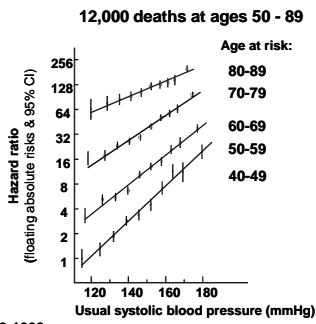


1

Facts about the Risk of Elevated Blood Pressure in the Elderly

2

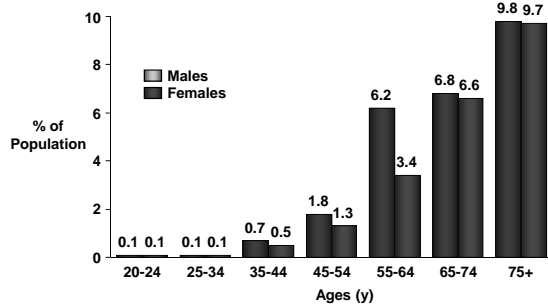
Stroke Mortality Rate in Each Decade of Age compared to Usual SBP at the Start of That Decade



Lancet. 2002;360:1903.

3

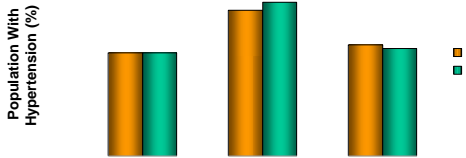
Heart Failure Prevalence by Age and Gender*



*United States: 1988-1994. American Heart Association. Heart Disease and Stroke Statistics - 2003 Update.

4

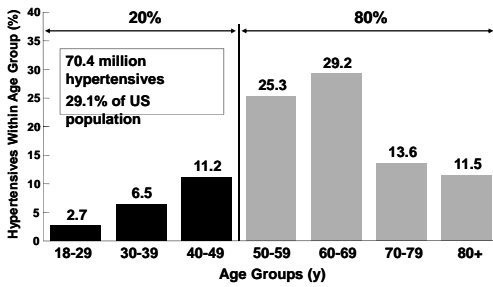
Hypertension Affects Approximately 65 Million Americans: 28% of Adults



Hypertension. October 2004;44:1-7

5

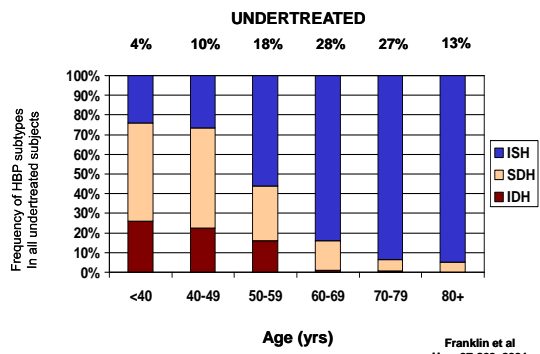
Age Distribution of Hypertensives in US Population From NHANES III and the Projected 2020 Census



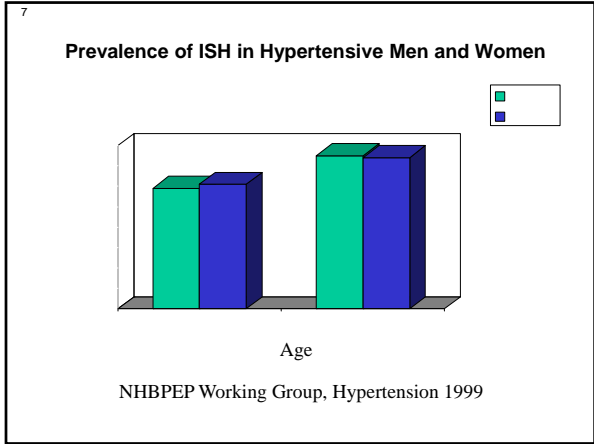
Franklin SS. J Hypertension. 1999;17(suppl 5):S29-S36.

