Hypertension in General Practice
Primary Prevention

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Perth Cardiovascular Institute
Hollywood Pvt Hospital
Joondalup Health Campus
Royal Perth Hospital (Director of Physician Education)
Key recommendation areas

- Diagnosis and classification
- Assessment
- Measurement of blood pressure (BP)
- Drug treatment
- Lifestyle advice
- When to intervene
- Absolute risk
Five Things You Need to Know
We treat hypertension poorly!

First thing you need to Know.
AusDiab: The majority of patients with treated hypertension don’t achieve BP guidelines goal

Uncontrolled 60%

Controlled 40%

6 out of 10 treated hypertensive patients in Australia are not at BP goal

Prevalence of Hypertension in Australian Adults: AusDiab (n=11105)

- Hypertension (overall): 28.6% (95% CI 25.0 - 32.3)
- Treated Hypertension: 13.4% (95% CI 11.4 - 15.5)
- Untreated Hypertension: 15.2% (95% CI 13.2 - 17.2)

Hypertension is the Number One Risk Factor for Global Mortality

Attributable mortality in millions (total: 55,861,000)

- High Blood Pressure (BP): 6
- Tobacco: 4.5
- High cholesterol: 3.9
- Underweight: 3.6
- Unsafe sex: 2.9
- High body mass index: 2.4
- Physical inactivity: 2.0
- Alcohol: 1.7

Ezzati et al. Lancet 2002;360:1347–60
Figure 1. The percentage of burden of disease in Indigenous Australians by broad cause groups, measured in disability adjusted life years (DALYs)

- Cardiovascular disease: 32%
- Mental disorders: 17%
- Chronic respiratory disease: 15%
- Diabetes mellitus: 8%
- Malignant neoplasms: 8%
- Unintentional injuries: 8%
- Intentional injuries: 5%
- Other: 7%
Figure 2. The relative risk of disease burden in Indigenous Australians compared to the total Australian population by broad cause groups

- All causes: 2.4
- Intentional injuries: 4.1
- Unintentional injuries: 2.5
- Cancers: 1.7
- Diabetes: 5.1
- Chronic respiratory disease: 2.5
- Mental disorders: 1.6
- Cardiovascular disease: 4.6

Level of DALYs in total population
HTN in Australia

• 1 in 4 Australians are hypertensive

• > 70yrs old All Australians: 1 in 2 hypertensive
  – Often incorrectly diagnosed

• > 50yrs OLD : 1 in 2 Indigenous Australians are hypertensive
  – 6% -8 % of health gap is attributed to HTN
  – 2 out of 3 hypertensive indigenous patients are not treated

Mild hypertension can kill you!
What do we do?

• Case 1: John
  • 40 y old, F
  • Ex Smoker
  • BMI 32
  • Alcohol 3-4 beers a day
  • FHx of IHD
  • BP 148/76

• Case 2: Jane
  • 45 y old, F
  • Ex Smoker
  • BMI 30
  • Alcohol 5-10 drinks weekend
  • Father – stents at 55
  • BP 137/80
<table>
<thead>
<tr>
<th>Diagnostic category*</th>
<th>Systolic (mmHg)</th>
<th>Diastolic (mmHg)</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 120</td>
<td>&lt; 80</td>
<td>Recheck in 2 years (or earlier as guided by patient’s absolute cardiovascular risk).†</td>
</tr>
<tr>
<td>High-normal</td>
<td>120–139</td>
<td>80–89</td>
<td>Recheck in 1 year (or earlier as guided by patient’s absolute cardiovascular risk).†</td>
</tr>
<tr>
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<td>140–159</td>
<td>90–99</td>
<td>Confirm within 2 months. See When to intervene (page 12)</td>
</tr>
<tr>
<td>Grade 2 (moderate) hypertension</td>
<td>160–179</td>
<td>100–109</td>
<td>Reassess or refer within 1–7 days as necessary. See When to intervene (page 12)</td>
</tr>
<tr>
<td>Grade 3 (severe) hypertension</td>
<td>≥ 180</td>
<td>≥ 110</td>
<td>Reassess or refer within 1–7 days as necessary. See When to intervene (page 12)</td>
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<tr>
<td>Isolated systolic hypertension</td>
<td>≥ 140</td>
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<td>≥ 160</td>
<td>≤ 70</td>
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</table>

* When a patient’s systolic and diastolic BP levels fall into different categories, the higher diagnostic category and recommended action/s apply.
† See Assessing absolute cardiovascular risk (page 14)
‡ In middle-aged and elderly patients with cardiovascular risk factors or associated clinical conditions, isolated systolic hypertension with large pulse pressure indicates high absolute risk for cardiovascular disease.³
Cardiovascular (CV) Mortality Risk Doubles with Each 20/10 mmHg Increment in Systolic/Diastolic BP (SBP/DBP)*

*Individuals aged 40–69 years
Coronary heart disease (CHD) mortality rate, pictured on a log scale with 95 percent confidence intervals, in each decade of age in relation to the estimated usual systolic and diastolic blood pressure at the start of that decade. CHD mortality increases with both higher pressures and older ages. For diastolic pressure, each age-specific regression line ignores the left-hand point (ie, at slightly less than 75 mmHg), for which the risk lies significantly above the fitted regression line (as indicated by the broken line below 75 mmHg).

