HYPERTENSION: 2015 UPDATE

Learning Objectives:

- Recognize that HTN is the leading contributor to global mortality and disability and is increasing in prevalence in the U.S. due to the obesity epidemic and population aging.
- Understand that while HTN control rates have improved in the past 30 years, these rates remain unacceptable.
  - Be able to look at your individual, group, and system practices to find both previously undetected as well as uncontrolled hypertensive patients.
- Be aware of key differences/controversies among the multitude of new HTN practice guidelines in 2013-2015.
  - Understand the different rationales for variable BP goals.
- Be able to make a more accurate diagnosis of HTN in view of new recommendations – including 2015 recommendations from the U.S. Preventive Services Task Force and the Canadian Hypertension Education Program – to routinely incorporate out-of-office BP measurement in all patients to confirm the diagnosis of hypertension.
- Be able to effectively use home BP monitoring (HBPM) for your patients.
- Be able to provide effective lifestyle modification – recognizing the controversies surrounding sodium restriction – to reduce BP.
- Be able to select optimal 1-4 drug regimens to improve HTN control rates.
- Be able to select the few patients who may benefit from evaluation and treatment of renal artery stenosis.

The Bottom Line:

HTN continues to be the leading risk factor for global mortality and disability at a cost of $94 billion/y in the U.S. One third of all adult Americans and two thirds of Americans age ≥ 60y have hypertension with prevalence likely to increase to 41% by 2030 due to the increasing obesity and aging of the population. Only 54% of hypertensive Americans have their BP controlled below 140/90 mm Hg, with lower control rates in blacks and Hispanics. Recent EHR studies indicate substantial numbers of undetected/untreated hypertensive persons in U.S. medical practices.

The accurate diagnosis of HTN requires correct BP measurement preparation and technique - infrequently accomplished in busy primary care practices – and detection of the 15-30% of patients with elevated office BP who have white-coat or isolated office HTN. Otherwise, many patients will be over-diagnosed and overtreated, an important patient safety issue. While office BP measurement (OBPM) has historically been the gold standard for HTN diagnosis, new 2015 recommendations from the U.S. Preventive Services Task Force, the Canadian Hypertension Education Program, and the French, UK, and Taiwan HTN guidelines now propose out-of-office BP measurement (24-hour ambulatory BP studies, or if not available, standardized home BP measurement) to confirm all office diagnoses of HTN prior to treatment.
There is no consensus among new HTN practice guidelines as to target treatment BP among various subpopulations of patients. While most guidelines have a target BP < 140/90 mm Hg for the general population, the JNC-8 task force – but only a majority of this group – favors a target BP < 150/90 mm Hg for persons age ≥ 60y. Their rationales include the absence of a definitive RCT that treated patients with BP = 140-149, a 2012 Cochrane Review that found no decrease in CVD events in such patients, and the presence of potential treatment side effects. However, many other groups favor the < 140/90 target, citing the considerable epidemiologic CVD risk of BP= 140-149 and other meta-analyses suggesting reduction of CVD events with BP = 140-149. Most guidelines now target a BP < 150/90 for persons age ≥ 80y. Most guidelines now target a BP < 140/90 for patients with diabetes or CKD, while a few others target a BP < 130/80 if diabetes, albuminuria, or high stroke risk is present.

With respect to treatment, controversy continues to surround the benefits, or lack of benefit, or even toxicity of very low sodium diets < 1500-2300 mg/d. Algorithms have been published in the new guidelines recommending optimal one, two, three, and four drug regimens to more effectively treat HTN; most guidelines have relegated beta-blockers to step 3 or step 4 therapy unless there are compelling indications for their use. Finally, recent studies suggest that evaluation and treatment of renal artery stenosis should be limited to a very small subgroup of patients with very high BP and/or declining eGFR and/or flash pulmonary edema.

Selected References:

- **Clinical Practice Guidelines:**
  5. The 2015 Canadian Hypertension Education Program Recommendations for the Diagnosis and Management of Hypertension. www.hypertension.ca
**BP measurement:**

**Home BP Monitoring:**

**How Low Should We Go?**

**Hypertension Treatment:**

**Lifestyle Modification:**

**Team Approach to Improve Hypertension Control Rates:**

**Renal Artery Stenosis and Hypertension Management:**

**Renal Artery Sympathetic Denervation:**
HYPERTENSION 2015 UPDATE

Barry Stults, M.D.
Division of General Medicine
University of Utah Medical Center
and
Salt Lake City, VA Medical Center
HYPERTENSION: MORBID, LETHAL!
TOP RF FOR GLOBAL MORTALITY/DISABILITY

Increases RR by 2.0-4.0 fold for:
- CAD, stroke, HF, PAD, AF, CKD
- Dementia: vascular, Alzheimers
- Mild cognitive deficits

Attributable risk for HTN:
- Stroke → 62%
- CKD → 56%
- HF → 49%
- MI → 25%
- Premature death → 24%

Aftermath:
- Shortens lifespan 5y – 16% of deaths
- $46.4 billion/y in U.S. ($94 billion/y, total)

HYPERTENSION: UNBELIEVABLY COMMON!

