1 Prevalence and causes

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In the population, blood pressure is a continuous, normally distributed variable. No separate subgroups of people with and without hypertension exist. A consistent continuous gradient exists between usual levels of blood pressure and the risk of coronary heart disease and stroke, and this gradient continues down to blood pressures that are well below the average for the population. This means that much of the burden of renal disease and cardiovascular disease related to blood pressure can be attributed to blood pressures within the so called "normotensive" or average range for Western populations.

The main concern for doctors is what level of blood pressure needs drug treatment. The pragmatic definition of hypertension is the level of blood pressure at which treatment is worthwhile. This level varies from patient to patient and balances the risks of untreated hypertension in different types of patients and the known benefits of reducing blood pressure, while taking into account the disadvantages of taking drugs and the likelihood of side effects.

"In an operational sense, hypertension should be defined in terms of a blood pressure level above which investigation and treatment do more good than harm" Grimley Evans J, Rose G. *Br Med Bull* 1971;27:37–42

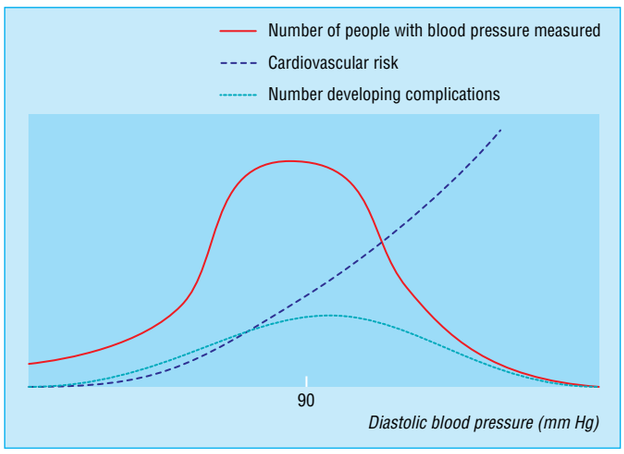
Systolic blood pressure has a strong tendency to increase with advancing age, so the prevalence of hypertension (and its complications) also increases with age. Hypertension thus is as much a disorder of populations as of individual people. Globally, high blood pressure accounts for more deaths than many common conditions and is a major burden of disease.

As hypertension is the most important risk factor for cardiovascular disease, achievement of a universal target systolic blood pressure of 140 mm Hg should produce a reduction of 28–44% in the incidence of stroke and 20–35% of coronary heart disease. This could prevent about 21 400 deaths from stroke and 41 400 deaths from coronary heart disease in the United Kingdom each year. It would also mean about 42 800 fewer fatal and non-fatal strokes and 82 800 fewer coronary heart disease events per year in the United Kingdom alone. Globally, as hypertension is becoming more common, coronary heart disease and stroke correspondingly are becoming common, particularly in developing countries.

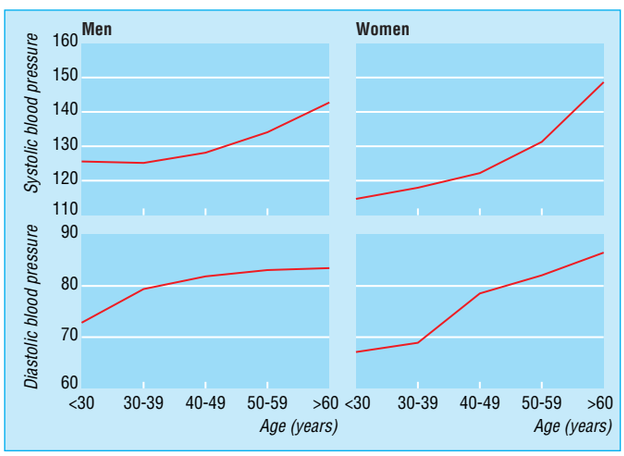
A recently published analysis of pooled data from different regions of the world estimated the overall prevalence and absolute burden of hypertension in 2000 and the global burden in 2025. Overall, 26.4% of the adult population in 2000 had hypertension and 29.2% were projected to have this condition by 2025. The estimated total number of adults with hypertension in 2000 was 972 million: 333 million in economically developed countries and 639 million in economically developing countries. The number of adults with hypertension in 2025 thus is predicted to increase by about 60% to a total of 156 billion.

