99Η ΕΠΙΣΤΗΜΟΝΙΚΗ ΣΥΝΑΝΤΗΣΗ ΤΗΣ ΕΝΕ ΚΟΙΝΗ ΕΚΔΗΛΩΣΗ ΜΕ ΕΔΕ

ΣΑΚΧΑΡΩΔΗΣ ΔΙΑΒΗΤΗΣ – ΧΝΝ

Σημασία της πρώιμης πολυπαραγοντικής παρέμβασης

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Τμήμα Ενδοκρινολογίας και Μεταβολισμού – Διαβητολογικό Κέντρο
Α’ Παθολογική Κλινική ΠΓΝΘ ΑΧΕΠΑ

Η διαβητική Νεφροπάθεια είναι η πρώτη αιτία Τελικού Σταδίου Νεφρικής Νόσου παγκοσμίως.

20-50% των ασθενών με ΣΔ έχουν Διαβητική Νεφροπάθεια.

Η επίπτωση του ΣΔ αυξάνεται. Αναμένουμε να αυξηθεί αντίστοιχα και η επίπτωση της Διαβητικής Νεφροπάθειας.

Για κάθε ↓ 20ml/min/1,73m² eGFR αυξάνεται κατά 50% ο κίνδυνος ανεπιθύμητου ΚΑ συμβάματος.

Η καρδιαγγειακή νόσος είναι η 1η αιτία θανάτου μεταξύ των ασθενών με ΣΔ.

Standards of Medical Care in Diabetes – 2022. Diabetes Care.2021
Cortese F et al. Vascular, cardiac and renal target organ damage associated to arterial hypertension: which noninvasive tools for detection? J Hum Hypertens 34, 420–431 (2020).

↓ Κινδύνου εμφάνισης/εξέλιξης ΧΝΝ σε ασθενείς με ΣΔ

Στρατηγικές ΠΡΩΙΜΗΣ ΠΟΛΥΠΑΡΑΓΟΝΤΙΚΗΣ ΠΑΡΕΜΒΑΣΗΣ

Table 1. Risk Factors for Diabetic Kidney Disease

Nonmodifiable
Genetic factors
Male sex
Age at onset of diabetes between 5 and 15 years
Long duration of diabetes
Increasing age
Family history of diabetic kidney disease, type 2 diabetes, hypertension, and insulin resistance
Modifiable
Poor glycemic control
Hypertension
Lipid abnormalities
Smoking
Metabolic syndrome
Insulin resistance
Low-grade inflammation
Endotoxins
Advanced glycation end products
Low intensity of physical activity
Salt intake

- *Genetic Risk Factors may play o major role in the development of DKD.*
- *Aggressive treatment of modifiable risk factors may prevent DKD.*

Harjutsalo V, Groop PH. Epidemiology and risk factors for diabetic kidney disease. Adv Chronic Kidney Dis. 2014 May;21(3):260-6.

ΣΔT1

Metabolic Memory Phenomenon

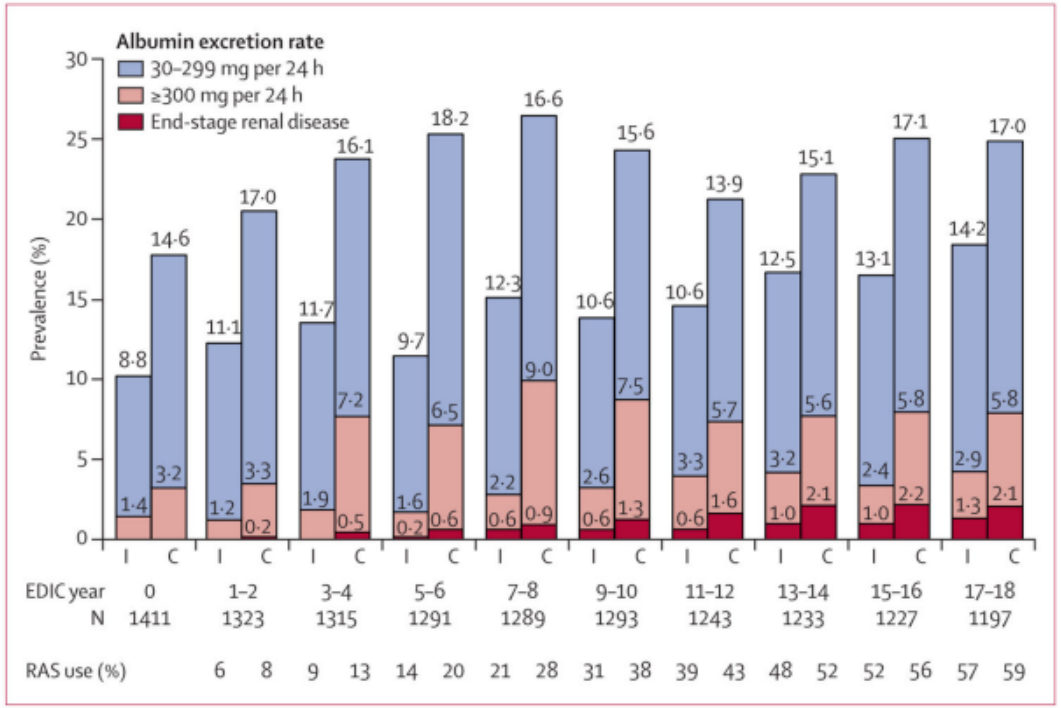
The New England
Journal of Medicine

Volume 329 SEPTEMBER 30, 1993 Number 14

THE EFFECT OF INTENSIVE TREATMENT OF DIABETES ON THE DEVELOPMENT AND PROGRESSION OF LONG-TERM COMPLICATIONS IN INSULIN-DEPENDENT DIABETES MELLITUS

The Diabetes Control and Complications Trial Research Group*

Intensive insulin therapy reduced the risk of albuminuria and microalbuminuria by 54 % and 39 %, respectively, in the combined cohort.



Diabetes Control and Complications Trial Research Group.The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993 Sep 30;329(14):977-86.

DCCT/EDIC research group. Effect of intensive diabetes treatment on albuminuria in type 1 diabetes: long-term follow-up of the Diabetes Control and Complications Trial and Epidemiology of Diabetes Interventions and Complications study. Lancet Diabetes Endocrinol. 2014 Oct;2(10):793-800.

ΣΔT2

Lowering blood glucose itself helps prevent CKD and its progression.

DIABETICMedicine

DOI: 10.1111/j.1464-5491.2008.02496.x

Review Article

Microvascular disease: what does the UKPDS tell us about diabetic nephropathy?

R. Bilous

Professor of Clinical Medicine, Newcastle University, Newcastle upon Tyne, UK

Accepted 23 April 2008

Table 1 Effect of intensive glycaemic control on cumulative incidence of micro- and macroalbuminuria at 9 years in the DDCT and UKPDS

DCCT	*n*	HbA_{1c}	Microalbuminuria	RRR	*P*	Macroalbuminuria	RRR	*P*
Primary prevention	346 I	7.2% I	16% I	34%	0.04	2.6% I	NS	NS
	378 C	9.2% C	27% C			2.3% C		
Secondary prevention	363 I	7.2% I	26% I	43%	< 0.001	5.2% I	56%	< 0.01
	352 C	9.2% C	42% C			11.3% C		
UKPDS	2408 I	7.0% I	19% I	24%	< 0.001	4.4% I	33%	0.026
	994 C	7.9% C (10-year data)	25% C			6.5% C		

Microalbuminuria defined as urinary albumin excretion > 28 μg/min from a single timed 4-h sample in the DCCT and median urinary albumin concentration from random samples > 50 mg/l in the UKPDS. Macroalbuminuria defined as > 208 μg/min or > 300 mg/l, respectively.
C, conventional glycaemic therapy; I, intensive; DCCT, Diabetes Control and Complications Trial; HbA_{1c}, glycated haemoglobin; RRR, relative risk reduction; UKPDS, UK Prospective Diabetes Study.

ΣΔT2

HbaA1c **6,8 %** **7,74%**

Lowering blood glucose itself helps prevent CKD and its progression.

