2016
Hypertension Canada CHEP Guidelines for the Management of Hypertension

What’s new in the treatment of hypertension?
What’s still really important?
Presenter Disclosure

• Relationships with commercial interests:
  • Grants/Research Support: Bayer
  • Speakers Bureau/Honoraria: Bayer, Servier, Valeant
  • Consulting Fees: GSK, Servier
  • Data Safety and Monitoring: NA
At the completion of this session, participants should be able to:

- Critically appraise and define how the SPRINT trial results will be incorporated into practice.
- Describe how the SPRINT trial results (outlined in the 2016 CHEP recommendations) will change the management of hypertensive patients.
- Summarize the importance of electronic blood pressure monitoring and out-of-office blood pressure measurement.

CanMeds Roles: Medical Expert, Scholar and Professional
Mitigating Potential Bias

- The information presented is based on recent information that is explicitly “evidence-based”.

- This presentation and all the recommendations involving clinical medicine are based on evidence that was vetted by the Canadian Hypertension Education Program. The presentation has been developed for dissemination by Hypertension Canada and is available in its entirety at http://guidelines.hypertension.ca
Mission:
• Advancing health through the prevention and control of high blood pressure and its complications.

Vision:
• Canadians will have the healthiest blood pressure in the world.
Evidence-Based Annual Guidelines

• Canada has the world’s highest reported national blood pressure control rates

• CHEP is known as the most credible source for evidence-based hypertension guidelines, with annual updates, a well-validated review process and effective dissemination techniques across Canada
2016 CHEP Guidelines Task Force
Guidelines Task Force

- Topic Sub-Group
- Topic Sub-Group
- Topic Sub-Group
- Topic Sub-Group

Central Review Committee

- Dissemination and Implementation Committee
- Outcomes Research Task Force
Hypertension Canada’s Annual KT Cycle For Developing Management Guidelines

- Monitor Guidelines Use
- CHEP Guidelines Creation
  - Systematic review and critical appraisal of studies
  - Synthesis into recommendations
  - Scientific Manuscripts and Summaries
- Evaluate Outcomes by Combining National and Provincial Administrative Data
- Knowledge Gaps, Best Practice Goals
- Identify New Knowledge, Select What is Still Important
- Adapt Knowledge to Local/Regional Context
- Address Barriers to Knowledge Use
- Tailor Tools for Interprofessional Team Members
What’s still important?

• The diagnosis of hypertension should be based on out-of-office measurements
• The management of hypertension is all about global cardiovascular risk management and vascular protection
• The most important step in prescription of antihypertensive therapy is achieving patient “buy-in” and adherence
What’s new?

• **New thresholds and targets for high risk patients (SPRINT)**
• *Assessing* clinic blood pressures using **automatic electronic** (oscillometric) monitors
• **Adopting** healthy behaviours is integral to the management of hypertension (focus on potassium supplementation)
• **Updating** the evaluation of patients with suspected secondary forms of hypertension (focus on primary hyperaldosteronism)
• **Updating** the treatment of patients with hypertension with concurrent coronary artery disease
• **New** recommendations on the diagnosis and management of hypertension in pediatric patients *(NOT the focus of this presentation)*
For high-risk patients, aged ≥ 50 years, with systolic BP levels ≥130 mm Hg, intensive management to target a systolic BP ≤120 mm Hg should be considered.

Intensive management should be guided by automated office BP measurements.

Patient selection for intensive management is recommended and caution should be taken in certain high-risk groups.
### Usual Office BP Threshold Values for Initiation of Pharmacological Treatment

<table>
<thead>
<tr>
<th>Population</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Risk (SPRINT population)</td>
<td>&gt;130</td>
<td>NA</td>
</tr>
<tr>
<td>Diabetes</td>
<td>&gt;130</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Moderate-to-high risk (TOD or CV risk factors)</td>
<td>&gt;140</td>
<td>&gt;90</td>
</tr>
<tr>
<td>Low risk (no TOD or CV risk factors)</td>
<td>&gt;160</td>
<td>&gt;100</td>
</tr>
</tbody>
</table>

TOD = target organ damage

*AOBP threshold ≥135/85
Recommended Office BP Treatment Targets

Treatment consists of health behaviour ± pharmacological management

<table>
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<tr>
<th>Population</th>
<th>SBP</th>
<th>DBP</th>
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<tbody>
<tr>
<td>High Risk</td>
<td>≤120</td>
<td>NA</td>
</tr>
<tr>
<td>Diabetes</td>
<td>&lt; 130</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>All others*</td>
<td>&lt; 140</td>
<td>&lt; 90</td>
</tr>
</tbody>
</table>

* Target BP with AOBP < 135/85
New Thresholds/Targets for the High Risk Patient Post-SPRINT: who does this apply to??