The development of hypertension reflects a complex and dynamic interaction between genetic and environmental factors. In some primitive communities in which obesity is rare and salt intake is low, hypertension is virtually unknown, and blood pressure does not increase with advancing age.

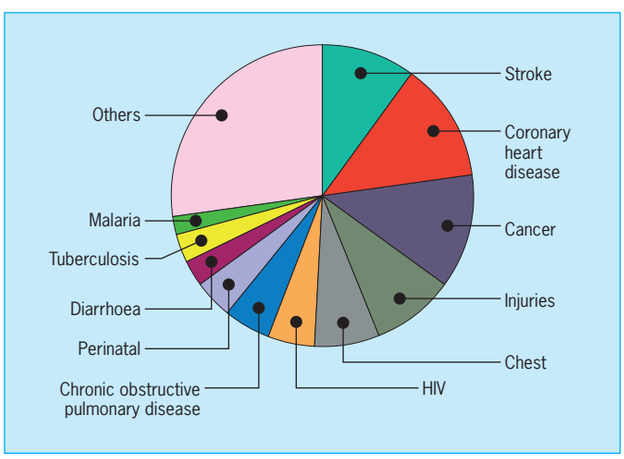
Studies have investigated Japanese people migrating from Japan to the west coast of America. In Japan, high blood



Hypertension: a disease of quantity not quality



Birmingham Factory Screening Project (figure excludes data from 165 patients on drugs that lower blood pressure). Adapted from Lane D, et al. *J Human Hypertens* 2002;16:267–73



Worldwide causes of death. Adapted from Mackay J, Mensah GA, WHO 2004

pressure is common and the incidence of stroke is high, but coronary heart disease is rare. When Japanese people moved across the Pacific Ocean, a reduction in the incidence of hypertension and stroke was seen, but the incidence of coronary heart disease increased. These studies strongly suggest that, although racial differences exist in the predisposition to hypertension, environmental factors still play a significant role. The United Kingdom also has a pronounced north–south gradient in blood pressure, with pressures higher in the north of the country. Studies that compare urban and rural populations in African populations also show clear differences in blood pressure between urban and rural societies with the same genetic composition.

Prevalence

The prevalence of hypertension in the general population depends on the arbitrary criteria used for its definition, as well as the population studied. In 2853 participants in the Birmingham Factory Screening Project, the odds ratios for being hypertensive after adjustment for age were 1.56 and 2.40 for African-Caribbean men and women, respectively, and 1.31 for South-Asian men compared with Europeans.

The Third National Health and Nutrition Examination Survey 1988–91 (NHANES III) showed that 24% of the adult population in the United States, which represents more than 43 million people, have hypertension (>140/90 mm Hg or current treatment for hypertension). The prevalence of hypertension varies from 4% in people aged 18–29 years to 65% in people older than 80 years. Prevalence is higher among men than women, and the prevalence in African-Americans is higher than in Caucasians and Mexican-Americans (32.4%, 23.3%, and 22.6%, respectively). Most cases of hypertension in young adults result from increases in diastolic blood pressure, whereas in elderly people, isolated increases in systolic blood pressure are more common and account for 60% of cases of hypertension in men and 70% in women. Hypertension generally affects ≤10% of the population up to the age of 34 years. By the age of 65, however, more than half of the population has hypertension.

Incidence

Unfortunately, few data are available on the incidence of new onset hypertension. The incidence of hypertension does increase sharply with age, with higher rates in men.

Follow up of people in the Framingham Heart Study after 30 years found that the two year incidence of new onset hypertension increases from 3.3% in men and 1.5% in women aged 30–39 years to 6.2% in men and 8.6% in women aged 70–79 years. People with "high normal" blood pressure at first examination were at greater risk of developing sustained hypertension over the ensuing years. Some authorities argue that high normal blood pressure should be reclassified as "prehypertensive."

