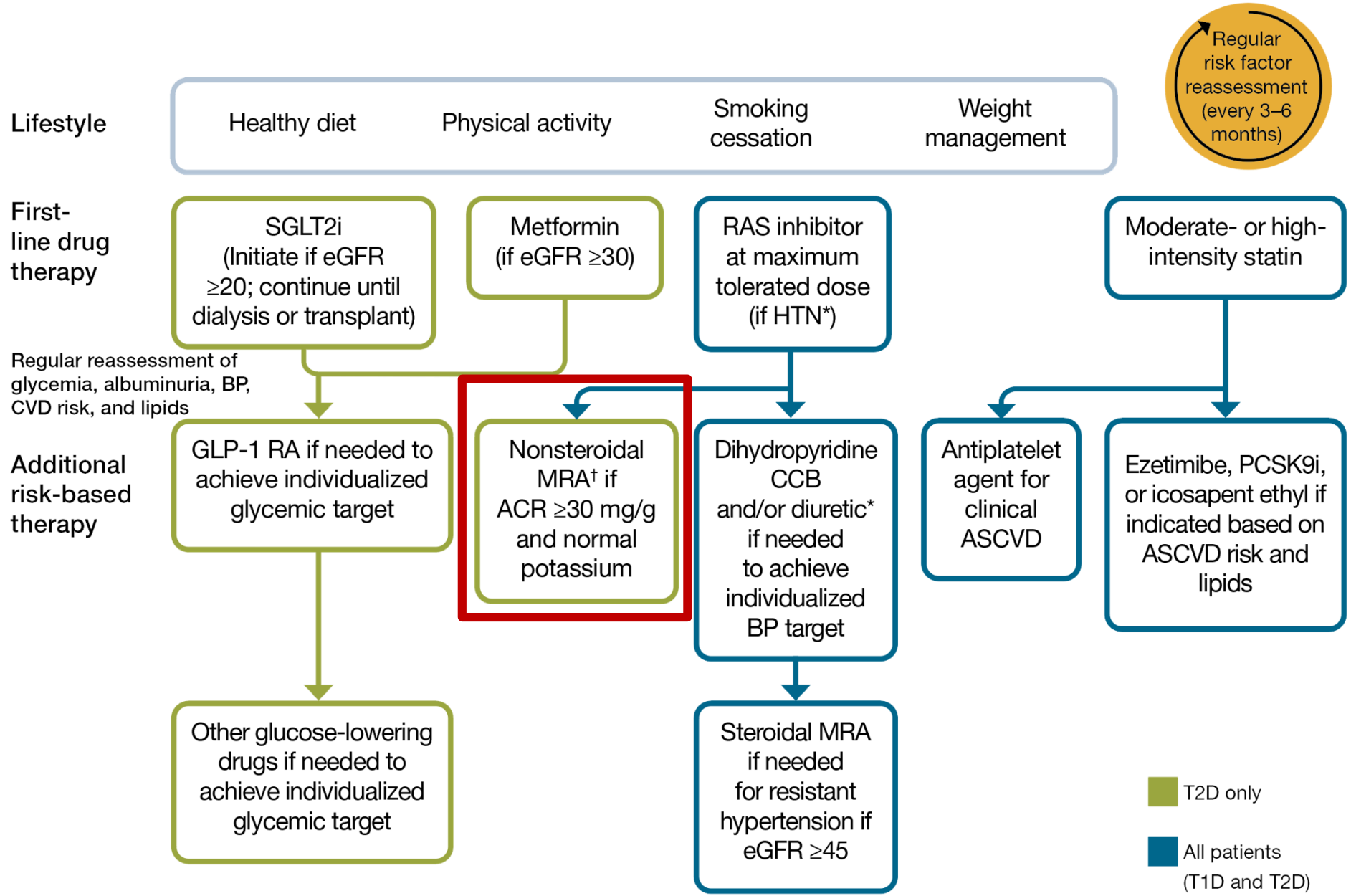
KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES — KDIGO

2024

ACE, angiotensin-converting enzyme inhibitor; ACR, albumin-creatinine ratio; ARB, angiotensin II receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CCB, calcium channel blocker; CGM, continuous glucose monitoring; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; HTN, hypertension; LDL-C, low-density lipoprotein cholesterol; MRA, mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; SGLT2, sodium-glucose cotransporter-2; T2D, Type 2 diabetes; TG, triglycerides

Kidney International 2024 105S117-S314DOI: (10.1016/j.kint.2023.10.018)

Holistic Approach to Improving Outcomes in People With Diabetes and CKD



American Diabetes Association

2025

American Diabetes Association Primary Care Advisory Group. 11. Chronic kidney disease and risk management: *Standards of Care in Diabetes—2024* abridged for primary care professionals. Clin Diabetes 2024;42:212–213 (doi: 10.2337/cd24-a011)

APPROACH PLAN

Approach and planning

Combination Strategies

Incidence of **UKPDS** composite endpoints in 4,320 patients, as rate per 1,000 person-years.

