

5 Hypertension

Richard J McManus and Jonathan Mant

1 Summary

Introduction

Hypertension – that is, raised blood pressure – affects up to a third of adults in England. It is asymptomatic in the majority of cases but predisposes to significant morbidity and mortality, particularly due to stroke and coronary heart disease (CHD). It is also a risk factor in some renal disease and may accelerate cognitive decline. Both the treatment of hypertension and its sequelae are associated with significant costs to the NHS: stroke and CHD alone consume almost 9% of the total budget.

Treatment can significantly reduce risk of stroke and CHD. However, achieving these gains depends on identification of cases and community surveys suggest that only a third of those with raised blood pressure receive treatment and only a third of these are controlled below commonly accepted targets.

The definition of thresholds for hypertension is problematic due to evidence of a log-linear relationship between blood pressure and risk at all levels of blood pressure. This had led to variations in definition between various national and international guidelines. Furthermore, evidence is emerging in stroke at least that lowering blood pressure is worthwhile whatever the baseline level.

Sub-categories

Due to the problems with definition of blood pressure we have taken a pragmatic approach to the sub-categories used and have broadly kept to those definitions recommended by the Joint British Societies Statement. The sub-categories used are as follows:

- **Group 1:** *Raised blood pressure – level sufficient to merit treatment regardless of cardiovascular risk.* Definition: For people without diabetes, blood pressure $\geq 160/100$ mmHg (either diastolic alone, systolic alone or both) *or* evidence of target organ damage with blood pressure below 160/100 mmHg. The level of blood pressure along with the overall cardiovascular risk dictates the degree of urgency.
- **Group 2:** *Raised blood pressure – treat on basis of underlying cardiovascular risk.* Definition: sustained systolic blood pressure in the range 140–159 *or* sustained diastolic blood pressure 90–99 mmHg with no evidence of target organ damage. In this group, overall cardiovascular risk dictates the need for treatment.
- **Group 3:** *Raised blood pressure and diabetes.* Definition: blood pressure $\geq 140/90$ mmHg with co-existing diabetes mellitus. In this group the presence of diabetes lowers the treatment threshold whatever other cardiovascular risk factors are present.

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- **Group 4:** *Malignant or accelerated hypertension.* Definition: hypertensive emergency with bilateral retinal haemorrhages and exudates.
- **Group 5:** *Secondary hypertension.* Definition: hypertension with clear underlying cause, often renovascular or endocrine.
- **Group 6:** *White coat hypertension.* Definition: blood pressure raised in the presence of medical personnel but not otherwise and with no evidence of target organ damage.

Literature on the epidemiology of hypertension tends to combine groups 1, 2 and 3 under the umbrella term of essential hypertension, i.e. hypertension with no discernible cause. This pragmatic grouping will also be used where applicable in this chapter.

Prevalence and incidence

The prevalence and incidence is summarised in **Table 1**.

Table 1: Prevalence and incidence of hypertension.

Category	Prevalence	Incidence	Comment
Essential hypertension (sub-categories 1–3)	36.5% >16 years raised or on treatment 9.6% >16 years on treatment (both figures from community survey)	<1% per year in under 30s 4–8% in those aged 60–79	Prevalence and incidence both rise with age. Community surveys tend to overestimate prevalence of hypertension.*
Diabetes and hypertension (sub-category 3)	Prevalence in newly presenting diabetics 40%	No data	Current prevalence probably higher as study quoted used conservative cut-off figure (>160/90).
Malignant or accelerated hypertension (sub-category 4)	1–2/100 000 population	No data	
Secondary hypertension (sub-category 5)	10%	No data	Primary hyperaldosteronism comprises half of all cases.
White coat hypertension (sub-category 6)	7–35%	No data	Wide variation between studies depending on definition and method of measurement.

*Blood pressure measured on one occasion will overestimate presence of hypertension compared to the recommended three occasions.

