Management of Blood Pressure
What are the new standards of care?

Bryan Williams, MD
Professor of Medicine
Department of Cardiovascular Sciences
& NIHR Biomedical Research Unit in Cardiovascular Diseases
University of Leicester, U.K
Hypertension Standards of Care

Defined by clear questions and a structured systematic review of the evidence, resulting in evidence-based guidance for clinical practice
Hypertension

The clinical management of primary hypertension in adults

NICE Guidance on Hypertension 2011

Prepared in collaboration with the British Hypertension Society

Bryan Williams, Professor of Medicine, University of Leicester
Chairman; NICE Hypertension Guideline Development Group

http://guidance.nice.org.uk/CG127
Hypertension remains one of the most important preventable cause of premature cardiovascular morbidity and mortality;
The “silent killer” – only detected by screening
In the world., ~25% of all adults are hypertensive;
~50% of adults over the age of 60yrs are hypertensive;
Clinical management of hypertension is a major component of primary care clinical work-load;
NICE Hypertension Guideline Update 2011

Areas Reviewed

• Diagnosis of hypertension;
• Treatment Thresholds and Targets;
• Treatment of the very elderly (>80yrs);
• Pharmacological treatment and its cost effectiveness;
• Which diuretic?
• Definition and treatment of resistant hypertension
How should hypertension be diagnosed?

**Current Practice**

- **Screening BP – High?**
  - **Repeat BP Measurement in Doctor’s Office**
  - **Repeat BP Measurement in Doctor’s Office**
  - **Repeat BP Measurement in Doctor’s Office**

- **± Diagnose Hypertension**

**CVD Risk & TOD Assessment**

*Weeks or Months*
How should hypertension be diagnosed?

New Guidance 2011

Days or weeks

- Screening BP – High?
- Offer Ambulatory BP Measurement (ABPM)
- Use Mean daytime BP to define hypertension
- ± Diagnose Hypertension

CVD Risk & TOD Assessment
Why ABPM ?
ABPM for the Diagnosis of Hypertension

- ABPM is a better predictor of clinical outcomes than clinic BP;
- ABPM is the reference standard used in clinical practice when there is uncertainty about the diagnosis;
- ABPM improves the specificity and sensitivity of diagnosis versus clinic and home BP measurement;
- Avoids treatment in people who are not hypertensive – as many as 25% with “white coat hypertension”;
ABPM for the Diagnosis of Hypertension

- Was **cost effective** (cost saving to the NHS) versus clinic and home BP measurement;
- **Home BP is an alternative** for those who do not tolerate ABPM but it is not as good as ABPM;
- **Use the Daytime average of least two measurements per hour** (minimum 14 measurements)
- Automated devices cannot be used for people with significant **pulse irregularity** – e.g. Atrial fibrillation – use **manual auscultation** in such patients:
Cost-effectiveness of options for the diagnosis of high blood pressure in primary care: a modelling study

Kate Lovibond, Sue Jowett, Pelham Barton, Mark Caulfield, Carl Heneghan, F D Richard Hobbs, James Hodgkinson, Jonathan Mant, Una Martin, Bryan Williams, David Wonderling, Richard J McManus

Interpretation Ambulatory monitoring as a diagnostic strategy for hypertension after an initial raised reading in the clinic would reduce misdiagnosis and save costs. Additional costs from ambulatory monitoring are counterbalanced by cost savings from better targeted treatment. Ambulatory monitoring is recommended for most patients before the start of antihypertensive drugs.
Home BP Monitoring Protocol

• For each blood pressure measurement, **two consecutive measurements** are taken, at least **1 minute apart** and with the person seated;

• Blood pressure measurements are taken **twice daily**, ideally in the morning and evening;

• Blood pressure **measurement** continues for at least **4 days**, ideally for **7 days**;

• Discard the measurements taken on the first **day** and use the average value of all the remaining measurements;
# Blood Pressure Thresholds for Diagnosis and Treatment of Hypertension

<table>
<thead>
<tr>
<th>Stage of Hypertension</th>
<th>Office BP (mmHg)</th>
<th>24hr. Daytime ABPM Average</th>
<th>Home ABPM Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 Hypertension</td>
<td>≥140 /90 but &lt;160/100</td>
<td>≥135/85</td>
<td>≥135/85</td>
</tr>
</tbody>
</table>

**Stage of Hypertension**

- **Stage 1 Hypertension**: ≥140 /90 but <160/100
- **Stage 2 Hypertension**: ≥160 /100
- **Severe Hypertension**: ≥180/110
- **Accelerated Hypertension**: Usually ≥180/110 + retinal haemorrhages and/or papilloedema
Cardiovascular Risk and Target Organ Damage Assessment

• **Assess Cardiovascular Risk:**
  - using CVD risk calculator (e.g. JBS, Q-Risk);
  - **Assess Target Organ Damage:**
    - Urine dipstick (blood/protein) and UACR;
    - Blood electrolytes, glucose, LDL and HDL-cholesterol, eGFR;
    - Fundoscopy for retinopathy;
    - 12-lead ECG.

