Modern Management of Hypertension: Where Do We Draw the Line?

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Associate Dean for GME and CME

Declaration of full disclosure: No conflict of interest

Blood Pressure and Risk

- Risk of Cardiovascular Disease (CVD) is linear to Systolic Blood Pressure (SBP) level. Starts at relatively low BP’s (118 mm Hg)

- Risk doubles for every 20/10 mm Hg

- 120-139/80-89 is “pre-hypertension” and merits lifestyle modifications
Current Status of Hypertension

- Prevalence 29.1%; Blacks 42.1%
- About 75.6% treated; 51.8% controlled (<140/90)
- Risk for poor control: Latinos, Blacks, age 18-44 and ≥80, <300% poverty, < college degree
- Better control: Any insurance, ≥2 visits, and a usual source of care

Hypertension Control by Cardiovascular Disease and Risk: NHANES, 2003-04

<table>
<thead>
<tr>
<th>Condition</th>
<th>%HTN</th>
<th>%Rx</th>
<th>% Not Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Risk</td>
<td>34</td>
<td>66</td>
<td>35</td>
</tr>
<tr>
<td>Diabetes</td>
<td>85</td>
<td>96</td>
<td>54</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>83</td>
<td>95</td>
<td>53</td>
</tr>
<tr>
<td>CHF</td>
<td>86</td>
<td>98</td>
<td>50</td>
</tr>
<tr>
<td>Cardiovascular Dis</td>
<td>85</td>
<td>95</td>
<td>51</td>
</tr>
<tr>
<td>Framingham Score ≥10</td>
<td>77</td>
<td>68</td>
<td>59</td>
</tr>
</tbody>
</table>

MMWR 2012; NCHS 2013
Bertoia ML, Hypertension 2011
Racial Differences in Impact of Elevated BP

- 27,748 patients followed for 4.5 years
- 715 strokes
- SBP 10 mm Hg: 8% increase for whites and 24% for blacks
- HR = 2.38 for stage 1 HTN, age 45-64

- Should blacks be treated more intensively?


Accurate BP Measurement

1) Seated for 5 minutes in chair
2) Arms bared and supported
3) No cigs, coffee; no talking
4) Correct fitting cuff for arm (small cuff results in elevated BP: 3/2 mm Hg - 12/8 mm Hg)
5) First appearance of sound is SBP; disappearance is DBP
6) Two or more reading in 2 minutes averaged
7) Two visits to define HTN
Treatment Based on What Blood Pressure Measurement?

- Office clinician measures are standard, used in trials
- Home BP measurement leads to less intensive drug Rx & BP control. Identifies “white-coat” HTN
- Ambulatory monitor measures higher correlation with CVD

Clinic, Home and Ambulatory BP in Diagnosis of Hypertension

- Systematic review comparing measures in initial diagnosis
- 20 studies with 5683 patients, compared to ambulatory monitor daytime mean ≥135/85

<table>
<thead>
<tr>
<th>Measure</th>
<th>Definition</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home</td>
<td>135/85 mean</td>
<td>85.7%</td>
<td>62.4%</td>
</tr>
<tr>
<td></td>
<td>+LR = 2.28</td>
<td>–LR= 0.23</td>
<td></td>
</tr>
<tr>
<td>Clinic</td>
<td>140/90 mean</td>
<td>74.6%</td>
<td>74.6%</td>
</tr>
<tr>
<td></td>
<td>+LR = 2.94</td>
<td>+LR = 0.34</td>
<td></td>
</tr>
</tbody>
</table>

Individual Lifestyle Modifications for Hypertension Control

- Weight loss if overweight: 5-20 mm Hg/10-kg weight loss
- Limit alcohol to ≤ 1 oz/day: 2-4 mm Hg
- Reduce sodium intake to ≤100 meq/d (2.4 g Na): 2-8 mm Hg in SBP
- DASH Diet: 6 mm alone; 14 mm plus Na
- Physical activity 30 min/day: 4-9 mm Hg
- Habitual caffeine consumption not associated with risk of HTN

Joint National Commission 8 (JNC 8)

Three questions:
1) Does Rx at specific BP thresholds improve outcomes?
2) Does Rx to a specific BP goal improve outcomes?
3) Do various meds differ on outcomes?

