Optimizing Blood Pressure Control in CKD Patients

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Chronic Kidney Disease (CKD)

Introduction

- Chronic kidney disease is a major public health problem with adverse outcomes:
  - Kidney failure (ESRD) .
  - Cardiovascular disease.
  - Premature death.

- Early detection and treatment can often prevent or delay such outcomes

Definition of CKD

Structural or functional abnormalities of the kidneys for ≥3 months,

Manifested by either:

1. Kidney damage, with or without decreased GFR:

- **Markers of kidney damage include:**
  - **abnormalities in the composition of the blood**
  - **or abnormalities in the composition of the urine**
  - **or abnormalities in imaging tests**

2. GFR <60 ml/min/1.73 m^2, with or without kidney damage

Stages of Chronic Kidney Disease NKF-K/DOQI

Stage	Description	GFR (ml/min/1.73 m^2)
1	Kidney Damage* with Normal or ↑ GFR	≥ 90
2	Kidney Damage* with Mild ↓ GFR	60-89
3 A	Moderate ↓ GFR	45-59
3B		30-45
4	Severe ↓ GFR	15-29
5	Kidney Failure	< 15 or Dialysis

C K D

* Proteinuria or Hematuria

Albuminuria categories in CKD

Category	AER (mg/24 hours)	ACR (approximate equivalent) (mg/mmol)	ACR (approximate equivalent) (mg/g)	Terms
A1	<30	<3	<30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased*
A3	>300	>30	>300	Severely increased**

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.

*Relative to young adult level.

**Including nephrotic syndrome (albumin excretion usually >2200 mg/24 hours [ACR >2220 mg/g; >220 mg/mmol]).

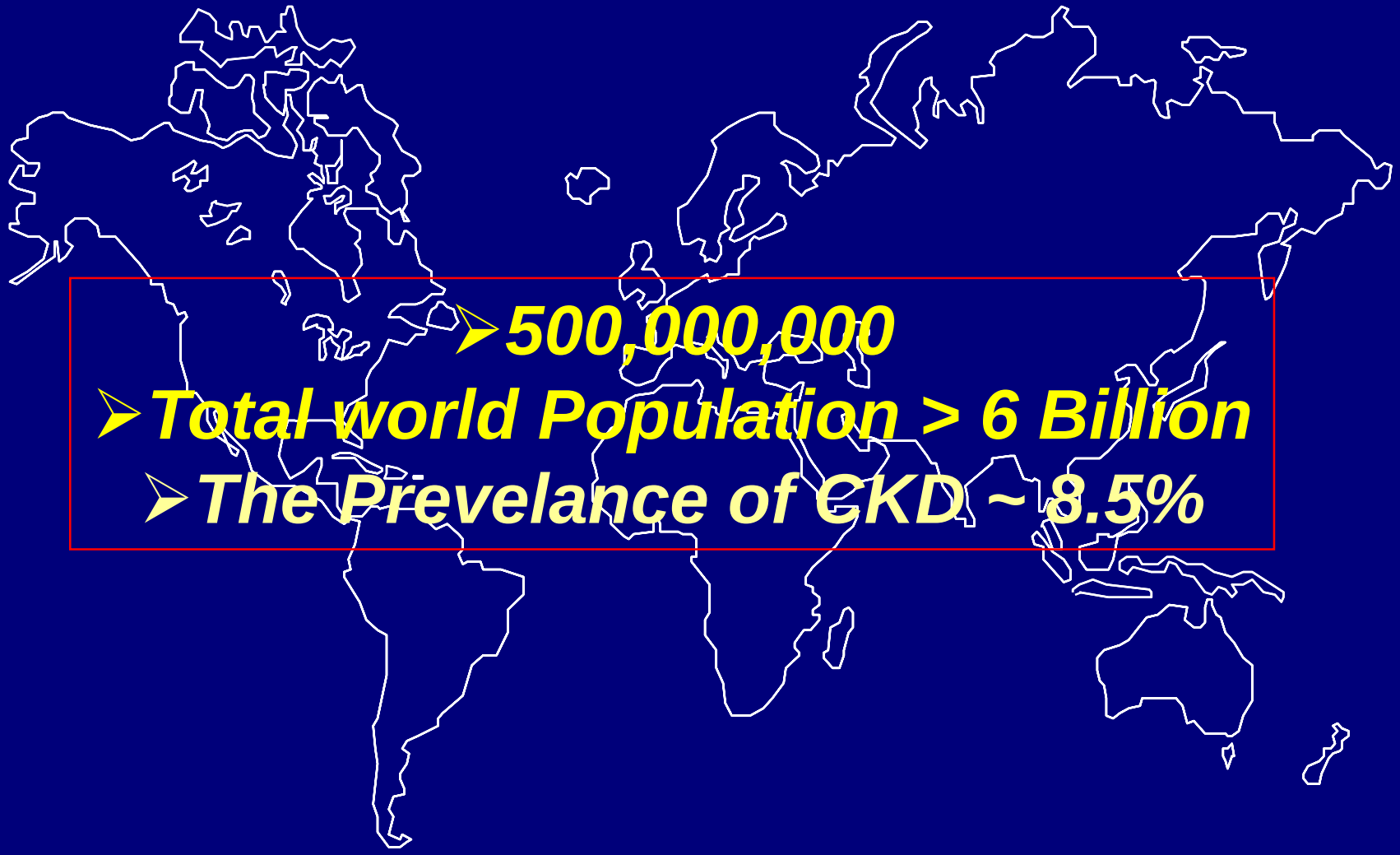
New classification of CKD

Stage	Description	Classification by severity: GFR mL/min/1.73 m^2	Classification by severity: Related terms	Classification by treatment
1	Kidney damage with normal or ↑ GFR	≥90	Albuminuria, proteinuria, hematuria	T if kidney transplant recipient
2	Kidney damage with mild ↓ GFR	60–89	Albuminuria, proteinuria, hematuria	
3	Moderate ↓ GFR	30–59	Chronic renal insufficiency, early renal insufficiency	
4	Severe ↓ GFR	15–29	Chronic renal insufficiency, late renal insufficiency, pre-ESRD	
5	Kidney failure	<15 (or dialysis)	Renal failure, uremia, end-stage renal disease	D if dialysis (hemodialysis, peritoneal dialysis)

Abbreviations are: GFR, glomerular filtration rate; ESRD, end-stage renal disease.
Related terms for CKD stages 3 to 5 do not have specific definitions, except ESRD.

Levey et al, KI, 67:2089-2100,2005

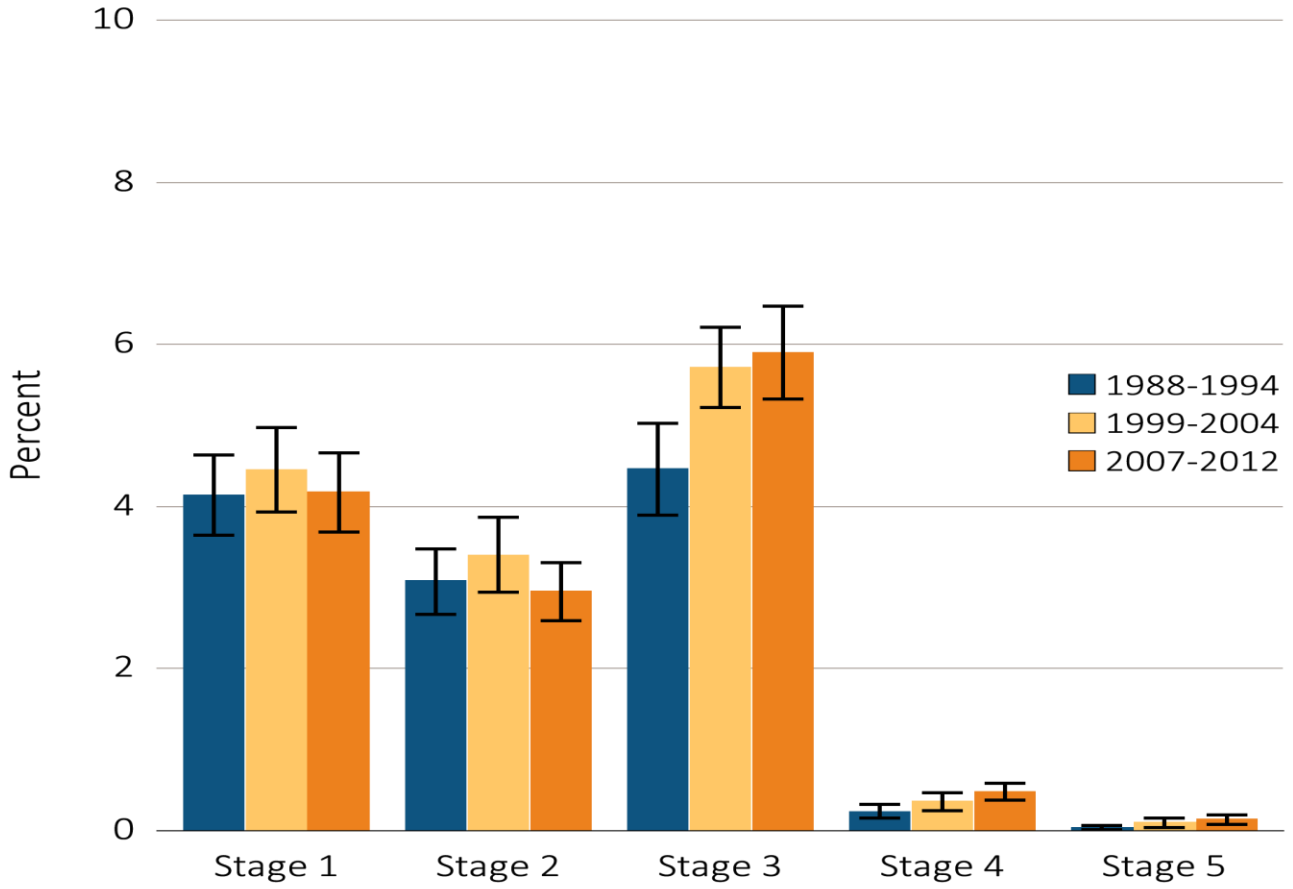
Prevelance of Chronic Kidney Disease Worldwide



- ***500,000,000***
- ***Total world Population > 6 Billion***
- ***The Prevelance of CKD ~ 8.5%***

Estrapolated from Coresh et al., *Am J Kidney Dis,* 2003

Prevalence of CKD by stage among NHANES participants (1988-2012) > 14%



Data Source: National Health and Nutrition Examination Survey (NHANES), 1988–1994, 1999-2004 & 2005–2012 participants age 20 & older. Whisker lines indicate 95% confidence intervals. Abbreviations: CKD, chronic kidney disease. This graphic also appears as Figure 1.1.

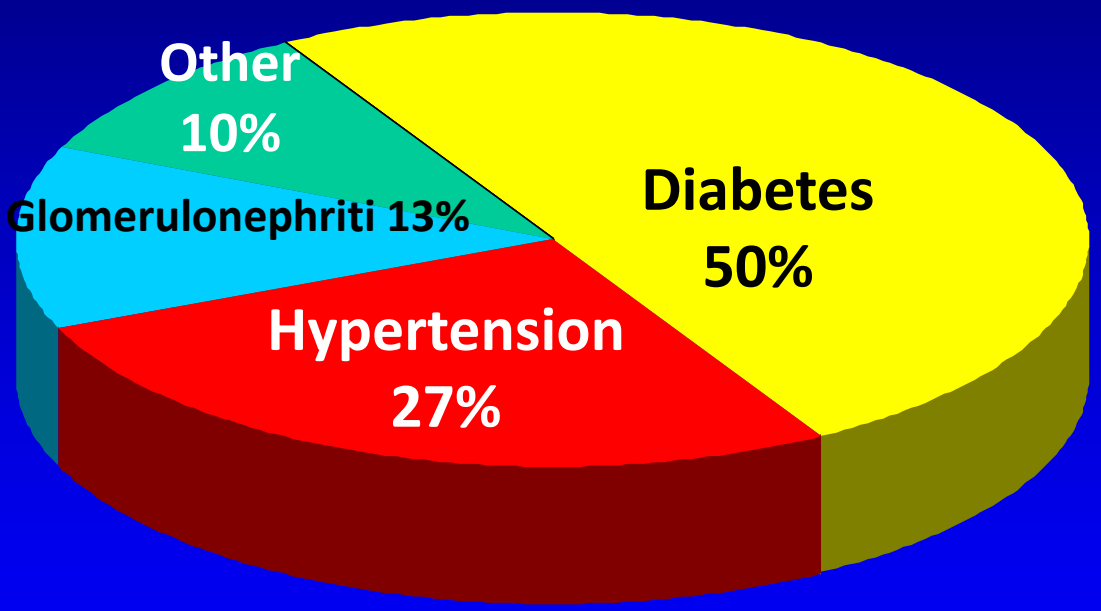
What Are Initiation Factors for CKD?

Initiation factors for CKD are diverse & include:

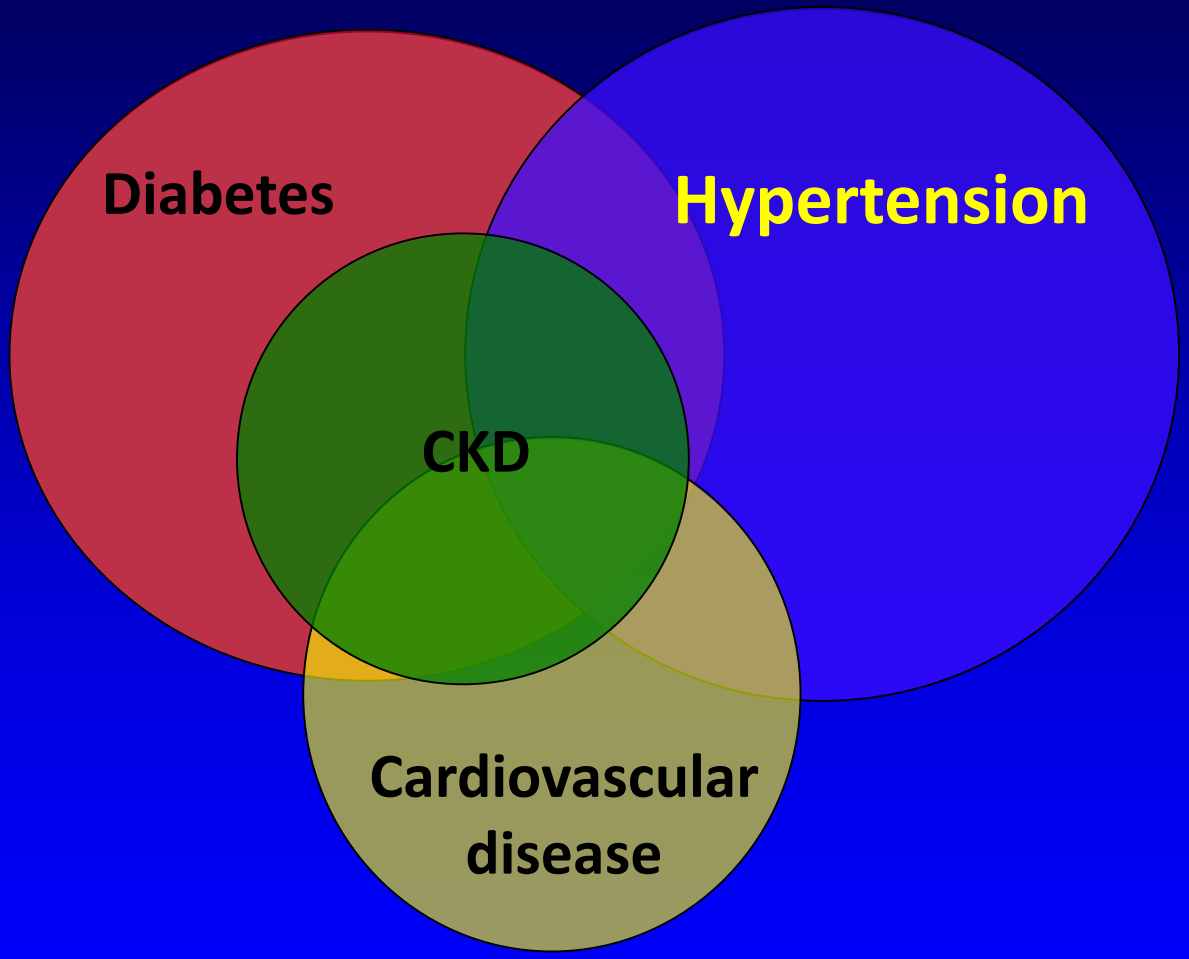
- **Diabetes**
- **Hypertension**
- **Autoimmune disease**
- **Glomerulonephritis**
- **Systemic infections**
- **Urinary tract infections**
- **Urinary stones**
- **Drug toxicity**

Levey et al. *Ann Intern Med.* 2003;139:137-147.

COMMON CAUSES OF CKD



CKD often coexists with other NCDs



Diabetes & Hypertension are the major risk factors for CKD.
Diabetes Increases the risk of developing ESRD by up to 13-fold

Overview of hypertension in CKD

- Hypertension is a frequent finding in both acute and chronic kidney disease, particularly with glomerular or vascular disorders .
- The pathogenesis and preferred treatment of hypertension in CKD patients vary with:
  - The **Type** of the Renal Disease
  - The **Severity** of the Renal Disease
  - The **Duration** of the Renal Disease
- The kidney is both a **Cause** and a **Victim** of hypertension.

The kidney is both a cause and a victim of hypertension

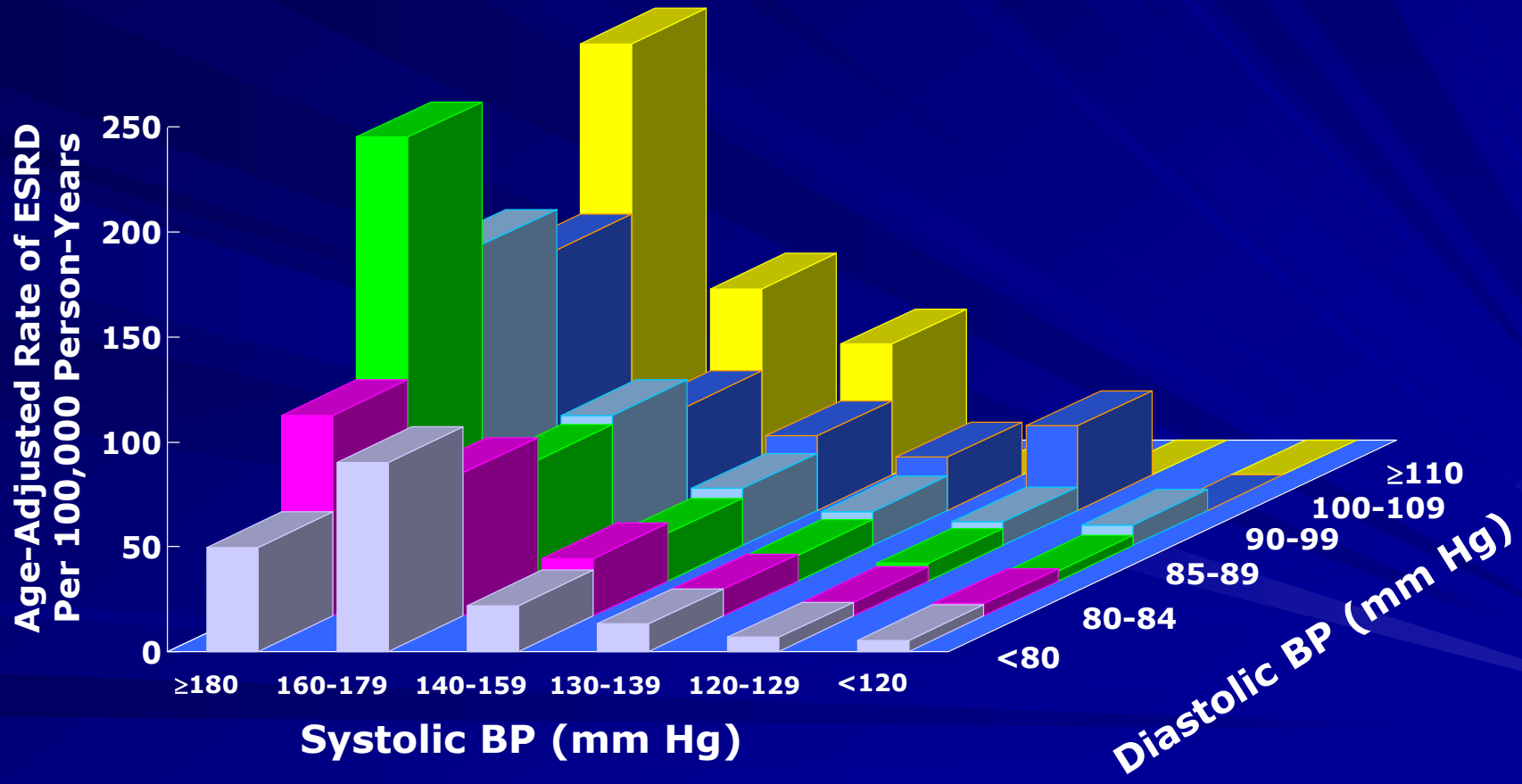
- **Victim :** High blood pressure is a key pathogenetic factor that contributes to deterioration of kidney function.

- **Cause:** The presence of kidney disease is a common and underappreciated preexisting medical cause of **Resistant hypertension**.

- Therefore, treatment of hypertension has become the most important intervention in the management of all forms CKD.

P.A. Sarafidis, G.L. Bakris : J Clin Hypertens 10 (2008), pp. 130–139

HTN Linked To Chronic Renal Disease Among 332,544 Men Screened for MRFIT



Adapted from Klag MJ, et al. N Engl J Med. 1996;334(1):13-18.

