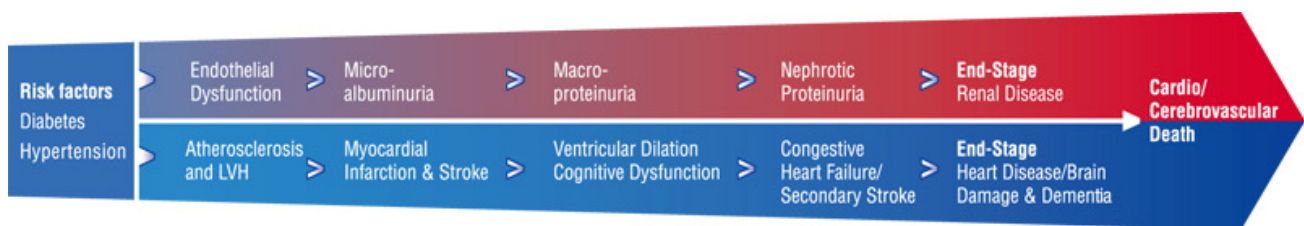


Cardiovascular Disease

- Cardiovascular disease (CVD) is one of the leading causes of death and disability. Worldwide, CVD results in approximately 17 million deaths each year which represents 30% of all global deaths – most significantly from myocardial infarction (7.2 million) and stroke (5.5 million). By 2015, global CVD deaths are predicted to reach approximately 20 million, according to an estimate of the World Health Organization (WHO). Currently being a leading cause of disability, by 2020 CVD is expected to be the largest cause of disability worldwide.
- There are many risk factors associated with CVD, including life-style (smoking, physical inactivity), modifiable factors (hypertension, dyslipidaemia, diabetes mellitus) and non-modifiable factors (age, sex). One of the main factors responsible for CVD is arterial hypertension.
- The World Health Organization (WHO) expects that 600 million people with high blood pressure bear an increased risk of myocardial infarction or stroke. The development of CVD from the onset to end-stage heart disease shows a stepwise progression: mechanical or biochemical changes lead to arteriosclerotic changes and thrombotic occlusion. The ischemic organ damage finally results in progressive functional impairment.

The Cardiovascular Continuum



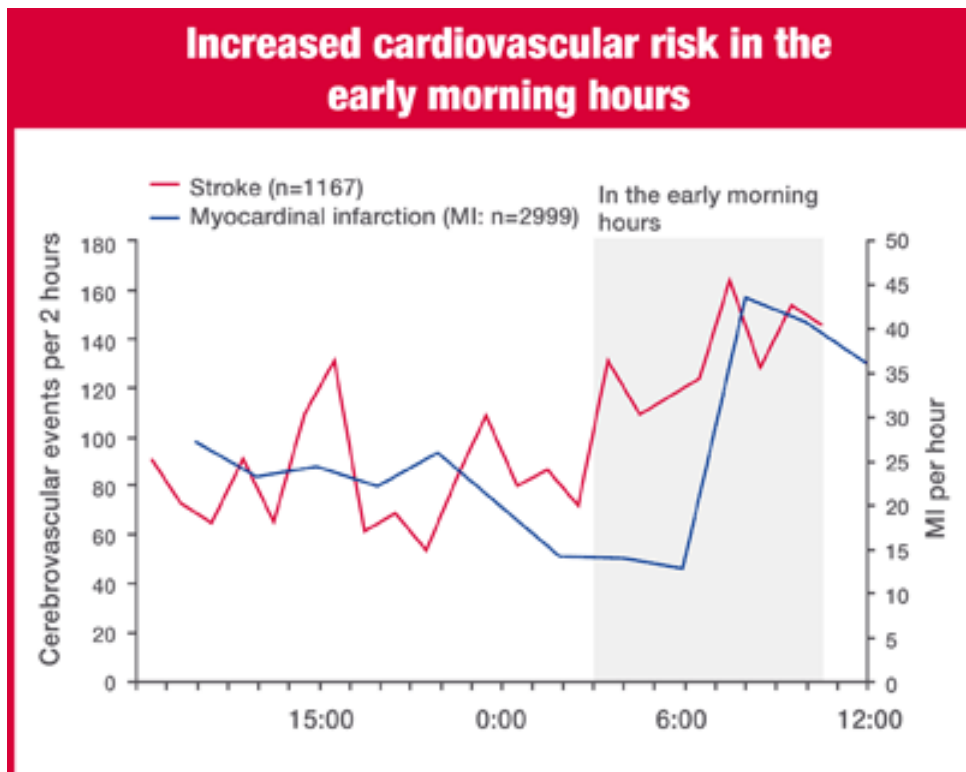
Adapted from Dzau, Braunwald. Am Heart J 1991;121:1244-1263