Nine recommendations
Recommendations for Management of Hypertension

Recommendation 1
≥60 years:

- Lower BP at SBP ≥150 mm Hg or DBP ≥90 mm Hg
- Treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg.

Strong Recommendation – Grade A (but not unanimous)

Evidence from 6 studies of patients over age 60, treated to goal ≤150/90: HYVET, Syst-Eur, SHEP, JATOS, VALISH, CARDIO-SIS

Some evidence (lower quality) comparing ≤160 to ≤140 and ≤150 to ≤140 showing no additional benefit
Hypertension in the Very Elderly Trial (HYVET)

- 3845 patients ≥ 80 y, 2 years
- >160 mm Hg – goal of 150/80 mm Hg BP=173/91
- Indapamide SR 1.5 mg vs. placebo
  Added perindopril if needed

HYVET Study Results

<table>
<thead>
<tr>
<th>End Point</th>
<th>Meds</th>
<th>Placebo</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>12.4</td>
<td>17.7</td>
<td>0.64 (0.46 -0.95)</td>
</tr>
<tr>
<td>CVA Death</td>
<td>6.5</td>
<td>10.7</td>
<td>0.55 (0.33 -0.93)</td>
</tr>
<tr>
<td>CHF</td>
<td>5.3</td>
<td>14.8</td>
<td>0.28 (0.17 -0.48)</td>
</tr>
<tr>
<td>CV Death</td>
<td>23.9</td>
<td>30.7</td>
<td>0.73 (0.55 -0.97)</td>
</tr>
<tr>
<td>Any Death</td>
<td>47.2</td>
<td>59.6</td>
<td>0.72 (0.59-0.88)</td>
</tr>
</tbody>
</table>
HYVET Conclusions and Implications

• Benefits appear at 1 year of Rx
• NNT = 20 to prevent one stroke
• NNT = 10 to prevent one CHF
• Never too old to treat SBP > 160
• Goal does not have to be < 140

73 yo woman. BP=148/88. No Diabetes, Kidney normal. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin beta blocker
73 yo woman. BP=148/88. No Diabetes, Kidney normal. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin beta blocker

Recommendations for Management of Hypertension

Corollary Recommendation
≥60 years:

❖ If treatment results in lower SBP (eg, <140 mm Hg) and is well tolerated treatment does not need to be adjusted.

Expert Opinion – Grade E

Recommendations for Management of Hypertension

Recommendation 2
<60 years:

¬ Treat to lower BP at DBP ≥90 mm Hg
¬ Treat to a goal DBP <90 mm Hg.

30-59 years, Strong Recommendation – Grade A
18-29 years, Expert Opinion – Grade E

Recommendations for Management of Hypertension

Recommendation 3
<60 years:

¬ Treat to lower BP at SBP ≥140 mm Hg
¬ Treat to a goal SBP <140 mm Hg.

(Expert Opinion – Grade E)
Recommendations for Management of Hypertension

Recommendation 4
≥18 years with chronic kidney disease (CKD) (GFR < 60 or proteinuria >30 mg alb/g creat):

- Treat to lower SBP ≥140 mm Hg or DBP ≥90 mm Hg
- Treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg.

Expert Opinion – Grade E

Recommendation 5
≥18 years with diabetes, treat to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg

- Treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg.

