Hypertensiology

Epidemiology of hypertension

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Cardiovascular disease is the main cause of death in virtually all industrialised countries.[1] The limited information available from developing countries suggests that a similar epidemic is inevitable if current trends go unchecked.[2] Treatment of patients with clinical manifestations is an important element in overall management but on its own is an insufficient and incomplete response. Sudden death is often the first manifestation of cardiovascular disease and, even when treatment of disease is applicable and effective, it is usually palliative rather than curative. Thus treatment and prevention directed at the underlying risk factors, including high blood pressure, constitute a complementary and more fundamental approach to reducing the burden of illness. Epidemiological studies provide the scientific foundation for such an approach by identifying the distribution and determinants of high blood pressure in the general population, by establishing the role of high blood pressure as a risk factor for cardiorenal complications, and by quantifying the potential value of treating and preventing high blood pressure in the general population.

Factors influencing average level of blood pressure

Many factors have been associated with blood pressure levels in epidemiological surveys—eg, age, sex, race, socioeconomic status, starting level of blood pressure, early life experiences, nutrition, alcohol consumption, physical activity, and exposure to various environmental agents. Cross-sectional surveys in countries with divergent cultures and at different stages of economic development have documented a strikingly consistent relation between age and blood pressure; the similarities in the four national surveys of adult blood pressure are shown in figure 1.

At birth, average values for systolic and diastolic blood pressure in westernised countries are about 70 and 50 mm Hg, respectively.[3] In most surveys, systolic blood pressure tends to rise progressively throughout childhood, adolescence, and adulthood to reach an average value of about 140 mm Hg by the seventh or eighth decade. Diastolic blood pressure also tends to increase with age but the rate of rise is less steep than that for systolic pressure and the average value tends to remain flat or to decline after the fifth decade. Consequently, pulse pressure widens and isolated increases of systolic pressure become more common with advancing age.

By contrast to the experience in most countries, in isolated populations there is little evidence of an age-related change in blood pressure.[4] This finding indicates that age-related changes are not a biological necessity. An equally important observation is that unacculturated societies acquire a predisposition to age-related increases in blood pressure when they adopt a western lifestyle; the explanation must lie in environmental alterations rather than genetic influences. Changes in diet seem to have an important role.[5,6]

The overall pattern of age-related increase in blood pressure conceals various trends in population subgroups. Early in life there is little evidence of a difference in pressure between the sexes, but beginning in adolescence men tend to display a higher average level. The discrepancy in blood pressure between the sexes is most evident in young and middle-aged adults. Late in life the difference narrows and the pattern is often reversed; this change partly reflects the premature death of men with high blood pressure in middle-age. Ethnicity also tends to modify the relation between blood pressure and age. In the USA, where national surveys have shown a progressive age-related trend toward higher pressures in African-Americans than in whites,[7] this difference becomes apparent around the second decade of life. Average differences in blood pressure vary from slightly less than 5 mm Hg during the second decade to nearly 20 mm Hg during the sixth. In many studies, socioeconomic status has been closely associated with average levels of blood pressure. For example, in the Whitehall Study of British civil servants, the average value for systolic pressure varied from 133·7 mm Hg in the highest grade of employment to 139·9 mm Hg in the lowest.[8]

In most longitudinal studies, blood pressure has tended to track along a steeper or flatter age/blood-pressure relation according to relative position in the blood pressure distribution at baseline. This tracking tendency is of particular interest and potential importance in childhood, since it would be helpful to identify those who are most likely to manifest hypertension later in life. Unfortunately, tracking is most effective in predicting group experience over short periods and the ability to predict adult levels of blood pressure in an individual child is limited.[3]

Do exposures early in life influence cardiovascular disease risk factors and outcomes in adulthood?[9-12] Barker and colleagues, especially, have been strong advocates for the view that an adverse environment during critical periods of development in fetal life and infancy predisposes an individual to an unfavourable profile of cardiovascular disease risk factors and mortality later in life.[9] In several non-concurrent cohort studies they have shown an inverse relation of weight (measured at 1 year or at birth) to adult levels of blood pressure and hypertension. In addition, they have shown an independent positive relation between placental weight and adult blood pressure in both men and women.[10] Based on these and other studies, they propose that retardation of growth in fetal life and infancy leads to high blood pressure and other cardiovascular disease risk factors in adulthood. However, others have questioned the causality of these relationships.[11,12] The fact that migrants tend to assume the pattern of disease in their host