Services available and their costs

Diagnosis

The diagnosis of hypertension depends on clinical evaluation usually in primary care, including blood pressure measurement with further investigations indicated if pressures remain consistently raised. More specialised investigations may be required if there is suspicion of secondary or white coat hypertension.

Screening

No national community screening programme exists for hypertension and blood pressure is commonly measured opportunistically in primary care. The prevalence of untreated hypertension suggests that current methods may be inadequate.

Treatment

Treatment for hypertension may be divided into three categories: non-pharmacological aimed at lowering blood pressure (diet, exercise and stop smoking), pharmacological aimed at lowering blood pressure (i.e. antihypertensive medication) and pharmacological aimed at reducing other cardiovascular risk factors (i.e. cholesterol lowering and anti-platelet agents).

Setting

The majority of care for hypertension (>90%) occurs in primary care on an outpatient basis. Smaller numbers are seen in hospital outpatients (mostly for assessment of possible secondary causes) with very few inpatient episodes per year.

Costs

The main direct costs of hypertension are due to medication which varies widely in costs depending on class of drug from £20/patient/year to over £300/patient/year. A typical PCT would expect to spend well over £1 million on antihypertensive medication per year.

Effectiveness of services and interventions

Diagnostic tests

Measurement of blood pressure using a sphygmomanometer is the standard method of diagnosis. More than one measurement on at least three occasions is required due to the natural variability of blood pressure. Measurement may be performed using a mercury, aneroid or electronic sphygmomanometer. All of these methods may be inaccurate, principally due to operator or device errors.

Screening for hypertension

Little evidence for systematic screening for hypertension over and above opportunistic case finding exists. The prevalence of untreated hypertension in the community suggests that current practice is not effective.

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Opportunistic screening has the potential to reach the vast majority of patients registered with a GP within a five year time period.

Non-pharmacological treatment

Evidence from small RCTs has shown that small but significant reductions of blood pressure (1–3 mmHg) are possible following non-pharmacological treatment including exercise, weight loss, reduced salt intake, and reduced alcohol intake. Stopping smoking does not reduce blood pressure but reduces overall cardiovascular risk.

Pharmacological treatment

Unequivocal evidence from numerous large RCTs and meta-analyses now exists that reduction of blood pressure using antihypertensive medication is effective at reducing stroke and CHD. This strong evidence applies to both men and women when analysed separately. The latest meta-analyses including data from the ALLHAT trial as well as other recent RCTs suggests that the major benefits from lowering blood pressure are proportional to the reduction in blood pressure achieved and are independent of the agent used, at least for diuretics, beta-blockers, ACE inhibitors and calcium antagonists.

Absolute benefit from lowering blood pressure in terms of absolute risk reductions is dependent on baseline risk and so most advantage comes from treating the elderly and those with co-morbidities such as diabetes. Evidence for current treatment targets is flawed but suggests that a target of <140/85 mmHg as suggested by the Joint British Societies is reasonable for those without diabetes.

Population treatment

Population approaches to lowering blood pressure are attractive in that relatively small reductions in pressure across a whole population can theoretically result in large gains for that population. Interventions such as supermarkets lowering salt content in food have the potential to realise such gains.

Cost-effectiveness

Most of the evidence for the cost-effectiveness of antihypertensive treatment comes from modelling exercises and suggests that treatment is most cost-effective for those who are older or at higher risk for some other reason.

Models of care and recommendations

Guidelines for hypertension treatment

The British Hypertension Society (BHS) recommends that treatment is required for all patients with a sustained blood pressure greater than 160/100 mmHg and not required for those with a blood pressure below 140/90 mmHg. Between these limits, treatment will depend on evidence of end organ damage, coronary heart disease risk $\geq 15\%$ over 10 years or the presence of diabetes. For those receiving treatment then target blood pressures should be 140/85 mmHg for those without diabetes and 140/80 mmHg for those with diabetes. Choice of antihypertensive agent may be influenced by co-morbidities but in general the evidence suggests that cheaper alternatives are as effective as more expensive classes. In combining

drugs, the BHS 'ABCD' rule (ACE inhibitor or beta-blocker first line for under-55s combined with a calcium antagonist or diuretic (which are first line for over-55s)) is a reasonable one.

