ΕΛΛΗΝΙΚΗ ΝΕΦΡΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ
HELLENIC SOCIETY OF NEPHROLOGY

25ο Πανελλήνιο Συνέδριο
ΝΕΦΡΟΛΟΓΙΑΣ

Bakris George
USA

Maximal slowing of diabetic nephropathy: using 4 pillars of therapy

ΚΑΛΑΪΤΖΙΔΗΣ ΡΗΓΑΣ

G. Bakris

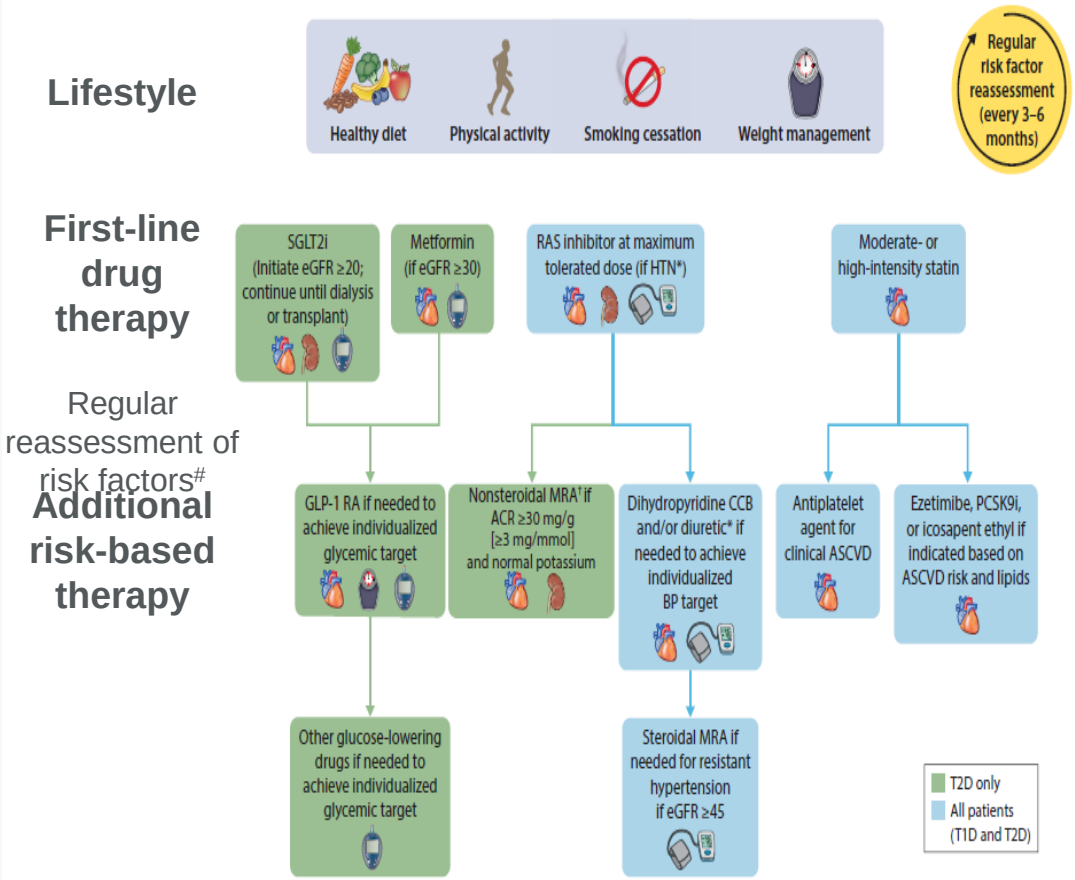
Maximal slowing of diabetic nephropathy

Using 4 pillars of therapy

ΕΛΛΗΝΙΚΗ ΝΕΦΡΟΛΟΓΙΚΗ ΕΤΑΙΡΕΙΑ
HELLENIC SOCIETY OF NEPHROLOGY
25ο Πανελλήνιο Συνέδριο
ΝΕΦΡΟΛΟΓΙΑΣ

What did the recent clinical guidelines suggest for the management of CKD in T2D

KDIGO 2022 guidelines recommend a holistic approach to improve outcomes in patients with CKD and T2D



The KDIGO 2022 guidelines position finerenone in **ALL** patients with diabetes and CKD (UACR ≥30 mg/g)§

*ACEi or ARB (at maximal tolerated doses) should be first-line therapy for hypertension when albuminuria is present. Otherwise, dihydropyridine calcium channel blocker or diuretic can also be considered; all three classes are often needed to attain BP targets; #glycaemia, albuminuria, BP, CVD risk and lipids; †finerenone is currently the only nonsteroidal MRA with proven clinical kidney and CV benefits; § after treatment with RASis in patients with UACR ≥30 mg/g and normal serum potassium.

ACR, albumin-to-creatinine ratio; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CCB, calcium channel blocker; CVD, cardiovascular disease;

GLP-1 RA, glucagon-like peptide-1 receptor agonist; HTN, hypertension; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAS, renin–angiotensin system; T1D, type 1 diabetes

Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2022;102:S1–S128

A consensus report from the ADA and KDIGO on the management of CKD in T2D was published in October 2022

Key focus of report

- **Screening and diagnosis** (screening for CKD with eGFR and UACR)
- **A holistic** approach including **treatment targets** and **pharmacotherapy**
- **Comprehensive patient care**

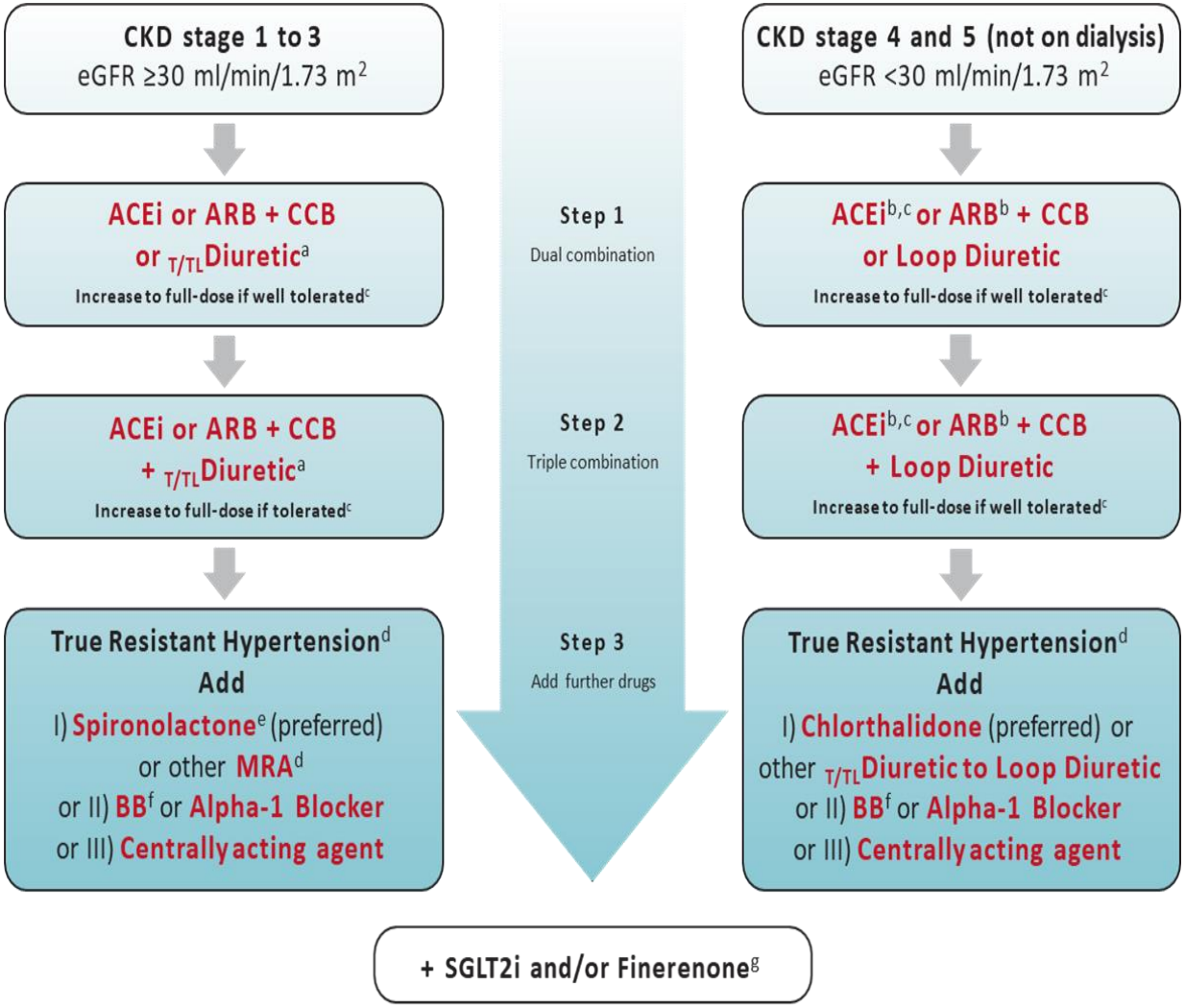
Finerenone consensus statement

*A **nonsteroidal MRA** with proven **kidney and CV benefit** is recommended for patients with T2D, eGFR ≥25 ml/min/1.73 m^2, normal serum [K^+], and albuminuria (ACR ≥30 mg/g) despite maximum tolerated dose of RASi*

Statements were based on the **FIDELIO-DKD** and **FIGARO-DKD** studies and the **FIDELITY** pooled analysis

de Boer IH, *et al. Diabetes Care* 2022;45:3075–3090

BP-lowering in patients with hypertension and chronic kidney disease



Recent clinical guidelines for the management of CKD in T2D recommend a combination of drug therapies to optimally reduce risks, with finerenone recommended as a core treatment pillar 1–3

KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES · KDIGO

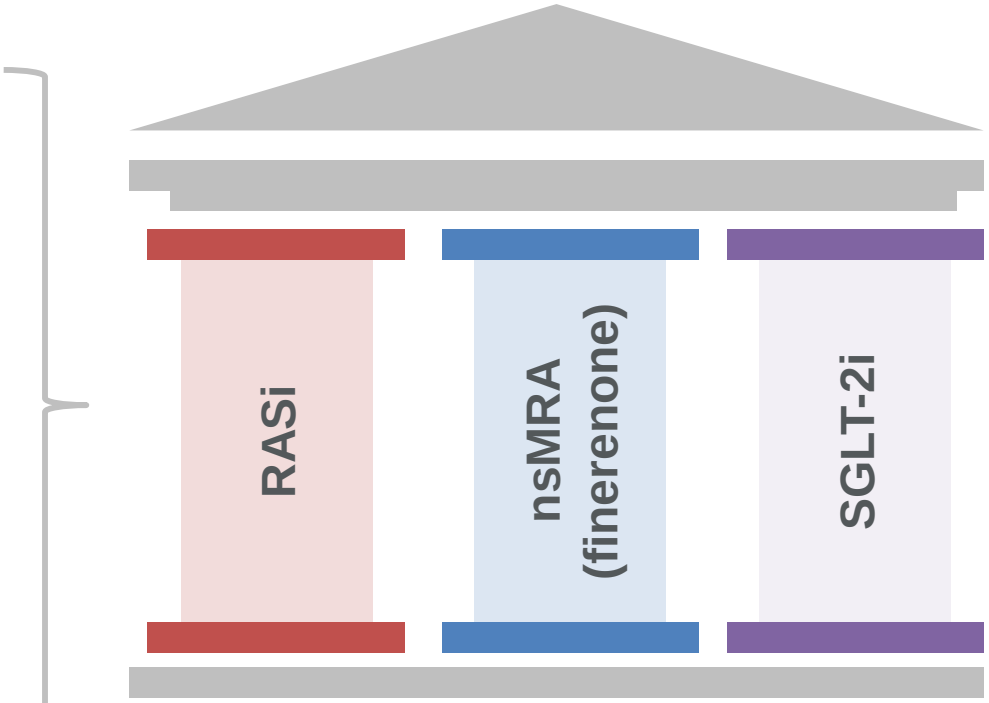
American Diabetes Association®

ADA KDIGO Consensus 2022

ERA ERBP European Renal Best Practice

ESH European Society of Hypertension

ESC European Society of Cardiology



Finerenone is indicated for the treatment of CKD (with albuminuria) associated with T2D in adults[4]