A- Any diabetes-related endpoint,

B- diabetes-related deaths,

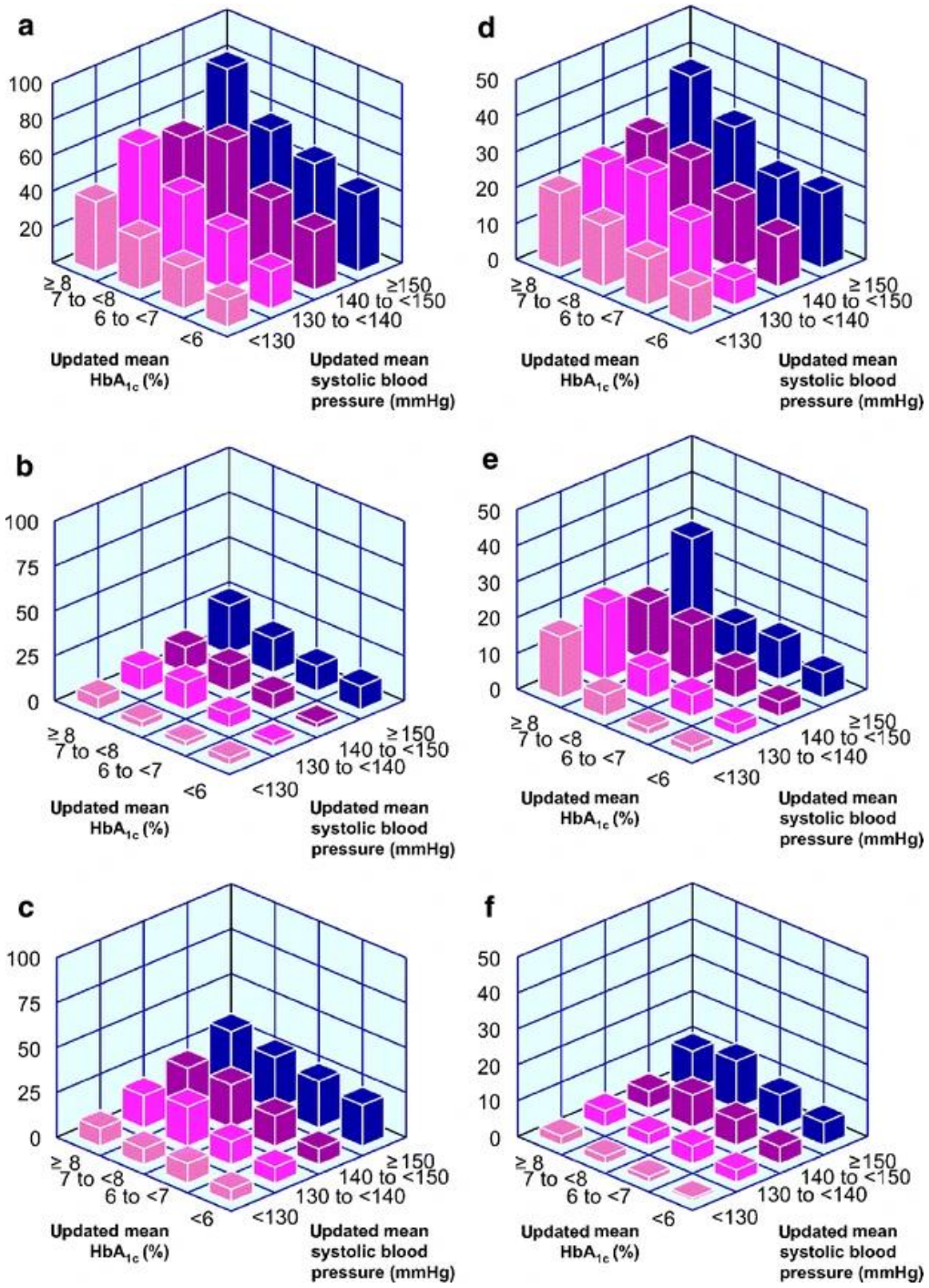
C- all-cause mortality, d myocardial infarction,

E- microvascular disease,

F- stroke.

