





Organizers:


 INSTITUTE OF INTERNAL MEDICINE & HEPATOLOGY, LARISSA, GREECE

 DEPARTMENT OF MEDICINE & RESEARCH LABORATORY OF INTERNAL MEDICINE
UNIVERSITY OF THESSALY MEDICAL SCHOOL, LARISSA, GREECE
Director: Professor G.N. Dalekos

In cooperation with:

 HELLENIC ASSOCIATION FOR THE STUDY OF THE LIVER  HSO HELLENIC STROKE ORGANIZATION

Under the auspices of the:

 UNIVERSITY OF THESSALY MEDICAL SCHOOL, LARISSA, GREECE

8th Larissa International Congress of Internal Medicine

March 17-19, 2016

Larissa Imperial Hotel

LARISSA, GREECE

<http://www.internalmedicine-uth.gr>

The Congress has been accredited with **16 Continuing Medical Education (C.M.E.) Credits**
by the Panhellenic Medical Association

Resistant Hypertension

Diagnosis & Evaluation

Larissa, March 18, 2016

Konstantinos P. Makaritsis
Associate Professor of Medicine
University of Thessaly
Medical School

Disclosures

Received scientific support and speaker
honorarium from Sanofi, Bayer,
WinMedica & Amgen

Presentation Outline

- **Introduction**
- **Definitions**
- **Pathophysiology**
- **Diagnosis – Evaluation**
- **Conclusions**

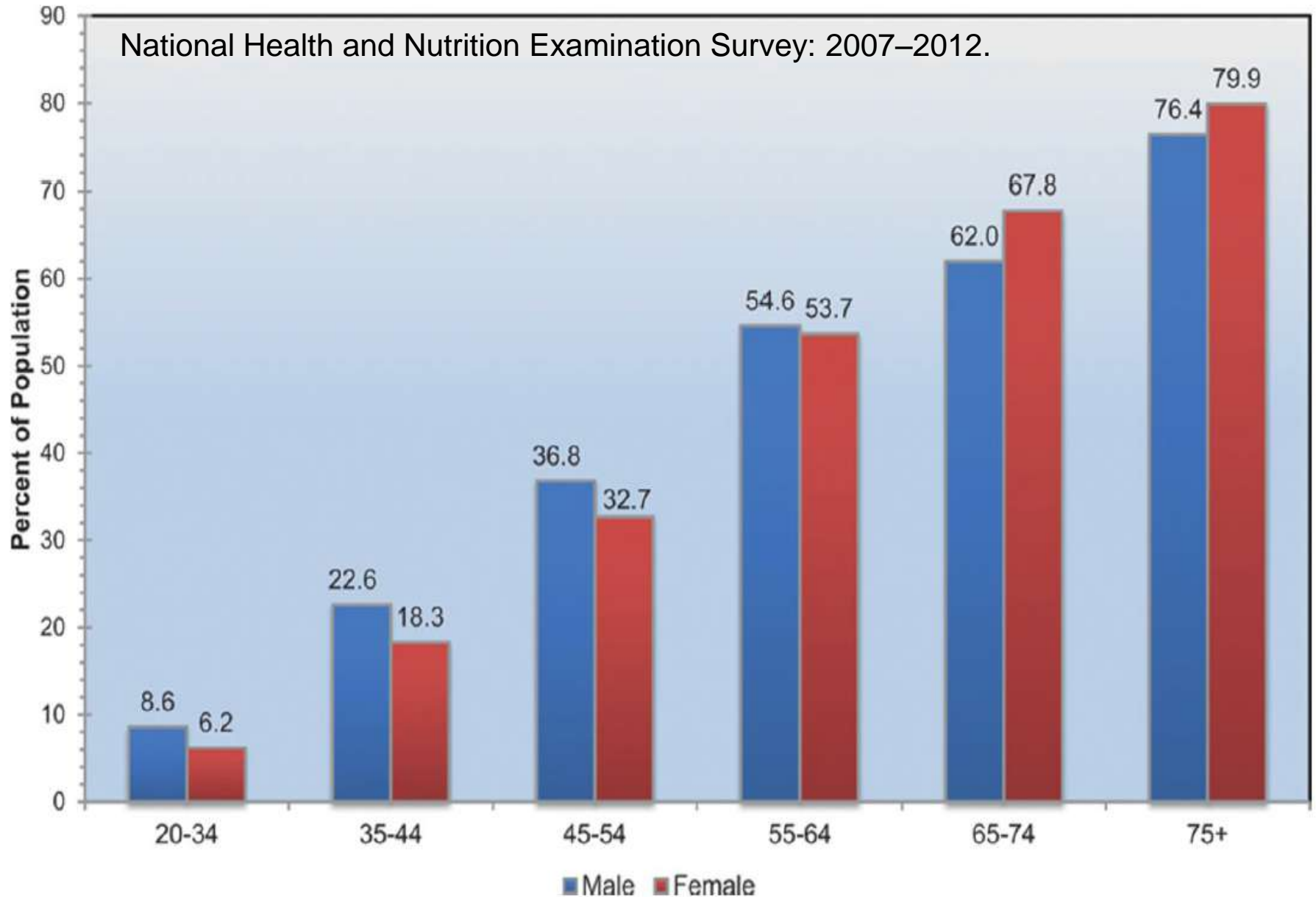
Introduction

Hypertension is the most common of the chronic diseases, affecting **an estimated 1 billion adults worldwide.**

The prevalence of hypertension is rising, owing in part to the increasing **age** of the population, the increased rates of **obesity** and the increased consumption of **sodium** in packaged and processed foods.

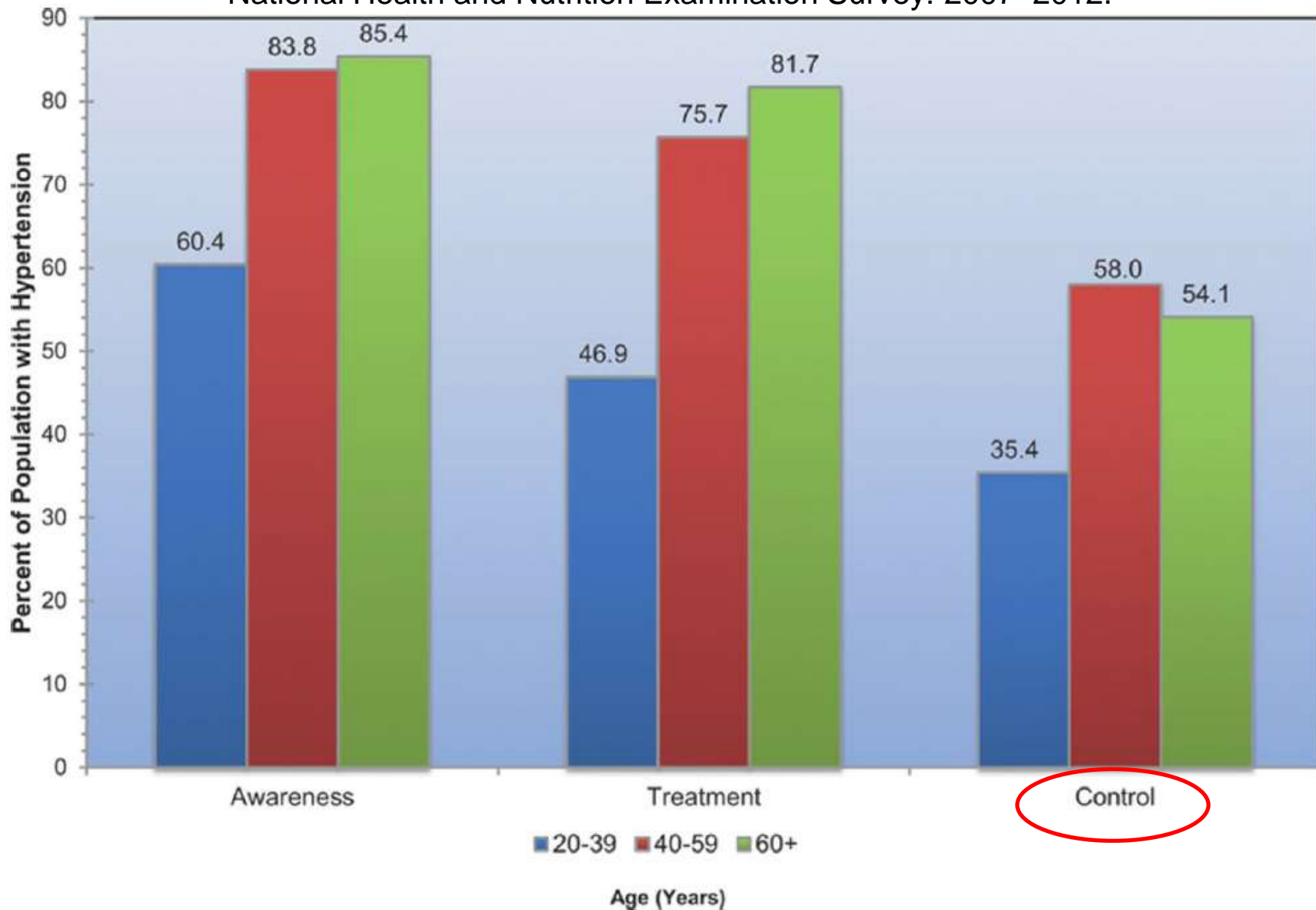
Kearney PM et al. *Lancet* 365, 217–223 (2005).
Fields LE et al. *Hypertension* 44, 398–404 (2004).

Prevalence of high blood pressure in adults ≥ 20 years of age by age and sex



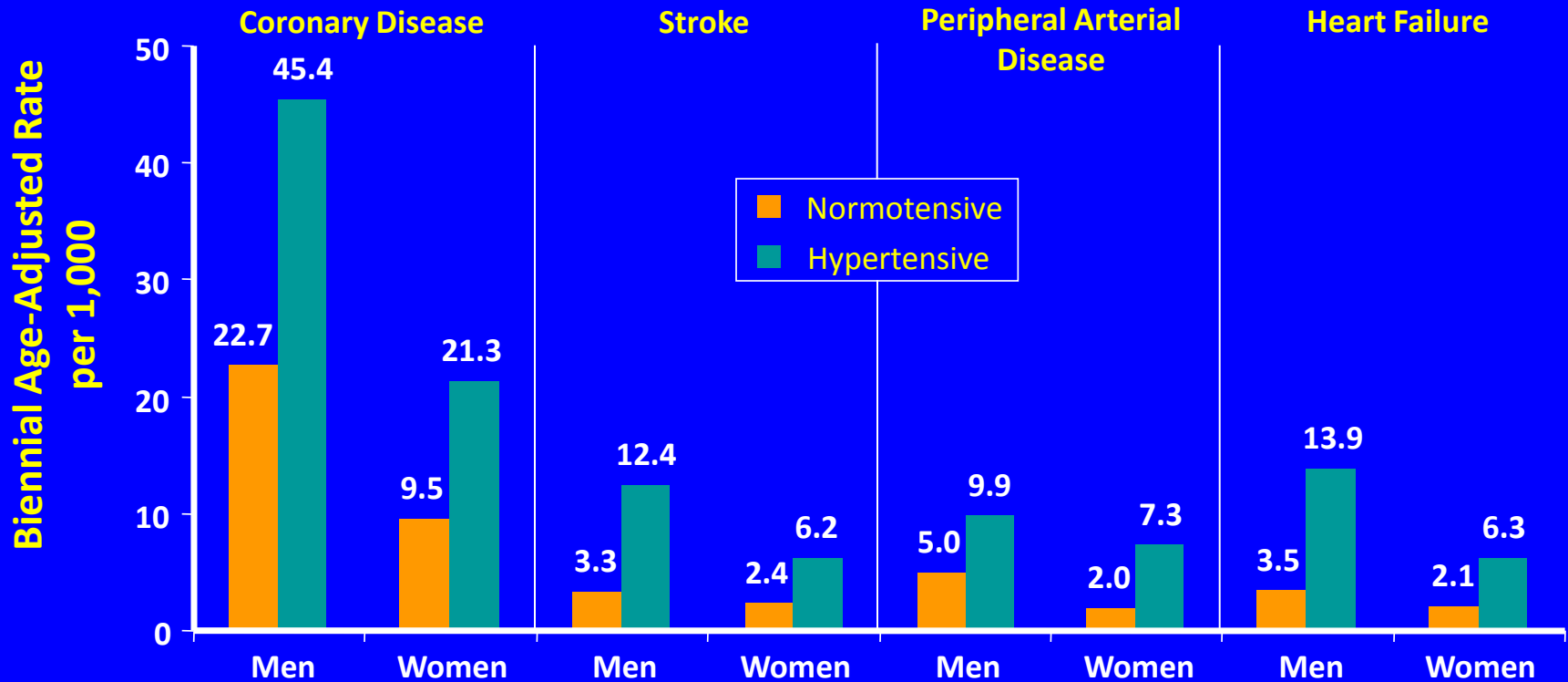
Extent of awareness, treatment, and control of high blood pressure by age

National Health and Nutrition Examination Survey: 2007–2012.