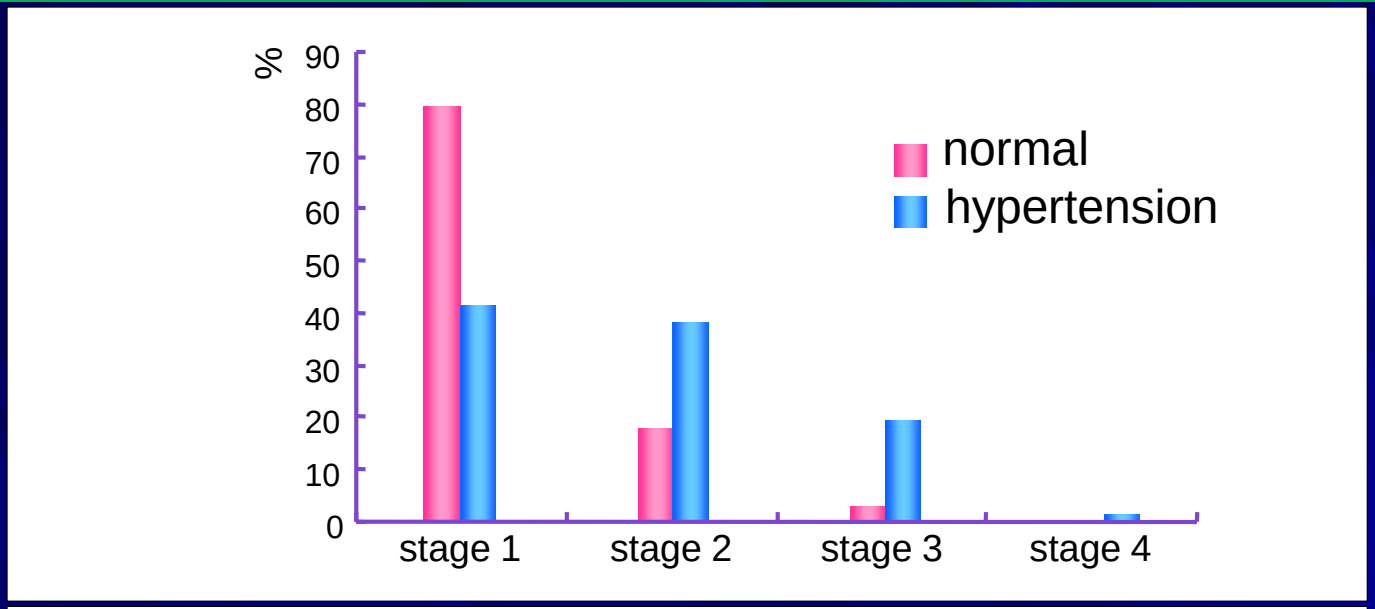
Hypertension in Chronic kidney disease

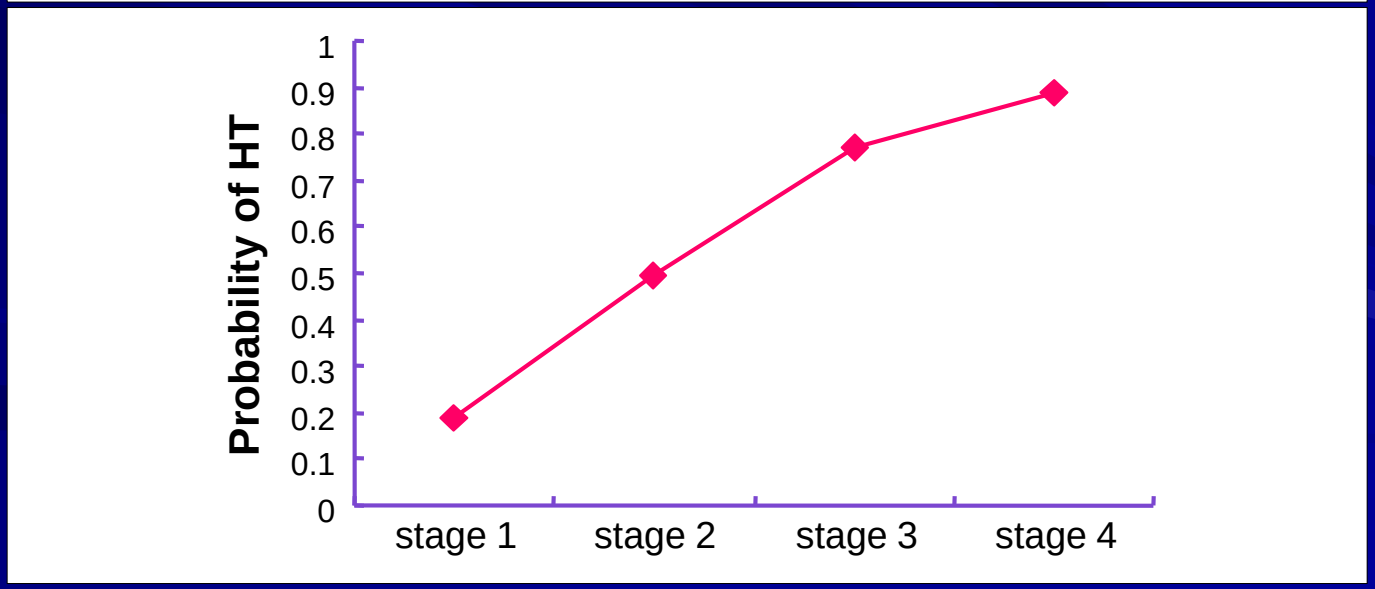
- Hypertension is present in approximately 80 - 85 % of patients with CKD.

  Whaley-Connell AT et al Am J Kidney Dis. 2008;51(4 Suppl 2):S13

- The prevalence of hypertension is elevated in patients with:
  - kidney damage and a normal glomerular filtration rate,
  - and increases further as the glomerular filtration rate falls.

Hypertension and renal function





Whaley-Connell AT et al Am J Kidney Dis. 2008;51(4 Suppl 2):S13

MDRD Study: Prevalence of high BP By level of GFR

- Data from the MDRD Study, showed that the prevalence of hypertension rose progressively:
  - from 65 - 95 % as the
  - GFR fell from 85 - 15 mL/min per 1.73 m^2

Buckalew VM Jr : Am J Kidney Dis. 1996;28(6):811

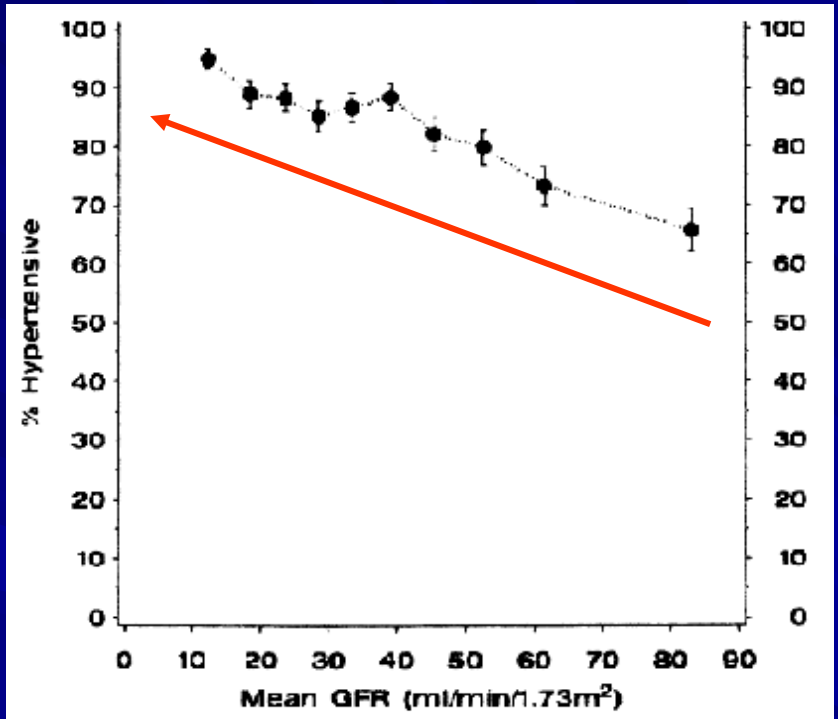
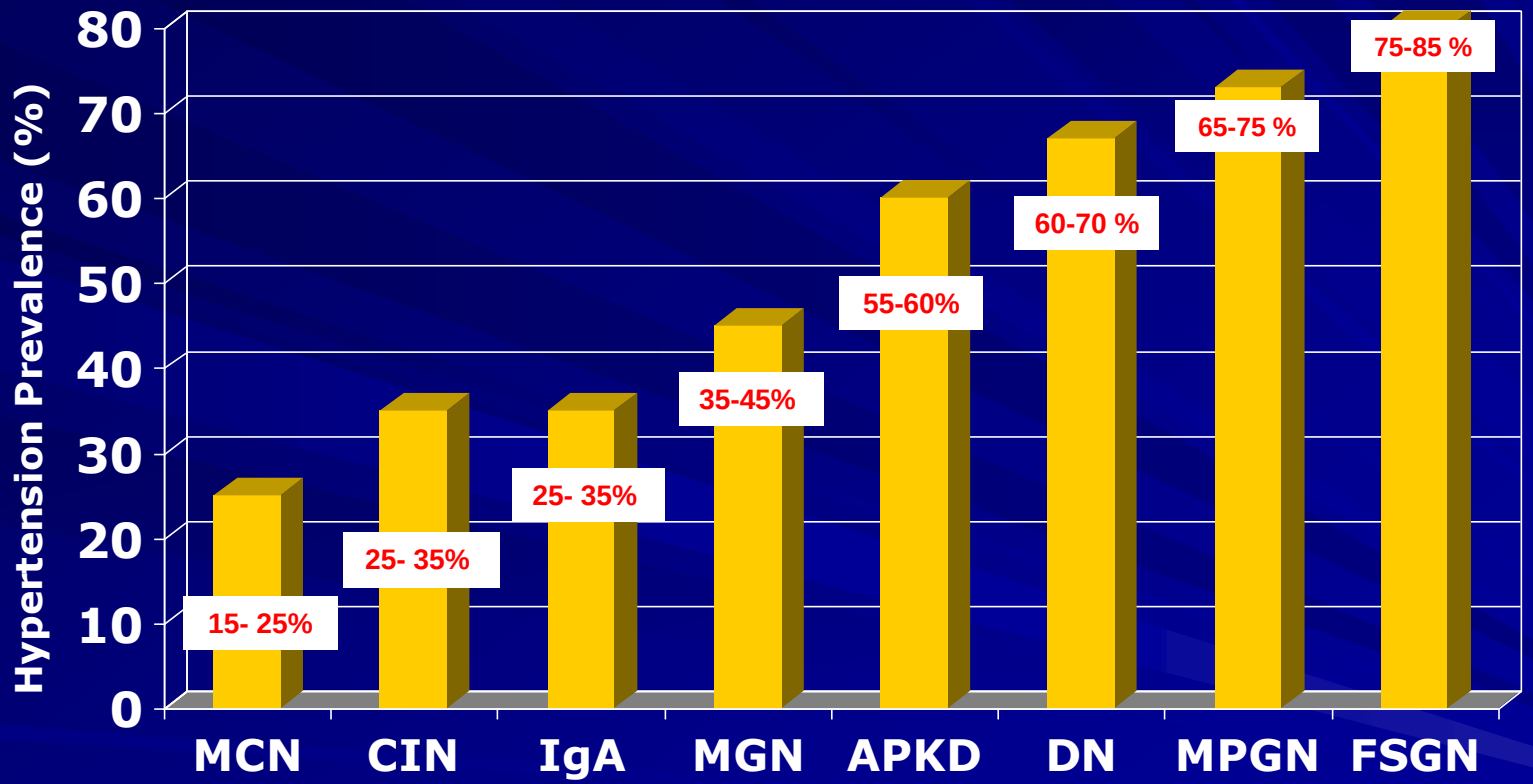


Figure 21 Prevalence of high blood pressure by level of GFR in the MDRD Study. High blood pressure was defined as classification by study investigators based on patient history (including the use of antihypertensive drugs) and review of medical records. GFR was measured by urinary clearance of 125I-iothalamate. Patients were ranked by GFR into 10 groups, each containing 179 or 180 patients. Data are presented as mean values ± standard errors.

Prevalence of Hypertension in Renal Parenchymal Disease



Rodicio JL & Alcazar JM. ESH Newsletter 2011, No. 4

MCN=minimal change nephropathy CIN=chronic interstitial nephritis IgA=IgA nephropathy MGN=membranous glomerulonephritis APKD=adult-onset polycystic kidney disease DN=diabetic nephropathyMPGN=membranoproliferative glomerulonephritis FSGN=focal segmental glomerulonephritis

Pathogenesis: Hypertension in CKD

Pathophysiology thought to be both ***pressor*- and *volume*-related**, thus CKD patients respond to both vasodilators as well as diuretics/sodium restriction.

As kidney function declines closer to ESRD, ***volume-dependent hypertension*** becomes more important.

Often on dialysis, we can remove antihypertensive agents as we bring the patient down to their dry weight with ultrafiltration.

Hypertension and Chronic Renal Disease: Hemodynamic Abnormalities

Mean BP = **Cardiac Output** x **Total Systemic Vascular Resistance**

Increased Cardiac Output ++

- ↑ **Intravascular Volume**
  - ↓ Glomerular filtration
  - ↓ Sodium excretion
  - ↑ Extracellular Fluid
  - ↑ Renal Nerve Activity
- ↑ **Myocardial Performance**
  - ↑ Adrenergic Activity

Increased Vasoconstriction ++++

- ↑ **Adrenergic Stimuli**
- ↑ **Angiotensin II**
- ↑ **Endothelin**
- ↑ **Endothelium-derived Contracting Factors**
- ↑ **Thromboxane**

Decreased Vasodilation

- ↓ Prostacyclin
- ↓ Nitric oxide
- ↓ EDHF*

***Endothelium-derived Hyperpolarizing Factors**

Textor SC. Atlas of Diseases of the Kidney, 2001.

Other Contributing factors to the increased prevalence of hypertension in patients with CKD

- Patients with ESRD are more likely to have an increase in central pulse pressure and isolated systolic hypertension due to increased aortic stiffness .

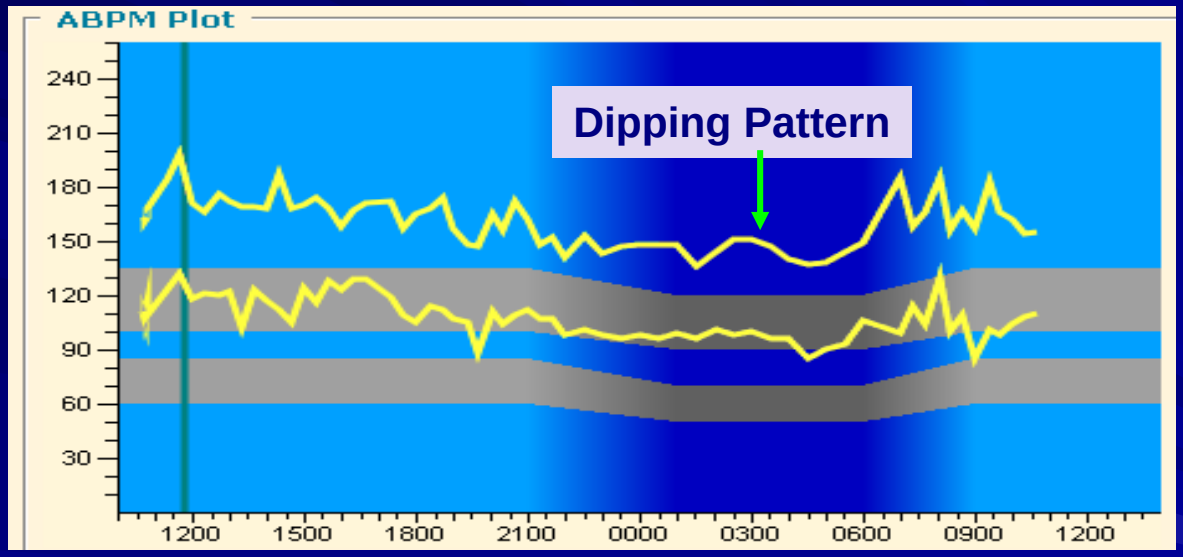
  London G Hypertension. 1992;20(1):10

- Patients with CKD may not demonstrate the normal nocturnal decline in blood pressure ("**nondippers**"), a possible risk factor for hypertensive complications.

  Portaluppi F : Am J Hypertens. 1991;4(1 Pt 1):20

Ambulatory blood pressure monitoring and CKD patients

24 Hour Average BP



Head GA et al: *J Hypertens 2012;30:253–266*

Ambulatory blood pressure monitoring: Non- dippers

- Non- dipping has also been associated with moderately **increased albuminuria**
- More rapid progression of nephropathy in patients with diabetes mellitus.

Lurbe E et al: ***N Engl J Med. 2002;347(11):797***

- More importantly, **Non-dipping** may be a risk factor for:
  - decline in glomerular filtration rate,
  - as well as for ESRD
  - and death among patients with chronic kidney disease
  - **BP Medications to be given at bed-time**

Agarwal R et al: Kidney Int. 2006;69(7):1175

Treatment Goals of Hypertension in CKD Patients

Treatment of even mild hypertension is important in patients with CKD *to protect against:*

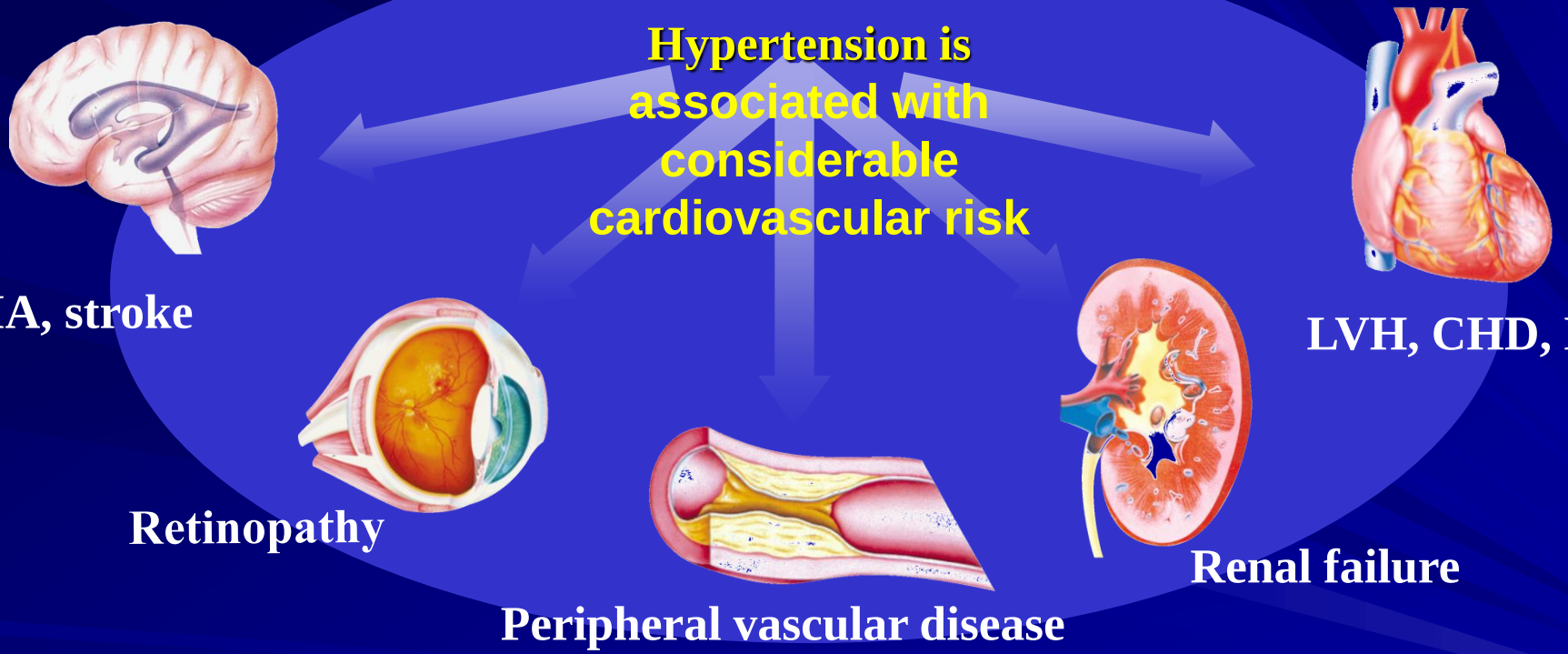
1. Cardiovascular disease

And

2. Progressive renal function loss

Target-Organ Damage

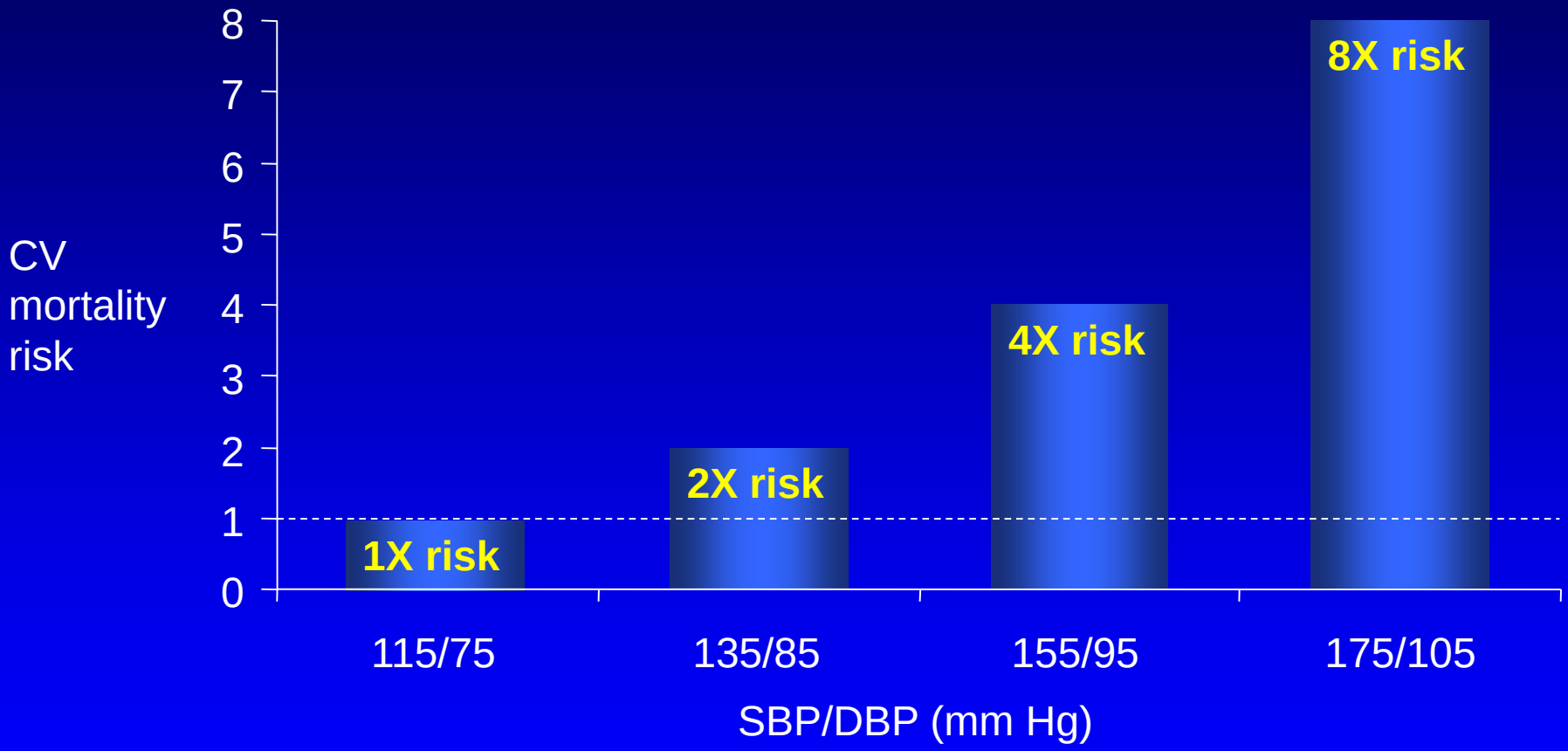
Cardiovascular disease



TIA = transient ischemic attack; LVH = left ventricular hypertrophy; CHD = coronary heart disease; HF = heart failure.

Cushman WC. J Clin Hypertens. 2003;5(Suppl):14-22.

