The Current Hype on Hypertension: Novel Concepts in the Evaluation and Management

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Immediate Past President
American Society for Preventive Cardiology

UC Irvine Health
“There is a lack of correlation in most cases between the severity and duration of hypertension and development of cardiac complications.”
'CAME OUT OF CLEAR SKY,' SAYS PRESIDENT'S PHYSICIAN

Adm. Ross T. McIntire asserts there was no indication of imminent danger.

DEATH DUE TO CEREBRAL HEMORRHAGE --- BLOOD VESSEL IN BRAIN BROKE

WASHINGTON, April 13 (AP). President Roosevelt died from what doctors call a cerebral hemorrhage.

Complications of Hypertension:

- TIA, stroke
- Retinopathy
- Peripheral vascular disease
- LVH, CHD, HF
- Renal failure

Hypertension is a risk factor

TIA = transient ischemic attack; LVH = left ventricular hypertrophy; CHD = coronary heart disease; HF = heart failure.
Global Mortality 2000: Impact of Hypertension and Other Health Risk Factors


Attributable Mortality (In thousands; total 55,861,000)

High blood pressure
Tobacco
High cholesterol
Underweight
Unsafe sex
High BMI
Physical inactivity
Alcohol
Indoor smoke from solid fuels
Iron deficiency

High mortality, developing region
Lower mortality, developing region
Developed region

0 1000 2000 3000 4000 5000 6000 7000 8000
Attributable Mortality

Increased BP: top attributable cause of global mortality

- 75 million deaths annually attributable to HTN (12.8% of all deaths)
- 57 million disability-adjusted life years
- 40% global prevalence of HTN in 2008
- Highest: 46% Africa; Lowest: 35% America
- Uncontrolled HTN: 1980: 600 million
  2010: 1 billion
Hypertension: How Big Is the Problem?

At Least 78 Million Americans Have Hypertension

81% are aware, 75% treated, but only 53% are controlled

Go A et al Circulation 2013
Hypertension Awareness, Treatment, and Control: US 1976 to 2000*

- NHANES II 1976-1980
  - Awareness: 51%
  - Treated: 31%
  - Control: 10%

- NHANES III (Phase 1) 1988-1991
  - Awareness: 55%
  - Treated: 29%

- NHANES III (Phase 2) 1991-1994
  - Awareness: 68%
  - Treated: 27%

- NHANES 1999-2000
  - Awareness: 73%
  - Treated: 55%
  - Control: 34%

Healthy People 2000/2010
Control Target = 50%


Dariush Mozaffarian et al. Circulation. 2016;133:e38-e360

Dariush Mozaffarian et al. Circulation. 2016;133:e38-e360
SBP-Associated Risks: MRFIT

SBP versus DBP in Risk of CHD Mortality

CHD Death Rate

Diastolic BP (mm Hg)

Systolic BP (mm Hg)

Adapted from Neaton JD et al. Arch Intern Med. 1992;152:56-64.
CV Mortality Risk Doubles with Each 20/10 mm Hg BP Increment

*Individuals aged 40-70 years, starting at BP 115/75 mm Hg.
CV, cardiovascular; SBP, systolic blood pressure; DBP, diastolic blood pressure
Distribution of Hypertension Subtype in the untreated Hypertensive Population in NHANES III by Age

Numbers at top of bars represent the overall percentage distribution of untreated hypertension by age.

<table>
<thead>
<tr>
<th>Category</th>
<th>JNC VI SBP (mm Hg)</th>
<th>JNC VI DBP (mm Hg)</th>
<th>JNC 7 Category</th>
<th>JNC 7 SBP (mm Hg)</th>
<th>JNC 7 DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt;120</td>
<td>80</td>
<td>Normal</td>
<td>&lt;120</td>
<td>80</td>
</tr>
<tr>
<td>Normal</td>
<td>120-129</td>
<td>80-84</td>
<td>Prehypertension</td>
<td>120-139</td>
<td>80-89</td>
</tr>
<tr>
<td>Hi-normal</td>
<td>130-139</td>
<td>85-89</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Hypertension**

- Stage 1: 140-159 or 90-99
- Stage 2: 160-179 or 100-109
- Stage 3: ≥180 or ≥110

Adapted with permission from Chobanian AV et al. *Hypertension.* 2003;42:1206-1252.
What’s Wrong with this Picture?

