“Hypertension is a global crisis with pandemic proportions that needs a commensurate and coordinated global response to its immense health and socioeconomic burden.”

World Hypertension League, 2021

1.1 billion persons have BP ≥ 140/90 mmHg

Leading risk factor for death/disability:
- 10.8 million deaths/y, ie, 30,000/d
- 218 million disability-adjusted life-years

Lancet 2018;392:1923  
Lancet 2020;396:1223
# Hypertension: Leading Risk for Death & Disability

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Attributable Risk</th>
<th>Outcome</th>
<th>Attributable Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strokes</td>
<td>60%</td>
<td>CKD</td>
<td>50%</td>
</tr>
<tr>
<td>CVD Events</td>
<td>55%</td>
<td>Atrial Fibrillation</td>
<td>34%</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>25%</td>
<td>Risk of valvular disease: AS, AR, MR</td>
<td>2-3x higher risk</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>50%</td>
<td>Dementia</td>
<td>≥ 5%</td>
</tr>
</tbody>
</table>

- HTN = 1,000 deaths per day in US
- Decrease of 5 years lifespan
- $130 Billion annually in U.S., $2,000/person
- #1 Dx for primary care visits
  - 34 million visits in 2018

References:

- Lancet 2015;386:399
- Lancet 2017;390:2673;1345
- JAMA 2018;7:e008731
- Hypertension 2017;70:854
- Circulation 2021;143:2244
- JAMA 2019;322:535
- Lancet Neuro 2019;18:942
- NCHS Data Brief 2017;No.289
- Lancet 2016;388:1659
- J Am Heart Assoc 2020;9:e017546
- Lancet 2017;317:165
- Lancet 2018;392:1923
- Circulation 2019;140:715
- J Am Heart Assoc 2018;7:e008731
- JAMA Cardiol 2019;4:788
ASSOCIATION BETWEEN SBP AND CVD MORTALITY

12.7x10^6 pt-yr in 61 prospective observational studies

From SBP = 115: ↑ SBP 2 mm Hg → ↑ Stroke/MI death by 10%/7%

Lewington, Lancet 2002

CHD mortality

Stroke mortality
HOW SHOULD WE DEFINE “HYPERTENSION?”

“The level of BP at which the benefits of treatment unequivocally outweigh the risks of treatment as documented by clinical trials.”
ESC/ESH, 2018

But what is that level of BP?
• Threshold to Rx?
• Target BP for Rx?

Eur Heart J 2018;39:3021
WHAT ARE THE BENEFITS OF LOWERING BP?

BPLTTC 2021 Meta-analysis: 48 RCTs; 344,716 pts

**Lower SBP by 5 mmHg x4.2 y:**

<table>
<thead>
<tr>
<th>Event</th>
<th>HR Prior CVD</th>
<th>HR No CVD</th>
<th>HR All Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major CVD Event</td>
<td>0.89</td>
<td>0.91</td>
<td>0.90</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.89</td>
<td>0.85</td>
<td>0.87</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>0.89</td>
<td>0.83</td>
<td>0.87</td>
</tr>
<tr>
<td>ASCVD</td>
<td>0.90</td>
<td>0.95</td>
<td>0.92</td>
</tr>
<tr>
<td>CV Death</td>
<td>0.98*</td>
<td>0.93</td>
<td>0.95</td>
</tr>
</tbody>
</table>

*Not significant

Lancet 2021;397:1625
WHAT ARE THE BENEFITS OF LOWERING BP?

BPLTTC 2021 Meta-analysis:

SBP 5 mm Hg x 4.2 y \rightarrow CVD 10%

SBP 15 mm Hg x 4.2 y \rightarrow CVD 20%

Lancet 2021;397:1625
WHAT ARE THE BENEFITS OF LOWERING BP?

BPLTTC 2021 Meta-analysis:
• BP-lowering beneficial whether baseline SBP < 120 or ≥ 170 mmHg!

Lower SBP by 5 mmHg x 4.2 ys

<table>
<thead>
<tr>
<th>Major CVD events</th>
<th>HR Prior CVD</th>
<th>HR No CVD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 120</td>
<td>0.77</td>
<td>0.83</td>
</tr>
<tr>
<td>120-129</td>
<td>0.89</td>
<td>0.94*</td>
</tr>
<tr>
<td>130-139</td>
<td>0.99*</td>
<td>0.89</td>
</tr>
<tr>
<td>140-149</td>
<td>0.89</td>
<td>0.95*</td>
</tr>
<tr>
<td>150-149</td>
<td>0.90</td>
<td>0.87</td>
</tr>
<tr>
<td>160-169</td>
<td>0.83</td>
<td>0.84</td>
</tr>
<tr>
<td>≥ 170</td>
<td>0.90</td>
<td>0.90</td>
</tr>
</tbody>
</table>

*Not significant

Lancet 2021;397:1625
WHAT ARE THE BENEFITS OF HTN RX?

**Dementia**

- Meta-analysis: 4 RCTs; 23,358 pts  
  ↓SBP ≥ 10 mmHg  
  12% risk reduction

- Prospective cohort: 6 studies; 31,090 pts  
  Use of any BP PharmRx  
  12%, all dementia  
  16%, Alzheimers

**Mild Cognitive Impairment**

- SPRINT RCT; 9361 pts.  
  ↓SBP 13 mmHg, 135→122  
  19% risk reduction

References:

Neurology 2019;92:1017  
Lancet Neurology 2019;19:61  
JAMA 2019;321:553
## NEW ACC/AHA 2017 CLASSIFICATION OF BP

<table>
<thead>
<tr>
<th>JNC-7, 2003</th>
<th>ACC/AHA, 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>&lt; 120/80</td>
<td>&lt; 120/80 (40%)*</td>
</tr>
<tr>
<td>Pre-HTN</td>
<td>Elevated</td>
</tr>
<tr>
<td>120-139/80-89</td>
<td>120-129/&lt; 80 (13%)*</td>
</tr>
<tr>
<td>HTN</td>
<td>HTN</td>
</tr>
<tr>
<td>≥ 140/90</td>
<td>≥ 130/80 (47%)*</td>
</tr>
<tr>
<td>• Stage 1</td>
<td>• Stage 1</td>
</tr>
<tr>
<td>140-159/90-99</td>
<td>130-139/80-89 (15%)*</td>
</tr>
<tr>
<td>• Stage 2</td>
<td>• Stage 2</td>
</tr>
<tr>
<td>≥ 160/100</td>
<td>≥ 140/90 (32%)*</td>
</tr>
</tbody>
</table>

