«Καρδιαγγειακή Νόσος,

Ρύθμιση και στόχος

Αρτηριακής Πίεσης»

Ρήγας Καλαϊτζίδης

Νεφρολόγος

Σάββατο 21 Οκτωβρίου 2023 και ώρα 09:00 - 09:20.

Δεν υπάρχει σύγκρουση συμφερόντων

1.<u>Ποιο από τα παρακάτω είναι το σωστό</u>:

α. Η μείωση της ΑΠ σε επίπεδα <130 mmHg σε ασθενείς με νεφρική νόσο μειώνει τη θνησιμότητα από κάθε αιτία

β. Ο στόχος ΑΠ για την πρωτεϊνουρική μη διαβητική ΧΝΝ είναι ίδιος και για ασθενείς με πρωτεϊνουρική διαβητική νεφρική νόσο

γ. Ο στόχος ΣΑΠ <130 mmHg και DBP <80 mmHg, σε ασθενείς με λευκωματουρία >30 mg/g με ή χωρίς διαβητική νεφρική νόσο εάν είναι καλά ανεκτός προστατεύει έναντι της εξέλιξής της

δ. Το α+β

ε. Όλα τα παραπάνω

2.<u>Ποιο από τα παρακάτω είναι το σωστό</u>:

α. Η επίτευξη των συνιστώμενων στόχων ΑΠ στη ΧΝΝ απαιτεί συνήθως θεραπεία συνδυασμού, η οποία θα πρέπει να αποτελείται από αναστολέα RAS με CCB ή θειαζιδικό διουρητικό, εάν τα επίπεδα του eGFR είναι 45 ml/min/1,73 m2 (Στάδια ΧΝΝ 3α)

β. Η μετάβαση από τη θεραπεία με θειαζιδικά σε διουρητικά της αγκύλης θα πρέπει να εξατομικεύεται σε ασθενείς με τιμές eGFR μεταξύ 30 και 45 ml/min/1,73m2

γ. Το α σωστό

δ. Όλα τα παραπάνω

3. <u>Ποιο από τα παρακάτω είναι λάθος;</u>

α. Στα άτομα με ΧΝΝ η επίπτωση της καρδιαγγειακής νόσου αυξάνει με το στάδιο της νεφρικής ανεπάρκειας

β. Στα άτομα με ΧΝΝ η επίπτωση της καρδιαγγειακής νόσου αυξάνει με την αύξηση της λευκωματουρίας

γ .Η επίπτωση της καρδιαγγειακής νόσου δεν σχετίζεται με το στάδιο της νεφρικής νόσου

δ. Οι ασθενείς με ΧΝΝ έχουν διπλάσιες πιθανότητες να εμφανίζουν καρδιαγγειακή νόσο σε σύγκριση με τα άτομα χωρίς ΧΝΝ

4. <u>Ποιο από τα παρακάτω είναι λάθος</u>;

α. Η νεφρική βλάβη από την επιθετική μείωση της ΑΠ είναι συνήθως αναστρέψιμη

β. Η επιθετική μείωση της ΑΠ στην ΧΝΝ προκαλεί μη αναστρέψιμη βλάβη του διάμεσου νεφρικού ιστού

γ. Η επιθετική μείωση της ΑΠ στην ΧΝΝ οδηγεί σε μείωση των καρδιαγγειακών συμβάματων και της θνητότητας

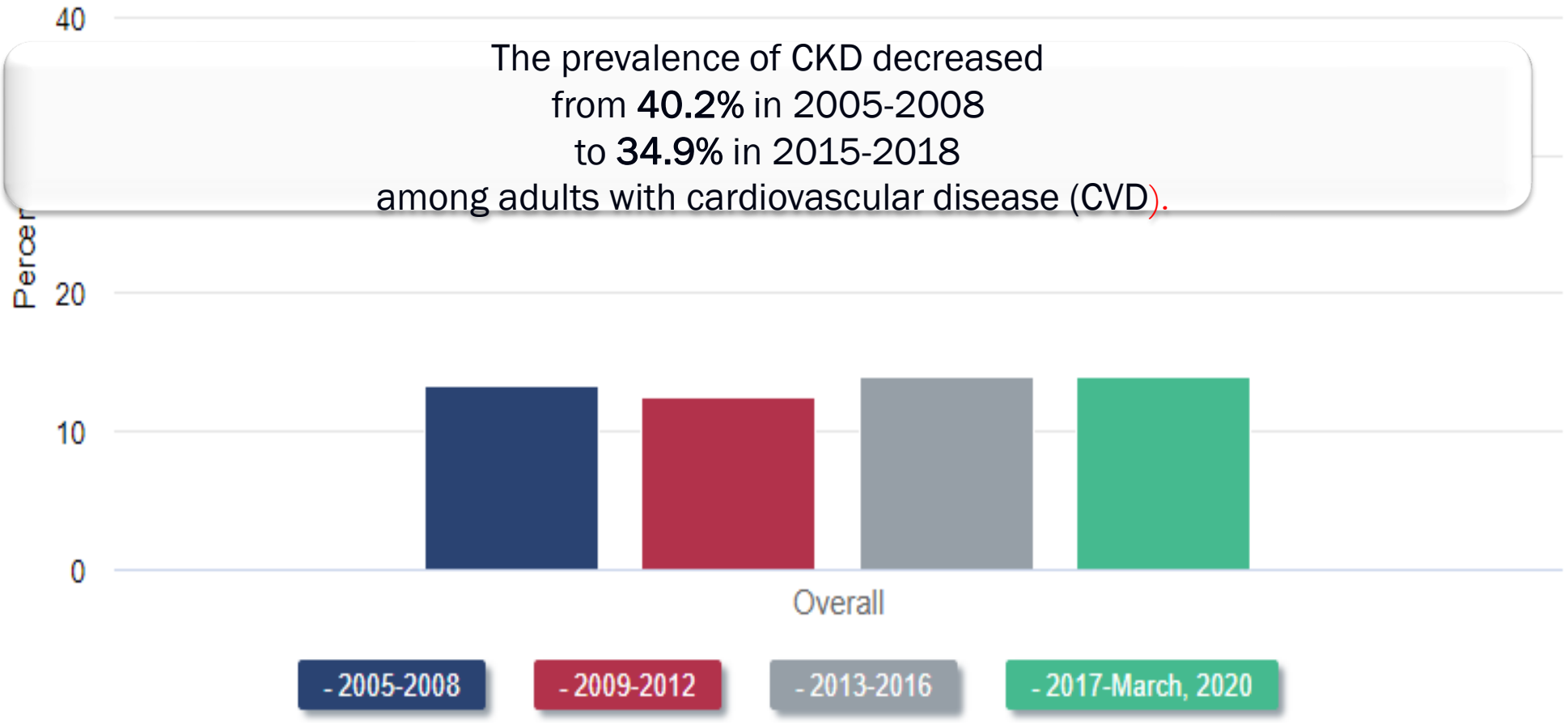
δ. Η επιθετική μείωση της ΑΠ στην ΧΝΝ οδηγεί σε επιτάχυνση της εξέλιξης της νεφρικής λειτουργιάς

Agenda

- Η Καρδιαγγειακή Νόσος στην Χρόνια Νεφρική Νόσο
- Ανεξάρτητα συστατικά ως παράγοντες καρδιαγγειακού κινδύνου στην ΧΝΝ
- Μηχανισμοί καρδιαγγειακών επιπλοκών στην ΧΝΝ
- Στόχος Αρτηριακής Πίεσης στην ΧΝΝ
- Αντιϋπερτασικά φάρμακα στην ΧΝΝ
- Επιδείνωση της νεφρικής λειτουργίας με την χρήση RAS blockers
- Συμπεράσματα

Η Καρδιαγγειακή Νόσος στην χρόνια Νεφρική νόσο

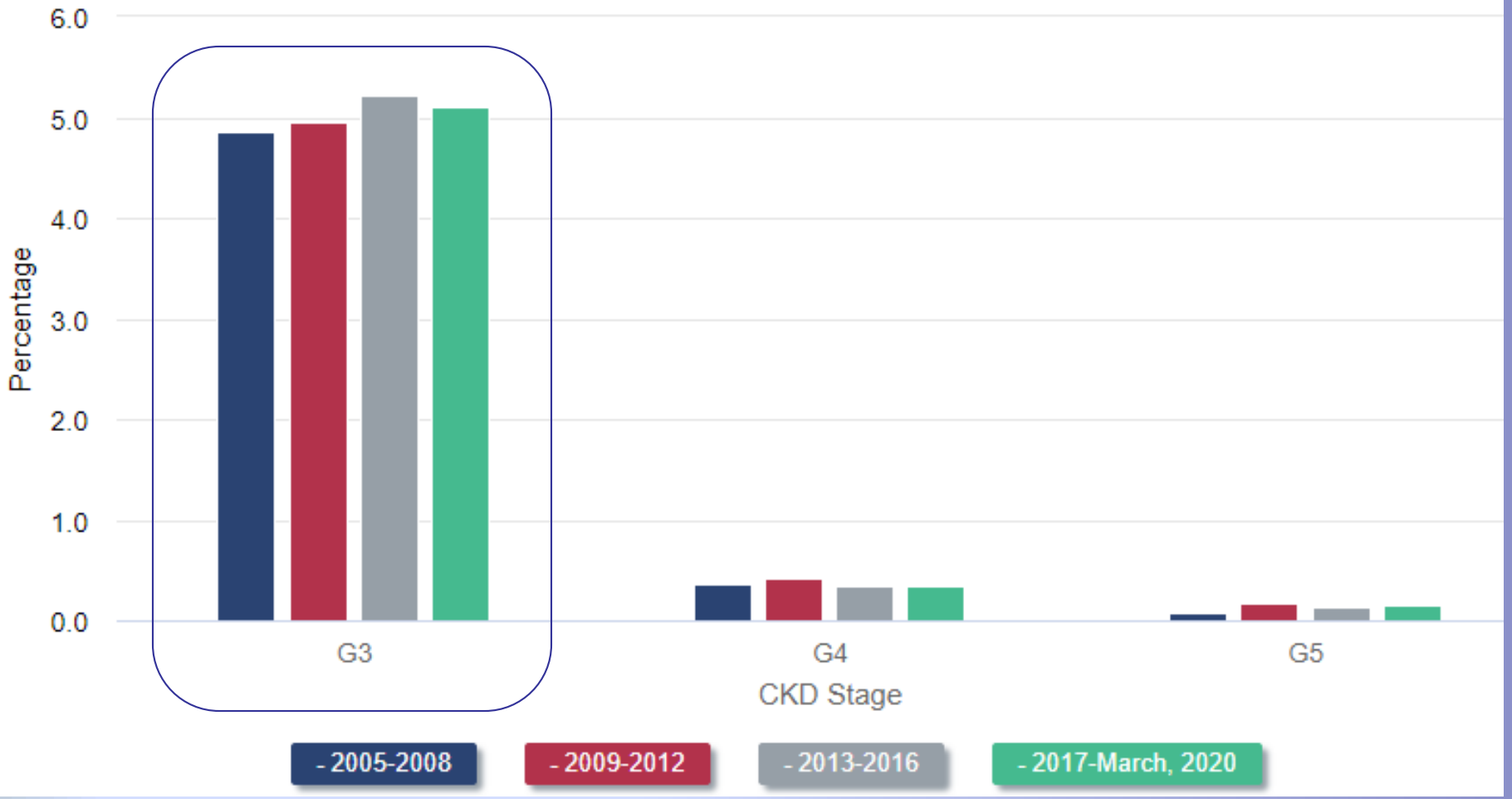
The prevalence of CKD decreased
from **40.2%** in 2005-2008
to **34.9%** in 2015-2018
among adults with cardiovascular disease (CVD).



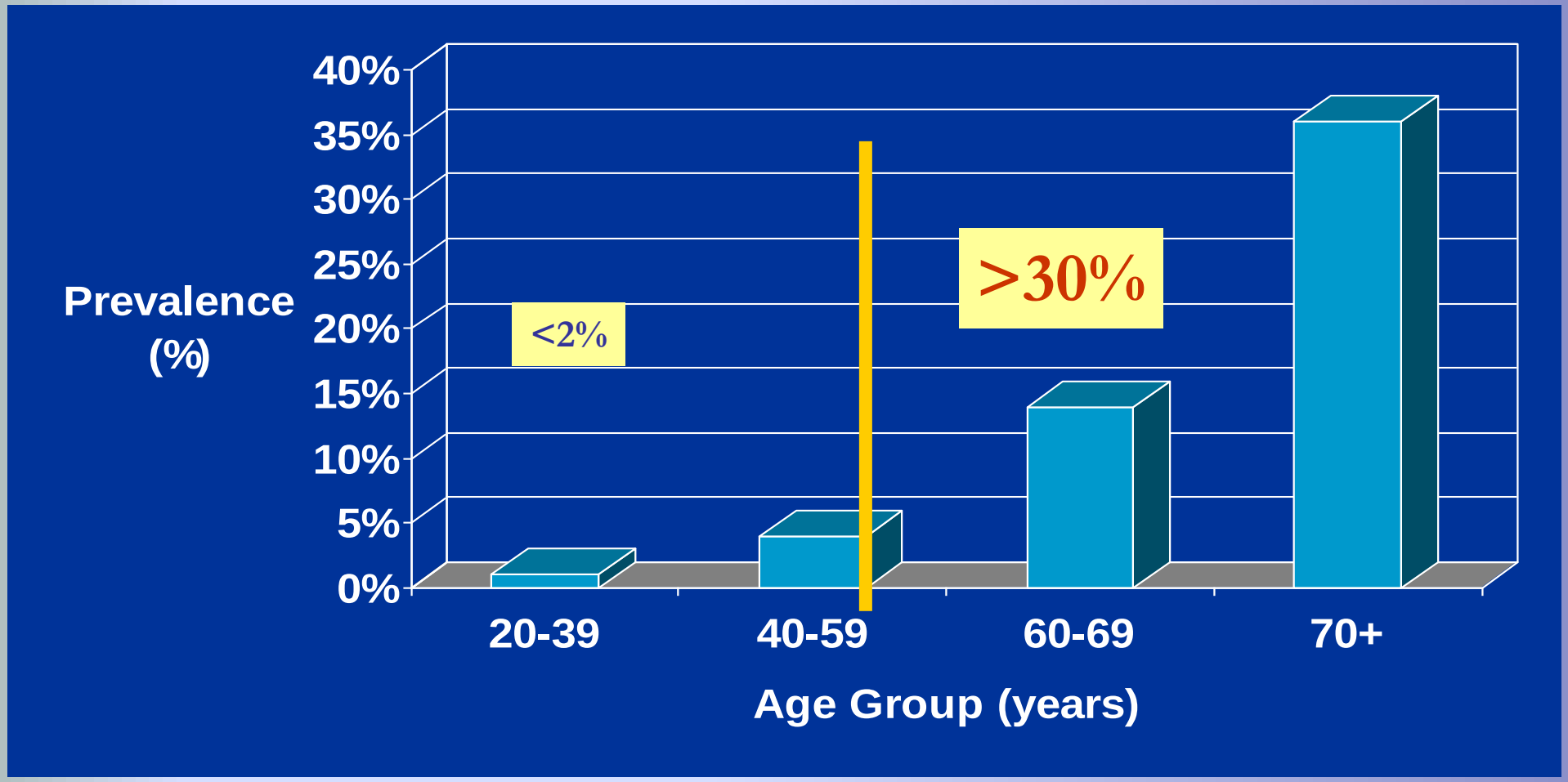
Data source: NHANES; Cohort: Participants aged ≥20 years with serum creatinine and urinary ACR measurements. Abbreviations: CKD, chronic kidney disease; ACR, albumin to creatinine ratio; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey.

For Researchers | ESRD Quarterly Update | Data Query Tools | USRDS News | About USRDS

Overall | Age | Sex | Race/Ethnicity

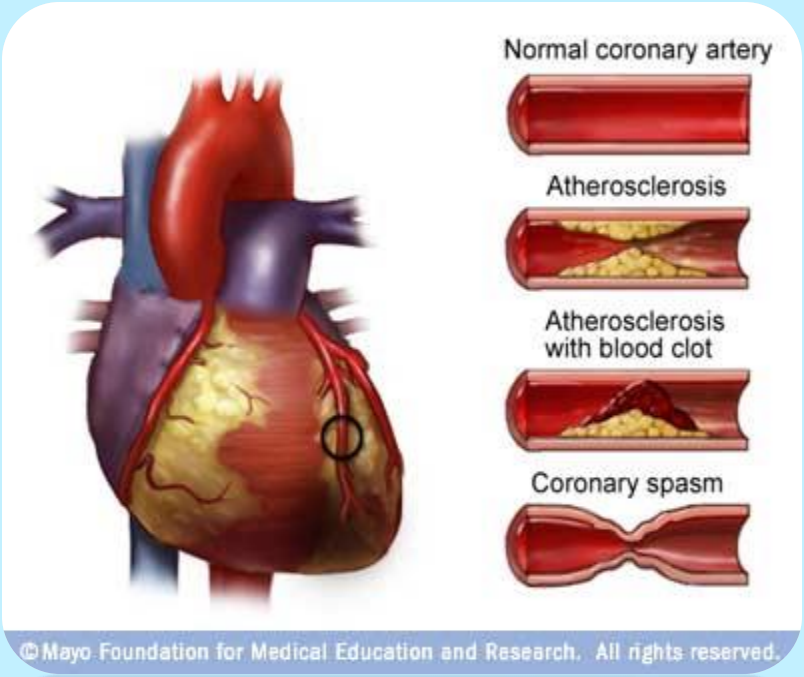


Επίπτωση της ΧΝΝ στους ηλικιωμένους



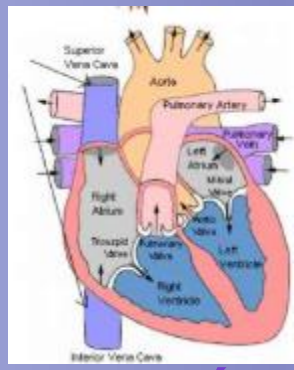
Καρδιαγγειακή νόσος

- Ισχαιμική καρδιακή νόσος
- Καρδιακή ανεπάρκεια
- Εγκεφαλική αγγειακή νόσος
- Περιφερική αγγειακή νόσος



NFK, K/DOQI, AJKD 2002; 39 (Suppl 1)

Types of Cardiovascular disease in patients with Chronic Kidney Disease



Διαταραχές της καρδιαγγειακής **αιμάτωσης**

- Coronary artery disease
- Cerebrovascular disease
- Peripheral vascular disease
- Renovascular disease

Διαταραχές της καρδιαγγειακής **λειτουργίας**

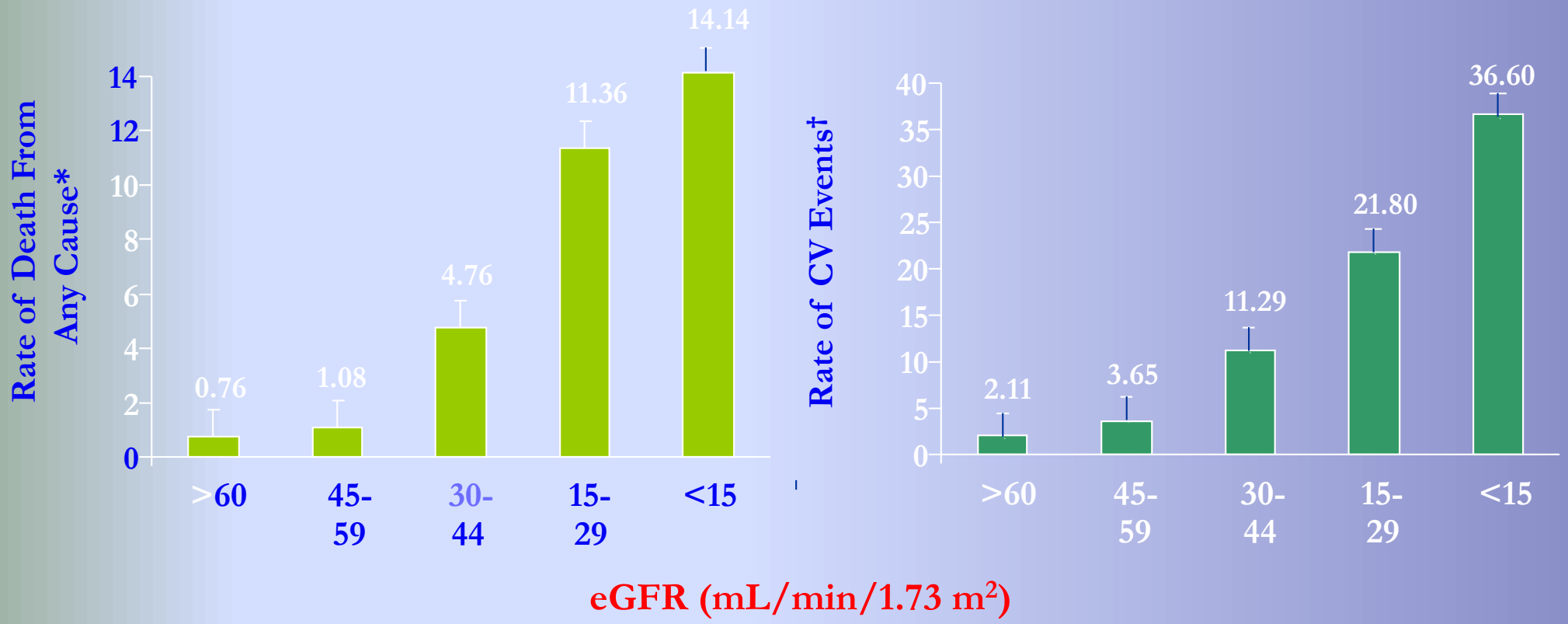
- Left ventricular hypertrophy
- Congestive heart failure
- Atrial fibrillation

Clinical manifestations of Cardiovascular disease in patients with chronic Kidney Disease

- Angina pectoris
- Myocardial infarction
- Congestive heart failure
- Stroke
- Arrhythmias
- Peripheral vascular disease
- Sudden death

Rates of Death and Cardiovascular Events in Patients According to eGFR

Data From Kaiser Permanente



N = 1,120,295 adults.

*Age-standardized rates per 100 person-years; †CV event defined as hospitalization for coronary heart disease, heart failure, ischemic stroke, and peripheral arterial disease per 100 person-years.

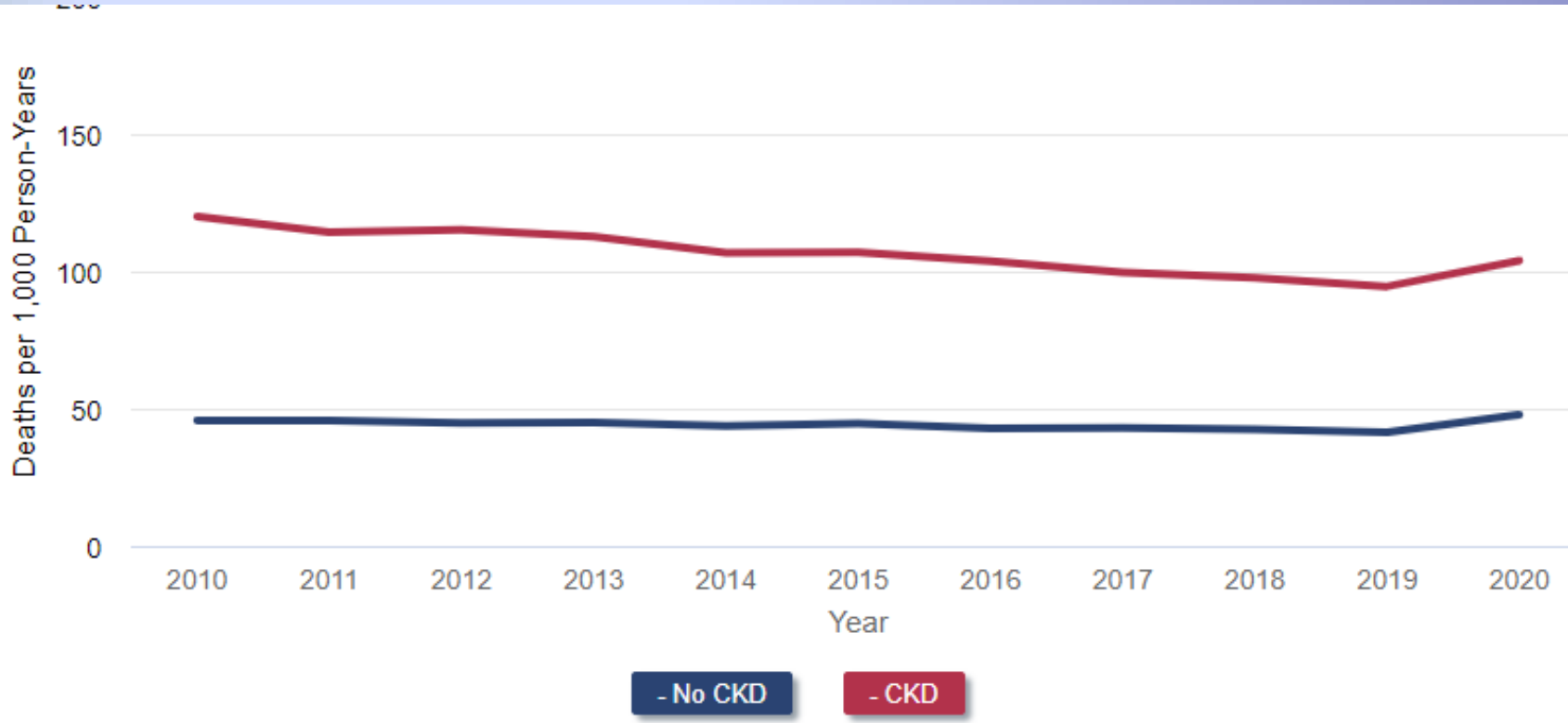
Go AS, et al. *N Engl J Med.* 2004;351:1296-1305.

chronic kidney disease: a KDIGO Controversies Conference report

Andrew S. Levey[1], Paul E. de Jong[2], Josef Coresh[3], Meguid El Nahas[4], Brad C. Astor[3], Kunihiro Matsushita[3], Ron T. Gansevoort[2], Bertram L. Kasiske[5] and Kai-Uwe Eckardt[6]

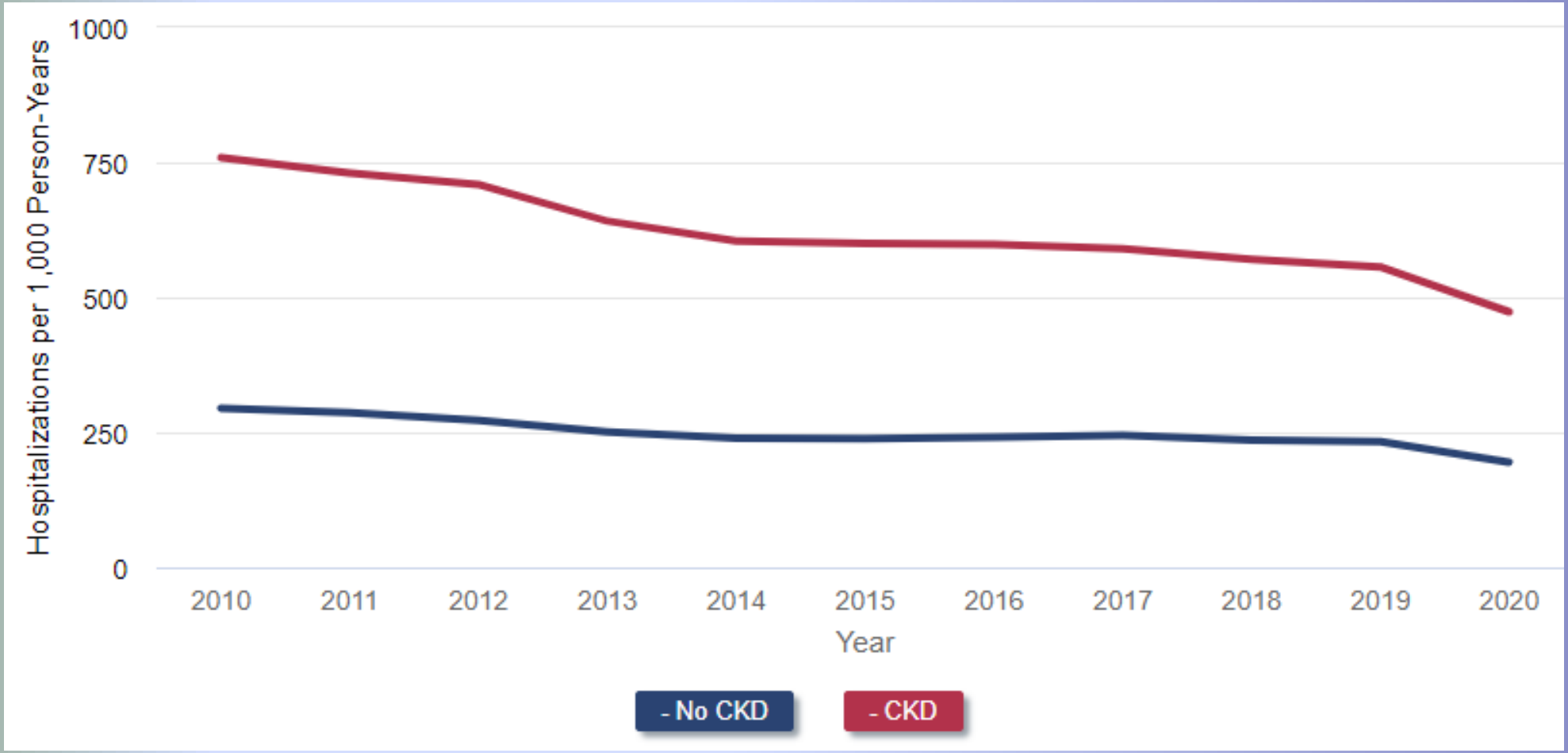
Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)

GFR stages, description and range (ml/min per 1.73 m^2)				Albuminuria stages, description and range (mg/g)				
				A1		A2	A3	
				Optimal and high-normal		High	Very high and nephrotic	
				<10	10–29	30–299	300–1999	⩾2000
	G1	High and optimal	>105					
			90–104					
	G2	Mild	75–89					
			60–74					
	G3a	Mild-moderate	45–59					
	G3b	Moderate-severe	30–44					
	G4	Severe	15–29					
	G5	Kidney failure	<15					



Data source: Medicare 5% random sample database. January 1 point prevalent Medicare FFS beneficiaries aged ≥66 years, 2010-2020. Age, sex, race/ethnicity, and comorbidity were used in adjusted analyses. Abbreviations: FFS, fee-for-service.

