Hypertension Update

ACOI 2016
John Prior
Disclosures

Nothing to declare
Hypertension - Introduction

US population incidence – 30% and growing due to an aging and increasingly obese population

Poorly controlled

Most common risk for CVD

Global Burden of Disease Study 2010 – HTN is the leading risk factor for death and DALY

Despite poor control, treatment of HTN has positively influenced stroke, CVD and CHF
<table>
<thead>
<tr>
<th>Report/MC</th>
<th>Publications/Year</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Report (JAMA, 1977)</td>
<td>6 pages</td>
<td></td>
</tr>
<tr>
<td>1980 Report (Archives)</td>
<td>6 pages</td>
<td></td>
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<tr>
<td>1984 Report (Archives)</td>
<td>13 pages</td>
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<tr>
<td>1988 Report (Archives)</td>
<td>16 pages</td>
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<tr>
<td>JNC V (Archives, ‘93)</td>
<td>30 pages</td>
<td></td>
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<tr>
<td>JNC VI (Archives ‘97)</td>
<td>34 pages</td>
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<tr>
<td>JNC 7 (Hypertension ‘03)</td>
<td>47 pages</td>
<td></td>
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<tr>
<td>NICE HTN 2011</td>
<td>36 pages</td>
<td></td>
</tr>
<tr>
<td>JNC 8 2013</td>
<td>14 pages</td>
<td></td>
</tr>
</tbody>
</table>
Primary HTN – BP > 140/90 without secondary cause (Stg 1 140-159/90-99; Stg 2 > 160/100 (benign if criteria for malignant HTN not met)

White Coat HTN – BP > 140/90 in office and home BP < 135/85 at home

Masked HTN – BP normal in office but > 140/90 at home (end organ damage)
HTN - Definitions

Secondary HTN – HTN with secondary cause such as renovascular HTN, ETOH etc

Malignant/Accelerated HTN – HTN associated with grade 3 or 4 hypertensive retinopathy with a thrombotic microangiopathy leading to acute tissue injury (brain, kidney, heart)

Resistant HTN - BP above goal (> 160/) despite 3 or more medications (including a diuretic)
HTN - Definitions

**HTN Emergencies** – HTN and acute end organ disease (malignant HTN etc)

**HTN Urgencies** – asymptomatic elevation of BP > 180/

**Non Dipper** – loss of normal BP decrease during sleep (predicts CV disease)

**Gestational HTN** – BP > 140/90 that occurs after the 20th week (chronic HTN occurs before and lacks proteinuria) (preeclampsia has proteinuria)
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>
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<tbody>
<tr>
<td></td>
<td>II (Phase 1)</td>
</tr>
<tr>
<td>Awareness</td>
<td>51</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>10</td>
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</table>

## Benefits of Lowering BP

<table>
<thead>
<tr>
<th>Condition</th>
<th>Average Percent Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke incidence</td>
<td>35–40%</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>20–25%</td>
</tr>
<tr>
<td>Heart failure</td>
<td>50%</td>
</tr>
</tbody>
</table>
HTN Evaluation

History and physical along with directed lab evaluation serve to screen for secondary HTN, assess end organ damage as well as assess CV risk. These serve to determine further workup and to tailor therapy types and goals.
Laboratory Tests

Routine Tests
   Electrocardiogram
   Urinalysis
   Blood glucose, and hematocrit
   Serum potassium, creatinine, or the corresponding estimated GFR, and calcium
   Lipid profile, after 9- to 12-hour fast, that includes high-density and low-density lipoprotein cholesterol, and triglycerides

Optional tests
   Measurement of urinary albumin/creatinine ratio

More extensive testing for identifiable causes is not generally indicated unless BP control is not achieved
Assess interarm difference when at first assessment of hypertension

Clark’s meta-analysis included a number of published studies in hypertensive patients or subgroups of hypertensive patients, in which BPs were taken from both arms, plus some unpublished data from his own group.

Differences in mortality between those with large differences in interarm SBP readings

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HR, ≥10-mm-Hg difference in SBP between arms a</th>
<th>Total subjects/deaths, n</th>
<th>p a</th>
<th>HR, ≥15-mm-Hg difference in SBP between arms b</th>
<th>Total subjects/deaths, n</th>
<th>p b</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>1.60</td>
<td>1990/420</td>
<td>0.01</td>
<td>1.60</td>
<td>2231/456</td>
<td>0.008</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>2.15</td>
<td>1516/151</td>
<td>0.007</td>
<td>1.34</td>
<td>2178/201</td>
<td>0.24</td>
</tr>
</tbody>
</table>
Ambulatory BP Monitoring

ABPM is warranted for evaluation of “white-coat” HTN in the absence of target organ injury. Also dx of masked HTN

Ambulatory BP values are usually lower than clinic readings.

