

# The global impact of hypertension

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According to the World Health Organization, hypertension is the most important and leading risk factor for global death and disability.

**It is estimated that hypertension is the** cause of about 50% of heart disease, stroke and heart failure (HF), 18% of deaths overall and more than 40% of deaths in people with diabetes. In addition, hypertension is a leading risk for dementia, renal failure and risk for foetal and maternal death in pregnancy.

Hypertension is very common as approximately four in 19 adults older than 25 years of age have hypertension, another one in five have prehypertension and nine in 10 adults living to 80 years of age will develop hypertension.

Hypertension also disproportionately impacts low-income and middle-income countries as 60% of those with hypertension are in these economically developing countries.

Effective life-style and drug treatments are available that could control blood pressure (BP) and improve the outcome of hypertension if we can overcome treatment inertia and improve adherence to these treatments.

## **DRUG THERAPY: WHAT ARE THE OUTCOMES?**

The results of the two most recent and both extensive meta-analyses show remarkable similar results:

**1** Law meta-analysis: For a standardised reduction of blood of systolic BP of 10mmHg and diastolic BP (DBP) of 5mmHg (10/5mmHg), the relative risk reduction for coronary heart disease (CHD) is 22% (95% confidence interval (CI): 17%-27%) and for stroke is 41% (95%CI: 33%-48%).

**2** Thomopoulos meta-analysis: For a standardised reduction of SBP of 10mmHg and DBP of 5mmHg, the relative risk reduction for CHD is 16% (95%CI: 9%-21%) and for stroke is 33% (95%CI: 27%-39%). This meta-analysis also showed that cardiovascular (CV) mortality and all-cause mortality are reduced in the treatment of hypertension. Treatment, even as little as 10/5mmHg can and does prolong life. The bottom line of both these very large meta-analyses is that reduction of BP is the most important aspect of the treatment and that specific drugs may not be the most important aspect.

**3** The Blood Pressure Lowering Treatment Trialists' Collaboration has shown in a meta-analysis of 31 randomised clinical trials (RCTs) on 190 606 people that





there are no clear differences between different age groups (<65 years and >65 years) in the effects of lowering BP or any difference between the effects of the drug classes on major CV events.

**4** A recent meta-analysis has shown benefit even in people with mild hypertension with no sign of CV disease.

### WHICH DRUG AS MONOTHERAPY IS THE BEST?

The Law meta-analysis did not find any particular drug class that was outstandingly better than another drug class and all drug classes had very similar effectiveness in reducing CV events for a given reduction in BP with the exception that calcium channel blockers, mainly of the dehidropiridine class, seem to be the slightly better in protecting from stroke than any other drug class.

Thomopoulos-meta-analysis, in another meta-analysis of 50 RCTs involving 247,006 patients, showed that the effects of all drug classes were not significantly different on most CV outcomes when their BP lowering effect is equivalent.

When compared to all other classes together, diuretics are superior in preventing HF, beta blockers less effective in preventing stroke, calcium channel blockers (CCB) superior in preventing stroke and all-cause death but inferior in preventing HF, angiotensin-converting-enzyme (ACE) inhibitors more effective in preventing CHB and less effective in preventing stroke and angiotensin receptor blockers (ARBs) inferior in preventing CHD and renin-angiotensin (RAS) blockers as group more effective in preventing HF.

When patients with different levels of cardiovascular risk were evaluated, no drug class was found to change in effectiveness with the level of risk. The bottom line is that as monotherapy, no single drug was superior in all CV outcome and all the drugs have strong points and weak points.

Low-dose hydrochlorothiazide (12.5mg) does not seem suitable as monotherapy because in a number of studies with 24-ambulatory BP monitoring, low-dose hydrochlorothiazide (HCTZ) did not reduce nocturnal BP.

Another problem with monotherapy is that in most clinical trials it was shown that control of BP was possible in only 20%-30% of patients and this under the strict supervision of the clinical trial.

### COMBINATION DRUG THERAPY

The increasing use of combination drug treatment of hypertension is probably a reflection of the need to achieve a specific target blood pressure and control of hypertension, which is not always possible with monotherapy and the fact that no single

drug is superior in reducing all cardiovascular outcomes equally well.

The use of a RAS blocker (e.g. ACE or ARB) plus a dehidropiridine CCB seems to be favoured by most if not all guidelines. The European and American guidelines also add a RAS blocker and a diuretic.