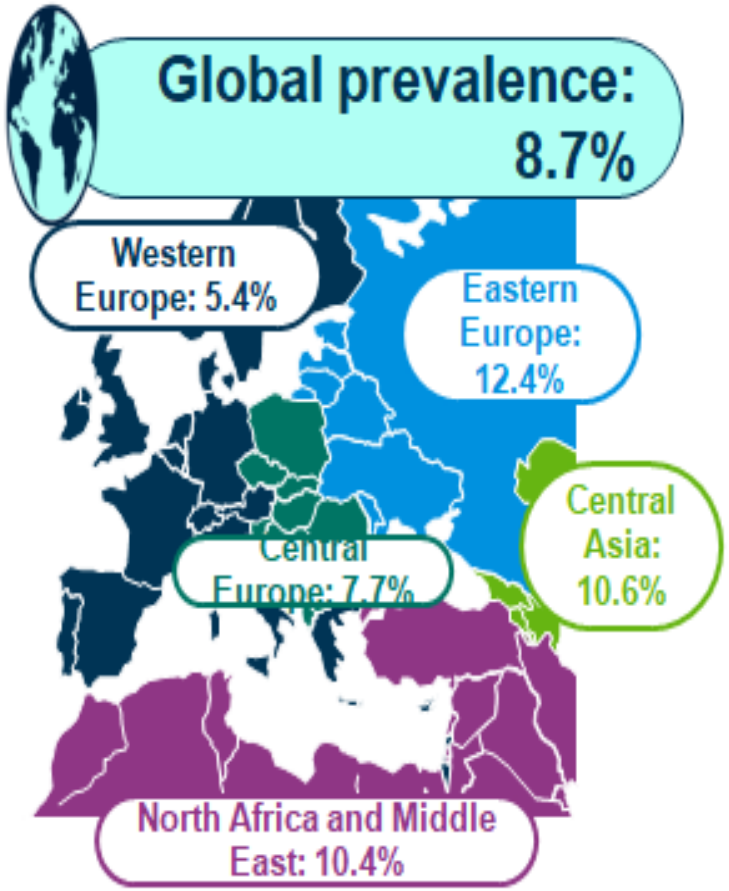
RASi, renin–angiotensin system inhibitor

1. Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2022;102(5S):S1–S128; 2. American Diabetes Association. *Diabetes Care* 2023;46(Suppl 1):S191–S202; 3. de Boer IH, *et al. Diabetes Care* 2022;45:3075–3090; 4. Blazek O, *et al. Am Heart J Plus* 2022;19:100187. 4. Bayer AG. KERENDIA®(finerenone) Summary of Product Characteristics. 2023. https://www.ema.europa.eu/documents/product-information/kerendia-epar-product-information_en.pdf [accessed October 2023]

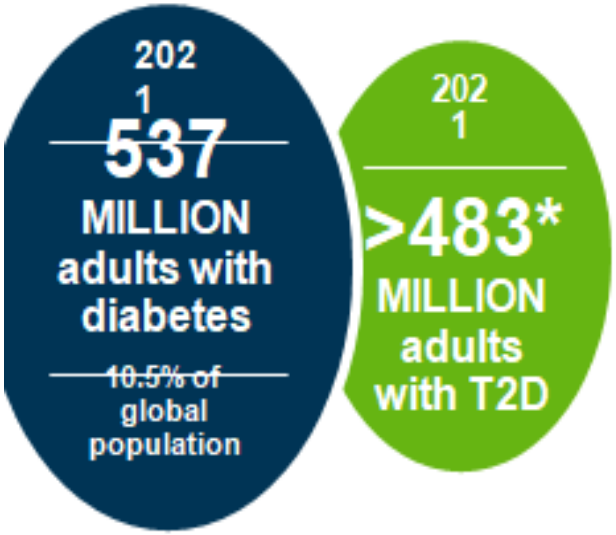
CKD and DM

CKD and T2D have a significant global disease burden

Global prevalence of diabetes in adults aged 20–79 years[1]



- Age-standardised prevalence of CKD globally and in Europe, 2017[2]



Diabetes and its associated complications accounted for an estimated **6.7 million deaths**[*#] in 2021[1]

Despite glycaemic and BP treatments,[‡] **>30%** of patients with T2D will develop CKD[3,4]

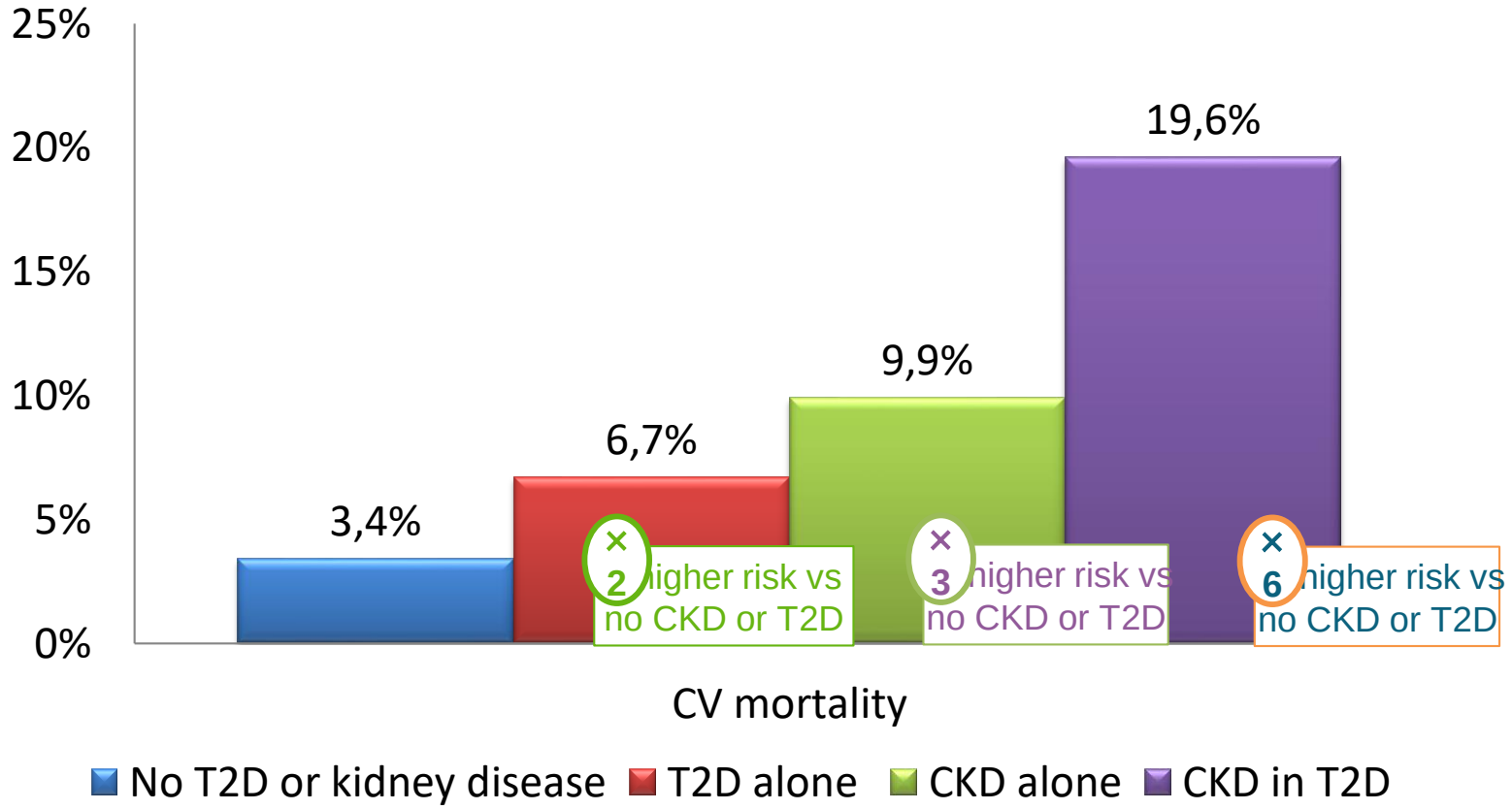
*In [illegible] aged 20-79 years; #T2D accounts for >90% of diabetes burden; ‡patients treated to achieve guideline-recommended glycaemic and BP [illegible]s under clinical trial conditions

BP, blood pressure

1. International Diabetes Federation. IDF Diabetes Atlas, 10th ed. Brussels, Belgium; 2021; 2. GBD Chronic Kidney Disease Collaboration. *Lancet* 2020;395:709–733;
3. Cherney DZ & Bakris GL. *Kidney Int* 2018;8:18–25; 4. Webster AC, *et al. Lancet* 2017;389:1238–1252

Patients with CKD and T2D are at an increased risk of **death from CV-related causes**

- Ten-year standardised CV mortality by diabetes and kidney disease status



CV, cardiovascular

Afkarian M, *et al. J Am Soc Nephrol* 2013;24:302–308

Στην Χρόνια νεφρική νόσο παρατηρείται Έλλειψη εξατομικευμένης θεραπείας

Σε ασθενείς **υψηλού κινδύνου** δεν χορηγείται η κατάλληλη θεραπεία και καταλήγουν σε αιμοκάθαρση

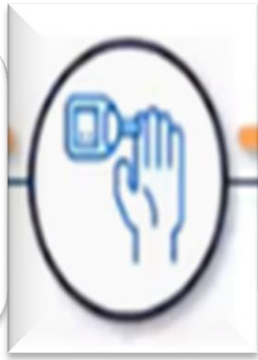
Σε ασθενείς χαμηλού κινδύνου χορηγούμε θεραπεία σε υπερβολικό βαθμό και οδηγούμαστε σε περιττές παρενέργειες

Σημαντική επιβάρυνση του κόστους νοσηλείας και των επισκέψεων στο τμήμα επειγόντων περιστατικών

Πρόσθετη επιβάρυνση στο σύστημα με αιμοκάθαρση που μπορεί να αποφευχθεί

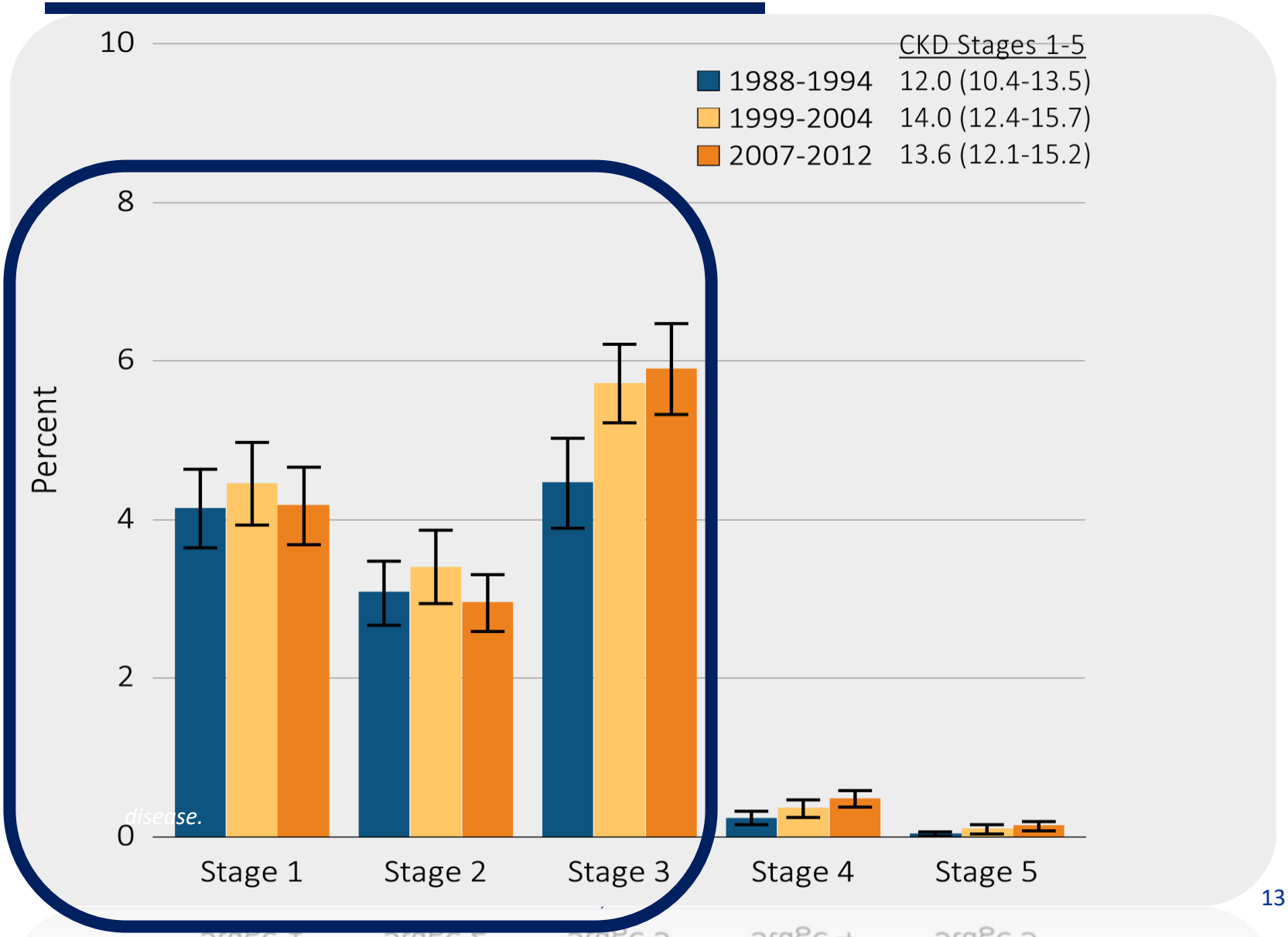
Στην Χρόνια νεφρική νόσο παρατηρείται Έλλειψη εξατομικευμένης θεραπείας