Expert Opinion – Grade E
Intensive BP Control in Type 2 DM: ACCORD

- RCT of 4733 patients with type 2 DM
- Compare BP less than 120 mm Hg vs 140

<table>
<thead>
<tr>
<th></th>
<th>120</th>
<th>140</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>119</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>CV events plus death</td>
<td>1.87%</td>
<td>2.09%</td>
<td>.20</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.28%</td>
<td>1.19%</td>
<td>.55</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.32%</td>
<td>0.53%</td>
<td>.01</td>
</tr>
<tr>
<td>Adverse events</td>
<td>3.3%</td>
<td>1.3%</td>
<td>.001</td>
</tr>
</tbody>
</table>

- In type 2 DM: treating to 120 mm Hg did not reduce the rate of composite fatal and non-fatal CV events

Recommendations for Management of Hypertension

Recommendation 6

Nonblack population, including diabetes:

Initial treatment:
- Thiazide-type diuretic
- Calcium channel blocker (CCB)
- Angiotensin-converting enzyme inhibitor (ACEI)
- Angiotensin receptor blocker (ARB).

(Moderate Recommendation – Grade B)
**Thiazide Diuretics**

- Very effective for systolic BP
- Do not increase sudden death
- Most effective in LVH regression
- Lipid effects are short lasting (1 y)
- Hyperglycemia only in high doses
- Still effective in early chronic kidney disease (to GFR 40-45)
- Erectile dysfunction in 20%
- More effective in Blacks and older

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**Efficacy of HCTZ**

Messerli FH, et al; JACC 2011; 57: 590-600

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Decrease in mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCTZ 12.5 -25 mg</td>
<td>6.5/4.5</td>
</tr>
<tr>
<td>HCTZ 50 mg</td>
<td>12.0/5.4</td>
</tr>
<tr>
<td>ACE-I</td>
<td>12.9/7.7</td>
</tr>
<tr>
<td>ARB</td>
<td>13.3/7.8</td>
</tr>
<tr>
<td>CCB</td>
<td>11.0/8.1</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>11.2/8.5</td>
</tr>
</tbody>
</table>
**Beta Blockers**

- Most effective as mono-therapy in younger persons and whites
- Adverse effects: no clear depression or sexual dysfunction, but + fatigue
- Glucose elevation with A1C increase by 0.2%
- No lasting effect on lipids
- Less efficacy in stroke prevention among those older than 60 years

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**Atenolol in hypertension: is it a wise choice?**

No benefit to prevent MI or All-cause mortality

*Bo Carlberg. LANCET 2004, Vol 364*
ACE–I or ARB

- 30% reduction of ESRD (dialysis) and of doubling of serum creatinine; optimal with GFR 30-60, proteinuria
- Not better tolerated than other drugs
- Regression of LVH not more than other drugs–SBP reduction
- Elevates K+
- Do not use in women < 50 y
- Works less well in Blacks as 1 drug
- Best choice in diabetes (in non-blacks)
- Don’t combine

Calcium Channel Blockers

- Effective in Blacks and elderly
- Effective in preventing CV events
- No increase risk of cancer
- Short acting CCB may be harmful
- Effective in systolic hypertension
- Better outcomes in latest trials
ACCOMPLISH
Calcium Blockers Combined with ACE

• Comparison of combinations: ACE-I + HCTZ vs. ACE-I + amlodipine. 3 yrs

• RCT, 11,506 patients, ≥ 65 y, 60% men, 83% White, 60% diabetes, BMI = 31

• Outcomes: CV death, MI, stroke, hospitalization for angina, resuscitation after cardiac arrest, CABG or PCI