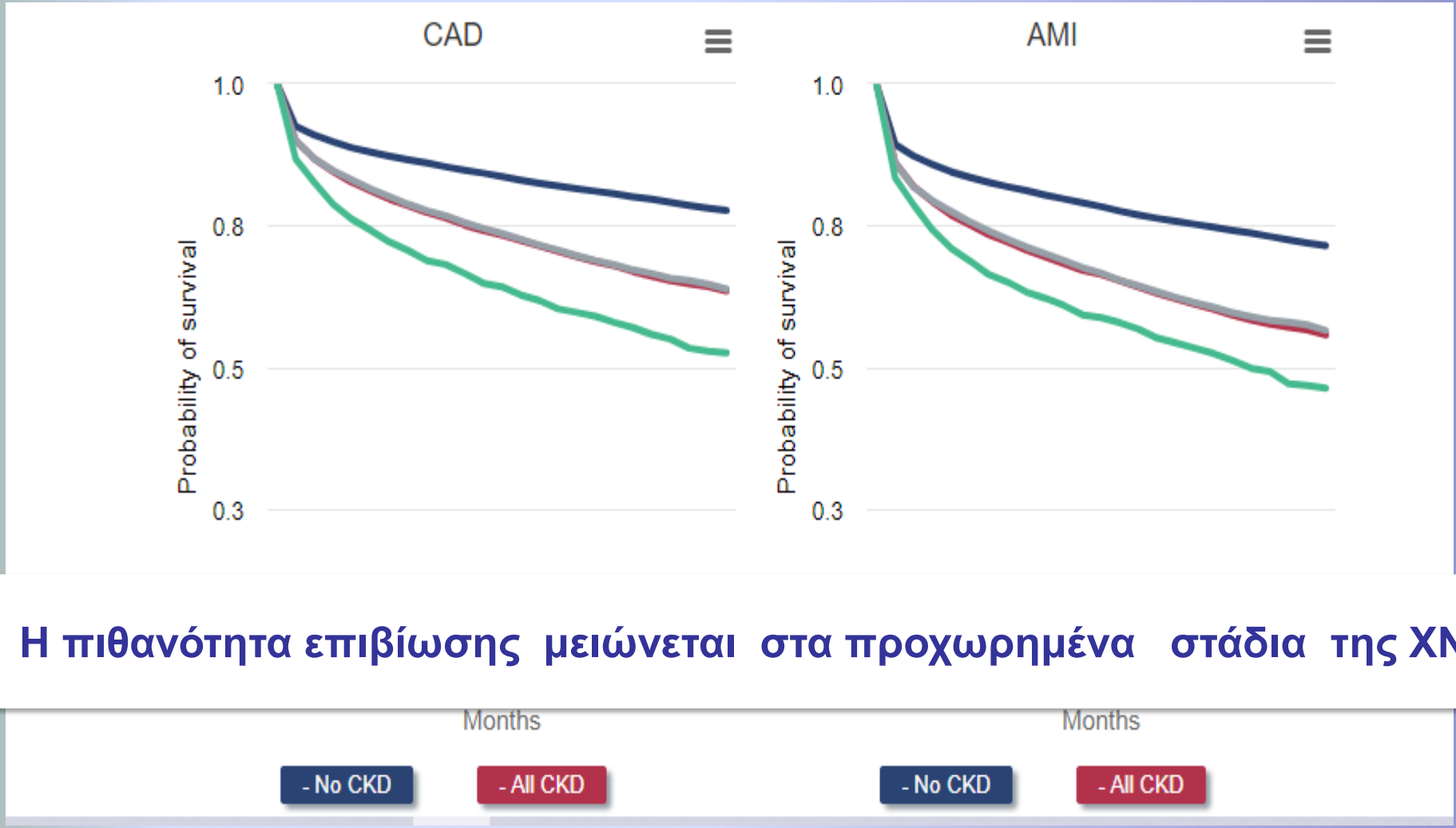
All-cause hospitalization rates in older adults, 2010-2020



All-cause hospitalization rates in older adults, by CKD status and CKD stage, 2020

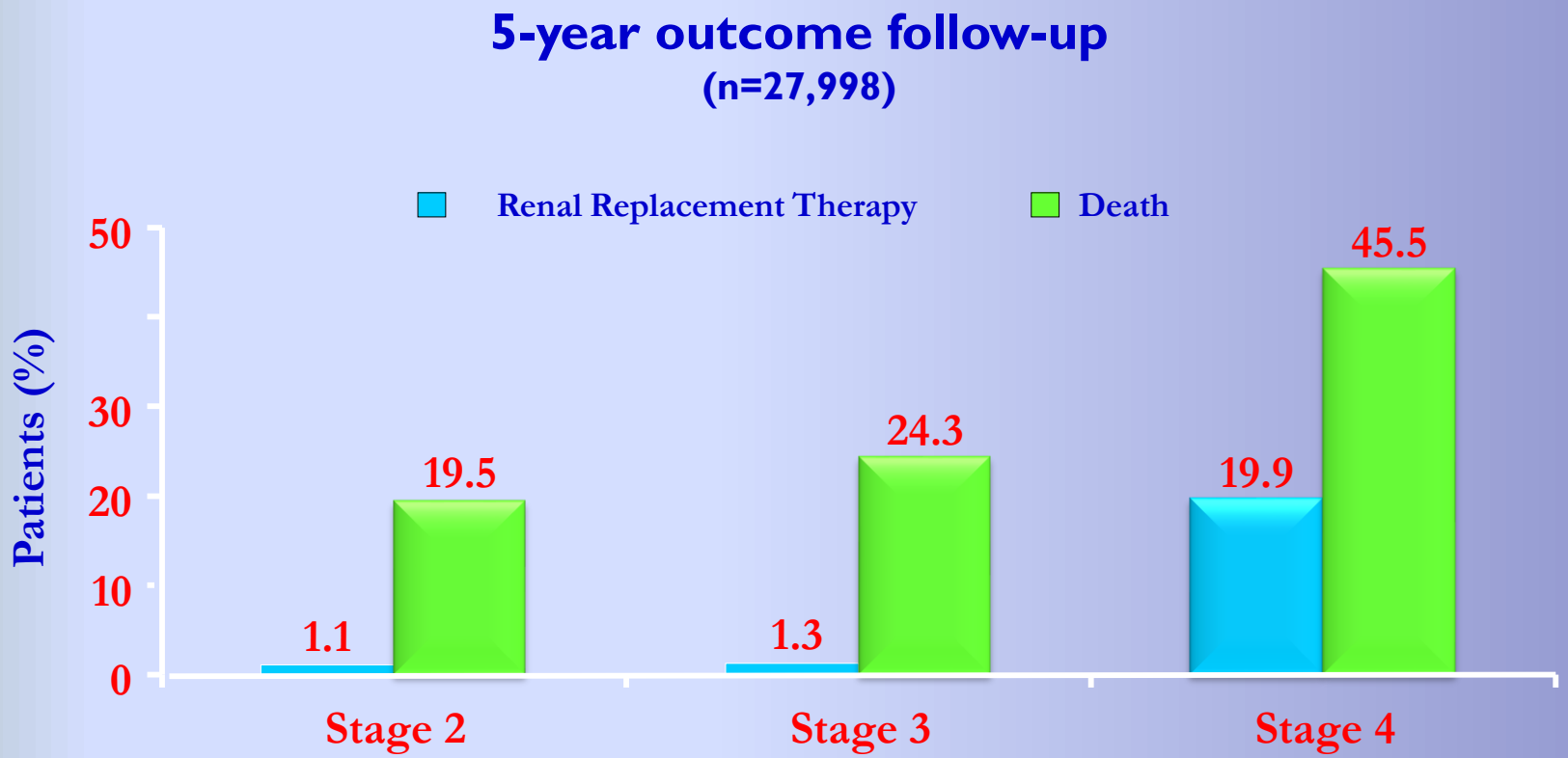
Η πιθανότητα νοσηλείας αυξάνεται στα προχωρημένα στάδια της ΧΝΝ

Survival probability in older adults following hospital admission for a cardiovascular disease, by CKD status and stage, 2018-2020



Η πιθανότητα επιβίωσης μειώνεται στα προχωρημένα στάδια της ΧΝΝ

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



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

CKD patients are more than twice as likely to have CVD compared to non CKD (CVD prevalence 66% versus 32%, respectively}

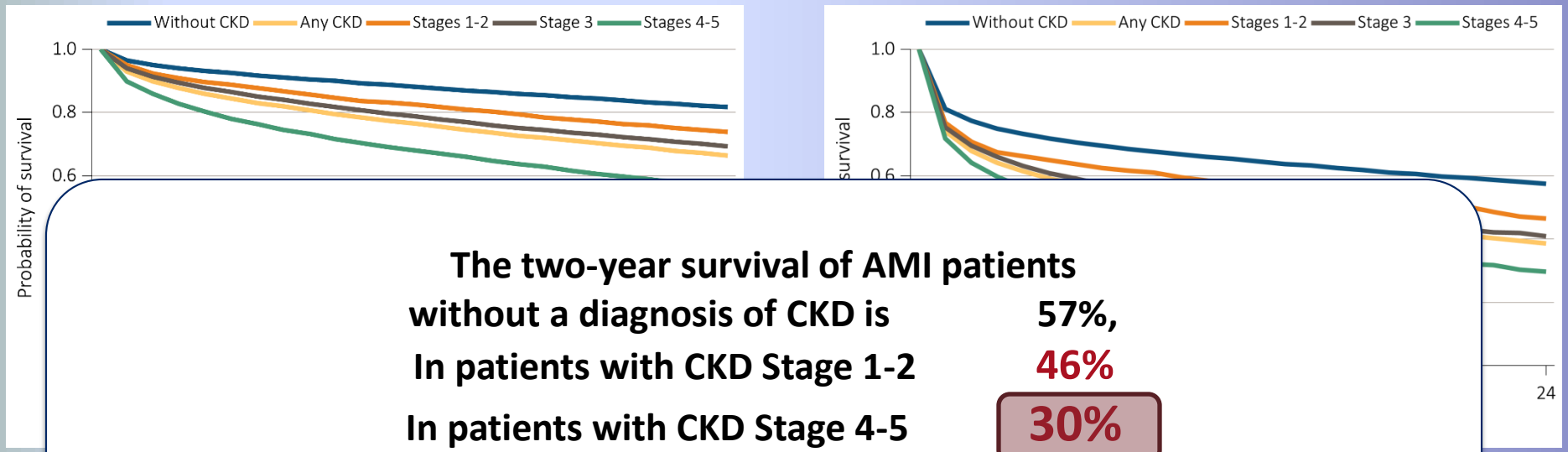
Heart failure prevalence increases dramatically with CKD severity

Nearly 40% of patients with Stages 4-5 CKD carried a diagnosis of Heart failure

Survival of patients with a cardiovascular diagnosis or procedure, by CKD status, 2011-2013

(a) *atherosclerotic heart disease*

(b) *acute myocardial infarction*



The two-year survival of AMI patients

without a diagnosis of CKD is 57%,

In patients with CKD Stage 1-2 46%

In patients with CKD Stage 4-5 30%

Data Source: Special analyses, Medicare 5 percent sample. Patients aged 66 and older alive without end-stage renal

Το ποσοστό επιβίωσης μετά από έμφραγμα μυοκαρδίου μειώνεται με την εξέλιξη των Σταδίων της ΧΝΝ

Atrial fibrillation

(g) AFIB (h) SCA / VA

Atrial fibrillation is common in patients with CKD **24.1%.**

The prevalence of atrial fibrillation rises for

1. males
2. with more advanced stages of CKD
3. age
4. hypertension
5. congestive heart failure

Nearly half of CKD patients with congestive heart failure have a diagnosis of atrial fibrillation.

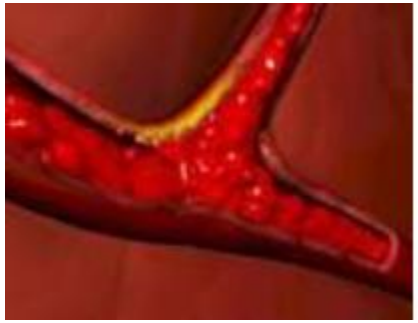
CKD as a coronary disease risk equivalent

CKD has been recognized as an independent

risk factor for cardiovascular disease

and has now been recognized

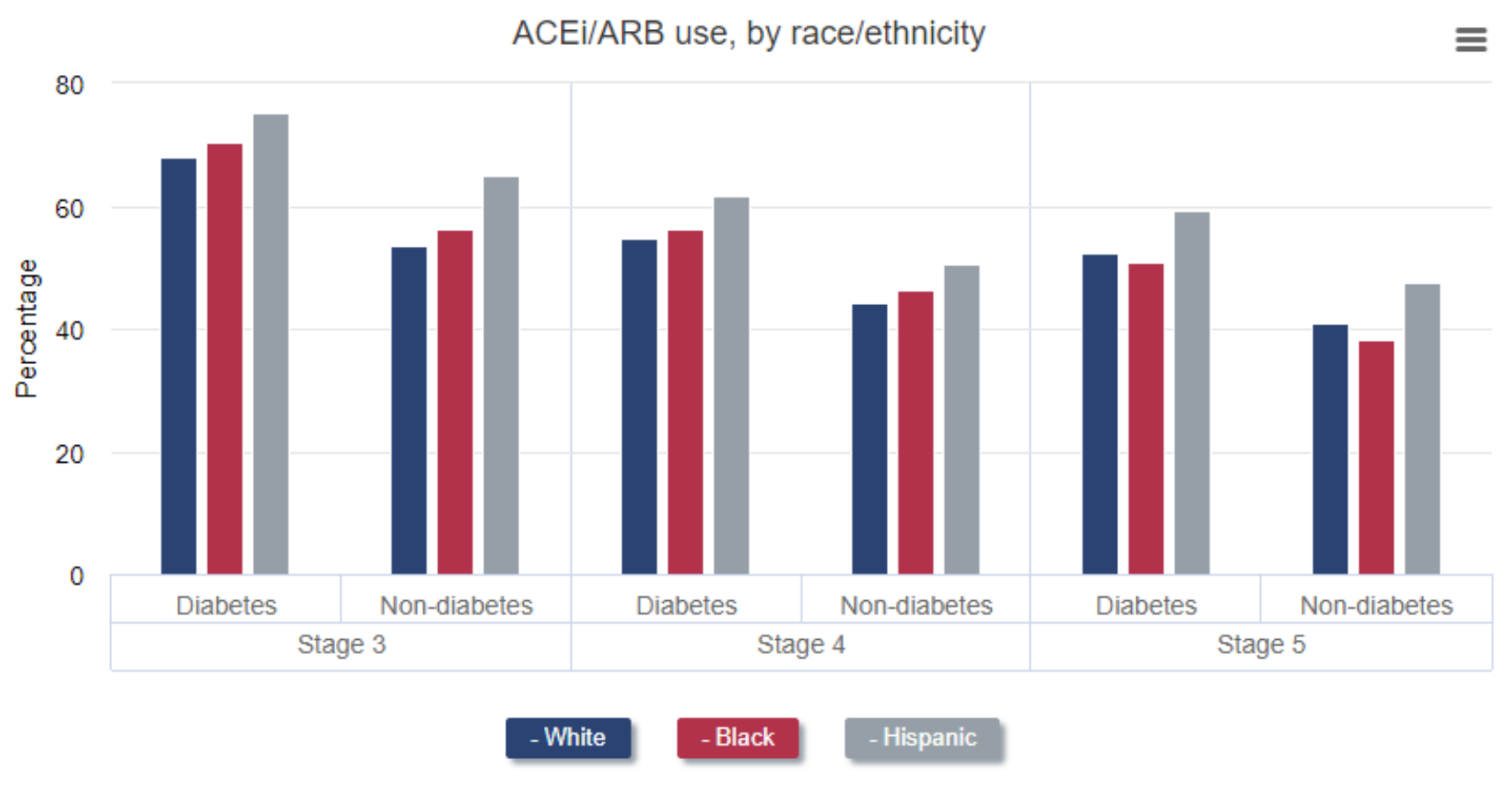
as a coronary disease risk



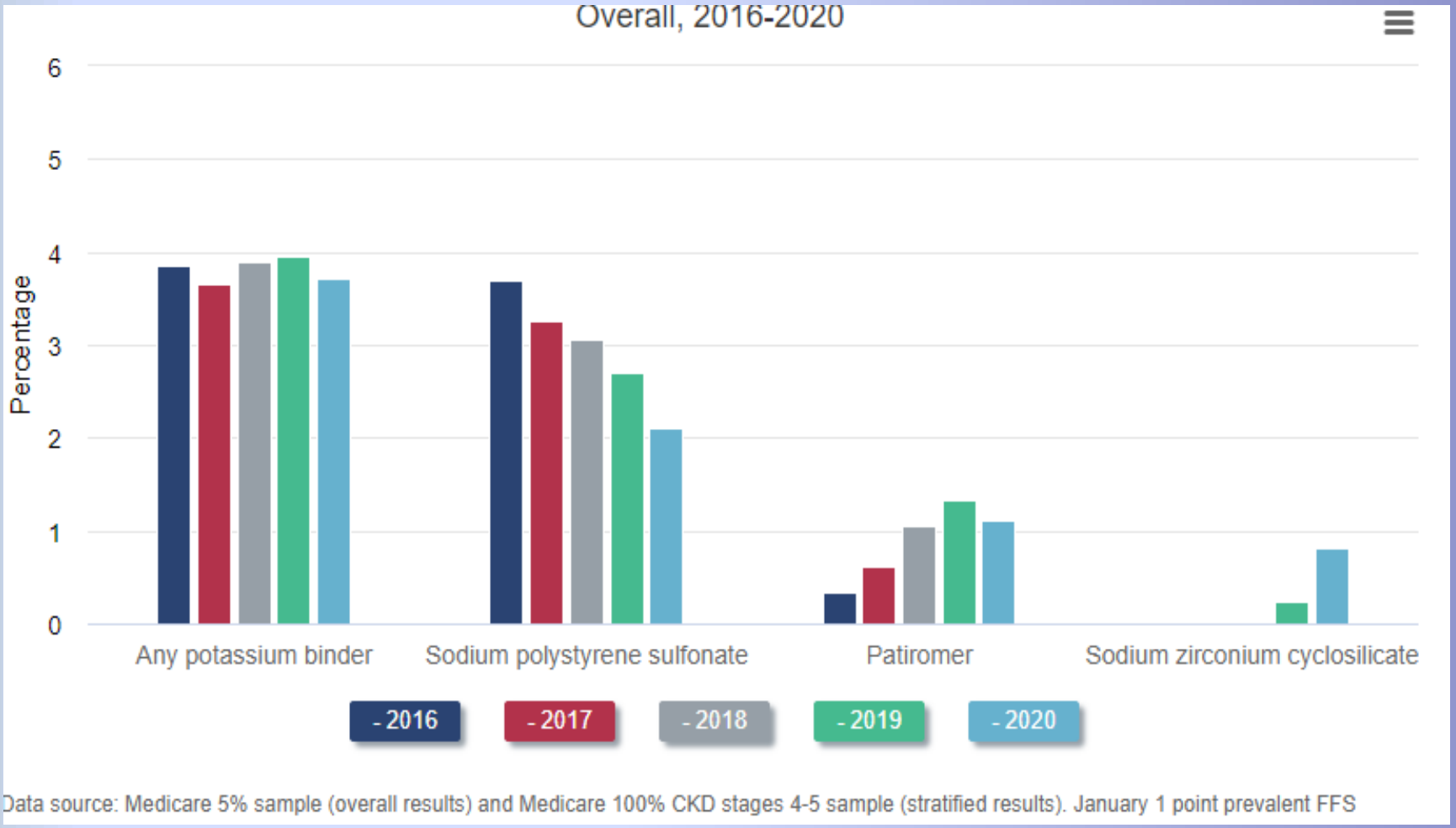
equivalent similar to diabetes mellitus.

(Briasoulis and Bakris, 2013),

Prescription Drug Coverage in Patients with CKD



Percentage of older adults with CKD stage 4-5 receiving potassium binders, 2016-2020

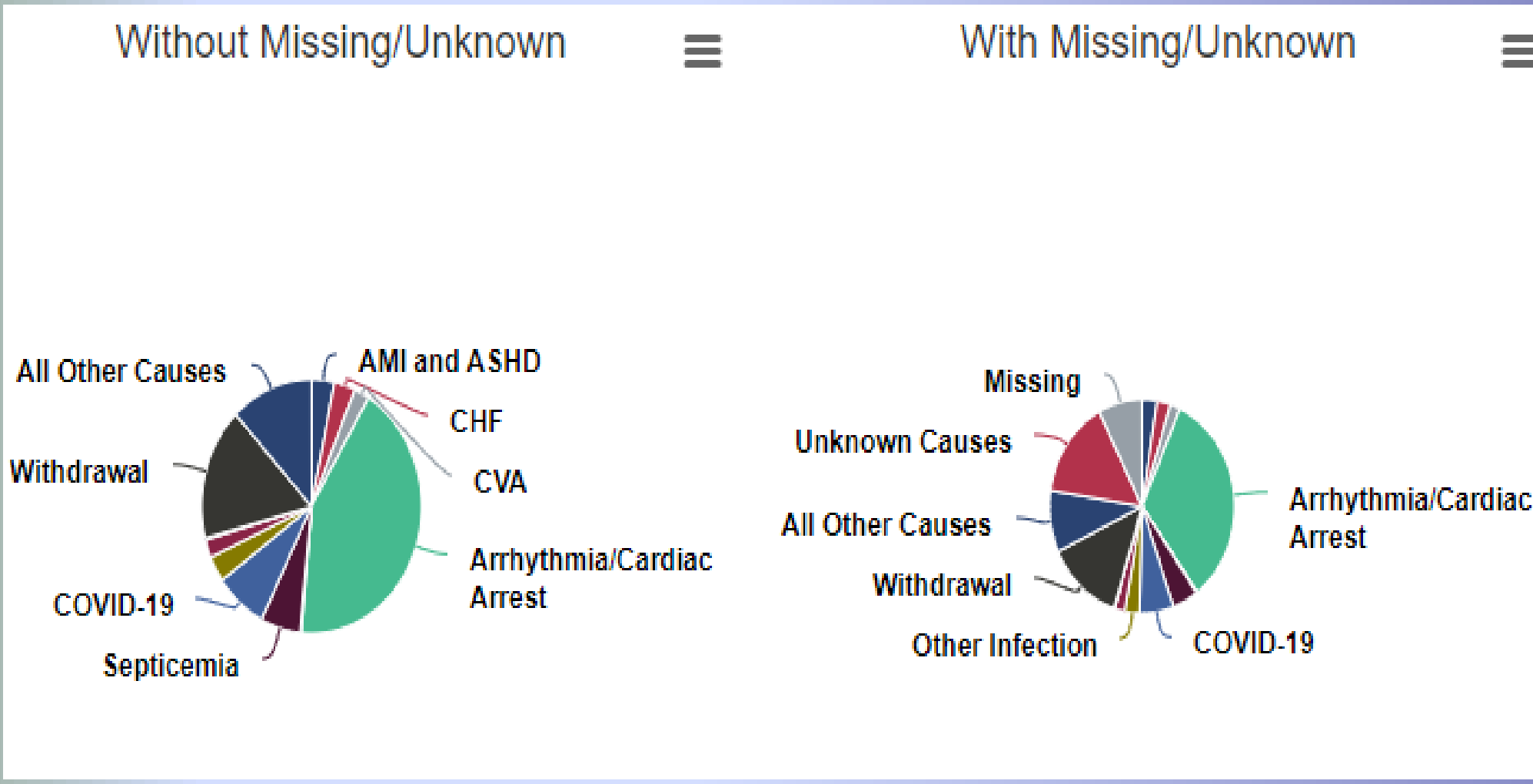


Data source: Medicare 5% sample (overall results) and Medicare 100% CKD stages 4-5 sample (stratified results). January 1 point prevalent FFS

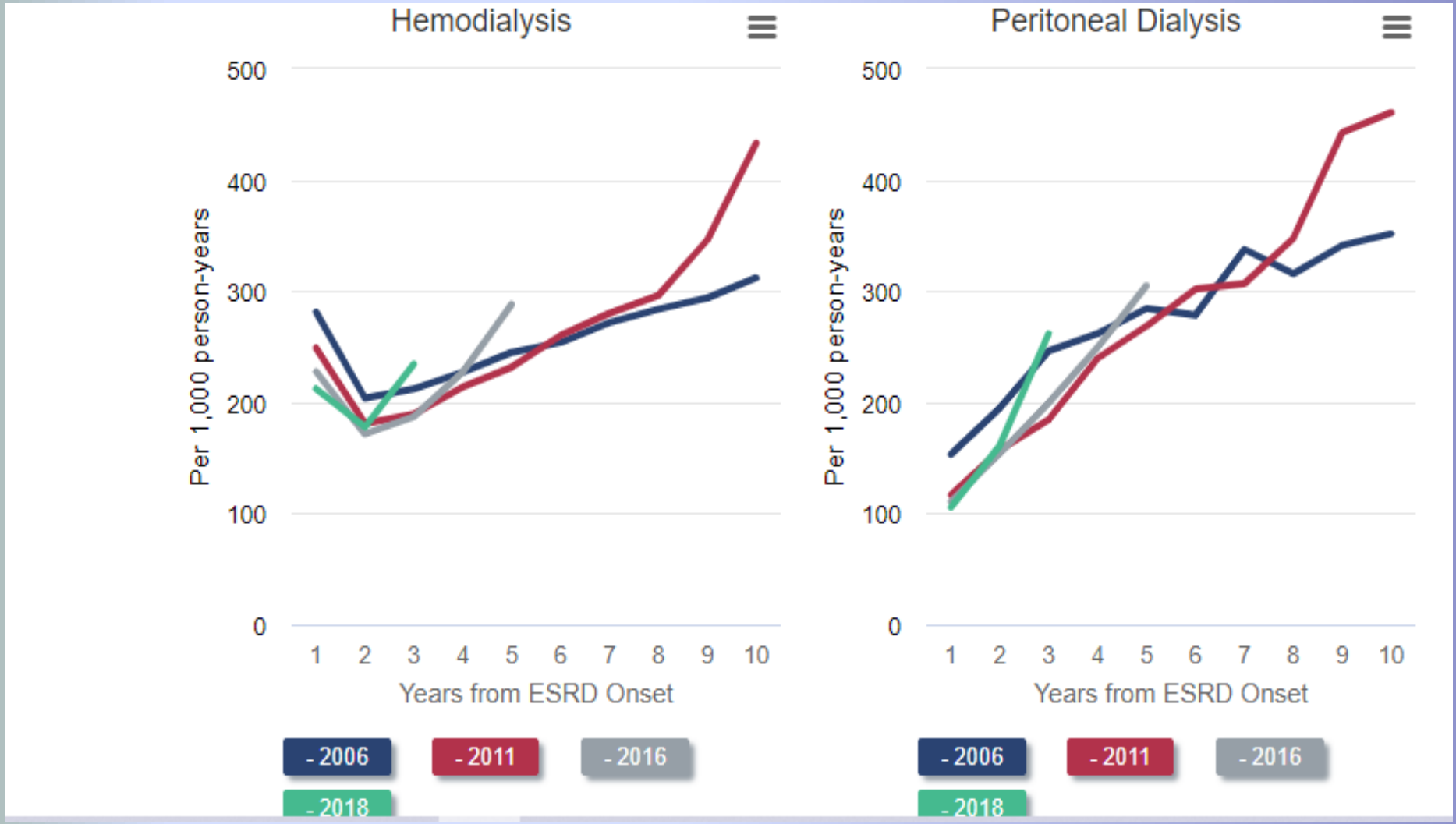
Percentage of older adults receiving medications for cardiovascular disease, 2020