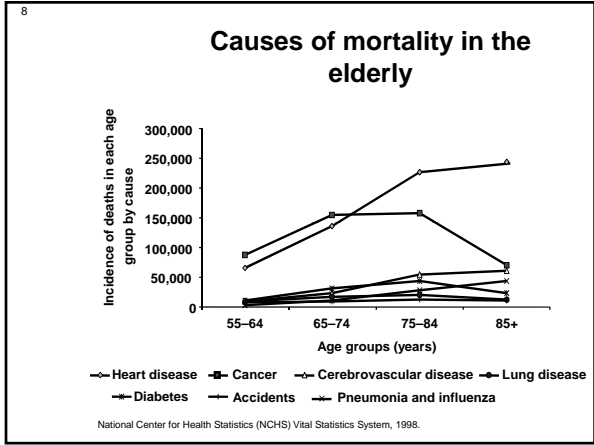
6

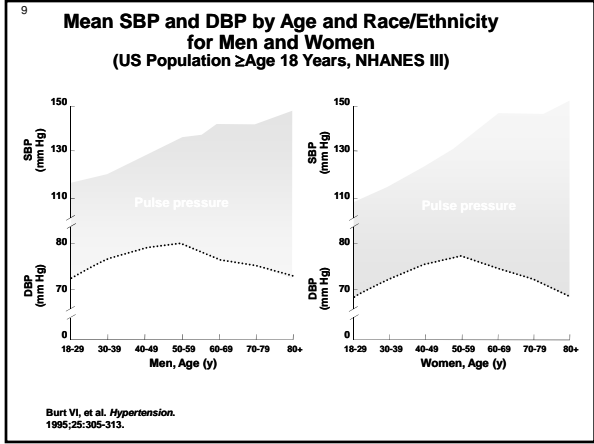
HYPERTENSION IN THE US - NHANES III



Franklin et al Hyp. 37:869, 2001







10

Isolated Systolic Hypertension

Definition: ≥ 140
 < 90 mm Hg

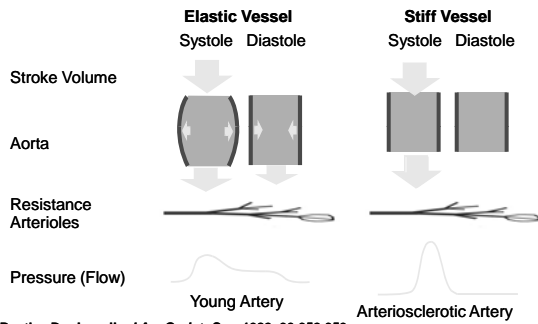
Etiology: Age related decrease in aortic compliance
(increase in vascular stiffness)

In rigid aorta $\left\{ \begin{array}{l} \text{Decrease in elastic tissue} \\ \text{Increase in collagen deposition} \\ \text{Intimal thickening} \end{array} \right.$

Diastolic pressure remains constant or decreases.
In rigid aorta elastic recoil that helps maintain DBP is decreased.

11

Arterial Wall Compliance and Pulse Pressure Wave



Bentley Dw, Izzo JL. *J Am Geriatr Soc.* 1982; 30:352-359.

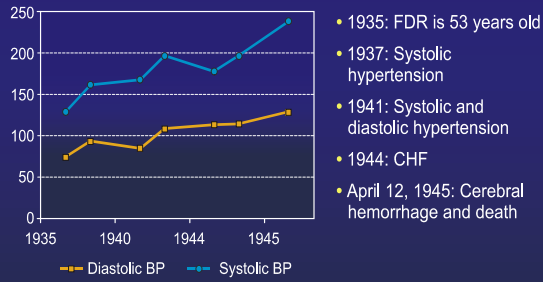
12

The Importance of Systolic Blood Pressure in the Elderly

- Isolated systolic hypertension (≥ 140 / < 90 mm Hg) is present in about two thirds of hypertensive individuals > 60 years old
- Systolic blood pressure:
 - Is almost always less well controlled than diastolic BP
 - Is more important than diastolic BP as a cardiovascular risk factor
 - Should become the major criterion for diagnosis and treatment decisions in middle-aged or older individuals

Hypertension. 2000;35:1021-1024.

Franklin Delano Roosevelt: A Case of Uncontrolled Hypertension



- 1935: FDR is 53 years old
- 1937: Systolic hypertension
- 1941: Systolic and diastolic hypertension
- 1944: CHF
- April 12, 1945: Cerebral hemorrhage and death

Bruenn HG. *Ann Intern Med.* 1970;72:579-591.

Franklin Delano Roosevelt



What if FDR Had Been Alive Today?