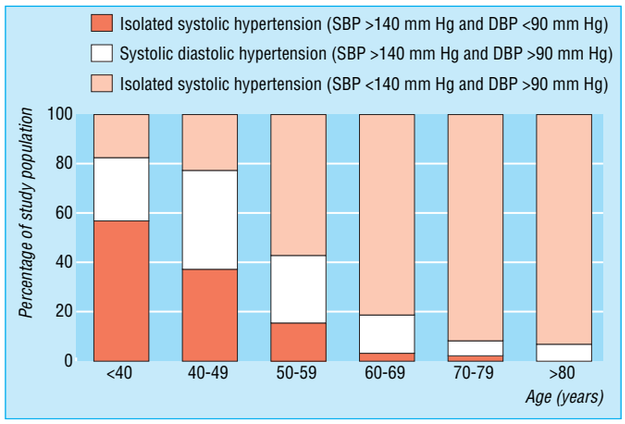
"High normal" blood pressure is one of the strongest predictors for the later development of hypertension. At the individual level, however, blood pressure in childhood is poorly predictive of later levels of blood pressure or the risk of hypertension.

Age

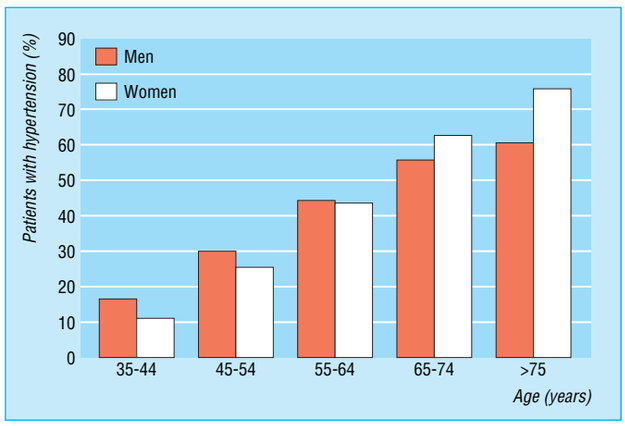
In western societies, blood pressure rises with increasing age, and people with high baseline blood pressures have a faster increase than those with normal or below average pressures. In rural non-Westernised societies, however, hypertension is rare, and the increase in pressure with age is much smaller. The level of blood pressure accurately predicts coronary heart disease and stroke at all ages, although in very elderly people, the

Prevalence of hypertension (>160/95 mm Hg or treated) in the Birmingham Factory Screening Project

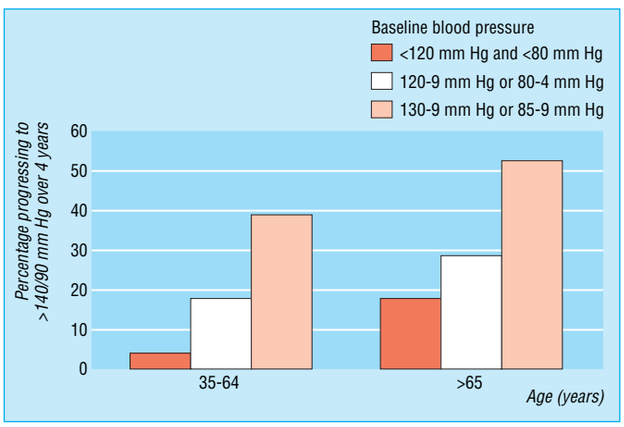
Population	Men (%)	Women (%)
African-Caribbean	30.8	34.4
European	19.4	12.9
South Asian	16.0	–



Hypertension subtypes from the NHANES III study (DBP = diastolic blood pressure, SBP = systolic blood pressure). Adapted from Franklin SS, et al. *Hypertension* 2001;37:869–74



Prevalence of hypertension in US citizens aged ≥35 years by age and sex in the NHANES III study (1988–94). Those classified as having hypertension had a systolic blood pressure ≥140 mm Hg or a diastolic blood pressure of ≥90 mm Hg, were taking antihypertensive drugs. Adapted from Wolz M, et al. *Am J Hypertens* 2000;13:104–4



Patients progressing to develop new hypertension in the Framingham Heart Study. Adapted from Vasan RS, et al. *Lancet* 2001;358:1682–6

relation is less clear. This may be because many people with increased blood pressures have died and those with lower pressure may have subclinical or overt heart disease that causes their blood pressure to decrease.