Percentage of older adults receiving medications for HF 2020

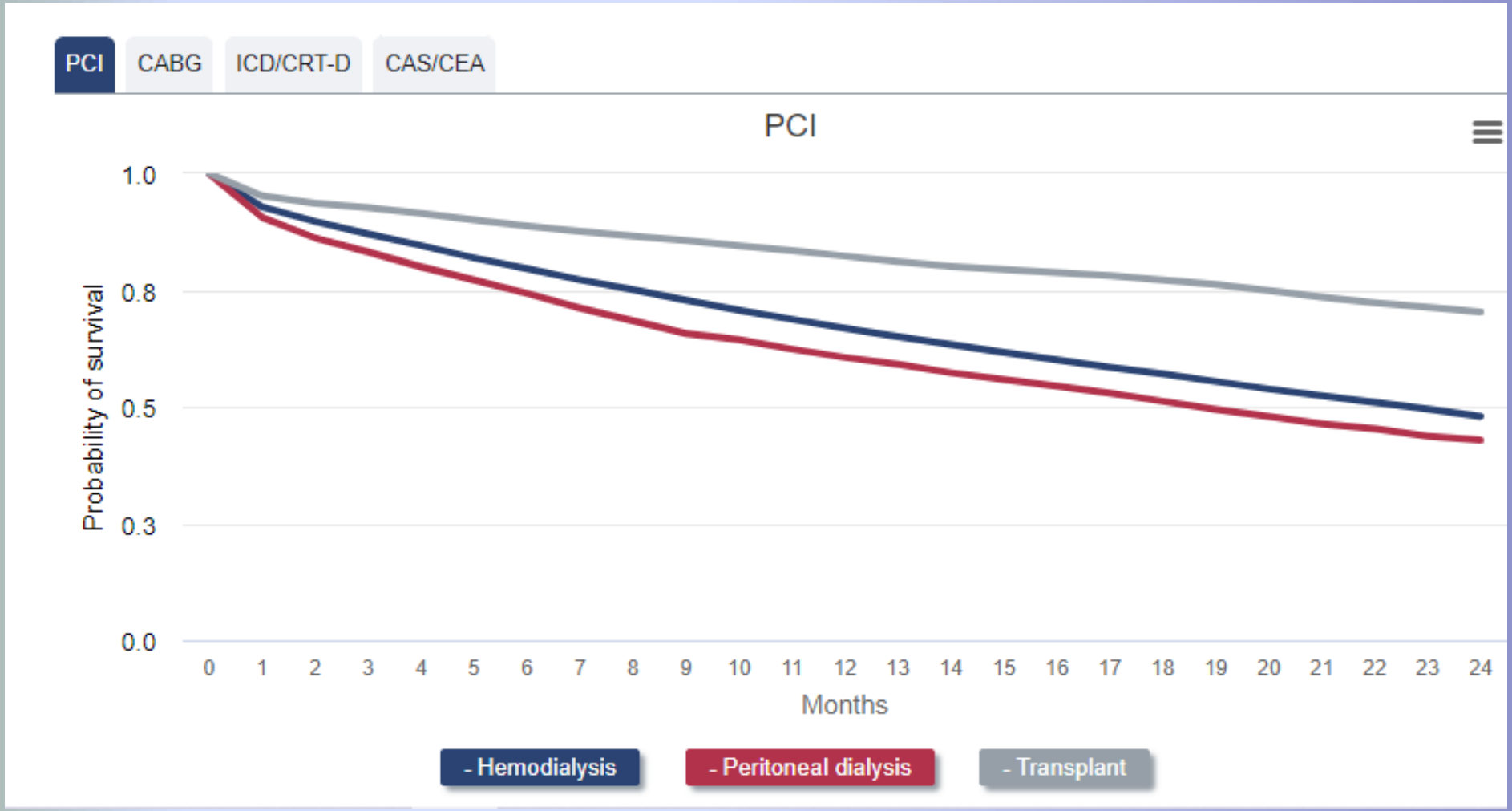
Percentages of cause-specific mortality, with and without inclusion of missing and unknown causes of death, in patients with ESRD receiving hemodialysis, who died in 2020



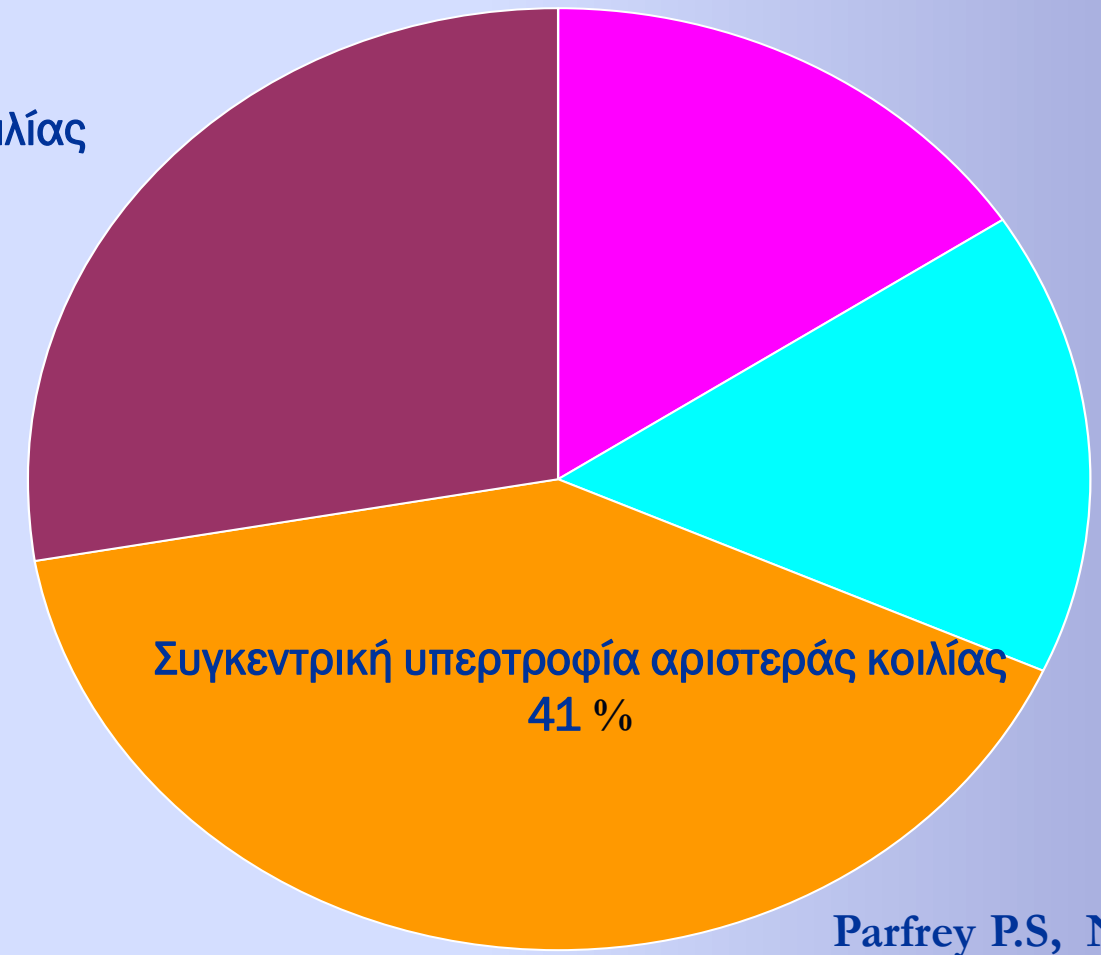
All-cause mortality after initiation of dialysis for ESRD, by treatment modality, 2006, 2011, 2016 and 2018



Unadjusted survival probability in adult patients with ESRD following a first cardiovascular procedure, by treatment modality, 2018-2020

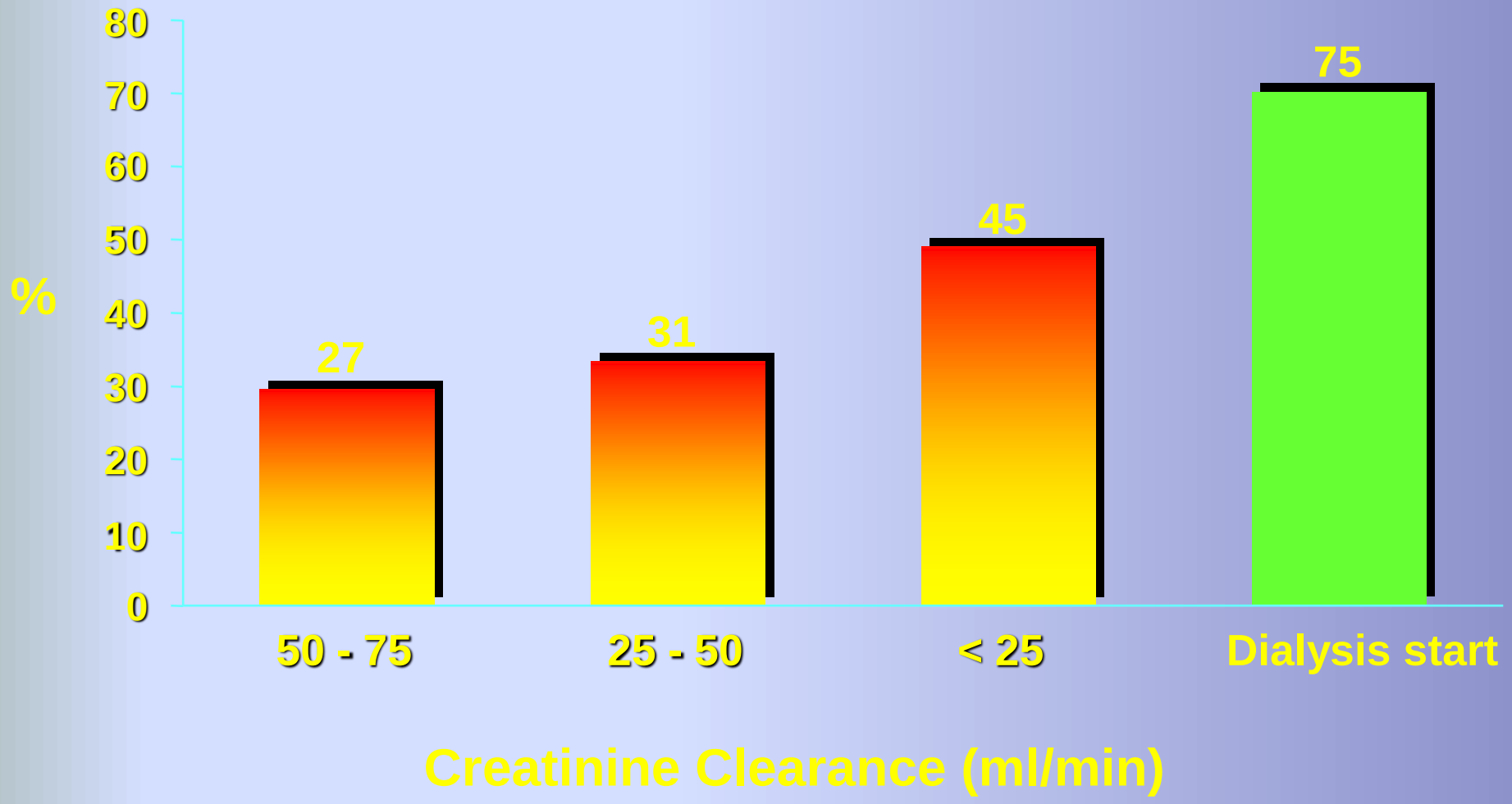


Υπερηχοκαρδιογραφικά ευρήματα κατά την έναρξη της αιμοκάθαρσης



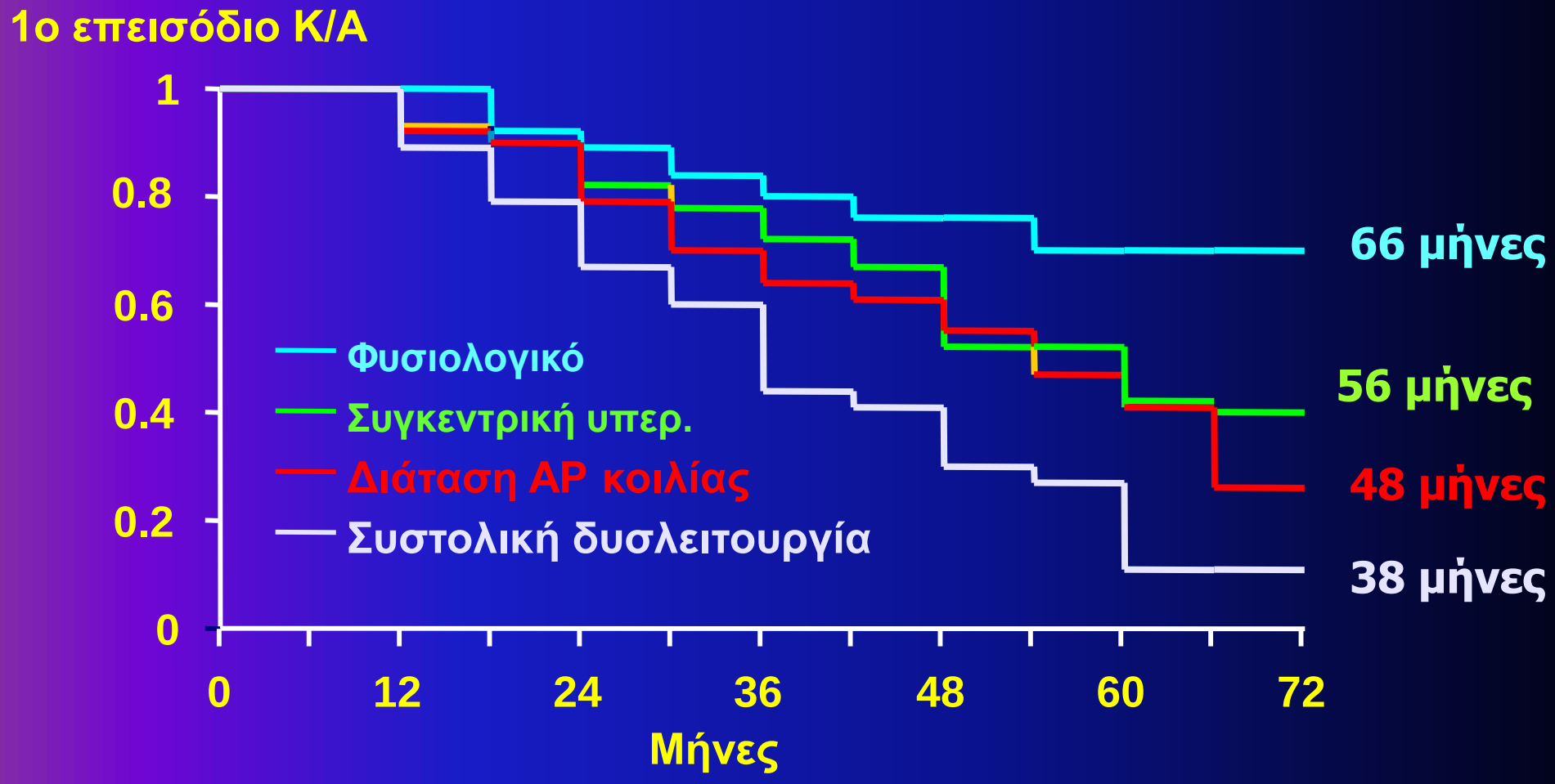
Parfrey P.S, NDT 1996; 11: 1277-1285

Prevalence of LVH According to GFR



Levin A, et al. AJKD 1999

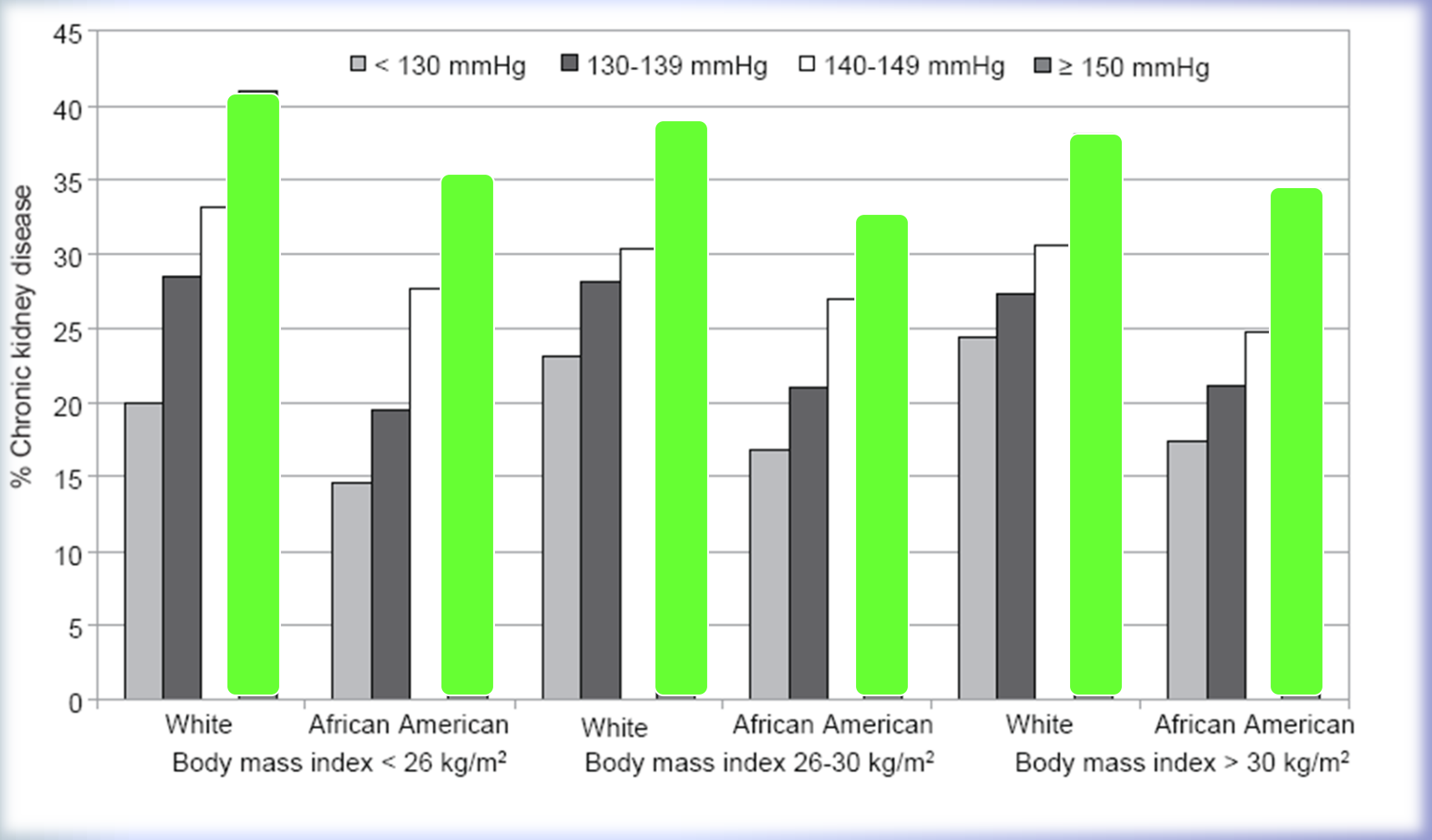
Η καρδιαγγειακή νόσος στη ΧΝΝ (στην έναρξη της αιμοκάθαρσης) ως παράγοντας κινδύνου



Parfrey P.S, NDT 1996; 11: 1277-1285

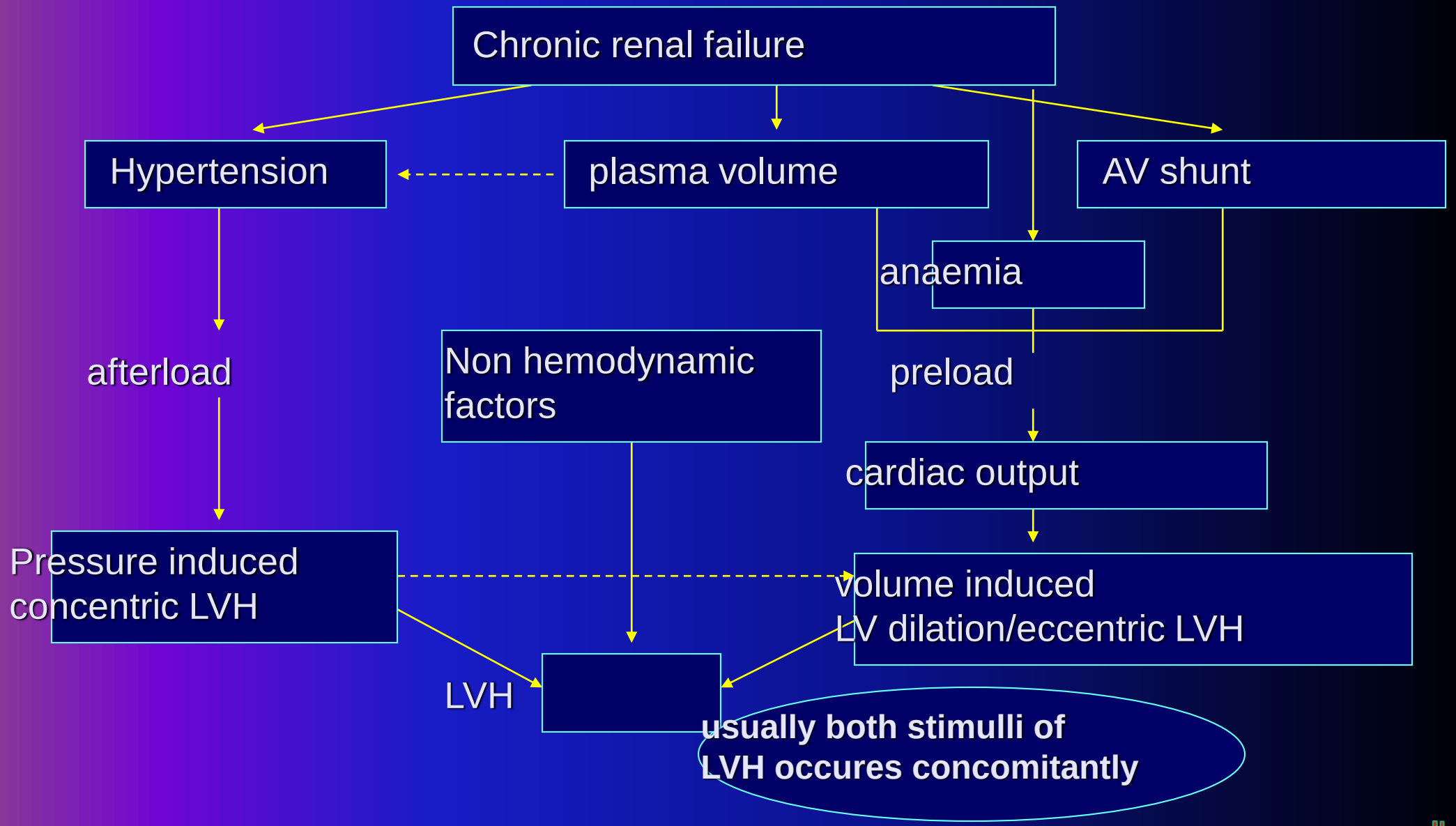
Ανεξάρτητα συστατικά ως παράγοντες καρδιαγγειακού κινδύνου στην ΧΝΝ

Percentage of CKD in white and African American participants stratified by SBP and BMI



Kalaitzidis et al, AJKD, May 2009

Pathophysiology of LVH



Πρωτεινουρία

Καρδιαγγειακά συμβάματα

Πρωτεινουρία και καρδιαγγειακά συμβάματα

Post hoc analyses

Moderately increased Albuminuria or Micro-A

In different populations

Risk factor for cardiovascular disease

and

early cardiovascular mortality

Observational Studies

Severely increased Albuminuria or Macro-A

chronic kidney disease

A graded increase

in coronary risk

Rapid Decline of Kidney Function Increases Cardiovascular Risk in the Elderly

Michael G. Shlipak,* Ronit Katz,† Bryan Kestenbaum,‡ David Siscovick,§ Linda Fried,‖ Anne Newman,¶ Dena Rifkin,** and Mark J. Sarnak**

Table 2. Association of rapid kidney function decline with CVD events in the elderly

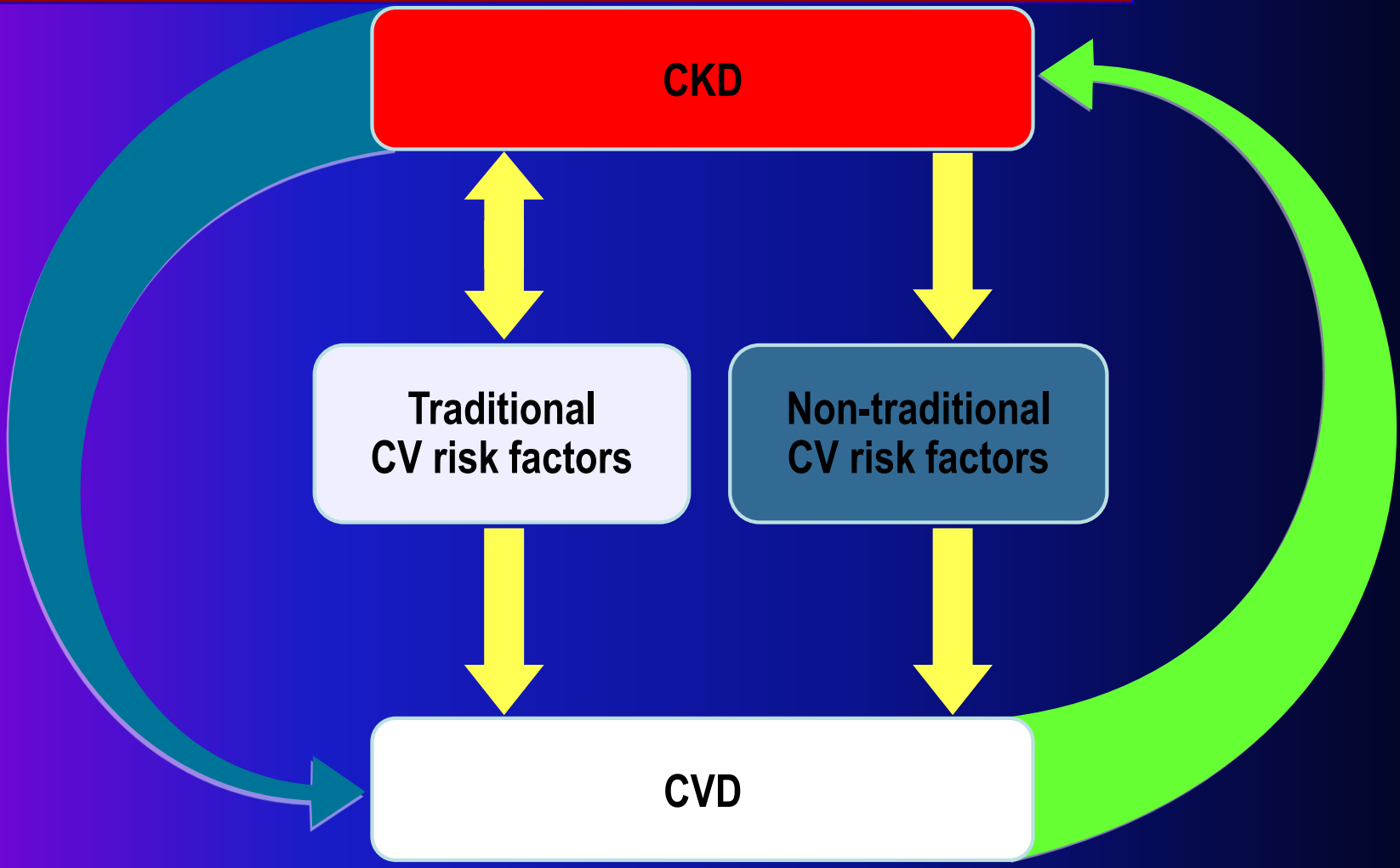
Parameter	No Rapid Decline	Rapid Decline
HF		
rates (events/1000 patient-years)	30	42
demographic adjusted HR	1.00 (reference)	1.40 (1.20 to 1.65)
multivariate adjusted HR	1.00 (reference)	1.24 (1.05 to 1.46)
MI		
rates (events/1000 patient-years)	16	24
demographic adjusted HR	1.00 (reference)	1.53 (1.24 to 1.88)
multivariate adjusted HR	1.00 (reference)	1.42 (1.14 to 1.76)
Stroke		
rates (events/1000 patient-years)	17	22
demographic adjusted HR	1.00 (reference)	1.29 (1.05 to 1.57)
multivariate adjusted HR	1.00 (reference)	1.11 (0.89 to 1.37)
PAD		