16

CARDIOVASCULAR THERAPY

**PEOPLE AT HIGHER RISK
ALWAYS BENEFIT MORE
FROM EFFECTIVE THERAPY**

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Management of Hypertension in the Elderly

- Identify and if possible correct secondary causes
 - Obesity
 - Renal artery stenosis
 - Sleep apnea
- Lifestyle modification
 - DASH-like diet
 - Exercise
 - Weight loss
- Drug therapy

18

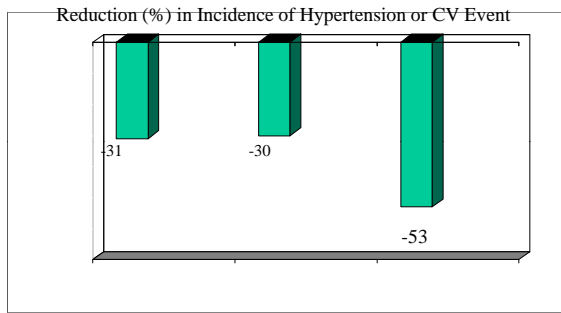
Laboratory Tests

- Routine Tests in the Evaluation of a Hypertensive Patient (JNC 7)
 - Electrocardiogram
 - Urinalysis
 - Blood glucose and hematocrit
 - Serum potassium, creatinine, or the corresponding estimated GFR, and calcium
 - Lipid profile (fasting)
- Optional Tests
 - Measurement of urinary albumin excretion or albumin/creatinine ratio

Lifestyle Interventions in the Management of Hypertension

<u>Intervention</u>	<u>Possible BP Effect</u>
Exercise	6-10 mm Hg (≥30 min ≥3x/wk)
Weight reduction	1-2 mm Hg/Kg ↓
Alcohol intake reduction	1 mm Hg/drink/d ↓
Sodium intake reduction	1-3 mm Hg/40 mmol/d ↓

Trial of Non Pharmacologic Interventions in the Elderly (TONE)

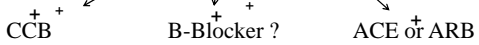


JAMA 1998;279:839-846

Algorithm for Management of the Elderly - Primarily Systolic Hypertension

1) Lifestyle changes

2) Low dose diuretic (12.5 mg HCTZ)



3) Stop, Look & Listen before increasing dosages

Let the Baroreceptors reset

4) ↑ Rx until goal achieved

Pharmacologic Management of Hypertension in the Elderly

- **Primary goal of reducing BP is to reduce CV events. This has been demonstrated in trials with**
 - Diuretics
 - ACE inhibitors and
 - Calcium antagonists **BUT**
 - Evidence for B-blockers is **less strong**
- Alpha blockers should not be used as initial antihypertensive therapy

Treatment Recommendations for the Elderly in JNC 7

Recommendations do not differ according to age for:

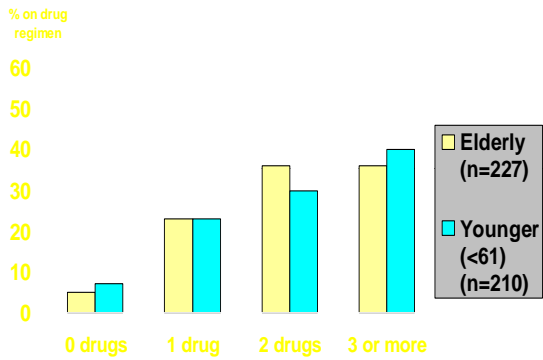
- BP classification
- BP goals
- Lifestyle interventions
- Selection of medications

Results of Therapy

in Elderly Hypertensive

Individuals

There are difficulties in reducing BPs to Goal levels in hypertensive patients



Pharmacologic Management of Hypertension in the Elderly

- A variety of drugs alone or in combination reduce BP; most patients will require 2-3 medications for adequate BP control (especially SBP).
- A diuretic should be included in most antihypertensive regimens:
 - to enhance efficacy
 - diuretics have the most evidence of benefit from morbidity trials in the elderly.

Blood Pressure (mm Hg) in SHEP and Syst-Eur Trials

	<u>SHEP -Diuretic based</u>	<u>Syst-Eur -CCB based</u>
Entry	160-219/<90	160-219/<95
Goal (SBP)	<160	<150
Baseline	170/77	174/86
Achieved: Rx	143/68	151/79
Achieved: Placebo	155/72	161/84

Swedish Trial in Old Persons (2+ years)

B-blockers vs diuretics vs placebo

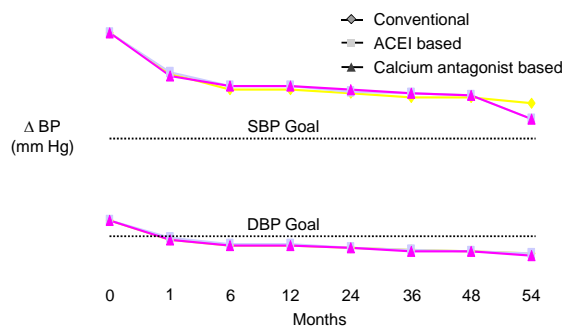
Age: 70-84

Achieved BPs: 167/87 mm Hg on Rx
186/96 mm Hg on placebo

Rx significantly reduced strokes, CV events and cardiac deaths

Benefits noted up to age 84

The Difficulty in Reducing SBP: STOP-2



Hansson L, et al. *Lancet*. 1999;354:1751-1756.