Awake, individuals with hypertension have an average BP of >135/85 mmHg and during sleep >120/75 mmHg.

BP drops by 10 to 20% during the night; if not, signals possible increased risk for cardiovascular events. Non dipper

BP highest 6-8 AM and 5-7 PM
Self-Measurement of BP

Provides information on:
- Response to antihypertensive therapy
- Improving adherence with therapy
- Evaluating white-coat HTN
- BP variability

Home measurement of >135/85 mmHg is generally considered to be hypertensive.

Home measurement devices should be checked regularly.

PREDICTS CV OUTCOMES BETTER THAN OFFICE BP
Causes of Resistant Hypertension

Improper BP measurement
Excess sodium intake
Inadequate diuretic therapy
Medication
  Inadequate doses or timing
  Drug actions and interactions (e.g., NSAIDs, illicit drugs, sympathomimetics, oral contraceptives)
  Over-the-counter (OTC) drugs and herbal supplements
Excess alcohol intake - > 14/wk men, > 7/wk women
Identifiable causes of HTN – sleep apnea, RAS, primary aldosteronism etc
Secondary HTN
CKD and HTN
Prevalence of Abnormalities at each level of GFR

- Hypertension* (>140/90 or antihypertensive medication)
- Hemoglobin < 12.0 g/dL
- Unable to walk 1/4 mile
- Serum albumin < 3.5 g/dL
- Serum calcium < 8.5 mg/dL
- Serum phosphorus > 4.5 mg/dL

*p-trend < 0.001 for each abnormality
Prevalence of Hypertension In Chronic Renal Diseases

MCN=minimal change nephropathy   CIN=chronic interstitial nephritis   IgA=IgA nephropathy
MGN=membranous glomerulonephritis   APKD=adult-onset polycystic kidney disease   DN=diabetic nephropathy
MPGN=membranoproliferative glomerulonephritis   FSGN=focal segmental glomerulonephritis
Pathogenesis HTN - CKD

1. **Volume Dependent**: Salt sensitive HTN
2. **Volume Independent**:
   A. Activation of the RAS
   B. Activation of the Sympathetic NS
   C. Nitric oxide deficiency
   D. Endothelin
   F. Hyperuricemia
   G. Sleep Apnea
   H. Renal artery stenosis
   I. Nephron number
Pathogenesis HTN – CKD
Na Sensitive HTN

Volume-dependent HTN is the most common type of HTN seen in CKD
Incidence inversely proportional to GFR
Defined as low or normal renin and response to dietary Na restriction
Always consider volume overload as a cause of poor HTN control (GFR < 30 and proteinuria)
Pathogenesis HTN – CKD
Uric Acid

Uric acid acts as a renal vasoconstrictor by decreasing NO and activating RAS

Vasculopathic

Treatment will improve angina in adults and HTN in adults and adolescents
Low nephron numbers in HTN
This leads to HTN and progressive HTN by maladaption
HTN mothers have small babies who have small kidneys (low nephrons) and develop HTN to have small babies and so on
Genetic influences as well
Summary of studies on nephropathy progression used in figure:

- Viberti GC et al. *JAMA*, 1993
- Bakris GL. *Hypertension*, 1997
- GISEN Group, *Lancet*, 1997*
<table>
<thead>
<tr>
<th>STUDIES</th>
<th>ARR</th>
<th>NNT</th>
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<tbody>
<tr>
<td>CAP</td>
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<tr>
<td>DCCT</td>
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<td>IBES</td>
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<tr>
<td>LOS</td>
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</table>
Kaplan-Meier Estimates of the Percentage of Patients Not Reaching the Primary Composite End Point of a Doubling of the Serum Creatinine Level, End-Stage Renal Disease, or Death
Summary of ACEI/ARB in Stage 3-5 CKD – Non Diabetic

EFFICACY – proteinuric best
Stage 3 – ARR 8-10%; NNT 10-11 for ACE or ARB (ARR 20%) (ARR 20%: NNT 5 if U P/C > 3)
Stage 4 – ARR 20%; NNT 5 for ACE
Stage 5D – ACE will preserve residual function even when on PD