- Clinical or sub-clinical cardiovascular disease
  - OR
- Chronic kidney disease (non-diabetic nephropathy, proteinuria <1 g/d, *estimated glomerular filtration rate 20-59 mL/min/1.73m²)
  - OR
- †Estimated 10-year global cardiovascular risk ≥15%
  - OR
- Age ≥ 75 years

Patients with one or more clinical indications should consent to intensive management.

* Four variable MDRD equation
† Framingham Risk Score, D'Agastino, Circulation 2008
Limited or No Evidence:
- Heart failure (EF <35%) or recent MI (within last 3 months)
- Indication for, but not currently receiving a beta-blocker
- Frail or institutionalized elderly

Inconclusive Evidence:
- Diabetes mellitus
- Prior stroke
- eGFR < 20 ml/min/1.73m2

Contraindications:
- Patient unwilling or unable to adhere to multiple medications
- Standing SBP <110 mmHg
- Inability to measure SBP accurately
- Known secondary cause(s) of hypertension
SPRINT: SBPs Achieved

Average no. of medications
Intensive care: 2.8
Standard care: 1.8

The SPRINT Research Group, NEJM, Nov 9th, 2015
SPRINT Primary Outcome

NNT=61

Hazard ratio with intensive treatment, 0.75 (95% CI, 0.64–0.89)

No. at Risk
- Standard treatment: 4683, 4437, 4228, 2829, 721
- Intensive treatment: 4678, 4436, 4256, 2900, 779

The SPRINT Research Group, NEJM, Nov 9th, 2015
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Office BP Measurement Methods

Office (attended):

• Auscultatory (mercury, aneroid) – not recommended
• Non-automated oscillometric (electronic)

Automated office (unattended): AOBP

• Oscillometric (electronic)
Automated Office BP Measurement

• Measurement using electronic (oscillometric) devices in the upper arm
• Provider can be outside the room/area (mitigates white coat effect)
• Multiple readings
• Mean automatically calculated
Recommendation for BP Measurement

Automated office blood pressure (AOBP) is the preferred method of performing in-office BP measurement.

Automated Office (unattended, AOBP)
Oscillometric (electronic)
Comparison of Automated Office, Ambulatory and Pharmacy BP measurements

AOBP is Not Affected by the Setting in Which BP is Recorded

- Readings recorded in an ABPM unit or in an office waiting room are similar to AOBP recorded in a physician’s examination room


- AOBP results obtained in the pharmacy were comparable with AOBP results from the physician’s office

AOBP More Closely Approximates ABP Than Routine Office BP

<table>
<thead>
<tr>
<th></th>
<th>Centre for Studies in Primary Care&lt;sup&gt;1&lt;/sup&gt;</th>
<th>ABPM referral unit&lt;sup&gt;2&lt;/sup&gt;</th>
<th>CAMBO trial&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine manual office BP</td>
<td>151/83</td>
<td>152/87</td>
<td>150/81</td>
</tr>
<tr>
<td>Automated office BP</td>
<td>140/80</td>
<td>132/75</td>
<td>135/77</td>
</tr>
<tr>
<td>Awake ambulatory BP</td>
<td>142/80</td>
<td>134/77</td>
<td>133/74</td>
</tr>
</tbody>
</table>

*The automated office blood pressure (BP) and awake ambulatory BP were similar, and both were lower than the routine manual BP obtained in community practice.*

Predictive value of AOBP

AOBP predicts end-organ damage

- Systolic AOBP correlates with LVMI similarly to awake ABPM
- AOBP and 24-h ABPM have similar predictive ability for microalbuminuria
- AOBP is more strongly associated with cIMT (compared to OBPM)

\[cIMT: \text{Carotid Intima Media Thickness}\]
\[LVMI: \text{Left Ventricular Mass Index}\]

Predictive Value of AOBP

*The CHAP Study*

AOBP Predicts Cardiovascular Events

- 3627 community-dwelling residents, aged >65 yrs, untreated for hypertension – part of the CHAP trial
- BpTRU® device in community pharmacies
- f/u 4.9 ± 1.0 yrs for **fatal and non-fatal CV events**