- Measurement error
- Small number of readings
- White coat effect
- No measure of the diurnal changes of BP
Prehypertension …

- Is not a disease,
- Is not “hypertension”,
- Is not an indication for drug treatment of HTN,
- Does not have a BP goal,
- Does predict a higher risk for developing CV events,
- Does predict a higher risk for developing HTN,
- Should be an incentive to improve lifestyle practices for prevention of HTN and CVD.
## Prevalence of Blood Pressure Categories in US Adults ≥20 Years of Age (NHANES 1999-2000)

<table>
<thead>
<tr>
<th>BP Category</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>39%</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>31%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>30%</td>
</tr>
</tbody>
</table>

4-Year Progression To Hypertension: The Framingham Heart Study

Participants age 36 and older

Relation of Non-Hypertensive Blood Pressure to Cardiovascular Disease

**10-year Age-Adjusted Cumulative Incidence**

<table>
<thead>
<tr>
<th>SBP</th>
<th>&lt;120/80 mm Hg</th>
<th>120-129/80-84 mm Hg</th>
<th>130-139/85-89 mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women</strong></td>
<td>1.9</td>
<td>2.8</td>
<td>4.4</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td>5.8</td>
<td>10.1</td>
</tr>
</tbody>
</table>

**Hazard Ratio***

<table>
<thead>
<tr>
<th>SBP</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120/80</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>120-129</td>
<td>1.5</td>
<td>1.3</td>
</tr>
<tr>
<td>130-139</td>
<td>2.5</td>
<td>1.6</td>
</tr>
</tbody>
</table>

H.R. adjusted for age, BMI, Cholesterol, Diabetes and smoking *P<.001

Framingham Study: Subjects Ages 35-90 yrs.
The shape of things to come
Risk factor clustering with hypertension, ages 18–74 years. Framingham offspring.

FRAMINGHAM STUDY (1983)
CV Risk In 40-Year-Olds

8 Year Probability Per 1,000

<table>
<thead>
<tr>
<th>Condition</th>
<th>Systolic B.P.</th>
<th>Cholesterol</th>
<th>Glucose Intol.</th>
<th>Cigarettes</th>
<th>ECG-LVH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>105</td>
<td>185</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>105</td>
<td>335</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>105</td>
<td>185</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>105</td>
<td>335</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>105</td>
<td>185</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td></td>
<td>105</td>
<td>335</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td></td>
<td>105</td>
<td>185</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>105</td>
<td>335</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Ref. Kennel, 1983
BP is a **risk marker** for “The Metabolic Syndrome”

**NCEP-ATP III Definition: ≥3 of the Following**

- **Abdominal obesity (waist circumference)**
  - Men: >102 cm (>40 in)
  - Women: >88 cm (>35 in)

- **Triglycerides**
  - ≥150 mg/dL

- **HDL-C**
  - Men: <40 mg/dL
  - Women: <50 mg/dL

- **Blood pressure**
  - ≥130/≥85 mm Hg

- **Fasting glucose**
  - ≥100 mg/dL

*Diagnosis is established when ≥3 of these risk factors are present.*

Long-Term Antihypertensive Therapy Significantly Reduces CV Events

- Stroke: 35%-40%
- Myocardial infarction: 20%-25%
- Heart failure: >50%

Clinical Trials in Hypertension

Should we treat diastolic HBP?  What is the goal of treatment?  Should we treat DBP in older persons?  What is the best way to treat HBP?  Should we treat ISH in older persons?  Can we prevent hypertension?


HDFP
VA Cooperative Studies
EWPHE MRC-1 ANHBPH-1
SHEP MRC-2 STOP-1
HAPPHY MAPHY
TOMHS VA MONORx
HOT UKPDS
Syst-Eur Syst-China
CAPPB STOP-2
INSIGHT NORDIL
SCOPE CONVENCE ALLHAT ANBP2 LIFE
VALUE ASCOT ACCOMPLISH TROPHY

Which is more important to minimize CV Events?

Blood Pressure Lowering Effect or Specific Drug Effect
### BP-Lowering Treatment Trialists’ Meta-analysis: Comparisons of Different Active Treatments