Hypertension is a leading cause for cardiovascular morbidity

36-Year Follow-up in Patients Aged 35-64 Years^{1,2}

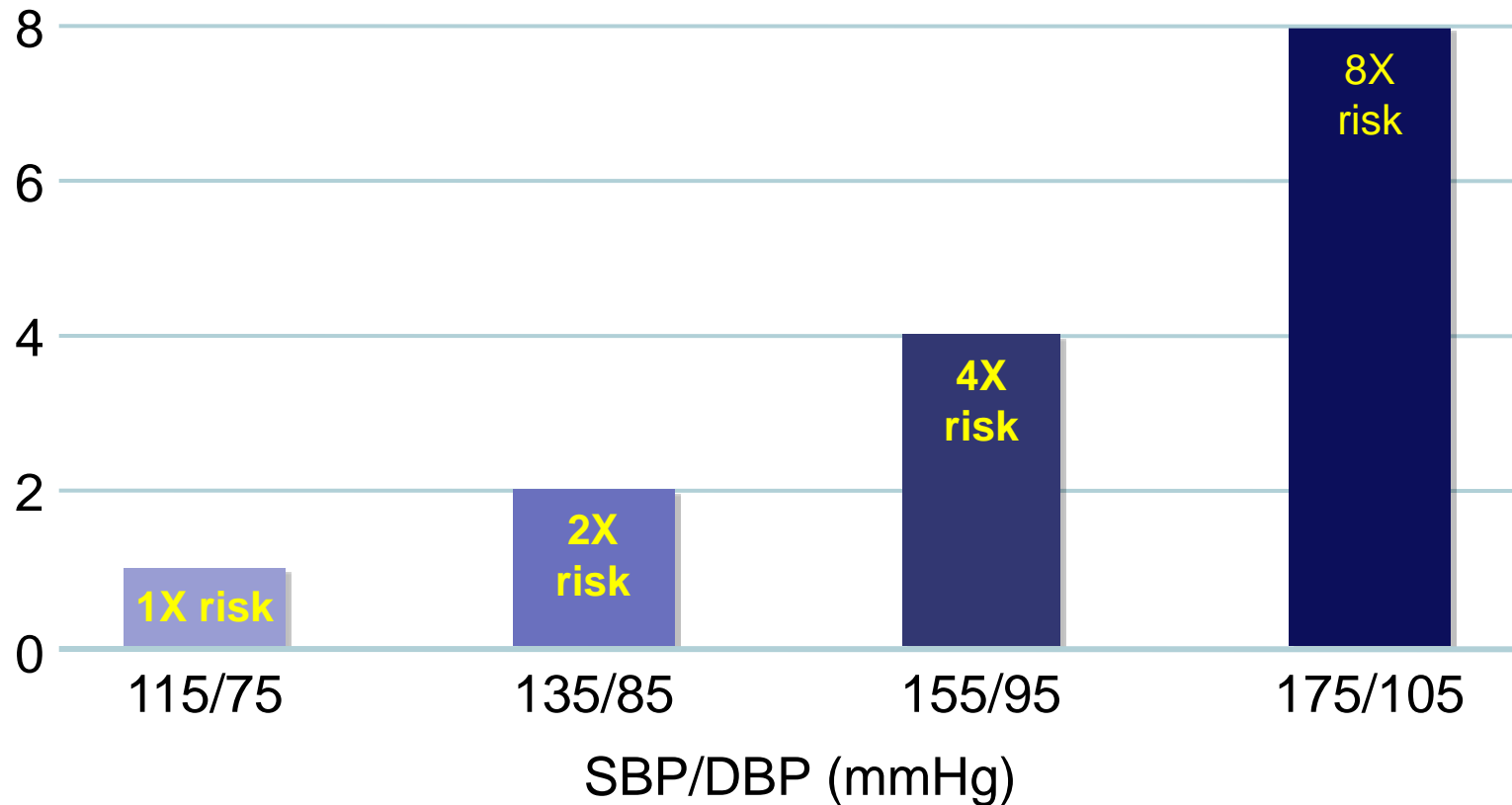


1. Kannel W.B. et al., JAMA 1996; 275: 1571-1576

2. Kannel W.B. et al., J Hum Hypertens 2000; 14: 83-90

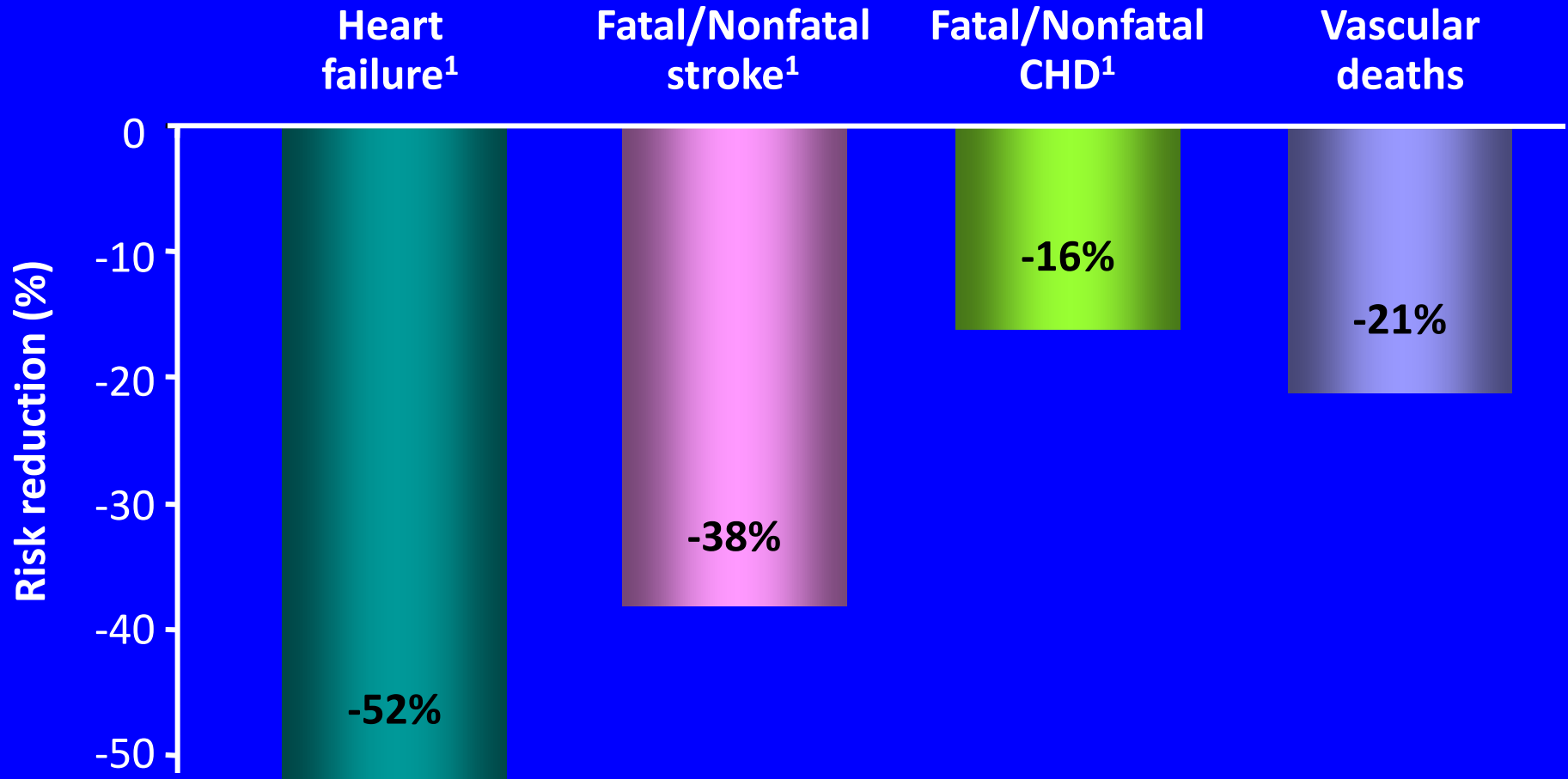
Cardiovascular (CV) Mortality Risk Doubles with Each 20/10 mmHg Increment in Systolic/Diastolic BP (SBP/DBP)*

CV mortality risk



*Individuals aged 40–69 years

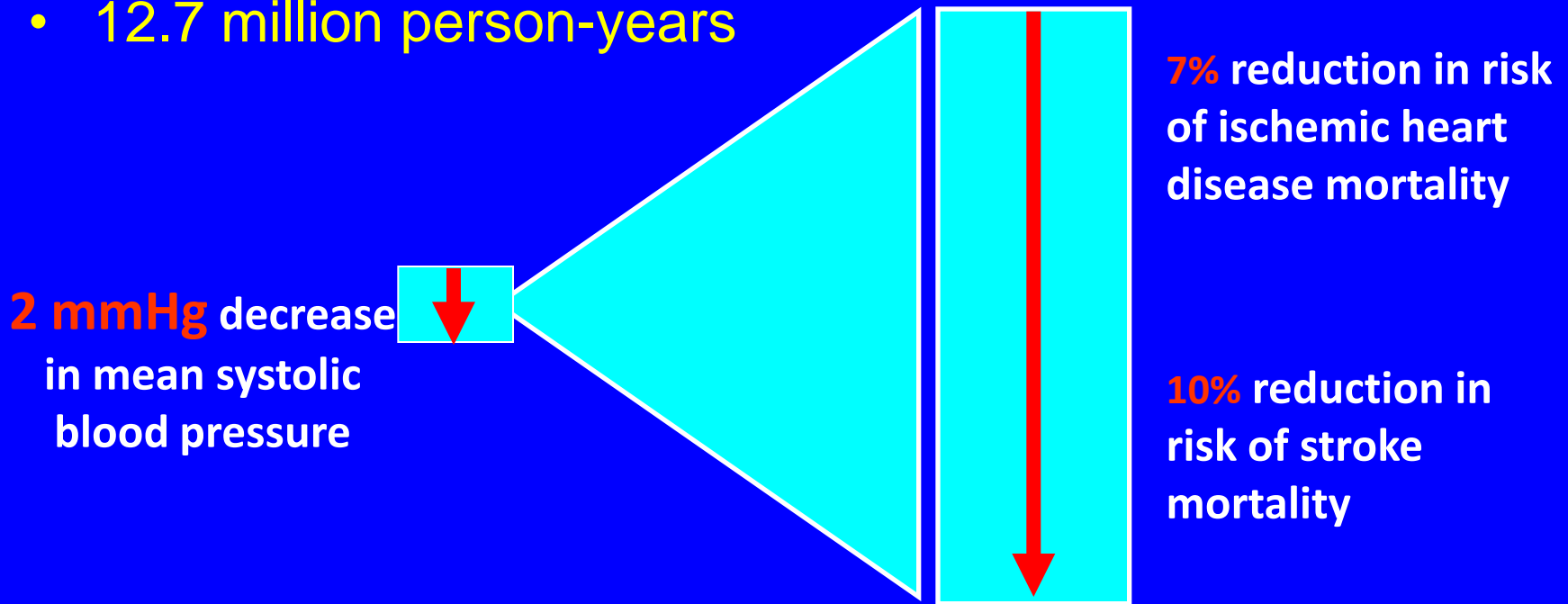
Antihypertensive drug therapy is effective at reducing risk of CV events



1. Moser and Herbert. *J Am Coll Cardiol.* 1996;
2. Collins R *et al. Lancet* 1990.

Blood pressure reductions of as little as 2 mmHg reduce the risk of cardiovascular events by up to 10%

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



Definitions

Updated ESH position paper on interventional therapy of resistant hypertension

EuroIntervention 2013;9:R58-R66

Roland E. Schmieder^{1*}, MD; Josep Redon², MD; Guido Grassi^{3,4}, MD; Sverre E. Kjeldsen⁵, MD; Giuseppe Mancia⁶, MD; Krzysztof Narkiewicz⁷, MD; Gianfranco Parati⁸, MD; Luis Ruilope⁹, MD; Philippe van de Borne¹⁰, MD; Costas Tsioufis¹¹, MD

Journal of the American Society of Hypertension 8(10) (2014) 743–757

ASH Scientific Statement

Detection, evaluation, and treatment of severe and resistant hypertension



Proceedings from an American Society of Hypertension Interactive Forum held in Bethesda, MD, USA, October 10th 2013

William B. White, MD, FASH, FAHA, FACP^{a,*}, J. Rick Turner, PhD^b, Domenic A. Sica, MD, FASH^c, John D. Bisognano, MD, PhD, FASH^d, David A. Calhoun, MD, FASH^e, Raymond R. Townsend, MD, FASH^f, Herbert D. Aronow, MD, MPH, FACC, FSCAI^g, Deepak L. Bhatt, MD, MPH, FACC, FAHA, FSCAI^h, and George L. Bakris, MD, FASHⁱ

