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HYPERTENSION AS A CARDIOVASCULAR RISK FACTOR

Hypertension is the most prevalent cardiovascular disorder, affecting 20–50% of the adult population worldwide, and ranking, in a comparative risk assessment of 84 risk factors and risk factor clusters, high for global disease burden (1). Likewise, it has been identified as a risk factor for coronary heart disease, stroke, peripheral arterial disease and heart and renal failure in both men and women in a large number of epidemiological studies (2–5). Hypertension has also been shown to increase the risk of atrial fibrillation (6). In addition, observational studies have found that blood pressure (BP) correlates inversely with cognitive function and that hypertension is associated with an increased incidence of dementia (7,8).

In the year 2001, the worldwide burden of disease attributable to high systolic BP (≥115 mmHg) was 54% for stroke, and 47% for ischaemic heart disease (9). About half of this burden was experienced by individuals with hypertension, the other part in those with a lesser degree of high BP. More than 80% of the attributable burden of the disease was found in low- and middle-income regions.

A meta-analysis of individual data of one million adults from 61 prospective observational studies found a continuous graded independent relationship with the risk of stroke and coronary events (10). Coronary heart disease (CHD) and stroke mortality increases progressively and linearly from BP levels as low as 115 mmHg systolic and 75 mmHg diastolic upward (Figures 2.1 and 2.2). The increased risks are seen in all age groups from 40 to 89 years of age.

For every 20 mmHg systolic or 10 mmHg diastolic BP increase, there is a doubling of mortality from CHD and stroke.

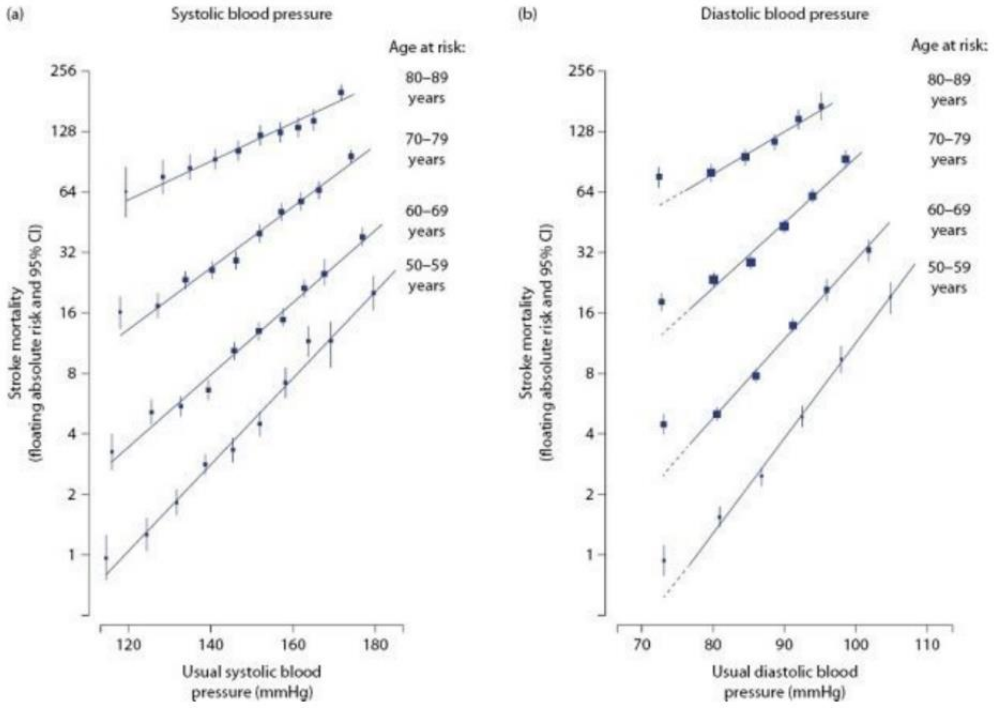

Figure 2.1 Stroke mortality rate in each decade of age plotted for the usual systolic (a) and diastolic (b) blood pressure at the start of that decade. Data from 1 million adults in 61 prospective studies. (Adapted from Lewington S et al. *Lancet* 2002; 360(10): 1903–1913.)

