Things that raise my blood pressure – how to make sense of dueling guidelines

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Outline

• BP targets
• Review recent guidelines
• Ambulatory BP monitoring
• A few drug caveats
• Alternative therapies
• How to live a happier life
HTN Stats

• One out of every 3 U.S. Adults\(^1\)

• Shortens lifespan by an average of 5 years, with increased CV disease burden during life\(^2\)

• WHO lists HTN as the leading risk factor for premature death worldwide\(^3\)

• Direct and indirect costs of $70 billion/yr\(^4\)

1. Circulation 2013;127:e6-e245  
4. Hypertension 2014;63(4):878-885

HTN Control – How are we doing?

• Currently, about half of people with HTN are treated to levels below 140/90 mmHg

Center for Disease Control and Prevention  
NCHS Data Brief 220, Nov 2015
What are the appropriate targets for blood pressure?

New Guidelines for HTN – Again?

• In Jan, 2017, ACP/AAFP released a joint guideline for hypertension, largely in support of JNC-8 recommendations of 2014

• In Nov, 2017, the ACC/AHA released their own blood pressure guidelines that differed from the above in important ways
ACC/AHA 2017 Guidelines

- Stricter parameters for definition of HTN
- Initiation of antihypertensive medication at lower levels of blood pressure
- A single BP target for all pts of < 130/80

Cardiovascular Mortality Risk Doubles With Each 20-mm Hg SBP or 10-mm Hg DBP Increment*

*Individually aged 40-69 years, starting at blood pressure 115/75 mm Hg
DBP=diastolic blood pressure; SBP=systolic blood pressure
2. Chobanian AV et al. JAMA. 2003;289:2560-2572
<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>JNC 7</th>
<th>2017 ACC/AHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120/80</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>120-129/80</td>
<td>Prehypertension</td>
<td>Elevated BP</td>
</tr>
<tr>
<td>130-139/80-89</td>
<td>Prehypertension</td>
<td>Stage 1 HTN</td>
</tr>
<tr>
<td>140-159/90-99</td>
<td>Stage 1 HTN</td>
<td>Stage 2 HTN</td>
</tr>
<tr>
<td>&gt;160/100</td>
<td>Stage 2 HTN</td>
<td>Stage 2 HTN</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>JNC 7</td>
<td>2017 ACC/AHA</td>
</tr>
<tr>
<td>------------------------</td>
<td>-------</td>
<td>--------------</td>
</tr>
<tr>
<td>Prevalence of HTN</td>
<td>31.9%</td>
<td>45.6%</td>
</tr>
<tr>
<td>Number with HTN (millions)</td>
<td>72.2</td>
<td>103.3</td>
</tr>
</tbody>
</table>


**CLINICAL SCENARIO**

- A 66 year old woman with a history of osteoporosis and borderline hypertension
- BPs average about 138/88
- Should we treat her BP?
Does lowering blood pressure substantially below the usual target of 140/90 improve outcomes?

Cardiovascular Mortality Risk Doubles With Each 20-mm Hg SBP or 10-mm Hg DBP Increment*

1 Million Adults in 61 Prospective Studies

*Individuals aged 40–69 years; starting at blood pressure 115/75 mm Hg;
SBP = systolic blood pressure; DBP = diastolic blood pressure
2009 Cochrane Review

• Does lowering of BP to targets below 135/85 reduce morbidity or mortality as compared to the usual target of <140/90?

Cochrane Database of Syst Rev 2009;3:CD004349

2009 Cochrane Review

• Seven randomized trials (n=22,089) identified

• Despite clear BP differences, there was no effect on any major endpoint

Cochrane Database of Syst Rev 2009;3:CD004349
AASK Trial

• 1,094 African American pts with HTN + CKD were randomized to intensive (<130/80) vs standard (<140/90) BP control

• Primary composite outcome of worsening CKD, new ESRD, or death

• Follow up ranged from 8.8 to 12.2 years

N Engl J Med 2010;363:918-29

AASK Trial - Results

• Despite a significant difference in BP achieved (130/78 vs 141/86), there were no differences in the primary outcome measure

N Engl J Med 2010;363:918-29
ACCORD Trial

- 4,733 diabetics were randomized to intensive blood pressure control (SBP < 120) vs. usual control (SBP <140) – followed for 4.7 years