Data from Prospective Studies Collaboration, Lancet 2002; 360:1903.
Stroke mortality rate, pictured on a log scale with 95 percent confidence intervals, in each decade of age in relation to the estimated usual systolic and diastolic blood pressure at the start of that decade. Stroke mortality increases with both higher pressures and older ages. For diastolic pressure, each age-specific regression line ignores the left-hand point (i.e., at slightly less than 75 mmHg), for which the risk lies significantly above the fitted regression line (as indicated by the broken line below 75 mmHg).

Data from Prospective Studies Collaboration, Lancet 2002; 360:1903.
Cumulative incidence of end-stage renal disease (ESRD), due to any cause, according to blood pressure category in 332,544 men screened for the MRFIT trial. The adjusted relative risk increased from 1.0 in those with optimal blood pressure (<120/<80) to 1.9 with high normal blood pressure, 3.1 with mild hypertension, 6.0 with moderate hypertension, and 11.2 with severe hypertension. Patients with stage 1 hypertension or lower blood pressure were at very low risk of ESRD at 16 years (≤0.34 percent).

Cardiovascular (CV) Mortality Risk Doubles with Each 20/10 mmHg Increment in Systolic/Diastolic BP (SBP/DBP)*

- Individuals aged 40–69 years


*Individuals aged 40–69 years
Blood Pressure Reduction of 2 mmHg Decreases the Risk of Cardiovascular Events by 7–10% 

- Meta-analysis of 61 prospective, observational studies 
- 1 million adults 
- 12.7 million person-years 

2 mmHg decrease in mean SBP 

- 7% reduction in risk of ischemic heart disease mortality 
- 10% reduction in risk of stroke mortality 

What do we do?

Case 1: John
- 40y old, M
- Smoker
- BMI 32
- Alcohol 3-4 beers a day
- FHx of IHD
- BP 148/76
- Mild HTN

Case 2: Jane
- 47 y old, F
- Ex Smoker
- BMI 34
- Alcohol 5-10 drinks weekend
- Father – stents at 50
- BP 137/80
- High normal
Cardiovascular risk increased with high-normal BP

Men

Women

Cumulative incidence, percent

Time, years

High normal
Normal
Optimal

High normal
Normal
Optimal
What are the absolute Risk of CVS in 5 years?

**Case 1**
- 1%
- 5%
- 10%
- 15%
- 20%
  - John: 40 y old,
  - Smoker
  - BMI 32
  - Alcohol 3-4 beers a day
  - FHx of IHD
  - BP 148/76
  - Mild HTN
  - TC 5.8, HDL 0.9

**Case 2**
- 1%
- 5%
- 10%
- 15%
- 20%
  - Jane: 45 y old
  - Ex Smoker
  - BMI 30
  - Alcohol 5-10 drinks weekend
  - Father –stents at 55
  - BP 137/80
  - High normal
  - TC 5.8, HDL 0.9
Individualized risk assessment improves outcome and compliance
Guide to management of hypertension 2008
Assessing and managing raised blood pressure in adults
Updated December 2010

Australian cardiovascular risk charts
Figure 1. Australian cardiovascular risk charts

People without diabetes

**Women**
- Non-smoker
- Smoker

**Men**
- Non-smoker
- Smoker

Systolic blood pressure (mm Hg)
- 179*
- 160
- 140
- 120

Age
- 65–74
- 55–64
- 45–54
- 35–44

Total cholesterol: HDL ratio*
- 4
- 5
- 6
- 7
- 8

*In accordance with Australian guidelines, patients with systolic blood pressure ≥ 180 mm Hg, or a total cholesterol of > 7.5 mmol/L, should be considered at increased absolute risk of CVD.