A more rapid loss of kidney function associates with greater risk for cardiovascular disease

Σε καταστάσεις που έχουμε ταχύτατη απώλεια της νεφρικής λειτουργίας ο κίνδυνος καρδιαγγειακής νόσου είναι μεγαλύτερος

Μηχανισμοί καρδιαγγειακών επιπλοκών στην ΧΝΝ

Relationship Between CKD and CVD



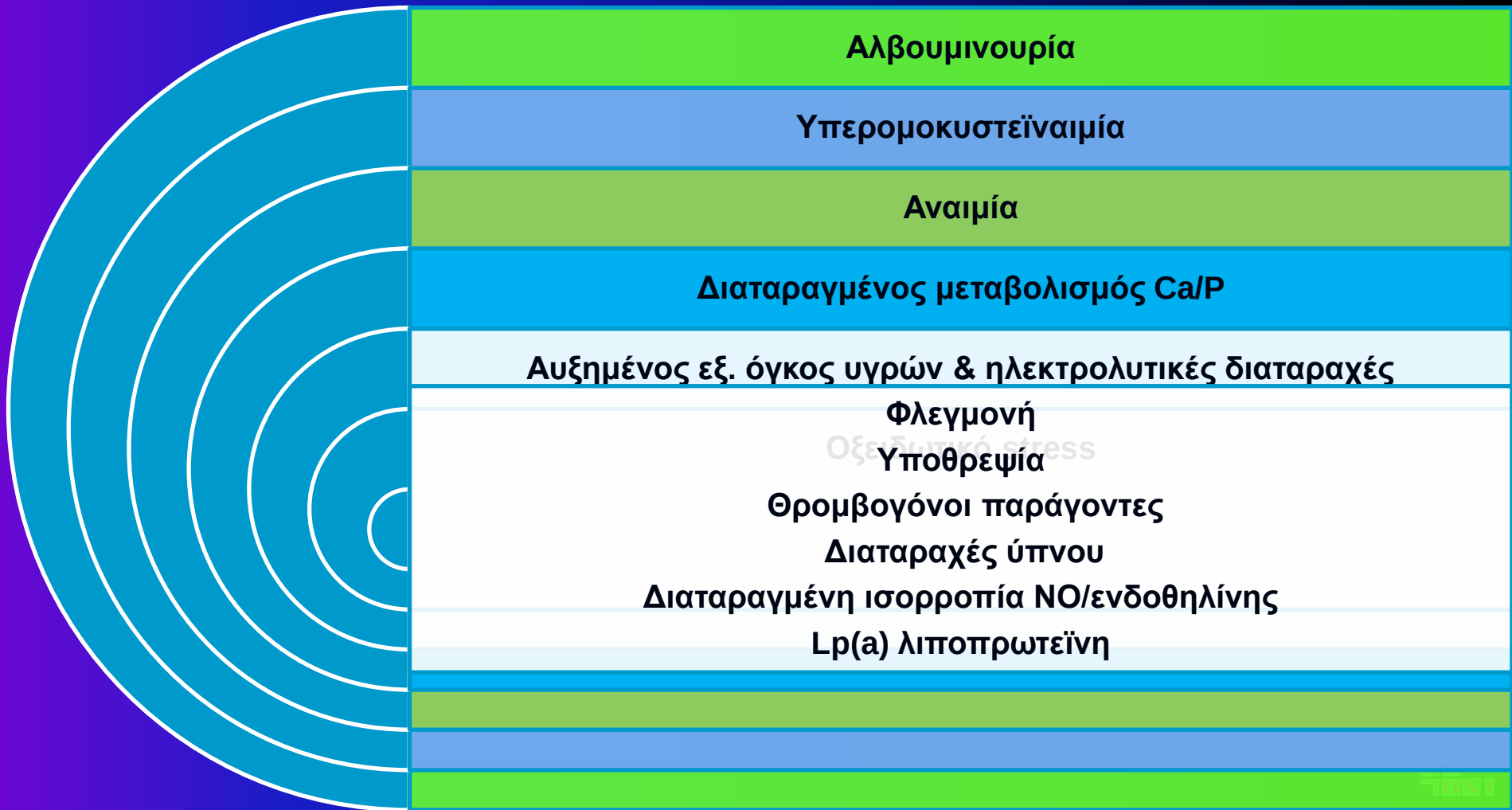
CKD is a risk factor for CVD, and CVD may be a risk factor for the progression of CKD

Traditional risk factors

- Diabetes mellitus,
- Hypertension
- Physical inactivity
- Left ventricular hypertrophy
- Smoking
- Family history
- Dyslipidemia

Καρδιαγγειακή Νόσος στην Χρόνια Νεφρική Νόσο

Μη συμβατικοί παράγοντες κινδύνου



Χαρακτηριστικά της καρδιαγγειακής νόσου στην ΧΝΝ

- Αρτηρίες
- Ενδοθηλιακή δυσλειτουργία
- Πάχυνση μέσου χιτώνα
- Επασβέστωση αθηρωματικής πλάκας
- Επασβέστωση μέσου χιτώνα

- Καρδιά
- Υπερτροφία ΑΡ κοιλιας
- Διάταση ΑΡ κοιλίας
- Ίνωση μυοκαρδίου
- Επασβέστωση σταφανιαίων
- Επασβέστωση βαλβίδων
- Διαταραχές αγωγιμότητας

Επιπλέον μεταβολικές διαταραχές στην ΧΝΝ

LVH που δεν εξηγείται από την υπέρταση

Διαταραχές του μεταβολισμού του μυοκαρδίου

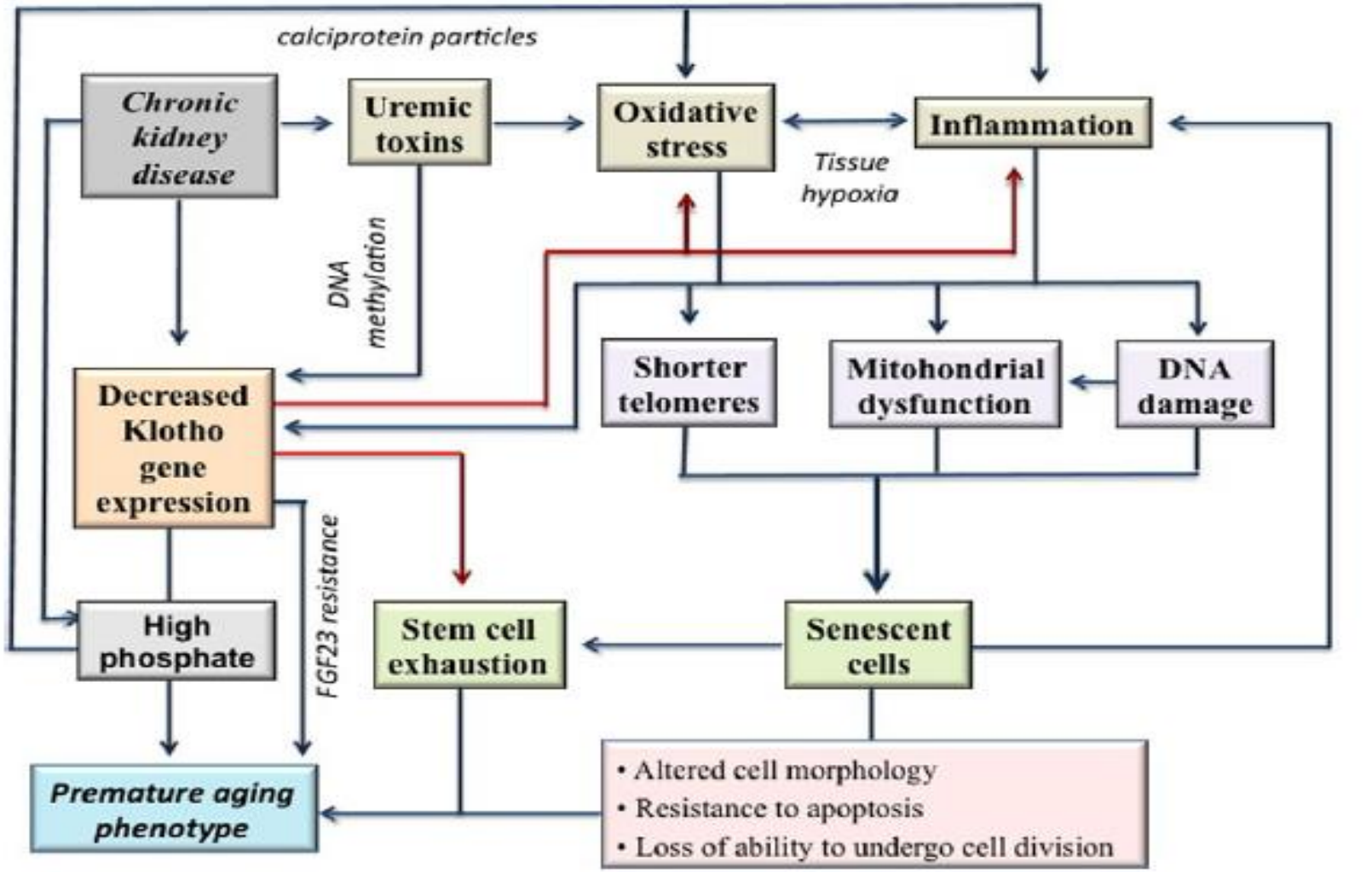
Λειτουργικές και δομικές αλλαγές αρτηριών μυοκαρδίου

Διάμεση μυοκαρδιακή ίνωση

Μειωμένη μυοκαρδιακή αιμάτωση

Chronic Kidney Disease: A Clinical Model of Premature Aging

Peter Stenvinkel, MD, PhD, and Tobias E. Larsson, MD, PhD



Η ΧΝΝ είναι ένα κλασικό μοντέλο επιταχυνόμενης γήρανσης

Accumulation of uremic toxins,
chronic inflammation
and oxidative stress
have been
identified to act as CKD-specific alterations
that increase cardiovascular risk.

Επιπλέον μεταβολικές διαταραχές στην ΧΝΝ

LVH που δεν εξηγείται από την υπέρταση

Διαταραχές του μεταβολισμού του μυοκαρδίου

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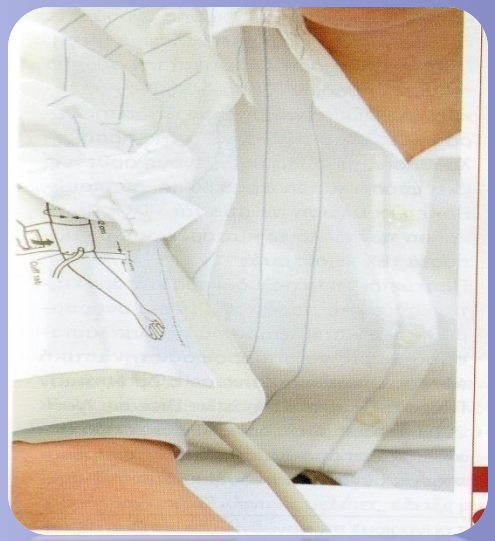
Διάμεση μυοκαρδιακή ίνωση

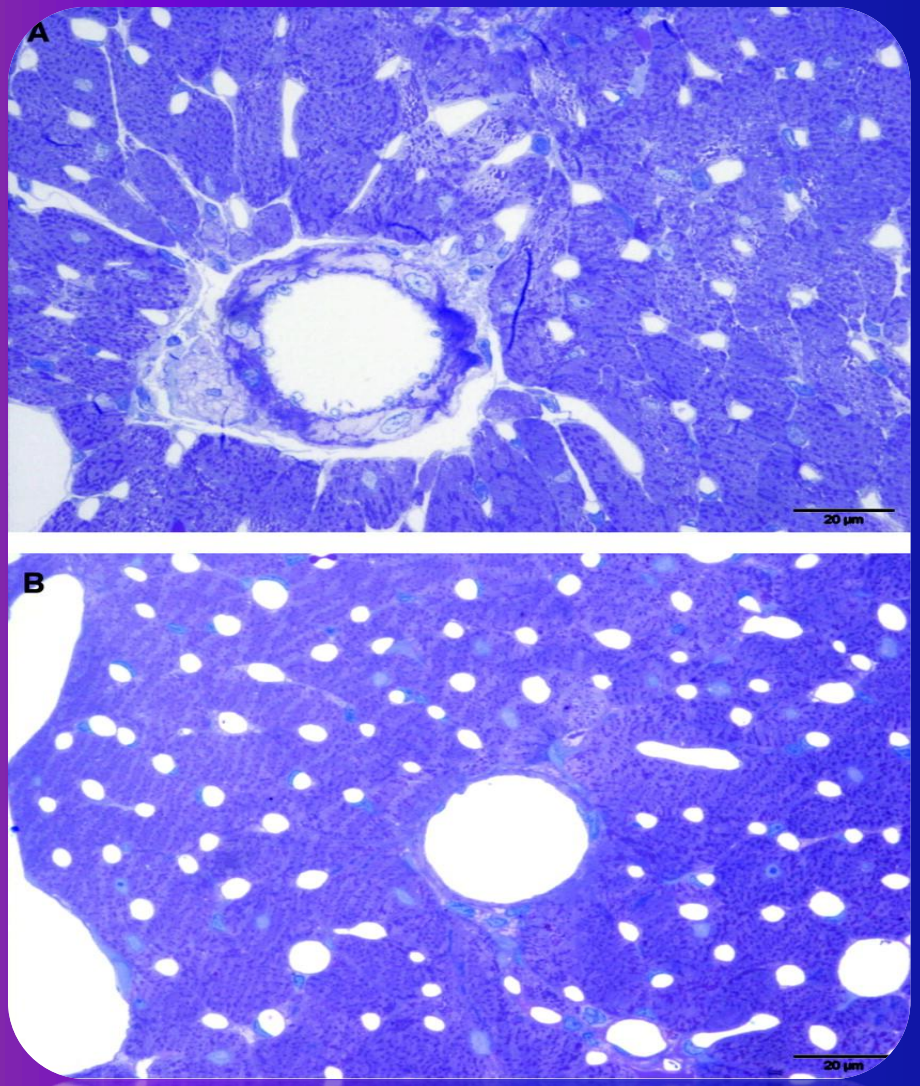
Μειωμένη μυοκαρδιακή αιμάτωση

Μηχανισμοί αύξησης της ΑΠ στη ΧΝΝ

- Προυπάρχουσα ιδιοπαθής υπέρταση
- **Αύξηση εξωκυτταρίου όγκου**
- Διέγερση του συστήματος RAS
- Αύξηση της δραστηριότητας του συμπαθητικού
- Αύξηση των παραγόντων με δράση δακτυλίτιδας
- Προσταγλανδίνες/βραδυκινίνες
- Τροποποίηση των παραγώγων ενδοθηλίου (NO/ενδοθηλίνη)
- Αύξηση σωματικού βάρους
- Χορήγηση EPO
- Υπερπαραθυρεοειδισμός/↑ ενδοκυττάριου Ca/υπερασβεστιαιμία
- Επασβέστωση αρτηριακού δένδρου
- Δυσλειτουργία χρόνιου μοσχεύματος
- Πτωματικό μόσχευμα από δότη με ιστορικό υπέρτασης
- Κυκλοσπορίνη, Tarcolimus,χορήγηση ανασοκατασταλτικών και κορτικοστεροειδών



Typical changes of the myocardium in a subtotally nephrectomized rat with moderate experimental renal failure



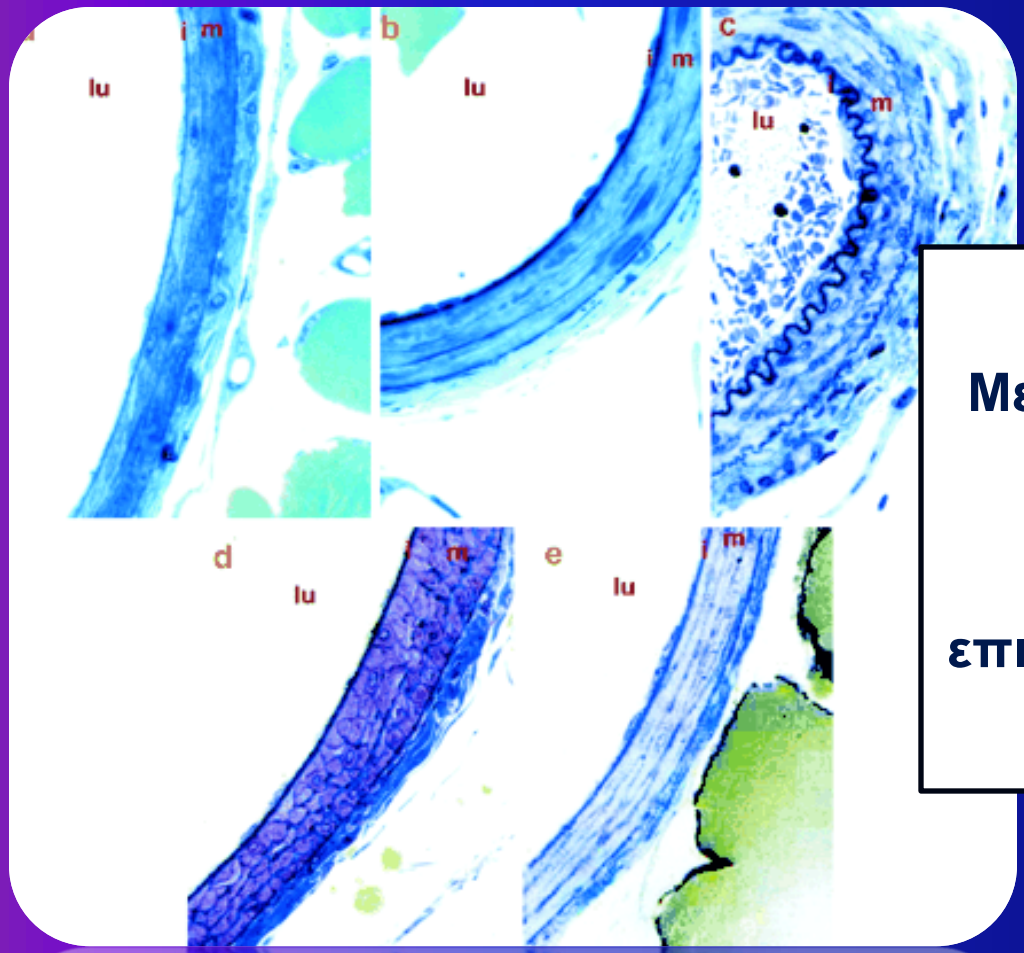
(A) compared with a sham-operated control animal (B). Semithin sections show methylene blue and basic fuchsin stain.

(B)Marked thickening of the wall of an intramyocardial arteriole with

(C) ***hypertrophy and hyperplasia*** of vascular smooth muscle cells, activation and ***expansion of the perivascular interstitial tissue*** with increased amounts of ***collagen fibers and interstitial fibroblasts***, and a lower number of capillary profiles per area of myocardium are demonstrable in renal failure (A) compared with the normal morphology in a sham-operated control rat (B).

Amann J Am Soc Nephrol
17: 2112-2119, 2006

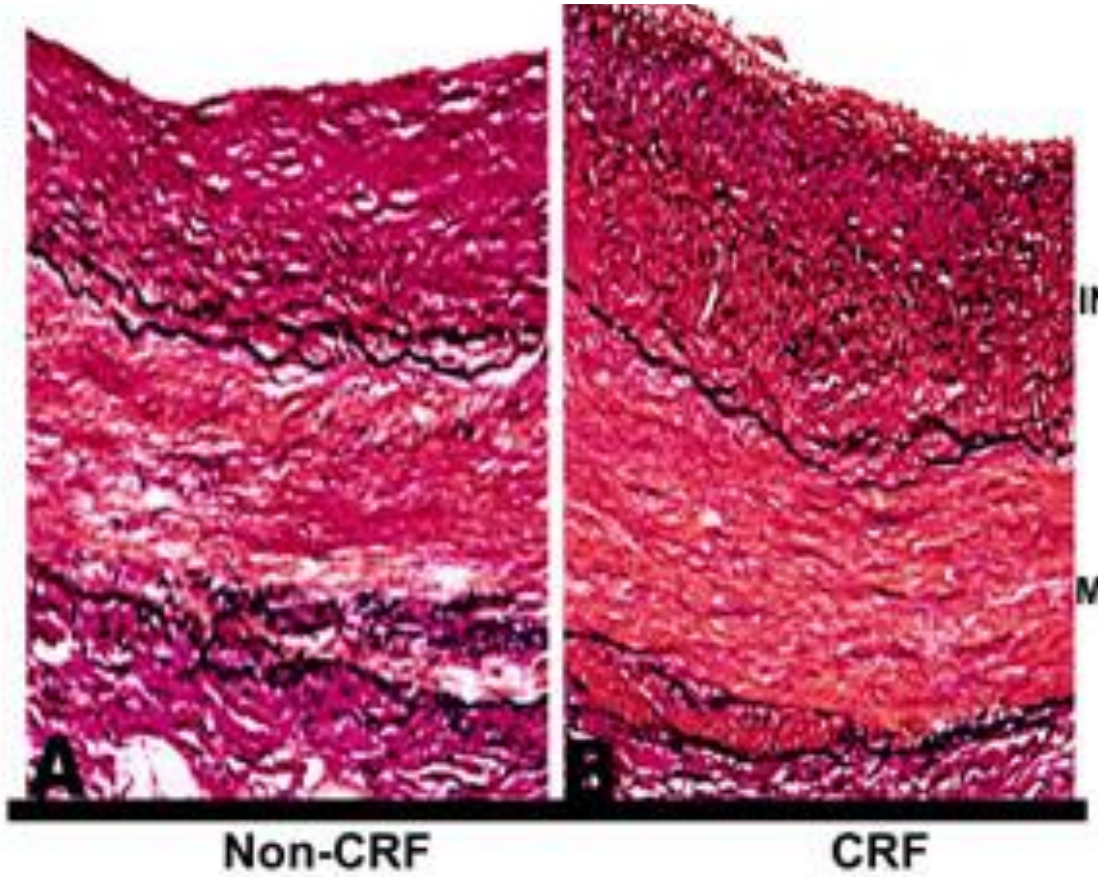
Remodeling of resistance arteries in renal failure: effect of endothelin receptor blockade



Μείωση της πυκνότητας των τριχοειδών και των εφεδρικών αγγείων σε άτομα με ΧΝΝ που εκτίθενται σε στεφανιαία ισχαιμία και τελικά επιδείνωση της κοιλιακής δυσλειτουργίας

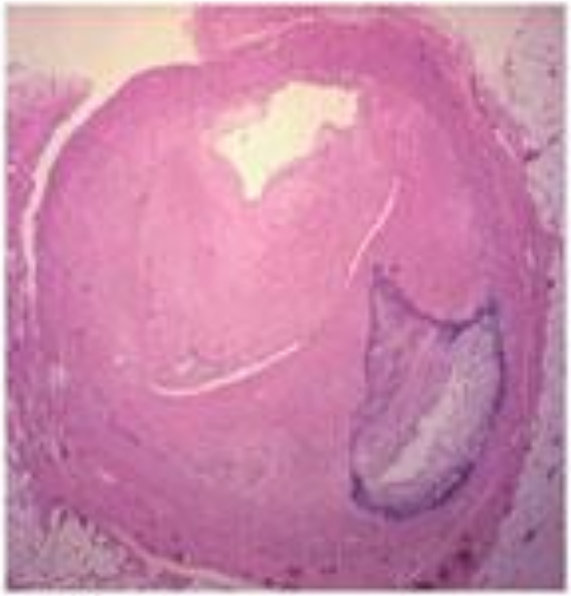
Vascular pathology in CRF

CKD affects the medial layer of blood vessels primarily through VC.



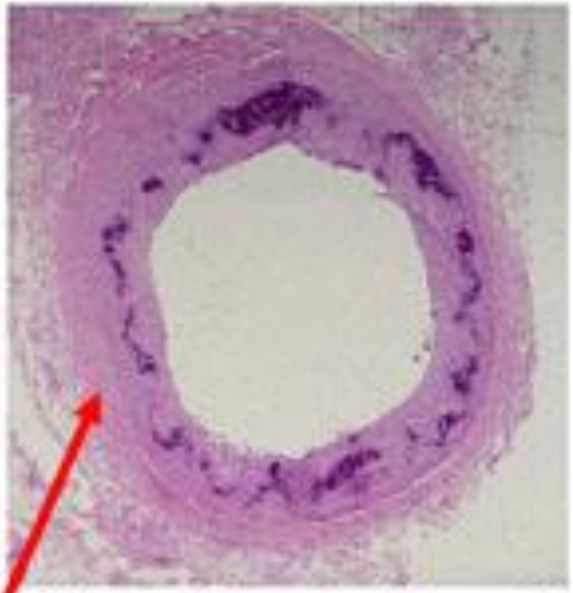
Schwarz et al, NDT 2000;15:218-23

Atherosclerosis vs. uremic arteriopathy



Atherosclerosis

- Inflammation
- Lipid
- Intimal calcification

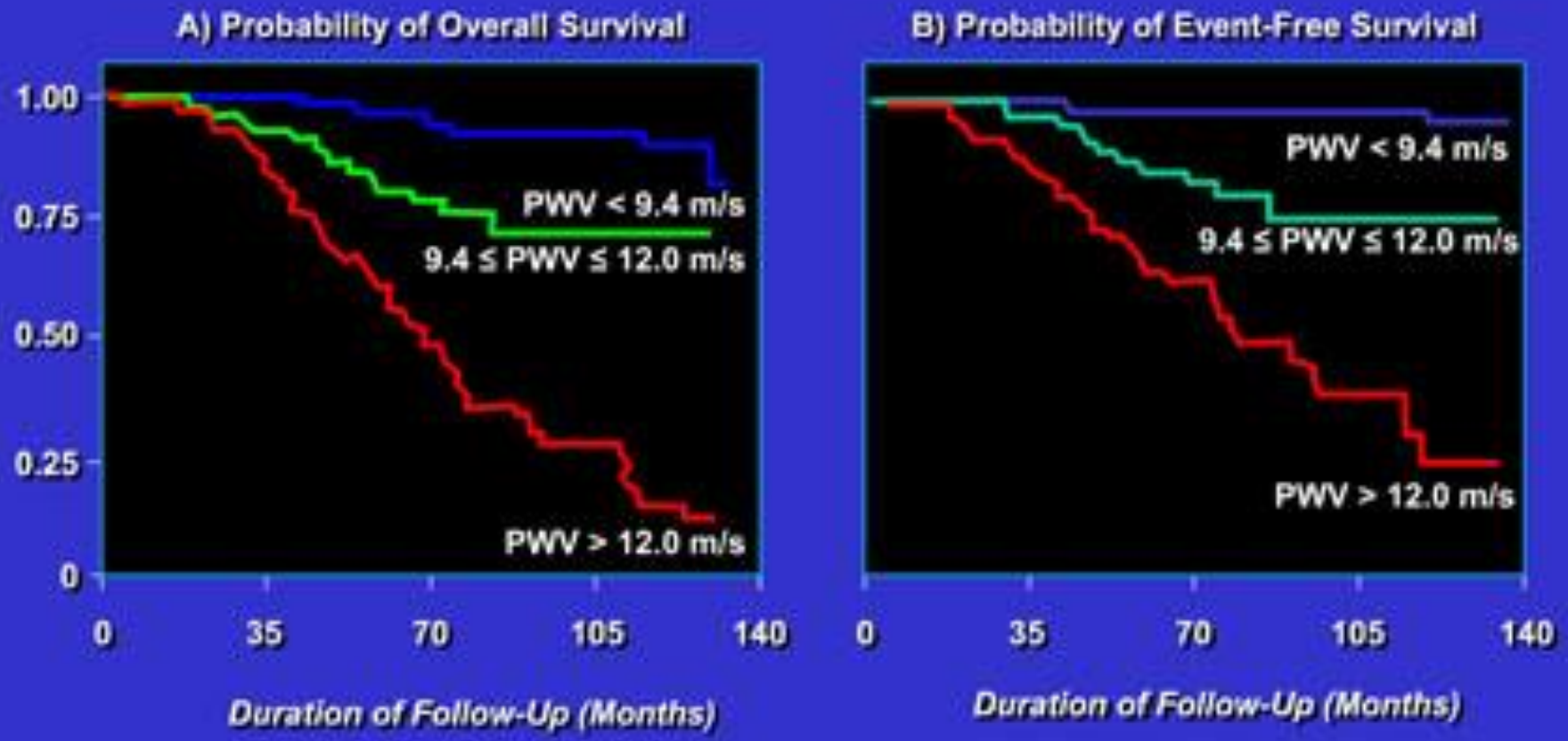


Uraemic arteriopathy

- +/- inflammation
- No lipid
- Medial calcification

increased collagen content and loss of elastic lamellae with secondary fibrosis and calcification of the media

Aortic Stiffness and Mortality in ESRD: PWV

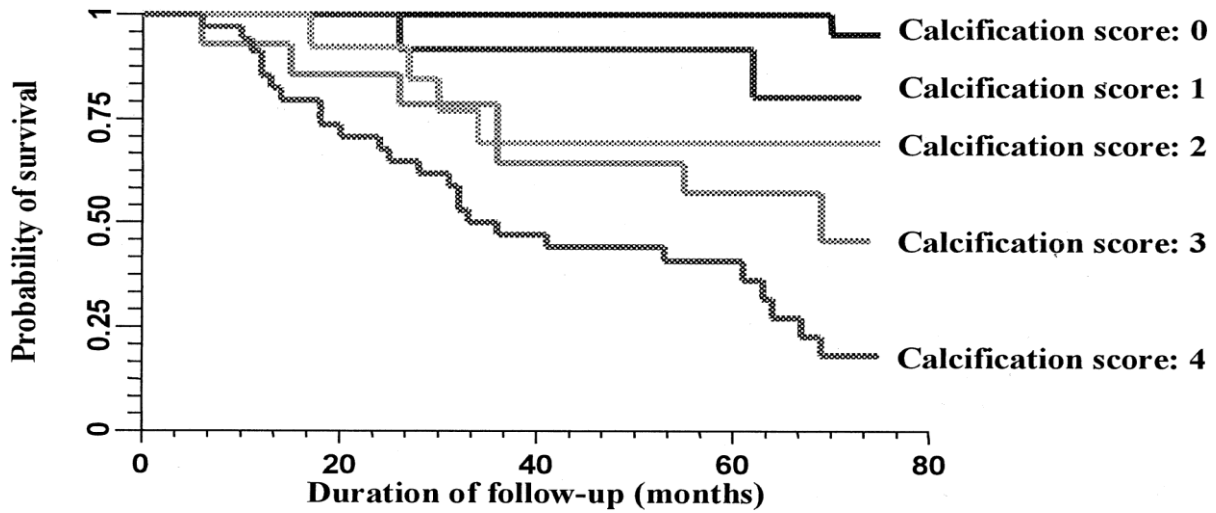


Blacher Circulation, 1999 (99); 2434

N = 241, F/U = 72+/-41 months

Probability of all-cause survival according to calcification score. Comparison between curves was highly significant (^{2}=42.66, *P*<0.0001).