- 1st composite outcome was nonfatal MI, nonfatal stroke, or CV death

- Starting average BP was 139/76


ACCORD – BP Results
ACCORD - Results

- No difference in primary outcome

- A small but significant decrease in stroke was noted in the intensive control group (NNT ≅ 450 over 5 years)


ACCORD - Adverse Events

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive Therapy</th>
<th>Standard Therapy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Adverse events</td>
<td>3.3%</td>
<td>1.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Important ↑ serum creatinine</td>
<td>23.8%</td>
<td>15.5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>New ESRD</td>
<td>4.2%</td>
<td>2.2%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Blood Pressure Treatment Trialists

• Meta-analysis of intensive versus standard BP control in patients with CKD (26 trials, n=152,290)

• No difference in CV outcomes

BMJ 2013;347:F5680

HOPE - 3

• 12,705 subjects with average risk for CV events randomized to combination BP med (candesartan 16 mg/HCTZ 12.5 mg) vs placebo

• Baseline BP 138/82
• Follow up = 5.6 years
• Primary outcome = CV death, MI or stroke

N Eng J Med 2016;374:2032-2043
HOPE - 3

• Despite a 6 mmHg difference in SBP (128 vs 134 mmHg) achieved, no differences seen for any outcome

N Eng J Med 2016;374:2032-2043

Longitudinal Cohort - Mild HTN

• 19,000 pts with mild HTN (140/90 – 159/99) who received BP meds were matched with another 19,000 pts who did not receive meds

• Excluded pts with CAD or any CV risks
• Average age = 55 years
• Median follow up = 5.8 years

Longitudinal Cohort - Mild HTN

- No difference in mortality or CVD events
- Pts on BP meds had significantly greater incidence of Adverse events:

<table>
<thead>
<tr>
<th>Event</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>1.69</td>
<td>1.30-2.20</td>
</tr>
<tr>
<td>Syncope</td>
<td>1.28</td>
<td>1.10-1.50</td>
</tr>
<tr>
<td>Electrolyte Abnormalities</td>
<td>1.72</td>
<td>1.12-2.65</td>
</tr>
<tr>
<td>AKI</td>
<td>1.37</td>
<td>1.00-1.88</td>
</tr>
</tbody>
</table>


Theme thus far – no benefits to going lower than SBP < 140
SPRINT

• RCT of 9,361 non-diabetic pts over age 50 with high risk for ASCVD events (>20% 10-year risk)
• Included many older pts (28% > 75 yrs)
• Mean SBP at baseline was 141.6 mmHg on 2 BP meds
• Pts randomized to aggressive BP control (SBP < 120) vs standard control (SBP<140)

N Eng J Med 2015;373:2103-2116

A side note on SPRINT...
SPRINT - How did they measure the blood pressure?

- Subjects were brought into rooms, asked to sit quietly alone for 5 minutes doing nothing. The caregiver then returns, does not speak to the patient, and inflates an automated BP cuff

N Eng J Med 2015;373:2103-2116

BP controversy with SPRINT

- BP measured in the SPRINT trial is estimated to be 10/7 mmHg lower than BP measured by traditional office practice methodology

Circulation 2016;134:904-905
SPRINT

• Primary composite outcome of MI, ACS, stroke, decompensated CHF, or CV death

• Average follow up of 3.2 years - stopped prematurely due to evidence of benefit

N Eng J Med 2015;373:2103-2116
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment n(%)</th>
<th>Standard Treatment n(%)</th>
<th>Hazard Ratio</th>
<th>P value</th>
<th>NNT over 3.26 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td>243(5.2)</td>
<td>319(6.8)</td>
<td>0.75</td>
<td>&lt;0.001</td>
<td>61</td>
</tr>
<tr>
<td>Heart failure</td>
<td>62(1.3)</td>
<td>100(2.1)</td>
<td>0.62</td>
<td>0.002</td>
<td>125</td>
</tr>
<tr>
<td>CV mortality</td>
<td>37(0.8)</td>
<td>65(1.4)</td>
<td>0.57</td>
<td>0.005</td>
<td>172</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>155(3.3)</td>
<td>210(4.5)</td>
<td>0.73</td>
<td>0.003</td>
<td>90</td>
</tr>
<tr>
<td>MI</td>
<td>97(2.1)</td>
<td>116(2.5)</td>
<td>0.83</td>
<td>0.19</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke</td>
<td>62(1.3)</td>
<td>70(1.5)</td>
<td>0.89</td>
<td>0.50</td>
<td>NS</td>
</tr>
</tbody>
</table>

