

Σακχαρώδης διαβήτης & ΧΝΝ



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Ιατρικής Σχολής ΕΚΠΑ

7-5-2026

Δήλωση σύγκρουσης συμφερόντων

- Η ομιλία εκφράζει τις απόψεις του ομιλητή
- Ο ομιλητής έχει λάβει αμοιβή για διαλέξεις & συμμετοχή σε συμβουλευτικές επιτροπές καθώς και χρηματοδότηση για έρευνα από τις ακόλουθες φαρμακευτικές εταιρείες:

Abbot, Astra Zeneca, Boehringer Ingelheim, Menarini, GSK, MSD, Novo Nordisk, Sanofi, Vianex

Δομή ομιλίας

- Επιδημιολογία - Διάγνωση
- Παθοφυσιολογία
- Θεραπευτικές παρεμβάσεις

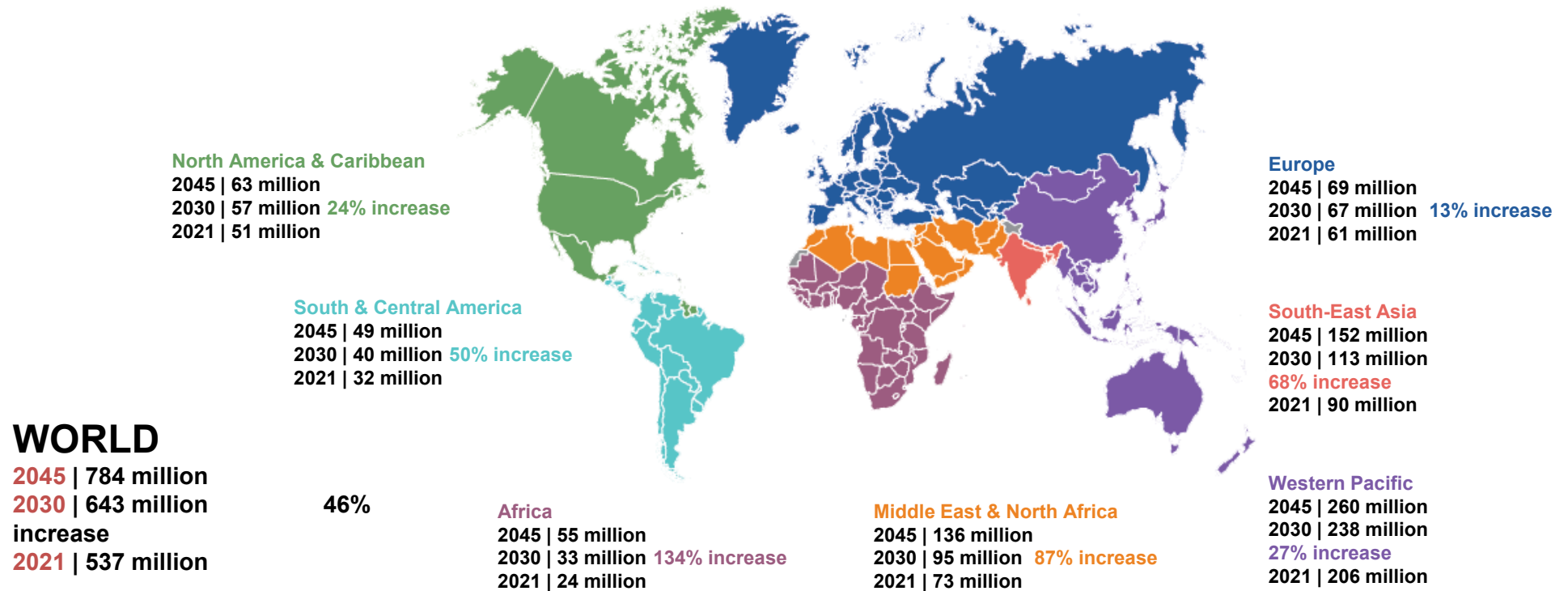
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Σακχαρώδης Διαβήτης τύπου 2 : Παγκόσμια Επιδημία

Number of people (aged 20–79 years) with diabetes worldwide and per IDF region and anticipated percentage increase



What is Chronic Kidney Disease?

KDIGO definition criteria

Definition

The National Kidney Foundation KDIGO define CKD as:¹
Duration of >3 months of either:

1. Kidney damage, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR manifest by either:
 - a. Pathological abnormalities; or
 - b. Markers of kidney damage, including albuminuria ≥ 30 mg/g (≥ 3 mg/mmol) or other abnormalities in the composition of urine, or abnormalities in histology or imaging tests, or history of kidney transplantation
2. GFR < 60 mL/min/1.73 m² with or without kidney damage

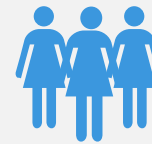


ESRD

ESRD* is the final stage of kidney disease, when the kidneys no longer function well enough to meet the needs of everyday life²

Chronic kidney disease – Global statistics³

- CKD has a global prevalence of 9.1%; prevalence is higher in women than in men



9.5%
of women



7.3%
of men

- CKD has a major effect on global health, both as a direct cause of global morbidity and mortality
- It is the 12th leading cause of death worldwide resulting in 1.2 million deaths and 35.8 million DALYs in 2017

*End-stage renal disease - defined by maintenance dialysis that is sustained for at least 30 days, renal transplantation, or eGFR < 15 mL/min per 1.73 m² sustained for at least 30 days^{1,4,5}

CKD, chronic kidney disease; DALY, disability-adjusted life year; GFR, glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcome

1. KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int.* 2020;98(4S):S1–S115 2. Rodger RSC et al. *Clin Med* 2012;12:472–475; 3. Carney EF. *Nat Rev Nephrol* 2020;16:251; 4. Perkovic V et al. *Lancet Diabetes Endocrinol* 2018;6:691–704; 5. Mann JFE et al. *N Engl J Med* 2017;377:839–848



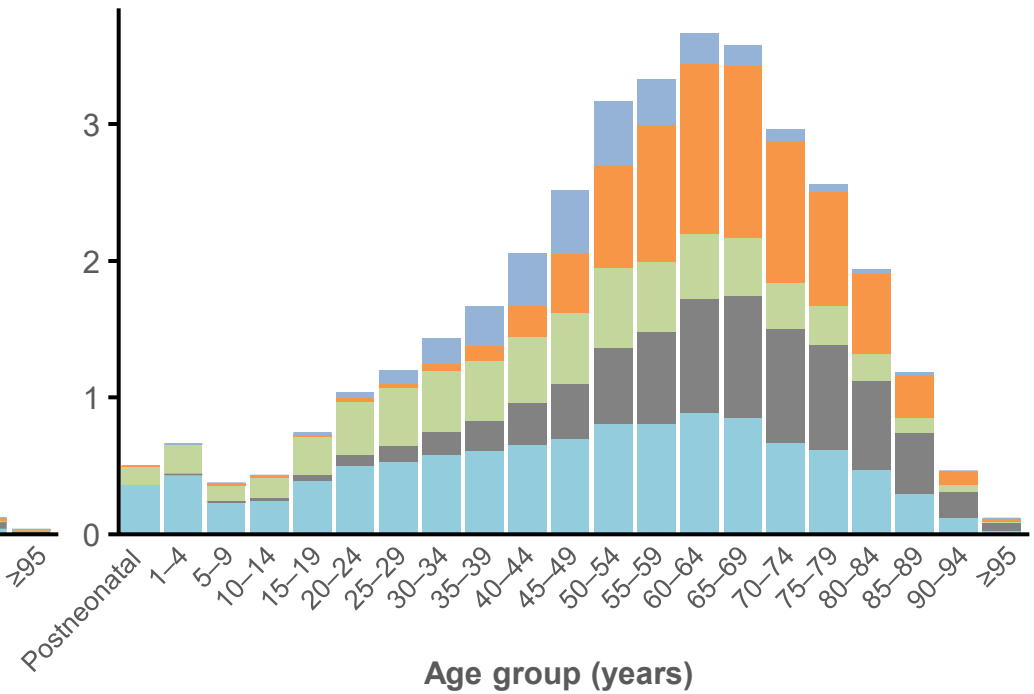
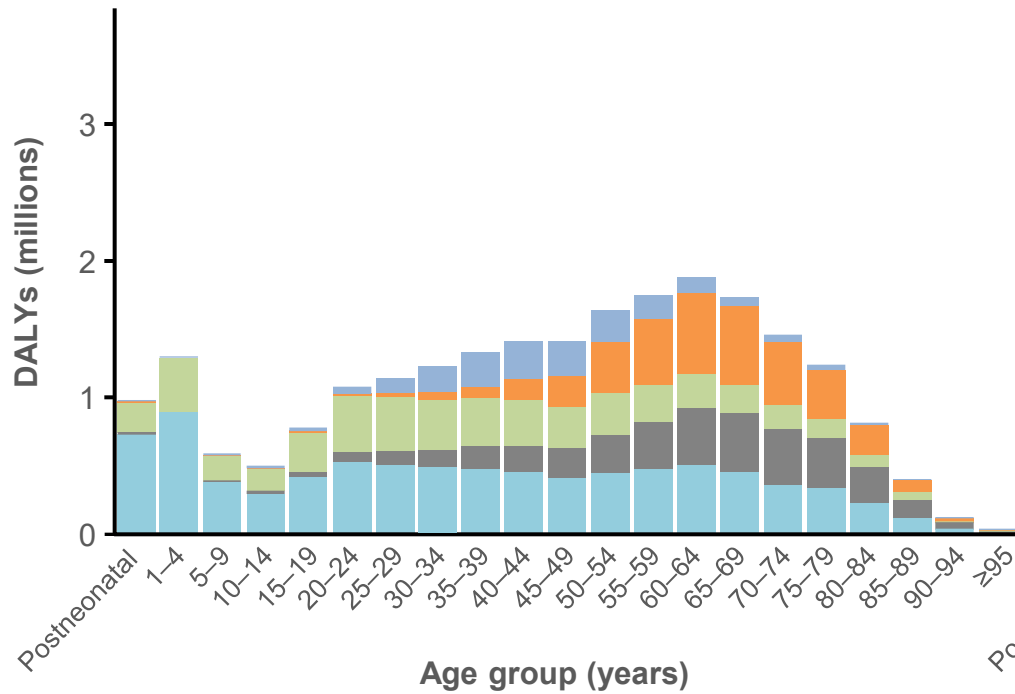
Επιπολασμός και αίτια της ΧΝΝ

1990

2017

Cause

- CKD due to T1D
- CKD due to T2D
- CKD due to glomerulonephritis
- CKD due to hypertension
- CKD due to other and unspecified causes



Data from 195 countries

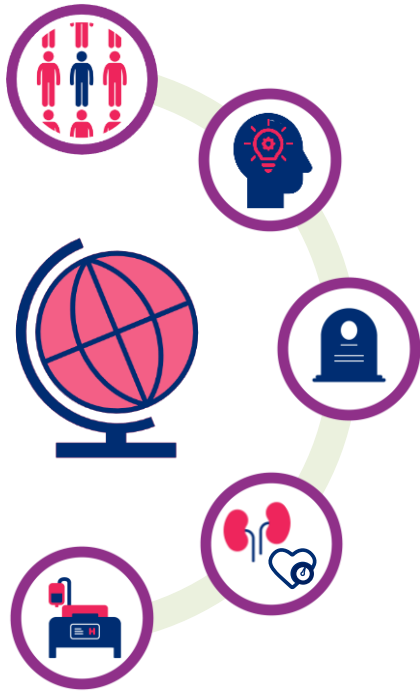
DALY, disability-adjusted life-year

GBD Chronic Kidney Disease Collaboration. *Lancet* 2020;395:709



Γιατί μας ανησυχεί η Χρόνια Νεφρική Νόσος;

Πρόκειται για ένα σημαντικό παγκόσμιο πρόβλημα δημόσιας υγείας



Η ΧΝΝ επηρεάζει περίπου **1 στους 10 ενήλικες** ή περίπου **850 εκατομμύρια άτομα** και πρόσφατα έχει αναγνωριστεί ως η «**κρυφή επιδημία**»

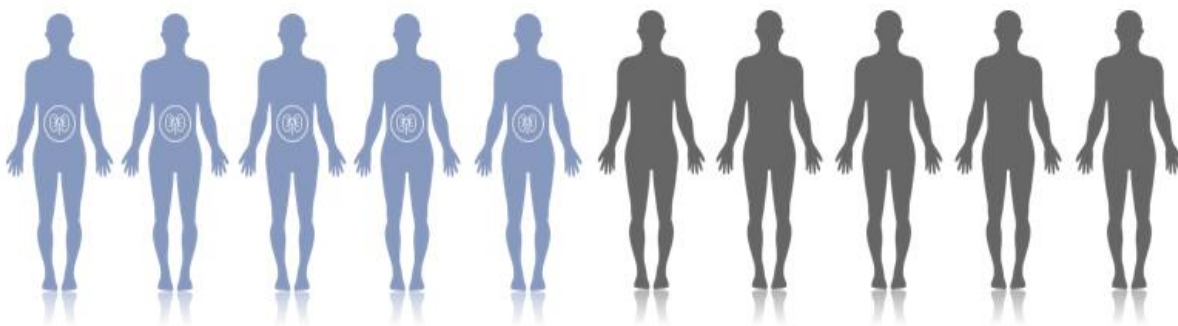
Σχεδόν το **90%** των ενηλίκων με ΧΝΝ **δεν γνωρίζουν** ότι έχουν την πάθηση

Ο **κίνδυνος θνησιμότητας στα 10 έτη** μπορεί να ξεπεράσει το **47%** και **5-10 εκατομμύρια άνθρωποι** πεθαίνουν κάθε χρόνο από ΧΝΝ

Σε χώρες υψηλού και μεσαίου εισοδήματος, η ΧΝΝ προκαλείται συχνότερα από **διαβήτη ή υπέρταση**

Η ΧΝΝ οδηγεί σε **αυξημένες νοσηλείες, δαπάνη πόρων υγειονομικής περίθαλψης και ανάπτυξη νεφρικής ανεπάρκειας**

Οι ασθενείς με διαβήτη διατρέχουν υψηλό κίνδυνο νεφρικής νόσου



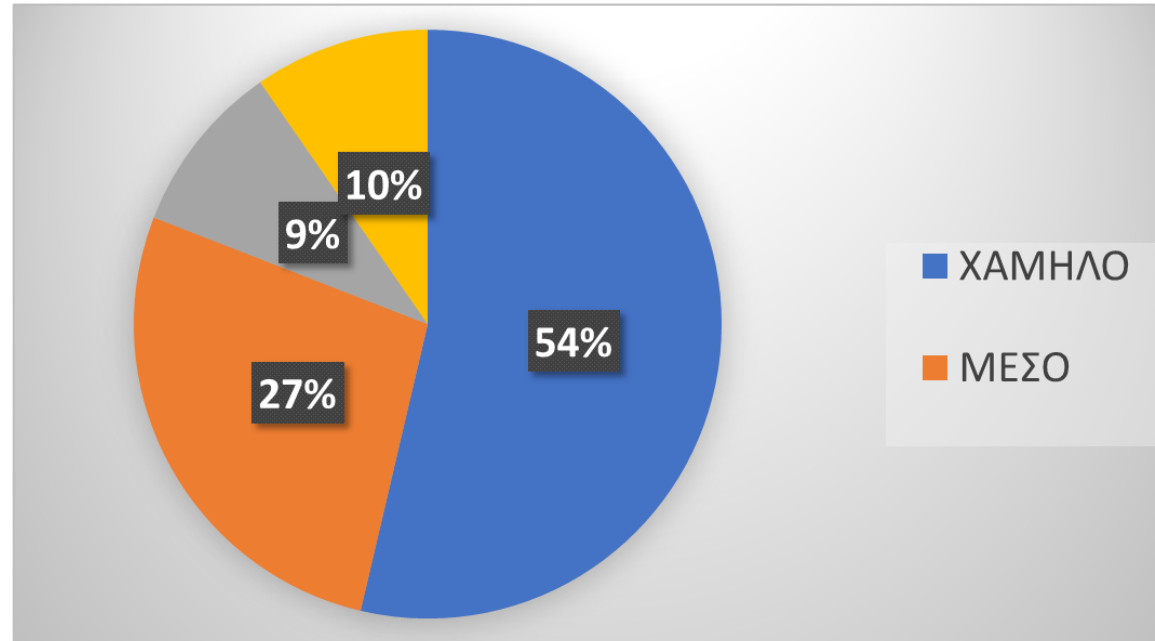
Η ΧΝΝ εκτιμάται ότι επηρεάζει το
~ **50%** των ασθενών με ΣΔτ2
παγκοσμίως...¹

...& είναι ο πιο συνηθισμένος
λόγος για εξέλιξη σε **νεφρική νόσο
τελικού σταδίου**
σε πολλά μέρη του κόσμου¹⁻³



The prevalence of diabetic chronic kidney disease in adult Greek subjects with type 2 diabetes mellitus: A series from hospital-based diabetes clinics

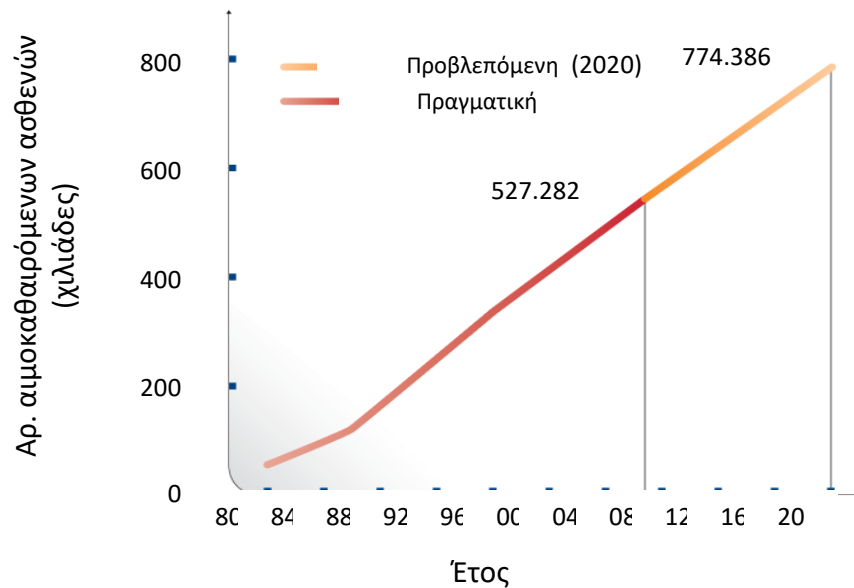
[Ilias N Migdalis¹](#), [Nikolaos Papanas²](#), [Athanasios E Raptis³](#), [Ioannis M Ioannidis⁴](#), [Alexios E Sotiropoulos⁵](#), [George D Dimitriadis³](#), [Hellenic Diabetic Nephropathy Study \(HDNS\) Group](#)



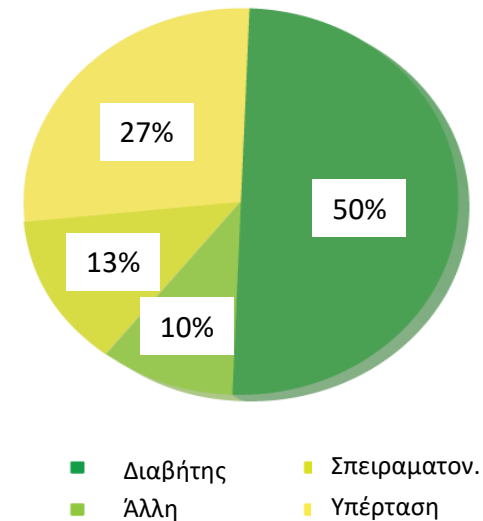
Αν εξαιρεθούν οι ελλιπείς τιμές (71 ασθενείς), τότε το ποσοστό των συμμετεχόντων πάσχει από μέτρια / σοβαρή / πολύ σοβαρή ΧΝΝ τροποποιείται από 46% σε 44.55%