Ethnic origin

People of African origin have been studied well in North America, but whether these data can be fully applicable to the African-Caribbean populations in the United Kingdom or similar populations in Africa or the West Indies is uncertain. All studies of people of African origin from urban communities, however, show a higher prevalence than in Caucasian people. Yet hypertension is rare in black people who live in rural Africa. Whether any particular level of blood pressure carries a worse prognosis in people of African origin or whether survival is much the same as in people of European origin but with more strokes and fewer heart attacks is uncertain.

Even when correction is made for obesity, socioeconomic, and dietary factors, ethnic factors remain in the predisposition to hypertension. These differences are probably related to ethnic differences in salt sensitivity. There is little evidence to show that people of African origin in the United Kingdom and United States consume more salt than people of European origin. There is evidence that salt loading raises blood pressure more in people of African origin and that salt restriction is more beneficial. These differences in salt sensitivity may also be related to the finding that plasma levels of renin and angiotensin in African-American people are about half those in Americans of European origin. As discussed later, differences in renin may explain ethnic differences in responses to antihypertensive drugs.

Sex

Before the age of about 50 years, hypertension is less common in women than men. After this age, blood pressure in women gradually increases to about the same level as in men. Consequently, the complications of hypertension are less common in younger women. This protection may be related to beneficial effects of oestrogens or a harmful effect of androgens on vascular risk.

Increasing evidence shows that women with a past history of pre-eclampsia and pregnancy induced or gestational hypertension have an increased risk of hypertension and cardiovascular disease in later life. Such women should be considered to be at higher risk and need regular monitoring.

Causes of hypertension

In around 5% of people with hypertension, the high blood pressure is explained by underlying renal or adrenal diseases. In the remaining 95%, no clear cause can be identified. Such cases of hypertension are described as “essential” or “primary” hypertension. Essential hypertension is related to the interplay of genetic and environmental factors, but the precise role of these is uncertain.

Environmental and lifestyle causes of hypertension

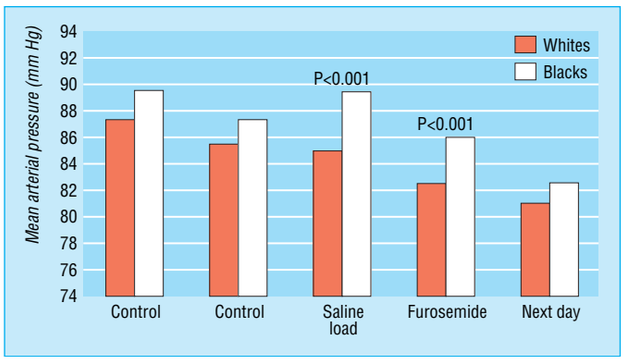
Salt

Salt intake has a consistent and direct effect on blood pressure. As stated earlier, migration studies in African and Japanese people have shown changes in blood pressure when moving from one environmental background to another. The factor most likely to be involved is a change in salt intake.

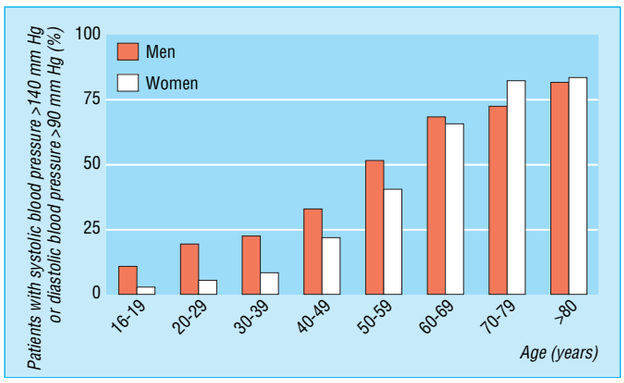
Many potential mechanisms for how salt causes hypertension have been suggested. Evidence from observational

Blood pressure in populations of African origin in the United Kingdom: review of 14 adult cross sectional studies in 1978

Blood pressure	Men	Women
Systolic higher than Europeans	10 of 14	10 of 12
Diastolic higher than Europeans	11 of 14	10 of 12
Hypertension more common	8 of 10	8 of 9