The worse the kidney function, the worse the proteinuria - the better the response
ACE and ARBs should be continued at all stages of CKD
A trial of ACE and/or ARBs should be considered for proteinuric patients regardless of the stage of CKD
Stopping ACE in nonproteinuric CKD may delay RRT
Initiation and Dose Escalation

<table>
<thead>
<tr>
<th>Baseline Value</th>
<th>SBP (mm Hg)</th>
<th>≥120*</th>
<th>110-119</th>
<th>&lt;110</th>
</tr>
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<tbody>
<tr>
<td>Baseline GFR</td>
<td>≥60</td>
<td>30-59</td>
<td>&lt;30</td>
<td></td>
</tr>
<tr>
<td>(mL/min/1.73 m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early GFR Decline (%)</td>
<td>&lt;15</td>
<td>15-30</td>
<td>&gt;30</td>
<td></td>
</tr>
<tr>
<td>Serum Potassium (mEq/L)</td>
<td>≤4.5</td>
<td>4.6-5.0</td>
<td>&gt;5.0</td>
<td></td>
</tr>
<tr>
<td>Interval (Weeks)</td>
<td>4-12</td>
<td>2-4</td>
<td>≤2</td>
<td></td>
</tr>
</tbody>
</table>
Renovascular HTN
Clinical Clues Suggesting Renovascular Hypertension

Onset of hypertension under age 25 or over age 55
An abdominal bruit, particularly in diastole
Refractory, accelerated, or malignant hypertension or worsening of previously controlled hypertension
Undiagnosed renal failure, with or without hypertension (particularly with normal urine sediment)
Acute renal failure precipitated by hypertension treatment, particularly with ACE inhibitors
A unilateral small kidney (by any prior investigational procedure)
“Flash” pulmonary edema
# Sensitivity and Specificity of Tests for Renovascular Hypertension

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doppler flow ultrasonography</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Magnetic resonance angiography</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>CT Angio</td>
<td>90</td>
<td>90</td>
</tr>
</tbody>
</table>

Anatomic Diagnosis not functional diagnosis
Renovascular Disease

Angiography, with or without digital subtraction, is the “gold standard” for diagnosis for renovascular disease

Drive by angio
A, Baseline selective renal angiogram showing tight ostial stenosis with normal filling of the renal arteries to the cortex.
Renovascular HTN

Outcomes

- Patency Rate at 12 months > 80%
- Progression of CKD – medical = intervention
- HTN Control – intervention = medication

Controversy – patient selection is key and we don’t have enough data to make recommendations

Recurrent flash pulm edema, refractory HTN and med intolerance

(7660 1996 to 35000 2005)

Cardiology vs. Nephrology

CORAL TRIAL
CORAL Trial - Results

BP goal met with medical treatment:
No DM or CKD – 93%
DM or CKD – 80%
2 year follow up
CORAL Kaplan–Meier Curves for the Primary Outcome.

Hazard ratio with stenting, 0.94 (95% CI, 0.76–1.17)
P=0.58 by log-rank test

<table>
<thead>
<tr>
<th>Years from Enrollment</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Event-free Survival (%)</td>
<td>100</td>
<td>95</td>
<td>88</td>
<td>83</td>
<td>78</td>
<td>75</td>
</tr>
</tbody>
</table>

No. at Risk
- Medical therapy alone: 472, 371, 314, 214, 115, 40
- Stent plus medical therapy: 459, 362, 318, 224, 131, 59