ACCORD
ADVANCE
UKPDS
VATD

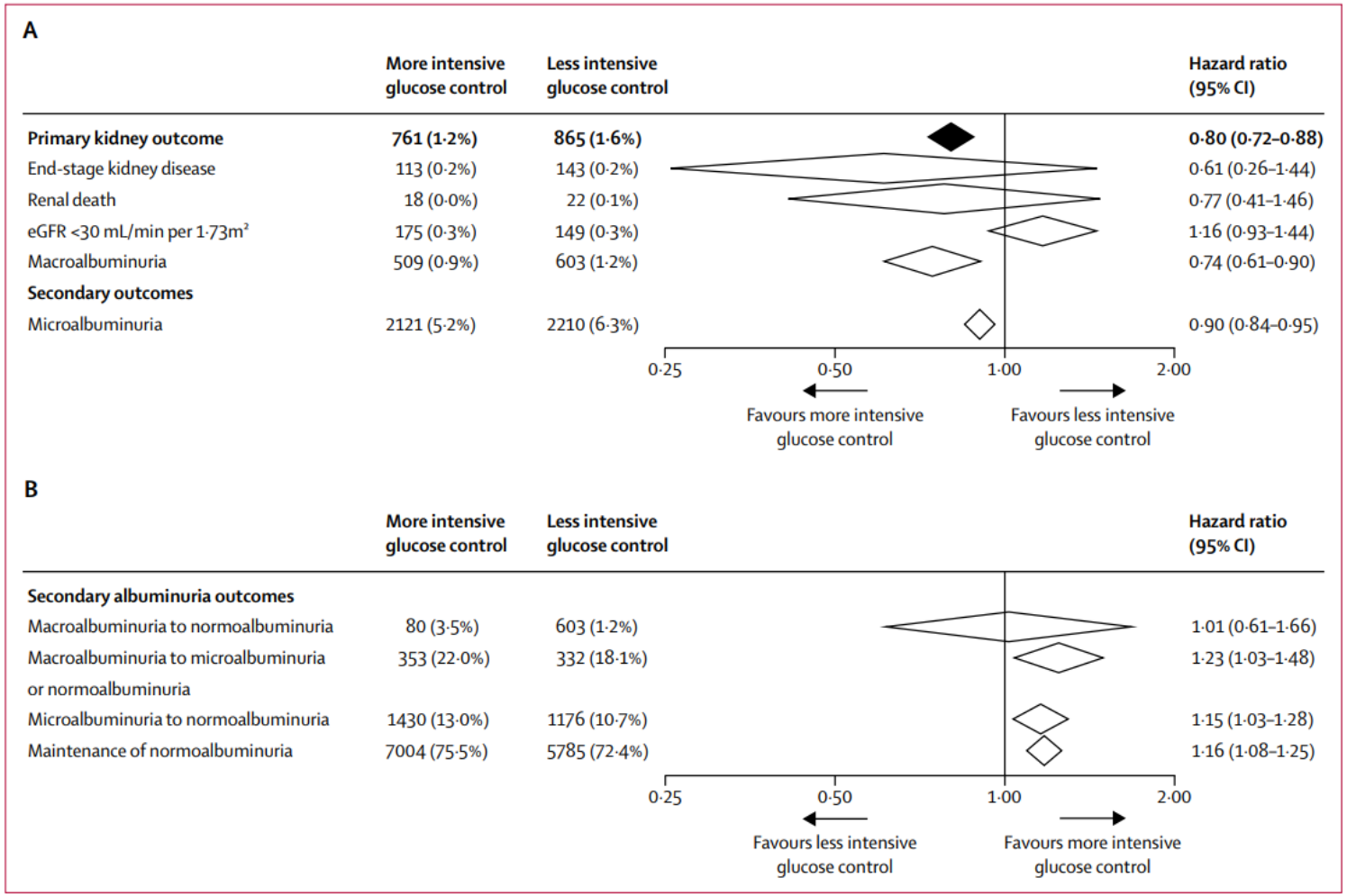
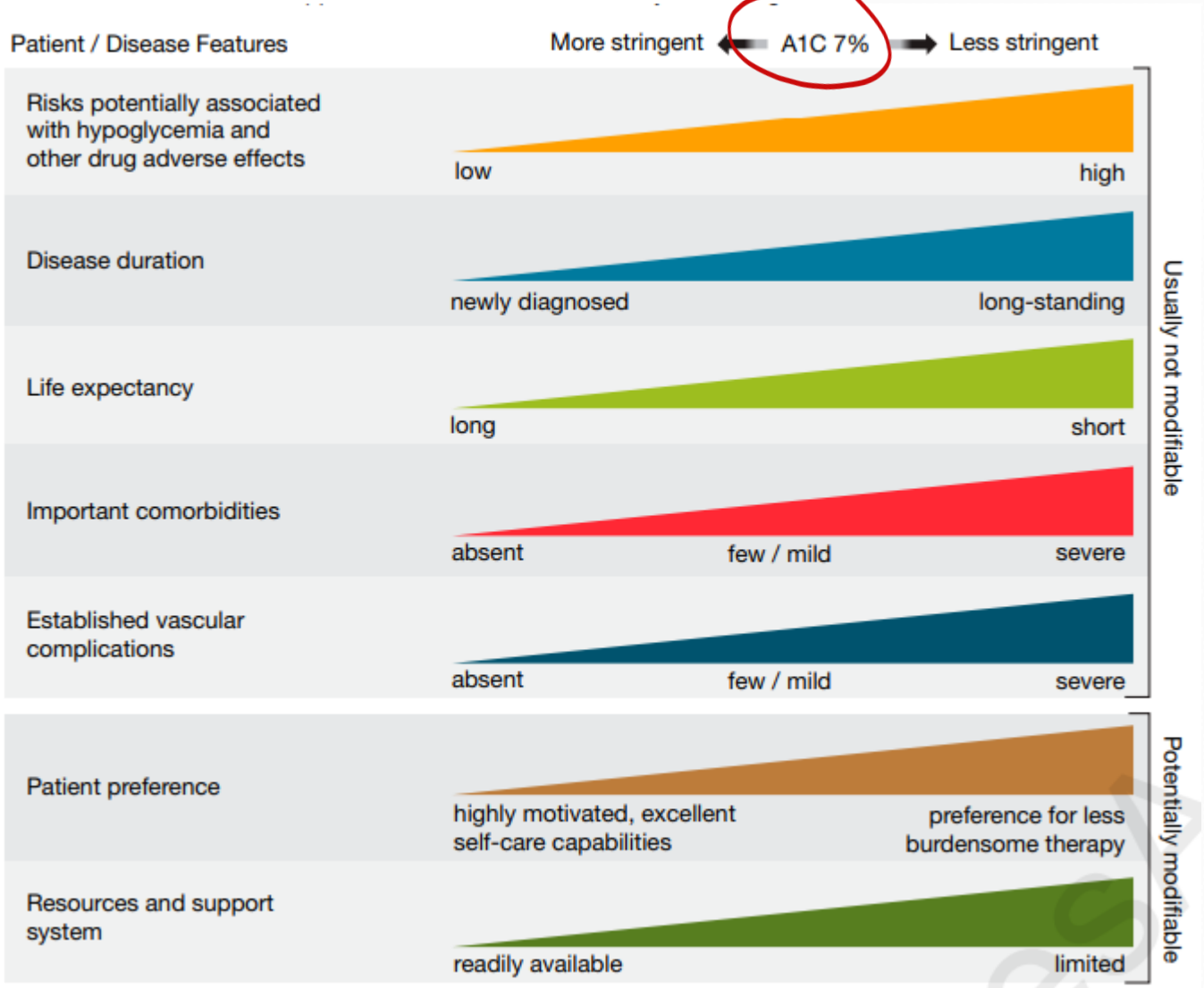


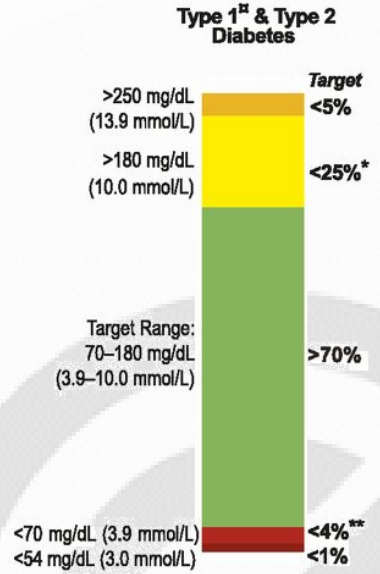
Figure 2: **Primary and secondary kidney outcomes**

Zoungas S, et al. Collaborators on Trials of Lowering Glucose (CONTROL) group. Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials. Lancet Diabetes Endocrinol. 2017 Jun;5(6):431-437.

Γλυκαιμικοί Στόχοι

Lowering blood glucose itself helps prevent CKD and its progression.





6.6 Achievement of lower A1C levels than goal of 7% may be acceptable and even beneficial if it can be achieved safely without significant hypoglycemia or other adverse effects.

Παράγοντες που καθορίζουν τον άριστο γλυκαιμικό στόχο. Η επίδραση των αντιυπεργλυκαιμικών φαρμάκων στην ΧΝΝ λήφθηκε υπόψιν κατά τον προσδιορισμό του άριστου γλυκαιμικού στόχου.

NA ElSayed et al; on behalf of the American Diabetes Association, Summary of Revisions: *Standards of Care in Diabetes—2023*. *Diabetes Care* 1 January 2023; 46 (Supplement_1): S5–S9

EASD
The European Association for the Study of Diabetes

American Diabetes Association.

KDIGO
KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES

GUIDELINES

+CKD

eGFR <60 mL/min per 1.73 m^2 OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). These measurements may vary over time; thus, a repeat measure is required to document CKD.

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

PREFERABLY

SGLT2i[§] with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m^2; once initiated should be continued until initiation of dialysis or transplantation

OR

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

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

First-line drug therapy

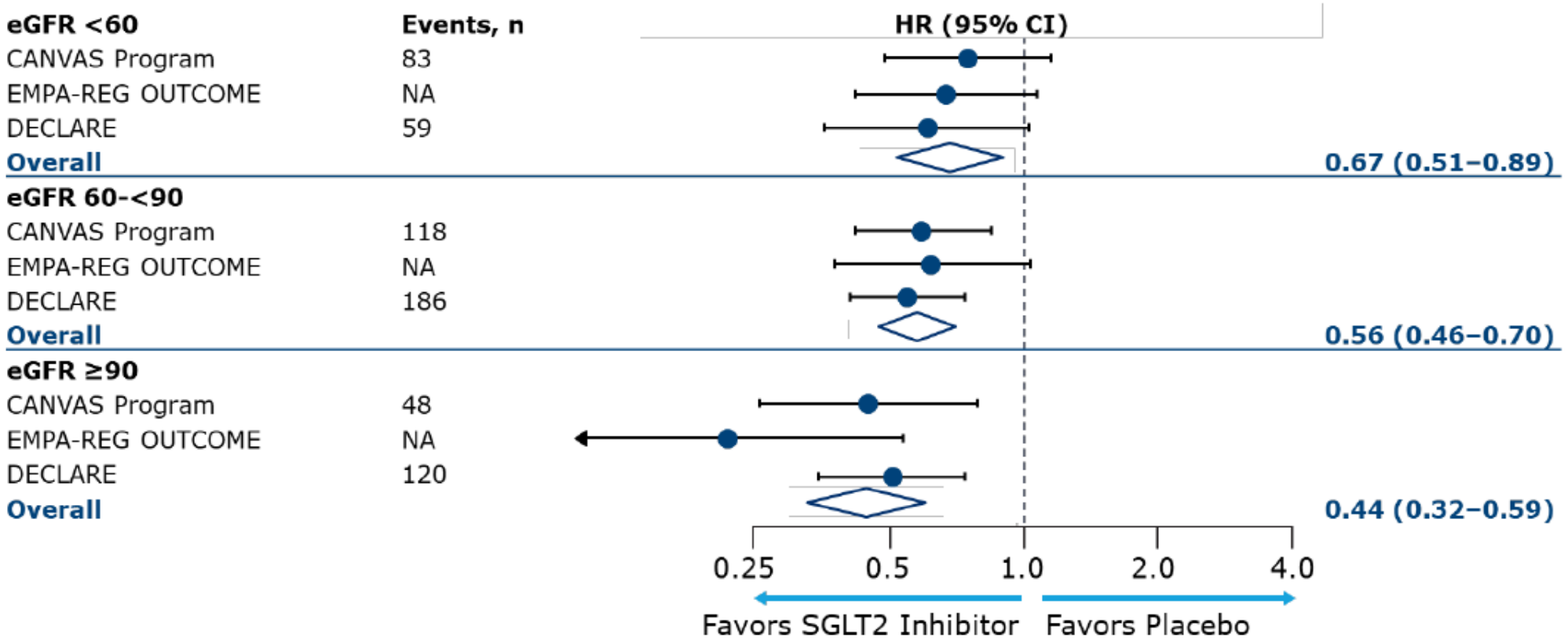
SGLT2i
(Initiate eGFR ≥20; continue until dialysis or transplant)