• **For people aged <40yrs** – consider specialist referral for:
  - Comprehensive assessment of potential underlying secondary causes for hypertension;
  - Detailed assessment of target organ damage
  - Assessment of CVD risk with lifetime risk projections
Thresholds for Diagnosis and Treatment of Hypertension

**Stage 1 Hypertension**

- Target organ Damage, CVD, or 10yr CVD risk ≥20% ?

- **YES = Treat**
- **No = Lifestyle and review 1 yr.**

*for people aged <40ys, 10yr CVD risk assessments underestimate lifetime risk – consider referral for exclusion of secondary causes and more detailed assessment of TOD*

**Stage 2 Hypertension**

Treat
Thresholds for Diagnosis and Treatment of Hypertension

Severe Hypertension

Treat
do not wait for ABPM confirmation if TOD or CVD

Accelerated Hypertension

Refer immediately for inpatient specialist care
Blood Pressure Treatment Targets

- There have been too few trials randomising patients to different BP treatment targets, especially for systolic BP;
- Guidelines have got ahead of the evidence in recommending the general application of more aggressive BP-lowering targets (e.g. <130/80mmHg) for people with CVD, CKD and/or Diabetes;
- Recent trials (e.g. ACCORD and post hoc analysis of INVEST and ONTARGET) do not support the general application of more aggressive BP lowering targets;
- Achieved BP <130/80mmHg may reduce the risk of stroke but at the expense of adverse effects and possible J curve for ischaemic heart disease events.
BP Treatment in the very elderly, i.e. aged over 80yrs

- New evidence suggests that BP lowering reduces the risk of stroke, heart failure and death in people aged over 80yrs;
- Offer people aged >80yrs same treatment as people aged >55yrs, taking account of co-morbidities;
- Initiate therapy in people aged >80yrs at stage 2 hypertension;
- Treat to a target of <150/90mmHg.
Pharmacological Treatment of Hypertension – Update 2011
Cost Effectiveness of Antihypertensive Treatment

“Treating high blood pressure is cheaper than doing nothing”
Evolution of Hypertension

**Pre-hypertensive**
- Vasoconstriction
- Increased Peripheral Resistance
- Vascular remodelling
- RAAS and SNS Activation

**Hypertensive + Damage**

**Hypertensive + Clinical Disease**
- Declining GFR
- Sodium retention
- Increased Cardiac output
- Stiff Aorta – systolic hypertension

**Younger**

**Older**

**Number of Drugs**

**Plasma Renin**

A: ACE-inhibition / ARB
B: β-blocker
C: CCB
D: Diuretic (thiazide-type)

B. Williams. 2007
Antihypertensive Drug Treatment

**Aged <55yrs**

- **Step 1**
  - A

- **Step 2**
  - A + C*

- **Step 3**
  - A + C + D

- **Step 4**
  - A + C* + D + Further Diuretic
  - Consider specialist Advice

**Aged ≥55yrs or Black AC**

- **Step 1**
  - C*

- **Step 2**
  - A + C*

- **Step 3**
  - A + C + D

- **Step 4**
  - A + C* + D + Further Diuretic
  - Consider specialist Advice

---

A = ACEi or ARB
C = CCB
D = Thiazide-like diuretic

C* = CCB preferred but D is an alternative in people intolerant of C or at high risk of heart failure

Further Diuretic:
Consider low dose spironolactine or higher dose thiazide
• Offer step 1 antihypertensive treatment with an ACE inhibitor or an ARB to people aged under 55 years. [new 2011]
• Do not combine an ACE inhibitor with an ARB to treat hypertension. [new 2011]
• 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]
Why is a CCB Preferred to Diuretic?

- CCB (usually amlodipine) was the most cost-effective treatment option for treating hypertension unless the patient had heart failure or was at high risk of developing heart failure – i.e. older patient ≥75yrs;
- CCB is metabolically neutral – easy to use;
- CCB is best at reducing blood pressure variability and BP variability is an independent predictor of clinical outcomes - especially stroke;
- At step 2, the combination of A + C was superior to A + D at preventing clinical outcomes (ACCOMPLISH).
But….have we been using the wrong diuretic or wrong dose?
Treatment Recommendations – Choice of Diuretic

• Which diuretic?

