Common Problems and Errors In Treating Hypertensive Urgencies and Emergencies

Colman Ryan, MD FACC

ASH Clinical Specialist in Hypertension

New Recommendations for Hypertension – JNC 8 - 2013

1. Start treatment in patients over age 60 at 150 mm Hg. or above

2. Aim for 140/90 as the upper limits in all patients (except for patients over 80 yrs. old in whom the aim is 150/90)

3. There is no evidence that lower is better in patients controlled to less than 140/90.

4. In those patients in whom the blood pressure is in the lower range of normal and are asymptomatic there is no indication to change medication or allow the pressure to drift up to higher levels.

5. Diastolic pressures in patients over 60 yrs. old may be harmful when consistently less than 60mm Hg

Home BP monitors (OMRON etc.) consistently need lower diastolic pressures in older individuals than either intra-arterial or audible Korotkoff sounds (C. Ryan)

Heart Disease and Stroke Statistics Update 2014.

Circ. 2014; 129: 399-410

Prevalence of Risk Factors	
High Blood Pressure	40.6%
Smoking	13.7%
Poor Diet	13.2%
Insufficient Activity	11.9%
Diabetes	8.8%
Abnormal Cholesterol	13.8% (> 240 mg / DL)
Obesity (BMI > 30%)	35%
Obesity in ages 6-11	18.8%

Death Rates - USA

- **2000 – 2010**
  - Death rates from CVD declined 31%
  - 2150 pts. die each day!
  - CAD caused 1/6th of deaths
  - Stroke deaths declined 22.8%
  - No decline in death from CHF

Cardiovascular Procedures + Costs

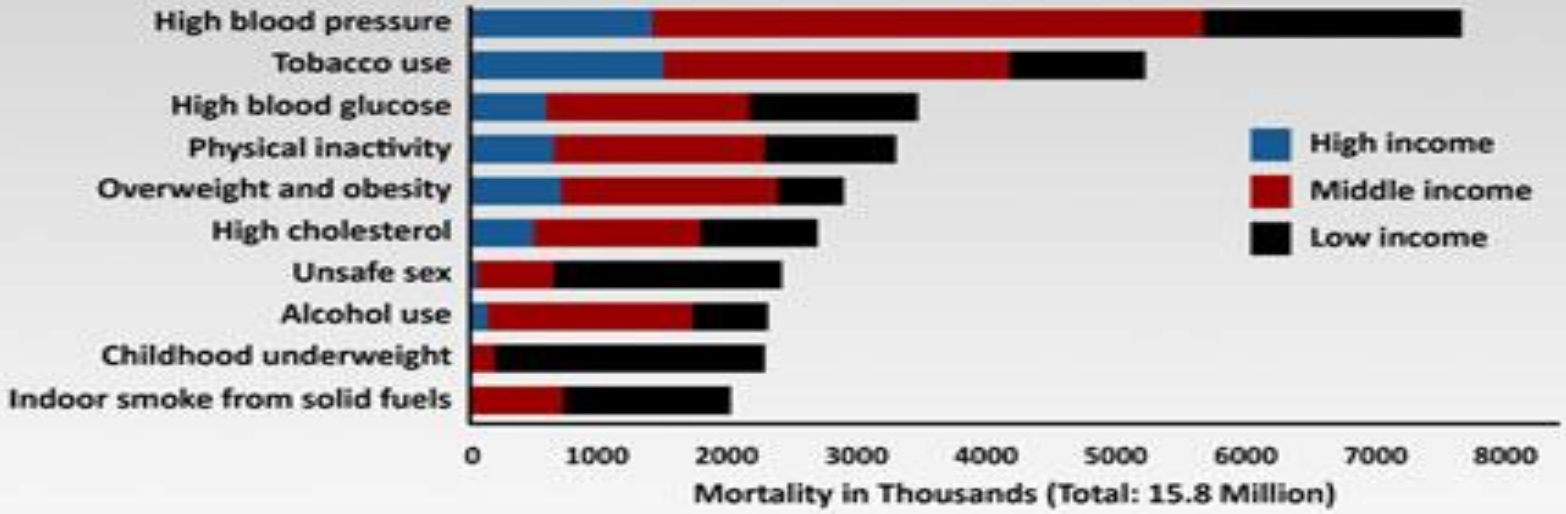
- **2000 - 5.9 million procedures done**
- **2010 - 7.6 million procedures done**
  - Cost for CVD Care in 2010
    - $315 Billion.
  - Cost for Cancer Care in 2010
    - $201 Billion.

1977	2013
1. Long hair	Longing for hair
2. KEG	EKG
3. Acid rock	Acid reflux
4. Seeds and stems	Roughage

1977	2013
5. Hoping for a BMW	Hoping for a BM
6. Going to a new, hip joint	Receiving a new hip joint
7. Rolling Stones	Kidney Stones
8. Disco	Costco

1977	2013
9. Passing the drivers' test	Passing the vision test
10. Whatever	Depends

Global Health Risks

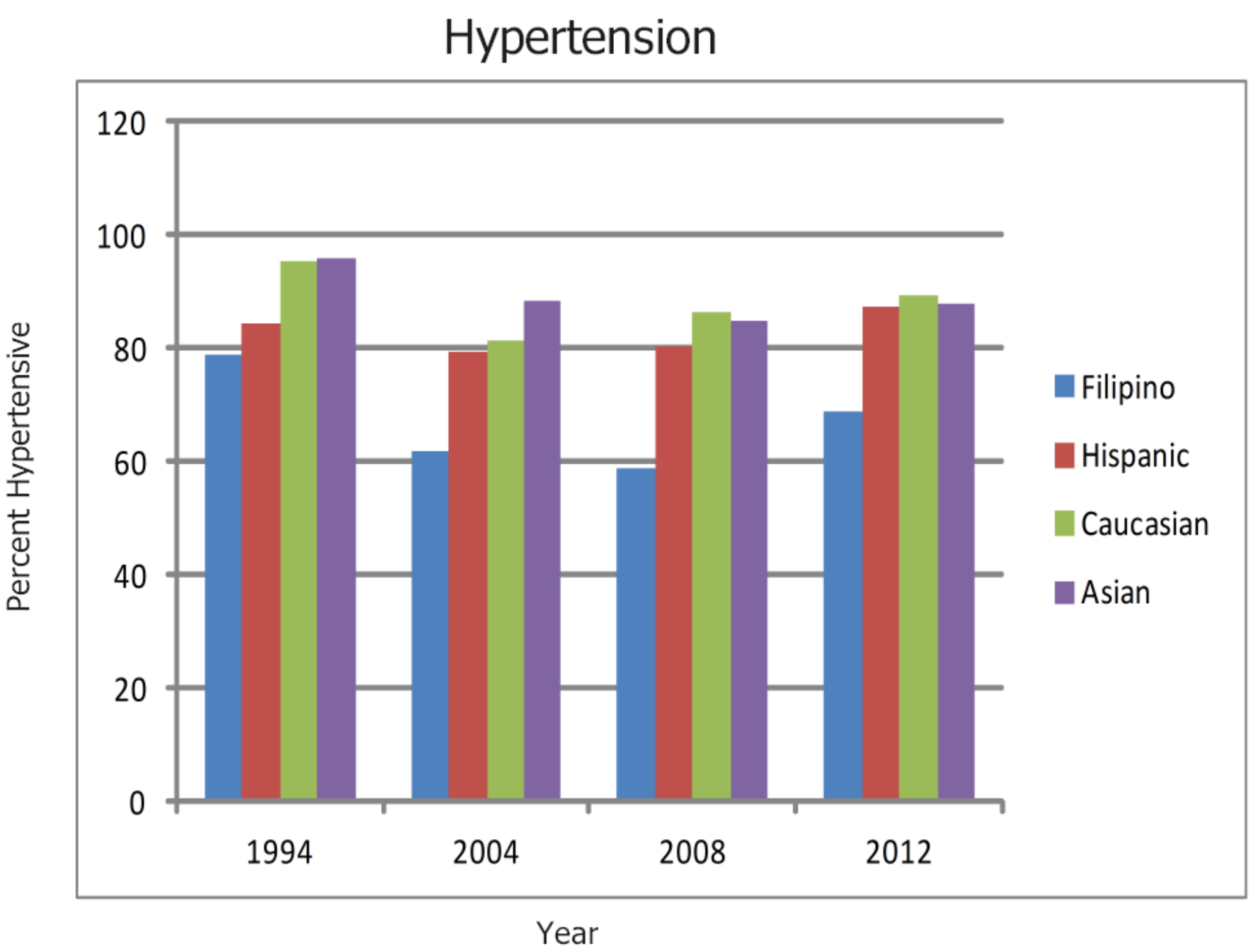


Deaths attributed to 10 leading risk factors, by country income level, 2004

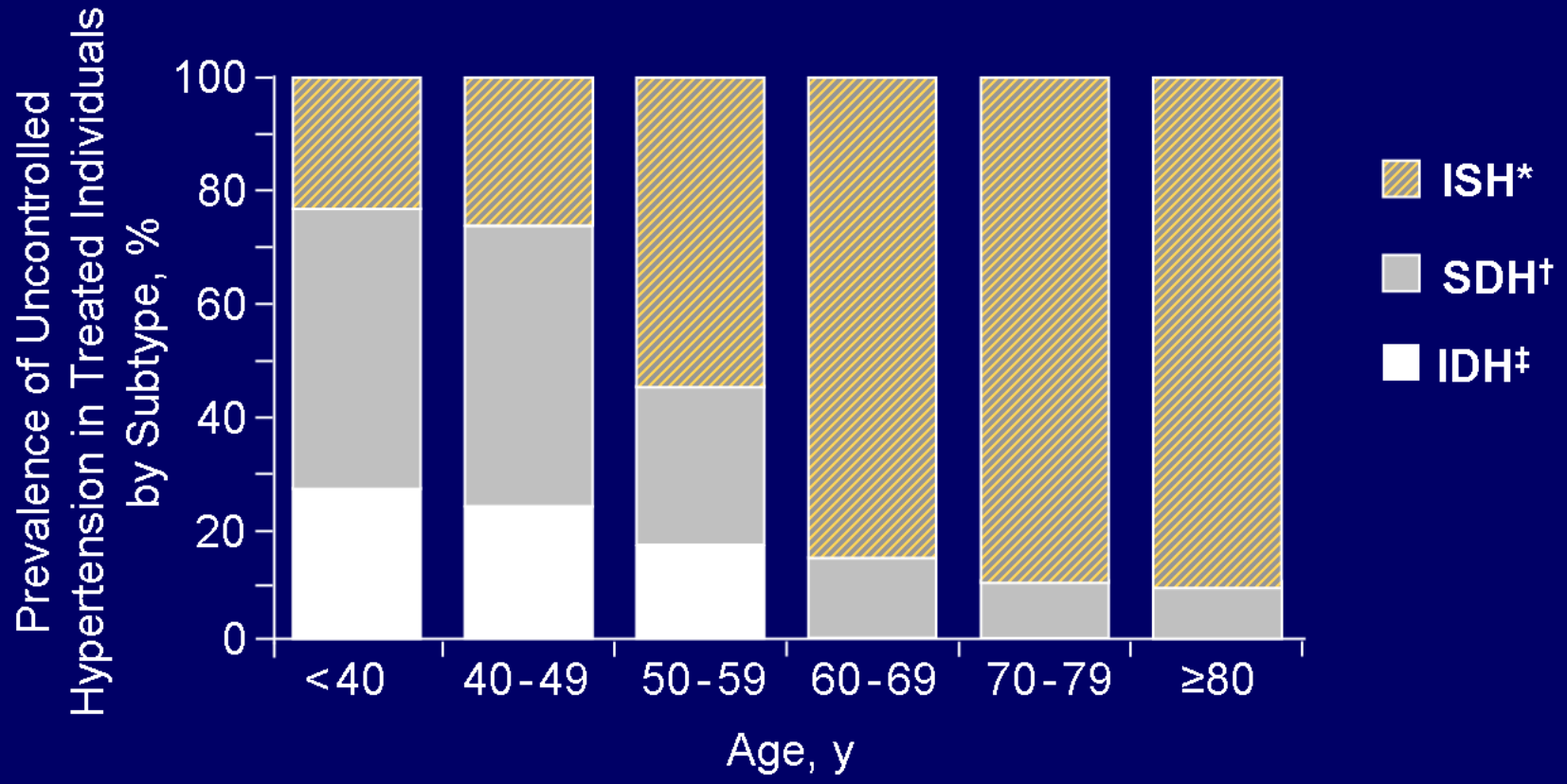
HYPERTENSION

World Health Organization. Global Health Risks: Mortality and burden of disease attributable to selected major risks. 2009.

theheart.org Medscape EDUCATION


Hypertension
120
100
80
60
40
20
0
Percent Hypertensive
1994
2004
2008
2012
Year
Filipino
Hispanic
Caucasian
Asian