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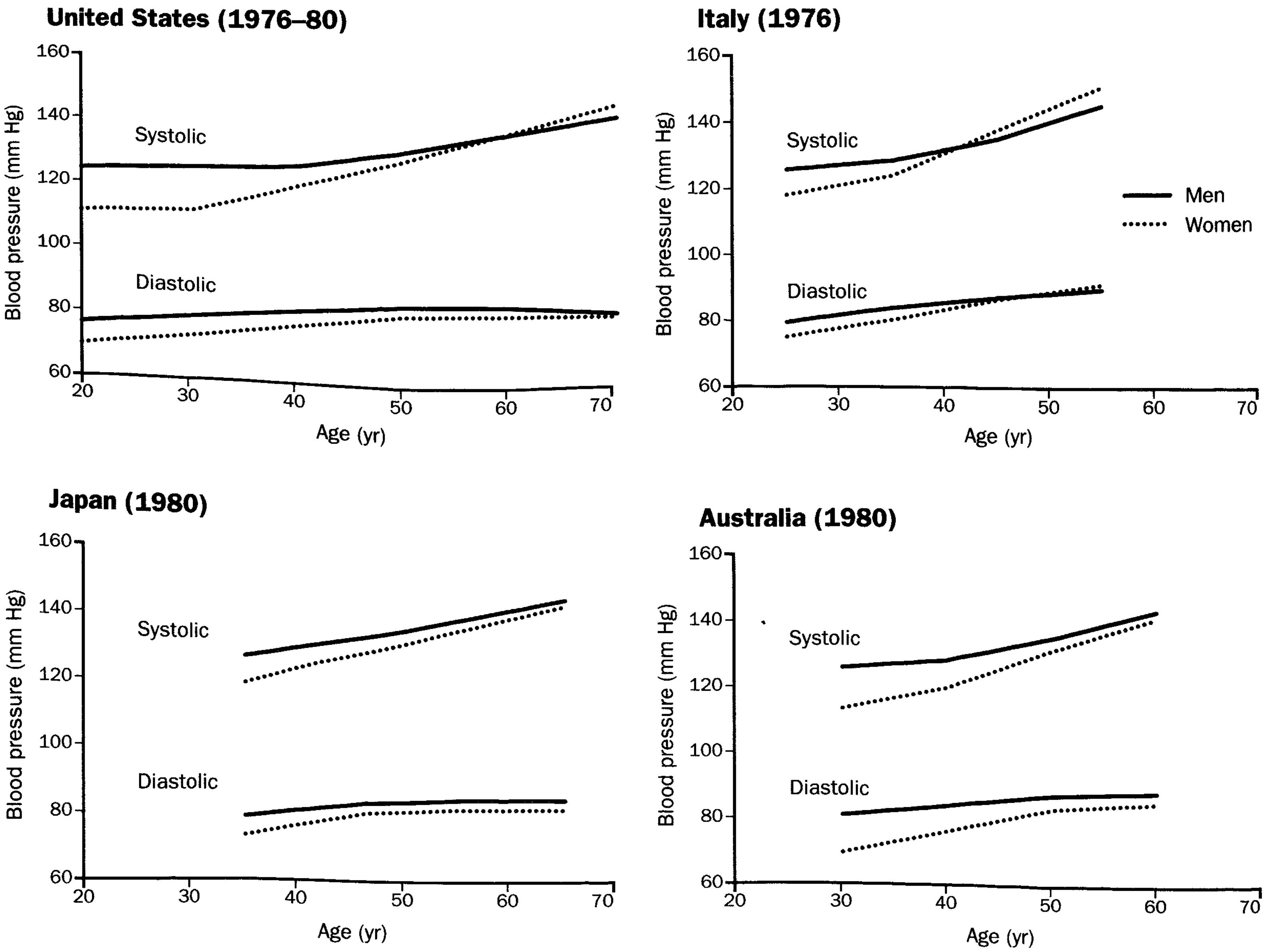