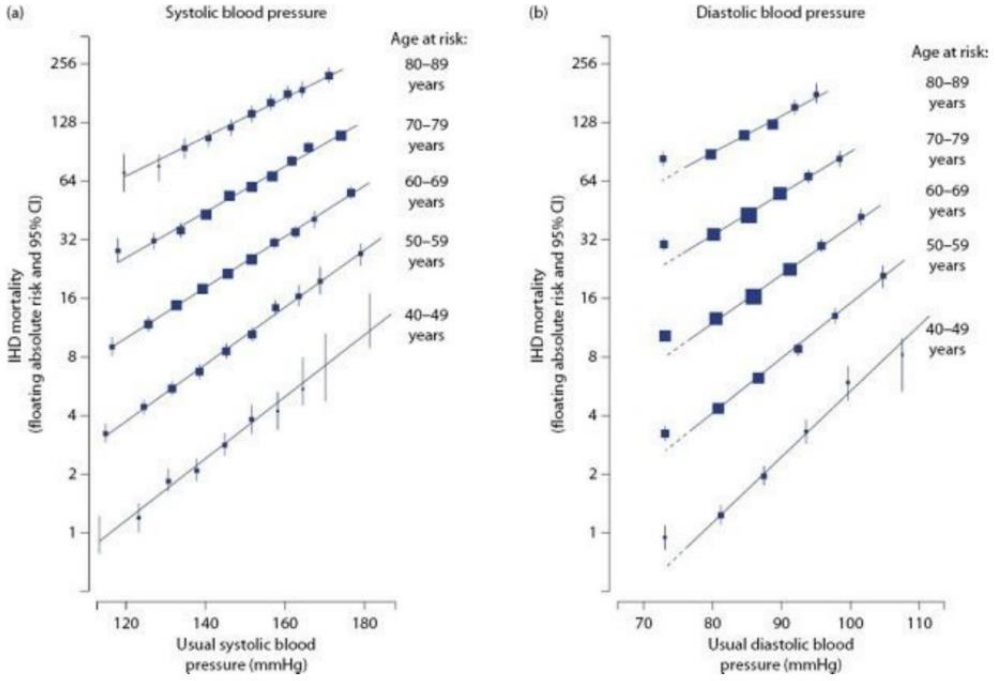

Figure 2.2 Ischaemic heart disease (IHD) mortality rate in each decade of age plotted for the usual systolic (a) and diastolic (b) blood pressure at the start of that decade. Data from one million adults in 61 prospective studies. (Adapted from Lewington S et al. *Lancet* 2002; 360(10): 1903–1913.)

ASSESSMENT OF TOTAL CARDIOVASCULAR RISK IN HYPERTENSION

INTRODUCTION

Historically, hypertension guidelines long focused on BP values as the only or main variables determining therapeutic interventions. Although this approach was maintained in the 2003 Joint National Committee (JNC) seven guidelines (11) and was found cost effective (12), the ESH-ESC guidelines have since 2003 (13–15) emphasized that management of hypertension should be related to quantification of total cardiovascular (CV) risk. Finally, this approach was also adopted by the most recent US hypertension guidelines (16). The rationale for this approach is that only a small proportion of the hypertensive population has an elevation of BP alone with the great majority exhibiting additional CV risk factors (17–21), with a relationship between the severity of BP elevation and that of alterations in glucose and lipid metabolism (22). When elevated BP and metabolic risk factors are concomitantly present, they potentiate each other risk (17,23,24). Thresholds and goals for antihypertensive treatment as well as treatment strategies for

concomitant risk factors may differ based on total CV risk. Therefore, estimation of total CV risk is essential for guiding patient management.

The use of total CV risk estimation may also improve physicians' behaviour in drug prescription and patient adherence (25,26); however, there are some reports showing no impact on provider behaviours (27) and inadequate use in routine clinical practice (28,29).

HOW TO ASSESS TOTAL CV RISK

A number of complex and computerized methods have been developed for estimating total CV risk, that is, the likelihood of experiencing a CV event, usually within the next 10 years. Many risk stratification systems are based on the Framingham study (30), estimating the 10-year risk for both fatal and nonfatal CHD by systolic BP and presence of other risk factors. The easy and rapid calculation of the Framingham risk score using published tables (National Cholesterol Education Program [NCEP]) (31) may assist the physician and patient in demonstrating the benefits of treatment.

The Framingham risk stratification has been shown to be reasonably applicable to some European populations (32) but requiring recalibration in other populations (33,34) due to geographic differences in the incidence of coronary and stroke events.

The latest US hypertension guidelines (16) recommend use of the ACC/AHA Pooled Cohort Equation (http://tools.acc.org/ASCVD-Risk-Estimator/) to estimate the 10-year risk of atherosclerotic CVD (ASCVD) to establish the BP threshold for treatment (35).

Given the need for a European model based on a large database, the SCORE (Systemic Coronary Risk Evaluation) project (36) was used to develop SCORE charts for high- and low-risk countries in Europe estimating the risk of dying from CV (not just coronary) disease over 10 years, and allowing calibration of the charts for individual countries provided that national mortality statistics and estimates of the prevalence of major CV risk factors are available. The SCORE model has also been used in the HeartScore, the official European Society of Cardiology management tool for implementation of CVD prevention in clinical practice (http://www.escardio.org).