Υπάρχουν θεραπείες που βελτιώνουν την εξέλιξη της ΧΝΝ αλλά δεν χρησιμοποιούνται σε ασθενείς που δεν αναγνωρίζουμε ότι είναι **υψηλού κινδύνου**



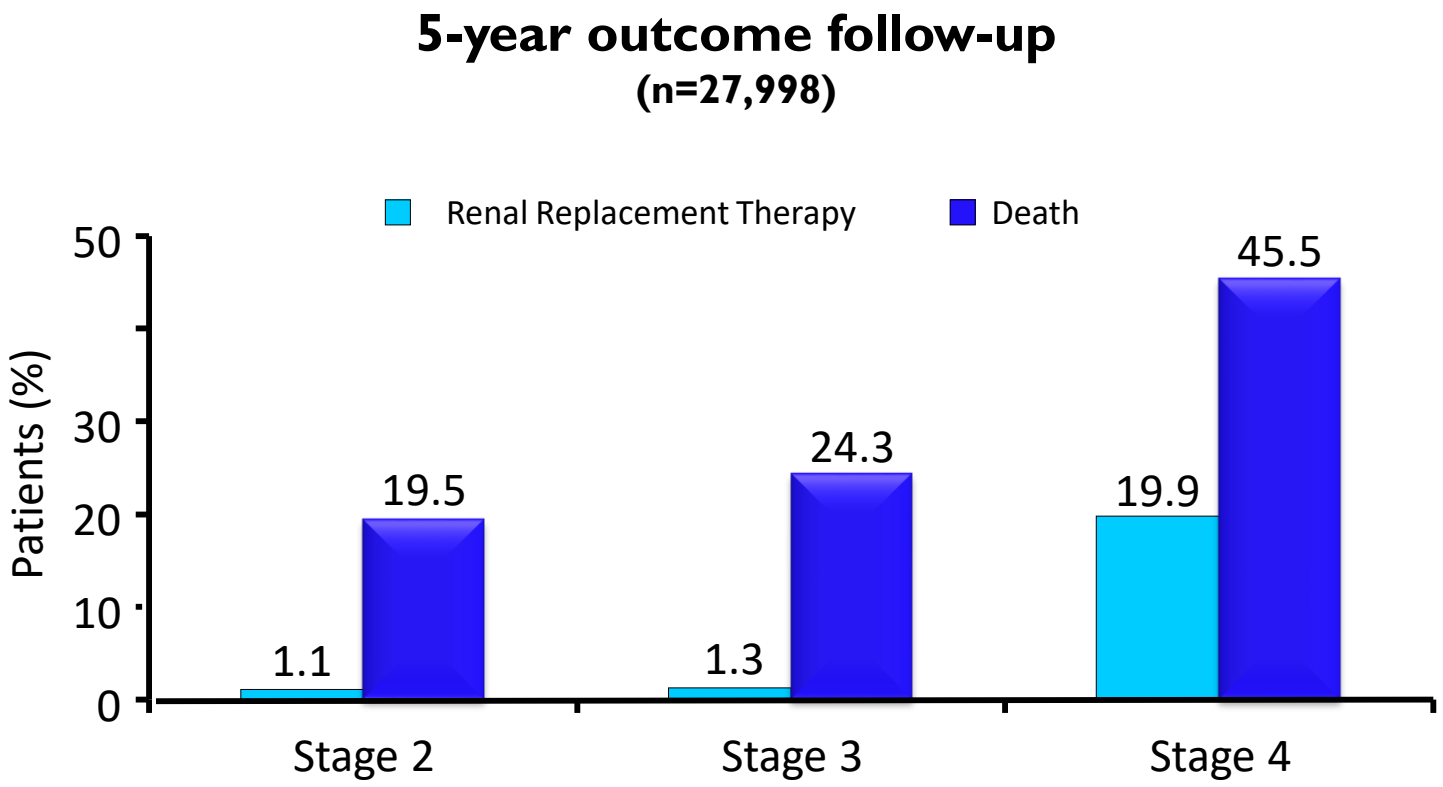
Οι γιατροί δεν έχουν ακριβή εργαλεία για την αξιολόγηση του κινδύνου εξέλιξης της ΧΝΝ από τα πρώιμα στάδια
Με αποτέλεσμα να υπάρχει ένα μοντέλο φροντίδας
“one size fits al care models”

Prevalence of CKD is higher in the early stages by stages among NHANES participants, 1988-2012



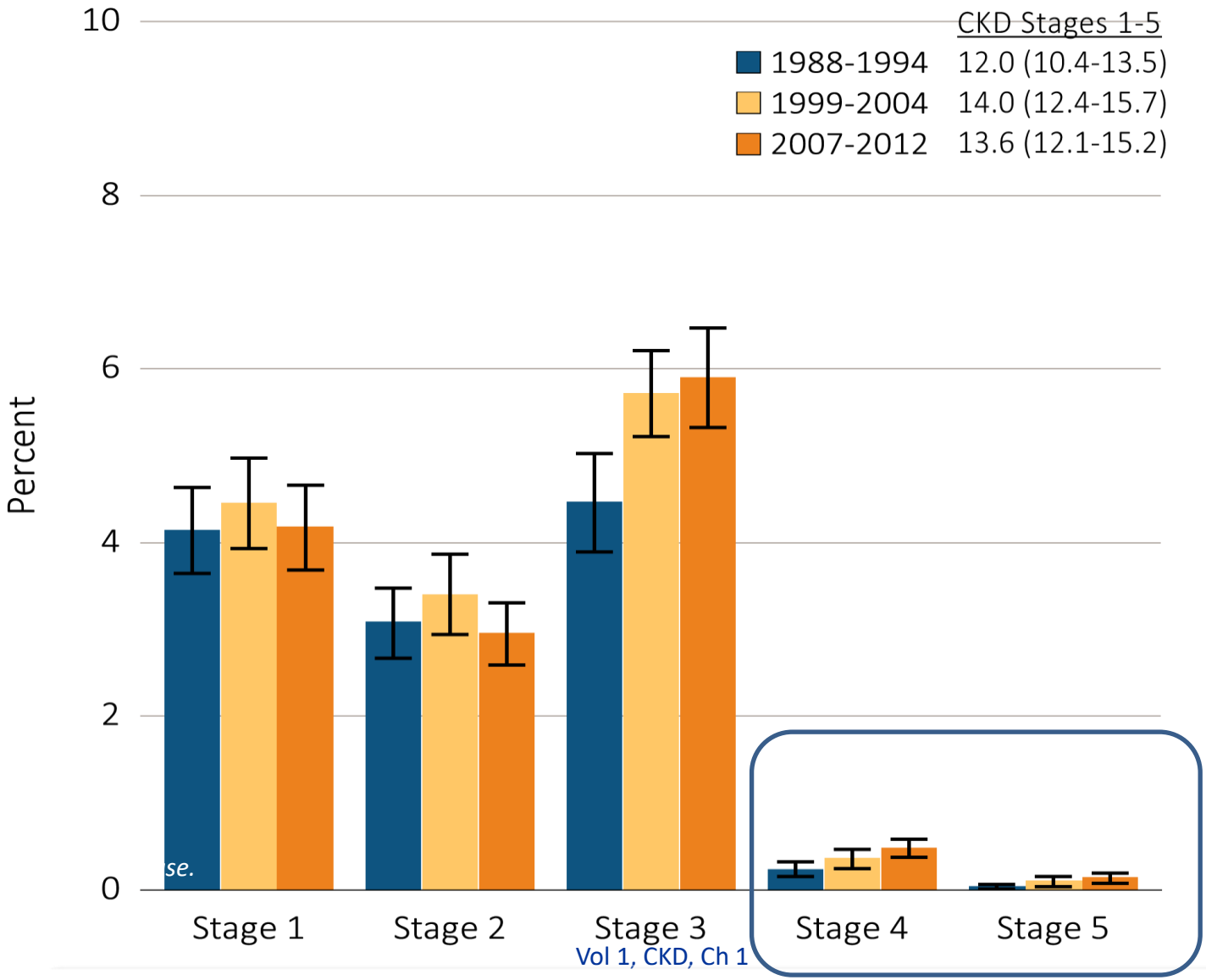
disease.

Death is a more common outcome than dialysis in patients with CKD



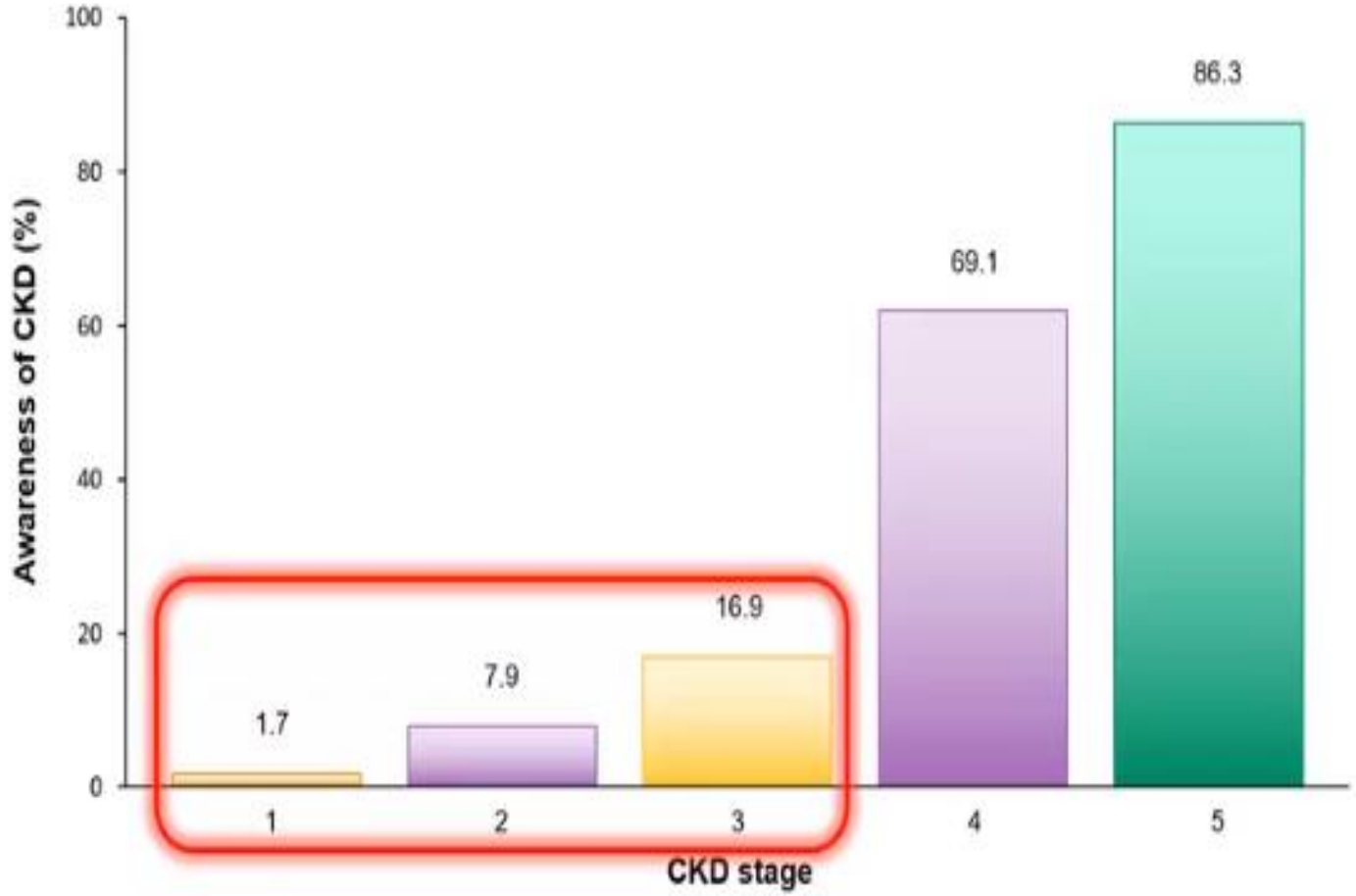
Keith et al. *Arch Intern Med*. 2004;164:659

Prevalence of CKD is higher in the early stages by stages among NHANES participants, 1988-2012



...with patient awareness of CKD significantly lower at early-stage CKI compared with late-stage CKD

CKD awareness by CKD stage in the NHANES population (2015–2018)[1,a]



[a]Awareness was assessed as those who reported being told that they had kidney disease

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; NHANES, National Health and Nutrition Examination Survey