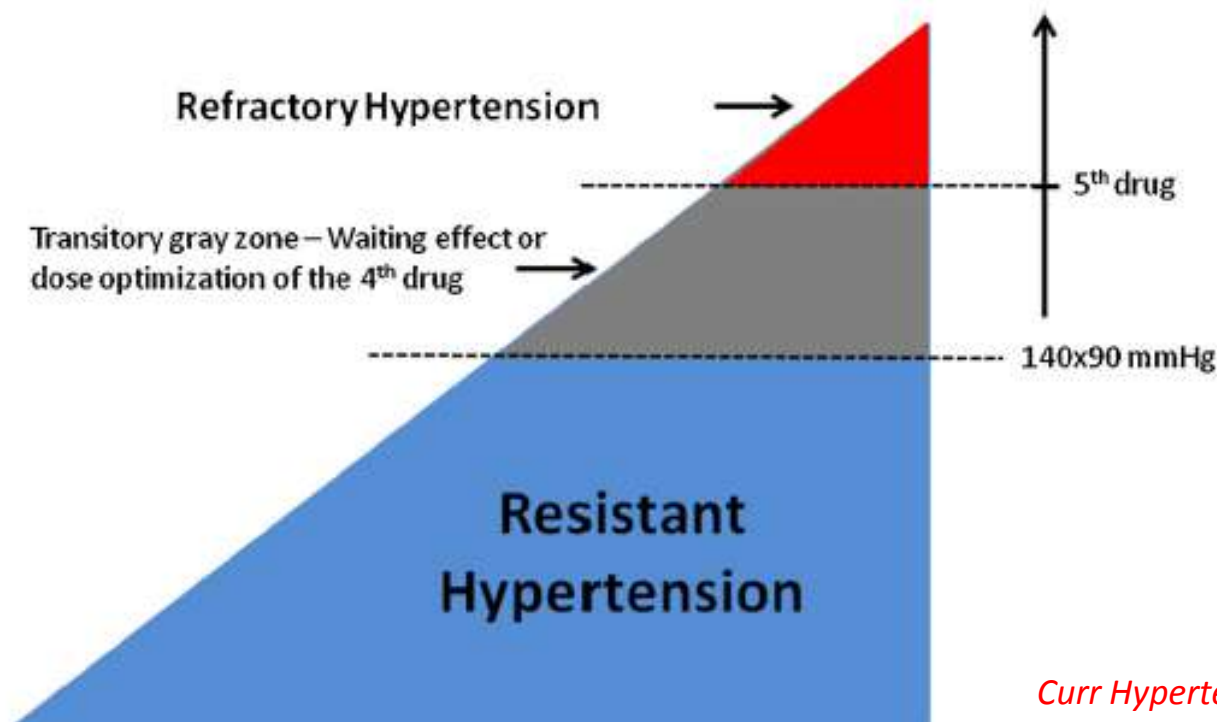
Resistant hypertension is defined as BP above goal (usually 140/90 mmHg) despite adherence to a combination of at least 3 optimally dosed antihypertensive medications of different classes, one of which ideally is a diuretic **OR** controlled BP with \geq 4 antihypertensive medication classes. The treatment regimen must be in place for at least 3 months.

Uncontrolled & Resistant Hypertension

- This definition does not apply to patients who have been recently diagnosed with hypertension.
- Moreover, resistant hypertension is not synonymous with uncontrolled hypertension.
- **Uncontrolled hypertension** includes all hypertensive patients who lack BP control under treatment, namely:
 - those receiving an inadequate treatment regimen
 - those with poor adherence
 - those with undetected secondary hypertension
 - those with true treatment resistance

Resistant & Refractory Hypertension

- The term **Refractory Hypertension** has been used almost concurrently with Resistant Hypertension for over 40 years and until the end of last decade they have been applied as synonymous.
- In 2014, Refractory Hypertension was defined as the Resistant Hypertension which remains uncontrolled despite the use of 5 or more antihypertensive agents.



Resistant & Refractory Hypertension

Patients with **refractory hypertension** are classified as having more:

1. cardiovascular risk
2. target organ damage
3. African-descending race
4. coronary heart disease
5. aldosterone excess
6. deregulation of adipokines
7. possible sympathetic hyperactivation

Epidemiology - Resistant Hypertension

- Prevalence of resistant hypertension ranges from 5% in general medical practice to 50% in nephrology clinics.
- The prevalence of resistant hypertension with office BP readings is estimated between 6–12% in the hypertensive population and 8–28% in all drug-treated hypertensive patients.
- When ABPM is used, at least 30–35% of patients labeled as resistant hypertensives turn out to have well-controlled BP on ambulatory basis.
- More recent data from the United States and Spain suggest a prevalence of resistant hypertension of approximately 10%.

Hypertension 2011; 57: 898-902.

Hypertension 2011;57:1076–80.

Curr Hypertens Rep 2015;17:78.

Pseudo-Resistant Hypertension

Pseudo-resistance refers to apparent lack of appropriate BP control in a patient who is prescribed ≥ 3 medications and is caused by several factors

Causes of Pseudo-Resistant Hypertension

Improper blood pressure measurement

Heavily calcified or arteriosclerotic arteries that are difficult to compress (in elderly persons)

White-coat effect

Poor patient adherence

J Am Coll Cardiol 2008;52:1749–57

Side effects of medication

Complicated dosing schedules

Poor relations between doctor and patient

Inadequate patient education

Memory or psychiatric problems

Costs of medication

Related to antihypertensive medication

Inadequate doses

Inappropriate combinations

Physician inertia (failure to change or increase dose regimens when not at goal)

American Society of Hypertension Self-Assessment Guide

Treatment: special conditions

Resistant hypertension

Henry R. Black, MD, MACP, FASH

- A resistant hypertensive patient is one whose
- **properly measured BP in the office**
 - **is above goal**
 - **on three or more appropriately chosen antihypertensive agents**
 - **administered at appropriate doses.**

One of these agents must be a diuretic.

American Society of Hypertension Self-Assessment Guide

Treatment: special conditions

Resistant hypertension

Henry R. Black, MD, MACP, FASH

A resistant hypertensive patient is one whose

- properly measured BP in the office

- Before classifying a patient as having resistant hypertension, the clinician must be sure that the office BP is measured properly.
- Many specialists suggest **home BP measurements or ABPM** before classifying a patient as a resistant hypertensive.

American Society of Hypertension Self-Assessment Guide

Treatment: special conditions

Resistant hypertension

Henry R. Black, MD, MACP, FASH

A resistant hypertensive patient is one whose

- Current guidelines define the treatment goal for office systolic BP to be <140 mm Hg and a diastolic BP of <90 mm Hg for most individuals. This goal level for treatment is not universally accepted.
- Most experts feel that a patient with an average 24h SBP of ≥ 135 mm Hg and/or a diastolic BP of ≥ 85 mm Hg, would be considered resistant.

American Society of Hypertension Self-Assessment Guide

Treatment: special conditions

Resistant hypertension

Henry R. Black, MD, MACP, FASH

A resistant hypertensive patient is one whose

- For most patients, a combination of
- a RAAS blocker,
- a CCB, and
- a diuretic, appropriate to the level of renal function (a thiazide for those with eGFR of ≥ 45 –50 mL/min/1.73 m²], or a loop active agent for those with a lower eGFR, must be part of the regimen.

American Society of Hypertension Self-Assessment Guide

Treatment: special conditions

Resistant hypertension

Henry R. Black, MD, MACP, FASH

A resistant hypertensive patient is one whose

- If **less than fully tolerated doses** of these agents are used or even if more than three drugs at **suboptimal doses** are prescribed, it does not mean the patient is resistant to therapy.
- Adjustments must be made to the regimen to get the patient to fully tolerated doses before classifying him/her as resistant.

American Society of Hypertension Self-Assessment Guide

Treatment: special conditions

Resistant hypertension

Henry R. Black, MD, MACP, FASH

A resistant hypertensive patient is one whose

Elevated blood pressure due to **incorrect choice of antihypertensive agents**

- **Inadequate dose(s)** of one or more agents
- **Incorrect diuretic** for the degree of renal insufficiency
- **Use** of two or more antihypertensives with same or **similar mechanism of action**

American Society of Hypertension Self-Assessment Guide

Treatment: special conditions

Resistant hypertension

Henry R. Black, MD, MACP, FASH

A resistant hypertensive patient is one whose

- **Non-adherence** to an appropriate regimen can make a patient appear to be a resistant hypertensive, and so adherence should be ascertained before classifying a patient as resistant.

Adherence to Treatment & Resistant Hypertension

- It has been found that approximately **50%** of patients with true resistant hypertension are non-adherent to treatment.
- Furthermore, among non-adherent patients, **30% are completely non-adherent** and 56% are taking less than half of the prescribed drugs.
- Thus, poor treatment adherence is actually exaggerated in patients with apparent resistant hypertension and this is a major problem.

*Burnier M et al. Seminars in Nephrology 2014;34(5),481-576.
Burnier M et al. Hypertension. 2013;62:218-225.
J Hypertens 2013; 31: 766-774 - J Hypertens 2013; 31: 2455-2461
World J Cardiol 2014; 6(10): 1080-1090*

Hints of nonadherence to pharmacologic therapy.

Prescription refill intervals longer than expected

Analytic measurements, e.g., with the use of HCTZ

Indirect indicators, e.g., low renin despite RAS

Questioning spouse or partner about adherence

Memory deficiency of patients

Complicated treatment regimen/high number of tablets to be taken daily

24h ABPM & Resistant Hypertension

The advantages of ABPM over clinic (office) BP measurements include improved reproducibility, the ability to determine BP during sleep, identification of the white-coat effect, and detection of masked hypertension.

Ambulatory BP is a stronger predictor of CV morbidity and mortality than clinic values.

However, one potential limitation should be noted: CV outcome data for ABPM have been derived from prospective cohorts and meta-analyses, whereas for clinic (office) BP they have been derived from randomized clinical trials.

Burnier M et al. Seminars in Nephrology 2014;34(5),481-576.

Journal of the American Society of Hypertension 2014;8(10):743-757

White coat Hypertension & Resistant Hypertension

- White coat hypertension is a commonly encountered factor that must always be ruled out.
- Using ambulatory BP monitoring, it was found that **only 62.5% of patients** with office RH actually had true RH, while the remaining **37.5% had white coat hypertension.**
- Apart from ambulatory BP monitoring, white coat hypertension may be excluded with the use of home BP measurements as well.

Physician Inertia & Resistant Hypertension

- Physician inertia can be defined as the failure of physicians to initiate, intensify or change therapy when BP values are above the therapeutic goal.
- Physicians do not start, intensify or switch antihypertensive therapy in about **30% of occasions**, reaching 50% in patients with comorbidities.
- In a recent study of more than 3500 patients with diagnosed RH, **treatment intensification (dose increase or drug addition) occurred in only 21.6% of visits with elevated BP.**
- Surprisingly, the study reported that diuretic use **was reduced** by 15% at 1 year after the diagnosis of RH.

Prognosis - Resistant Hypertension

- Patients with RH might be at a much higher CV risk
- In a large retrospective observational study of more than 200,000 patients and a median follow-up of 3.8 years, it was found that CV event rates were almost 50% higher in patients with RH compared to those without RH.
- In another study of almost 2000 hypertensive patients with a mean follow-up of 3.9 years, it was found that RH was associated with a 2.2-fold increased risk of CV morbidity compared to control patients without RH.