The use of single-pill combinations (commonly but inaccurately referred to as fixed-dose combinations) has the proven advantage of an increased adherence rate of up to 26%. These single-pill combinations have different dosages of the pills so that uptitration is possible.

The use of a RAS blocker plus a CCB or a diuretic sometimes is not enough to reach target BP. The most recommend a combination of all three (RAS-blocker+CCB+diuretic). This is currently also the definition of resistant hypertension.

The question is now what to add if there is resistant hypertension. The current favourite is spironolactone, an aldosterone antagonist in a low dose of 25mg/day to 50 mg/day. In a recent trial, the PATHWAY-2 study, the usefulness of this drug was demonstrated to improve BP control in resistant hypertension and it may be that the definition of resistant hypertension may have to be changed after this trial.

### TARGET OR GOAL BLOOD PRESSURE

Current recommendations are that the goal BP of all hypertensive patients up to the age of 80 years is to be below 140/90mmHg and that above the age of 80 years those mobile non-frail elderly should have blood pressure levels of below 150/90 mmHg.

The Eight Joint National Committee Guidelines have recently raised the target BP of all patients above 60 years to below 150/90mmHg. This recommendation has sparked a huge debate of whether this is advisable. There were two pieces of evidence recently published which has clarified some aspects of the target BP.

A meta-analysis of 19 trials involving 44 989 people with hypertension was evaluated to examine different blood pressure levels. The BP in the intensive group was 133/76mmHg and in the standard group the BP was 140/81mmHg.

Intensive blood pressure reduction in high-risk patients was associated with a reduction of 14% (95%CI: 4%-22%) in major CV events, myocardial infarction reduction of 13%, stroke reduction of 22%, albuminuria reduction of 10% - all statistically significant. There was no effect on HF or mortality.

In the Systolic Blood Pressure Intervention Trial, a randomised study, reducing SBP pressure to 121.4 mmHg as compared to SBP of 136.2mmHg in nondiabetic hypertensive

patients was associated with significant reduction of major CV events and mortality. These lower levels of treated BP were also associated with significant serious side-effects. It appeared that older people benefitted more than younger people.

These two trials have shown that there need to be a re-evaluation of target or goal BP levels.


### CONCLUSIONS

- 1** Hypertension is a common clinical problem.
- 2** Hypertension is a very significant treatable risk factor, but inertia in treatment and poor adherence to treatment are significant stumbling blocks in the management of hypertension.
- 3** Monotherapy does not favour a specific universal excellent drug as all classes have their advantages and disadvantages.
- 4** Combination therapy is probably the way forward and increasing use is made of single-pill combinations.
- 5** Target BP levels are currently in debate but increasing evidence favours lower BP levels than currently advocated.

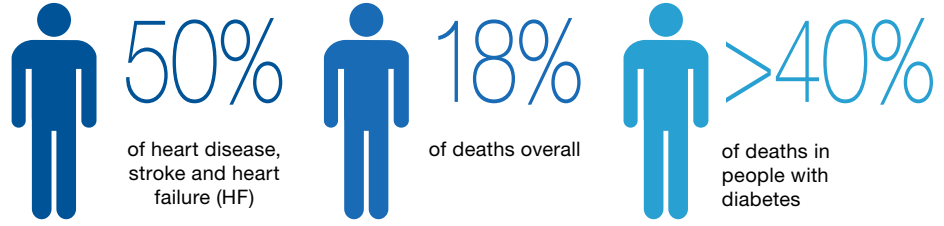
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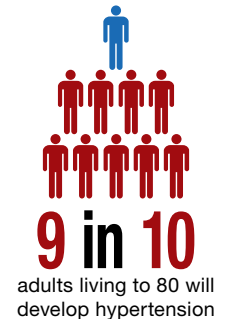
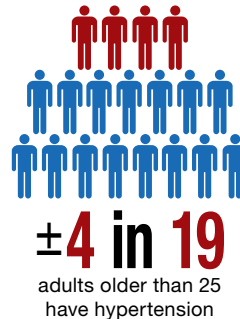
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### Hypertension is the cause of about



Hypertension is the leading risk for dementia, renal failure and risk for foetal and maternal death in pregnancy

Hypertension is very common in adults



An estimated **53** men and **78** women die in South Africa each day from the impact of hypertension.