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Benefits of Lowering BP by

About $\frac{-12}{-4-5}$ mmHg

Average Percent Reduction

Stroke incidence	35–40%
Myocardial infarction	20–25%
Heart failure	50%

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Public Health Implications of SHEP Study

Reduction in Events on Active Treatment (per 1000 patients/5 years)

CVA	30
CAD	16
CHD	55

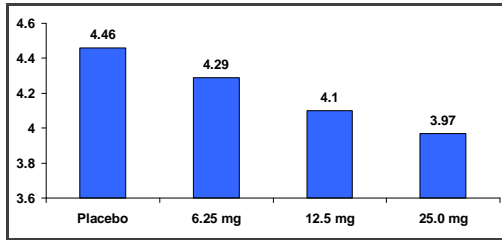
Annually in USA: 24,000 fewer strokes
 44,000 fewer major CV events
 84,000 fewer hospital admissions

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In the SHEP study the beneficial effect on cardiovascular events was attenuated in patients with potassium levels below 3.5 mmol d/L but were no greater than placebo

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Serum Potassium in SHEP Trial



n = 1989 n = n = 1070 n = 734

chlorthalidone daily dose

Fransse et al Hyper. 35:1025, 2000

35

Effect of low potassium on outcome in the SHEP trial

Relative risk- ACTIVE Rx GROUP by SERUM K⁺

K ⁺ < 3.5 mEq/LCVD (n = 151)	CHD	CVA
1.0	1.0	1.0
K ⁺ ≥ 3.5 mEq/L (n = 1951)	0.49	0.28

Hyper. 35:1025, 2000

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Injuries and Symptoms in the SHEP Trial

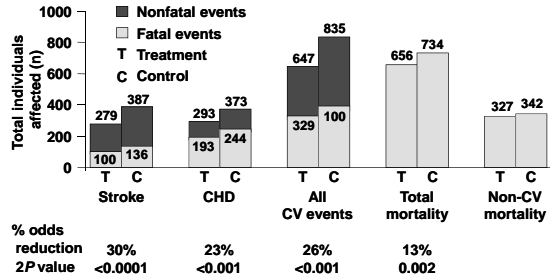
Fractures - no difference in hip fractures
2.4% vs 2.0% (active/placebo)

Orthostatic symptoms
24% - faintness on standing
3% - loss of consciousness
(no relationship to medication)

37

ISH: META-ANALYSIS OF OUTCOME TRIALS

n=15,693—3.8 -yr follow-up



Lancet 2000;355:865

38

Studies with different mediations.

- The Antihypertensive and Lipid Lowering to Prevent Heart Attack Trial. [ALLHAT]
- Comparative trial with a diuretic compared to an ACE Inhibitor, Alpha blocker or CCB based treatment.
- double blinded---- >44,000 patients

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ALLHAT Trial Results

Alpha blocker arm of trial stopped early-----More congestive heart failure and strokes than in Diuretic group