Prognosis - Resistant Hypertension

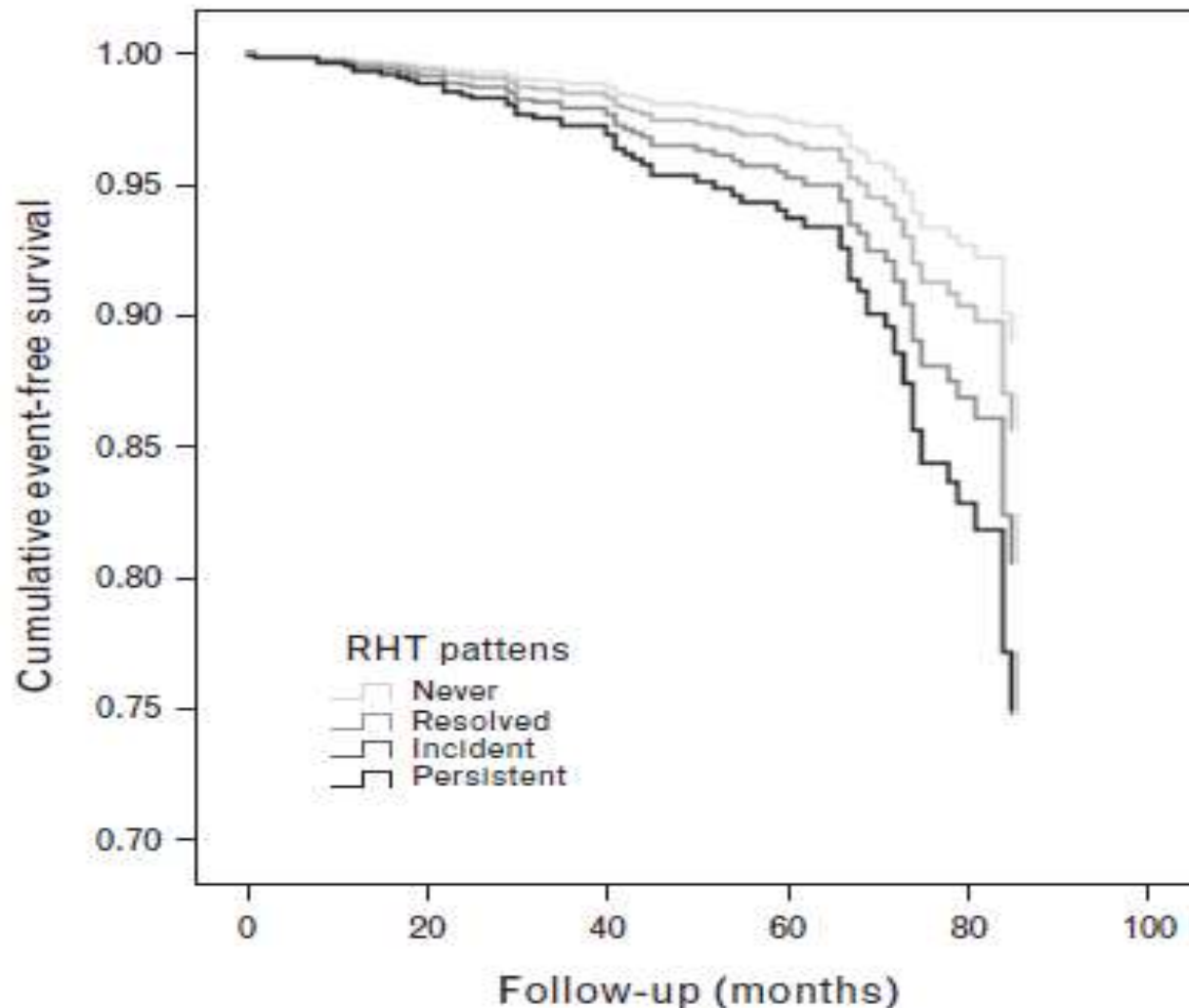


FIGURE 3 Probability of cardiovascular event-free survival in patients never having resistant hypertension, resolved resistant hypertension, incident resistant hypertension and persistent resistant hypertension. The comparison of the survival curves shows significant differences among groups (overall log-rank $P=0.011$).

Resistant Hypertension

Factors Contributing to Resistant Hypertension

Drug-induced

Nonsteroidal anti-inflammatory drugs (including cyclo-oxygenase-2 inhibitors)

Sympathomimetics (decongestants, anorectics)

Cocaine, amphetamines, other illicit drugs

Oral contraceptive hormones

Adrenal steroid hormones

Erythropoietin

Cyclosporine and tacrolimus

Licorice (included in some chewing tobacco)

Over-the-counter dietary and herbal supplements (e.g., ginseng, yohimbine, ma huang, bitter orange)

Excess alcohol intake

Volume overload

Excess sodium intake

Volume retention from kidney disease

Inadequate diuretic therapy

Resistant Hypertension

Factors Contributing to Resistant Hypertension

Associated conditions

Obesity- CKD

Diabetes mellitus

Older age

Identifiable causes of hypertension (Undetected Secondary Hypertension)

Renal parenchymal disease

Renovascular disease

Primary aldosteronism

Obstructive sleep apnea

Pheochromocytoma

Cushing's syndrome

Thyroid diseases

Aortic coarctation

Intracranial tumors

In pts with resistant hypertension, the presence of secondary hypertension must be considered.

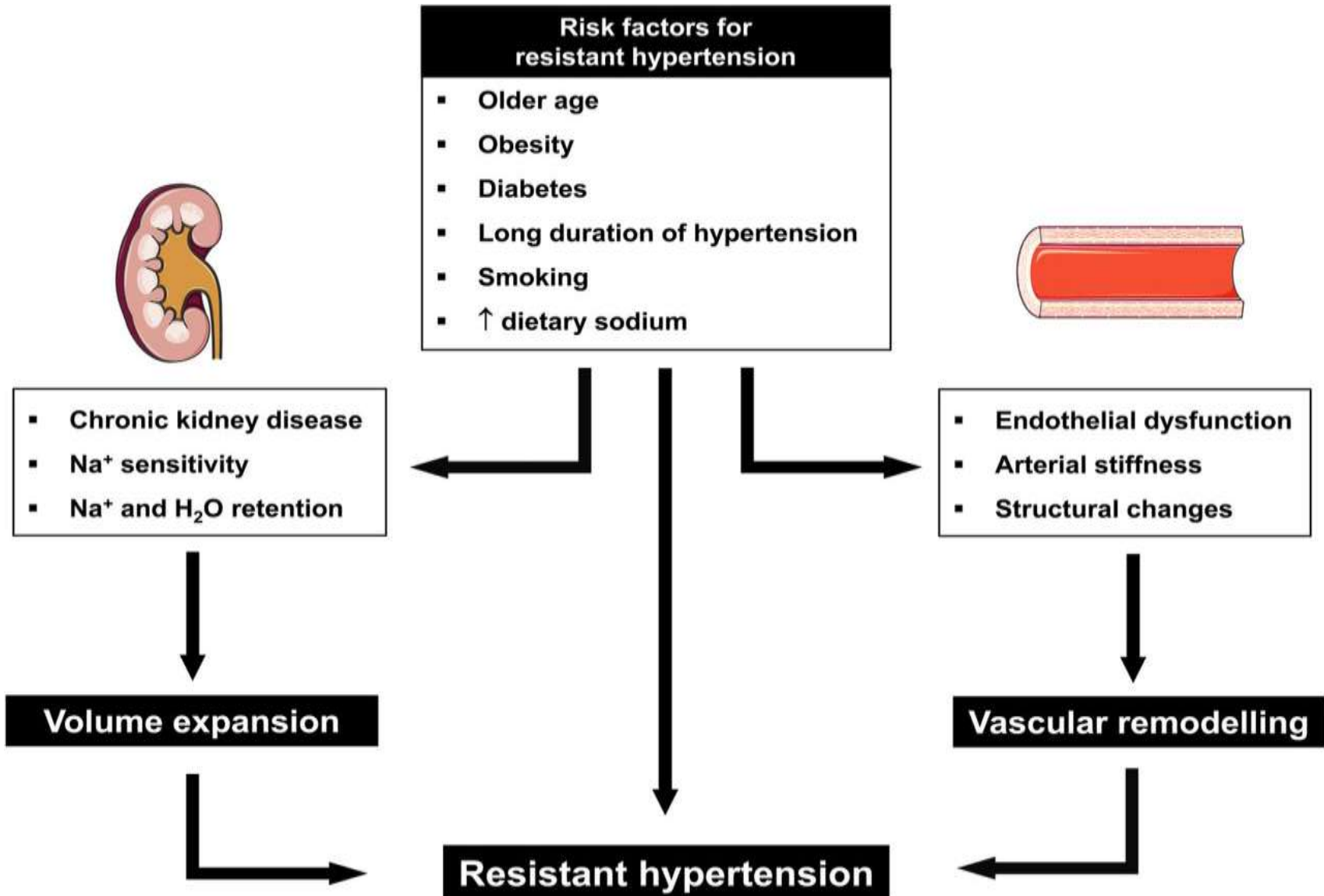
Although its prevalence is largely unknown, previous studies have shown that **5% to 10%** of patients with resistant hypertension have an identifiable cause.

Pathophysiology

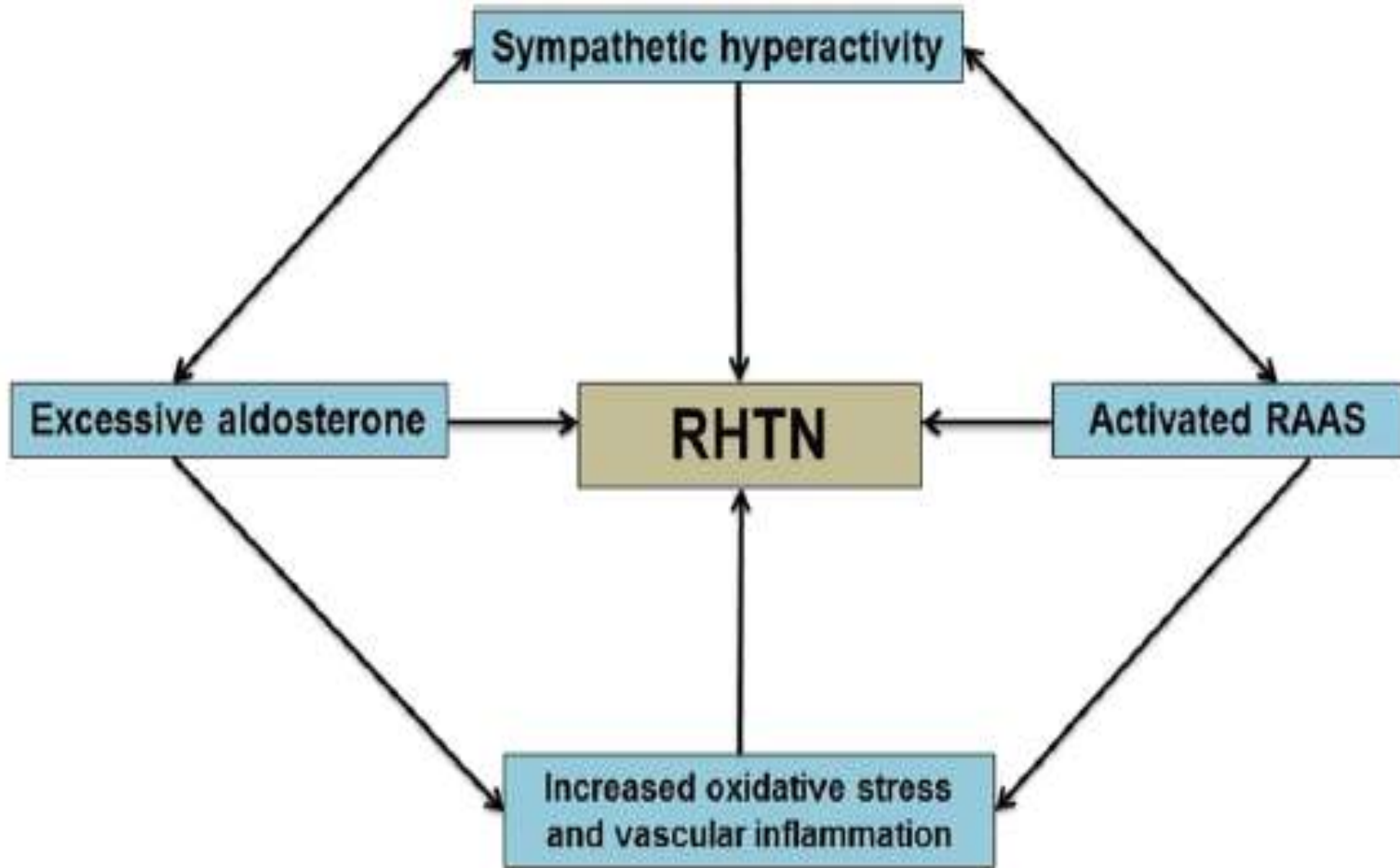
Risk factors and pathogenic mechanisms associated with treatment-resistant hypertension

- The underlying mechanisms in TRH are unclear but appear to be multifactorial.
- Factors associated with TRH include
 - Older age
 - Impaired renal function
 - Diabetes mellitus
 - Obesity
- Patients with TRH are known to have an **increased plasma volume and elevated systemic vascular resistance with a normal cardiac output.**

Risk factors and pathogenic mechanisms associated with treatment-resistant hypertension