# Predictive Value of AOBP

## Cardiovascular Events

### Systolic Blood Pressure

<table>
<thead>
<tr>
<th>Systolic BP</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 110</td>
<td>1.35 (0.8-2.3)</td>
</tr>
<tr>
<td>110-119 (referent)</td>
<td>1.00</td>
</tr>
<tr>
<td>120-129</td>
<td>1.08 (0.7-1.7)</td>
</tr>
<tr>
<td>130-139</td>
<td>1.30 (0.9-2.0)</td>
</tr>
<tr>
<td>135-144</td>
<td>1.66 (1.1-2.5)</td>
</tr>
<tr>
<td>140-149</td>
<td>1.79 (1.2-2.8)</td>
</tr>
<tr>
<td>150-159</td>
<td>1.96 (1.2-3.2)</td>
</tr>
<tr>
<td>160+</td>
<td>2.06 (1.3-3.4)</td>
</tr>
</tbody>
</table>

### Diastolic Blood Pressure

<table>
<thead>
<tr>
<th>Diastolic BP</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 60</td>
<td>1.06 (0.6-1.9)</td>
</tr>
<tr>
<td>60-69 (referent)</td>
<td>1.00</td>
</tr>
<tr>
<td>70-79</td>
<td>1.15 (0.8-1.6)</td>
</tr>
<tr>
<td>80-89</td>
<td>1.72 (1.2-2.5)</td>
</tr>
<tr>
<td>90+</td>
<td>2.07 (1.3-3.2)</td>
</tr>
</tbody>
</table>

What’s new?

• New thresholds and targets for high risk patients (SPRINT)
• Assessing clinic blood pressures using automatic electronic (oscillometric) monitors
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• Updating the evaluation of patients with suspected secondary forms of hypertension (focus on primary hyperaldosteronism)
• Updating the treatment of patients with hypertension with concurrent coronary artery disease
• New recommendations on the diagnosis and management of hypertension in pediatric patients (NOT the focus of this presentation)
## Health Behaviour Management

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduce foods with added sodium</td>
<td>→ 2000 mg /day</td>
</tr>
<tr>
<td>Weight loss</td>
<td>BMI &lt;25 kg/m²</td>
</tr>
<tr>
<td>Alcohol restriction</td>
<td>≤ 2 drinks/day</td>
</tr>
<tr>
<td>Physical activity</td>
<td>30-60 minutes 4-7 days/week</td>
</tr>
<tr>
<td>Dietary patterns</td>
<td>DASH diet</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>Smoke-free environment</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>Men &lt; 102 cm      Women &lt; 88 cm</td>
</tr>
<tr>
<td>Potassium supplementation</td>
<td>NEW RECOMMENDATION</td>
</tr>
</tbody>
</table>
New 2016 Recommendation: Health Behaviours

Potassium intake:

- In patients *not* at risk of hyperkalemia, increase dietary potassium intake to reduce blood pressure.
# Systematic Reviews Showing Significant Effect of Potassium on BP

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>RCTs</th>
<th>Total N</th>
<th>Pooled effect SBP</th>
<th>Pooled effect DBP</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cappuccio</td>
<td>1991</td>
<td>19</td>
<td>586</td>
<td>-5.9 (-6.6 to -5.2)</td>
<td>-3.4 (-4.0 to -2.8)</td>
<td>Mixed status, 5-112 days, 10-150 participants; ?all RCTs</td>
</tr>
<tr>
<td>Whelton</td>
<td>1997</td>
<td>33</td>
<td>2609</td>
<td>-3.11 (-4.3 to -1.9)</td>
<td>-1.97 (-3.4 to -0.5)</td>
<td>Mixed status; 4d-3yrs; 10-484 N</td>
</tr>
<tr>
<td>Geleijnse</td>
<td>2003</td>
<td>27</td>
<td>NR</td>
<td>-2.4 (-3.8 to -1.1)</td>
<td>-1.57 (-2.6 to -0.5)</td>
<td>Mixed status; &gt;2 wks duration</td>
</tr>
<tr>
<td>Dickinson</td>
<td>2006</td>
<td>5</td>
<td>425</td>
<td>-3.9 (-8.6 to 0.8)</td>
<td>-1.5 (-6.2 to 3.1)</td>
<td>Cochrane; hypertensive only; &gt;8wks; 12-212 N; still significant heterogeneity; one trial not pooled – no ss dec in BP</td>
</tr>
<tr>
<td>van Bommel</td>
<td>2012</td>
<td>10</td>
<td>563</td>
<td>-7.12 (-8.5 to -5.7)</td>
<td>-4.9 (-5.8 to -4.0)</td>
<td>Hypertensive pts with high Na diet; heterogeneity dec. after exc. of outlier</td>
</tr>
<tr>
<td>Aburto</td>
<td>2013</td>
<td>22</td>
<td>1606</td>
<td>-3.49 (-5.2 to -1.8)</td>
<td>-1.96 (-3.1 to -0.9)</td>
<td>Mixed status; &gt;4 wks; measured urinary K</td>
</tr>
<tr>
<td>Binia</td>
<td>2015</td>
<td>15</td>
<td>917</td>
<td>-4.7 (2.4 to -7)</td>
<td>- 3.5 (1.3 to 5.7)</td>
<td>Pts not on anti-htn Rx; mixed status; &gt;=4wks;</td>
</tr>
</tbody>
</table>
Increased Potassium Intake Decreases BP