Considerations for Diagnosis and Staging

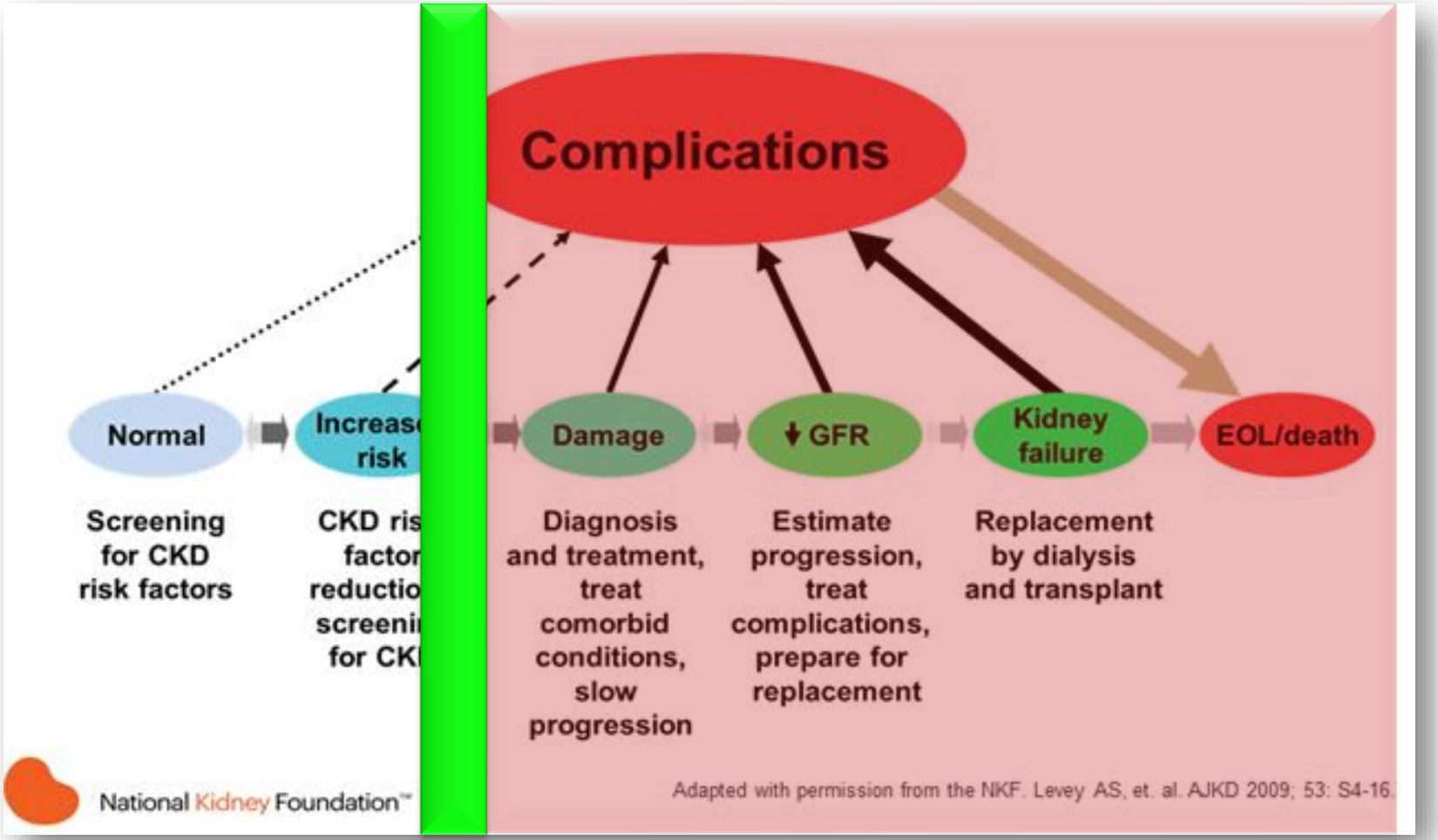
In developed countries, CKD is most commonly attributed to **diabetes and hypertension**

Less than 5% of patients with early CKD
Report **awareness** of their disease

The diagnosis of chronic kidney disease is most likely to occur with the onset of symptoms

JAMA. 2019 October 01; 322(13): 1294–1304. d

Conceptual model of CKD



Conceptual model of CKD

Η νεφρική νόσος συνήθως εξελίσσεται σιωπηλά συχνά καταστρέφοντας το μεγαλύτερο μέρος της νεφρικής λειτουργίας πριν προκαλέσει οποιαδήποτε συμπτώματα

Ωστόσο, εάν εντοπιστεί νωρίς μέσω προληπτικού ελέγχου μπορεί να **επιβραδυνθεί η εξέλιξη της νόσου** με τον έλεγχο και την αντιμετώπιση των παραγόντων της εξέλιξης

Prognosis of CKD by GFR and Albuminuria Categories

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/1.73m^2) 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			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Modified with permission from Macmillan Publishers Ltd. Levey AS, de Jong PE. Coresh J, et. al. Kidney Int 2011; 80: 17-28.

National Kidney Foundation™

Early detection of changes in kidney function facilitates timely diagnosis of CKD in T2D

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

Early detection of kidney injury or damage 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)

and/
or

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

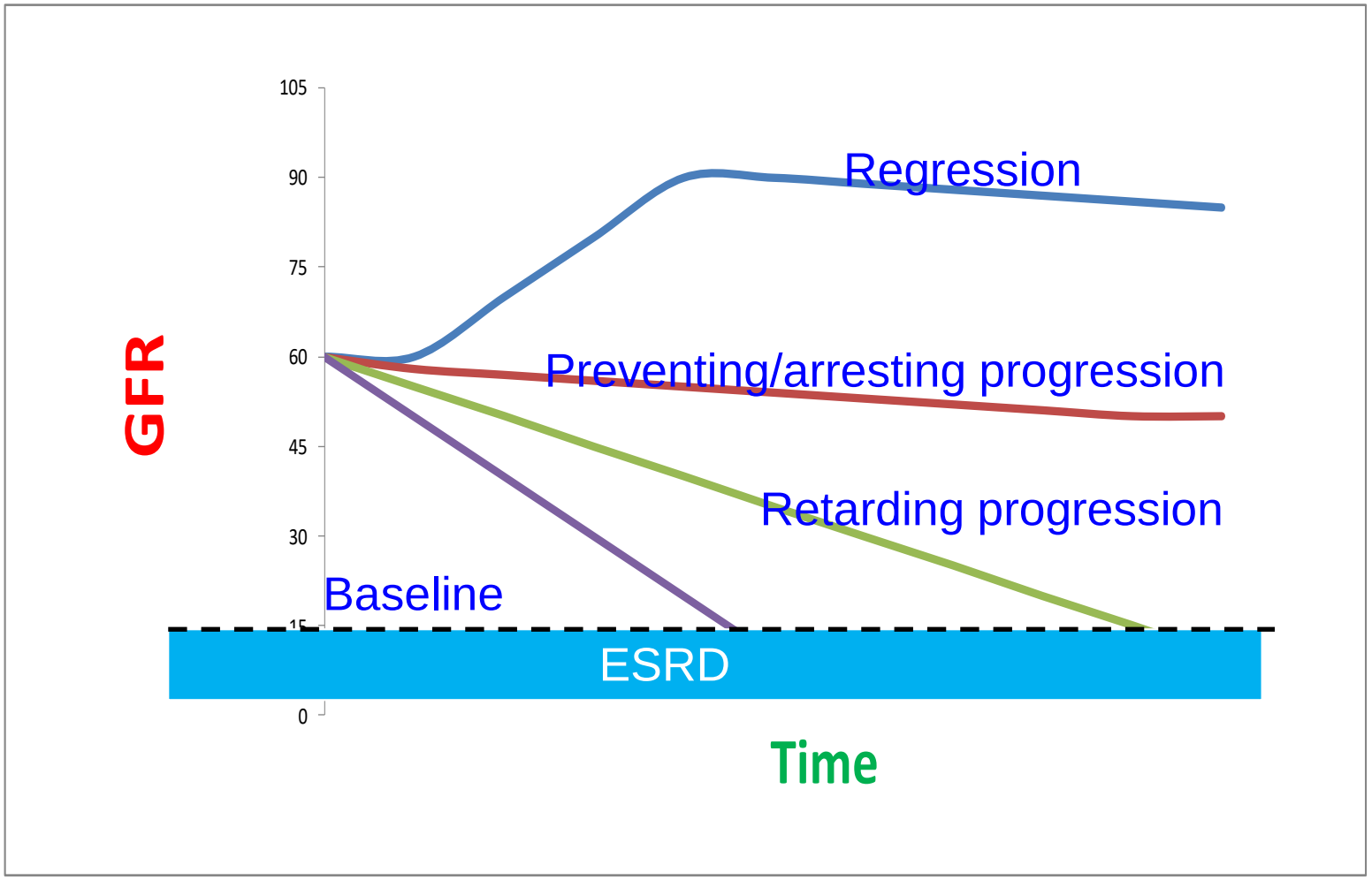
in the absence of signs or symptoms of other primary causes of kidney damage

*Elevated UACR should be confirmed in the absence of urinary tract infection with two additional early morning urine samples collected over the next 2 months

eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio

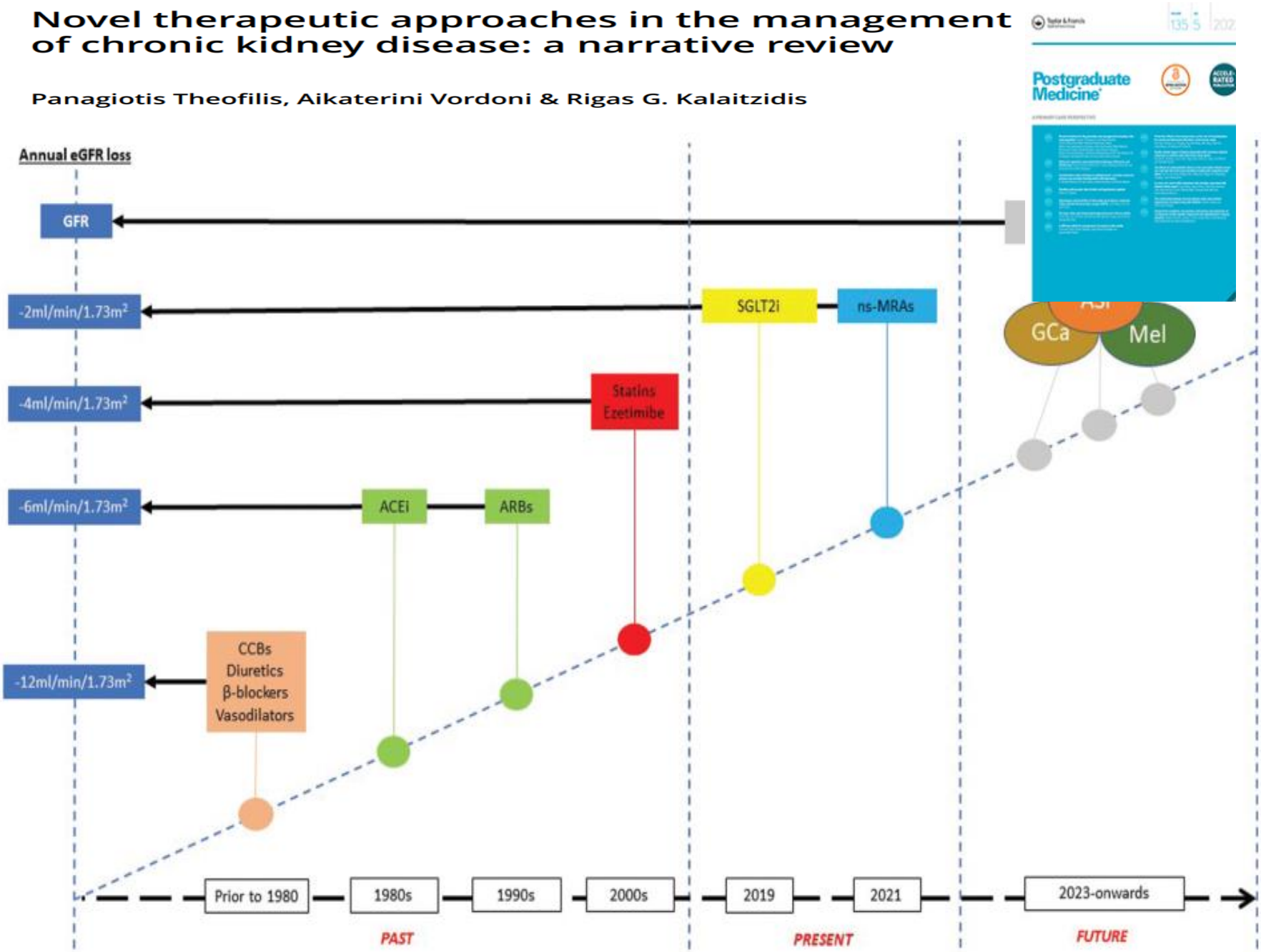
1. Kidney Disease Improving Global Outcomes. *Kidney Int Suppl* 2013;3:1–163; 2. Levey AS, *et al. JAMA* 2015;313:837–846; 3. National Kidney Foundation. *Am J Kidney Dis* 2007;49(Suppl 2):S1–S180; 4. American Diabetes Association. *Diabetes Care* 2022;45(Suppl 1):S175–S184