Probability of all-cause survival according to calcification score



Blacher, J. et al. Hypertension 2001;38:938-942

Hypertension

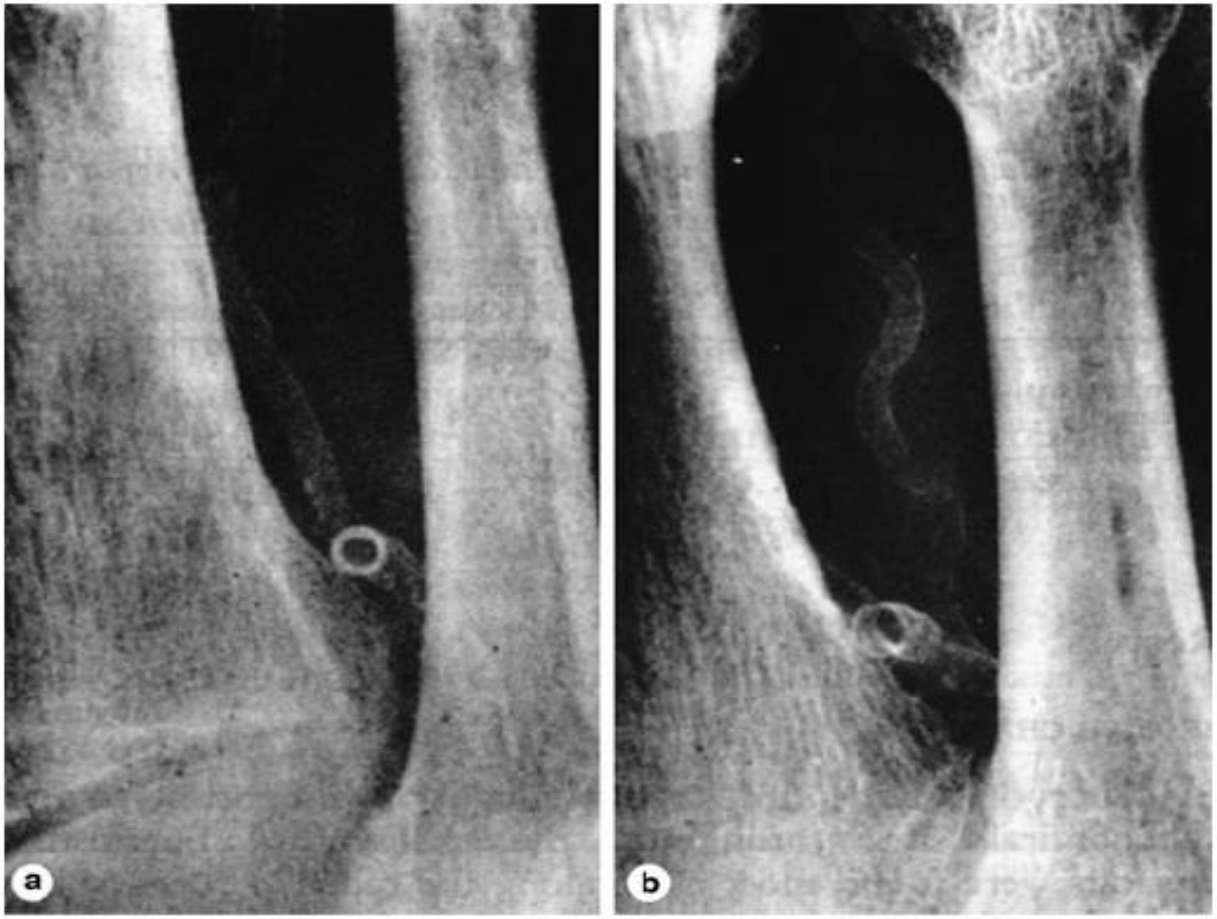
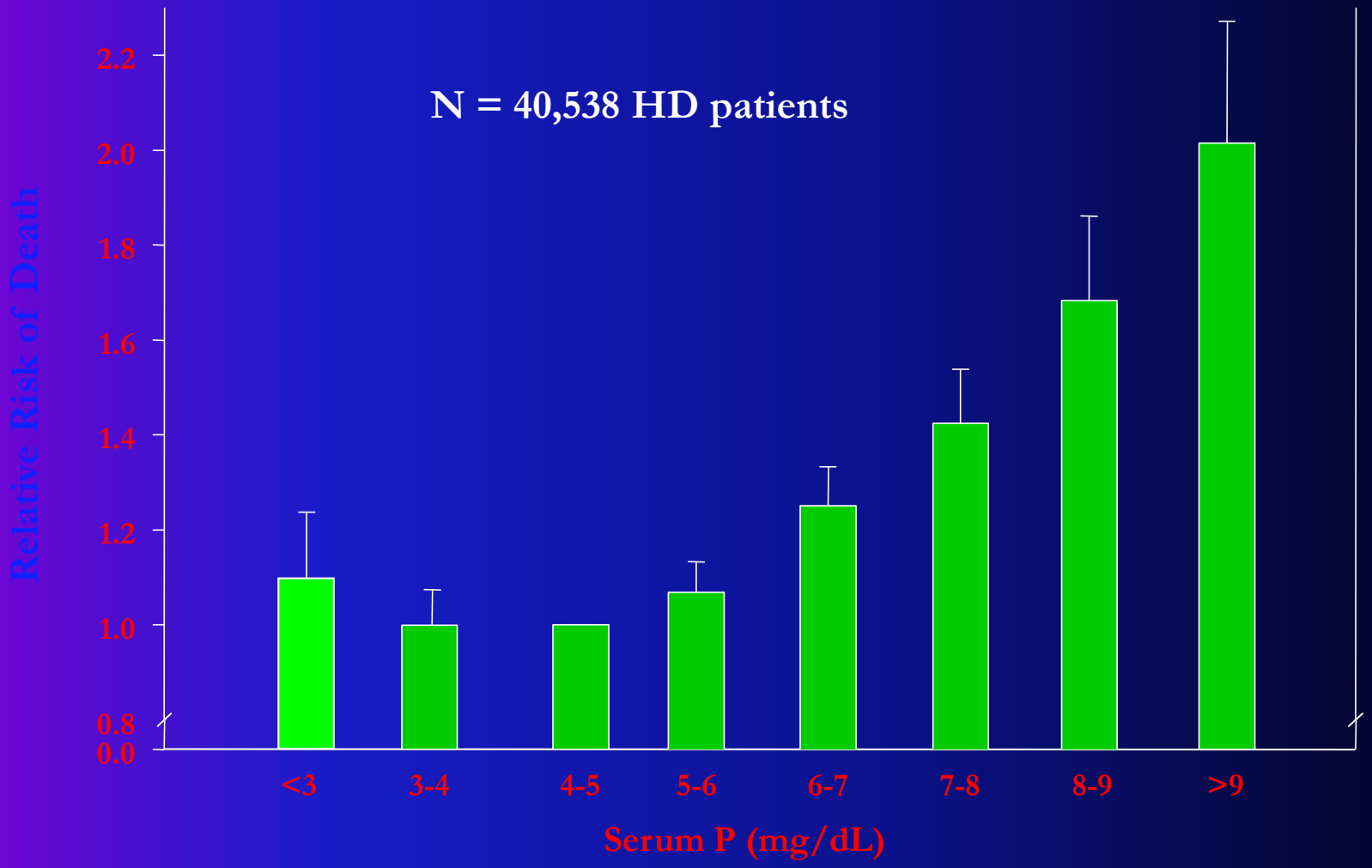


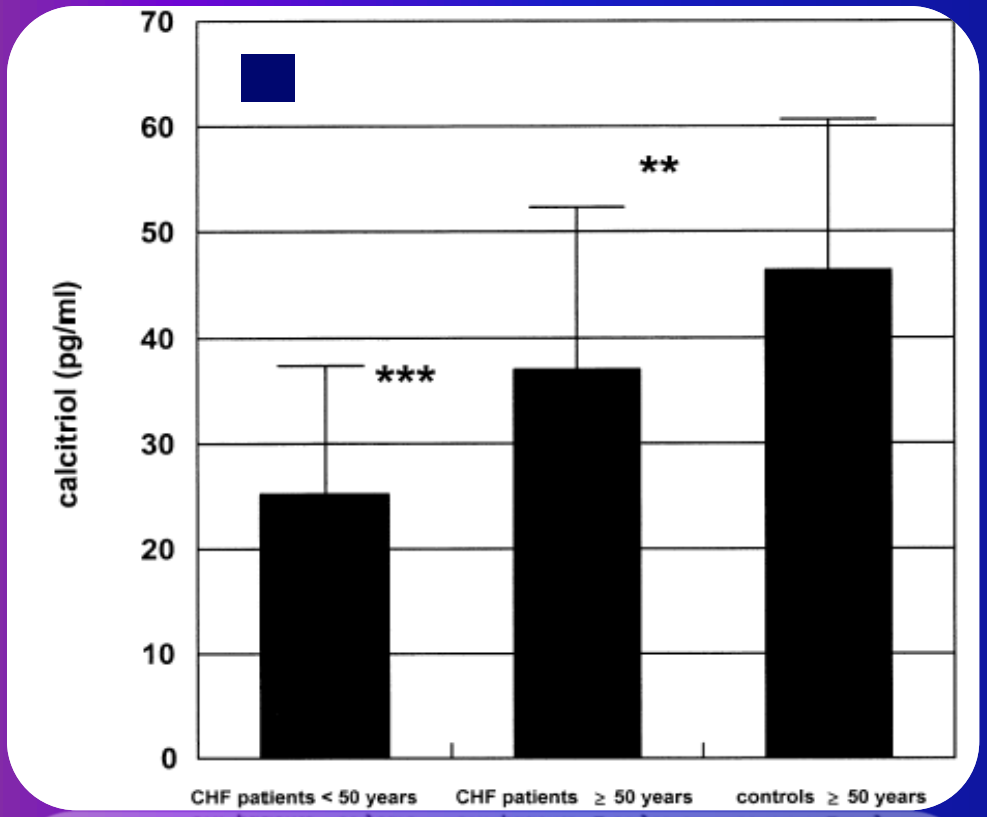
Fig. 1. X-rays of the foot of a dialysis patient showing "ring" and "tubular" patterns of arterial calcification as described by Tatler et al. (1) in 1973. Reproduced from their original publication with permission from the BMJ Publishing Group.

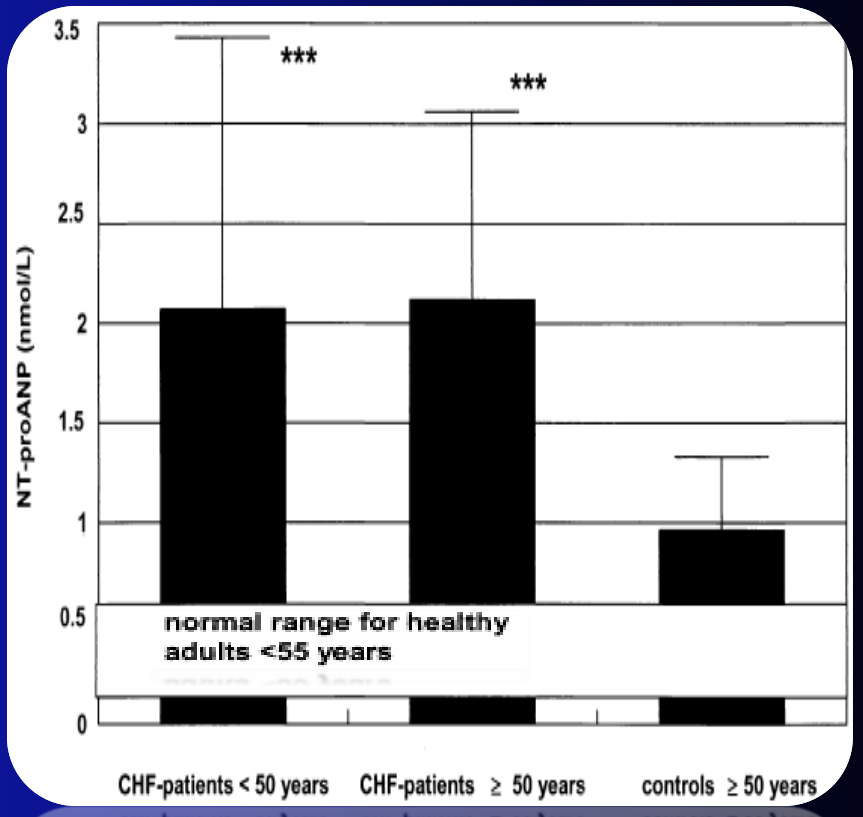
Mortality Risk by Serum P Levels



Block et al. *J Am Soc Nephrol.* 2004;15:2208-2218.

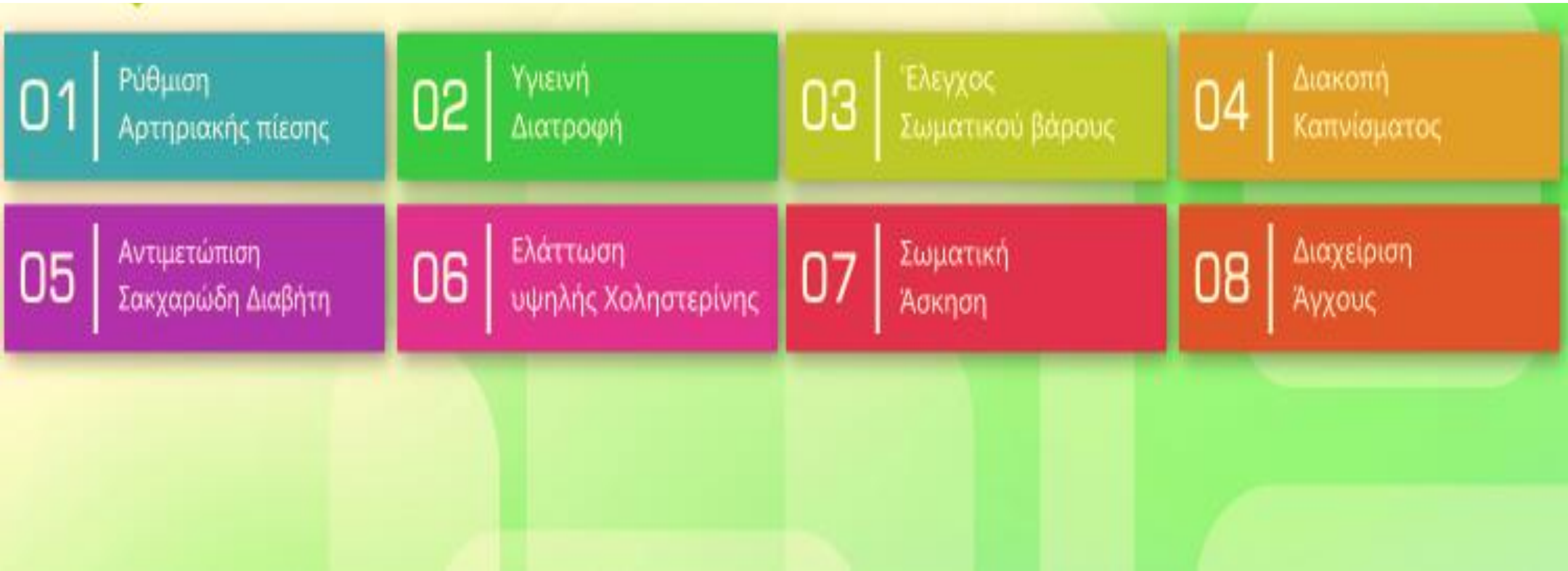
Vitamin D Deficiency in Humans is Associated with Heart Failure





Zitterman A, et al. *JACC.* 2003;41.

Βήματα για την πρόληψη της εξέλιξης της Καρδιαγγειακής Νόσου στη ΧΝΝ



Στόχοι αντι-υπερτασικής θεραπείας στη ΧΝΝ

1.1 Antihypertensive therapy should be used in CKD to:

1.1.a Lower blood pressure (A)

1.1.c Slow progression of kidney disease, in patients with or without hypertension (A) = (reduce proteinuria)

1.1.b Reduce the risk of CVD, in patients with or without hypertension (B)

K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis 2004

Stages of CKD & relationship to hypertension

GFR (mL/min/1.73 m²)	With Kidney Damage*		Without Kidney Damage*	
	With Hypertension	Without Hypertension	With Hypertension	Without Hypertension
≥90	1	1	"Hypertension"	"Normal"
60–89	2	2	"Hypertension with ↓ GFR"	"↓ GFR"[a]
30–59	3	3	3	3
15–29	4	4	4	4
<15 (or dialysis)	5	5	5	5

Shaded area represents CKD; numbers designate stage of CKD.

* Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

[a] May be normal in infants and in the elderly.

Reproduced with permission.[1]

KDOQI Am J Kidney Dis 2004

Ρύθμιση και στόχος Αρτηριακής Πίεσης

COMMENTARY

Blood Pressure in Chronic Kidney Disease: A Moving Target

Uncertainty remains on what the best blood pressure target is in patients with CKD

ary of Guidelines/Position Papers for Goal Blood e in People with Kidney Disease or Diabetes from us Consensus Committees around the World

Group	Goal BP	Initial Therapy
American Diabetes Assoc	<130/80	ACE Inhibitor/ARB*#
Am. Society of HTN (2008)	<130/80	ACE Inhibitor/ARB
National Kidney Foundation.	<130/80	ACE Inhibitor/ARB*
Japanese HTN Society (2006)	≤130/80	ARB*#
National Kidney Foundation	<130/80	ACE Inhibitor/ARB*
British HTN Society (2004)	<130/80	ACE Inhibitor/ARB
JNC 7 (2003)	<130/80	ACE Inhibitor/ARB*
ISH/ESC (2003)	<130/80	ACE Inhibitor/ARB
Australia-New Zealand (2002)	<130/85	ACE Inhibitor
WHO/ISH (1999)	<130/85	ACE Inhibitor

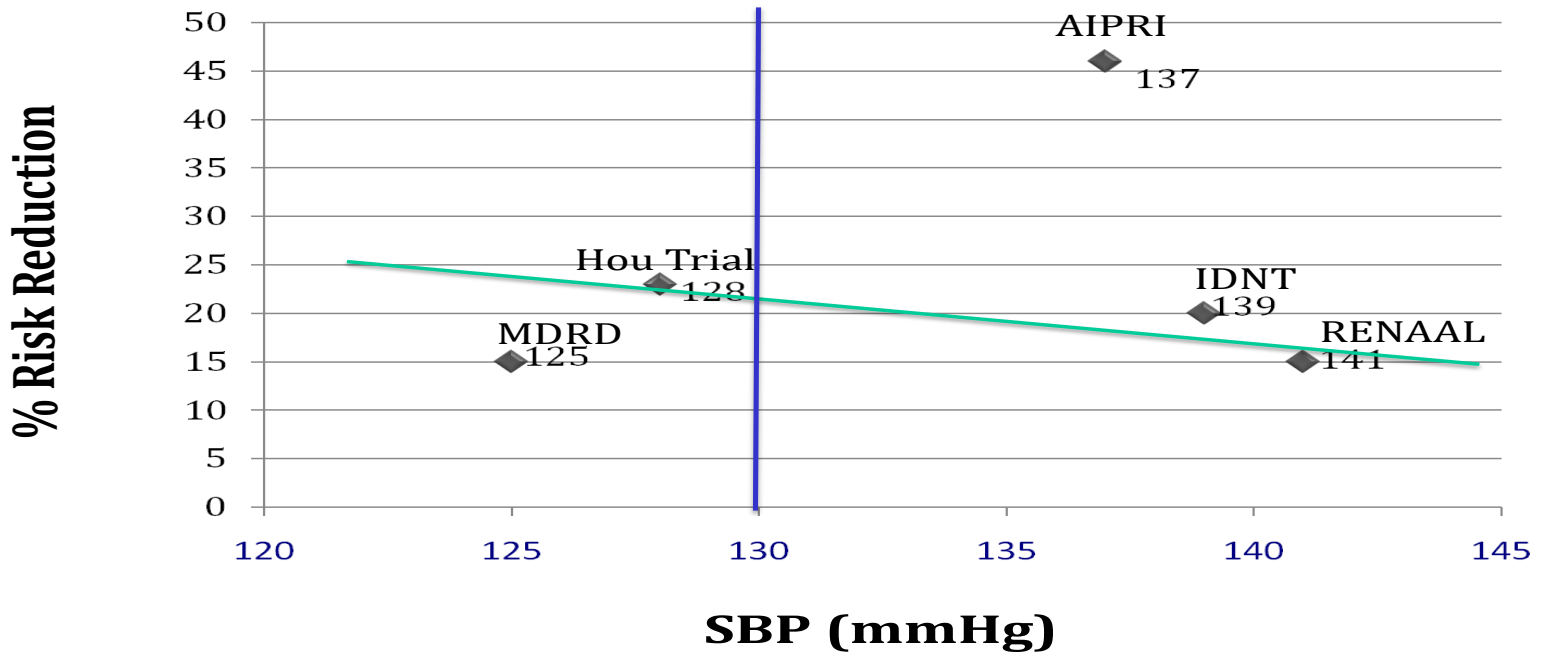
Khosla N, Kalaitzidis R et al Med Clin North Am 2009

2009

BP GOAL OF LESS THAN 130/80 mmHg : DOES THE EVIDENCE SUPPORT THIS BP IN CKD patients

Rigas Kalaitzidis, and George L. Bakris, J Clin Hypertens 2009

Lower Blood Pressure Goals for Cardiovascular and Renal Risk Reduction: Are They Defensible?



Rigas Kalaitzidis, and George L. Bakris, J Clin Hypertens May 2009

Three major goal blood pressure trials of patients with CKD

AASK | MDRD | SPRINT

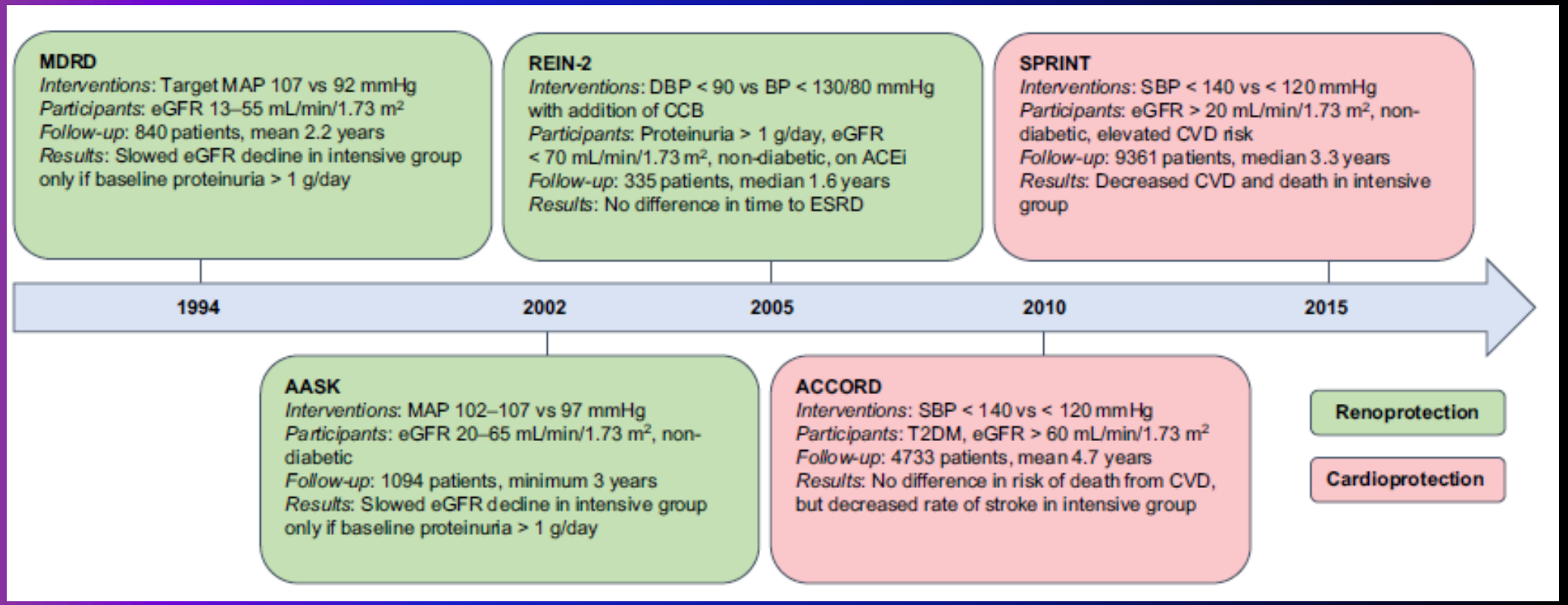
Included different patient populations

Examined different blood pressure targets

Used different methodology to measure blood pressure

All three reached **similar conclusions** about the benefit of more intensive blood pressure lowering

Timeline of landmark randomised trials comparing standard with intensive blood pressure control.



