

# Pathophysiology of Hypertension and Hypertension Management

Texas Hypertension Conference 2017

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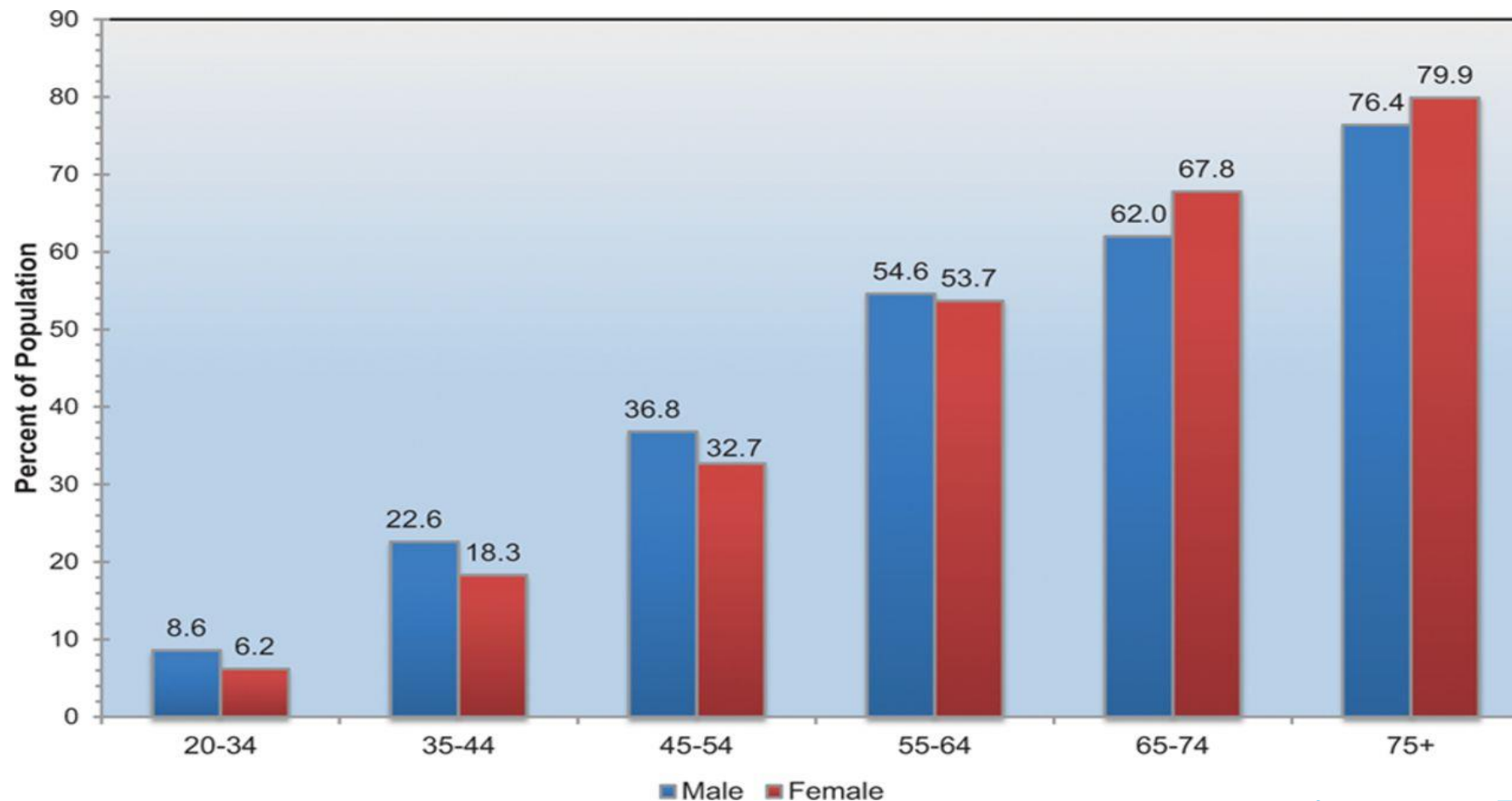
# Background

Epidemiology

Cost Burden

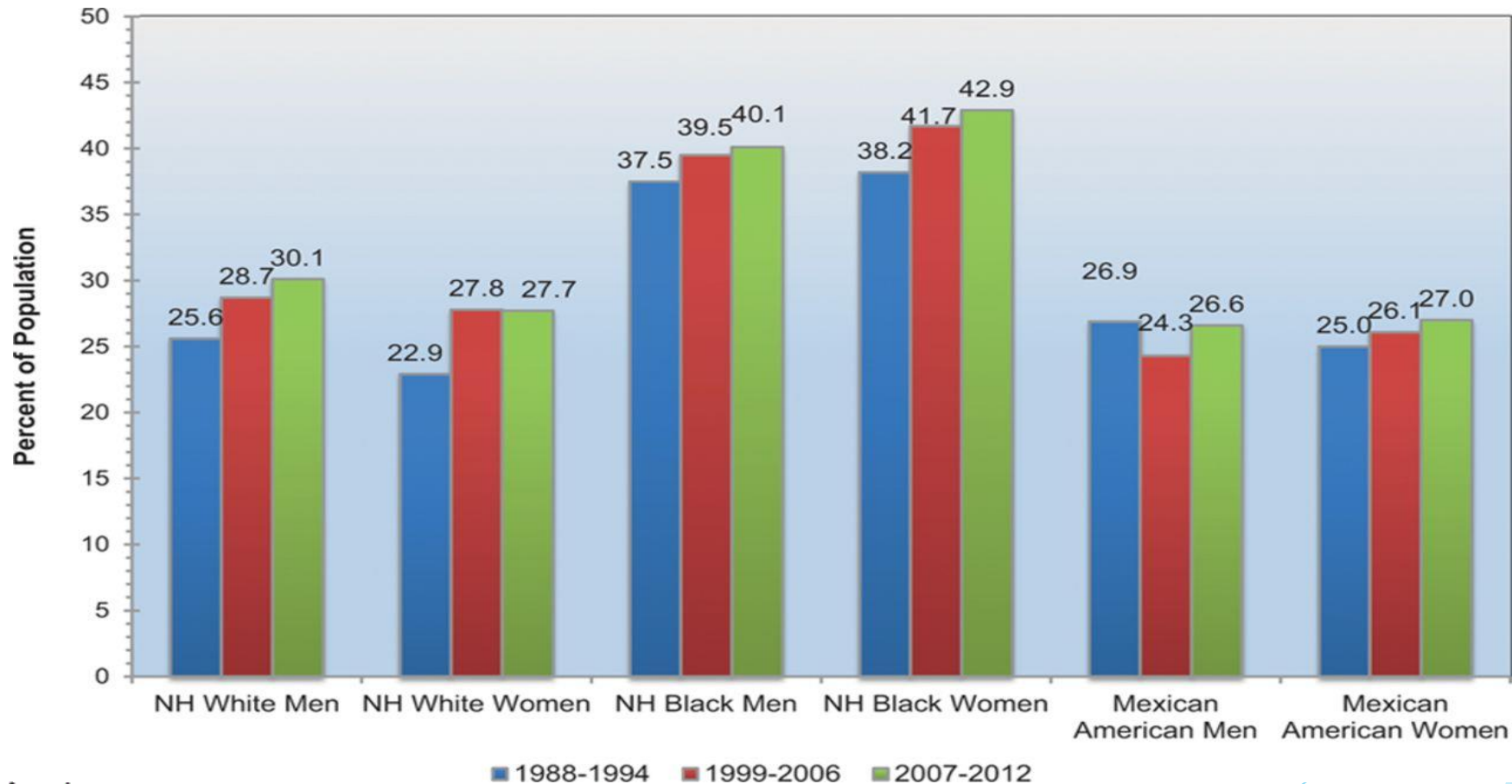
# High Blood Pressure Prevalence Adults $\geq 20$ Years Stratified by Age/Sex

National Health and Nutrition Examination Survey: 2007-2012



# Age-Adjusted Trends for High Blood Pressure Prevalence Adults $\geq 20$ years Stratified by Age/Race/Ethnicity/Sex

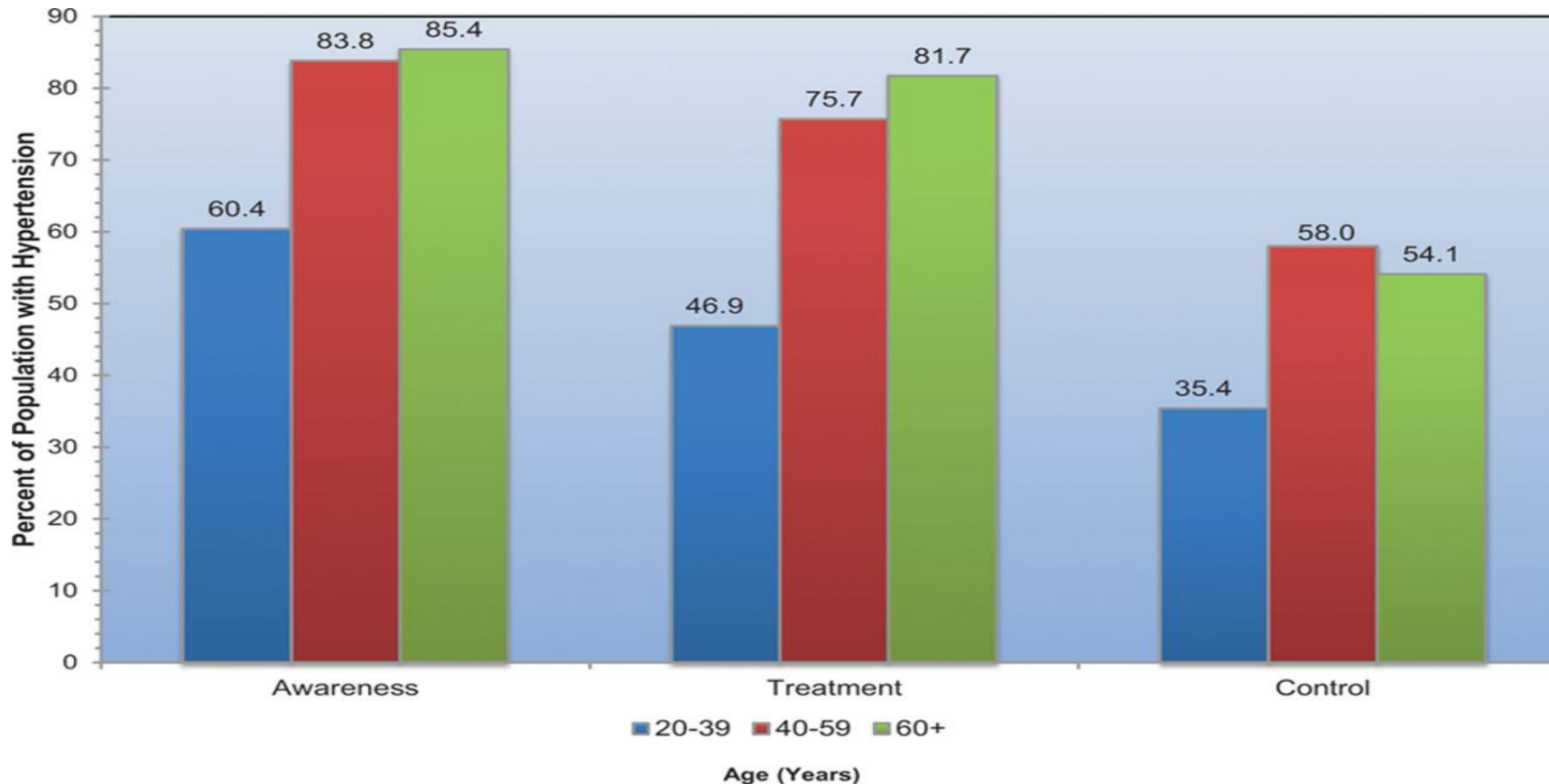
National Health and Nutrition Examination Survey: 1988-1994, 1999-2006, and 2007-2012