<table>
<thead>
<tr>
<th>Major CV Events</th>
<th>Relative Risk</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI vs D/BB</td>
<td>2/0</td>
<td>1.02 (0.98, 1.07)</td>
</tr>
<tr>
<td>CA vs D/BB</td>
<td>1/0</td>
<td>1.04 (0.99, 1.08)</td>
</tr>
<tr>
<td>ACEI vs CA</td>
<td>1/1</td>
<td>0.97 (0.95, 1.03)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CV Mortality</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI vs D/BB</td>
<td>2/0</td>
<td>1.03 (0.95, 1.11)</td>
</tr>
<tr>
<td>CA vs D/BB</td>
<td>1/0</td>
<td>1.05 (0.97, 1.13)</td>
</tr>
<tr>
<td>ACEI vs CA</td>
<td>1/1</td>
<td>1.03 (0.94, 1.13)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Mortality</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI vs D/BB</td>
<td>2/0</td>
<td>1.00 (0.95, 1.05)</td>
</tr>
<tr>
<td>CA vs D/BB</td>
<td>1/0</td>
<td>0.99 (0.95, 1.04)</td>
</tr>
<tr>
<td>ACEI vs CA</td>
<td>1/1</td>
<td>1.04 (0.98, 1.10)</td>
</tr>
</tbody>
</table>

D=diuretic; BB=β-blocker.

BP-Lowering Treatment Trialists’ Meta-analysis: Comparisons of Different Active Treatments

<table>
<thead>
<tr>
<th></th>
<th>BP Difference Between Rx (SBP/DBP mm Hg)</th>
<th>Relative Risk</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACEI vs D/BB</td>
<td>2/0</td>
<td></td>
<td>1.09 (1.00, 1.18)</td>
</tr>
<tr>
<td>CA vs D/BB</td>
<td>1/0</td>
<td></td>
<td>0.93 (0.86, 1.01)</td>
</tr>
<tr>
<td>ACEI vs CA</td>
<td>1/1</td>
<td></td>
<td>1.12 (1.01, 1.25)</td>
</tr>
<tr>
<td><strong>Coronary heart disease</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACEI vs D/BB</td>
<td>2/0</td>
<td></td>
<td>0.98 (0.91, 1.05)</td>
</tr>
<tr>
<td>CA vs D/BB</td>
<td>1/0</td>
<td></td>
<td>1.01 (0.94, 1.08)</td>
</tr>
<tr>
<td>ACEI vs CA</td>
<td>1/1</td>
<td></td>
<td>0.96 (0.88, 1.05)</td>
</tr>
<tr>
<td><strong>Heart failure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACEI vs D/BB</td>
<td>2/0</td>
<td></td>
<td>1.07 (0.96, 1.19)</td>
</tr>
<tr>
<td>CA vs D/BB</td>
<td>1/0</td>
<td></td>
<td>1.33 (1.21, 1.47)</td>
</tr>
<tr>
<td>ACEI vs CA</td>
<td>1/1</td>
<td></td>
<td>0.82 (0.73, 0.92)</td>
</tr>
</tbody>
</table>

**SPRINT Research Question**

Examine effect of more intensive high blood pressure treatment than is currently recommended

Randomized Controlled Trial

Target Systolic BP

- **Intensive Treatment**
  - Goal SBP < 120 mm Hg

- **Standard Treatment**
  - Goal SBP < 140 mm Hg

**SPRINT design details available at:**
- ClinicalTrials.gov (NCT01206062)
Major Inclusion Criteria

- ≥50 years old

- Systolic blood pressure: 130 – 180 mm Hg (treated or untreated)

- Additional cardiovascular disease (CVD) risk
  - Clinical or subclinical CVD (excluding stroke)
  - Chronic kidney disease (CKD), defined as eGFR 20 – <60 ml/min/1.73m²
  - Framingham Risk Score for 10-year CVD risk ≥ 15%
  - Age ≥ 75 years
SPRINT: Enrollment and Follow-up Experience

Screened (N=14,692)

Randomized (N=9,361)

Intensive Treatment (N=4,678)

- Consent withdrawn 154
- Discontinued intervention 224
- Lost to follow-up 111

Analyzed 4,678

(Vital status assessment: entire cohort)

Standard Treatment (N=4,683)