- **Prevalence:**
  - 33% of adult Americans
  - 45% of adult black Americans – highest in world
  - 65% of Americans age ≥ 60y
  - 90% of Americans age ≥ 85y

- **CKD:**
  - eGFR ≤ 60: 67% < 30: 92%
  - Hemodialysis: 60% Peritoneal: 30%

↓

80 million Americans with HTN!
Projected prevalence in 2030: 41% of adults

Circulation 2015; 131:e86  
Am J Kid Dis 2010; 55:441  
AJM 2003; 115:291
HYPERTENSION: VERY TREATABLE

Meta-analysis: 68 RCTs; 245,885 pts; 4.3y FU

- ↓ SBP/DBP by 10/5 mm Hg for 5y:

<table>
<thead>
<tr>
<th>Complication</th>
<th>% Risk Reduction</th>
<th>NNT x 5y</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD events</td>
<td>25%</td>
<td>36</td>
</tr>
<tr>
<td>Heart failure</td>
<td>43%</td>
<td>73</td>
</tr>
<tr>
<td>Stroke</td>
<td>36%</td>
<td>58</td>
</tr>
<tr>
<td>MI</td>
<td>16%</td>
<td>160</td>
</tr>
<tr>
<td>Mortality</td>
<td>11%</td>
<td>125</td>
</tr>
<tr>
<td>Dementia</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

J Hypertension 2014; 32:2285
**HTN CONTROL: IMPROVING, BUT STILL UNACCEPTABLE**

**NHANES:**

<table>
<thead>
<tr>
<th></th>
<th>1980</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aware</td>
<td>51%</td>
<td>83%</td>
</tr>
<tr>
<td>Treated</td>
<td>31%</td>
<td>77%</td>
</tr>
<tr>
<td>Controlled (&lt; 140/90)</td>
<td>10%</td>
<td>54%</td>
</tr>
<tr>
<td>- Blacks</td>
<td></td>
<td>41%</td>
</tr>
<tr>
<td>- Hispanics</td>
<td></td>
<td>34%</td>
</tr>
</tbody>
</table>

- **18% Unaware**
- **46% Not Controlled**
- **7% Aware, Not Treated**
- **22-38% Treated, Not Controlled**

Circulation 2015; 131:e86  
JACC 2012; 60:599  
JAMA 2010; 303:204
UNDIAGNOSED HYPERTENSION: HIDING IN Plain SIGHT IN OUR OFFICES?

• Geisinger Health System:
  – EHR search of 400,000 pts with ≥ 3 visits over 4y
    • 29,000 pts had ≥ 2 BP readings ≥ 140/90 but no evaluation

• Palo Alto Medical Foundation:
  – EHR search of 250,000 pts over 2y
    • 37% with ≥ 2 BP readings ≥ 140/90 had no evaluation

• North Shore University Health System:
  – 47% of recalled pts from EHR search had HTN previously undiagnosed

NEW HYPERTENSION GUIDELINES, 2015

- JNC-8 Panel: JAMA 2014; 311:507
- AHA/ACC/CDC Advisory: J Am Coll Card 2014; 63:1230
- Am Society of Hypertension: J Clin Hypertens 2014; 16:14
- Canadian Hypertension Education Program: Can J Card 2014; 30:485
- Joint British Societies 3: Heart 2014; 100 (Suppl 2):1
- ESH/ESC: J Hypertens 2013; 31:1281
- KDIGO Blood Pressure Work Group: Kid Int 2012; Suppl 2
- Taiwan Hypertension Society: J Clin Med Assoc; on-line 12/26/2014
HYPERTENSION GUIDELINES 2015: NOT SO MUCH CLARITY

“Hypertension guidelines – clear as mud.” TheHeart.org

“Why doctors are fighting over blood pressure guidelines.” Time, 2014

“The multitude of guidelines from respected professional bodies and individuals have caused needless confusion bordering on chaos.” Editorial, J Clin Hypertens 2014; 16:251
HOW TO DIAGNOSE HYPERTENSION IN 2015?

• Essential to measure office BP accurately!

“Blood pressure reading does not seem to be done correctly in any clinic...It appears to be so simple that anyone can do it, but they can’t...”

JAMA 2008; 299:2842

• 9 studies with 9000 patients, 1995-2011:
  Routine clinical practice vs Guideline-based
  BP measurement

  – Accurate BP measurement ↓ BP ≈ 10/7 mm Hg
    and doubled HTN control rates!

BP MEASUREMENT: KEY TECHNIQUES

△ BP (mm Hg) if not done

Rest ≥ 5 min, quiet
Seated, back supported
Cuff at midsternal level
Correct cuff size
Bladder center over artery
Deflate 2 mm Hg/sec
No talking during measurement

If initial BP > goal BP:

3 readings, 1 min apart
Discard 1st, average last 2

1st reading higher

- “Alerting response”
- Reclassify 18-34% as normotensive

Recommends 8-11 minutes!

