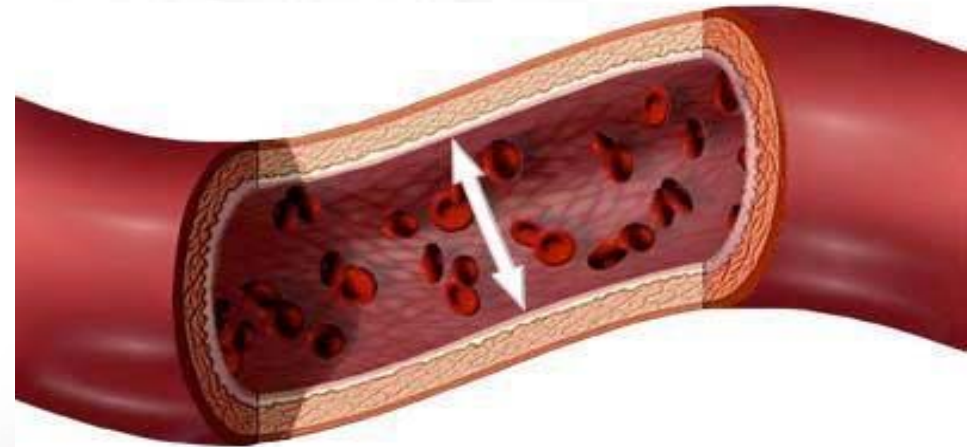
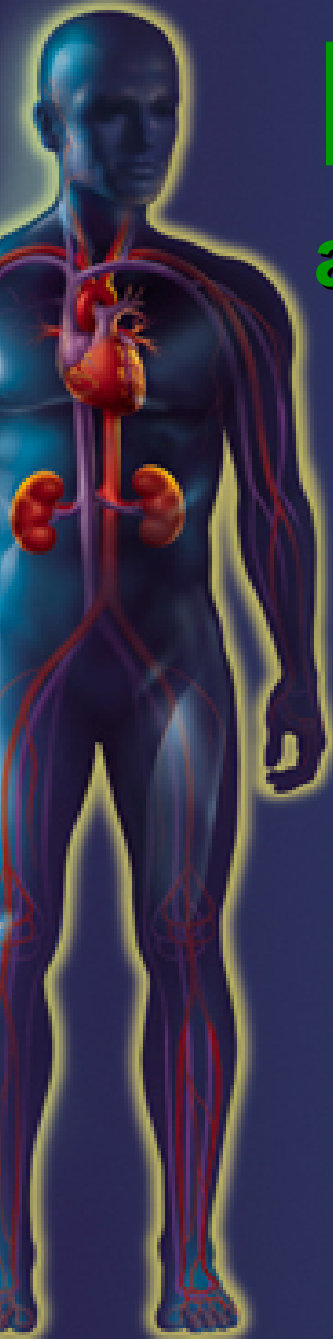