### CORAL Forest Plot of Treatment Effects within Subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Stent plus Medical Therapy Alone</th>
<th>Medical Therapy Alone</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td>161/459 (35.1)</td>
<td>169/472 (35.8)</td>
<td>0.94 (0.76–1.17)</td>
<td>0.09</td>
</tr>
<tr>
<td>Creatinine level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1.6 mg/dl</td>
<td>43/84 (51.2)</td>
<td>34/87 (39.1)</td>
<td>1.35 (0.86–2.11)</td>
<td></td>
</tr>
<tr>
<td>≤1.6 mg/dl</td>
<td>112/352 (31.8)</td>
<td>128/367 (34.9)</td>
<td>0.87 (0.67–1.12)</td>
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</tr>
<tr>
<td>Estimated GFR</td>
<td></td>
<td></td>
<td></td>
<td>0.80</td>
</tr>
<tr>
<td>≥45 ml/min/1.73 m²</td>
<td>91/288 (31.6)</td>
<td>105/311 (33.8)</td>
<td>0.93 (0.70–1.23)</td>
<td></td>
</tr>
<tr>
<td>&lt;45 ml/min/1.73 m²</td>
<td>64/148 (43.2)</td>
<td>57/143 (39.9)</td>
<td>0.98 (0.68–1.40)</td>
<td></td>
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<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>Yes</td>
<td>69/148 (46.6)</td>
<td>66/162 (40.7)</td>
<td>1.15 (0.82–1.61)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>92/309 (29.8)</td>
<td>103/310 (33.2)</td>
<td>0.84 (0.64–1.12)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>0.64</td>
</tr>
<tr>
<td>Male</td>
<td>75/234 (32.1)</td>
<td>78/231 (33.8)</td>
<td>0.89 (0.65–1.22)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>86/225 (38.2)</td>
<td>91/241 (37.8)</td>
<td>0.99 (0.74–1.33)</td>
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<tr>
<td>Global ischemia</td>
<td></td>
<td></td>
<td></td>
<td>0.32</td>
</tr>
<tr>
<td>Yes</td>
<td>39/89 (43.8)</td>
<td>20/51 (39.2)</td>
<td>1.07 (0.62–1.83)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>119/356 (33.4)</td>
<td>106/264 (40.2)</td>
<td>0.78 (0.60–1.01)</td>
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<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>0.62</td>
</tr>
<tr>
<td>Black</td>
<td>11/29 (37.9)</td>
<td>10/30 (33.3)</td>
<td>1.01 (0.42–2.43)</td>
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</tr>
<tr>
<td>Other</td>
<td>126/356 (35.4)</td>
<td>136/357 (38.1)</td>
<td>0.88 (0.69–1.13)</td>
<td></td>
</tr>
<tr>
<td>Baseline systolic blood pressure</td>
<td></td>
<td></td>
<td></td>
<td>0.55</td>
</tr>
<tr>
<td>&gt;160 mm Hg</td>
<td>66/148 (44.5)</td>
<td>58/139 (41.7)</td>
<td>1.02 (0.71–1.45)</td>
<td></td>
</tr>
<tr>
<td>≥160 mm Hg</td>
<td>95/309 (30.7)</td>
<td>108/328 (32.9)</td>
<td>0.90 (0.68–1.18)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
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<td>0.56</td>
</tr>
<tr>
<td>&gt;70 yr</td>
<td>91/226 (40.3)</td>
<td>94/220 (42.7)</td>
<td>0.87 (0.65–1.16)</td>
<td></td>
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<tr>
<td>≥70 yr</td>
<td>70/233 (30.0)</td>
<td>75/252 (29.8)</td>
<td>1.00 (0.72–1.39)</td>
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<td>U.S. sites</td>
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<td>0.38</td>
</tr>
<tr>
<td>Yes</td>
<td>137/385 (35.6)</td>
<td>146/387 (37.7)</td>
<td>0.90 (0.71–1.14)</td>
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<tr>
<td>No</td>
<td>24/74 (32.4)</td>
<td>23/85 (27.1)</td>
<td>1.22 (0.69–2.16)</td>
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</tr>
<tr>
<td>Maximal diameter stenosis</td>
<td></td>
<td></td>
<td></td>
<td>0.66</td>
</tr>
<tr>
<td>≥80%</td>
<td>77/198 (38.9)</td>
<td>64/166 (38.6)</td>
<td>0.93 (0.67–1.30)</td>
<td></td>
</tr>
<tr>
<td>&lt;80%</td>
<td>77/231 (33.3)</td>
<td>79/208 (38.0)</td>
<td>0.84 (0.61–1.14)</td>
<td></td>
</tr>
</tbody>
</table>
Prospective observational cohort study comparing RAS patients treated (n=62) or not treated (n=133) with ACEs inhibitors (mean follow-up: 4.5 years)
RAS – Principles of Treatment

Don’t poke the skunk
Unless you’ve already been sprayed
USE ACEI or ARBs
Primary Aldosteronism
Spironolactone-induced reduction in systolic (black square) and diastolic BP (square) at 6-wk, 3-mo, and 6-mo follow-up in patients with resistant hypertension.