Ο διαβήτης είναι το κύριο αίτιο νεφρικής ανεπάρκειας τελικού σταδίου

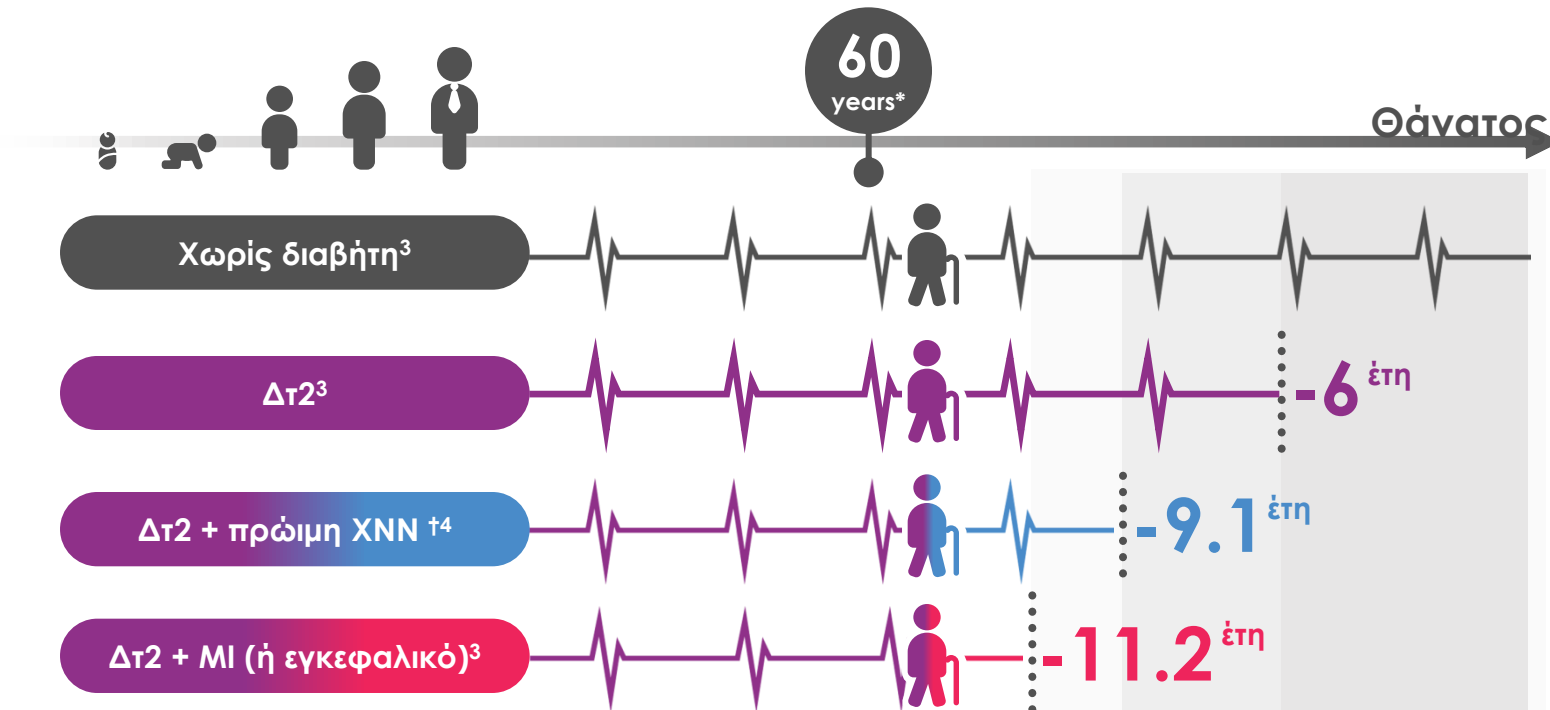
- Η επίπτωση αυξάνεται δραματικά



- Αρχική διάγνωση για ασθενείς που ξεκινούν αιμοδιύλιση

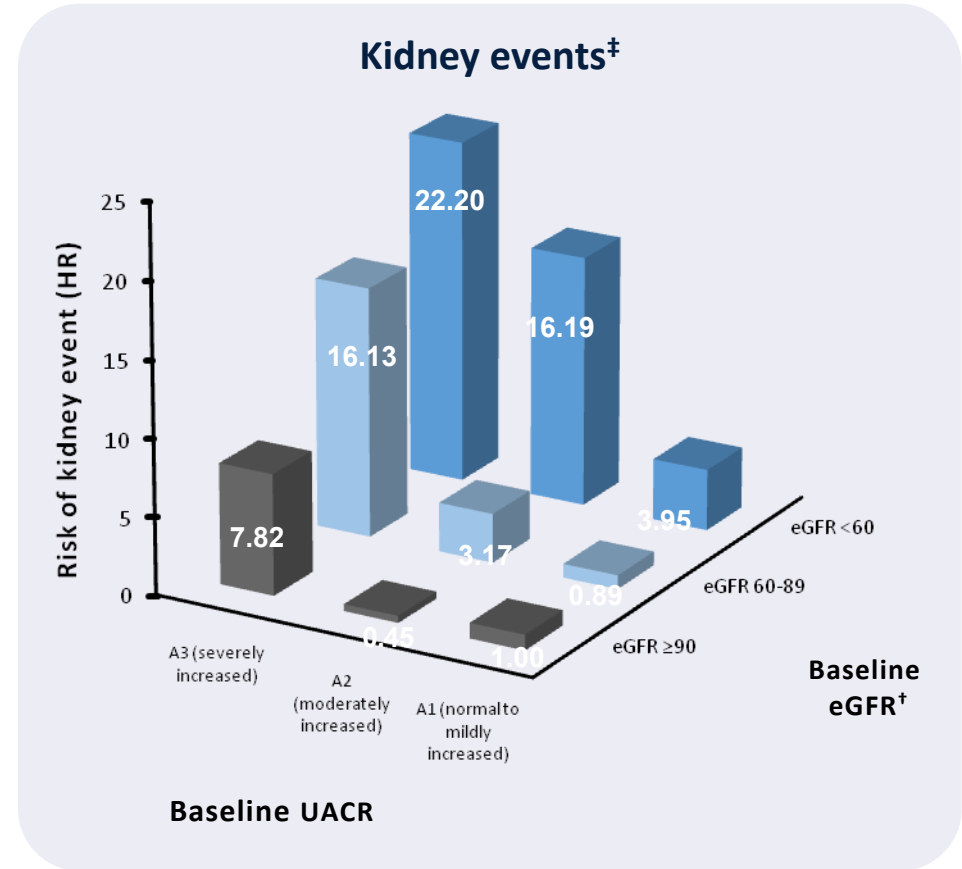
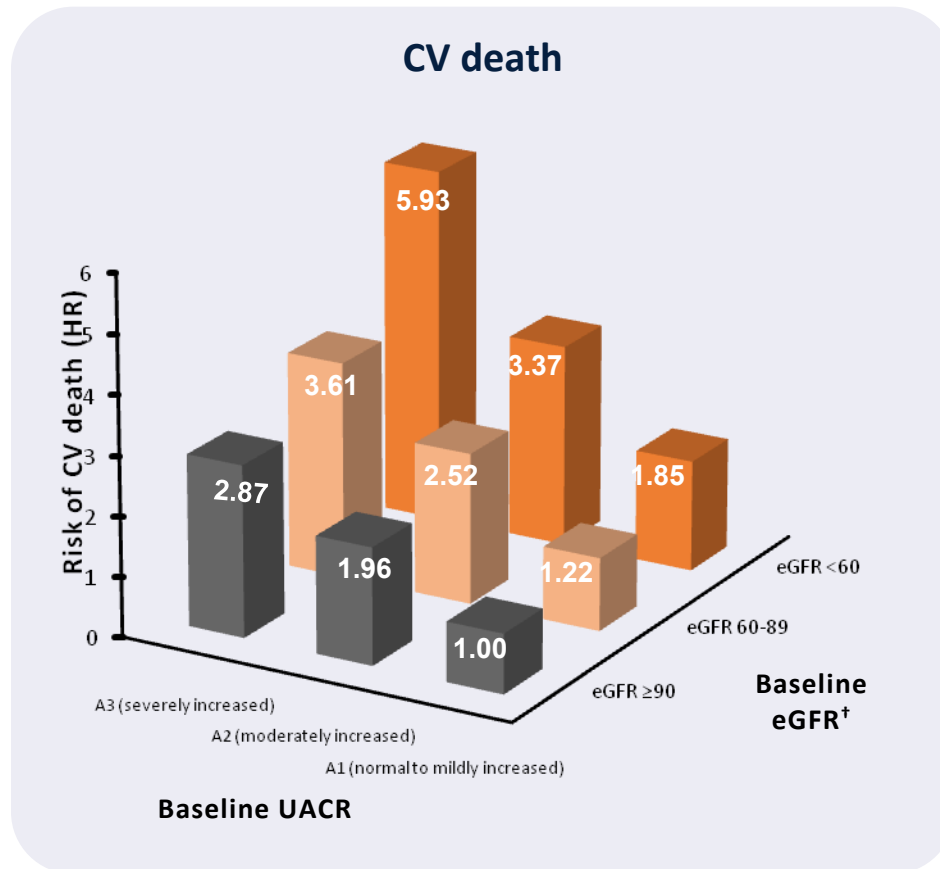


Οι παθήσεις των Καρδιο-Νεφρο-Μεταβολικών συστημάτων είναι μεταξύ των κυριότερων αιτιών πρόωρου θανάτου



1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet* 2018;392:1789;
2. GBD 2015 Mortality and Causes of Death Collaborators. *Lancet* 2016;388:1459;
3. The Emerging Risk Factors Collaboration. *JAMA* 2015;314:52; 4. Wen C *et al.* *Kidney Int* 2017;92:388

Reduced eGFR and increased albuminuria are independently associated with 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 m²; [‡]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

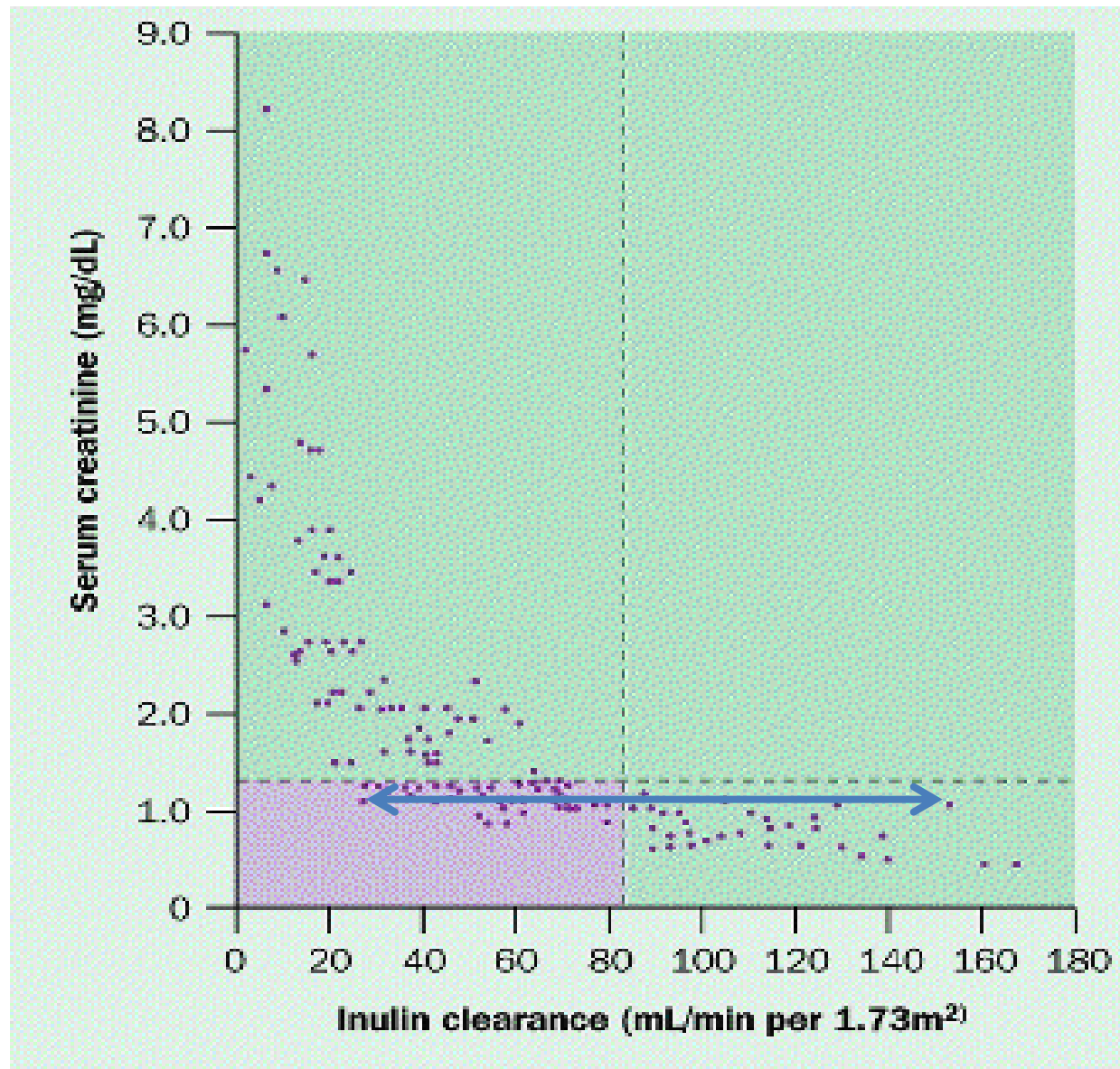
Εκτίμηση Χρόνιας Νεφρικής Νόσου

ΝΕΦΡΟΛΟΓΙΚΗ ΕΚΤΙΜΗΣΗ (1)

- Ρυθμός σπειραματικής διήθησης
Glomerular Filtration Rate



Αξιολόγηση κρεατινίνης ορού



Υπολογισμός σπειραματικής διήθησης (ml/min)

➤ **MDRD**

➤ **CKD-EPI**



Εκτίμηση Χρόνιας Νεφρικής Νόσου

Early-stage kidney disease is usually asymptomatic, requiring laboratory tests for detection³



UACR urine test^{1,2,4}

Tests for albumin in the urine, which is one of the earliest indicators of **kidney damage**



eGFR blood test^{1,2}

Measures the amount of **kidney function** remaining

1. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. *Kidney Int Suppl* 2022;102:S1; 2. Polkinghorne KR *et al. Clin Biochem Rev* 2014;35:67;
3. Shang N *et al. NPJ Digit Med* 2021;4:70; 4. Liu R *et al. J Clin Lab Anal* 2011;25:324



CKD-EPI Equations for Glomerular Filtration Rate (GFR) ☆

Estimates GFR based on serum creatinine, serum cystatin C, or both.

IMPORTANT

The 2021 CKD-EPI equation is now the recommended standard. This version does not include race, as do the 2009 and 2012 CKD-EPI creatinine and creatinine-cystatin C equations. [See here \(https://www.mdcalc.com/race\)](https://www.mdcalc.com/race) for more on our approach to addressing race and bias on MDCalc.

With the 2021 equation, for the same creatinine value, the 2021 equation will estimate a lower GFR for Black patients and a higher GFR for non-Black patients.

INSTRUCTIONS

For use in patients with stable kidney function. While the combined creatinine and cystatin C equation can add accuracy, cystatin C is not available in all laboratories and the creatinine-based equation is adequate for many clinical purposes.

2021 CKD-EPI creatinine is currently recommended by the ASN and NKF for GFR reporting in the United States.

When to Use ▾

Pearls/Pitfalls ▾

Why Use ▾

Equation

2021 CKD-EPI Creatinine

2021 CKD-EPI Creatinine-Cystatin C

2009 CKD-EPI Creatinine

2012 CKD-EPI Cystatin C

2012 CKD-EPI Creatinine-Cystatin C

Sex

Female

Male

Age

48

years

Serum creatinine

1.3

mg/dL 49

51 ml/min/1.73 m²

Estimated GFR by 2021 CKD-EPI Creatinine

ΝΕΦΡΟΛΟΓΙΚΗ ΕΚΤΙΜΗΣΗ (2)

- Απώλεια αλβουμίνης* και λευκωμάτων στα ούρα





Στοιχεία Παραπεμπτικού

Τύπος ΤΥΠΙΚΟ
Παραπεμπτικού

Κατηγορία Εξετάσεων Εξετάσεις Βιολογικών Υλικών 1 (Βιοπαθολογίας) (Α)

* Αιτιολογία ΕΛΕΓΧΟΣ

Παραπεμπτικού

Σημειώσεις

Περιπτώσεις Μηδενικής Συμμετοχής

Προσθήκη Διάγνωσης ICD-10

Κωδικός ICD-10	Διάγνωση
Z10.8	Γενικός προσυμπτωματικός έλεγχος ρουτίνας άλλων καθορισμένων υποπληθυσμών

Εξετάσεις

Ιατρικές Εξετάσεις

Αγαπημένες Εξετάσεις

Καθαρισ

Εξέταση

Διάγνωση

ΜΙΚΡΟΛΕΥΚΩΜΑΤΙΝΗ ΟΥΡΩΝ

Z10.8

Κρεατινίνη ούρων (CREAT)

Z10.8



ΒΙΟΧΗΜΙΚΕΣ

77

ΜΙΚΡΟΛΕΥΚΩΜΑΤΙΝΗ ΟΥΡΩΝ

5



ΒΙΟΧΗΜΙΚΕΣ

88

Καμπύλη καλοσακχάρου

4.75



ΒΙΟΧΗΜΙΚΕΣ

92

Ολική Χολερυθρίνη (TBIL)

2.88



ΒΙΟΧΗΜΙΚΕΣ

94

Κρεατινίνη αίματος (CREAT)

4.05



ΒΙΟΧΗΜΙΚΕΣ

95

Κρεατινίνη ούρων (CREAT)

4.05



ΗΛΕΚΤΡΟΦΟΡΗΣΕΙΣ

97

Ηλεκτροφόρηση λευκωμάτων ορού - Ηλεκτροφόρηση ορού επί οξικής κυτ...

10.8



ΜΙΚΡΟΒΙΟΛΟΓΙΚΕΣ

105

Καλλιέργεια ούρων

5.00

Albuminuria are used to assess kidney function and damage

Albuminuria^{6,7}

Albuminuria is the increased urinary albumin excretion and is commonly used as an indirect measure of kidney damage and marker of risk for kidney disease progression

Assessment:

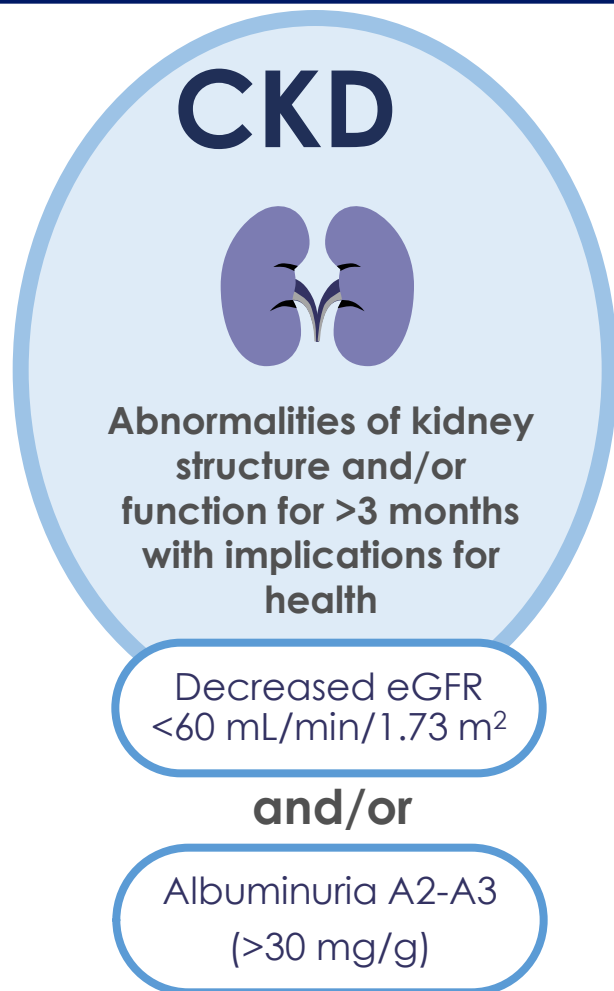
- In a spot urine measured by dipstick method or by laboratory assessment of the ratio of urinary albumin and creatinine (UACR). UACR is used to correct for variation in urinary albumin concentrations related to hydration and is widely used in clinical trials
- In urine collected over a 24-hour period as the albumin excretion rate (AER; mg/24 hours); AER is considered to be the gold standard method for assessing albuminuria

Category	AER (mg/day)	ACR (approximate equivalent)		Terms
		mg/mmol	mg/g	
A1	<30	<3	<30	Normal
A2	30–300	3–30	30–300	Microalbuminuria [†]
A3	>300	>30	>300	Macroalbuminuria [‡]

[†]Moderately increased; [‡]Severely increased; AER, albumin excretion rate; CKD, chronic kidney disease; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate, GI, gastrointestinal; MDRD, Modification of Diet in Renal Disease; UACR, urinary albumin-to-creatinine ratio

1. National Kidney Foundation. Frequently asked questions about GFR estimates. 2014. Available at: http://www.kidney.org/sites/default/files/12-10-4004_FAQ-ABE.pdf. Accessed June 2020; 2. National Kidney Foundation. Kidney Int Suppl 2013;3:1–150; 3. Traynor J et al. BMJ 2006;333:733–737; 4. Gowda S et al. N Am J Med Sci. 2010 Apr; 2(4): 170–173. 5. Mula-Abed WS et al. Oman Med J. 2012 Mar; 27(2):108–113; 6 National Kidney Foundation. Kidney Int Suppl 2013;3:1-150; 7. Johnson DW et al. Med J Aus 2012;197:224–225

Criteria for diagnosis and risk stratification of CKD require both eGFR and UACR



KDIGO: Classification and prognosis of CKD				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased <30 mg/g <3 mg/mmol	Moderately increased 30-300 mg/g 3-30 mg/mmol	Severely increased >300 mg/g >30 mg/mmol
eGFR categories (mL/min/1.73 m ²) Description and range	G1	Normal or high	≥90	Low*	Moderately increased	High
	G2	Mildly decreased	60-89	Low*	Moderately increased	High
	G3a	Mildly to moderately decreased	45-59	Moderately increased	High	Very high
	G3b	Moderately to severely decreased	30-44	High	Very high	Very high
	G4	Severely decreased	15-29	Very high	Very high	Very high
	G5	Kidney failure	<15	Very high	Very high	Very high

Risk of progression

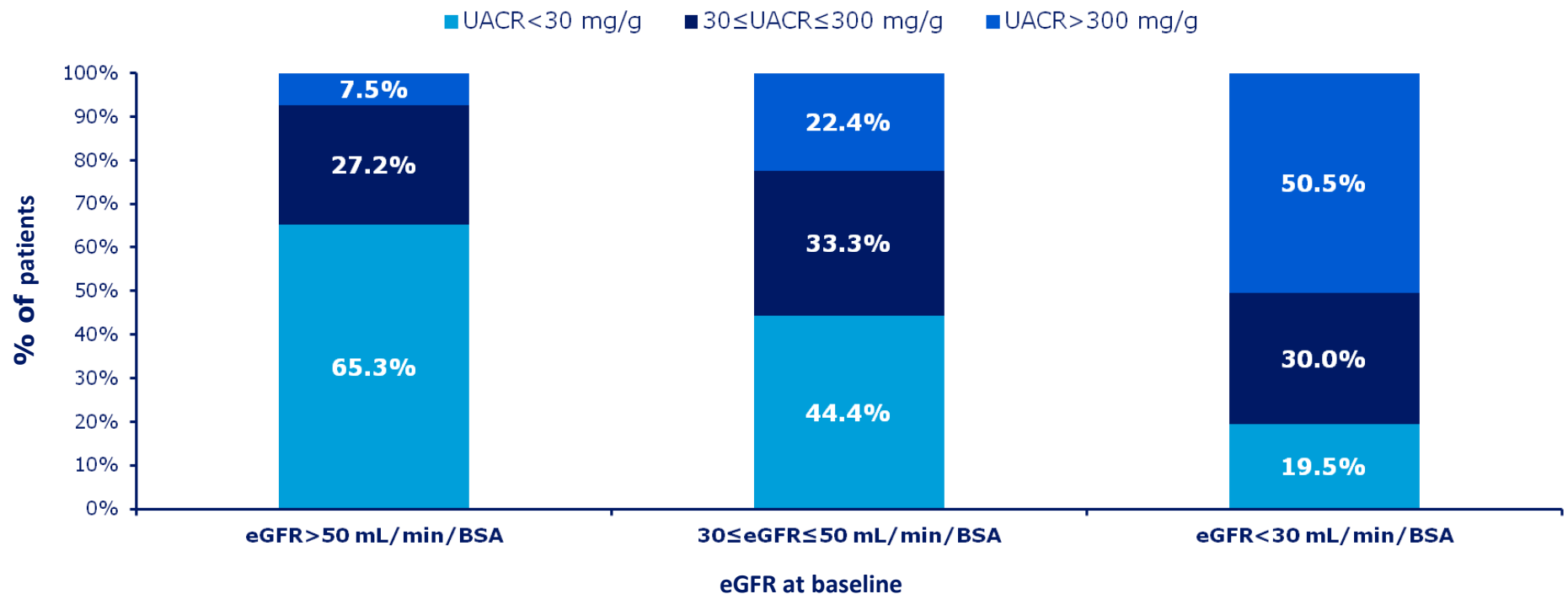
Risk of progression

*If no other markers of kidney disease, no CKD.

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate. KDIGO, Kidney Disease: Improving Global Outcomes. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. *Kidney Int.* 2020;98(suppl):S1-S115.

eGFR and UACR do not always correlate

SAVOR TIMI-53 study (n=16,492)





Τι είναι ΧΝΝ ;

Στάδιο ΧΝΝ	eGFR (mL/min)
Χωρίς ΧΝΝ	≥90*
1	≥90**
2	60–89
3α	45–59
3β	30–44
4	15–29
5	<15 ή ΕΝΥ

Νεφρική βλάβη

Νεφρική νόσος

Χωρίς σημεία νεφρικής βλάβης
** Λευκωματινουρία – νεφρική βλάβη

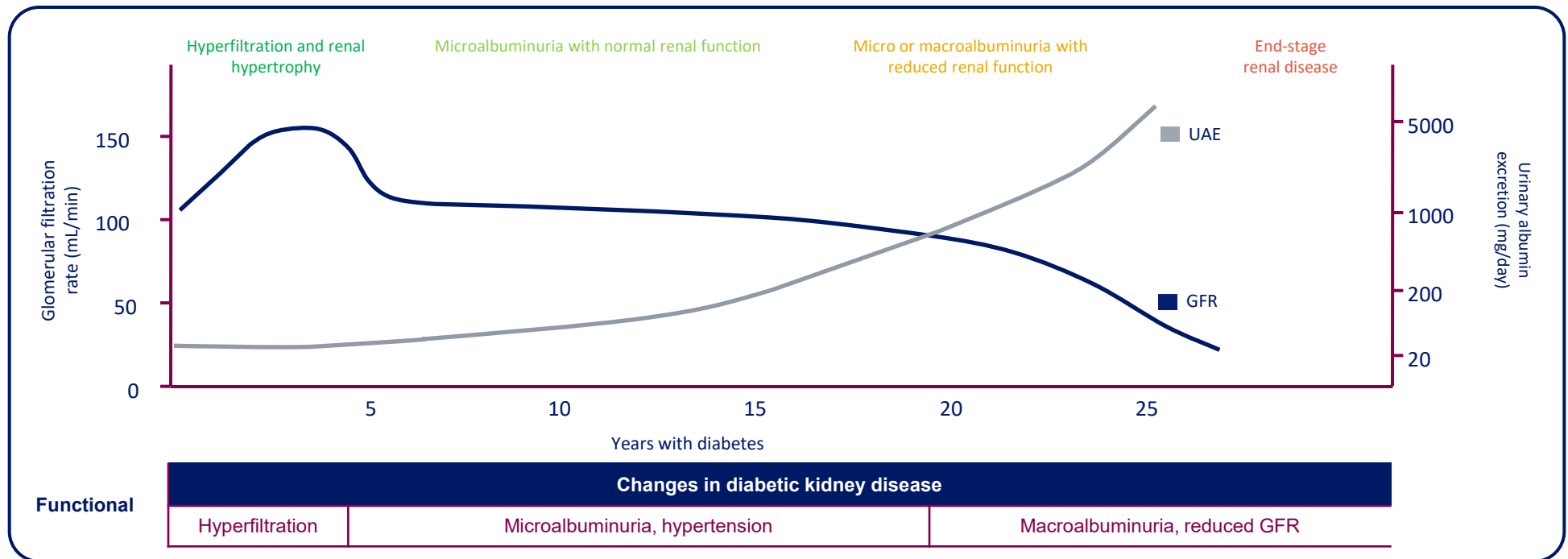
- National Kidney Foundation.
- Am J Kidney Disease 2007.