Figure 1: **Association between age and average levels of systolic and diastolic blood pressure in four economically developed countries from four continents**

Diastolic blood pressure reflects the use of phase 5 Korotkoff sounds. Adapted, with permission, from Whelton et al.[3]

environment emphasises the importance of adult rather than childhood environmental and cultural exposures.[4–6]

Observational and experimental studies provide strong evidence for an important role for common lifestyle-related exposures in the genesis of high blood pressure and hypertension.[13] These factors include high body weight and central obesity, sodium intake that greatly exceeds physiological needs, excessive consumption of alcohol, and insufficient physical activity. Taken together, these exposures probably account for much of the high blood pressure found in the general population and are an important focus for treatment and prevention of high blood pressure. Other factors including stress and general environmental exposures may also have an important aetiological role but the evidence is insufficient to warrant strong recommendations concerning treatment or prevention.[13,14]

Classification and prevalence of high blood pressure

It is convenient and pragmatically useful to classify individuals as being hypertensive or normotensive on the basis of their blood pressure levels. Such categorisation helps to establish prognosis, facilitates therapeutic decision-making, and tends to concentrate preventive efforts on those individuals who are most likely to benefit from the attention. In the recently revised system recommended by the US Joint National Committee for Detection, Evaluation and Treatment of High Blood Pressure (JNC V),[14] optimal blood pressure is defined as a systolic blood pressure less than 120 mm Hg and a diastolic blood pressure less than 80 mm Hg (table 1). Individuals with a systolic reading between 130 and 139 mm Hg or a diastolic reading between 85 and 89 mm Hg are designated as having a high normal blood pressure. Hypertension is diagnosed when a high systolic (⩾140 mm Hg) or diastolic (⩾90 mm Hg) pressure is confirmed at two or more visits. Hypertension is further categorised, as shown in table 1, into four stages according to the patient's level of systolic and diastolic blood pressure. Stage 1 is the most common

Category	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Optimal	<120	<80
Normal	120–129	80–84
High normal	130–139	85–89
Hypertension		
Stage 1	140–159	90–99
Stage 2	160–179	100–109
Stage 3	180–209	110–119
Stage 4	⩾210	⩾120

*Based on an average of two or more readings on two or more occasions in individuals not taking antihypertensive medications and not acutely ill. When average falls in different categories of systolic and diastolic blood pressure the higher category applies. Table based on recommendations of Fifth Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure.[14]