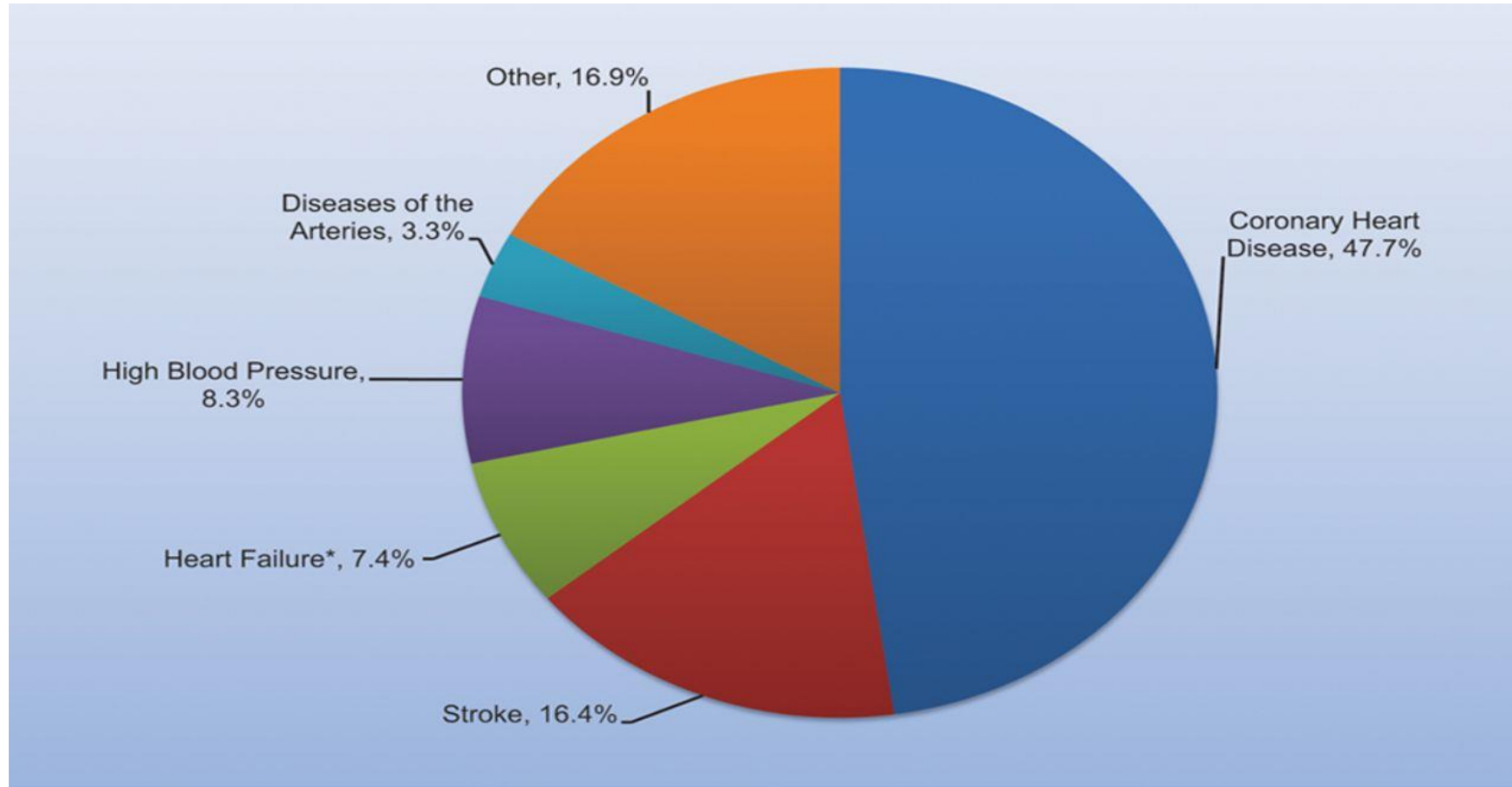
# High Blood Pressure Stratified by Age

## Awareness/Treatment/Control of Blood Pressure

National Health and Nutrition Examination Survey: 2007- 2012

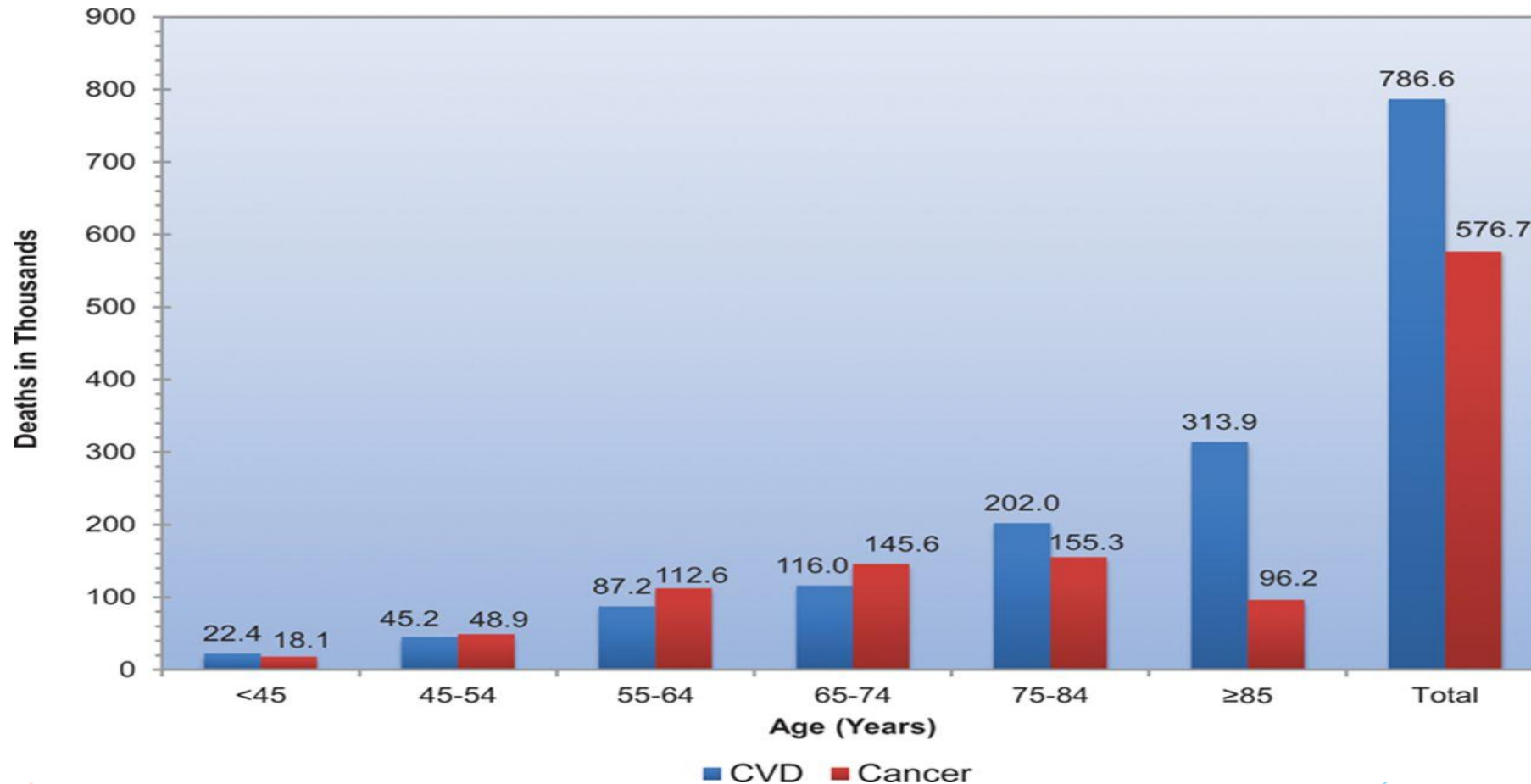


# Percentage Breakdown of Deaths Attributable to Cardiovascular Disease United States 2011



# Cardiovascular Disease (CVD) Deaths Versus Cancer Deaths by Age

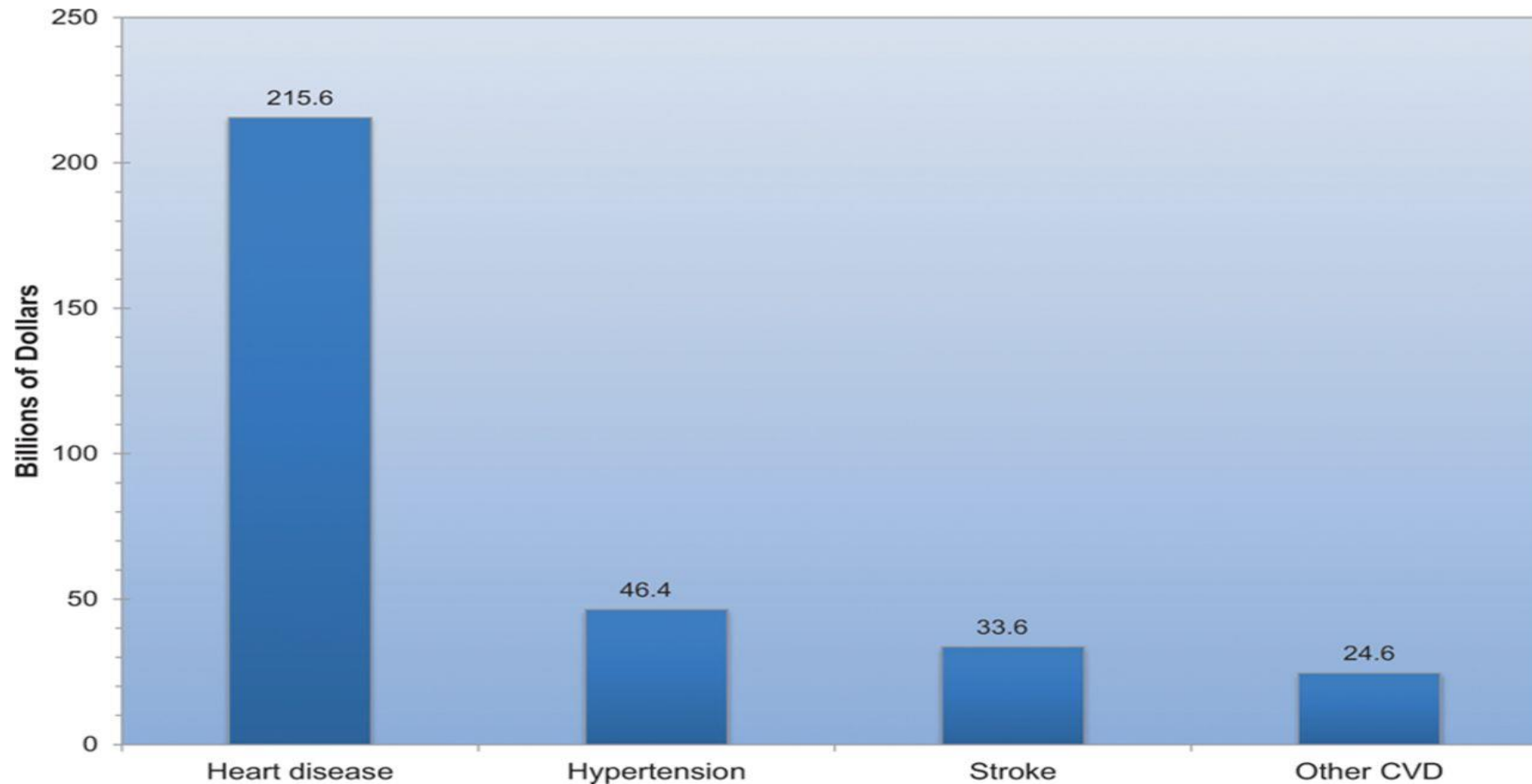