40

ALLHAT

Baseline BPs and Outcome in Subjects >75 Yrs

BP: 149/81 mm Hg

Achieved BPs, mm Hg at 5 Years

Chlorthalidone	Amlodipine	Lisinopril
134.5/72.3	135.3/71.8	137.5/72.4

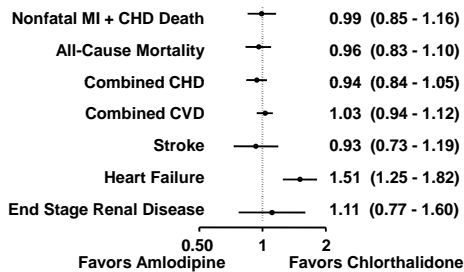
41



AHT Age < 65

Amlodipine/Chlorthalidone

Relative Risk and 95% Confidence Intervals



05/14/03

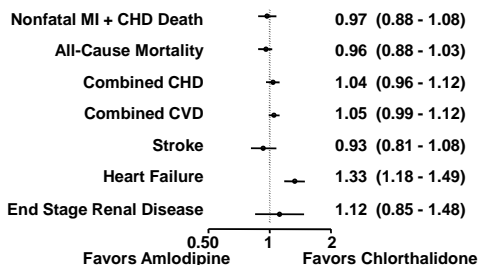
42



AHT Age 65+

Amlodipine/Chlorthalidone

Relative Risk and 95% Confidence Intervals



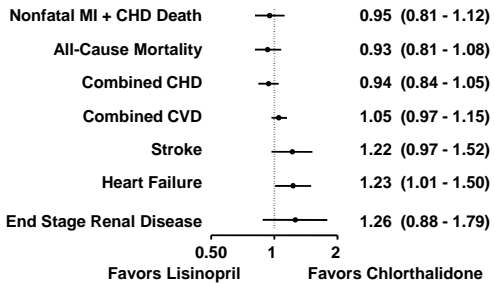
05/15/03

43



AHT Age < 65 Lisinopril/Chlorthalidone

Relative Risk and 95% Confidence Intervals



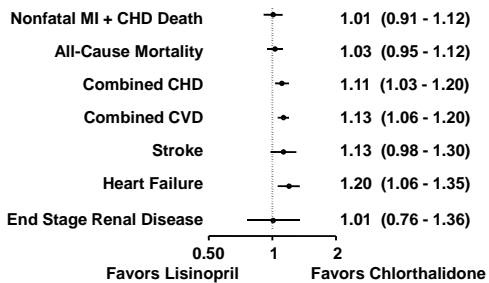
05/14/03

44



AHT Age 65+ Lisinopril/Chlorthalidone

Relative Risk and 95% Confidence Intervals



05/15/03

45

ALLHAT Trial - Age ≥ 75

Similar results as in younger groups

There was no difference among drugs for primary outcome (fatal and nonfatal MI)

Chlorthalidone →
less CHF than Amlodipine or Lisinopril

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**Double-Blind Placebo-Controlled Outcome Trials
in the Elderly: Risk Reduction (%) with
Antihypertensive Therapy**

Trial	Total Mortality	CV Mortality	Stroke Mortality	Heart Failure	All Myocardial Infarctions	Fatal and Nonfatal Stroke
EWPHE (>60)	-26	-38*	-43	-63*	NS	-46
HYVET (≥80)	-21*	-23	-39*	-64*	-28	-30
SHEP (≥60)	-13	-20	-29	-54*	-27*	-36*
STOP-Hypertension (70-84)	-43*	NS	-73*	-51*	-13	-47*
Syst-Eur (≥60)	-14	-27	-27	-29	-30	-42*

*Significant reduction (PS .05)

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Treatment of hypertensive patients
> 80 years of age. Should it be
pursued vigorously?

YES----with certain caveats

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**MANAGEMENT PROBLEMS
in the Elderly**

- DIZZINESS,-FATIGUE,-
 - POSTURAL HYPOTENSION --
- Patients may feel like a ZOMBIE

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What is a Zombie ?



- Snake God of Voodoo cults in West Africa
- A corpse revived by a supernatural power or spell (Voodoo)
- A tall mixed drink made of various rums, liqueur, and fruit juice

50

Treatment of ISH: How Low Should We Go?

Lower systolic BP to <150 mm Hg? <140 mm Hg? Or lower?

In SHEP

Decreasing SBP to <160 mm Hg decreased stroke rate by 33%

Decreasing SBP to <150 mm Hg reduced stroke rate by 38%

No further benefit below 140 mm Hg

Reducing DBP below 55-60 mmHg may negate benefit

51

Outcome benefit should be evaluated differently in the very elderly

- Less emphasis on mortality outcomes
- More emphasis on quality of life and disabilities outcomes

HYPERTENSION IN THE VERY ELDERLY

Do data support treatment in hypertensive patients > 80 years of age?

Are there benefits? – decrease in strokes, CV events, CHF or mortality?