Effect of salt loading in black and white normotensive people. Adapted from Luft FC, et al. *Circulation* 1979;59:643–50



Prevalence of secondary hypertension in the Health Survey for England 1998. Adapted from Primatesta P, et al. *Hypertension* 2001;38:827–32

Prevalence of secondary hypertension in three published surveys

Type of hypertension	Study		
	Rudnick, 1977	Sinclair, 1987	Anderson, 1994
Essential hypertension	94.0%	92.1%	89.5%
Renal disease	5.0%	5.6%	1.8%
Renal artery disease	0.2%	0.7%	3.3%
Cushing’s syndrome	0.2%	0.1%	–
Oral contraceptives	0.2%	1.0%	–
Phaeochromocytoma	–	0.1%	0.3%
Coarctation	0.2%	–	–

How does salt cause hypertension?

- Increased circulating fluid volume
- Inappropriate sodium:renin ratio, with failure of renin to suppress increased intracellular sodium
- Waterlogged, swollen endothelial cells that reduce the interior diameter of arterioles
- Permissive rise in intracellular calcium, which leads to contraction of vascular smooth muscle

epidemiological studies, animal models, and randomised controlled trials in patients with hypertension and normal blood pressure all point to a causal relation between salt and blood pressure. The potential clinical and public health impact of relatively modest salt restriction thus is substantial.

The Intersalt project, which involved more than 10 000 men and women aged 20–59 years in 52 different populations in 32 countries, quite clearly showed that the increase in blood pressure with advancing age in urban societies was related to the amount of salt in the diet. Positive associations between urinary excretion of sodium (a marker of salt intake) and blood pressure were observed within and between populations. In men and women of all ages, an increase in sodium intake of 100 mmol/day was estimated to be associated with an average increase in systolic blood pressure of up to 6 mm Hg. The association was larger for older people.

This finding was supported by a meta-analysis of the many individual population surveys of blood pressure in relation to salt intake. Law et al performed a meta-analysis of 78 trials of the effect of sodium intake on blood pressure and reported that a reduction in daily salt intake of about 3 g (attainable by moderate reductions in dietary intake of salt) in people aged 50–59 years should lower systolic blood pressure by an average of 5 mm Hg. An average reduction in blood pressure of this magnitude in the general population of most Western countries would reduce the incidence of stroke by 25% and the incidence of ischaemic heart disease by 15%.

A number of clinical trials also show reductions in blood pressure after restriction of salt intake (see chapter 8). In a recent study in the United Kingdom, a reduction in daily salt intake from 10 g to 5 g over one month in a group of men and women aged 60–78 years with hypertension resulted in an average fall in systolic blood pressure of 7 mm Hg.

The value of the restriction of salt intake in people without hypertension is more controversial. Data pooled from the limited studies available suggest that reduction of salt intake to about 6 g/day should reduce systolic blood pressure by about 2 mm Hg and diastolic pressure by 1 mm Hg. Although clinically unimportant, this reduction, if genuine and sustained, would be expected to bring about a 17% reduction in the prevalance of hypertension.

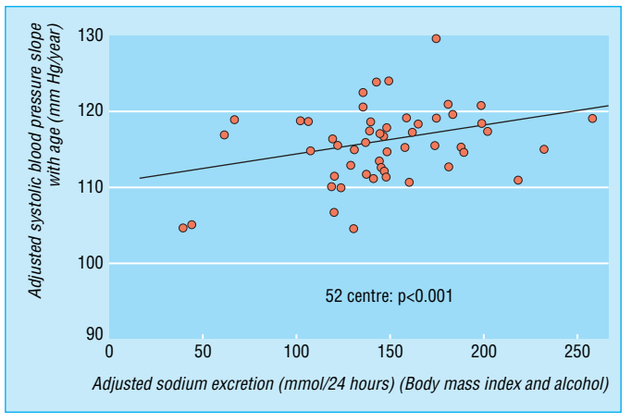
Potassium

The relation between intake of sodium, intake of potassium, and blood pressure is complex and has not been resolved completely. The effect of dietary intake of potassium on blood pressure is difficult to separate from that of salt.