## United States 2011





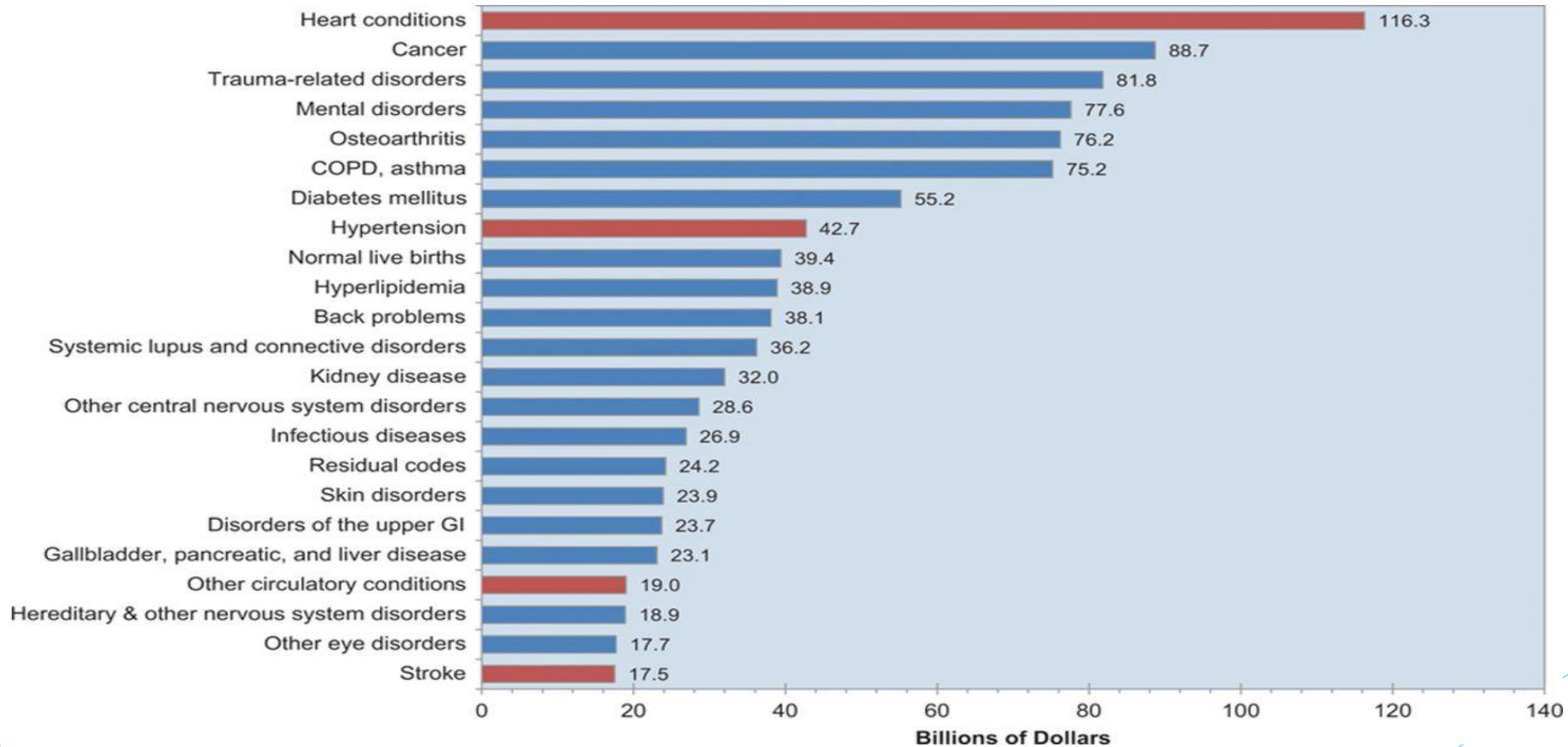
# Direct and Indirect Costs of Cardiovascular Disease (CVD) and Stroke *(in billions of dollars)*

## United States 2011



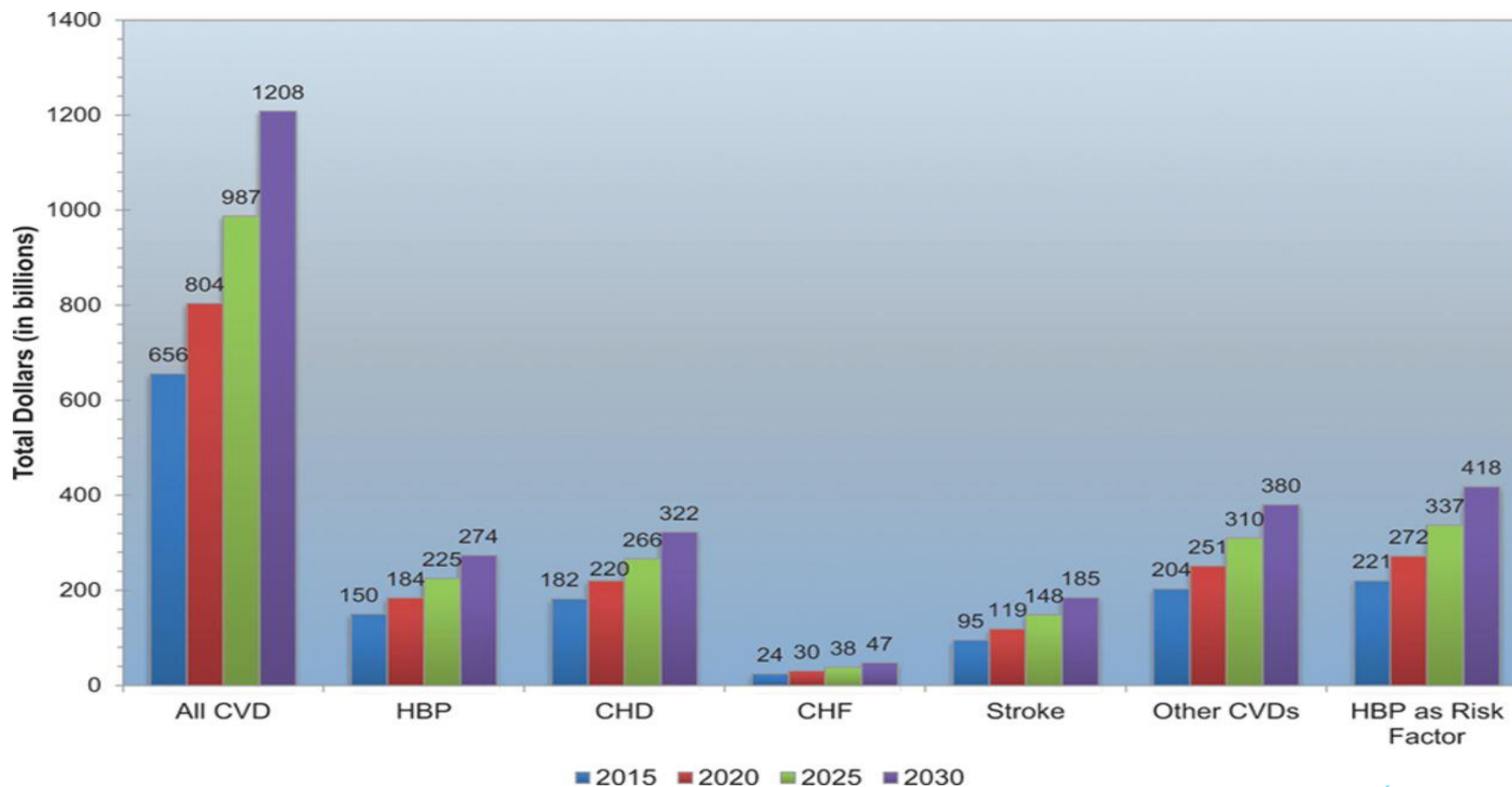
# The 23 Leading Diagnoses for Direct Health Expenditures *(in billions of dollars)*

## United States 2011



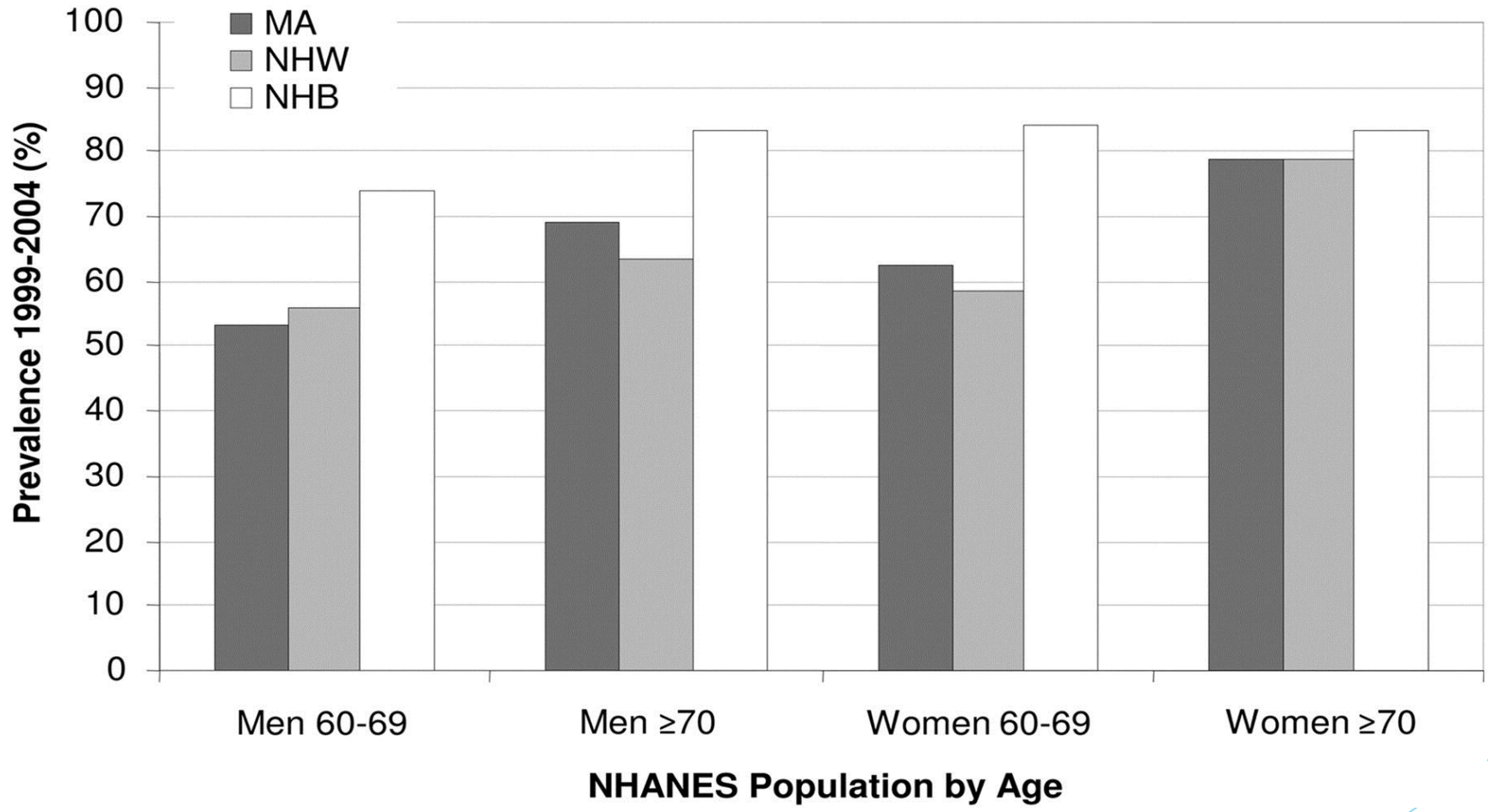
# Projected Total Costs of Cardiovascular Disease (CVD), 2015 to 2030 *(in billions of dollars)*