References:

J Clin Hypertens 2012;14:751
Hypertension 2005; 45:142
J Gen Int Med 2012; 27:623
J Hypertens 2005; 23:697
Can J Card 2014; 30:485
OFFICE BP MEASUREMENT: HOW TO DO IT?

• Can we teach/implement accurate manual BP measurement?
  – **Doubtful**: repetitive training/monitoring/time too difficult
• Automated electronic BP measurement favored by ASH, 2014 and by CHEP 2015
  – **Only** accurate devices validated by AAMI/BHS/IP protocols
    ▪ [www.dableducational.org](http://www.dableducational.org)
  – **Consider** unattended AOBP devices taking 3-6 measurements automatically
    ▪ ↑ accuracy and reproducibility, and ↓ white-coat effect
    ▪ BpTRU(6), Omron HEM-907 (3), MicroLife Watch BP Office (3)

  Canadian Hypertension Education Program 2015
OUT-OF-OFFICE BP MEASUREMENT: ESSENTIAL TO DX HTN?

- **White-coat (isolated office) HTN very common!**

<table>
<thead>
<tr>
<th>WCH Prevalence</th>
<th>General population</th>
<th>Office BP ≥ 140/90</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10-15%</td>
<td>20-30%</td>
</tr>
<tr>
<td>• Office BP = 140-159</td>
<td></td>
<td>55%</td>
</tr>
<tr>
<td>• Office BP ≥ 180</td>
<td></td>
<td>10%</td>
</tr>
</tbody>
</table>

*References*

- BMJ 2011; 343:d5421
- Hypertension Res 2014; 37:791
- J Clin Hypertens 2014; 16:4
OUT-OF-OFFICE BP MEASUREMENT: ESSENTIAL TO DX HTN?

AHRQ 2014 Systematic Review:

• Predicts CVD events superior to OBPM:

<table>
<thead>
<tr>
<th>Measurement</th>
<th>HR for CVD vs OBPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABPM (11 studies)</td>
<td>1.28-1.40</td>
</tr>
<tr>
<td>HBPM (4 studies)</td>
<td>1.17-1.39</td>
</tr>
</tbody>
</table>

• Diagnoses HTN more accurately than OBPM:

  Measurement error of OBPM → 5-65% of office HTN not confirmed by ABPM in 27 studies

  Regression to mean

  White-coat HTN in 15-30%

OUT-OF-OFFICE BP MEASUREMENT: ESSENTIAL TO DX HTN?

USPSTF Draft Statement, January, 2015:

“The USPSTF recommends screening for HTN in adults ≥ 18y old. Ambulatory BP monitoring is recommended to confirm high BP before the diagnosis of HTN, except in cases for which immediate initiation of therapy is necessary...Good quality evidence suggest that confirmation of hypertension using home BP monitoring may be acceptable...More research is needed on the best home BP monitoring protocols for followup of elevated office BP measurements...”

## HOW TO DIAGNOSE HYPERTENSION IN 2015?

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Gold Standard to Dx HTN</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASH/ISH 2014; ESH 2013</td>
<td>OBPM ≥ 2 visits</td>
</tr>
<tr>
<td>CHEP 2015</td>
<td>• ABPM/HBPM if suspect WCH, “borderline” BP, variable BP</td>
</tr>
<tr>
<td>Taiwan 2015; FSH 2013</td>
<td>• OBPM x 2 visits if TOD, CKD, DM, or BP ≥ 180/110</td>
</tr>
<tr>
<td>NICE (UK) 2011; USPSTF 2015</td>
<td>• Confirm with ABPM &gt; HBPM</td>
</tr>
<tr>
<td></td>
<td>• OBPM x 2 visits if TOD</td>
</tr>
<tr>
<td></td>
<td>• Confirm Dx in all others with ABPM or HBPM</td>
</tr>
<tr>
<td></td>
<td>Confirm with ABPM &gt; HBPM</td>
</tr>
</tbody>
</table>

*J Hypertens* 2014; 32:3  *Eur Heart J* 2013; 34:2159  *Can J Card* 2014; 30 485

<table>
<thead>
<tr>
<th></th>
<th>Routine Office BP</th>
<th>BpTRU AOBP</th>
<th>Daytime ABPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beckett, 2005</td>
<td>151/83</td>
<td>140/80</td>
<td>142/80</td>
</tr>
<tr>
<td>• 481 pts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myers, 2009</td>
<td>152/87</td>
<td>132/75</td>
<td>134/77</td>
</tr>
<tr>
<td>• 309 pts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myers, 2010</td>
<td>150/89</td>
<td>133/80</td>
<td>135/81</td>
</tr>
<tr>
<td>• 254 pts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Godwin, 2011</td>
<td>149/83</td>
<td>138/80</td>
<td>141/80</td>
</tr>
<tr>
<td>• 654 pts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Myers, 2011</td>
<td>150/81</td>
<td>136/78</td>
<td>133/74</td>
</tr>
<tr>
<td>• 303 pts</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**AOBP, isolated pt, is within 1-2 mm Hg of daytime ABPM: reduces WCH**

