Blood Pressure: Thresholds and Treatment

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Management of hypertension: the issues

• Measurement
• Classification
• Investigations
• Risk assessment
• Non-pharmacological measures
• Treatment thresholds
• Drug therapy - 1st line
  - sequencing
  - beyond BP
• Treatment targets
• Concomitant therapy
# BP treatment threshold

<table>
<thead>
<tr>
<th>JNC VII</th>
<th>ESH-ESC</th>
<th>WHO-ISH</th>
<th>BHS IV 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
<td>160/100</td>
</tr>
<tr>
<td>All risk strata</td>
<td>All risk strata</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inc? low risk</td>
<td>Inc? low risk</td>
<td>Consider resources</td>
<td>140/90</td>
</tr>
<tr>
<td>130/85 v high and high risk</td>
<td>130/85 v high and high risk</td>
<td>Consider resources</td>
<td>140/90</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10 year CV risk (\geq 20%)</td>
</tr>
</tbody>
</table>
Thresholds and targets
Thresholds for intervention?

• 30 studies since 2003
• Excluded studies if no stratified by threshold
• 3 systematic reviews – high quality
• 27 prognostic studies – mainly low quality
• 1 study that compared thresholds

9.1.2 Evidence statement - clinical
Details of all the included studies are summarised in Table 28, Table 29 and Table 30.
• Most studies showed a continuous relationship between BP and risk of developing clinical outcomes (i.e. an increased risk of outcome with increasing BP value)
• This was true regardless of BP measurement method (office, ABPM, self-reported/ not specified)
• The MA of Law et al., 349 showed that BP treatment reduced CVD risk regardless of pre-treatment BP
• The Head 2010 study, 267 provided equivalent threshold values for ABPM and clinic BP measurements for the diagnosis and treatment of HT. Evidence statements
Thresholds
Evidence to recommendations

• Head et al, 2010 - 8575 people - CBPM cf ABPM
• Used thresholds for sensitivity/specificity analysis
• CBPM 140/90 = ABPM daytime average 135/85 mm Hg
• CBPM 160/100 = ABPM daytime average 150/95 mm Hg

• Treat all stage 2
• Treat stage 1 at 20% 10 year risk or CVD or TOD
• Recognised bias towards older – few below 40 yrs
• Under 40 consider specialist evaluation
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• **Drug therapy** - 1st line
  - sequencing
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Choosing drugs for patients newly diagnosed with hypertension: NICE/BHS

**Abbreviations:**
- A = ACE inhibitor (consider angiotensin-II receptor antagonist if ACE intolerant)
- C = calcium-channel blocker
- D = thiazide-type diuretic

Black patients are those of African or Caribbean descent, and not mixed-race, Asian or Chinese patients

**Flowchart:**
1. **Younger than 55 years**
   - A
     - **Step 1**
2. **55 years or older or black patients of any age**
   - C or D
     - **Step 1**
   - **A + C or A + D**
     - **Step 2**
3. **A + C + D**
   - **Step 3**
   - **Add**
     - further diuretic therapy
     - alpha-blocker
     - beta-blocker
   - Consider seeking specialist advice
     - **Step 4**

**NICE/BHS algorithm: June 2006**
Treatment Recommendations – General Concepts

• 39. Prescribe non-proprietary drugs appropriate, where these are appropriate and minimise cost. [2004]

• 40. Offer people with isolated systolic hypertension (systolic BP 160 mmHg or more) the same treatment as people with both raised systolic and diastolic blood pressure. [2004]

• 41. Offer people older than 80 years the same antihypertensive treatment as people aged 55–80 years, taking into account any comorbidities. [new 2011]
Step 1 Treatment Recommendations

• 42. Offer step 1 antihypertensive treatment with an ACE inhibitor or a low-cost ARB to people aged under 55 years. If an ACE inhibitor is used and not tolerated, offer an ARB. [new 2011]

• 43. Do not combine an ACE inhibitor with an ARB to treat hypertension. [new 2011]

• 44. Offer step 1 antihypertensive treatment with a CCB to people aged 55 years and older and to black people of African and Caribbean descent of any age. If a CCB is not suitable, for example because of oedema or intolerance, or if there is evidence of heart failure, or a high risk of heart failure, offer a thiazide-like diuretic. [new 2011]
45. If a diuretic is required, choose a thiazide-like diuretic, such as chlortalidone (12.5 mg–25.0mg once daily) or indapamide (2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide or hydrochlorothiazide. [new 2011]
Thiazides

• Do NOT include chlorthalidone and inpadamide
• Low dose: HCTZ 12.5 – 25mg
  : BFZ 1.25 – 2.5mg
• Do show a dose response effect on BP
• Are not equivalent dose for dose with thiazide-like diuretics
## HCTZ vs Chlorthalidone