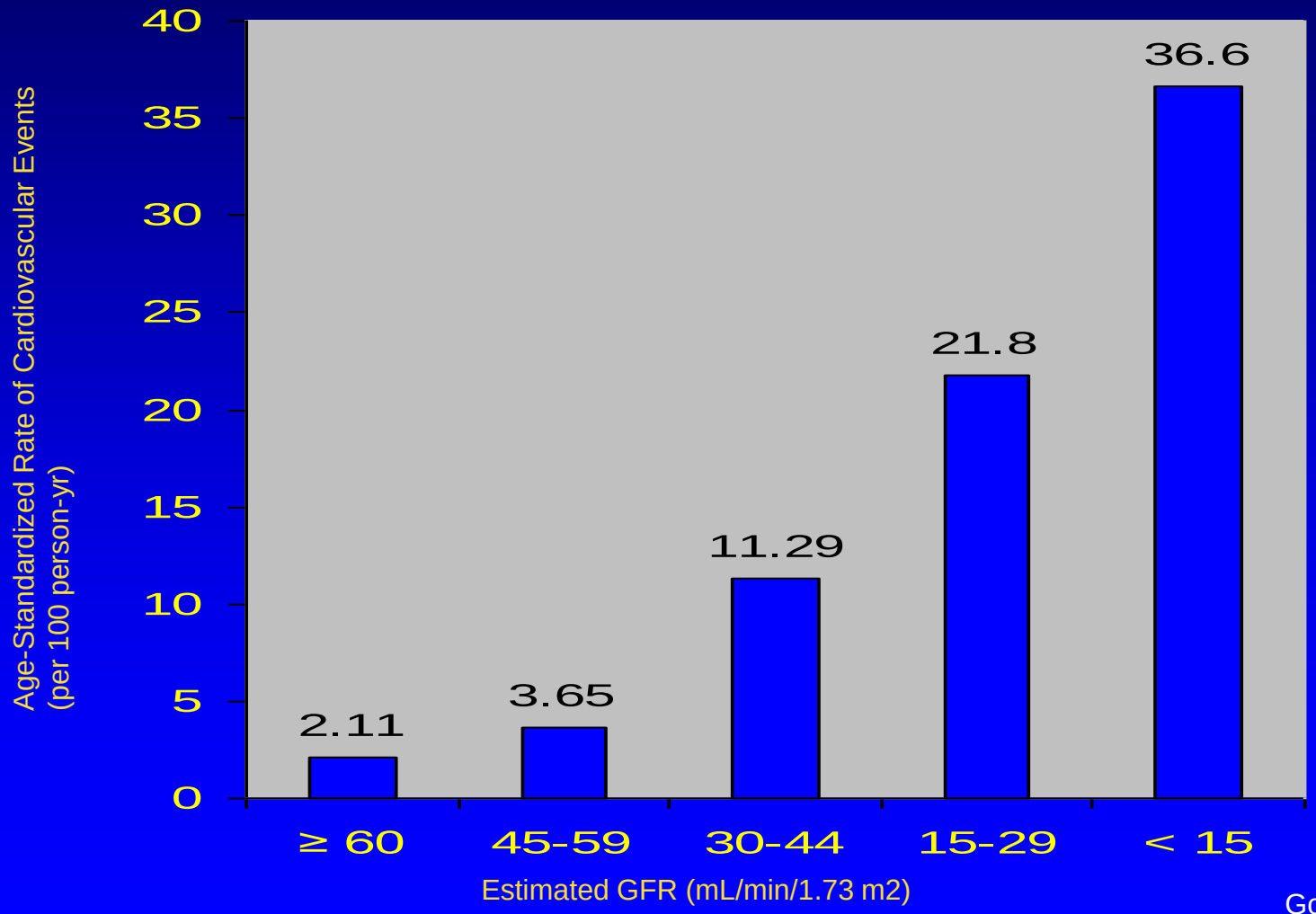
CV Mortality Risk Doubles with Each 20/10 mm Hg BP Increment*



*Individuals aged 40-70 years, starting at BP 115/75 mm Hg.
CV, cardiovascular; SBP, systolic blood pressure; DBP, diastolic blood pressure

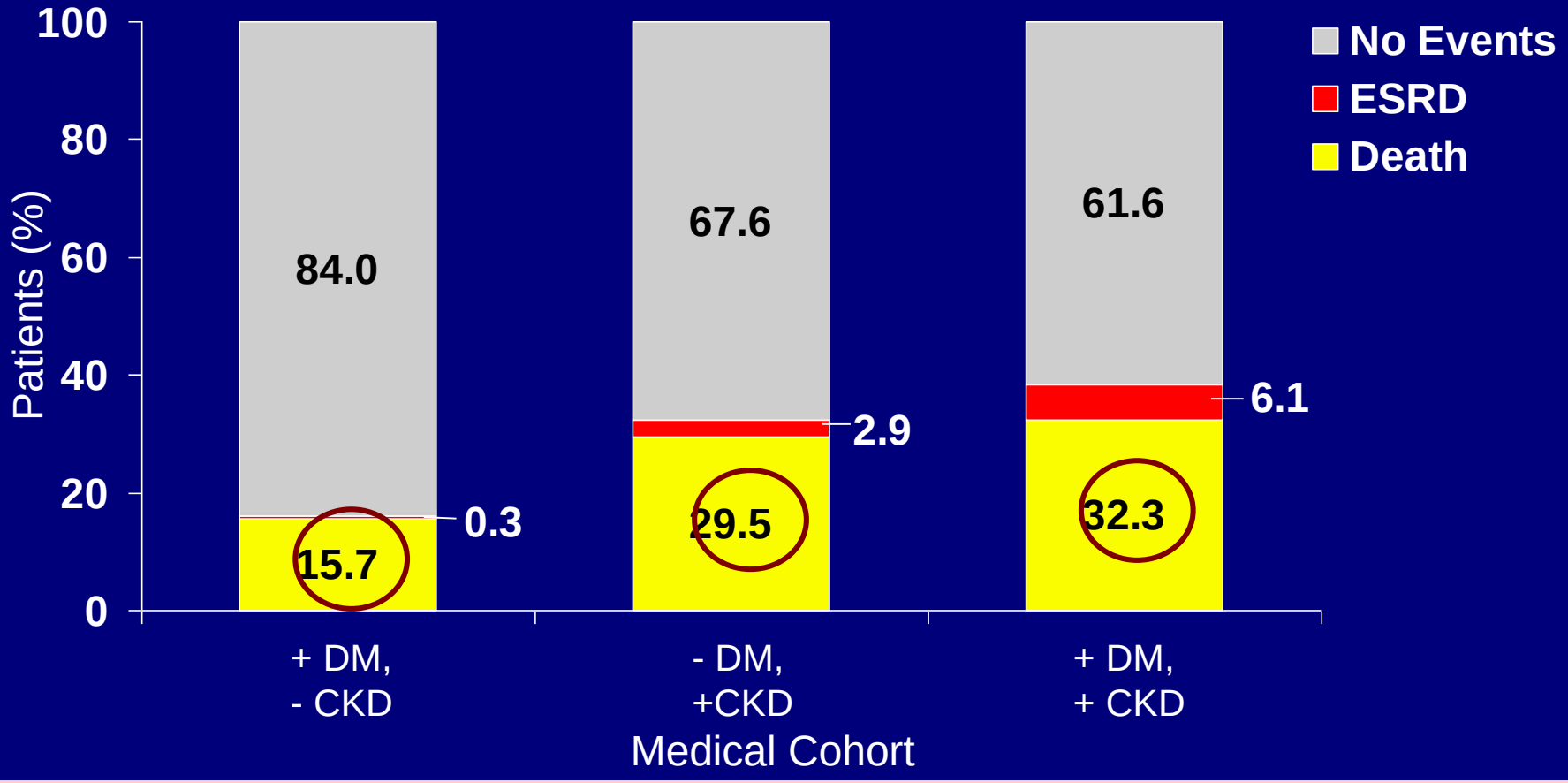
Lewington S, et al. Lancet. 2002; 60:1903-1913.
JNC 7. JAMA. 2003;289:2560-2572.

Premature cardiovascular death is a major risk for people with CKD



Go, et al., 2004

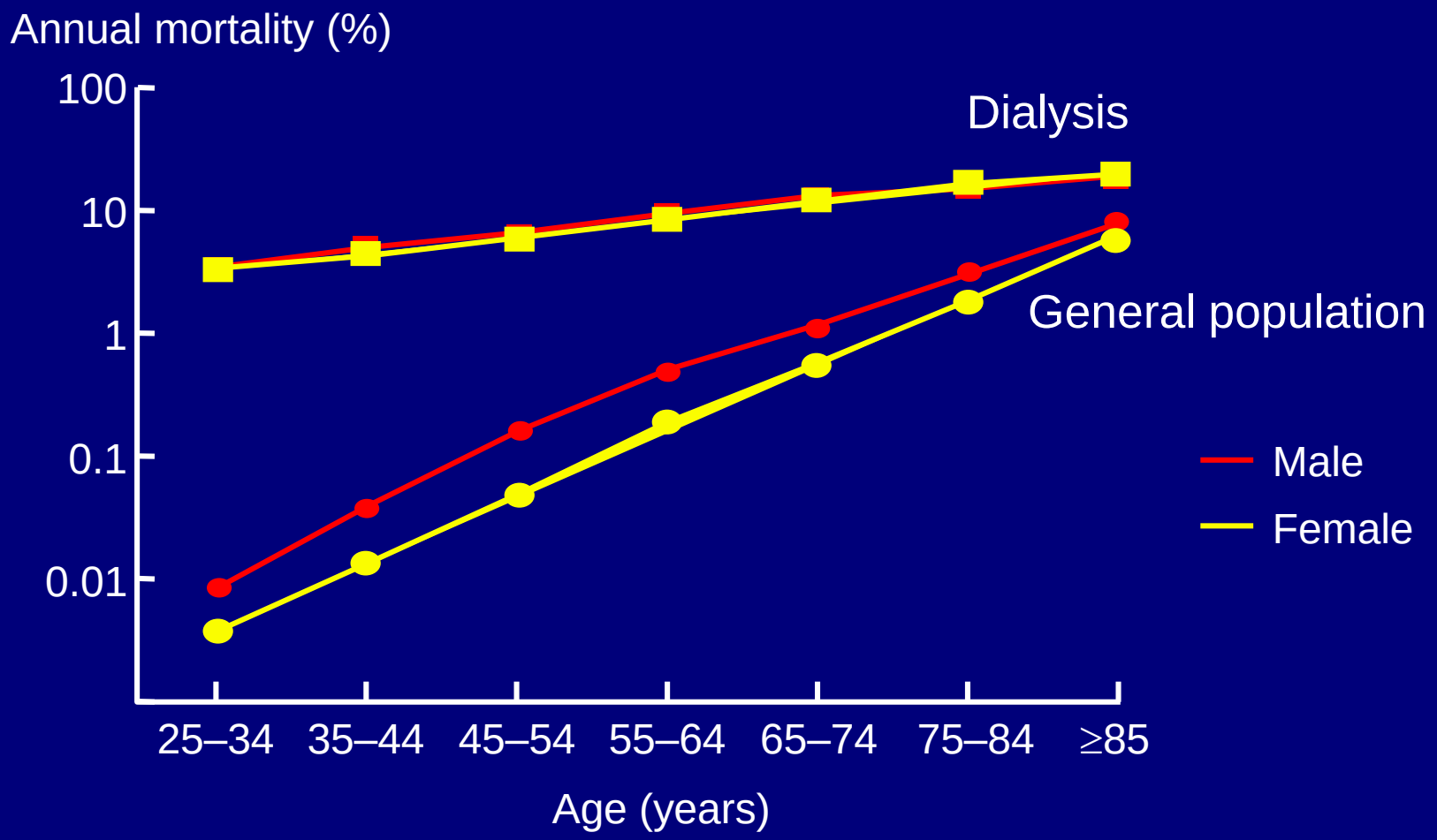
Patients with CKD are more likely to Die than go on Dialysis



"Only the lucky CKD patients reach ESRD."

Collins et al. *Kidney Int*. 2003;64(suppl 87):S24-S31

Cardiovascular Mortality in the General Population and in ESRD Treated by Dialysis



Sarnak . Am J Kidney Dis. 2000;35(suppl1):S117

The most common cause of death among ESRD patients is CVD

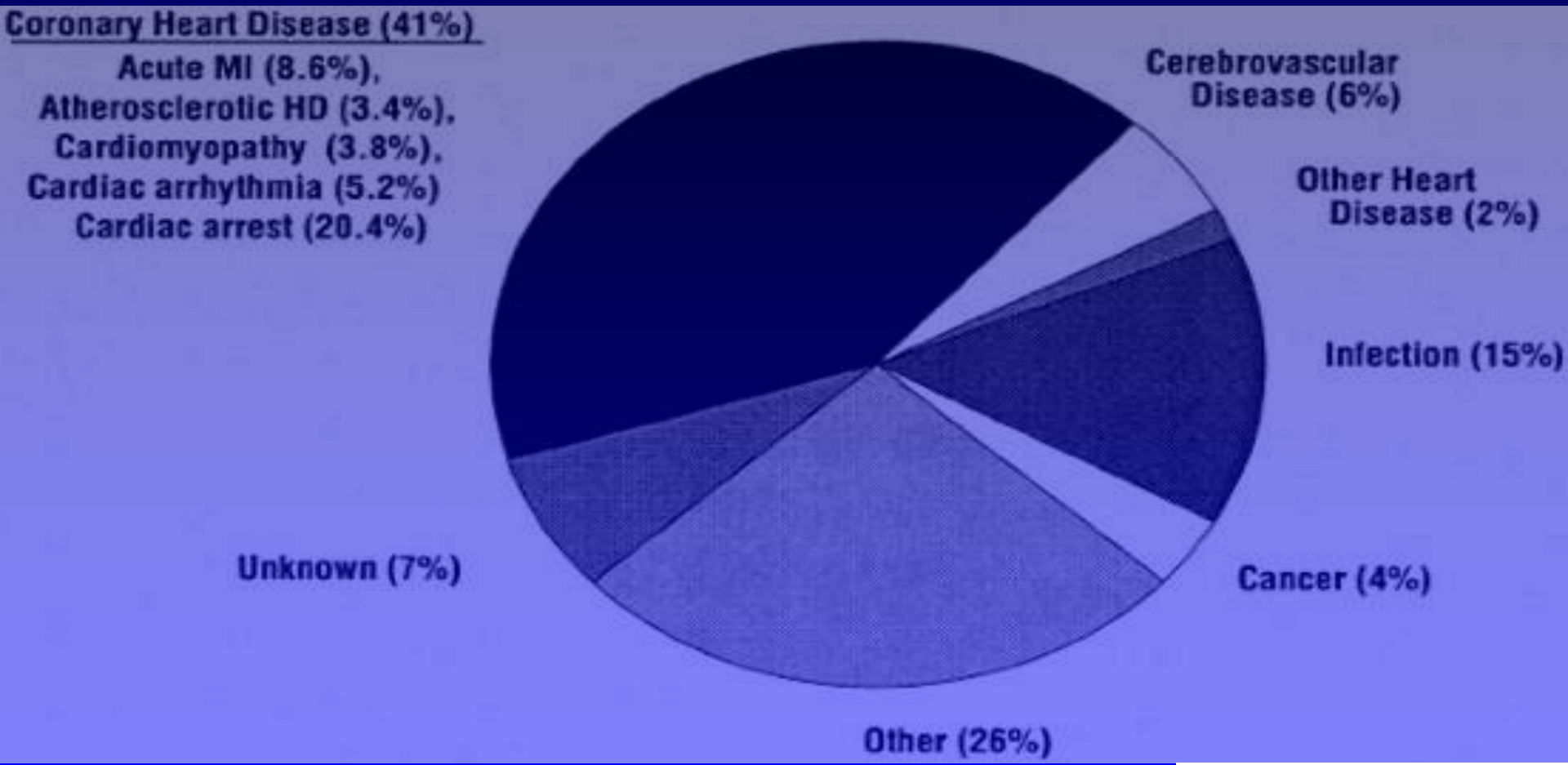


Fig 5. Causes of death among period prevalent patients 1997–1999, treated with hemodialysis, peritoneal dialysis, or kidney transplantation. Data are from the USRDS 2001 Annual Data Report (www.usrds.org). Abbreviations: MI, myocardial infarction; HD, heart disease.

National Kidney Foundation
of the NATIONAL CAPITAL AREA

Dialysis Facts from the US Renal Data System (USRDS)

- A 40-year old who starts dialysis will have an expected survival of 9.3 years compared to 37.4 years for the general population.

- The situation is even worse for the 59-year old who has just a 4.3-year life expectancy compared to 20.4 years for someone in the general population.

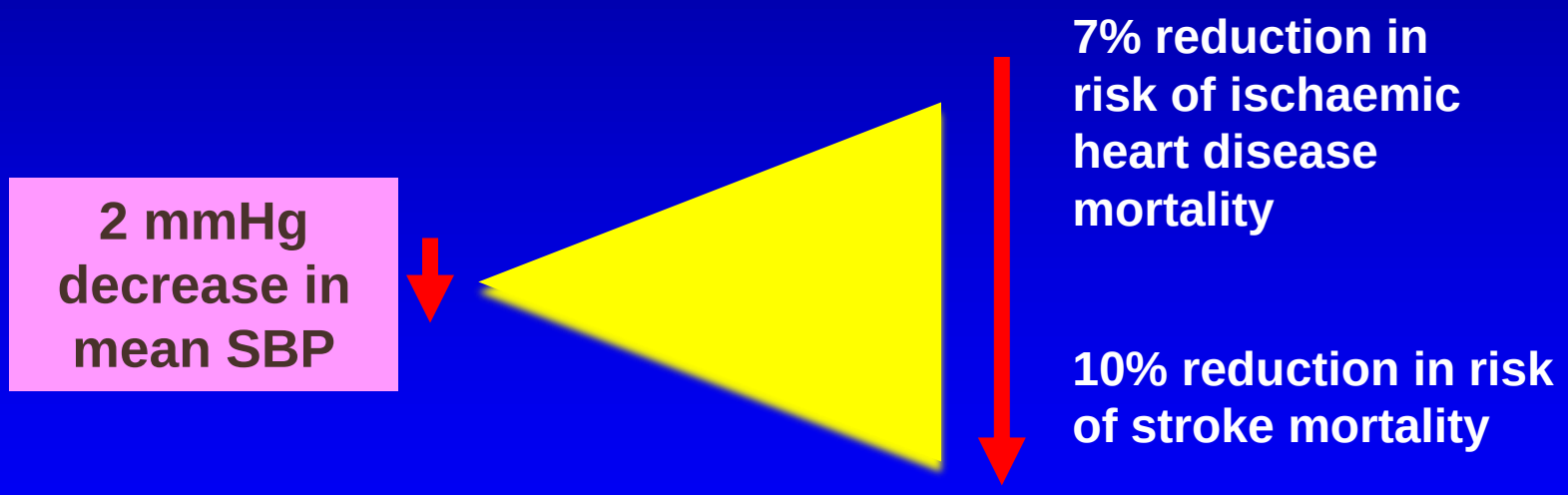
Treatment of Hypertension

Controlling BP with medication is unquestionably one of the most cost-effective methods of reducing premature CV morbidity and mortality.

Elliott. J Clin Hypertens 2003;5(Suppl. 2):3–13

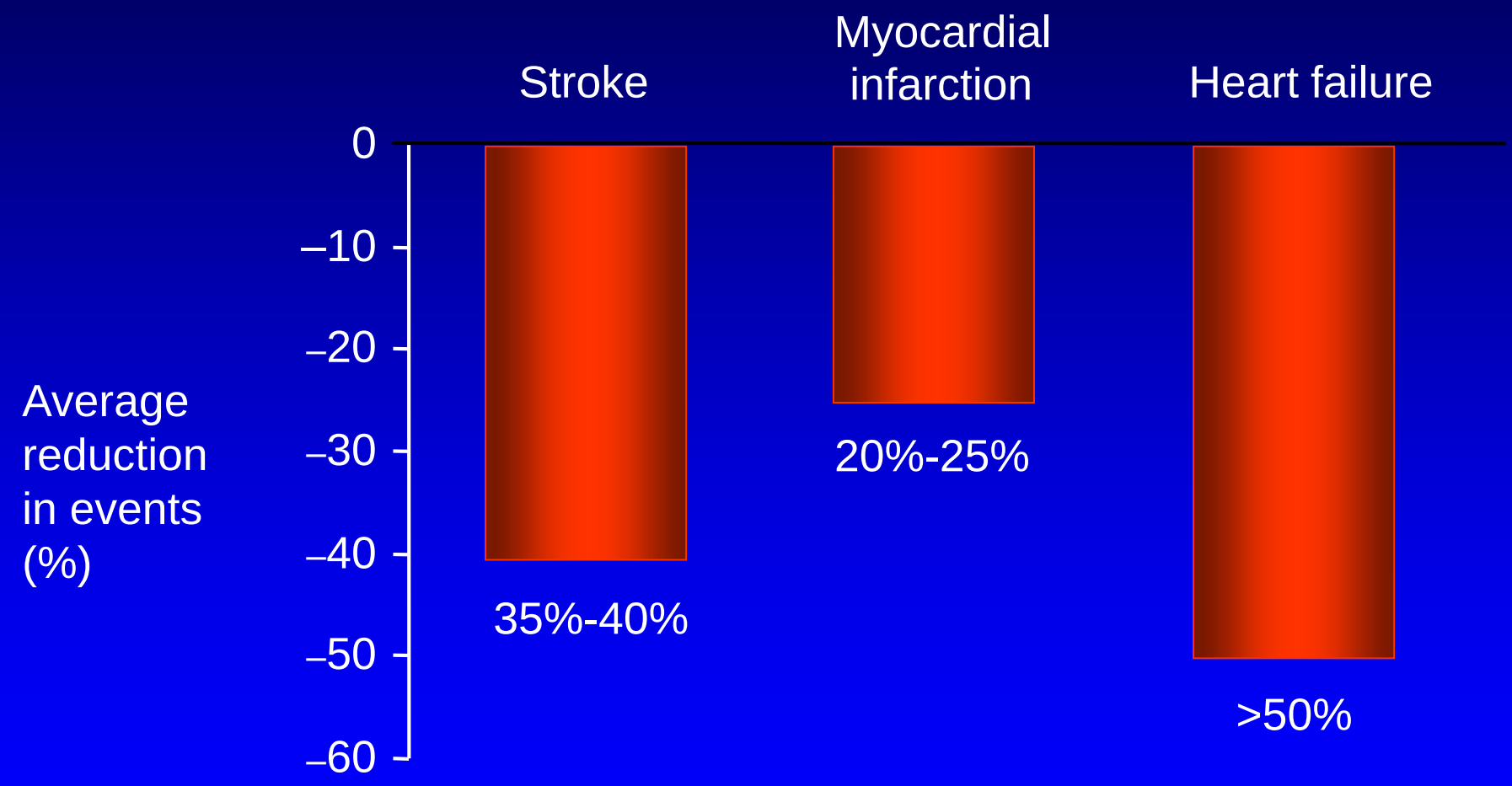
Blood Pressure Reduction of 2 mmHg Decreases the Risk of Cardiovascular Events by 7–10%

- Meta-analysis of 61 prospective, observational studies
- 1 million adults
- 12.7 million person-years



Lewington et al. Lancet 2002;360:1903–13

Long-Term Antihypertensive Therapy Significantly Reduces CV Events



Blood Pressure Lowering Treatment Trialists' Collaboration. Lancet. 2000;355:1955-1964.