Metformin
(if eGFR ≥30)

CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (mL/min/1.73 m^2) Description and range	G1	Normal to high	≥90	1 if CKD	Treat 1	Refer* 2
	G2	Mildly decreased	60-89	1 if CKD	Treat 1	Refer* 2
	G3a	Mildly to moderately decreased	45-59	Treat 1	Treat 2	Refer 3
	G3b	Moderately to severely decreased	30-44	Treat 2	Treat 3	Refer 3
	G4	Severely decreased	15-29	Refer* 3	Refer* 3	Refer 4+
	G5	Kidney failure	<15	Refer 4+	Refer 4+	Refer 4+

Υποαναλύσεις των μελετών καρδιαγγειακών εκβάσεων των SGLT2i έχουν προτείνει πιθανά νεφρικά οφέλη των φαρμάκων αυτών.

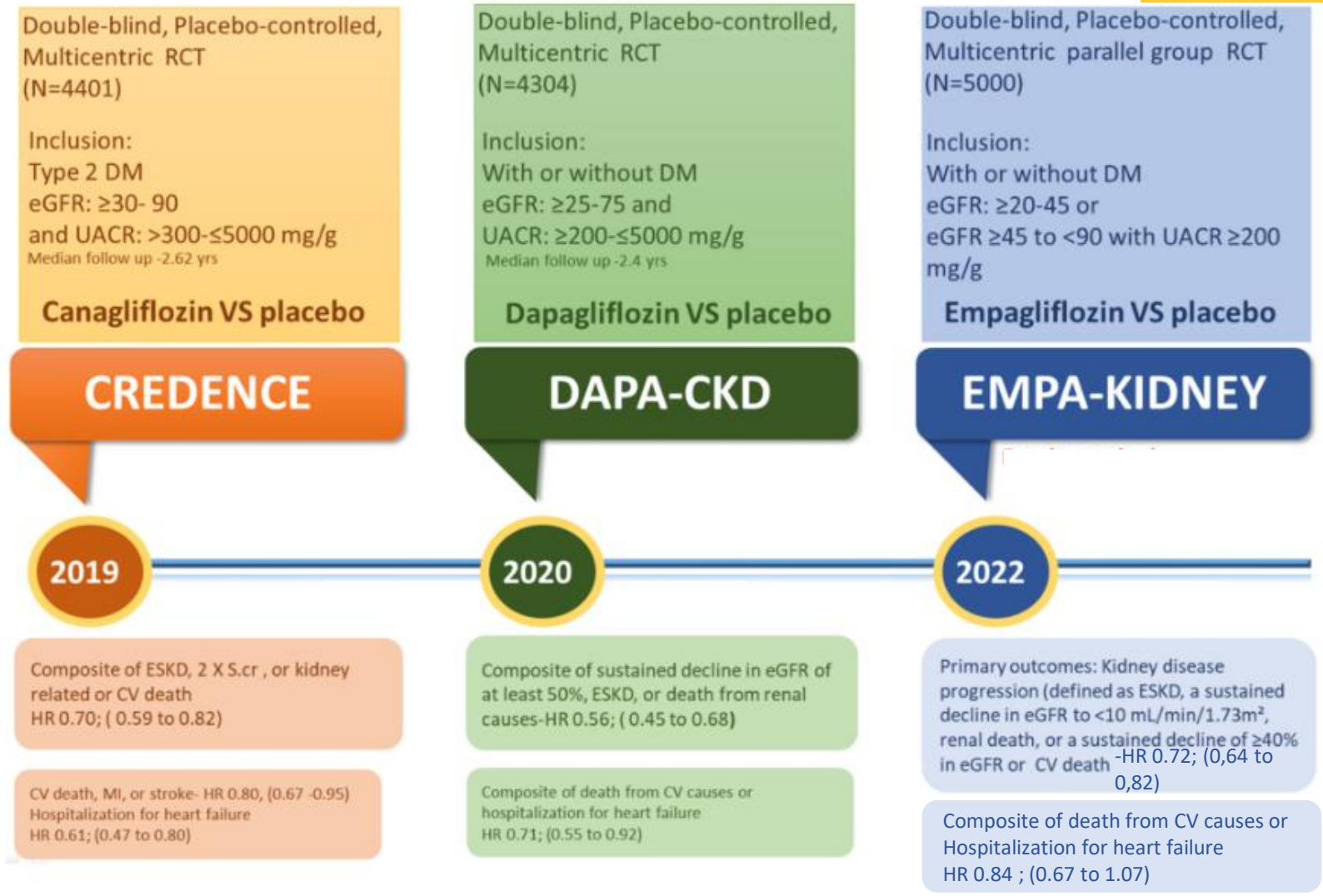
Composite of worsening of renal function, ESKD, or renal death



Zelniker TA, et al. *Lancet.* 2019;393(10166):31-39.

SGLT2i Kidney Outcomes Trials in Patients with T2DM

SGLT2i Kidney Outcomes Trials in Patients with T2DM



EASD
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American Diabetes Association

KDIGO
KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES

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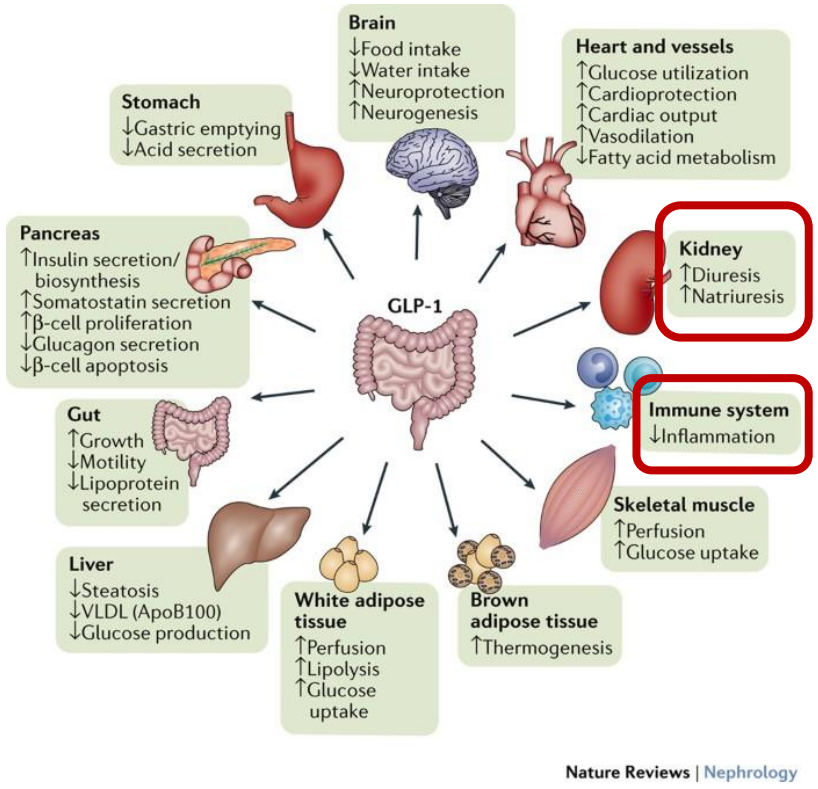
	G4	Severely decreased	15-29	Refer* 3	Refer* 3	Refer 4+
	G5	Kidney failure	<15	Refer 4+	Refer 4+	Refer 4+

Μια σειρά από πειραματικές μελέτες έχουν αναδείξει ευεργετικές επιδράσεις των GLP-1RA στη Διαβητική Νεφρική Νόσο ανεξάρτητες από τα υπογλυκαιμικά αποτελέσματα.