A quantified model for hypertension care

An opportunistic but systematically carried out method for screening in primary care is suggested. Treatment costs of those diagnosed with this method will vary dependent on the choice of medication. Assuming a five year cycle of screening, a PCT of 100 000 population will require 14 300 screening blood pressure checks per year and will treat an additional 2100 individuals per year over and above those currently receiving treatment. Total yearly additional costs will vary between £440 000 and £1.35 million depending on the choice of antihypertensives used. Overall, a five year screening programme will cost approximately £2.4 million – £8.9 million per 100 000 population over and above current costs, depending on the drugs used (i.e. more than doubled from current levels).

Approaches to audit and outcome measures

Most audit for hypertension on a national basis will now be geared towards the new General Medical Services contract for primary care which came into force in April 2004. This includes the following criteria for people with hypertension:

- **BP 1:** The practice can produce a register of patients with established hypertension (Yes/No).
- **BP 2:** The percentage of patients with hypertension, whose notes record smoking status at least once (standard max 90%).
- **BP 3:** The percentage of patients with hypertension who smoke, whose notes contain a record that smoking cessation advice has been offered at least once (standard max 90%).
- **BP 4:** The percentage of patients with hypertension in which there is a record of the blood pressure in the past 9 months (standard max 90%).
- **BP 5:** The percentage of patients with hypertension in whom the last blood pressure (measured in last 9 months) is 150/90 or less (standard max 70%).

Research priorities

Key areas for research in hypertension include:

- robustly powered studies with appropriate clinically relevant end points (i.e. mortality and major morbidity) to determine the efficacy of non-pharmacological measures in the treatment of hypertension
- further studies examining the effect of increased user involvement in the treatment and control of hypertension
- community-based studies evaluating the benefit of generic antihypertensive medication post stroke
- long-term community-based studies with clinically relevant end points evaluating the implementation of treatment for hypertension on the basis of risk rather than blood pressure thresholds.

2 Introduction and statement of the problem

Hypertension as a major health issue

Over a third of adults in England can be categorised as having hypertension.¹ Hypertension is asymptomatic, but is associated with significant morbidity and premature mortality, primarily from stroke and coronary heart disease.² It is also an important cause of renal disease,³ and may have a role in accelerating cognitive decline.⁴ Both the treatment of hypertension and its sequelae are associated with significant costs to the NHS – coronary heart disease has been estimated to account for 2.5% and stroke 6% of total NHS expenditure.⁵

Treatment of hypertension is associated with important reductions in risk of stroke and coronary heart disease. A 10–12 mmHg reduction in systolic and a 5–6 mmHg reduction in diastolic blood pressure has been shown to lead to a highly significant reduction in relative risk of stroke (38%, 95% CI 31–45%) and coronary heart disease (16%, 95% CI 8–23%) – *see* section 6.⁶ Therefore in theory, substantial reductions in the burden of coronary heart disease and stroke could be achieved by optimal treatment of blood pressure. However, to translate this trial-demonstrated efficacy into community-based effectiveness, people with hypertension need to be identified, treated, and their blood pressure controlled. The ‘Rule of Halves’ as stated in 1972 was that: ‘50% of hypertensives are unknown; 50% of the known hypertensives are untreated and that 50% of those treated are not controlled’.⁷ Ebrahim estimated that if the rule of halves still applied, the effect on stroke risk reduction of treating hypertension in the community will have been reduced to 5%.⁸ Similarly, the risk reduction for coronary heart disease will have been lessened from 16% to 2%. While there is some evidence that a greater proportion of hypertensive people have been identified and treated in recent years, there is still substantial under-treatment of hypertension in the community as described in section 5.