Risk level for 5-year cardiovascular (CVD) risk

<table>
<thead>
<tr>
<th>High risk</th>
<th>Moderate risk</th>
<th>Low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 30%</td>
<td>10–15%</td>
<td>5–9%</td>
</tr>
<tr>
<td>25–29%</td>
<td>10–15%</td>
<td>&lt; 5%</td>
</tr>
<tr>
<td>20–24%</td>
<td>4–5%</td>
<td>5–9%</td>
</tr>
<tr>
<td>16–19%</td>
<td>4–5%</td>
<td>&lt; 5%</td>
</tr>
</tbody>
</table>
Case 1:
40 y old, M
Smoker
BMI 32
Alcohol 3-4 beers a day
FHx of IHD
BP 148/76
Mild HTN

Case 2
45 y old, F
Ex Smoker
BMI 30
Alcohol 5-10 drinks weekend
Father – stents at 55
BP 137/80
High normal
If Diabetic
Case1: 10 - 15%
Case2: 15 - 19%

*In accordance with Australian guidelines, patients with systolic blood pressure \( \geq 180 \text{ mm Hg}\), or a total cholesterol of \( > 7.5 \text{ mmol/L} \), should be considered at increased absolute risk of CVD.

Risk level for 5-year cardiovascular (CVD) risk

<table>
<thead>
<tr>
<th>High risk</th>
<th>Moderate risk</th>
<th>Low risk</th>
</tr>
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<tbody>
<tr>
<td>( \geq 30% )</td>
<td>10 - 15%</td>
<td>5 - 9%</td>
</tr>
<tr>
<td>25 - 29%</td>
<td>( &lt; 5% )</td>
<td></td>
</tr>
</tbody>
</table>
Absolute Risk of CVD in 5 Y

• Case 1
  • 5% -9% in 5 Years
  • 42 y old, M
  • Boiler maker
  • Smoker
  • BMI 32
  • Alcohol 3-4 beers a day
  • FHx of IHD
  • BP 148/76
  • Mild HTN
  • TC 5.8, HDL 0.9

• Case 2
  • 5%-9% 5 Years
  • 45 y old, F
  • Accountant
  • Ex Smoker
  • BMI 30
  • Alcohol 5-10 drinks weekend
  • Father –stents at 55
  • BP 137/80
  • High normal
  • TC 5.8, HDL 0.9
High cardiovascular risk can be assumed for the following groups of patients without using a risk calculator:

**Group A. Patients aged 75 years and over**
For almost all individuals aged ≥ 75 years, the absolute risk of a cardiovascular event in the next 5 years is > 15%.

**Group B. Patients with existing cardiovascular disease**
Assume risk of a cardiovascular event > 15% in the next 5 years if either of the following present:
- symptomatic cardiovascular disease (e.g. angina, myocardial infarction, chronic heart failure, stroke, transient ischaemic attack, peripheral arterial disease)
- left ventricular hypertrophy diagnosed with electrocardiography or echocardiography.

**Group C. Patients with associated clinical conditions and/or end-organ disease (see Table 3 – see fold out)**
For this group, assume risk of a cardiovascular event > 15% in the next 5 years. Antihypertensive drug treatment is required (e.g. to preserve renal function).

For all other patients, estimate absolute risk using the chart (Figure 1 – see centrefold).
What are the end organ damages?
<table>
<thead>
<tr>
<th>End-organ disease</th>
<th></th>
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<tbody>
<tr>
<td><strong>Left ventricular hypertrophy</strong></td>
<td>(diagnosed by electrocardiogram, echocardiogram)</td>
</tr>
<tr>
<td><strong>Microalbuminuria</strong></td>
<td>Defined as either of following:</td>
</tr>
<tr>
<td></td>
<td>• albumin:creatinine ratio $\geq 2.0$ mg/mmol (males) or $\geq 2.5$ mg/mmol (females) on spot urine screening test$^\dagger$</td>
</tr>
<tr>
<td></td>
<td>• 24-hour urinary albumin excretion rate $\geq 20 \mu$g/minute</td>
</tr>
<tr>
<td><strong>Chronic kidney disease</strong></td>
<td>Presence of either of the following:</td>
</tr>
<tr>
<td></td>
<td>• Proteinuria defined as either protein/creatinine ratio $\geq 30$ mg/mmol$^\dagger$ on spot urine test or urine protein $&gt; 300$ mg/day on timed urine sample</td>
</tr>
<tr>
<td></td>
<td>• Glomerular filtration rate (eGFR)$^\dagger$ $&lt; 60$ mL/minute/1.73m$^2$</td>
</tr>
<tr>
<td><strong>Vascular disease</strong></td>
<td>• Atherosclerotic plaque (aorta, carotid, coronary, femoral and iliac arteries) evident on ultrasound or radiology</td>
</tr>
<tr>
<td></td>
<td>• Hypertensive retinopathy (grade II or greater)</td>
</tr>
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</table>
Cumulative absolute risk of cardiovascular disease (CVD) at five years according to systolic blood pressure and specified levels of other risk factors. The reference category is a nondiabetic, nonsmoking 50 year-old woman with a serum total cholesterol (TC) of 154 mg/dL (4.0 mmol/L) and HDL-cholesterol of 62 mg/dL (1.6 mmol/L). The CVD risks are given for systolic blood pressure levels of 110, 130, 150, and 170 mmHg. In the other categories, the additional risk factors are added consecutively. As an example, the diabetes category is a 50-year-old diabetic man who is a smoker and has a total cholesterol (TC) of 270 mg/dL (7 mmol/L) and HDL-cholesterol of 39 mg/dL (1 mmol/L).