GLP-1RA σε ΣΔΤ2 και ΧΝΝ – νεφρικό όφελος



	ELIXA	LEADER	SUSTAIN	EXSCEL	HARMONY	REWIND	PIONEER 6	AMPLITUDE-O	AWARD-7
Drug	Lixisenatide	Liraglutide	Semaglutide	Exenatide	Albiglutide	Dulaglutide	Semaglutide (oral)	Efpeglenatide	Dulaglutide
Total number of participants	6068	9340	3297	14,752	9463	9901	3183	4076	577
% with CVD	100	81.3	83	73	100	31.5	84.7	89.6	Not reported
eGFR criteria for enrollment (ml/min per 1.73 m²)	≥30	Most had eGFR ≥30, but did include 220 patients with eGFR 15 to 30	Not reported	≥30	≥30	≥15	≥30 (however 0.9% had eGFR <30)	25–59.9	Not reported
Mean eGFR at enrollment (ml/min per 1.73 m²)	76	80	~75	76	79	76.9	74	72.4	38
% with eGFR <60 ml/min per 1.73 m²	23	20.7 with eGFR 30 to 59 ml/min per 1.73 m², 2.4 with eGFR <30 ml/min per 1.73 m²	28.5	22.9	Not reported	22.2	26.9	31.6	100 with CKD G3a–G4
ACR	19% with moderately increased albuminuria and 7% with severely increased albuminuria	Not reported	Not reported	3.5% with severely increased albuminuria	Not reported	7.9% with severely increased albuminuria	Not reported	Median 28.3 mg/g [2.83 mg/mmol]	44% with severely increased albuminuria
Follow-up time (yr)	2.08	3.8	2.1	3.2	1.6	5.4	1.36	1.81	1
CV outcome definition	CV death, MI, stroke, or hospitalization for unstable angina	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	MACE	NA
CV outcome results	HR: 1.02; 95% CI: 0.89–1.17	HR: 0.87; 95% CI: 0.78–0.97	HR: 0.74; 95% CI: 0.58–0.95	HR: 0.91; 95% CI: 0.83–1.00	HR: 0.78; 95% CI: 0.68–0.90	HR: 0.88; 95% CI: 0.79–0.99	HR: 0.79; 95% CI: 0.57–1.11	HR: 0.73; 95% CI: 0.58–0.92	NA
Kidney outcome (secondary end points)	New-onset severely increased albuminuria and doubling of SCr	New-onset persistent severely increased albuminuria, persistent doubling of the SCr level, kidney failure, or death due to kidney disease	Persistent severely increased albuminuria, persistent doubling of SCr, a CrCl of <45 ml/min, or need for KRT	Two kidney composite outcomes: 1) 40% eGFR decline, kidney replacement, or renal death, 2) 40% eGFR decline, kidney replacement, renal death, or severely increased albuminuria	Not reported	New severely increased albuminuria ACR of >33.9 mg/mmol [>339 mg/g], a sustained fall in eGFR of 30% from baseline, or use of KRT	Not reported	Composite of incident severely increased albuminuria (ACR >300 mg/g or >33.9 mg/mmol), increase in ACR ≥30%, sustained decrease in eGFR by ≥40% for ≥30 days, or kidney replacement therapy for ≥90 days, or a sustained eGFR of <15 ml/min per 1.73 m² for ≥30 days	eGFR, ACR
Kidney outcome results	New-onset macroalbuminuria: adjusted HR: 0.81; 95% CI: 0.66–0.99, *P*=0.04; Doubling of SCr: adjusted HR: 1.16; 95% CI: 0.74–1.83, *P*=0.51	HR: 0.78; 95% CI: 0.67–0.92	HR: 0.64; 95% CI: 0.46–0.88	40% eGFR decline, kidney replacement, or renal death: adjusted HR: 0.87; 95% CI: 0.73–1.04, *P*=0.13; 40% eGFR decline, kidney replacement, renal death, or severely increased albuminuria: adjusted HR: 0.85; 95% CI: 0.74–0.98, *P*=0.03	Not reported	HR: 0.85; 95% CI: 0.77–0.93 Similar for eGFR ≥60 vs. <60 ml/min per 1.73 m², no albuminuria vs. albuminuria, no ACEi/ARB vs. ACEi/ARB	Not reported	Kidney composite outcome: HR: 0.68; 95% CI: 0.57–0.79	eGFR did not significantly decline (–0.7 ml/min per 1.73 m²) with dulaglutide 1.5 mg or dulaglutide 0.75 mg, whereas eGFR decreased by –3.3 ml/min per 1.73 m² with insulin glargine

Figure 28| Cardiovascular and kidney outcome trials for glucagon-like peptide-1 receptor agonists (GLP-1 RA). ACEi, angiotensin-converting enzyme inhibitor; ACR, albumin–

Daiji Kawanami D et al. GLP-1 Receptor Agonists in Diabetic Kidney Disease: From Clinical Outcomes to Mechanisms. Front. Pharmacol. 2020.

GLP-1RA Kidney Outcomes Trials in Patients with T2DM

GLP-1RA Kidney Outcomes Trials in Patients with T2DM

FLOW

semaglutide | renal outcomes trial

company announcement

Novo Nordisk will stop the once-weekly injectable semaglutide kidney outcomes trial, FLOW, based on interim analysis

Bagsværd, Denmark, 10 October 2023 – Novo Nordisk today announced the decision to stop the kidney outcomes trial FLOW (Effect of semaglutide versus placebo on the progression of renal impairment in people with type 2 diabetes and chronic kidney disease).

The decision to stop the trial is based on a recommendation from the independent Data Monitoring Committee (DMC) concluding that the results from an interim analysis met certain pre-specified criteria for stopping the trial early for efficacy.

Based on the decision to stop the trial at interim, the process of closing the trial will be initiated. To protect the integrity of the trial, Novo Nordisk remains blinded to the results until trial completion. Novo Nordisk expects that FLOW will read out during the first half year of 2024.

Με στόχο την πρωτογενή πρόληψη ΔΝΝ→

Όλες οι κατευθυντήριες οδηγίες συστήνουν επίτευξη του στόχου HbA1c<7% ή χαμηλότερα αν αυτό μπορεί να γίνει με ασφάλεια.

Με στόχο τη 2ογενή πρόληψη ΔΝΝ→

Όλες οι κατευθυντήριες οδηγίες προκρίνουν την έναρξη χορήγησης SGLT2i σε ασθενείς με ΣΔΤ2 και ΧΝΝ με eGFR≥20 ml/min/1,73m^2

Επί αδυναμίας χορήγησης SGLT2i, μη επίτευξης γλυκαιμικού στόχου ή συννοσηροτήτων συστήνουν τη χορήγηση GLP-1RA.

- ❖Χορήγηση SGLT2i σε ασθενείς με ΣΔΤ1 και ΔΝΝ?
- ❖Χορήγηση GLP-1RA σε ασθενείς με ΣΔΤ1 και ΔΝΝ?
- ❖Επιλογή κατηγορίας αντιδιαβητικού παράγοντα με στόχο την 1ογενη πρόληψη της ΔΝΝ?

Εφαρμόζονται οι κατευθυντήριες οδηγίες;

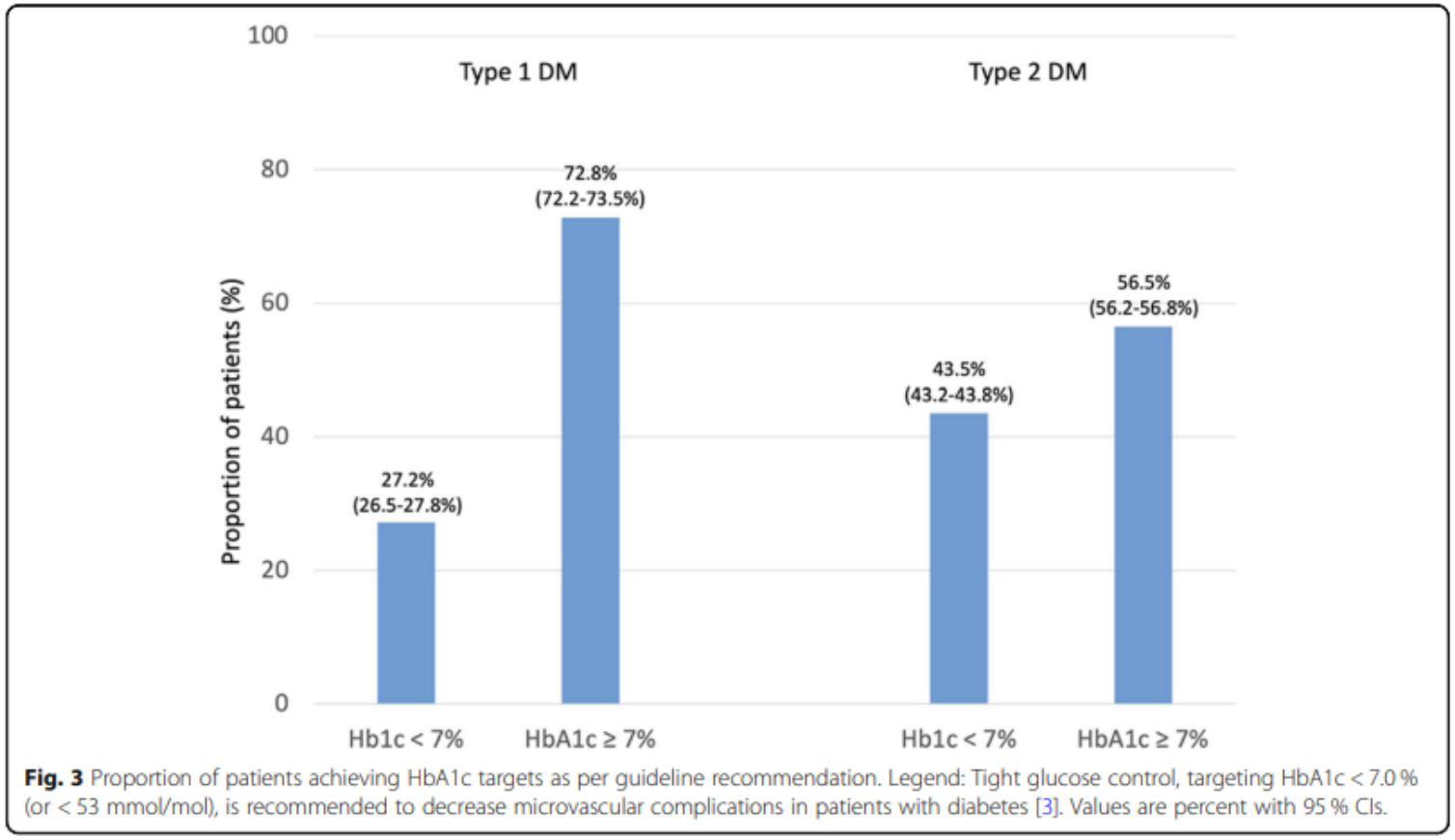


Fig. 3 Proportion of patients achieving HbA1c targets as per guideline recommendation. Legend: Tight glucose control, targeting HbA1c < 7.0 % (or < 53 mmol/mol), is recommended to decrease microvascular complications in patients with diabetes [3]. Values are percent with 95 % CIs.