Treatment Goals of Hypertension in CKD Patients

Protection against progressive renal function loss

Progression of chronic kidney disease

- CKD progression as defined by a reduction in GFR, occurs at a variable rate,
  - ranging from <1 to >12 mL/min per 1.73 m^2 per year,
- *This progression depends upon*:
  - the level of blood pressure control,
  - the degree of proteinuria,
  - the previous rate of GFR decline,
  - And the underlying kidney disease, including diabetes

Remuzzi G et al :Ann Intern Med. 2002;136(8):604

Pathophysiology: CKD Progression

Hyperfiltration theory: *The Final Common Pathway*

RENAL INJURY

↓

Reduction in nephron mass (Hyperfiltration of remaining nephron ↑ SNGFR)

↓

1. Glomerular capillary hypertension

↓

Increased glomerular permeability to macromolecules

↓

3. Increased BP

Increased filtration of plasma proteins — **2. Proteinuria**

↓

Excessive tubular protein reabsorption

↓

Tubulointerstitial inflammation

↓

RENAL SCARRING

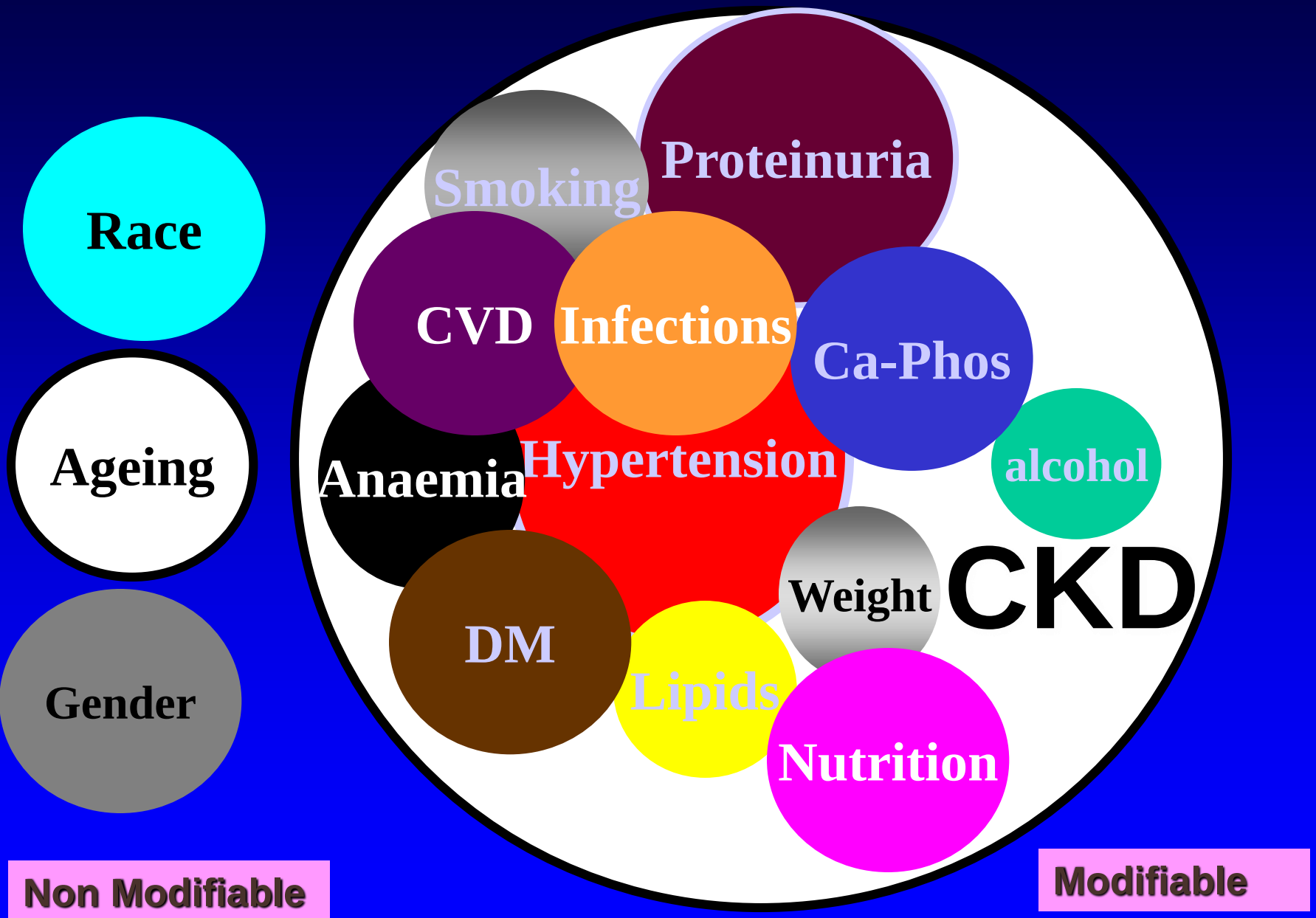
National Kidney Foundation of the National Capital Area

Progression of CKD

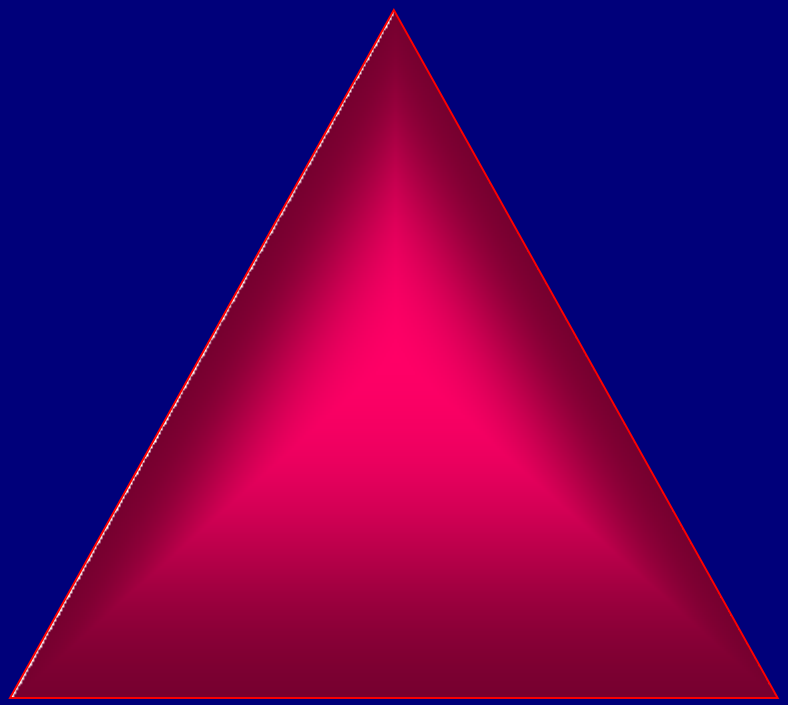
Regardless of CKD Etiology

the prognosis best correlates with the degree of renal interstitial fibrosis

Risk Factors / Markers for progressive CKD



The Renal Injury Triad



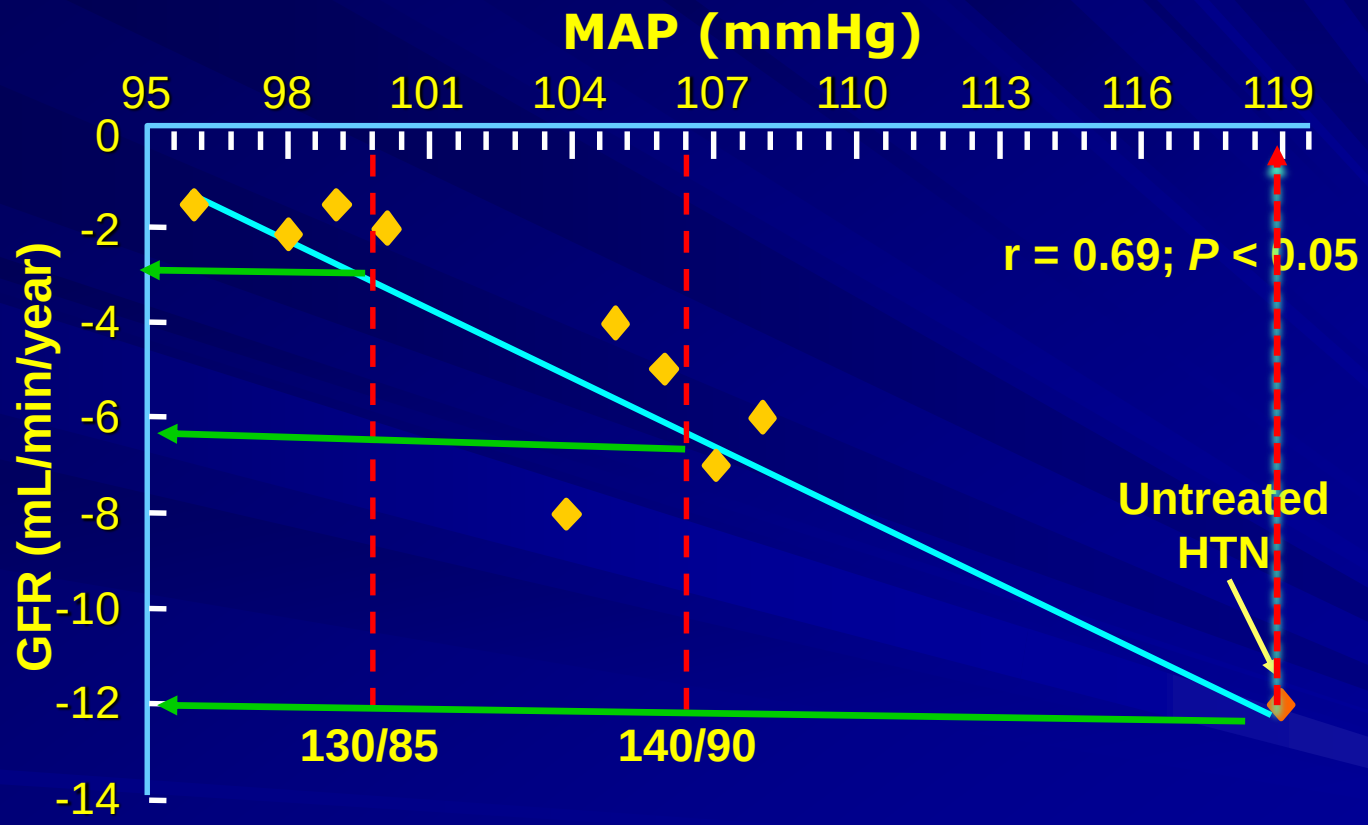
Progression of chronic kidney disease

There are Two Major components to slowing the rate of progression of CKD:

- **Treatment of the underlying disease, if possible !!!**

- **Treatment of secondary factors that are predictive of progression:**
  - **Elevated blood pressure**
  - **Proteinuria**

Long-term Decline in GFR is Correlated With Poor Control of BP



9 Studies on Nephropathy Progression in Diabetics and Non-Diabetics

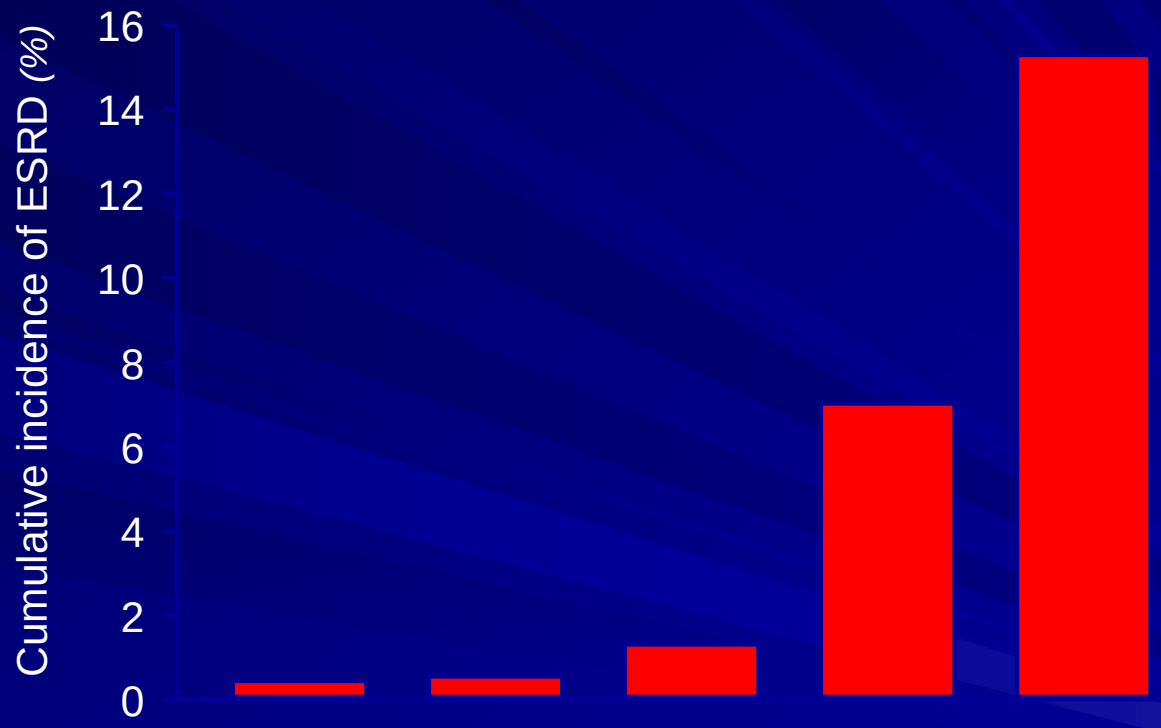
Parving HH, et al. Br Med J. 1989.
Viberti GC, et al. JAMA. 1993.
Klahr S, et al. N Eng J. Med 1994.
Hebert L, et al. Kidney Int. 1994.
Moschio G, et al. N Engl J Med. 1996.
Bakris GL, et al. Kidney Int. 1996.
Bakris GL. Hypertension. 1997.
The GISEN Group. Lancet. 1997.
ebovitz H, et al. Kidney Int. 1994.

L

Bakris GL, et al. Am J Kidney Dis. 2000;36(3):646-661.

Proteinuria Predicts Risk for ESRD?

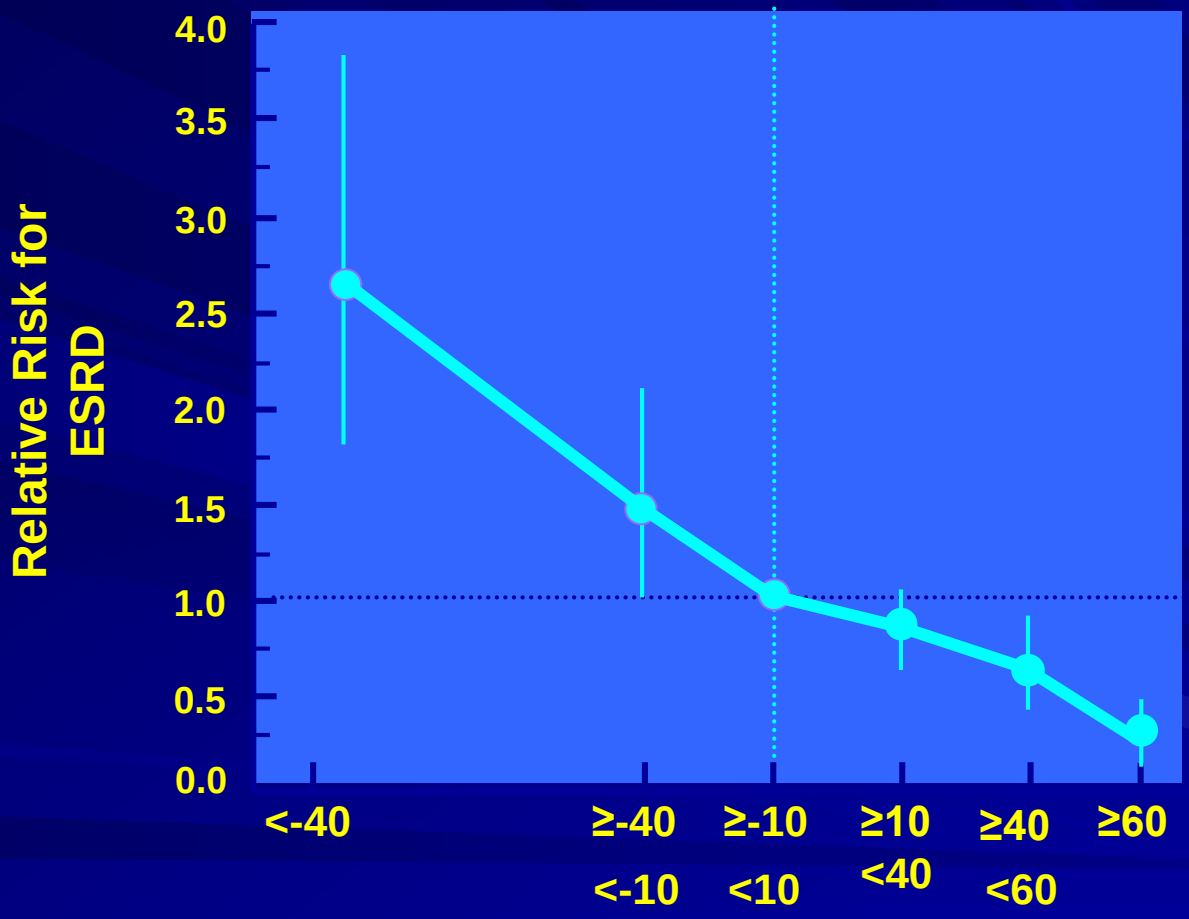
Community-based screening in 106,177 General Population : Follow-up: 17 years



Proteinuria	-	±	+	2+	≥3+
Number of screened	86,253	10,000	4,007	1,072	357
Number of ESRD	185	38	55	76	55

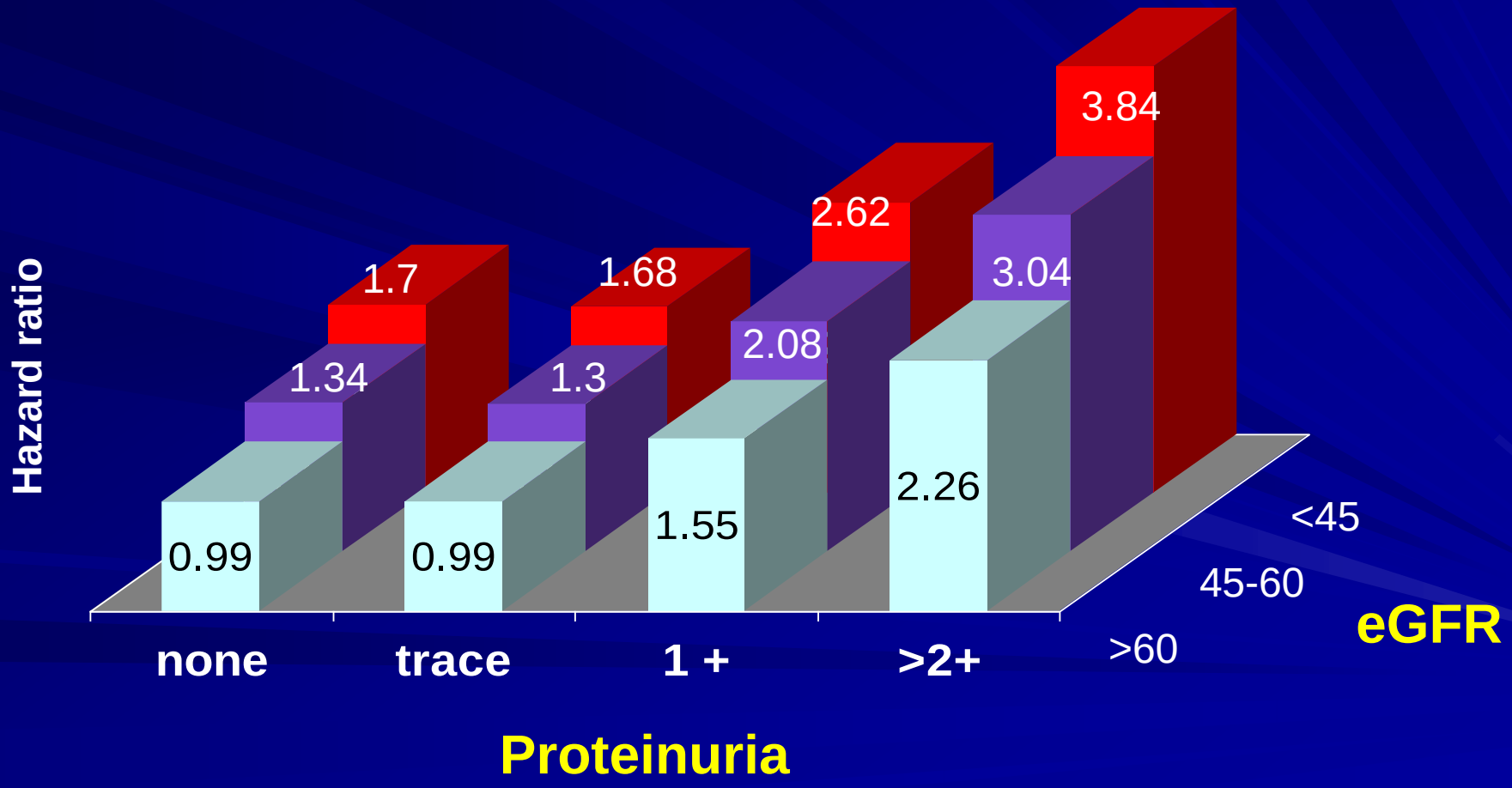
Iseki et al., *Kidney Int,* 2003

Reduction in Proteinuria is Associated with Reduced Risk for ESRD in Diabetic Nephropathy