Drugs (2019) 79:365–379

2023 ESH Guidelines for the management of arterial hypertension

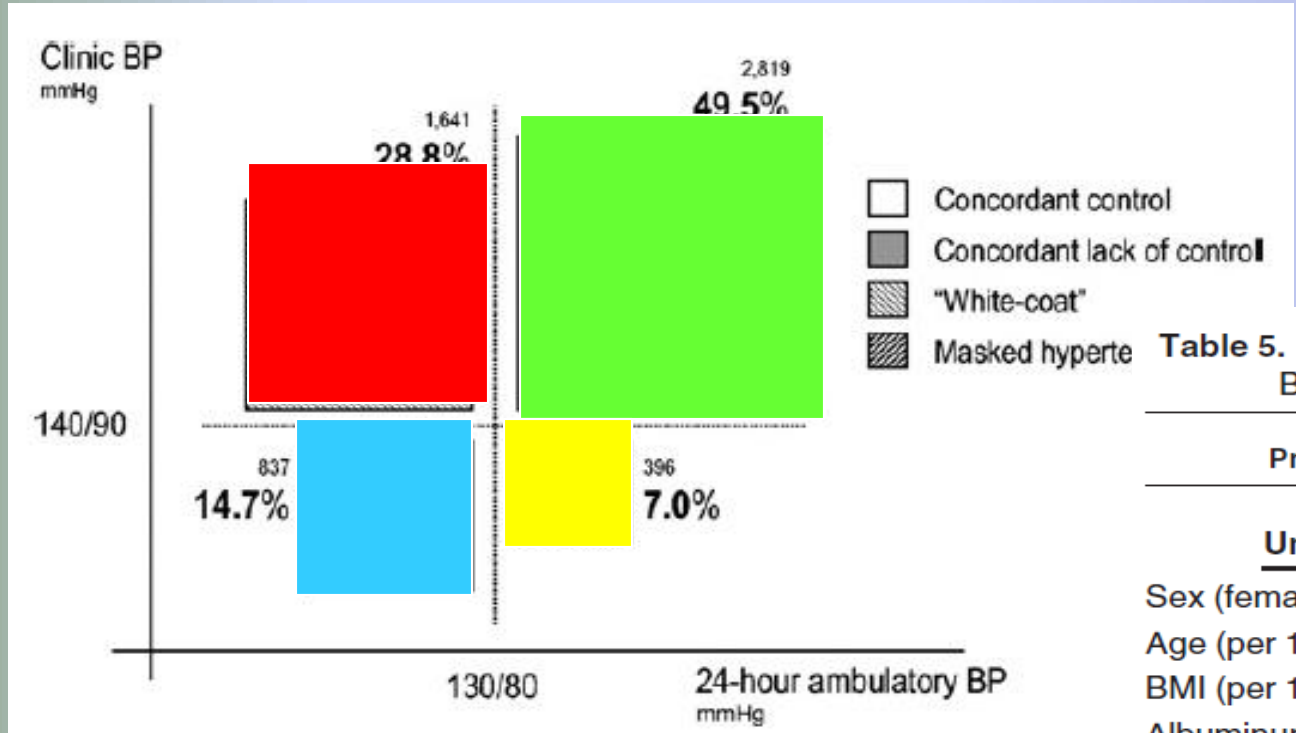
Treatment strategies in patients with kidney disease

Recommendations and statements	CoR	LoE
BP should be monitored at all stages of CKD, because hypertension is the second most important risk factor for end-stage kidney disease (ESKD).	I	A
Non-dipping or elevated night-time BP are frequent in CKD patients and should be monitored by ABPM or HBPM.	I	B
In both diabetic and non-diabetic CKD with hypertension, BP-lowering treatment slows the decline of kidney function and reduces the risk of ESKD and CV outcomes.	I	A
Immediate lifestyle interventions and antihypertensive drug treatment are recommended in most patients with CKD independently of the CKD stage if SBP≥ 140mmHg or DBP ≥90mmHg	I	C

Ambulatory Blood Pressure in Chronic Kidney Disease

Home blood pressure measurements in Chronic Kidney Disease: Ready for Prime Time?

White Coat and Masked Hypertension in CKD



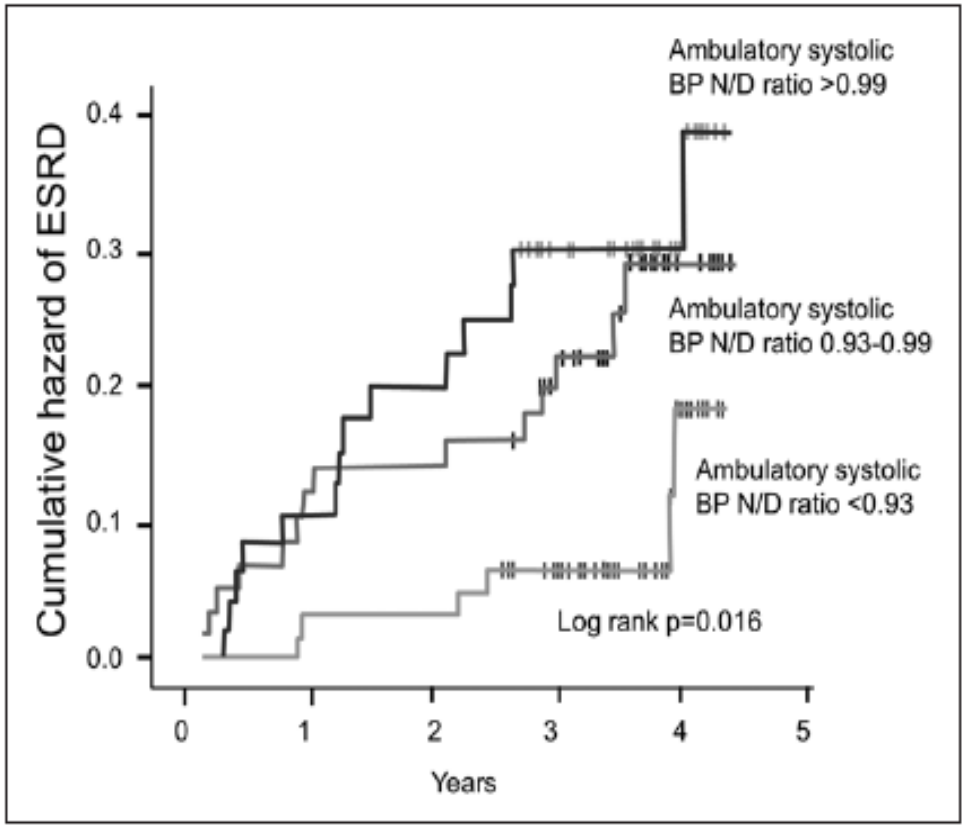
N=5693 CKD patients

Table 5. Predictors of Underestimation and Overestimation of BP Control From Multivariate Logistic Analysis

Predictor	OR (95% CI)	*P*
Underestimation ("white-coat" hypertension)		
Sex (female vs male)	1.217 (1.040-1.424)	0.02
Age (per 1-y older)	1.009 (1.003-1.015)	0.004
BMI (per 1-kg/m^2 higher)	1.022 (1.005-1.040)	0.01
Albuminuria (per 1-mg/g greater ACR)	1.001 (1.001-1.002)	<0.001
Target-organ damage (yes vs no)	1.201 (1.065-1.339)	0.02
Overestimation (masked hypertension)		
Age (per 1-y older)	1.017 (1.009-1.025)	<0.001
BMI (per 1-kg/m^2 higher)	1.032 (1.009-1.057)	0.008

Gorostidi, Sarafidis, de la Sierra, et al. Am J Kidn Dis 2013

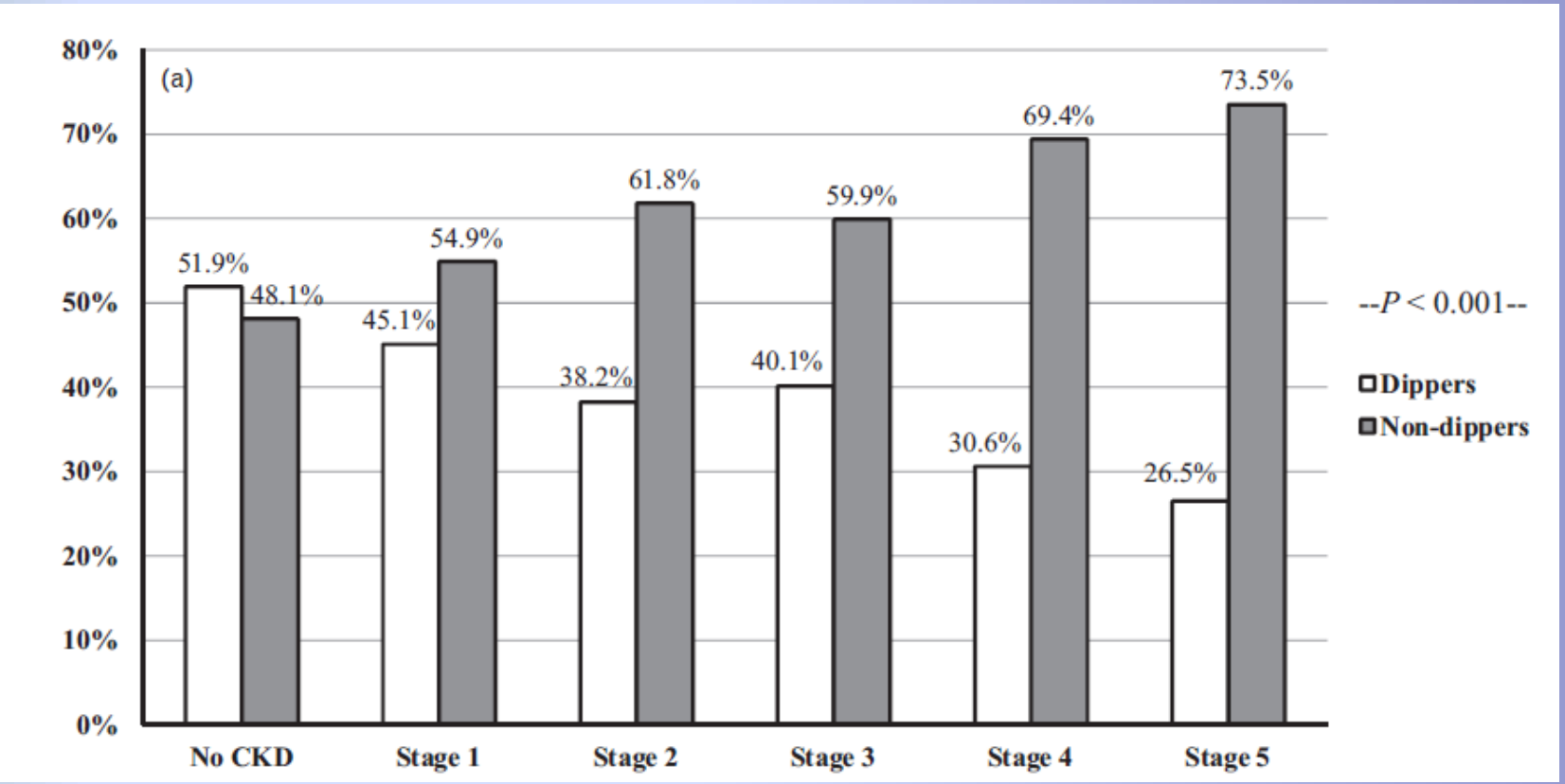
Blood Pressure Variability in Renal Disease



Association of dipping and end-stage renal disease (ESRD) events: night/day systolic ambulatory blood pressure was divided into 3 tertiles. Increasing severity of nondipping was associated with increasing ESRD events (P<0.016, log-rank test).

Hypertension. 2016;67:1102-1110.

Blood pressure variability increases with advancing chronic kidney disease stage: a cross-sectional analysis of 16 546 hypertensive patients



Abnormal dipping patterns are more common in CKD patients and worsen with advancing CKD stages

P Sarafidis et al Journal of Hypertension 2018, 36:1076–1085

2023 ESH Guidelines for the management of arterial hypertension

Treatment strategies in patients with kidney disease

In all patients with CKD the primary goal is to lower office BP to <140 mmHg systolic and <90 mmHg diastolic.	I	A
In most CKD patients (young patients, patients with an albumin/creatinine ratio ≥ 300 mg/g, high CV risk patients) office BP should be lowered to <130/80 mmHg if tolerated.	II	B
In kidney transplant patients with hypertension, office BP should be lowered to <130 mmHg systolic and <80 mmHg diastolic	II	B
In patients with CKD regardless of the presence of albuminuria, BP should not be lowered below 120/70 mmHg.	III	C
An ACEi or an ARB, titrated to the maximum tolerated	I	A

2023 ESH Guidelines for the management of arterial hypertension

Treatment strategies in patients with kidney disease

doses is recommended for patients with CKD and moderate (UACR 30 to 300 mg/g) or severe (UACR > 300 mg/g) albuminuria.		
Dual combination of an ACEi with an ARB is not recommended.	III	A
BP control is difficult in CKD and resistant hypertension is very frequent. Therefore combination treatment is almost always recommended.	I	B

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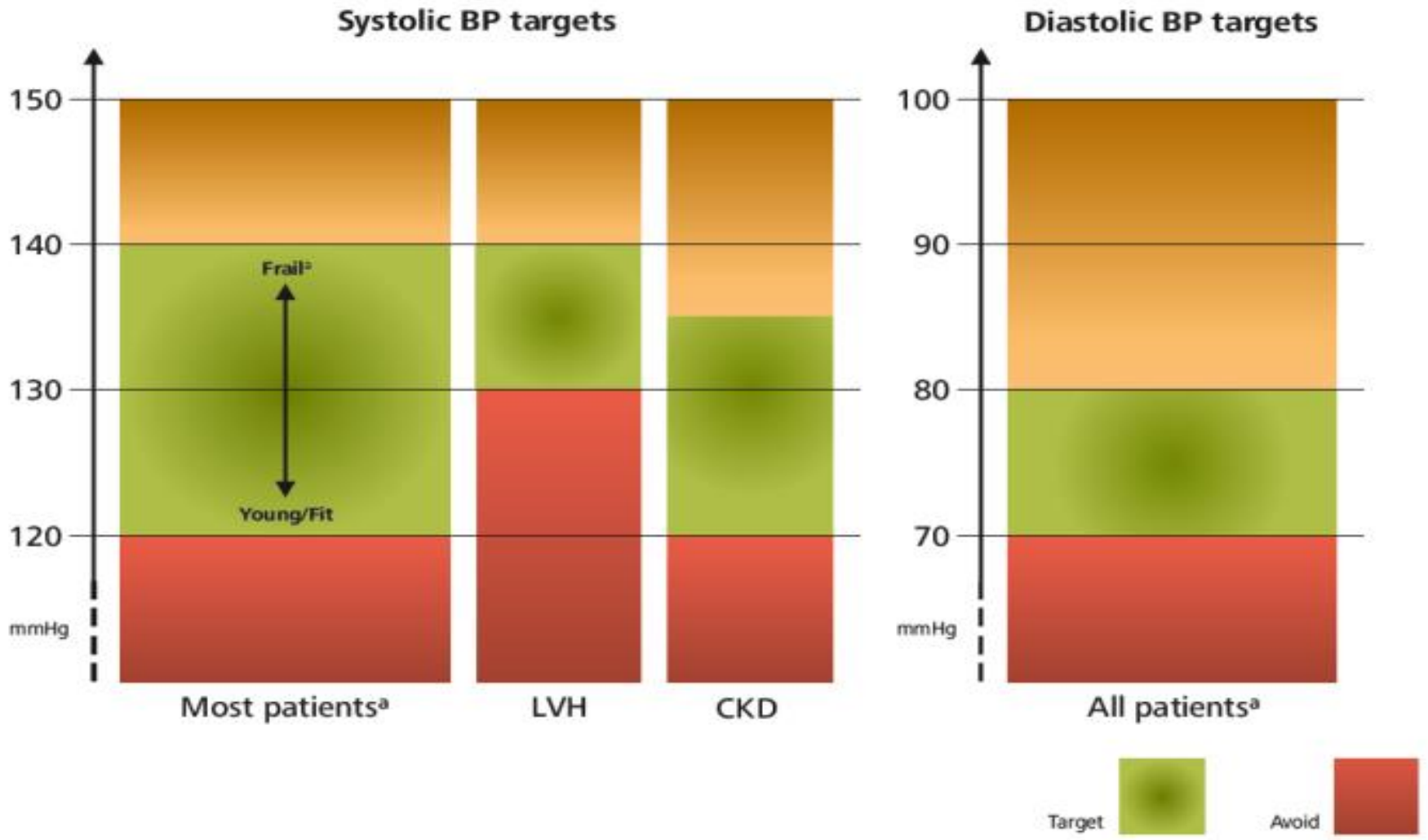

Figure 10. Office BP targets in most patients and selected patient groups

2023 ESH Guidelines for the management of arterial hypertension

Treatment strategies in patients with kidney disease

SGLT-2 inhibitors are recommended for patients with CKD due to type-2 diabetes or some non-diabetic nephropathies and moderately or severely increased albuminuria, independent of eGFR, and in those patients with CKD and eGFR < 45 ml/min/1.73²	I	A
The non-steroidal MRA finerenone can be used, because of its nephroprotective and cardioprotective properties and some BP lowering effect in patients with diabetic CKD and moderately or severely increased albuminuria.	I	A
In CKD patients with hyperkalemia a potassium binder can be used to maintain normal or near normal serum potassium levels (<5.5 mmol/L) in order to allow optimal treatment with a RAS-blocker or a MRA to continue.	II	B

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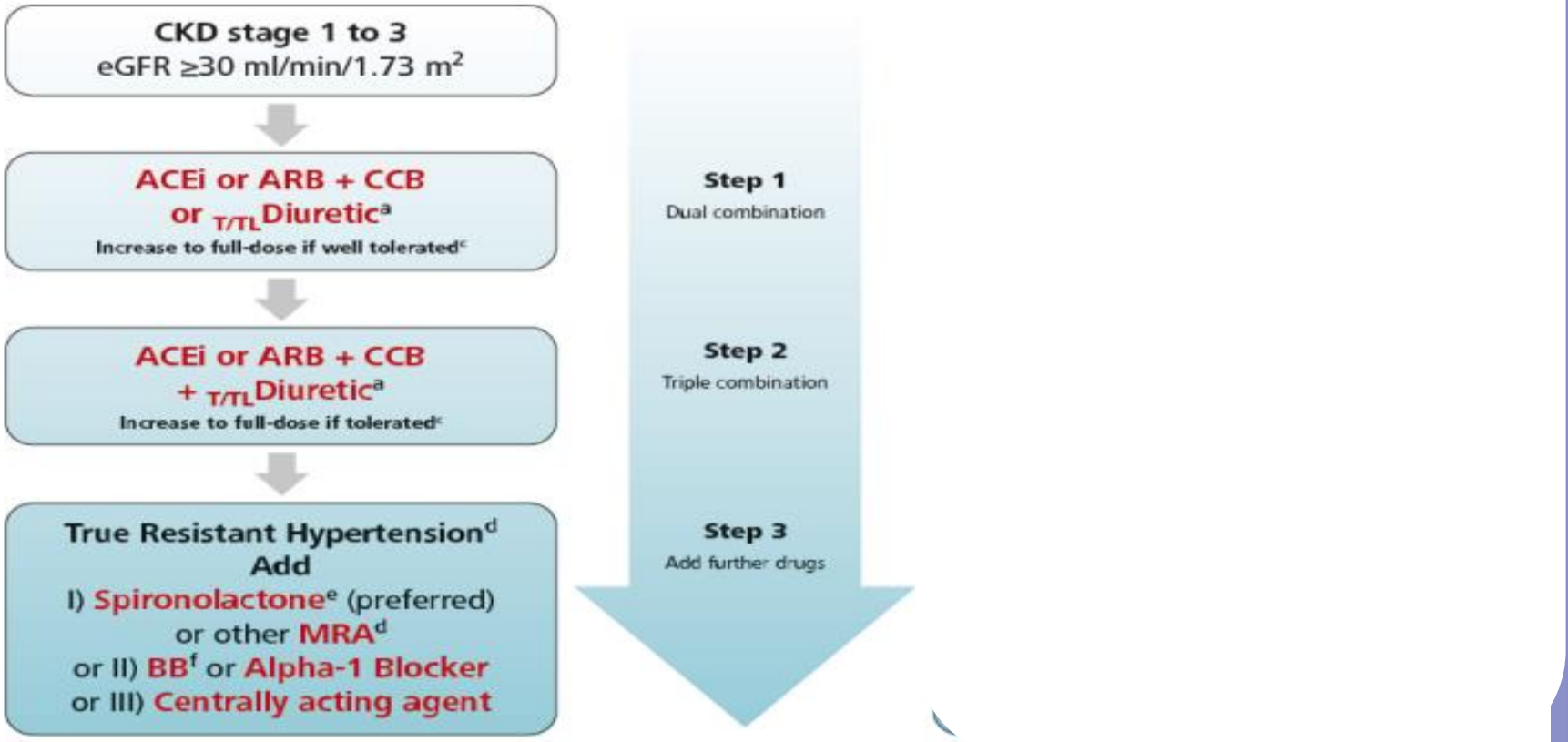
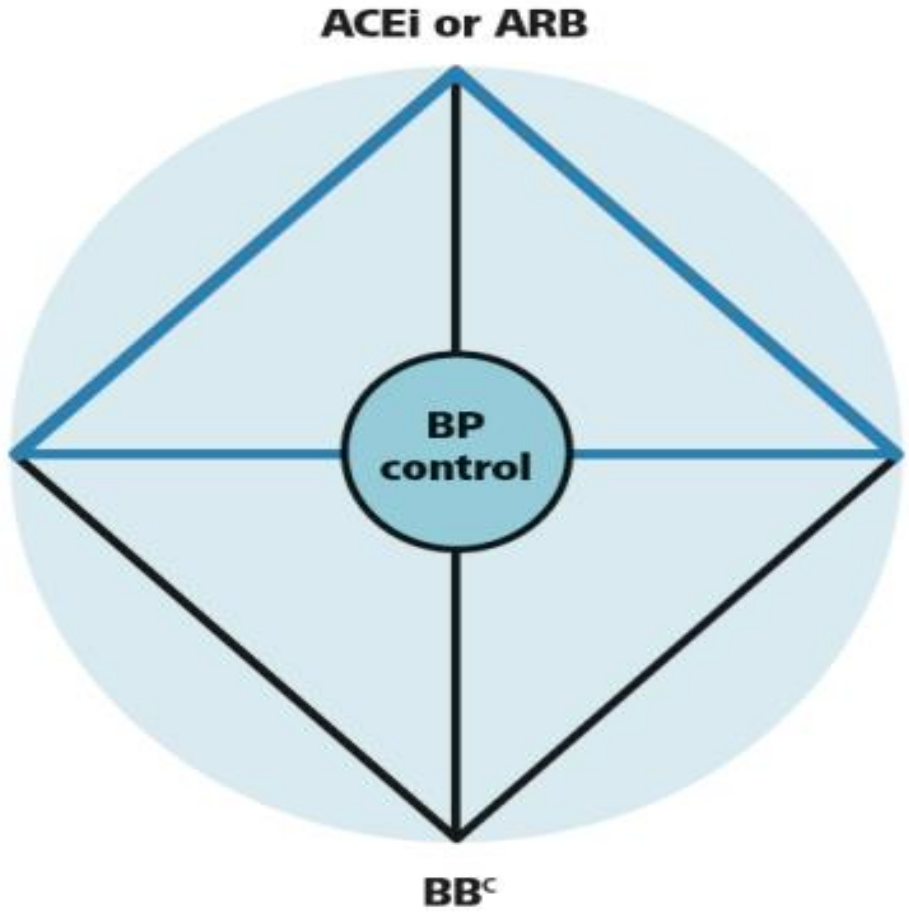


Additional therapy: SGLT2i as GDMT in CKD or Finerenone as GDMT in CKD with Type 2 Diabetes mellitus

2023 ESH Guidelines for the management of arterial hypertension

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**



Additional drug classes

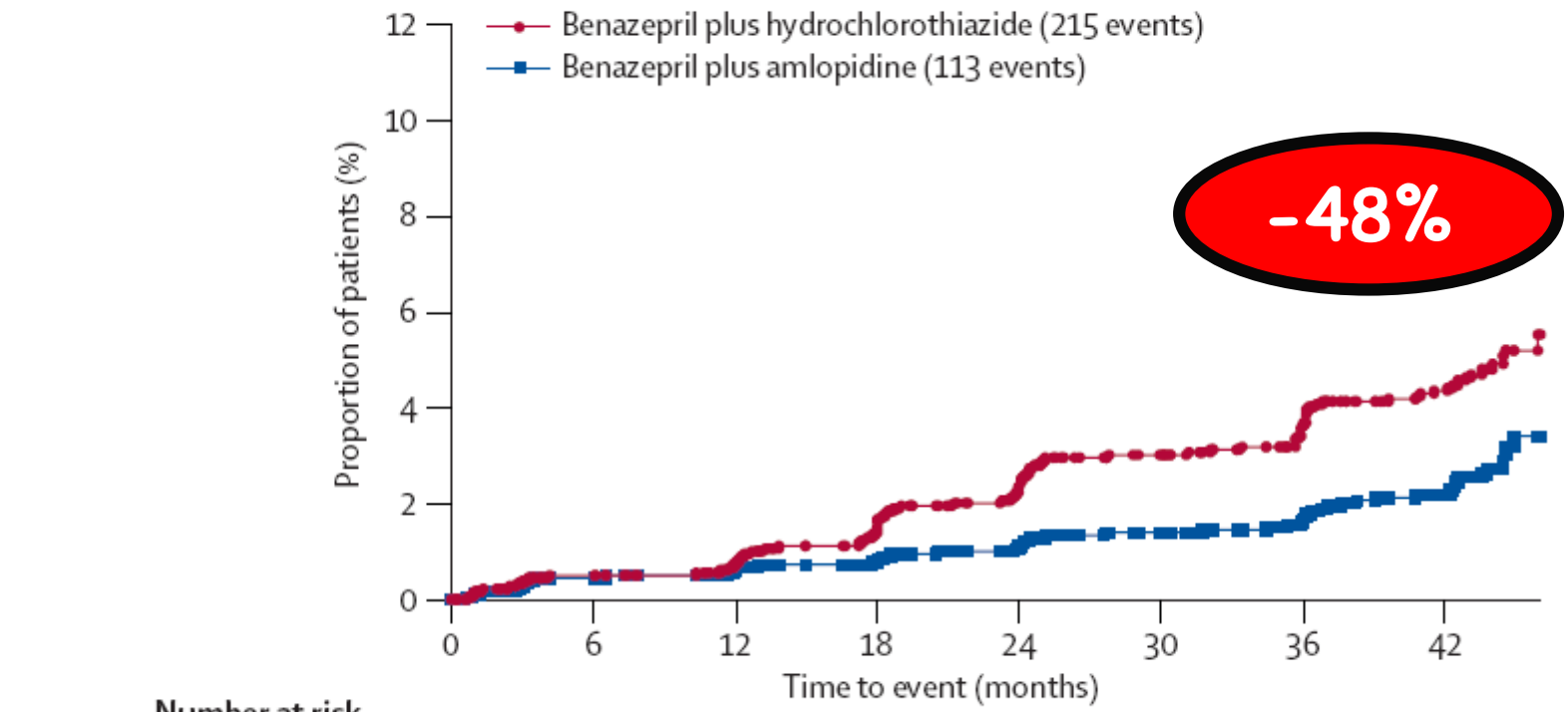
General antihypertensive therapy:

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

Special comorbidities:

- ARNi
- SGLT2i
- Non-Steroidal MRA

Progression of chronic kidney disease



Number at risk								
Benazepril plus hydrochlorothiazide	5762	5576	5459	5307	5139	4936	2956	1506
Benazepril plus amlopidine	5744	5578	5452	5336	5203	5022	3016	1559

Lancet 2010;375:1173-81

Diuretics Used to Treat Hypertension

		BA (%)	$T_{½}$ (hours)	DOA (hours)
Thiazide and Thiazide-like Diuretics	Hydrochlorothiazide	65 – 75	3.0 – 10.0	6 – 12
	Chlorothiazide	30 – 50	15.0 – 25.0	6 – 12
	Chlorthalidone	65	24.0 – 55.0	24 – 72
	Bendroflumethiazide	90	2.5 – 5.0	18 – 24
	Indapamide	90	6.0 – 15.0	24 – 36
	Metolazone	65	14	12 – 24
Loop Diuretics	Bumetanide	80 – 90	0.3 – 1.5	4-6
	Furosemide	10 – 100	0.3 – 3.4	6-8
	Torsemide	80 – 100	3.0 – 4.0	6-8
Potassium-Sparing Diuretics	Amiloride	15-20	17.0 – 26.0	24
	Triamterene	83 (55)*	3.0 (3.0)*	7-9
	Spironolactone	>90	1.5 – 15.0†	48-72
	Eplerenone	69	2.2 – 9.4	NA

*

Reprinted from Brater DC. In: *Principles of Pharmacology: Based Concepts and Clinical Applications*. 1995:657-672, with permission from Springer Science and Business Media; Delyani JA, et al. *Cardiovasc Drug Rev*. 2001;19:185-200; Rosenberg J, et al. *Cardiovasc Drug Ther*. 2005;19:301-306; Sica DA. *Congest Heart Fail*. 2003;9:100-105.

2023 ESH Guidelines for the management of arterial hypertension

Diuretics

Diureticcs are particularly useful in CKD patients, because these patients are most often sodium-sensitive (especially if older, diabetic or obese) and have a high prevalence of treatment-resistant hypertension.