Δομή ομιλίας

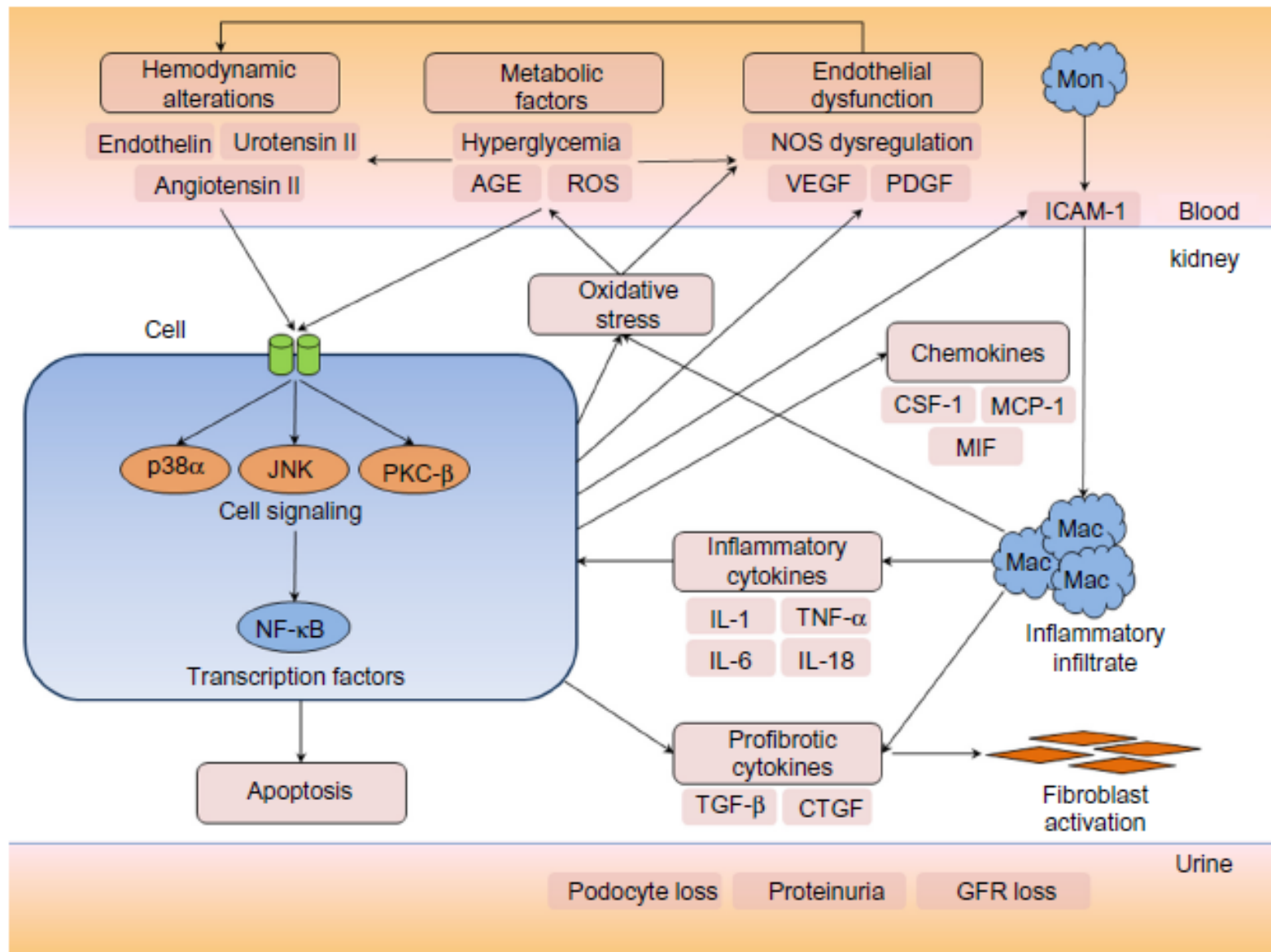
- Επιδημιολογία - Διάγνωση
- Παθοφυσιολογία
- Θεραπευτικές παρεμβάσεις

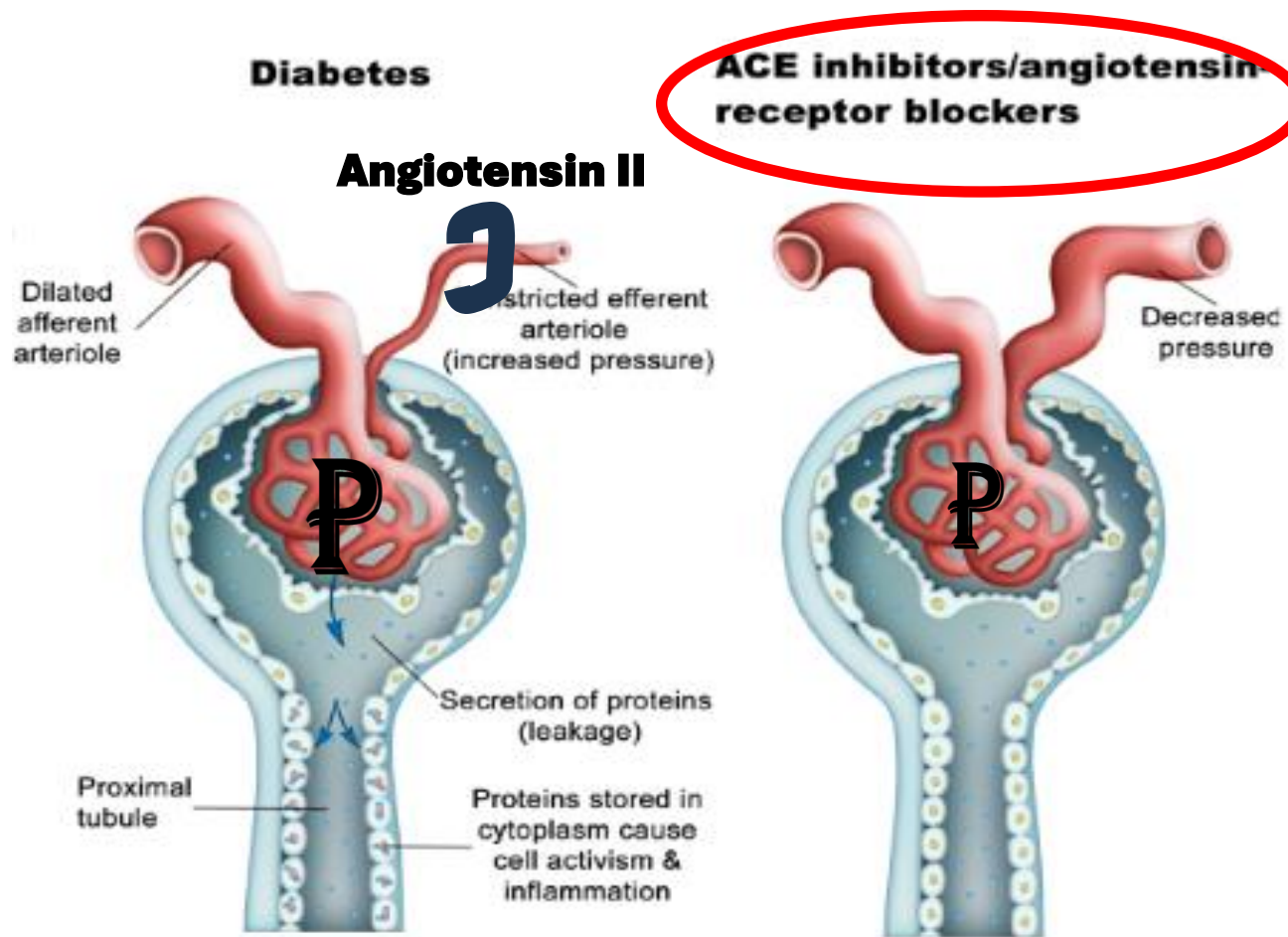
Progression of CKD in diabetes

An initial hyperfiltration is followed by progressive decline in GFR accompanied by microalbuminuria progressing to macroalbuminuria

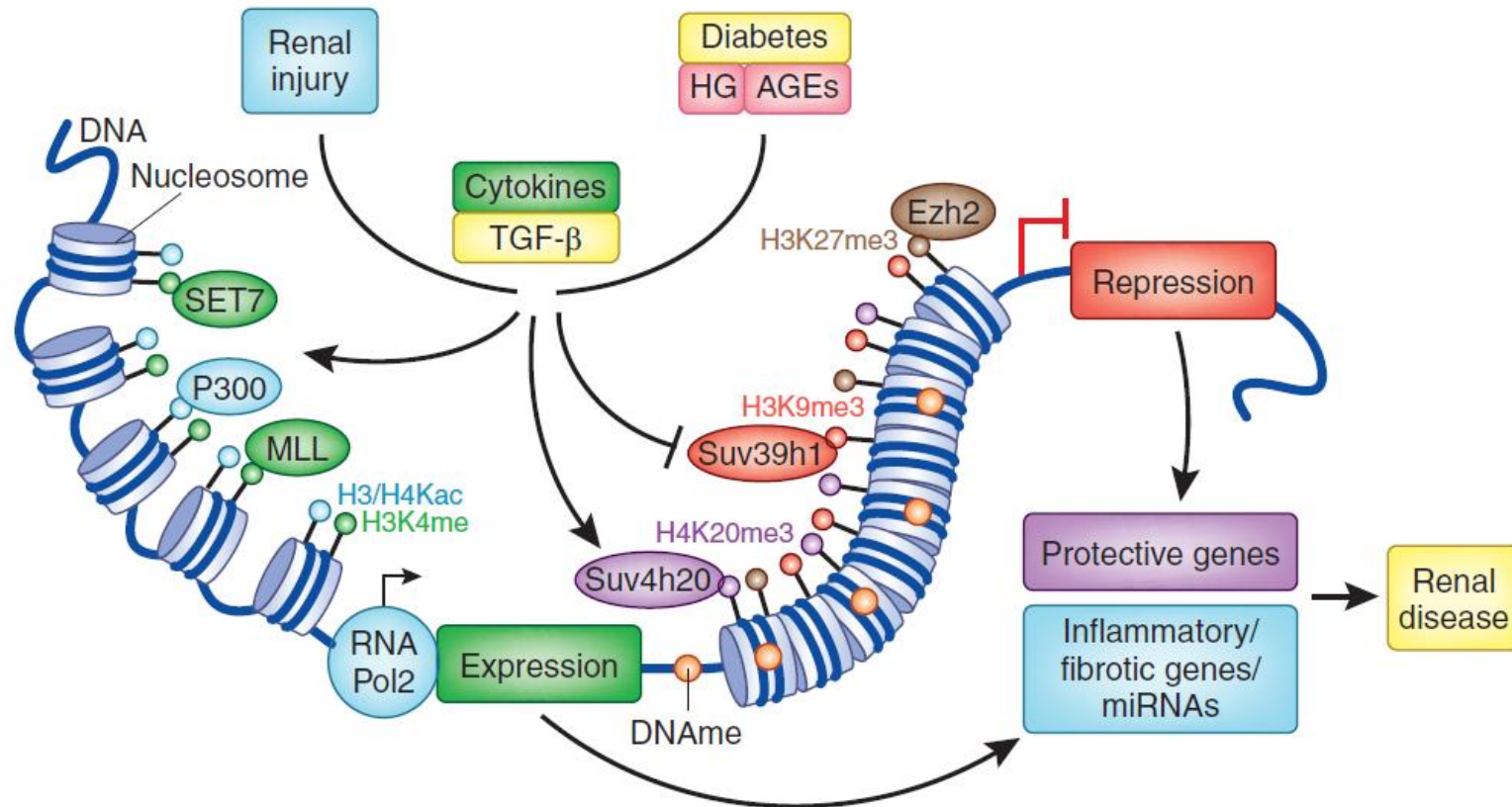


Παθοφυσιολογία





Epigenetics in Diabetic Kidney Disease



ΔΙΑΦΟΡΙΚΗ ΔΙΑΓΝΩΣΗ ΧΝΝ

- Μέγεθος νεφρών
- Ίζημα ούρων - κύλινδροι
- Ρυθμός απώλειας GFR
- Ρυθμός αύξησης λευκωματινουρίας



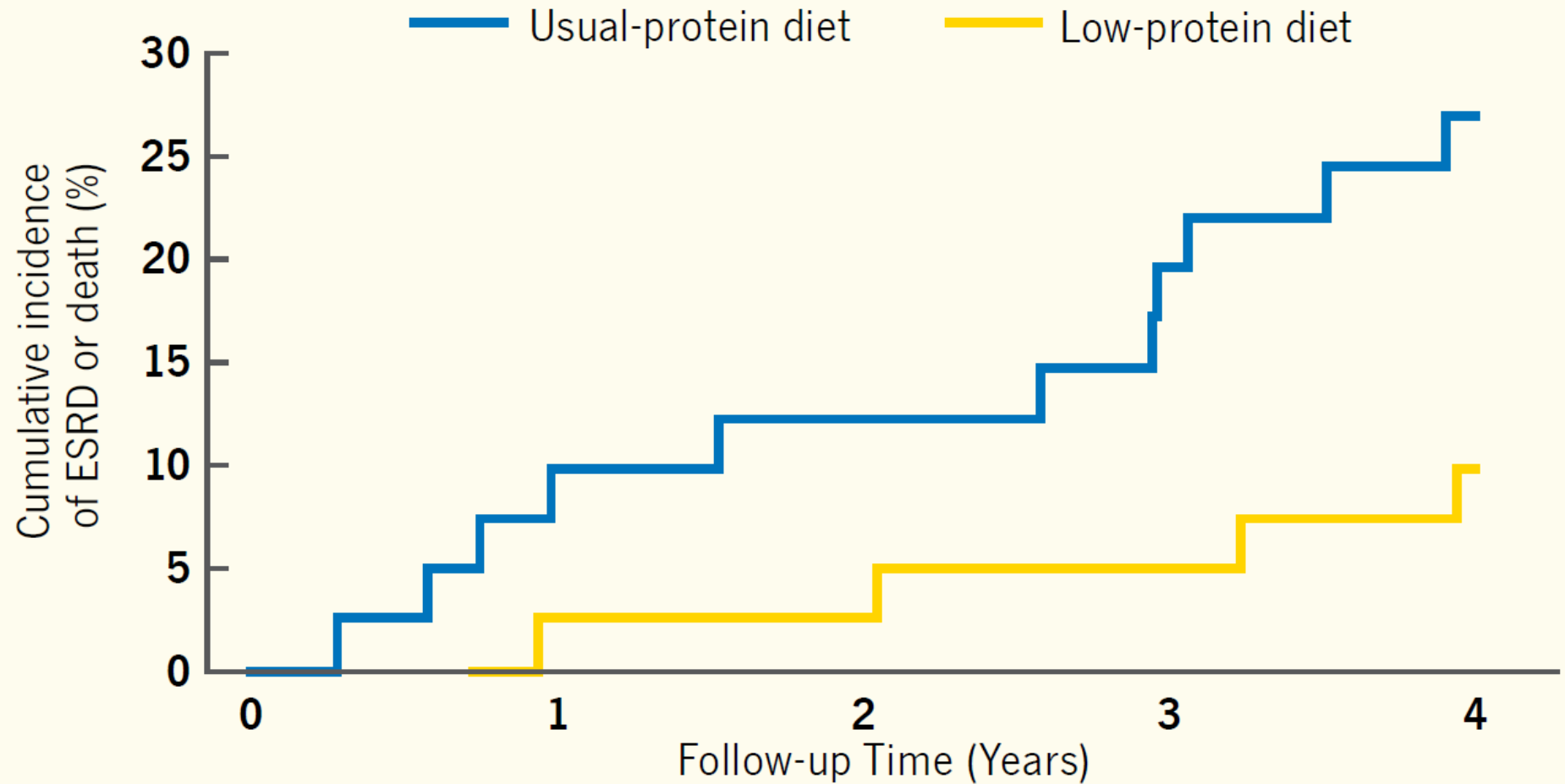
Kidney Biopsy Findings Among Patients With Diabetes in Q1 the Cleveland Clinic Kidney Biopsy Epidemiology Project

- 1,242 patients
- 462 (**37.2%**) had DKD alone
- 780 (**62.8%**) had non-DKD
- Among those with non-DKD, the most common diagnoses were:
 - focal segmental glomerulosclerosis (24%)
 - global glomerulosclerosis otherwise not specified (13%)
 - acute tubular necrosis (9%)
 - IgA nephropathy (8%)
 - antineutrophil cytoplasmic antibody vasculitis (7%)
 - membranous nephropathy (5%)

Δομή ομιλίας

- Επιδημιολογία
- Παθοφυσιολογία
- Θεραπευτικές παρεμβάσεις

Cumulative incidence of ESRD or Death in persons with T1DM, by protein intake



Usual-protein diet	41	40	37	37	36	36	33	31	30
Low-protein diet	41	41	40	40	40	39	39	38	37

Risk Factors for Development of Incipient and Overt Diabetic Nephropathy in T1DM

A 10-year prospective observation study

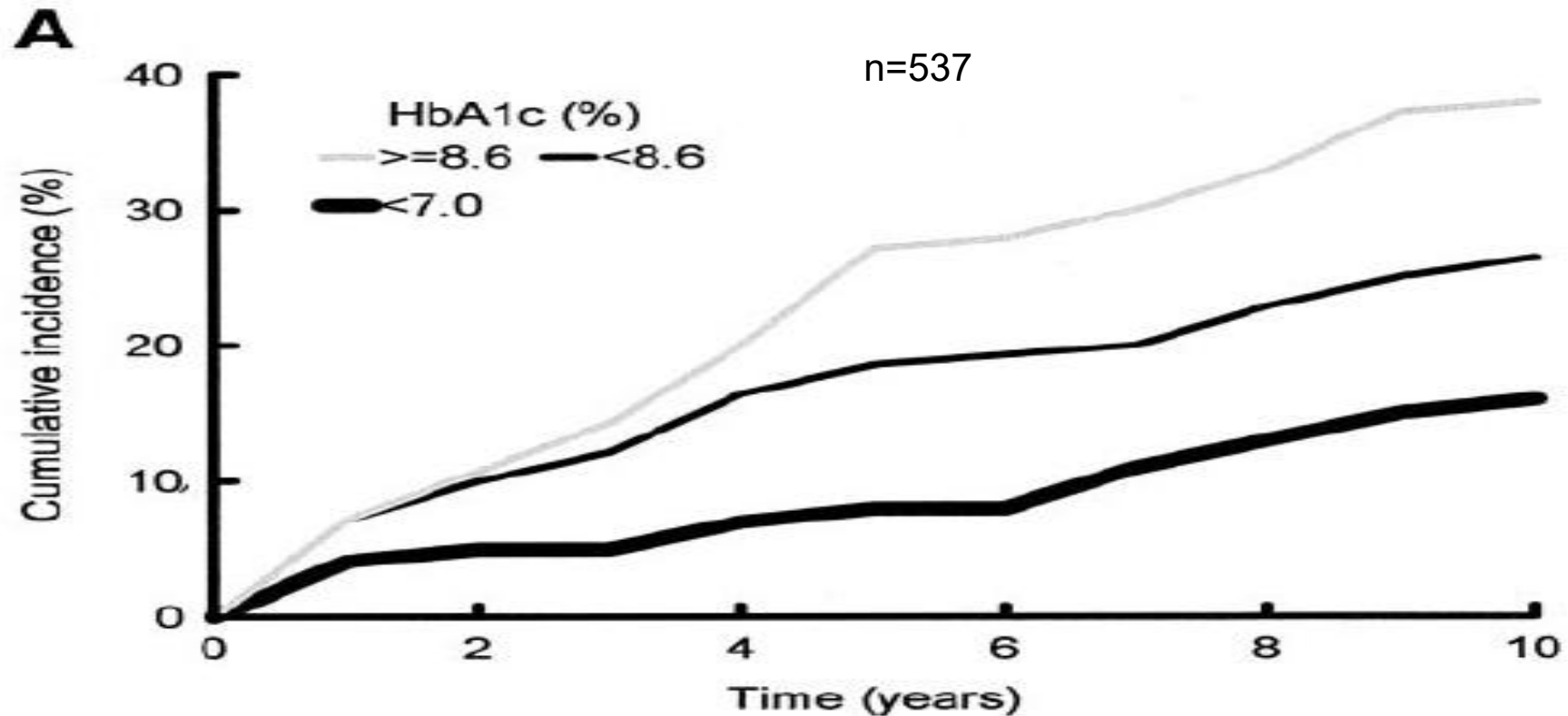
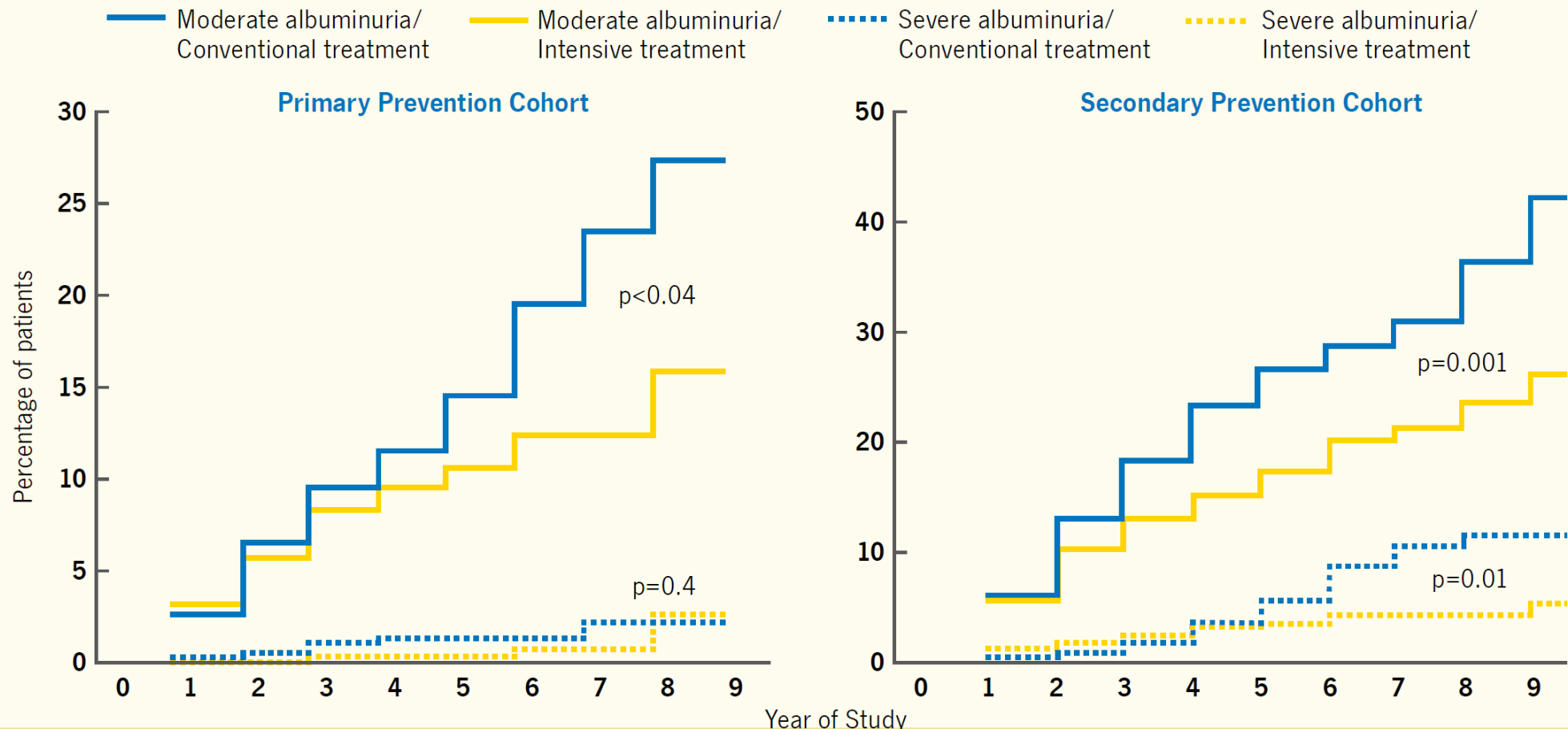


FIGURE 22.49. Cumulative Incidence of Moderately Elevated Albuminuria and Severe Albuminuria in Participants With Type 1 Diabetes, Diabetes Control and Complications Trial



- DCCT: 1441 ασθενείς με ΣΔ τύπου 1 τυχαιοποιημένοι σε εντατική και συμβατική ινσουλινοθεραπεία.
- Η αυστηρή ρύθμιση του σακχάρου βελτιώνει τη μικρολευκωματινουργία (κατά 39%) και την λευκωματινουργία (κατά 54%).

The Diabetes Control and Complications Trial Research Group. N Engl J Med. 1993;329:977-86.