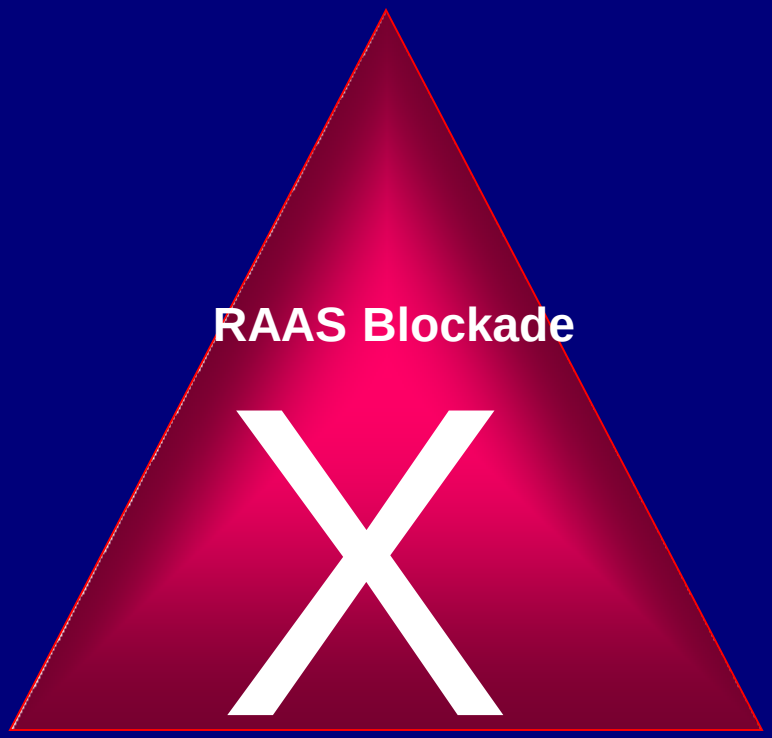
de Zeeuw et al. *Kid. Int.* June 2004

Relationship of Proteinuria, eGFR and Mortality

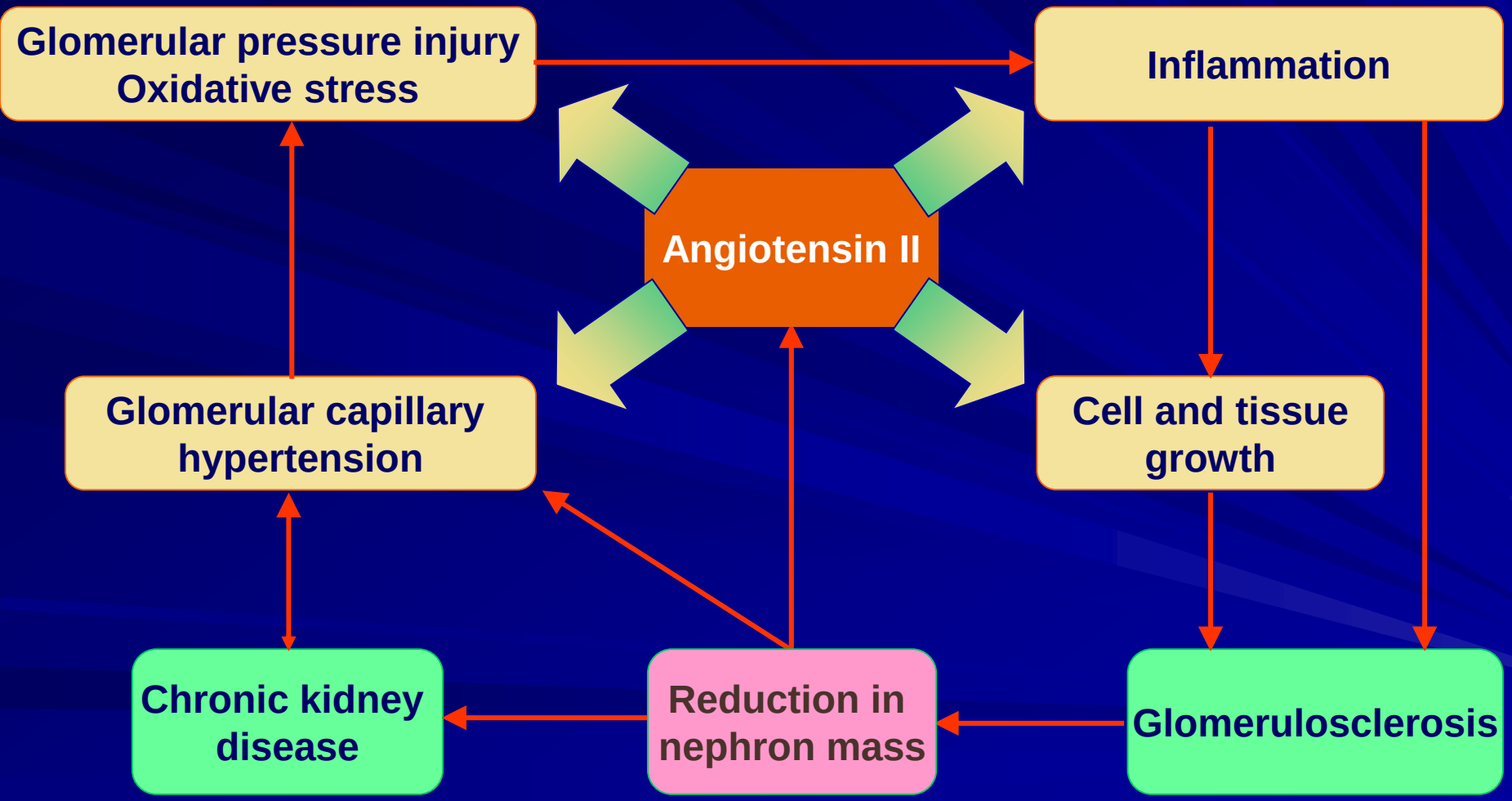


Tonelli et al. CARE investigators. BMJ 2005. In Print

The Renal Injury Triad

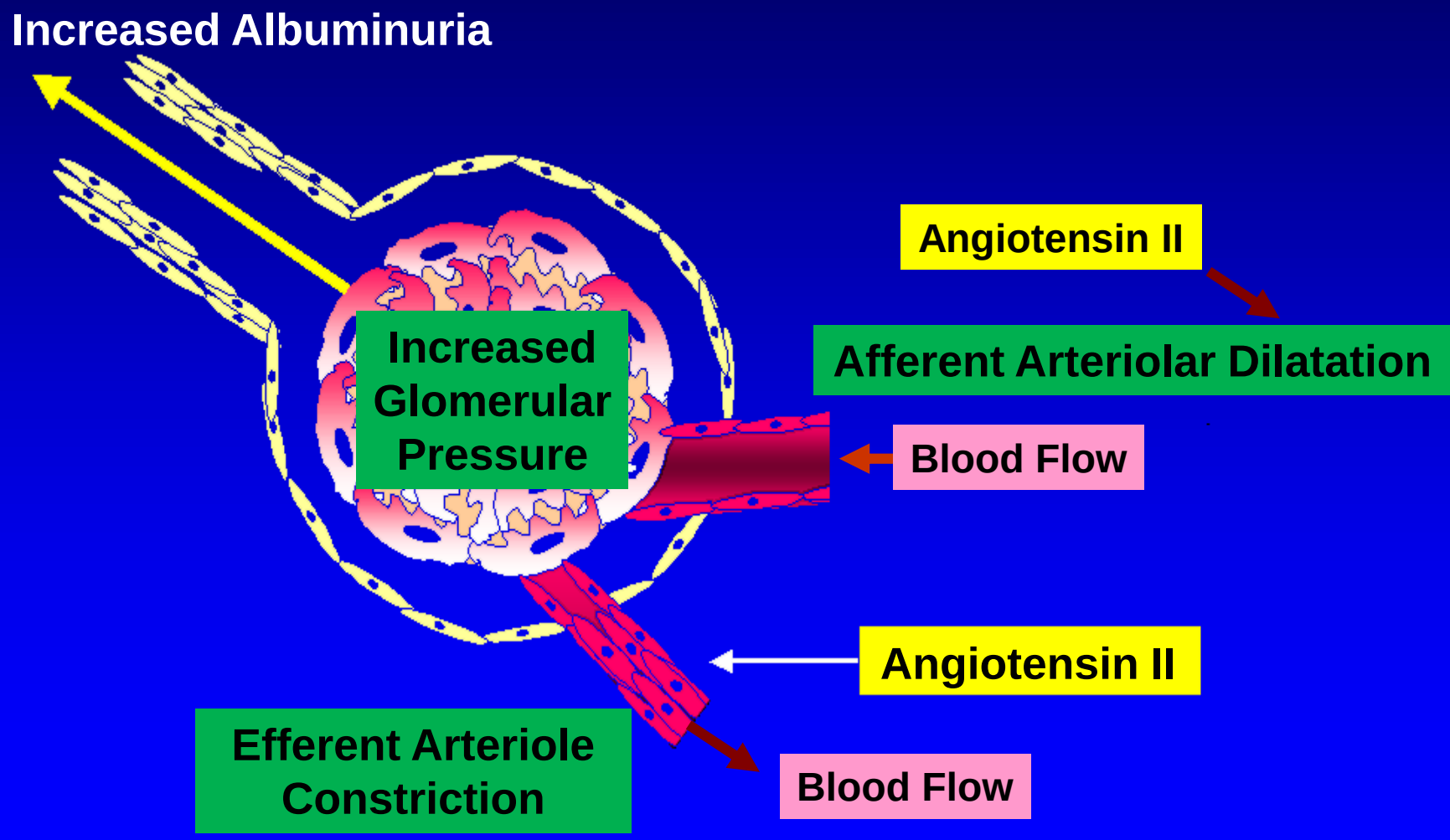


Angiotensin II is central to the pathophysiology of renal disease

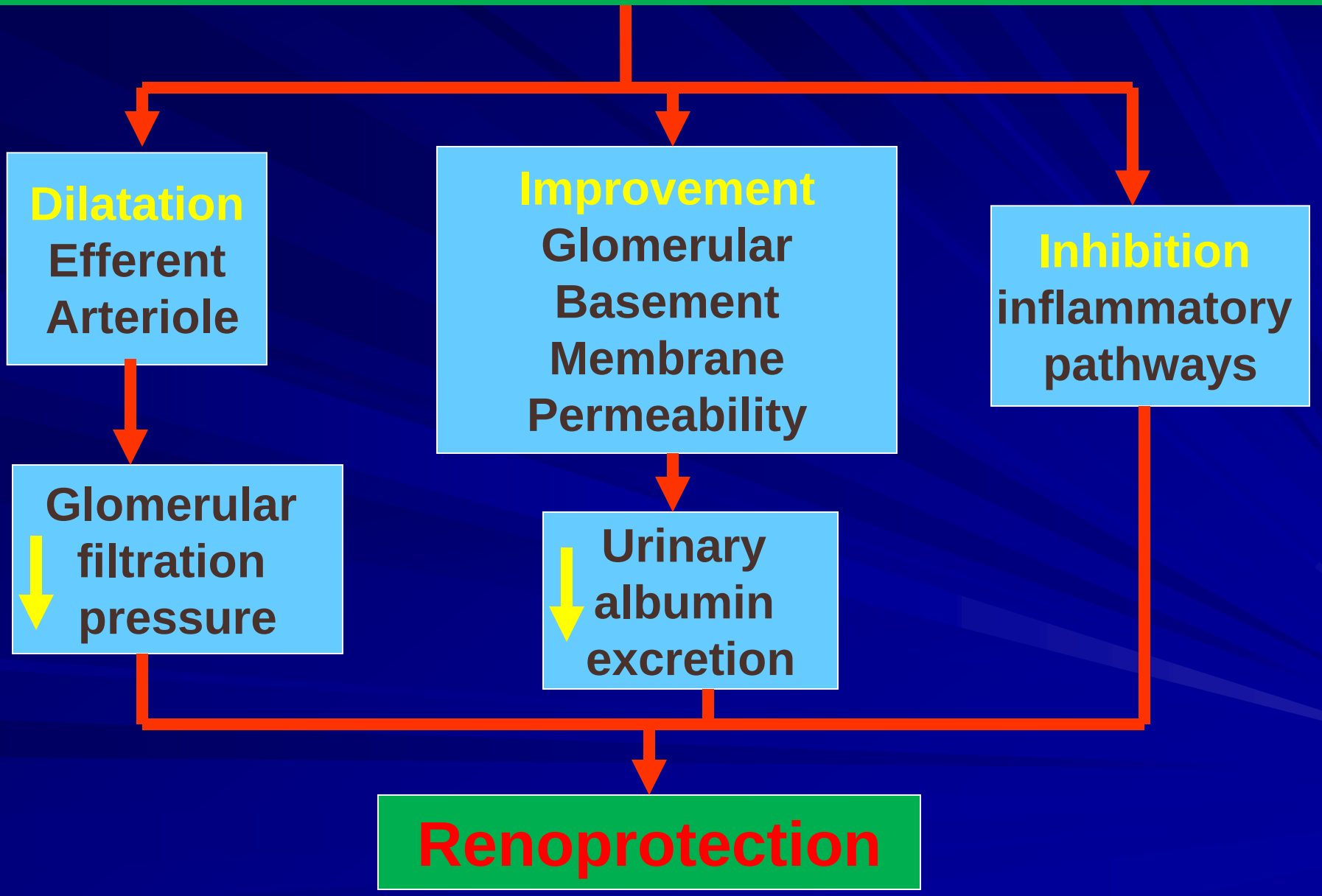


Brewster, Perazella. *Am J Med* 2004;116:263–272

Theoretical Hemodynamic Role of Angiotensin II in Diabetic Glomerular Injury



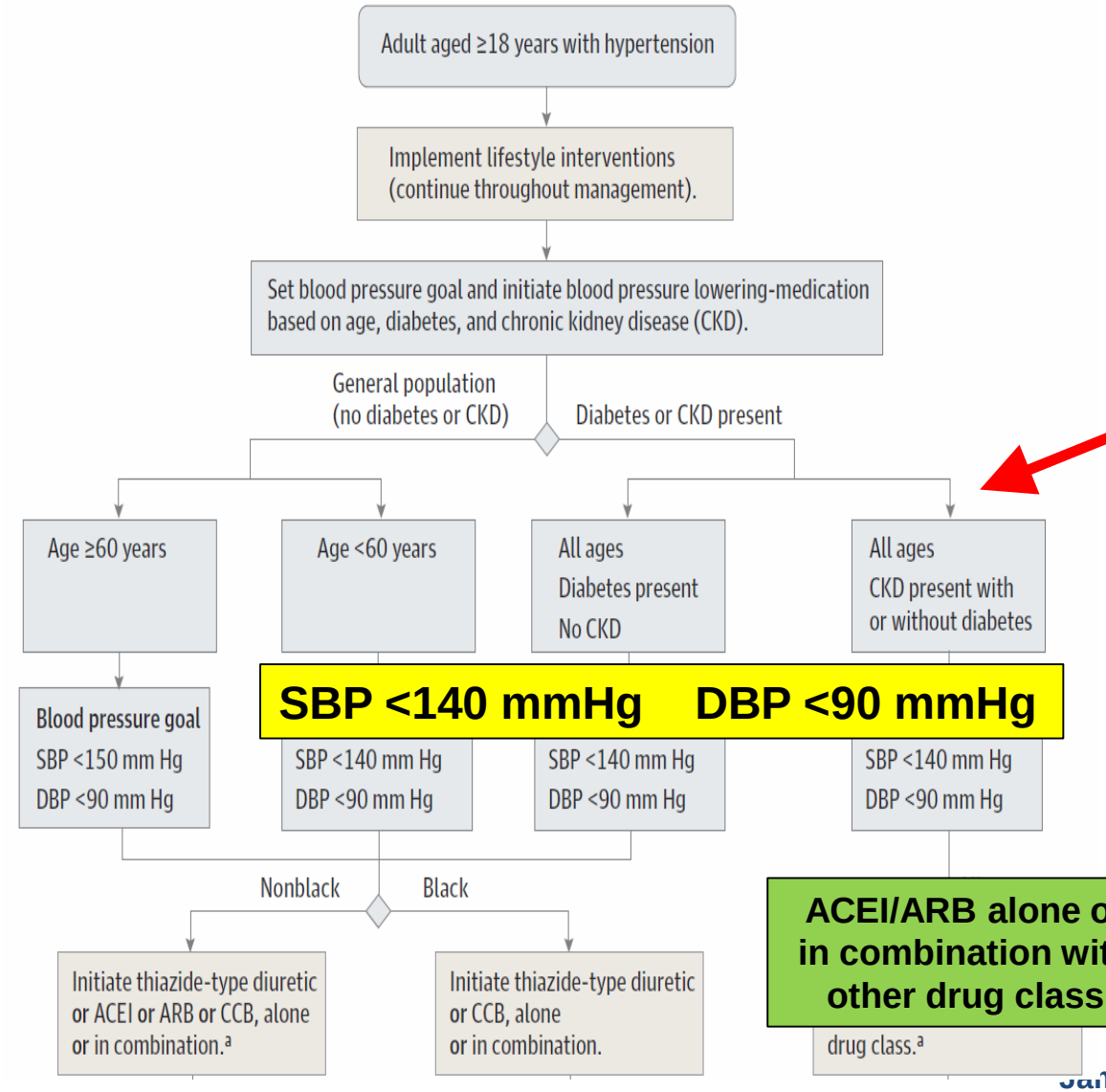
RAAS Blockade



Management of Hypertension in CKD Patients

- Blood pressure goal
- Non-pharmacological treatment
- Pharmacological treatment

JNC 8



James PA et al. JAMA 2014

ESH/ESC

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
1–2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
≥3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs	• Lifestyle changes • BP drugs	• Lifestyle changes • Immediate BP drugs
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90

CKD

SBP <140 mmHg DBP <90 mmHg

2013 ESH/ESC Guidelines. J Hypertens 2013

ESH/ESC

Type of kidney disease	Protein excretion < 0.3 g/day (normoalbuminuria, microalbuminuria, 30–150 mg/day)	Protein excretion 0.3–1 g/day (microalbuminuria 150–300 mg/day, macroalbuminuria 300–500 mg/day)	Protein excretion > 1 g/day (macroalbuminuria > 500 mg/day)
Non-diabetic kidney disease	< 140/90 mm Hg	< 130/80 mm Hg	<125/75 mm Hg*
Diabetic kidney disease	SBP < 130–140 mm Hg** DBP < 80 mm Hg**	< 130/80 mm Hg***	<130/80 mm Hg*** (<125/75 mm Hg*** for young patients with heavy proteinuria)

*As evident from MDRD study B trial phase and MDRD long-term study (see *text*); **from cardiovascular outcome trials (see *text*); ***through extrapolation from data in non-diabetic CKD and post-hoc or observational analyses in diabetic CKD (see *text*)

Sarafidis PA & Ruilope LM. ESH Newsletter 2013, No. 55

- **Non-diabetic adults with CKD:**
  ≤140 mmHg systolic and ≤90 mmHg diastolic if norm… …inuric
  ≤130 mmHg systolic and ≤80 mmHg diastolic if … macroalbuminuric

- **Diabetic adults with non dialysis-depend… D:**
  ≤140 mmHg systolic and ≤90 mmHg… …c if normoalbuminuric
  ≤130 mmHg systolic and ≤80 m… …stolic if micro or macroalbuminuric

- **Kidney transplant recipi…**
  ≤130 mmHg systoli… …0 mmHg diastolic

- **Elderly pe… …CKD:**
  probak… …mmHg systolic and ≤90 mmHg diastolic, but set targets after co…sideration of co-morbidities

Aim for <130/80 mmHg if albuminuria is present

KDIGO Blood Pressure Work Group. Kidney Int Suppl 2012

Blood Pressure Goals in CKD

There is little evidence among patients with CKD that a BP goal of less than 130/80mmHg saves lives, saves kidneys or reduces cardiovascular events.

Nonetheless, BP control is important. Therefore, as in the general population, BP should be targeted to less than 140/90mmHg.

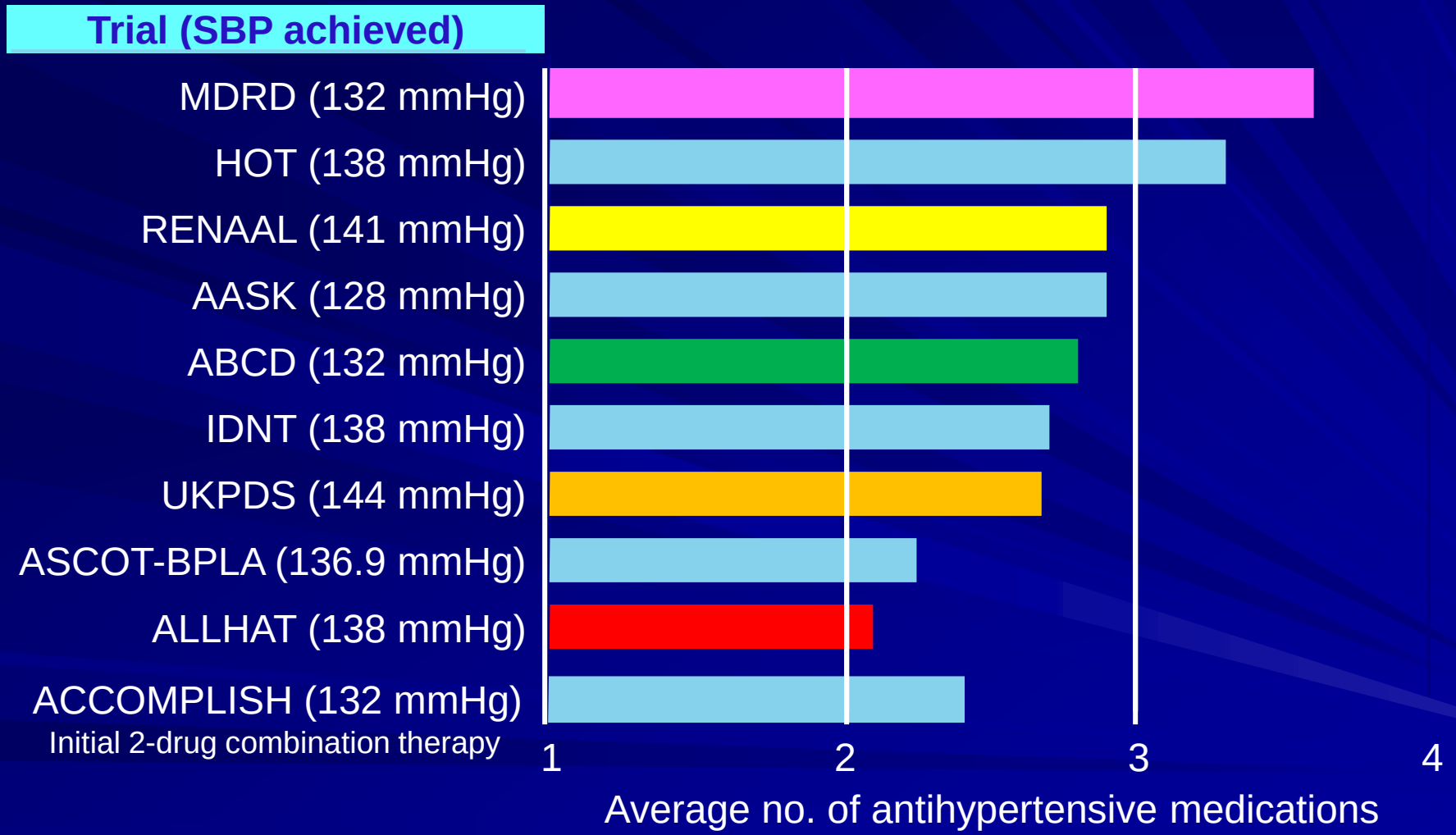
Hypertension therapy personalized and individualized using home BP monitoring holds great promise.