Definitions of hypertension

As outlined in section 3, the definition of hypertension is problematic. Blood pressure is a continuous variable, and any cut-off between normal and abnormal is to some extent arbitrary. Indeed, in the last decade, emphasis in treating hypertension has changed from consideration of the blood pressure alone, to consideration of blood pressure in the context of the underlying risk of cardiovascular disease in a given individual. The higher the risk of cardiovascular disease, the greater the potential benefit in terms of absolute risk reduction for an individual in lowering their blood pressure. Thus, guidelines recommend lower treatment thresholds for initiating antihypertensive therapy in people with other risk factors for cardiovascular disease (*see* section 7), such as diabetes, hyperlipidaemia and smoking. Indeed, the implications of the PROGRESS trial are that in people who have had a stroke, treatment should be considered in people who are traditionally thought to be normotensive.⁹ Thus, the terminology is switching from ‘treating hypertension’ to ‘lowering blood pressure’.

Purpose and scope of this chapter

The aim of this chapter is to provide the background information for commissioners of health care – a responsibility being taken over by primary care trusts in England – to inform their decision making on policy with regard to hypertension services. The chapter does not address the sequelae of hypertension, which are dealt with in separate chapters in this series. The chapter does comment on treatment of hypertension in the context of some specific diseases, such as diabetes, but readers should cross-refer to the other chapters that address these diseases (including diabetes, coronary heart disease and stroke).

Key questions for commissioners of health care include:

- choice of antihypertensive agents, which has significant cost implications, given the ten-fold difference in costs of different drugs (*see* section 5)
- how to improve population coverage, given the evidence from the Health Survey for England of significant under-diagnosis and under-treatment of hypertension (*see* section 5)
- how to ensure optimal blood pressure lowering in people at high risk of cardiovascular disease.

A particular issue in relation to the latter point is blood pressure lowering in the elderly. There is good evidence from systematic reviews of randomised controlled trials that treatment of elderly people with hypertension is an effective way to reduce risk of stroke and coronary heart disease (*see* section 6).^{10,11} Despite this, surveys have consistently demonstrated, as shown in section 5, that general practitioners have a higher threshold for treating hypertension in older patients.¹²

There are two complementary strategies to reducing morbidity from hypertension. One is to identify and treat individuals with high blood pressure. This is sometimes referred to as the 'high risk' approach.¹³ An alternative strategy is to aim to lower blood pressure in the population as a whole, the so-called 'population strategy'. The attraction of the population strategy is that it will lower risk in the whole population, and not just in high risk individuals, and therefore has the potential to lead to greater reductions in stroke and coronary heart disease than strategies focusing on those individuals with higher blood pressure. While the focus of much preventive health care is on identifying and treating at-risk individuals, commissioners of health care have important public health responsibilities, which include taking this broader population-based perspective on preventive strategy. Therefore, population-based strategies to lower blood pressure in the population are included within the scope of this chapter, although the responsibility for implementation is wider than health care commissioners alone.

3 Sub-categories

The categorisation of blood pressure is of necessity an arbitrary exercise, as there is a continuum of cardiovascular risk associated with the level of blood pressure: the higher the blood pressure, the higher the risk of both stroke and coronary events.^{2,14} Within this continuum, all but the highest blood pressures produce little in the way of symptoms for the patient and so these cannot form the basis of a categorisation. Qualitative terms such as mild, moderate and severe have been used to label increasing levels of blood pressure but without universal acceptance of the definition of these terms.¹⁵

In the majority of patients with asymptomatic hypertension, it has become commonplace to use level of cardiovascular risk to guide the level at which intervention to lower blood pressure is required.^{16–18} In determining cardiovascular risk, two broad categories of risk factor must be taken into account: fixed and modifiable. Age, sex and family history are the most important fixed risk factors, whilst modifiable factors include smoking, serum cholesterol, diabetes (in terms of control), blood pressure, left ventricular hypertrophy, diet and exercise status.¹⁹ Many of these risk factors have been combined in a set of risk equations derived from multifactorial analysis of the results from 12 years of follow-up of the subjects in the Framingham Heart Study.²⁰ Estimations of the risk of a number of cardiovascular end points can then be made for patients without current cardiovascular disease and may be used to inform thresholds for intervention at various levels of blood pressure.