*Adapted from Jackson, R, Lawes, CM, Bennett, DA, et al, Lancet 2005; 365:434*
Four-year, age-adjusted incidence of cardiovascular events in men and women in the Framingham Study according to left ventricular mass determined by echocardiography. Subjects with increased left ventricular mass (far right panel) had a marked increase in cardiovascular risk.

Minimum investigations

- **Proteinurea** - DipStick
  - > 1+ Proteine then 24hr Urine
  - > 300mg/Day or 30mg/mmol protein Cr ratio

- **Microalbuminuria**
  - All and Specially diabetics
  - Albimin/Cr ratio
    - > 2mg/mmol for Male
    - > 2.5mg/mmol for Female

- **ECG +/- Echo**
- **U&E, Cr, Na, K**
- **Fasting Lipid Profile, TC/HDL ratio**
- **Fasting BSL**
When to start Therapy?
When to intervene in patients with confirmed hypertension – Recommendations

The decision to intervene and the development of a comprehensive management plan (including lifestyle advice and drug treatment) should be based on a thorough clinical investigation to identify associated clinical conditions and/or end-organ damage and assessment of absolute cardiovascular risk.

Initiate antihypertensive drug treatment immediately in hypertensive patients with any of the following:

- grade 3 hypertension or isolated systolic hypertension with widened pulse pressure (SBP ≥ 160 mmHg and DBP ≤ 70 mmHg)
- associated conditions or evidence of end-organ damage (regardless of BP)
- high absolute risk of cardiovascular disease, based on the presence of markers of high risk or as estimated using a risk calculator.

Advise lifestyle risk reduction for all patients, especially those with high-normal BP or hypertension (see Lifestyle modification, page 13).

Also consider drug therapy for:

- patients with moderate risk of a cardiovascular event (10–15% probability within the next 5 years) as estimated using a risk calculator
- Aboriginal and Torres Strait Islander adults.

Explain the health implications of current risk and the potential benefits of the recommended treatment.

> 15%
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† See Assessing absolute cardiovascular risk (page 14)

‡ In middle-aged and elderly patients with cardiovascular risk factors or associated clinical conditions, isolated systolic hypertension with large pulse pressure indicates high absolute risk for cardiovascular disease.
Immediate Medical therapy

1. Grade 3 HTN
2. End organ effects
3. High risks > 15%
4. Age > 60
5. Also - Indigenous Patients
What are the therapies?

- Non pharmacological
- Pharmacological
Lifestyle – Recommendations

Manage identified lifestyle risk factors in all patients, whether or not BP is elevated.

Advise patients to aim for healthy targets:

- **At least 30 minutes of moderate-intensity physical activity on most, if not all, days of the week (daily total can be accumulated e.g. three 10-minute sessions).** Advise patients of all ages to become more active.

- **Smoking cessation.** Refer patients to Quitline. Consider recommending nicotine replacement therapy and/or prescribing oral therapy (bupropion or varenicline) in patients who smoke more than 10 cigarettes per day and have no contraindications.

- **Waist measurement** < 94 cm for men and < 80 cm for women, body mass index (BMI) < 25 kg/m². When recommending weight loss, advise patients on reducing kilojoule intake as well as increasing physical activity.

- **Dietary salt restriction:** ≤ 4 g/day (65 mmol/day sodium). Recommend low-salt and reduced-salt foods as part of a healthy eating pattern.

- **Limited alcohol intake:** maximum of two standard drinks per day for men or one standard drink per day for women.
Weight loss-induced reduction in blood pressure

<table>
<thead>
<tr>
<th>Weight change, kg</th>
<th>Fall in diastolic BP, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; -9.5</td>
<td>10</td>
</tr>
<tr>
<td>-4.5 to -9.5</td>
<td>8</td>
</tr>
<tr>
<td>-2 to -4.5</td>
<td>6</td>
</tr>
<tr>
<td>+1 to -2</td>
<td>4</td>
</tr>
<tr>
<td>&gt; +1</td>
<td>2</td>
</tr>
</tbody>
</table>

Relationship between the quantity of weight lost and the fall in diastolic blood pressure in 308 moderately obese patients given a weight reduction regimen for 18 months. The patients began with a diastolic pressure between 80 and 89 mmHg; those who lost the most weight had the largest reduction in diastolic pressure. The decreases in the systolic pressure were similar.