A K-Rich Diet Has Additive Effects to Na Restriction

Potassium supplementation leads to a decrease in BP
Effect most consistently seen in patients with hypertension
Effect of K is modified by Na intake, with greater effect at higher baseline Na
Risk of Hyperkalemia with K Supplementation

Identify those at risk of hyperkalemia with potassium supplementation

Prior to advising increase in potassium intake, the following kinds of patients – who are at high risk of hyperkalemia, should be assessed for suitability, and monitored closely:

• Patients taking renin-angiotensin-aldosterone inhibitors
• Patients on other drugs that can cause hyperkalemia (trimethoprim and sulfamethoxazole, amiloride, triamterene)
• Patients with CKD (GFR < 45mL/min)
• Patients with baseline serum potassium > 4.5 mmol/L
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Recommendation: Endocrine Hypertension

• In patients with primary hyperaldosteronism and a definite adrenal mass who are eligible for surgery, adrenal venous sampling (AVS) is recommended to assess for lateralization of aldosterone secretion. AVS should be performed exclusively by experienced teams working in specialized centres.
Role for Adrenal Venous Sampling in Primary Aldosteronism

- Cohort of 203 patients from Mayo Clinic with PA, receiving CT and AVS
- 41% of those with normal CT had unilateral hypersecretion
- Only 51% of those with unilateral micronodules (<1 cm) had ipsilateral hypersecretion; 66% of those with unilateral macronodules (>1 cm) had ipsilateral hypersecretion
- 15% with micronodules and 3% with macronodules had contralateral hypersecretion
- 49% with bilateral micronodules and 33% with bilateral macronodules had unilateral hypersecretion

CT alone would incorrectly exclude 21% of patients for surgery
Based on CT alone, 25% would have received unnecessary surgery

What’s new?

• *Updating* the treatment of patients with hypertension with concurrent coronary artery disease

• *New* recommendations on the diagnosis and management of hypertension in pediatric patients (*NOT the focus of this presentation*)
What’s new?

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Prior recommendation:
For patients with stable angina, β-blockers are preferred as initial therapy. *CCBs may also be used.*

New recommendation:
For patients with hypertension and stable angina pectoris but without prior HF, MI or coronary artery bypass surgery, *either a beta blocker or a calcium channel blocker can be used as initial therapy.*
Beta blocker vs CCB in Treatment of CAD

The TIBET Trial

Events = MI, CV death, HF, ACS
Hard events + ischemic ST changes on 24 h ECG

Total Ischaemic Burden European Trial (TIBET): Effects of atenolol (N=226), nifedipine SR (N=232) or combination (N=224) on outcome in chronic stable angina. Dargie et al. EHJ 1996;17:104-112
The curves were not extended beyond 5 years as few patients were followed thereafter

APSIS: metoprolol vs verapamil in stable angina pectoris
No difference: CV events (30.8% v 29.3%) CV mortality 4.7% vs 4.7%), Non-fatal CV events 26.1 v 24.3%

*Hjemdahl P. et al. Favourable long term prognosis in stable angina pectoris: an extended follow up of the angina prognosis study in Stockholm (APSIS); Heart 2006;92:177-182*
CCB vs. Non-CCB in Treatment of CAD

The INVEST trial

As required to achieve blood pressure control:

CCB strategy:
Verapamil sustained release + Trandolapril + HCTZ

Non-CCB strategy:
Atenolol + HCTZ, + Trandolapril

- 22,000 HT patients with CAD
- Primary Outcome:
  Alive, Free of MI or Stroke
- Total FU: 61,807 pt-y, mean FU 2.7y,
- Annual event rate = 3.6%
What’s still important?