Furthermore, diuretics can effectively reduce proteinuria when added to RAS blockers in proteinuric CKD [1366]. When GFR falls below 45 ml/min/1.73 m2,

Thiazide diuretics become less effective, because they cannot reach their tubular site of action because of competition for tubular secretion with other substances that accumulate in CKD

Τορασεμίδη έναντι Φουροσεμίδης

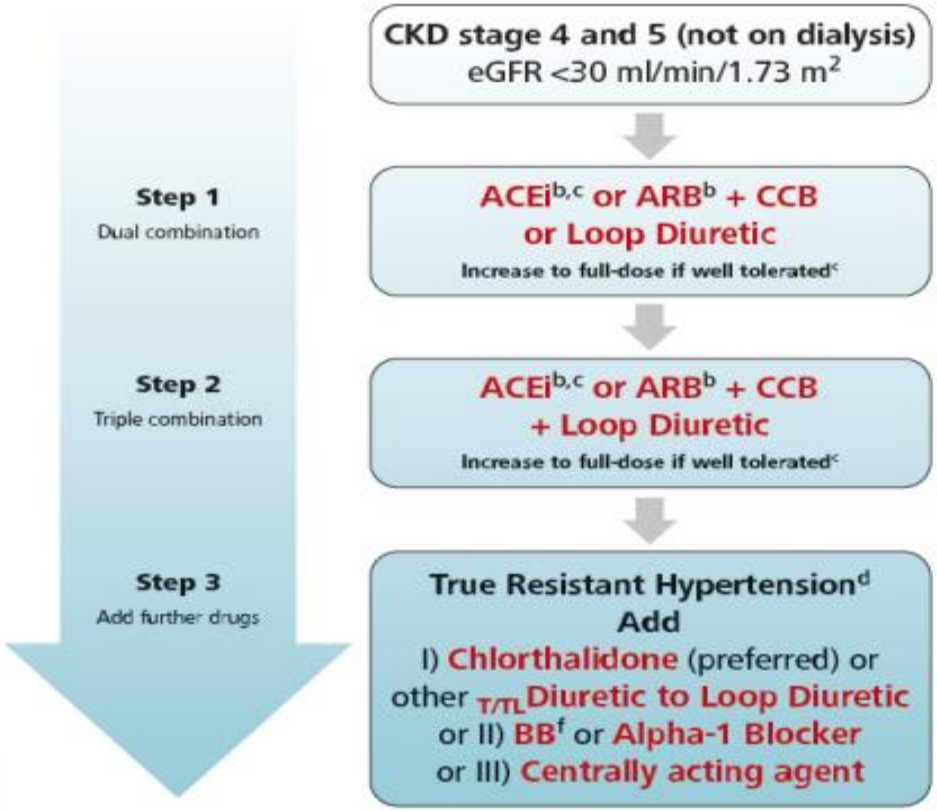
	Φουροσεμίδη	Τορασεμίδη
Βιοδιαθεσιμ. (%)	10-100	**80-100**
Μεταβολισμός	50% νεφροί	80% ηπαρ
Σύνδεση με πρωτεΐνες	95%	97-99%
Διάρκεια δράσης (ώρες)	4-6	**18-24**

Μεγαλύτερη μείωση της θνητότητας στην ΧΚΑ
Μεγαλύτερη μείωση συχνότητας επανεισαγωγών και διάρκειας νοσηλείας
Μεγαλύτερη μείωση τάξης κατά NYHA
Ταχύτερη και πιο αποτελεσματική υποχώρηση συμπτωμάτων

Βελτίωση αιμοδυναμικών παραμέτρων (LVEF, LVESV, LVEDV)
Αντι-αλδοστερονική και αντι-ινωτική δράση

Ισχυρότερη αντι-υπερτασική δράση
Καλύτερη ποιότητα ζωής (νυκτουρία, μικρουρία)
Λιγότερη καλλιούρηση

2023 ESH Guidelines for the management of arterial hypertension



Additional therapy: SGLT2i as GDMT in CKD or Finerenone as GDMT in CKD with Type 2 Diabetes mellitus

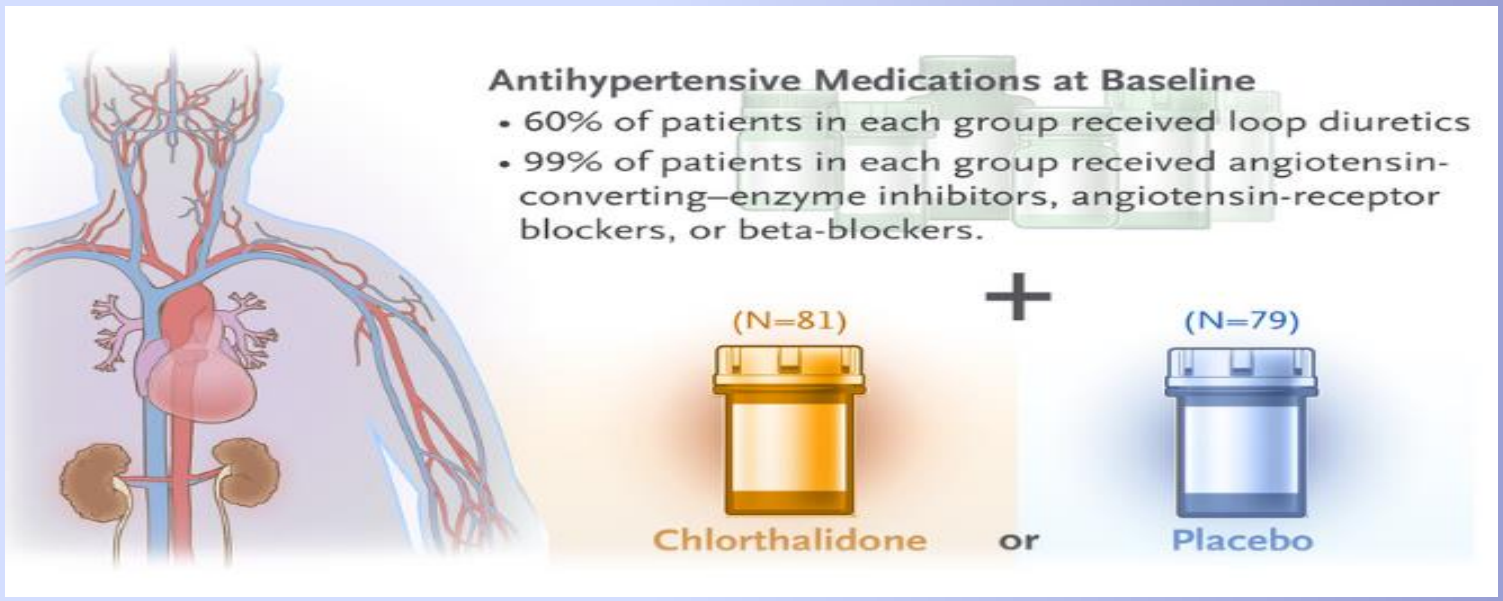
diuretics

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 30, 2021 VOL. 385 NO. 27

Chlorthalidone for Hypertension in Advanced Chronic Kidney Disease

Rajiv Agarwal, M.D., Arjun D. Sinha, M.D., Andrew E. Cramer, B.S., Mary Balmes-Fenwick, M.S., Jazmyn H. Dickinson, B.S., Fangqian Ouyang, M.S., and Wanzhu Tu, Ph.D.



diuretics

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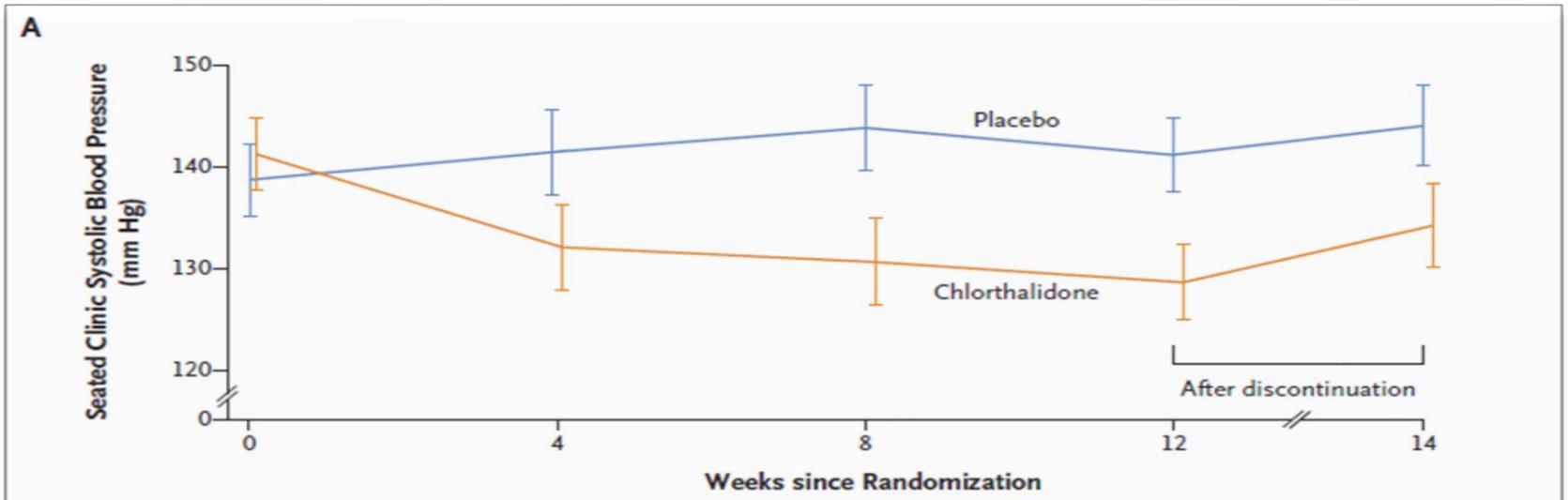


Mean Change from Baseline (95% CI) — mm Hg				
Placebo	2.7 (−0.9 to 6.3)	5.1 (1.4 to 8.8)	2.4 (−0.6 to 5.5)	5.3 (1.8 to 8.8)
Chlorthalidone	−9.2 (−12.9 to −5.5)	−10.6 (−14.5 to −6.8)	−12.6 (−15.8 to −9.5)	−7.0 (−10.7 to −3.3)
Difference	−11.9 (−17.1 to −6.7)	−15.7 (−21.0 to −10.5)	−15.1 (−19.4 to −10.7)	−12.3 (−17.5 to −7.2)

diuretics

The NEW ENGLAND JOURNAL of MEDICINE

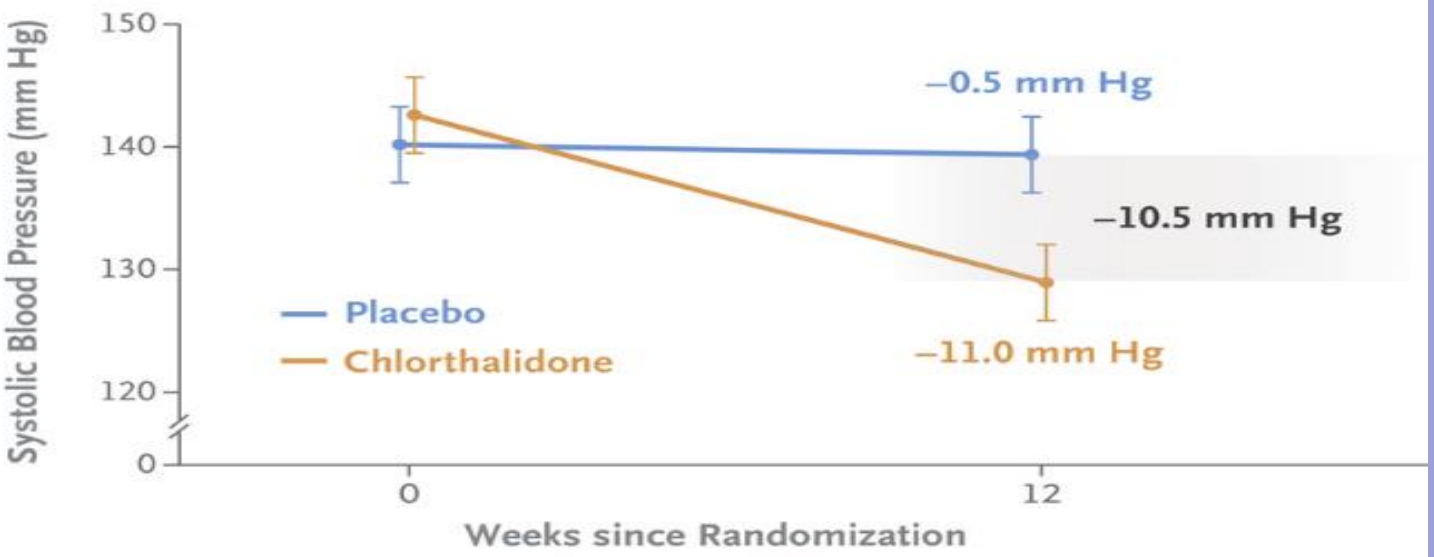
ESTABLISHED IN 1812 DECEMBER 30, 2021 VOL. 385 NO. 27

Chlorthalidone for Hypertension in Advanced Chronic Kidney Disease

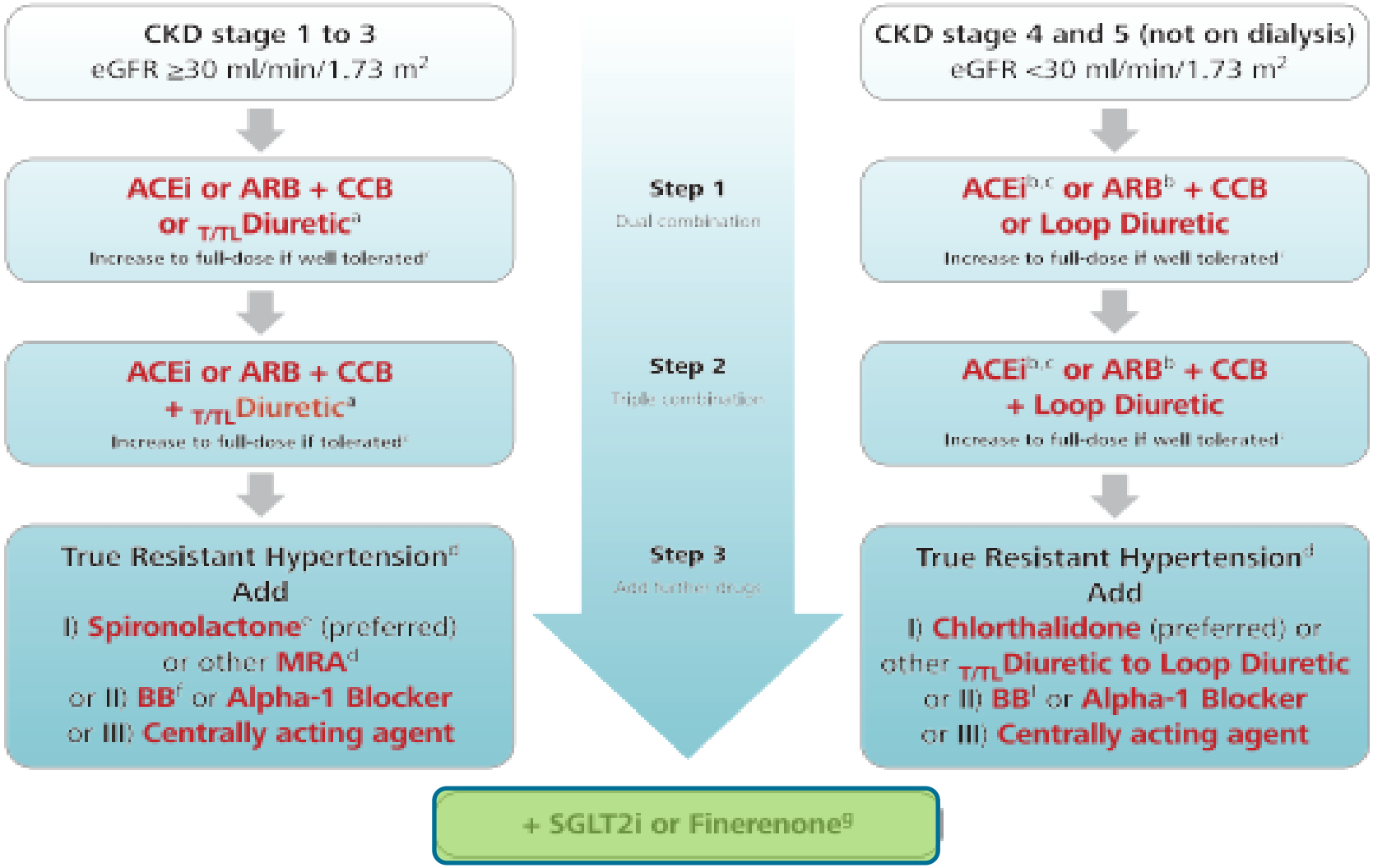
k, M.S.,

Adjusted Change in 24-Hour Ambulatory Systolic Blood Pressure from Baseline to 12 Weeks

Mean difference, −10.5 mm Hg; 95% CI, −14.6 to −6.4; P<0.001



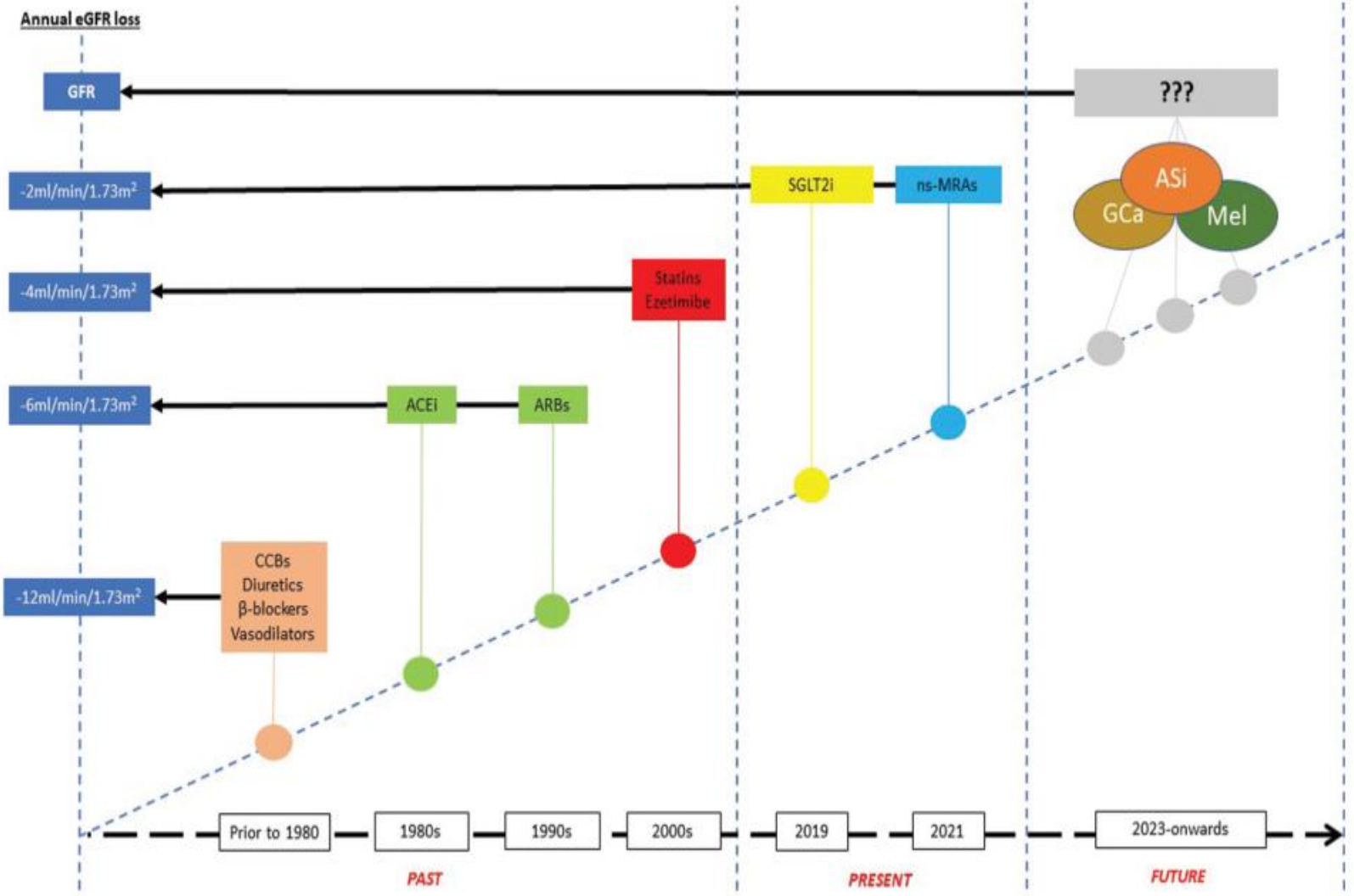
2023 ESH Guidelines for the management of arterial hypertension



Στρατηγικές μείωσης της Αρτηριακής Πίεσης

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

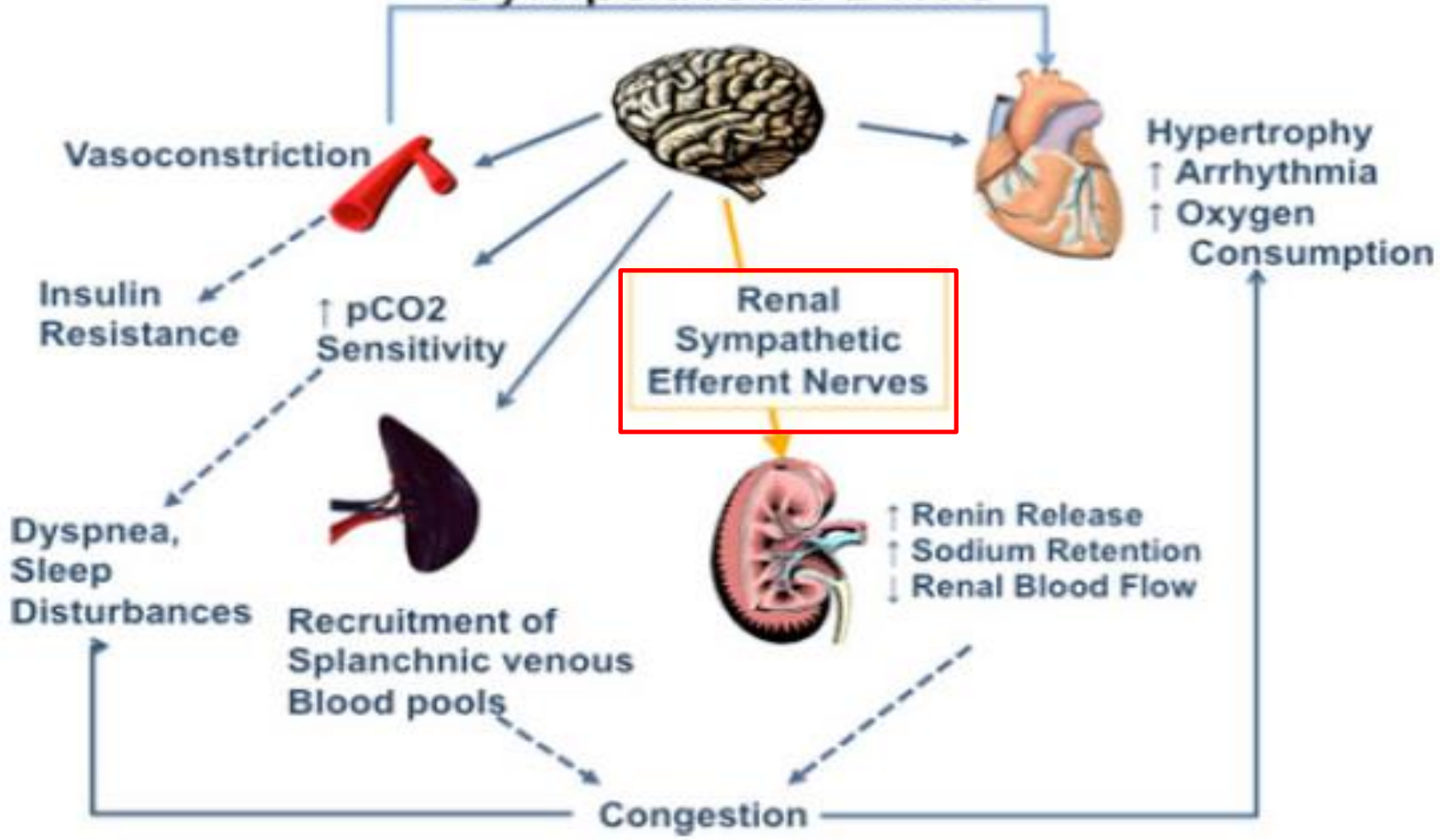
Panagiotis Theofilis, Aikaterini Vordoni & Rigas G. Kalaitzidis



https://doi.org/10.1080/00325481.2023.2233492

β-blockers & CKD

Consequences of Chronic Elevated Central Sympathetic Drive



Clin Res Cardiol (2011) 100:1049–1057

Nephrol Dial Transplant (2009) 24: 701–702
doi: 10.1093/ndt/gfn695
Advance Access publication 10 December 2008

Should nephrologists use beta-blockers? A perspective

Rigas Kalaitzidis and George Bakris

- **…sympathetic over-activity is part of CKD and contributes to the maintenance of hypertension and associated cardiac complications. Larger prospective trials are needed to determine whether the properties of the vasodilating β-blockers will translate into improved cardiovascularoutcomes in CKD.**

- **Until then, given the high prevalence of cardiovascular disease in people with CKD and mortality benefits observed for some β-blockers, there is clearly a need for their use in CKD patients.**

Kalaitzidis R et al Nephrol Dial Transplant 2009

2023 ESH Guidelines for the management of arterial hypertension

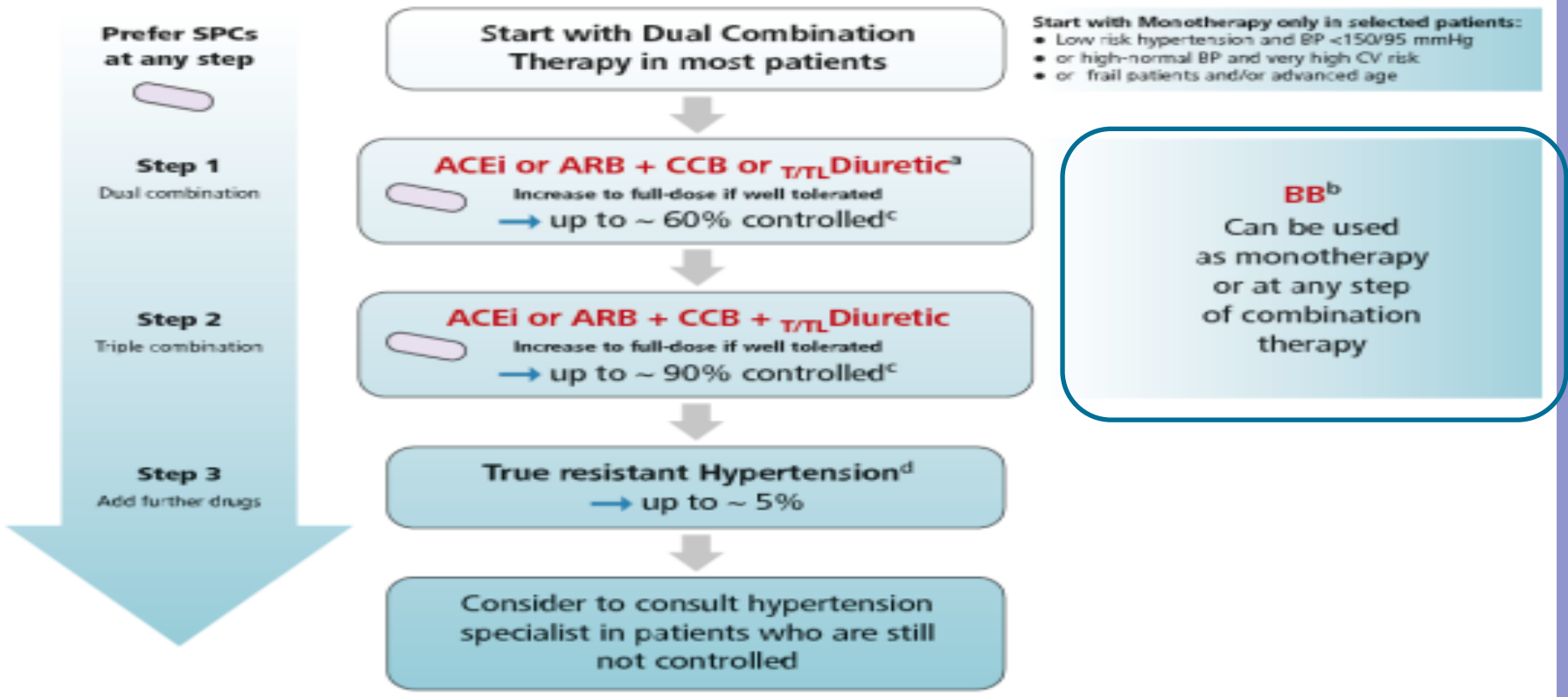
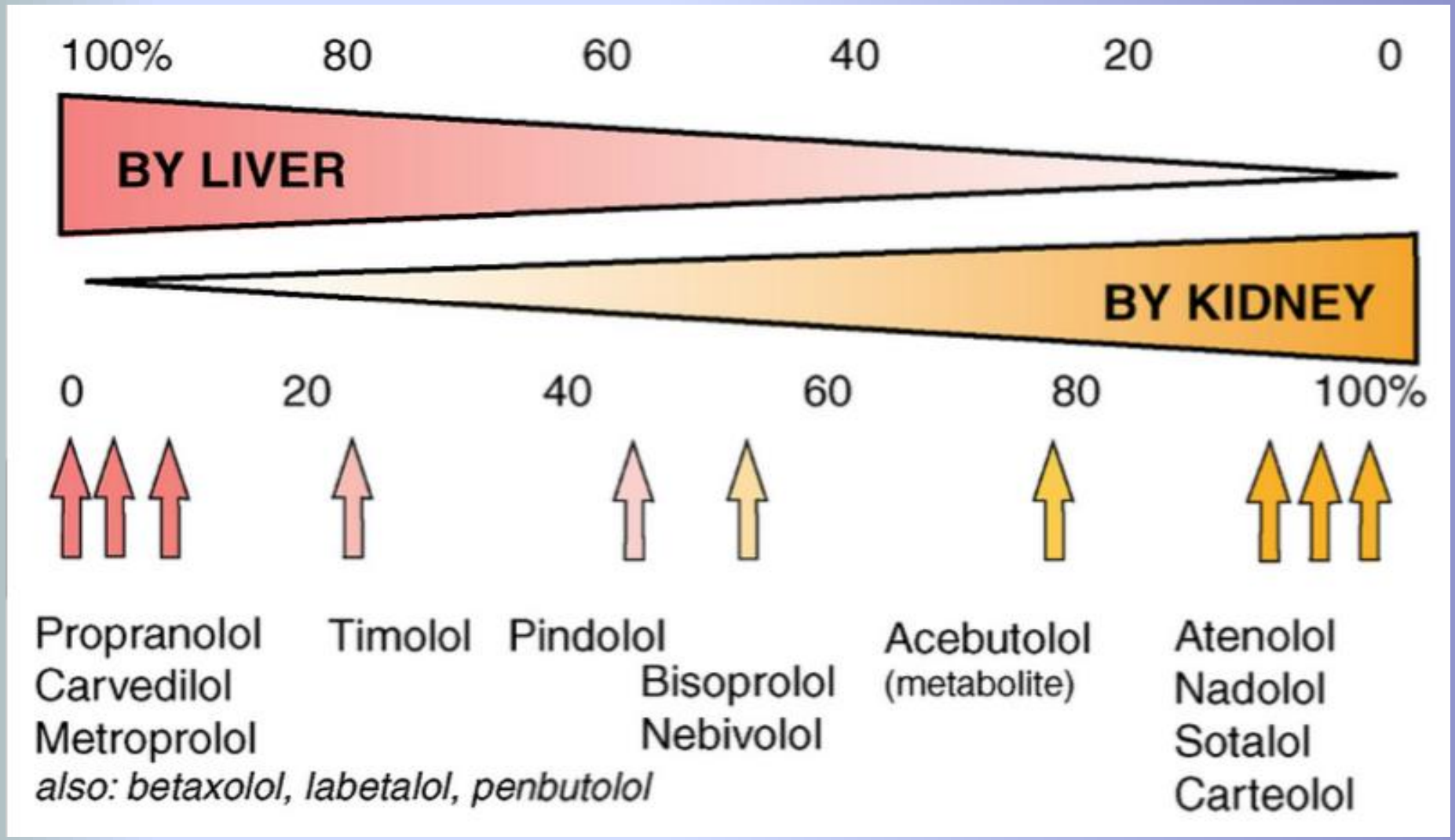
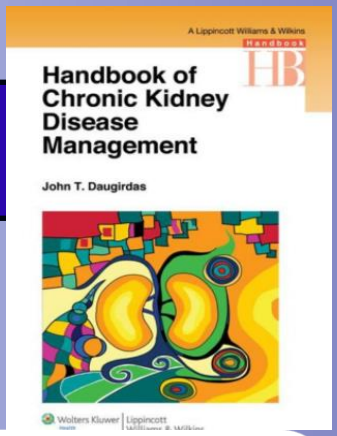


Figure 12. General BP lowering strategy in patients with hypertension

Comparative routes of elimination of β-blockers.