N Eng J Med 2015;373:2103-2116

<table>
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<th>Hazard Ratio</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>110(2.4)</td>
<td>66(1.4)</td>
<td>1.67</td>
<td>0.01</td>
</tr>
<tr>
<td>Syncope</td>
<td>107(2.3)</td>
<td>80(1.7)</td>
<td>1.33</td>
<td>0.05</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td>144(3.1)</td>
<td>107(2.3)</td>
<td>1.35</td>
<td>0.02</td>
</tr>
<tr>
<td>Acute Kidney Injury</td>
<td>193(4.1)</td>
<td>117(2.5)</td>
<td>1.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Injurious falls</td>
<td>105(2.2)</td>
<td>110(2.3)</td>
<td>1.00</td>
<td>0.97</td>
</tr>
</tbody>
</table>

N Eng J Med 2015;373:2103-2116
For every 1,000 high risk pts treated with intensive strategy over 3.2 yrs:

- 16 persons will benefit (CHF, CV and all-cause mortality)
- 22 persons will be harmed (hypotension, syncope, AKI, electrolyte imbalance, ED visits)
- 962 persons - no apparent benefit or harm


Meta-analysis in Diabetics

- Examined 49 trials (n=73,738) in diabetics to assess the effect of more vs less intensive BP control on CV events and mortality
- Mean follow up: 3.7 years
- Stratified pts according to baseline systolic BP

BMJ 2016;352: Published Feb 25, 2016
<table>
<thead>
<tr>
<th>Baseline SBP (mmHg)</th>
<th>All-cause mortality</th>
<th>CV mortality</th>
<th>MI</th>
<th>Stroke</th>
<th>CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;150</td>
<td>0.89</td>
<td>0.75</td>
<td>0.74</td>
<td>0.77</td>
<td>NS</td>
</tr>
<tr>
<td>140-150</td>
<td>0.87</td>
<td>NS</td>
<td>0.84</td>
<td>NS</td>
<td>0.80</td>
</tr>
<tr>
<td>&lt; 140</td>
<td>NS</td>
<td>1.15</td>
<td>1.12</td>
<td>NS</td>
<td>NS</td>
</tr>
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</table>

BMJ 2016;352: Published Feb 25, 2016

What do the 2014 JNC-8 HTN guidelines recommend?
**JNC 8 Recommendations**

<table>
<thead>
<tr>
<th>Initiate Therapy</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 60</td>
<td>&gt;150/90 &lt;150/90</td>
</tr>
<tr>
<td>Ages 18 - 59</td>
<td>&gt;140/90 &lt;140/90</td>
</tr>
<tr>
<td>DM or CKD</td>
<td>&gt;140/90 &lt;140/90</td>
</tr>
</tbody>
</table>

1. JAMA 2014;311:507-520

**JNC 8 Recommendations**

<table>
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<tr>
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<td>Age ≥ 60</td>
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<tr>
<td>Ages 18 - 59</td>
<td>&gt;140/90 &lt;140/90</td>
</tr>
<tr>
<td>DM or CKD</td>
<td>&gt;140/90 &lt;140/90</td>
</tr>
</tbody>
</table>

Controversial!

1. JAMA 2014;311:507-520
Why 150/90 for older adults?

- Cochrane review of RCTs comparing BP target <150-160 mmHg vs more strict control of <140 mmHg
- 3 RCTs (n=8,221) with average age of 75
- Results: No differences in mortality or CV events after 2-4 years

Cochrane Database Syst Rev 2017; 8:CD011575

How have guidelines changed since the SPRINT trial?
### ACP/AAFP Joint Guidelines

<table>
<thead>
<tr>
<th>Age ≥ 60</th>
<th>Initiate Therapy</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;150/90</td>
<td>&lt;150/90</td>
</tr>
</tbody>
</table>

- Age ≥ 60: >140/90 <140/90
- with CVA or TIA, or high CV risk

1. Ann Intern Med 2017;166:430-437

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### Canadian and Australian Guidelines

- Consider treatment to SBP target < 120 for high risk pts > 50 yrs without DM

1. Can J Cardiol 2016;32:569-88
63 year old healthy ♀, BP = 144/70

Initiate Therapy Target

• ACP/AAFP 2017¹ >150/90 <150/90 No Treatment
• ACC/AHA 2017² >140/90 <130/80 Treat

1. Ann Intern Med 2017;166:430-437
2. JACC 2017;doi10.1016/j.jacc.2017.11.006

67 ♂ with DM and CAD, BP = 146/86

Initiate Therapy Target

• ACP/AAFP 2017¹ & ADA² >140/90 <140/90
• ACC/AHA 2017³ >130/80 <130/80

1. Ann Intern Med 2017;166:430-437
2. Diabetes Care 2018;41:S86-S104
3. JACC 2017;doi10.1016/j.jacc.2017.11.006
BP Targets – My take...