AOBP superior to Office BP to predict target organ damage

* 1° care

AOBP ON ISOLATED PATIENT IS LOWER THAN MANUAL ACCURATE BP ON OBSERVED PATIENT

<table>
<thead>
<tr>
<th>Equivalent BPs to Dx HTN:</th>
<th>BP (mm/Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research quality manual office BP</td>
<td>140/90</td>
</tr>
<tr>
<td><strong>AOBP on isolated patient</strong></td>
<td>135/85</td>
</tr>
<tr>
<td>Home BP, mean of 3-7 days</td>
<td>135/85</td>
</tr>
<tr>
<td>24 hour ABPM study:</td>
<td></td>
</tr>
<tr>
<td>- Mean daytime awake</td>
<td>135/85</td>
</tr>
<tr>
<td>- Full 24 hour mean</td>
<td>130/80</td>
</tr>
</tbody>
</table>

AOBP IN OFFICE PRACTICE: ALGORITHM

High quality manual or electronic 1st BP measurement
- Rest 5 min
- Correct cuff size
- Etc.

BP ≤ Goal
- Record
  (Goal unattended AOBP is < 135/85!)
  
BP > Goal
- AOBP: exam/waiting room
  - no rest period
  - ± Observe 1st measurement
    - 6 → Yes; 3 → No
  - Leave patient in isolation

Return in 5 min
SEQUENTIAL BpTRU READINGS IN 284 HTN PATIENTS IN PRIMARY CARE

<table>
<thead>
<tr>
<th>Reading No.</th>
<th>AOBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (observer present)</td>
<td>147/82</td>
</tr>
<tr>
<td>2 (observer absent)</td>
<td>140/79</td>
</tr>
<tr>
<td>3</td>
<td>136/78</td>
</tr>
<tr>
<td>4</td>
<td>134/77</td>
</tr>
<tr>
<td>5</td>
<td>132/76</td>
</tr>
<tr>
<td>6</td>
<td>133/77</td>
</tr>
<tr>
<td>Mean 2-6</td>
<td>136/78</td>
</tr>
</tbody>
</table>

BMJ 2011; 342:d286
Criteria for the diagnosis of hypertension and recommendations for follow-up: overview

Measurement using electronic (oscillometric) upper arm devices is preferred over auscultation
ABPM: Ambulatory Blood Pressure Measurement
AOBP: Automated Office Blood Pressure
HBPM: Home Blood Pressure measurement
OBPM: Office Blood Pressure measurement
HBPM MONITORS

• **Must** be validated: AAMI, BHS, and/or IP protocols
  – Omron ([www.omronhealthcare.com](http://www.omronhealthcare.com))
  – A&D – Lifesource ([www.andmedical.com](http://www.andmedical.com))
  – MicroLife ([www.microlife.com](http://www.microlife.com))

• Arm cuffs only (unless massive obesity)

• **Correct cuff size for mid-arm circumference**
  – < 33 cm  → regular cuff
  – 33-43 cm  → large adult or self-adjusting
  – > 43 cm  → wrist cuff (if wrist < 22 cm)
HBPM: PRECISE PREPARATION/MEASUREMENT TECHNIQUE

Same careful preparation/technique as required in office:

• Home BP technique video from CHEP
  – www.youtube.com/watch?v=eqajdX5XU9Y&feature=plcp

• Home BP technique written instructions:
  – UUMC/VAMC Home BP Measurement handouts

• Check patient technique, cuff accuracy in office
  – Pt R arm/Office L arm → Office R arm/Pt L arm
  – < 5 mm hg difference between averages
### HBPM: RECOMMENDED MONITORING PROTOCOL

<table>
<thead>
<tr>
<th>Morning</th>
<th>Work</th>
<th>Evening</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1h post-awaken</td>
<td>?</td>
<td>6-9 PM</td>
</tr>
<tr>
<td>Post-micturition</td>
<td></td>
<td>---</td>
</tr>
<tr>
<td>Pre-breakfast</td>
<td></td>
<td>Pre-supper (or pre-bed?)</td>
</tr>
<tr>
<td>Pre-BP med</td>
<td></td>
<td>Pre-BP med</td>
</tr>
<tr>
<td>Rest quietly 3-5 min</td>
<td></td>
<td>Rest quietly 3-5 min</td>
</tr>
<tr>
<td>Measure X 2, 1 min apart</td>
<td></td>
<td>Measure X 2, 1 min apart</td>
</tr>
</tbody>
</table>

- **Dx/FU Rx △**: FU controlled BP
- **BID x 3-7d**: 12-28 readings
- **BID x 3-7d**: q 3 mo

**Goal BP < 135/85**

- J Hum Hypertens 2010; 24:779
- Hypertension 2011; 57:9081
- Hypertens Res 2012; 35:777
TREATMENT OF HYPERTENSION
TARGET BP 2014: STILL NO CONSENSUS!