Pooled results from all sodium-reduction trials concerning the mean net change in blood pressure due to restrictions in sodium intake among various subsets of patients.

* The mean change is compared with control values.

SBP: systolic blood pressure; DBP: diastolic blood pressure.

Data from Cutler, JA, Follmann, D, Allender, PS. Am J Clin Nutr 1997; 65:643S.
## Lifestyle modifications in the management of hypertension

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate systolic BP reduction, range*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (BMI, 18.5 to 24.9 kg/m²)</td>
<td>5-20 mmHg per 10-kg weight loss</td>
</tr>
<tr>
<td>Adopt DASH eating plan</td>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat</td>
<td>8 to 14 mmHg</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to no more than 100 meq/day (2.4 g sodium or 6 g sodium chloride)</td>
<td>2 to 8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)</td>
<td>4 to 9 mmHg</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>Limit consumption to no more than 2 drinks per day in most men and no more than 1 drink per day in women and lighter-weight persons</td>
<td>2 to 4 mmHg</td>
</tr>
</tbody>
</table>
Blood Pressure Reduction of 2 mmHg Decreases the Risk of Cardiovascular Events by 7–10%:

- Meta-analysis of 61 prospective, observational studies
- 1 million adults
- 12.7 million person-years

- 2 mmHg decrease in mean SBP
- 7% reduction in risk of ischemic heart disease mortality
- 10% reduction in risk of stroke mortality

Is there White coat HTN?

• 30% HTN in office -> **Normotensive** on home recordings (“White Coat Effect”)

• Normal BP variability makes “snapshot” office recordings often unreliable

• Target organ damage and cardiac events correlate better with home recordings than office recordings.
Hypertensive response to physician visit

Increase in systolic pressure, determined by continuous intraarterial monitoring, in 30 hypertensive patients as the blood pressure is taken with a sphygmomanometer by an unfamiliar doctor or nurse. A new doctor's visit raised the systolic pressure by a mean of 22 mmHg within the first few minutes, an effect that attenuated within five to 10 minutes and that was less pronounced with a nurse's visit. The alerting effect of the new physician's visit persisted for four daily visits in this study, but typically diminished with increasing familiarity. A similar pattern was seen with the diastolic pressure, with the peak increase being 13 mmHg during a physician's visit.

### DIURNAL VARIATION

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime (awake)</td>
<td>&lt; 135/85 mmHg</td>
</tr>
<tr>
<td>Night-time (asleep)</td>
<td>&lt; 120/70 mmHg</td>
</tr>
<tr>
<td>Over 24 hours</td>
<td>&lt; 130/80 mmHg</td>
</tr>
</tbody>
</table>
HT: Diagnostic Criteria

- Office: > 140/90
- Personal electronic: > 135/85
- ABPM: (Day) > 135/85
- ABPM: (Sleep) > 120/75
- ABPM: (24hr) > 130/80

Use “Mean BP’s”
“Nocturnal Non Dipping”

- ABPM studies
- Loss of nocturnal dipping is high risk
- More end organ effects at low BPs
- 24hr up titration of Renin Aldosterone system

<table>
<thead>
<tr>
<th>Table 1. Associated conditions and other influences</th>
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<tbody>
<tr>
<td><strong>Endocrine conditions</strong></td>
</tr>
<tr>
<td>Aldosteronism 5-10</td>
</tr>
<tr>
<td>Hypercortisolism 61,64</td>
</tr>
<tr>
<td>Pheochromocytoma 69</td>
</tr>
<tr>
<td>Acromegaly 71</td>
</tr>
<tr>
<td>Hyperthyroidism 75</td>
</tr>
<tr>
<td>Hyperparathyroidism 78</td>
</tr>
<tr>
<td><strong>Renal dysfunction</strong></td>
</tr>
<tr>
<td>Chronic kidney damage 11-14</td>
</tr>
<tr>
<td>Renal transplantation 12,18</td>
</tr>
<tr>
<td>Unilateral nephrectomy 33</td>
</tr>
<tr>
<td><strong>Disturbances of the autonomic nervous system</strong></td>
</tr>
<tr>
<td>Pure autonomic failure 57-60</td>
</tr>
<tr>
<td>Diabetic neuropathy 65-67</td>
</tr>
<tr>
<td>Uraemic neuropathy 12</td>
</tr>
<tr>
<td>Familial amyloidotic polyneuropathy 72</td>
</tr>
<tr>
<td>Obstructive sleep apnoea syndrome 76</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
</tr>
<tr>
<td>Salt-sensitive hypertension 41,44,61,62</td>
</tr>
<tr>
<td>Pre-eclamptic toxaemia 68</td>
</tr>
<tr>
<td>Malignant hypertension 70</td>
</tr>
<tr>
<td>Cardiac transplantation 71,74</td>
</tr>
<tr>
<td>Ethnicity 77**</td>
</tr>
<tr>
<td>Disturbances in circadian plasma melatonin changes 79</td>
</tr>
</tbody>
</table>
Does the Treatment benefits extend to Prehypertension?