UKPDS: Αποτελέσματα γλυκαιμικού ελέγχου

- Εντατικοποιημένη θεραπεία μείωσε την HbA_{1c} κατά 0.9% εντός 11 ετών, με αποτέλεσμα την μείωση των επιπλοκών (κυρίως των μικροαγγειακών)

Μεταβολές
στον κίνδυνο*

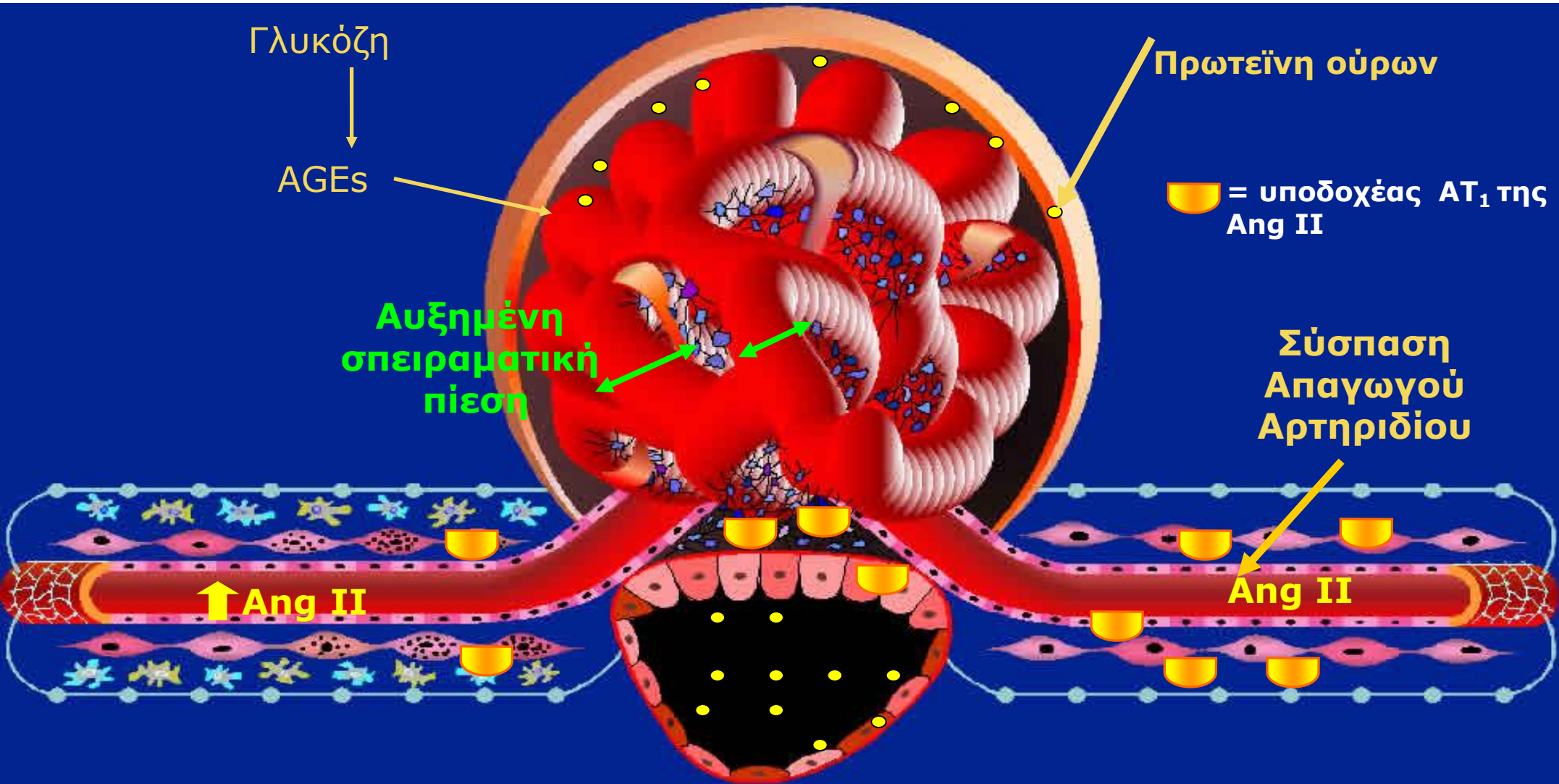
P value

Μικρολευκωματινουρία στα 12 έτη

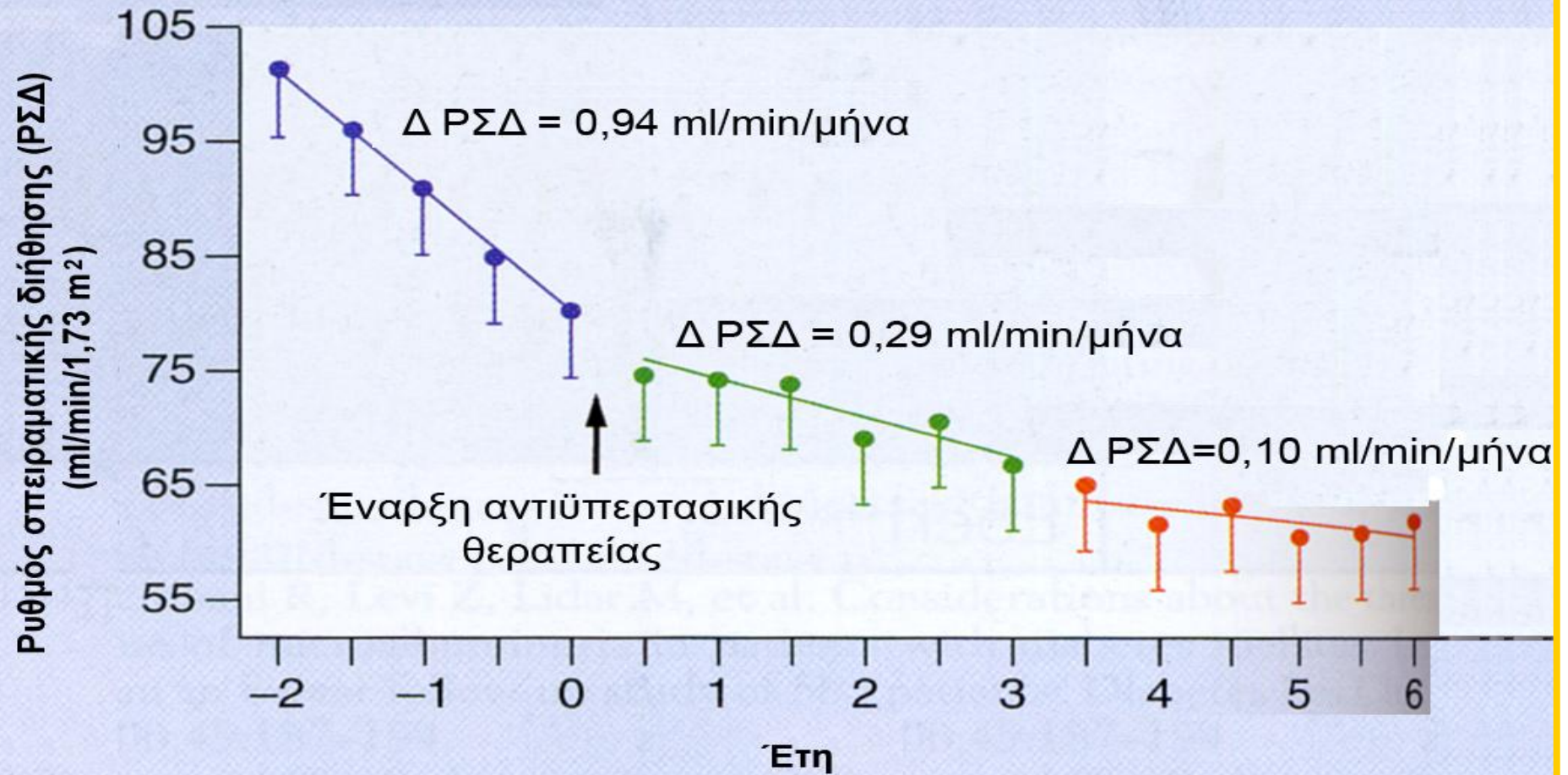
33% ↓

<0.001

Παθογενετικοί μηχανισμοί που οδηγούν σε βλάβη του σπειράματος και πρωτεϊνουρία

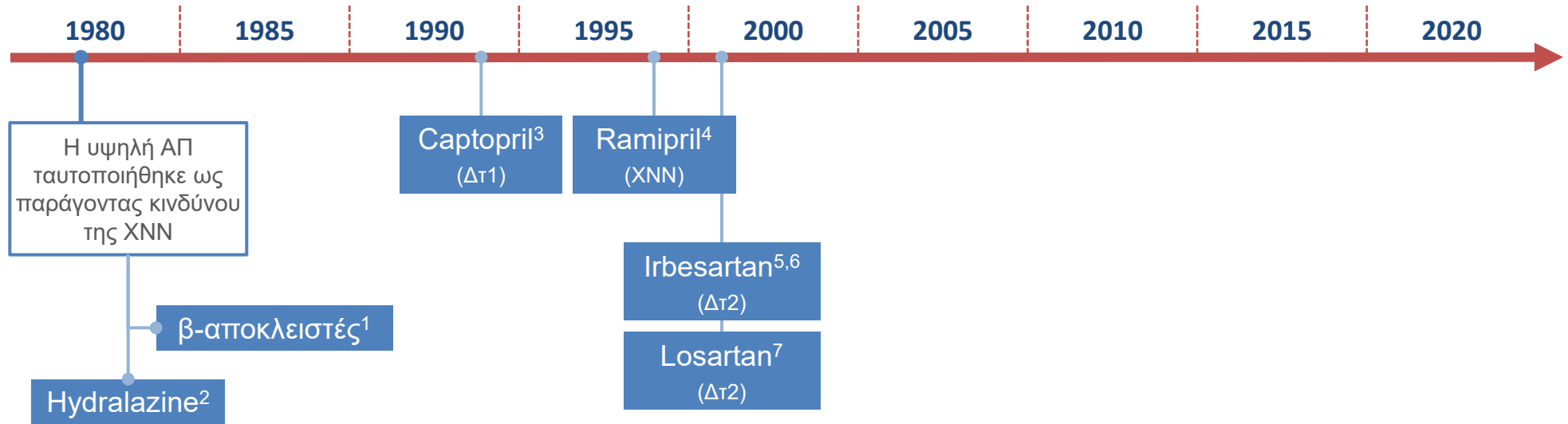


Ο έλεγχος της αρτηριακής πίεσης επιβραδύνει την εξέλιξη της διαβητικής νεφροπάθειας τύπου 1





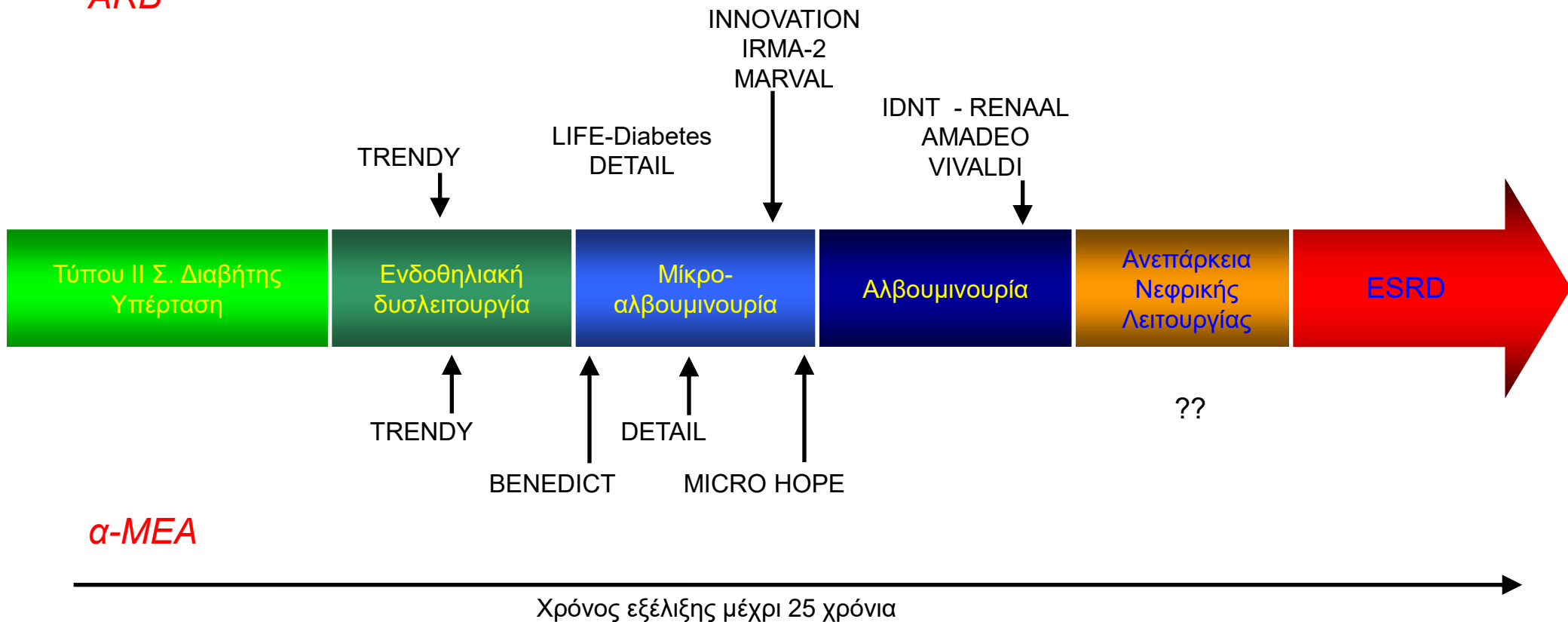
Λίγες ειδικές για τη ΧΝΝ θεραπείες εγκρίθηκαν κατά τη διάρκεια των προηγούμενων δύο δεκαετιών



1. Mogensen CE *et al. Br Med J (Clin Res Ed)* 1982;285:685; 2. Parving H-H *et al. Lancet* 1983;1:1175; 3. Lewis EJ *et al. N Engl J Med* 1993;329:1456; 4. The GISEN Group. *Lancet* 1997;349:1857; 5. Lewis EJ *et al. N Engl J Med* 2001;345:851; 6. Parving H-H *et al. N Engl J Med* 2001;345:870; 7. Brenner BM *et al. N Engl J Med* 2001;345:861

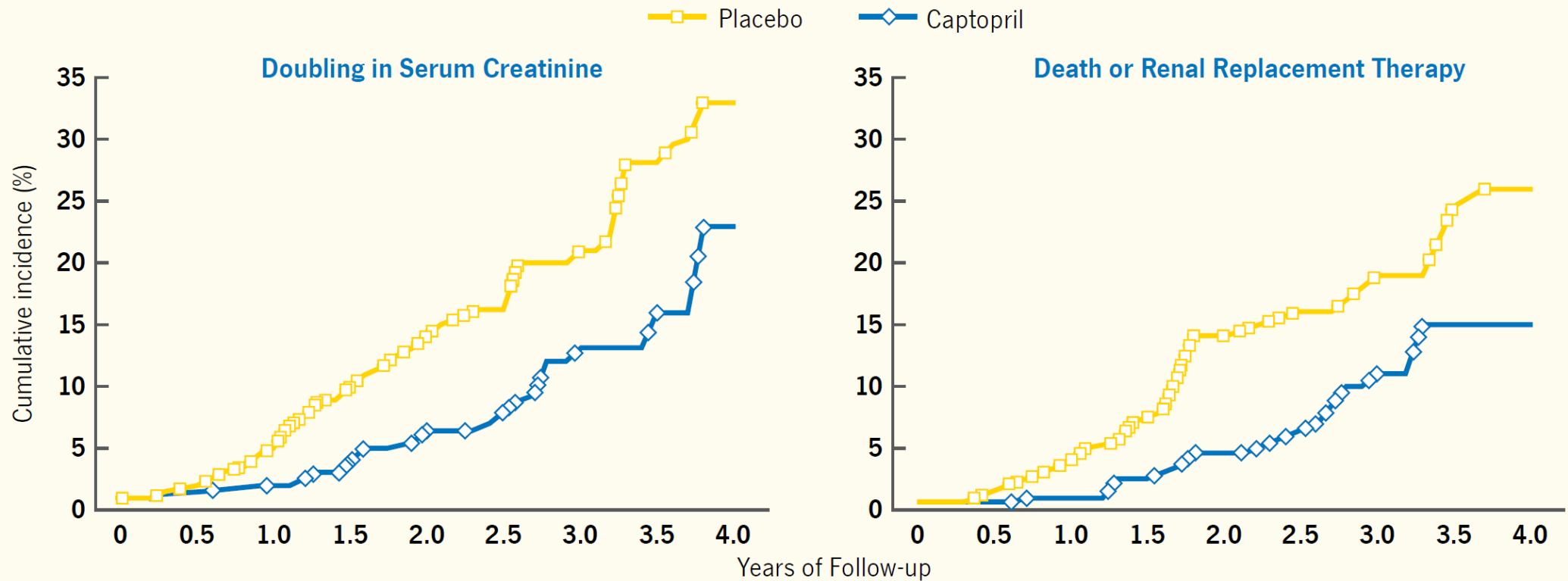
Αναστολή της εξέλιξης της διαβητικής νεφροπάθειας μέσω του αποκλεισμού του RAS

ARB



α -MEA

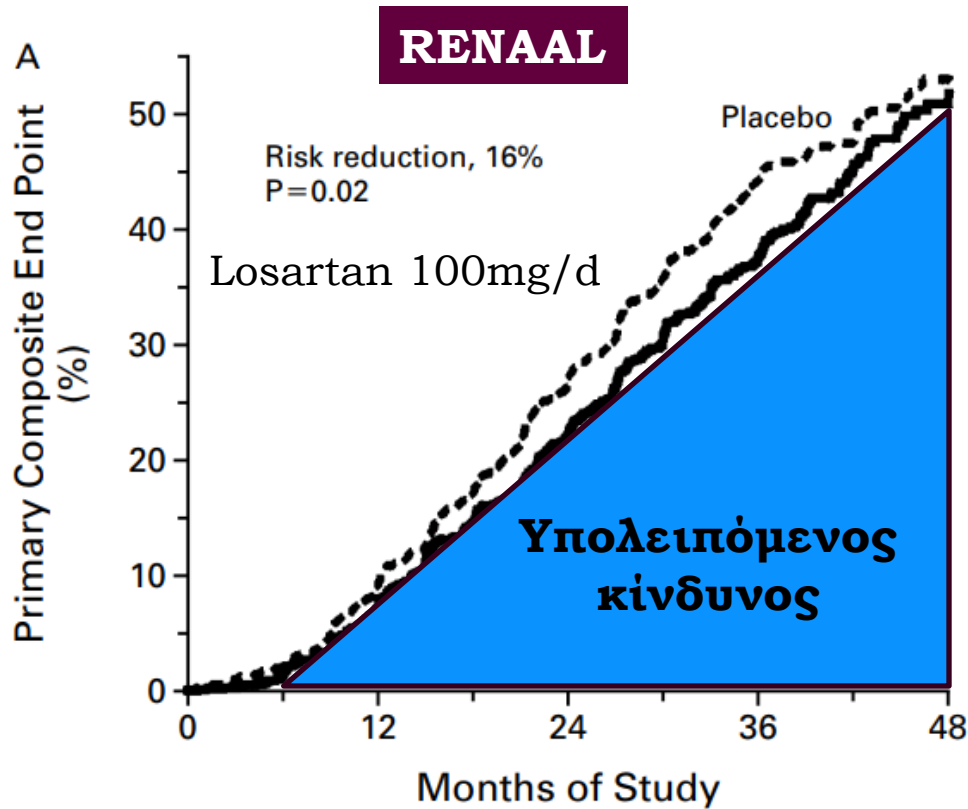
Effects of Captopril on incidence of Kidney disease in persons with T1DM and proteinuria, 1987-1992



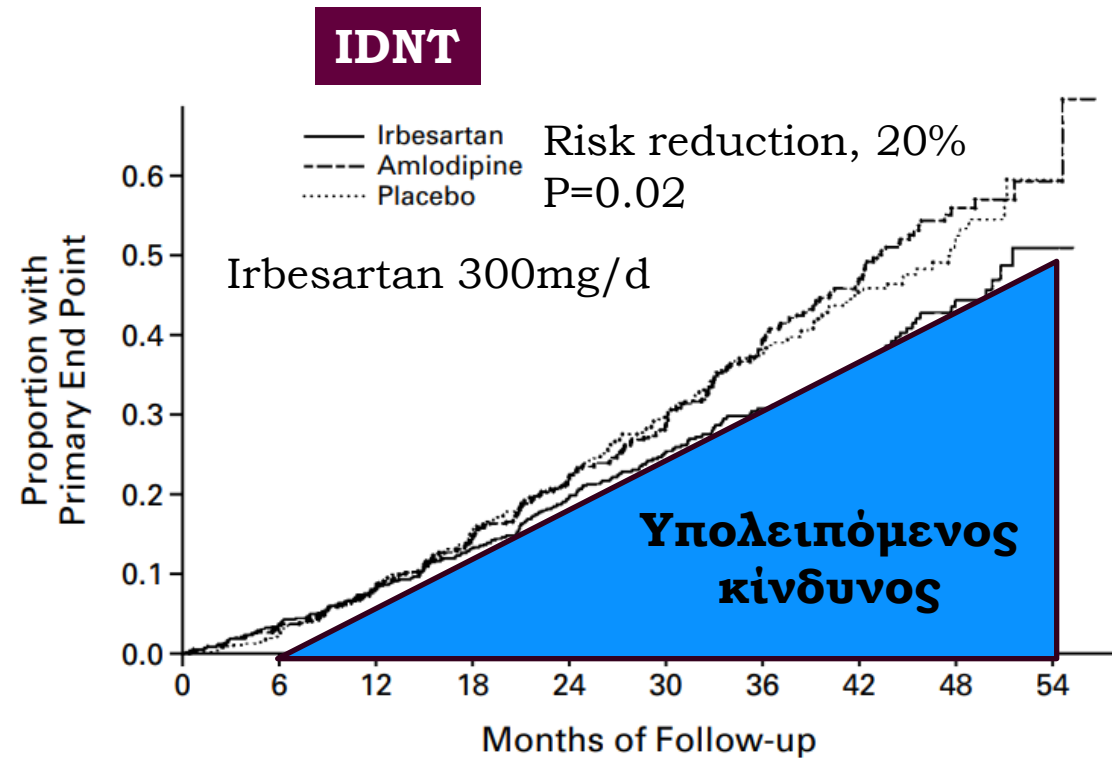


Νεφροπρασσία στα άτομα με ΣΔτ2- RAS BLOCKERS : RENAAL & IDNT

Διπλασιασμός κρεατινίνης, ΤΣΧΝΑ ή Θάνατος



Brenner B., et.al., NEJM 2001



Lewis E.J., NEJM 2001



ESH Guidelines 2023

Prescribing patterns:

- Start with dual combination therapy in most patients
- Uptitrate to maximum well tolerated doses and to triple therapy if needed
- Once daily (preferred in the morning)
- Add further drugs if needed
- Preferred use of SPCs at any step



T/TL **Diuretic^a**

ACEi or ARB

CCB^b

**BP
control**

BB^c

Additional drug classes

General antihypertensive therapy:

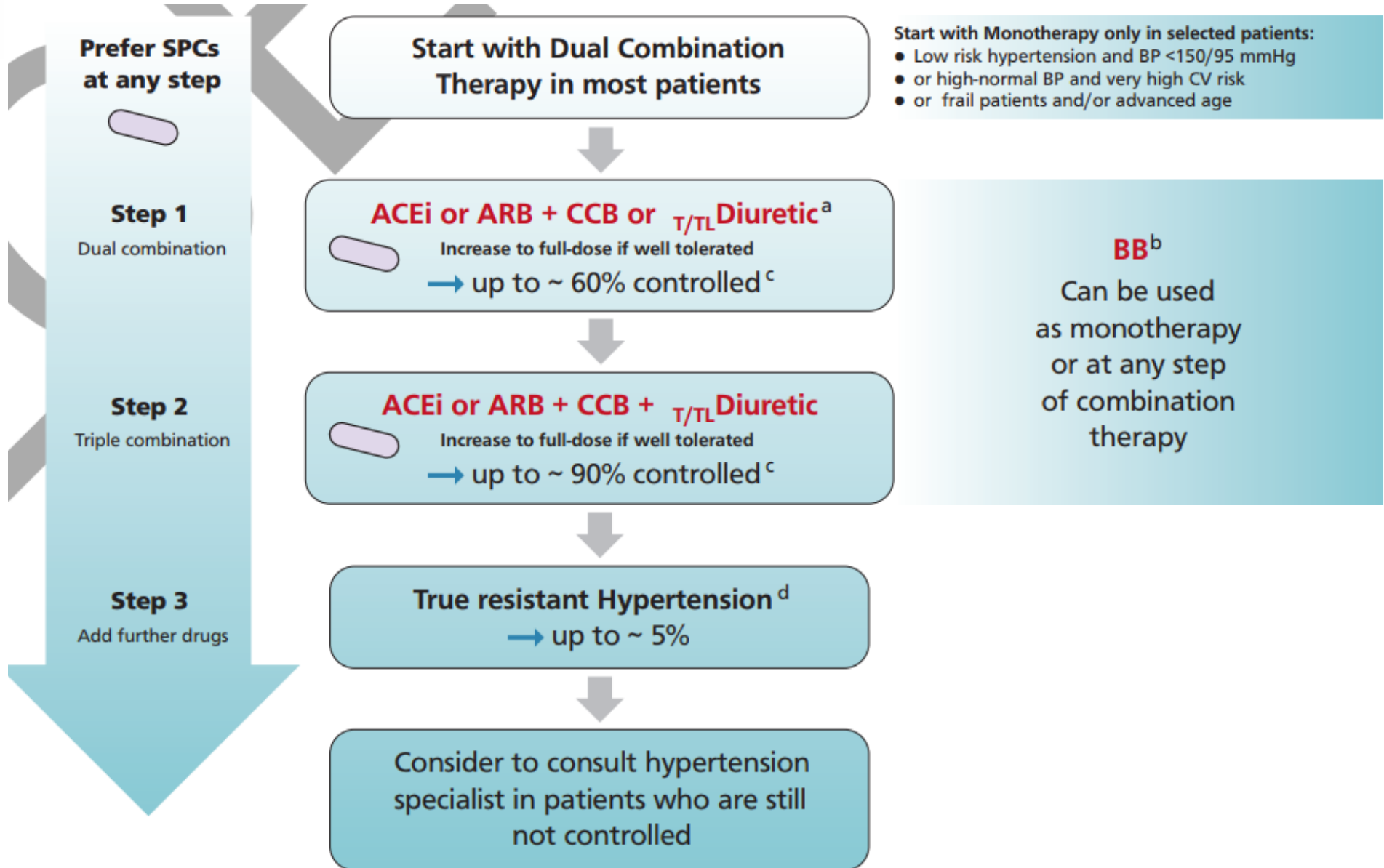
- Steroidal MRA
- Loop Diuretic
- Alpha-1 Blocker
- Centrally acting agent
- Vasodilator

Special comorbidities:

- ARNi
- SGLT2i
- Non-Steroidal MRA

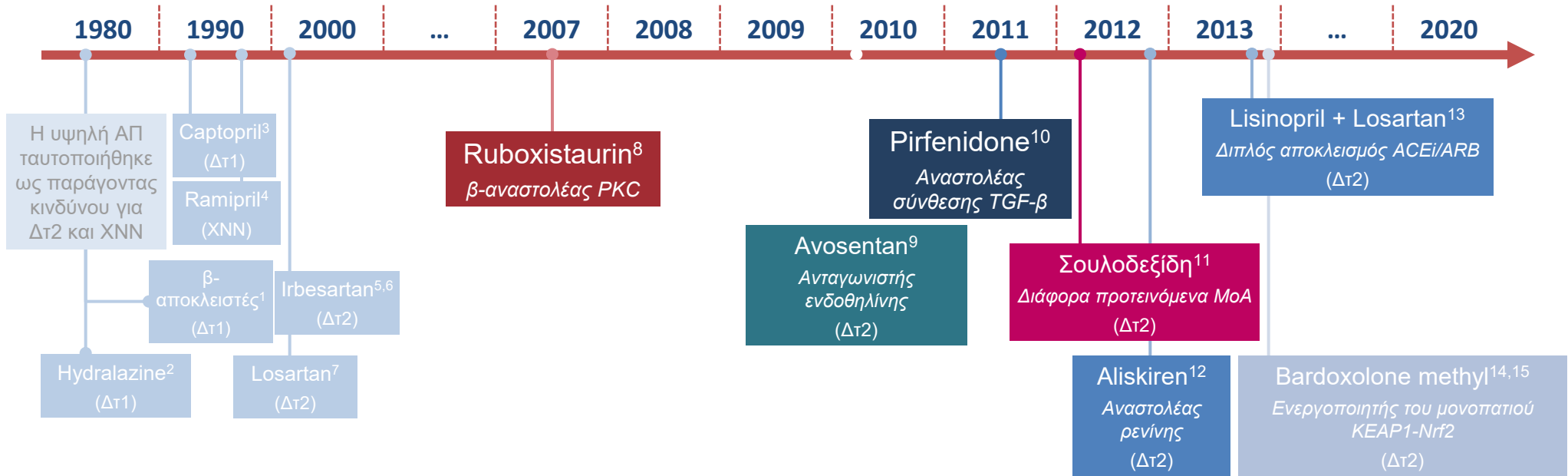


ESH Guidelines 2023





Διάφορες στρατηγικές έχουν διερευνηθεί από τότε σε ασθενείς με Δτ2 και ΧΝΝ ώστε να επιβραδυνθεί η εξέλιξη της ΝΝΤΣ, με μικρή επιτυχία



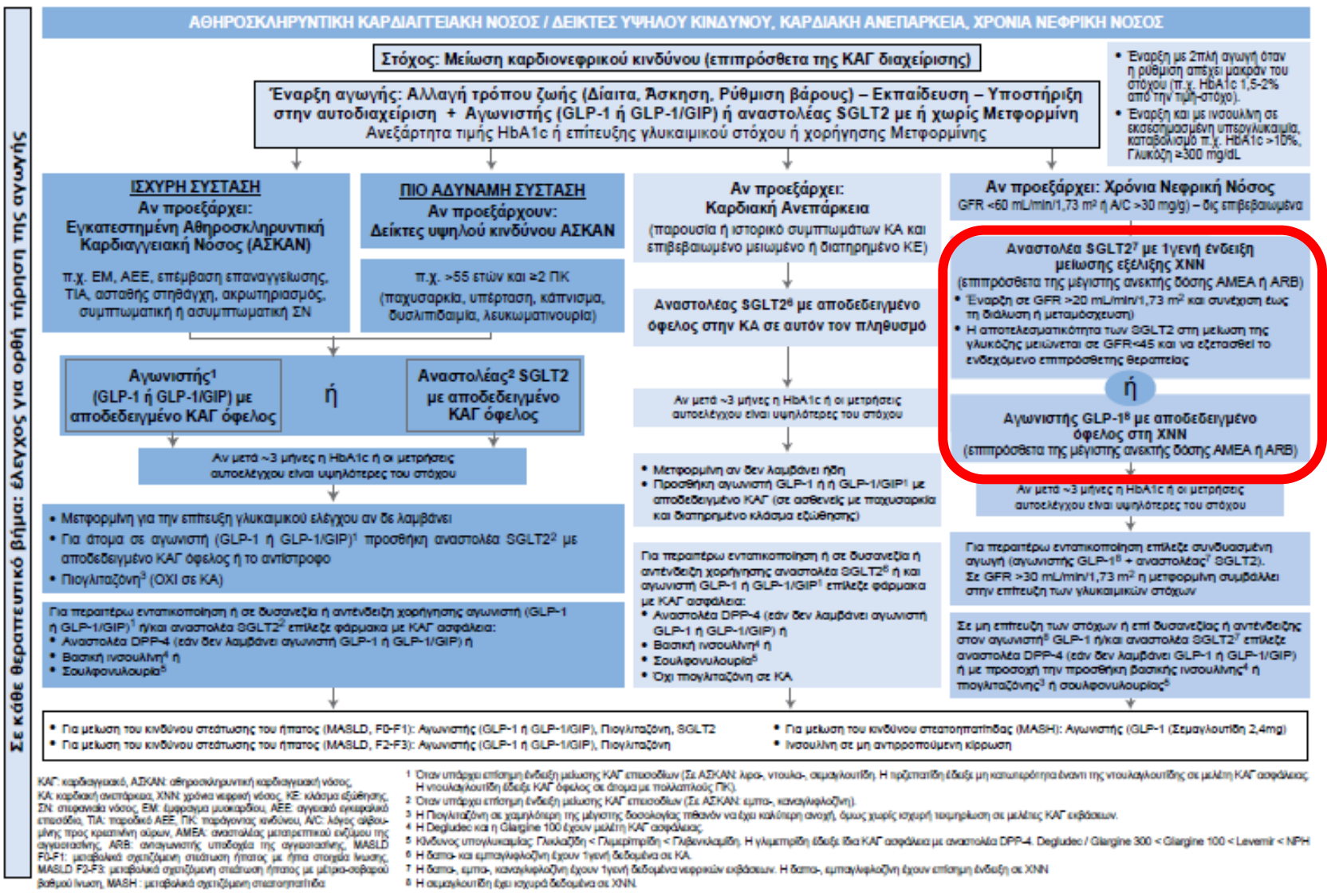
ACEi, αναστολέας του μετατρεπτικού ενζύμου αγγειοτενσίνης. ARB, αποκλειστής του υποδοχέα της αγγειοτενσίνης. ΝΝΤΣ, νεφρική νόσος τελικού σταδίου. KEAP1, Kelch-like ECH-associated protein 1. MoA, Μηχανισμός δράσης. Nrf, πυρηνικός παράγοντας. PKC-β, πρωτεϊνική κινάση C τύπου βήτα. Δτ1, διαβήτης τύπου 1. Δτ2, διαβήτης Τύπου 2. TGF-β, αυξητικός παράγοντας μετασχηματισμού τύπου β

1. Mogensen CE *et al. Br Med J (Clin Res Ed)* 1982;285:685; 2. Parving HH *et al. Lancet* 1983;1:1175; 3. Lewis EJ *et al. N Engl J Med* 1993;329:1456; 4. The GISEN Group. *Lancet* 1997;349:1857; 5. Lewis EJ *et al. N Engl J Med* 2001;345:851; 6. Parving HH *et al. N Engl J Med* 2001;345:870; 7. Brenner BM *et al. N Engl J Med* 2001;345:861; 8. Tuttle KR *et al. Clin J Am Soc Nephrol* 2007;2:631; 9. Mann JFE *et al. J Am Soc Nephrol* 2010;21:527; 10. Sharma K *et al. J Am Soc Nephrol* 2011;22:1144; 11. Packham DK *et al. J Am Soc Nephrol* 2012;23:123; 12. Parving HH *et al. N Engl J Med* 2012;367:2204; 13. Fried LF *et al. N Engl J Med* 2013;369:1892; 14. de Zeeuw D *et al. N Engl J Med* 2013;369:2492; 15. Wang Y *et al. Drug Des Devel Ther* 2014;8:2075

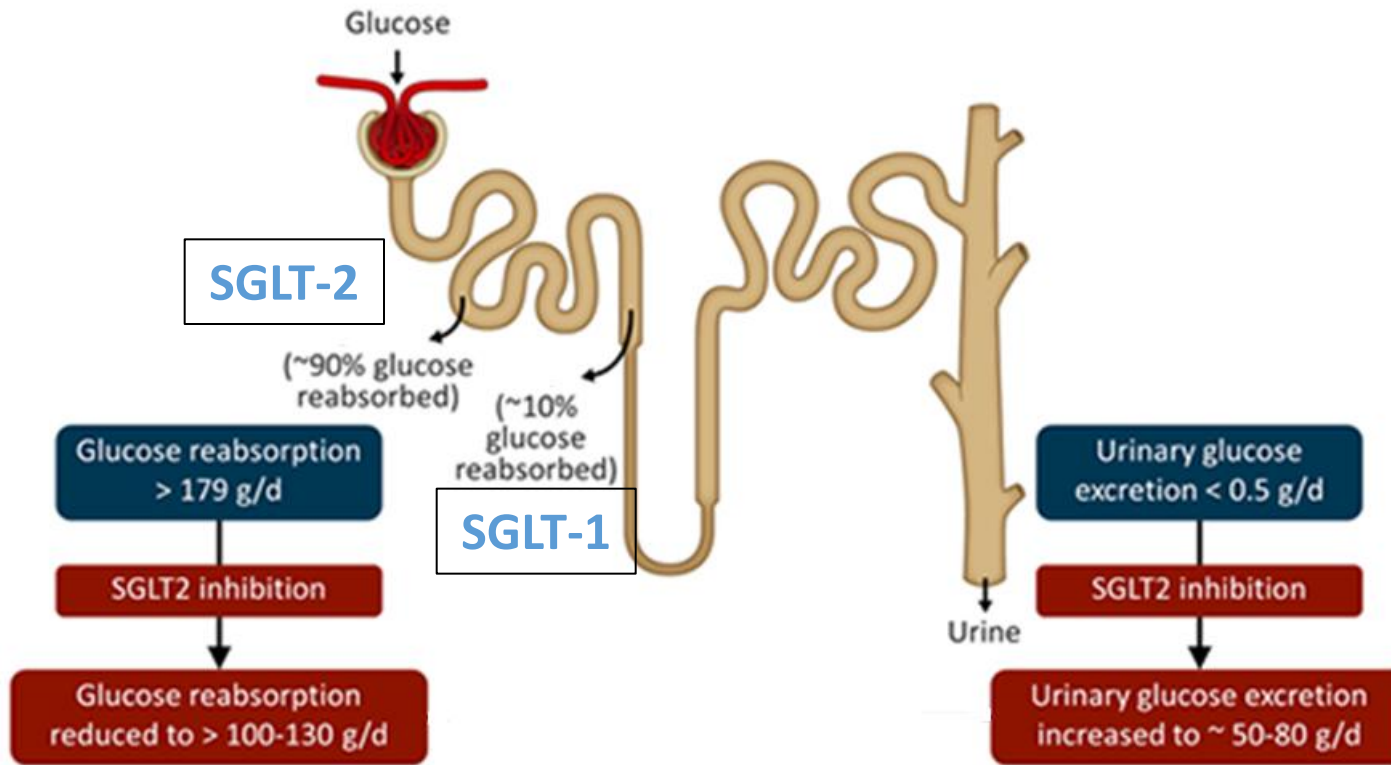


Κατευθυντήριες Οδηγίες για το Σακχαρώδη Διαβήτη 2026

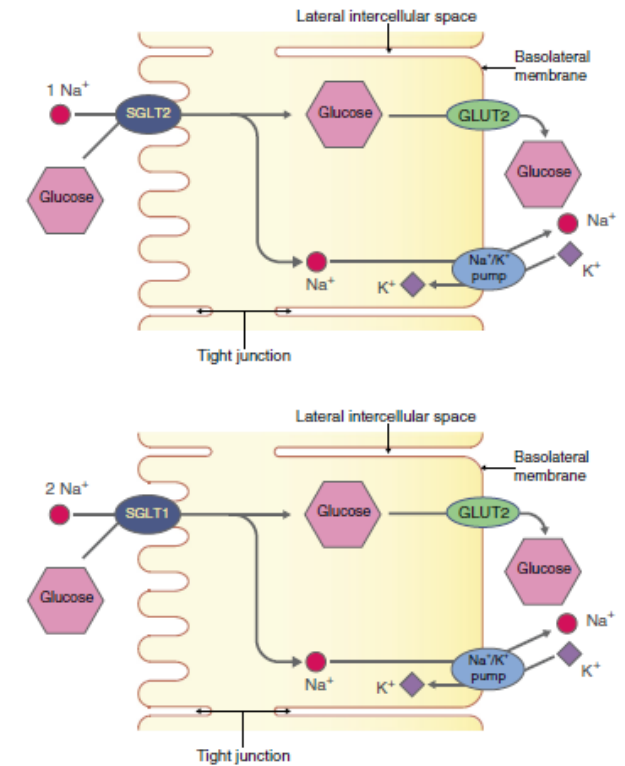
2026, Κατευθυντήριες
οδηγίες για το Σακχαρώδη
Διαβήτη, Ελληνική
Διαβητολογική Εταιρεία



Αναστολείς SGLT

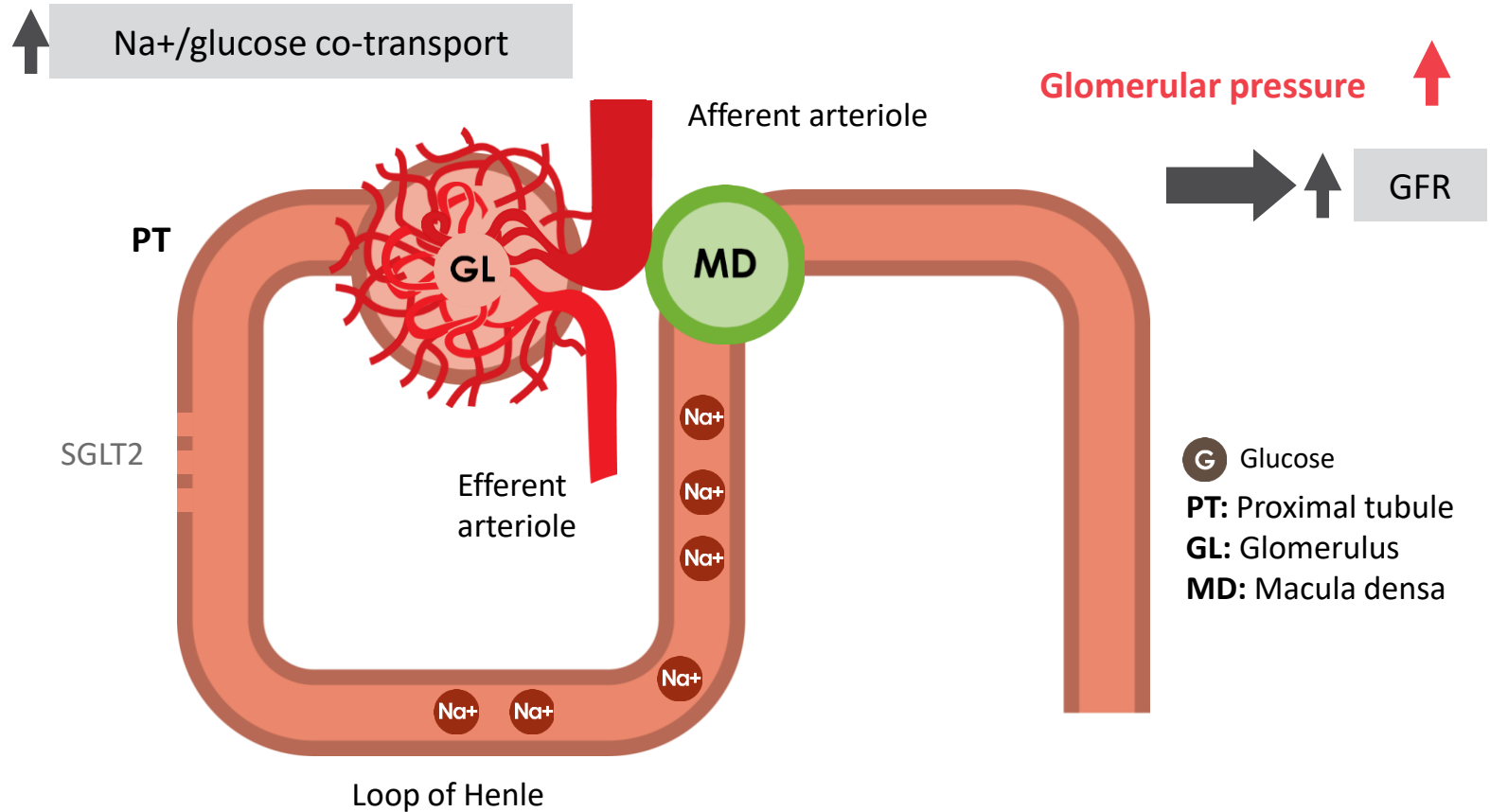


Nauck Drug Design, Development and Therapy. 2014;8:1335



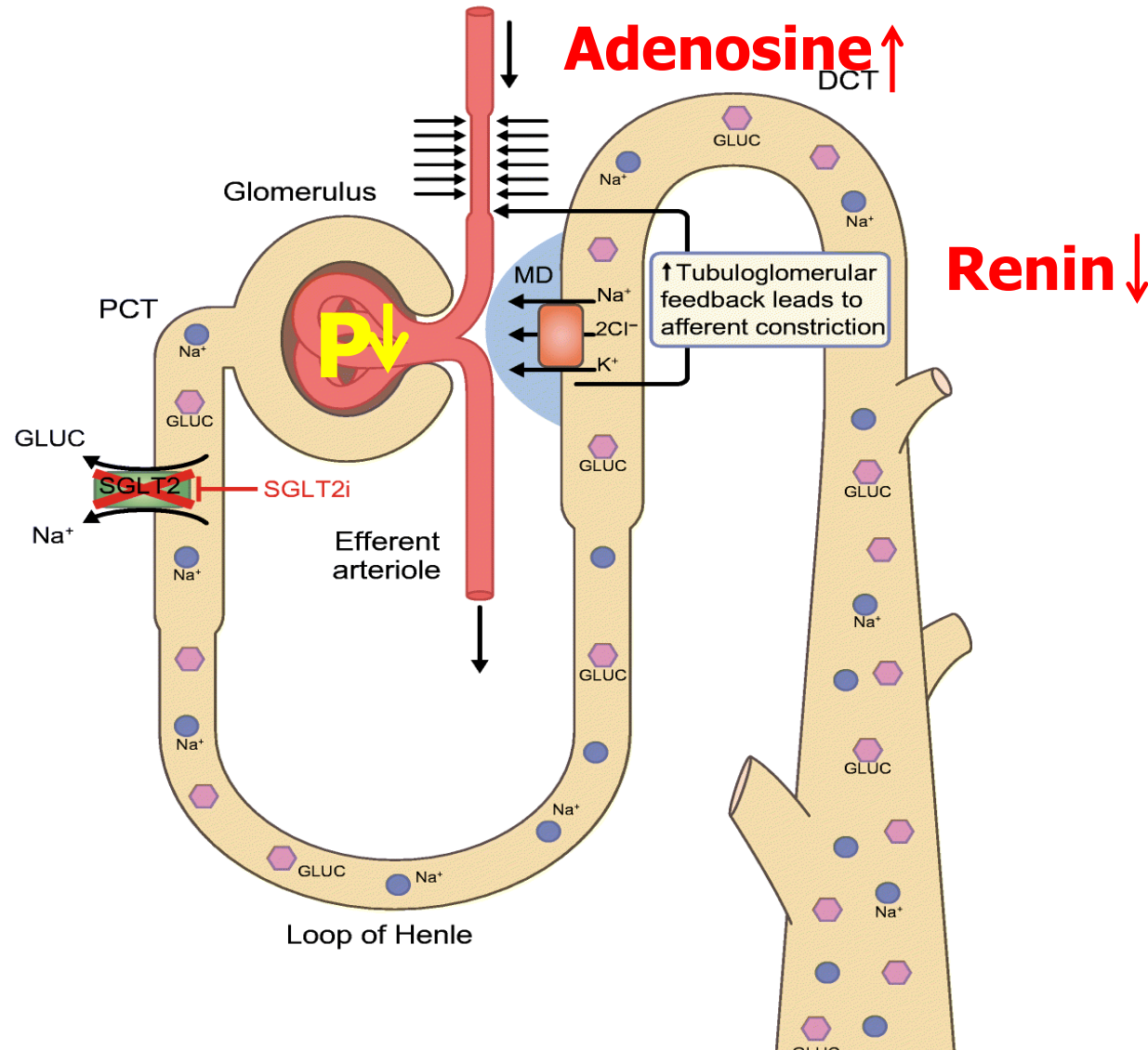
Ghezzi Diabetologia (2018) 61:2087

Diabetes may cause glomerular hypertension



Renal hemodynamics under hyperglycemia

Αναστολείς SGLT-2



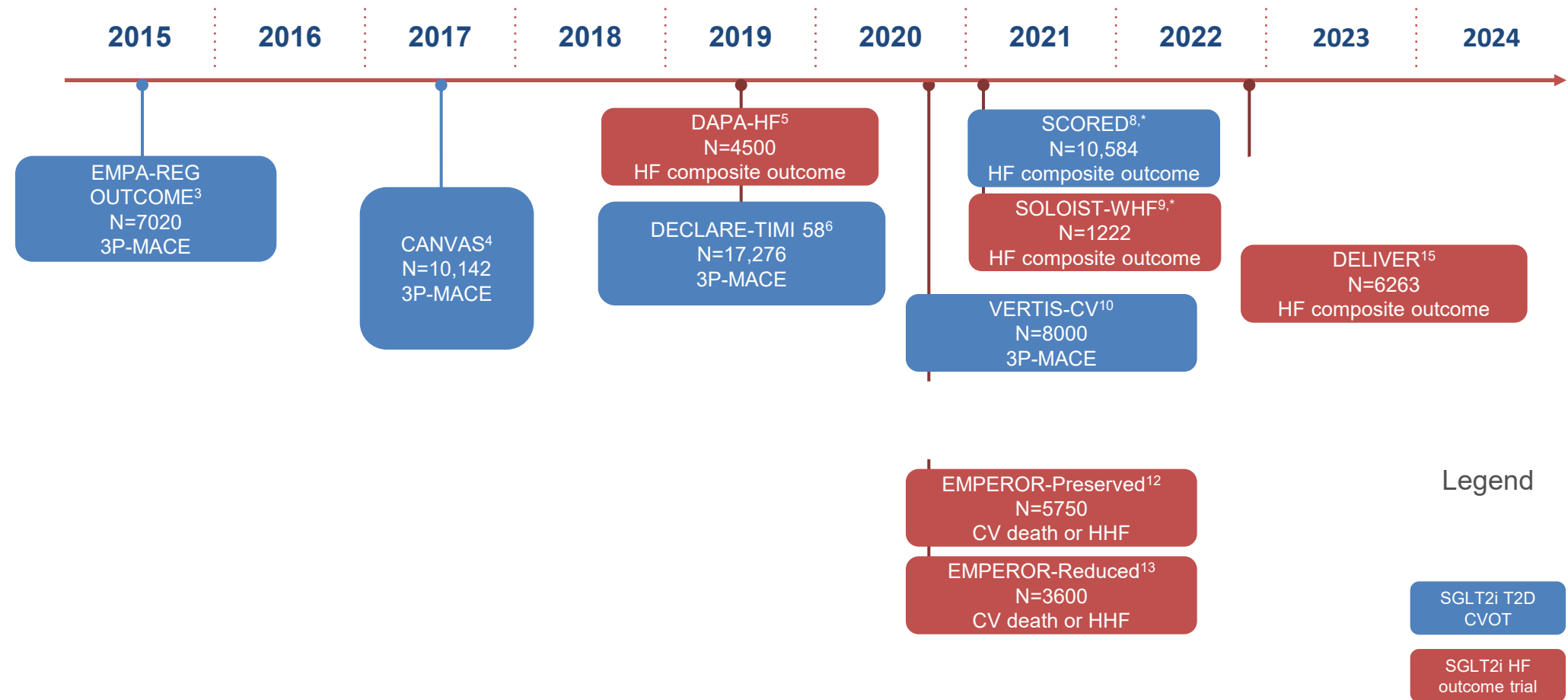


Αναστολείς SGLT-2

	Αναστολή SGLT	Δοσολογία (pos)	Συχνότητα χορήγησης	Μεταβολισμός	Ηπατική λειτουργία	Νεφρική λειτουργία
Dapafliflozin	2	5mg, 10mg	1 φορά ημερησίως	ήπαρ, νεφροί	Child-Pugh class C 5mg→10mg	έναρξη $>25 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$
Empagliflozin	2	10mg, 25mg	1 φορά ημερησίως	Glucuronosyl transferases UG2B7, UGT1A3, UGT1A8, UGT1A9	Child-Pugh class C δεν συνιστάται	έναρξη $>30 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$
Canagliflozin	1 και 2	100mg, 300mg	1 φορά ημερησίως	ήπαρ	Child-Pugh class C δεν συνιστάται	έναρξη $>30 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$