<table>
<thead>
<tr>
<th>Guideline</th>
<th>General Population</th>
<th>Age ≥ 80y</th>
<th>CKD</th>
<th>DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASH 2014</td>
<td>&lt; 140/90</td>
<td>&lt; 150/90</td>
<td>&lt; 140/90</td>
<td>&lt; 140/90</td>
</tr>
<tr>
<td>ACC/AHA 2014</td>
<td>&lt; 140/90</td>
<td>&lt; 150/90</td>
<td>&lt; 140/90</td>
<td>&lt; 140/90</td>
</tr>
<tr>
<td>CHEP 2015, JBS3 2014</td>
<td>&lt; 140/90*</td>
<td>&lt; 150/90</td>
<td>&lt; 140/90</td>
<td>&lt; 130/80</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>JNC-8 2014</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Majority:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Age &lt; 60</td>
<td>&lt; 140/90</td>
<td>---</td>
<td>&lt; 140/90</td>
<td>&lt; 140/90</td>
</tr>
<tr>
<td>- Age ≥ 60</td>
<td>&lt; 150/90***</td>
<td>&lt; 150/90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Minority:</td>
<td>&lt; 140/90</td>
<td>&lt; 150/90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADA 2015</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>&lt; 140/90****</td>
</tr>
<tr>
<td>NKF/KDIGO 2012</td>
<td>---</td>
<td>&lt; 150/90?</td>
<td>&lt; 140/90</td>
<td>&lt; 140/90</td>
</tr>
<tr>
<td>- ACR ≥ 30</td>
<td>---</td>
<td>?</td>
<td>&lt; 130/80</td>
<td>&lt; 130/80</td>
</tr>
</tbody>
</table>

* < 160/100 if no TOD or CVD risk factors
** If no TOD or DM; otherwise Rx if ≥ 140/90
*** No down-titration needed if tolerate < 140/90
**** < 130 if ↑ stroke risk
WHEN TO INITIATE HTN TREATMENT?

Support for ≥ 150/90 For Age ≥ 60y, No CKD/DM

- No definitive RCT for 140-149
  - Cochrane 2012 meta-analysis:
    - No ↓ CVD events for 140-149
  - Marginal benefits/side effects

Support for ≥ 140/90 For Age ≥ 60y, No CKD/DM

- One RCT, CARDIO-SIS
  - 2014 meta-analysis:
    - ↓ Stroke, CHD for 140-149
  - Epidemiologic data:
    - ↑ CVD begins at SBP=90

JAMA 2014; 311:507
JACC 2014; 64:394
Heart 2014; 100:317
J Hypertens 2014; 32:2296
Cochrane Syst Rev 2012; 8:CD006742
STAGE 1 HTN: SUBSTANTIAL CVD RISK!

• 1.3 million 1° care pts, 1997 → 2010:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Age 30-59</th>
<th>Age 60-79</th>
<th>Age ≥ 80</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>1.89</td>
<td>1.69</td>
<td>1.44 (NS)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>2.57</td>
<td>1.38</td>
<td>1.14 (NS)</td>
</tr>
<tr>
<td>Stroke, ischemic</td>
<td>2.05</td>
<td>1.23</td>
<td>1.04 (NS)</td>
</tr>
<tr>
<td>Stroke, hemorrhagic</td>
<td>2.49</td>
<td>1.34 (NS)</td>
<td>1.19 (NS)</td>
</tr>
</tbody>
</table>

Lifetime CVD risk at age 30:
- BP ≥ 140/90 → 63%
  - CVD occurs 5y earlier
- BP < 140/90 → 46%

*Lancet* 2014; 383:1899
# HOW LOW TO GO?

## 2014 Meta-analysis of RCTs of Achieved SBP:

<table>
<thead>
<tr>
<th></th>
<th>RRR</th>
<th>NNT/5y</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stroke</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>140-149 vs 150-159*</td>
<td>↓ 35%</td>
<td>52</td>
</tr>
<tr>
<td>130-139 vs 140-149**</td>
<td>↓ 27%</td>
<td>90</td>
</tr>
<tr>
<td>120-129 vs 130-139***</td>
<td>↓ 31%</td>
<td>106</td>
</tr>
<tr>
<td><strong>Coronary Heart Disease:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>140-149 vs 150-159*</td>
<td>↓ 21%</td>
<td>169</td>
</tr>
<tr>
<td>130-139 vs 140-149**</td>
<td>↓ 23%</td>
<td>122</td>
</tr>
<tr>
<td>120-129 vs 130-139***</td>
<td>↓ 12% (NS)</td>
<td>---</td>
</tr>
</tbody>
</table>

*5 RCTs; 12,406 pts  **13 RCTs; 79,736 pts  ***4 RCTs; 24,404 pts

J Hypertension 2014; 32:2296
Projected Average Cost-Effectiveness of Full Implementation of the 2014 Guidelines for Hypertension Treatment in Patients without Cardiovascular Disease, According to Sex, Age, Hypertension Stage, and Status with Respect to Diabetes and Chronic Kidney Disease.