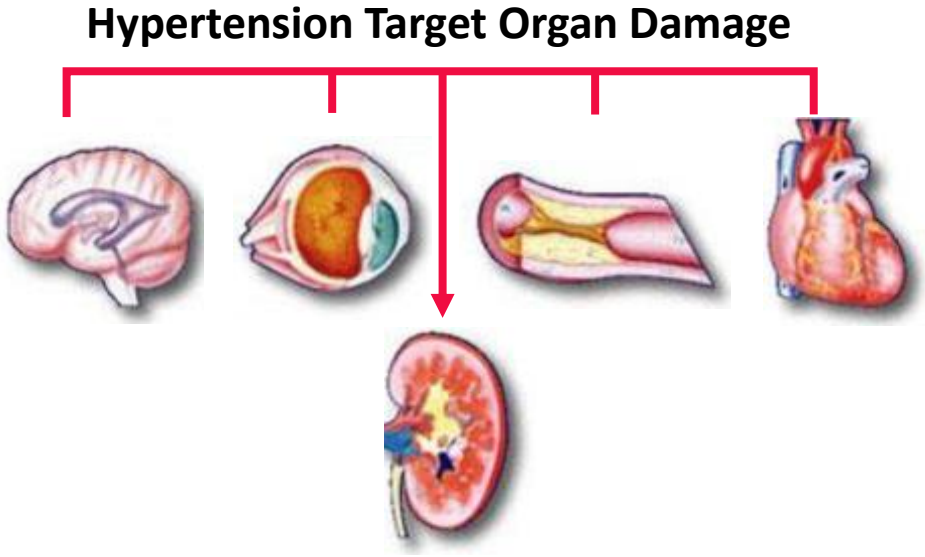
Bramlage P. *et al.* Guidelines adherence in the prevention and management of chronic kidney disease in patients with diabetes mellitus on the background of recent European recommendations – a registry-based analysis. *BMC Nephrol* **22**, 184 (2021).

Αρτηριακή Υπέρταση (Ι)

Οι νεφροί αποτελούν ένα από τα όργανα στόχους της Αρτηριακής Υπέρτασης

Η υψηλή Αρτηριακή Πίεση, μαζί με το ΣΔ, αναγνωρίζονται παγκοσμίως ως οι κύριες αιτίες ΧΝΝ και ΤΣΝΑ.

Αποτελεί ταυτόχρονα αιτία ΧΝΝ και επιπλοκή της ΔΝΝ.



AH related kidney damage: microalbuminuria and reduction of glomerular filtration rate:
- Endothelial dysfunction
- Increased oxidative stress
- Increased arterial stiffness

increase of the glomerular hydrostatic pressure and of permeability of the glomerular membrane

Cortese F et al. Vascular, cardiac and renal target organ damage associated to arterial hypertension: which noninvasive tools for detection? J Hum Hypertens 34, 420–431 (2020).

Αρτηριακή Υπέρταση (Ι)

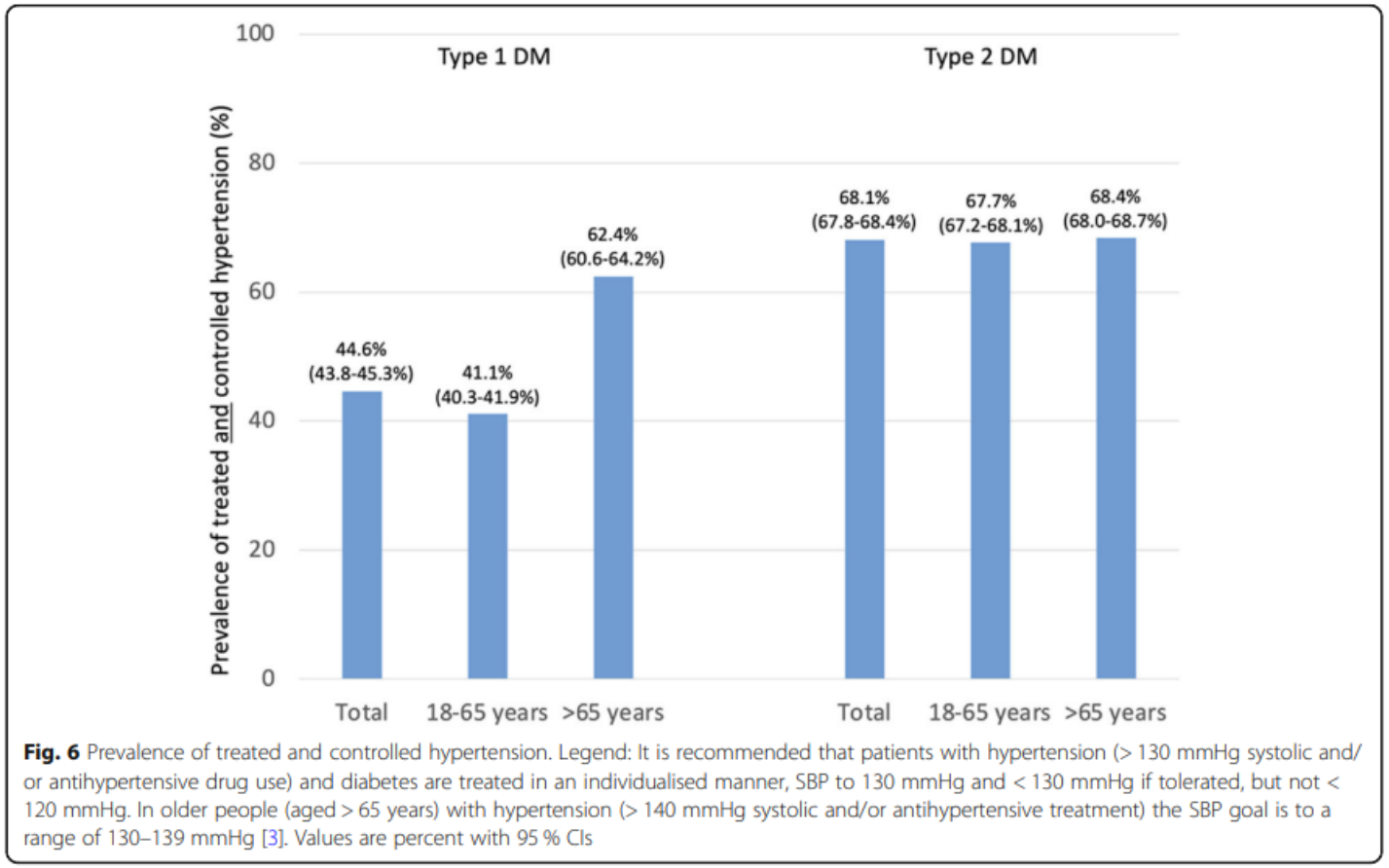


Fig. 6 Prevalence of treated and controlled hypertension. Legend: It is recommended that patients with hypertension (> 130 mmHg systolic and/or antihypertensive drug use) and diabetes are treated in an individualised manner, SBP to 130 mmHg and < 130 mmHg if tolerated, but not < 120 mmHg. In older people (aged > 65 years) with hypertension (> 140 mmHg systolic and/or antihypertensive treatment) the SBP goal is to a range of 130–139 mmHg [3]. Values are percent with 95 % CIs

Bramlage P. *et al.* Guidelines adherence in the prevention and management of chronic kidney disease in patients with diabetes mellitus on the background of recent European recommendations – a registry-based analysis. *BMC Nephrol* **22**, 184 (2021).

Classification of office BP and definitions of hypertension grade

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	< 120	and	< 80
Normal	120–129	and/or	80–84
High normal	130–139	and/or	85–89
Grade 1 hypertension	140–159	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥ 180	and/or	≥ 110
Isolated systolic hypertension	≥ 140	and	< 90

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Summary of office BP thresholds for treatment

Age group	Office SBP treatment threshold (mmHg)					Office DBP treatment threshold (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/TIA	
18–65 years	≥ 140	≥ 140	≥ 140	≥ 140	≥ 140	≥ 90
65–79 years	≥ 140	≥ 140	≥ 140	≥ 140	≥ 140	≥ 90
≥ 80 years	≥ 160	≥ 160	≥ 160	≥ 160	≥ 160	≥ 90
Office DBP treatment threshold (mmHg)	≥ 90	≥ 90	≥ 90	≥ 90	≥ 90	

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Office BP treatment target range