Incidence of Systolic Hypertension Increases With Age

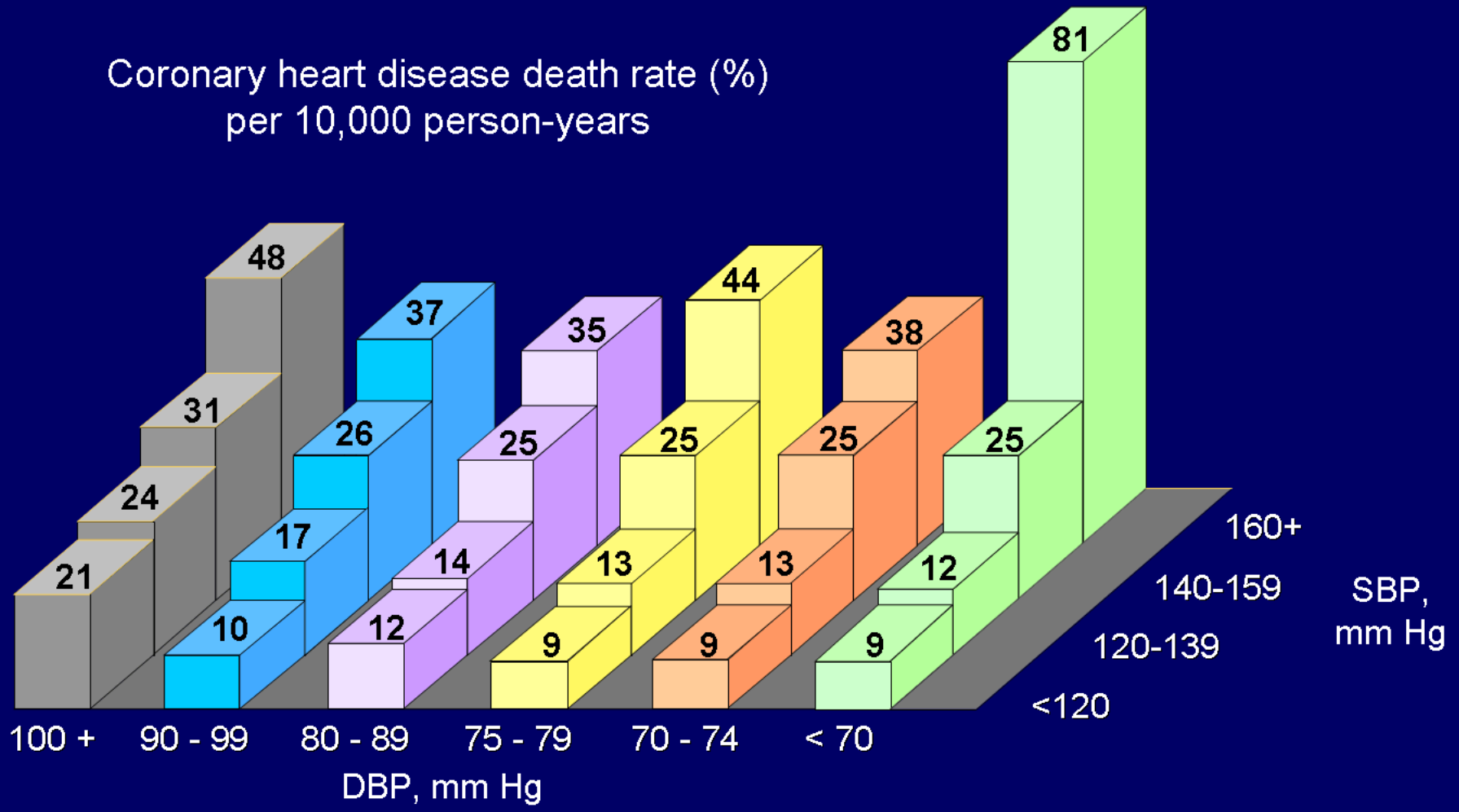


*SBP ≥140 mm Hg and DBP <90 mm Hg.
†SBP ≥140 mm Hg and DBP ≥90 mm Hg.
‡SBP <140 mm Hg and DBP ≥90 mm Hg.

ISH, isolated systolic hypertension; SDH, systolic/diastolic hypertension; IDH, isolated diastolic hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Adapted from Franklin SS et al. *Hypertension*. 2001;37:869-874.

Systolic Blood Pressure Is a More Important Cardiovascular Risk Factor Than Diastolic Blood Pressure

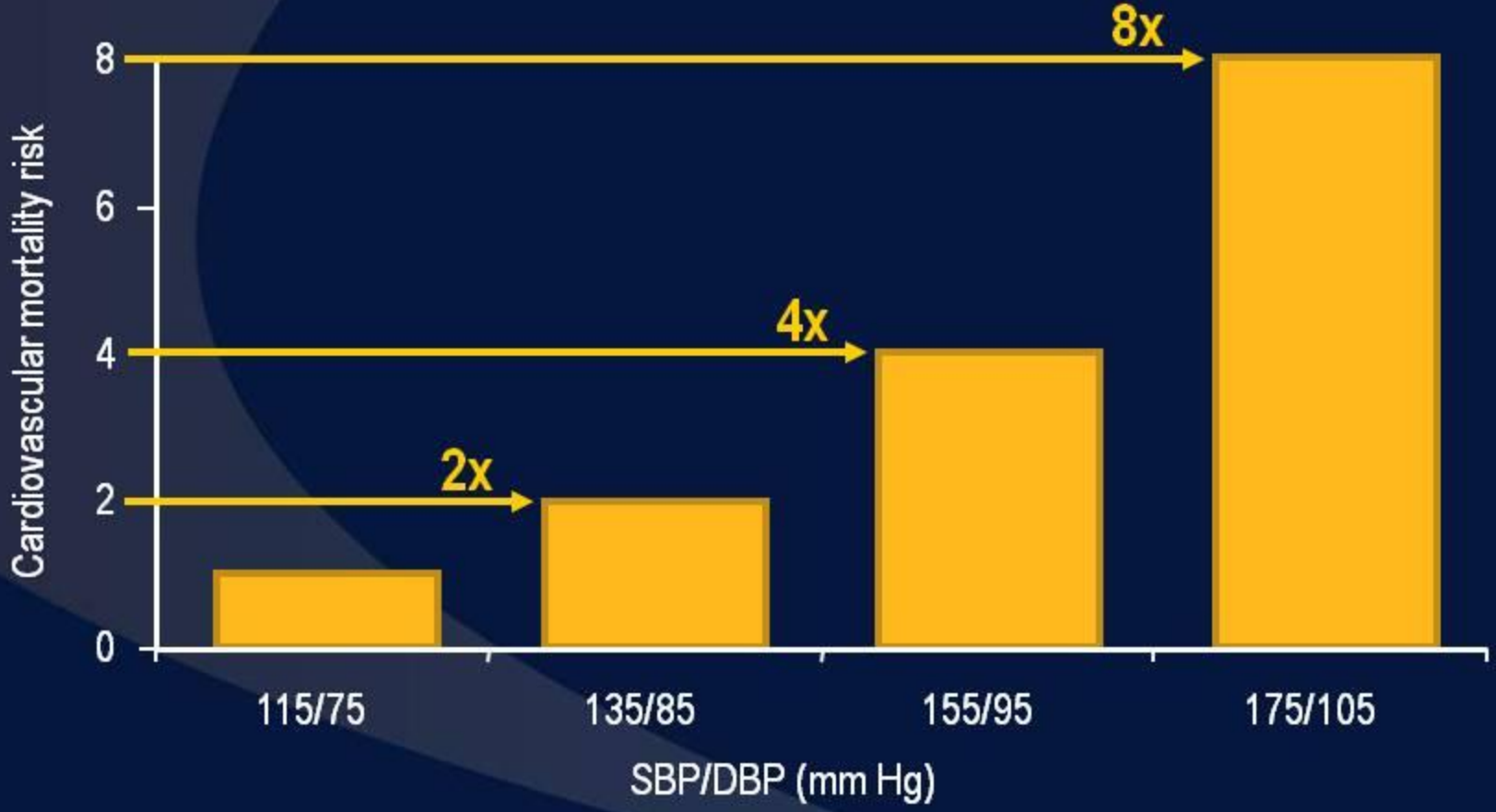


SBP, systolic blood pressure; DBP, diastolic blood pressure.

Neaton JD et al. *Arch Intern Med.* 1992;152:56-64.

BP and Cardiovascular Mortality

*Risk Doubles With Every 20/10-mm Hg Increment**

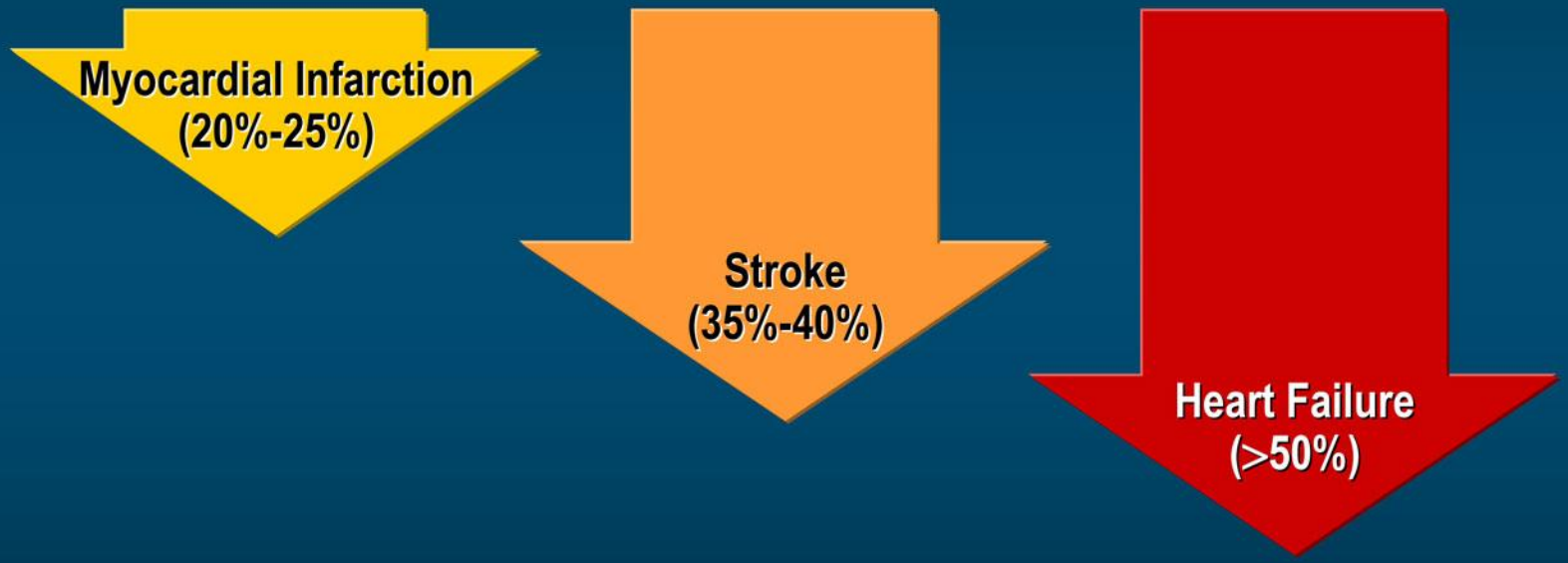


*Individuals aged 40-69 years, starting at blood pressure 115/75 mm Hg.
BP=blood pressure; SBP=systolic BP; DBP=diastolic BP.

1. Prospective Studies Collaboration. *Lancet*. 2002;360:1903-1913.
2. Chobanian AV et al. *JAMA*. 2003;289:2560-2572.

According to JNC 7, Lowering BP Is Important in Reducing CV Risk

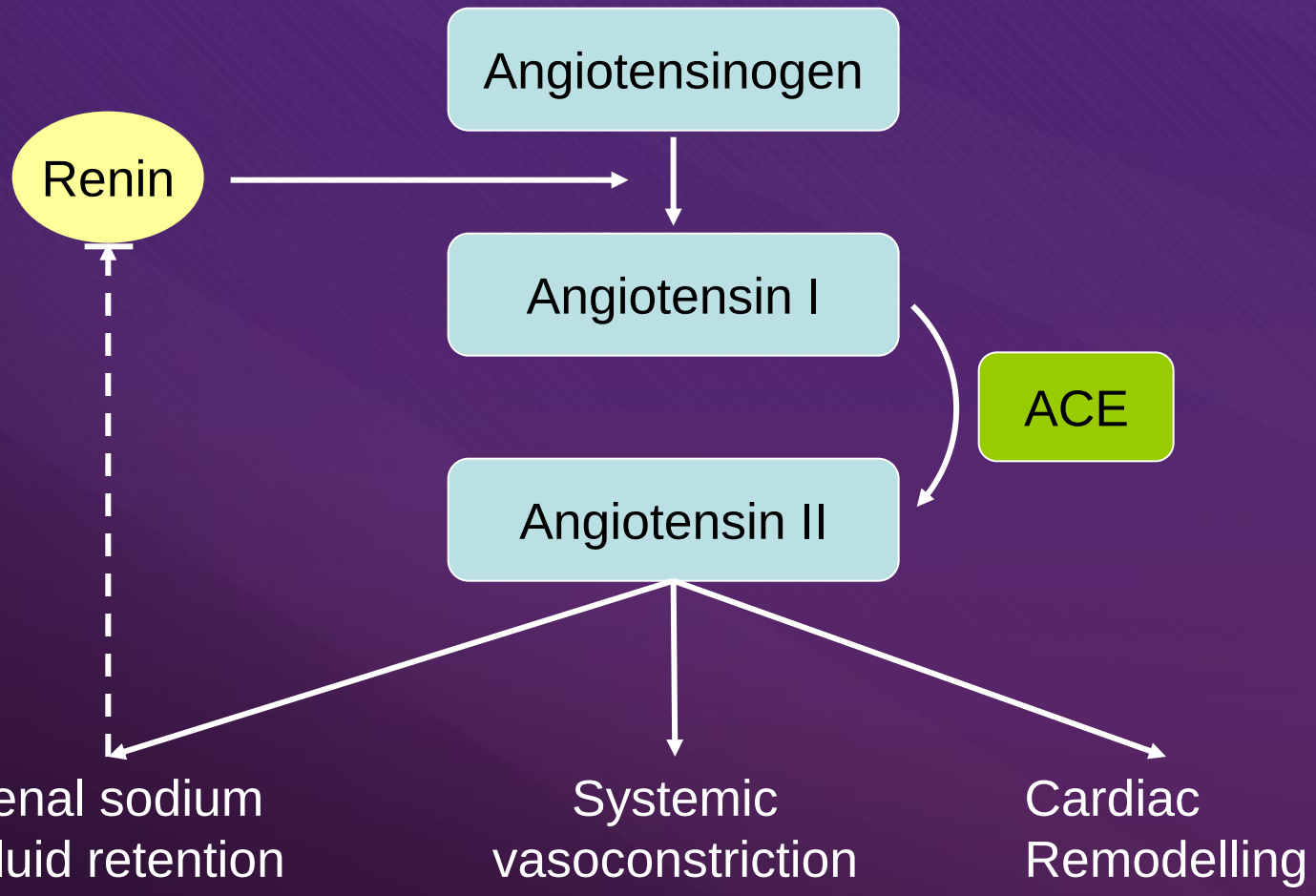
In Clinical Trials, Antihypertensive Therapy Has Been Associated With Reductions in



- Each 20–mm Hg increase in SBP or 10–mm Hg increase in DBP doubles the risk of CVD

Chobanian AV et al. *JAMA*. 2003;289:2560-2572.