**NEJM 2015; 372:447**
CAN WE GO TOO LOW? J-CURVE FOR DBP?

Framingham HS: recurrent CVD events in 791 survivors

<table>
<thead>
<tr>
<th></th>
<th>DBP &lt; 70 mm Hg</th>
<th>DBP 70-89 mm Hg</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent CVD events</td>
<td>68%</td>
<td>48%</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Hazard ratio vs DBP = 70-89 mm Hg:

<table>
<thead>
<tr>
<th></th>
<th>DBP &lt; 70 mm Hg</th>
<th>DBP 70-89 mm Hg</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treated</td>
<td>5.1</td>
<td>---</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Untreated</td>
<td>11.7</td>
<td>---</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

- ↑CVD events with DBP < 70 only if PP ≥ 68 mm Hg regardless of Rx – ie, reflects ↑SBP
  - Antihypertensive Rx may not increase CVD events
  - Arterial stiffness → low DBP as cause of CVD events
- Caution ↓DBP < 60 if CAD?

CMAJ 2015; 187:116
Hypertension 2015; 655:299
LIFESTYLE MODIFICATION FOR HYPERTENSION

Select ≥ 1 Intervention $\bowtie$ Motivation

- DASH Diet
  - Na < 2.3 g/d
  - Exercise 30-60 min/d
  - Wt loss, 1Kg
  - ETOH ≤ 2/d
  - ↓ 11/5, 5/3, 3/2, 1/1/Kg, 3/3

- Low CVD risk and BP < 160/100
  - Lifestyle Rx X 3-6 mo
  - BP ≥ 140/90
  - Pharm Rx

- High CVD risk or BP ≥ 160/100
  - Lifestyle Rx
  - Pharm Rx

www.hypertension.ca
Can J Card 2013; 29:528
Circulation 2010; 122:406
## AHA 2013: RECOMMENDED ALTERNATIVE APPROACHES TO LOWER BP IN CLINICAL PRACTICE

<table>
<thead>
<tr>
<th>Approach</th>
<th>$\Delta$ BP (mm Hg)</th>
<th>Class of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transcendental meditation</td>
<td>$\downarrow$ 5/3</td>
<td>IIB</td>
</tr>
<tr>
<td>Device-guided breathing</td>
<td>$\downarrow$ 4/3</td>
<td>IIA</td>
</tr>
</tbody>
</table>

**Candidates:** Low CVD risk and BP < 160/100, for 6-12 mo
- Multiple drug side effect pts
- Desire to $\downarrow$ drug doses
- Refractory HTN

**Not useful:**
- Other meditation/relaxation techniques
- Yoga; biofeedback; acupuncture

Hypertension 2013; 61:1360
JAMA Int Med 2014; 174:1815
Am J Hypertens 2008; 21:310
J Hypertens 2012; 30:852
DOES ↓ DIETARY Na REDUCE CVD?
(IT CLEARLY LOWERS BP!)

Minimal RCT data:
• Require 30,000 pts x 5y

Cohort data: 31 analyses of 285,530 pts
• Substantial methodologic deficiencies in most
  13 studies ↓ CVD
  8 studies ↑ CVD
  2 studies J-curve
  8 studies No effect

Post-hoc 15y FU of TOHP: 2275 pts
> 3600 vs < 2300 mg/d → low Na ↓ CVD by 32%
### Na RESTRICTION: CURRENT GUIDELINES

<table>
<thead>
<tr>
<th>Source</th>
<th>Na (mg/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHA, 2012/2014</td>
<td>&lt; 1500</td>
</tr>
<tr>
<td>WHO, 2012</td>
<td>&lt; 2000</td>
</tr>
<tr>
<td>CHEP, 2015</td>
<td>&lt; 2000</td>
</tr>
<tr>
<td>DHSS, 2010</td>
<td>&lt; 2300</td>
</tr>
<tr>
<td>IOM, 2013</td>
<td>2300</td>
</tr>
<tr>
<td>Graudal, et al 2014</td>
<td>2600-4900</td>
</tr>
</tbody>
</table>

SELECTING INITIAL PHARMACOLOGIC THERAPY

- Pregnancy Potential
  - Compelling Indications for Specific Drugs
  - General HTN Population
    - J Hypertens 2013; 31:1925
    - JAMA 2013; 310:1274

- Age ≥ 80y
SELECTING INITIAL PHARMACOLOGIC THERAPY

Pregnancy Potential

- **No** ACE-I or ARB
- **OK:**
  - Thiazides
  - CCBs
  - BBs

SELECTING INITIAL PHARMACOLOGIC THERAPY

Pregnancy Potential

Compelling Indications for Specific Drugs

- **DM or CKD:**
  - Albuminuria → ACE-I or ARB
  - No albuminuria → ACE-I, ARB, CCB, Thiazide*
- **Recent MI or Systolic HF** → ACE-I (ARB) ⊕ BB
- **Stable CAD** → ACE-I (BB/CCB if angina)