• Funded by Novartis: USA and 4 N Europe

Jamerson K, NEJM 2008; 359:2417-28

ACCOMPLISH Results

<table>
<thead>
<tr>
<th>Primary Outcomes</th>
<th>Benazepril + Amlodipine N=5744</th>
<th>Benazepril + HCTZ N=5762</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Events</td>
<td>552 (9.6%)</td>
<td>679 (11.8%)</td>
<td>0.80 (0.72-0.90)</td>
</tr>
<tr>
<td>CV Death</td>
<td>107 (1.9%)</td>
<td>134 (2.3%)</td>
<td>0.80 (0.62-1.03)</td>
</tr>
<tr>
<td>All MI</td>
<td>125 (2.2%)</td>
<td>159 (2.8%)</td>
<td>0.78 (0.62-0.99)</td>
</tr>
<tr>
<td>All Strokes</td>
<td>112 (1.9%)</td>
<td>133 (2.3%)</td>
<td>0.84 (0.65-1.08)</td>
</tr>
<tr>
<td>Revasc procedure</td>
<td>334 (5.8%)</td>
<td>386 (6.7%)</td>
<td>0.86 (0.74-1.00)</td>
</tr>
</tbody>
</table>
ACCOMPLISH Conclusions

• Combination of CCB and ACE was superior to ACE/HCTZ
• BP differences of 1 mm only
• Different populations may matter
• Chlorthalidone vs. HCTZ?
• Recommendation to change practice in highest risk patients – ACE and CCB may have special benefits

53 yo African-American woman, BP=148/88. Has Diabetes Type 2, Kidney normal. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin angiotensin receptor blocker
53 yo African-American woman, BP=148/88. Has Diabetes Type 2, Kidney normal. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin angiotensin receptor blocker

Recommendations for Management of Hypertension

Recommendation 7
Black population, including diabetes:

Initial treatment:
✓ Thiazide-type diuretic
✓ Calcium Channel Blocker (CCB)

General black population: Moderate Rec – Grade B
Black patients with diabetes: Weak Rec – Grade C

Recommendation 8
≥18 years with CKD, initial (or add-on) treatment:

- ACEI or ARB to improve kidney outcomes.
- For all CKD patients with HTN regardless of race or diabetes

Moderate Recommendation – Grade B

Recommendation 9
- If goal BP not reached within 1 month, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB).
- Assess BP and adjust the treatment regimen until goal is reached.
- If goal cannot be reached with 2 drugs, add and titrate a third drug from the list provided.
Recommendations for Management of Hypertension

Recommendation 9

- Do not use and ACE and an ARB in the same patient.
- If goal cannot be reached using the drugs in rec 6 drugs from other classes can be used.
- Referral to a specialist may be indicated
- Expert Opinion – Grade E

Evidence-based Medications

ACE inhibitors
- Captopril
- Enalapril
- Lisinopril

Angiotensin receptor blockers
- Eprosartan
- Candesartan
- Losartan
- Valsartan
- Irbesartan
Evidence-based Medications

**Beta blockers**
- Atenolol,
- Metoprolol

**Calcium channel blockers**
- Amlodipine,
- Diltiazem ER
- Nitrendipine

**Thiazide-type diuretics**
- Bendroflumethiazide,
- Chlorthalidone,
- Hydrochlorothiazide,
- Indapamide

Strategies to Dose BP Meds

1) **One drug, titrate to max, add second**

2) **One drug, add second before max of initial**

3) **Two drugs at same time, separate or as combo**
Resistant Hypertension

• Not reaching goal BP despite three medications from different classes (including one diuretic)
• Adherence is number one cause
• Avoid NSAID, decongestants, speed
• Other causes not common

What About Other Drugs?

• Spironolactone
• Beta blockers
• CNS sympatholytics: Clonidine
• Methyldopa: Little reason to use
• Alpha-1 blockers: OK but inferior as single drug and tachyphylaxis
• Labetalol good 5th or 6th choice
• Direct vasodilators - hydralazine or minoxidil - need more diuretics
• Peripheral adrenergic antagonists
British Management of Hypertension

- If BP 140/90 in office, use ambulatory monitor to confirm
- Estimate CV risk, evaluate for target organ effects (LVH, CKD, retinopathy)
- Treat stage 1 with meds only if target organ damage, known CVD, diabetes, 10-year CV risk ≥ 20%
- Offer meds to all at any age with stage 2 (>155/95) independent of other effects