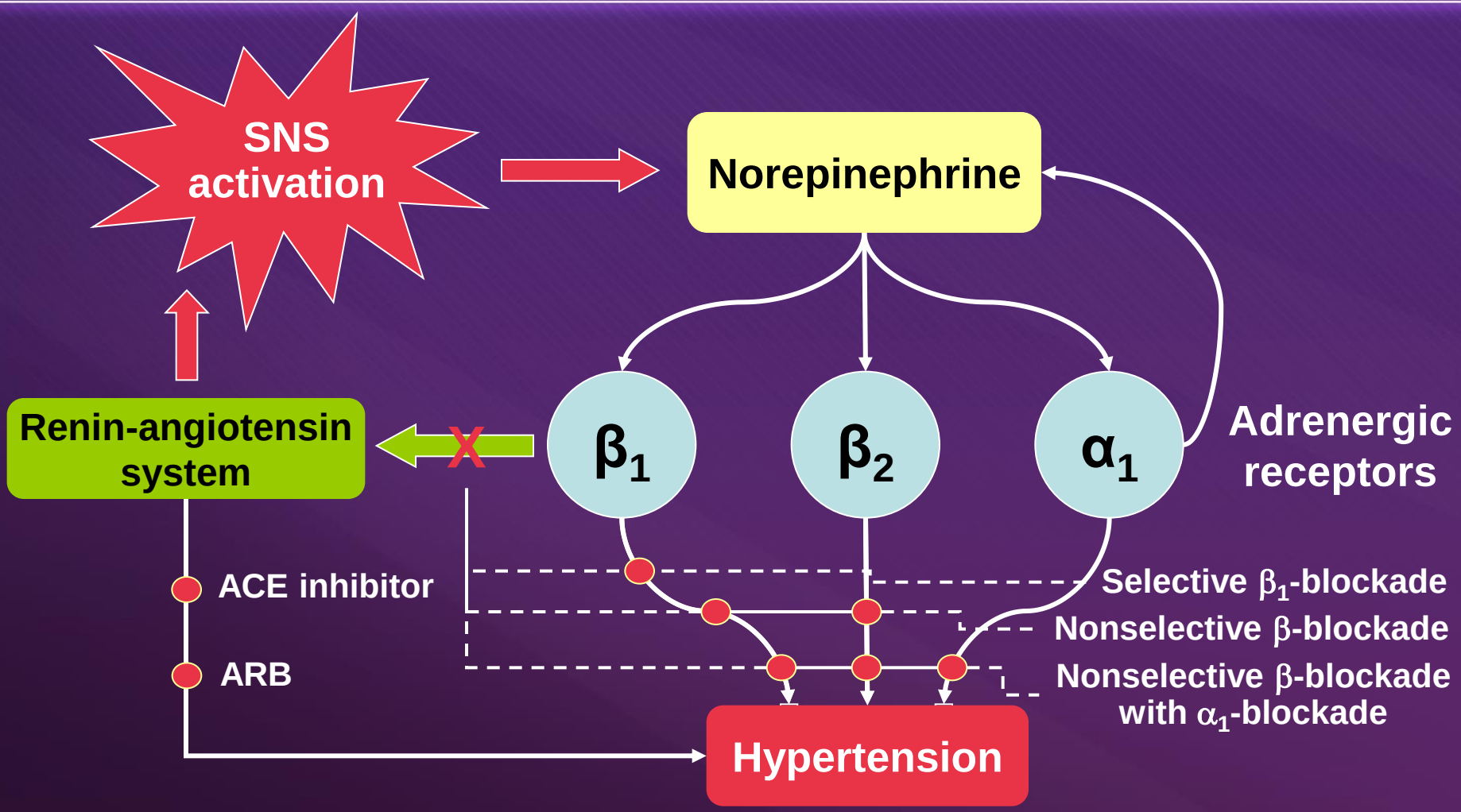
RAAS: An Important Pathway in Hypertension



RAAS=Renin-angiotensin-aldosterone system; ACE=Angiotensin-converting enzyme.

Atlas SA. *J Manag Care Pharm*. 2007;13:S9-S20.

Intersection of the SNS and RAAS Pathways

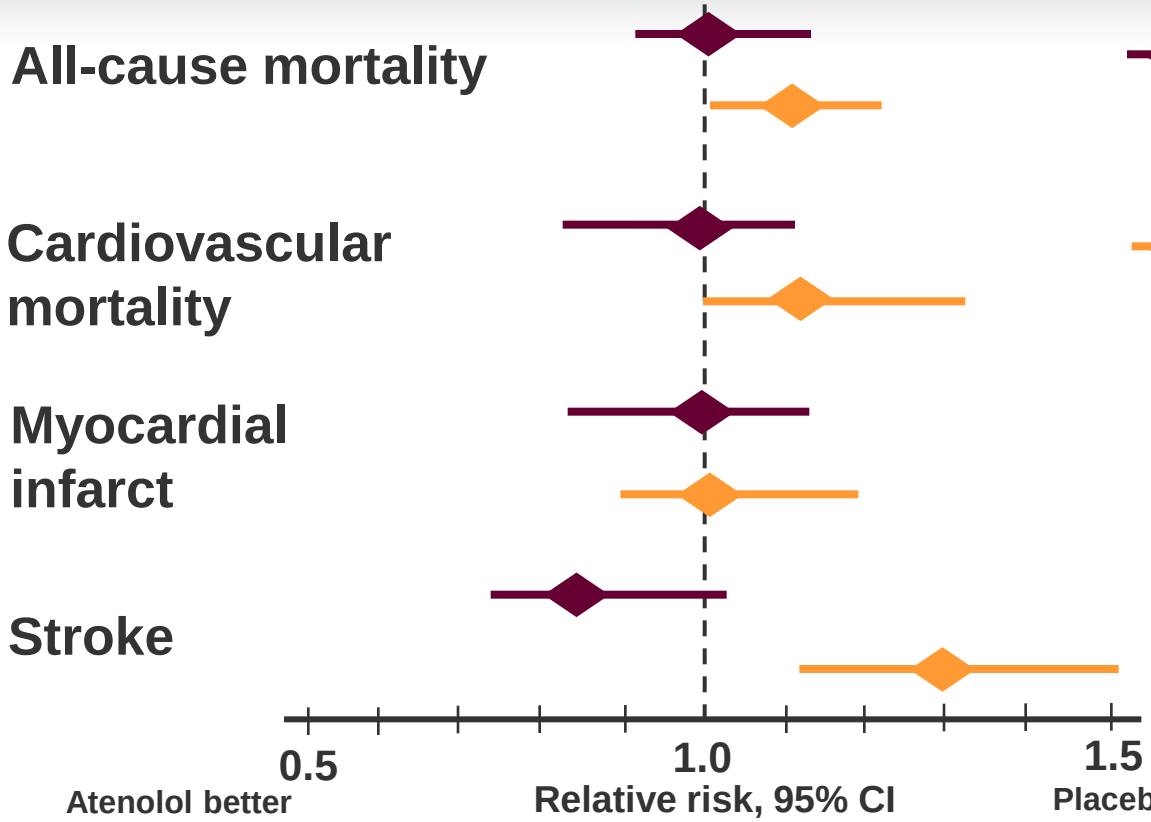


ACE=Angiotensin-converting enzyme; ARB=Angiotensin-receptor blocker.

Atlas SA. *J Manag Care Pharm*. 2007;13:S9-S20.

Adapted from Packer M. *Prog Cardiovasc Dis*. 1998;41:39-52.

Use of β_1-Selective Atenolol and Adverse Outcomes in Patients With Hypertension



Atenolol vs placebo or no treatment

4 studies included (n=6825)

Atenolol vs other antihypertensive therapy

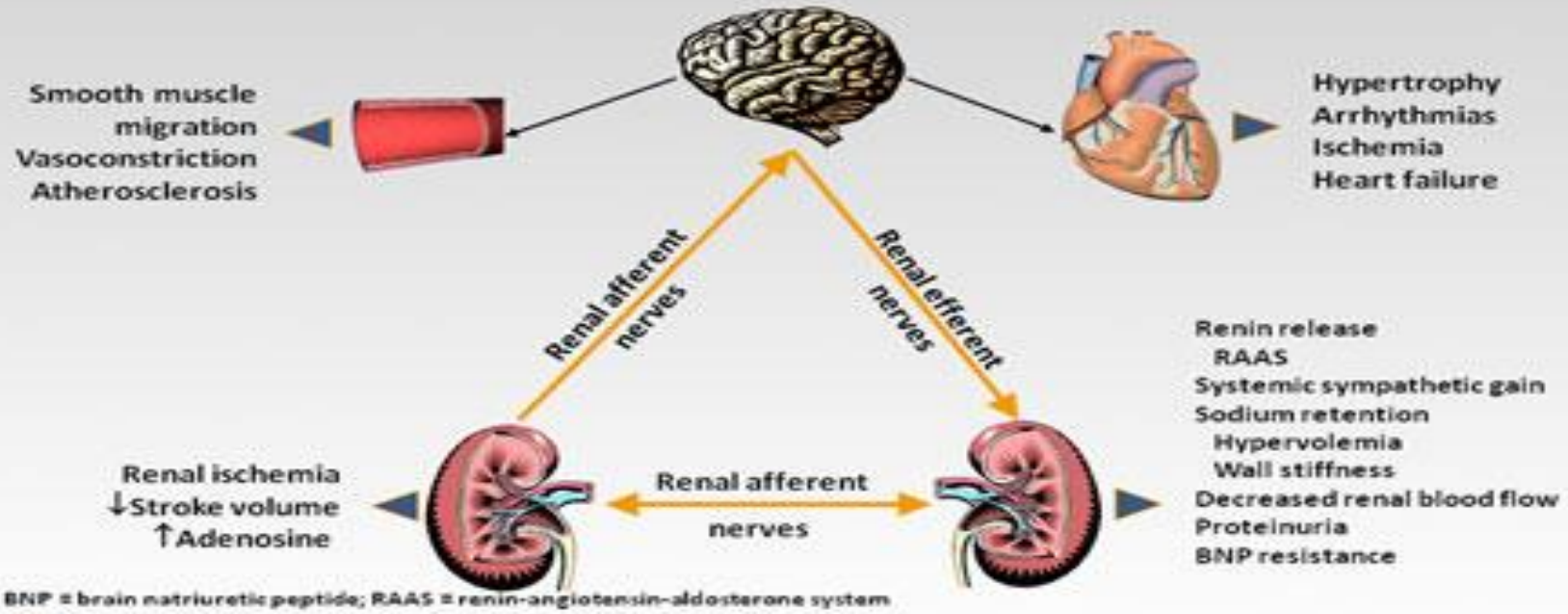
5 studies included (n=17,671)

Primary outcomes studies in hypertension have not been conducted with COREG CR.

Trials included in meta-analysis vs placebo: Treatment of Hypertension in Elderly Patients in Primary Care (HEP); Dutch Transitory Ischemic Attack Trial; Tenormin After Stroke and TIA (TEST); Medical Research Council Trial of Treatment of Hypertension in Older Adults (MRC Old). Trials included in meta-analysis vs other antihypertensive agent: MRC Old; UKPDS; European Lacidipine Study of Atherosclerosis (ELSA); Heart Attack Primary Prevention in Hypertension Trial (HAPPHY); Losartan Intervention for Endpoint Reduction Study (LIFE).

Carlberg B, et al. *Lancet*. 2004;364:1684-1689.

Renal Sympathetic Activation in Hypertension



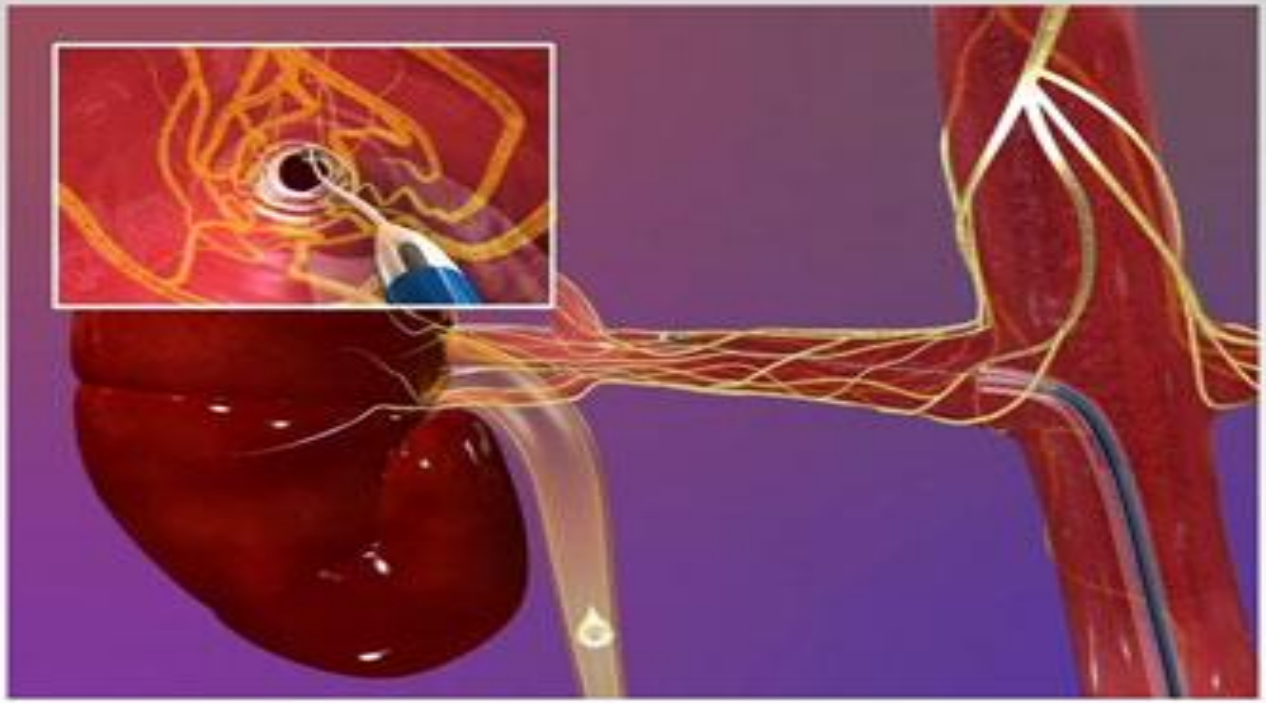
BNP = brain natriuretic peptide; RAAS = renin-angiotensin-aldosterone system

HYPERTENSION

From Krum H, et al. *Circulation*. 2011;123:209-215.
Republished with permission.