- Angiotensin II (All) - acting through the AT₁-receptor - is involved in every step of this multi-factorial process. Therefore, blocking the AT₁-receptor can be expected to significantly reduce cardiovascular morbidity and mortality by retarding the progression of CVD.

- CVD places a heavy burden on the patient and the community:
 - At least 20 million people survive heart attacks and strokes every year, many of whom require clinical care afterwards.
 - Heart disease impacts quality of life through chronic pain or discomfort, activity restriction, disability and unemployment.
 - Of the estimated 10 million people who survive a stroke each year, over half are permanently disabled, placing a burden on the family and community.
 - A major stroke is viewed by more than half of those at risk as being worse than death.
 - Disability due to stroke may include loss of vision and/ or speech, paralysis and confusion.

Essential Hypertension

- Essential hypertension can be defined as a rise in blood pressure of unknown cause that increases the risk for cerebral, cardiac and renal events.¹
- When blood pressure is too high, it can lead to end-organ damage and end-stage disease. Subtle target-organ damage such as left-ventricular hypertrophy, microalbuminuria and cognitive dysfunction takes place early in the course of hypertensive cardiovascular disease, whereas catastrophic events such as stroke, heart attack, renal failure and dementia usually happen after long periods of uncontrolled hypertension.¹
- Blood pressure follows a circadian rhythm in a normal individual: it falls during sleep and rises rapidly just before awakening.^{2, 3} In hypertensive patients, the early morning sharp rise in blood pressure coincides with a higher incidence of cardiovascular events.^{4, 5}