*NHANES 2018

---

*JACC 2017;69:2446  Circulation 2022;145:e00  JAMA Cardiol 2018;3:427  Hypertension 2018;71:e13*
**ACC/AHA 2017 HTN GUIDELINE:**
**RECOMMENDATIONS FOR LIFESTYLE/PHARMACOLOGIC RX**

**Accurate BP Assessment in and out of office**

- **Elevated BP:** 120-129/< 80

- **Stage 1 HTN:**
  - BP = 130-139/80-89

- **Stage 2 HTN:**
  - BP ≥ 140/90

- **Clinical CVD**
  - Lacunar stroke
  - or
  - 10y CVD risk ≥ 10%* (19% of U.S. adults)
  - or
  - DM or CKD
  - or
  - Age ≥ 65y: Ambulatory in community

- **Follow-up q 1 mo until control to <130/80 (I-B) home/office!**

- **Lifestyle Rx 3-6 mo (I-B)**

- **BP ± 130-139/80-89**

- **10y CVD risk < 10%**

- **Lifestyle Rx 3-6 mo (I-B)**

- **BP ± 130-139/80-89**

- **?**

- **Individualize target BP if age ≥ 65 ⊕ limited lifespan/comorbidities**

*ACC/AHA Pooled Cohort Equation

Hypertension 2021;77:e58

Hypertension 2018;71:e13
AHA 2021 SCIENTIFIC STATEMENT: RX FOR STAGE 1 HTN AND 10-Y CVD RISK <10%

BP=130-139/80-89 ⊕ PCE 10y CVD risk <10%
(≈69% of Stage 1 patients)

Lifestyle Rx for 6 mo
BP=130-139/80-89

Consider Pharm Rx for all, especially:
• Stage 1 HTN during adolescence
• Family Hx of premature CVD
• Hx of HTN in pregnancy
• Personal Hx of premature birth

Based on observational data

Hypertension 2021;77:e58
## HYPERTENSION GUIDELINES: ACP/AAFP 2017

<table>
<thead>
<tr>
<th>Age &lt; 60y</th>
<th>Threshold BP, Drug Rx</th>
<th>Target BP, Drug Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not addressed</td>
<td>Not addressed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age ≥ 60y:</th>
<th>Threshold BP, Drug Rx</th>
<th>Target BP, Drug Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Lower Risk”</td>
<td>≥ 150/(90)*</td>
<td>&lt; 150/(90)*</td>
</tr>
<tr>
<td>Prior Stroke/TIA</td>
<td>≥ 140/(90)**</td>
<td>&lt; 140/(90)**</td>
</tr>
<tr>
<td>“High CV risk,” eg,</td>
<td>≥ 140/(90)***</td>
<td>&lt; 140/90***</td>
</tr>
<tr>
<td>– CVD, CKD (eGFR &lt; 45)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>– DM, metabolic syndrome</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Strong recommendation; high quality evidence
**Weak recommendation; moderate quality evidence
***Weak recommendation; low quality evidence

Ann Int Med 2017;166:430
**SOLUTION TO VARIABLE HTN GUIDELINES: PERSONALIZED TARGET BP?**

<table>
<thead>
<tr>
<th>“Lower” Target BP</th>
<th>“Higher” Target BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>(&lt; 120-130/80)</td>
<td>(&lt; 140-150/90)</td>
</tr>
</tbody>
</table>

- Younger, long life span
- Cardiovascular disease
- High cardiovascular risk
- CKD ± albuminuria
- Diabetes ± albuminuria
- Patient preference to reduce risk
- Tolerant of lower target BP

- Limited life expectancy
- Severe cognitive impairment
- Standing BP < 110 mmHg
- High fall risk
- Polypharmacy
- Less motivated, non-adherent, poor self-care capacity
- Patient preference
- Not tolerant of lower target BP

*Circulation* 2018;138:128
## U.S. HTN CONTROL: UGLY TRUTH 2017-2018!

**NHANES, 1999 → 2018:**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>&lt; 140/90:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>31.8%</td>
<td>53.8%</td>
<td>43.7%</td>
</tr>
<tr>
<td>On Rx</td>
<td>53.4%</td>
<td>72.2%</td>
<td>64.8%</td>
</tr>
<tr>
<td><strong>&lt; 130/80:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>9.7%</td>
<td>25.0%</td>
<td>19.0%</td>
</tr>
<tr>
<td>On Rx</td>
<td>27.6%</td>
<td>48.5%</td>
<td>38.9%</td>
</tr>
</tbody>
</table>

- Similar ↓ control rates: white, black, Hispanic
  - ↑ control rate: Asians

*References:*

JAMA 2020;324:1190  
NEJM 2021;384:2219  
Hypertension 2022; 79:207  
Am J Hypertens 2021;34:591
<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Prevalence</th>
<th>Awareness</th>
<th>Rx (Intensity DR)</th>
<th>Control &lt; 130/80</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Am.</td>
<td>46%</td>
<td>62%</td>
<td>52% (1.00)</td>
<td>23% (32%)</td>
</tr>
<tr>
<td>Black Am.</td>
<td>58%</td>
<td>67%</td>
<td>55% (1.45)</td>
<td>20% (25%)</td>
</tr>
<tr>
<td>Hispanic Am.*</td>
<td>46%</td>
<td>52%</td>
<td>41% (0.86)</td>
<td>16% (25%)</td>
</tr>
<tr>
<td>Asian Am.</td>
<td>47%</td>
<td>53%</td>
<td>44% (0.60)</td>
<td>15% (19%)</td>
</tr>
</tbody>
</table>

- Dismal control rates in all-unacceptable race/ethnic disparities

*Varies greatly by background

Circulation 2022;145;Heart Disease and Stroke Statistics, 2022 update
HOW TO IMPROVE HTN CONTROL RATES

Unaware of HTN: 16-35% \( \propto \) definition
- ↑ Media outreach
- ↑ Alternative screening sites
- ↑ Access to care

Uncontrolled ≥ 140/90: 56%
Uncontrolled ≥ 130/80: 81%

Treated but Uncontrolled: 35-60% \( \propto \) definition
- Measure office BP accurately
- Detect white-coat BP elevation
- Optimize Rx medication regimens
- Intensify follow-up: ↑ office visits, HBPM
- Team care:
  - ↓ Clinician inertia to intensify Rx
  - ↑ Patient Rx adherence
OFFICE BP MEASUREMENT TO CONFIRM HTN?: NO!