Οι μελέτες εκβάσεων των SGLT2 αναστολέων συμπεριέλαβαν περισσότερους από 90.000 ασθενείς από το 2015^{1,2} έως σήμερα



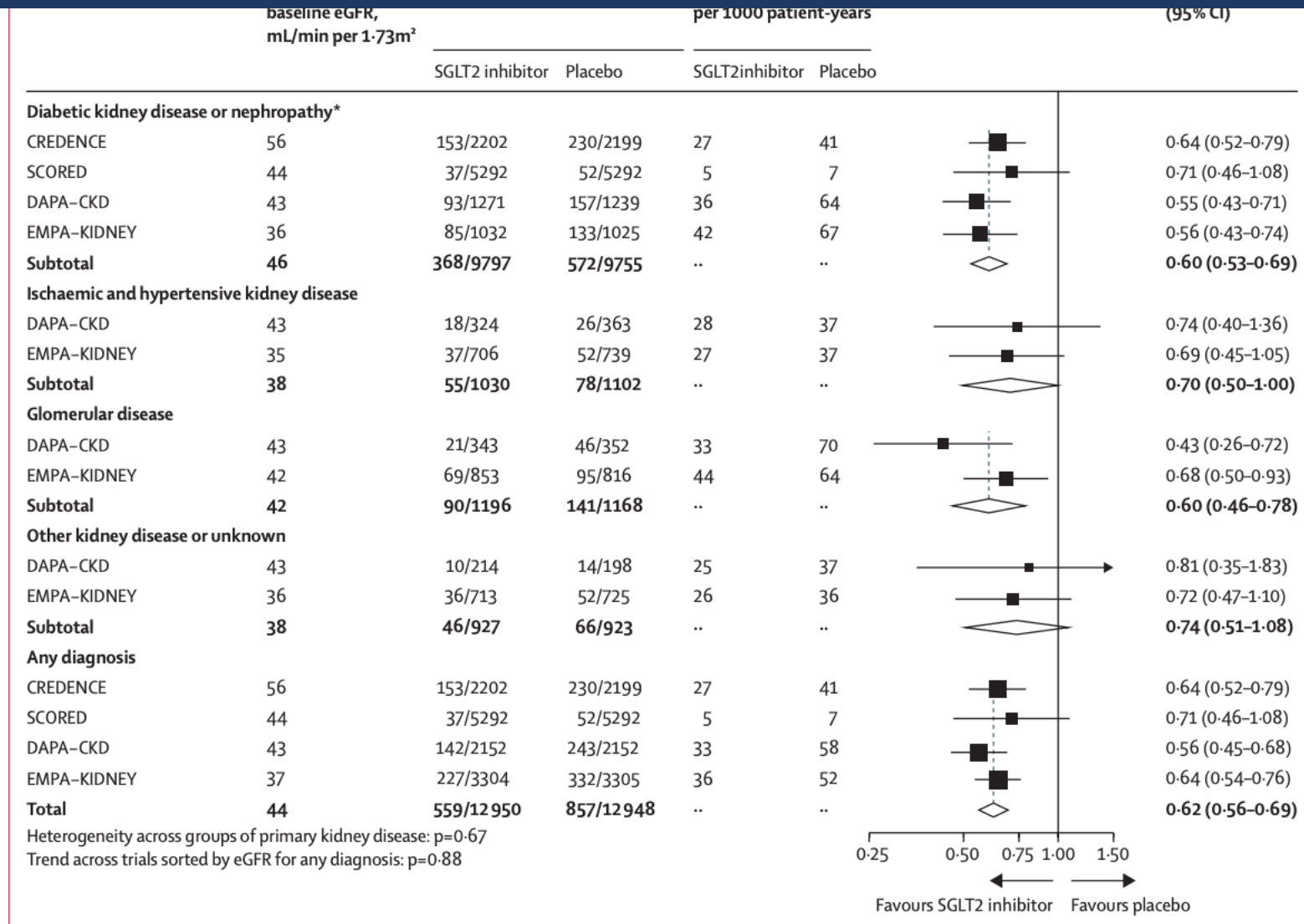
*The trial ended early because of loss of funding from the sponsor. Although the SCORED population was people with T2D and CKD, the primary endpoint was a composite of the total number of CV deaths, hospitalisations for HF, and urgent visits for HF; the secondary endpoints were a sustained decrease of $\geq 50\%$ in the eGFR from baseline for at least 30 days, long-term dialysis, renal transplantation, or a sustained eGFR of <15 ml/min/1.73 m² for at least 30 days. The SOLOIST-WHF population was people with T2D who were recently hospitalised for worsening HF; the primary endpoint of the total number of deaths from CV causes and hospitalisations, and urgent visits for HF (first and subsequent events). Sotagliflozin has been withdrawn in the European Union

Figure adapted from Z. Rangaswami J *et al. Circulation* 2020;142:e265

Please refer to slide notes for abbreviations and references

Effects of SGLT2 on kidney disease progression

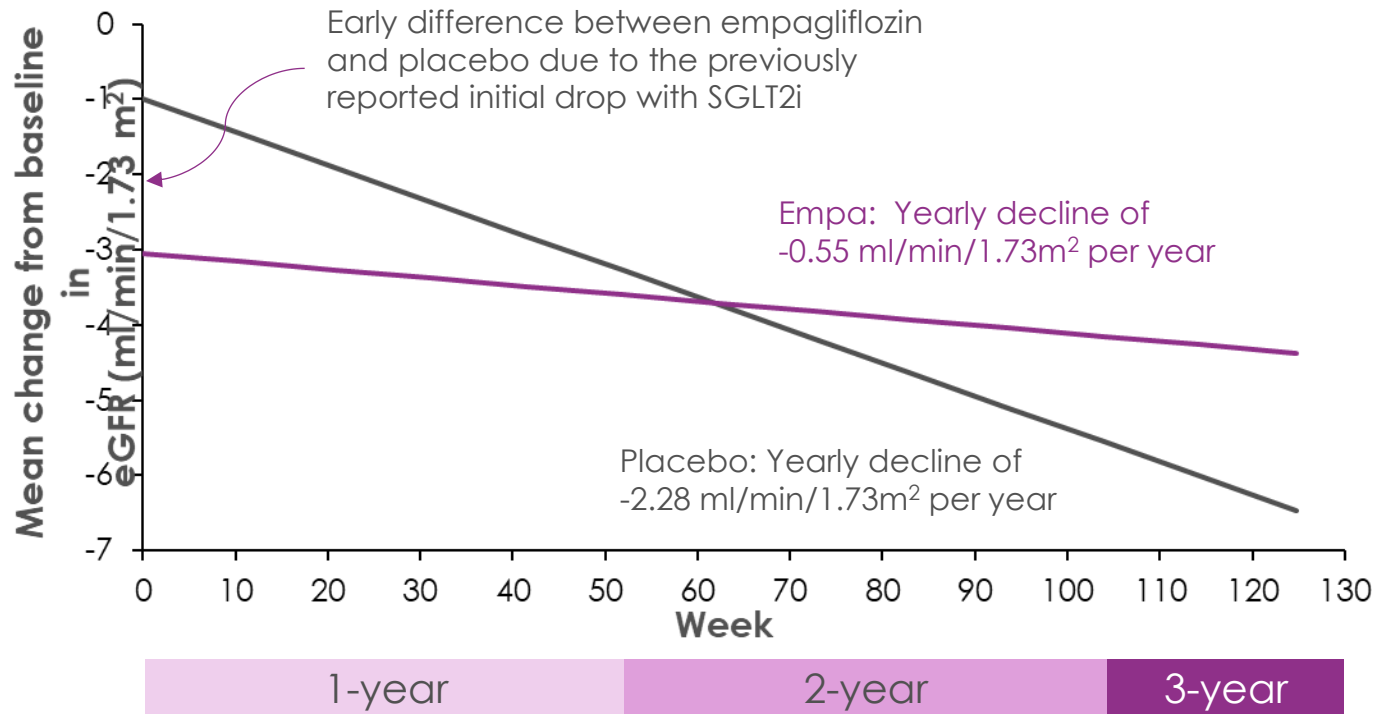
Collaborative meta-analysis of large placebo-controlled trials





Key secondary endpoint: eGFR slope

Empagliflozin protected the kidney by slowing the progression of kidney disease



eGFR Slope = **rate of decline**

eGFR slope is a measure for **long-term renal function**

+1.73

eGFR slope difference
ml/min/1.73 m² per year

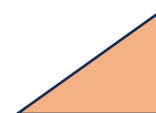
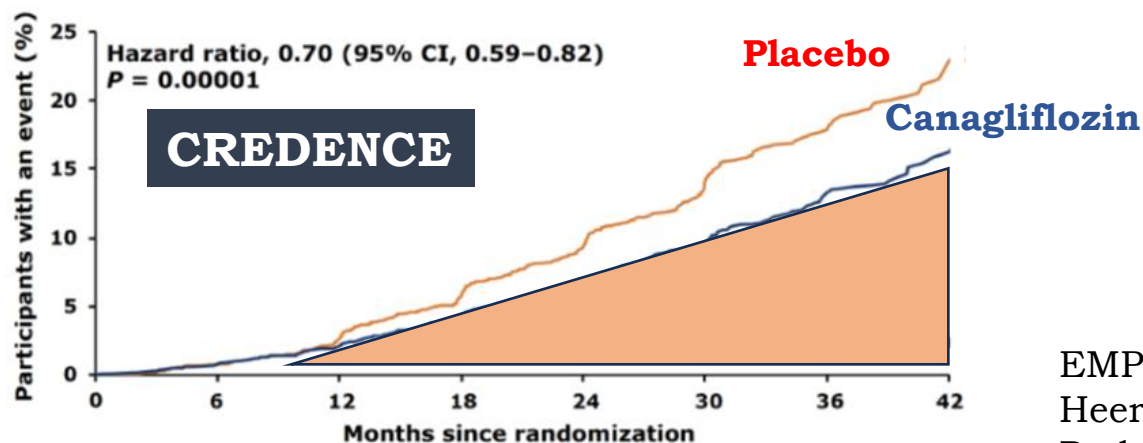
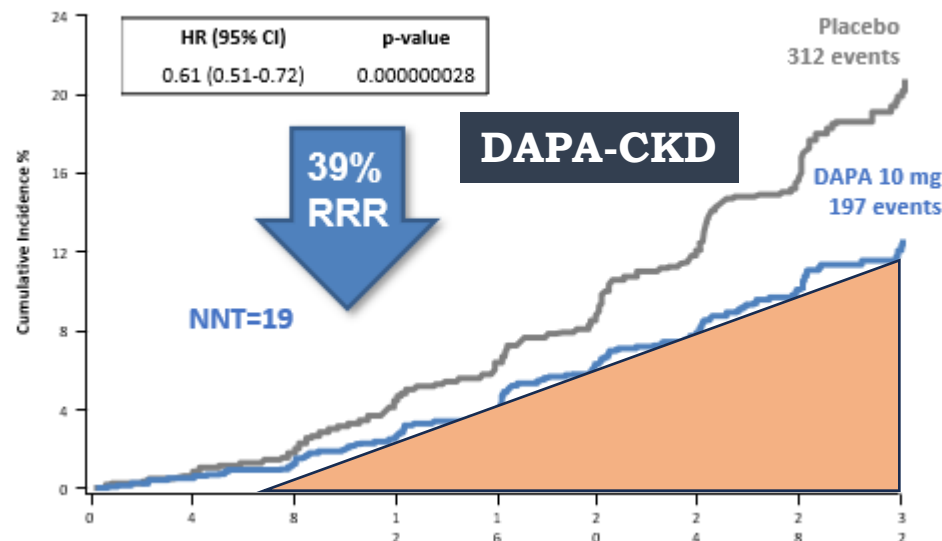
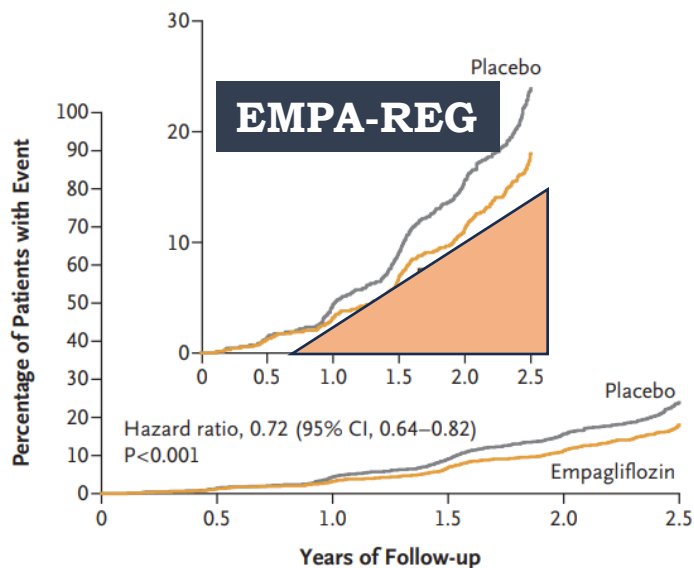
p<0.001





Νεφροπρασασία στα άτομα με ΣΔτ2- SGLT2i: EMPA-REG, DAPA-CKD, CREDENCE

διπλασιασμός κρεατινίνης, τελικού σταδίου νεφρική νόσος ή θάνατος



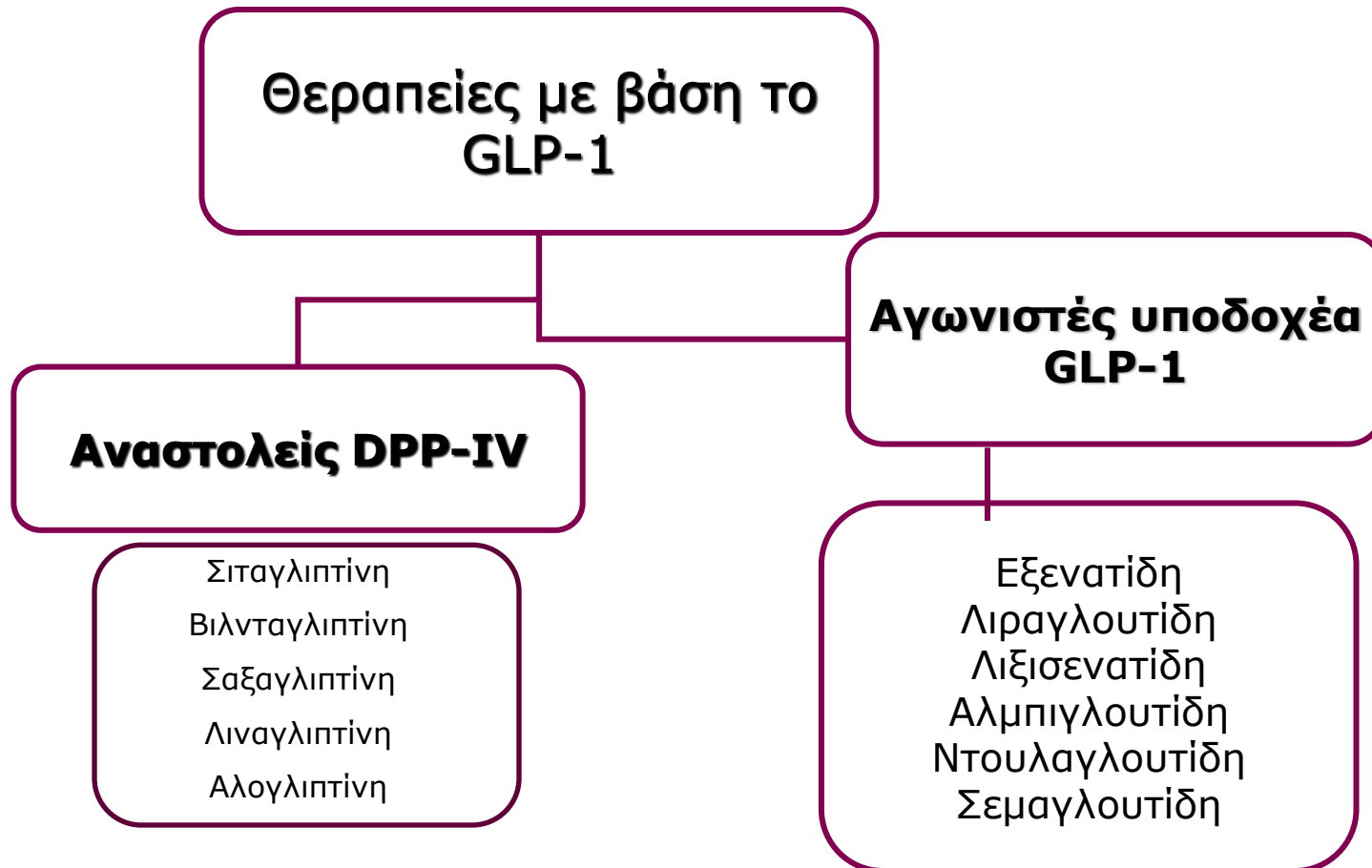
Υπολειπόμενος κίνδυνος

EMPA-KIDNEY, NEJM, 2023

Heerspink HJL et.al., Nephrol. Dial. Transpl, 35,2020

Perkovic. Et.al., NEJM., 2019

Ταξινόμηση θεραπειών που βασίζονται στο GLP-1



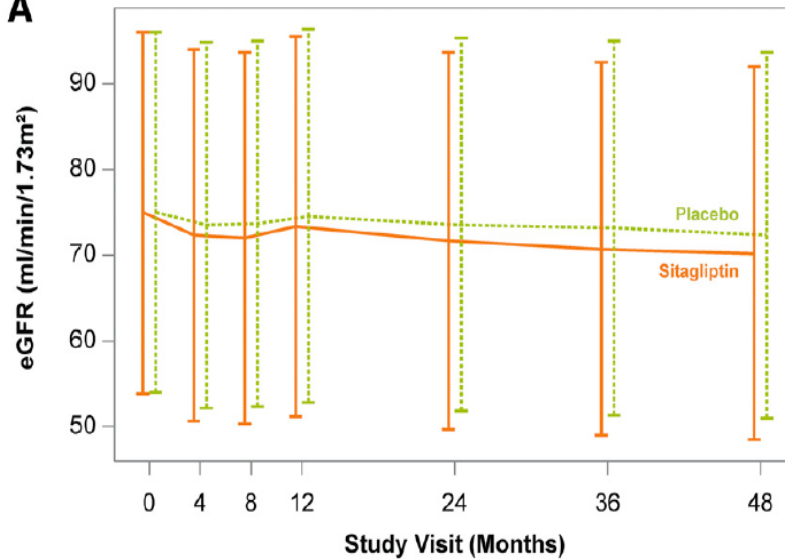


Effect of Sitagliptin on Kidney Function and Respective Cardiovascular Outcomes in Type 2 Diabetes: Outcomes From TECOS

DOI: 10.2337/dc16-1415

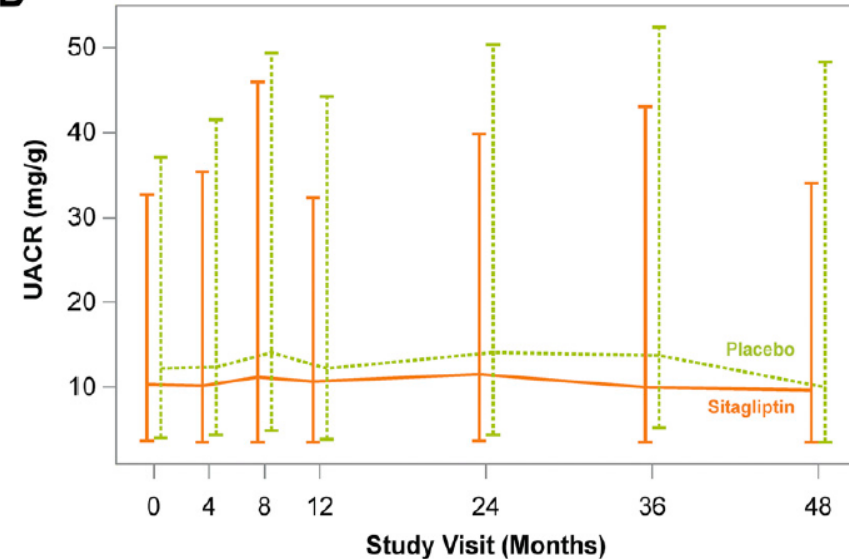


Jan H. Cornel,¹ George L. Bakris,²
 Susanna R. Stevens,³ Michael Alvarsson,⁴
 Willem A. Bax,⁵ Lee-Ming Chuang,⁶
 Samuel S. Engel,⁶ Renato D. Lopes,³
 Darren K. McGuire,⁷ Axel Riefflin,⁸
 Helena Wachslicht Rodbard,⁹
 Isaac Sinay,¹⁰ Tsvetelina Tankova,¹¹
 Julia Wainstein,¹² Eric D. Peterson,⁸ and
 Rury R. Holman,¹³ on behalf of the TECOS
 Study Group

A

Number of Patients:

Sitagliptin	6,809	4,135	3,809	5,263	5,553	3,291	1,360
Placebo	6,795	4,169	3,772	5,197	5,482	3,165	1,335

B

Number of Patients:

Sitagliptin	1,949	687	664	1,171	1,054	562	276
Placebo	1,883	730	640	1,129	1,006	580	273

A: eGFR over 4 years (N = 13,604). B: UACR over 4 years (N = 3,832)