## United States 2012



# Age-Specific Prevalence of Hypertension in US Adults

NHANES 1999-2004



# Pathophysiology

Essential Hypertension

Secondary Hypertension

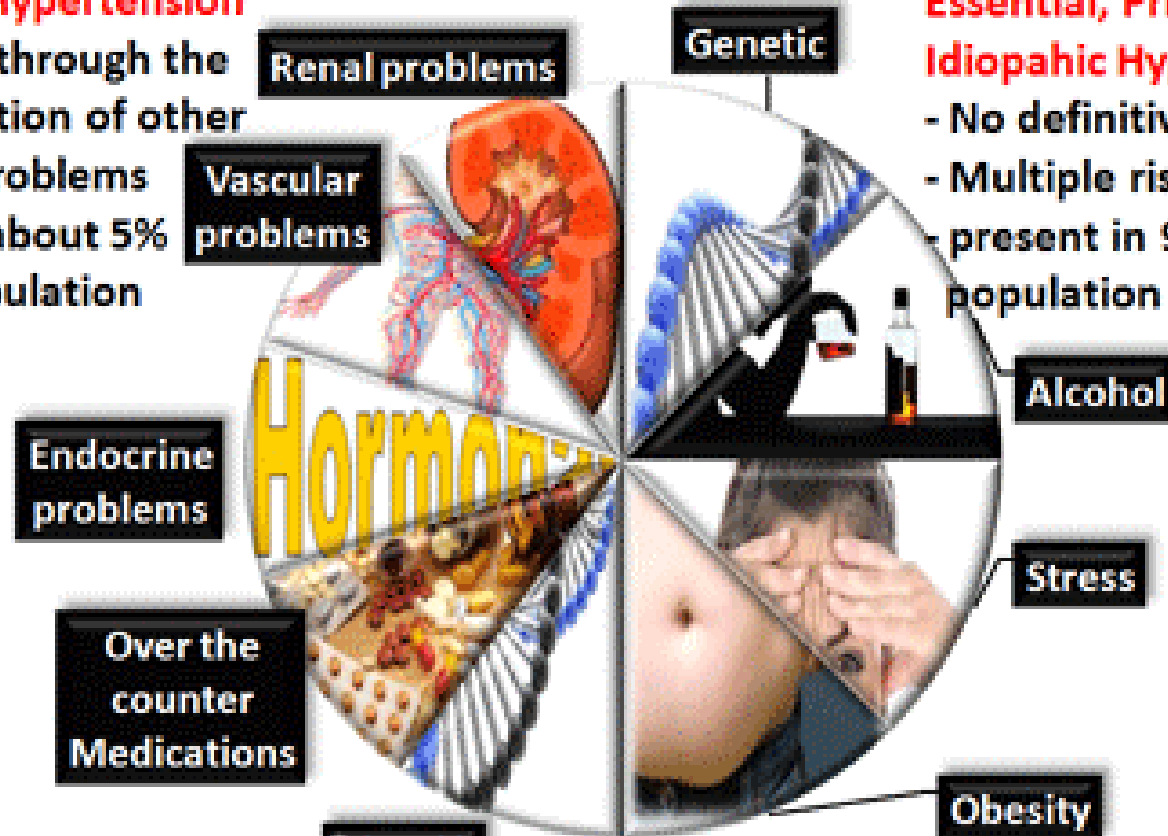
## Causes of Hypertension

### Secondary Hypertension

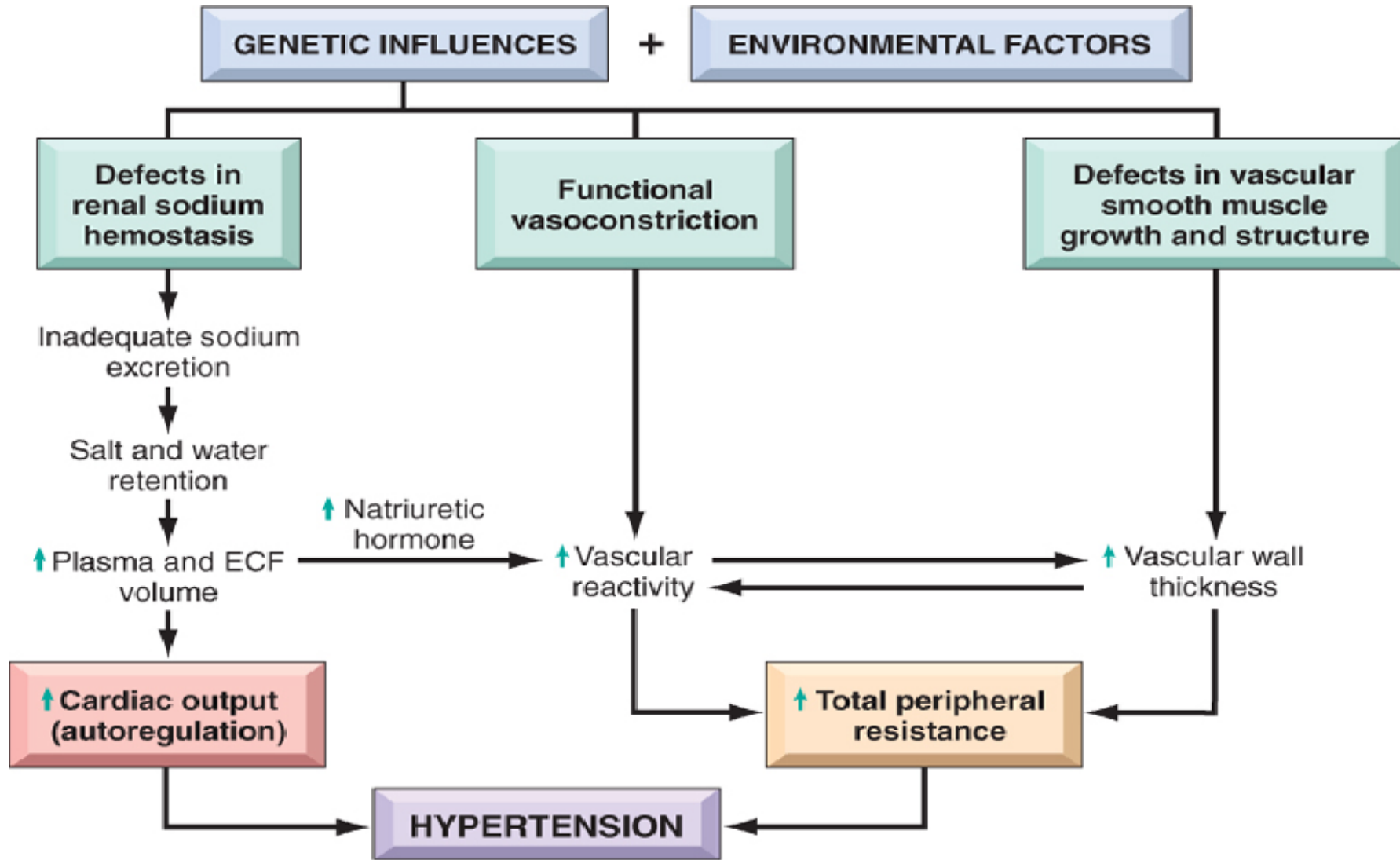
- Develops through the manifestation of other medical problems
- Occurs in about 5% of the population

### Essential, Primary or Idiopathic Hypertension

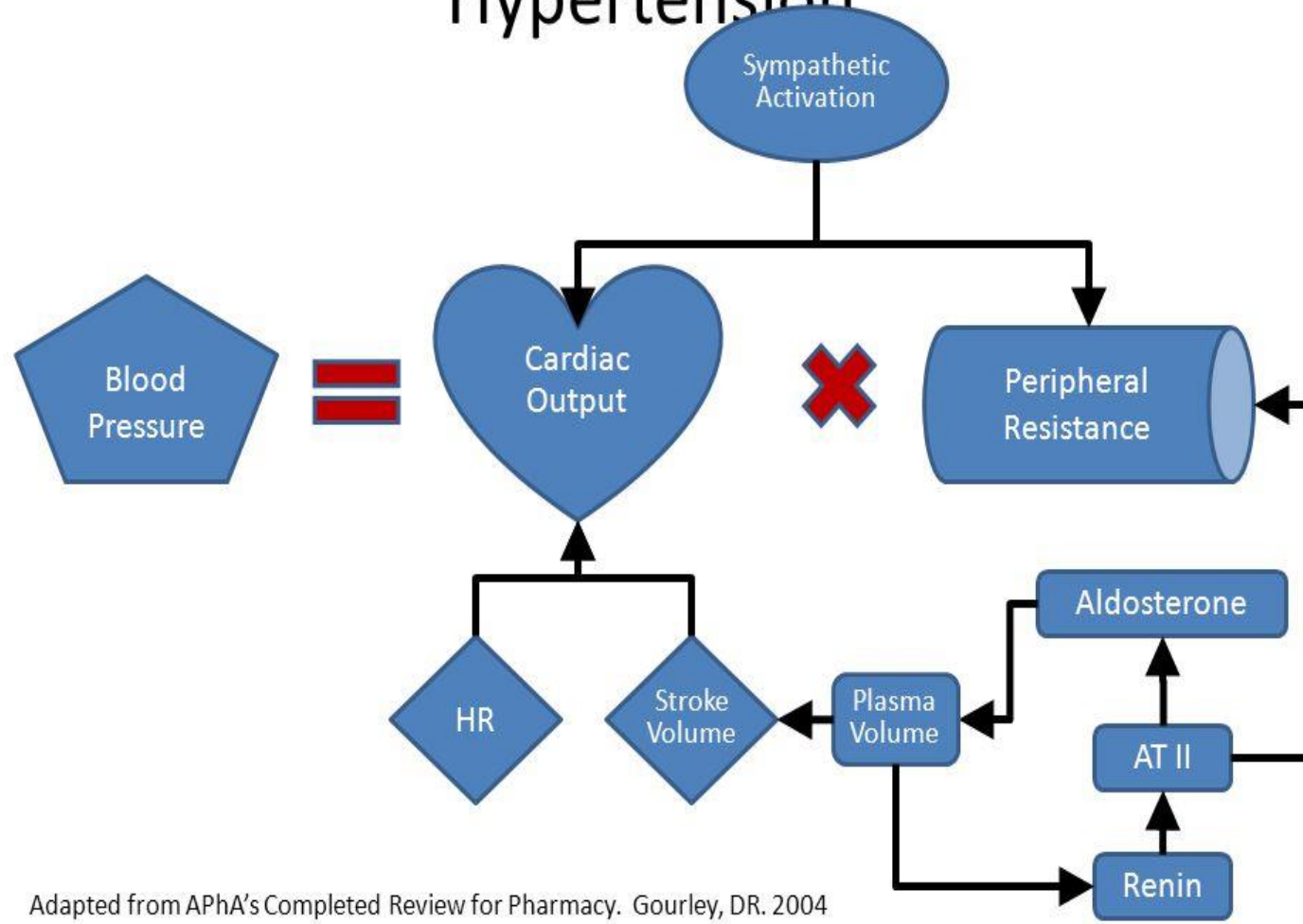
- No definitive causes
- Multiple risk factors present in 95% of the population