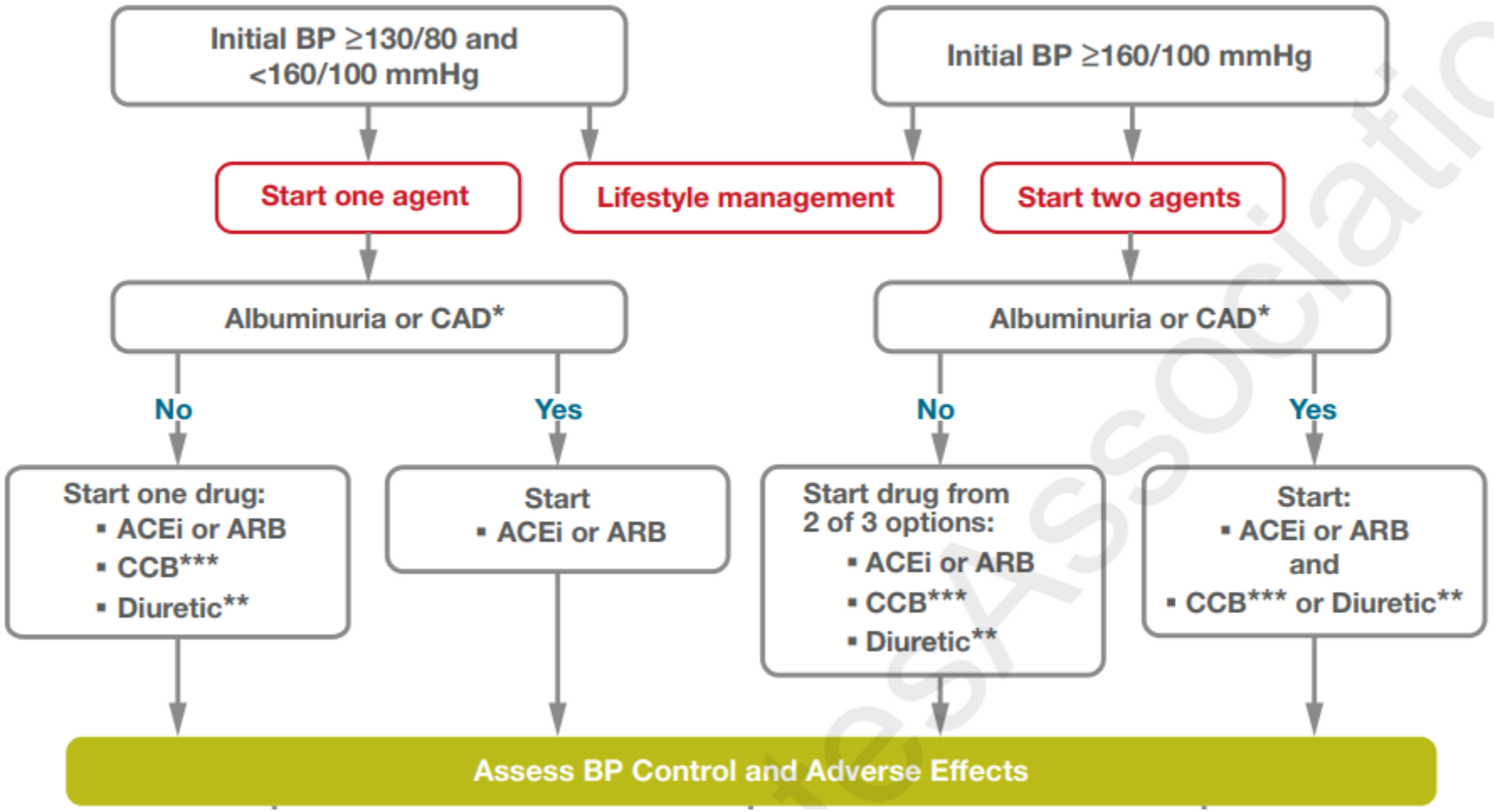
Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/TIA	
18–65 years	**Target to 130** *or lower if tolerated* Not < 120	**Target to 130** *or lower if tolerated* Not < 120	**Target to < 140 to 130** *if tolerated*	**Target to 130** *or lower if tolerated* Not < 120	**Target to 130** *or lower if tolerated* Not < 120	70-79
65–79 years	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	70-79
≥ 80 years	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	70-79
Office DBP treatment target range(mmHg)	70-79	70-79	70-79	70-79	70-79	

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Treatment strategies in people with diabetes

Recommendations	Class	Level
Antihypertensive drug treatment is recommended for people with diabetes when office BP is ≥ 140/90 mmHg.	I	A
In people with diabetes receiving BP-lowering drugs it is recommended:		
• To target SBP to 130 mmHg and lower, if tolerated, but not lower than 120 mmHg.	I	A
• In older people (aged ≥ 65 years), to target to an SBP range of 130 - 139 mmHg.	I	A
• To target the DBP to < 80 mmHg, but not lower than 70 mmHg.	I	C
It is recommended to initiate treatment with a combination of a RAS blocker with a CCB or thiazide/thiazide-like diuretic.	I	A
Simultaneous administration of two RAS blockers, e.g. and ACE inhibitor and ARB, is not indicated.	III	A

Recommendations for the Treatment of Confirmed Hypertension in People With Diabetes



Standards of Care in Diabetes—2023. *Diabetes Care* 1 January 2023; 46 (Supplement_1): S5–S9

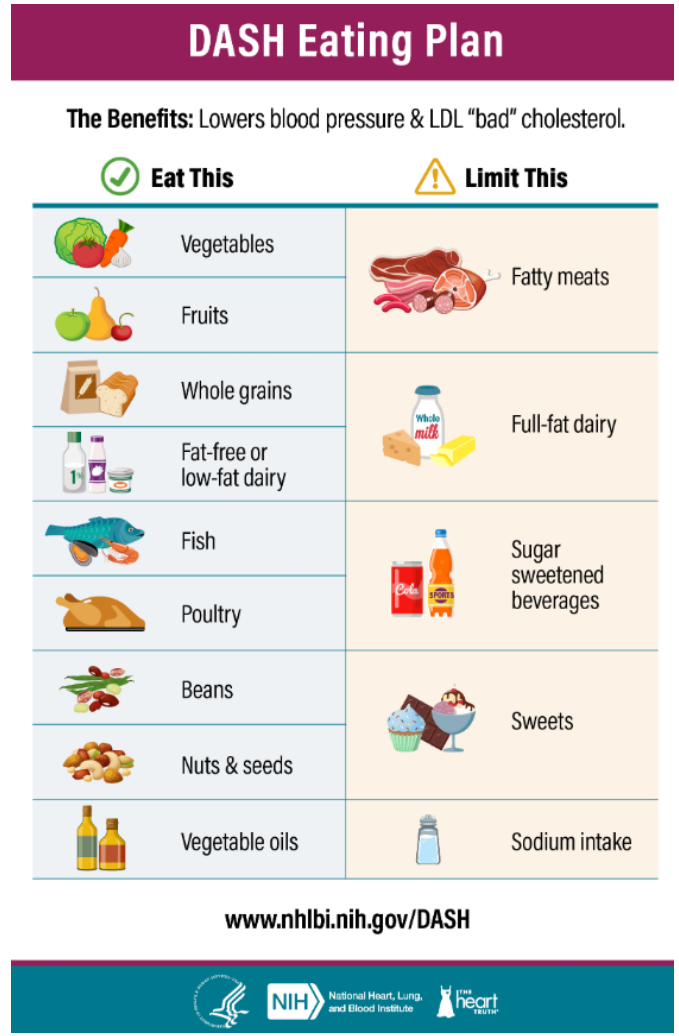
Παρεμβάσεις στον τρόπο ζωής (I) (Lifestyle Management)

Αν η ΣΑΠ>120 mmHg και η ΔΑΠ> 80 mmHg τότε απαιτούνται:

- Απώλεια Βάρους (παχύσαρκους/υπέρβαρους)
- Δίαιτα τύπου DASH(Dietary Approaches to Stop Hypertension)
- Περιορισμός της κατανάλωσης αλκοόλ
- Αύξηση σωματικής δραστηριότητας
- Διακοπή Καπνίσματος

DASH Eating Plan—Number of Food Servings by Calorie Level

Food Group	1,200 Cal.	1,400 Cal.	1,600 Cal.	1,800 Cal.	2,000 Cal.	2,600 Cal.	3,100 Cal.
Grains[a]	4–5	5–6	6	6	6–8	10–11	12–13
Vegetables	3–4	3–4	3–4	4–5	4–5	5–6	6
Fruits	3–4	4	4	4–5	4–5	5–6	6
Fat-free or low-fat dairy products[b]	2–3	2–3	2–3	2–3	2–3	3	3–4
Lean meats, poultry, and fish	3 or less	3–4 or less	3–4 or less	6 or less	6 or less	6 or less	6–9
Nuts, seeds, and legumes	3 per week	3 per week	3–4 per week	4 per week	4–5 per week	1	1
Fats and oils[c]	1	1	2	2–3	2–3	3	4
Sweets and added sugars	3 or less per week	3 or less per week	3 or less per week	5 or less per week	5 or less per week	≤2	≤2
Maximum sodium limit[d]	2,300 mg/day	2,300 mg/day	2,300 mg/day	2,300 mg/day	2,300 mg/day	2,300 mg/day	2,300 mg/day



Standards of Care in Diabetes—2023. *Diabetes Care* 1 January 2023; 46 (Supplement_1): S5–S9

Παρεμβάσεις στον Τρόπο Ζωής (Lifestyle Management)

- Μείωση Αρτηριακής πίεσης
- Καθυστέρηση της εξέλιξης σε Αρτηριακή Υπέρταση
- Ενίσχυση των αποτελεσμάτων των αντιυπερτασικών φαρμάκων
- Ευνοϊκή επίδραση σε μεταβολική και αγγειακή υγεία
- ↓ Κινδύνου εμφάνισης επιπλοκών (συμπεριλαμβανομένης και της ΔΝΝ)

Όλες οι κατευθυντήριες οδηγίες προκρίνουν την τη χρήση ΑΜΕΑ ή ΑΤΙΙ για ασθενείς με ΣΔ και ΑΥ και αλβουμινουρία (δευτερογενής πρόληψη) και την παράλληλη εφαρμογή παρεμβάσεων στον τρόπο ζωής.

Ορισμένες κατευθυντήριες οδηγίες προκρίνουν τη χρήση ΑΜΕΑ ή ΑΤΙΙ και για ασθενείς με ΣΔ και ΑΥ χωρίς αλβουμινουρία.

Χορήγηση Αντιυπερτασικών φαρμάκων της κατηγορίας των ΑΜΕΑ ή ΑΤΙΙ σε ασθενείς με ΣΔ και ΧΝΝ χωρίς ΑΥ.

Χορήγηση Αντιυπερτασικών φαρμάκων σε ασθενείς με ΣΔ χωρίς ΑΥ – χωρίς ΧΝΝ?

Όλες οι κατευθυντήριες οδηγίες προκρίνουν την τη χρήση ΑΜΕΑ ή ΑΤΙΙ για ασθενείς με ΣΔ και ΑΥ και αλβουμινουρία (δευτερογενής πρόληψη) και την παράλληλη εφαρμογή παρεμβάσεων στον τρόπο ζωής.