• If a diuretic is required, choose a thiazide-like diuretic, such as chlortalidone (12.5 mg–25.0 mg once daily) or indapamide (1.5 mg SR, or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide or hydrochlorothiazide. [new 2011]
Why Change the Diuretic?

• No need to change diuretic in people stable on treatment and in whom BP is controlled;
• Evidence review found limited evidence in clinical outcome trials of benefits with hydrochlorthiazide or bendroflumethiazide 2.5mg daily;
• Most recent trials showing benefits with lower dose diuretics have used thiazide-like diuretics, eg. chlortalidone or indapamide
If step 2 antihypertensive treatment is required, offer a CCB in combination with either an ACE Inhibitor or an ARB. [new 2011]

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 (e.g. elderly over 75yrs), offer a thiazide-like diuretic [new 2011]
Added Value of Combination Therapy in Hypertension

- Improved blood pressure lowering efficacy;
- Restores dose response to the component drugs;
- Reduces heterogeneity in the blood pressure response in individual patients – all patients respond;
- Reduces side effects associated with higher dose monotherapy (e.g. less oedema with A+C or less hypokalaemia with A + D.)
If treatment with three drugs is required, the combination of ACE inhibitor or an ARB, a CCB and a thiazide-like diuretic should be used. [2006]
DEFINITION OF RESISTANT HYPERTENSION

A clinic blood pressure that remains higher than 140/90 mmHg – confirmed by ABPM, despite treatment with *optimal or best tolerated doses* of A + C + D

Consider adding a fourth antihypertensive drug and/or seeking expert advice. [new 2011]
For treatment of resistant hypertension, consider further diuretic therapy with low-dose spironolactone (25 mg once daily) if blood potassium levels are lower than 4.5 mmol/l. Caution is required in patients with impaired renal function who are at higher risk of developing hyperkalaemia.

If blood potassium levels are higher than 4.5 mmol/l, consider therapy with a higher-dose thiazide-like diuretic treatment.[new 2011]

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]
RESISTANT HYPERTENSION
Treatment Recommendations

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

• 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]
Antihypertensive Drug Treatment

- **Aged <55yrs**
  - Step 1: A
  - Step 2: A + C*
  - Step 3: A + C + D
  - Step 4: A + C + D + Further Diuretic
  - Consider specialist Advice

- **Aged ≥55yrs or Black AC**
  - Step 1: C*
  - Step 2: A + C*
  - Step 3: A + C + D
  - Step 4: A + C + D + Further Diuretic

**Step 4: Resistant Hypertension**

- A = ACEi or ARB
- C = CCB
- D = Thiazide-like diuretic

- C* = CCB preferred but D is an alternative in people intolerant of C or at high risk of heart failure

- Further Diuretic: Consider low dose spironolactine or higher dose thiazide
Going Beyond Blood Pressure to Reduce CVD Risk

- Many hypertensive patient even when treated to recommended BP goals remain at increased risk of stroke and coronary heart disease;
- Assessment of CVD risk can identify patients who might also benefit from concomitant statin and antiplatelet therapies;
- Offer these treatment in all patients for secondary prevention;
- Offer these treatments for patients at increased CVD risk, i.e. diabetes, CKD and estimated CVD risk ≥20% over 10 years – lifetime risk assessments may prompt even earlier interventions.
ASCOT-LLA: Non-fatal MI and Fatal CHD
– Impact of Atorvastatin 10mg o.d. in people with controlled BP

HR=0.64 (0.50–0.83)
p=0.0005

Atorvastatin 10mg: Number of events: 100
Placebo: Number of events: 154

36% reduction

ASCOT-LLA: Fatal and Non-fatal Stroke
– Impact of Atorvastatin 10mg o.d. in people with controlled BP

- Atorvastatin 10mg: Number of events: 89
- Placebo: Number of events: 121

HR = 0.73 (0.56–0.96)
p = 0.0236

27% reduction

NICE Draft Hypertension Guidance: Summary and Reflections

• Evolution rather than revolution;
• Pragmatic guidance – focus on implementation;
• Simpler treatment algorithm;
• ABPM for diagnosis is the most controversial aspect;
• Recognition of need to look more closely at younger people before deciding not to treat;
• Continued recognition of the need to assess and treat CVD risk factors (including lifestyle) beyond blood pressure.
GUIDELINES

Management of hypertension: summary of NICE guidance

Taryn Krause senior project manager, research fellow¹, Kate Lovibond senior health economist¹, Mark Caulfield professor of clinical pharmacology², Terry McCormack general practitioner³, Bryan Williams professor of medicine⁴⁵, on behalf of the Guideline Development Group

BMJ, August 24th 2011