Central Alpha-Adrenergic Agonists



The most commonly used drug in this group is clonidine

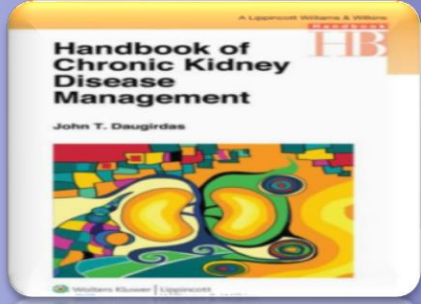
Other members of the class include guanfacine and methyldopa.

The rationale for their use is to mitigate the increase in sympathetic activity

Clonidine causes sedation, dry mouth, bradycardia, and can worsen depression

Rigas G. Kalaitzidis and George L. Bakris, 2017

Vasodilators



As fourth-line agents, minoxidil or hydralazine sometimes are required when other antihypertensive treatment with calcium antagonists, RAAS blockers, and diuretics has failed

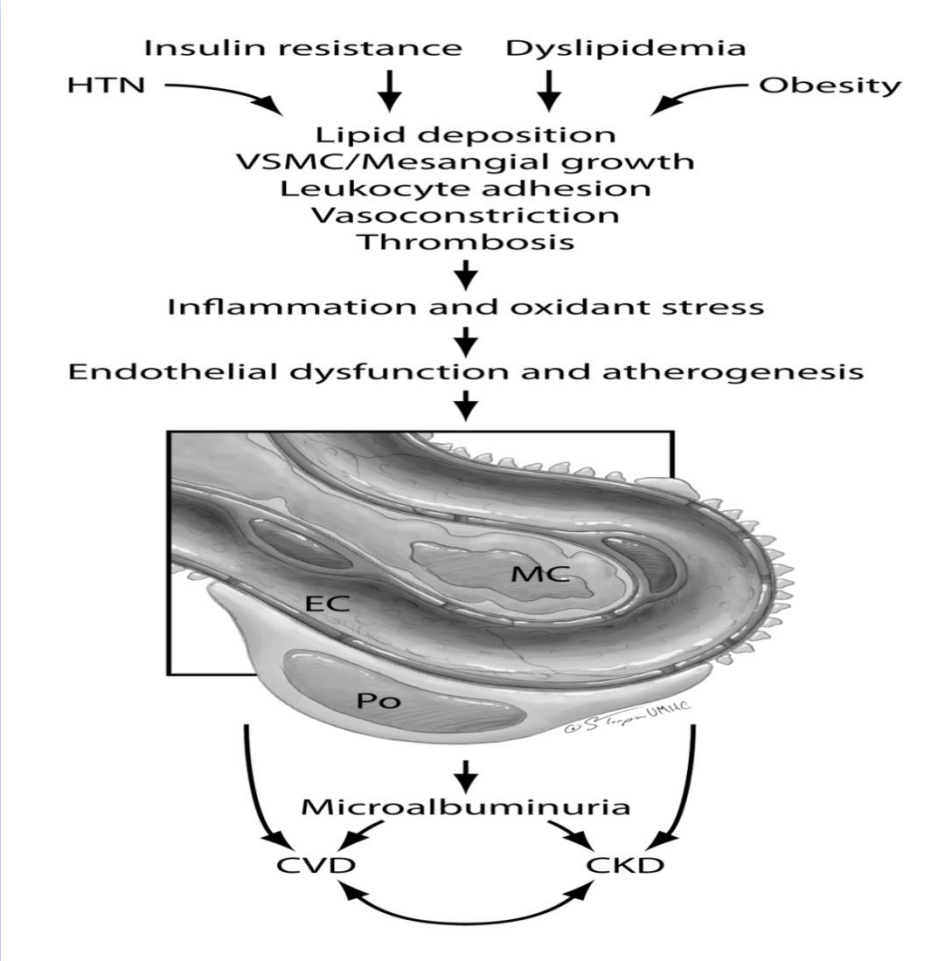
Vasodilator use is associated with reflex tachycardia that can worsen angina pectoris, and these vasodilators should always be combined with a beta-adrenergic blocker

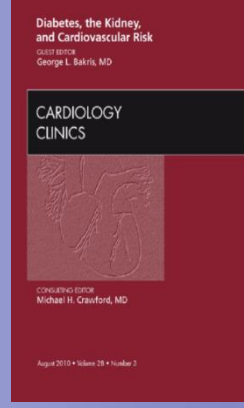
Weight gain, increased hair growth, pericardial effusion

Rigas G. Kalaitzidis and George L. Bakris, 2017

Albuminuria as a Appropriate Therapeutic Target

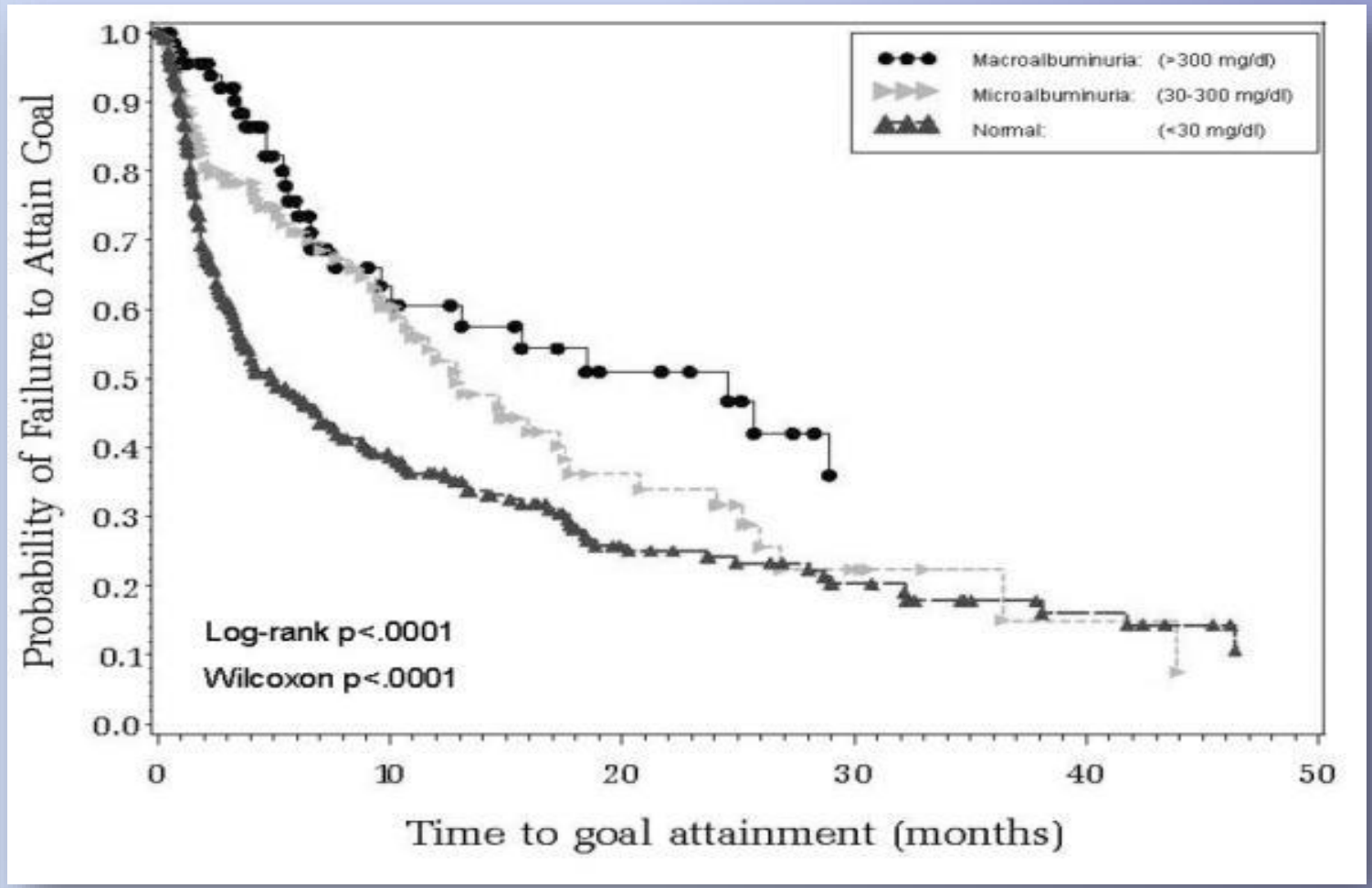
Should targeting Albuminuria Be Part of Cardiovascular risk Reduction Paradigm?





Whaley-Connell and Kalaitzidis R Cardiology Clinics 2010

Influence of albuminuria on blood pressure response to antihypertensive therapy



Flack, Vasc Risk Manag 2007

Special therapeutic challenges

2023 ESH Guidelines for the management of arterial hypertension

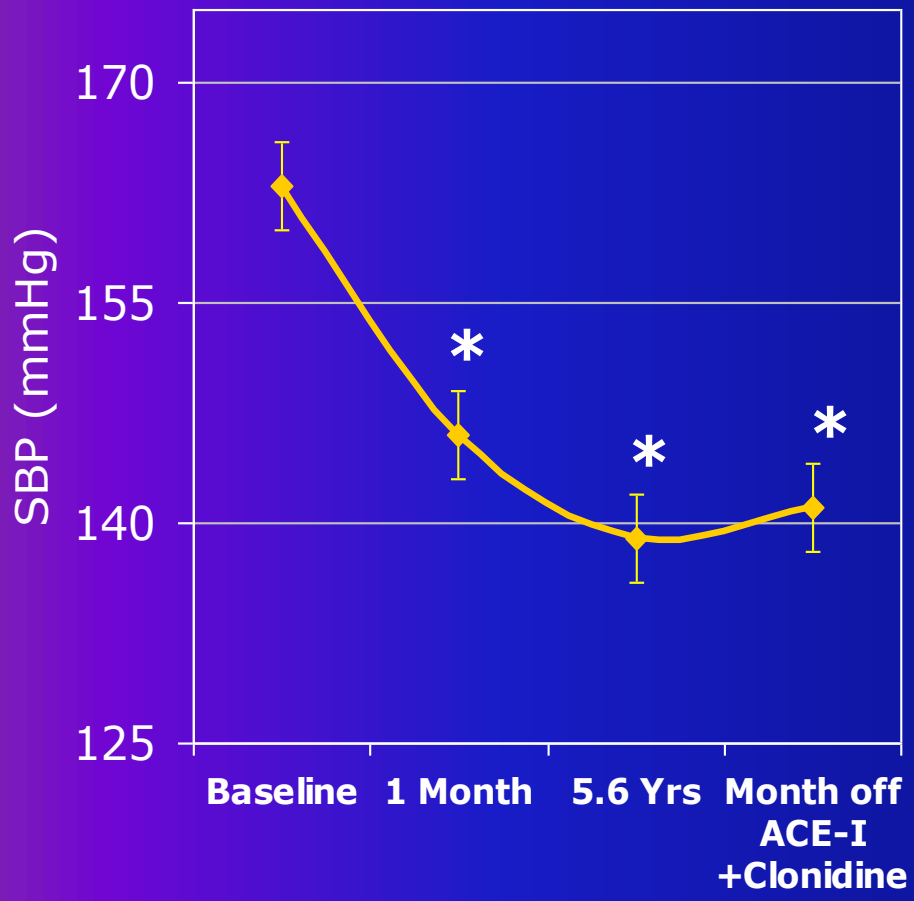
ACEis or ARBs on the efferent arteriole reduces intraglomerular pressure.

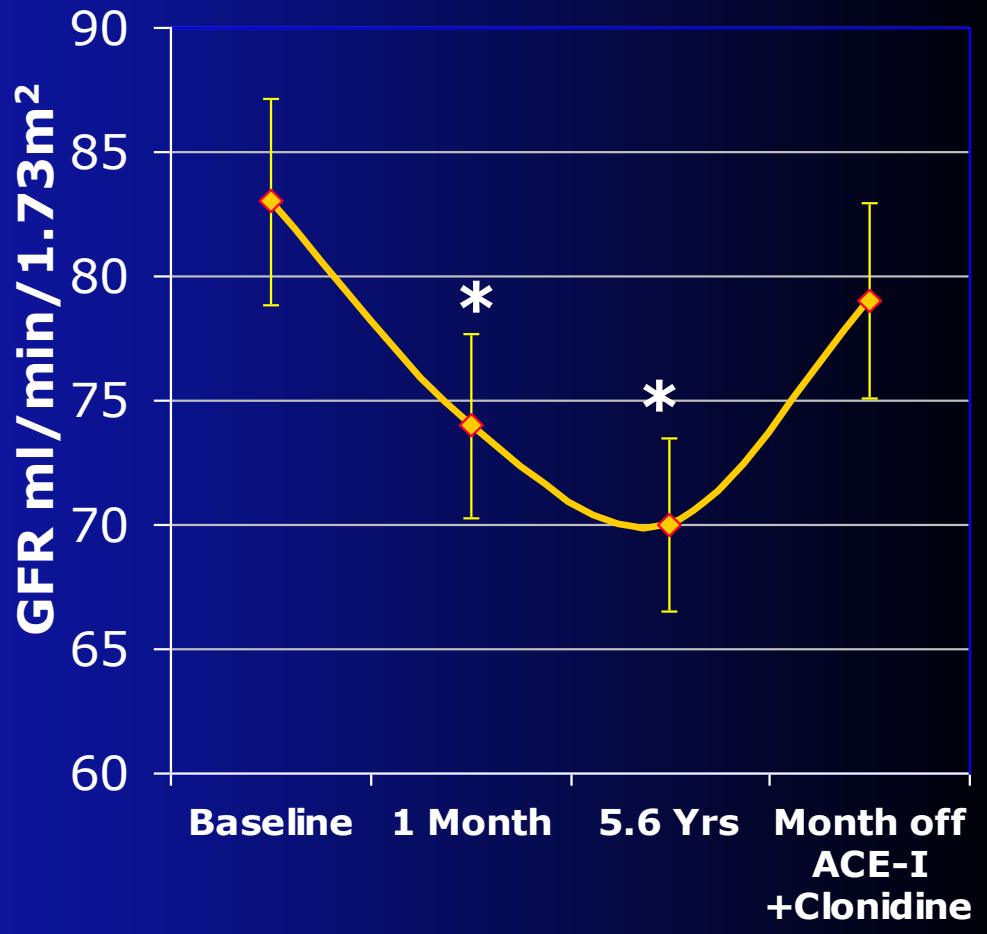
GFR reductions on average 10–15% in the first weeks of treatment

Monitoring of eGFR (as well as serum electrolytes, see the following) within the first 4–8 weeks

If the decline in GFR continues or becomes more severe (>30%), the RAS blocker should be stoppd and the epatient should be investigated for the presence of renovascular disease

Impact of ACE-I on BP and GFR: Acute and Chronic Effects





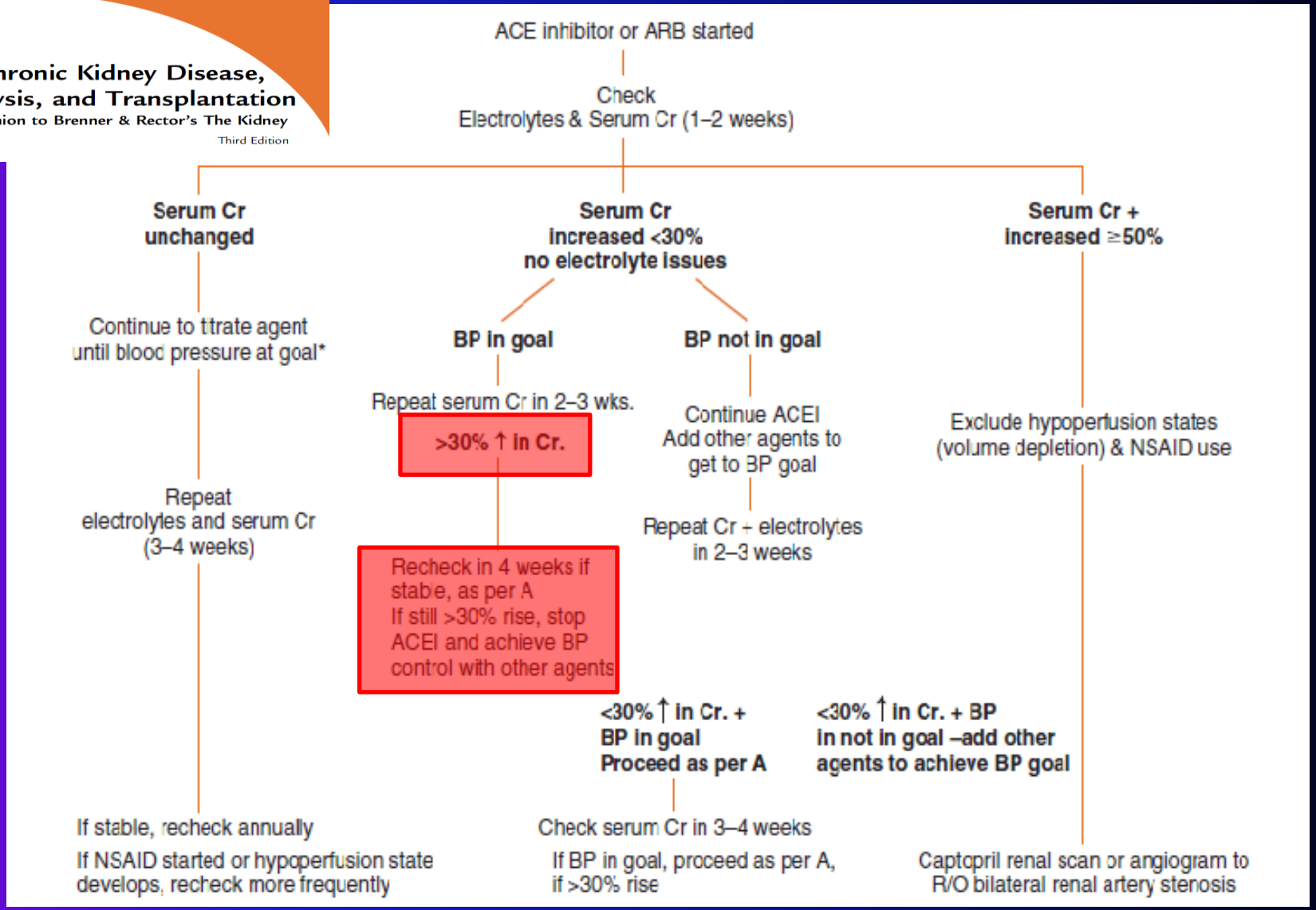
*P<0.05 compared to baseline

Bakris GL, Weir MR. Arch Intern Med. 2000;160(5):685-93.

Hypertensive Kidney Disease

kidney dysfunction with RAS blockers

Chronic Kidney Disease, Dialysis, and Transplantation
Companion to Brenner & Rector's The Kidney
Third Edition



Nitin Khosla, M.D., Rigas Kalaitzidis, M.D., and George L. Bakris, M.D.

2023 ESH Guidelines for the management of arterial hypertension

Use RAS blockers in CKD patients further increases the risk of hyperkalemia

Incident hyperkalemia is associated with increased mortality

The most frequent reason for dose reduction or discontinuation

Reducing the dose or discontinuing RAS blockers has been associated with increased risk of CV events

Novel potassium binders (patiromer and sodium zirconium cyclosilicate) were shown to normalize elevated serum potassium

Adherence to guidelines for creatinine and potassium monitoring and discontinuation following renin–angiotensin system blockade: a UK general practice-based cohort study

Table 4 Proportion of new users of ACE inhibitors or angiotensin receptor blockers who continue or discontinue treatment according to guideline recommended cut-off levels of serum creatinine and potassium at follow-up testing*

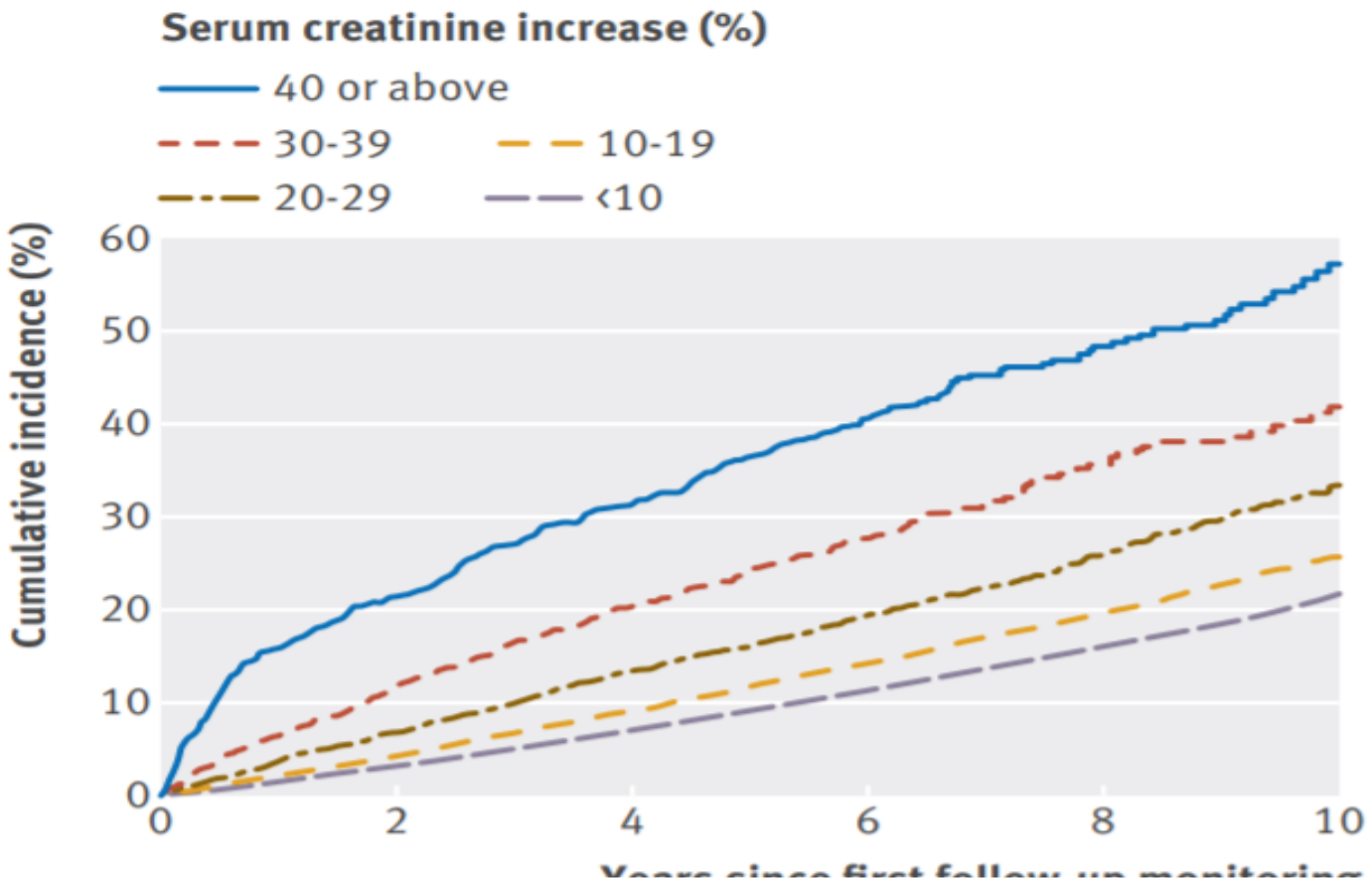
	Continuation†	Discontinuation†	Total
Total number, %	42 942 (93.1)	3178 (6.9)	46 120 (100)
Serum creatinine increase ≥30%, n (%)	462 (81.5)	105 (18.5)	567 (100)
Serum potassium >6 mmol/L, n (%)	150 (78.5)	41 (21.5)	191 (100)

*Calculated from the most recent measurements within 1 month before and 2 months after drug initiation.
†A patient was considered a continuous user when the end date of the first continuous course of therapy was larger than the date of the first follow-up monitoring +30 days (to allow for stockpiling and irregular use).

Only one-tenth of patients initiating ACEI/ARB therapy receive the guideline-recommended creatinine monitoring. Moreover, the vast majority of the patients fulfilling postinitiation discontinuation criteria for creatinine and potassium increases continue on treatment.

BMJ Open 2017;7:e012818.

Serum creatinine elevation after renin-angiotensin system blockade and long term cardiorenal risks: cohort study



Cumulative mortality according to levels of creatinine increase after renin-angiotensin system blockade

Graduated increased risk of end stage renal disease, adverse cardiac outcomes, and death for each 10% increase in creatinine, even below the 30% threshold

BMJ 2017;356:j791 | doi: 10.1136/bmj.j791

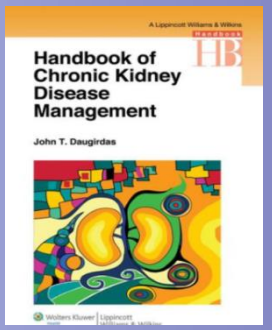
Serum creatinine elevation after renin-angiotensin system blockade and long term cardiorenal risks: cohort study

Increases in creatinine after starting ACEI/ARB treatment

identify a high risk group

needing close monitoring and in whom the risks and benefits of ACEI/ARB prescribing should be considered

BMJ 2017;356:j791 | doi: 10.1136/bmj.j791



Dosage adjustment of hypertensive drugs in patients with reduced glomerular filtration rate

Rigas G. Kalaitzidis and George L. Bakris, 2019
Handbook of Chronic Kidney Disease Managment

Ευχαριστώ