“More often than not, the measurement of office BP is not only inaccurate but also downright misleading.”

Editorial, J Clin Hypertens 2016; 18:616

• Incorrect office technique is the rule:
  – 6 studies; 8249 pts; 1995-2011: usual office vs guideline technique
  – Correct technique ↓ BP ≈ 10/7 mm Hg
    • More than doubles HTN control rate

• White-coat BP elevation highly prevalent:

  Office BP ≥ 140/90 → 15-30%
  Office SBP = 140-159 → 40-50%
  Office SBP ≥ 180 → 10%

  Inaccurate office HTN Dx in 20-65%

IMPROVING OFFICE SCREENING FOR HYPERTENSION

Increase office BP accuracy: automated oscillometric devices

• Guideline recommended: ACC/AHA 2017; HTN Canada 2020; Eur Soc HTN 2018; AHA Scientific Statement, 2019

• Validated for accuracy: AAMI, BHS, IP-ESH protocols or new AAMI/ESH/ISO universal protocol
  - [https://www.validateBP.org/](https://www.validateBP.org/) (AMA, 2020)
  - [www.stridebp.org](http://www.stridebp.org) (ESH; ISH; WHL)
  - [http://bihsoc.org/bp-monitors](http://bihsoc.org/bp-monitors)
  - J Hypertens 2018;36:479

Only a few devices validated in pregnancy

• Take/average 3 BP measurements automatically, ≥ 30 sec. intervals, over 3-5 min.

• Auscultatory BP only when electronic BP may be inaccurate:
  - Mid-arm circumference > 42 cm
IMPROVING OFFICE SCREENING FOR HTN

Reduce office “white-coat” BP elevation: ✓ BP with patient alone

• Sequential automated BP on isolated patients: “u-AOBP”
  • Alone in exam room/quiet corner of waiting room

• Three validated devices perform/average 3 measurements
  • Microlife Watch BP Office ($380)
  • Omron HEM-907 ($750)
  • Welch Allyn PRO BP 2400 ($380) (Welch Allyn Connex Spot BP)
  • BpTRU off market (perform 6/average 5)
  • u-AOBP values similar to out-of-office daytime ABPM/HBPM

### 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>

- **Meaning of this 11/4 ↓ BP? → ↓ White-coat HTN**

BMJ 2011;342:d286
u-AOBP COMPARED TO OTHER BP MEASUREMENT METHODS

2019 meta-analysis:
• 31 studies; 9279 participants with systolic u-AOBP ≥ 130 mmHg

<table>
<thead>
<tr>
<th>Comparator</th>
<th>Studies</th>
<th># Participants</th>
<th>Comparator SBP Θ AOBP, mmHg</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine Office BP</td>
<td>9</td>
<td>2570</td>
<td>14.5</td>
<td>Routine BP higher</td>
</tr>
<tr>
<td>Guideline-recommended BP</td>
<td>9</td>
<td>1484</td>
<td>7.0</td>
<td>Guideline BP higher</td>
</tr>
<tr>
<td>Out-of-office Daytime ABPM</td>
<td>19</td>
<td>4146</td>
<td>-0.3</td>
<td>u-AOBP = Day ABPM</td>
</tr>
</tbody>
</table>

AOBP nearly eliminates white-coat BP elevation

JAMA Int Med 2019;179:351
U-AOBP: EFFICIENT IN REAL-WORLD CLINICS?

Five minute rest period **not** required!

- RCT: 618 pts referred for 24h ABPM

  Omron HEM-907 for u-AOBP

<table>
<thead>
<tr>
<th></th>
<th>All pts</th>
<th>0-min rest</th>
<th>5-min rest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean u-AOBP</td>
<td>141.2/83.1</td>
<td>138.2/81.7</td>
<td></td>
</tr>
<tr>
<td>Mean awake ABPM</td>
<td>141.3/83.8</td>
<td>143.4/83.6</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>HTN pts on meds</th>
<th>0-min rest</th>
<th>5-min rest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean u-AOBP</td>
<td>140.5/82.3</td>
<td>131.5/80.4</td>
<td></td>
</tr>
<tr>
<td>Mean awake ABPM</td>
<td>141.2/81.1</td>
<td>142.3/81.1</td>
<td></td>
</tr>
</tbody>
</table>

0-minute wait time optimal for u-AOBP

Hypertension 2021;78:353
u-AOBP: EFFICIENT IN REAL-WORLD CLINICS?

Can be performed at 30 sec. rather than 60 sec. intervals:

• Omron HEM-907: 51 pts with 3 BPs at 60 sec. intervals
  51 pts with 3 BPs at 30 sec. intervals
  – Nearly identical correlations with daytime awake ABPM

4.5 min for 60 sec interval sequence → 2.25 min for 30 sec
**u-AOBP IN OFFICE PRACTICE: ALGORITHM**

High quality observed automated/manual 1\textsuperscript{st} BP measurement, 2 visits

- BP < 130/80 (ACC/AHA 2017)
- BP < 140/90 (JNC-7, 2003)

Record*
Consider masked HTN risk

- BP ≥ 130/80 (ACC/AHA 2017)
- BP ≥ 140/90 (JNC-7, 2003)

Perform u-AOBP in exam room or in quiet area of waiting room

- No rest period
- 30 sec between readings
- No observation of 1st reading
- Patient alone

Return in 3-4 min
MA attends to other duties

u-AOBP ≥ 130/80 (ACC/AHA 2017)
u-AOBP ≥ 135/85 (JNC-7, 2003)

Out-of-office BP:

- 24h ABPM or 3-7d HBPM

*≤ 3% chance that average of 3 measurements > goal BP

\textit{Hypertension} 2021;78:353 \hspace{1cm} \textit{Hypertension} 2021;78:on-line,Jurashe
### BP SUBSETS: OFFICE/OUT-OF-OFFICE BP MONITORING, UNTREATED PATIENTS

<table>
<thead>
<tr>
<th>Masked HTN***: 12-15%</th>
<th>Sustained HTN:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Normal office BP</td>
<td>• High office BP</td>
</tr>
<tr>
<td>• High out-office BP</td>
<td>• High out-of-office BP</td>
</tr>
<tr>
<td>• CV prognosis ≈ Sustained HTN</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Normotension:</th>
<th>White-coat HTN**: 15-40%</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Normal office BP</td>
<td>• High office BP</td>
</tr>
<tr>
<td>• Normal out-of-office BP</td>
<td>• Normal out-of-office BP</td>
</tr>
<tr>
<td><strong>CV prognosis = Normotension</strong></td>
<td></td>
</tr>
</tbody>
</table>

*Varies according to guideline recommended threshold BP to Dx HTN

***“White-coat effect” in treated persons

****“Masked uncontrolled HTN” in treated persons
OUT-OF-OFFICE BP TO CONFIRM HTN DIAGNOSIS

USPSTF Guideline, 2021:
“Ambulatory BP monitoring (ABPM) and home BP monitoring (HBPM) with validated and accurate devices should be used outside of a clinical setting to confirm a diagnosis of hypertension before starting treatment.”

- Level A recommendation

- Detect white-coat/masked HTN
- Superior CVD prediction vs OBPM
- ABPM > HBPM for CVD prediction?

JAMA 2021;325:1650  Hypertension 2018:71:e13
### THRESHOLDS TO DX HTN WITH OBSERVED BP, AOBP AND OUT-OF-OFFICE BP MONITORING

#### Equivalent 10y CVD risk:

<table>
<thead>
<tr>
<th></th>
<th>ACC/AHA 2017</th>
<th>JNC-7 2003</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BP (mm/Hg)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guideline quality observed office BP</td>
<td>130/80</td>
<td>140/90</td>
</tr>
<tr>
<td><strong>u-AOBP on isolated patient</strong></td>
<td>130/80</td>
<td>135/85</td>
</tr>
<tr>
<td>Home BP, mean of 3-7 days and 12-28 accurate readings</td>
<td>130/80</td>
<td>135/85</td>
</tr>
<tr>
<td>24 hour ABPM study:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mean daytime awake</td>
<td>130/80</td>
<td>135/85</td>
</tr>
<tr>
<td>- Full 24 hour mean</td>
<td>125/75</td>
<td>130/80</td>
</tr>
<tr>
<td>- Sleep BP</td>
<td>110/65</td>
<td>120/70</td>
</tr>
</tbody>
</table>

**Hypertension** 2018;72:1312  **Hypertension** 2019;73:e35  ↓ **Hypertens** 2013;31:1731  **Hypertension** 2018;71:e13  ↓ **J Clin Hypertens** 2018;20:1696
HOME BP MONITORING: EVIDENCE-BASED ADVANTAGES

Home BP ⊕ Office BP vs Office BP only:

• At 12 mo: ↓ SBP 6 mmHg/↑ HTN control 43-56% **IF:**
  – One-to-one communication patient/clinic team
  – Systematic medication intensification

• ↑ HTN Rx adherence absolute 18%

• Cost-effective

References:

PLOS Med 2017;14(9):e1002389
Ann Int Med 2015;162:192
Hypertension 2014;63:675
J Hypertens 2015;33:755
Ann Int Med 2013;159:185
Am J Hypertens 2014;27:184
J Hum Hypertens 2014;28:229
J Am Soc Htn 2014;8:732
Am J Hypertens 2015;28:1209
Am J Hypertens 2020;33:243
JACC 2020;76:2911
HOME BP MONITORING: CHALLENGES IN PRACTICE

Patient issues:
• 20% refuse HBPM; 20% accept but do not provide follow-up BP’s
• Incorrect technique, 63-87%; fabricate/omit readings, 12-36%
• Patient anxiety in some – unnecessary ER visits documented

Clinic issues:
• Initially labor-intensive to establish HBPM program
  – Train/retrain staff and patients
  – Follow-up mechanisms: phone, visit, EMR, FAX

Device issues:
• ≥85% of devices on the market not validated in study
• Increased rate of inaccuracy after 4y use

Listings of validated devices:

- AMA 2020: https://www.validateBP.org/
- https://hypertension.ca/bpdevices
  - Gold/Silver
- www.stridebp.org: “preferred”; “validated”
- Specific companies (others as well)
  - A&D-Lifesource (www.andmedical.com)
  - Microlife (www.microlife.com)
  - Omron (www.omronhealthcare.com)
- For pregnancy: www.stridebp.org and Journal of Hypertension 2018;71:326

Desirable characteristics:

- Memory to store ≥ 30 readings, automatic averaging, and internet connectivity
- Automatically take/average 3 readings q 1 min

J Hypertension 2018;36:479
J Hypertens 2020;38:21
Pregnancy Hypertension 2017;8:9
J Hypertens 2020;38:394
Hypertension 2018;71:326
HOME BP MONITORING DEVICES

Upper arm cuffs for most patients: wrist cuffs less accurate

- **Correct cuff size** \( \propto \) mid-arm circumference
  
  - 22-26 cm → small adult
  - 27-34 cm → regular adult
  - 35-44 cm → large adult
  - 27-44 cm (9”-17”) → “self-adjusting” or “wide-range” cuff

- 45-52 cm:
  - Welch Allyn Monitor, 1700 series
    - XL 40-54 cm (validated) upper arm cuff
  - Validated wrist cuff often needed: Omron BP 4350, 6100, 8000M
    - Wrist at heart level, not flexed/extended, arm supported

- **Only 2-3 cuff sizes from most manufacturers**
  - “Wide-range” cuffs for mid-arm circumference 22-42 cm
    - Validation studies of inadequate quality for wide range cuffs?