Prevalence of primary aldosteronism in patients with resistant hypertension from multiple clinics worldwide

Prevalence of Primary Aldosteronism in Subjects with Resistant Hypertension

- Seattle: 17% (n=90)
- Birmingham: 20% (n=88)
- Oslo: 22% (n=90)
- Prague: 19% (n=402)

Prevalence of primary aldosteronism in patients according to Sixth Joint National Committee (JNC VI) stages of severity of hypertension.
Diagnosis of Primary Aldosterone Excess

AM plasma aldosterone/ plasma renin ratio of >30 (esp. if aldo > 20) = 90% sens/spec

Confirmation

24 hr urine for aldosterone after 72 hrs of > 5 grams/day Na diet

plasma aldosterone after 2000 cc NSS
(<6 nl, > 10 primary aldo)

CT – hyperplasia more common than adenoma
Algorithm for Treatment of Hypertension

Not at Goal Blood Pressure (<140/90 mmHg) (<130/80 mmHg for those with diabetes or chronic kidney disease)

Initial Drug Choices

Without Compelling Indications

Stage 1 Hypertension (SBP 140–159 or DBP 90–99 mmHg)
Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.

Stage 2 Hypertension (SBP ≥160 or DBP ≥100 mmHg)
2-drug combination for most (usually thiazide-type diuretic and ACEI, or ARB, or BB, or CCB)

Optimize dosages or add additional drugs until goal blood pressure is achieved.
Consider consultation with hypertension specialist.

With Compelling Indications

Drug(s) for the compelling indications
Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.
Importance of Stroke Risk Factors

![Graph showing prevalence of stroke risk factors.](image)

- **HTN**: 3-5
- **Smoking**: 2-2.5
- **Obesity**: 1.5
- **Afib**: 2
- **Prevalence**: 5-17
### Primary Prevention

<table>
<thead>
<tr>
<th>Treatment</th>
<th>RRR</th>
<th>NNT (1 stroke/yr)</th>
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<tbody>
<tr>
<td>HTN</td>
<td>42%</td>
<td>7937</td>
</tr>
<tr>
<td>Statins</td>
<td>25%</td>
<td>13,333</td>
</tr>
<tr>
<td>Aspirin</td>
<td>7% increase</td>
<td>NA</td>
</tr>
<tr>
<td>ACE-I</td>
<td>30%</td>
<td>11,111</td>
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</table>

Straus et al, JAMA, 2002
## Secondary Prevention

<table>
<thead>
<tr>
<th>Treatment</th>
<th>RRR (%)</th>
<th>NNT (1 stroke/yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTN</td>
<td>28%</td>
<td>51</td>
</tr>
<tr>
<td>Statins</td>
<td>25%</td>
<td>57</td>
</tr>
<tr>
<td>Aspirin</td>
<td>28%</td>
<td>77</td>
</tr>
<tr>
<td>Thieno vs ASA</td>
<td>13%</td>
<td>64</td>
</tr>
<tr>
<td>Smoking D/C</td>
<td>33%</td>
<td>43</td>
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<tr>
<td>CEA</td>
<td>44%</td>
<td>26</td>
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## Lifestyle Modifications

### Table 3. Lifestyle Modifications to Manage Hypertension

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate Systolic BP Reduction, Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (BMI, 18.5-24.9)</td>
<td>$5-20$ mm Hg/10-kg weight loss$^{2,3}$</td>
</tr>
<tr>
<td>Adopt DASH eating plan</td>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat</td>
<td>$8-14$ mm Hg$^{4,5}$</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to no more than $130$ mEq/L (2.4 g sodium or 6 g sodium chloride)</td>
<td>$2-8$ mm Hg$^{6,7}$</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)</td>
<td>$4-9$ mm Hg$^{8,9}$</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>Limit consumption to no more than 2 drinks per day (1 oz or 30 mL ethanol [eg, 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey]) in most men and no more than 1 drink per day in women and lighter weight persons</td>
<td>$2.4$ mm Hg$^{10}$</td>
</tr>
</tbody>
</table>

**Abbreviations:** BMI = body mass index; calculated as weight in kilograms divided by the square of height in meters; BP = blood pressure; DASH = Dietary Approaches to Stop Hypertension.