Toward Regression of Chronic Kidney Disease



Novel therapeutic approaches in the management of chronic kidney disease: a narrative review

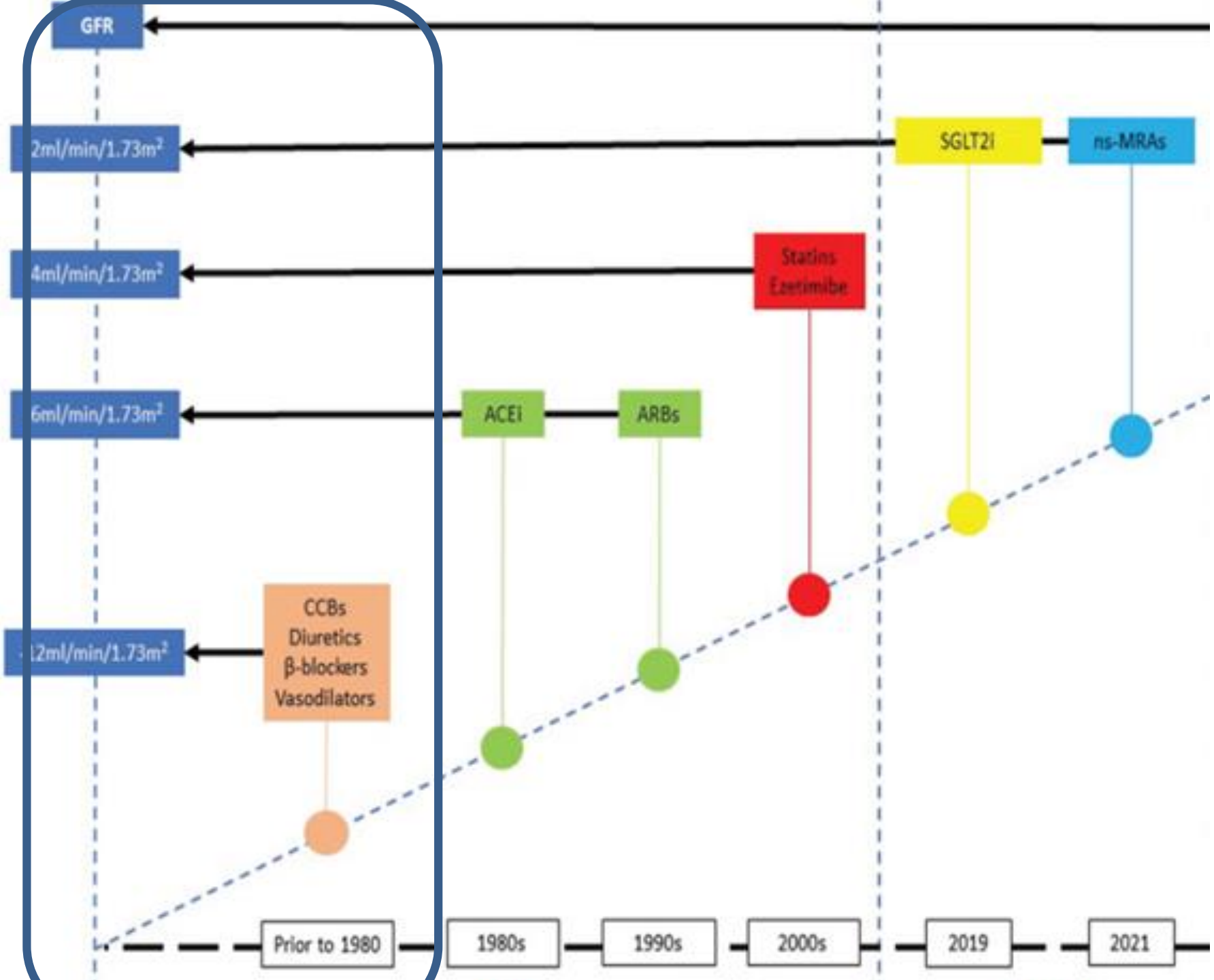
Panagiotis Theofilis, Aikaterini Vordoni & Rigas G. Kalaitzidis

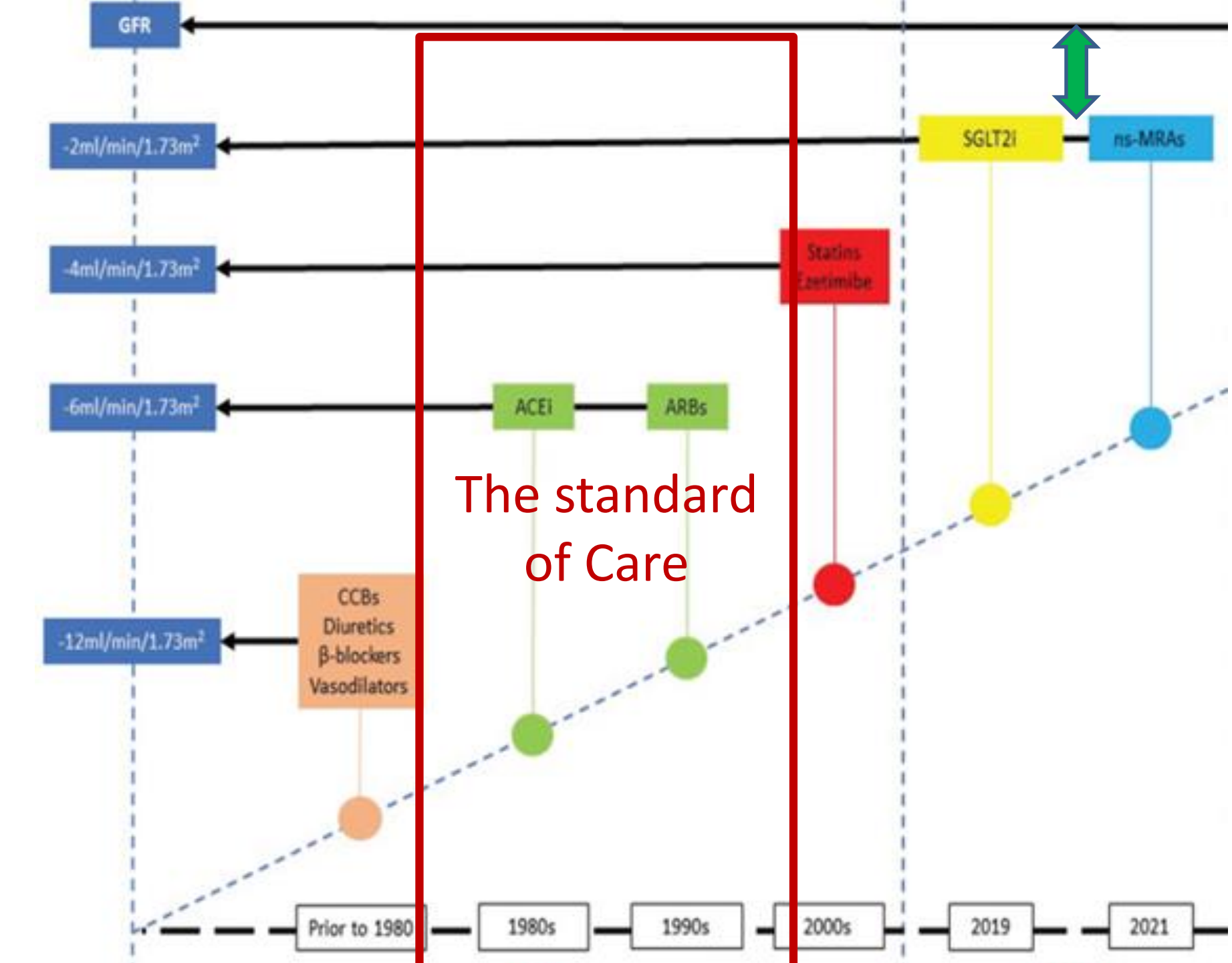


https://doi.org/10.1080/00325481.2023.2233492

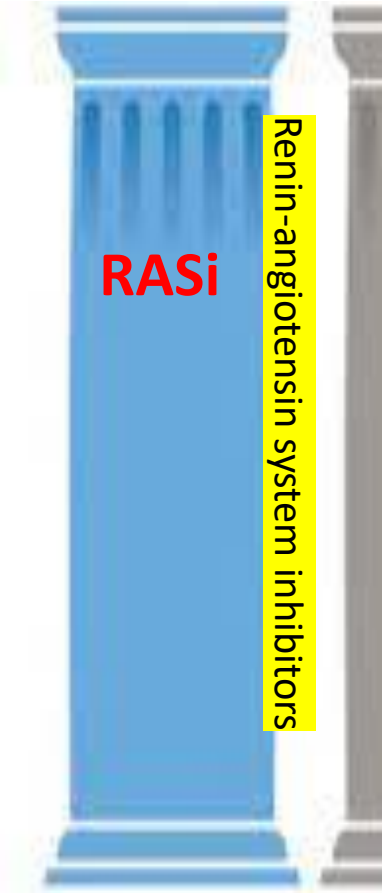
Prior to “80-90 “

Besides hypertension
and
proteinuria
no other targets to stop glomerular filtration rate decrease
existed in the nephrologist’s armamentarium


GFR
2ml/min/1.73m²
4ml/min/1.73m²
6ml/min/1.73m²
2ml/min/1.73m²
CCBs
Diuretics
β-blockers
Vasodilators
ACEi
ARBs
Statins
Ezetimibe
SGLT2i
ns-MRAs
Prior to 1980
1980s
1990s
2000s
2019
2021


GFR
-2ml/min/1.73m²
-4ml/min/1.73m²
-6ml/min/1.73m²
-12ml/min/1.73m²
SGLT2i
ns-MRAs
Statins
Ezetimibe
ACEi
ARBs
CCBs
Diuretics
β-blockers
Vasodilators
The standard of Care
Prior to 1980
1980s
1990s
2000s
2019
2021

Πυλώνες καρδιονεφρικής προστασίας στη ΧΝΝ-ΣΔ



The first pillar

In people with T2D and very high albuminuria, the use of losartan or irbestartan slows kidney disease progression.

The relative risk reduction was

16% in RENAAL

19% in IDNT

Rajiv Agarwal and Denis Fouque

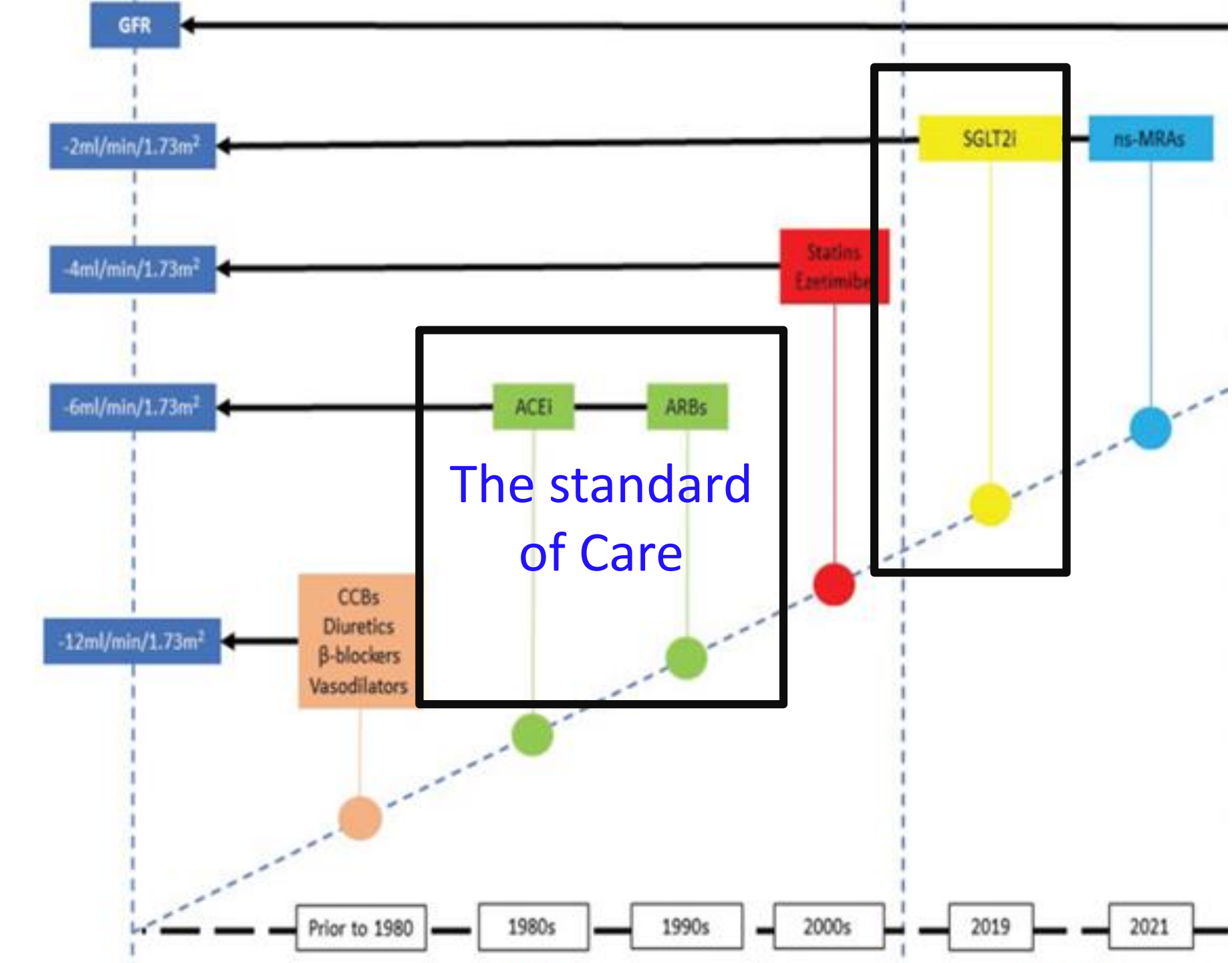
For the next **18 years** there were many attempts to end cardiorenal disease in T2D but these were unsuccessful