J Clin Hypertens 2018;20:1100  
Blood Press Monit 2018;23:219  
J Hypertens 2019;37:37
**HBPM: RECOMMENDED MONITORING PROTOCOL**

- Routine work days preferred if only 3-5 days monitoring

---

### Morning

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1h post.awaken</td>
<td>?</td>
</tr>
<tr>
<td>Post-micturition</td>
<td></td>
</tr>
<tr>
<td>Pre-breakfast</td>
<td></td>
</tr>
<tr>
<td>Pre-BP med</td>
<td></td>
</tr>
</tbody>
</table>

- Rest quietly 5 min
- No reading, cell phone, talking

- Measure X 2-3, 1 min apart

---

### Work

- ?

### Evening

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-9 PM</td>
<td>Post-micturition</td>
</tr>
<tr>
<td>Pre-supper/pre-bed</td>
<td></td>
</tr>
<tr>
<td>Pre-BP med</td>
<td></td>
</tr>
</tbody>
</table>

- Rest quietly 5 min
- No reading, cell phone, talking

- Measure X 2-3, 1 min apart

---

### Routine work days preferred if only 3-5 days monitoring

- **Dx/FU Rx △**
- **FU controlled BP**
- **BID, 2X-3X/time, x 3-7d**
- **Average 12-28 readings ∝ Dx threshold**
- **BID x 3-7d q 3 mo. vs 1-3d/wk**
- **vs weekly/monthly if ↓ adherence**

- **Goal Home BP:**
  - <135/85 for office goal
  - <130/80 for office goal < 130/80 and < 140/90

- 24h ABPM if home/clinic discrepancy

---

**References**

- J Hypertens 2021;39:1742
- J Hypertens 2015;33:755; 693
- Hypertens Res 2018;41:738
- Am J Hypertens 2015;28:595
- Am J Hypertens 2019;32:350
- Blood Press Monit 2018;23:1
- Am J Hypertens 2020;33:154
- Hypertens Res 2012;35:777
- Can J Card 2020;36:596
HBPM: NEW 1/1/2020 CMS BILLING CODES

99473: one-time code, $11.19
  • MA education in HBPM/✓ HBPM device accuracy

99474: once/month code, $15.16
  • Clinician receives/evaluates ≥ 12 HBPM readings:
    – Documents change in BP medications, or
    – Diagnoses white-coat BP elevation
HOME BP MONITORING: KEY COMPONENTS

Purchase **validated** device
- A few commercial and Medicaid plans reimburse device

Instruct ⊕ Assess Skill ⊕ Reinforcement: preparation/technique
- Written instructions: [https://targetbp.org](https://targetbp.org) (AHA/AMA)
- Patient video: [https://targetbp.org](https://targetbp.org) (AHA/AMA)
- Direct observation: individual/group

Provide monitoring protocol (prior slide)
- Patient logbook to record BP: [https://targetbp.org](https://targetbp.org) (AHA/AMA)

Communication pathway: patient ↔ clinic
- Clinic visit, telephone, mail/FAX, Website upload, EHR

Clinic action on BP results: confirm Dx, intensify Rx
Repeat education/assess skill q 6-12 mo

LIFESTYLE MODIFICATION FOR HYPERTENSION

Select ≥ 1 Intervention \( \propto \) Motivation

- DASH Diet
- Na \( \downarrow \) by 2.3 g/d (<2.3 g/d)
- Exercise 150-330 min/wk
- Wt loss, 1Kg
- ETOH \( \leq \) 2/d

\( \downarrow \) 11/5
\( \downarrow \) 8/3
\( \downarrow \) 5/3
\( \downarrow \) 1/1/Kg
\( \downarrow \) 3/3

\( \downarrow \) 7/5 mm Hg if proper prescription/pt. adherence

- Minority \( \Delta \) lifestyle post-HTN Dx
- Few sustain \( \geq \) 1y
- 3-6 mo. trial as only Rx limited to Stage 1 (130-139/80-89) and 10y CVD risk <10%

Hypertension 2016;68:78  Hypertension 2018;71:e13  www.hypertension.ca
Hypertension 2021;78:online, Hall ME  Hypertension 2021;78:e26
PHARMACOLOGIC THERAPY

• ACC/AHA 2017 Guideline approach adopted by WHO, 2021

R/O White-coat HTN
✓ Standing BP for orthostatic hypotension

BP = 130-139
10y CVD risk ≥ 10%

Mono-Rx (IIa-C)
• CCB***/Diuretic if AA unless compelling
  Indication for ACE-I/ARB (I-B)
• If not AA
  – ≤ 55-65: ACE-I/ARB?
  – > 55-65: Diuretic/CCB?
• BB only if compelling indication of IHD or HF

BP = 140-149

Consider 2-drug Rx (low-dose) (I-C) *

• ACE-I/ARB** ⊕ CCB***
  – Higher CVD risk; gout
• ACE-I/ARB ⊕ Diuretic

BP ≥ 150/90

2-drug Rx (low-dose)* (I-C)

*Caution/Mono-Rx if very elderly/frail or Hx of ↓ BP, drug intolerance
**Avoid ACE-I/ARB in pregnancy
***Long-acting dihydropyridine preferred

Hypertension 2022;79:293  Hypertension 2018;71:e13
# Relative Efficacy of Monotherapy to Reduce Cardio-Renal Events

Meta-analysis: 123 RCTs; 613,815 pts.

<table>
<thead>
<tr>
<th>Drug</th>
<th>CVD events</th>
<th>Stroke</th>
<th>CHD</th>
<th>HF</th>
<th>Renal Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBs</td>
<td>1.17 (1.11–1.24)</td>
<td>1.24 (1.14–1.35)</td>
<td>NS</td>
<td>NS</td>
<td>1.19 (1.05–1.34)</td>
</tr>
<tr>
<td>CCBs</td>
<td>NS</td>
<td>0.90 (0.85–0.95)</td>
<td>NS</td>
<td>1.17* (1.11–1.24)</td>
<td>NS</td>
</tr>
<tr>
<td>ACE-I</td>
<td>NS</td>
<td>1.08 (1.01–1.16)</td>
<td>NS</td>
<td>NS</td>
<td>0.85 (0.72–0.99)</td>
</tr>
<tr>
<td>ARB</td>
<td>NS</td>
<td>0.92 (0.85–0.99)</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Diuretic</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>0.81 (0.75–0.88)</td>
<td>NS</td>
</tr>
</tbody>
</table>

**BBs Step 4 unless compelling indication**

*Possible study artifact*
DO WE FOLLOW 2017 ACC/AHA GUIDELINE FOR MONO-RX: BP=130-139/80-89, 10y CVD RISK ≥10%?