An Evaluation of the Effects of an Angiotensin Receptor Blocker on Health-Related Quality of Life in Patients With High-Normal Blood Pressure (Prehypertension) in the Trial of Preventing Hypertension (TROPHY)

Setareh A. Williams, PhD; Eric L. Michelson, MD; Valerie A. Cain, MS; Min Yang, MD, PhD; Shawna D. Nesbitt, MD; Brent M. Egan, MD; Stevo Julius, MD, ScD; for the TROPHY Study Investigators

Prehypertension: should we be treating with pharmacologic therapy?

Brent M. Egan, Shawna D. Nesbitt and Stevo Julius
Does the Treatment benefits extend to Prehypertension?

- 2/3 in placebo developed HTN
- Protection for 2 years after treatment
- ? End point data

Figure 1. Kaplan-Meier analysis of new-onset clinical hypertension. (From Julius et al. [2], with permission. Copyright © 2007 Massachusetts Medical Society. All rights reserved.)

An Evaluation of the Effects of an Angiotensin Receptor Blocker on Health-Related Quality of Life in Patients With High-Normal Blood Pressure (Prehypertension) in the Trial of Preventing Hypertension (TROPHY)
Cardiovascular benefit of treating mild hypertension

Reduced incidence of fatal and total coronary heart disease (CHD) events and strokes following antihypertensive therapy in 17 controlled studies involving almost 48,000 patients with mild to moderate hypertension. The number of patients having each of these events is depicted, with active treatment lowering the incidence of coronary events by 16 percent and stroke by 40 percent. However, the absolute benefit - as shown, in percent, by the numbers at the top of the graph - was much less. Treatment for approximately 4 to 5 years prevented a coronary event or a stroke in two percent of patients (0.7 + 1.3), including prevention of death in 0.8 percent.

## Prehypertension: should we be treating with pharmacologic therapy?

Brent M. Egan, Shawna D. Nesbitt and Stevo Julius

*Ther Adv Cardiovasc Dis 2008 2: 305*

DOI: 10.1177/1753944708094226

<table>
<thead>
<tr>
<th>Study</th>
<th>Hazard ratio(^1) PHT2 vs NT</th>
<th>Absolute diff, %/yr(^2) PHT2 vs NT</th>
<th>NNT (10 yrs) 50%(^4)</th>
<th>NNT (10 yrs) 100%(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARIC [Kshirsagar, et al. 2006]</td>
<td>2.33, 1.85–2.92</td>
<td>~0.42%</td>
<td>48</td>
<td>24</td>
</tr>
<tr>
<td>Framingham [Nasan et al. 2001]</td>
<td>men 1.6, 1.1–2.2</td>
<td>~0.54% (0.43%)</td>
<td>47</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>women 2.5, 1.6–4.1</td>
<td>~0.51% (0.25%)</td>
<td>80</td>
<td>40</td>
</tr>
<tr>
<td>NHANES I [Liszka et al. 2005]</td>
<td>1.42, 1.09–1.84</td>
<td>~0.53%</td>
<td>38</td>
<td>19</td>
</tr>
<tr>
<td>NHEFS 1 [Ogden et al. 2000]</td>
<td></td>
<td></td>
<td>46(26)(^5)</td>
<td>23(13)(^5)</td>
</tr>
<tr>
<td>Strong Heart [Zhang et al. 2006]</td>
<td>1.80, 1.28–2.54</td>
<td>~0.61%</td>
<td>33</td>
<td>17</td>
</tr>
</tbody>
</table>

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**Compliance & Efficacy**

PHT2 = Prehypertension  130 – 139 : JNC7 (High normal in Australia)
Are we too relaxed with high normal/pre-hypertension group?

