Success and Predictors of Blood Pressure Control in Diverse North American Settings: The Antihypertensive and Lipid-lowering Treatment to Prevent Heart Attack Trial (ALLHAT)

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J Clinical Hypertens 2002; 4:393-404
The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial

Geographic distribution of ALLHAT Clinical Sites that enrolled participants in the trial.
February 14, 1994 - January 31, 1998

ALLHAT is sponsored by the National Heart, Lung, and Blood Institute, National Institutes of Health, in collaboration with the Department of Veterans Affairs.
Blood Pressure Control (<140/90 mm Hg) Rates in The United States in the 1990s

- NHANES III:
  - 27% for adults with hypertension.
  - Among those on treatment in NHANES III: 30 to 45% in older adults from various sex-race/ethnicity groups.

- In treated patients in Olmstead County, MN:
  - 33% among persons 45 years and older.

- At a group of New England Veterans Affairs Medical Centers:
  - < 25% in older (mostly white) males

Randomized Design of ALLHAT BP Trial

42,418 High-risk hypertensive patients

Consent / Randomize

Amlodipine
Chlorthalidone
Doxazosin
Lisinopril

Follow until death or end of study (4-8 years, mean 4.9 years)
ALLHAT Inclusion Criteria

- Men and women aged $\geq$ 55 years
- Seated blood pressure (2 categories):
  1) Treated for @ least 2 months.
  2) Not on drugs or on drugs < 2 months.
- Additional risk factor or target organ damage.
# ALLHAT BP Eligibility Criteria

<table>
<thead>
<tr>
<th>Status at Visit 1 and Visit 2</th>
<th>Lower Limit (mm Hg)</th>
<th>Upper Limit (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>On 1-2 drugs used for hypertension &gt;= 2 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visit 1</td>
<td>---</td>
<td>160</td>
</tr>
<tr>
<td>Visit 2</td>
<td>---</td>
<td>180</td>
</tr>
<tr>
<td>On drugs for &lt; 2 months or currently untreated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visit 1 &amp; Visit 2</td>
<td>140</td>
<td>180</td>
</tr>
</tbody>
</table>

SBP or DBP lower limit must be met at Visit 1 and Visit 2
SBP and DBP upper limit must be met at Visit 1 and Visit 2
### Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size</td>
<td>33,357</td>
</tr>
<tr>
<td>Mean SBP/DBP</td>
<td>145 / 83</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>67</td>
</tr>
<tr>
<td>Black, %</td>
<td>35</td>
</tr>
<tr>
<td>Women, %</td>
<td>47</td>
</tr>
<tr>
<td>Current smoking %</td>
<td>22</td>
</tr>
<tr>
<td>ASCVD, %</td>
<td>47</td>
</tr>
<tr>
<td>Type II diabetes, %</td>
<td>36</td>
</tr>
<tr>
<td>LVH by ECG, %</td>
<td>3</td>
</tr>
<tr>
<td>Mean BMI, kg/m²</td>
<td>30</td>
</tr>
<tr>
<td>Test</td>
<td>Value</td>
</tr>
<tr>
<td>--------------------------</td>
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</tr>
<tr>
<td>Serum Creatinine, mg/dL</td>
<td>1.02</td>
</tr>
<tr>
<td>Fasting Glucose, mg/dL</td>
<td>125</td>
</tr>
<tr>
<td>Total Cholesterol, mg/dL</td>
<td>216</td>
</tr>
<tr>
<td>LDL-Cholesterol, mg/dL</td>
<td>136</td>
</tr>
<tr>
<td>HDL-Cholesterol, mg/dL</td>
<td>47</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>172</td>
</tr>
</tbody>
</table>
## Antihypertensive Treatment Regimen

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorthalidone</td>
<td>12.5 mg</td>
<td>12.5 mg</td>
<td>25 mg</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2.5 mg</td>
<td>5 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>10 mg</td>
<td>20 mg</td>
<td>40 mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reserpine</td>
</tr>
<tr>
<td>Clonidine</td>
</tr>
<tr>
<td>Atenolol</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Step 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydralazine</td>
</tr>
</tbody>
</table>
Mean Systolic and Diastolic Blood Pressure

Compared to chlorthalidone:

SBP significantly higher in the amlodipine group (~1 mm Hg) and the lisinopril group (~2 mm Hg).

Compared to chlorthalidone:

DBP significantly lower in the amlodipine group (~1 mm Hg).