<http://papahealth.com/> Genetic

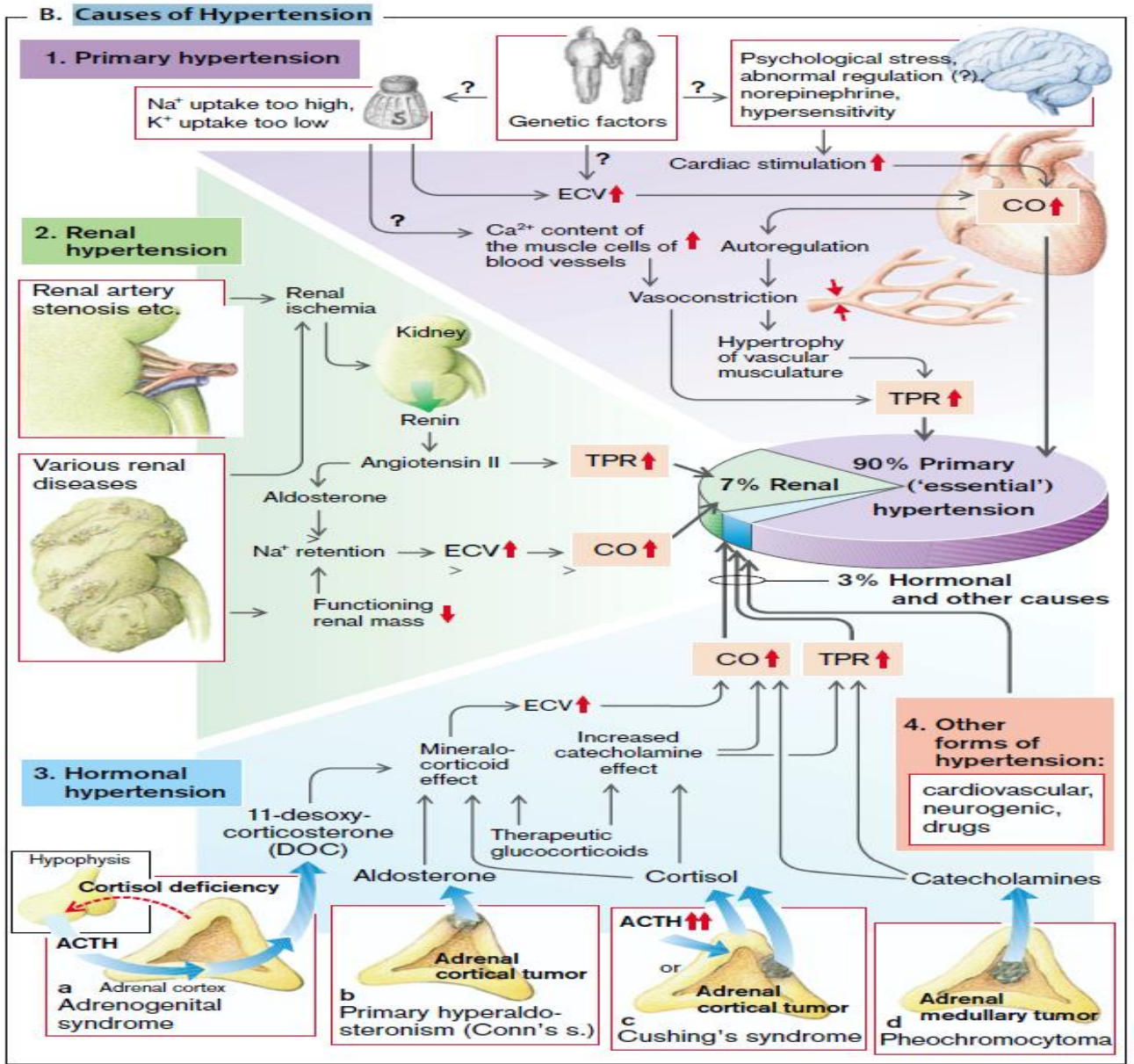


# Schematic of the Pathophysiology of Hypertension

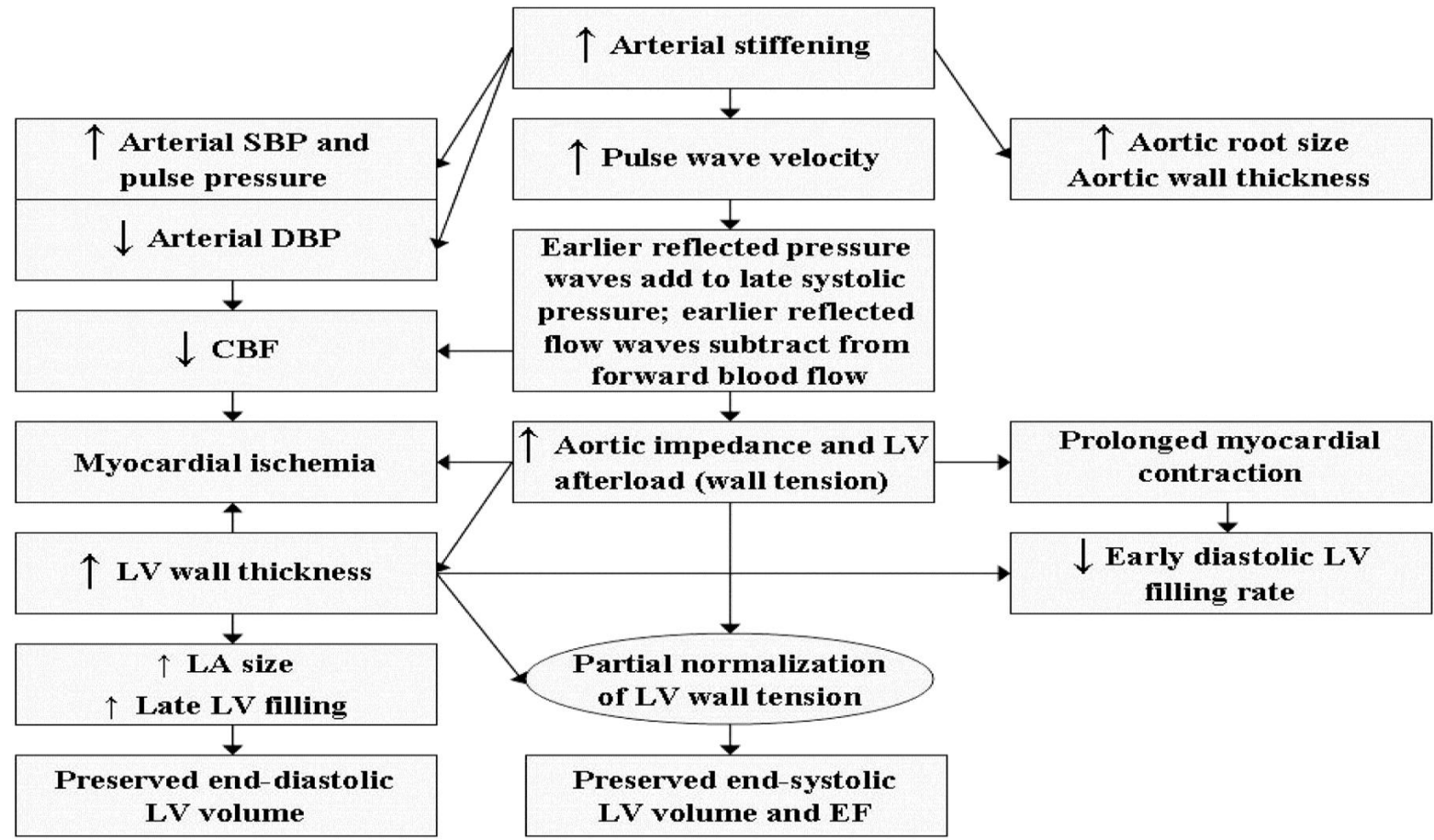


Adapted from APhA's Completed Review for Pharmacy. Gourley, DR. 2004

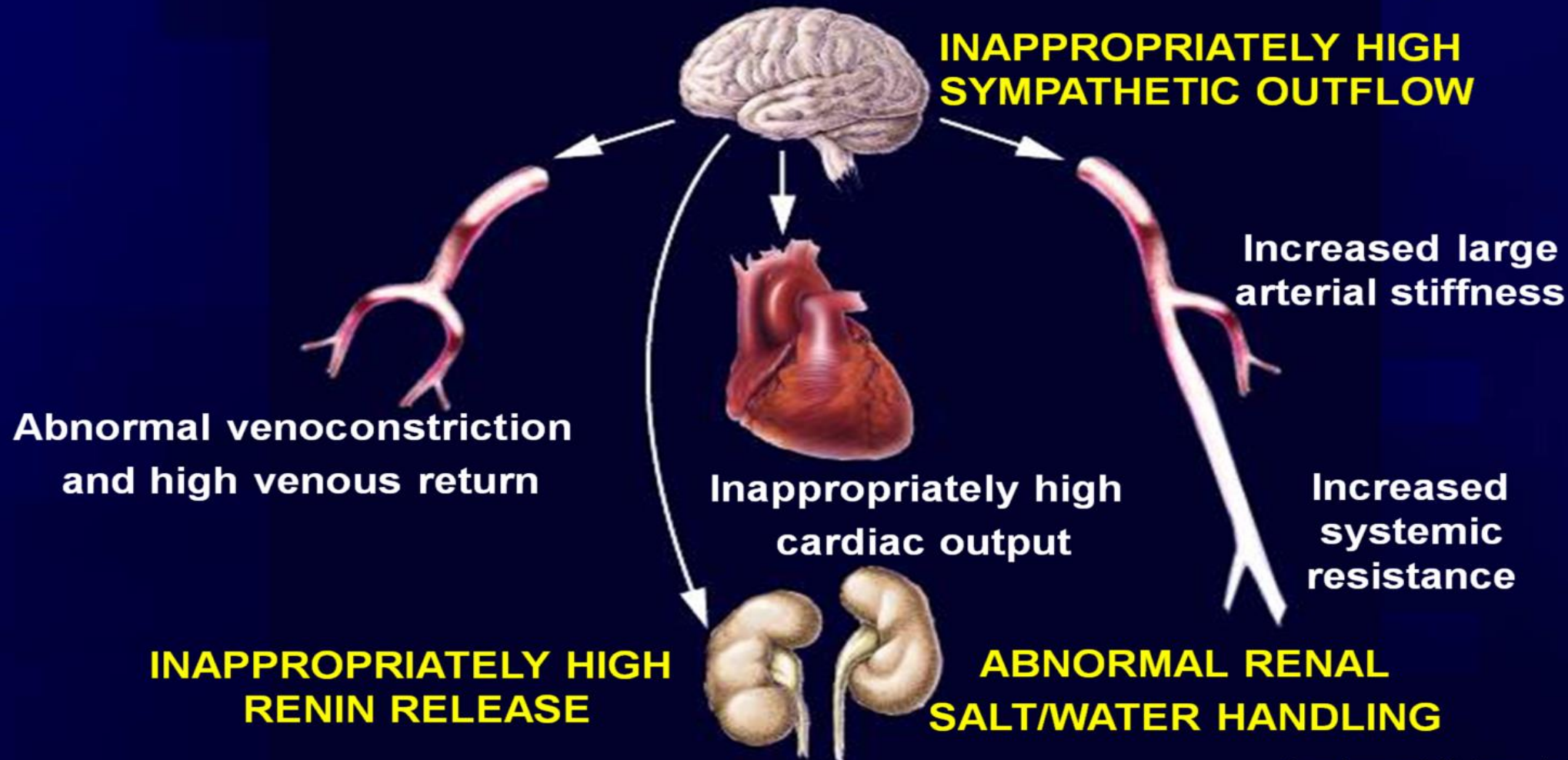




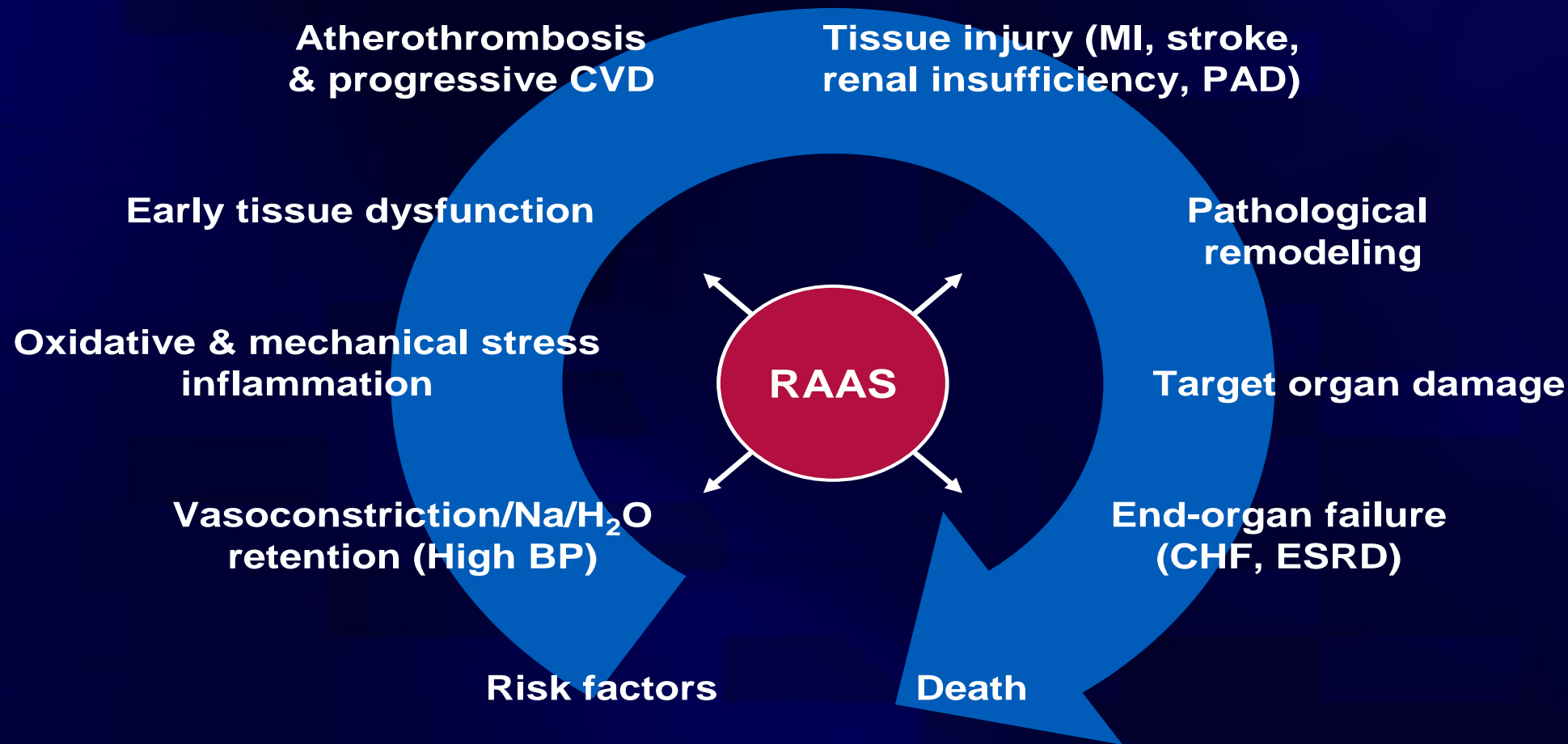