Do we document the target BP and 5 y risks for everyone?
<table>
<thead>
<tr>
<th>Patient group</th>
<th>Target (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>People with proteinuria $&gt;1 \text{ g/day}$ (with or without diabetes)</td>
<td>$&lt; 125/75$</td>
</tr>
<tr>
<td>People with associated condition/s or end-organ damage:*</td>
<td>$&lt; 130/80$</td>
</tr>
<tr>
<td>• Coronary heart disease</td>
<td></td>
</tr>
<tr>
<td>• Diabetes</td>
<td></td>
</tr>
<tr>
<td>• Chronic kidney disease</td>
<td></td>
</tr>
<tr>
<td>• Proteinuria ($&gt; 300 \text{ mg/day}$)</td>
<td></td>
</tr>
<tr>
<td>• Stroke/TIA</td>
<td></td>
</tr>
<tr>
<td>People with none of the following:</td>
<td>$&lt; 140/90$ or lower if tolerated</td>
</tr>
<tr>
<td>• Coronary heart disease</td>
<td></td>
</tr>
<tr>
<td>• Diabetes</td>
<td></td>
</tr>
<tr>
<td>• Chronic kidney disease</td>
<td></td>
</tr>
<tr>
<td>• Proteinuria ($&gt; 300 \text{ mg/day}$)</td>
<td></td>
</tr>
<tr>
<td>• Stroke/TIA</td>
<td></td>
</tr>
</tbody>
</table>
Are any of the following present?
- Grade 3 hypertension (SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg)
- Isolated systolic hypertension with widened pulse pressure (SBP ≥ 160 mmHg and DBP ≤ 70 mmHg)
- Associated conditions or target-organ damage (Table 3)

**Yes**
- Start drug treatment immediately (See Figure 3: Initiating drug treatment)
  - Lifestyle modification
  - Manage associated conditions

**No**
- Confirmed hypertension grades 1–2 (SBP 140–179 mmHg or DBP 90–109 mmHg)
- All other adults
  - Assess 5-year absolute cardiovascular risk (Figure 1)

**High**
- (>15%)
  - Start drug treatment immediately (See Figure 3: Initiating drug treatment)
    - Lifestyle modification
    - Manage associated conditions

**Moderate**
- (10–15%)
  - Lifestyle modification
  - Monitor BP
  - Reassess 5-year absolute cardiovascular risk in 3–6 months

**Low**
- (<10%)
  - Lifestyle modification
  - Monitor BP
  - Reassess 5-year absolute cardiovascular risk in 6–12 months
First choice
ACE inhibitor (or angiotensin II receptor antagonist)*
or
calcium channel blocker
or
low-dose thiazide diuretic (consider for people aged ≥ 65 years only)†

If target BP not reached
ACE inhibitor (or angiotensin II receptor antagonist)*
+ calcium channel blocker
or
ACE inhibitor (or angiotensin II receptor antagonist)*
+ low-dose thiazide diuretic

If target BP not reached
ACE inhibitor (or angiotensin II receptor antagonist)*
+ calcium channel blocker + low-dose thiazide diuretic

If target BP not reached
Consider seeking specialist advice
Antihypertensive drug treatment initiated

- Target BP achieved
  - **Medium – low risk**
    - Check every 6 months
    - Monitor BP and risk factors
    - Reinforce lifestyle measures

- Target BP not achieved at 3 months
  - **Medium – low risk**
    - Intensify lifestyle advice
    - If partial BP response: add drug from another class at low dose

- Significant adverse effects or no BP reduction
  - If monotherapy, change to another agent.
  - If adverse effects occur with combination therapy, identify agent responsible and replace with an agent from another class

**High risk**
- Check every 3 months
- Monitor BP and risk factors
- Reinforce lifestyle measures

**High risk**
- Add second agent from another class
- Increase doses to achieve target BP

If target still not achieved despite treatment adjustments
- Consider specialist care
- Further investigations as indicated
Fifth thing you should know

More is More.
Less is also More.
More agents are more effective than single agent

Less pills confer more compliance

• Multiple agents are needed to achieve target BP

• Combination pills achieve better results.
Multiple Antihypertensive Agents are Needed to Reach BP Goal

<table>
<thead>
<tr>
<th>Trial</th>
<th>SBP achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDRD</td>
<td>132 mmHg</td>
</tr>
<tr>
<td>HOT</td>
<td>138 mmHg</td>
</tr>
<tr>
<td>RENAAL</td>
<td>141 mmHg</td>
</tr>
<tr>
<td>AASK</td>
<td>128 mmHg</td>
</tr>
<tr>
<td>ABCD</td>
<td>132 mmHg</td>
</tr>
<tr>
<td>IDNT</td>
<td>138 mmHg</td>
</tr>
<tr>
<td>UKPDS</td>
<td>144 mmHg</td>
</tr>
<tr>
<td>ASCOT-BPLA</td>
<td>136.9 mmHg</td>
</tr>
<tr>
<td>ALLHAT</td>
<td>138 mmHg</td>
</tr>
<tr>
<td>ACCOMPLISH</td>
<td>132 mmHg</td>
</tr>
</tbody>
</table>

Initial 2-drug combination therapy

Average no. of antihypertensive medications

Choice of antihypertensive drug does not predict outcome

In the ALLHAT trial, cumulative event rates for the primary outcome (fatal coronary heart disease or nonfatal myocardial infarction) according to primary treatment with chlorthalidone, amlodipine, or lisinopril. Compared to chlorthalidone, there was no significant difference with amiodipine (relative risk 0.98) or lisinopril (relative risk 0.99 percent) at a mean of 4.9 years. 

