The Hypertension, Detection, and Follow-up Program (HDFP)

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

Sponsored by the National Heart, Lung, and Blood Institute (NHLBI)

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Rationale

• By the early 1970s, several data sets from US population surveys had found hypertension to be one of the most prevalent chronic diseases for which treatment was available.

• About 85% of individuals with high BP were undetected, untreated, or inadequately controlled.

• The VA Study Group trial (‘67,’70,’71) showed a significant reduction of mortality/morbidity from treating middle-aged, male hypertensive patients with DBP of 115-129 mm Hg.
The VA study, which had involved highly selected patients, left unanswered several questions:

1. Could hypertensives in an entire community be identified, brought and kept under pharmacologic management?
2. Would intervention of hypertension identified in the population of the community at large reduce the occurrence of associated disease and death?
Rationale

3. Would therapeutic efficacy exceed toxicity in the mild hypertensive and justify long-term treatment?

4. Would pharmacologic control of elevated BP be effective in young adults and women?

5. Would the occurrence of myocardial infarction and coronary death be decreased by antihypertensive therapy?
Trial Design

- Randomized, multi-center clinical trial
- Determine whether antihypertensive therapy can reduce occurrence of all-cause mortality in hypertensive participants screened from the general population
- 10,940 hypertensive participants 30-69 years old; Half the participants were to be randomly assigned to Stepped Care (SC) and half to Referred Care (RC).
Trial Design

- The SC group was offered antihypertensive therapy in special centers. Therapy was increased stepwise to achieve and maintain reduction of BP to or below set normotensive goals.
- The RC group was referred for treatment to usual sources of care, with special referral efforts for those with more severe hypertension or pre-existing organ system damage.
Secondary Outcomes

- CV mortality
- Stroke
- MI
- LVH
- Adverse effects
- Success of drug treatment
Fig. 2  Hypertension Detection and Follow-Up Program clinical sites and support centers.
**Table 1**  HDFP Inclusion and Exclusion Criteria

*Inclusion Criteria*
1. Men and women aged 30–69 years
2. Average home screening DBP ≥ 95 mm Hg
3. Confirmed follow-up DBP ≥ 90 mm Hg

*Exclusion Criteria*
1. Terminally ill patients
2. Institutionalized patients
Each clinical center defined a population base for enumeration and screening of potential participants.

13 centers identified target populations on the basis of residential areas (census tracts, probability samples of larger areas, or entire housing projects).

1 center used employment rolls of industries.

Census enumeration was used to prepare a roster of all household members and to identify those between the ages of 30 and 69.
Enumeration, Screening, and Recruitment

- Home screening of those ages 30 to 69, which included a health status and health care interview plus BP measurements,
- Interviewers were trained to conduct these tasks in a standardized manner.
- Interview included education and employment status, basic demographic information, information on history of hypertension and its treatment, smoking history, history of heart attack, stroke, and diabetes, information on health beliefs, and status of current health care.
Fig. 3 Number of persons enumerated, screened, and randomized by Hypertension Detection and Follow-Up Program.
Sample Size Assumptions & Statistical Methods

- 90% power to detect 17.7% reduction in risk for all-cause mortality
- 2-sided $\alpha=.05$
- Analysis according to “intent to treat”
- Cumulative event rates
- Differences between event curves - Log-rank tests
- Sample size 10,500
Step 1 SC Treatment Protocol

<table>
<thead>
<tr>
<th>Step 1 Agent</th>
<th>Initial Dose*</th>
<th>Step-up Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorthalidone</td>
<td>25</td>
<td>50-100</td>
</tr>
</tbody>
</table>

* mg/day
### Step Up SC Treatment Protocol

<table>
<thead>
<tr>
<th>Step 2 Agent:</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reserpine</td>
<td>0.1 – 0.25 qd</td>
</tr>
<tr>
<td><strong>Step 3 Agent:</strong></td>
<td></td>
</tr>
<tr>
<td>Hydralazine</td>
<td>30-200 qd</td>
</tr>
<tr>
<td><strong>Step 4 Agent:</strong></td>
<td></td>
</tr>
<tr>
<td>Guanethidine</td>
<td>10-200 qd</td>
</tr>
<tr>
<td><strong>Step 5 Agent:</strong></td>
<td></td>
</tr>
<tr>
<td>Additional drugs as needed</td>
<td></td>
</tr>
</tbody>
</table>