*For overall cardiovascular risk reduction, stop smoking. The effects of implementing these modifications are dose and time dependent and could be higher for some individuals.
Diet and HTN

![Graph showing the effect of diet on HTN over years.](Image)
Diet Durability
<table>
<thead>
<tr>
<th>Study, Year, Reference</th>
<th>Target SBP (mm Hg)</th>
<th>Achieved SBP (mm Hg)</th>
<th>Mean Number of Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDNT, 2001&lt;sup&gt;139&lt;/sup&gt;</td>
<td>&lt;135</td>
<td>138</td>
<td>2.6</td>
</tr>
<tr>
<td>RENAAL, 2001&lt;sup&gt;338&lt;/sup&gt;</td>
<td>&lt;140</td>
<td>141</td>
<td>2.7</td>
</tr>
<tr>
<td>ABCD, 2000&lt;sup&gt;407&lt;/sup&gt;</td>
<td>&lt;75 or 80-89*</td>
<td>128 and 137</td>
<td>2.4</td>
</tr>
<tr>
<td>CSG Captopril Trial, 1993&lt;sup&gt;329&lt;/sup&gt;</td>
<td>&lt;140</td>
<td>136</td>
<td>1-3#</td>
</tr>
</tbody>
</table>

* Includes studies of progression of diabetic kidney disease randomized by DBP.<sup>#</sup> no data given on SBP in reference; there were approximately 25% normotensive participants.
Antihypertensive Medicine and Risk of Diabetes

Beta blockers and thiazides diuretics increase risk for DMII

ARBs and ACEI decrease risk for DMII
HTN 2010-2016 Update

ONTARGET
SIMPLICITY
JNC 8
AASK
ACCORD
SPRINT
Kaplan-Meier Curves for the Primary Outcome in the Three Study Groups

Conclusion

Telmisartan was equivalent to Ramipril in patients with vascular disease or high-risk diabetes and was associated with less angioedema.

The combination of the two drugs was associated with more adverse events without an increase in benefit.
SIMPLICITY HTN

Use of catheter based renal sympathetic nerve ablation
Already widely used in Europe
SYMPPLICITY HTN-1

Change in Blood Pressure (mmHg)

-60 -50 -40 -30 -20 -10 0 10

6 Months n = 144
1 Year n = 132
2 Years n = 105
3 Years n = 88

Systolic
Diastolic

-22 -27 -29 -32

p < 0.01 for Δ from baseline for all time points.
Data is reported only on the patients available at each time point.
Medtronic's U.S. Renal Denervation Trial Fails to Meet Efficacy Endpoint
Safety Endpoint is Met; All Symplicity Trials Suspended, Pending Review

January 9, 2014 -- In a definite blow to the entire field of renal denervation, Medtronic reported this morning that its pivotal U.S. clinical trial for the Symplicity™ Renal Denervation System has failed to meet its endpoint for efficacy.

Pending review by a panel of invited experts, the company has suspended enrollment in all of its renal denervation clinical studies worldwide.

The negative results were posted by Medtronic, prior to presentation at a scientific symposium or publication in a peer-reviewed journal. In a press release, Dr. Rick Kuntz, chief medical officer for Medtronic, stated: "We believe this course of action is the most prudent and will help us thoroughly evaluate these findings and determine the appropriate next steps for renal denervation therapy."

Positive Results and a Hoped-for "Fix" for Treatment-Resistant Hypertension
Renal denervation has been considered to be one of the most highly-anticipated advances for treatment-resistant hypertension: high systolic blood pressure $\geq 160$mm Hg that is not reduced, even when three anti-hypertensive drugs are used. The procedure involves threading a special catheter to the renal arteries and utilizing a controlled "burn" to disable the sympathetic nerves that control blood pressure.

A number of worldwide trials have shown positive results for this technology over the past two years. The European Society of Cardiology even authored a consensus statement on renal denervation in April 2013.
JNC 8 Etal. Summary

JNC 8 published in close temporal proximity with ASH/ISH and AHA/ACC/CDC guidelines
Confusion reigns supreme
All agree with:
1. Use of ACE/ARB, thiazides and CCB 1\textsuperscript{st}
2. BB, aldactone etc used for pts who fail this
3. AA should use thiazides or CCB 1\textsuperscript{st}
4. Avoid ACE/ARB combination
5. ACE for all CKD (JNC8)
JNC 8 Etal. Summary