Values are for 16 different combinations of updated mean HbA1c and updated mean SBP. Unadjusted rates are shown for the three primary and three secondary composite endpoints

I. M. Stratton et al., Diabetologia 2006



Chapter 3: SGLT2 inhibitors

1A

3.7.1: We recommend treating patients with type 2 diabetes, CKD, and an eGFR ≥ 20 ml/ min per 1.73 m^2 with an SGLT2i.

1A

3.7.2: We recommend treating adults with CKD with an SGLT2i for the following: ≥ 20 ml/ min per 1.73 m^2 with urine ACR ≥ 200 mg/g (≥ 20 mg/mmol), or heart failure, irrespective of level of albuminuria.

2B

3.7.3: We suggest treating adults with eGFR 20 to 45 ml/min per 1.73 m^2 with urine ACR <200mg/g (20 mg/mmol) with an SGLT2i.

Chapter 3: Non-Steroidal MRAs

2A

3.8.1: We suggest a nonsteroidal mineralocorticoid receptor antagonist with proven kidney or cardiovascular benefit for adults with T2D, an eGFR >25 ml/min per 1.73 m^2, normal serum potassium concentration, and albuminuria (>30 mg/g [>3 mg/mmol]) despite maximum tolerated dose of RAS inhibitor.

Chapter 3: GLP1-RA

1B

3.9.1: In adults with T2D and CKD who have not achieved individualized glycemic targets despite use of metformin and SGLT2 inhibitor treatment, or who are unable to use those medications, we recommend a long-acting GLP-1 RA.

KDIGO 2024 Clinical Practice Guideline for Evaluation and Management Chronic Kidney Disease. Kidney Int. 2024

Chapter 3: Statins

1A

3.15.1.1: In adults aged ≥50 years with eGFR <60 ml/min per 1.73 m^2 but not treated with chronic dialysis or kidney transplantation (GFR categories G3a–G5), we recommend treatment with a statin or statin/ezetimibe combination (1A)

1B

3.15.1.2: In adults aged ≥50 years with CKD and eGFR ≥ 60 ml/min per 1.73 m^2 (GFR categories G1–G2), we recommend treatment with a statin (1B).

2A

3.15.1.3: In adults aged 18–49 years with CKD but not treated with chronic dialysis or kidney transplantation, we suggest statin treatment in people with one or more of the following (2A):

- known coronary disease (myocardial infarction or coronary revascularization),
- diabetes mellitus, prior ischemic stroke, or
- estimated 10-year incidence of coronary death or
- nonfatal myocardial infarction >10%

KDIGO 2024 Clinical Practice Guideline for Evaluation and Management Chronic Kidney Disease. Kidney Int. 2024