*All doses in mg*
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Measure</th>
<th>SC (5485)</th>
<th>RC (5455)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean SBP/DBP</td>
<td>159 / 101</td>
<td>159 / 101</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>Black, %</td>
<td>44</td>
<td>45</td>
</tr>
<tr>
<td>Women, %</td>
<td>46</td>
<td>46</td>
</tr>
<tr>
<td>Current smoking %</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>History of MI, %</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Type 2 diabetes, %</td>
<td>7</td>
<td>8</td>
</tr>
</tbody>
</table>
Fig. 6  Percentage of stepped care (SC) (n = 5485) participants with clinic follow-up visits (active SC) by month of follow-up; the percentage of “active SC” on specific drug steps and at or below their goal diastolic blood pressure.
Fig. 7  Hypertension Detection and Follow-Up Program cumulative, life table, all-causes death rates in stepped care (n = 5485) and referred care (n = 5455) participants. All participants were followed up to a common 5-year trial termination date. Deaths beyond 5 years were excluded from the trial’s final report (4) because mortality follow-up of referred care participants ended with their year-5 (60-month) visit. Subsequent mortality surveillance identified post-5-year deaths, allowing life table analysis of the trial’s full follow-up (17).
Fig. 8  Hypertension Detection and Follow-Up Program cumulative, life table, all-causes death rates in stepped care (n = 5485) and referred care (n = 5455) participants (1973–1982).
Operational Factors Acceptance of Antihypertensive Therapy

- The HDFP shaped its program for SC participants to attempt to reduce barriers to patient cooperation.
- Center staffs attuned to need for long-term antihypertensive treatment, help communicate this to patients.
- Hours of operation, transportation arrangements, treatment center location organized to increase accessibility for participants.
Operational Factors
Acceptance of Antihypertensive Therapy

- Treatment was without cost to the patient.
- Visits by appointment, minimum waiting time.
- Missed appointments monitored; early renewed contact.
- SC treatment, frequent visits at early stages of treatment, plus giving time and encouragement for patients to discuss problems aimed at minimizing side effects that can deter discontinuation of treatment.
Socioeconomic Factors Acceptance of Antihypertensive Therapy

- Full-time employed more likely to be active
- Higher education levels more likely to be participate
- Married persons more likely to be active
Motivational Factors
Acceptance of Antihypertensive Therapy

- Factors related to health status and behavior (history of more days sick, more hospitalizations, a positive history of comorbid conditions, current smoking) had a modest negative association with participation in some age-sex-race groups
- Promptness of follow-up of initial findings tends to increase participation – quickly schedule follow-up appointments
HDFP

Accomplishments

- Hypertension could be
  - identified in the community
  - brought under pharmacological treatment
  - effectively treated among
    - young and old
    - blacks and white
    - men and women
- Through antihypertensive treatment total morality could be reduced
  - overall
  - in age, race, and sex subgroups
  - in those with mild hypertension
  - in those with uncomplicated mild hypertension
- A large-scale clinical trial could be conducted successfully in the community
- Landmark trial
- Implications and influence are still strong in the medical and public health communities
- Demonstrated that hypertension in the community could be identified by enumeration and screening
- Demonstrated that systematic management of hypertension could reduce mortality in people with high BP.
Impact

- Demonstrated that antihypertensive treatment reduces morbidity/mortality in
  - age, race, and sex subgroups
  - those with uncomplicated mild hypertension
- Treatment had an enormous public health benefit, as more than 70 million Americans have high BP.
- Reduction in deaths, strokes, and CHD events, and the economic impact, are substantial.
Influence on Practice

- Major effect on guidelines for hypertension management from the Joint National Committee
- Heightened awareness of hypertension as a public health problem
- Played a major role in resulting in large decreases in stroke mortality, hypertensive renal failure and heart failure in the United States
Influence on Practice

- Resulted in the large-scale institution of treatment for patients with mild hypertension
- Demonstrated efficacy of using diuretics in treating hypertension.
- Although the use of diuretics deceased after the Multiple Risk Factor Intervention Trial (MRFIT) results, the success of the SHEP trial, which used chlorthalidone as a first-line drug, revitalized the use of diuretics.
Disseminating Clinical Trial Results to Promote Public Health: Case Study from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)
Antihypertensive Trial Design

- Largest hypertension trial – 42,418 participants randomized at 623 clinical sites in a variety of clinical settings
- Tested 3 newer antihypertensive drug classes (ACE inhibitors, calcium channel blockers, alpha blockers) against diuretic
- Primary endpoint combined fatal CHD or nonfatal MI
- Sponsored by NHLBI
Summary of Outcomes
Relative Risks and 95\% CI