Hypertension

a timeless problem with new frontiers

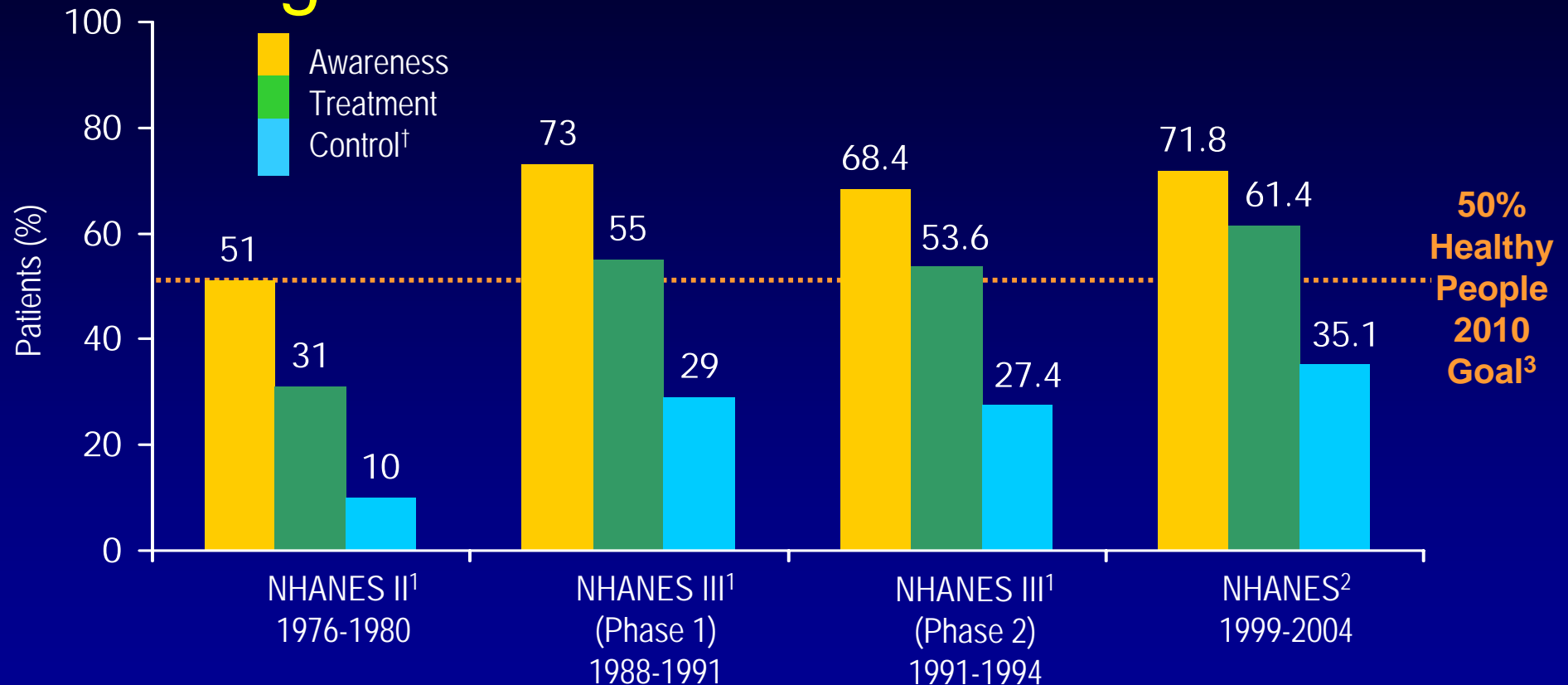


A. Oussama Rifai, MD
Vice President of Medical Affairs
The Virtual Nephrologist, Inc.

Hypertension at a glance

- The number one modifiable risk factor for 12% of all deaths worldwide.
- Hypertension is the number one risk factor for cardiovascular disease, with ample evidence that active reduction of BP to target leads to improvement in cardiovascular morbidity and mortality.
- Since 1900, except for the year 1918 (flu-pneumonia epidemics) CVD is the number one cause of death.
- One death every 36 seconds
- One out of three American adults has HTN.
- 70 millions American have HTN, one billion worldwide

Awareness, Treatment, and Control of High Blood Pressure in Adults*



*Adults aged 18 to 74 years with SBP \geq 140 mm Hg or DBP \geq 90 mm Hg or who are taking antihypertensive medication.

†SBP <140 mm Hg and DBP <90 mm Hg. NHANES=National Health and Nutrition Examination Survey.

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

2. Rosamond W et al. *Circulation*. 2007;115:e69-e171.

3. US Department of Health and Human Services. *Health People 2010: Understanding and Improving Health*. 2nd ed. Washington, DC: US Government Printing Office, November 2000.

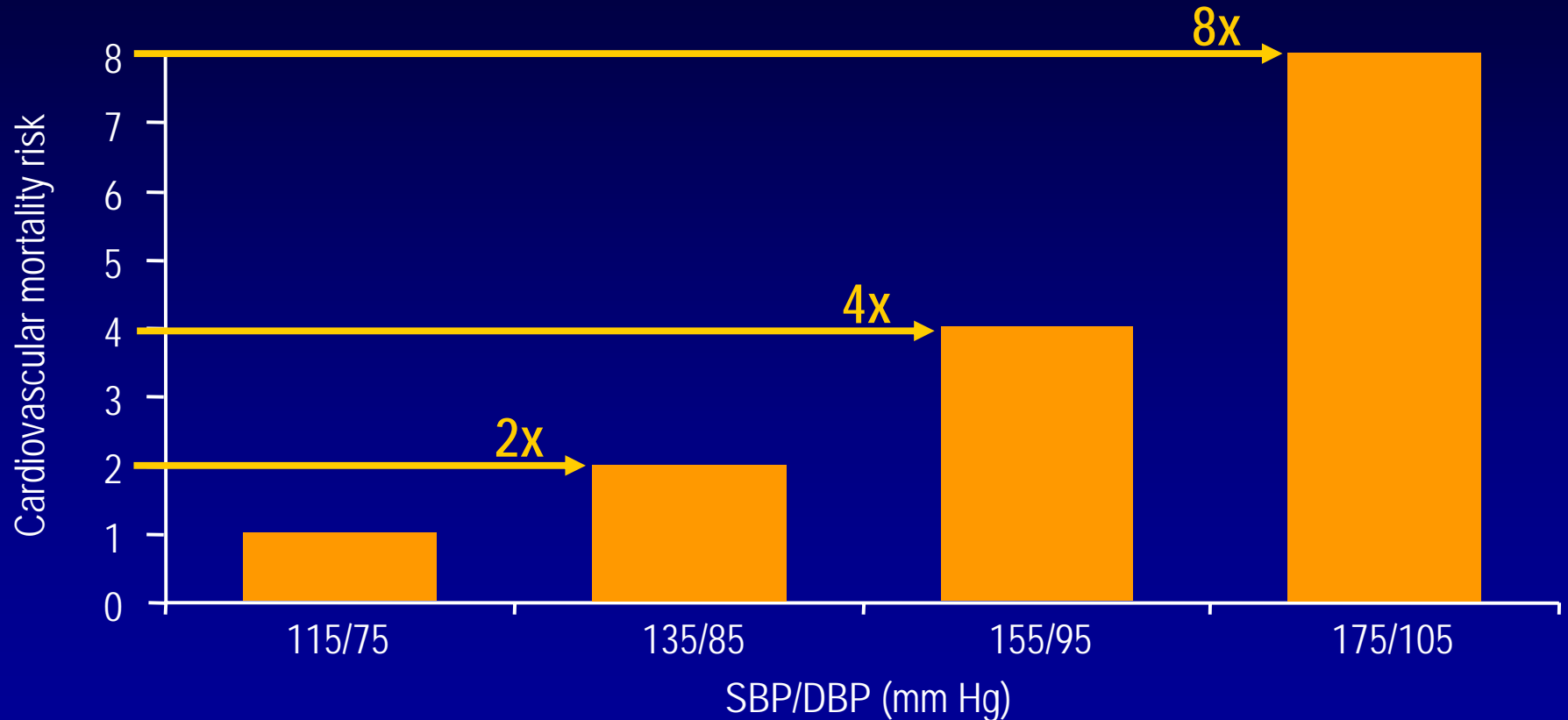
Blood Pressure Classification

JNC VII

BP Classification	SBP mmHg		DBP mmHg
Normal	<120	and	<80
Pre HTN	120–139	or	80–89
Stage I HTN	140–159	or	90–99
Stage II HTN	≥ 160	or	≥ 100