The Intersalt project showed that high intake of potassium was associated with a lower prevalence of hypertension. Urinary sodium and potassium ratios in the United States showed marked differences between black and white people, despite little difference in their sodium intake or excretion. Dietary intake of potassium also has been related inversely to the risk of stroke. The antihypertensive effects of potassium chloride and other potassium salts are the same, which indicates that it is the potassium that matters. Most of the potassium in the diet is not in the form of potassium chloride but potassium citrate and potassium bicarbonate.

Calcium and magnesium

A weak inverse association exists between intake of calcium and blood pressure. Nonetheless, data from clinical trials of calcium supplementation on blood pressure are inconsistent, and the overall effect probably is minimal. A weak relation also exists between intake of magnesium and blood pressure, but the use of magnesium supplements has been disappointing.



Intersalt project. Adapted from INTERSALT cooperative research group. *BMJ* 1988;297:319–28

INTERSALT project: sodium excretion and systolic blood pressure in individual centres

Variable	Adjusted for	
	Age, sex	Age, sex, body mass index (kg/m^2), alcohol, and potassium
Centres with positive change	39	33
Centres with significantly positive change	15	8
Combined centre coefficient per mm Hg per 100 mmol of sodium	1.63*	1.00*
Combined centre coefficient corrected for reliability	3.54	2.17

*P < 0.001.

Adapted from INTERSALT cooperative research group. *BMJ* 1988;297:319–28

INTERSALT project: within centre coefficients for potassium in 24 hour urine sampling adjusted for age and sex

Variable	Blood pressure	
	Systolic	Diastolic
Positive coefficients:	24	29
Significant	0	2
Negative coefficients:	28	23
Significant	2	2
Centres	52	52

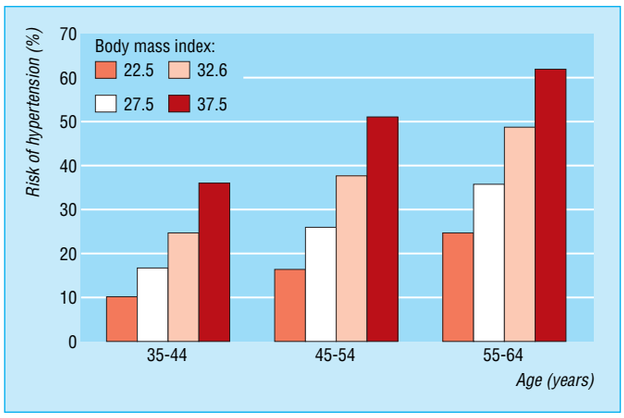
Adapted from INTERSALT cooperative research group. *BMJ* 1988;297:319–28

Weight

People who are obese or overweight tend to have higher blood pressures than thin people. Even after taking into account the confounding effects of obese arms and inappropriate cuff sizes on blood pressure measurement, a positive relation still exists between blood pressure and obesity—whether expressed as body mass index (weight (kg)/(height (m)^2)), relative weight, skinfold thickness, or waist to hip ratio. An increase in body weight from childhood to young adulthood is a major predictor of adult hypertension.

This association is clearly related to a high energy diet, although other dietary factors may be implicated (for example, high intake of sodium). The risk is greater in patients with truncal obesity, which may be a marker for insulin resistance, activation of the sympathetic nervous system, or other pathophysiological mechanisms that link obesity and hypertension. The close association of obesity with diabetes mellitus, insulin resistance, and impaired glucose tolerance and high levels of plasma lipids also partly explains why obesity is such a powerful risk factor for cardiovascular disease.

In general, trials of weight reduction show changes in mean systolic blood pressure and diastolic blood pressure of about 5.2 mm Hg in patients with hypertension and 2.5 mm Hg in people with normal blood pressure. This translates roughly to a reduction in blood pressure of 1 mm Hg for each kilogram of weight loss.