GLP-1 ανάλογα



Βραχείας
δράσης

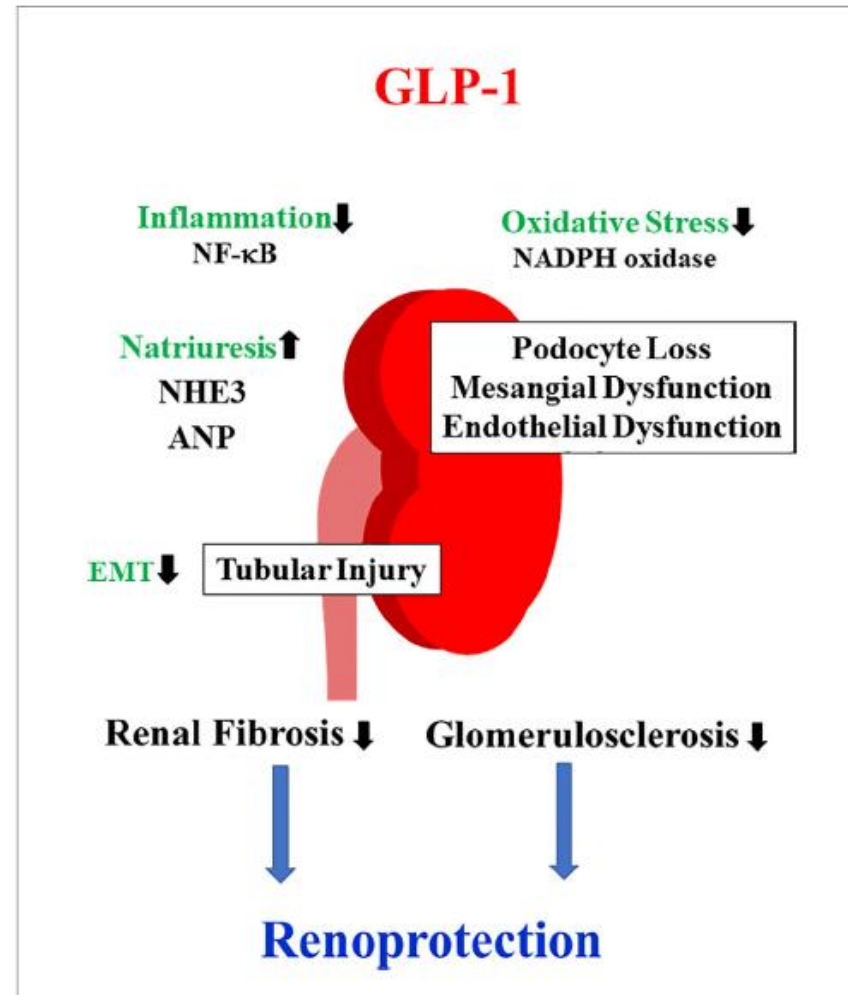
	Δοσολογία (sc)	Συχνότητα χορήγησης	Χορήγηση πριν το γεύμα	Μεταβολισμός	Ηπατική λειτουργία	Νεφρική λειτουργία
Exenatide standard release	5μg → 10μg	2 φορές ημερησίως	Ναι	νεφροί	Ίδια δόση	$>30 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ 30-50: 5μg → 10μg <30 όχι
Lixisenatide	10μg → 20μg	1 φορά ημερησίως	Ναι	νεφροί	Ίδια δόση	$>30 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ <30 όχι
Liraglutide	0,6mg → 1,2mg → 1,8mg	1 φορά ημερησίως	Όχι	μεταβολισμός πεπτιδίων	Ίδια δόση	$>15 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ <15 περιορισμένα δεδομένα
Exenatide modified release	2 mg	1 φορά εβδομαδιαία	Όχι	νεφροί	Ίδια δόση	$>50 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ 30-50: περιορισμένα δεδομένα <30 όχι
Albiglutide	30 mg → 50mg	1 φορά εβδομαδιαία	Όχι	μεταβολισμός πεπτιδίων	Ίδια δόση	$>30 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ <30 περιορισμένα δεδομένα
Dulaglutide	0,75mg → 1,5mg	1 φορά εβδομαδιαία	Όχι	μεταβολισμός πεπτιδίων	Ίδια δόση	$>15 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ <15 περιορισμένα δεδομένα
Semaglutide *	0,25mg → 0,5mg – 1mg	1 φορά εβδομαδιαία	Όχι	μεταβολισμός πεπτιδίων	Ίδια δόση	$>15 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ <15 περιορισμένα δεδομένα

* υπό ανάπτυξη χορήγηση semaglutide από το στόμα

Μακράς δράσης

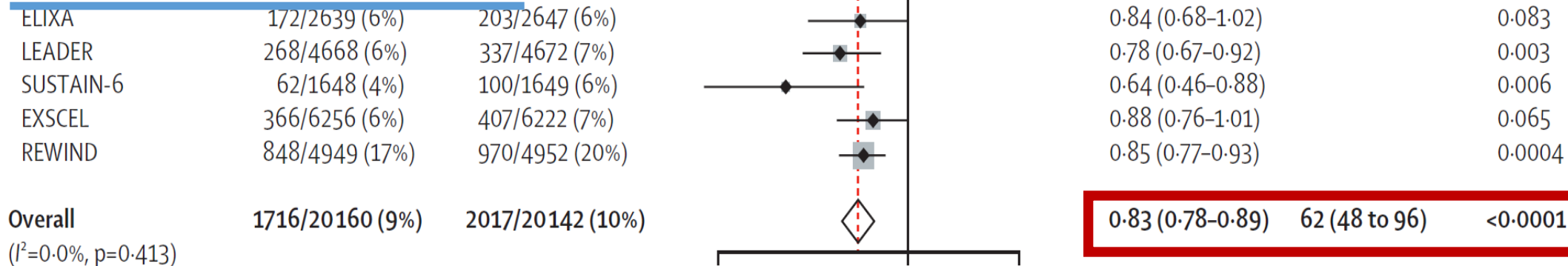


GLP-1 analogues – mechanisms of renoprotective effects

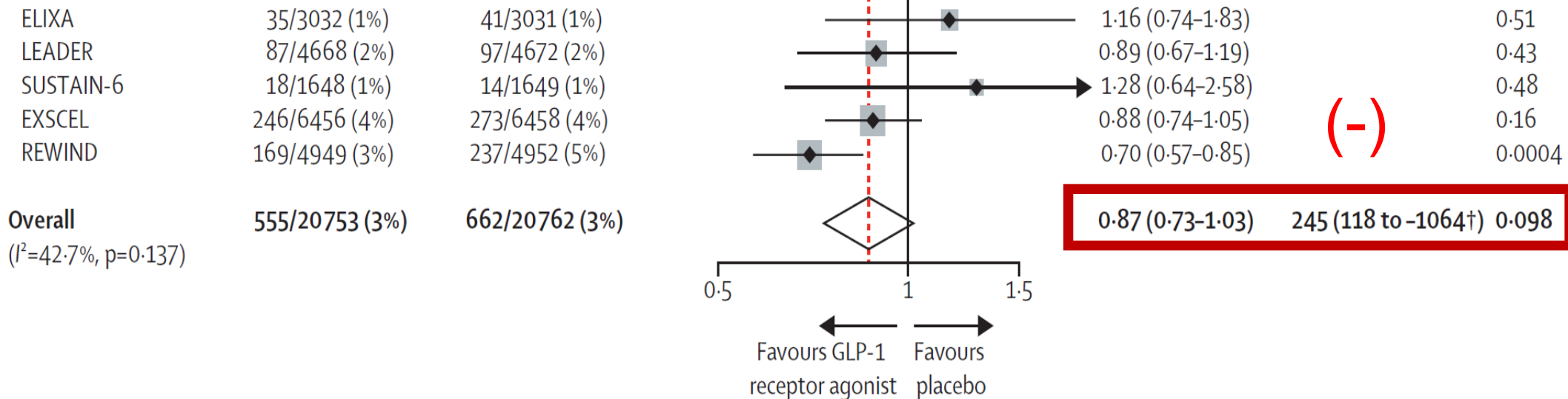


GLP-1RA vs placebo στις CVOT μελέτες : Η επίδραση στις νεφρικές εκβάσεις

Composite kidney outcome including macroalbuminuria



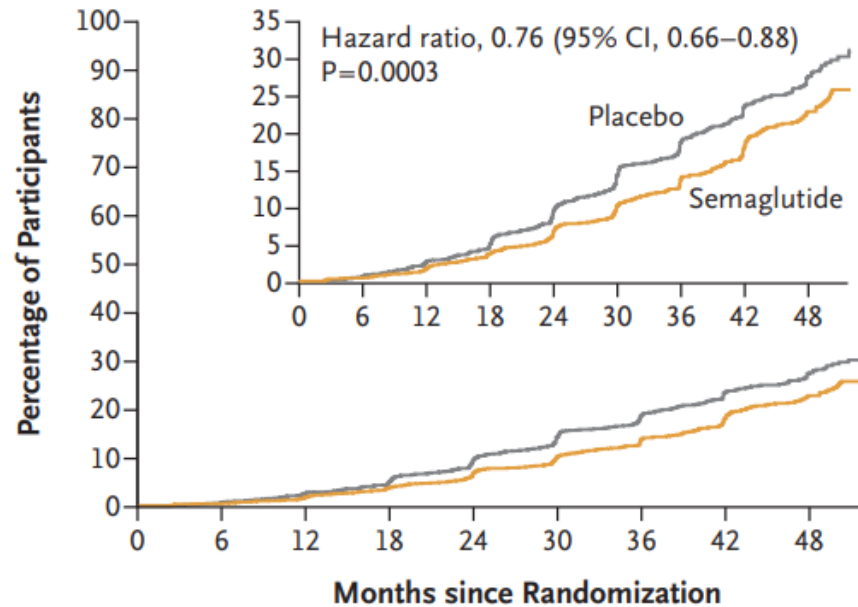
Worsening of kidney function





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

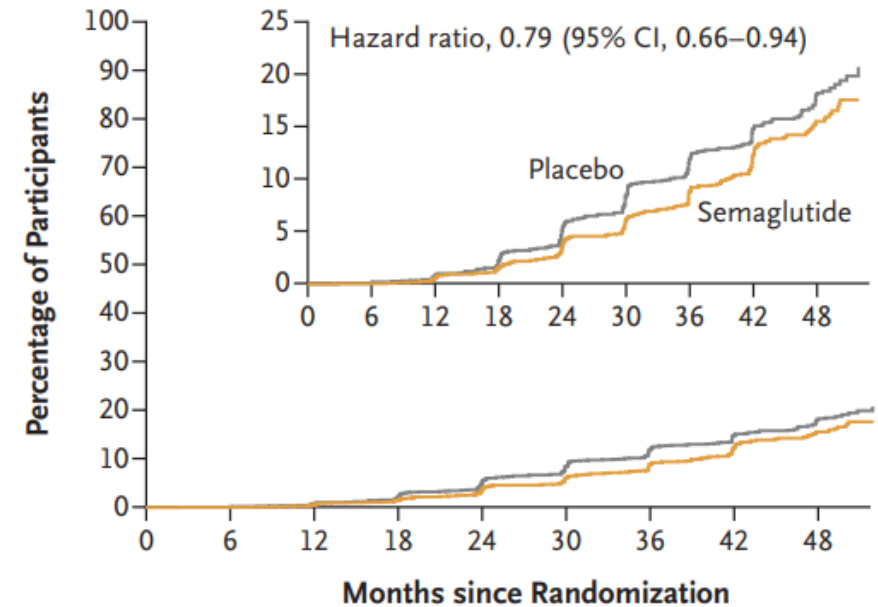
A First Major Kidney Disease Event



No. at Risk

Placebo	1766	1736	1682	1605	1516	1408	1048	660	354
Semaglutide	1767	1738	1693	1640	1572	1489	1131	742	392

B First Kidney-Specific Component Event



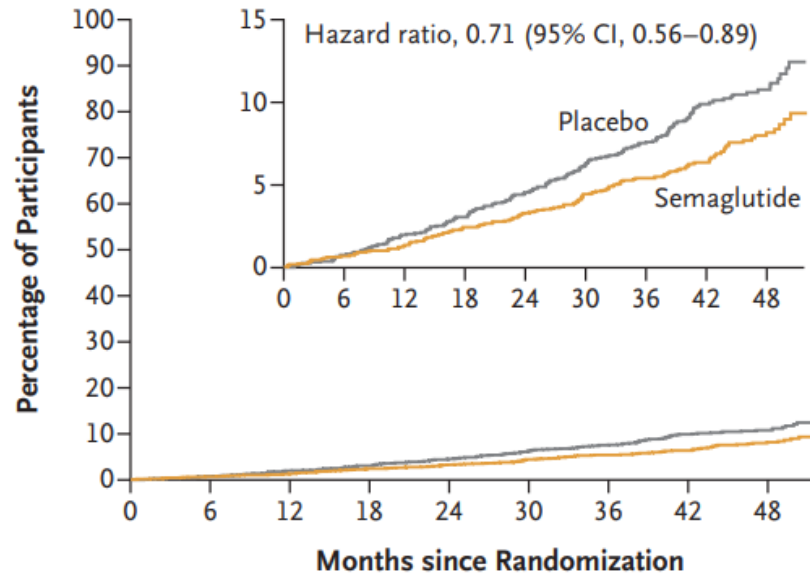
No. at Risk

Placebo	1766	1736	1682	1605	1516	1408	1048	660	354
Semaglutide	1767	1738	1693	1640	1572	1489	1131	742	392



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

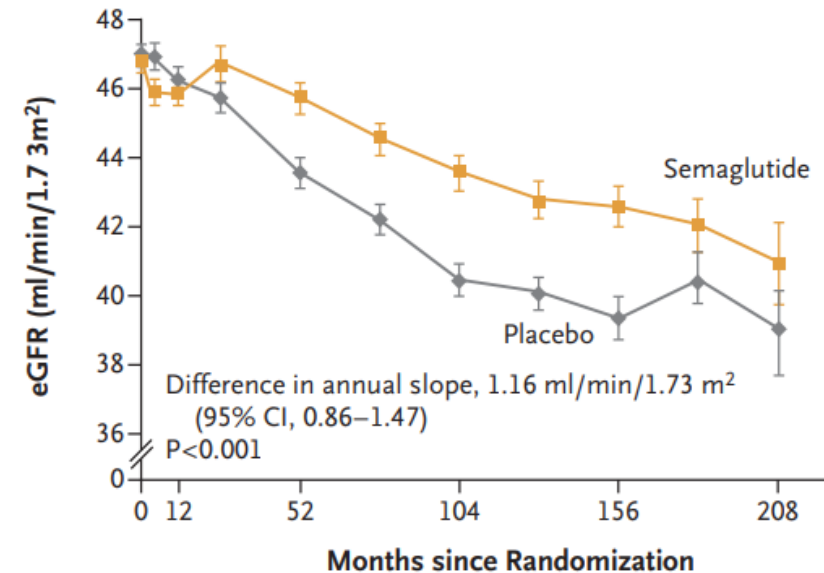
C Death from Cardiovascular Causes



No. at Risk

Placebo	1766	1737	1697	1641	1601	1544	1185	772	437
Semaglutide	1767	1739	1703	1665	1627	1583	1234	838	460

D Total eGFR Slope

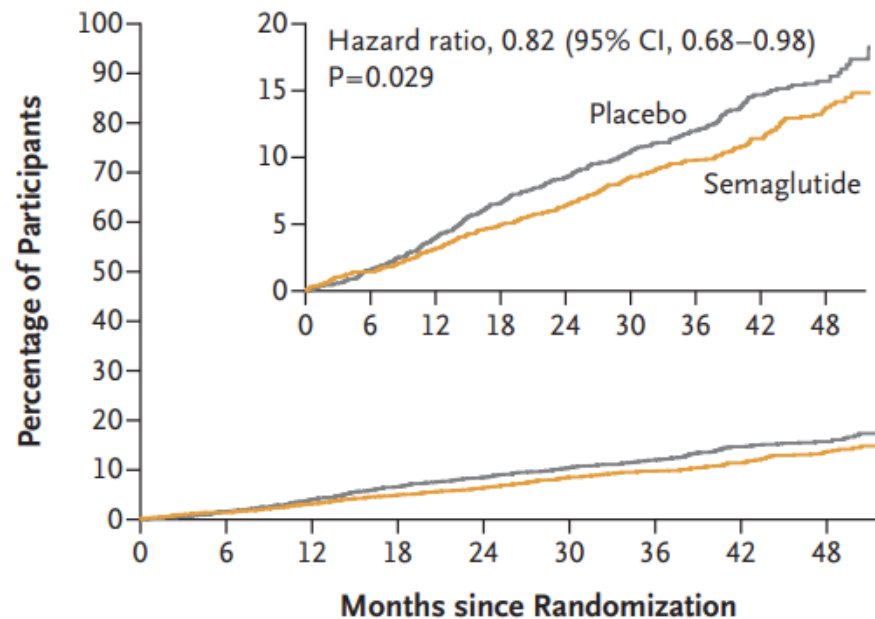


No. at Risk

Placebo	1766	1663	1573	1609	1490	1441	1284	876	609	199
Semaglutide	1766	1665	1590	1606	1521	1468	1345	952	651	218

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

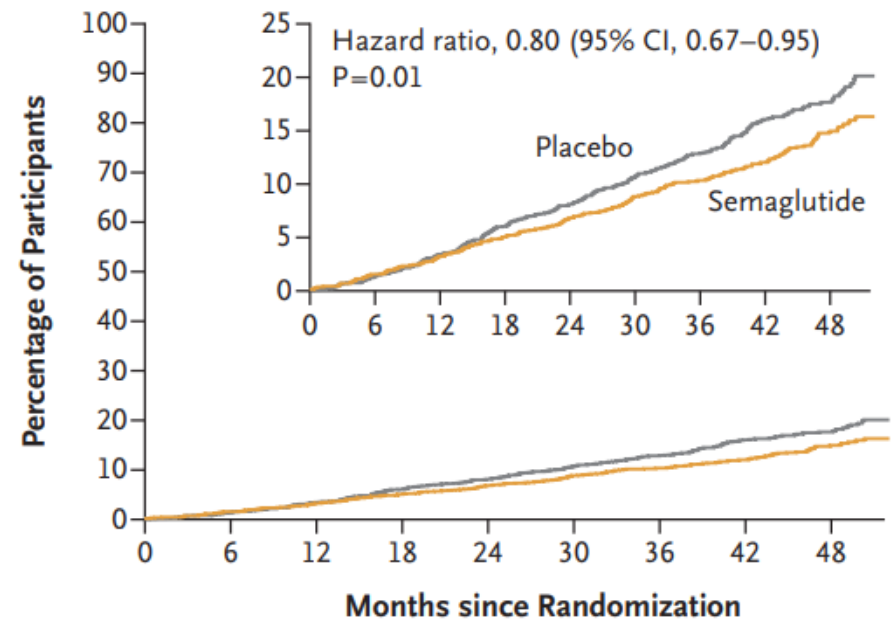
E First Major Cardiovascular Event



No. at Risk

Placebo	1766	1721	1663	1583	1535	1478	1133	731	418
Semaglutide	1767	1725	1672	1622	1575	1515	1176	793	430

F Death from Any Cause



No. at Risk

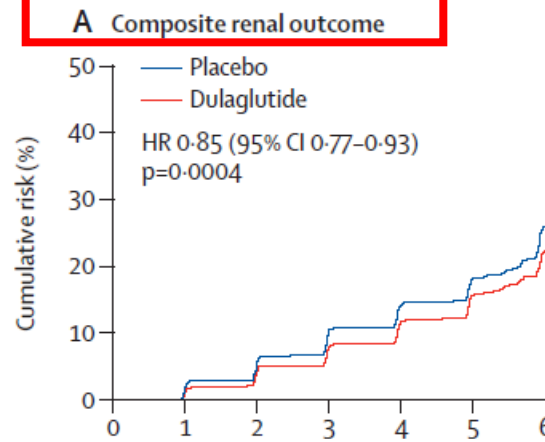
Placebo	1766	1737	1697	1641	1601	1544	1185	772	437
Semaglutide	1767	1739	1703	1665	1627	1583	1234	838	460



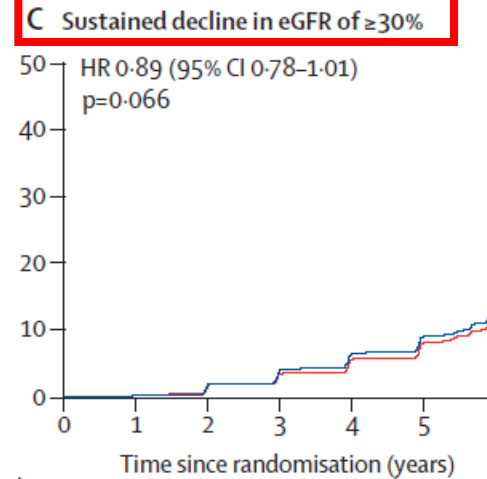
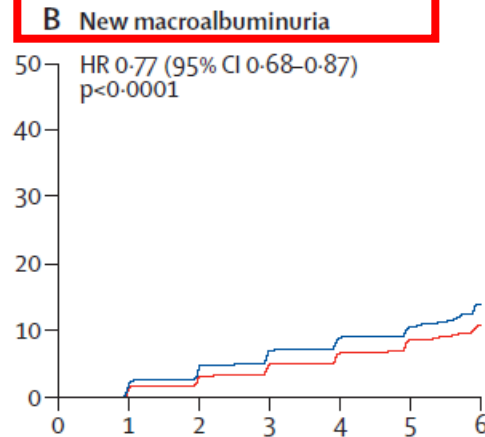
Ντουλαγλουτίδη – Μελέτη REWIND

Επίδραση στο νεφρό

↓
15%



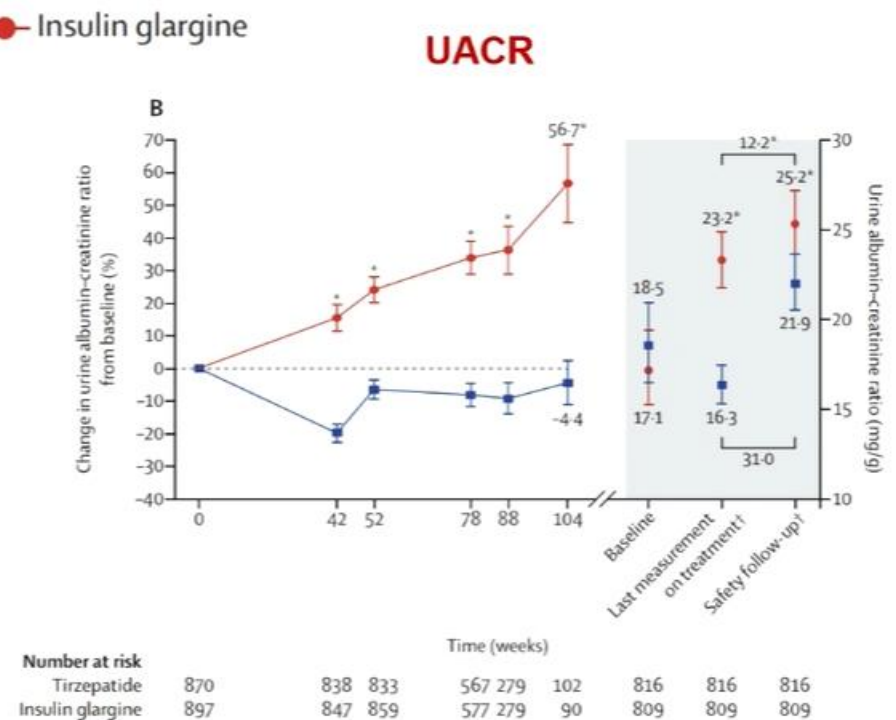
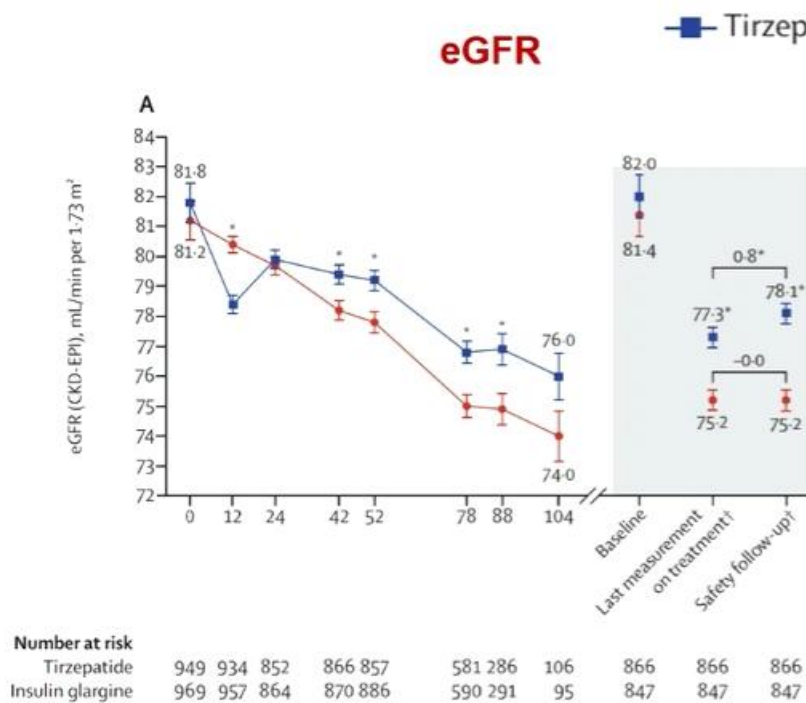
↓
23%