The discovery of cardiorenal protection with the

sodium– glucose cotransporter 2 inhibitors

in people with T2D and very high albuminuria led to approval of this drug for this indication

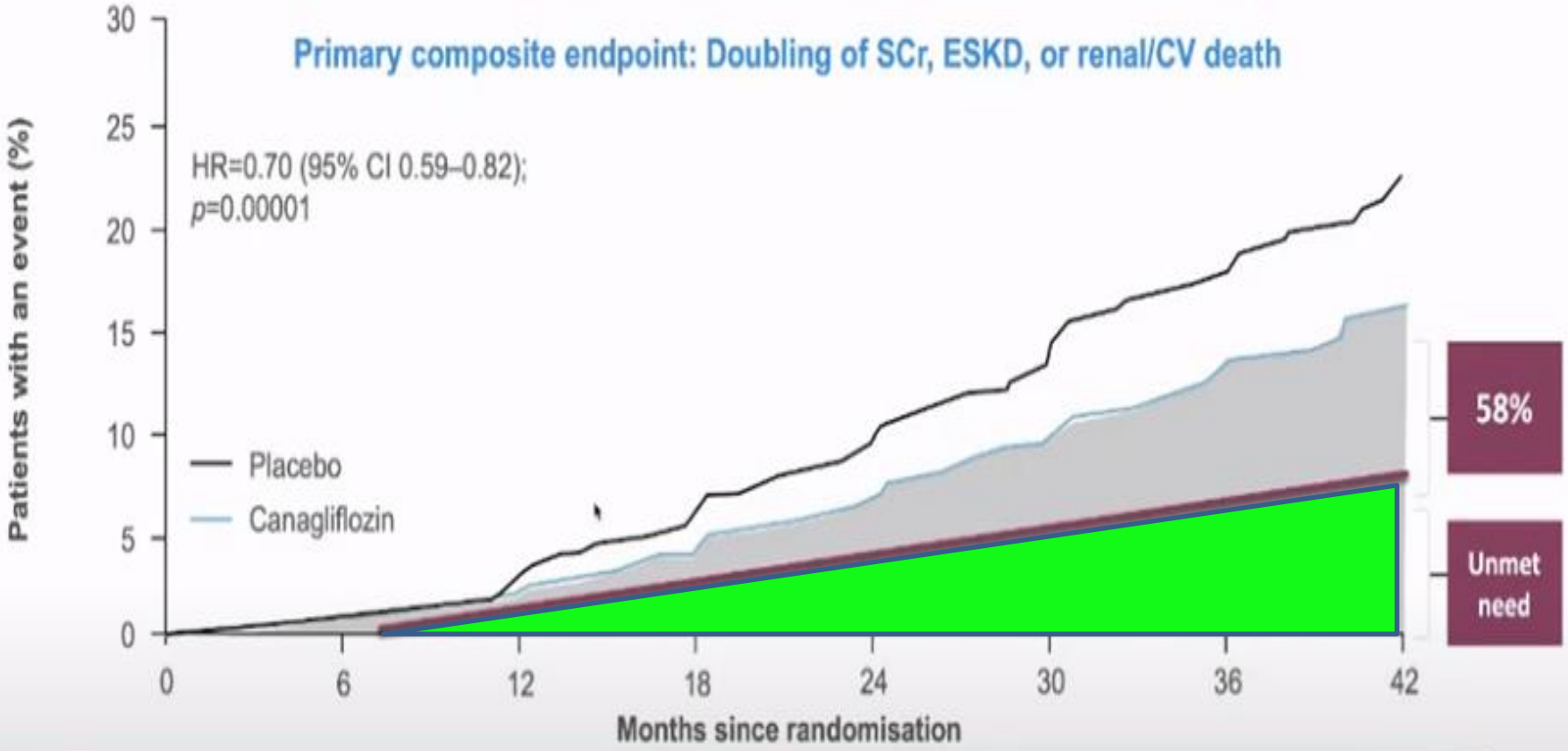
The second pillar


GFR
-2ml/min/1.73m²
-4ml/min/1.73m²
-6ml/min/1.73m²
-12ml/min/1.73m²
SGLT2i
ns-MRAs
Statins
ACEi
ARBs
The standard of Care
CCBs
Diuretics
β-blockers
Vasodilators
Prior to 1980
1980s
1990s
2000s
2019
2021

Πυλώνες καρδιονεφρικής προστασίας στη ΧΝΝ-ΣΔ

Rajiv Agarwal and Denis Fouque

REMAINING RESIDUAL RISK AFTER SGLT2 INHIBITORS



No. at risk								
Canagliflozin	2202	2181	2145	2081	1786	1211	646	196
Placebo	2199	2178	2132	2047	1725	1129	621	170

CV, cardiovascular; ESKD, end-stage kidney disease; SCr, serum creatinine; HR, hazard ratio

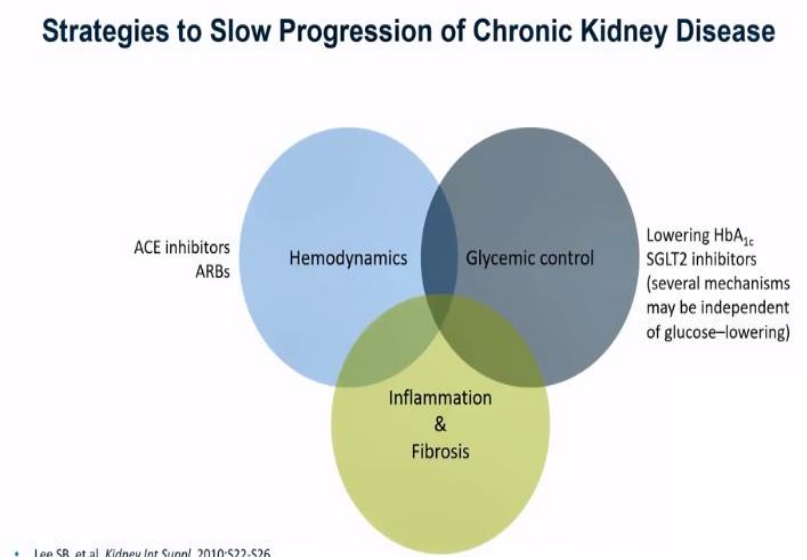
Perkovic V, *et al. N Engl J Med* 2019;380:2295–2306

“2020 “

Besides hypertension and proteinuria, no other targets to stop glomerular filtration rate decrease exist in the nephrologist’s armamentarium

Inflammation, oxidative stress and fibrosis

are three new targets that show promising results in experimental models and clinical trials

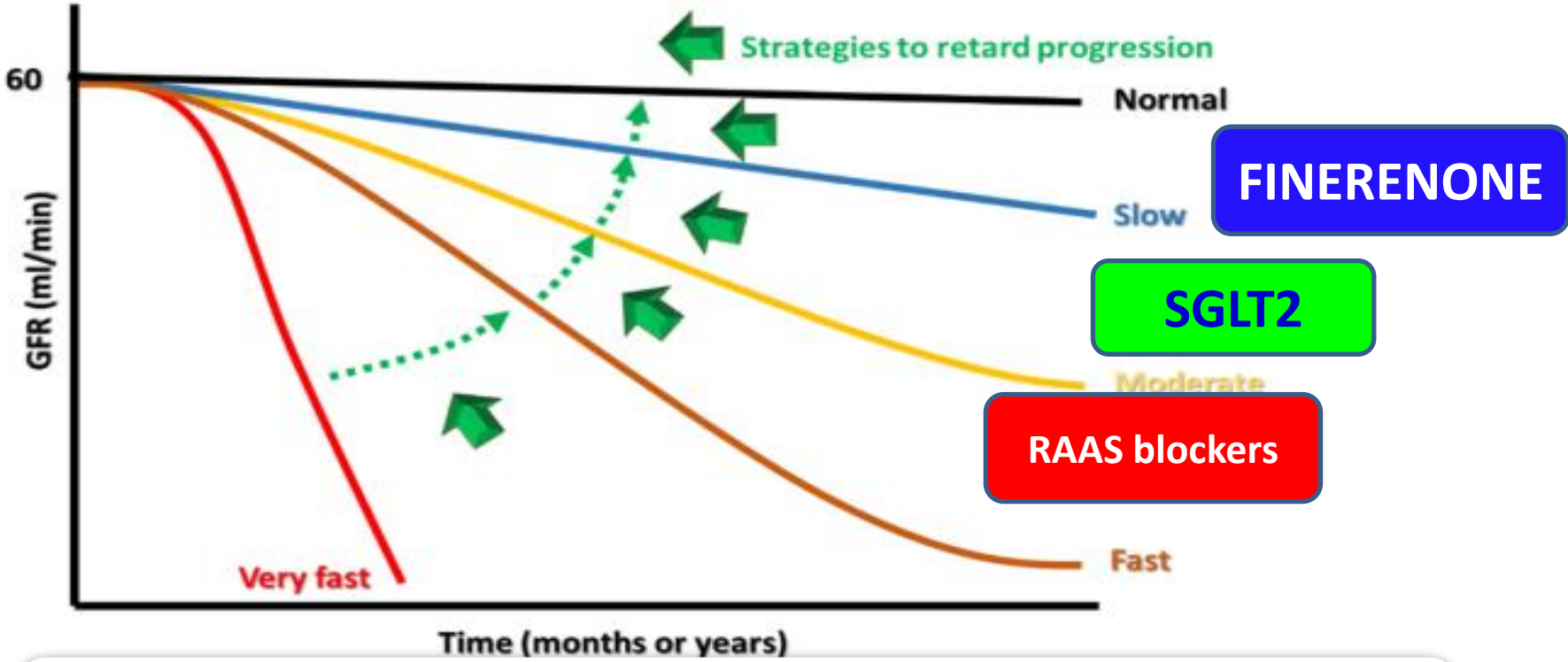


Novel nonsteroidal MRAs,
have been developed with
better anti-fibrotic and anti-inflammatory
effects

Πυλώνες καρδιονεφρικής προστασίας στη ΧΝΝ-ΣΔ

Rajiv Agarwal and Denis Fouque

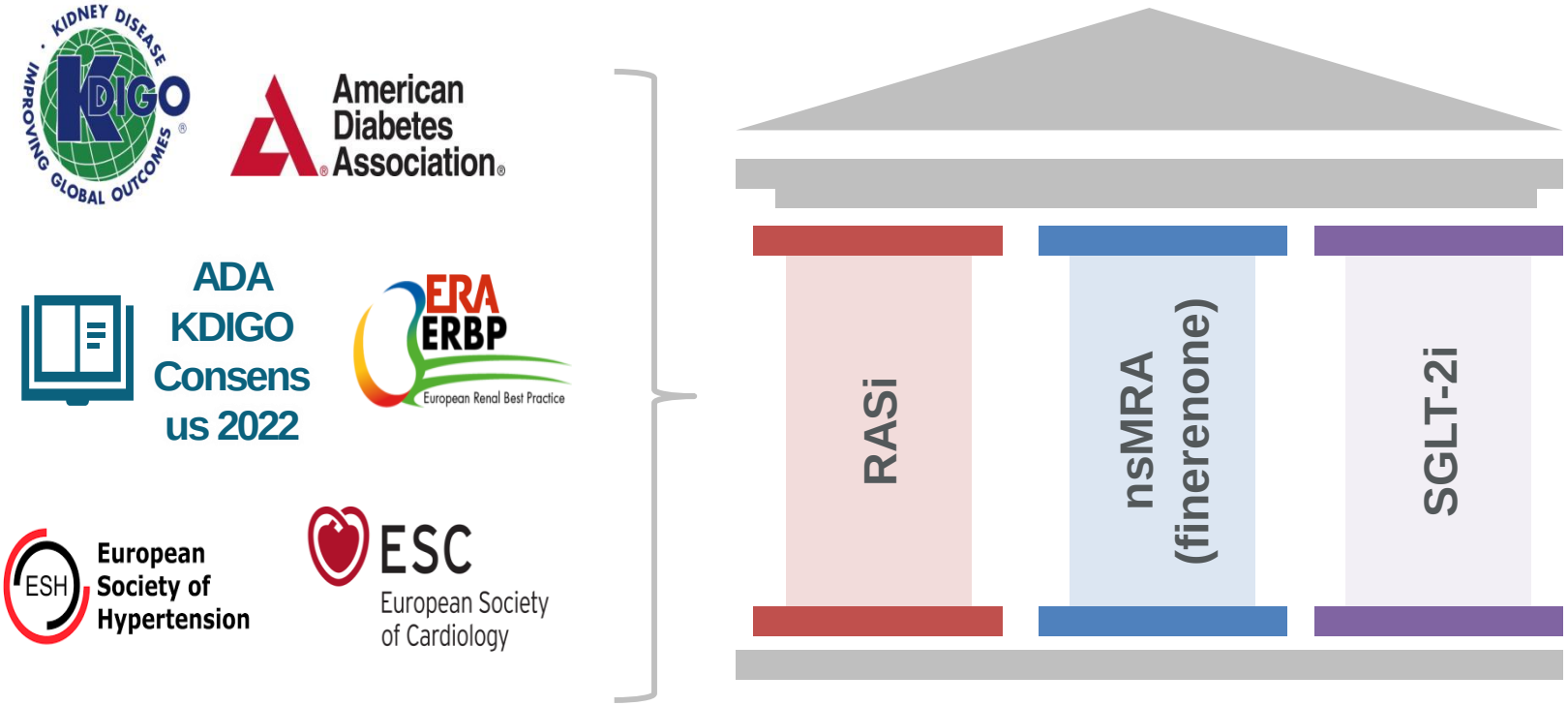
CHRONIC KIDNEY DISEASE: STRATEGIES TO RETARD PROGRESSION



Th e different declined rates of renal function in CKD with the target switch from superfast to slow rate.