Hypertension and body mass index (BMI) observed in the NHANES III study. Adapted from Thompson PD, et al. *Arch Intern Med* 1999;159:2177–83

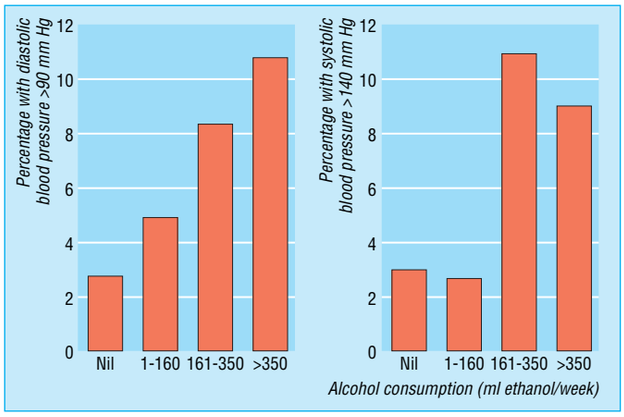
Alcohol

Epidemiological studies have shown a positive relation between alcohol consumption and blood pressure, which is independent of age, obesity, cigarette smoking, social class, and sodium excretion. In the British Regional Heart Study, about 10% of cases of hypertension (blood pressure ≥160/95 mm Hg) could be attributed to moderate or heavy drinking. Generally, the greater the alcohol consumption, the higher the blood pressure, although teetotallers seem to have slightly higher blood pressures than moderate drinkers.

The reversibility of hypertension related to alcohol has been shown in population surveys and alcohol loading and restriction studies. A reduction in weekly alcohol consumption is associated with clinically significant decreases in blood pressure, independent of weight loss, in people with normal blood pressure and those with hypertension. A reduction in intake of about three drinks per week was estimated to result in an average fall in supine systolic blood pressure of 3.1 mm Hg.

The mechanisms of the relation between alcohol and blood pressure are uncertain, but they are not explained by body mass index or salt intake. The effects of alcohol on blood pressure may include:

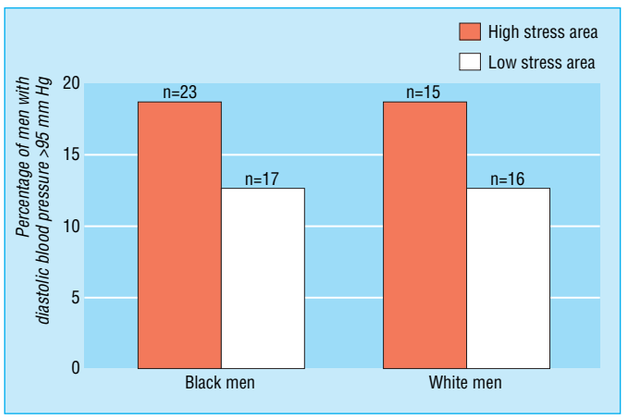
- A direct pressor effect of alcohol
- Sensitisation of resistance vessels to pressor substances
- Stimulation of the sympathetic nervous system (possibly as a result of fluctuating levels of alcohol in blood)
- Increased production of adrenocorticoid hormones.



Alcohol and hypertension. in a working population. Adapted from Arkwright P, et al. *Circulation* 1982;66:60–6

Stress

Psychological or environmental stress may play a small part in the aetiology of hypertension, although studies frequently have been confounded by other environmental or lifestyle factors. Although research has focused on possible direct effects of psychosocial "stress" on blood pressure, "stressors" such as poverty, unemployment, and poor education are involved, as are other aspects of lifestyle that are linked to hypertension (including obesity, a diet high in salt, and physical inactivity).



Stress, ethnicity, and hypertension in men. Stress was classified by residential area and crime rates. Adapted from Harburg E, et al. *J Chronic Dis* 1973;26:595–611

Although stressful stimuli may cause an acute rise in blood pressure, whether this has any significance in the long term is doubtful. A reduction in psychological stress through biofeedback techniques may reduce blood pressure in the clinic, although little effect on ambulatory blood pressure recordings at home is seen. In a recent meta-analysis of trials that involved stress management techniques such as meditation and biofeedback with at least six months of follow up, only eight trials that met the inclusion criteria were identified and the findings were inconsistent, with very small pooled falls in systolic and diastolic blood pressure (1.0/1.1 mm Hg).

Exercise

Blood pressure increases sharply during physical activity, but people who undertake regular exercise are fitter and healthier and have lower blood pressures. Such people, however, also may have a healthier diet and more sensible drinking and smoking habits.