theheart.org Medscape EDUCATION

Placement of Renal RF Catheter



HYPERTENSION

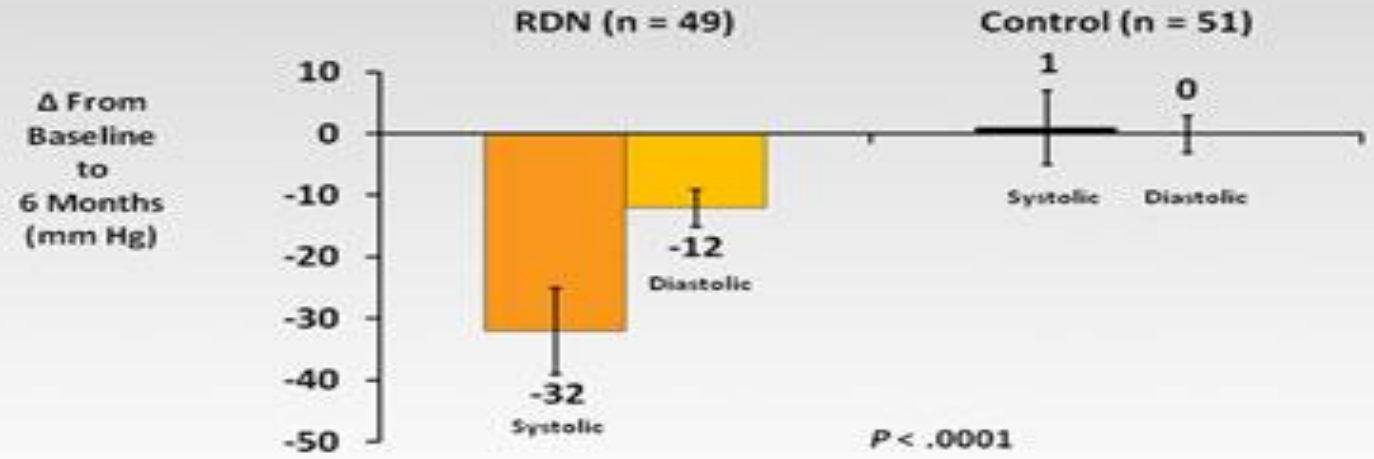
From Krum H, et al. *Circulation*. 2011;123:209-215.
Republished with permission.

theheart.org Medscape EDUCATION

Symplicity HTN-2: Background Medications

	Renal denervation group (n = 52)	Control group (n = 54)
Number of antihypertensive medications, mean (SD)	5.2 (1.5)	5.3 (1.8)
Patients on medication for hypertension for more than 5 years	37 (71%)	42 (78%)
Patients on 5 or more medications	35 (67%)	31 (57%)
Patients receiving (drug class)		
Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker	50 (96%)	51 (94%)
Direct renin inhibitor	8 (15%)	10 (19%)
Beta-blocker	43 (83%)	37 (69%)
Calcium channel blocker	41 (79%)	45 (83%)
Diuretic	46 (89%)	49 (91%)
Aldosterone antagonist	9 (17%)	9 (17%)
Vasodilator	8 (15%)	9 (17%)
Alpha-1 blocker	17 (33%)	10 (19%)
Centrally acting sympatholytic	27 (52%)	28 (52%)

Symplicity HTN-2: Change in 6-Month Blood Pressure Measured in Office



RDN = renal denervation

HYPERTENSION

Reprinted from Symplicity HTN-2 Investigators, et al. *Lancet*. 2010; 376:1903-1909. With permission from Elsevier.

theheart.org

Medscape EDUCATION

Symplicity HTN-1

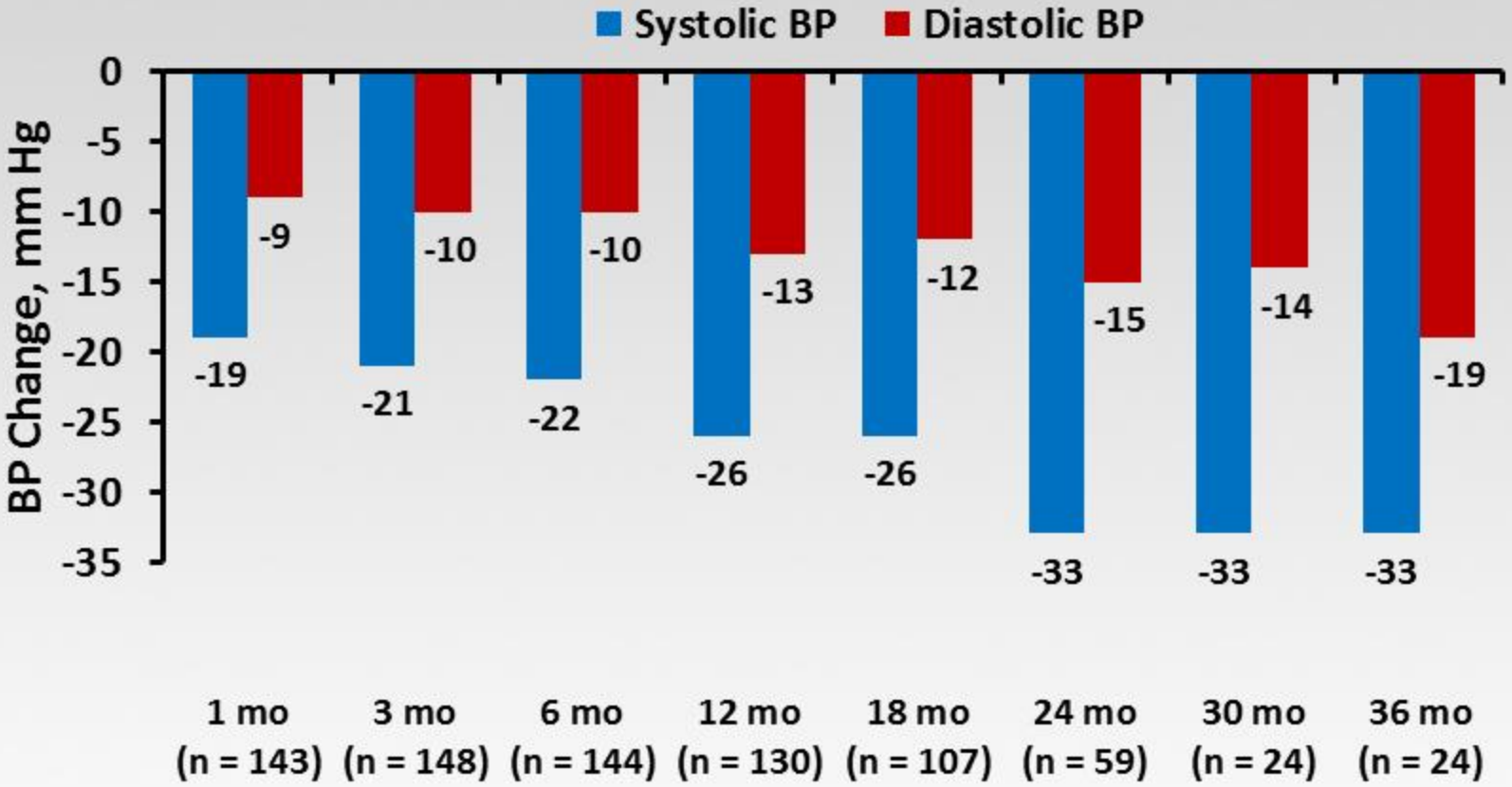
Inclusion Criteria

- Office SBP ≥ 160 mm Hg
- ≥ 3 antihypertensive medications (1 of them a diuretic)

Exclusion Criteria

- Significant renal artery abnormalities or prior renal artery intervention
- eGFR < 45 mL/min/1.7 3m^2 (MDRD formula)
- Type 1 diabetes mellitus
- Stenotic valvular heart disease, for which reduction of blood pressure would be hazardous
- Secondary cause of hypertension other than sleep apnea or chronic kidney disease

Symplicity HTN-1: 36-Month Follow-up Sustained Reductions in Blood Pressure



P < .001 for systolic and diastolic BP changes from baseline

HYPERTENSION

Krum H, et al.[10]

Slide courtesy of Dr Murray Esler

theheart.org from WebMD

Medscape EDUCATION

Symplicity HTN-2

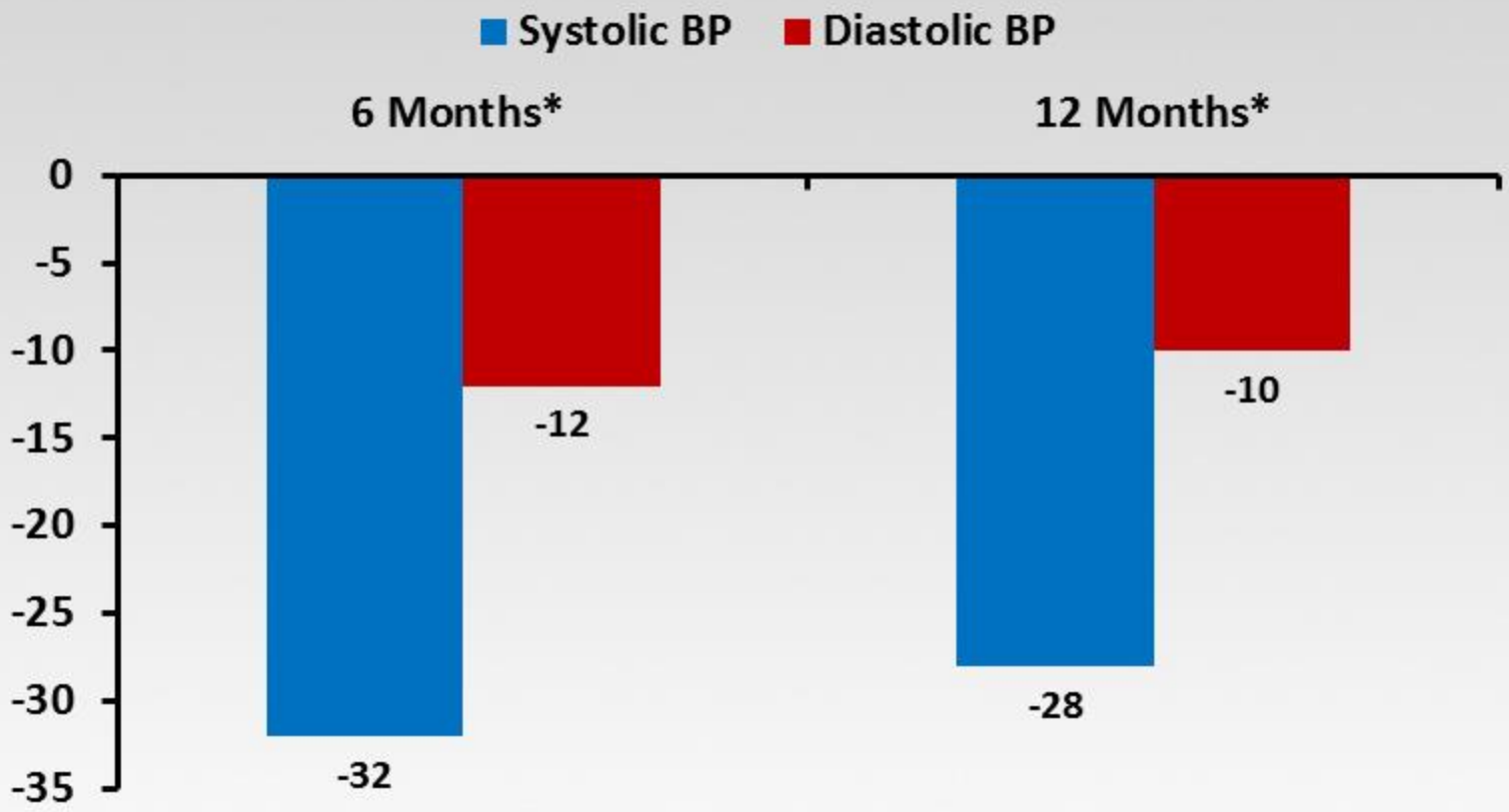
Inclusion Criteria

- Office SBP ≥ 160 mm Hg (≥ 150 mm Hg with type 2 diabetes mellitus)
- ≥ 3 antihypertensive medications (1 of them a diuretic)

Exclusion Criteria

- Significant renal artery abnormalities or prior renal artery intervention
- eGFR < 45 mL/min/1.73 m^2 (MDRD formula)
- Type 1 diabetes mellitus
- Stenotic valvular heart disease, for which reduction of blood pressure would be hazardous
- MI, stroke, or unstable angina in the prior 6 months

Symplicity HTN-2: 12-Month Follow-up Change in Office Blood Pressure (mm Hg)



*$P < .001$ for systolic diastolic BP changes from baseline

Esler MD, et al.[12]
Slide courtesy of Dr Murray Esler

Different Approaches That Target the Sympathetic Nervous System in RH

Catheter-based radiofrequency renal nerve ablation (approved for use in Europe, Australia, and other countries; phase 3 trial ongoing in the USA)

Other methodology for renal denervation (under investigation):

- Focused ultrasound
- Heat therapy

Carotid baroreceptor stimulation (under investigation)

Different Approaches That Target the Sympathetic Nervous System in RH

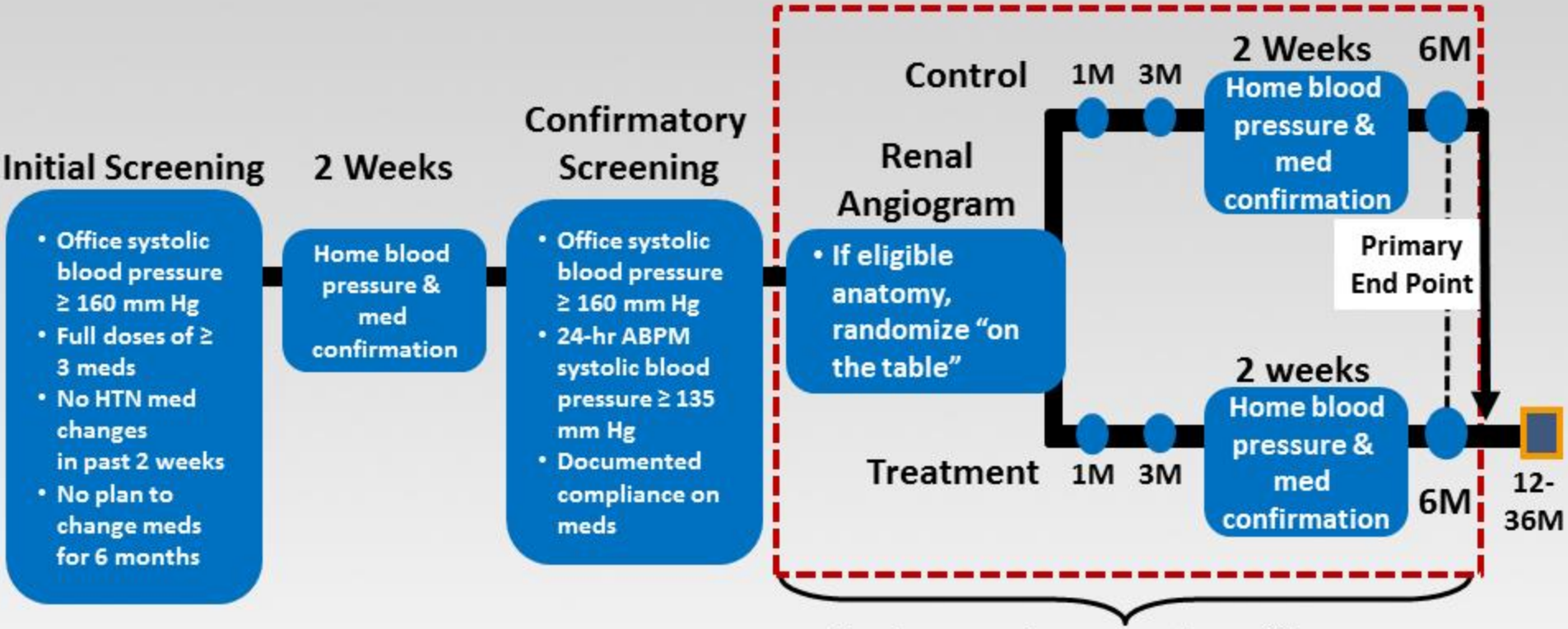
Catheter-based radiofrequency renal nerve ablation (approved for use in Europe, Australia, and other countries; phase 3 trial ongoing in the USA)

Other methodology for renal denervation (under investigation):

- Focused ultrasound
- Heat therapy

Carotid baroreceptor stimulation (under investigation)

SYMPLICITY-3: Study Design



- Patient and research staff assessing blood pressure and performing follow-ups are blinded to treatment status
- No changes in medications for 6 months

http://clinicaltrials.gov/ct2/show/NCT01418261[14]

Problems with response to severe hypertension.