- Consent withdrawn 121
- Discontinued intervention 242
- Lost to follow-up 134

Analyzed 4,683

(Vital status assessment: entire cohort)
## Demographic and Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total N=9361</th>
<th>Intensive N=4678</th>
<th>Standard N=4683</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD) age, years</strong></td>
<td>67.9 (9.4)</td>
<td>67.9 (9.4)</td>
<td>67.9 (9.5)</td>
</tr>
<tr>
<td>% ≥75 years</td>
<td>28.2%</td>
<td>28.2%</td>
<td>28.2%</td>
</tr>
<tr>
<td><strong>Female, %</strong></td>
<td>35.6%</td>
<td>36.0%</td>
<td>35.2%</td>
</tr>
<tr>
<td><strong>White, %</strong></td>
<td>57.7%</td>
<td>57.7%</td>
<td>57.7%</td>
</tr>
<tr>
<td><strong>African-American, %</strong></td>
<td>29.9%</td>
<td>29.5%</td>
<td>30.4%</td>
</tr>
<tr>
<td><strong>Hispanic, %</strong></td>
<td>10.5%</td>
<td>10.8%</td>
<td>10.3%</td>
</tr>
<tr>
<td><strong>Prior CVD, %</strong></td>
<td>20.1%</td>
<td>20.1%</td>
<td>20.0%</td>
</tr>
<tr>
<td><strong>Mean 10-year Framingham CVD risk, %</strong></td>
<td>20.1%</td>
<td>20.1%</td>
<td>20.1%</td>
</tr>
<tr>
<td><strong>Taking antihypertensive meds, %</strong></td>
<td>90.6%</td>
<td>90.8%</td>
<td>90.4%</td>
</tr>
<tr>
<td><strong>Mean (SD) number of antihypertensive meds</strong></td>
<td>1.8 (1.0)</td>
<td>1.8 (1.0)</td>
<td>1.8 (1.0)</td>
</tr>
<tr>
<td><strong>Mean (SD) Baseline BP, mm Hg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Systolic</strong></td>
<td>139.7 (15.6)</td>
<td>139.7 (15.8)</td>
<td>139.7 (15.4)</td>
</tr>
<tr>
<td><strong>Diastolic</strong></td>
<td>78.1 (11.9)</td>
<td>78.2 (11.9)</td>
<td>78.0 (12.0)</td>
</tr>
</tbody>
</table>
Systolic BP During Follow-up

Year 1
Mean SBP
136.2 mm Hg Standard

Mean SBP
121.4 mm Hg Intensive

Average SBP (During Follow-up)
Standard: 134.6 mm Hg

Intensive: 121.5 mm Hg

Average number of antihypertensive medications

Number of participants
Hazard Ratio = 0.75 (95% CI: 0.64 to 0.89)

During Trial (median follow-up = 3.26 years)
Number Needed to Treat (NNT) to prevent a primary outcome = 61
**SPRINT Primary Outcome and its Components**

*Event Rates and Hazard Ratios*

<table>
<thead>
<tr>
<th></th>
<th>Intensive</th>
<th>Standard</th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Outcome</strong></td>
<td>243</td>
<td>319</td>
<td>0.75 (0.64, 0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>All MI</strong></td>
<td>97</td>
<td>116</td>
<td>0.83 (0.64, 1.09)</td>
<td>0.19</td>
</tr>
<tr>
<td><strong>Non-MI ACS</strong></td>
<td>40</td>
<td>40</td>
<td>1.00 (0.64, 1.55)</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>All Stroke</strong></td>
<td>62</td>
<td>70</td>
<td>0.89 (0.63, 1.25)</td>
<td>0.50</td>
</tr>
<tr>
<td><strong>All HF</strong></td>
<td>62</td>
<td>100</td>
<td>0.62 (0.45, 0.84)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>CVD Death</strong></td>
<td>37</td>
<td>65</td>
<td>0.57 (0.38, 0.85)</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Age 75+ Results for Systolic Blood Pressure (SBP) Intervention Trial (SPRINT) (Williamson et al., JAMA 2016)

• Participants Aged >=75 Years with SBP 130-180 mm Hg if <1 medication, 130-170 mm Hg if taking 2 medications, 130-160 mm Hg if taking 3 medications, and 130-150 if taking >=4 medications.
• 1317 randomized to SBP<120 and 1319 to SBP<140 mmHg, mean age 79.9 years, median follow-up 3.1 years
• Intensive vs. standard treatment group had lower risk of primary outcome of non-fatal MI, ACS, nonfatal stroke, nonfatal HF, and CVD death (HR=0.66 [0.51-0.85])
• No difference in primary outcome by frailty status (p-interaction=0.84)
• All cause mortality also lower, HR=0.67 [0.49-0.91]
• Serious adverse events similar (48.4% vs. 48.3%)
• Hypotension rates were 2.4% vs. 1.4%
Kaplan-Meier Curves for the Primary Cardiovascular Disease Outcome in Systolic Blood Pressure Intervention Trial (SPRINT) in Participants Aged 75 Years or Older by Baseline Frailty Status

Tinted regions indicate 95% confidence intervals; FI, 37-item frailty index; HR, hazard ratio. The primary cardiovascular disease outcome was a composite of nonfatal myocardial infarction, acute coronary syndrome not resulting in a myocardial infarction, nonfatal stroke, nonfatal acute decompensated heart failure, and death from cardiovascular causes.