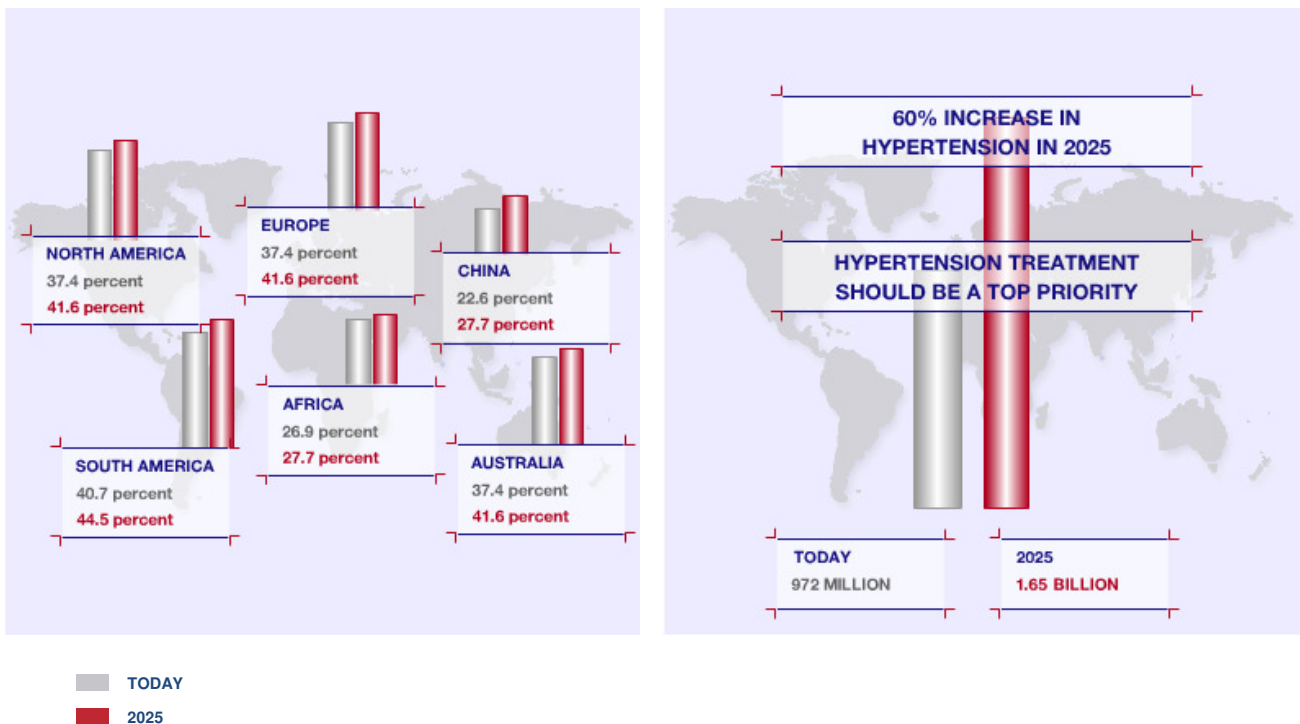


Epidemiology of Hypertension

- Essential hypertension is highly prevalent and is often associated with concomitant risk factors for cardiovascular disease. Therefore, it is an important public health issue worldwide.

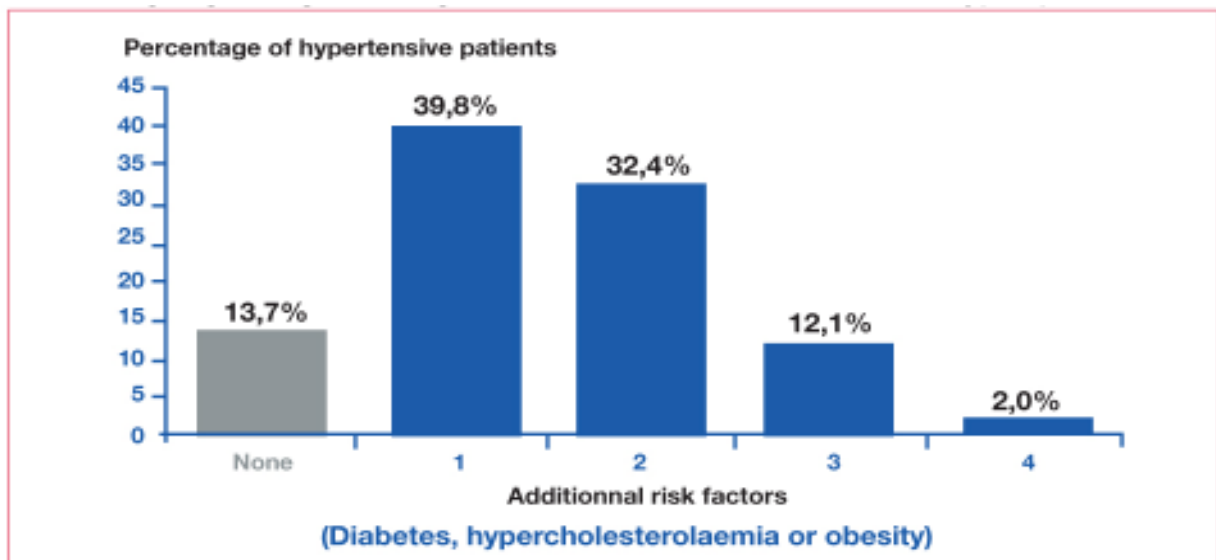
Prevalence⁶

- In 2000, the total number of adults with hypertension was estimated at 972 million, 333 million in economically developed countries and 639 million in economically developing ones.
- This number is expected to increase by 60% and reach a total of 1.56 billion in 2025, mainly because of population aging, increased demographics and lifestyle changes (diet rich in sugar and high-fat processed foods, and sedentary behaviour).