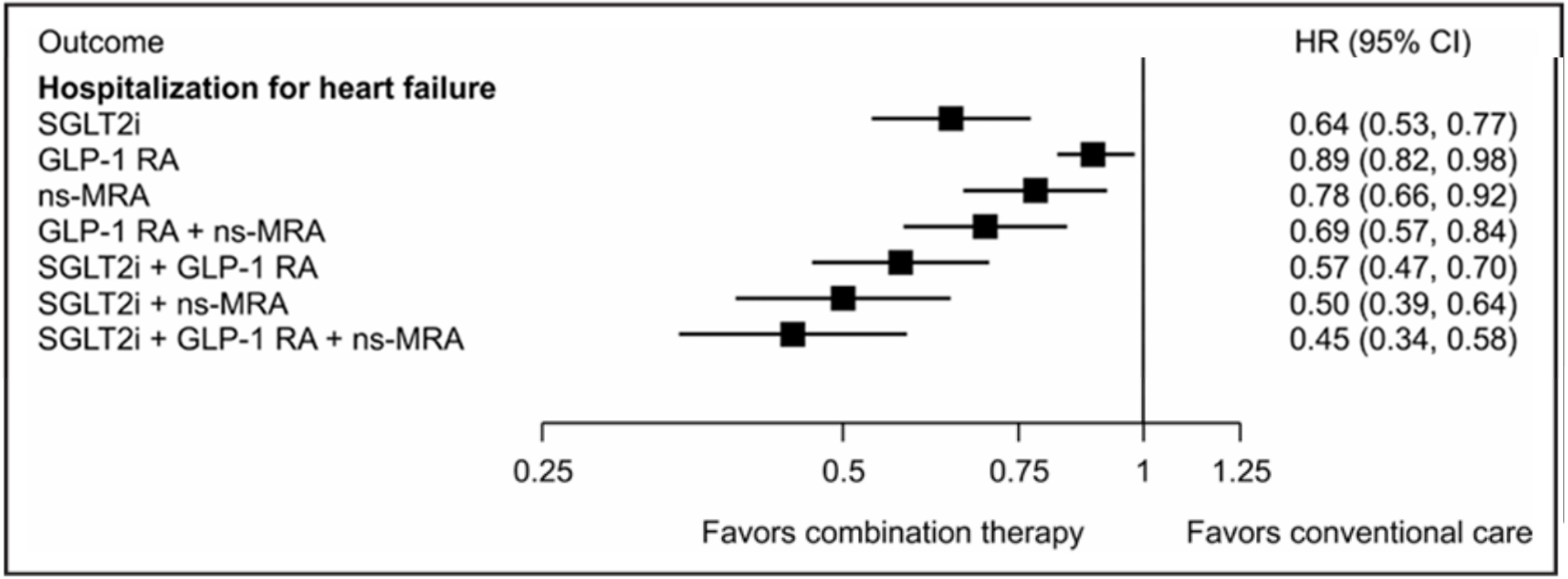
Circulation 2024

ORIGINAL RESEARCH ARTICLE

Estimated Lifetime Cardiovascular, Kidney, and Mortality Benefits of Combination Treatment With SGLT2 Inhibitors, GLP-1 Receptor Agonists, and Nonsteroidal MRA Compared With Conventional Care in Patients With Type 2 Diabetes and Albuminuria

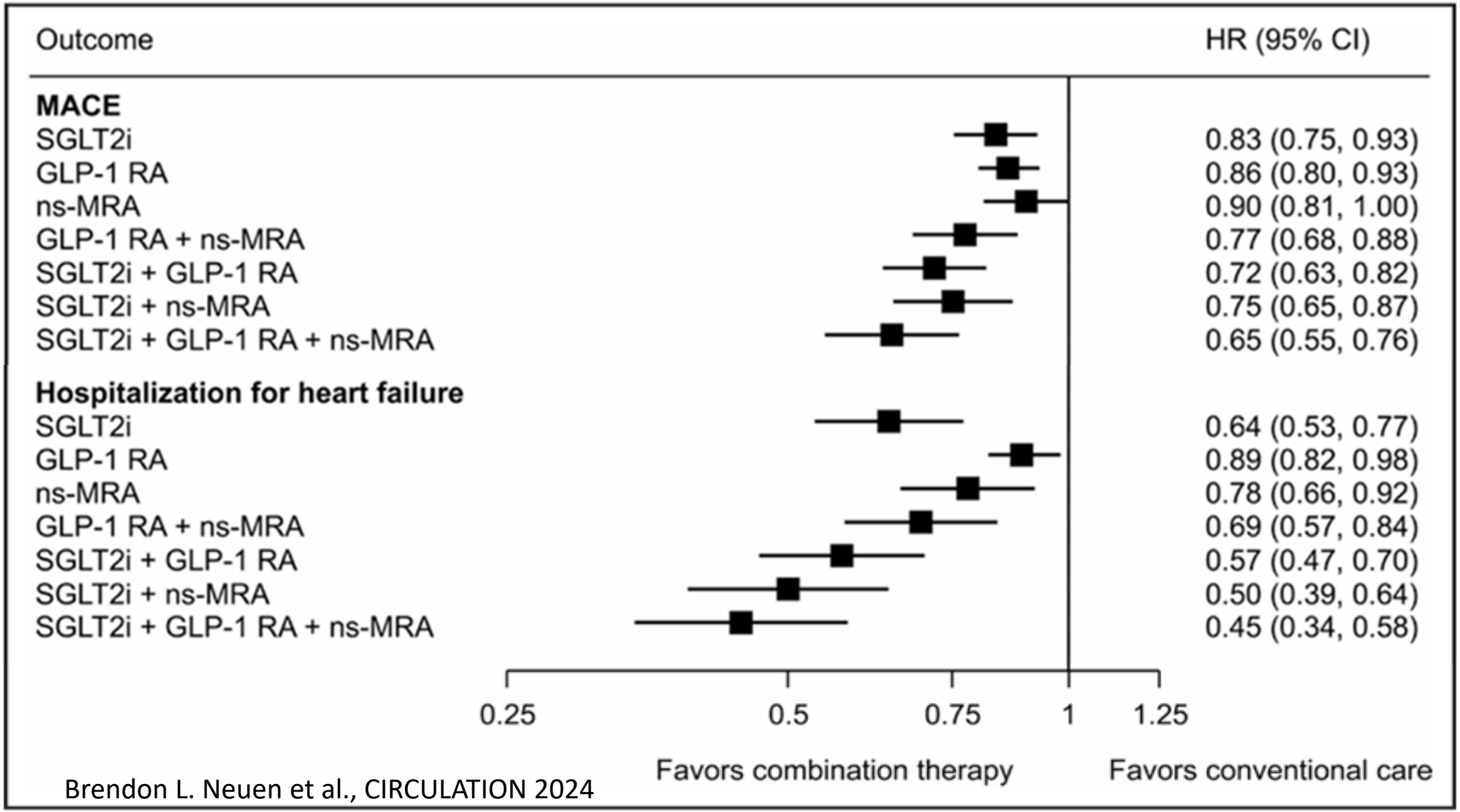
Brendon L. Neuen, MBBS, MSc, PhD; Hiddo J.L. Heerspink, PhD; Priya Vart, PhD; Brian L. Claggett, PhD; Robert A. Fletcher, MSc; Clare Arnott, MBBS, PhD; Julianna de Oliveira Costa, PhD; Michael O. Falster, PhD; Sallie-Anne Pearson, PhD; Kenneth W. Mahaffey, MD; Bruce Neal, MB ChB, PhD; Rajiv Agarwal, MD; George Bakris, MD; Vlado Perkovic, MBBS, PhD; Scott D. Solomon, MD; Muthiah Vaduganathan, MD, MPH