NHANES 2015-2018 Mono-Rx:

<table>
<thead>
<tr>
<th></th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-I or ARB</td>
<td>44%</td>
<td>31%</td>
</tr>
<tr>
<td>CCB</td>
<td>9%</td>
<td>30%</td>
</tr>
<tr>
<td>TD</td>
<td>8%</td>
<td>14%</td>
</tr>
<tr>
<td>BB</td>
<td>32%</td>
<td>15%</td>
</tr>
</tbody>
</table>

- Optimum Mono-Rx: 61% whites; 44% blacks
- Too much BB
ACE-Is OR ARBs FOR INITIAL THERAPY?

ACC/AHA 2017, ESC/ESH 2018: ACE-Is = ARBs, Level A

- Limited database:
  - 4 RCTs: <2000 pts; <40 CVD events
  - Registries: ARBs ↑ or ↓ MI 10% vs ACE-Is

- AHRQ, 2011: comparative effectiveness studies needed

---

LEGEND-HTN large-scale observational study:

- 8 databases in U.S., Germany, South Korea
- 3 million pts. initiating ACE-Is (2.3 m) vs ARBs (0.7 m)
- 785,000y FU with >24,000 CVD events
- Comprehensive stats to reduce residual bias

Hypertension 2021;78:591
### LEGEND-HTN Observational Study:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD events</td>
<td>1.06 (0.90-1.25)</td>
</tr>
<tr>
<td>Acute MI</td>
<td>1.11 (0.95-1.32)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.07 (0.91-1.27)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>1.03 (0.87-1.24)</td>
</tr>
<tr>
<td>Angioedema</td>
<td><strong>3.31</strong> (2.55-4.51)</td>
</tr>
<tr>
<td>Cough</td>
<td><strong>1.32</strong> (1.11-1.59)</td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td><strong>1.32</strong> (1.04-1.70)</td>
</tr>
<tr>
<td>Weight loss (abnormal)</td>
<td><strong>1.18</strong> (1.01-1.41)</td>
</tr>
<tr>
<td>GI bleed</td>
<td><strong>1.18</strong> (1.01-1.41)</td>
</tr>
</tbody>
</table>

- **Favor ARBs?**
## THIAZIDE-LIKE DIURETICS SUPERIOR TO THIAZIDES

<table>
<thead>
<tr>
<th></th>
<th>Thiazide-like:</th>
<th>Thiazides:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Indapamide</td>
<td>Chlorthalidone</td>
</tr>
<tr>
<td><strong>Duration of action</strong></td>
<td>&gt; 24h</td>
<td>48-72h</td>
</tr>
<tr>
<td><strong>“Equipotency” office SBP</strong></td>
<td>1.25 mg</td>
<td>12.5 mg</td>
</tr>
<tr>
<td><strong>↓ Office SBP</strong></td>
<td>↓ 5.1 mmHg</td>
<td>↓ 3.6-6.3 mmHg</td>
</tr>
<tr>
<td><strong>↓ Night ABPM</strong></td>
<td>—</td>
<td>↓ 6.9 mmHg, 25 mg</td>
</tr>
<tr>
<td><strong>↓ 24h ABPM</strong></td>
<td>—</td>
<td>↓ 5 mmHg, 25 mg</td>
</tr>
<tr>
<td><strong>↓ K, ↓ Na</strong></td>
<td>Minimal</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>↑ glu, ↑ lipids</strong></td>
<td>No</td>
<td>Some</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>$4/mo</td>
<td>$21-41/mo</td>
</tr>
<tr>
<td><strong>Fixed dose combos</strong></td>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td><strong>Skin cancers</strong></td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

J Hypertens 2019;37:1574  
Hypertension 2015;65:1033;1041  
J Am Acad Derm 2018;78:673  
JAMA Int Med 2018;178:1120  
Am J Hypertens 2016;29:1130
# THIAZIDE-LIKE DIURETICS SUPERIOR TO THIAZIDES

## RCT meta-analyses vs placebo, adjusted for ↓ BP

<table>
<thead>
<tr>
<th></th>
<th>Thiazide-Like:</th>
<th>Thiazide:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Indapamide</td>
<td>Chlorthalidone</td>
</tr>
<tr>
<td>CVD events</td>
<td></td>
<td>↓ 12%</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td>↓ 14%</td>
</tr>
<tr>
<td>↓ LV mass</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

- BP-independent effects of thiazide-like diuretics?
- No head-to-head RCTs for clinical events – VA RCT in progress
- Thiazide-like diuretics favored by:
  
  ACC/AHA 2017; HTN Canada, 2020; NICE 2019; ADA, 2020

**References**

- J Hypertens 2019;37:1574
- Ann Int Med 2016;165:63
- Can J Card 2020;36:596
- Diabetes Care 2020;43(Suppl1):S111
- BMJ 2019;367:15310
HTN THERAPY: CHOOSE “BEST” DIURETIC

Thiazide hyponatremia

eGFR < 15

Thiazide hyponatremia

eGFR > 15**

FDC convenience

Efficacy

CVD prevention

Loop diuretic*:

- Torsemide 5-40 mg qd
- Titrate to 3-4 lb wt loss
- K⁺, Creatinine often
  (Furosemide 20-80 mg bid impractical)