Agarwal R. Curr Opin Nephrol Hypertens 2011

Management of Hypertension in CKD Patients

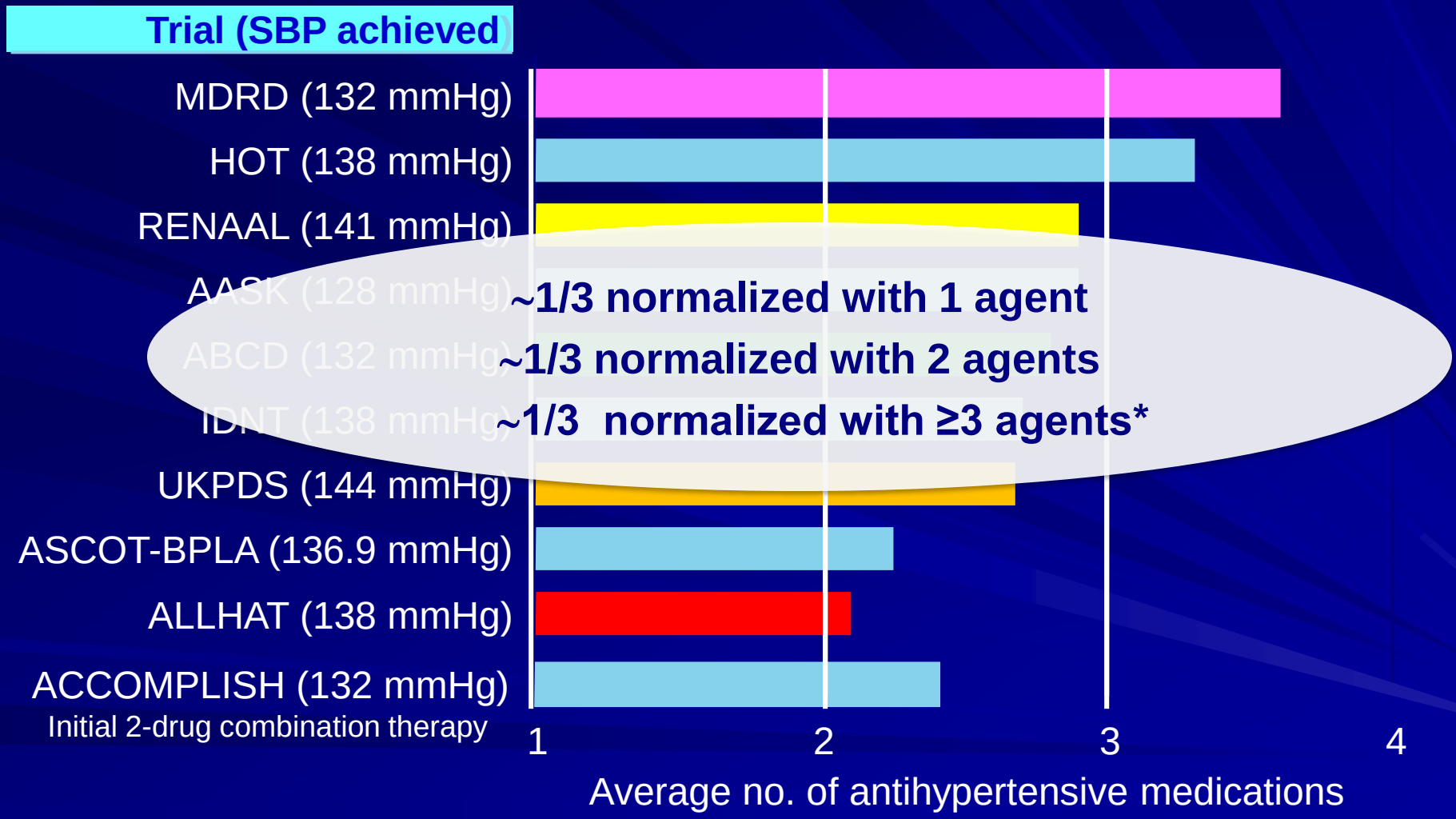
- Blood pressure goal
- **Pharmacological treatment**

Multiple Antihypertensive Agents are Needed to Reach BP Goal



Bakris et al. Am J Med 2004;116(5A):30S–8; Dahlöf et al. Lancet 2005;366:895–906
Jamerson et al. Blood Press 2007;16:80–6; Jamerson et al. N Engl J Med 2008;359:2417–28

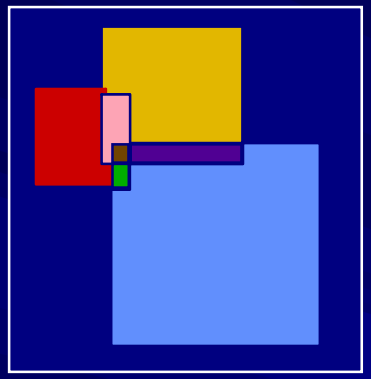
Multiple Antihypertensive Agents are Needed to Reach BP Goal



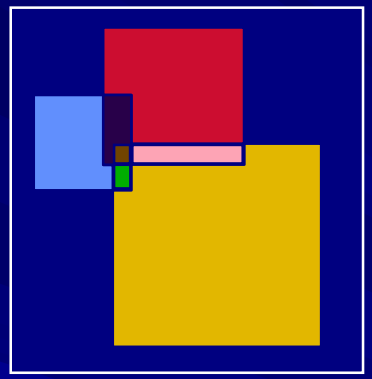
Bakris et al. Am J Med 2004;116(5A):30S–8; Dahlöf et al. Lancet 2005;366:895–906
Jamerson et al. Blood Press 2007;16:80–6; Jamerson et al. N Engl J Med 2008;359:2417–28

Blood Pressure has Multiple Regulatory Pathways

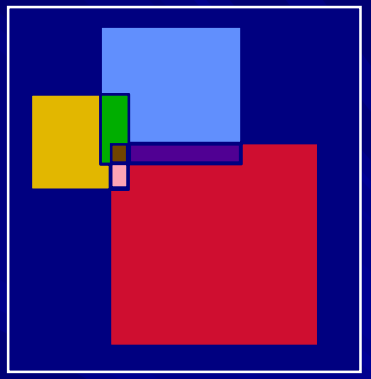
Patient 1



Patient 2



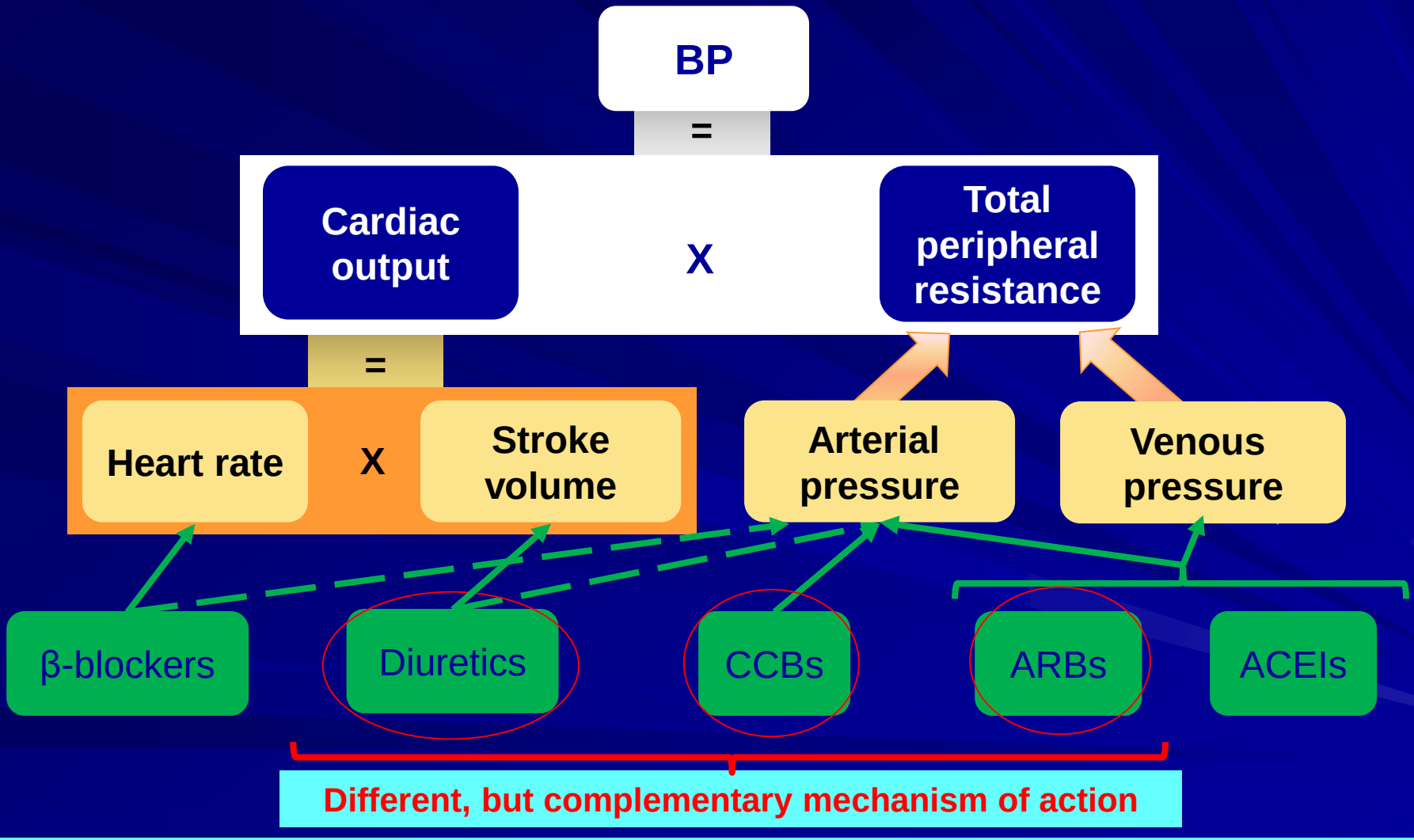
Patient 3



- Sympathetic nervous system
- Renin-angiotensin system (**RAAS**)
- Total body sodium (Volume)

B. Waeber, March 2007, with permission

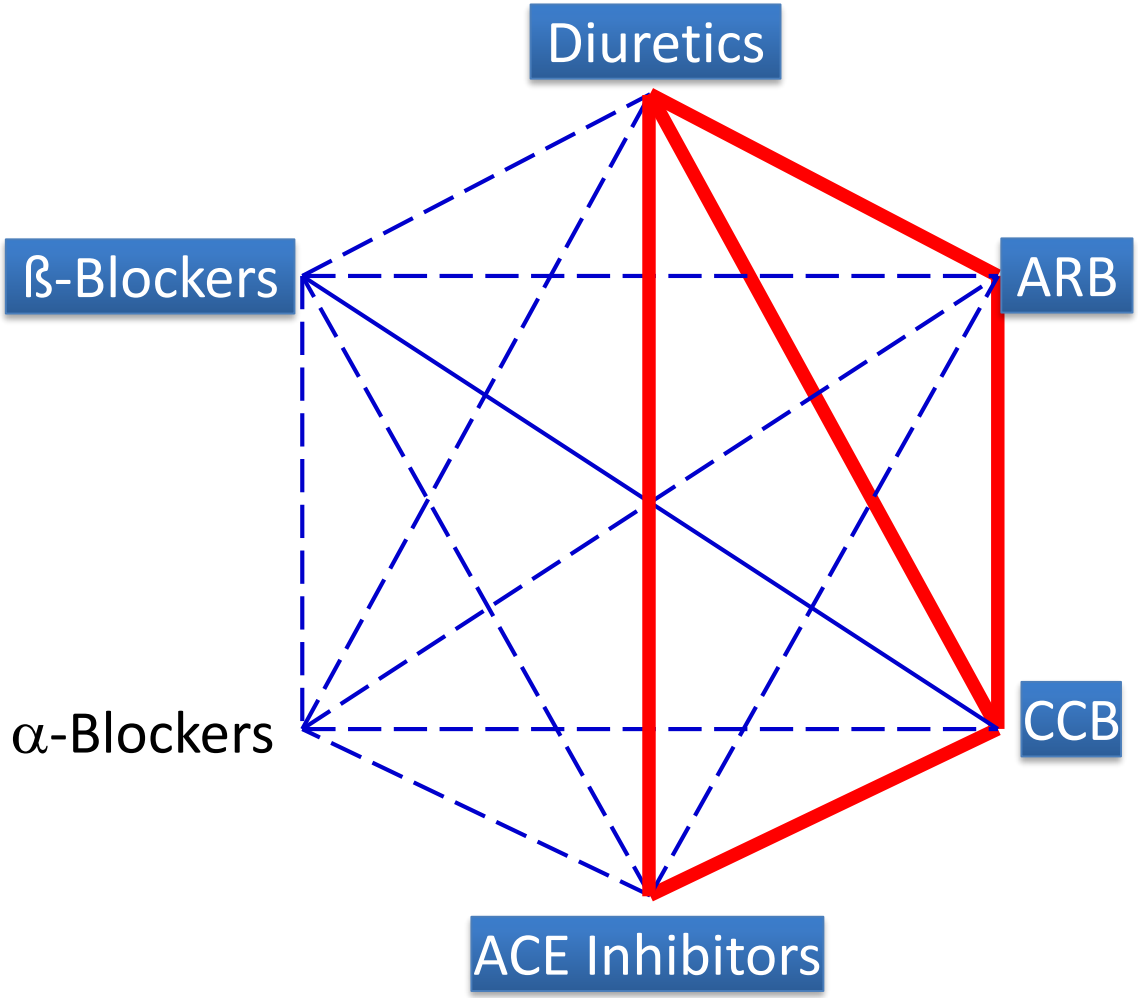
Different Classes of Drugs have Different Sites of Action



ACEI = angiotensin-converting enzyme inhibitor;
ARB = angiotensin Type II receptor blocker;
CCB = calcium channel blocker

Beevers, et al. BMJ 2001;322:912–6;
McGhee, et al. Crit Care Nurse 2002;22:60–4;
Goodman & Gilman's Pharmacological Basis of Therapeutics. 9th ed. 1995.

ESH/ESC 2009 vs. 2007
first-line antihypertensives and combination therapy



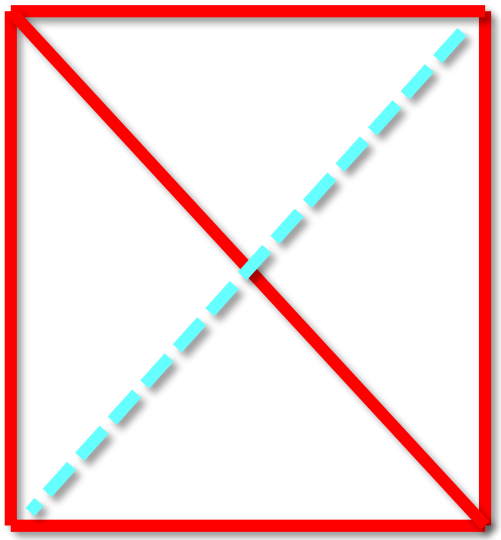
— most rational combinations

ESH/ESC, J Hypertens 2007;25:1105–87
ESH/ESC, J Hypertens 2009;27:2121–58

ESH/ESC 2009: Recommendations for Dual Combination Therapy

Diuretic

ARB



ACE-I

CCB

Note that among the four groups of antihypertensives only the combination of ARB and ACE-I is not recommended

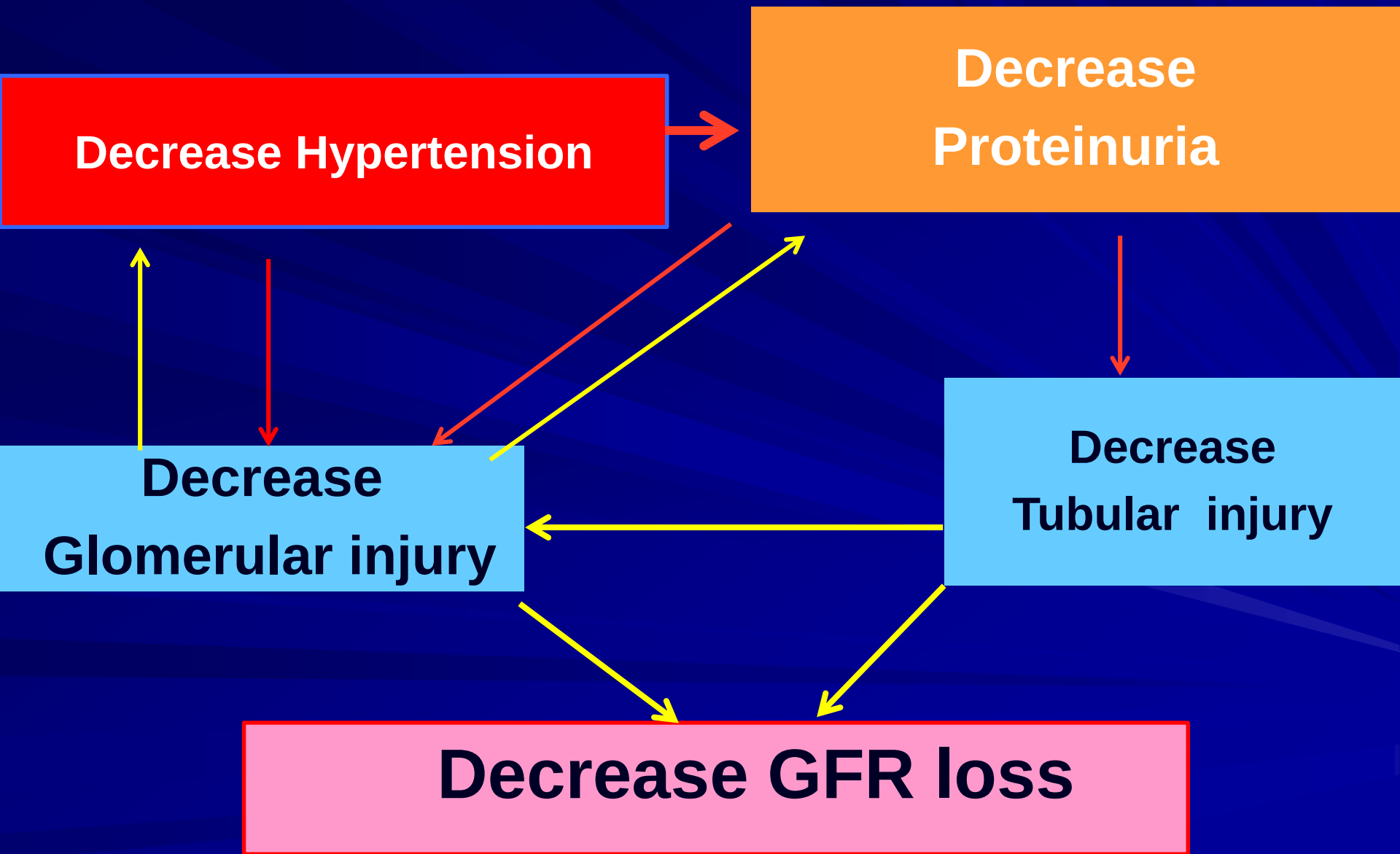
ESH/ESC, J Hypertens 2009;27:2121–58

Advantages of Fixed Versus Free Combinations of Two Antihypertensive Drugs

	Fixed	Free
Simplicity of treatment	+	–
Compliance	+	–
Efficacy	+	+
Tolerability	+*	–
Price	+	–
Flexibility	–	+

*Lower doses generally used in fixed-dose combinations
+ = potential advantage

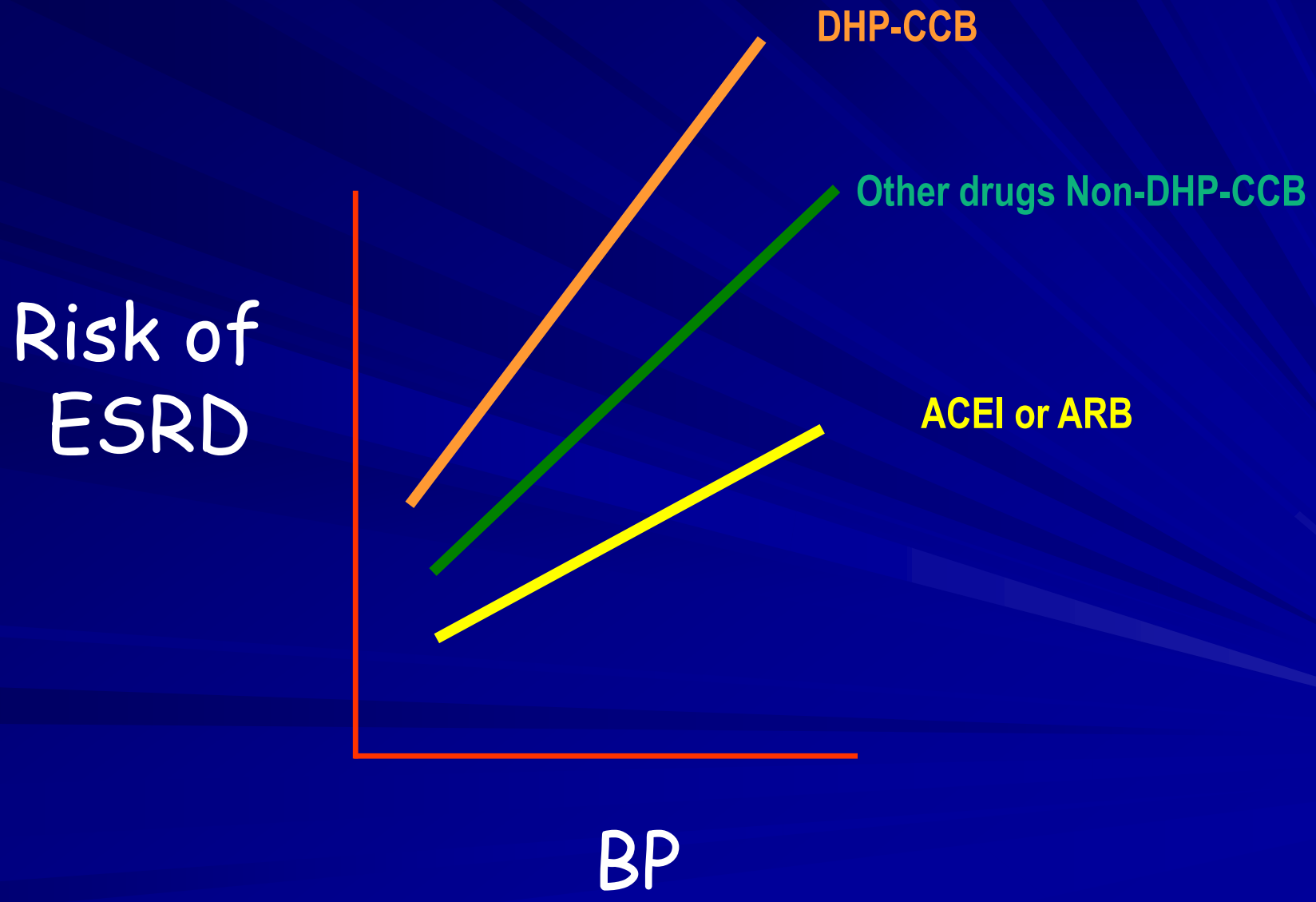
Renoprotection: One or Many Therapies ?