Estimated treatment effects on **cardiovascular outcomes** with **SGLT2i, GLP-1 RA, and ns-MRA**, alone and in combination, when added to renin-angiotensin system blockade in patients with type 2 diabetes.



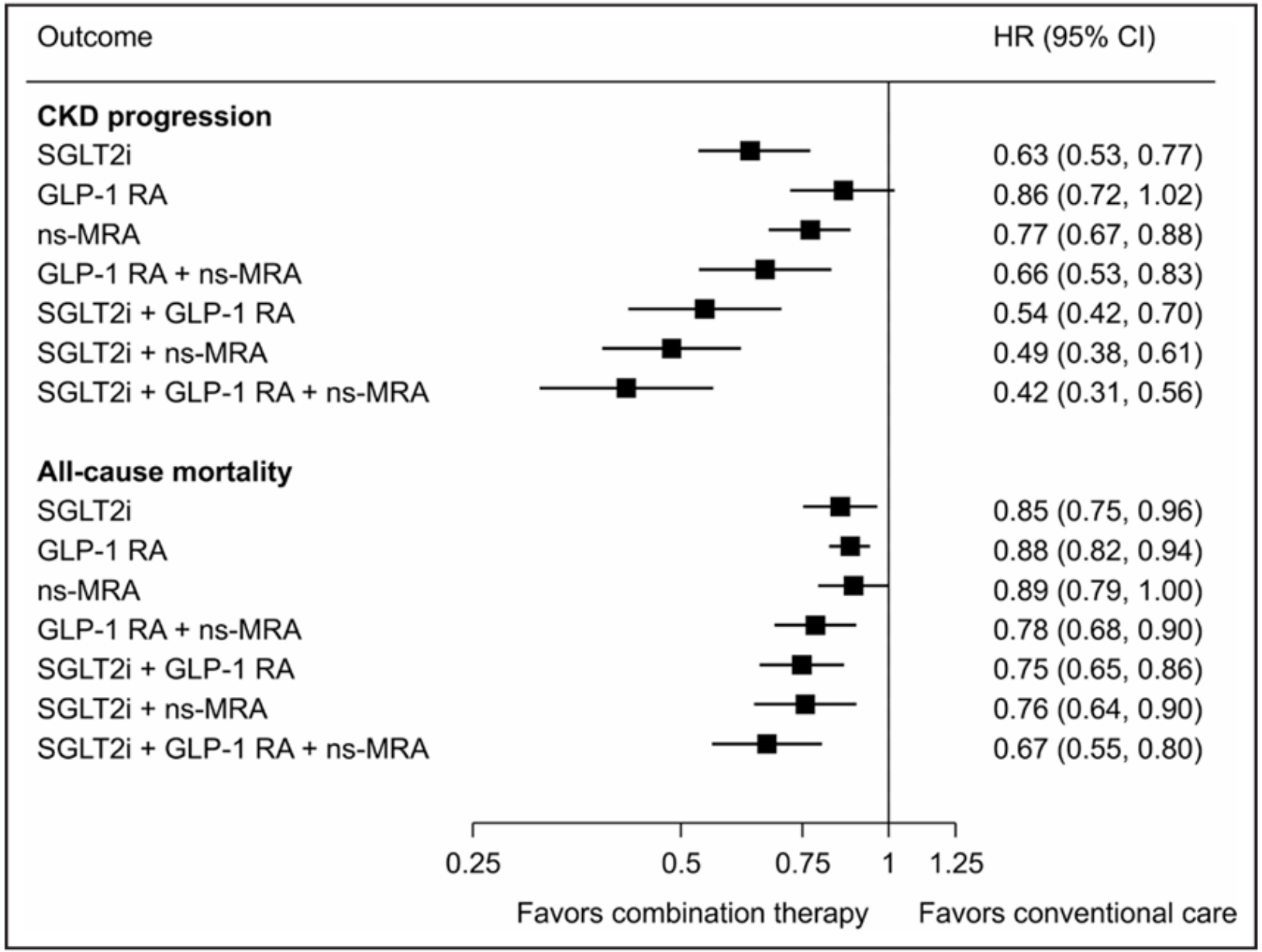
Brendon L. Neuen et al., CIRCULATION 2024