- Data are conflicting – SPRINT vs most other studies
- Target < 150 seems too high, except in very elderly
- Target < 140 seems good in DM, CKD, CVA, TIA and for most lower risk pts
- Target < 130 reasonable for non-diabetic pts with very high ASCVD risk

Clinical Scenarios

- 1) 60 year old man with an incidental finding of LVH on EKG, but clinic BPs in the 120s
- 2) 64 year old woman with elevated office BPs, but normal BPs at home
- 3) 48 year old man with controlled BPs on HCTZ
- 4) 58 year old man with 3 normal office BPs
New Guideline recommendations

• Newer guidelines all agree on one thing:
  
  – some form of out of office BP measurements to better establish the diagnosis of HTN

What is the role of 24 hour Ambulatory BP Measurements?
Current Indications for ABPM

- Suspected white coat HTN
- Suspected episodic HTN (pheo)
- Resistant HTN
- Hypotensive sx while on BP meds
- Autonomic dysfunction

J Hypertens 2013;31:1281-1357
J Hypertens 2014;32:3-15

Who recommends ABPM?1-3

- US (ACC/AHA, USPSTF, ASH)
- Canada (CHEP)
- Europe (ESH/ESC and NICE)

Is Ambulatory BP a better predictor of mortality risk than office BP?

Clinic vs 24\(^0\) ambulatory BPs

- Analysis of 63,910 individuals with 24\(^0\) ambulatory BP monitoring data in primary care practice
- Comparison of clinic vs ambulatory BP measurements as a predictor of CV and all-cause mortality
- Mean follow up: 4.7 years

Clinic vs 24h ambulatory BPs

- Ambulatory BP was strongly predictive of all-cause and CV mortality (HR 1.58 for each SD above normal BP)

- Clinic BP was not predictive of mortality after adjustment for ambulatory BP readings


<table>
<thead>
<tr>
<th>Group</th>
<th>Clinic BP (NI &lt;140/90)</th>
<th>Ambulatory BP (NI &lt;130/80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>White Coat HTN</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Masked HTN</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Sustained HTN</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>CV Mortality Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotensive</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>White Coat HTN</td>
<td>1.79</td>
<td>1.38 – 2.32</td>
</tr>
<tr>
<td>Masked HTN</td>
<td>2.83</td>
<td>2.12 – 3.79</td>
</tr>
<tr>
<td>Sustained HTN</td>
<td>1.80</td>
<td>1.41 – 2.31</td>
</tr>
</tbody>
</table>

Masked Hypertension

- A 50 year old with masked HTN has an all-cause mortality rate equivalent to someone 14 years older!
So how common is masked HTN?

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Masked HTN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy Adults&lt;sup&gt;1-2&lt;/sup&gt;</td>
<td>888</td>
<td>15.7%</td>
</tr>
<tr>
<td></td>
<td>63,910</td>
<td>3.6%</td>
</tr>
<tr>
<td>DM&lt;sup&gt;3&lt;/sup&gt;</td>
<td>266</td>
<td>26.5%</td>
</tr>
<tr>
<td>Obesity&lt;sup&gt;4&lt;/sup&gt;</td>
<td>323</td>
<td>17.1%</td>
</tr>
<tr>
<td>African Americans&lt;sup&gt;5&lt;/sup&gt;</td>
<td>1,016</td>
<td>25.4%</td>
</tr>
<tr>
<td>Chronic Kidney Dz&lt;sup&gt;6-7&lt;/sup&gt;</td>
<td>1492</td>
<td>27.8%</td>
</tr>
<tr>
<td></td>
<td>377</td>
<td>70%</td>
</tr>
</tbody>
</table>

Clinic vs 24\(^0\) ambulatory BPs

- Analysis of 24\(^0\) ambulatory BP monitoring data in 1,191 elderly pts with treated HTN
- Outcome: Combined CV events
- Mean follow up: 9.1 years