- Jumping too fast: responding to single or multiple blood pressures under circumstances of pain, distress, or anxiety – “Emergency room pseudohypertension”
- Reacting too slowly: persistent severe elevations of hypertension being ignored.
- Inappropriate responses…
  Oral medications, Nitropaste, and failure to move to an intensive care setting.

Choice of Medication

- **Oral Nifedipine or Clonidine alone are inappropriate. Sublingual Nitroglycerine and Nifedipine are dangerous.**

- **Hydralazine (IV or IM) is also dangerous as it may not work at all or work too well. Hydralazine is also associated with tachycardia which is dangerous for most patients.**

Choice of Medication (cont…)

- IV Nitroglycerine is not the drug of choice at anytime except when hypertension accompanies pulmonary edema or acute coronary syndromes in conjunction wit a beta blocker. This is a venodilator with poor arteriolar dilatation.
- Diuretics e.g. IV Furosemide are not useful for hypertensive emergencies or urgencies.
- Relief of pain alone may allow blood pressure to no longer be urgent.

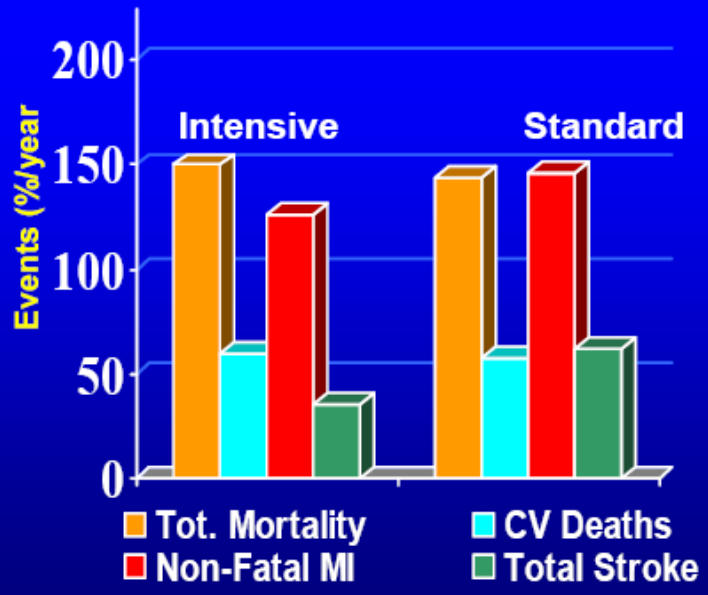
ACCORD – Blood Pressure

Action to Control Cardiovascular Risk in Diabetes

American Heart Association. | American Stroke Association.
Learn and Live.

BACKGROUND: Adults who have diabetes mellitus and hypertension are at increased risk for cardiovascular disease. Evidenced-based guidelines from the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) recommends blood pressure goals of less than 130/80 mmHg in people with diabetes. **PURPOSE:** To assess cardiovascular risk reduction in high risk adults with type 2 diabetes when systolic blood pressure is maintained below 120mmHg. **METHODS:** 4,733 patients with T2DM, high BP, and either pre-existing CVD or a high risk for developing it from 77 US and Canadian based medical centers were randomly assigned to a target systolic BP of either <120 mmHg or <140 mmHg. Various combinations of blood-pressure-lowering medications were used to achieve goals.

Outcome Events



Primary Endpoint: Combined rate for a major CVD event, specifically nonfatal MI, nonfatal stroke, or CV death.

Secondary Endpoints: Total mortality, cardiovascular deaths, nonfatal MI, nonfatal stroke and total stroke.

Results: Systolic BP averaged 119 mm Hg in the intensive-therapy group, 134 mm Hg in the standard-therapy group.

Primary Endpoint: No significant difference between the groups in the combined rate of NF heart attack, NF stroke, or CV death (p=.20) after 4.7 y avg. follow up. Stroke risk was significantly lower with intensive therapy (36 vs. 62 strokes; p=.01).

Conclusion: This study does not support the reduction of CV risk by achieving systolic BP goals < 120mmHg in high risk type II diabetic patients.

ACCORD Study, ACC, Atlanta , GA

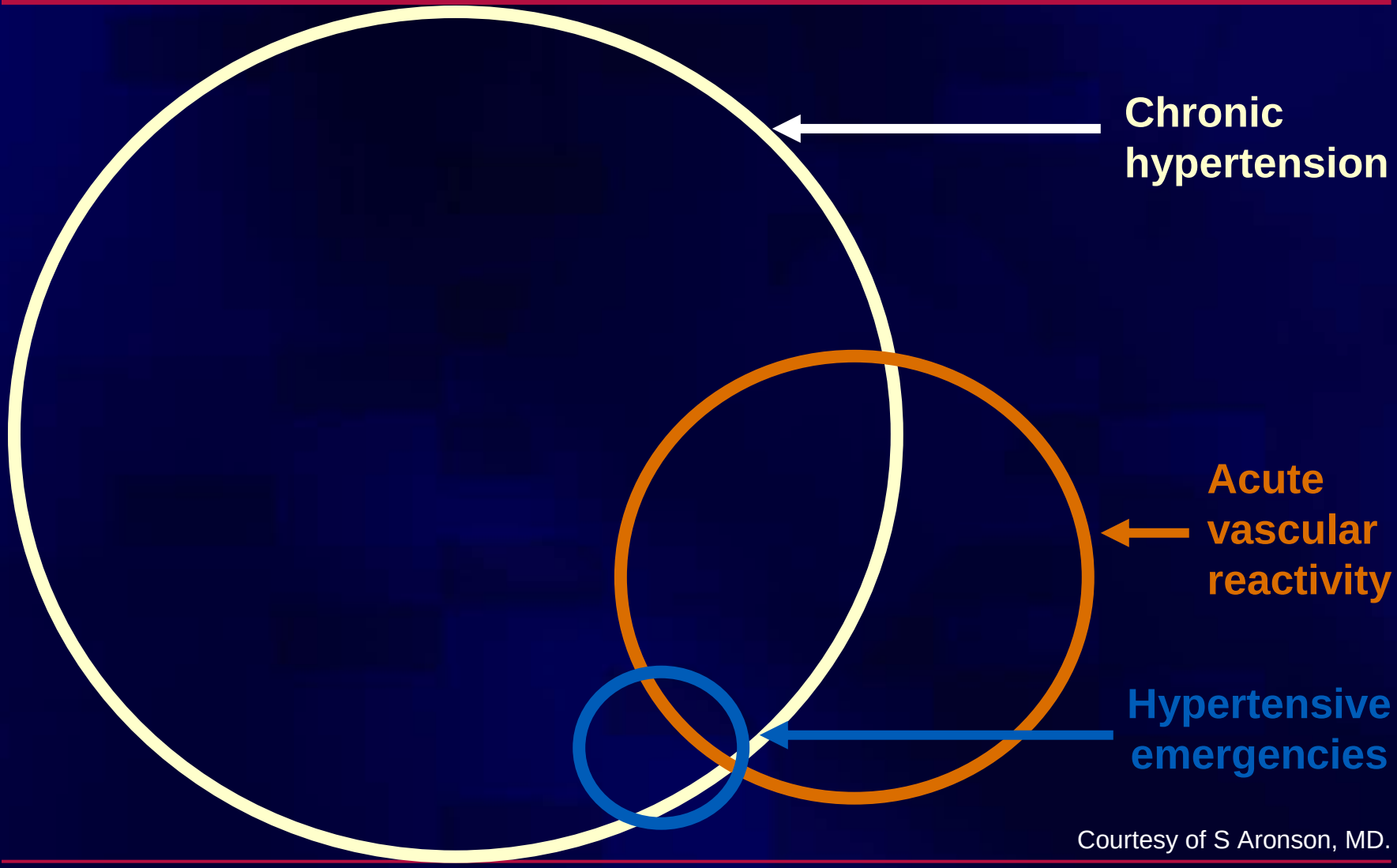
Vascular Biology Working Group

Management of Hypertensive Emergencies

Vascular Biology Working Group

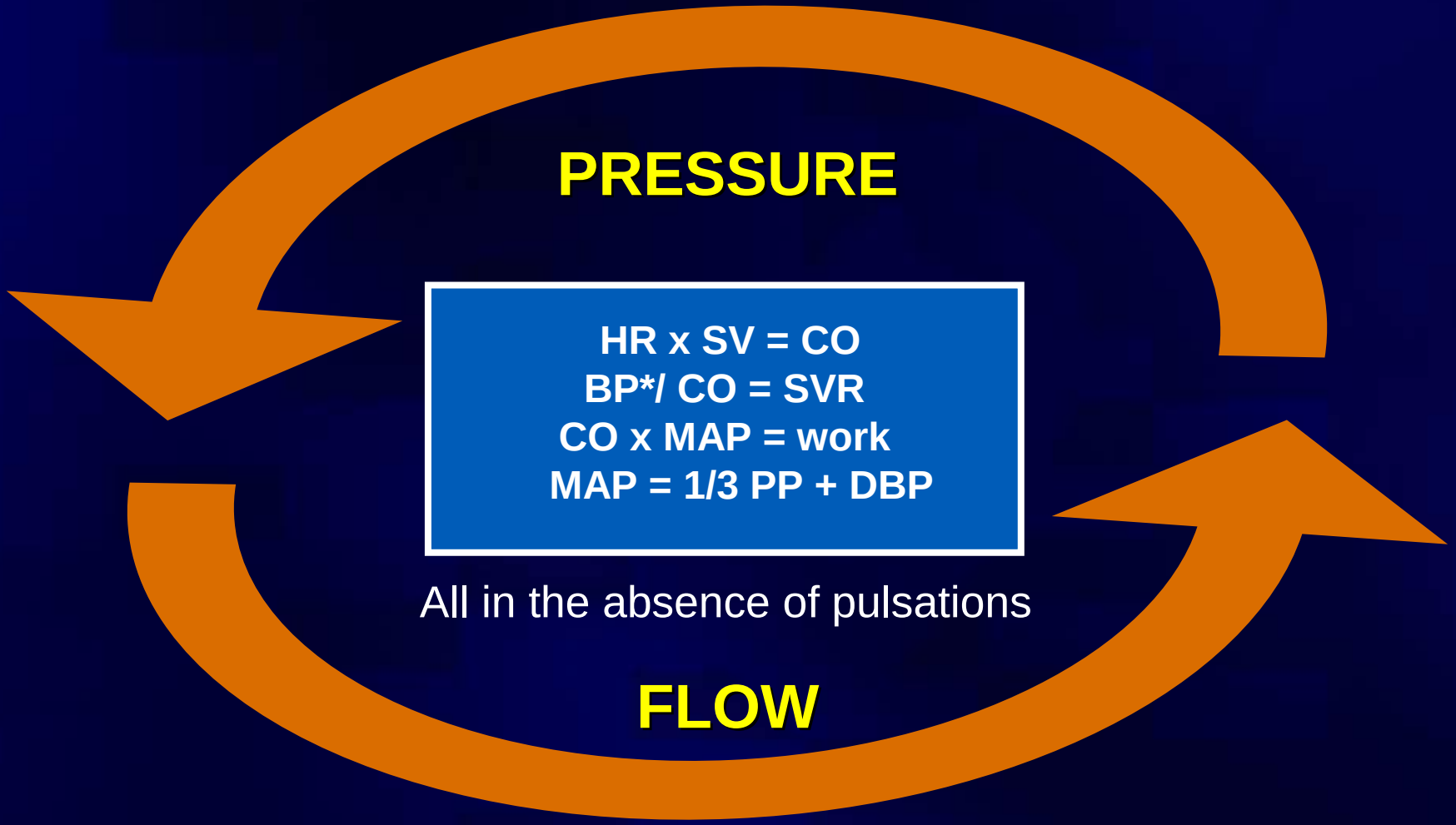
Vascular Dysfunction: Sequelae of Acute Hypertension