P-interaction between frailty groups = 0.84 indicating no difference in primary CVD outcome by frailty status.
<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate SBP Reduction Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (BMI=18.5-24.9)</td>
<td>5-20 mmHg/10 kg weight lost</td>
</tr>
<tr>
<td>Adopt DASH eating plan</td>
<td>Diet rich in fruits, vegetables, low fat dairy and reduced in fat</td>
<td>8-14 mmHg</td>
</tr>
<tr>
<td>Restrict sodium intake</td>
<td>&lt;2.4 grams of sodium per day</td>
<td>2-8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Regular aerobic exercise for at least 30 minutes on most days of the week</td>
<td>4-9 mmHg</td>
</tr>
<tr>
<td>Moderate alcohol consumption</td>
<td>≤2 drinks/day for men and ≤1 drink/day for women</td>
<td>2-4 mmHg</td>
</tr>
</tbody>
</table>

BMI=Body mass index, SBP=Systolic blood pressure

Chobanian AV et al. *JAMA*. 2003;289:2560-2572
Effect of Moderate Weight Loss On Cardiometabolic Risk Factors

Percent changes are initial visit to final visit.

Mediterranean Diet and BP

• Counseling to eat a Mediterranean-style dietary pattern compared to minimal advice to consume a low-fat dietary pattern, in free-living middle-aged or older adults (with type 2 diabetes mellitus or at least 3 CVD risk factors):
  \[ \downarrow \text{BP by 6–7/2–3 mm Hg} \]

• In an observational study of healthy younger adults, adherence to a Mediterranean-style dietary pattern was associated with:
  \[ \downarrow \text{BP 2–3/1–2 mm Hg} \]

*Strength of Evidence: Low*
DASH Fact Sheet

The DASH Eating Plan

Research has found that diet affects the development of high blood pressure, or hypertension (the medical term). Recently, two studies showed that following a particular eating plan—called the DASH eating plan—and reducing the amount of sodium consumed lowers blood pressure.

While each step alone lowers blood pressure, the combination of the eating plan and a reduced sodium intake gives the biggest benefit and may help prevent the development of high blood pressure.

This fact sheet, based on the DASH research findings, tells about high blood pressure, and how to follow the DASH eating plan and reduce the amount of sodium you consume. It offers tips on how to start and stay on the eating plan, as well as a week of menus and some recipes. The menus and recipes are given for two levels of daily sodium consumption—2,400 milligrams (the upper limit of current recommendations by the Federal Government’s National High Blood Pressure Education Program, or NHBPEDP, and the amount used to figure food labels’ Nutrition Facts Daily Value) and 1,500 milligrams.

Those with high blood pressure may especially benefit from following the eating plan and reducing their sodium intake, but the combination is a heart-healthy recipe that all adults can follow.
DASH: Dietary Approaches to Stop Hypertension

- 2 RCTs (6 citations) evaluating the DASH pattern met eligibility criteria.

- DASH dietary pattern description:
  - high in vegetables, fruits, and low-fat dairy products
  - high in whole grains, poultry, fish, and nuts
  - low in sweets, sugar-sweetened beverages, and red meats
  - low in saturated fat, total fat, and cholesterol
  - high in potassium, magnesium, calcium
  - rich in protein and fiber
DASH and BP

When all food was supplied to adults with BP 120–159/80–95 mm Hg and both body weight and sodium intake were kept stable, the DASH dietary pattern, compared with a typical American diet of the 1990s:

↓BP 5–6/3 mm Hg

Strength of Evidence: High
Diet Evidence: Effect on Blood Pressure

Dietary Approaches to Stop Hypertension (DASH) Group

459 hypertensive patients randomized to 1 of 3 diets for 8 weeks

Systolic blood pressure (mm Hg)

Diastolic blood pressure (mm Hg)

A diversified diet improves blood pressure

Appel LJ et al. *NEJM* 1997;336:1117-24
Sodium and BP: Overall Results

In adults aged 25–80 years with BP 120–159/80–95 mm Hg, reducing sodium intake lowers BP.

Strength of Evidence: High
Different Levels of Sodium Intake

In adults aged 25–75 years with BP 120–159/80–95 mm Hg, relative to approximately 3,300 mg/day ↓ sodium intake that achieved a mean 24-hour urinary sodium excretion of approximately 2,400 mg/day:

↓ BP by 2/1 mm Hg
↓ Sodium intake that achieved a mean 24-hour urinary sodium excretion of approximately 1,500 mg/day
↓ BP by 7/3 mm Hg

Strength of Evidence: Moderate
Sodium and Dietary Pattern Changes

In adults aged 25–80 with BP 120–159/80–95 mm Hg, the combination of ↓ sodium intake + eating the DASH dietary pattern lowers BP more than ↓ sodium intake alone.