Table 1: **Classification of blood pressure for adults age 18 years or older**

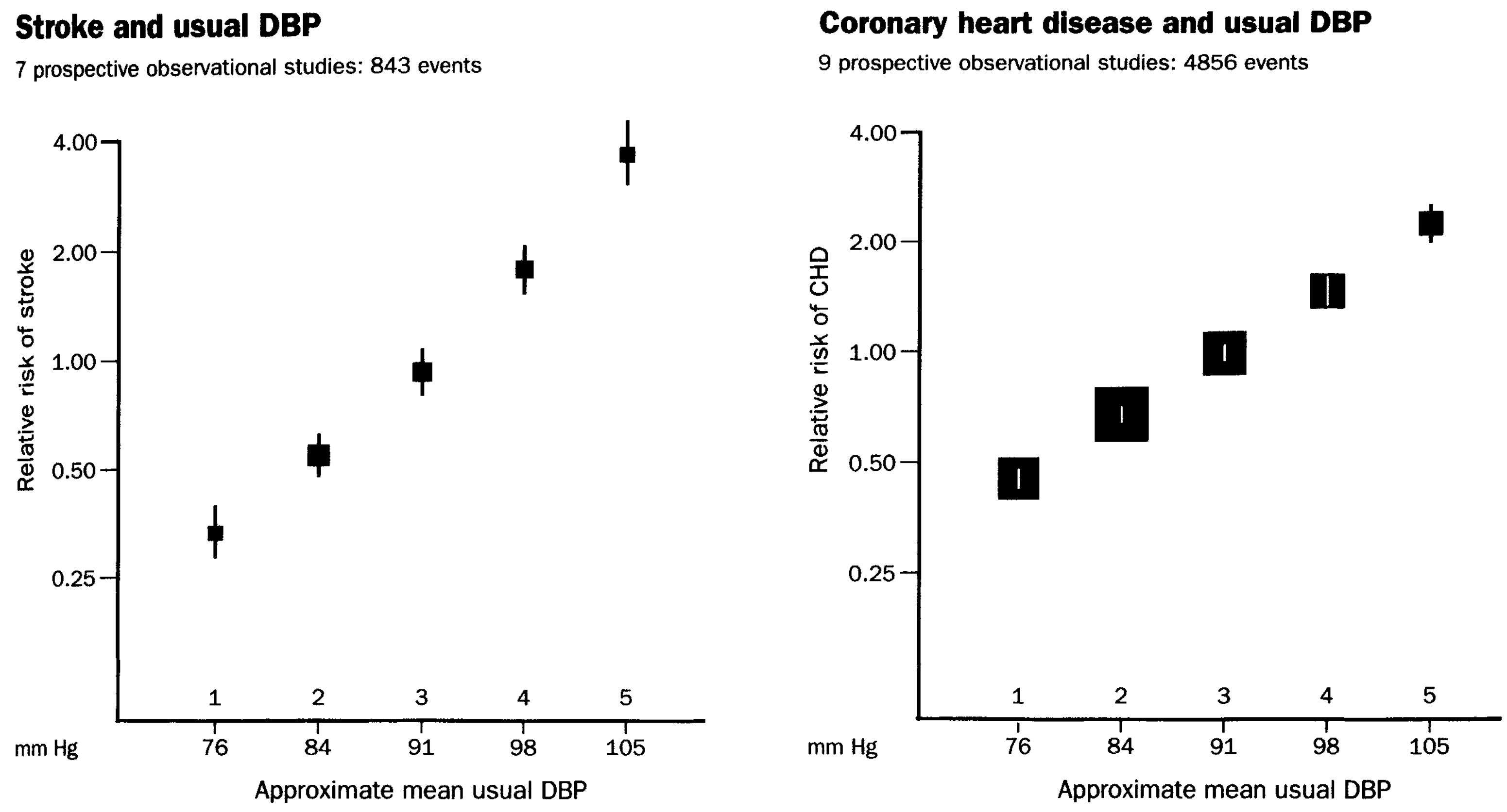

Figure 2: **Relation between diastolic blood pressure (in five categories 1–5 defined by baseline DBP) and subsequent coronary heart disease and stroke during an average of 10 years of follow-up**

Pooled estimates from nine prospective observational studies of 418 343 persons who were initially free of CHD (Multiple Risk Factor Intervention Trial Screenee Cohort Study, Chicago Heart Association Study, Framingham Heart Study, Honolulu Heart Study, Lipid Research Clinics Screenee Study, Peoples Gas Study, Chicago Electric Study, Puerto Rico Heart Study, and Whitehall Study). CHD (n=4856) includes fatal events that were monitored in all nine studies (n=4260) and non-fatal myocardial infarction that was measured in only three of the studies (n=596). The size of the squares is proportional to the number of events in each category of blood pressure and the vertical lines within the boxes reflect 95% CIs for each estimate of relative risk. Reproduced, with permission, from MacMahon et al.[16]

(80%) form of hypertension in the community whereas stage 4 is the least common (3%).