J. Mol. Sci. **2021**, *22*, 10084. https:// doi.org/10.3390/ijms221810084

Recent clinical guidelines for the management of CKD in T2D recommend a combination of drug therapies to optimally reduce risks, with finerenone recommended as a core treatment pillar 1–3

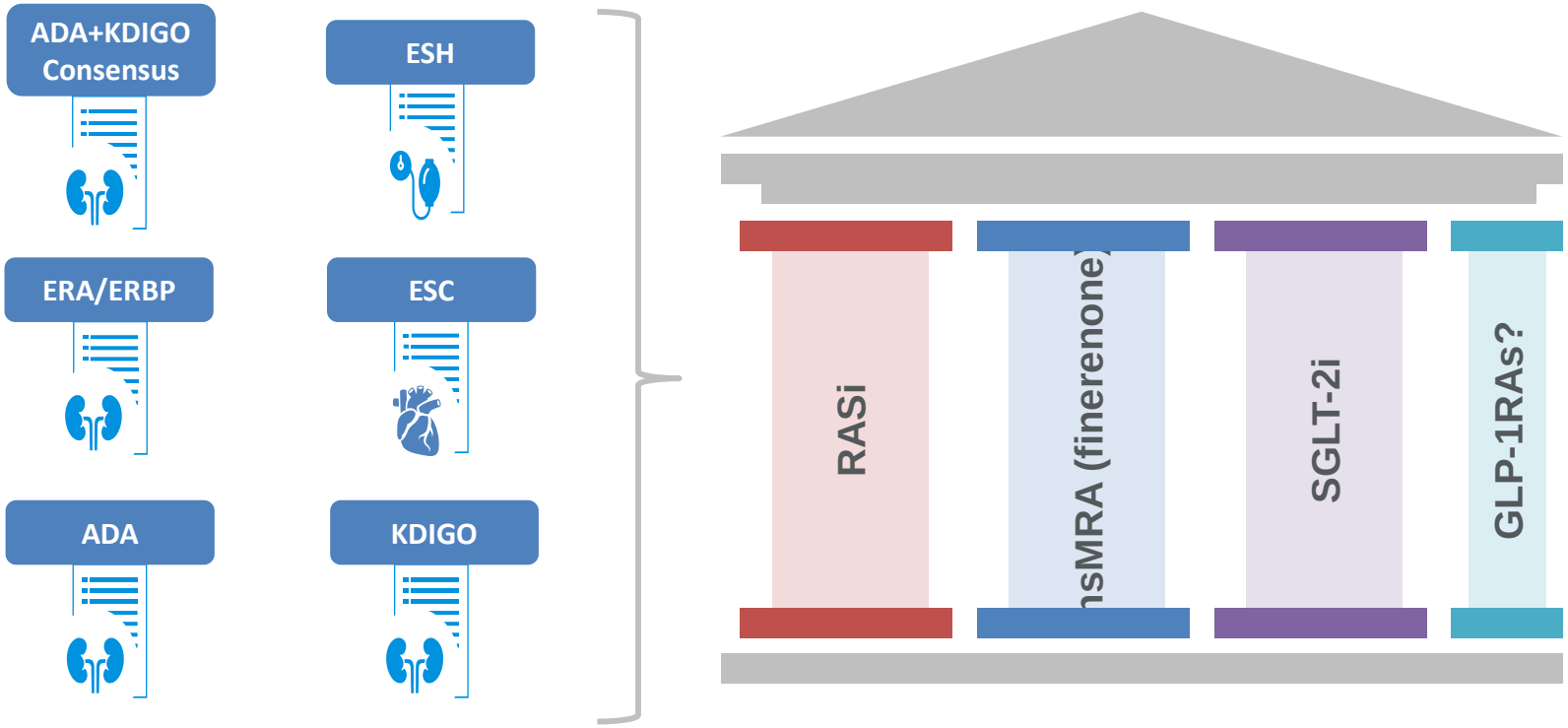


nerenone is indicated for the treatment of CKD (with albuminuria) associated with T2D in adults[4]

ASi, renin–angiotensin system inhibitor

Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int* 2022;102(5S):S1–S128; 2. American Diabetes Association. *Diabetes Care* 2023;46(Suppl 1):S191–S202; 3. de oer IH, *et al. Diabetes Care* 2022;45:3075–3090; 4. Blazek O, *et al. Am Heart J Plus* 2022;19:100187. 4. Bayer AG. KERENDIA®(finerenone) Summary of Product Characteristics. 023. https://www.ema.europa.eu/documents/product-information/kerendia-epar-product-information_en.pdf [accessed October 2023]

Clinical guidelines for the management of CKD in T2D recommend a combination of drug therapies to optimally reduce risks,[1–8] with finerenone proposed as a core treatment pillar[8]

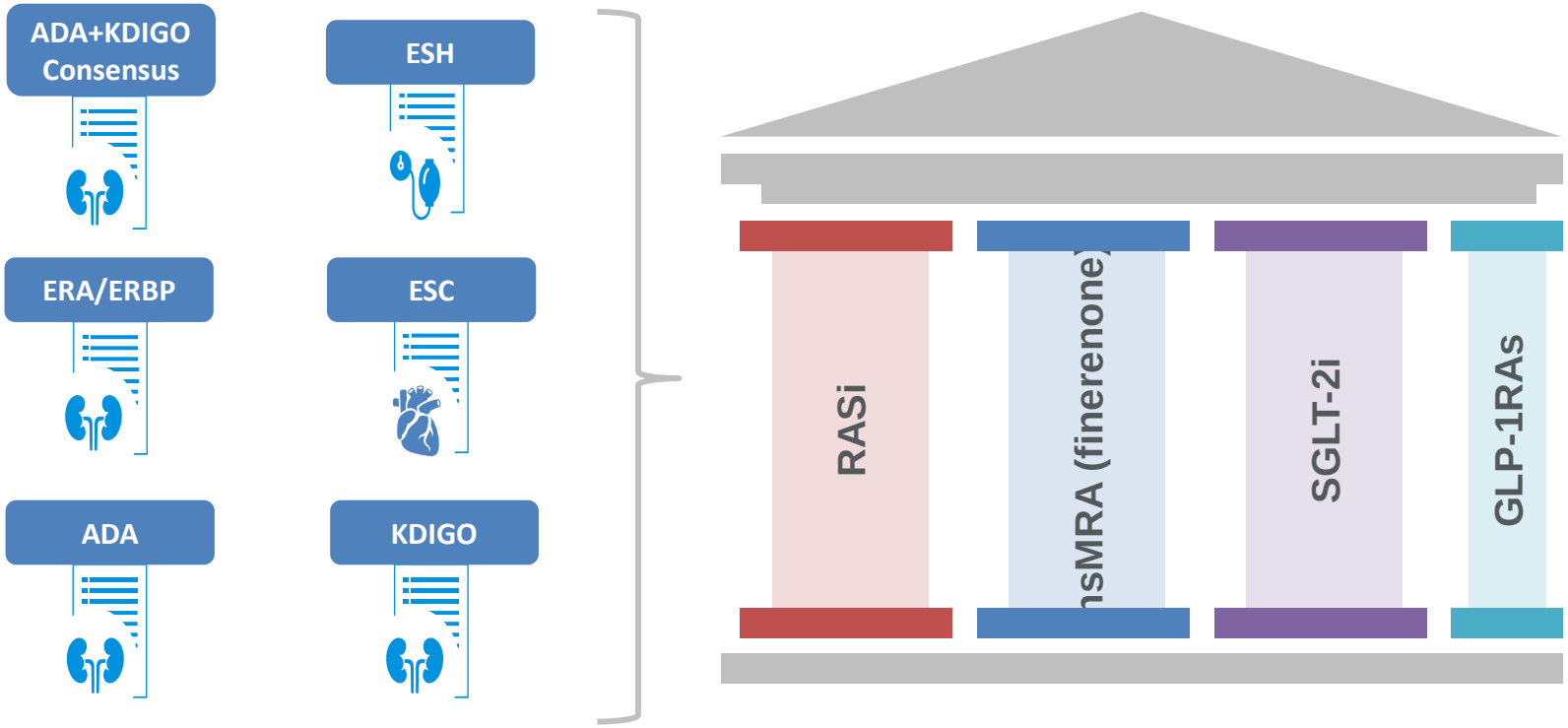


This ‘pillar approach’ is aligned with the multifactorial and holistic approaches for the treatment of CKD and T2D recommended by ADA and KDIGO, respectively[1–3]

Finerenone is indicated in the EU for the treatment of CKD (with albuminuria) associated with T2D in adults. CV prevention is not an approved indication for finerenone in the EU

1. KDIGO Diabetes Work Group. *Kidney Int* 2022;102:S1–S127; 2. Kidney Disease: Improving Global Outcome (KDIGO): *Kidney Int* 2024;105;S117–S314;
3. American Diabetes Association. *Diabetes Care* 2024;47(Suppl 1):S179; 4. de Boer IH, *et al. Diabetes Care* 2022;45:3075–3090; 5. Sarafidis PA, *et al. Clin Kidney J* 2023;16:1885–1907;
6. Mancia G, *et al. J Hypertens* 2023;41:1874–2071; 7. Marx N, *et al. Eur Heart J* 2023;44:4043–4140; 8. Blazek O & Bakris GL. *Am Heart J Plus* 202 2;19:100187

Clinical guidelines for the management of CKD in T2D recommend a combination of drug therapies to optimally reduce risks,[1–8] with finerenone proposed as a core treatment pillar[8]



38

This 'pillar approach' is aligned with the multifactorial and holistic approaches for the treatment of CKD and T2D recommended by ADA and KDIGO, respectively[1–3]