*JNC-8: ACE-I/ARB for all CKD

SELECTING INITIAL PHARMACOLOGIC THERAPY

- Pregnancy Potential
- Compelling Indications for Specific Drugs
  - Gout, Urinary Incontinence, ↓ Serum Na, SSRI Rx
    - No
      - Low dose: Thiazide, ACE-I, CCB, ARB
    - Yes
      - Goal BP < 150/90
        - ACE-I, CCB, ARB
SELECTING INITIAL PHARMACOLOGIC THERAPY

General HTN Population

Initial 1-drug Rx  Initial low-dose 2-drug Rx

Black pts  Non-black pts  No Gout  Gout

CCB or Thiazide  JNC-8, 2014  ASH, 2014  ACE-I (ARB)  ACE-I (ARB)

ACE-I, ARB, CCB, or Thiazide  Age < 60  Age ≥ 60  Thiazide  CCB*

ACE-I or ARB  CCB or Thiazide

*Consider this Rx if high CVD risk (ACCOMPLISH RCT, 2008)

### GUIDELINE COMPARISONS: BBs AND DRUGS FOR BLACKS

<table>
<thead>
<tr>
<th>Guideline</th>
<th>BB Use*</th>
<th>1st Drug in Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESH/ESC 2013</td>
<td>Step 1 Alt. (carvedilol, nebivolol)</td>
<td>Thiazide/CCB</td>
</tr>
<tr>
<td>CCS 2015</td>
<td>• Step 1 Alt if age &lt; 60y</td>
<td>Thiazide/CCB</td>
</tr>
<tr>
<td></td>
<td>• Step 4 Age ≥ 60y</td>
<td></td>
</tr>
<tr>
<td>JNC-8, 2014</td>
<td>Step 4</td>
<td>Thiazide/CCB</td>
</tr>
<tr>
<td>ACC/AHA 2013</td>
<td>Step 3, 4</td>
<td>---</td>
</tr>
<tr>
<td>ASH/ISH 2014</td>
<td>Step 4</td>
<td>Thiazide/CCB</td>
</tr>
<tr>
<td>JSH 2014</td>
<td>Step 4</td>
<td>---</td>
</tr>
</tbody>
</table>

- **BBs provide less stroke protection over age 60**

*Unless special indication*
“OPTIMAL” 2-DRUG RX: GENERAL HTN POPULATION

Effectively ↓ BP, ↓ CVD events, ↓ side effects

ACE-I (ARB) + Thiazide
- ↓ BP additively, many studies
- ↓ CVD in RCTs: HYVET, PROGRESS, ADVANCE
- ↓ hypokalemia

ACE-I (ARB) + CCB (amlodipine)
- ↓ BP additively, many studies
- ↓ CVD in RCTS: ASCOT, ACCOMPLISH
- ↓ CCB-induced edema

ACCOMPLISH RCT, 2008: 11,056 high CVD risk pts x 36 mo
ACE-I + Thiazide vs ACE-I + Amlodipine
- ACE-I + amlodipine ↓ CVD events 20%, CKD by 48%

“OPTIMAL” 3-DRUG RX: GENERAL HTN POPULATION

- Effectively ↓ BP, ↓ CVD events, ↓ side effects
  - Less evidence

- ACE-I (ARB) ⊕ CCB ⊕ Thiazide diuretic
  - ↓ BP additively in several studies
  - ↓ side effects of △ potassium, CCB-induced edema
  - ? ↓ CVD events: post-hoc analysis of ADVANCE

Hypertension 2009; 54:19; 32  Hypertension 2014; 63:220; 259
J Hypertens 2014; 32:3  Diabetes Care 2013; 36:S4
General HTN Population: Control BP in < 8-12 wks

 Older, no gout, not high CVD risk or DM-prone

 - Lisinopril 20 mg/HCTZ 25 mg tabs:
  - \( \frac{1}{2} \) tab \( \frac{2-4}{wk} \) \( \rightarrow \) 1 tab \( \frac{2-4}{wk} \) \( \rightarrow \) 2 tabs, prn
  - Not controlled, 2-4 wk
  - Add Amlodipine 5 mg tabs:
    - \( \frac{1}{2} \) tab \( \frac{2-4}{wk} \) \( \rightarrow \) 1 tab, prn
    - Not controlled, 2-4 wk
  - Increase amlodipine to 10 mg tab qd

 Younger, gout, high CVD risk, or DM-prone

 - Lisinopril 20 mg tabs \( \oplus \) Amlodipine 5 mg tabs:
  - \( \frac{1}{2} \) tab each \( \frac{2-4}{wk} \) \( \rightarrow \) 1 tab each, prn
  - Not controlled, 2-4 wk
  - 2 tab Lisinopril \( \oplus \) 10 mg amlodipine tab
  - Not controlled, 2-4 wk
  - 1 tab Lisinopril 20 mg/HCTZ 25 mg
    - \( \oplus \) Amlodipine 10 mg
    - Not controlled, 2-4 wk
  - 2 tab Lisinopril 20 mg/HCTZ 25 mg
    - \( \oplus \) Amlodipine 10 mg