HCTZ 12.5-25/Other

if eGFR ≥30 ml/min

Indapamide, 1.25-2.5 mg qd

Chlorthalidone,**

12.5-50 mg qd

*Loop diuretics less effective to ↓ BP

**Chlorthalidone lowers BP 10/5 mmHg

with eGFR = 15-30 ml/min

J Am Soc Htn 2016;10:282;285;288

Curr Hypertens Rep 2016;18:27

Cochrane Data Syst Rev 2015;5:CD003825

NEJM 2021;385:2507
**“STANDARD” DOSES OF ANTI-HTN DRUGS**

Mean reduction in BP = 9/5 mm Hg in ≥ 100 patients:
from baseline BP = 150/95

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCTZ</td>
<td>25 mg</td>
<td>Amlodipine</td>
<td>5 mg</td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>12.5 mg</td>
<td>Diltiazem</td>
<td>240 mg</td>
</tr>
<tr>
<td>Indapamide</td>
<td>1.25 mg</td>
<td>Verapamil</td>
<td>240 mg</td>
</tr>
<tr>
<td>Amiloride</td>
<td>10 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lisinopril</td>
<td>10 mg</td>
<td>Metoprolol</td>
<td>50 mg bid</td>
</tr>
<tr>
<td>Benazepril</td>
<td>20 mg</td>
<td>Carvedilol</td>
<td>12.5 mg bid</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>150 mg</td>
<td>Nebivolol</td>
<td>5 mg</td>
</tr>
<tr>
<td>Losartan</td>
<td>50 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valsartan</td>
<td>80 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Telmisartan</td>
<td>40 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candesartan</td>
<td>8 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• **Individual** response to given drug varies markedly due to ∆ Htn mechanisms

WHY INITIAL LOW-DOSE 2 DRUG RX?

- ≥75% of HTN patients need ≥ 2 drugs to ↓ BP < 140/90

- >BP lowering than maximal MonoRx: dose-response studies

<table>
<thead>
<tr>
<th>Dose</th>
<th>↓ BP, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>¼ Standard</td>
<td>5/3</td>
</tr>
<tr>
<td>½ Standard</td>
<td>7/4</td>
</tr>
<tr>
<td>Standard</td>
<td>10/5</td>
</tr>
<tr>
<td>Maximal (2X Standard)</td>
<td>12/7</td>
</tr>
<tr>
<td>2 Drugs ½ Standard</td>
<td>14/8</td>
</tr>
<tr>
<td>3 Drugs ½ Standard</td>
<td>29/14</td>
</tr>
<tr>
<td>4 Drugs ¼ Standard</td>
<td>22-24/11-15</td>
</tr>
</tbody>
</table>

- Fewer/equal side effects (log-linear ∝ dose)

WHY INITIAL LOW-DOSE 2 DRUG RX?

Greater efficacy than MonoRx: RCTs

• BP-lowering: 26-39% greater at 2-24 mo.
• HTN control: absolute 20% greater at 3-12 mo

Greater CVD event reduction than MonoRx: obs. Studies

• ↓ CVD events: 10-34% fewer at 1-2 y

Mechanisms for benefits:

• 2-drug Rx corrects for variable BP response to MonoRx
• Improved adherence—absolute 10-21% obs. studies
  ↑ BP-lowering → ↓ drug titrations → ↓ visits

Hypertension 2021;77:103
J Hypertension 2019;37:1768
J Hypertension 2019;38:1572
J Gen Int Med 2017;32:619
Hypertension 2018;72:846
Eur Heart J 2018;39:3654
Am J Hyperters 2021;34:1083
SELECTING INITIAL PHARMACOLOGIC THERAPY

**Pregnancy Potential:** consider pregnancy test

- **No** ACE-I or ARB unless compelling indication + birth control
- **OK:**
  - DHP-CCB 1st
  - Labetalol or other BB 2nd
  - Thiazides 3rd
- **Planning pregnancy:**
  - Nifedipine ER
  - Labetalol
  - Alpha-methyldopa
- **Lactation:**
  - Nifedipine ER
  - Enalapril
  - Labetalol-avoid atenolol, propranolol
  - Alpha-methyldopa

SELECTING INITIAL PHARMACOLOGIC THERAPY

Pregnancy Potential

Compelling Indications to Use/Avoid Specific Drugs

- Pre-DM → ACE-I/ARB ↓ progression to T2DM by 16%
- DM or CKD:
  - Albuminuria ≥ 300 mg/g ACR → ACE-I or ARB
  - No albuminuria → ACE-I ARB, CCB, Thiazide
- Recent MI or Systolic HF → ACE-I (ARB) + BB ± MRA
- Stable CAD → ACE-I (ARB); BB or CCB if stable angina
- Paroxysmal AF → ARB?
- Thoracic aortic aneurysm → BB, ARB
- Asthma prefer ARB > ACE-I; limit BB
- Gout → prefer losartan, amlodipine–avoid/minimize diuretics
- HIV → drug interactions with CCBs
SELECTING INITIAL PHARMACOLOGIC THERAPY

Pregnancy Potential

- Compelling Indications for specific drugs
- Contraindications for specific drugs
  - CHF → verapamil, diltiazem
  - CAD → short-acting nifedipine
  - LVH → hydralazine, minoxidil
  - Severe PAD → BBs
  - Bilateral RAS → ACE-I, ARB
    Unilateral RAS, 1 Kidney → ACE-I, ARB
  - Always → ACE-I ⊕ ARB
DESIRABLE 2-DRUG REGIMENS: ADDITIVE BP-LOWERING ⊕ CVD REDUCTION

Effective:
- ACE-I (ARB) ⊕ CCB: ACCOMPLISH RCT, ASCOT, CREOLE*
- CCB ⊕ Thiazide: FEVER, VALUE, CONVINCE, ELSA RCTs, CREOLE*
  *Especially in black patients
- ACE-I (ARB) ⊕ Thiazide: ADVANCE, PROGRESS RCTs

Less Effective:
- Thiazide ⊕ BB
  - Lesser CVD reduction vs above: LIFE, ASCOT RCTs
  - More diabetogenic
- ACE-I (ARB) ⊕ BB
  - Not additive BP-lowering
  - Optimal Rx for systolic HF, post-MI

Unknown:
- DHP-CCB ⊕ BB: lowers BP; no CVD data

Avoid:
- ACE-I ⊕ ARB: ON-TARGET; VA NEPHRON-D RCTs
- Clonidine ⊕ BB: bradycardia, rebound HTN
- Non-DHP CCB ⊕ BB: bradycardia
OPTIMAL 2-DRUG RX: ACE-I (ARB) ⊕ CCB