JAMA 2002;288:2981-2997
ALLHAT
SBP Distribution at Baseline and 36 Months of Follow-up

Baseline:
- 31% < 140 mm Hg
- 14% ≥ 160 mm Hg

36 Months:
- 64% < 140 mm Hg
- 8% ≥ 160 mm Hg

ALLHAT: DBP Distribution at Baseline and 36 Months of Follow-up

**Baseline**
- 68% < 90 mm Hg
- 4% ≥ 100 mm Hg

**36 Months**
- 90% < 90 mm Hg
- 2% ≥ 100 mm Hg

ALLHAT

SBP Distribution at 36 Months of Follow-up

64% < 140 mm Hg
36% ≥ 140 mm Hg
8% ≥ 160 mm Hg
Of those ≥ 140 mm Hg:
53% 140-149 mm Hg
24% 150-159 mm Hg
(77% 140-159 mm Hg)

BP Control (<140/90 mm Hg) at 5 Years by Randomized Group

JAMA 2002;288:2981-2997
Blood Pressure Control

ALLHAT

Blood Pressure Control 1.6 = mean number of drugs

@ 5 years: 62% were on ≥2 drugs, 30% were on 1 drug with BP <140/90 mm Hg

Proportion of Uncontrolled ALLHAT Participants Not Stepped Up at Annual Visits

Multiple Logistic Regression Analysis: Relative Odds (95% CI) of BP Control at 36 Months

- Baseline SBP (10 mmHg ↑)
- Age (10 year ↑)
- Black
- Type 2 Diabetic
- Smoker
- BMI ≥ 30 kg/m²
- Prior Rx
- Cr ≥ 1.5 mg/dL
- ECG LVH
- Clinic Research Exp.

BP Control Worse More (*) or less (†) likely to be on 2+ drugs

BP Control Better

Male
ASCVD

Logistic Regression Analysis of Relative Odds (95% CI) of Being On 2+ Drugs at 36 Months

- Age (10 year ↑)
- Black
- Smoker
- Baseline SBP (10 mmHg ↑)
- Male
- Type 2 Diabetic
- ASCVD
- BMI ≥ 30 kg/m²
- Cr ≥ 1.5 mg/dL
- ECG LVH
- Clinic Research Exp.

Less Likely To Be On 2+ Drugs

More Likely To Be On 2+ Drugs

Relative Odds (95% CI) of BP Control or Being On 2+ Drugs at 36 Months of Follow-Up, by Geographic Region (Compared with West)

Other Large Trials and BP Control

- LIFE (4.8 years of f/u):
  - 46%: atenolol arm
  - 49%: losartan arm

- CONVINCE (30 and 36 months of f/u):
  - 67% overall and similar in verapamil HS and standard therapy arms
The ALLHAT trial provides compelling evidence that BP control rates can be markedly increased to at least 2/3 of the treated hypertensive population.

These control rates were achieved in a multiethnic hypertensive population in diverse practice settings.

Most of the participants who did not achieve goal had persistent elevation of SBP.
Conclusions - 2

- At least 2 antihypertensive medications are required for most patients to achieve BP control.
- Various factors that are associated with lower BP control rates were identified.
- It is likely that the majority of people with hypertension could achieve BP < 140/90 mm Hg with the antihypertensive medications available today.
BP Inadequately Controlled† in Nearly 75% of Adult Hypertensives* in the US

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<tbody>
<tr>
<td>Aware</td>
<td>51%</td>
<td>73%</td>
<td>68%</td>
</tr>
<tr>
<td>Treated</td>
<td>31%</td>
<td>55%</td>
<td>54%</td>
</tr>
<tr>
<td>Controlled†</td>
<td>10%</td>
<td>29%</td>
<td>27%</td>
</tr>
</tbody>
</table>

†SBP <140 mm Hg and DBP <90 mm Hg.
NHANES = National Health and Nutrition Examination Surveys.
•Age 18 to 74 years with SBP 140 mm Hg or DBP 90 mm Hg or taking antihypertensive medication.

Participants were randomized to chlorthalidone (15,255), amlodipine (9,048), lisinopril (9,054), or doxazosin (9,061) between 2/94-1/98. [Sponsored by NHLBI]

Over 15,000 (>3000/drug group) of ALLHAT participants had DM at baseline and a similar # were African Americans.

The doxazosin arm was stopped in January 2000 due to higher CV events and virtually no chance to show a difference in CHD.

The remaining 3 arms continued to scheduled completion and were reported in December 2002.
Inclusion Criteria - 2

At least one of the following:

- Myocardial infarction or stroke: age-indeterminate or at least 6 months old
- History of revascularization procedure
- Other documented ASCVD
- Major ST segment depression or T-wave inversion
- Type II diabetes mellitus
- HDL cholesterol < 35 mg/dl on any 2 or more determinations in past 5 years
- Left ventricular hypertrophy (past 2 years) on ECG or echo
- Current cigarette smoking
Exclusion Criteria for Antihypertensive Trial

- Angina pectoris or recent MI or Stroke (within past 6 months)
- Heart failure and/or LVEF < 35%, if known
- Renal insufficiency (serum creatinine > 2.0 mg/dL)
- Requiring diuretics, calcium channel blockers, ACE inhibitors, or alpha adrenergic blockers for reasons other than high blood pressure
- Requiring more than two antihypertensive agents to achieve blood pressure control
- Factors suggesting inability to comply with protocol
Number of Antihypertensive Drugs Used and BP Control (<140/90 mm Hg)