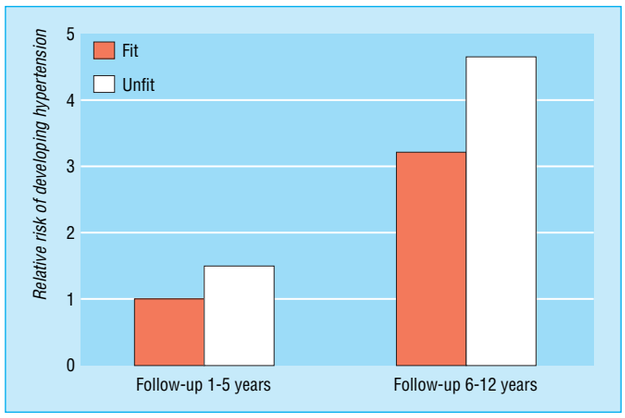
Recent studies suggest an independent relation between increased levels of exercise and lower blood pressures; vigorous exercise might be harmful, but all other grades of exercise increasingly are beneficial. Observational epidemiological studies also show that physical activity reduces the risk of heart attack and stroke, which may be mediated by beneficial effects on blood pressure. In the British Regional Heart Study, an inverse association between physical activity and systolic and diastolic blood pressure was seen in men who did not have evidence of ischaemic heart disease. This association was independent of age, body mass index, social class, smoking status, total levels of cholesterol, and levels of high density lipoprotein cholesterol.

Other dietary factors

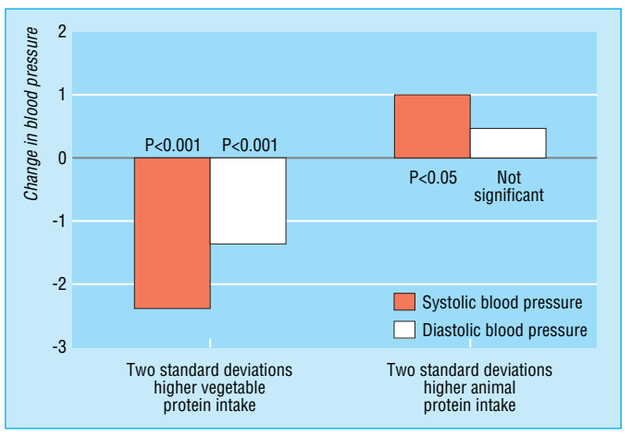
Blood pressure in vegetarians is generally lower than in non-vegetarians. Substitution of animal products with vegetable products reduces blood pressure. The mechanisms of this beneficial effect of a vegetarian diet are uncertain. It may, in part, be related to a lower intake of dairy products or salt. Alternatively the lower blood pressures may be related to a higher dietary intake of potassium, fibre, flavinoids, or vegetable protein (see Elliott P, et al. *Arch Intern Med* 2006;166:79–87).

Large amounts of omega 3 fatty acids from fish oils may reduce blood pressure in people with hypertension. In observational studies, important inverse associations of blood pressure with intake of fibre and protein have been reported.

Although caffeine acutely increases blood pressure, tolerance to this pressor effect is generally believed to develop rapidly. A recent report suggests an association of raised blood pressure with an excessive intake of cola drinks, with an effect seen with "diet" and high energy cola drinks. This may be related to their caffeine content.



Physical fitness and later hypertension. Adapted from Blair SN, et al. *JAMA* 1984;252:487–90



Vegetable protein and blood pressure in the INTERMAP study. Adapted from Elliot P, et al. *Arch Intern Med* 2006;166:79–87 and Stamler J, et al. *J Human Hypertens* 2003;17:591–608

The table of prevalence of hypertension is adapted from Lane D, et al. *J Human Hypertens* 2002;16:267–73. The table of blood pressure in populations of African origin in the UK is adapted from Agyemang C, Bhopal, RS. *J Human Hypertens* 2003;17:523–34. The table of secondary hypertension is adapted from Rudnick NR, et al. *CMAJ* 1977;117:492–7; Sinclair AM, et al. *Arch Intern Med* 1987;147:1289–93; and Anderson GH, et al. *J Hypertens* 1994;12:609–15.