Cardiovascular Mortality Risk Doubles With Each 20-mm Hg SBP or 10-mm Hg DBP Increment*

1 Million Adults in 61 Prospective Studies



*Individuals aged 40-69 years, starting at blood pressure 115/75 mm Hg.

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

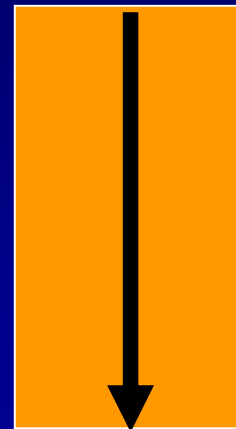
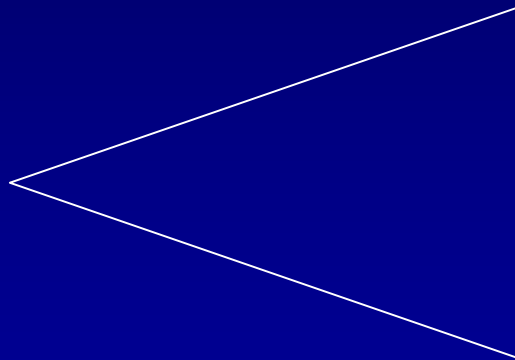
1. Prospective Studies Collaboration. *Lancet*. 2002;360:1903-1913.

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

BP Reductions as Small as 2 mmHg Reduce the Risk of CV events by Up to 10%

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

**2 mmHg
decrease in
mean SBP**



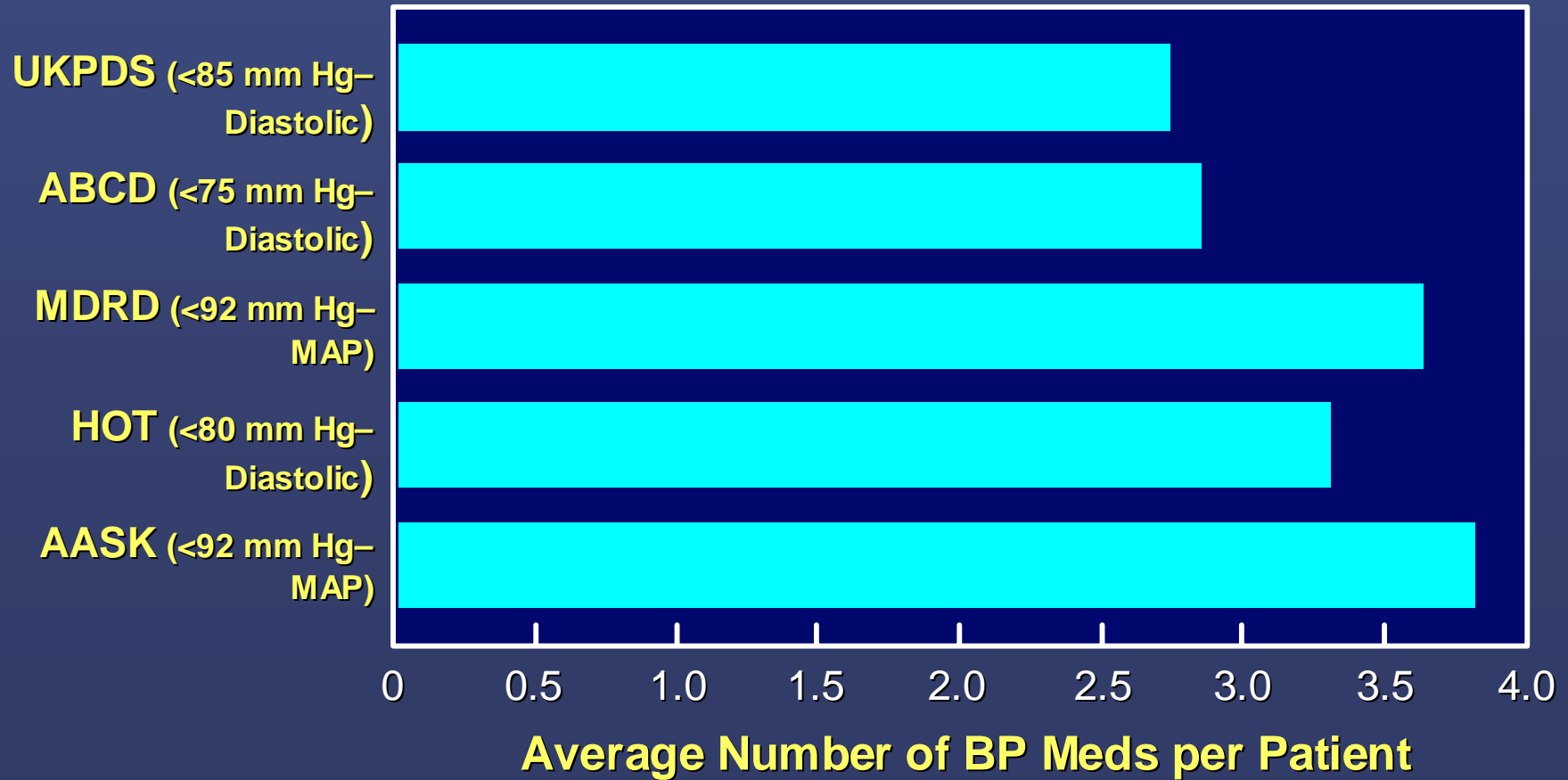
**7% reduction in
risk of IHD
mortality**