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Table 6. Guideline Comparisons of Goal BP and Initial Drug Therapy for Adults With Hypertension

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Population</th>
<th>Goal BP, mm Hg</th>
<th>Initial Drug Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014 Hypertension guideline</td>
<td>General ≥60 y</td>
<td>&lt;150/90</td>
<td>Nonblack: thiazide-type diuretic, ACEI, ARB, or CCB; black: thiazide-type diuretic or CCB</td>
</tr>
<tr>
<td></td>
<td>General &lt;60 y</td>
<td>&lt;140/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;140/90</td>
<td>Thiazide-type diuretic, ACEI, ARB, or CCB</td>
</tr>
<tr>
<td></td>
<td>CKD</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>General nonelderly</td>
<td>&lt;140/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>General elderly &lt;80 y</td>
<td>&lt;150/90</td>
<td>Diuretic, β-blocker, CCB, ACEI, or ARB</td>
</tr>
<tr>
<td></td>
<td>General ≥80 y</td>
<td>&lt;150/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;140/85</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD no proteinuria</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD + proteinuria</td>
<td>&lt;130/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>CHEP 2013</td>
<td>General &lt;80 y</td>
<td>&lt;140/90</td>
<td>Thiazide, β-blocker (age &lt;60y), ACEI (nonblack), or ARB</td>
</tr>
<tr>
<td></td>
<td>General ≥80 y</td>
<td>&lt;150/90</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>&lt;130/80</td>
<td>ACEI or ARB with additional CVD risk ACEI, ARB, thiazide, or DHPPCBB without additional CVD risk</td>
</tr>
<tr>
<td></td>
<td>CKD</td>
<td>&lt;140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>ADA 2013</td>
<td>Diabetes</td>
<td>&lt;140/80</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>KDOQI 2012</td>
<td>CKD no proteinuria</td>
<td>≤140/90</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD + proteinuria</td>
<td>≤130/80</td>
<td>ACEI or ARB</td>
</tr>
<tr>
<td>NICE 2011</td>
<td>General &lt;80 y</td>
<td>&lt;140/90</td>
<td>&lt;55 yr: ACEI or ARB</td>
</tr>
<tr>
<td></td>
<td>General ≥80 y</td>
<td>&lt;150/90</td>
<td>≥55 yr or black: CCB</td>
</tr>
<tr>
<td>ISHIB 2010</td>
<td>Black, lower risk</td>
<td>&lt;135/85</td>
<td>Diuretic or CCB</td>
</tr>
<tr>
<td></td>
<td>Target organ damage or CVD risk</td>
<td>&lt;130/80</td>
<td>Diuretic or CCB</td>
</tr>
</tbody>
</table>

Abbreviations: BP, blood pressure; CV, cardiovascular; CVD, cardiovascular disease; LVH, left ventricular hypertrophy; CKD, chronic kidney disease; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; DHPPCBB, dihydropyridine calcium channel blocker; JNC, Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; KDIGO, Kidney Disease: Improving Global Outcomes; KDOQI, Kidney Disease Outcomes Quality Initiative; NICE, National Institute for Health and Care Excellence.
Kaiser Northern California HTN Program

- 80% control

**Key elements**

- Patient registry
- Sharing of performance metrics
- Evidence-based guidelines
- Medical assistant/pharmacist visits
- Single pill combination therapy

Jaffe, JAMA 2013

**Key Points of JNC 8**

1) ≥60 yo: goal ≤150
2) Others <140/<90 (including DM, CKD, race/ethnicity)
3) Non blacks: thiazide, CCB, ACEI, ARB
4) Blacks: thiazide, CCB
5) CKD: ACEI or ARB
Other Take Home Points

- Most patients will need two or more drugs to achieve goal SBP
- Control only occurs with motivated patients who trust their clinician

One Other Key Point

Take the BP accurately yourself, and record it in the medical record.