Evidence of end organ damage is another factor which affects the intervention threshold for blood pressure control. High blood pressure affects the heart, kidneys, brain and eye – so-called 'end organs' – via vascular damage to both the small (resistance) arteries and arterioles and large (conduit) arteries. Whilst

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there is universal agreement that end organ damage is important, there is no agreed definition of what constitutes damage. One scheme adapted from that proposed in Canadian guidelines is shown in **Table 2**.²¹

Table 2: Definitions of hypertensive end organ damage (adapted from Myers *et al.* 1989²¹).

Target organ	Evidence of damage
Heart and peripheral vasculature	a) Left ventricular hypertrophy with strain demonstrated by electrocardiography or echocardiography. b) A history or symptoms of angina pectoris. c) A history or electrocardiographic evidence of myocardial infarction. d) A history or symptoms of intermittent claudication.
Brain	Previous history of transient ischaemic attack or cerebrovascular accident.
Kidney	Serum creatinine >150mmol/l.
Eye	Evidence of hypertensive retinopathy.

This difficulty in categorisation is reflected in the differences in recommendations from various national and international bodies for the diagnosis and treatment of hypertension. Of these recommendations, those of the World Health Organization,²² and the national guidelines of New Zealand,¹⁷ Canada,²¹ US¹⁶ and UK¹⁸ are the best known and most cited. Whilst there are many similarities between these guidelines there are also important differences. These differences include the definitions of both treatment thresholds and target blood pressure.

The key differences between the guidelines in terms of definition of hypertension that warrants treatment are summarised in **Table 3**.

Table 3: Blood pressure thresholds for treatment (adapted and updated version of Swales, 1994 to include current versions of guidelines¹⁴).

Guideline	Absolute treatment threshold: Diastolic blood pressure (mmHg)	Absolute treatment threshold: Systolic blood pressure (mmHg)	Period of observation (months)	Treatment threshold in presence of other risk factors (mmHg)
Canada ²³	90 if aged under 60 105 if over 60	160	3–6	90
Britain ¹⁸	100	160	4–6	140/90
USA ²⁴	90	140	1 week–2 months	120/80
New Zealand ¹⁷	100	170	6	150/90–170/100 depending on overall cardiovascular risk
WHO/ISH ²²	95	150	3–6	140/90

All of the guidelines recognise that overall cardiovascular risk affects treatment threshold. Both the New Zealand and British guidelines advocate formally estimating risk, using a series of tables or a computer program, before considering treatment for patients lying within their definition of mild hypertension. All of the authorities agree on the need for treatment of sustained hypertension above the threshold of 170/100 and none recommend treatment below 130/85. Between these two values there is considerable variation in the level and associated cardiovascular risks at which treatment is advocated.

The importance of blood pressure control in diabetes is now well established. People with diabetes derive more benefit from blood pressure reduction than those without diabetes.^{18,25} Moreover, there is good evidence that lowering blood pressure in those with type 2 diabetes reduces both micro and macrovascular changes.²⁶ In view of this we have separated outpatients in this group as a separate sub-category.

A special sub-category of hypertension is malignant hypertension, which is defined by WHO as the presence of bilateral retinal haemorrhages and exudates in the presence of severe hypertension – typically with a diastolic blood pressure greater than 130 mmHg.²⁷ Malignant hypertension is accompanied by a number of clinical features, the most common of which are left ventricular hypertrophy, headache, visual impairment and renal failure.²⁸ The relevance of this sub-category is that urgent treatment is required to limit the risk of serious complications, most notably the onset of renal failure.