**10% reduction in
risk of stroke
mortality**

Few points from JNC VII

- For persons over age 50, SBP is a more important than DBP as CVD risk factor.
- Thiazide-type diuretics should be initial drug therapy for most, either alone or combined with other drug classes.
- Certain high-risk conditions are compelling indications for other drug classes.
- The responsible physician's judgment remains paramount.
- 2/3 of patients need 2 or more antihypertensive agents.
- Failure to titrate or combine medications, despite knowing the patient is not at goal BP, represents clinical inertia and must be overcome.

Medication Requirements in Large Recent Trials of Diabetes and/or Hypertension



Pre Hypertension

HTN and Damage

HTN and clinical Dz

Vasoconstriction
Increased peripheral resistance
Vascular remodeling
RAAS and SNS activation



Declining GFR
Sodium Retention
Increased cardiac output
Stiff Aorta-Systolic HTN

PRA

of drugs

ARB

ACE-I

β-blocker

CCB

Diuretics (Thiazide-Type)



The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)

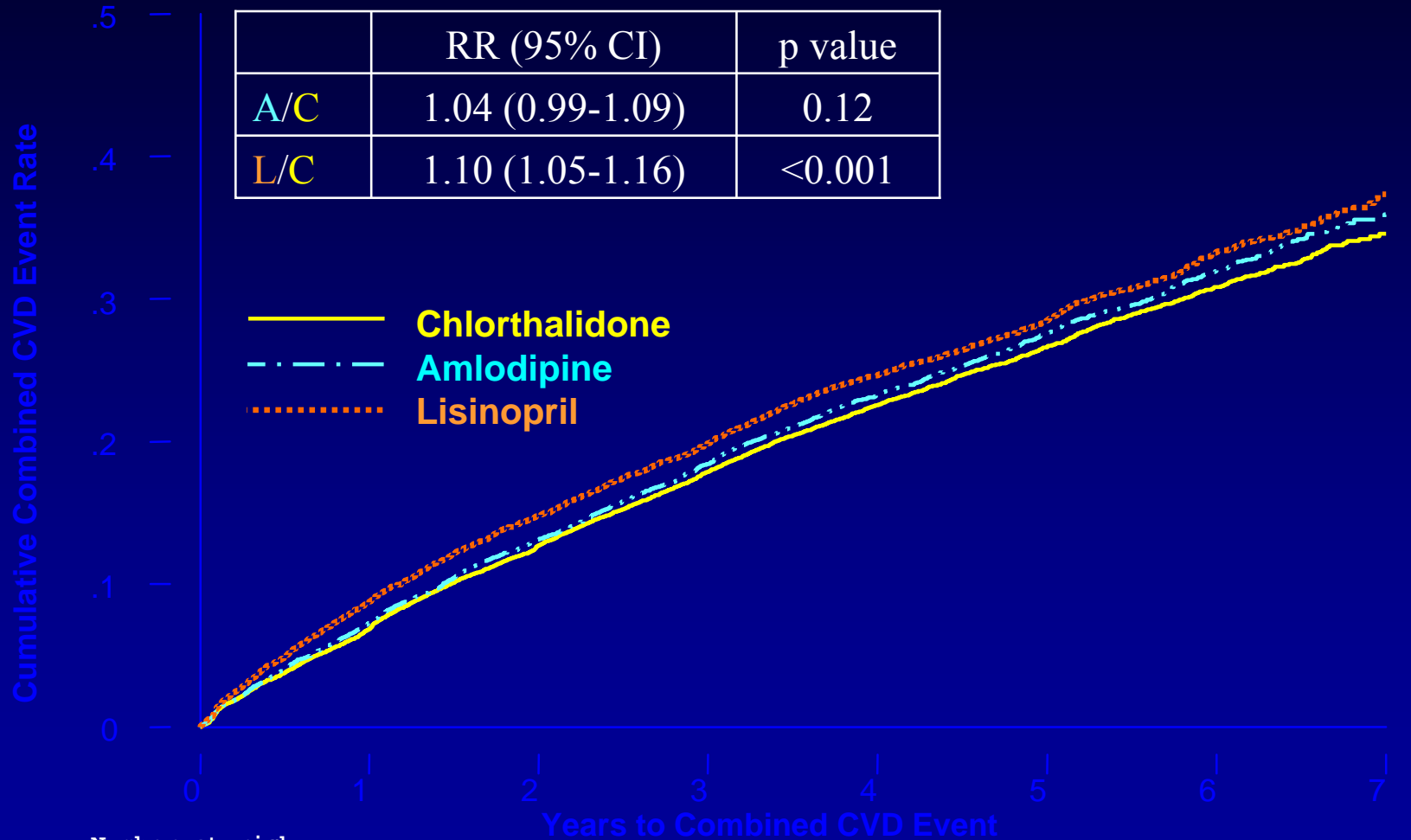


Antihypertensive Treatment Regimen

Step 1	Dose 1	Dose 2	Dose 3
Chlorthalidone	12.5 mg	12.5 mg	25 mg
Amlodipine	2.5 mg	5 mg	10 mg
Lisinopril	10 mg	20 mg	40 mg
Step 2			
Reserpine	0.05 mg qd	0.1 mg qd	0.2 mg qd
Clonidine	0.1 mg bid	0.2 mg bid	0.3 mg bid
Atenolol	25 mg qd	50 mg qd	100 mg qd
Step 3			
Hydralazine	25 mg bid	50 mg bid	100 mg bid



Cumulative Event Rates for **Combined CVD** by ALLHAT Treatment Group

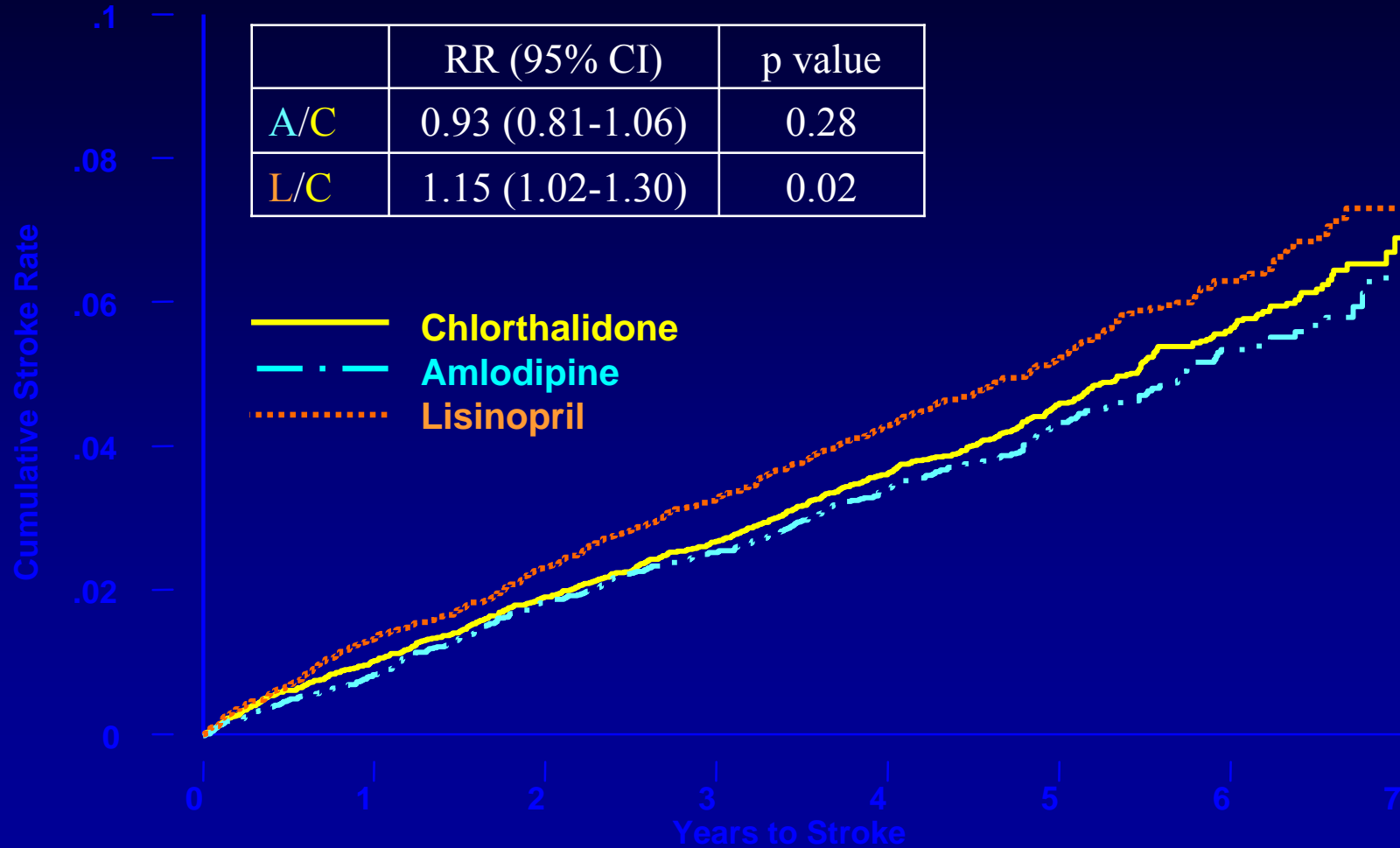


Number at risk:

Chlor	15,255	13,752	12,594	11,517	9,643	5,167	2,362	288
Amlo	9,048	8,118	7,451	6,837	5,724	3,049	1,411	153
Lisin	9,054	7,962	7,259	6,631	5,560	3,011	1,375	139