<table>
<thead>
<tr>
<th>Condition</th>
<th>Amlodipine / Chlorthalidone</th>
<th>Lisinopril / Chlorthalidone</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>0.98 (0.91, 1.08)</td>
<td>0.99 (0.91, 1.08)</td>
</tr>
<tr>
<td>Death</td>
<td>0.96 (0.89, 1.02)</td>
<td>1.00 (0.94, 1.08)</td>
</tr>
<tr>
<td>CCHD</td>
<td>1.00 (0.94, 1.07)</td>
<td>1.05 (0.98, 1.11)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.93 (0.82, 1.06)</td>
<td>1.15 (1.02, 1.30)</td>
</tr>
<tr>
<td>CCVD</td>
<td>1.04 (0.99, 1.09)</td>
<td>1.10 (1.05, 1.16)</td>
</tr>
<tr>
<td>HF</td>
<td>1.38 (1.25, 1.52)</td>
<td>1.19 (1.07, 1.31)</td>
</tr>
</tbody>
</table>

Amlodipine Better | Chlorthalidone Better | Lisinopril Better | Chlorthalidone Better

4/17/2006
BP goal <140/90 mm Hg.
Lifestyle modifications.
For better BP control & long term CVD risk:
- Start with thiazide-type diuretic for untreated SBP 140-159 or DBP 90-99 mm Hg (Stage 1 hypertension).
- Use multi-drug regimen including a thiazide-type diuretic for untreated SBP > 160 or DBP > 100 mm Hg (Stage 2).
- For uncontrolled hypertension, add thiazide-type diuretic to regimen.
Traditional Approaches to Dissemination & Implementation of Clinical Trial Results and Guidelines

- Press release/press conference
- Short burst of media coverage
- Presentations at scientific meetings
- Publications in peer-reviewed journals
“People do a wonderful press conference, publish in prestigious journals, present at important meetings – and nothing happens”, says Paul Whelton, professor of epidemiology and medicine at Tulane University Health Sciences Center (New Orleans, LA, USA), who was on the ALLHAT Steering Committee. Publishing your data will not get doctors to change their practice, Whelton says.
BP Control Rates

Trends in awareness, treatment, and control of high blood pressure in adults ages 18–74

<table>
<thead>
<tr>
<th></th>
<th>National Health and Nutrition Examination Survey, Percent</th>
</tr>
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<tbody>
<tr>
<td>Awareness</td>
<td>51 73 68 70</td>
</tr>
<tr>
<td>Treatment</td>
<td>31 55 54 59</td>
</tr>
<tr>
<td>Control</td>
<td>10 29 27 34</td>
</tr>
</tbody>
</table>

ALLHAT Dissemination – Features & Challenges

- NHLBI requires a detailed dissemination & evaluation plan for trials with potential for immediate public health applicability
- ALLHAT Steering Committee packaged and published recommendations based on trial results
- NHLBI has an existing HBP education infrastructure (NHBPEP)
  - JNC has packaged recommendations based on a synthesis of all available evidence in HBP prevention and treatment
- Dissemination plan must meld both
Branding of the Dissemination Project

Improving Blood Pressure Treatment in the Community: How the JNC7 Recommendations and ALLHAT Results Relate to Your Practice
Multi-faceted Intervention

- **Furthers traditional approaches**
  - Press release/press conference
  - Media coverage (usually short bursts)
  - Presentation at scientific meetings
  - Publications in peer-reviewed journals

- **New approaches**
  - Health care providers (academic detailing)
  - Formulary systems approach
  - Patient-oriented approach
  - Professional society approach
  - Prespecified evaluation component
## Selected Factors that Influence Dissemination and Implementation of New Treatment Trial

### Findings – Providers

<table>
<thead>
<tr>
<th>Influences</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge</td>
<td>Face-to-face colleague contact (academic detailing)</td>
</tr>
<tr>
<td>Conviction</td>
<td>Contact through NHBPEP member organizations</td>
</tr>
<tr>
<td>Recall of results</td>
<td>Inquiries from patients</td>
</tr>
<tr>
<td>Interest in innovation</td>
<td></td>
</tr>
<tr>
<td>Marketing influences</td>
<td></td>
</tr>
<tr>
<td>Influences</td>
<td>Approach</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Access to care</td>
<td>Formulary approach – 8 major systems</td>
</tr>
<tr>
<td>Insurance coverage</td>
<td></td>
</tr>
<tr>
<td>Marketing influences</td>
<td></td>
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</tbody>
</table>
# Selected Factors that Influence Dissemination and Implementation of New Treatment Trial