Despite the pragmatic value of this system for case-definition and therapeutic decision-making, we need to remember that the cut-off points used for identification of hypertension and its stages are chosen for their operational suitability and not as a reflection of a clear biological distinction between hypertension and normotension—ie, all persons within the so-called normotensive range do not have an optimum risk of blood-pressure-related complications. It is also worth emphasising that the prevalence of hypertension varies considerably depending on the cut-off-points chosen and on the methods of blood pressure measurement. In addition, the prevalence of hypertension is influenced by population characteristics such as age, race, gender, and socioeconomic status.[3] Age has the greatest impact: by use of the JNC V criteria,[14] the prevalence of hypertension in the general US population varied from 4% in those aged 18–29 years to 65% in those aged ⩾80 years during the 1988–91 National Health and Nutrition Examination Survey.[13]

Blood pressure and risk

Epidemiological studies have repeatedly identified an important and independent risk relation between high blood pressure and various disorders including coronary heart disease, stroke, congestive heart failure, and renal insufficiency.[15] Quantitative estimates of the association between usual levels of diastolic pressure and coronary heart disease and stroke are shown in figure 2. These estimates come from the pooling of information from 418 343 adults aged 25–70 years who participated in nine prospective observational studies.[16] None had a history of coronary heart disease or stroke at baseline and each was followed for an average of about 10 years. The data have been corrected for the effect of regression dilution bias resulting from imprecision in blood pressure measurement. The difference between the highest (105 mm Hg) and lowest (76 mm Hg) stratum of blood pressure was only about 30 mm Hg. However, even within this rather narrow range the risk of coronary heart disease was nearly five times higher and the risk of stroke more than ten times higher for those in the highest than for those in the lowest stratum of mean overall diastolic pressure during follow-up. The data suggest that a 5–6 mm Hg lower level of diastolic pressure is typically associated with a 20–25% lower risk of incident coronary heart disease.[17]

The relation between blood pressure and risk of congestive heart failure and end-stage renal disease is equally impressive. In a 34-year follow-up of the Framingham Heart Study cohort, the risk of congestive heart failure was 2–4 times higher for those in the highest than for those in the lowest quintile of blood pressure at entry into the study.[18] During a 15·3 year follow-up of 361 639 individuals screened for the Multiple Risk Factor Intervention Trial, the risk (95% CI) of end-stage renal disease for a 10 mm Hg higher level of systolic pressure at baseline was 1·65 (1·57, 1·76) after adjustment for age, race, cigarette smoking, serum cholesterol concentration, treatment for diabetes, previous myocardial infarction, and income.[19]

The relation between blood pressure and cardiovascular disease outcomes has been consistent in studies conducted in women[20] and men,[15] and in groups with diverse geographic, cultural, and ethnic backgrounds.[15,21,22] In most large epidemiological studies, cardiorenal risk

Systolic BP (mm Hg)	No (%)	No of CHD deaths (rate per 10 000 person-years)*	Relative risk†	No of excess CHD deaths (%)‡
<110	21 379 (6 1)	197 (9 8)	1 00	
110–119	66 080 (19 0)	712 (11 1)	1 12	77 (1 3)
120–129	98 834 (28 4)	1349 (12 9)	1 32§	319 (9 9)
130–139	79 308 (22 8)	1587 (17 0)	1 76§	669 (20 7)
140–149	44 388 (12 8)	1328 (22 8)	2 35§	755 (23 4)
150–159	21 477 (6 2)	938 (30 5)	3 14§	631 (19 5)
160–169	9308 (2·7)	470 (34 0)	3 41§	328 (10 1)
170–179	4013 (1 2)	286 (47 6)	4 30§	221 (6 8)
≥180	3191 (0 9)	283 (57 2)	5 65§	232 (7 2)

*Adjusted for age, race, serum cholesterol, cigarettes per day, use of medication for diabetes, and income; average follow-up 11 6 years.
†Adjusted by proportional hazards regression for age, race, serum cholesterol, cigarettes per day, use of medication for diabetes, and income.
‡Estimated number of excess deaths compared with the baseline systolic BP category of less than 110 mm Hg during 11 6 years of follow-up.
Excess deaths were derived by first calculating expected number of deaths within deciles of a risk score based on age, race, serum cholesterol, cigarettes per day, use of medication for diabetes, and income, then summing these estimates across risk score deciles within each blood pressure category and subtracting this number from the observed number of deaths.
§p<0 001.
Adapted, with permission, from Stamler, et al.[15]