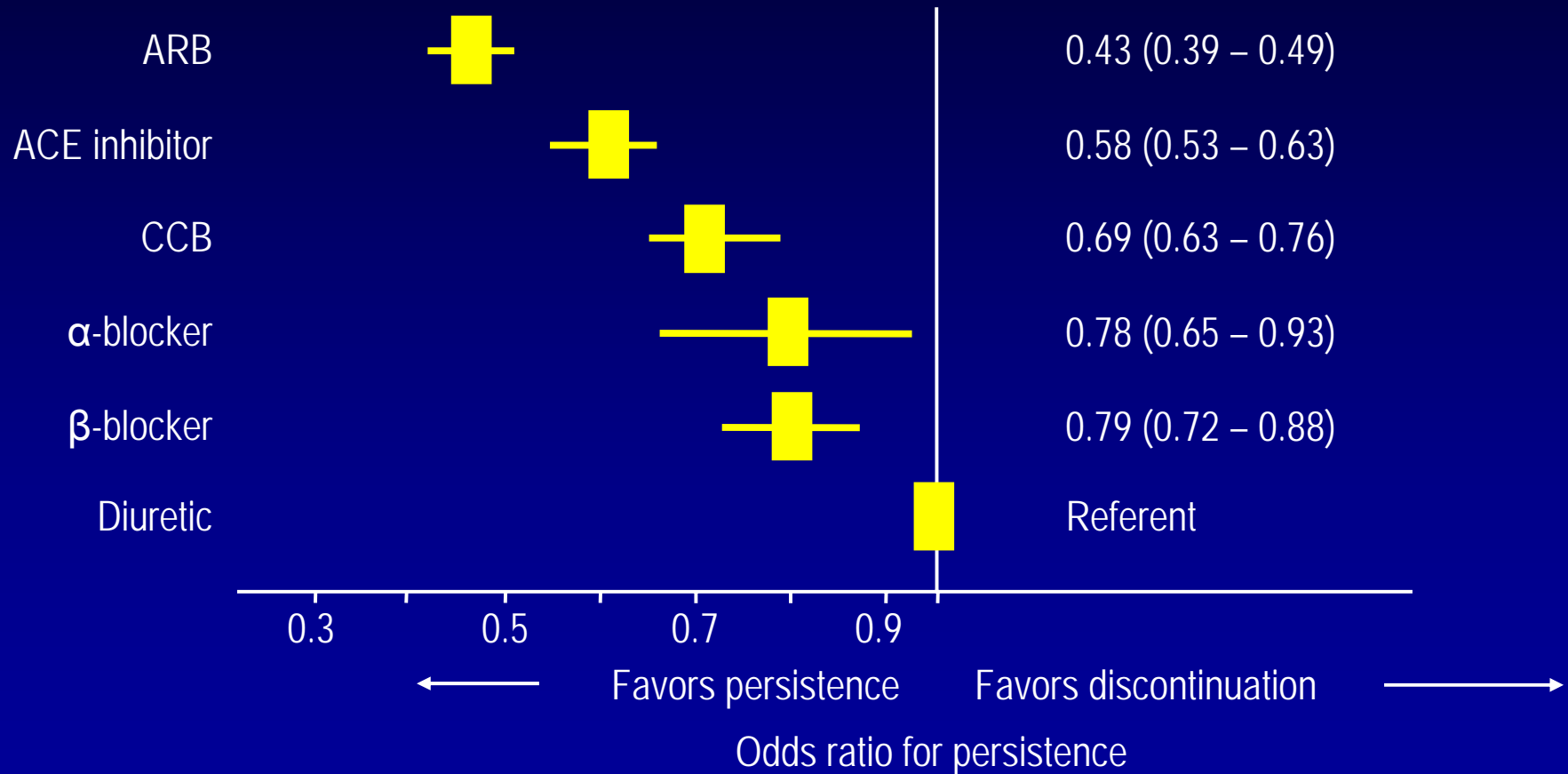
Cumulative Event Rates for Stroke by ALLHAT Treatment Group



Number at risk:	0	1	2	3	4	5	6	7
Chlor	15,255	14,515	13,934	13,309	11,570	6,385	3,217	567
Amlo	9,048	8,617	8,271	7,949	6,937	3,845	1,813	506
Lisin	9,054	8,543	8,172	7,784	6,765	3,891	1,828	949

One-Year Discontinuation Rates of Antihypertensive Drugs in Clinical Practice (N=631,579)