Meta-analysis: 8 RCTs; 20,451 pts

- ACE-I or ARB ⊕ CCB
- ACE-I or ARB ⊕ Diuretic
- BB ⊕ CCB
- BB ⊕ Diuretic

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative Risk</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVD events</td>
<td>0.80 (0.70-0.91)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>GFR reduction</td>
<td>⊕ 4.2 ml/min</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total mortality</td>
<td>0.90 (0.77-1.04)</td>
<td>0.09</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>0.85 (0.73-0.95)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

• Predominance of higher CVD risk pts in these RCTs

J Clin Hypertens 2016;18:801
“OPTIMAL” 3-DRUG RX: GENERAL HTN POPULATION

• Effectively ↓ BP, ↓ CVD events, ↓ side effects
  2017 AHA recommended

• ACE-I (ARB) ⊕ CCB ⊕ Thiazide diuretic
  – ↓ BP additively in several studies
    ▪ Most effective:
      Azilsartan ⊕ CTD/Indap ⊕ Amlodipine
  – ↓ side effects of △ potassium, CCB-induced edema
  – ? ↓ CVD events: post-hoc analysis of ADVANCE
    Need confirmatory RCT
  – Need inexpensive 3-drug SPCs

Hypertension 2009;54:19;32
J Hypertens 2014;32:3
Hypertension 2018;72:e53

Hypertension 2014;63:220;259
Diabetes Care 2013;36:S4
Am J Med 2021;134:1195
APPROACH TO UNCONTROLLED HTN ON 3 DRUGS: APPARENT RESISTANT HTN

✓ for suboptimal Rx regimen: best 3-drug Rx
  – \(\triangle HTZ \rightarrow\) chlorthalidone 25 mg/d or indapamide, 2.5 mg/d
  – Single pill 2-3 drug combinations

✓ 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, serum/urine drug level

✓ for drugs that \(\uparrow\) BP: NSAIDS, estrogen, \(\uparrow\) ETOH, epogens

• Review (± testing) for 2° causes of HTN
• Consider consultation
OPTIMAL 4-DRUG RX FOR RESISTANT HTN

PATHWAY-2 RCT, 2015:

285 pts on A ⊕ C ⊕ D: clinic SBP ≥ 140; home SBP ≥ 130
- Each pt for 3 mo: spironolactone, 25-50 mg/d;
  doxazosin, 4-8 mg/d; bisoprolol, 5-10 mg/d; placebo
- eGFR ≥ 45 ml/min.

<table>
<thead>
<tr>
<th></th>
<th>Change in BP</th>
<th>% Controlled to</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clinic SBP</td>
<td>Home SBP</td>
<td>Home SBP &lt; 130</td>
</tr>
<tr>
<td>Spironolactone, 50 mg/d</td>
<td>- 21</td>
<td>- 14</td>
<td>58%</td>
</tr>
<tr>
<td>Doxazosin, 8 mg/d</td>
<td>- 16</td>
<td>- 9</td>
<td>42%</td>
</tr>
<tr>
<td>Bisoprolol, 10 mg/d</td>
<td>- 16</td>
<td>- 8</td>
<td>43%</td>
</tr>
<tr>
<td>Placebo</td>
<td>- 11</td>
<td>- 4</td>
<td>24%</td>
</tr>
</tbody>
</table>

- Best drug: spirono. 60%; dox. 20%; bisop. 20%
  - Hyperkalemia (≥ 6.0) in 2%
  - Spironolactone efficiency $1/\infty$ plasma renin

Lancet Diab Endo 2018;6:464
Lancet 2015;386:2059
RESISTANT HYPERTENSION ON ACE-I (ARB) ⊕ INDAP./CHLORTHAL ⊕ AMLODIPINE

Torsemide if eGFR < 15 ml/min

✓ eGFR/K+

≥ 45 ml/min and < 4.5 mEq/L

Yes

Spironolactone*
12.5 → 50 mg/d
q 4 wks, prn

• ✓ K+/creatinine at 1 and 4 wks

‡ eGFR < 45 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

‡ eGFR < 45 ml/min or K+ > 4.5 and HR < 84-90/min

Doxazosin hs
2 → 4 → 8 mg
q 2-4 wks prn

Diltiazem ER
180 → 240 mg/d
q 2-4 wks, prn

• ✓ for edema

Amiloride 10-20 mg/d = Spironolactone 25-50 mg/d
Eplerenone 50 mg bid 4-6 mmHg less effective than spironolactone

2. RESISTANT HTN ON ≥ 4-DRUG THERAPY

ACE-I or ARB ⊕ Indap. or Chlorthal. ⊕ Amlodipine
⊕
MRA and/or BB and/or AB and/or 2nd CCB and/or 2nd Diuretic

OSA

CPAP
(↓ 5/4 mmHg 24h ABPM)

T2DM

SGLT-2 Inhibitor
(↓ 4-7/2-3 mmHg 24h ABPM)

HF-PEF

Sacubitril-Valsartan
(↓ SBP 4-6 mmHg, OBPM)

Hypertens Res 2022;45:167
Am J Hypertens 2020;33:1071
Eur Heart J 2021;42:3741
Sleep Med Rev 2021;58:101446
CAN WE DO BETTER?
TEAM-BASED CARE IMPROVES HTN CONTROL!

1° Care Clinician

New Role for Existing Staff

Add New Staff – Clinical Pharmacist

ID Uncontrolled HTN:
- Paper/EMR registries
- Pt. call-back

Improve Clinical BP Measurement:
- Accurate electronic > Manual
- AOBP on pts in isolation

Therapeutic Inertia:
- Initial low-dose 2-drug Rx for most
- Algorithm-guided Rx
- Optimal 3,4 drug Rx
- Adjust q 2-4 wk
- HBPM program
- Pharmacist/RN guided
- Performance feedback:
  - Clinician level
  - Clinic level

Rx Adherence
- Phone FU
- Walk-in BP √’s
- Education:
  - HTN outcomes
  - BP goals
  - HBPM
  - Side effects

Kaiser Perm HTN control rate:  
- 650,000 HTN pts
- 44%, 2001 → 90%, 2013

J Clin Hypertens 2016;18:260  
Curr Hypertens Rep 2019;21(12):91