BP Goals

1. Age > 80 – SBP < 150/
2. Age 60 – 80 – SBP < 150/ (JNC8);
   SBP < 140/ (ASH)
3. Age < 60 – SBP < 140/ and DBP < 90 (JNC8)(ASH)
4. CKD/Albuminuria - < 130/ (ASH)
Regardless of intervention, CKD progressed in African-American patients. This was despite good BP control. Genetic differences – APOL-1 Gene (MYH9 gene (nonmuscle myosin heavy chain))
Effect of Blood Pressure Lowering and Antihypertensive Drug Class on Progression of Hypertensive Kidney Disease: Results From the AASK Trial
ACCORD Trial

DM II patients with HTN and normal GFR and normal albuminuria randomized to SBP control of < 140/ and < 120/ (4733 participants)

High risk for CV events
Lower BP did not decrease the risk of fatal and non-fatal CV events
Lower BP did decrease the incidence of stroke (p 0.001)
Kaplan–Meier Analyses of Selected Outcomes.

SPRINT Trial

High CV risk patients with HTN randomized to SBP < 140/ or < 120/ (9361 participants)
Inclusion – HTN and increased CV risk
Exclusion = DM, GFR < 20, ADPCKD, stroke
< 120/ resulted in a decrease in primary outcome (MI, ACS, CVA, HF or CV death) NNT 61
< 120/ resulted in a decrease in all cause mortality NNT 90
< 120/ resulted in decreased death from CV cause NNT 172
Primary Outcome and Death from Any Cause.

A Primary Outcome

Hazard ratio with intensive treatment, 0.75 (95% CI, 0.64–0.89)
Standard treatment
Intensive treatment

Cumulative Hazard

No. at Risk
Standard treatment
Intensive treatment

Years
0 1 2 3 4 5

B Death from Any Cause

Hazard ratio with intensive treatment, 0.73 (95% CI, 0.60–0.90)
Standard treatment
Intensive treatment

Cumulative Hazard

No. at Risk
Standard treatment
Intensive treatment

Years
0 1 2 3 4 5

2015;373:2103-2116
# Forest Plot of Primary Outcome According to Subgroups


<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>243/4678 (5.2)</td>
<td>319/4683 (6.8)</td>
<td>0.75 (0.64–0.89)</td>
<td>0.36</td>
</tr>
<tr>
<td>Previous CKD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>135/3348 (4.0)</td>
<td>193/3367 (5.7)</td>
<td>0.70 (0.56–0.87)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>108/1330 (8.1)</td>
<td>126/1316 (9.6)</td>
<td>0.82 (0.63–1.07)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td>0.32</td>
</tr>
<tr>
<td>&lt;75 yr</td>
<td>142/3361 (4.2)</td>
<td>175/3364 (5.2)</td>
<td>0.80 (0.64–1.00)</td>
<td></td>
</tr>
<tr>
<td>≥75 yr</td>
<td>101/1317 (7.7)</td>
<td>144/1319 (10.9)</td>
<td>0.67 (0.51–0.86)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>0.45</td>
</tr>
<tr>
<td>Female</td>
<td>77/1684 (4.6)</td>
<td>89/1648 (5.4)</td>
<td>0.84 (0.62–1.14)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>166/2994 (5.5)</td>
<td>230/3035 (7.6)</td>
<td>0.72 (0.59–0.88)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>0.83</td>
</tr>
<tr>
<td>Black</td>
<td>62/1454 (4.3)</td>
<td>85/1493 (5.7)</td>
<td>0.77 (0.55–1.06)</td>
<td></td>
</tr>
<tr>
<td>Nonblack</td>
<td>181/3224 (5.6)</td>
<td>234/3190 (7.3)</td>
<td>0.74 (0.61–0.90)</td>
<td></td>
</tr>
<tr>
<td>Previous cardiovascular disease</td>
<td></td>
<td></td>
<td></td>
<td>0.39</td>
</tr>
<tr>
<td>No</td>
<td>149/3738 (4.0)</td>
<td>208/3746 (5.6)</td>
<td>0.71 (0.57–0.88)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>94/940 (10.0)</td>
<td>111/937 (11.8)</td>
<td>0.83 (0.62–1.09)</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td></td>
<td></td>
<td></td>
<td>0.77</td>
</tr>
<tr>
<td>≤132 mm Hg</td>
<td>71/1583 (4.5)</td>
<td>98/1553 (6.3)</td>
<td>0.70 (0.51–0.95)</td>
<td></td>
</tr>
<tr>
<td>&gt;132 to &lt;145 mm Hg</td>
<td>77/1489 (5.2)</td>
<td>106/1549 (6.8)</td>
<td>0.77 (0.57–1.03)</td>
<td></td>
</tr>
<tr>
<td>≥145 mm Hg</td>
<td>95/1606 (5.9)</td>
<td>115/1581 (7.3)</td>
<td>0.83 (0.63–1.09)</td>
<td></td>
</tr>
</tbody>
</table>