Pathways involved in the Pathogenesis of Treatment Resistant Hypertension



Sympathetic Nervous System

&

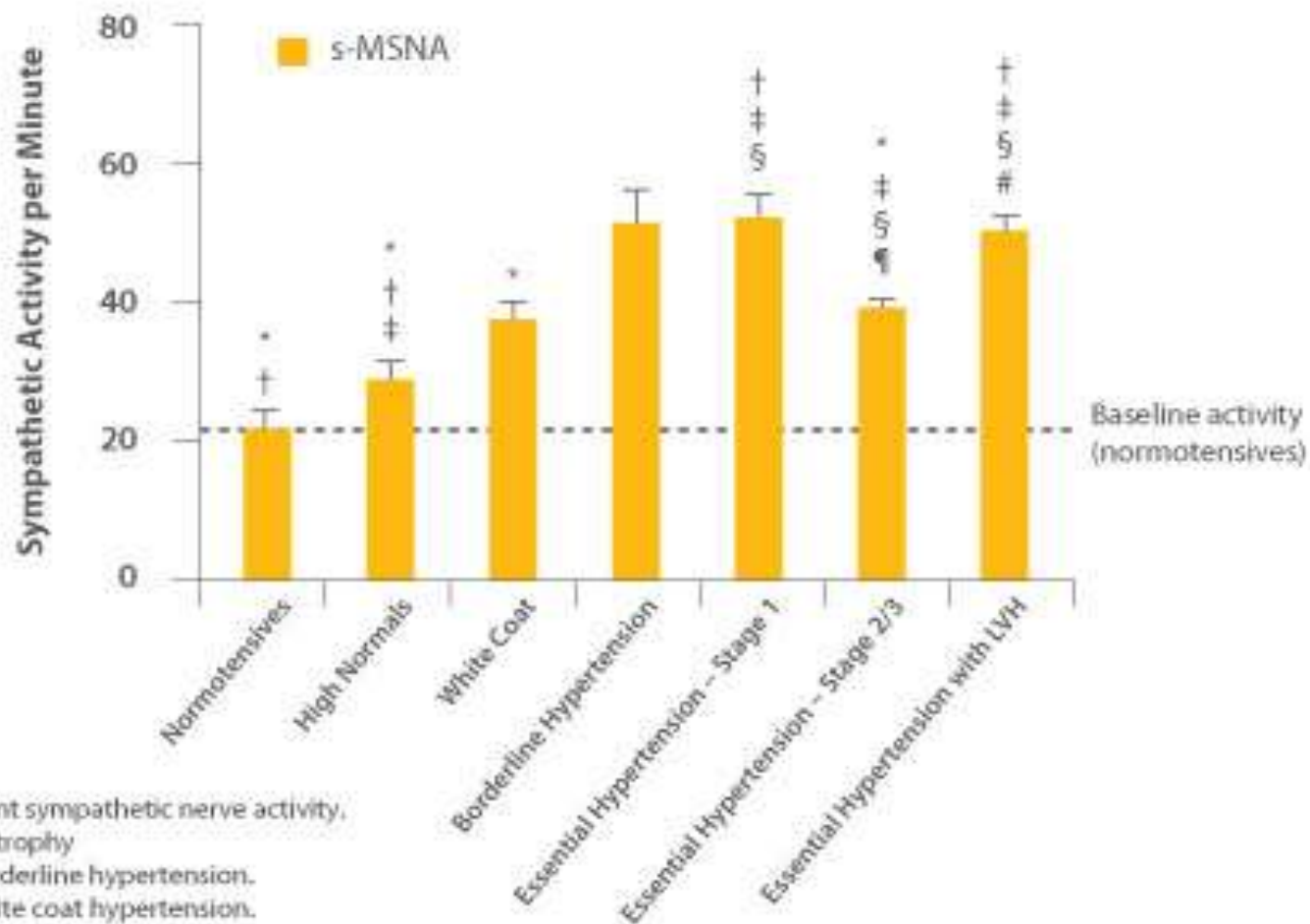
Hypertension

Sympathetic nerve activity in Hypertension

- Once it was thought that the SNS was not of importance in the pathogenesis of hypertension.
- There is ample evidence for elevated sympathetic nerve activity in experimental and human primary (essential) hypertension.
- Norepinephrine spillover and muscle sympathetic nerve activity (MSNA) are elevated (2 - 3 x) in essential hypertensive patients compared to normotensive controls.

Increased Central Sympathetic Drive in Hypertension

- Sympathetic drive is elevated in multiple types of hypertension



s-MSNA = single-unit efferent sympathetic nerve activity,
 LVH = left ventricular hypertrophy

* $P < 0.05$ Compared with borderline hypertension.

† $P < 0.05$ Compared with white coat hypertension.

‡ $P < 0.05$ Compared with normal pressure.

§ $P < 0.05$ Compared with high-normal pressure

¶ $P < 0.05$ Compared with essential hypertension-stage 1.

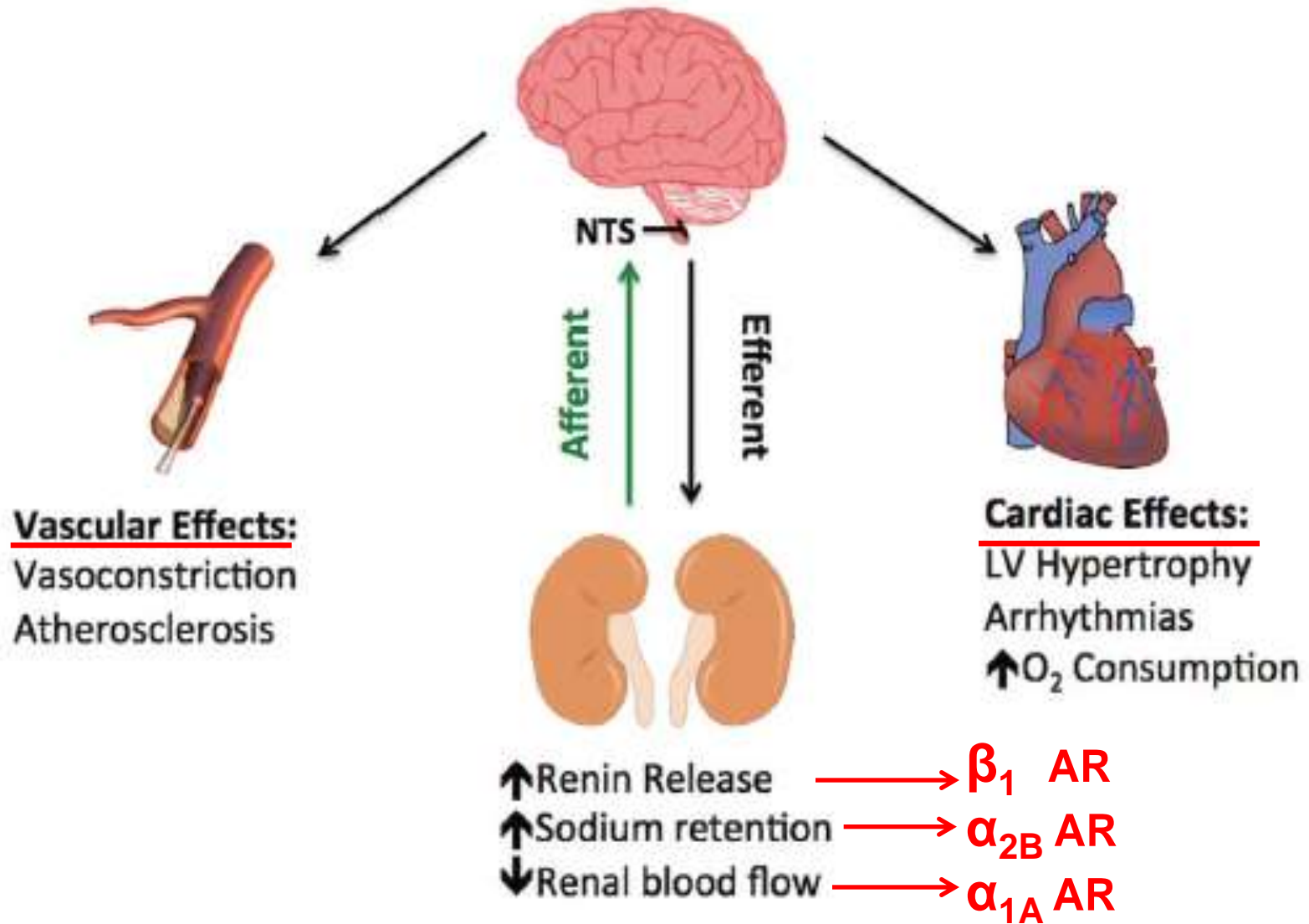
‡ $P < 0.05$ Compared with essential hypertension-stage 2/3.

Adapted from Smith P, et al. *Am J Hypertens*, 2004; 17:217-222.

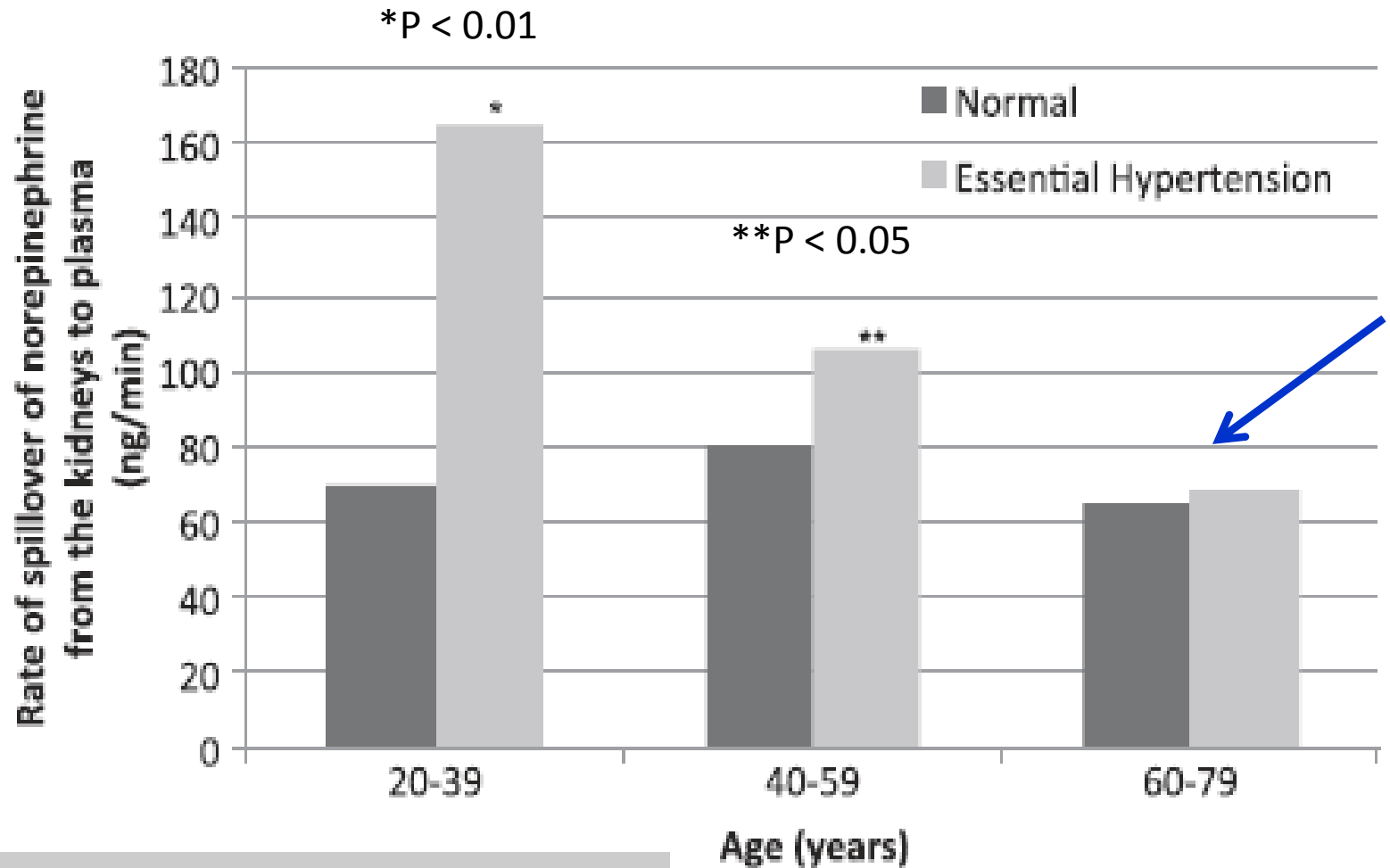
Renal Sympathetic nerve activity in Hypertension

- Renal sympathetic activity is also elevated and the SNS may act through the kidney to cause or maintain arterial hypertension.
- It now seems certain that the **renal sympathetic nerves** are pivotal in the pathogenesis of experimental and essential hypertension, through influences on
 1. renin release
 2. renal tubular reabsorption of sodium
 3. glomerular filtration rate – (renal blood flow)

Chronic Effect of Increased Sympathetic Nerve Activity



Renal sympathetic activity in **untreated** hypertensive patients and age-matched controls by tertiles of age.