Estimated treatment effects on **cardiovascular outcomes** with **SGLT2i, GLP-1 RA, and ns-MRA**, alone and in combination, when added to renin-angiotensin system blockade in patients with type 2 diabetes.

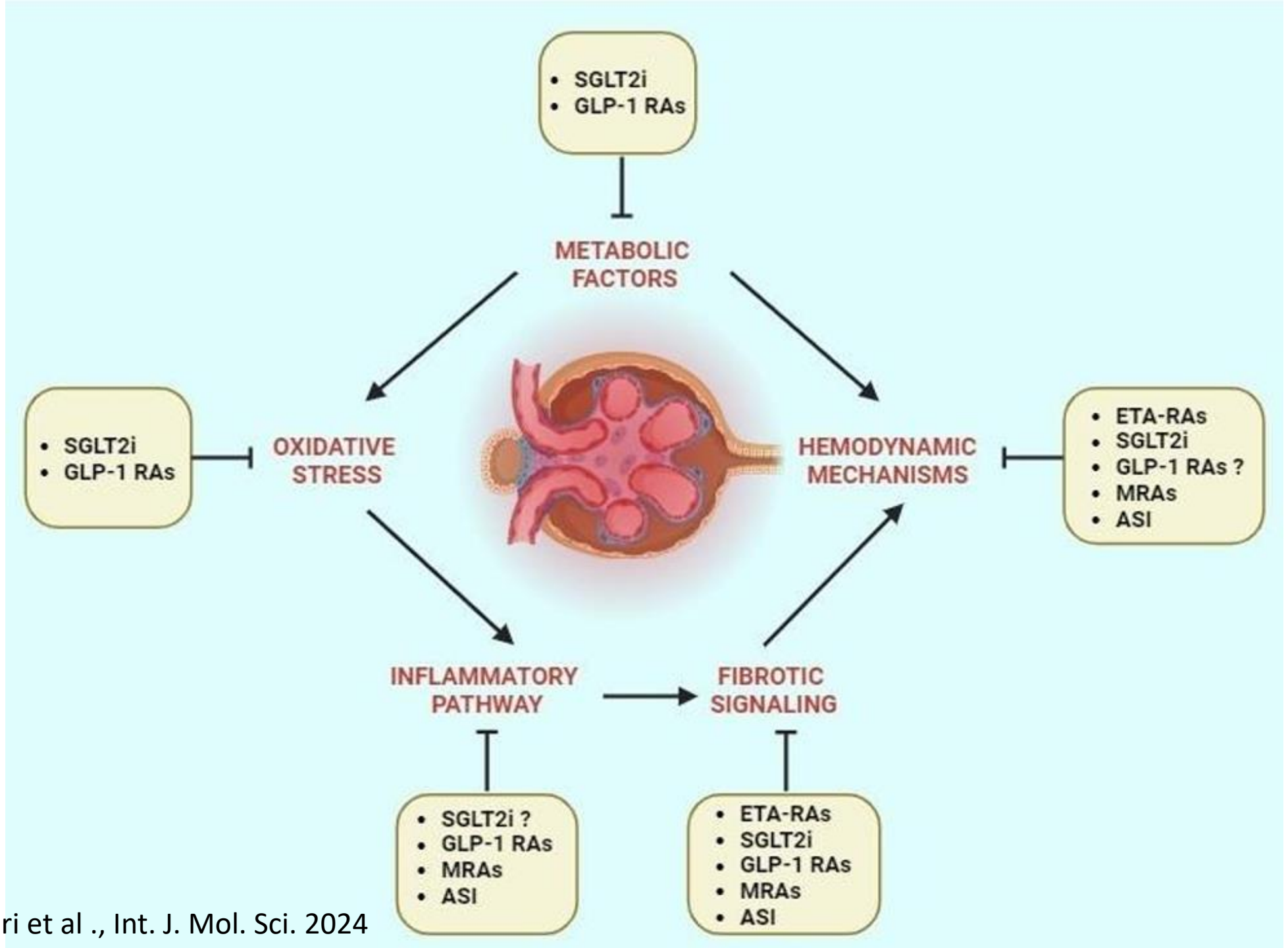


Brendon L. Neuen et al., CIRCULATION 2024