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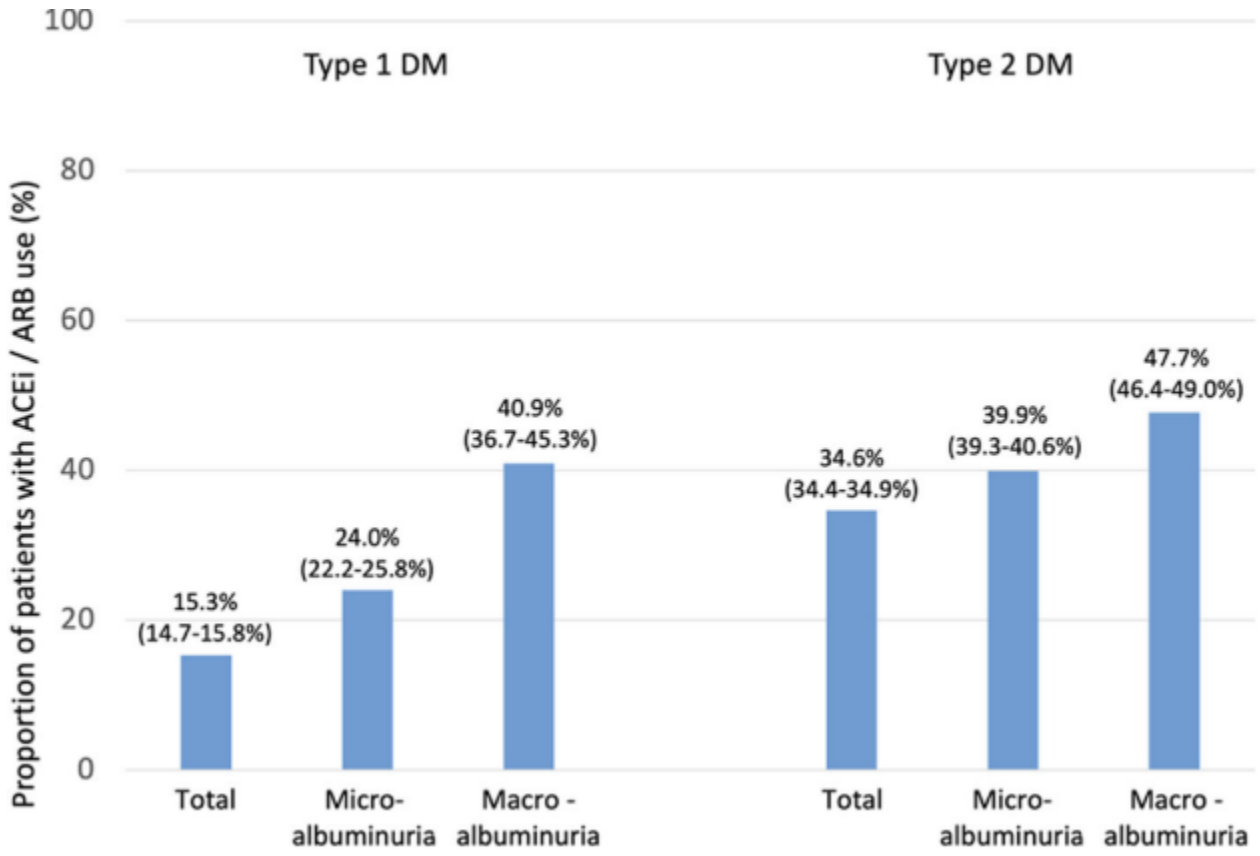
Χορήγηση Αντιυπερτασικών φαρμάκων της κατηγορίας των ΑΜΕΑ ή ΑΤΙΙ σε ασθενείς με ΣΔ και ΧΝΝ χωρίς ΑΥ.

Χορήγηση Αντιυπερτασικών φαρμάκων σε ασθενείς με ΣΔ χωρίς ΑΥ – χωρίς ΧΝΝ?

Εφαρμόζονται οι κατευθυντήριες οδηγίες;



Bramlage P. *et al.* Guidelines adherence in the prevention and management of chronic kidney disease in patients with diabetes mellitus on the background of recent European recommendations – a registry-based analysis. *BMC Nephrol* **22**, 184 (2021).

Δυσλιπιδαιμία και ΔΝΝ

ΣΥΣΧΕΤΙΣΕΙΣ

↑TGL και ↓HDL έχουν συσχετισθεί με την εμφάνιση αλβουμινουρίας

↑ TGL με ↓ του eGFR

↑ LDL-C με ↑ACR.

ΓΕΓΟΝΟΤΑ

Συσσώρευση λιπιδίων στα επιθηλιακά κύτταρα των νεφρικών σωληναρίων προκαλεί λιποτοξικότητα και ίνωση.

Η διαβητική δυσλιπιδαιμία επιταχύνει την εξέλιξη της ΔΝΝ.

ΚΛΙΝΙΚΕΣ ΜΕΛΕΤΕΣ

Η διαβητική δυσλιπιδαιμία ↑ τον CVD κίνδυνο ασθενών με ΔΝΝ

Οι στατίνες ↓ των CVD κίνδυνο ασθενών με ΔΝΝ.

Η φαινοφιμπράτη ↓ τον CDV κίνδυνο, την αλβουμινουρία και την 5ετή απώλεια eGFR σε ασθενείς με ΣΔ (αν και στην αρχή προκαλεί ήπια αλλά αναστρέψιμη αύξηση της Cr).

IN VITRO ΜΕΛΕΤΕΣ

Πλειοτρόπες νεφροπροστατευτικές δράσεις στατινών και φιμπρατών (αντιοξειδωτικές, αντιινωτικές, αντιφλεγμονώδεις) ανεξάρτητες από τις υπολιπιδαιμικές τους δράσεις.

M Kitada et al. Clinical therapeutic strategies for early stage of diabetic kidney disease. World J Diabetes. 2014 Jun 15; 5(3): 342–356.

Table 4 **Cardiovascular risk categories**

Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. DM with target organ damage,[a] or at least three major risk factors, or early onset of T1DM of long duration (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.
High-risk	People with: Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage,[a] with DM duration ≥10 years or another additional risk factor. Moderate CKD (eGFR 30–59 mL/min/1.73 m^2). A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors. Calculated SCORE ≥1 % and <5% for 10-year risk of fatal CVD.
Low-risk	Calculated SCORE <1% for 10-year risk of fatal CVD.

Table 7 **Treatment targets and goals for cardiovascular disease prevention**

Smoking	No exposure to tobacco in any form.
Diet	Healthy diet low in saturated fat with a focus on wholegrain products, vegetables, fruit, and fish.
Physical activity	3.5–7 h moderately vigorous physical activity per week or 30–60 min most days.
Body weight	BMI 20–25 kg/m^2, and waist circumference <94 cm (men) and <80 cm (women).
Blood pressure	<140/90 mmHg.[a]
LDL-C	**Very-high risk in primary or secondary prevention:** A therapeutic regimen that achieves ≥50% LDL-C reduction from baseline[b] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL). No current statin use: this is likely to require high-intensity LDL-lowering therapy. Current LDL-lowering treatment: an increased treatment intensity is required. **High risk:** A therapeutic regimen that achieves ≥50% LDL-C reduction from baseline[b] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL). **Moderate risk:** A goal of <2.6 mmol/L (<100 mg/dL). **Low risk:** A goal of <3.0 mmol/L (<116 mg/dL).
Non-HDL-C	Non-HDL-C secondary goals are <2.2, 2.6, and 3.4 mmol/L (<85, 100, and 130 mg/dL) for very-high-, high-, and moderate-risk people, respectively.
ApoB	ApoB secondary goals are <65, 80, and 100 mg/dL for very-high-, high-, and moderate-risk people, respectively.
Triglycerides	No goal, but <1.7 mmol/L (<150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
Diabetes	HbA1c: <7% (<53 mmol/mol).

Apo = apolipoprotein; BMI = body mass index; HbA1c = glycated haemoglobin; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.
[a]Lower treatment targets are recommended for most treated hypertensive patients, provided that the treatment is well tolerated.[118]
[b]The term 'baseline' refers to the LDL-C level in a person not taking any lipid-lowering medication, or to the extrapolated baseline value for those who are on current treatment.

Κάπνισμα

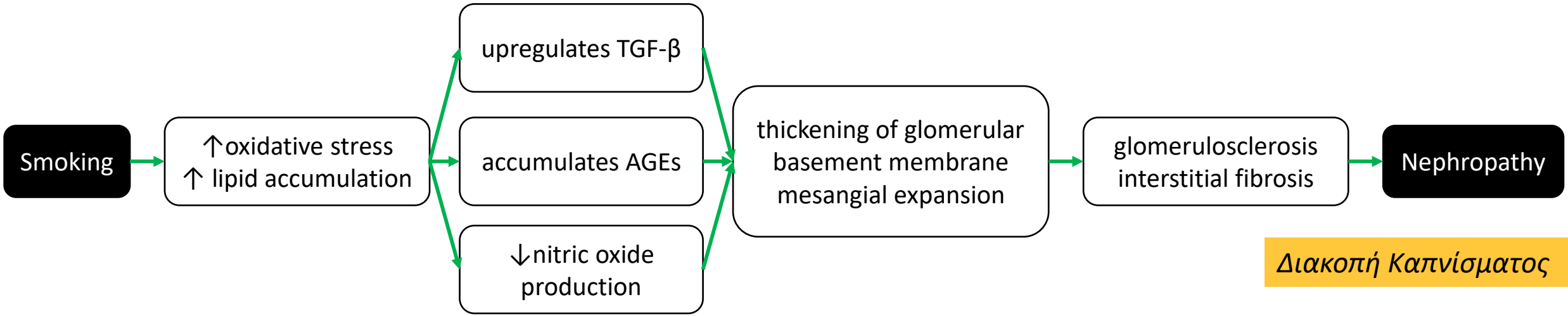
Στο γενικό πληθυσμό
↑απέκκριση αλβουμίνης στα ούρα (ακόμα και κάτω από το όριο της αλβουμινουρίας) → σε νορμοτασικούς και σε μη διαβητικούς
↑κίνδυνο έκπτωσης της νεφρικής λειτουργίας (άνδρες και ηλικιωμένους)

Ασθενείς με ΑΥ

Ανεξάρτητος παράγοντας κινδύνου αλβουμινουρίας

Ασθενείς με ΣΔΤ1/ΣΔΤ2
↑κίνδυνο διαβητικής νεφροπάθειας
↑κίνδυνο μικροαλβουμνουρίας
↑κίνδυνο εξέλιξης σε μακροαλβουμινουρία
Επιταχύνει την εξέλιξη σε νεφρική ανεπάρκεια (ανεξάρτητα από ηλικία και διάρκεια νόσου)

Ασθενείς με μη διαβητική νεφρική νόσο
↑κίνδυνο μακροαλβουμινουρίας
↑ κίνδυνο εξέλιξης σε ΤΣΝΑ



Διακοπή Καπνίσματος

Orth SR. Smoking and the kidney. J Am Soc Nephrol. 2002;13(6):1663-1672.
Chakkarwar VA. Smoking in diabetic nephropathy: sparks in the fuel tank? World J Diabetes 2012; 3(12): 186-195.