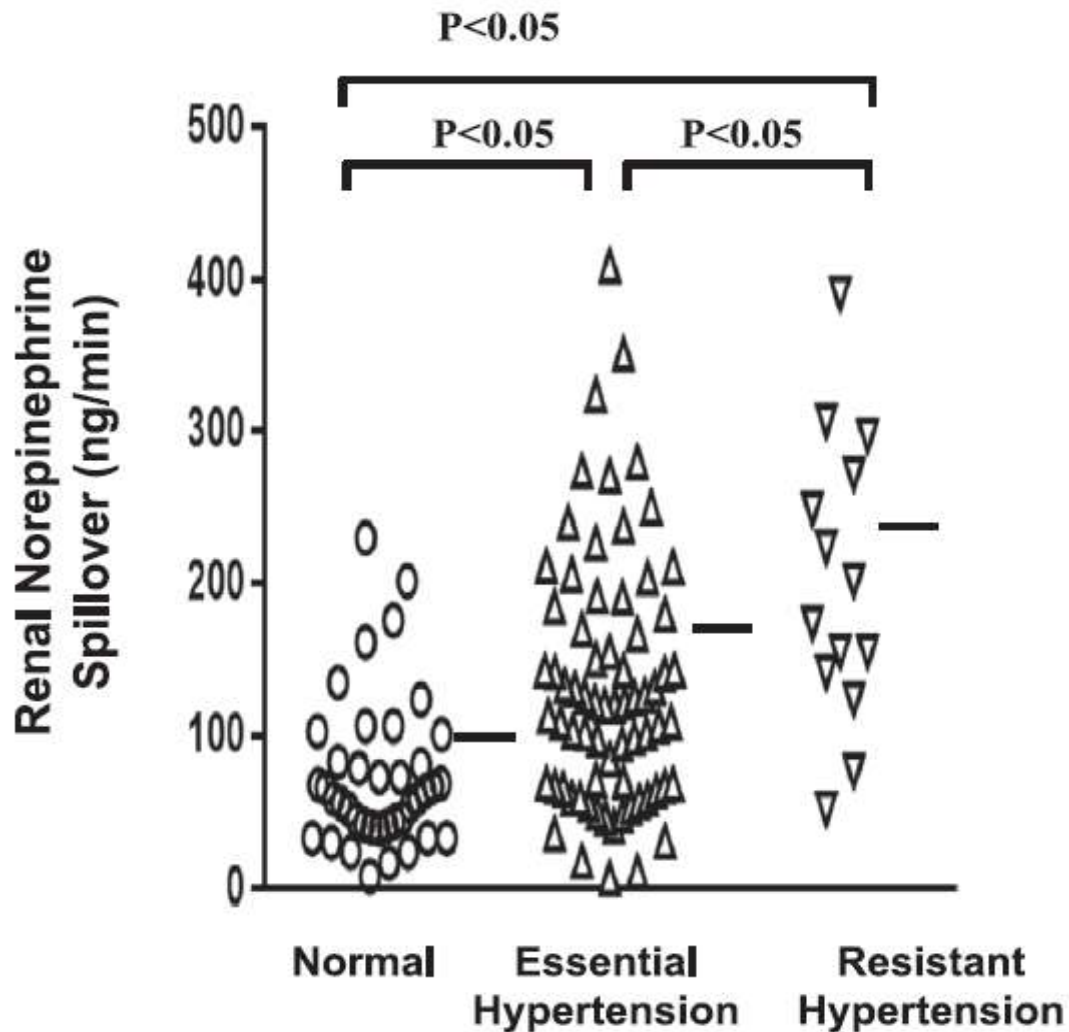
In pts with essential HT aged > 60 years, their renal sympathetic activity was not different from their age-matched controls

*Esler M. et al. Hypertension 1988;11:3-20.
Cardiovascular Therapeutics 2015;33:9-14.*

Renal Sympathetic nerve activity in Resistant Hypertension

- Until recently, there were no data implicating an overactive sympathetic nervous system in TRH.
- This is difficult to assess in the presence of various medications that alter the sympathetic activity such as alpha and beta blockers.
- However, recent data indicate that among hypertensive patients of all ages, there may be an increase in the activation of renal sympathetic outflow in those with TRH as compared with essential hypertension.

Preferential Activation of Renal Sympathetic Outflow in Essential Hypertension

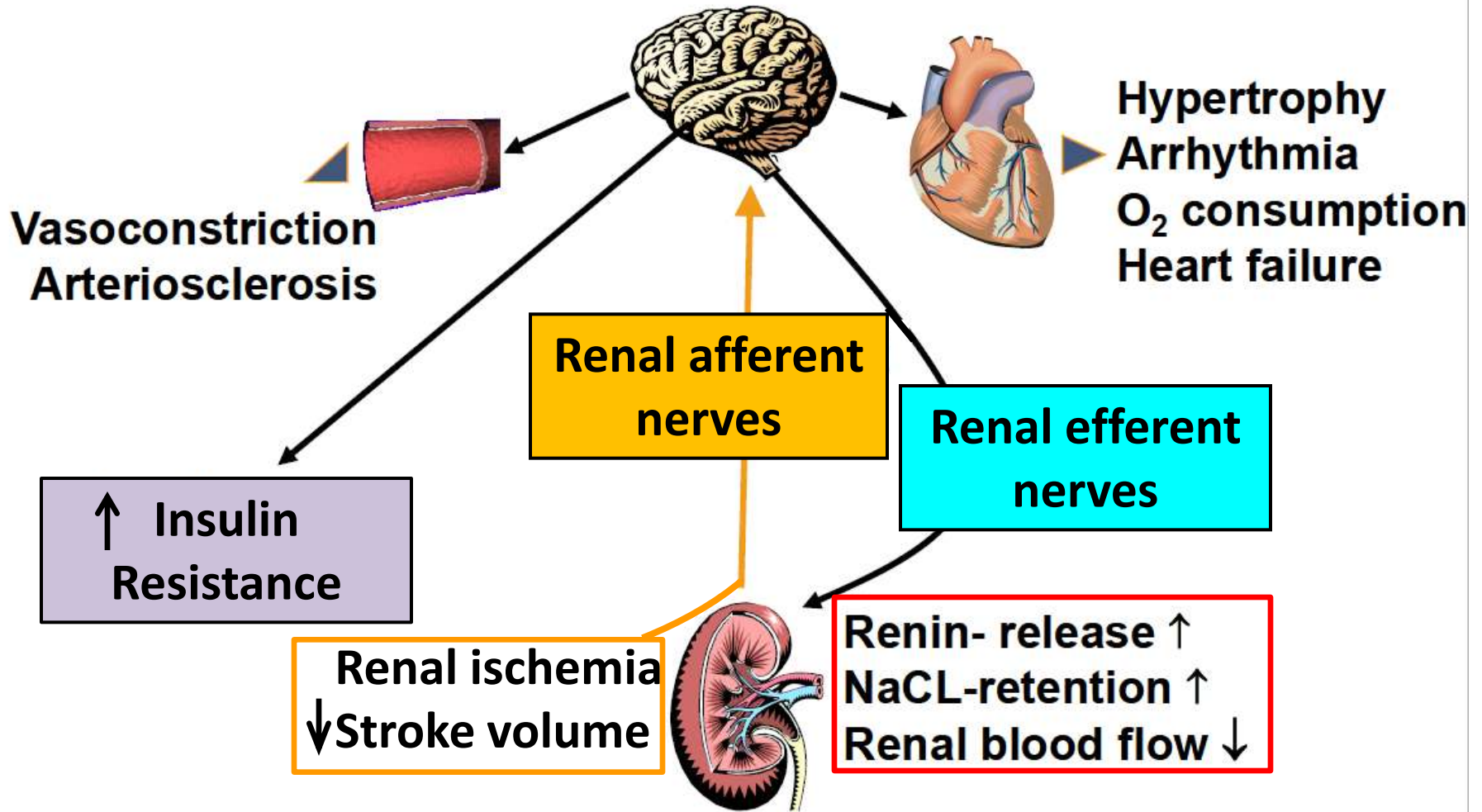


Combined Melbourne Experience 1981- 2014

In untreated patients with mild-moderately severe essential hypertension, renal NE spillover was increased overall, and elevated in approximately 50%. In resistant hypertension, with patients administered on average 5 antihypertensive drug classes, renal NE spillover was higher again, attributable to their hypertension, and its treatment; vasodilators, calcium channel blockers and diuretics stimulate the sympathetic nervous system. (From unpublished results of the author, Markus Schlaich, Gavin Lambert, and Dagmara Hering.)

Crosstalk between Renal Nerves and CNS

Kidney as the origin of central sympathetic drive



RAAS Activity - Aldosterone

&

Resistant Hypertension

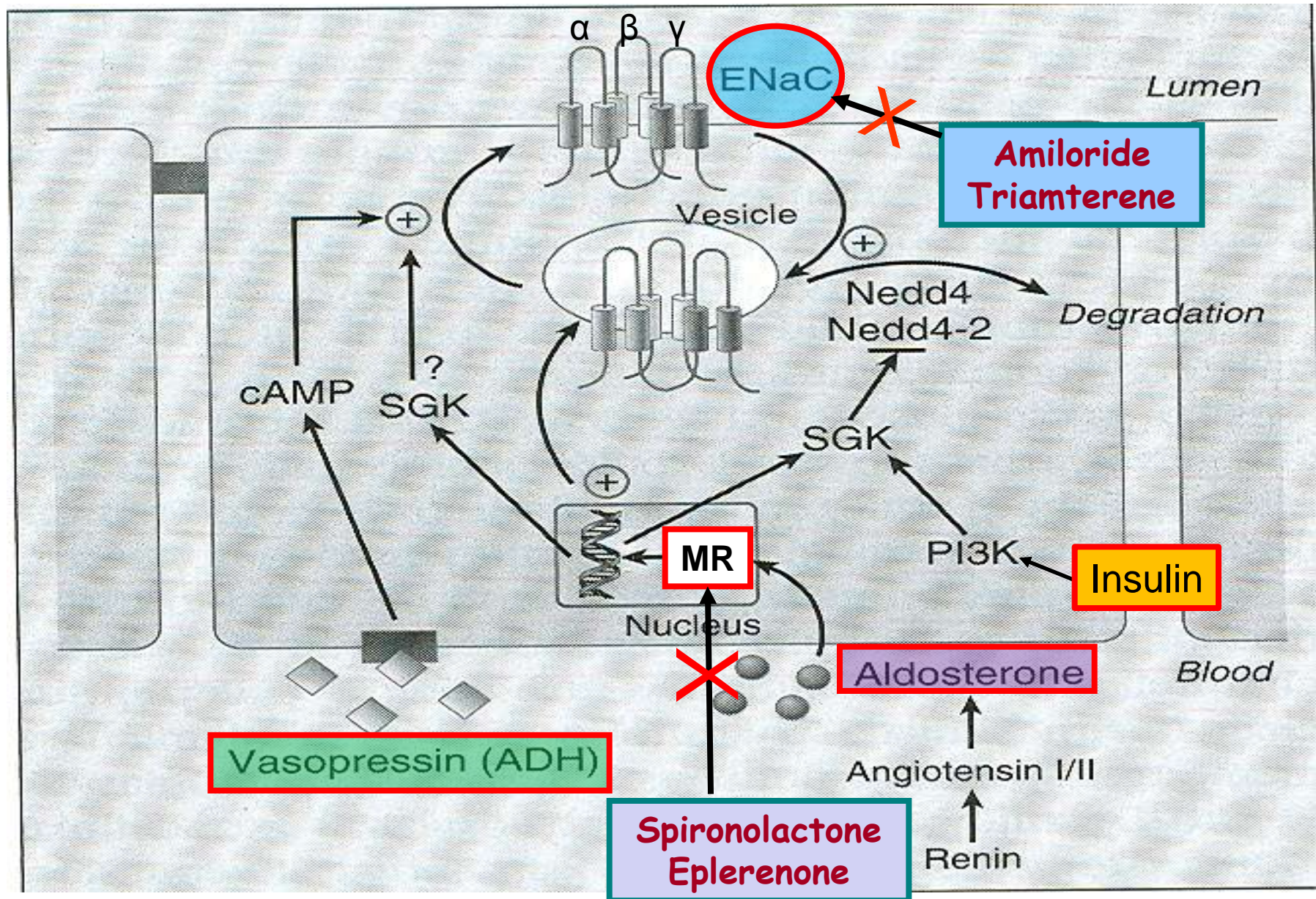
Aldosterone & Resistant Hypertension

- Primary hyperaldosteronism is more prevalent in HTN than generally recognized and is estimated to be present in **15-20 % of patients with RHTN**.
- Even in the absence of primary hyperaldosteronism, **patients with RHTN demonstrate higher levels of aldosterone** and volume overload than individuals without RHTN.
- Activation of the renin-angiotensin aldosterone system (RAAS) may constitute the mechanistic link between elevated aldosterone levels and the sympathetic hyperactivity.