Strength of Evidence: Moderate

There is insufficient evidence from RCTs to determine whether ↓ sodium intake + changing dietary intake of any other single mineral (for example, increasing potassium, calcium, or magnesium) ↓ BP more than ↓ sodium intake alone.
Special Communication

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults
Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD; Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH; Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS; Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD; Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH
Important to Note…

• JNC 7 was “The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.”

• JNC 8 is the “2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults.”

• In JNC 8 they give 9 Evidence based Recommendations

• “… these recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient.”

• RCTs
  • conducted 1966 to present
  • Minimum 1-year follow-up period
  • Sample size > 100
Recommendation #1

1. In patients aged ≥60 years, initiate pharmacologic treatment in systolic BP ≥150mmHg or diastolic BP ≥90mmHg and treat to a goal systolic BP <150mmHg and goal diastolic BP <90mmHg.

(Strong Recommendation – Grade A)

In other words:

Ease up on Hypertension Treatment in Older Adults (60 years of age or older)

Treat if BP >150/90
Aim for <150/90
Corollary Recommendation

• In the general population aged 60 or older, if pharmacologic treatment for high BP results in lower achieved SBP (for example <140 mm Hg) and treatment is not associated with adverse effects on health or quality of life, treatment does not need to be adjusted. Expert Opinion-Grade E
Recommendation #1 JNC 8 (Minority report) (Wright et al, Ann Intern Med 2014)

- Concern that new cutpoint of <150/90 mmHg for most persons 60 years of age and over will result in poorer BP control and possibly higher CVD (especially stroke) rates.
- Many older persons are at higher CVD risk and should not have a higher BP target goal.
- Evidence supporting ↑ SBP target from <140 to < 150 mm Hg in persons ≥ 60 yrs. was insufficient and inconsistent with evidence supporting panel’s recommendation for a SBP target of < 140 mm Hg in those < age 60 Yrs.
Other Guidelines Still Endorse BP Goal of <140/90 for Adults <80 Years of Age

- ACC/AHA/CDC Scientific Advisory on an Effective Approach to High BP Control (November 2013)
- ASH/ISH Guideline – December 2013
- ESH Guideline – June 2013
Hypertension in Diabetes

- JNC 7 said: Treat to <130/80
- Evidence says: No overall cardiovascular benefit with lower BP goals (although there was a stroke benefit)
- JNC 8 says: <140/90
- Both ESH and ADA maintain goal at <140/80
UKPDS: Effects of Tight vs. Less-Tight Blood Pressure Control

![Graph showing risk reduction percentages for various outcomes.]

*P=0.0046; †P=0.019; ‡P=0.0092; §P=0.0038; ¶P=0.0036; ‖P=0.013; **P=0.0043

Controlling Hypertension in Adults

AHA/ACC/CDC Science Advisory for Effective Approach to High Blood Pressure Control (Hypertension 2013)
American Heart Association’s My Life Check Assessment (www.mylifecheck.org)

My Life Check™

Life’s Simple 7 Success Plan

This assessment is based on the knowledge and experience of American Heart Association medical experts.

It can help you:
- Understand your current level of cardiovascular health
- Assess your individual health needs
- Commit to steps to improve your health and quality of life
- Move closer to your personal health goals
# My Life Check Assessment

## QUESTIONS 1 TO 9

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you male or female?</td>
<td>Male, Female</td>
</tr>
<tr>
<td>What is your age?</td>
<td>[ ]</td>
</tr>
<tr>
<td>What is your ethnicity?</td>
<td>[ ]</td>
</tr>
<tr>
<td>How tall are you?</td>
<td>[ ]</td>
</tr>
<tr>
<td>What is your zip code?</td>
<td>[ ]</td>
</tr>
<tr>
<td>Have you been diagnosed by a healthcare provider as having any of these conditions?</td>
<td>Yes, No</td>
</tr>
<tr>
<td>Do you have diabetes? (either type 1 or type 2)</td>
<td>Yes, No</td>
</tr>
<tr>
<td>What is your weight?</td>
<td>[ ]</td>
</tr>
<tr>
<td>How much physical activity do you get in a week?</td>
<td>[ ]</td>
</tr>
<tr>
<td>- You can include both moderate and vigorous activity levels.</td>
<td>[ ]</td>
</tr>
<tr>
<td>- All types of activity count, such as gardening, walking briskly, or bicycling.</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

**More about physical activity**

- **Moderate intensity**
  A person doing moderate-intensity aerobic activity can usually talk, but not sing, during the activity.