Περισσότεροι Τροποποιήσιμοι Παράγοντες Κινδύνου

Παχυσαρκία/ BMI

-Απώλεια Βάρους σε Υπέρβαρα και Παχύσαρκα άτομα
-Εφαρμογή Medical Nutrition Therapy
-Επιλογή αντιδιαβητικών φαρμάκων με ωφέλιμη/ουδέτερη επίδραση στο ΒΣ.

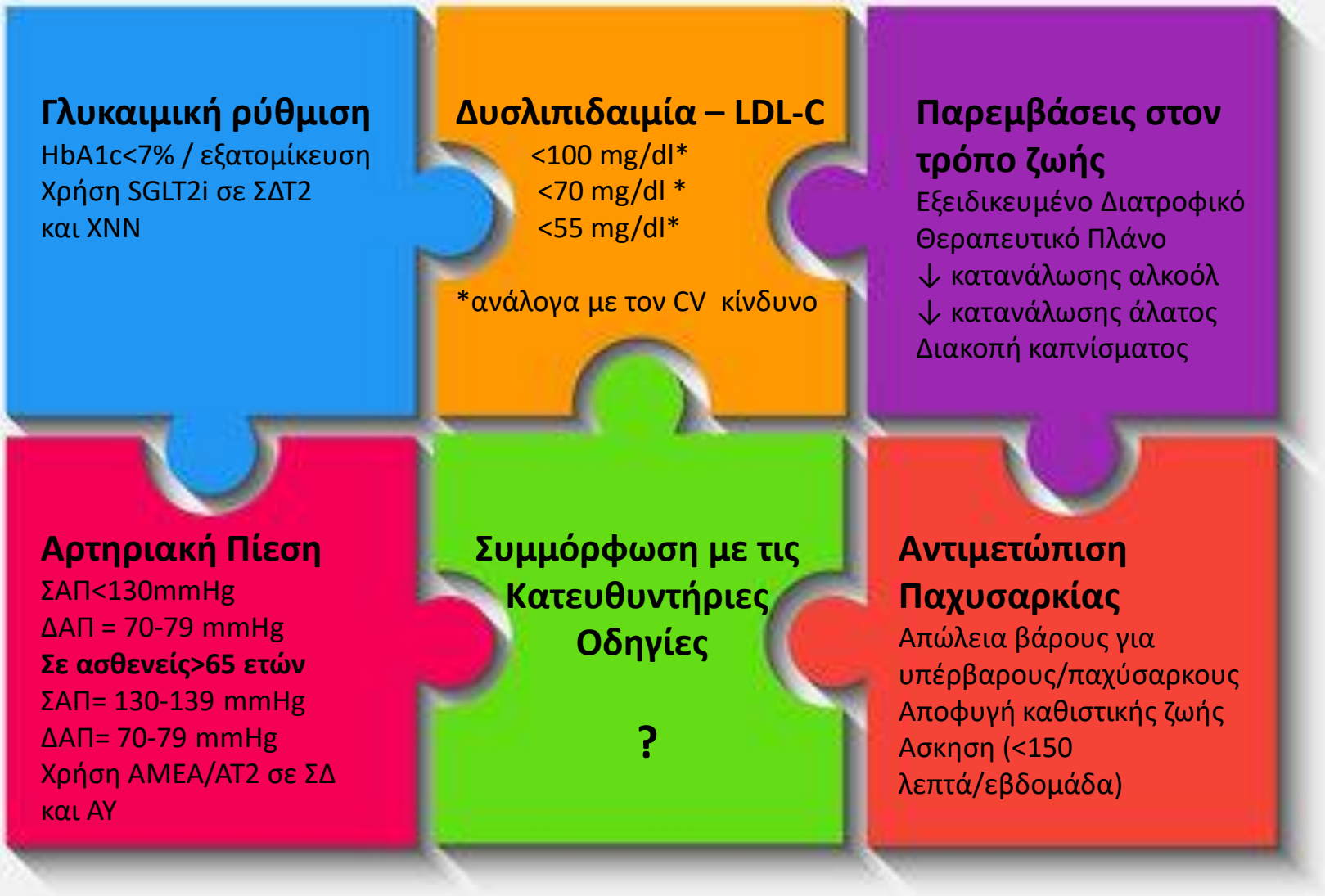
Σωματική Δραστηριότητα

-Μείωση της ΑΠ
-Βελτίωση λιπιδαιμικού προφίλ
-Βελτίωση γλυκαιμικής ρύθμισης
-Μείωση αντίστασης στην ινσουλίνη
-Βελτίωση ενδοθηλιακής λειτουργίας

AGEs

Απαιτούνται
-διατροφικές παρεμβάσεις (Όχι αναψυκτικά και τροφές μαγειρεμένες σε υψηλές θερμοκρασίες)
-καλή γλυκαιμική ρύθμιση

Πρωιμή (1ογενής και 2ογενής) πολυπαραγοντική παρέμβαση



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Genetic and epigenetic background of diabetic kidney disease

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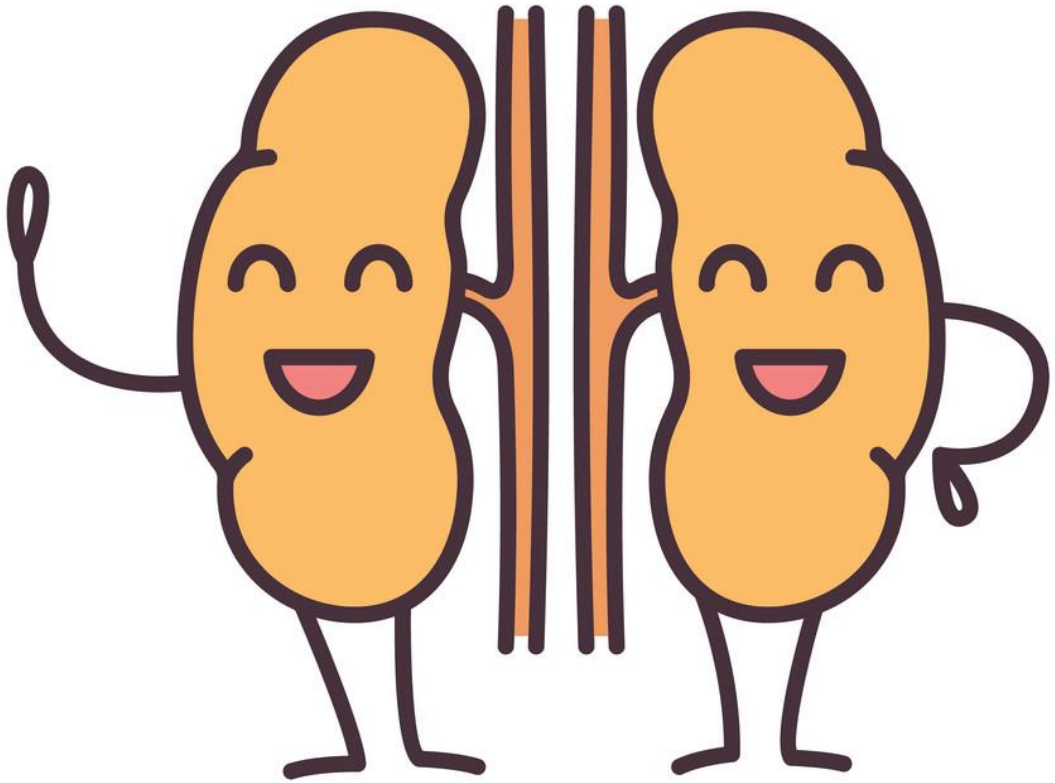
Diabetic kidney disease (DKD) is a severe diabetic complication that affects up to half of the individuals with diabetes. Elevated blood glucose levels are a key underlying cause of DKD, but DKD is a complex multifactorial disease, which takes years to develop. Family studies have shown that inherited factors also contribute to the risk of the disease. During the last decade, genome-wide association studies (GWASs) have emerged as a powerful tool to identify genetic risk factors for DKD. In recent years, the GWASs have acquired larger number of participants, leading to increased statistical power to detect more genetic risk factors. In addition, whole-exome and whole-genome sequencing studies are emerging, aiming to identify rare genetic risk factors for DKD, as well as epigenome-wide association studies, investigating DNA methylation in relation to DKD. This article aims to review the identified genetic and epigenetic risk factors for DKD.

KEYWORDS

diabetic kidney disease, kidney failure, GWAS, genome sequencing, exome sequencing, epigenetics, epigenome-wide association study, EWAS

Πρώιμη (1ογενής και 2ογενής) πολυπαραγοντική παρέμβαση

Η ευρύτερη χρήση των σκορ εκτίμησης γενετικού κινδύνου θα βοηθήσει στην αναγνώριση των πιο ευάλωτων – στην εμφάνιση ΔΝΝ – ασθενών.
Σε αυτές τους ασθενείς θα έχει ακόμη μεγαλύτερη αξία η πρώιμη 1ογενής πολυπαραγοντική παρέμβαση.



Thank you!