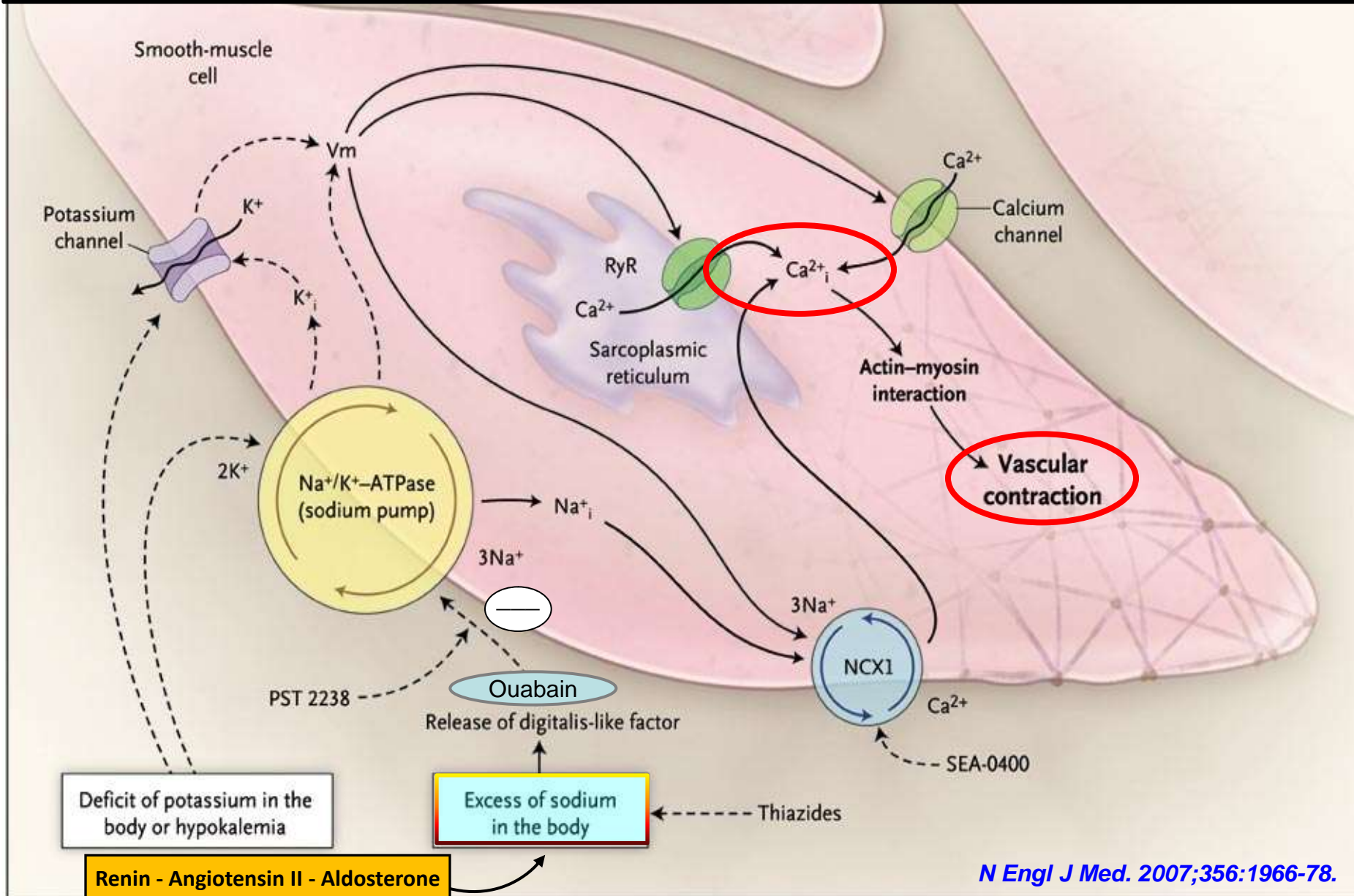
Hypertension. 2002;40(6):892–6.

Arch Intern Med. 2008;168(11):1159–64.

Aldosterone & ENaC membrane expression



Molecular Pathways Implicated in the Generation of Increased Arterial and Arteriolar Smooth-Muscle Tone by an Excess of Sodium



Diagnostic recommendations & Evaluation

Step-by-Step Physician Guide for Evaluation and Management of Patients Appearing to Have Resistant Hypertension

J Am Coll Cardiol 2008;52:1749–57

A. Become familiar with and adhere to the most recent hypertension guidelines.

B. Identify and reverse “pseudo-resistance.”

1. Perform proper measurements of BP in the office, following the relevant guidelines, to confirm the diagnosis of resistant hypertension.
2. Exclude the “white-coat effect” with the use of home or ambulatory BP measurements.
3. Evaluate patient’s adherence to the treatment regimens; in case of poor adherence, determine the causes of it. Educate the patient on the risks of uncontrolled hypertension and the benefits of drug treatment and motivate the patient to work toward an appropriate BP goal.
4. Closely follow-up nonadherent patients to ensure their compliance.

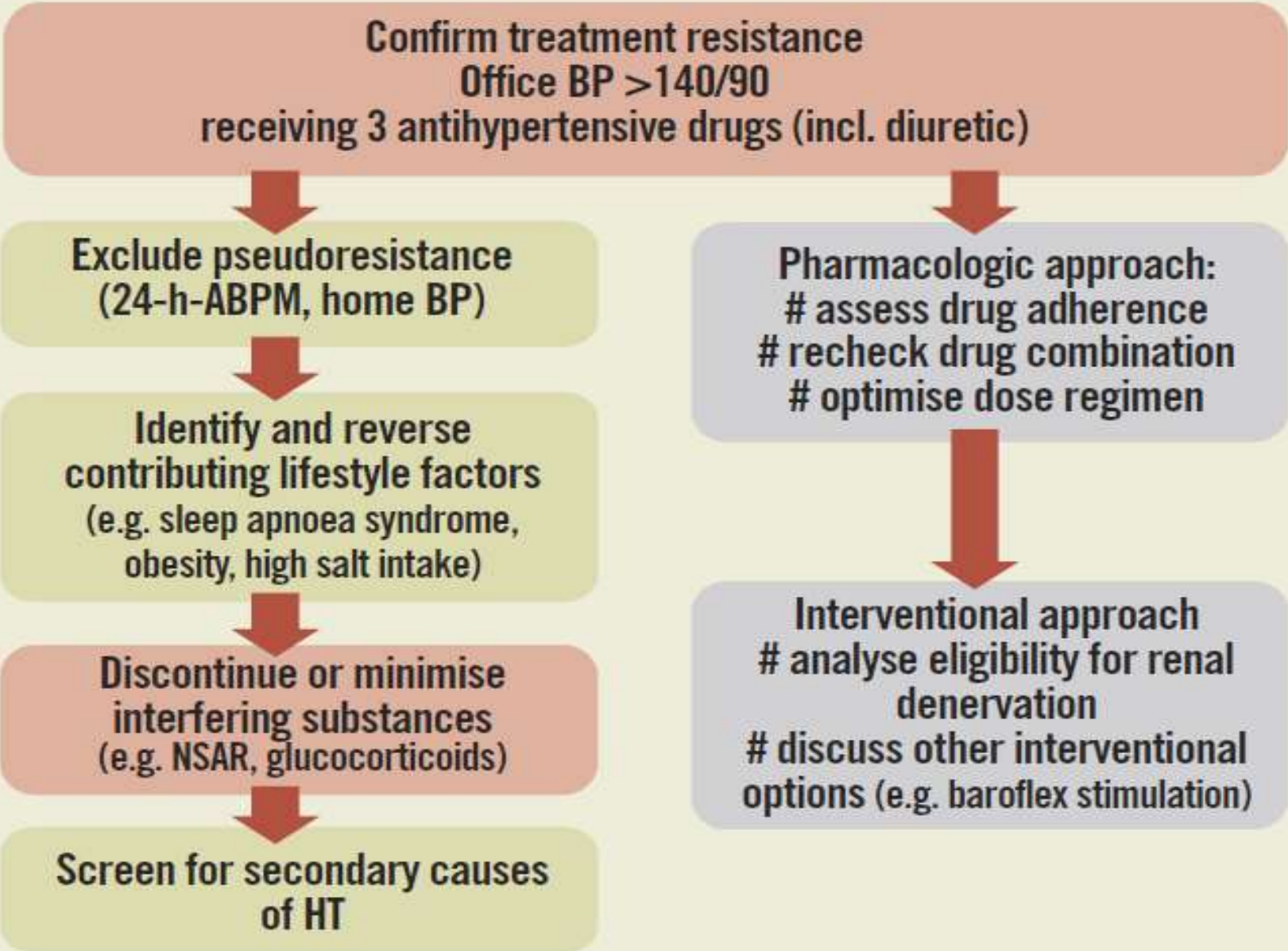
Step-by-Step Physician Guide for Evaluation and Management of Patients Appearing to Have Resistant Hypertension

J Am Coll Cardiol 2008;52:1749–57

C. Identify and reverse factors contributing to true resistance.

1. Specifically ask the patient about use of any pharmacological agents that may increase BP; in case of identification of such a substance, discontinue or minimize its use.
2. Evaluate the amount of alcohol intake and counsel the patient on the benefits of ceasing alcohol consumption.
3. Perform a reliable evaluation of dietary salt intake and recommend sodium restriction to <100 mmol (2.4 g) per day.
4. Assess the degree of obesity, abdominal obesity, and physical activity and recommend weight reduction and regular aerobic exercise (at least 30 min/day, most days of the week).
5. Evaluate the level of renal function with estimation of glomerular filtration rate and modify treatment accordingly.
6. Perform a thorough search for secondary hypertension; if an identifiable cause is present, treat accordingly or refer the patient to a hypertension center.

Diagnostic and treatment algorithm for resistant hypertension



Concluding Remarks

Concluding Remarks

- Resistant hypertension is defined as a condition where BP remains uncontrolled despite the use of at least 3 drugs (one diuretic) or if the control happens with four or more drugs.
- In evaluating such patients, it is most important to exclude “pseudo”-resistance (confirm the diagnosis-evaluate patient’s compliance-search for secondary hypertension).
- Factors associated with resistant hypertension include older age, obesity, diabetes, increased sodium consumption and impaired renal function.
- Sympathetic hyperactivity and excessive aldosterone and RAAS activation are the pathways usually involved.
- Regardless of the exact underlying mechanisms, resistant hypertension has been shown to increase a patient’s risk of death, cardiovascular events, and the development of renal failure, and thus, better therapies are required.

Questions

1. Which of the following is **NOT** a necessary part of the definition of resistant hypertension?
 - a. An elevated BP on an ambulatory blood pressure monitoring.
 - b. Adherence to the medication regimen.
 - c. At least three appropriately chosen drugs.
 - d. Appropriate doses of the appropriate drugs.

1. Which of the following is **NOT** a necessary part of the definition of resistant hypertension?
 - a. **An elevated BP on an ambulatory blood pressure monitoring.**
 - b. Adherence to the medication regimen.
 - c. At least three appropriately chosen drugs.
 - d. Appropriate doses of the appropriate drugs.

2. Which of the following are commonly used substances that can raise blood pressure and may explain why a patient is a resistant hypertensive?

a. Anti-inflammatory agents

b. Oral contraceptives

c. Corticosteroids

d. All of the above

2. Which of the following are commonly used substances that can raise blood pressure and may explain why a patient is a resistant hypertensive?

a. Anti-inflammatory agents

b. Oral contraceptives

c. Corticosteroids

d. All of the above

3. All of the following statements regarding resistant hypertension are true EXCEPT:

a. White coat hypertension can be excluded by ABPM

b. Patients with resistant hypertension carry a much higher risk for cardiovascular events

c. Renal sympathetic activity is much higher in elderly untreated hypertensives

d. Erythropoietin administration might explain why a patient is a resistant hypertensive