Outcomes of Antihypertensive Treatment in 1566 Subjects Aged 80 and Older in Double -Blind Trials - 3 Year Follow-up

Outcome	Number of Events		RR
	Treatment (n=824)	Control (n=742)	
Stroke*	51	69	0.64*
Coronary events*	39	41	0.85
Heart failure*	33	50	0.58*
CV deaths	104	93	1.11
All deaths*	208	180	1.14*

*Significant difference

Hypertension in People >80 Years of Age

- Increasing number of octogenarians
- Many have hypertension
- Does it increase risk? --- Yes (although some debate)
- Can BP be lowered? – probably
- Does this reduce disability? --- Yes
- Should hypertension >80 be treated? --- **Yes**

55

Hypertension in the Very Elderly Trial (HYVET)

Average age: 83.5
 No. of patients 3845
 Double Blind: 1933
 Placebo: 1912
 Baseline BP: 113 / 90.8 mm Hg
 Target BP: 150 / 80 mm Hg
 Indapamide SR 1.5 mg add Perindopril 2-4 mg
 Relatively healthy older aged population
 65% already on Rx

56

Hypertension in the Very Elderly Trial (HYVET)

Conclusions

- Antihypertensive treatment based on a diuretic, Indapamide (SR) 1.5 mg, ± an ACE inhibitor, Perindopril, reduced stroke mortality and total mortality in the very elderly
- NNT (2 yrs) = 94 for stroke and 40 for mortality
- Large and significant benefit in reduction of heart failure events and for combined endpoint of cardiovascular events
- Benefits seen early
- Treatment regime employed was safe

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Hypertension in the Very Elderly Trial (HYVET)

Results: BP difference: -15/-6 mm Hg Active compared to

Placebo - Mean achieved BP: 144/78 mm Hg

	HR (%)	95% CI	P
All stroke	-34	0.46 – 0.95	0.025
Total mortality	-28	0.59 – 0.88	0.001
Fatal stroke	-45	0.33 – 0.93	0.021
CV mortality	-27	0.55 – 0.97	0.029
Heart failure	-72	0.17 – 0.48	<0.001
CV events	-37	0.51 – 0.71	<0.001

Postural Hypotension

- Decrease in standing SBP >10 mmHg, when associated with dizziness/fainting, is more frequent in older SBP patients, patients with diabetes or on diuretics, and patients on some psychotropic drugs
- BP in most elderly individuals should be monitored in the upright position

Orthostatic BP Changes in HYVET

- N = 1283
- Age: 83.8
- Entry BP: 182/100 mm Hg
- Average decrease in BP: 8/1.3 mm Hg
- **7.7% ≥ 20 mm Hg SBP**
- **5.4% > 10 mm Hg DBP**
- 1.6% BOTH

J of Hum Hyper 1999;13:839-840

Status of BP Control Among 800 Elderly Men in a 2-year Study

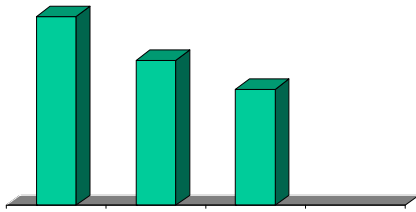
- **More than 40 percent of subjects had BPs > 160/90 mm Hg**
- Patient visits averaged 5-6/year
- Medication was increased only 26% of the time in patients with BPs > 155/90 mm Hg
- Medication was increased only 22% of the time in patients with BPs <90 but > 165 mm Hg

N Engl J Med. 1998;339:1957.

61

Many Older Patients with SBP of 160 mm Hg are not being Treated

% Likely to be Treated



Age Group

Am J Geriatr Cardiol 1997;5:21-36

62

DEMENTIA

- Rate of Dementia is projected to increase dramatically in the next 20 years
- Increase will be primarily in those ≥ 75 years of age
- Hypertensives have some evidence of impaired mental activity compared to normotensives

NEJM 2001;344:1160

63

DEMENTIA AND HYPERTENSION

PREVALENCE

AGE 70-74 - 2.8 %

AGE 90-95 - 38.6%

INCIDENCE

10.7/1000 person-years

Harrington et al 36:1079, 2000

DEMENTIA AND HYPERTENSION

Compared to Normotensive individuals

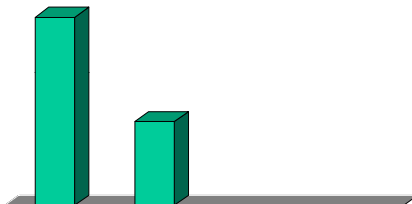
**HYPERTENSIVES ARE SLOWER
IN standardized mental activity tests**

(number vigilance, reaction times, word and picture recognition, spatial memory and memory scanning)

Hypertension 36:1079, 2000

Better BP Control Reduces Dementia by 55% in ISH

Dementia /1000 pt yrs



(n = 1417) (n = 1485)

Arch Intern Med 2002;162:2046-2052