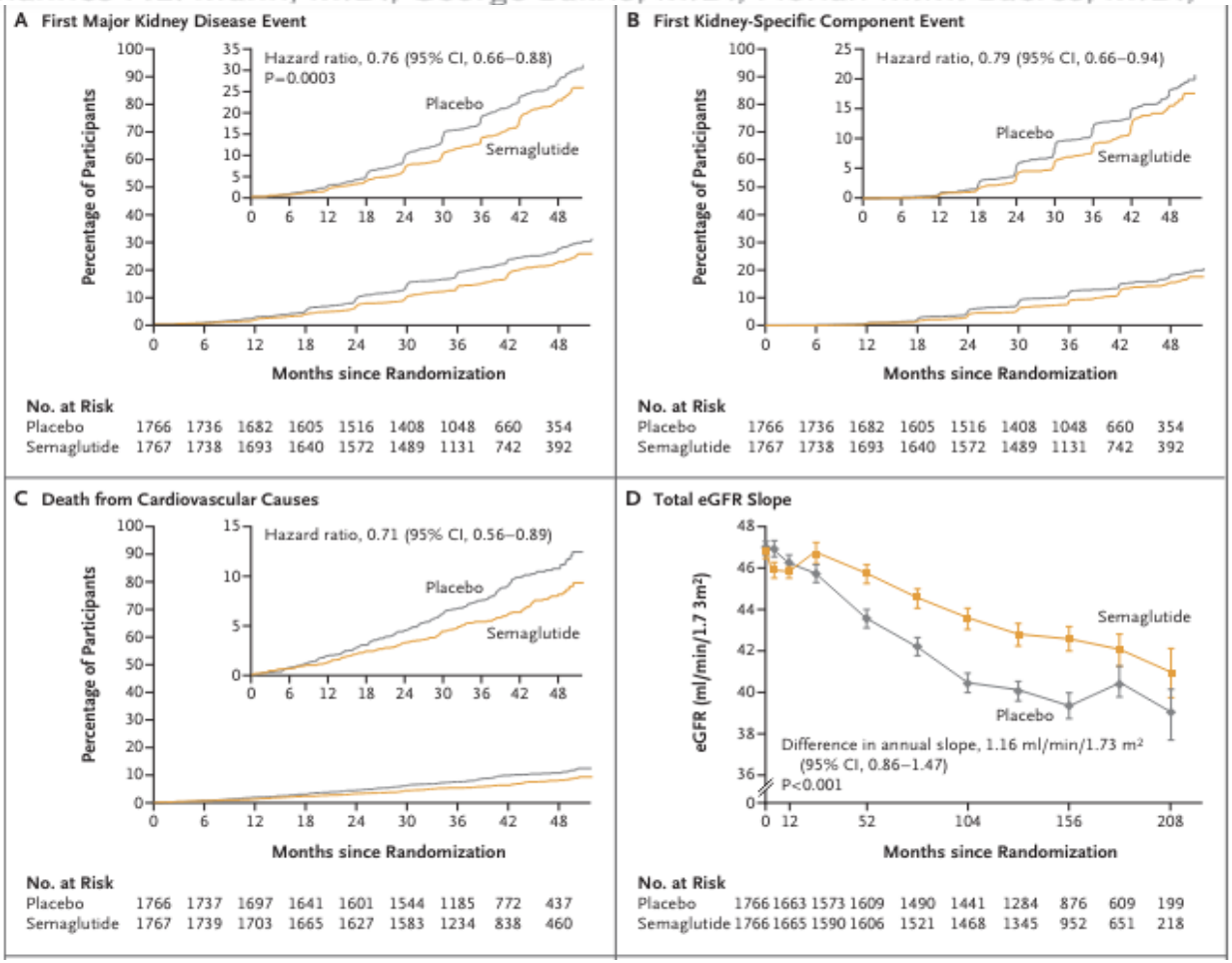
Finerenone is indicated in the EU for the treatment of CKD (with albuminuria) associated with T2D in adults. CV prevention is not an approved indication for finerenone in the EU

1. KDIGO Diabetes Work Group. *Kidney Int* 2022;102:S1–S127; 2. Kidney Disease: Improving Global Outcome (KDIGO): *Kidney Int* 2024;105;S117–S314;
3. American Diabetes Association. *Diabetes Care* 2024;47(Suppl 1):S179; 4. de Boer IH, *et al. Diabetes Care* 2022;45:3075–3090; 5. Sarafidis PA, *et al. Clin Kidney J* 2023;16:1885–1907;
6. Mancia G, *et al. J Hypertens* 2023;41:1874–2071; 7. Marx N, *et al. Eur Heart J* 2023;44:4043–4140; 8. Blazek O & Bakris GL. *Am Heart J Plus* 202 2;19:100187

ORIGINAL ARTICLE

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

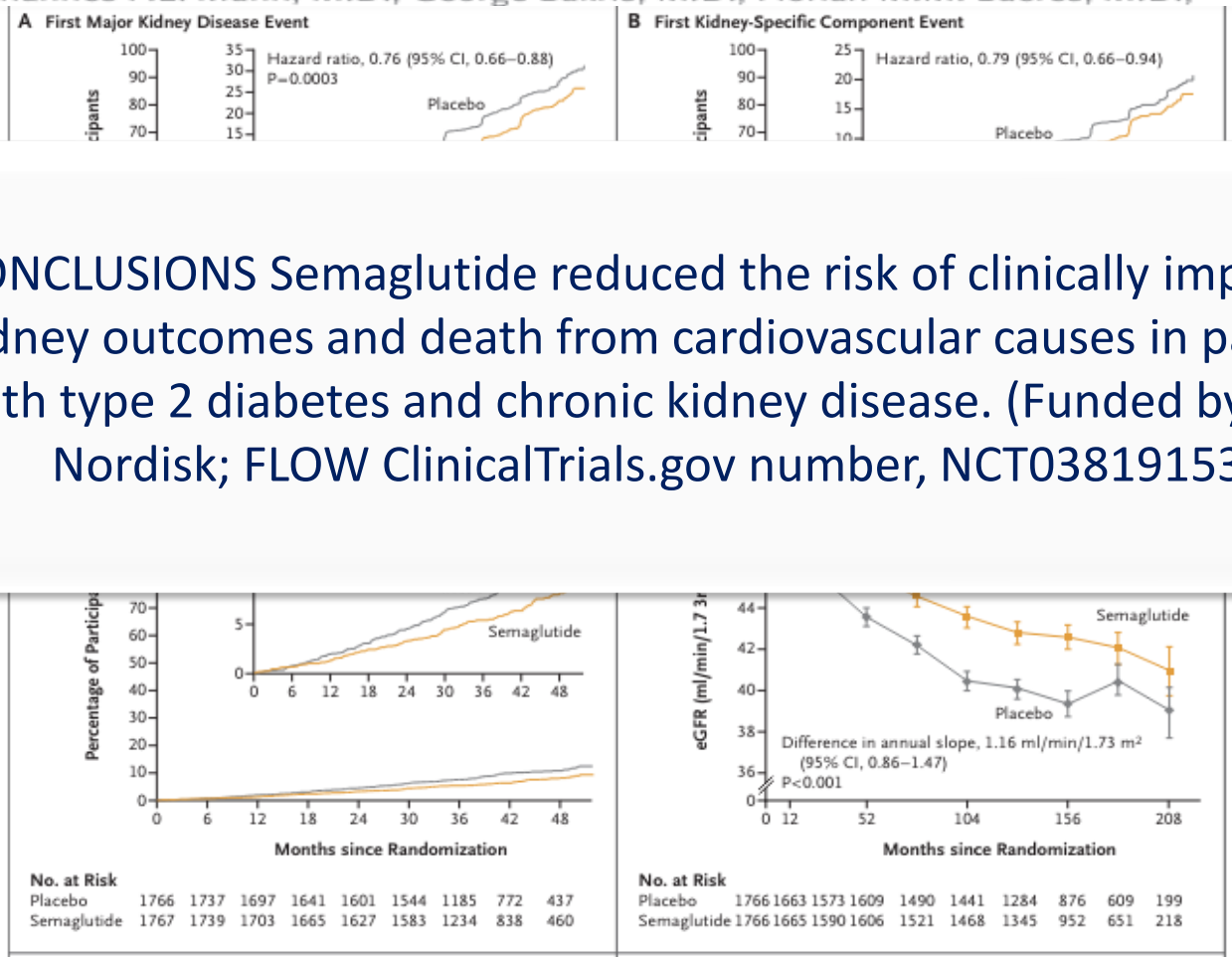
Vlado Perkovic, M.B., B.S., Ph.D., Katherine R. Tuttle, M.D., Peter Rossing, M.D., D.M.Sc., Kenneth W. Mahaffey, M.D., Johannes F.E. Mann, M.D., George Bakris, M.D., Florian M.M. Baeres, M.D.,



ORIGINAL ARTICLE

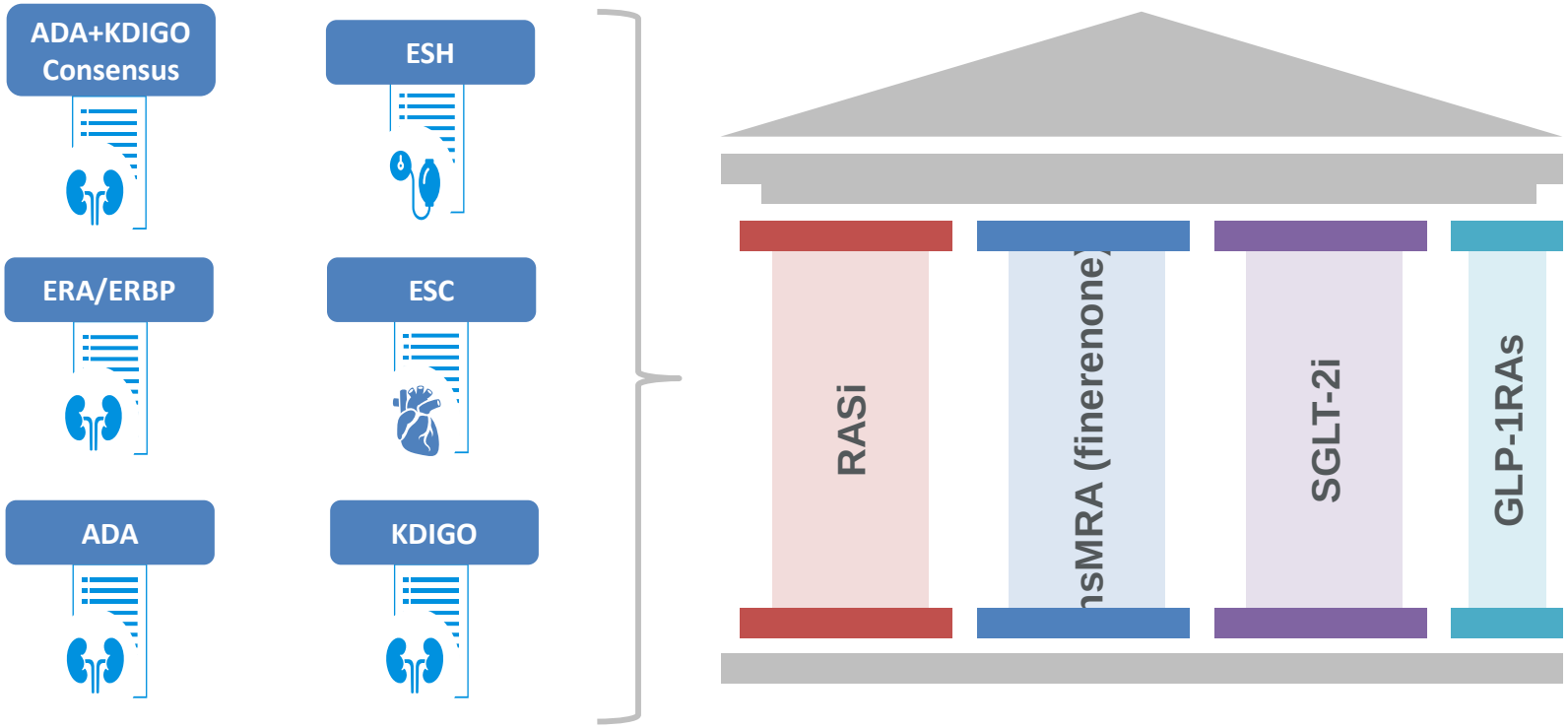
Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes

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.,



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.)

Clinical guidelines for the management of CKD in T2D recommend a combination of drug therapies to optimally reduce risks,[1–8] with finerenone proposed as a core treatment pillar[8]



41

This ‘pillar approach’ is aligned with the multifactorial and holistic approaches for the treatment of CKD and T2D recommended by ADA and KDIGO, respectively[1–3]

Finerenone is indicated in the EU for the treatment of CKD (with albuminuria) associated with T2D in adults. CV prevention is not an approved indication for finerenone in the EU

1. KDIGO Diabetes Work Group. *Kidney Int* 2022;102:S1–S127; 2. Kidney Disease: Improving Global Outcome (KDIGO): *Kidney Int* 2024;105;S117–S314;
3. American Diabetes Association. *Diabetes Care* 2024;47(Suppl 1):S179; 4. de Boer IH, *et al. Diabetes Care* 2022;45:3075–3090; 5. Sarafidis PA, *et al. Clin Kidney J* 2023;16:1885–1907;
6. Mancia G, *et al. J Hypertens* 2023;41:1874–2071; 7. Marx N, *et al. Eur Heart J* 2023;44:4043–4140; 8. Blazek O & Bakris GL. *Am Heart J Plus* 202 2;19:100187

bakris g

Search

Advanced Create alert Create RSS User Guide

Save Email Send to Sort by: Most recent Display options

1,026 results

Page 1 of 103

1

Cite

Share

Design and baseline characteristics of the Finerenone, in addition to standard of care, on the progression of kidney disease in patients with Non-Diabetic Chronic Kidney Disease (FIND-CKD) randomized trial.

Heerspink HJL, Agarwal R, **Bakris GL**, Cherney DZI, Lam CSP, Neuen BL, Sarafidis PA, Tuttle KR, Wanner C, Brinker MD, Dizayee S, Kolkhof P, Schloemer P, Vesterinen P, Perkovic V; FIND-CKD investigators.

Nephrol Dial Transplant. 2024 Jun 11:gfae132. doi: 10.1093/ndt/gfae132. Online ahead of print.

PMID: 38858818

THANK YOU GEORGE