# Conceptual Framework for Cardiovascular Adaptations to Arterial Stiffening that Occur with Aging



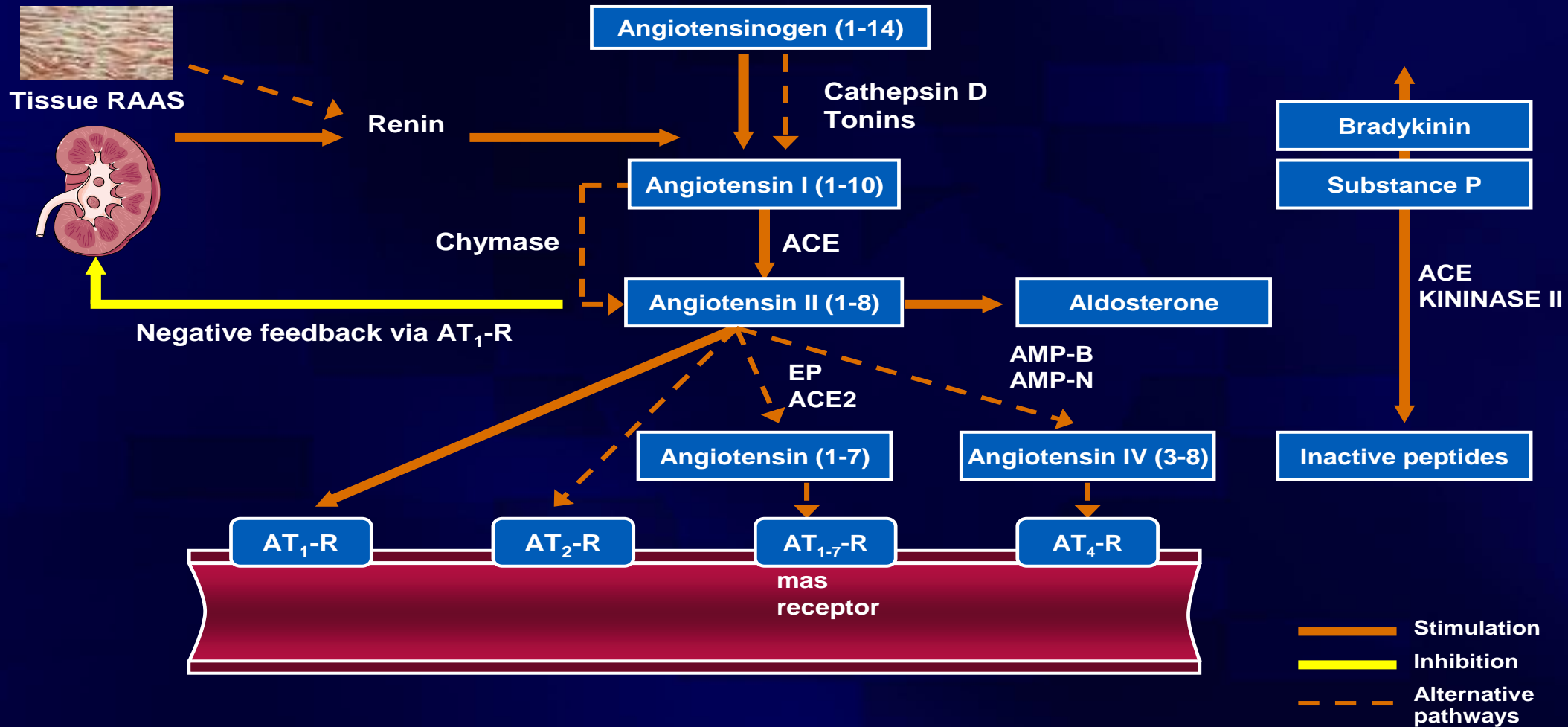
# Pathophysiology of hypertension



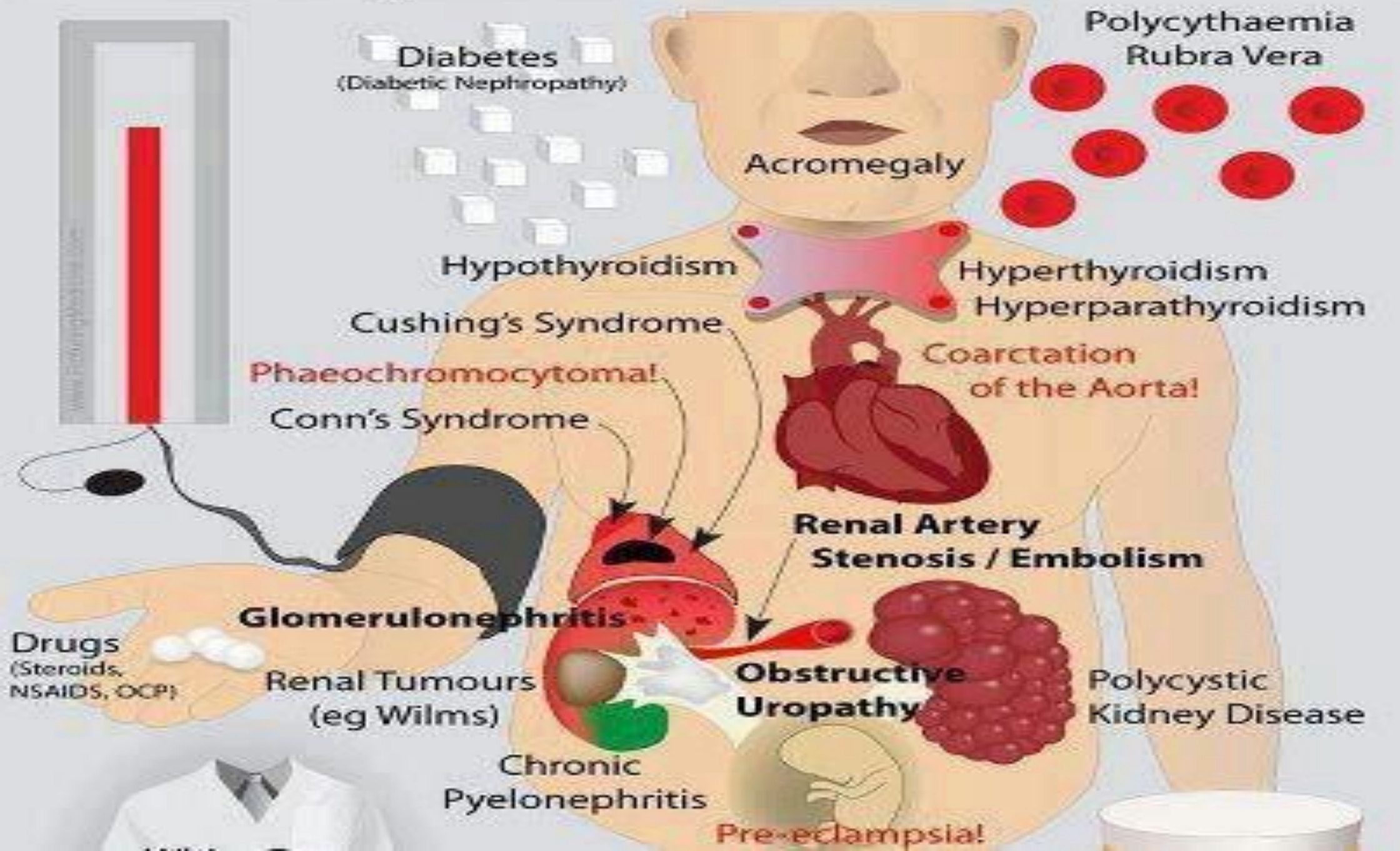
# CV and renal continuum: RAAS as a mediator of pathophysiology