Table 2: **Baseline systolic blood pressure and coronary heart disease (CHD) death rates for men screened for the Multiple Risk Factor Intervention Trial**

increases progressively throughout the entire range of blood pressure, with no evidence of a threshold in risk or of the J-shaped relation that features in some secondary analyses of smaller data sets.[23] In virtually every study, both systolic and diastolic pressures have been independent predictors of risk. However, almost without exception, systolic pressure has been the more important, being associated with a higher relative risk of both cardiovascular and renal disease for a similar range of blood pressure. In the Multiple Risk Factor Intervention Trial, individuals in the highest deciles of systolic and disastolic pressure had a relative risk of coronary heart disease of 3·66 whereas those in the lowest deciles had a risk of 2·78.[15] In a cross-tabulation of systolic and diastolic pressures, relative risk increased progressively from 1·0 in those with an optimum level of blood pressure (systolic <120, diastolic <80) to 3·23 in those with an isolated increase of diastolic pressure (diastolic ≥100, systolic <120), 4·19 in those with an isolated increase of systolic blood pressure (systolic ≥160, diastolic <80), and 4·57 in those with a combined increase (systolic ≥160, diastolic ≥100).

High blood pressure is a potent cardiovascular disease risk factor, independent of the presence or absence of other factors that predict the likelihood of disease. However, the risk of high blood pressure is substantially modified by the presence and levels of other risk factors. For example, among individuals screened for the Multiple Risk Factor Intervention Trial, there was more than a twenty-fold difference in risk between those who were smokers and in the upper quintiles for both blood pressure and serum cholesterol and their counterparts who were non-smokers and in the lowest quintiles for both blood pressure and serum cholesterol. Findings such as these emphasise the importance of a multifactorial approach to risk reduction in patients with high blood pressure. Since the relative benefits of antihypertensive therapy remain constant across a wide spectrum of absolute risk,[24] quantification of overall cardiovascular disease risk has important implications for clinical management. Thus, the risk-benefit relation of antihypertensive therapy becomes progressively more appealing with increasing absolute risk.[25] For example, a 70-year-old man with hypertension and a high serum cholesterol should derive greater benefit from a period of antihypertensive therapy than a 40-year-old woman with an identical blood pressure and a normal serum cholesterol. This reasoning does not, however, take into account the relative value of avoiding events at different stages of life.

Population excess risk

In view of the risk for subsequent morbidity and mortality if hypertension is untreated, and the value of antihypertensive therapy in reducing that risk,[24,26] detection, treatment, and control of individuals with hypertension should be assigned a high priority. Nevertheless, the burden of illness due to any risk factor in the community depends on the prevalence of the factor as well as on its importance as a predictor of risk in the individual. Table 2 shows the baseline blood pressure and subsequent coronary heart disease mortality for 347 978 men who were screened for the Multiple Risk Factor Intervention Trial.[15] The risk of death from coronary heart disease increased steadily with progressively higher levels of blood pressure: compared with those in the lowest stratum of blood pressure (<110 mm Hg systolic), individuals in the highest stratum (≥180 mm Hg systolic) had a 5·65 times higher risk. Less than a quarter of the cohort had hypertension, but this group accounted for more than two-thirds of the presumed excess risk of coronary heart disease mortality related to excess systolic blood pressure. The 5% with stage 2–4 hypertension accounted for almost a quarter of the population excess risk. On average, the relative risk in those with stage 1 hypertension was less than in their counterparts with more severe hypertension. However, nearly 80% of the hypertensives had stage 1 hypertension, so this stage accounted for about 43% of the overall population excess risk and or nearly two-thirds of the hypertension-related population excess risk. Although the relative risk of coronary heart disease mortality was lower in the normotensive individuals, it increased steadily with progressively higher levels of blood pressure—eg, 1·76 for those in the 130–139 mm Hg stratum *vs* those in the <100 mm Hg stratum of systolic blood pressure. Nearly 75% of those with a systolic blood pressure ≥110 mm Hg were in the normotensive category, so this group accounted for almost one-third of the overall population excess risk.