- **Vigorous intensity**
  A person doing vigorous-intensity activity usually cannot say more than a few words without pausing for a breath.
My Life Check Assessment

My Life Check™

Your Heart Score

Blood Cholesterol: Warning
Healthy Diet: Excellent
Blood Pressure: Needs Improvement
Healthy Weight: Excellent
Blood Sugar: Excellent
Physical Activity: Needs Improvement
Smoking Status: Excellent

You're doing well, but consider all the aspects of your behaviors that lead to good health.
Make adjustments to strengthen your position.

Result Report
Includes your Simple 7, your action plans, and heart score.

Note: Print or save a PDF of this report for your records.
Use your email program to send the PDF anywhere you want.

Print or Save PDF
CONCLUSIONS

1) Hypertension is the leading cause of death worldwide and increases the risk of numerous CVD-related outcomes

2) Many persons are misclassified on the basis of clinic BP measurements (white coat vs. masked HTN)

3) Many persons, especially with comorbidities, remain inadequately controlled for HTN

4) Combination therapy can improve BP control, and in resistant HTN, emerging invasive therapies such as renal denervation hold promise.
Thank You!

www.aspconline.org

www.heart.uci.edu

ndwong@uci.edu

UC Irvine Health

714-456-6699

Preventive Cardiology Program
Take control of your health

Life-threatening cardiac events often can be prevented through early diagnosis, risk assessment, treatment and lifestyle changes.

The UC Irvine Health Preventive Cardiology Program uses the latest evidence-based guidelines for cardiovascular disease prevention. Services include:

- Initial evaluation by cardiologist, plus follow-up to track progress
- Comprehensive laboratory measures for cardiac risk factors and biomarkers, plus further evaluation with optional imaging tests
- Computerized cardiovascular risk profiles and risk scoring
- Comprehensive dietitian consultation with a specific focus on cardiovascular risk factor management
- Physical activity prescriptions and consultations with an exercise specialist
- A full report sent to the patient’s referring physician when the program is finished

Our preventive cardiology program’s multidisciplinary team includes:

- Cardiologists
- Registered dietitian
- Exercise physiologist
- Prevention researchers/specialists

Our program can help you if you have been diagnosed with at least one risk factor for cardiovascular disease, including:

- Hypertension
- Hypercholesterolemia/dyslipidemia
- Metabolic syndrome
- Diabetes
- Cigarette smoking

Patients with pre-existing cardiovascular disease who need more guidance with risk factor modification to prevent disease

To learn more, call 714-456-6699.

UC Irvine Health
101 The City Drive South
Orange, CA 92868
ucirvinehealth.org/heart
THANK YOU!

www.aspconline.org
Definition of Resistant Hypertension

Defined as failure of a rational 3-drug regimen, including an adequate dose of a diuretic or requiring ≥ 4 drugs.

To reduce BP to <140/90 mm Hg
Prevalence of “True” Resistant Hypertension

- Egan, et al. (NHANES: 1 or 2 Rx) 33-50% (Rx inertia)
- Egan, et al. (NHANES: 3 Rx) 15.9%
- Persell (NHANES: ≥ 4 Rx) 8.9%
- del la Sierra, et al. (ABM) 7.6%
- Hanselin, et al. (optimal Rx selection) 2.7%
1. Risk factors associated with resistant HTN

- Higher baseline SBP (ISH with wide PP)
- Older age (increased arterial stiffness)
- Black race
- Female sex (worst control in black women)
- CKD (eGFR < 45-60 cc/min) & ↑ U_{protein}
- Living in Southeastern United States
- Obesity
- Diabetes
- Excessive alcohol intake
- Excessive salt intake

Therapeutic Approaches for Resistant HTN

- Most people need combination Rx (rule of 1/3rds)
- If 20/10 mm Hg above goal, start with 2 drugs
- RAAS blockade is logical foundation of Rx
- ARBs = ACEIs re CV protection
- ARBs better tolerated than ACEIs
- Simplifying combination Rx (A+C or A+ D):
  -- Scientifically logical
  -- restores dose responsiveness
  -- removes unpredictability of response
    (all respond)
Physiological and pathophysiological actions of renal sympathetic afferent and efferent nerves.