<table>
<thead>
<tr>
<th>Study</th>
<th>Diurectic</th>
<th>Dose (mg)</th>
<th>BP Reduction (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowlus &amp; langford</td>
<td>HCTZ, Chlorthalidone</td>
<td>100, 50</td>
<td>18.1 / 8.0, 25.1 / 10.1</td>
</tr>
<tr>
<td>Finnerty</td>
<td>HCTZ, Chlorthalidone</td>
<td>100, 50</td>
<td>22.2 / 16.4, 18.2 / 15.1</td>
</tr>
<tr>
<td>Ernst et al (meta-anal)</td>
<td>HCTZ, Chlorthalidone</td>
<td>33, 25</td>
<td>17*, 26</td>
</tr>
<tr>
<td>Ernst et al (clinic)</td>
<td>HCTZ, Chlorthalidone</td>
<td>25-50, 12.5-25</td>
<td>10.8 / 6.9, 17.5 / 8.1</td>
</tr>
<tr>
<td>Ernst et al (ABPM)</td>
<td>HCTZ, Chlorthalidone</td>
<td>25-50, 12.5-25</td>
<td>7.4 / 5.1, 12.4 / 7.1</td>
</tr>
</tbody>
</table>

* = median SBP
### ABPM: HCTZ vs. All Other Antihypertensive Drug Classes

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>ABPM Reduction (mmHg)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
<td></td>
</tr>
<tr>
<td>HCTZ (12.5-25mg)</td>
<td>7.5</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>ACE-Inhibitors</td>
<td>12.9</td>
<td>7.6</td>
<td></td>
</tr>
<tr>
<td>ARB’s</td>
<td>13.3</td>
<td>7.8</td>
<td></td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>11.2</td>
<td>8.5</td>
<td></td>
</tr>
<tr>
<td>CCB</td>
<td>11.0</td>
<td>8.1</td>
<td></td>
</tr>
</tbody>
</table>

*Messerli et al: ESH: 2009*
Summary of the efficacy of Diuretics in the Hypertension Trials

- No evidence for benefit of truly low-dose thiazides vs. placebo

- Low-dose thiazides vs. anything was inferior (ANBP2, ASCOT, ACCOMPLISH)

- Good evidence of CV benefits for
  a) higher dose Thiazides (+/- K+ sparing)
  b) Chlorthalidone
  c) Indapamide
Step 2 Treatment Recommendations

• 52. If step 2 antihypertensive treatment is required, offer a CCB in combination with either an ACE Inhibitor or a low-cost ARB. If a CCB is not suitable, for example because of oedema or intolerance, or if there is evidence of heart failure or a high risk of heart failure, offer a thiazide-like diuretic [new 2011]
Titrated to achieve BP<140/90 mmHg; <130/80 mmHg in patients with diabetes or renal insufficiency

*Beta blockers; alpha blockers; clonidine; (loop diuretics).
Step 3 Treatment Recommendations

53. If treatment with three drugs is required, the combination of ACE inhibitor or angiotensin-II receptor blocker, calcium-channel blocker and thiazide-like diuretic should be used. [2006]
Antihypertensive Drug Treatment

People aged < 55 years

A = ACE inhibitor or angiotensin II receptor blocker

People aged ≥ 55 years and all black people of African or Caribbean descent

C = calcium-channel blocker (CCB)

D = thiazide-like diuretic

C* = CCB preferred but consider thiazide-like diuretics in people with oedema or a high risk of heart failure

Further diuretic** = consider low-dose spironolactone or higher doses of a thiazide-like diuretic

Step 1

A

C*

Step 2

A + C*

Step 3

A + C + D

Step 4 (resistant hypertension)

A + C + D + further diuretic** or alpha-blocker or beta-blocker

Consider seeking specialist advice.
Step 4 Treatment Recommendations
RESISTANT HYPERTENSION

55. For treatment of resistant hypertension at step 4, consider further diuretic therapy with low-dose spironolactone (25 mg once daily) if blood potassium levels are lower than 4.5 mmol/l and eGFR is higher than 60 ml/min/1.73m². If blood potassium levels are higher than 4.5 mmol/l, consider therapy with a higher-dose thiazide-like diuretic treatment. [new 2011]

56. When using further diuretic therapy for resistant hypertension at step 4, monitor blood sodium and potassium and renal function within 1 month and repeat as required thereafter. [new 2011]
Step 4 Treatment Recommendations

RESISTANT HYPERTENSION

• 57. If further diuretic therapy for resistant hypertension at step 4 is not tolerated, contraindicated or ineffective, consider an alpha- or beta-blocker. [new 2011]

• 58. If blood pressure remains uncontrolled with the optimal or maximum tolerated doses of four drugs, seek expert advice if it has not yet been obtained.[new 2011]
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## BP Targets in Various Guidelines

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>Uncomplicated hypertension</th>
<th>Diabetes</th>
<th>Chronic renal failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA (JNC VII [2003])</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;130/80 mmHg</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>Europe (ESH 2007)</td>
<td>&lt;140/90 mmHg (lower if tolerated)</td>
<td>&lt;130/80 mmHg</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>China (CSH 2005)</td>
<td>&lt;140/90 mmHg (≤150 mmHg SBP for elderly)</td>
<td>&lt;130/80 mmHg</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>Russia</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;130/80 mmHg</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>Korea (KSH 2004)</td>
<td>&lt;140/90 mmHg</td>
<td>&lt;130/80 mmHg</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>WHO^ISH</td>
<td>SBP &lt;140 mmHg</td>
<td>&lt;130/80 mmHg</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>BHS IV 2004</td>
<td>&lt;140/85 mmHg</td>
<td>&lt;130/80 mmHg</td>
<td>&lt;130/80 mmHg</td>
</tr>
</tbody>
</table>
TARGETS?

• Pragmatic recommendations based on poor evidence
• Systolic 140mmHg (150 in 80+)
• Diastolic 90mmHg (90 in 80+)