



Disease backgrounder

Hypertension

What is hypertension?

- Essential hypertension can be defined as a rise in blood pressure (BP) of unknown cause that increases the risk for cerebral, cardiac and renal events.¹
- Elevated BP can lead to end-organ damage and end-stage disease. Subtle target-organ damage such as left-ventricular hypertrophy (LVH), microalbuminuria and cognitive dysfunction takes place early in the course of hypertensive cardiovascular disease (CVD), whereas catastrophic events such as stroke, heart attack, renal failure and dementia usually happen after long periods of uncontrolled hypertension.¹
- For the general population, hypertension is defined as repeated elevation of systolic BP (SBP) ≥ 140 mmHg and diastolic BP (DBP) ≥ 90 mmHg.
- However, this threshold for hypertension (and the need for therapy) is flexible and should be based on the total cardiovascular (CV) risk of the individual.² For example, in patients with additional risk factors for CVD such as diabetes, coronary artery disease (CAD) or hyperlipidemia, the threshold for treating high BP will be $< 140/90$ mmHg.
- Most patients with hypertension have additional CV risk factors, which increase the overall risk of CVD and renal disease, necessitating tighter BP control.
- There is a continuous relationship between both DBP and SBP and CV morbidity and mortality, and there is no evidence of a threshold down to at least 115/75mmHg.^{3,4}
 - A 20mmHg increase in SBP or a 10mmHg increase in DBP doubles the risk of death from stroke, ischemic heart disease and other vascular diseases.
- Both SBP and DBP show a graded independent relationship with end-stage renal disease.⁵ For example, a BP of 130–139/85–89mmHg almost doubles the risk of end-stage renal disease compared with a BP of $< 120/80$ mmHg, and moderate hypertension (160–179/100–109mmHg) increases the risk by 6-fold.⁵
- Hypertension is called the silent killer due to the fact that it is a disease without symptoms which ultimately, when untreated, will cause death.



The impact of hypertension

- Hypertension affects nearly 1 billion people worldwide – about 25% of the total adult population.⁶
- Prevalence of hypertension is similar in both men and women⁷ and consistently increases with age in all world regions. As BP tends to increase with age and as the trend for longer life continues, hypertension is likely to become more prevalent in the future.
- It is estimated that by 2025, 29% of all adults worldwide will have hypertension – that is 1.56 billion people.⁷
- Hypertension also has a major impact on morbidity and is ranked third as a cause of disability-adjusted life-years (DALY).⁸ DALY are a measure of disease burden based on the estimated rate of premature death, disability and infirmity caused by a given disease.
- In 2002, the DALY for hypertension was estimated at 64 million – to put this into context, globally tobacco is associated with 59 million DALY, high cholesterol is associated with 40 million DALY, and global climate change is associated with 6 million DALY. The burden of hypertension is second to the burden of alcohol in lower-mortality, developing regions and second to tobacco in the developed world – it therefore represents a tremendous burden in many regions of the world.⁸
- The estimated direct and indirect cost of hypertension in 2009 is \$73.4 billion in the US alone.⁹

Therapeutic approach

- Hypertension control is suboptimal around the world, and the level of control varies between regions. For example, 29% of hypertensive patients in the USA have controlled BP below 140/90mmHg compared with 17% in Canada and less than 10% in Europe.¹⁰
- The decision to start therapy depends not only on the BP of the individual, but also on the overall level of CV risk.² The target should be <140/90mmHg and lower if tolerated, and <130/80mmHg in patients with diabetes or other additional risk factors for CVD.
- A large number of clinical trials have shown that BP reduction in patients with hypertension significantly reduces morbidity and mortality.²
- Even small reductions in BP can have a large impact on the future health of people with hypertension. A mean 2mmHg reduction in DBP in the general population would result in up to¹¹:
 - 17% reduction in the prevalence of hypertension
 - 14% reduction in the risk of stroke or transient ischemic attack
 - 6% reduction in the risk of coronary heart disease.



- Lifestyle changes should be encouraged, where appropriate, to manage hypertension and/or CV risk, including:
 - Smoking cessation
 - Weight reduction or stabilization
 - Reduction in excessive alcohol intake
 - Physical exercise
 - Reduced salt intake
 - Increased fruit and vegetable intake, decreased saturated and total fat intake.
- Most patients with hypertension will also require pharmacotherapy to reduce BP. Delaying therapy can result in poorer outcomes; therefore, the most recent recommendations suggest that prompt pharmacotherapy is optimal.²

Pharmacotherapy to treat hypertension

- There are five main classes of antihypertensive agent – thiazide diuretics, calcium channel blockers (CCBs), angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and β -blockers.
- Monotherapy with any of these drugs achieves target BP in a limited number of patients; in high-risk patients, combination therapy is nearly always required.¹²
- Starting a patient on monotherapy or combination therapy depends on the initial CV risk and the target BP but both are valid treatment options for hypertension.
- Optimal BP control may be achieved with the combination of more than one antihypertensive agent. Drugs for hypertension can be combined if they have different and complementary mechanisms of action and if the combination has a favorable tolerance profile. Preferred combinations that are effective and well tolerated include²:
 - CCB and ARB
 - CCB and ACE inhibitor
 - CCB and thiazide diuretic
 - CCB and β -blocker
 - Thiazide diuretic and ARB
 - Thiazide diuretic and ACE inhibitor.
- In addition to the BP-lowering effects of the five main classes of antihypertensive agents, some trial data show improvements in subclinical organ damage. For example, CCBs have been shown to reduce LVH, and slow the progression of atherosclerosis,¹³ and ARBs and ACE inhibitors reduce LVH, microalbuminuria and proteinuria.^{14–16}



- European Society of Hypertension/European Society of Cardiology guidelines for the management of hypertension² stipulate that the choice of specific antihypertensive drugs or drug combinations should take into account the following considerations:
 - Patient's previous experience with particular drug class(es)
 - The effects of particular drugs on the individual's CV risk profile
 - Presence of subclinical organ damage, CVD, renal disease or diabetes
 - Presence of other disorders that may limit the use of particular antihypertensive drug classes
 - Possible drug interactions
 - Cost of drugs (but never a consideration over efficacy, tolerability or patient safety)
 - Preference for drugs that have a 24-hour effect with once-daily administration
 - Continued attention to side effects.

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