Acute and chronic hypertension: Clinical context



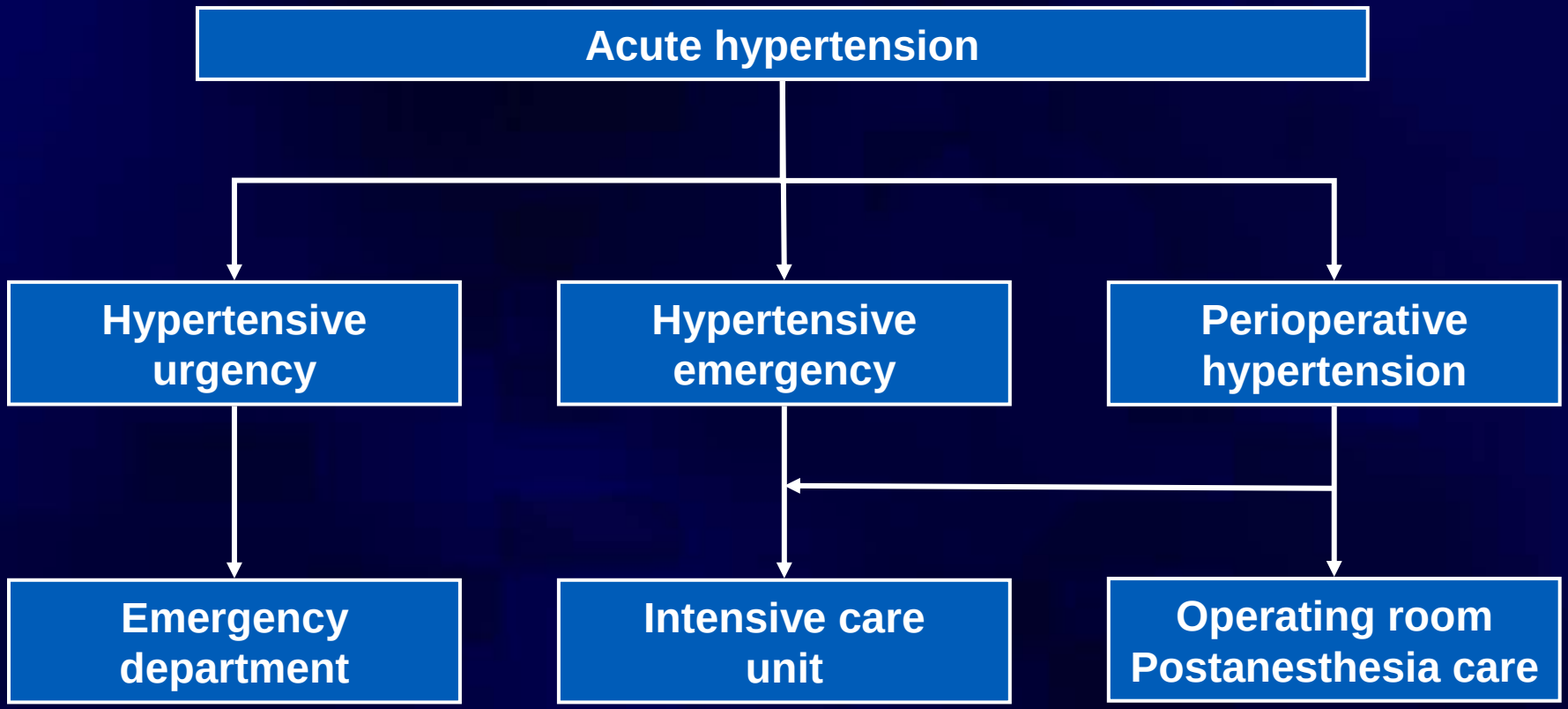
Courtesy of S Aronson, MD.

Components of blood pressure: New focus on pulse pressure



Courtesy of S Aronson, MD.

Acute hypertension: Subgroups and settings



JNC 7 definitions

Hypertensive emergency	**BP >180/120 mm Hg complicated by evidence of impending or progressive end-organ damage**
Hypertensive urgency	**Severe elevation in BP without progressive end-organ damage**

Chobanian AV et al. *Hypertension.* 2003;42:1206-52.

Hypertensive urgencies/emergencies: Patients and organ systems at risk

1% of hypertensives (1990 data). Contemporary prevalence may be lower

Cardiopulmonary
- ADHF
- ACS
- Acute pulmonary edema
- Acute aortic syndromes

Neurovascular
- Hypertensive encephalopathy
- Stroke

Ocular
- Papilloedema

Renal
- Acute renal dysfunction

ACS = acute coronary syndrome
ADHF = acute decompensated heart failure

Calhoun DA, Oparil S. *N Engl J Med.* 1990;323:1177-83.
Marik PE, Varon J. *Chest.* 2007;131:1949-62.

Hypertensive urgencies/emergencies: Prevalence of organ system complications

N = 449 presenting to Emergency Department with hypertensive urgency/emergency

	Incidence (%)
CNS	
Cerebral infarction	24.5
Hypertensive encephalopathy	16.3
Intracerebral/subarachnoid hemorrhage	4.5
CV	
Pulmonary edema	22.5
Acute congestive heart failure	14.3
ACS	12.0
Eclampsia	4.5
Aortic dissection	2.0

Zampaglione B et al. *Hypertension.* 1996;27:144-7.

Hypertensive urgencies/emergencies: Most common presenting symptoms

Urgencies

- Headache (22%)
- Epistaxis (17%)
- Faintness and psychomotor agitation (10%)

Emergencies

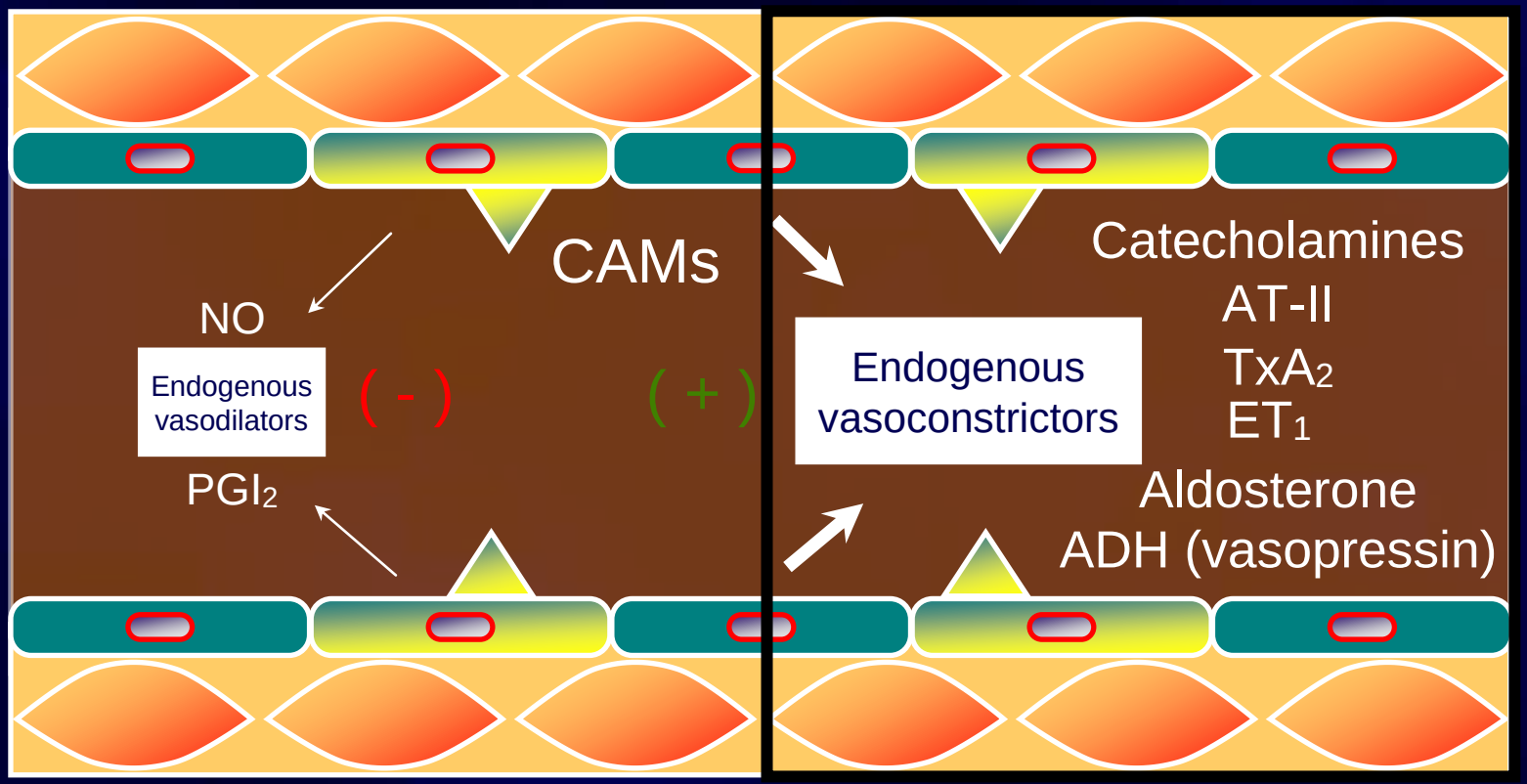
- Chest pain (27%)
- Dyspnea (22%)
- Neurological deficit (21%)

Zampaglione B et al. *Hypertension.* 1996;27:144-7.

Vascular Biology Working Group

Effects of Acute BP Elevation on the Vessel Wall

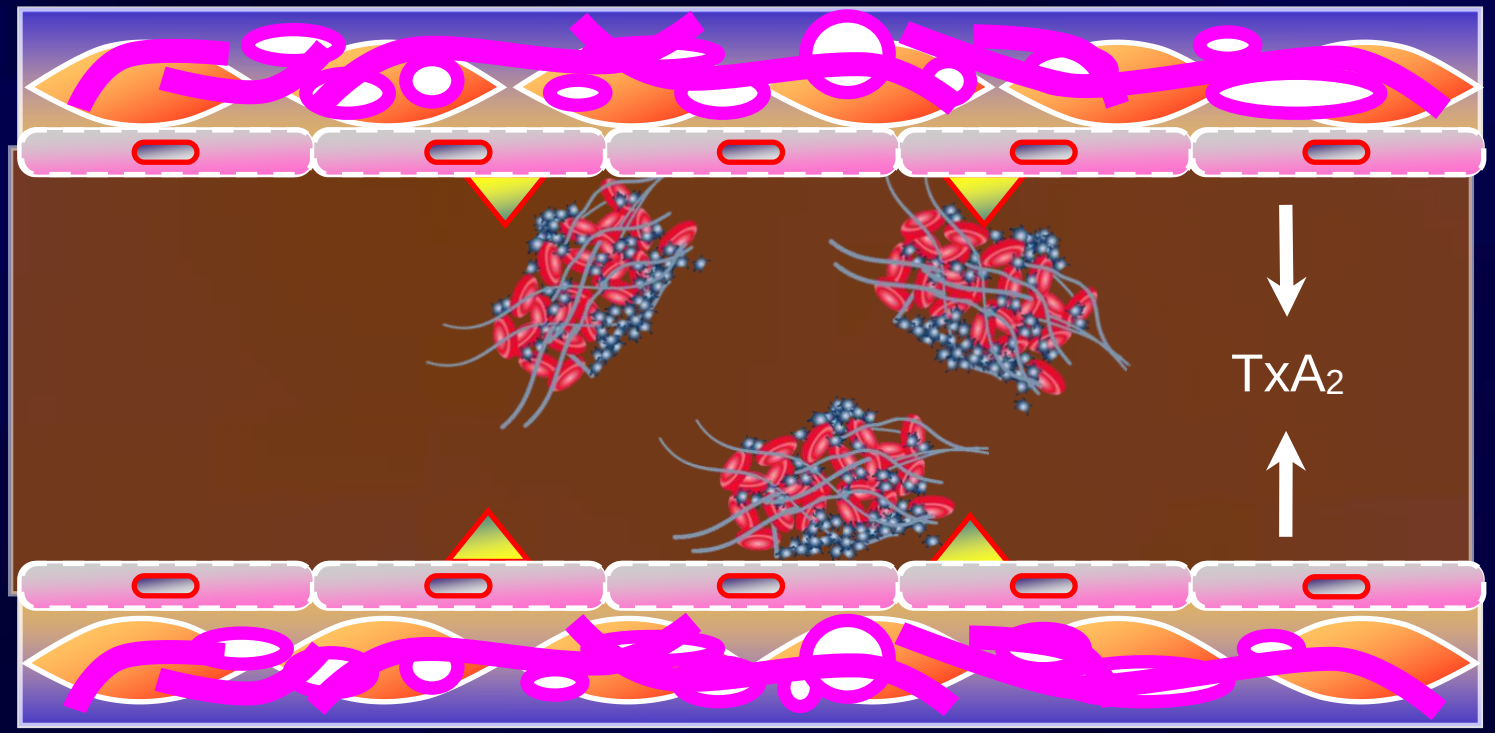
Proposed vascular pathophysiology of hypertensive urgency



Acute ↑ BP triggers ↑ cellular adhesion molecular expression

Vaughan CJ, Delanty N. *Lancet.* 2000;356:411-7.
Courtesy of JJ Ferguson III, MD.

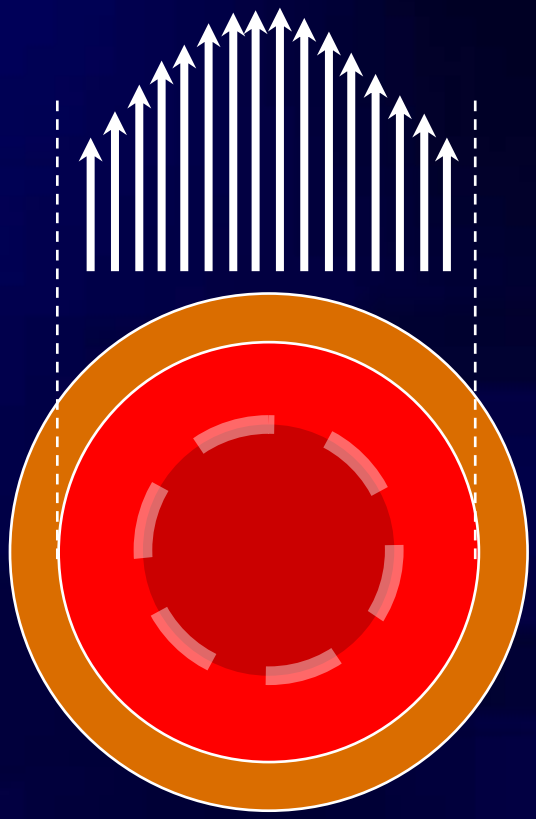
Proposed vascular pathophysiology of hypertensive emergency



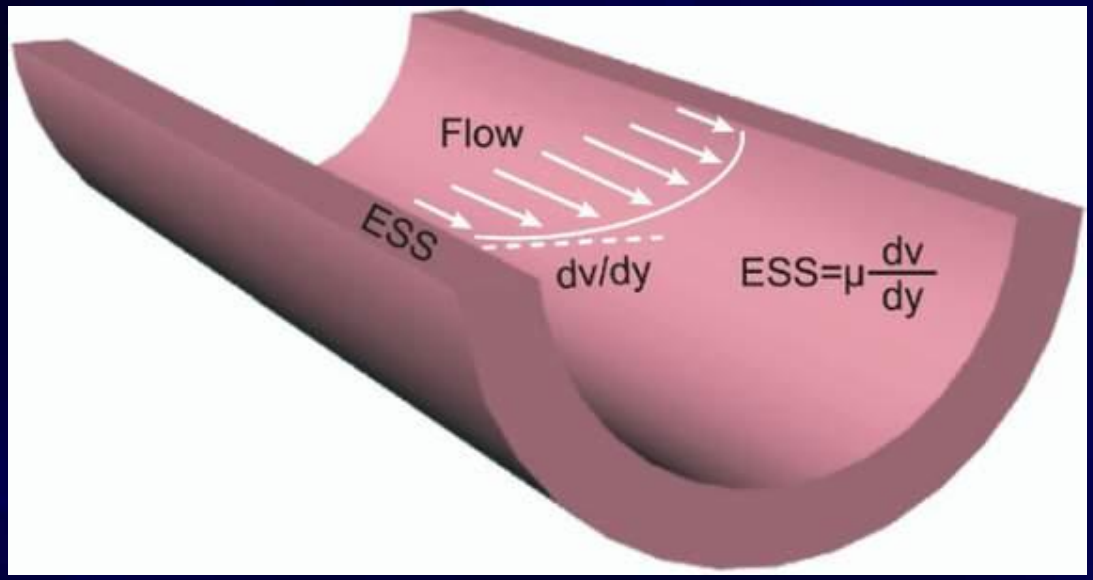
- Overwhelmed control of vascular tone leads to coagulation cascade activation
- Loss of endothelial activity coupled with coagulation and platelets promotes DIC

Vaughan CJ, Delanty N. *Lancet.* 2000;356:411-7.
Courtesy of JJ Ferguson III, MD.