Data from The ALLHAT Officers, JAMA 2002; 288:2981.
Avoid these combinations:

- ACE inhibitor (or angiotensin II receptor antagonist) plus potassium-sparing diuretic
- beta-blocker plus verapamil
- ACE inhibitor plus angiotensin II receptor antagonist.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Potentially beneficial</th>
<th>Potentially harmful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>Beta-blockers (except oxprenolol, pindolol), calcium channel blockers, ACE inhibitors</td>
<td>Caution</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Remodelling: ACE inhibitors, angiotensin II receptor antagonists¹</td>
<td>Contraindicated</td>
</tr>
<tr>
<td></td>
<td>Rate control: verapamil, diltiazem, beta-blockers</td>
<td></td>
</tr>
<tr>
<td>Asthma/COPD</td>
<td>Cardioselective beta-blockers, (e.g. atenolol, metoprolol): use cautiously in mild/moderate asthma/COPD only</td>
<td>Beta-blockers (except cardioselective agents)</td>
</tr>
<tr>
<td>Bradycardia, second-or third-degree atroventricular block</td>
<td>Beta-blockers, clonidine, methyldopa, moxonidine</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>Losartan</td>
<td>Thiazide diuretics</td>
</tr>
<tr>
<td>Gout</td>
<td>ACE inhibitors, angiotensin II receptor antagonists¹, thiazide diuretics, beta-blockers¹ (bisoprolol, carvedilol, metoprolol controlled release), spironolactone</td>
<td>Calcium channel blockers (especially verapamil, diltiazem) Alpha blockers in aortic stenosis Beta-blockers in uncontrolled heart failure</td>
</tr>
<tr>
<td>Heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post myocardial infarction</td>
<td>Beta-blockers (except oxprenolol, pindolol), ACE inhibitors, eplerenone</td>
<td></td>
</tr>
</tbody>
</table>
Excluding Hyperaldosteronism

- Hyperaldosteronism is more common than previously thought, and particularly common in “Resistant HT”
- A normal Renin/Aldosterone ratio effectively excludes hyperaldosteronism
- Many antihypertensive drugs affect the ratio
- Test before commencing antihypertensive treatment
Renal Sympathetic Afferent Nerves: Kidney as Origin of Central Sympathetic Drive

- Vasoconstriction
- Atherosclerosis
- Insulin Resistance
- Renal Ischemia
  - ↑ Adenosine production
- Contributing factors:
  - Obesity
  - Hyperlipidemia
  - Hypercapnia
  - Smoking
- Renin Release → RAAS activation
- Sodium Retention
- Renal Blood Flow
- Hypertrophy
- Arrhythmia
- Oxygen Consumption
- Heart Failure
PAC/PRA ratio in hypertension and hypokalemia

- Hypertension and hypokalemia
  - Plasma renin activity (PRA)
  - Plasma aldosterone concentration (PAC)
    - ↑ PRA
    - ↓ PAC
    - PAC-PRA ratio ≈ 10
      (277 in SI units)
    - Investigate for causes of secondary hyperaldosteronism
      - Renovascular hypertension
      - Diuretic use
      - Renin-secreting tumor
      - Malignant hypertension
      - Coarctation of the aorta
    - ↓ PRA
    - ↑ PAC
    - PAC-PRA ratio ≥ 20
      (≥ 555 in SI units)
      and
      - PAC ≥ 15 ng/dL (≥ 416 pmol/L)
    - Investigate for primary aldosteronism
    - Congenital adrenal hyperplasia
    - Exogenous mineralocorticoid
    - DOC-producing tumor
    - Cushing's syndrome
    - 11-beta-HSD deficiency
    - Altered aldosterone metabolism
    - Liddle's syndrome
    - Glucocorticoid resistance

Use of the plasma aldosterone concentration (PAC)-to-plasma renin activity (PRA) ratio to differentiate among different causes of hypertension and hypokalemia.

Resistant HTN

- Consider secondary HTN
- Compliance
- Change to different class /combinations
  - Alpha blockers, Beta Blockade, Aldosterone Blockers
- Specialist review
- Renal Nerve Denervation
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