<table>
<thead>
<tr>
<th>Group</th>
<th>CV Events Hazard Ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled HTN</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>White Coat HTN</td>
<td>1.09</td>
<td>0.74 – 1.60</td>
<td>0.66</td>
</tr>
<tr>
<td>Masked HTN</td>
<td>1.60</td>
<td>1.12 – 2.29</td>
<td>0.01</td>
</tr>
<tr>
<td>Sustained HTN</td>
<td>1.81</td>
<td>1.35 – 2.42</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Am J Hypertens 2017;30:1106-1111
White Coat Hypertension - tips

- Have a medical assistant or nurse measure BPs rather than the doctor\(^1\)
- Use automated BP cuffs without anyone else in the room\(^2\)

2. Can J Cardiol 2012;28:341-346

Doctor vs Nurse BP readings

Hypertension 1987;9:209-215
Don’t Judge too quickly!

• In patients diagnosed with HTN on an initial clinic visit, BP drops an average of 15/7 mmHg by the 3rd visit, and often does not reach a steady state until the 6th visit\(^1\)\(^-\)\(^2\)

1. JAMA 2003;289:2560-2572
2. J Hypertens 1987;5:207-211

White Coat Hypertension – Prevalence

• White coat HTN occurs in \(\approx\)10-20\% of the general population\(^1\)\(^-\)\(^4\)

2. JAMA 1988;259(2):225-228
3. J Hypertens. 2006;24(3):463-70
White Coat Hypertension - Prognosis

• Pts with WCH appear to have a CV risk somewhere in between that of sustained HTN and normotensives\(^1\)\(^-\)\(^2\)
• Increased risk to develop comorbidities (DM, LVH, RVH, and albuminuria)\(^3\)
• Increased risk for progression to chronic HTN\(^4\)

1. J Hypertens 2016;34:593-599
2. Uptodate Oct 2018 – White coat Hypertension in adults

White Coat Hypertension - Prognosis

• Meta-analysis of 14 studies (n=29,100) comparing outcomes of normotension, sustained HTN, and white coat HTN

• Mean age = 59 years
• Mean follow up = 9 years

J Hypertens 2016;34:593-599
What are the barriers to obtaining 24-hour ambulatory BP monitoring?

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Normal BP</th>
<th>White coat HTN</th>
<th>Sustained HTN</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV Events</td>
<td>4.0%</td>
<td>5.7%</td>
<td>11.4%</td>
</tr>
<tr>
<td>CV Mortality</td>
<td>1.2%</td>
<td>4.2%</td>
<td>6.6%</td>
</tr>
<tr>
<td>All-cause Mortality</td>
<td>7.7%</td>
<td>10.8%</td>
<td>14.4%</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.7%</td>
<td>3.4%</td>
<td>6.4%</td>
</tr>
</tbody>
</table>

Am J Hypertens 2017;30:1106-1111
Ambulatory BP costs - 2011

• Monitoring equipment - $2500-5000
• Computer software - $2000-3000

UptoDate – Ambulatory and home blood pressure monitoring – accessed Oct 1, 2018

Ambulatory BP costs - 2018
How accurate are wrist BP cuffs?

- 50 subjects with equal BP in each arm assigned to simultaneous 24-hour ambulatory BP with a wrist cuff vs arm cuff
- Wrist SBP was about 5 mmHg lower than that of arm BP cuffs (p<0.01)

Conclusions

- Ambulatory or home BP readings can yield important information regarding BP control and need for further intervention
- White coat HTN confers elevated risk compared to normotensives
- In patients with white coat HTN, minimizing risk factors and monitoring closely for development of sustained HTN are key
Conclusions

- Masked HTN appears to represent a major underrecognized CV disease risk factor
- Home monitoring devices are evolving and will soon be a regular part of practice
- Further studies are needed to ensure accuracy of these devices

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendations</th>
<th>↓ in SBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Reduction</td>
<td>Maintain Normal BMI (18.5-24.9)</td>
<td>5-20 mmHg per 10kg wt loss</td>
</tr>
<tr>
<td>DASH Diet</td>
<td>↑ fruits, vegetables and low fat dairy</td>
<td>8-14 mmHg</td>
</tr>
<tr>
<td>Dietary Sodium</td>
<td>Reduce sodium to &lt; 2.4 g/d</td>
<td>2-8 mmHg</td>
</tr>
<tr>
<td>Restriction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetarian Diet</td>
<td>Eliminate meats</td>
<td>5 mmHg</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>Regular aerobic exercise most days</td>
<td>4-9 mmHg</td>
</tr>
<tr>
<td>Moderation of Alcohol</td>
<td>No more than 1-2 drinks per day</td>
<td>2-4 mmHg</td>
</tr>
</tbody>
</table>

Spironolactone

- For patients with resistant hypertension, addition of spironolactone can substantially improve blood pressure control

- Monitor carefully for hyperkalemia and breast discomfort

Additional BP control with Spironolactone in Refractory HTN

Cardiol 2007;88(6):604-613
Is there a difference between ACE & ARB?