Endothelial shear stress



Proportional to the product of blood viscosity (μ) and spatial gradient of blood velocity at the wall (dv/dy).



ESS = endothelial shear stress

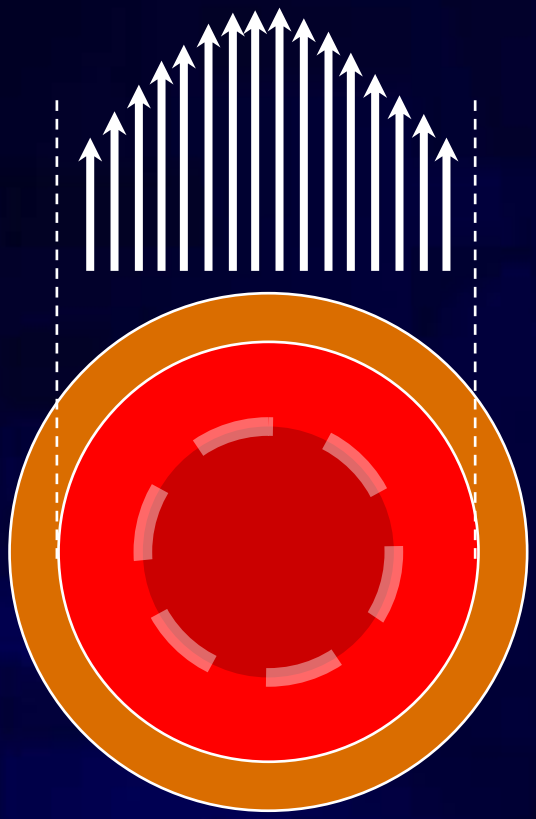
Chatzizisis YS et al. *J Am Coll Cardiol.* 2007;49:2379-93.

Implications of low and high shear stress

Effects of *low* shear stress

Atherosclerosis

Plaque rupture



Effects of *high* shear stress

Endothelial dysfunction

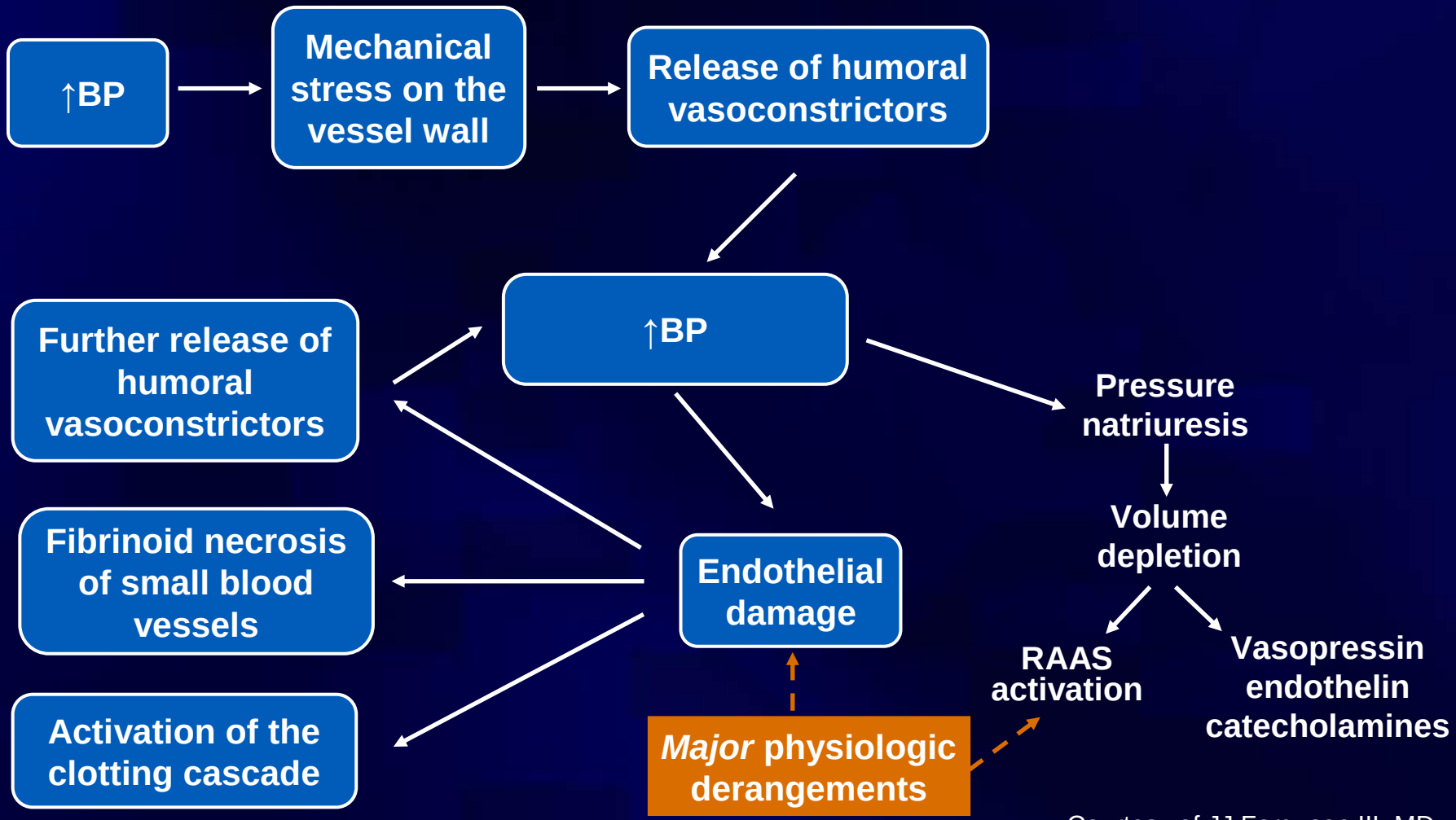
Vascular injury

Thrombosis

Neurohumoral activation

Chatzizisis YS et al. *J Am Coll Cardiol.* 2007;49:2379-93.

Summary: The pathophysiology of acute hypertensive syndromes



Courtesy of JJ Ferguson III, MD.

Profile of an ideal parenteral antihypertensive

- Treats underlying pathophysiology
- Rapid onset of action
- Predictable dose response
- Minimal dosage adjustments
- Highly selective
- No increase in intracranial pressure
- Rapidly reversible
- Low risk of overshoot hypotension or adverse reaction
- Easy conversion to oral agents
- Acceptable cost-benefit ratio

Levy JH. *Anesthesiol Clin North Am.* 1999;17:567-79.
Oparil S et al. *Am J Hypertens.* 1999;12:653-64.

JNC 7: Parenteral antihypertensive treatment

Currently available

Drug	Class	Onset / Duration
Sodium nitroprusside	Vasodilator	Faster
Esmolol	β-blocker	
Phentolamine	α-blocker	
Nitroglycerin	Vasodilator	
Fenoldopam	D1 agonist	
Labetalol	α/β-blocker	
Nicardipine	CCB	
Hydralazine	Vasodilator	
Enalaprilat	ACEI	Slower

D1 = dopamine receptor

Chobanian AV et al. *Hypertension*. 2003;42:1206-52.

Sodium nitroprusside: Profile

- Arterial and venodilator
  - ↓Preload and afterload
- Onset: Immediate
- Duration of action: 1-2 min
- Adverse effects
  - Nausea, vomiting, muscle twitching, sweating, thiocyanate and cyanide intoxication, coronary steal, maldistribution of blood flow
- Light sensitive: requires special delivery system

Chobanian AV et al. *Hypertension.* 2003;42:1206-52.
Aggarwal M, Khan IA. *Cardiol Clin*. 2006;24:135-146.

Esmolol: Profile

- Blocks β_1 receptors of heart and vasculature
  - ↓Heart rate, cardiac output, and stroke volume
- Onset: 1-2 min
- Duration of action: 10-30 minutes
- Adverse effects:
  - Hypotension, nausea, asthma, 1st degree heart block, HF

Chobanian AV et al. *Hypertension.* 2003;42:1206-52.
Aggarwal M, Khan IA. *Cardiol Clin*. 2006;24:135-146.

Fenoldopam: Profile

- Selective dopamine-1 receptor agonist
  - ↓Peripheral vascular resistance
  - ↑Renal blood flow, natriuresis, and diuresis
- Onset: <5 min
- Duration of action: 30 min
- Adverse effects:
  - Tachycardia, headache, nausea, flushing

Chobanian AV et al. *Hypertension.* 2003;42:1206-52.
Oparil S et al. *Am J Hypertens*. 1999;12:653-664.

Labetalol: Profile

- α_1- and β_1-receptor blocker
  - ↓Peripheral vascular resistance (α_1 blockade)
  - No reflex tachycardia (β_1 blockade)
  - Maintains coronary, cerebral, and renal blood flow
- Onset: 5-15 min
- Duration of action: 4-6 hours
- Adverse effects:
  - Vomiting, scalp tingling, bronchoconstriction, dizziness, nausea, heart block, orthostatic hypotension

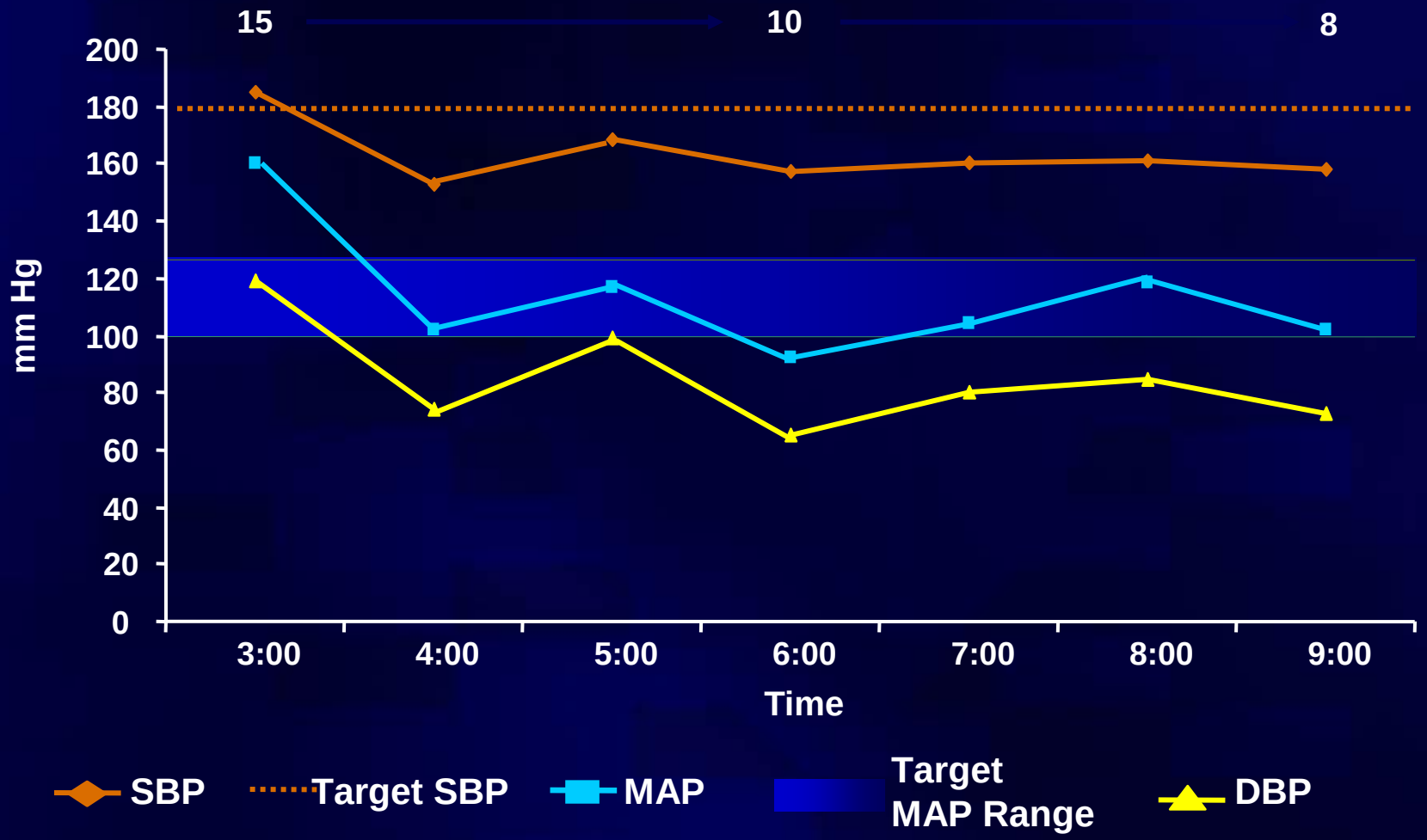
Chobanian AV et al. *Hypertension.* 2003;42:1206-52.
Marik P, Varon J. *Chest.* 2007;131:1949-62.