**Findings – Patients**

<table>
<thead>
<tr>
<th>Influences</th>
<th>Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferences</td>
<td>Major publications, e.g., Prevention, Modern Maturity, etc.</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
</tr>
<tr>
<td>Marketing influences</td>
<td></td>
</tr>
</tbody>
</table>
Academic Detailing

- 147 Investigator Educators (ALLHAT Investigators)
- Centralized training
- Materials
- Remuneration for IE and staff
- Website
Investigator Educator Disclaimer

• I am not:
  – Employed or paid by any pharmaceutical company for this presentation

• I am:
  – An ALLHAT investigator
  – Personally committed to blood pressure control and evidence-based hypertension treatment
  – Being paid a nominal amount by NHLBI to talk to you today about blood pressure treatment guidelines
  – Intending to dispel some misperceptions about the current guidelines for blood pressure treatment
Academic Detailing - Pilot

- Feasibility of achieving the number of presentations (1 presentation per investigator per month)
- 24 Investigator Educators, 6 months
Academic Detailing – Full Scale

- 147 Investigator Educators (IE’s)
- Materials
  - Handouts, posters, worksheets
  - PowerPoint presentations & FAQs
  - IE newsletters & discussion board
- Evaluation – 2007
Improving Blood Pressure Treatment
in the Community

A Joint Project of the National High Blood Pressure
Education Program and the Antihypertensive
and Lipid-Lowering Treatment to
Prevent Heart Attack Trial Collaborative Group
Are you in Control?

BLOOD PRESSURE

Your doctor knows something new.

ASK.
Clinician – Patient Worksheet

ARE YOU IN CONTROL?

Name: ________________________________
Date: ________________________________

My blood pressure today: _____ / _____
My goal: _____ / _____

If your blood pressure today is below your goal, congratulations! Continue with your healthy lifestyle and take your blood pressure medicines as prescribed by your doctor.

If your blood pressure today is not below your goal pressure, talk to your doctor about healthy lifestyle changes and about your blood pressure medicine. Use the tips below to check off how you and your doctor decide to help lower your blood pressure:

<table>
<thead>
<tr>
<th>Your healthy lifestyle can help to lower your blood pressure:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achieve and maintain a healthy weight. (Goal: _____ pounds)</td>
</tr>
<tr>
<td>Be physically active for 30 minutes most days of the week.</td>
</tr>
<tr>
<td>Eat a diet high in fresh fruits and vegetables and low fat dairy products with reduced saturated and total fat.</td>
</tr>
<tr>
<td>Choose foods that are lower in salt and other forms of sodium. Read food labels.</td>
</tr>
<tr>
<td>If you drink alcohol, have no more than one drink a day for women, two drinks a day for men. For example, one drink = 5 ounces of wine or one 12-ounce beer.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood pressure medicine can also help:</th>
</tr>
</thead>
<tbody>
<tr>
<td>If you are not already taking blood pressure medicine, ask your doctor if you need to be on medication, such as a diuretic (water pill).</td>
</tr>
<tr>
<td>If you are already on blood pressure medicine, ask your doctor if the dose of your blood pressure medicine should be increased or if a new medicine should be added.</td>
</tr>
<tr>
<td>If your medicine does not include a diuretic (water pill), ask your doctor if this would be a good addition to your blood pressure medicine regimen.</td>
</tr>
<tr>
<td>Remember to take your blood pressure medicine exactly as prescribed by your doctor.</td>
</tr>
</tbody>
</table>
Results

- **IE approach**
  - 1698 presentations
  - 18,500+ clinicians reached
  - 41 states plus D.C.

- **Direct patient messages (e.g., AARP)** – 14 contacts

- **Formulary approach** – 10 contacts

- **Materials for professional society use** – 20 contacts
Evaluations

- **Process evaluation**
  - Pretest and posttest data from attendees
  - Feedback from IE’s and coordinators
  - Specific data collected about presentations

- **Outcome evaluation from closed health systems**
  - VA monitoring of drug use & BP control
  - Oschner Health Plan, Louisiana
  - Kaiser
  - BP control and medication use

- **Outcome evaluation based on national prescription data** – NDTI, NPA, Integrated Promotional Services Audit
Hypertension Treatment by Drug Class

- Calcium Channel Blockers
- Beta Blockers
- Diuretics
- ACE Inhibitors
- ARBs

ALLHAT Results

IMS Health NDTI, 1978-2004
Key Lessons Learned

- Outside influences
- Dissemination partners
- Planning and lead time for strategies
- A large multi-method dissemination of clinical trial results is feasible