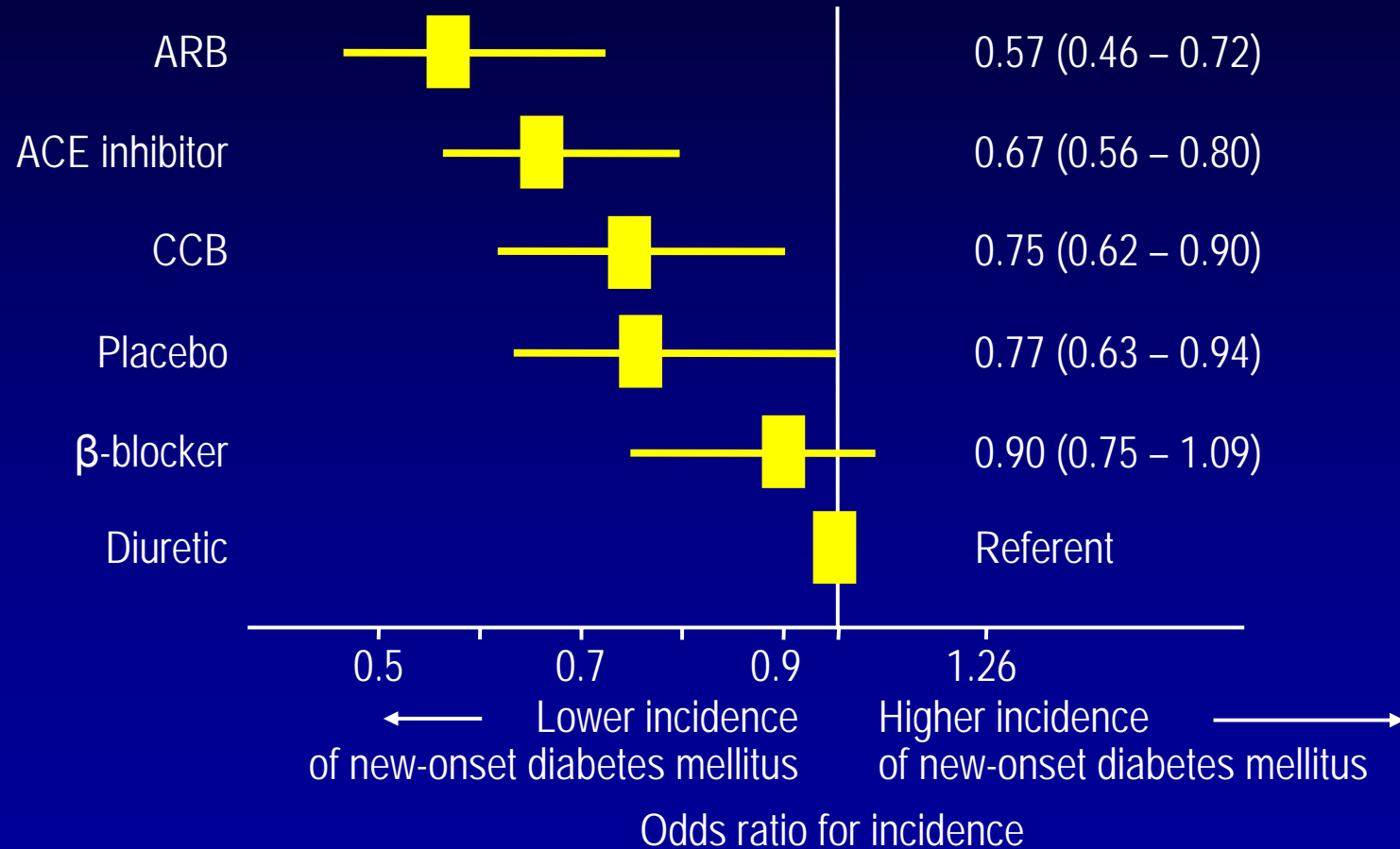
A Network Meta-analysis



ARB=angiotensin receptor blocker; ACE=angiotensin converting enzyme; CCB=calcium channel blocker.
Elliott W. *J Clin Hypertens*. 2007;9:A210.

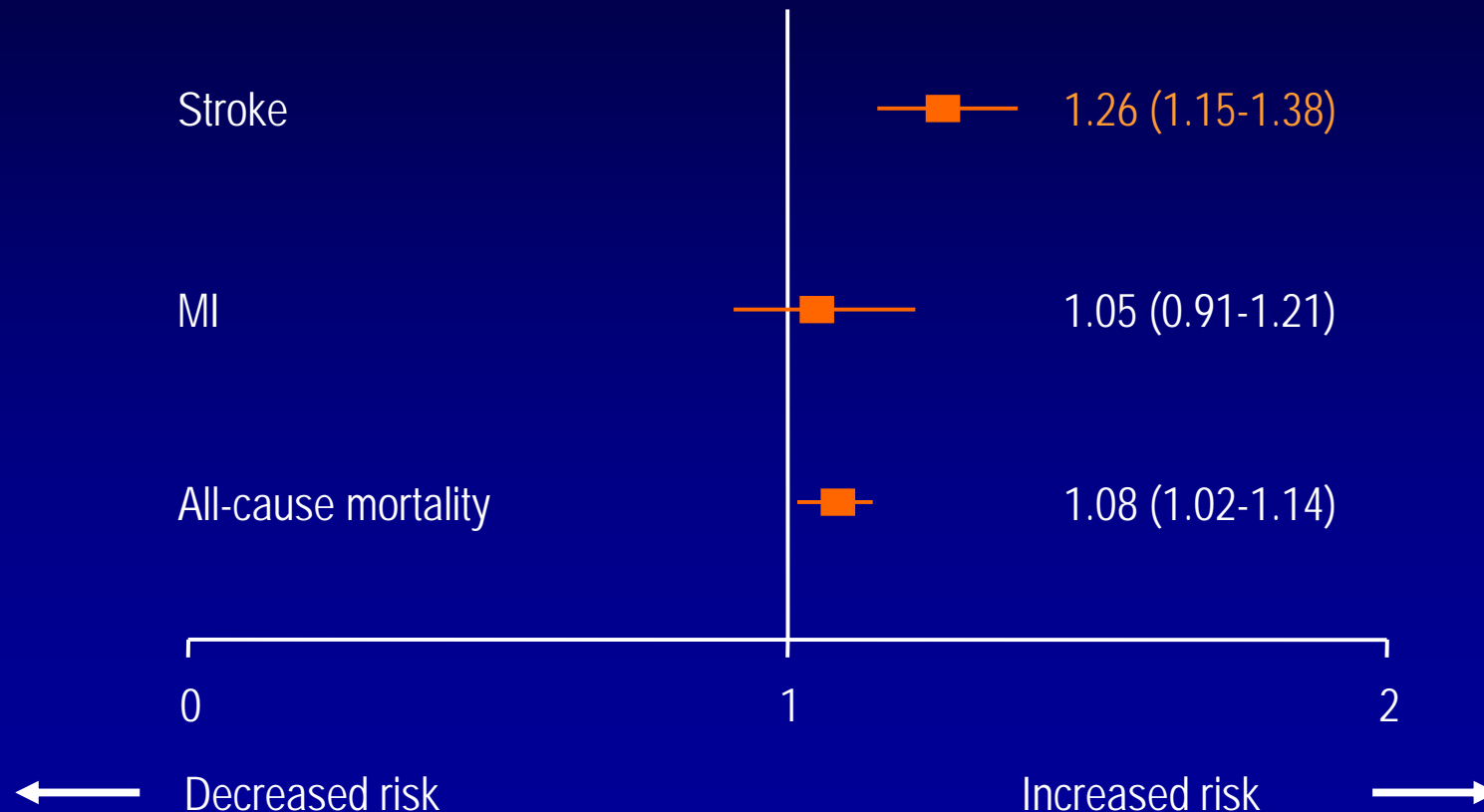
Odds of Developing Diabetes by Initial Antihypertensive Class (N=143,153)