↓
11%



Change from baseline in eGFR and UACR in SURPASS 4





**Υπάρχει συνεργική δράση στην ΧΝΝ με τον συνδυασμό
SGLT-2i και GLP-1a ;**



Combined GLP-1 RA + SGLT2i: Meta-analysis

12 SGLT2i CVOTs (Apperloo et al. Lancet D&E 2024;12:545)

Clinical Implications

- No GLP-1RA interactions with diabetes status (T2DM vs. non-DM) on outcomes
- No SGLT2i interactions with diabetes status (T2DM vs. non-DM) on outcomes
- No GLP-1RA interactions with SGLT2i on outcomes
- Therefore, for T2DM or non-DM people:

Event	GLP-1RA & SGLT2i	~ 5y Risk (No Rx)	~ 5y Risk (Rx)	NNT for 5y
MI, Stroke, CV death	0.77	20%	15.4%	22
Heart failure	0.64	20%	12.8%	14
Kidney Function Decline	0.42	20%	8.4%	9

Άλλες θεραπευτικές παρεμβάσεις

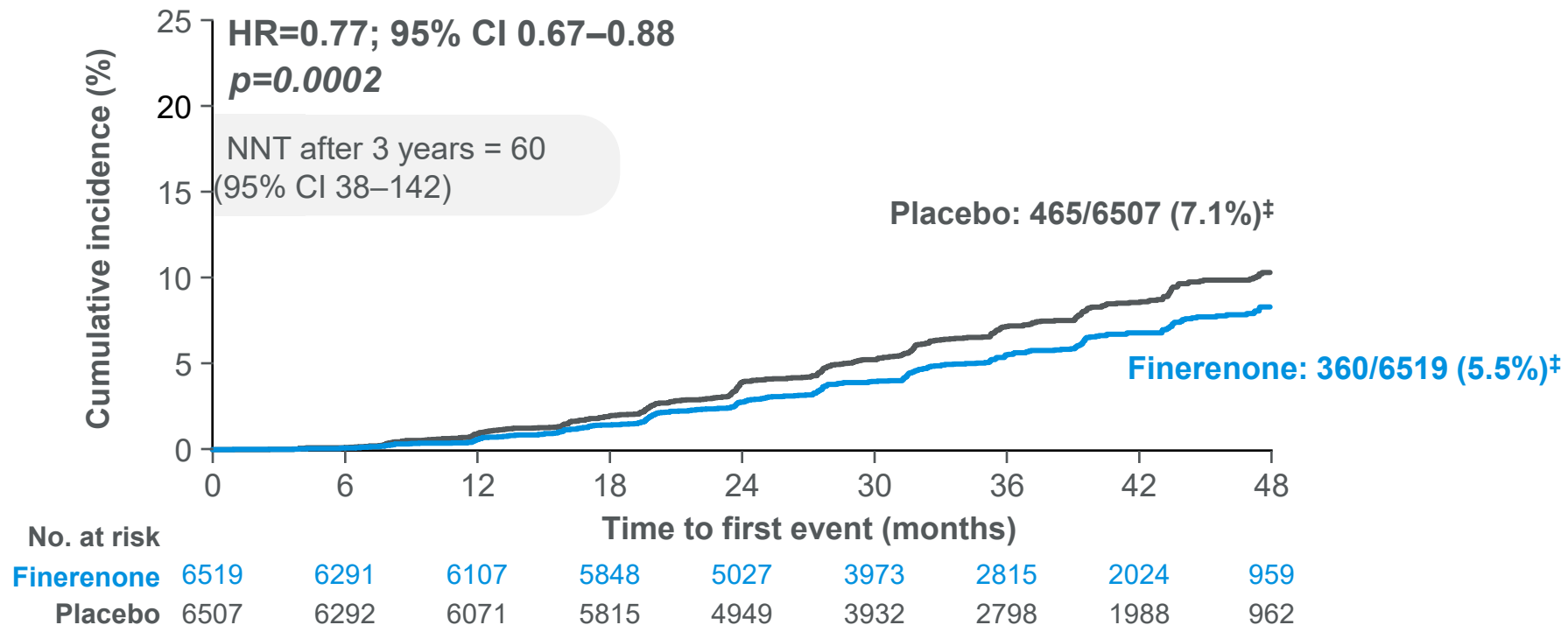
Comparison of MRA inhibitors: Steroidal and Non-steroidal



	Spironolactone	Eplerenone	Finerenone
Structural properties	Flat (steroidal)	Flat (steroidal)	Bulky (nonsteroidal)
Potency to MR	+++	+	+++
Selectivity to MR	+	++	+++
CNS penetration	+	+	-
Sexual side effects	++	(+)	-
Half-life	> 20 hours	4-6 hours	2-3 hours
Active metabolites	++	-	-
Effect on BP	+++	++	+

Finerenone significantly reduced the risk of the $\geq 57\%$ eGFR kidney composite outcome by 23%

Time to kidney failure,* sustained $\geq 57\%$ decrease in eGFR from baseline, or renal death[#]



*ESKD or an eGFR <15 ml/min/1.73 m²; [#]events were classified as renal death if: (1) the patient died; (2) kidney replacement therapy had not been initiated despite being clinically indicated; and (3) there was no other likely cause of death; [‡]cumulative incidence calculated by Aalen–Johansen estimator using deaths due to other causes as competing risk;

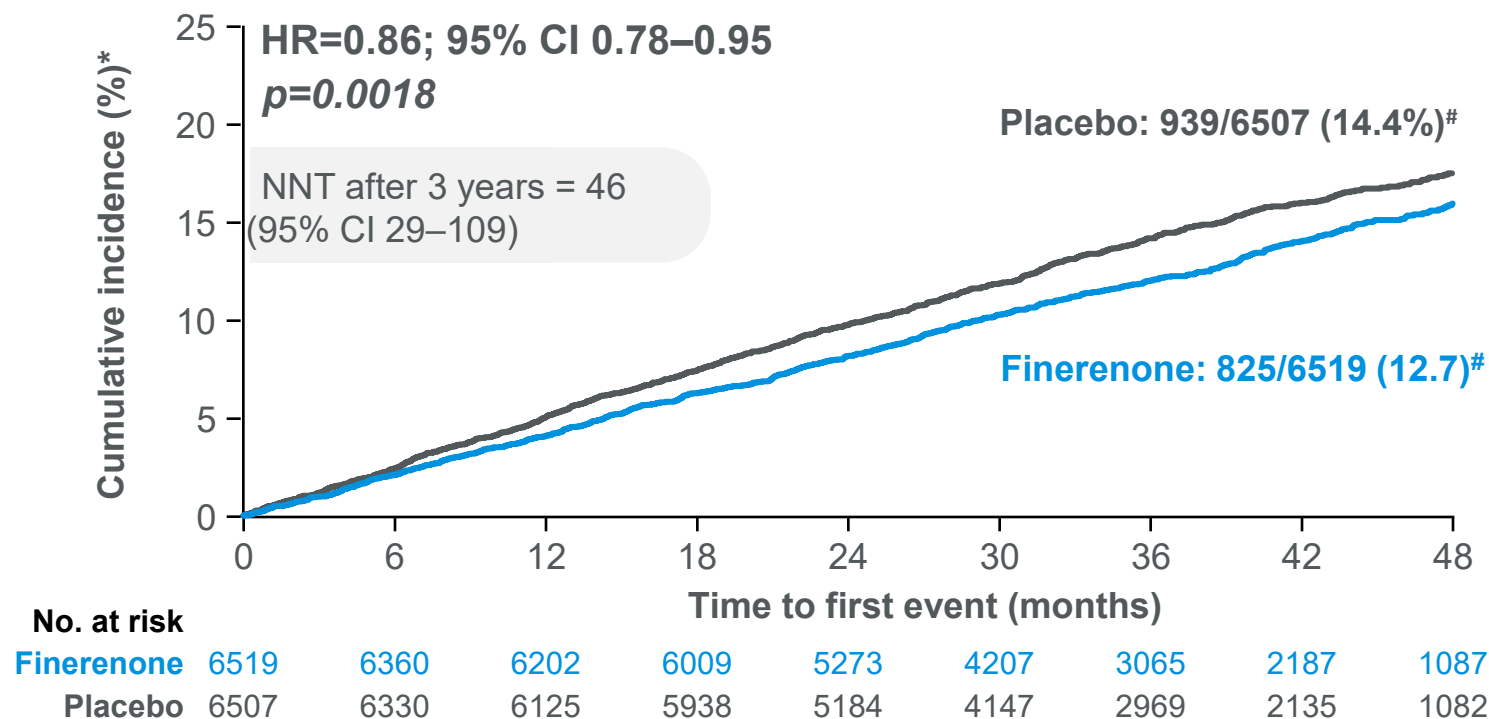
[†]number of patients with an event over a median of 3.0 years of follow-up

CI, confidence interval; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HR, hazard ratio; NNT, number needed to treat

Agarwal R, et al. Eur Heart J 2021; doi:10.1093/eurheartj/ehab777

On top of optimised RAS blockade, finerenone significantly reduced the risk of the composite CV outcome by 14%

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

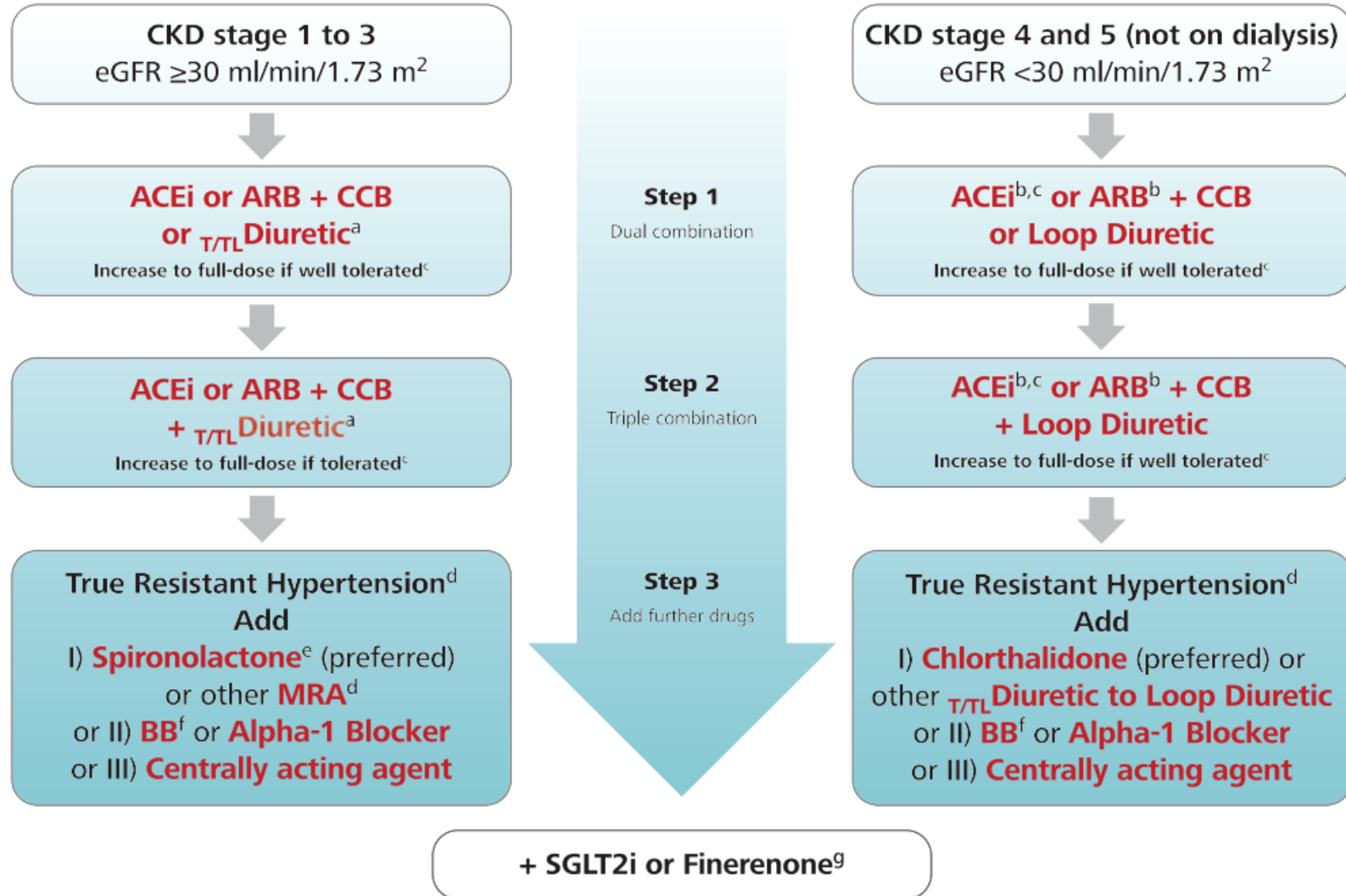


*Cumulative incidence calculated by Aalen–Johansen estimator using deaths due to other causes as competing risk; [#]number of patients with an event over a median of 3.0 years of follow-up
 CI, confidence interval; CV, cardiovascular; HF, heart failure; HR, hazard ratio; MI, myocardial infarction; NNT, number needed to treat; RAS, renin–angiotensin system
 Agarwal R, et al. Eur Heart J 2021; doi:10.1093/eurheartj/ehab777



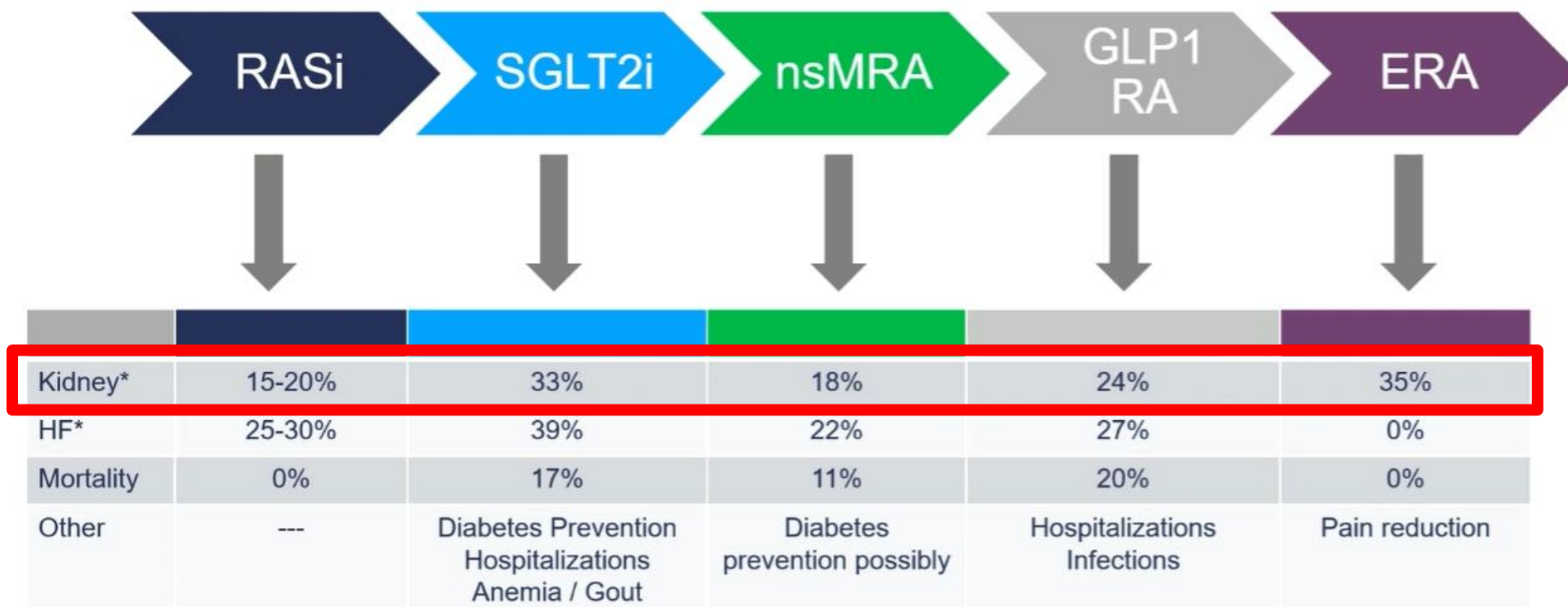
ESH Guidelines 2023

HYPERTENSION AND THE KIDNEY





Effects of different drug classes on kidney / CV outcomes in DKD



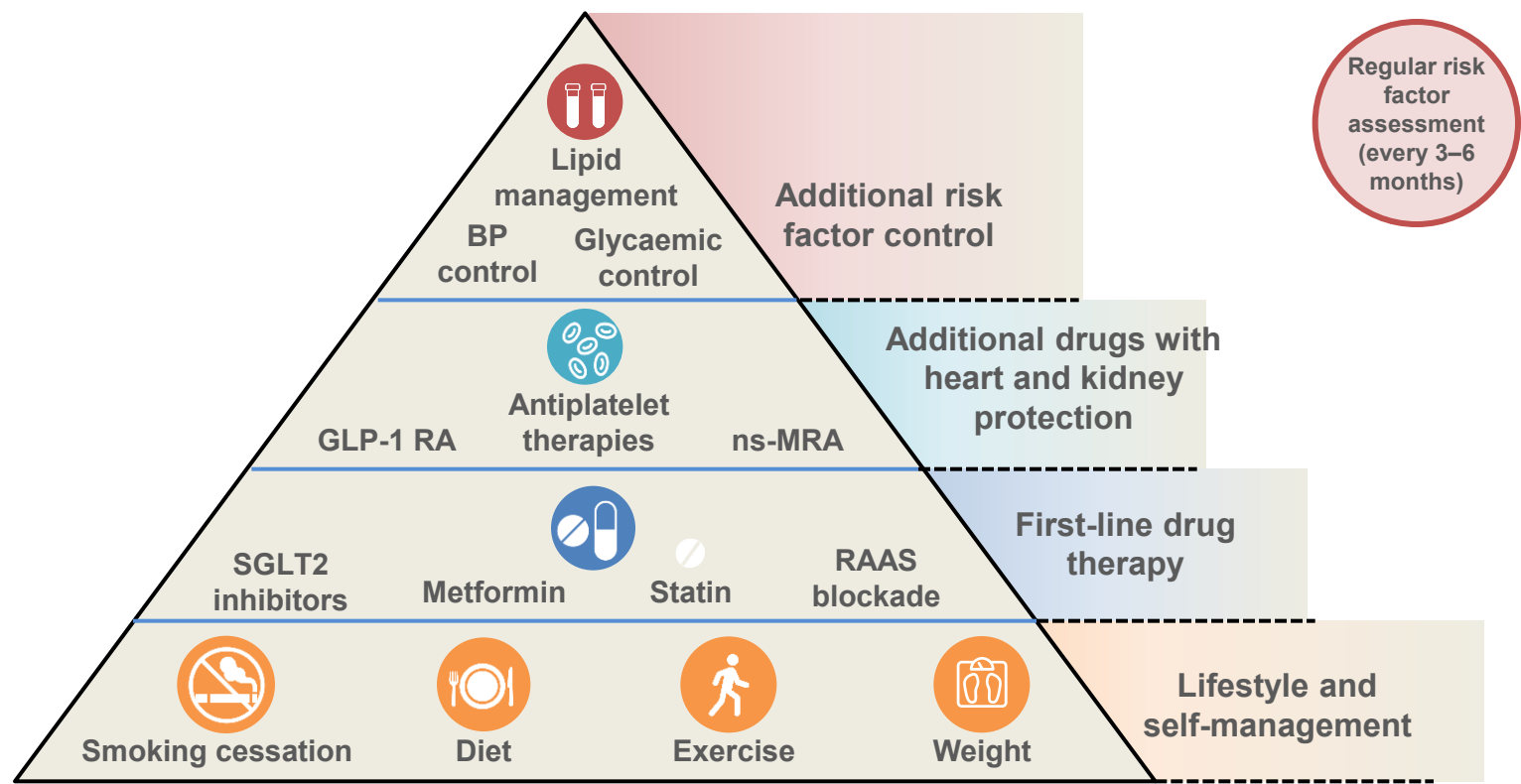
RENAAL; CREDENCE; FIDELIO/FIGARO; FLOW; SONAR

Κατευθυντήριες οδηγίες



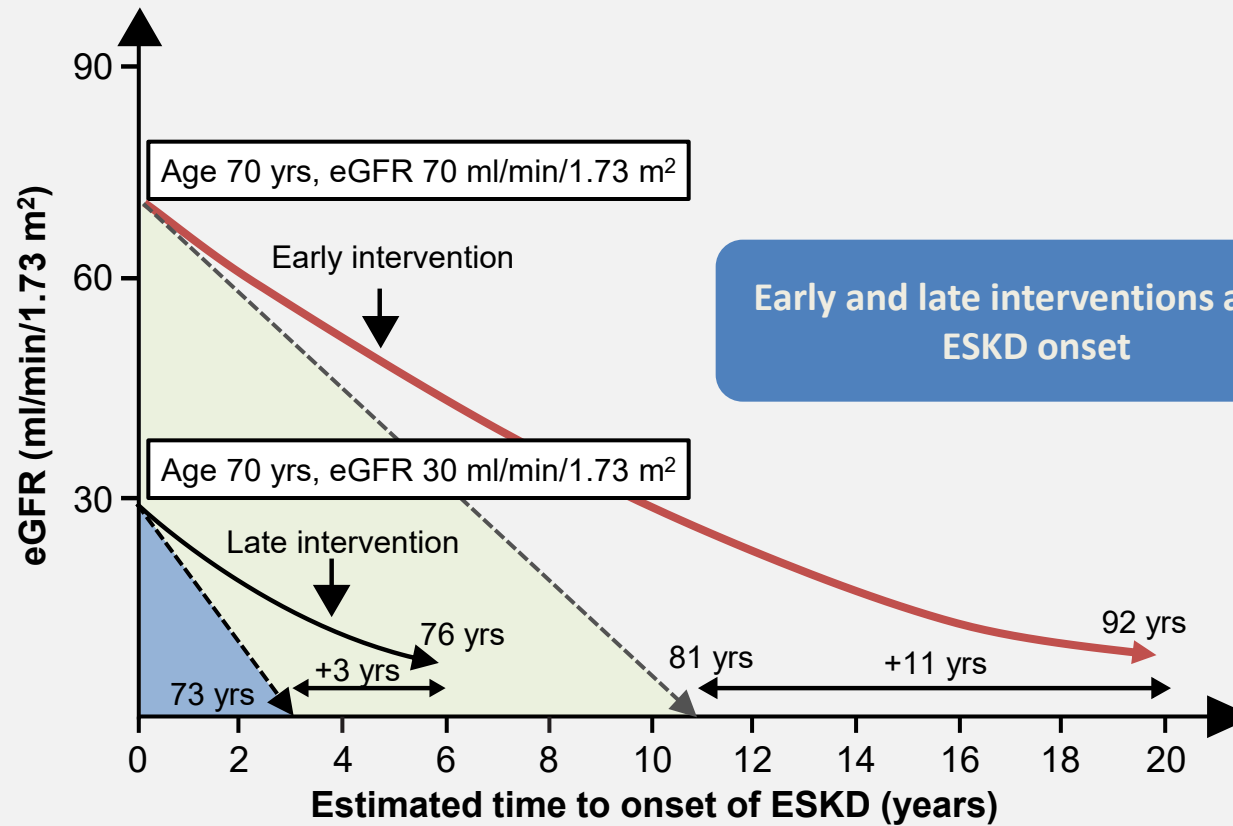
2024 KDIGO guidelines recommend comprehensive treatment of people with T2D and CKD to reduce risks of kidney disease progression and CV disease

Kidney–heart risk factor management





Early intervention in CKD may slow disease progression



CKD, chronic kidney disease; ESKD, end-stage kidney disease; yrs, years

Gohda T *et al. Int J Mol Sci* 2022;23:13749



Ευχαριστώ για την προσοχή σας