Intensive Treatment Better | Standard Treatment Better
Outcomes Data from SPRINT and the ACCORD Trial and Combined Data from Both Trials.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Event Rate per Year with Standard Treatment</th>
<th>Risk Ratio (95% CI)</th>
<th>P Value for Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonfatal myocardial infarction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPRINT</td>
<td>1.0%</td>
<td>0.89 (0.74–1.07)</td>
<td>0.8</td>
</tr>
<tr>
<td>ACCORD trial</td>
<td>1.1%</td>
<td>0.75 (0.58–0.97)</td>
<td>0.1</td>
</tr>
<tr>
<td>Combined</td>
<td>1.1%</td>
<td>0.77 (0.62–0.95)</td>
<td>0.07</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.0%</td>
<td>0.81 (0.72–0.92)</td>
<td>0.2</td>
</tr>
<tr>
<td>SPRINT</td>
<td>1.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACCORD trial</td>
<td>1.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>1.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>1.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPRINT</td>
<td>1.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACCORD trial</td>
<td>1.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>1.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary outcome as defined in each trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPRINT</td>
<td>1.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACCORD trial</td>
<td>1.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>1.3%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Legend:
- Coronary event
- Stroke
- Heart failure
- Unexpected or presumed cardiovascular death
- Other

HTN Treatment Summary

BP Goals - <140/90 in all but elderly (<150/80).
GFR < 60 ml + proteinuria goals < 130/80
Lifestyle modification effective but not durable
Expect to use 2-3 drugs to achieve goals
Nocturnal dosing better than AM dosing
ACE/ARB combination should not be used
Spironolactone effective for resistant HTN
People who don’t think too good should not think too much

Ted Williams
Nephrolithiasis - Facts

The lifetime incidence of kidney stones is approximately 13 percent for men and 7 percent for women.

Among adults with kidney stones, approximately 80 percent consist predominately of calcium oxalate and/or calcium phosphate stones.

Following an initial stone event, the 5-year recurrence rate in the absence of specific treatment is 35 to 50 percent.
Nephrolithiasis - Facts

Genetic factors are thought to account for about half the risk of developing kidney stones.

Environmental risk factors include low fluid intake, low calcium intake, and high fructose intake.

The evidence for a role for increased animal protein intake, high sodium intake, increased sucrose intake, and low magnesium intake as risk factors for kidney stones is mixed.

Risk of kidney stones may be increased by medical conditions such as obesity, diabetes, primary hyperparathyroidism, gout, paralysis, and anatomic abnormalities of the kidney and bowel.
Nephrolithiasis - Workup

Standard workup for stones is comprehensive metabolic panel, UA, PTH, and Vitamin D 24 HR urine for volume, Na, UA, Ca, PO4, oxalate, citrate, and Mg

Limited evidence to support that therapy directed by workup is better than empiric tx alone (exception serum and urine uric acid)
Nephrolithiasis - Treatment

Fluid intake to maintain urine excretion of > 2 liters per day may provide a clinically significant reduction in risk of stone recurrence.

Abstaining from soft drinks or eliminating soft drinks acidified solely with phosphoric acid but not by citric acid (based on a single study in men) reduces risk of stone recurrence in frequent consumers.

A normal-calcium, low-sodium, low-animal protein diet may reduce the risk for stone recurrence, but the independent effect of increasing dietary calcium has not been determined.

High-fiber and reduced-animal protein diets may or may not help prevent stone recurrence.

The effectiveness of other dietary interventions is not clear.
Nephrolithiasis - Treatment

Thiazide diuretics (any) reduce the risk of calcium stone recurrence (ARR = 29 percent; (NNT) = 3

Citrate reduces the risk of calcium stone recurrence ARR = 41 percent; NNT = 3

Allopurinol reduces the risk of calcium stone recurrence in patients with elevated blood and urine UA levels ARR = 22 percent; NNT = 5

Treatment with magnesium did not reduce the risk of stone recurrence