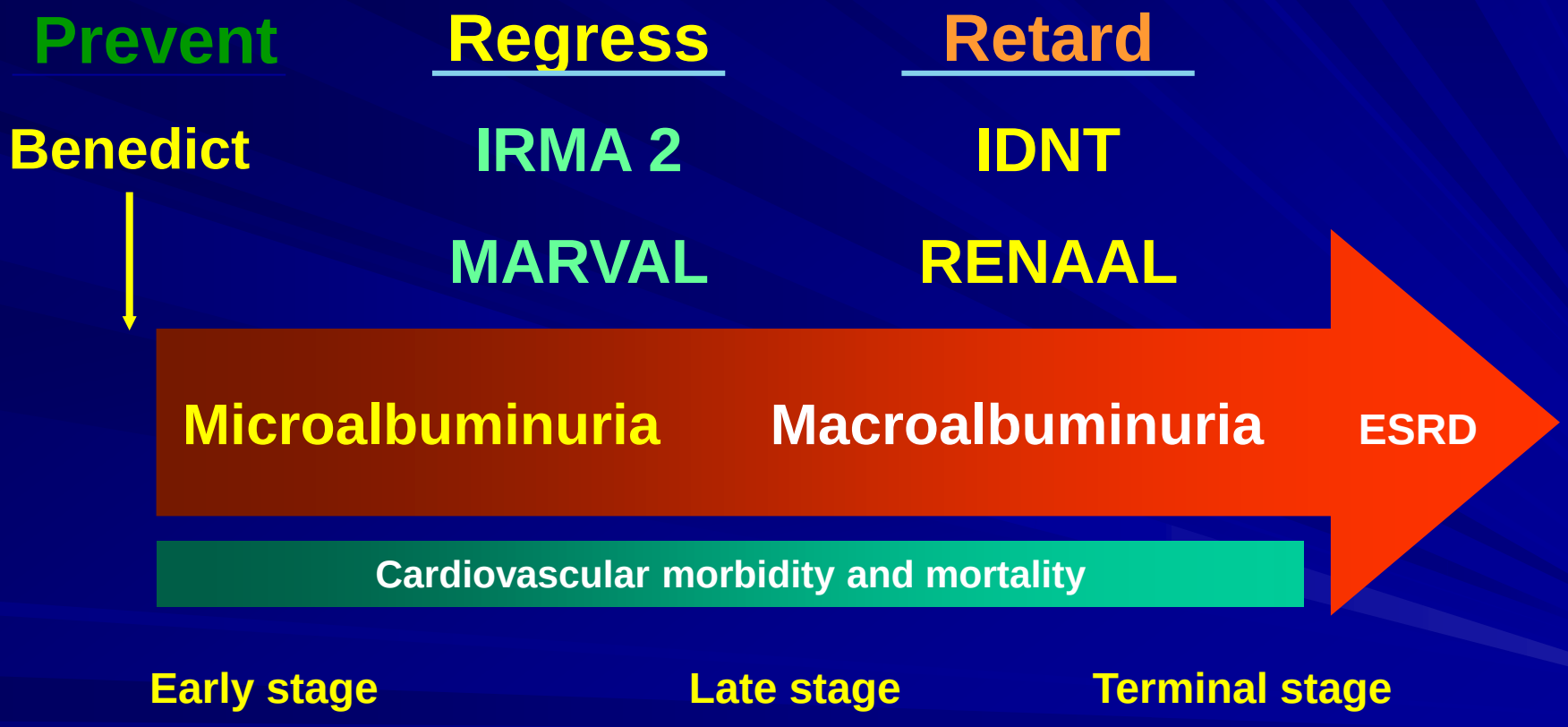
Proteinuria Reduction and Choice of Antihypertensive

- ACE Inhibitors and ARBs
  - equivalent 30-40% reduction; effect greater when exposed to a diuretic or salt restricted diet
- Non-dihydropyridine calcium antagonists
  - 20 - 30% reduction (variable)
- Diuretics, beta-blockers, alpha-blockers
  - variable, small reduction
- Dihydropyridine calcium antagonists
  - variable, may increase protein excretion

Renal protection beyond BP?



Renoprotection



Severity of renal disease

Prevent: BENEDICT Study in Type 2 DM

- This is the largest study ever to compare an ACE I with a calcium channel blocker.
- 1204 patients
- 3 years of treatment with
  - trandolapril alone,
  - trandolapril and verapamil combined,
  - verapamil alone,
  - or placebo.

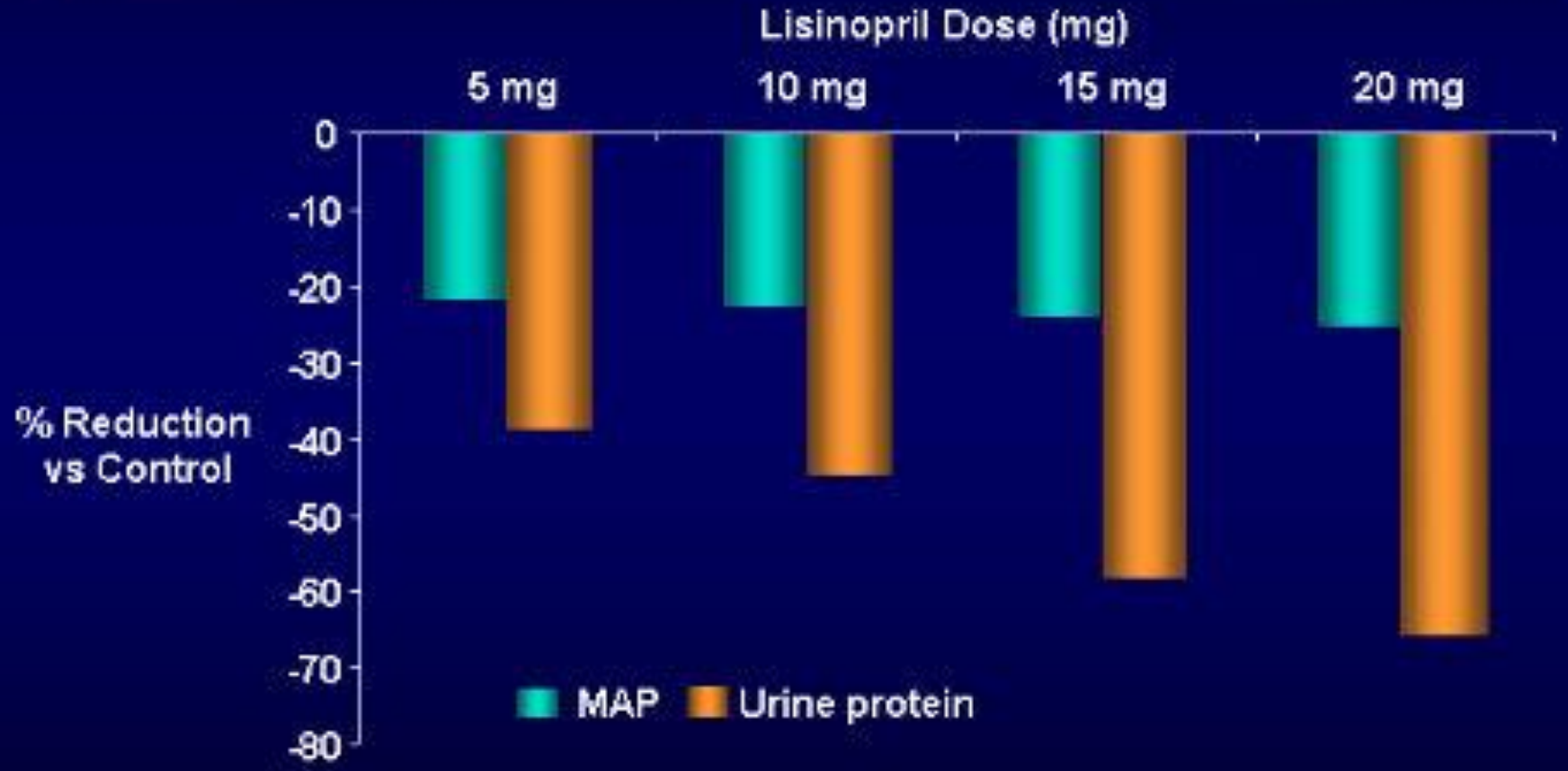
- In normoalbuminuric patients with type 2 diabetes and hypertension (BP >130/85 mm Hg), treatment with ACEI prevents development of microalbuminuria.

Assal JP Int J of Metab 2004

Antiproteinuric Effects of ACE.I / ARBs

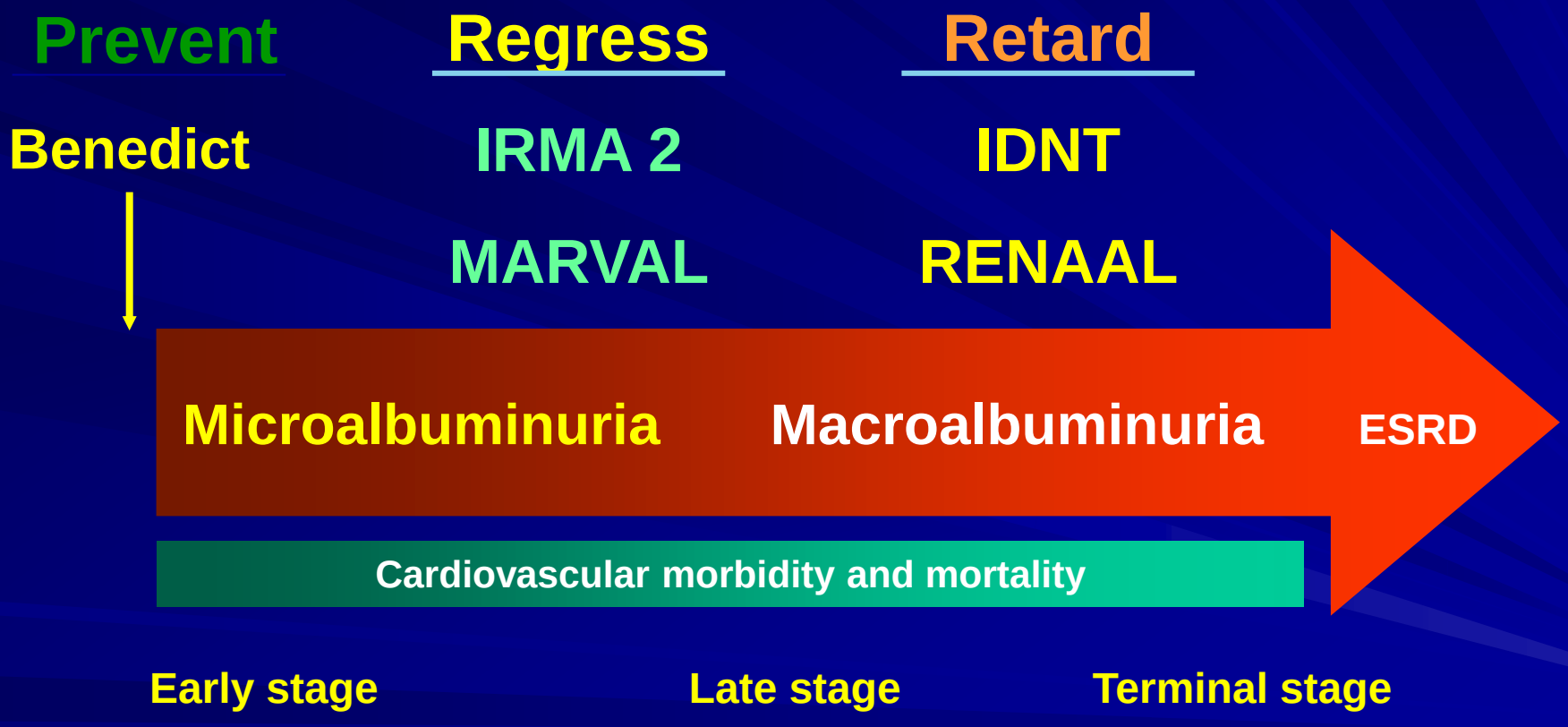
- It occres early within 7 days after treatment is started
- Independent of blood pressure reduction
- They have a dose-response effect
- The doses are higher than needed to control BP

Blood Pressure and Proteinuric Responses to Increasing Dose of ACE-Is



Adapted from Palla R et al. *Int J Clin Pharmacol Res* 1994;14:35-43.

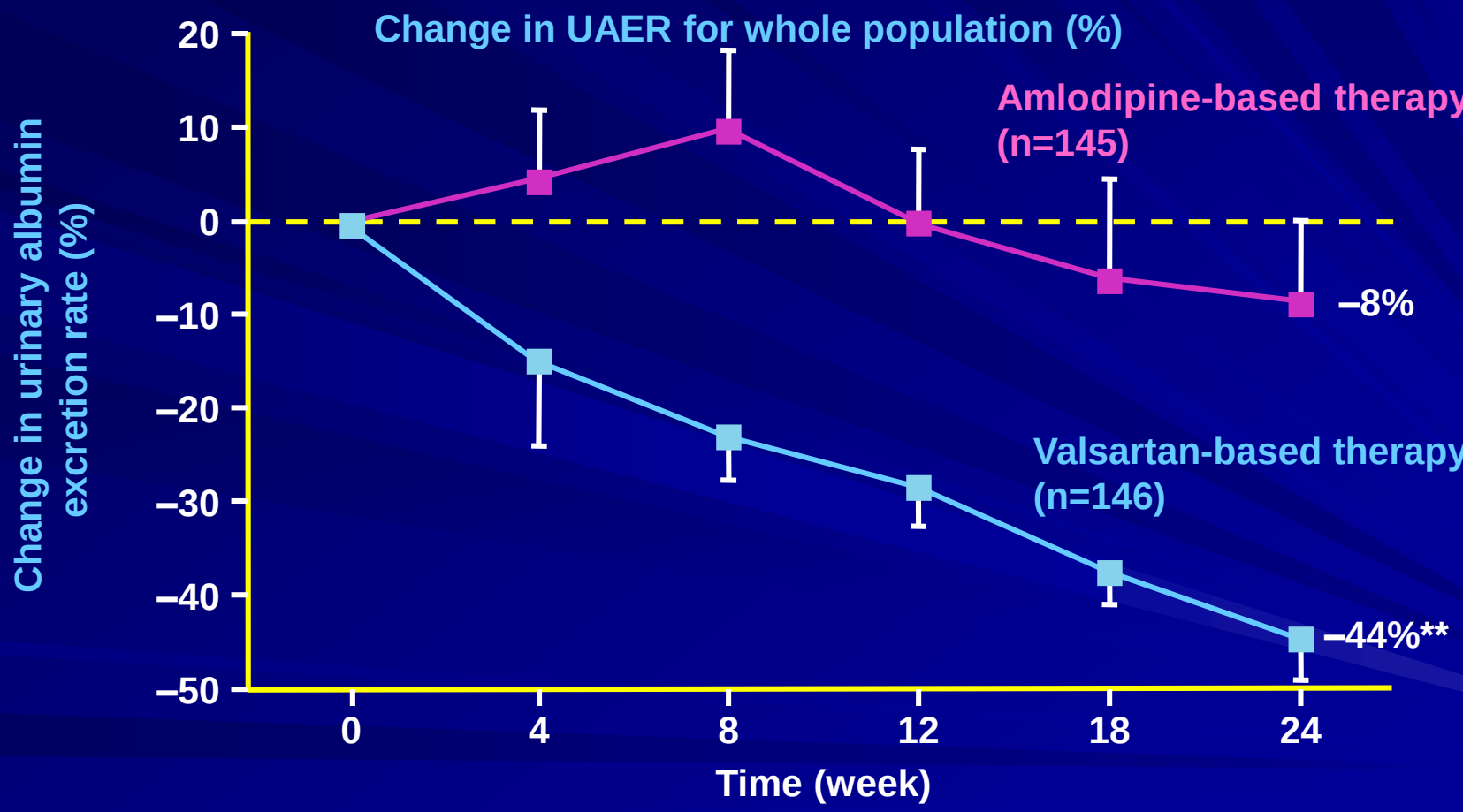
Renoprotection



Severity of renal disease

MARVAL: Microalbuminuria Reduction with Valsartan

Valsartan is Effective in Reducing Urinary Albumin Excretion Rate



MARVAL = Microalbuminuria Reduction with Valsartan

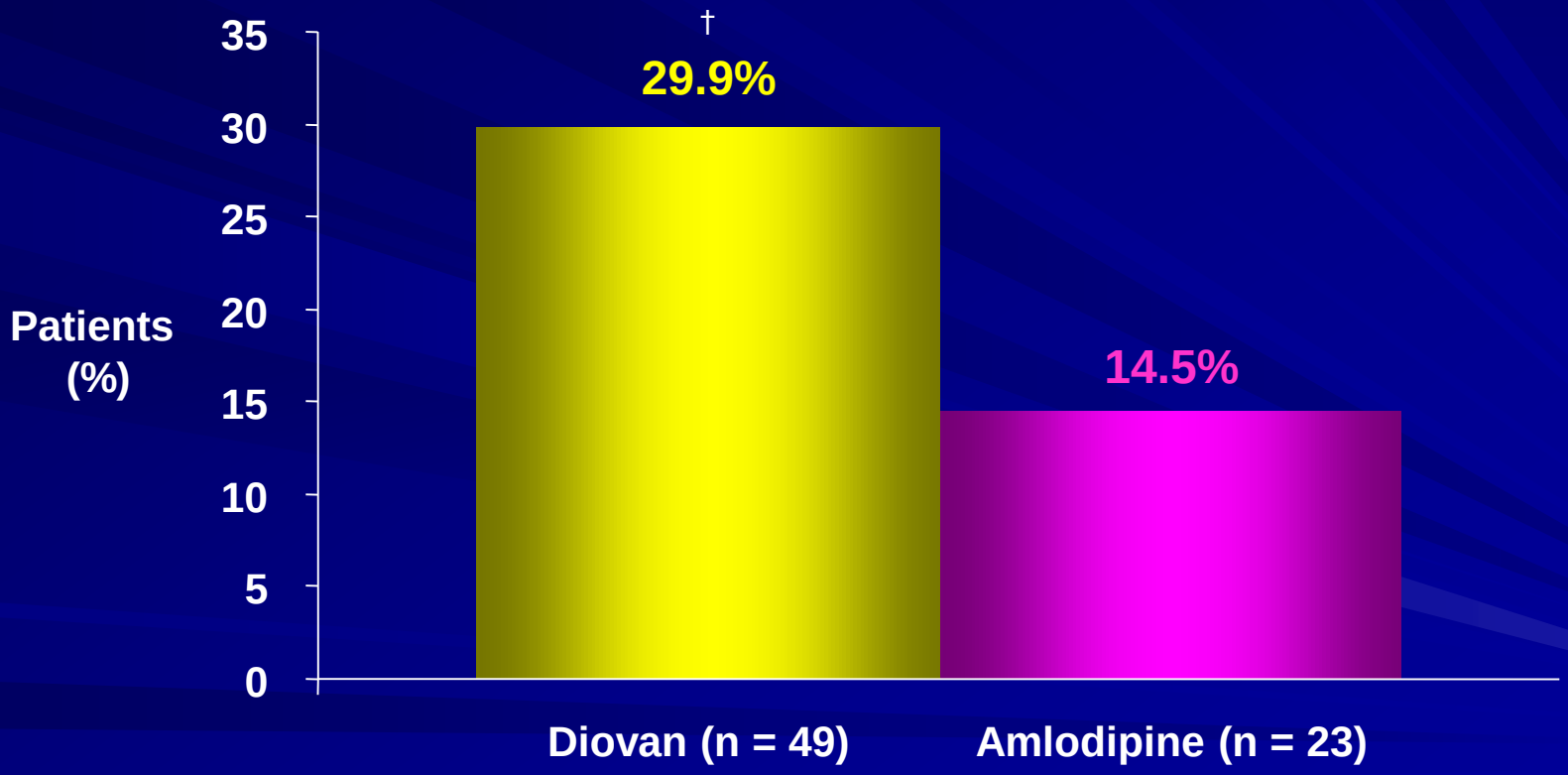
**p<0.001 vs amlodipine

UAER = urinary albumin excretion rate

Viberti et al. Circulation 2002;106:672–8

MARVAL: Significantly More Valsartan-Treated Patients Than Amlodipine-Treated Patients Exhibit Regression to Normoalbuminuria

Percentage of Patients Returning to Normoalbuminuria* at 24 Weeks



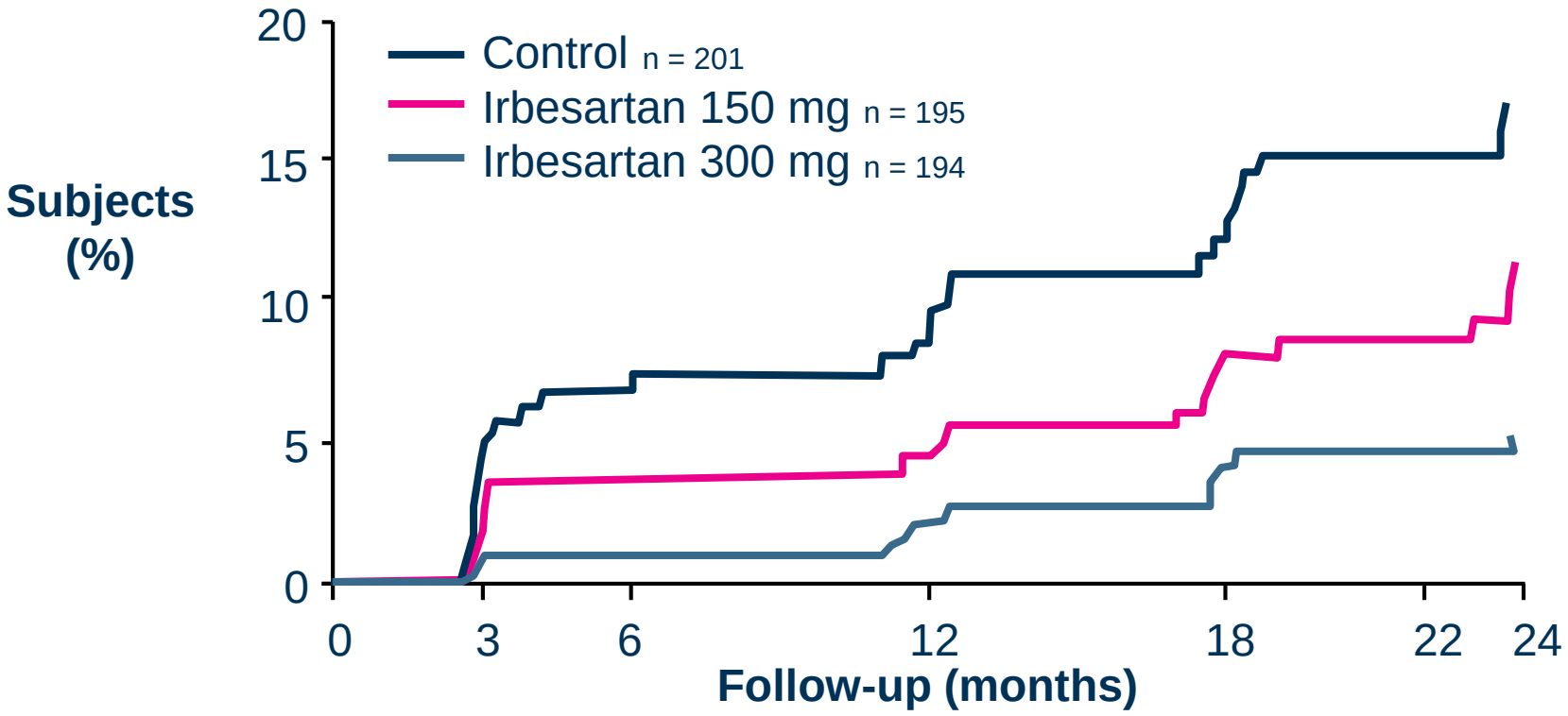
*Defined as urinary albumin excretion rate <20 µg/min; †*P*<0.001 vs amlodipine.

Viberti G et al. *Circulation.* 2002;106:672-678.