The main disadvantage associated with an intervention threshold based on relatively short-term absolute risk is that younger adults (particularly women), while having more than one risk factor, are unlikely to reach treatment thresholds despite being at high risk relative to their peers. By contrast, most elderly men (e.g., those aged 65) will often reach treatment thresholds whilst being at very little increased risk relative to their peers. This situation results in most resources being concentrated on the oldest subjects whose potential

lifespan, despite intervention, is relatively limited, while young subjects at high relative risk remain untreated despite, in the absence of intervention, a predicted significant shortening of their otherwise much longer potential lifespan (37,38).

Use of the SCORE chart for estimating total CV risk in hypertension should be considered a minimal requirement taking into account the fact that total CV risk can be underestimated (39).

On the basis of these considerations, the 2013 ESH-ESC guidelines (15) suggest total CV risk be stratified as shown in Table 2.1. The terms *low* (<1%), *moderate* (≥1 and <5%), *high* (≥5 and <10%) and *very high* (≥10%) *risk* refer to the 10-year risk of CV mortality as defined by the 2012 ESC prevention guidelines (40). The factors on which this stratification is based are listed in Table 2.2. They include risk factors, asymptomatic organ damage, diabetes mellitus and established CV or renal disease.

Table 2.1 Stratification of total CV risk

Other risk factors, asymptomatic organ damage or disease	Blood pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF		Low risk	Moderate risk	High risk
1–2 RF	Low risk	Moderate risk	Moderate to high risk	High risk
≥3 RF	Low to moderate risk	Moderate to high risk	High risk	High risk
OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

BP = blood pressure; CKD = chronic kidney disease; CV = cardiovascular; CVD = cardiovscular disease; DBP = diastolic blood pressure; HT = hypertension; OD = organ damage; RF = risk factor; SBP = systolic blood pressure.

Table 2.2 Factors – other than office BP – influencing prognosis; used for stratification of total CV risk

Risk factors
- Male sex
- Age (men ≥55 years; women ≥65 years)
- Smoking
- Dyslipidemia
  - Total cholesterol >4.9 mmol/L (190 mg/dL); and/or
  - LDL-cholesterol >3.0 mmol/L (115 mg/dL); and/or
  - HDL-cholesterol: men <1.0 mmol/L (40 mg/dL), women <1.2 mmol/L (46 mg/dL); and/or
  - Triglycerides >1.7 mmol/L (150 mg/dL)
- Fasting plasma glucose 5.6–6.9 mmol/L (102–125 mg/dL)
- Abnormal glucose tolerance test
- Obesity (BMI ≥30 kg/m^2)
- Abdominal obesity (waist circumference: men ≥102 cm, women ≥88 cm in Caucasians)
- Family history of premature CV disease (men aged <55 years; women aged <65 years)

Asymptomatic organ damage
- Pulse pressure (in the elderly) ≥60 mmHg
- Left ventricular hypertrophy
  - Electrocardiogram: Sokolow-Lyon index >3.5 mV; RaVL >1.1 mV; Cornell voltage duration product >244 mV × ms; or
  - Echocardiogram: LVM index[a]: men >115 g/m^2; women >95 g/m^2
- Carotid wall thickening (IMT >0.9 mm) or plaque
- Carotid-femoral pulse wave velocity >10 m/s
- Ankle-brachial index <0.9
- CKD with eGFR (30–60 mL/min/1.73 m^2)
- Microalbuminuria

30–300 mg/24 h or albumin-creatinine ratio 30–300 mg/g; 3.4–34 mg/mmol preferentially in morning spot urine

Diabetes mellitus
- Fasting plasma glucose ≥7.0 mmol/L (126 mg/dL) on 2 repeated measurements; and/or
- HbA_{1c} >7% (53 mmol/mol); and/or
- Post-load plasma glucose >11.0 mmol/L (198 mg/dL)

Established CV or renal disease
- Cerebrovascular disease:

Ischaemic stroke
Cerebral haemorrhage
Transient ischaemic attack
- *CHD*:

Myocardial infarction
Angina
Coronary revascularization with PCI or CABG
Heart failure
- Heart failure, including heart failure with preserved EF
- Symptomatic lower extremities PAD
- CKD with eGFR <30 mL/min/1.73 m^2; proteinuria (>300 mg/24 h)
- *Advanced retinopathy*:

Haemorrhages or exudates
Papilledema

Source: Adapted from Mancia G et al. *J Hypertens* 2013; 31(15): 1281–1357.
Abbreviations: BMI, body mass index; CABG, coronary artery bypass grafting; CHD, coronary heart disease; CKD, chronic kidney disease; CV, cardiovascular; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HbA_{1c}, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; IMT, intima-media thickness; LDL-C, low-density lipoprotein cholesterol; LVM, left ventricular mass; PCI, percutaneous coronary intervention; PWV, pulse wave velocity.

[a] Risk maximal for concentric LVH: increased LVM index with a wall thickness to radius ratio of 0.42.