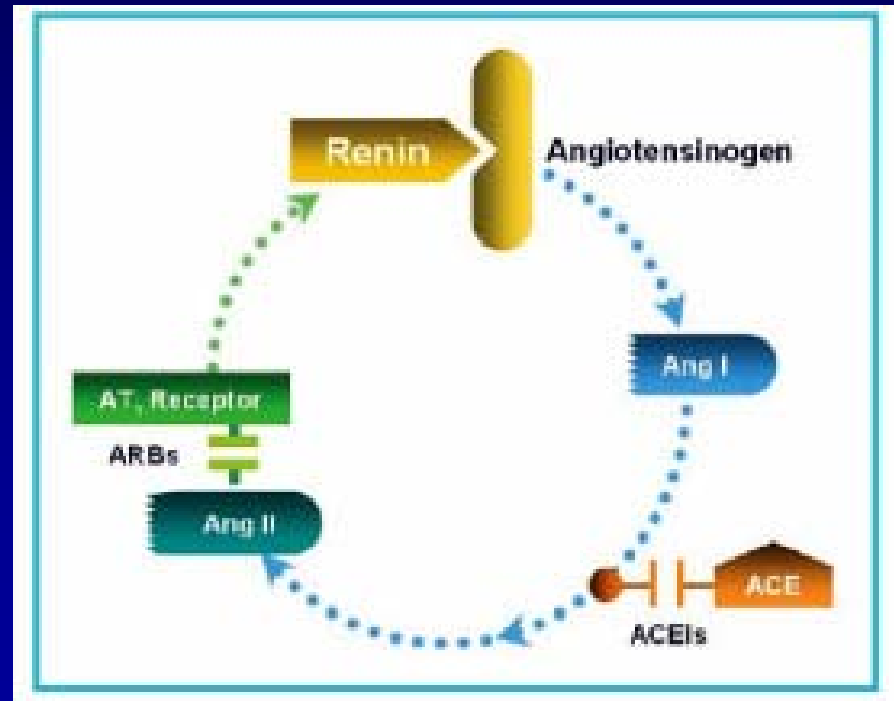
A Network Meta-analysis



ARB=angiotensin receptor blocker; ACE=angiotensin converting enzyme; CCB=calcium channel blocker.
Elliott WJ, Meyer PM. *Lancet*. 2007;369:201-207.

Meta-analysis of β -blockers in Hypertension: Outcome Data for Atenolol vs. Other Antihypertensive Therapy







**NOW
ENROLLING**



ONGOING CLINICAL TRIALS IN RESISTANT HYPERTENSION

DORADO INCLUDES TWO PHASE 3 CLINICAL TRIALS OF DARUSENTAN*

Darusentan is an experimental oral endothelin receptor antagonist being studied for the treatment of resistant hypertension.

THE DORADO STUDIES ARE NOW ENROLLING

The DORADO clinical trials, DORADO and DORADO-AC, are each 14-week, randomized, double-blind, multicenter, parallel-group clinical trials.

DORADO: Patients are randomized to receive darusentan at 1 of 3 fixed doses or placebo

DORADO-AC: Patients are randomized to receive darusentan at an individually optimized dose, an active comparator (guanfacine), or placebo

The objective of these trials is to determine if darusentan can be effective in reducing blood pressure in patients with resistant systolic hypertension despite treatment with full doses of 3 or more antihypertensive drugs, including a diuretic.

GET INVOLVED

Your patients may be eligible to participate in these resistant hypertension clinical trials. To learn more, call 1-877-320-7583 or visit ClinicalTrials.gov for more details.

***Darusentan is under investigation and is not approved for use.**



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What is coming in the next few years

- ARBs will become generic one at a time
- Outcome data for DRI
- JNC VIII with 2 concepts:
 - GPA: Global Patient assessment
 - e-Prescribing : Economic prescribing
- New anti Endothelin 1 and devices
- New group of physicians will become **VIP**
Vascular **I**nternal Medicine **P**hysicians