*Monitor potassium/sodium/creatinine with dose changes

  - Delays > 6 weeks to intensify Rx increase CVD risk

SELECT DIURETIC $\propto$ eGFR

✓ for optimal 3-drug Rx – **maximal tolerated doses** of:

- CCB $\oplus$ ACE-I (ARB) $\oplus$ diuretic $\propto$ eGFR

\[ < 30 \text{ ml/min} \quad \text{vs} \quad \geq 30 \text{ ml/min} \]

\[ \uparrow \text{total body Na} \]

Furosemide/bumetanide bid (8AM, 5PM)  

or

Torsemide qd

\[ \downarrow \text{Titrare dose to 4-5 lb wt loss only} \]

Monitor creatinine/potassium carefully

---

Eur Heart J 2013; 34:1175  
BMJ 2012; 345:e7473  
Hypertension 2012; 60:303
APPROACH TO UNCONTROLLED HTN ON 3 DRUGS: “RESISTANT HYPERTENSION”

- ✓ for suboptimal Rx regimen
- ✓ for white-coat resistant HTN: present in ≥ 30%
  - Home BP monitoring bid x 3-7d
  - 24h ambulatory BP monitor study
- ✓ for medication non-adherence: present in ≥ 30%
  - Ask, Morisky questionnaire, ✓ refill use
- ✓ for drugs that ↑ BP: NSAIDS, estrogen, ↑ ETOH, epogens
- Review (± testing) for 2° causes of HTN
- △ HCTZ → chlorthalidone 25 mg/d: ↓ SBP 5-6 mm Hg
- Consider consultation
ALDOSTERONE ANTAGONISTS ↓ BP IN RESISTANT HTN

Meta-analysis: 13 studies; 2505 patients

Mean BP Reduction, mm Hg

3 RCTs: 17/4
135 pts

10 Observational studies: 20/9
2208 pts

J Hum Hypertens 2015; 29:159
Resistant Hypertension On ACE-I (ARB) ⊕ Chlorthalidone ⊕ Amlodipine

- eGFR/K+ ≥ 50 ml/min and < 4.5 mEq/L
- Spironolactone, 12.5 → 25 mg/d q 4 wks, prn
  - √ K+/creatinine at 1 and 4 wks

- eGFR < 50 ml/min or K+ ≥ 4.5 mEq/L
- HR ≥ 84-90/min?
  - Yes
    - Carvedilol 25 → 50 mg bid or Metoprolol 50 → 100 mg bid q 2-4 wks, prn
    - Monitor HR
  - No
    - Yes
      - Doxazosin hs 2 → 4 → 8 mg q 2-4 wks prn
      - Diltiazem ER 180 → 240 mg/d q 2-4 wks, prn
        - √ for edema
RENAL ARTERY STENOSIS ≥ 60%

Epidemiology
- Gen. pop. ≥ 65y: 7%
- CAD at cath: 9%
- HTN ⊕ CKD: 20%
- HF-ASCVD: 50%

Clinical Syndromes
- Incidental: < 80% stenosis and < 20 mm Hg gradient
- Flash Pulm. Edema: Acute HF, EF > 40%, ↑↑ BP
- Resistant HTN
- ↑↑ ASCVD
- Ischemic CKD

Theory:
- Restore Renal Q
- ↓ HF
- ↓ BP
- ↓ CVD events
- Preserve GFR
**RA STENTING ⊕ MEDICAL RX vs MEDICAL RX**

Meta-analysis: 8 RCTs; 2223 pts; 34 mo follow-up

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative Risk (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ BP</td>
<td>0.99 (0.97-1.21)</td>
<td>0.83</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.91 (0.75-1.11)</td>
<td>0.98</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0.89 (0.68-1.17)</td>
<td>0.80</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.80 (0.54-1.21)</td>
<td>0.85</td>
</tr>
<tr>
<td>↓ GFR</td>
<td>0.96 (0.79-1.16)</td>
<td>0.71</td>
</tr>
</tbody>
</table>

- Only CORAL (2014) with all pts > 60-80% stenosis
- Few pts with bilateral stenoses, stenosis to solitary kidney
- Mild HTN and Stage 3 CKD in most pts
- Highest risk pts excluded: ↑↑↑↑ BP, progressively ↓ eGFR, recurrent flash pulm. edema

*JAMA Int Med* 2014; 174:1818
RA STENTING ⊕ MEDICAL RX vs MEDICAL RX

Observational data: 234 “high risk” pts; 50% stented; 3.8y FU

• Recurrent flash pulmonary edema subset:
  – Mortality HR = 0.4 favoring stenting
    ▪ Class I AHA recommendation, 2013

• Resistant HTN ⊕ ↓ eGFR over 6 mo.
  – Mortality HR = 0.15 favoring stenting
  – CVD HR = 0.23 favoring stenting

• Bilateral severe RAS??
Severe RAS to solitary functioning kidney??