# RAAS overview: Key targets

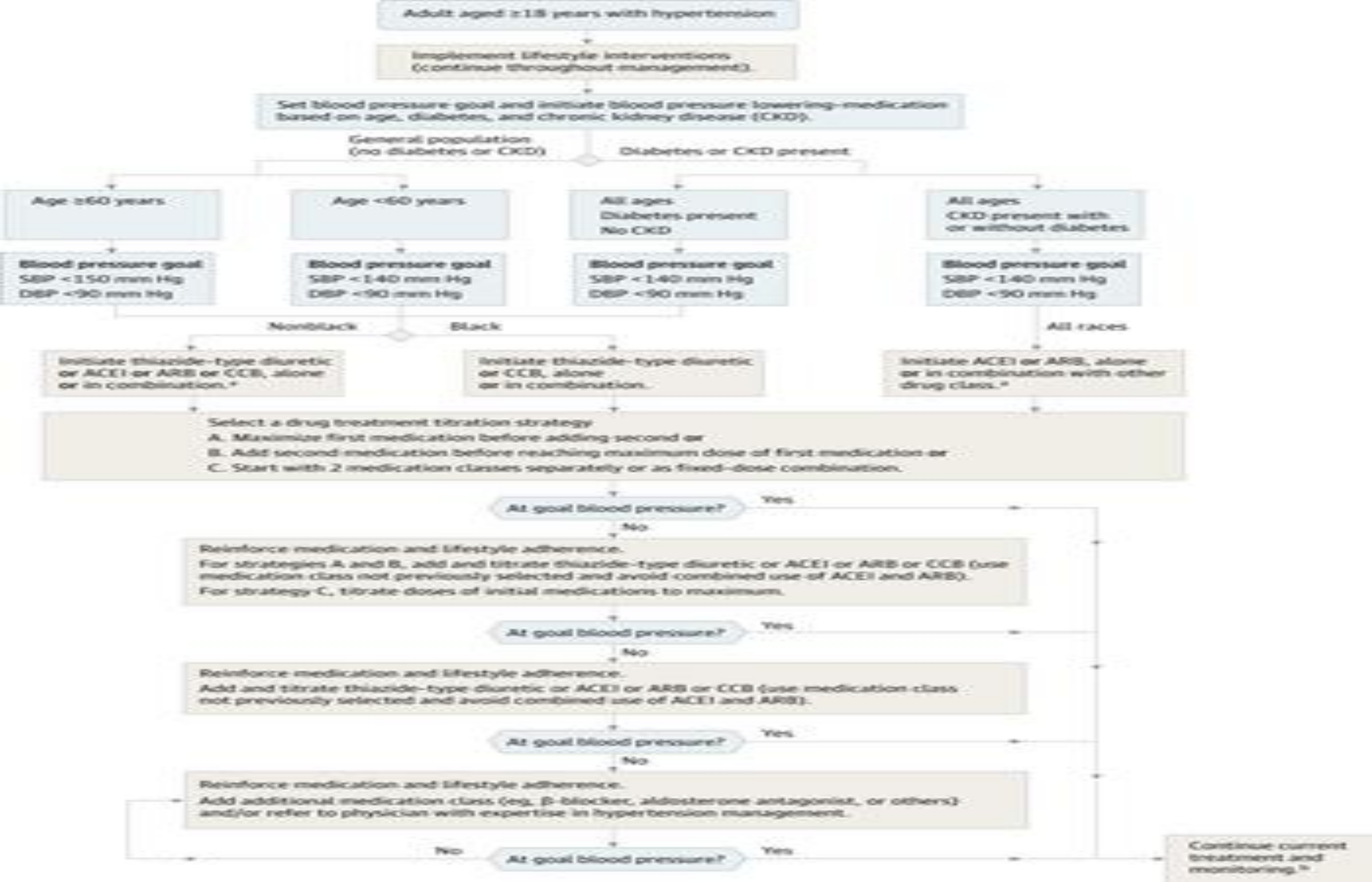


# The causes of Hypertension



# Treatment

Lifestyle Modification





**Blood Pressure  $\geq 140/90$  in Adults Aged  $>18$  years**  
(For age  $\geq 80$  years, pressure  $\geq 150/90$  or  $\geq 140/90$  if high risk [diabetes, kidney disease])

**Start Lifestyle Changes**  
(Lose weight, reduce dietary salt and alcohol, stop smoking)

**Drug Therapy**  
(Consider a delay in uncomplicated Stage 1 patients)\*

**Start Drug Therapy**  
(In all patients)

**Stage 1**  
140-159/90-99

**Stage 2**  
 $\geq 160/100$

**Special Cases**

**Black Patients**

**non-Black Patients**

**All Patients**

- Kidney disease
- Diabetes
- Coronary disease
- Stroke history
- Heart failure  
*[see table of recommended drugs for these conditions]*

CCB or Thiazide

Age  $<60$  Years

Age  $\geq 60$  Years

Start With 2 Drugs

If Needed, Add ...

ACE-i or ARB

CCB or Thiazide

CCB or Thiazide + ACE-i or ARB

ACE-i or ARB OR combine CCB+Thiazide

If Needed, Add ...

If Needed, Add ...

If Needed ...

If Needed ...

CCB or Thiazide

ACE-i or ARB

If Needed ...

If Needed ...

If Needed ...

CCB+Thiazide+ACE-i (or ARB)

CCB+Thiazide+ACE-i (or ARB)

CCB+Thiazide+ACE-i (or ARB)

If Needed, add other drugs e.g. spironolactone; centrally acting agents;  $\beta$ -blockers

If Needed, Refer to a Hypertension Specialist

\* In stage 1 patients without other cardiovascular risk factors or abnormal findings, some months of regularly monitored lifestyle management without drugs can be considered.



**Exercise and maintenance of a healthy weight**

**Lifestyle changes and/or medication may reduce high blood pressure to healthy levels:**

**Medications such as diuretics, beta-blockers, potassium replacements, calcium channel blockers and ACE inhibitors**

**A healthy, low sodium (salt) diet rich in natural sources of potassium, calcium, and fiber**



**ADAM.**

# RAAS Blockade With ARBs Can Be Considered a Foundation of Antihypertensive Therapy



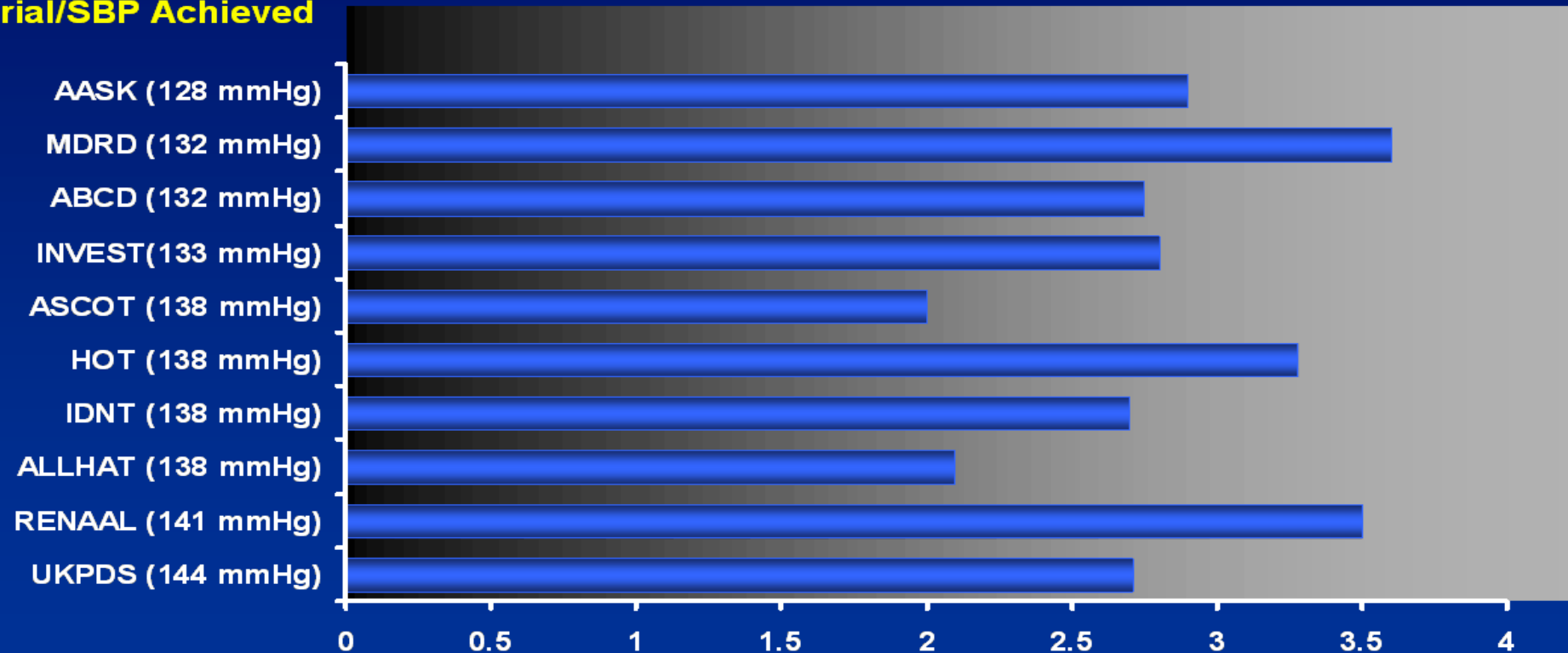
## ARB Foundation

ARB=angiotensin receptor blocker; BP=blood pressure; CCB=calcium channel blocker; RAAS=renin-angiotensin-aldosterone system.

# BP Control Usually Requires Combination Therapy

Most patients require  $\geq 2$  antihypertensives to reach BP goal

## Trial/SBP Achieved



**BP=**blood pressure; **SBP=**systolic blood pressure.

1. Copley JB et al. *Dis Mon.* 2005;51:548–614.
2. Dahlof B et al. *Lancet.* 2005;366:895–906.

# Special Populations

Treatment of Hypertension in Patients With Coronary Artery Disease

# Summary of BP Goals

BP Goal, mm Hg	Condition	Class/Level of Evidence
<140/90	CAD	IIa/B
	ACS	IIa/C
	HF	IIa/B
<130/80	CAD	IIb/B
	Post-myocardial infarction, stroke or TIA, carotid artery disease, PAD, AAA	IIb/B

Abdominal Aortic Aneurysm(AAA)  
Blood Pressure (BP)  
Heart Failure (HF)  
Ischemic Attack (TIA)

Acute Coronary Syndrome (ASC)  
Coronary Artery Disease (CAD)  
Peripheral Arterial Disease (PAD)

Transient

# Pharmacological Treatment of Hypertension in the Management of Ischemic Heart Disease

	ACEI or ARB	Diuretic	β-Blocker	Non-DHP CCB	DHP CCB	Nitrat es	Aldosteron e Antagonist	Hydralazine/ Isosorbide Dinitrate
Stable Angina	1*	1†	1	2‡	2	1	2	
ACS	1*	1†	1§	2‡	2	2	2	
HF	1	1†	1¶			2	1	2

ACEI indicates angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DHP, dihydropyridine; HF, heart failure; 1, drug of choice; and 2, “add-on,” alternative drug, or special indications.

\* Especially if prior myocardial infarction, left ventricular systolic dysfunction, diabetes mellitus, or proteinuric chronic kidney disease is present.

† Chlorthalidone is preferred. Loop diuretic should be used in the presence of HF (New York Heart Association class III or IV) or chronic kidney disease with glomerular filtration rate  $<30 \text{ mL} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ . Caution should be exercised in HF with preserved ejection fraction.

‡ If β-blocker is contraindicated, a non-DHP CCB can be substituted, but not if left ventricular dysfunction or HF is present. Caution should be exercised if combining a non-DHP CCB with a β-blocker

# Recommendations:

- The <140/90-mm Hg BP target is reasonable for the secondary prevention of cardiovascular events in patients with hypertension and CAD (Class IIa; Level of Evidence B).
- A lower target BP (<130/80 mm Hg) may be appropriate in some individuals with CAD, previous MI, stroke or transient ischemic attack, or CAD risk equivalents (carotid artery disease, PAD, abdominal aortic aneurysm) (Class IIb; Level of Evidence B).
- In patients with an elevated DBP and CAD with evidence of myocardial ischemia, the BP should be lowered slowly, and caution is advised in inducing decreases in DBP to <60 mm Hg in any patient with diabetes mellitus or who is >60 years of age. In older hypertensive individuals with wide pulse pressures, lowering SBP may cause very low DBP values (<60 mm Hg). This should alert the clinician to assess carefully any untoward signs or symptoms, especially those resulting from myocardial ischemia (Class IIa; Level of Evidence C).