IRMA-2 Results: Irbesartan Significantly Delays Progression To Overt Proteinuria

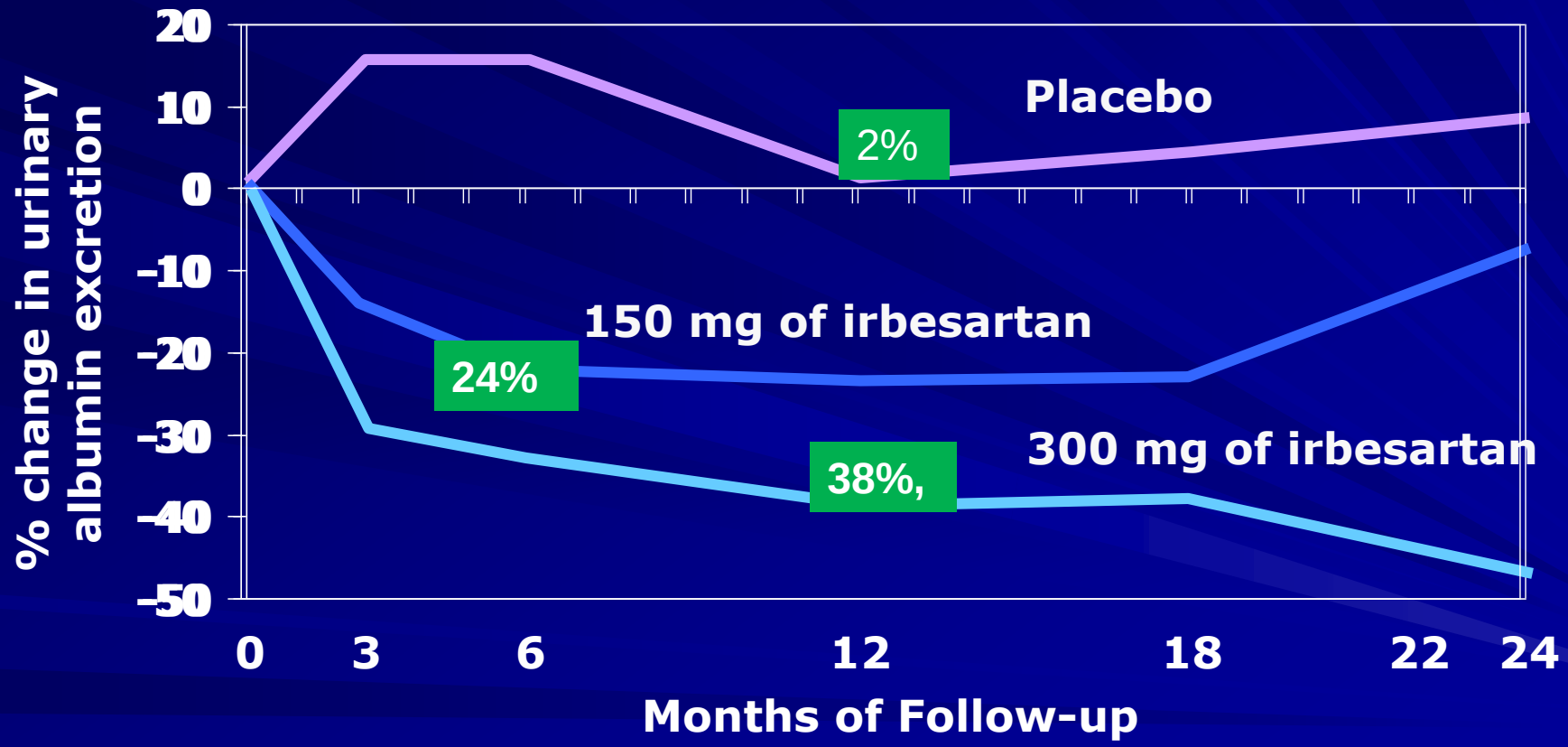
Primary endpoint: Time to overt proteinuria

(urinary albumin excretion rate [AER] > 200 μg/min, or 300 mg/day, and an increase of urinary AER from baseline by at least 30%),



Parving H-H *et al*. *N Engl J Med* 2001;**345:** 870–8.

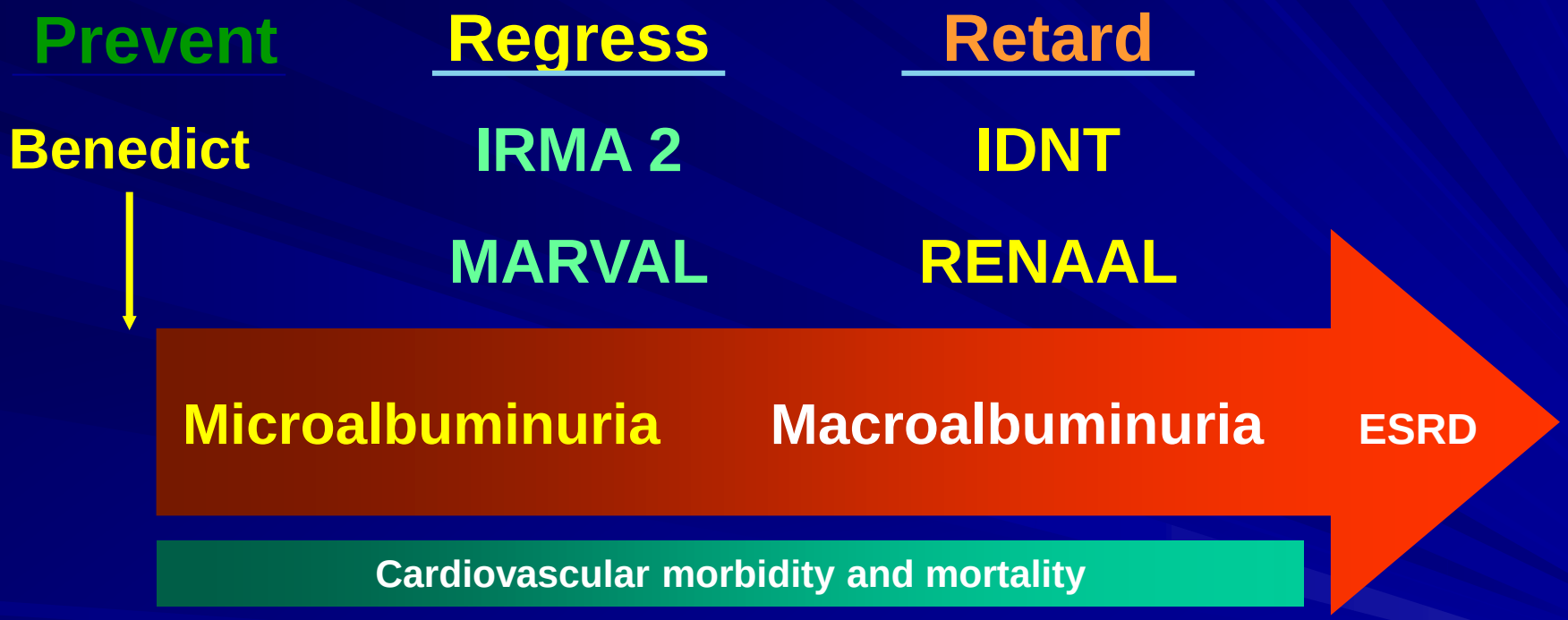
IRMA II Change in Urinary Albumin Excretion*



*P<0.001 for difference between both irbesartan groups and placebo

Parving HH, et al. N Engl J Med. 2001;345(12):870-878.

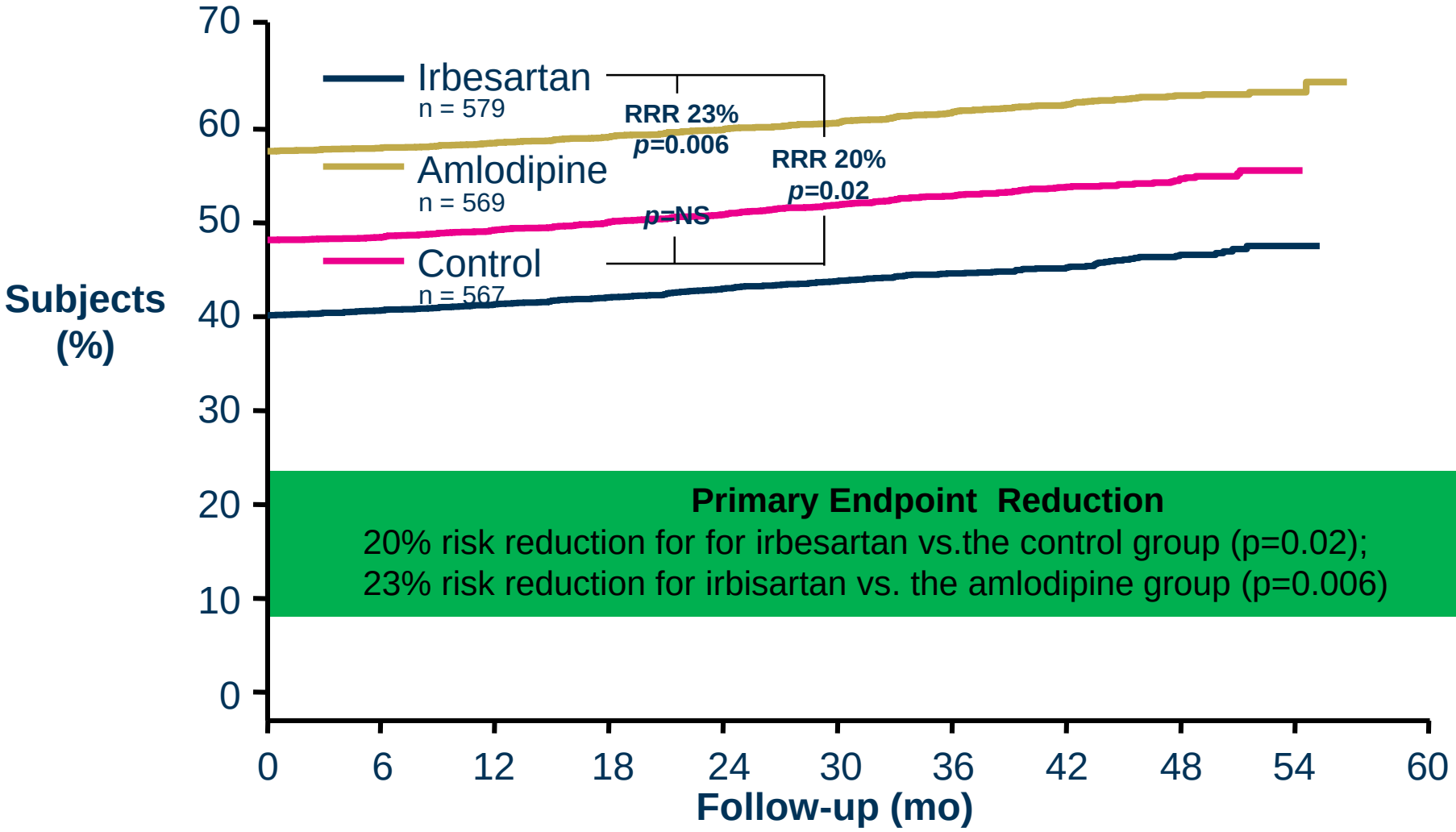
Renoprotection



Severity of renal disease

IDNT Results: Irbesartan Reduces the Progression of Diabetic Nephropathy (Combined Endpoint)

IDNT primary endpoint: Time to doubling of serum creatinine, ESRD, or death



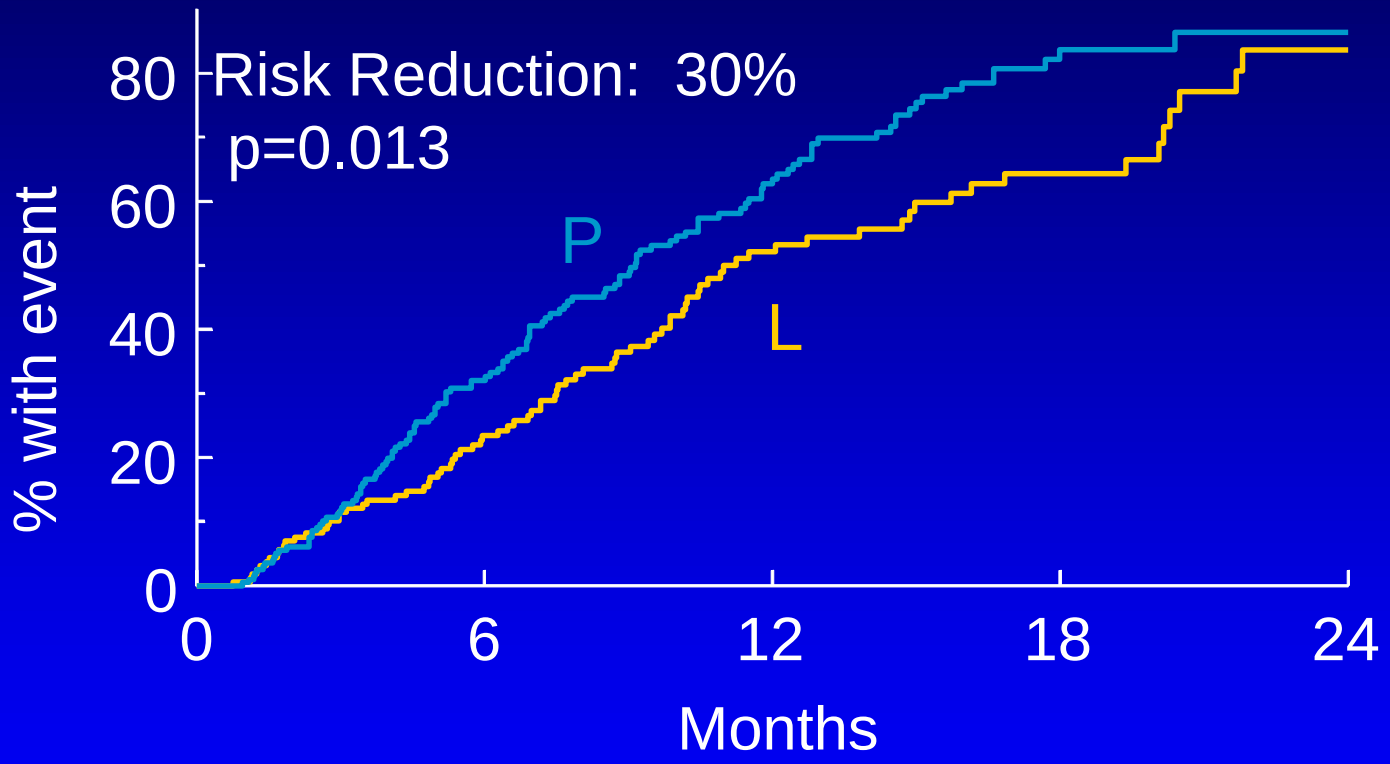
Primary Endpoint Reduction

20% risk reduction for for irbesartan vs.the control group (p=0.02);
23% risk reduction for irbisartan vs. the amlodipine group (p=0.006)

Lewis EJ, *et al*. *N Engl J Med* 2001;**345:** 851–60

RENAAL

Time to ESRD from Doubling of Serum Creatinine



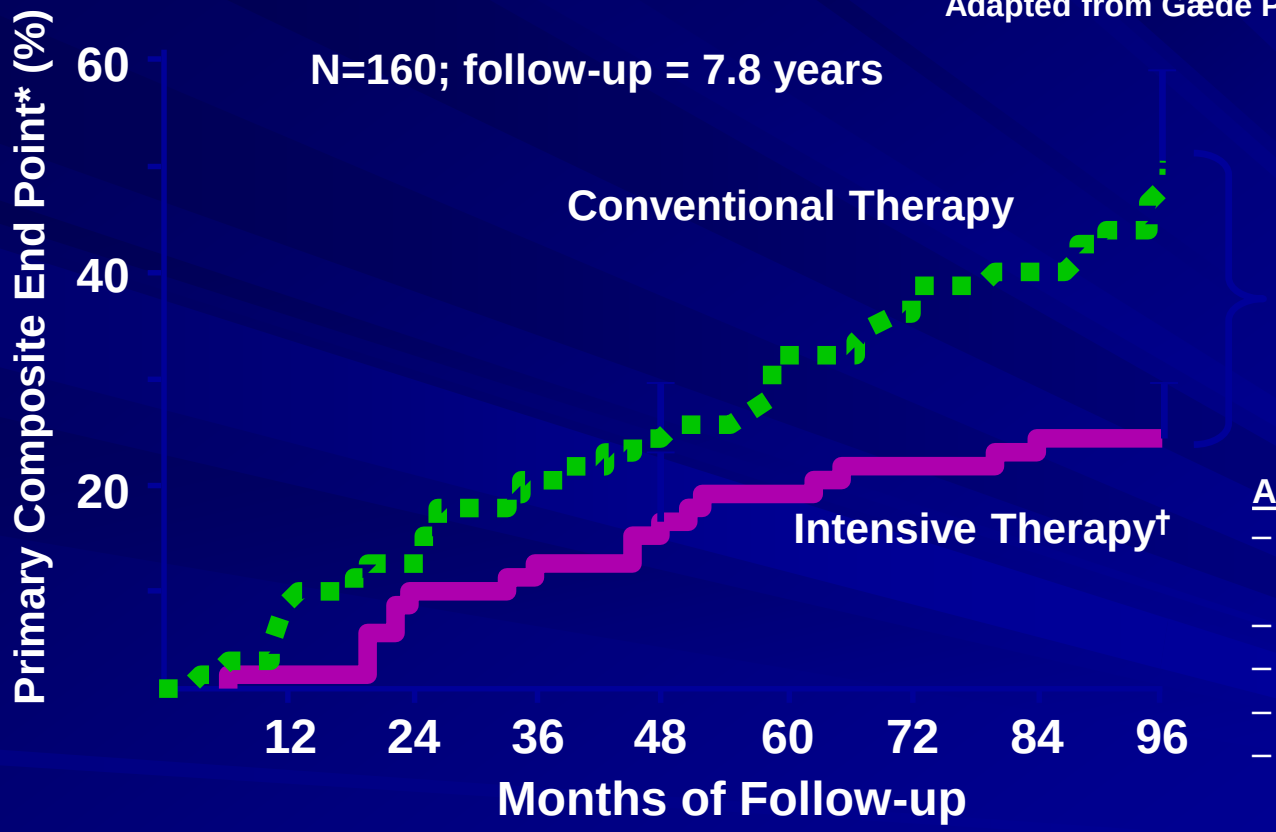
P (+CT)	198	111	48	11	4
L (+CT)	162	104	43	19	3

Presented by Brenner B. Reduction of endpoints in non-insulin-dependent diabetes mellitus with angiotensin II antagonist losartan. Program and abstracts of the 16th Annual Meeting of the American Society of Hypertension; May 16-19, 2001; San Francisco, California.

Intensive Multiple Risk Factor Management

Patients with Type 2 Diabetes and Microalbuminuria

Adapted from Gæde P et al. *N Eng J Med*. 2003;348:383-393



20% Absolute Risk Reduction

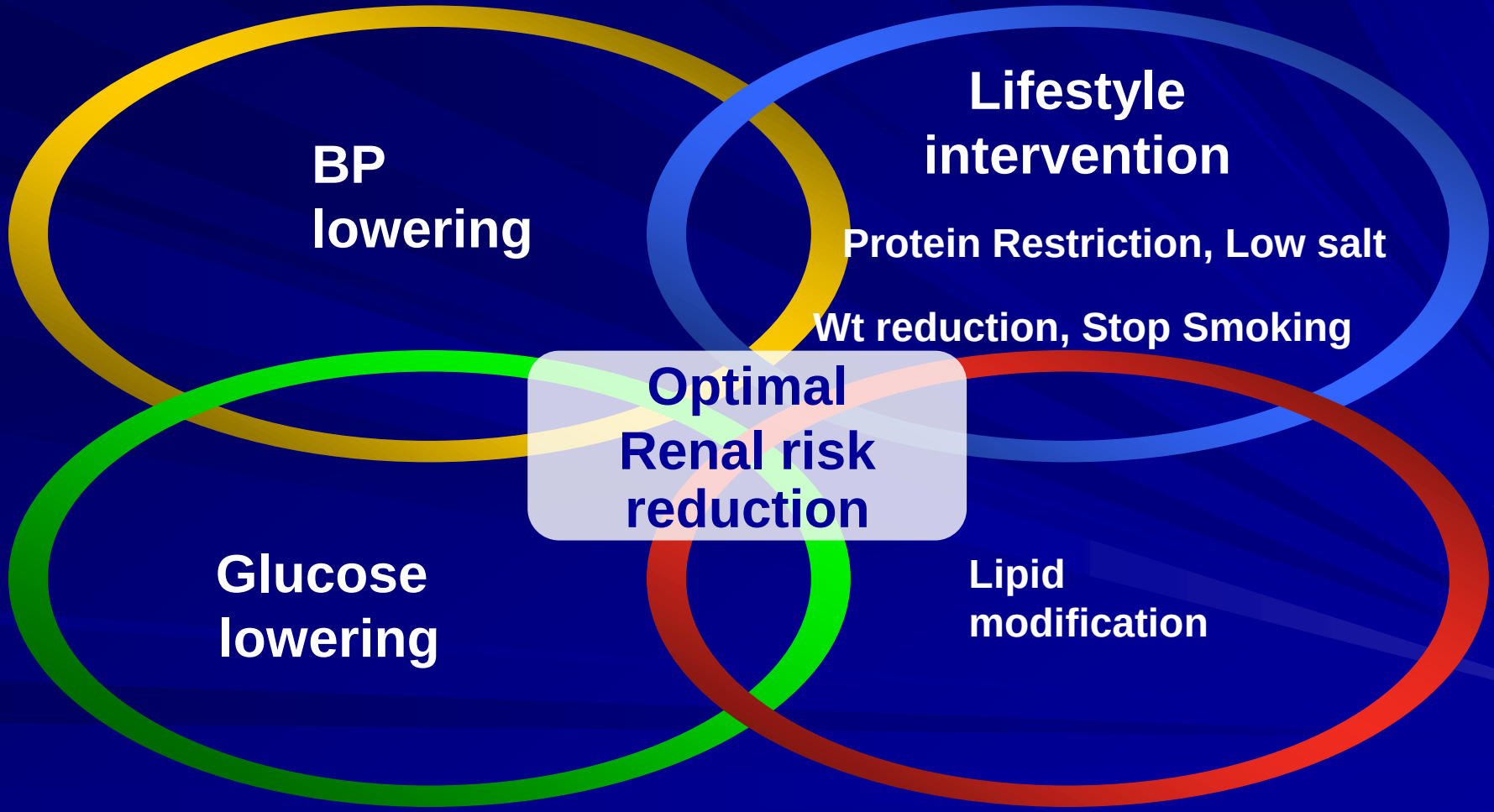
Aggressive treatment of†:
- Microalbuminuria with ACEIs, ARBs, or combination
- Hypertension
- Hyperglycemia
- Dyslipidemia
- Secondary prevention of CVD

Primary composite endpoint: conventional therapy (44%) and intensive therapy (24%).

*Death from CV causes, nonfatal myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, nonfatal stroke, amputation, or surgery for peripheral atherosclerotic artery disease.

†Behavior modification and pharmacologic therapy.

Benefit of Multifactorial Interventions



Conclusion

The message for World Kidney Day 2009

Hypertension and kidney disease:
a marriage that should be prevented.

Bakris GL, Ritz E : Kidney Int. 2009;75(5):449.


Thank You