ACE vs ARBs – Direct Comparison

• Direct comparison trials (n=11,007) demonstrated similar efficacy with slightly lower SE profile for ARBs

• NNT to prevent one episode of cough was 55 with use of ARB instead of ACE

ACE vs ARBs – Indirect Comparison

- Two meta-analyses (n=158,998 and n=56,704) looked at studies of ACE or ARB vs placebo
- Overall, use of an ACE or ARB reduced mortality by 5%
- On further analysis, pts on ACE had a 10% mortality benefit, whereas pt on ARB had none


CLINICAL BOTTOM LINE

- While imperfect, a large volume of indirect evidence suggests superiority of ACE over ARBs for HTN
- Never combine ACE and ARB due to adverse renal outcomes1-3

My hypertensive patient has a cold – what should I advise?

Pseudoephedrine and BP

• Review of 24 trials (n=1,285) revealed a significant increase in SBP and HR with use of pseudoephedrine

• Average SBP: ↑ 1 mmHg
• Average heart rate: ↑ 3 bpm

Arch Intern Med 2005;165:1684-1694
Double the dose or add a second agent?

Titrate single drug vs combo?

- Meta-analysis of 11,000 patients from 42 trials comparing single dose with up titration vs switch to combo therapy

Adding a second agent is about 5-fold more effective


Number of BP Agents Utilized

Cardiol Clin 2007;25:507-522
Based on RCTs of HTN, at least 75% of patients will require combination therapy to achieve BP targets

Am J Hypertens 2010;4:42-50

Does Timing Matter?
Morning vs Evening Meds

• Lack of nighttime “dipping” of BP and morning BP surges have both been associated with increased cardiac events

• Non-dippers comprise 25% of pts with HTN


Morning vs Evening Meds

• Review of 21 RCTs (n=1,993) comparing am vs pm dosing of BP meds (-1.7/-1.4) when at least one BP med taken at night

Cochrane Database Syst Rev 2011, Issue 10 CD004184
Chronotherapy

• 60 pts with uncontrolled HTN and non-dipper status on 1-2 BP meds in the am
  - Randomized to usual am BP meds vs switching BP meds to night administration
  - No changes made to BP regimen

• Outcome: 240 Ambulatory BP at 2 and 4 mos


Chronotherapy

• 86% of subjects given nighttime meds achieved BP control, compared to none of the control subjects (p<0.005)

• BP improved by a mean of -6.2/-2.6 mmHg (p<0.009)

Chronotherapy

• 1,109 pts with HTN randomized to receive all BP meds in am vs ≥ 1 BP med at night

• Follow up 5.4 years

• Outcomes measured were night time and ambulatory BPs as well as major CV events

1. Diabetes Care 2011;34:1270-1276

Chronotherapy

• Patients taking ≥ 1 med at night:
  – Lower night time and ambulatory BPs
  – 72-75% RRR in major CV events (p = 0.003)

1. Diabetes Care 2011;34:1270-1276
Chronotherapy - Conclusions

• Timing appears to matter!

• ADA Standards of Care recommends administering ≥ 1 BP med at night

• More studies are needed...

Diabetes Care 2015;38:S1-99

What if my patient has gout?
HTN and Gout

- Losartan decreases serum uric acid levels by 20-25% by its uricosuric effects
- Other ARBs do not share this property

BMJ 2012;344:d8190

Gout and Antihypertensives

<table>
<thead>
<tr>
<th>Antihypertensive Class</th>
<th>RR of Gout Flare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losartan</td>
<td>0.81 (0.70 – 0.94)</td>
</tr>
<tr>
<td>Calcium Channel Blockers</td>
<td>0.87 (0.82-0.93)</td>
</tr>
<tr>
<td>ACE Inhibitors</td>
<td>1.24 (1.17 – 1.32)</td>
</tr>
<tr>
<td>Non-Losartan ARBs</td>
<td>1.29 (1.16-1.43)</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>1.48 (1.40 – 1.57)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>2.36 (2.21-2.52)</td>
</tr>
</tbody>
</table>

BMJ 2012;344:d8190
Clinical Question

I heard a renal bruit on my patient with hypertension. Should I look for renal artery stenosis?