Nicardipine: Profile

- 2nd generation dihydropyridine calcium channel blocker
  - Coronary and cerebral arterial vasodilation
  - No negative inotropic or dromotropic effects
  - ↓Systemic vascular resistance
- Onset: 5-15 min
- Duration of action: 15-30 mins
- Adverse effects:
  - Tachycardia, headache, flushing, local phlebitis

Chobanian AV et al. *Hypertension.* 2003;42:1206-52.
Levy JH. *Tex Heart Inst J.* 2005;32:467-71.

BP reduction with IV nicardipine



Courtesy of WF Peacock, MD

Nicardipine vs SNP for perioperative hypertension

N = 139 following cardiac or noncardiac surgery

	Time to response (min)	# Dose changes		Adverse events
		Cardiac patients	Noncardiac patients	
Nicardipine	14.1 ± 1* (n = 51)	1.5 ± 0.2† (n = 18)	1.6 ± 0.1‡ (n = 33)	7% (5/71)
SNP	30.4 ± 3.5 (n = 51)	5.1 ± 1.4 (n = 15)	4.6 ± 0.6 (n = 36)	18% (12/68)

*P = 0.0029 vs SNP, †P ≤ 0.05 vs SNP
‡Significant treatment differences in 2/5 centers (P < 0.05)

Halpern NA et al. *Crit Care Med*. 1992;20:1637-43.

Vascular Biology Working Group

Newer Parenteral Antihypertensive Treatment

Pharmacology

Parenteral antihypertensive treatment

Approved	Class	Investigational	Class
SNP	Vasodilator	Nesiritide	B-type natriuretic peptide
Esmolol	β-blocker	Diazoxide*	K^+ channel agonist
Phentolamine	α-blocker	Torsemide*	Loop diuretic
Nitroglycerin	Vasodilator		
Fenoldopam	D1 agonist		
Nicardipine	CCB		
Labetalol	α/β-blocker		
Hydralazine	Vasodilator		
Enalaprilat	ACEI		
Clevidipine	CCB		

*Limited data only

Chobanian AV et al. *Hypertension.* 2003;42:1206-52.
Nordlander M et al. *Cardiovasc Drug Rev.* 2004;22:227-50.
Peacock WF et al. *Am J Emerg Med.* 2005;23:327-31.
Hennessy A et al. *ANZJOG.* 2007;47:279-85.

Calcium channel blockers in acute hypertension

1st generation: Nifedipine

2nd generation: Nicardipine

3rd generation: Clevidipine

Marik PE, Varon J. *Chest.* 2007;131:1949-62.

Clevidipine: Pharmacokinetic overview

- Dihydropyridine calcium channel blocker (CCB)
- $T_{½} \approx 1$ min
- Selective arteriolar dilation
  - ↓Systemic vascular resistance
  - ↓Afterload
  - ↑Stroke volume
  - ↑Cardiac output
- No venous dilation
  - No effect on cardiac filling pressure
- No effect on HR

Nordlander M et al. *Cardiovasc Drug Rev.* 2004;22:227-50.

Clevidipine: Principles of use

- Clevidipine is indicated for the reduction of blood pressure when oral therapy is not feasible or not desirable
- Linear relationship between dosage and arterial blood concentrations
  - Relationship maintained for dose rates up to 7 nmol/kg per min
- Rapid clearance following infusion discontinuation
  - BP returns to baseline within 10 min

Ericsson H et al. *Anesthesiology*. 2000;92:993-1001.
Clevidipine prescribing information. http://www.cleviprex.com/media/ClevidipinePI.pdf.

Nesiritide: Pharmacokinetic overview

- Recombinant B-type natriuretic peptide (BNP)
- Venous and arteriolar dilation
  - ↓Preload
  - ↓Afterload
  - ↑Cardiac output
- No direct inotropic effects
- Approved only for treatment of acute decompensated heart failure

Marcus LS et al. *Circulation.* 1996;94:3184-9.
Zellner C et al. *Am J Physiol*. 1999;276:H1049-57.

Vascular Biology Working Group

Hypertensive Urgencies/Emergencies: Guidelines

Hypertensive emergencies: JNC 7 consensus recommendations*

- Admit to ICU
- Administer short-acting parenteral antihypertensive with close monitoring
  - ↓BP by ≤25% within 1 hour
  - ↓BP to 160/100-110 mm Hg over next 2-6 hours
  - ↓BP to 130/85 mm Hg over next 24-48 hours

*Expert opinion

Chobanian AV et al. *Hypertension.* 2003;42:1206-52.

Hypertensive urgencies: JNC 7 consensus recommendations*

- Some patients may benefit from short-acting oral antihypertensive treatments
  - However, in one recent study, resting for 60 min was associated with ↓BP of >20% in 1/3 of patients
  - In addition, no evidence that failure to ↓BP in emergency department is associated with ↑short-term risk
- Adjust or reinstitute antihypertensive regimen to gradually ↓BP over next few days

*Expert opinion

Chobanian AV et al. *Hypertension.* 2003;42:1206-52.
Duarte M et al. Presented at ASH. 2006.

JNC 7: Treatment of acute hypertension in preeclampsia

Consider if childbirth is imminent

	Dosing	Precautions
Hydralazine	5 mg IV bolus, then 10 mg q20-30 min to max 25 mg; Repeat in several hr	
Labetalol (second-line)	20 mg IV bolus, then 40 mg 10 min later, 80 mg q10 min for 2 additional doses to max 220 mg	
Nifedipine (controversial)	10 mg po, repeat q20 min to max 30 mg	Precipitous ↓BP when using with $MgSO_4$
SNP (rarely-when others fail)	0.25 µg/kg per min to max 5 µg/kg per min	Cyanide poisoning may occur if used >4 hr

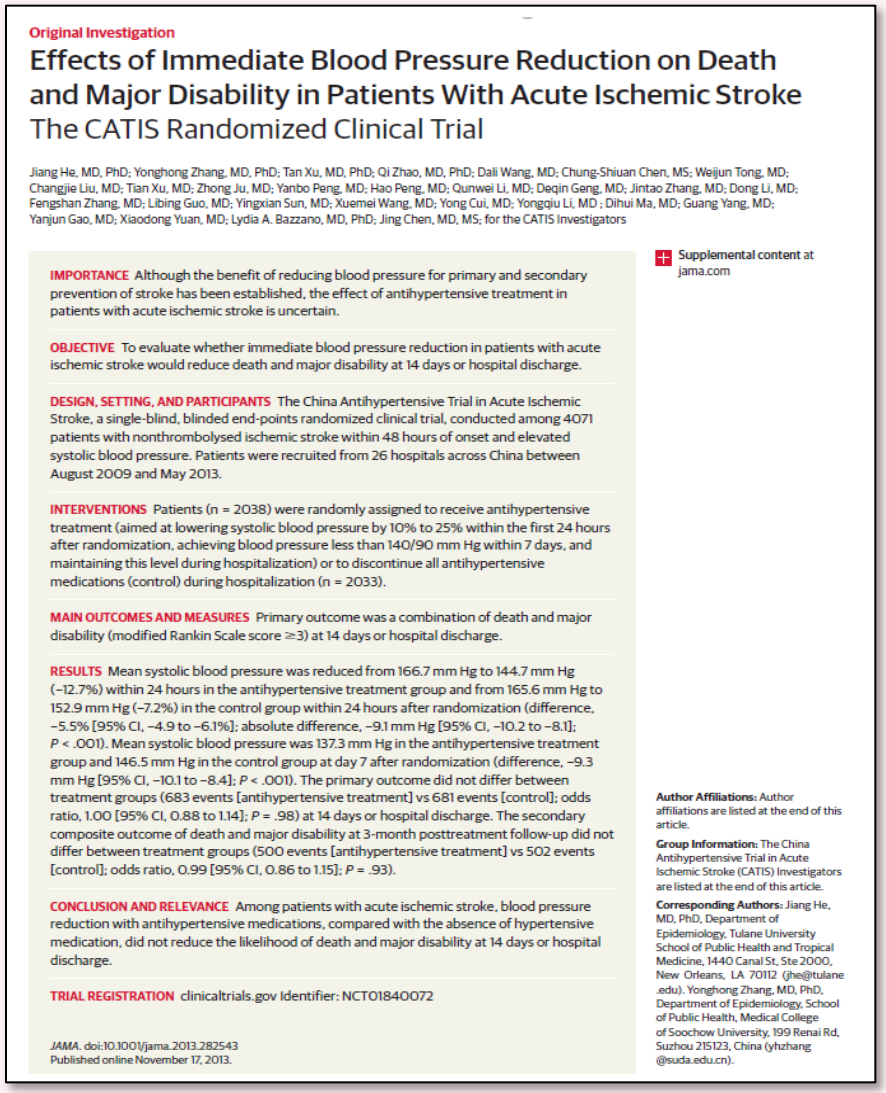
Chobanian AV et al. *Hypertension.* 2003;42:1206-52.

NEW DATA PRESENTED SEPT.2013 EUROPEAN STROKE CNFERENCE,LONDON.

- INTERACT 2 TRIAL….LOWERING BLOOD PRESSURE RAPIDLY TO LESS THAN 140 MM HG.IMPROVED THE MODIFIED RANKIN SCALE BUT NOT DEATH OR DISABILITY

Conclusion

- Among patients with acute ischemic stroke, BP reduction with antihypertensive medications compared with the absence of antihypertensive medications did not reduce death and major disability at 14 days or hospital discharge.
- These findings suggest that unless a patient's BP ≥220/120 mmHg, the decision to lower BP with antihypertensive treatment in patients with acute ischemic stroke should be based on individual clinical judgment.



Original Investigation

Effects of Immediate Blood Pressure Reduction on Death and Major Disability in Patients With Acute Ischemic Stroke

The CATIS Randomized Clinical Trial

Jiang He, MD, PhD; Yonghong Zhang, MD, PhD; Tan Xu, MD, PhD; Qi Zhao, MD, PhD; Dali Wang, MD; Chung-Shiuan Chen, MS; Weijun Tong, MD; Changjie Liu, MD; Tian Xu, MD; Zhong Ju, MD; Yanbo Peng, MD; Hao Peng, MD; Qunwei Li, MD; Deqin Geng, MD; Jintao Zhang, MD; Dong Li, MD; Fengshan Zhang, MD; Libing Guo, MD; Yingxian Sun, MD; Xuemei Wang, MD; Yong Cui, MD; Yongqiu Li, MD ; Dihui Ma, MD; Guang Yang, MD; Yanjun Gao, MD; Xiaodong Yuan, MD; Lydia A. Bazzano, MD, PhD; Jing Chen, MD, MS; for the CATIS Investigators

IMPORTANCE Although the benefit of reducing blood pressure for primary and secondary prevention of stroke has been established, the effect of antihypertensive treatment in patients with acute ischemic stroke is uncertain.

OBJECTIVE To evaluate whether immediate blood pressure reduction in patients with acute ischemic stroke would reduce death and major disability at 14 days or hospital discharge.

DESIGN, SETTING, AND PARTICIPANTS The China Antihypertensive Trial in Acute Ischemic Stroke, a single-blind, blinded end-points randomized clinical trial, conducted among 4071 patients with nonthrombolysed ischemic stroke within 48 hours of onset and elevated systolic blood pressure. Patients were recruited from 26 hospitals across China between August 2009 and May 2013.

INTERVENTIONS Patients (n = 2038) were randomly assigned to receive antihypertensive treatment (aimed at lowering systolic blood pressure by 10% to 25% within the first 24 hours after randomization, achieving blood pressure less than 140/90 mm Hg within 7 days, and maintaining this level during hospitalization) or to discontinue all antihypertensive medications (control) during hospitalization (n = 2033).

MAIN OUTCOMES AND MEASURES Primary outcome was a combination of death and major disability (modified Rankin Scale score ≥3) at 14 days or hospital discharge.

RESULTS Mean systolic blood pressure was reduced from 166.7 mm Hg to 144.7 mm Hg (−12.7%) within 24 hours in the antihypertensive treatment group and from 165.6 mm Hg to 152.9 mm Hg (−7.2%) in the control group within 24 hours after randomization (difference, −5.5% [95% CI, −4.9 to −6.1%]; absolute difference, −9.1 mm Hg [95% CI, −10.2 to −8.1]; $P < .001$). Mean systolic blood pressure was 137.3 mm Hg in the antihypertensive treatment group and 146.5 mm Hg in the control group at day 7 after randomization (difference, −9.3 mm Hg [95% CI, −10.1 to −8.4]; $P < .001$). The primary outcome did not differ between treatment groups (683 events [antihypertensive treatment] vs 681 events [control]; odds ratio, 1.00 [95% CI, 0.88 to 1.14]; $P = .98$) at 14 days or hospital discharge. The secondary composite outcome of death and major disability at 3-month posttreatment follow-up did not differ between treatment groups (500 events [antihypertensive treatment] vs 502 events [control]; odds ratio, 0.99 [95% CI, 0.86 to 1.15]; $P = .93$).

CONCLUSION AND RELEVANCE Among patients with acute ischemic stroke, blood pressure reduction with antihypertensive medications, compared with the absence of hypertensive medication, did not reduce the likelihood of death and major disability at 14 days or hospital discharge.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01840072

JAMA. doi:10.1001/jama.2013.282543
Published online November 17, 2013.

Supplemental content at jama.com

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The China Antihypertensive Trial in Acute Ischemic Stroke (CATIS) Investigators are listed at the end of this article.

Corresponding Authors: Jiang He, MD, PhD, Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, 1440 Canal St, Ste 2000, New Orleans, LA 70112 (jhe@tulane.edu). Yonghong Zhang, MD, PhD, Department of Epidemiology, School of Public Health, Medical College of Soochow University, 199 Renai Rd, Suzhou 215123, China (yhzhang@suda.edu.cn).

JAMA®

The Journal of the American Medical Association

J He and coauthors for the CATIS Investigators

Effects of Immediate Blood Pressure Reduction on Death and Major Disability in Patients With Acute Ischemic Stroke: The CATIS Randomized Clinical Trial

Published online November 17, 2013

Available at jama.com and mobile.jamanetwork.com

The JAMA Network

TRIALS IN HYPERTENSION NEVER DONE !

- 1:TREATMENT OF Systolic Hypertension 140-160 mmHg IN ANY GROUP.
  2: TREATMENT of PREHYPERTENSION 120/80 TO 140/90.
  3:TREATMENT of WHITE COAT HYPERTENSION.