As already discussed, most patients with hypertension are asymptomatic and have no discernible cause for their raised blood pressure. However, around 10% have a clearly defined cause for their hypertension.^{29,30} These form another important sub-group. In most cases, the underlying cause is endocrine (principally normokalaemic hyperaldosteronism), renal or vascular.^{29,30} These will be discussed as a separate sub-group as they are important not only in their own right, but in view of the implications for the investigation of the majority of patients with hypertension.

White Coat Hypertension is a description of the phenomenon whereby the blood pressure rises simply in association with the procedure of having it measured. This can be effectively identified using ambulatory blood pressure measurement and although patients do not generally need treatment, it is appropriate to consider this as a separate sub-category, since patients with this condition are at higher risk of subsequently developing true hypertension.³¹

In view of a lack of a universally accepted sub-categorisation of hypertension, this document has used the following sub-categories. The first three groups correspond to the blood pressure thresholds suggested in 1998 by the Recommendations of the Joint British Societies:³²

- **Group 1:** *Raised blood pressure – level sufficient to merit treatment regardless of cardiovascular risk.* Definition: For people without diabetes, blood pressure $\geq 160/100$ mmHg (either diastolic alone, systolic alone or both) *or* evidence of target organ damage with blood pressure below 160/100 mmHg. The level of blood pressure along with the overall cardiovascular risk dictates the degree of urgency.
- **Group 2:** *Raised blood pressure – treat on basis of underlying cardiovascular risk.* Definition: sustained systolic blood pressure between 140–159 *or* sustained diastolic blood pressure 90–99 mmHg with no evidence of target organ damage. In this group, overall cardiovascular risk dictates the need for treatment.
- **Group 3:** *Raised blood pressure and diabetes.* Definition: blood pressure $\geq 140/90$ mmHg with co-existing diabetes mellitus. In this group the presence of diabetes lowers the treatment threshold whatever other cardiovascular risk factors are present.
- **Group 4:** *Malignant or accelerated hypertension.* Definition: hypertensive emergency with bilateral retinal haemorrhages and exudates.
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Literature on the epidemiology of hypertension tends to combine groups 1, 2 and 3 under the umbrella term of essential hypertension, i.e. hypertension with no discernible cause. This pragmatic grouping will also be used where applicable in this chapter.

4 Prevalence and incidence

Essential hypertension (sub-categories 1–3)

Most community surveys measuring the prevalence of hypertension do not differentiate patients on the basis of cause of hypertension, but rather by other criteria such as age, sex and ethnicity. Essential hypertension (sub-categories 1–3) makes up around 95% of all cases and so the overall figures are presented here as broadly representative of the population burden of essential hypertension. The major sources of data are the Health Survey for England (HSE) 1998¹ and the General Practice Research Database (GPRD).³³ The Health Survey for England sampled a population of almost 16 000 drawn from 720 postcode districts stratified for health authority and social class of head of household. Hypertension was defined as a mean resting blood pressure $\geq 140/90$ mmHg or receiving treatment for hypertension. Blood pressure readings were taken on one occasion and although multiple measurements were made, this does not correspond to the definition of true hypertension, which requires that the elevation of blood pressure is sustained.¹⁸ Furthermore, the threshold adopted by the Joint British Societies and in the sub-categories of this chapter for hypertension was 160/100 or 140/90 in the presence of significant coronary heart disease risk due to presence of other risk factors. For both of these reasons, the estimates from the HSE are likely to overestimate the true prevalence of hypertension. The GPRD comprises electronic data from the computer records of over 350 general practices throughout the UK.³³ It provides an alternative estimate of the prevalence of treated hypertension, defined as an ever-recorded diagnosis of hypertension in combination with treatment with an antihypertensive agent.