3. All of the following statements regarding resistant hypertension are true EXCEPT:

a. White coat hypertension can be excluded by ABPM

b. Patients with resistant hypertension carry a much higher risk for cardiovascular events

c. Renal sympathetic activity is much higher in elderly untreated hypertensives

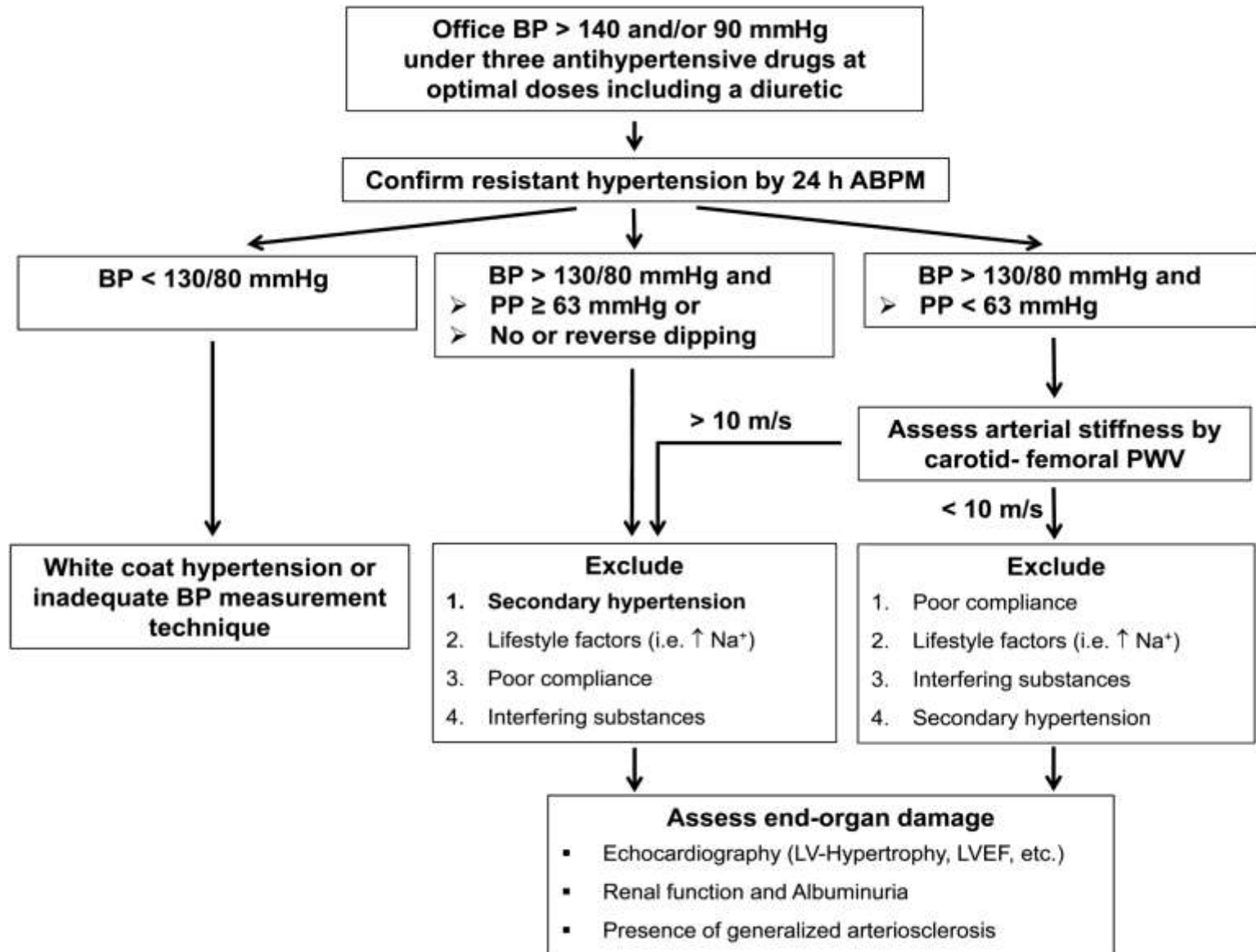
d. Erythropoietin administration might explain why a patient is a resistant hypertensive

Thank You



The Ancient Theatre of Larissa, Greece
3rd Century B.C.

Work-up of patients with suspected treatment-resistant hypertension



Stefano F. Rimoldi et al. Eur Heart J 2015;36:2686-2695

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2015. For permissions please email: journals.permissions@oup.com.

Hints of nonadherence to pharmacologic therapy.

Prescription refill intervals longer than expected

Analytic measurements, e.g., with the use of HCTZ

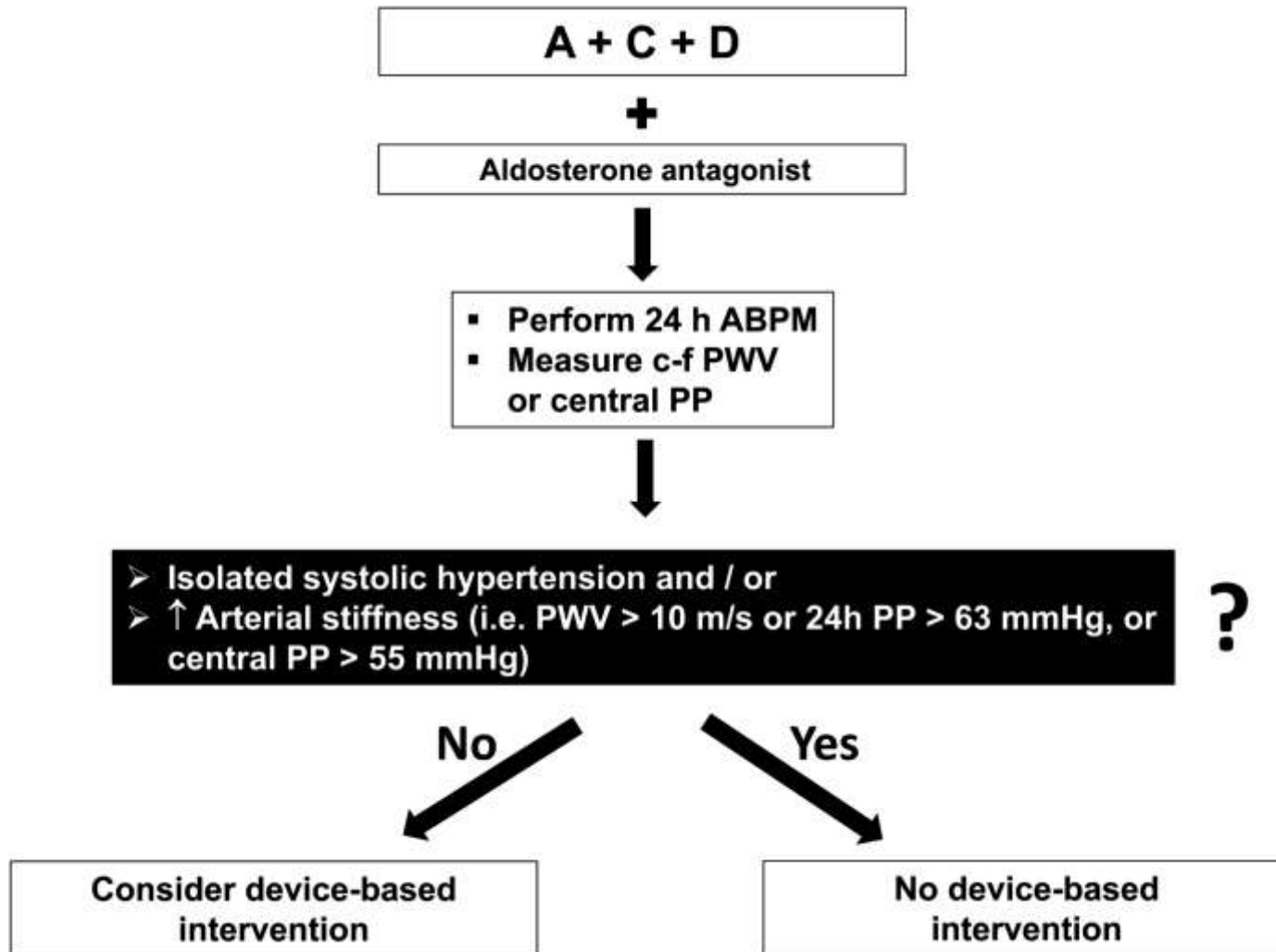
Indirect indicators, e.g., low renin despite RAS

Questioning spouse or partner about adherence

Memory deficiency of patients

Complicated treatment regimen/high number of tablets to be taken daily

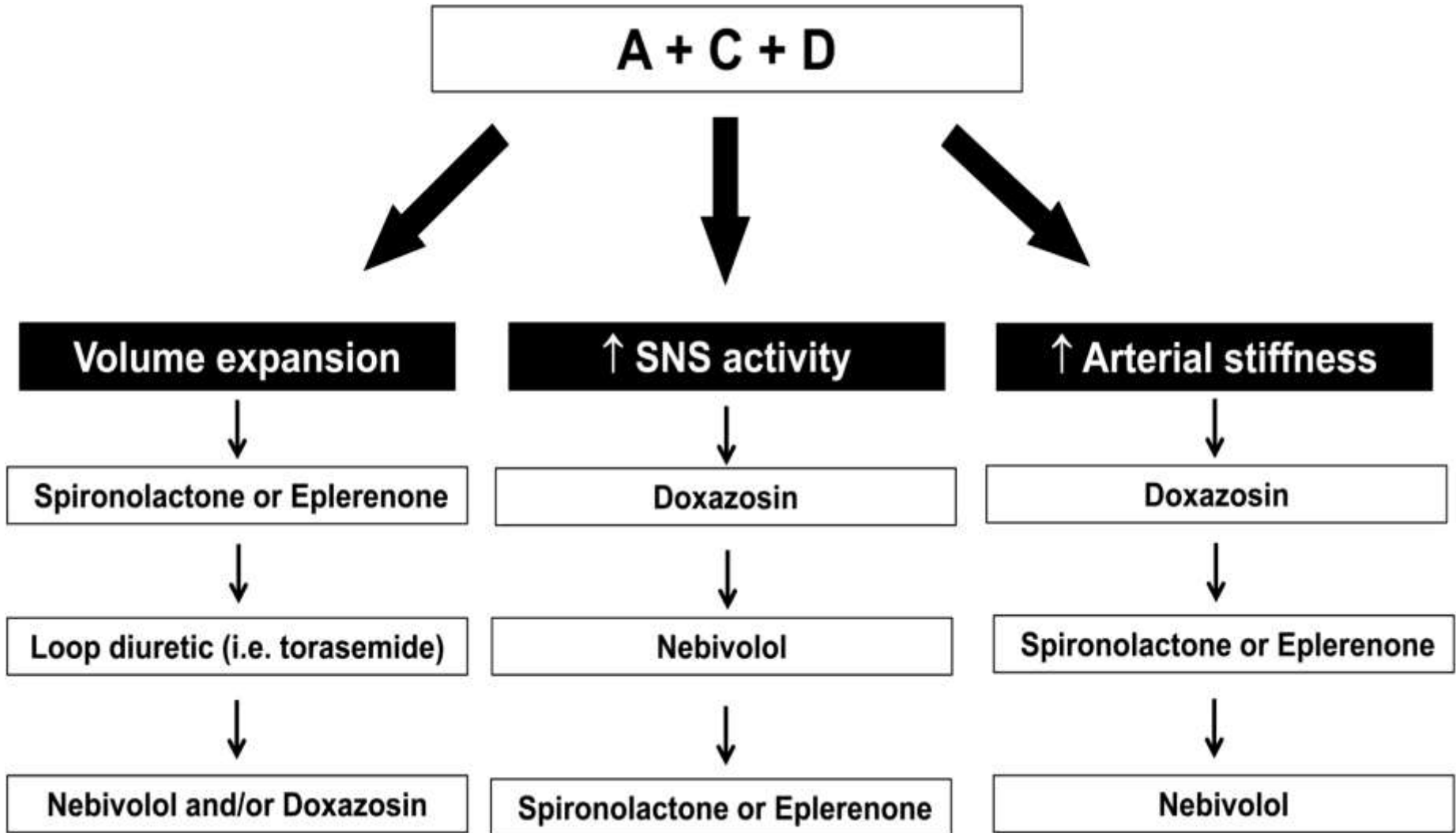
Screening for device-based interventions



Stefano F. Rimoldi et al. Eur Heart J 2015;36:2686-2695

Published on behalf of the European Society of Cardiology. All rights reserved. © The Author 2015. For permissions please email: journals.permissions@oup.com.

Antihypertensive drug therapy in patients with resistant hypertension



Stefano F. Rimoldi et al. Eur Heart J 2015;36:2686-2695

Diagnostic recommendations

Confirm Treatment Resistance

Office blood pressure $>140/90$ or $130/80$ mm Hg in patients with diabetes or chronic kidney disease
and
Patient prescribed 3 or more antihypertensive medications at optimal doses, including if possible a diuretic
or
Office blood pressure at goal but patient requiring 4 or more antihypertensive medications



Exclude Pseudoresistance

Is patient adherent with prescribed regimen?
Obtain home, work, or ambulatory blood pressure readings to exclude white coat effect



Identify and Reverse Contributing Lifestyle Factors

Obesity
Physical inactivity
Excessive alcohol ingestion
High salt, low fiber diet



Diagnostic recommendations

Discontinue or Minimize Interfering Substances

Non-steroidal anti-inflammatory agents
Sympathomimetics (diet pills, decongestants)
Stimulants
Oral contraceptives
Licorice
Ephedra



Screen for Secondary Causes of Hypertension

Obstructive sleep apnea (snoring, witnessed apnea, excessive daytime sleepiness)
Primary aldosteronism (elevated aldosterone/renin ratio)
Chronic kidney disease (creatinine clearance <30 ml/min)
Renal artery stenosis (young female, known atherosclerotic disease, worsening renal function)
Pheochromocytoma (episodic hypertension, palpitations, diaphoresis, head ache)
Cushing's syndrome (moon facies, central obesity, abdominal striae, inter-scapular fat deposition)
Aortic coarctation (differential in brachial or femoral pulses, systolic bruit)