Atherosclerotic Renal Artery Stenosis

• Atherosclerotic Renal Artery Stenosis (ARAS) is implicated as a cause of CKD and resistant HTN

• Common disorder - 6.8% of people age ≥ 66 yrs¹

• 21 cohort studies failed to show benefit from revascularization²

• 3 additional RCTs have shed further light

ASTRAL Trial

• 806 patients with ARAS were randomized to undergo stent + medical therapy versus medical therapy alone


ASTRAL Study Design

• 1st outcome measure was renal function
• 2nd outcomes were BP control, time to renal or major CV events, and mortality
• Follow up = 34 months

ASTRAL Study Results

- No important clinic differences were seen

ASTRAL – Early Complications

- 38 periprocedural complications occurred (19 serious) including embolizations resulting in peripheral gangrene and amputations

- 55 late events occurred in the revascularization group, including 2 CV deaths

STAR Trial

- 140 patients with ARAS randomized to stent + medical therapy vs medical therapy alone
  - 1\textsuperscript{st} outcome - decline in renal function
  - 2\textsuperscript{nd} outcomes - CV morbidity and mortality

- Follow up = 2 yrs

*Ann Intern Med 2009;150:840-48*

STAR Study Results

- No important clinic differences were seen
STAR - Complications

• 3 of the 46 patients receiving a stent died from the procedure, and another patient required chronic dialysis due to a cholesterol embolism

CORAL Trial

• 947 pts with ARAS (+ HTN or CKD) randomized to stent + medical therapy vs medical therapy alone

• Composite end point – (death, MI, stroke, CHF, ↓ kidney function, dialysis)

• Mean follow up of 43 months

CORAL Trial Results

- No important clinic differences were seen

CORAL Trial

- SBP in stent group was 2.3 mmHg lower (p=0.03)

- 11 Renal artery dissections occurred in the 434 patients receiving stents
Current Status

• Systematic review of 83 studies showed no overall benefit to revascularization procedures for ARAS

• Despite these data, roughly 20,000 renal revascularization procedures per year in US!

Ann Intern Med 2016;165:635-649

CLINICAL BOTTOM LINE

• Revascularization for ARAS causes greater harm than good!

• In most cases, evaluation of patients for possible renal artery stenosis in the setting of resistant hypertension is not warranted*

*Fibromuscular dysplasia is still a good reason to look for RAS in young people with refractory HTN
# Alternative Approaches to Hypertension

## Alternative Therapies

<table>
<thead>
<tr>
<th>Agent</th>
<th>BP Δ (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green tea</td>
<td>-2.1/1.7</td>
</tr>
<tr>
<td>Hibiscus tea*</td>
<td>-5.9/2.6</td>
</tr>
<tr>
<td>Coffee</td>
<td>NS</td>
</tr>
<tr>
<td>Transcendental meditation</td>
<td>-5/3</td>
</tr>
<tr>
<td>Biofeedback</td>
<td>-2/2</td>
</tr>
<tr>
<td>Yoga, classical music, acupuncture, Yo-Yo Ma</td>
<td>Inconclusive</td>
</tr>
</tbody>
</table>

*J Hypertension 2013;61:1360-83*  *J Nutr 2010;140:298-303*
Dark Chocolate

- Cochrane review of 20 studies involving 856 subjects randomized to dark chocolate vs placebo

- Outcome: Blood pressure at 2-18 weeks

Cochrane Database of Systematic Reviews 2012, Issue 8

Dark Chocolate

- Dark chocolate consumption resulted in BP reduction by 2.8/2.2 mmHg

- Adverse effects (GI complaints and distaste) were reported in 5% of the dark chocolate group and 1% of the control group

Cochrane Database of Systematic Reviews 2012, Issue 8
Blueberries

• Study of postmenopausal women with borderline HTN (n=48) randomized to blueberry powder vs placebo x 8 weeks

• BP significantly decreased by 7/5 mmHg with use of blueberries

J Acad Nutr Diet 2015; published online Jan 8, 2015