These data and similar findings for other blood-pressure-related complications[27,28] have important implications for prevention of blood-pressure-related disease. First, they indicate a strong epidemiological basis for efforts aimed at detection, treatment, and control of hypertension. Treatment of established hypertension not only targets individuals at high risk but also provides the potential for a reduction in the overall burden of cardiorenal disease in the population. Second, they emphasise the importance of treating those with the least severe stage of hypertension since most hypertension-related coronary heart disease occurs within this range of blood pressure. Finally, the data indicate that treatment of hypertension represents only a partial response to the overall burden of blood-pressure-related cardiovascular disease in the general population. Even under optimum conditions, treatment and control of hypertension will influence no more than 70% of the blood-pressure-related cardiovascular disease in the community.

Treatment must be accompanied by equally vigorous preventive efforts.[13] In the Multiple Risk Factor Intervention Trial, for the 11 908 screened individuals who had optimum levels of both systolic (<120 mm Hg) and

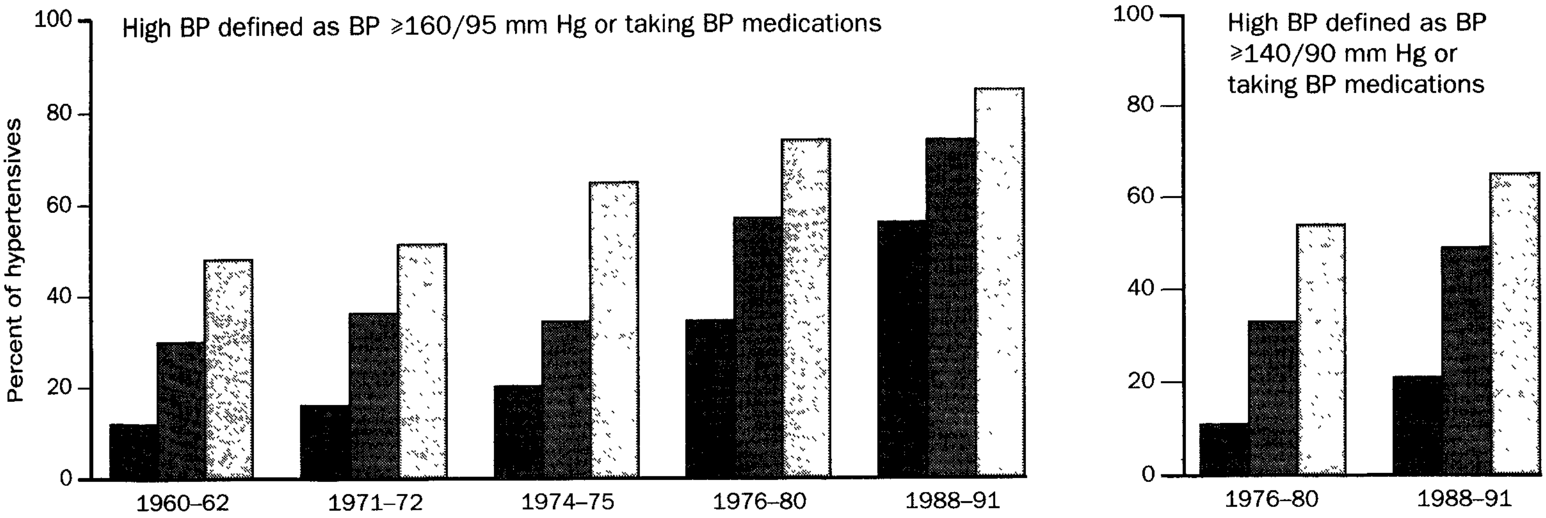

Figure 3: **Hypertension control (left-hand columns), treatment (middle), and awareness (right) rates for US adults aged 18–74 years in five sequential national prevalence surveys, 1976–91**

Hypertension was defined as use of antihypertensive drug therapy or raised systolic (≥160 or ≥140 mm Hg) or diastolic (≥95 or ≥90 mm Hg) blood pressure on a single occasion. Adapted, with permission, from Whelton and Brancati.[29]

diastolic (<80 mm Hg) pressure and a favourable profile for other major coronary heart disease risk factors (no diabetes, no history of cigarette smoking or myocardial infarction, and a serum cholesterol in the lowest quintile), the age-adjusted rate of coronary heart disease mortality was 2·1 per 10 000 person-years of follow-up. This figure was about 10% of that in the remainder of the cohort (20·4 per 10 000 person-years). Only about 8% of the deaths in the low-risk group were from coronary heart disease *vs* 35% in the rest of the cohort. This result suggests that the vast majority of coronary heart disease deaths can be attributed to a few conventional risk factors and that achievement of optimum levels of these factors would virtually eliminate the epidemic of premature coronary heart disease.