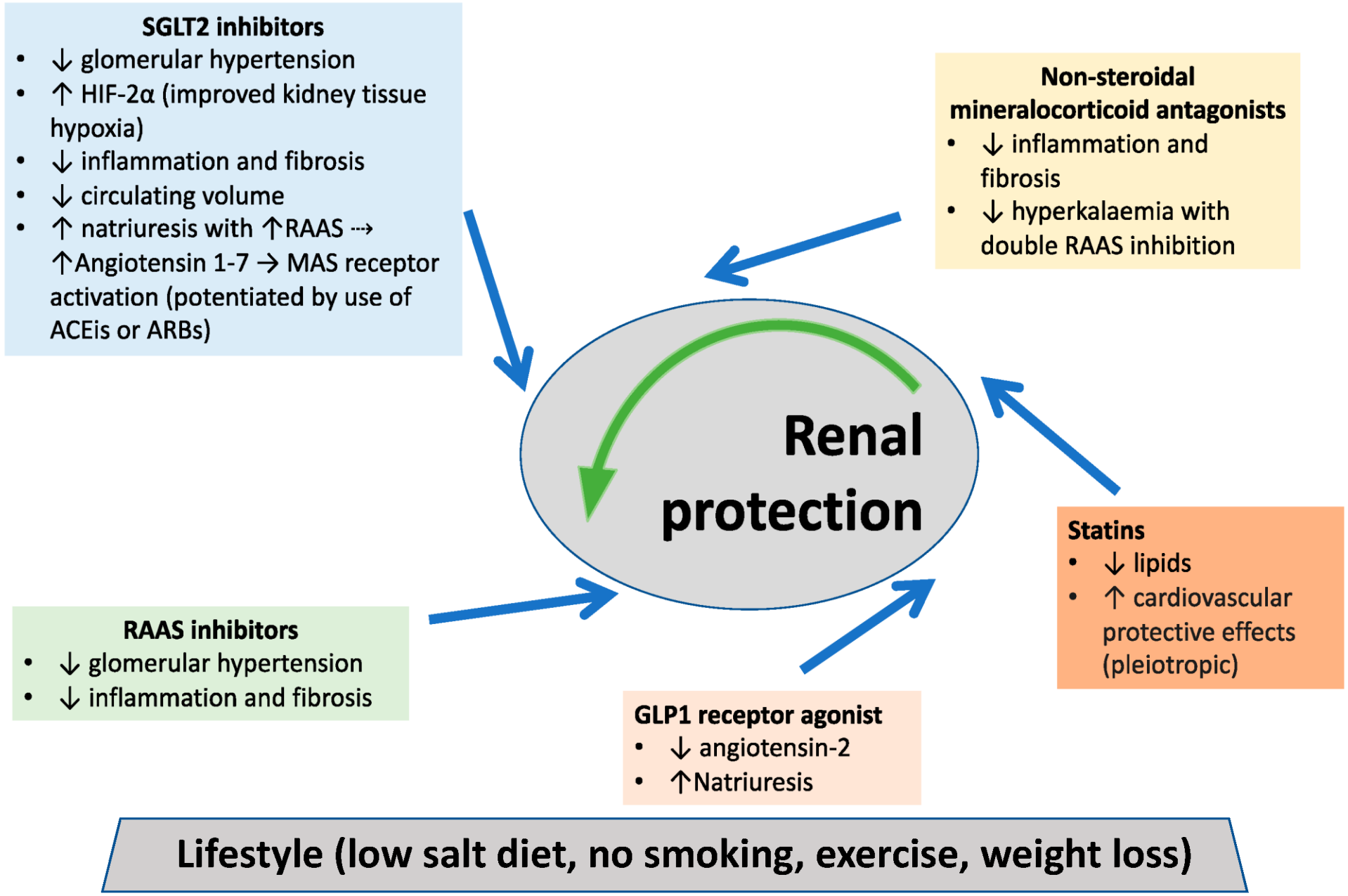
Estimated treatment effects on CKD progression and all-cause mortality with SGLT2i, GLP-1 RA, and ns-MRA, alone and in combination, when added to renin-angiotensin system blockade in patients with type 2 diabete