• The diagnosis of hypertension should be based on out-of-office measurements

• The management of hypertension is all about global cardiovascular risk management and vascular protection

• The most important step in prescription of antihypertensive therapy is achieving patient “buy-in” and adherence
1. **Out of office** assessment is the preferred means of hypertension Dx
2. **Measurement using electronic** (oscillometric) upper arm devices is preferred over auscultation

**ABPM**: Ambulatory Blood Pressure Measurement  
**AOBP**: Automated Office Blood Pressure
Out-of-Office BP Measurements

- ABPM has better predictive ability than OBPM and is the recommended out-of-office measurement method.
- HBPM has better predictive ability than OBPM and is recommended if ABPM is not tolerated, not readily available or due to patient preference.
- Identifies white coat hypertension and masked hypertension.
Out-of-Office BP Measurements are More Highly Correlated with BP-Related Risk

Value of Home Blood Pressures as Predictor of Target Organ Damage in Mild Arterial Hypertension

White Coat and Masked Hypertension

### Criteria for the Diagnosis of Masked Hypertension

<table>
<thead>
<tr>
<th></th>
<th>BP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office BP</td>
<td>&lt; 140/90</td>
</tr>
<tr>
<td>Awake Ambulatory</td>
<td>≥ 135/85</td>
</tr>
<tr>
<td>24-hour Ambulatory BP</td>
<td>≥ 130/80</td>
</tr>
</tbody>
</table>
Prevalence of Masked Hypertension

about 10% in the general population

about 30% in treated hypertensive patients*

higher in patients with diabetes and chronic kidney disease patients

One out of three treated hypertensive patients has masked hypertension

The Prognosis of White Coat and Masked Hypertension

![Graph showing CV events per 1000 patient-year for Normal, White coat, Uncontrolled, and Masked.]

- Normal: 23/685
- White coat: 24/656
- Uncontrolled: 41/462
- Masked: 236/3125

Okhubo et al. J. Am. Coll. Cardiol. 2005;46;508-515
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Impact of Discussing CAD Risk for Patients With Hypertension

Informing Patients of Their Global Risk improves BP Control
Cardiovascular Age™ www.myhealthcheckup.com

Statins are recommended in high risk hypertensive patients based on having established atherosclerotic disease or at least 3 of the following:

- Male
- 55 y or older
- Smoking
- Type 2 Diabetes
- Total-C/HDL-C ratio of 6 or higher
- Premature Family History of CV disease
- Previous Stroke or TIA
- LVH
- ECG abnormalities
- Albuminuria or CKD
- Peripheral Vascular Disease

The Treatment of Hypertension is All About Vascular Protection

ASCOT-LLA Lancet 2003;361:1149-58
Low dose ASA in hypertensive patients is recommended for patients >50 years.

*Caution should be exercised if BP is not controlled.*

Strong Evidence for Vascular Protection: Smoking Cessation

• **Tobacco use status** of all patients should be updated on a regular basis and health care providers should clearly advise patients to quit smoking.

• **Advice** in combination with pharmacotherapy (e.g., varenicline, bupropion, nicotine replacement therapy) should be offered to all smokers with a goal of smoking cessation.

*Cochrane network meta-analysis 2014
Kate Cahill et al*
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Adherence in Hypertensive Patients

Adherence Can Be Improved by a Multi-Pronged Approach

• Educate patients and patients' families about their disease/treatment regimens verbally and in writing
• Use an interdisciplinary care approach coordinating with work-site health care givers and pharmacists if available
• Healthcare practitioner-based telephone contact, particularly, over the first three months of therapy
• Encourage greater patient responsibility/autonomy in regular monitoring of their blood pressure
Adherence in Hypertensive Patients-II

Adherence Can Be Improved by a Multi-Pronged Approach

• Assess adherence to pharmacological and health behaviour therapies at every visit
• Teach patients to take their pills on a regular schedule associated with a routine daily activity e.g. brushing teeth.
• Simplify medication regimens using long-acting once-daily dosing
• Utilize single pill combinations
• Utilize unit-of-use packaging e.g. blister packaging
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hypertension.ca

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For professionals:
• Accredited 15.5 hour interdisciplinary training program
• Free monthly news updates, featured research and educational resources
• Become a member for special privileges and savings
2016 Hypertension Canada CHEP Guidelines for the Management of Hypertension

What’s new in the treatment of hypertension? What’s still really important?