Treatment and control of hypertension in the community

Surveys provide a means to assess the extent to which hypertension is being treated in the community. In the USA, five national probability surveys of hypertension awareness, treatment, and control have been conducted over the past 30 years,[29] and have documented a trend toward greater awareness, treatment, and control of hypertension in the community, independent of the cut-off points for definition of hypertension (figure 3). However, if one uses the definition of hypertension now favoured (antihypertensive drug therapy or a systolic pressure ≥140 mm Hg or a diastolic pressure ≥90 mm Hg), about one-third of the general population was unaware of their hypertension in 1988–91 and only about one in every five hypertensives was being controlled adequately. These surveys may have overestimated the prevalence of hypertension in the community since blood pressure was measured only once. In addition, the data presented in figure 3 underestimate the extent to which hypertension is being treated since they do not reflect the use of non-pharmacological therapy. Nonetheless, they suggest that efforts to increase awareness of hypertension should not be relaxed. Rates for detection, treatment, and control of hypertension are probably lower in other countries.[29]

Recent population surveys have also identified a changing pattern of antihypertensive drug prescription in the community. In the USA, there has been a rapid increase in the percentage of antihypertensive prescriptions for angiotensin converting enzyme inhibitors and calcium channel blockers, and a concurrent decline in the number and percentage of prescriptions for diuretics, and to a lesser extent beta-blockers.[30] These changes probably reflect a perception that the newer agents are better tolerated and provide more protection against end-organ damage. Ongoing population-based trials such as the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial and the African American Study of Kidney Disease and Hypertension should help to resolve the latter issue.

So far, surveillance systems have provided limited information on the extent to which lifestyle modification is being used to treat hypertension. There are indicators that both health care providers and patients are attracted to the concept of lifestyle modification but are frustrated by the difficulty of achieving and maintaining the goals of therapy.[31] Achievement of these goals should be facilitated by increasing commitment to food labelling, by making available more foods that are lower in calories and salt content, by mounting public education campaigns that promote healthy lifestyles (eg, better nutrition, moderation in alcohol consumption, and increased physical activity), and by enhancing the motivation and support of health care providers. It will be important to ensure that substitution of lifestyle modification interventions for pharmacological therapy does not diminish the level of hypertension control in the community.

Primary prevention of hypertension

Blood pressure reduction efforts have been focused almost exclusively on detection and treatment of hypertension. To achieve the broader goal of eliminating all blood-pressure-related complications in the community, treatment must be complemented by preventive strategies. The interventions recommended for primary prevention are the same as those already being used for non-pharmacological treatment of hypertension.[13] Consequently, both risk reduction approaches complement and reinforce one other

In the USA, the National Heart, Lung, and Blood Institute is promoting a nationwide effort to prevent high blood pressure.[13] This includes a population strategy to achieve a slight downward shift in the entire distribution of blood pressure in the community and a more intensive targeted strategy to lower pressure in those who are at greatest risk of hypertension. Because large segments of the population are candidates for primary prevention interventions, small changes in blood pressure are likely to yield substantial health benefits. Thus a downward shift of about 2 mm Hg in the blood pressure distribution of the general population should result in an annual reduction in stroke, coronary heart disease, and all-cause mortality of about 6%, 4%, and 3%, respectively.[32] Likewise, a 2–3 mm Hg average reduction in those with a high normal blood pressure should result in a 25–50% decrease in the incidence of hypertension.[33-35] This clear potential for benefit makes primary prevention of hypertension an important goal, for society.

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