Association with Concomitant Cardiovascular Risk Factors

- Essential hypertension also often clusters with other cardiovascular risk factors such as ageing, being overweight, insulin resistance, diabetes and hyperlipidaemia.¹ In fact, only a small fraction of the hypertensive population has an elevation of blood pressure alone, with the great majority exhibiting additional cardiovascular risk factors.⁷



Blood Pressure Measurement

- Because blood pressure is characterized by large spontaneous variations during the day, the diagnosis of hypertension should be based on multiple blood pressure measurements.⁸
- Although office blood pressure should be used as a reference, the new 2007 ESH Hypertension Guidelines acknowledge that ambulatory blood pressure monitoring (ABPM) may improve prediction of cardiovascular risk in both, treated and untreated patients.⁸ They recommend ABPM particularly if office blood pressure measurements vary widely or are unexpectedly high in patients at otherwise low cardiovascular risk. In addition, self-measurement of blood pressure at home is encouraged, as it not only yields more information on the therapeutic coverage throughout the dose-to-dose time interval but it may also improve patients' adherence to treatment regimens.⁸

Other Risk Factors and Disease History	Blood Pressure (mmHg)				
	Normal SBP 120-129 or DBP 80-84	High Normal SBP 130-139 or DBP 85-89	Grade 1 SBP 140-159 or DBP 90-99	Grade 2 SBP 160-179 or DBP 100-109	Grade 3 SBP ≥ 180 or DBP ≥ 110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1-2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors or TOD or diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Associated Clinical Conditions	High added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk
	< 15%	15%-20%	20%-30%	>30%	

Total Cardiovascular Risk Assessment

- Hypertension diagnosis should not only be based on repeated blood pressure measurement, but also on the evaluation of the patient's family and clinical history, as well as on the search for associated risk factors and subclinical organ damage.⁸ Dysmetabolic risk factors and subclinical organ damage are common in hypertensive patients.⁸ When concomitantly present, blood pressure and metabolic risk factors potentiate each other, leading to a higher total cardiovascular risk.⁸
- Furthermore, the importance of subclinical organ damage as an intermediate stage in the cardiovascular disease continuum and as a determinant of total cardiovascular risk underlines the need to carefully search for signs of organ involvement.⁸

Total Therapeutic approach

- In order to maximize cost-efficacy of the management of hypertension, the intensity of the therapeutic approach should be graded as a function of total cardiovascular risk.⁸ Therefore, hypertensive patients should be classified not only in relation to the grades of hypertension, but also in terms of the total cardiovascular risk resulting from the coexistence of different risk factors, organ damage and disease.⁸
- As before, one of the central themes that the guidelines stress is that the threshold for hypertension and the need for drug treatment should be considered as flexible, based on the level of total (global) cardiovascular risk.⁸ In line with this, the 2003 classification of cardiovascular risk, as low, moderate, high, and very high to indicate the 10-year risk of cardiovascular morbidity and mortality, is also retained in the 2007 guidelines.⁸
- The "flexible threshold" for initiating drug treatment should be $\geq 140/90$ mmHg for all hypertension patients and $< 140/90$ mmHg in high-risk patients, while stressing that drug treatment should never be delayed unnecessarily, especially in patients at higher level of risk.⁸
- The guidelines stipulate that the choice of specific antihypertensive drugs or drug combinations should take into account the following considerations:⁸
 - Patient's previous experience with particular drug class(es)
 - The effects of particular drugs on the specific details of a given patient's cardiovascular risk profile
 - Presence of subclinical organ damage, cardiovascular disease, 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 protection of the patient)
 - Preference for drugs that have a 24-hour effect with once-daily administration
 - Continued attention to side effects

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