Brendon L. Neuen et al., CIRCULATION 2024



Alessio Mazzieri et al ., Int. J. Mol. Sci. 2024



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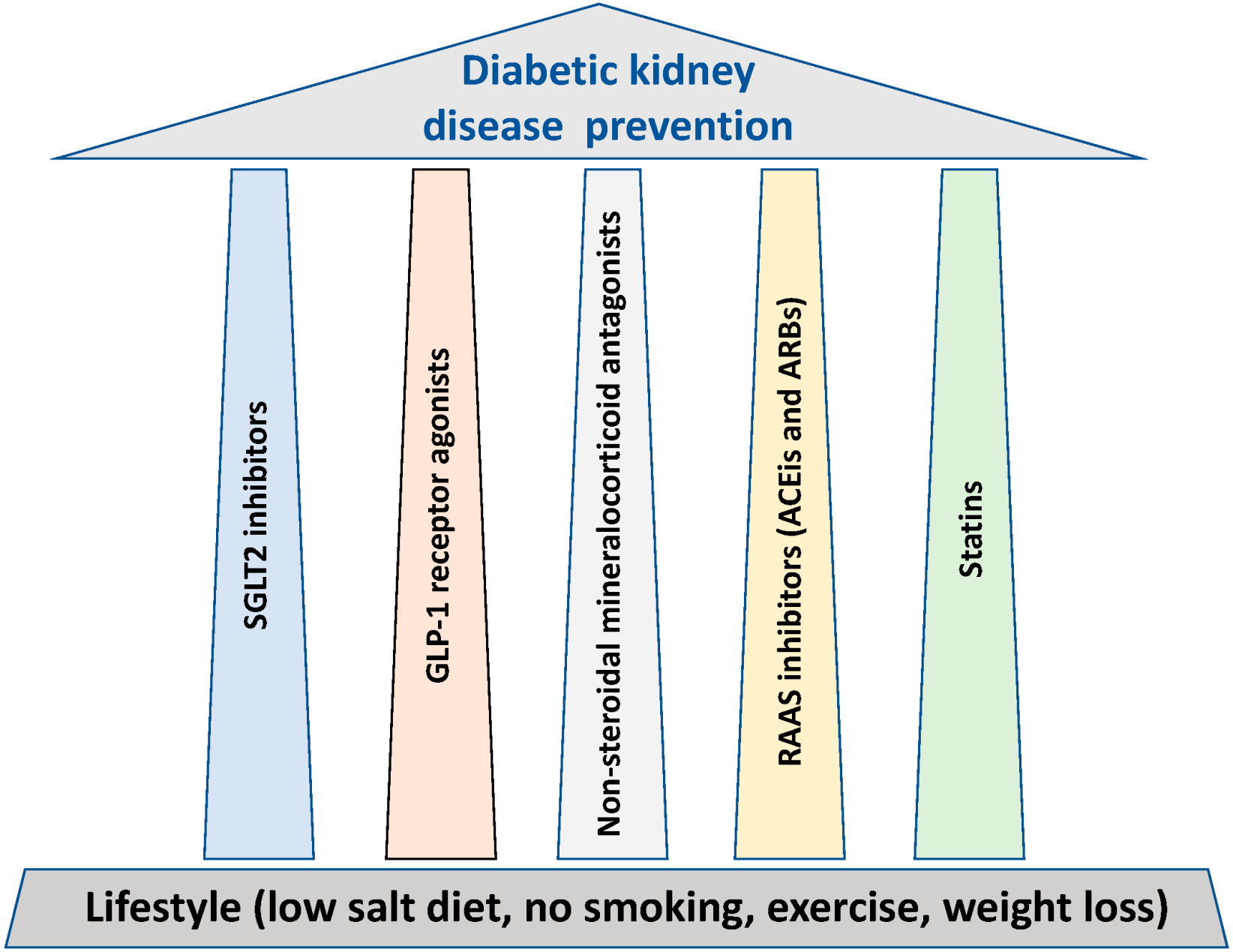

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Thank You