# Special Populations

**Treatment of Hypertension in Patients With Heart Failure**

# Recommendation for Prevention

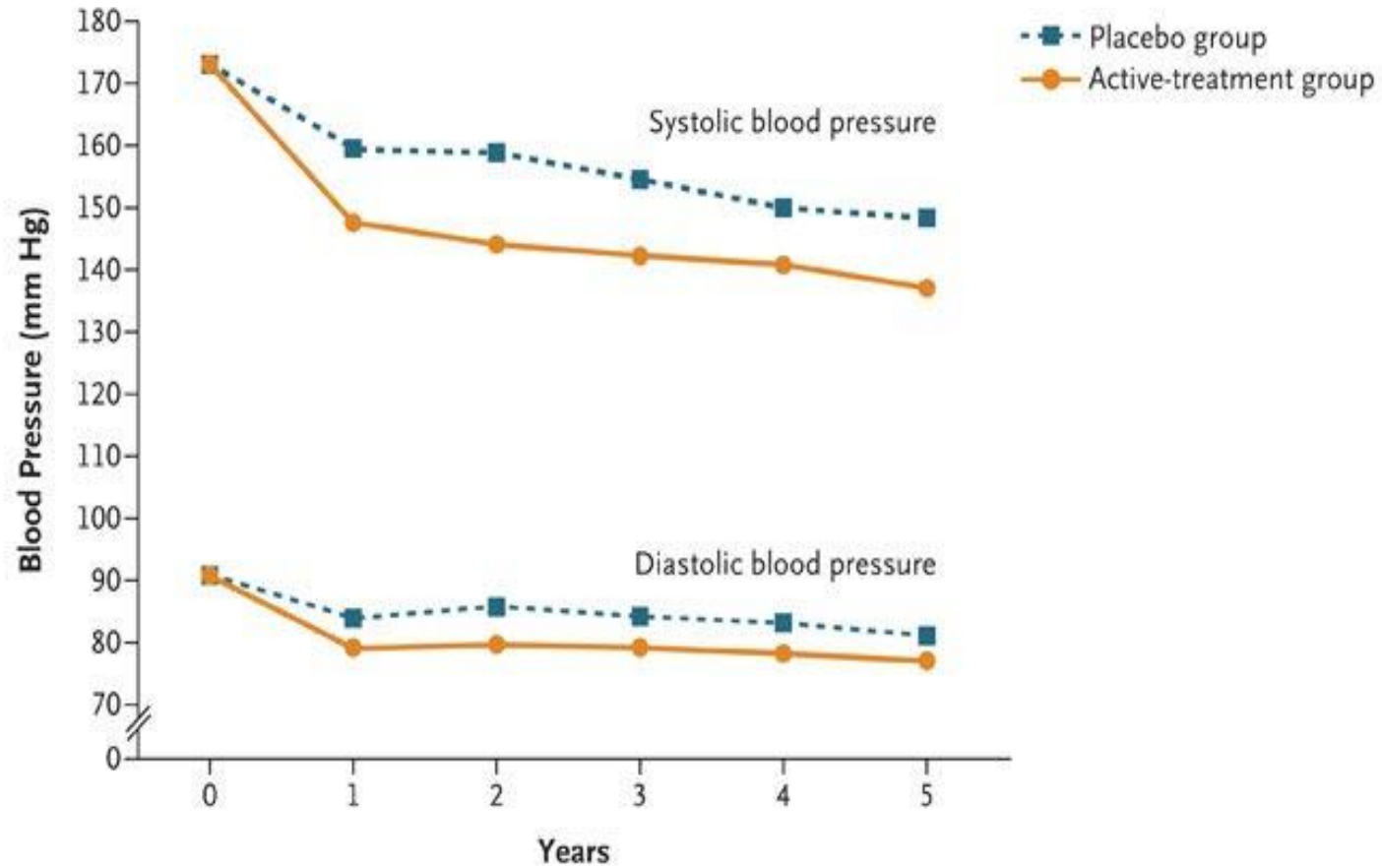
COR	LOE	Recommendations	Comment/Rationale
I	B-R	In patients at increased risk, stage A HF, the optimal blood pressure in those with hypertension should be less than 130/80 mm Hg. <sup>189-193</sup>	<b>NEW:</b> Recommendation reflects new RCT data.
See Online Data Supplements E and F.			
<p>A large RCT demonstrated that in those with increased cardiovascular risk (defined as age &gt;75 years, established vascular disease, chronic renal disease, or a Framingham Risk Score &gt;15%), control of blood pressure to a goal systolic pressure of &lt;120 mm Hg, as determined by blood pressure assessment as per research protocol, was associated with a significant reduction in the incidence of HF<sup>191</sup> and an overall decrease in cardiovascular death. Blood pressure measurements as generally taken in the office setting are typically 5 to 10 mm Hg higher than research measurements; thus, the goal of &lt;130/80 mm Hg is an approximation of the target blood pressure in conventional practice. <i>Targeting a significant reduction in systolic blood pressure in those at increased risk for cardiovascular disease is a novel strategy to prevent HF.</i></p>			

# Recommendation for Hypertension in Stage HFrEF

COR	LOE	Recommendation	Comment/Rationale
I	C-EO	Patients with HFrEF and hypertension should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg. <sup>191</sup>	<b>NEW:</b> Recommendation has been adapted from recent clinical trial data but not specifically tested per se in a randomized trial of patients with HF.
See Online Data Supplements E and F.			
<p>Clinical trials evaluating goal blood pressure reduction and optimal blood pressure–lowering agents in the setting of HFrEF and concomitant hypertension have not been done. However, it is apparent that in those patients at higher risk, blood pressure lowering is associated with fewer adverse cardiovascular events. GDMT for HFrEF with agents known to lower blood pressure should consider a goal blood pressure reduction consistent with a threshold now associated with improved clinical outcomes but not yet proven by RCTs in a population with HF.</p>			

# Recommendation for Hypertension in Stage HFpEF

COR	LOE	Recommendation	Comment/Rationale
I	C-LD	Patients with HFpEF and persistent hypertension after management of volume overload should be prescribed GDMT titrated to attain systolic blood pressure less than 130 mm Hg. <sup>9,167,169,170,195-199</sup>	<b>NEW:</b> New target goal blood pressure based on updated interpretation of recent clinical trial data.
See Online Data Supplements E and F.		<p>The use of nitrates in the setting of HFpEF is associated with a signal of harm and, in most situations, should be avoided. For many common antihypertensive agents, including alpha blockers, beta blockers, and calcium channel blockers, there are limited data to guide the choice of antihypertensive therapy in the setting of HFpEF.<sup>172</sup> Nevertheless, RAAS inhibition with ACE inhibitor, ARB (especially mineralocorticoid receptor antagonists), and possibly ARNI would represent the preferred choice. A shared decision-making discussion with the patient influenced by physician judgment should drive the ultimate choice of antihypertensive agents.</p>	

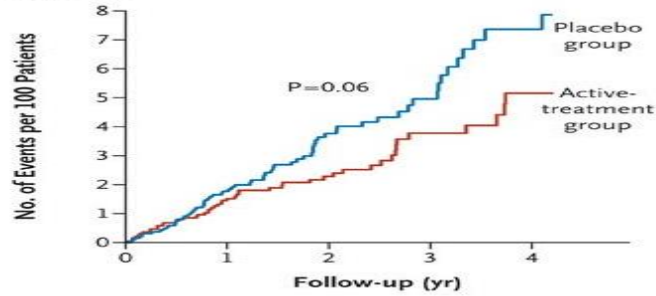


**No. at Risk**

Placebo group	1912	1468	701	330	191	116
Active-treatment group	1933	1540	754	373	207	118

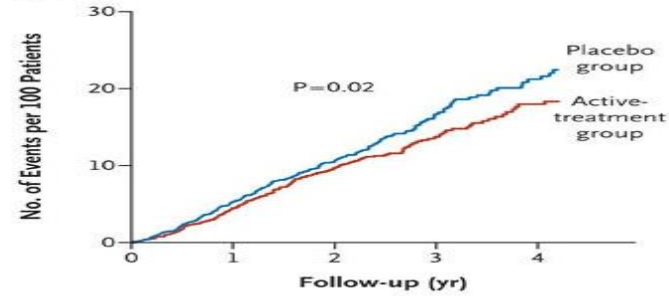


**A Fatal or Nonfatal Stroke**



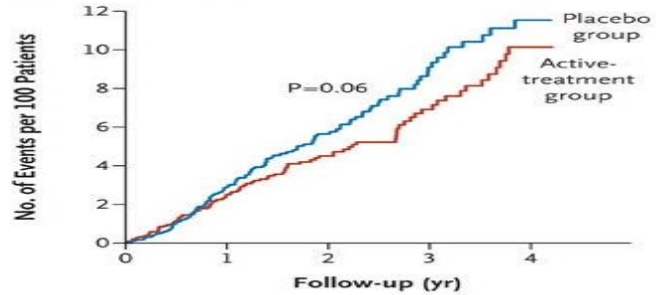
No. at Risk		0	1	2	3	4
Placebo group	1912	1484	807	374	194	
Active-treatment group	1933	1557	873	417	229	

**B Death from Any Cause**



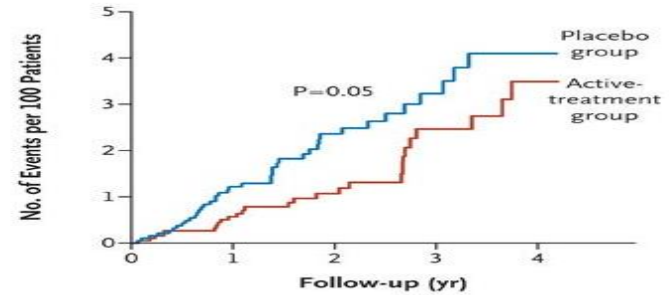
No. at Risk		0	1	2	3	4
Placebo group	1912	1492	814	379	202	
Active-treatment group	1933	1565	877	420	231	

**C Death from Cardiovascular Causes**



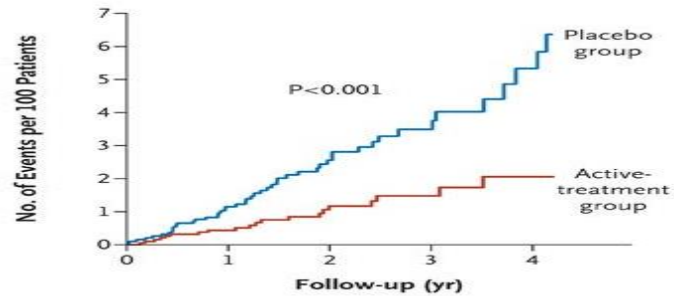
No. at Risk		0	1	2	3	4
Placebo group	1912	1492	814	379	202	
Active-treatment group	1933	1565	877	420	231	

**D Death from Stroke**



No. at Risk		0	1	2	3	4
Placebo group	1912	1492	814	379	202	
Active-treatment group	1933	1565	877	420	231	

**E Heart Failure**



No. at Risk		0	1	2	3	4
Placebo group	1912	1480	794	367	188	
Active-treatment group	1933	1559	872	416	228	

# Conclusion

- Evidence based data concludes the use of antihypertensive treatment with indapamide (sustained release), with or without perindopril, is beneficial for hypertensive persons  $\leq 80$  years of age