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Renal artery denervation

Renal nerves on the adventitial surface of the renal artery

Intraluminal *Simplicity* catheter
Simplicity HTN-2 Trial

Renal denervation group:

<table>
<thead>
<tr>
<th></th>
<th>Office BP</th>
<th>Home BP</th>
<th>ABPM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-32/-12</td>
<td>-20/-12</td>
<td>-11/-7</td>
</tr>
<tr>
<td>(n=49)</td>
<td></td>
<td>(n=32)</td>
<td>(n=20)</td>
</tr>
</tbody>
</table>

Simplicity HTN-2 Investigators, Lancet 2010
A Controlled Trial of Renal Denervation for Resistant Hypertension

Deepak L. Bhatt, M.D., M.P.H., David E. Kandzari, M.D., William W. O’Neill, M.D., Ralph D’Agostino, Ph.D., John M. Flack, M.D., M.P.H., Barry T. Katzen, M.D., Martin B. Leon, M.D., Minglei Liu, Ph.D., Laura Mauri, M.D., Manuela Negoita, M.D., Sidney A. Cohen, M.D., Ph.D., Suzanne Oparil, M.D., Krishna Rocha-Singh, M.D., Raymond R. Townsend, M.D., and George L. Bakris, M.D., for the SYMPPLICITY HTN-3 Investigators*
SYMPPLICITY HTN-3 Trial Design

Screening Visit 1
- Office SBP ≥160 mm Hg
- Full doses ≥3 meds
- No med changes in past 2 weeks
- No planned med changes for 6 M

Screening Visit 2
- Office SBP ≥160 mm Hg
- 24-h ABPM SBP ≥135 mm Hg
- Documented med adherence

Sham Procedure
Renal angiogram; Eligible subjects randomized

Home BP & HTN med confirmation

Primary endpoint

2 weeks
- Patients, BP assessors, and study personnel all blinded to treatment status
- No changes in medications for 6 M

Efficacy Endpoints

Primary Effectiveness Endpoint:

• Comparison of office SBP change from baseline to 6 months in RDN arm compared with change from baseline to 6 months in control arm

$$\text{Endpoint} = (\text{SBP}_{\text{RDN 6 month}} - \text{SBP}_{\text{RDN Baseline}}) - (\text{SBP}_{\text{CTL 6 month}} - \text{SBP}_{\text{CTL Baseline}})$$

• **Superiority margin of 5 mm Hg**

Powered Secondary Effectiveness Endpoint:

• Comparison of mean 24-hour ambulatory (ABPM) SBP change from baseline to 6 months in RDN arm compared with change from baseline to 6 months in control arm

• **Superiority margin of 2 mm Hg**

Primary Efficacy Endpoint

$\Delta = -2.39$ (95% CI, -6.89 to 2.12)  
P=0.26*

$\Delta = -14.1 \pm 23.9$  
P<0.001

$\Delta = -11.7 \pm 25.9$  
P<0.001

*P value for superiority with a 5 mm Hg margin; bars denote standard deviations

**Powered Secondary Efficacy Endpoint**

\[ \Delta = -1.96 \text{ (95\% CI, -4.97 to 1.06)} \]

\[ P = 0.98^* \]

\[ \Delta = -6.8 \pm 15.1 \]

\[ P < 0.001 \]

\[ \Delta = -4.8 \pm 17.3 \]

\[ P < 0.001 \]

*P value for superiority with a 2 mm Hg margin; bars denote standard deviations

Conclusions

• In a prospective, multicenter, randomized, blinded, sham controlled trial of patients with uncontrolled resistant hypertension, percutaneous renal denervation was safe but not associated with significant additional reductions in office or ambulatory blood pressure.

• These results underscore the importance of blinding and sham controls in evaluations of new devices.

• Further study in rigorously designed clinical trials will be necessary to confirm previously reported benefits of renal denervation in patients with resistant hypertension or to validate alternate methods of renal denervation.
### European Society of Hypertension Guidelines Regarding Renal Denervation, 2013

<table>
<thead>
<tr>
<th>In case of ineffectiveness of drug treatment invasive procedures such as renal denervation and baroreceptor stimulation may be considered.</th>
<th>IIb</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Until more evidence is available on the long-term efficacy and safety of renal denervation and baroreceptor stimulation, it is recommended that these procedures remain in the hands of experienced operators and diagnosis and follow-up restricted to hypertension centers.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>It is recommended that the invasive approaches are considered only for truly resistant hypertensive patients, with clinic values ≥160 mmHg SBP or ≥110 mmHg DBP and with BP elevation confirmed by ABPM.</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>