Prevalence by age and sex

Overall hypertension is more common in men than women and rises in prevalence with age. The rise with age is more pronounced in women who have a higher prevalence in the over-65 age group. Using the HSE definition of hypertension, over a third of the adult population have raised blood pressure, and the majority of people over the age of 55. Figures are presented in **Table 4** for men, women and overall derived from the Health Survey for England 1998.¹

Despite the higher prevalence of hypertension in men than women, the prevalence of treated hypertension is higher in women than men. This finding is echoed in the GPRD data (*see Table 5*), which shows a similar pattern of age specific prevalence of treated hypertension to that of the HSE. The overall standardised rate is lower in the GPRD as this is a prevalence for all ages, whereas the HSE gives an overall prevalence for adults (aged 16 or over).

Prevalence by region

Table 6 shows age and sex standardised prevalence by region. Prevalence varies in men from 35% in the North West Region, to 43% in Northern and Yorkshire Region.

Prevalence by socioeconomic group

There is an association between social class and hypertension, with higher rates in the lower social classes – see **Table 7**.

Table 4: Prevalence (%) of hypertension by age and sex.¹

	Age							Total
	16-24	25-34	35-44	45-54	55-64	65-74	>75	
<i>Males</i>								
Overall	16.0	20.5	26.1	42.3	59.8	69.9	72.8	40.8
On treatment	0	0.3	2.3	7.2	17.4	20.6	22.6	8.5
>140/90, untreated	16.0	20.2	23.8	35.4	42.4	49.3	50.2	32.3
<i>Females</i>								
Overall	4.2	6.9	13.2	30.8	51.6	72.8	77.6	32.9
On treatment	0.1	0.5	2.4	6.2	15.5	30.0	31.8	10.5
>140/90, untreated	4.0	6.4	10.8	24.6	36.0	42.9	45.8	22.5
Overall	9.7	13.2	19.0	36.1	55.4	71.4	75.7	36.5
On treatment	0.1	0.4	2.4	6.7	16.4	25.6	28.1	9.6
>140/90, untreated	9.5	12.8	16.7	29.5	38.9	45.9	47.6	27.0

Table 5: Prevalence (%) of treated hypertension by age and sex: GPRD data for 1998.³³

	Age							Overall (standardised)
	0-34	35-44	45-54	55-64	65-74	75-84	>85	
Males	0.2	2.0	7.3	16.4	25.9	28.1	20.1	6.0
Females	0.2	2.1	7.9	18.8	30.2	37.5	29.1	7.1

Table 6: Standardised prevalence (%) of hypertension by region.¹

	Northern & Yorks	North West	Trent	West Midlands	Anglia & Oxford	North Thames	South Thames	South & West
Males	43.0	35.1	38.4	39.2	38.3	36.5	38.5	42.2
Females	36.0	30.6	32.9	32.4	33.8	31.2	32.4	34.2

Table 7: Standardised prevalence (%) of hypertension^a by social class.¹

	I	II	IIINM	IIIM	IV	V
Men	34.3	38.0	37.2	41.8	35.2	40.2
Women	31.4	31.3	34.4	34.2	34.4	35.9

^a Defined as BP >140/90 mmHg or on treatment for hypertension.

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Prevalence by ethnic group

The data presented in **Table 8** are taken from the HSE minority ethnic group report 1999.³⁴ Some of these figures are likely to be imprecise due to the small numbers of representatives in a number of ethnic groups surveyed, most notably the Chinese. In general, the prevalence of hypertension is lower in minority ethnic groups than it is in the general population. The exception to this is the high prevalence of hypertension in the Black Caribbean group associated with cardiovascular disease. It is difficult to judge whether the prevalence of hypertension is genuinely lower in minority ethnic groups, or whether this reflects treatment patterns.

Table 8: Observed prevalence (%) of hypertension^a by ethnic group amongst those with and without CVD conditions.^{b 34}

	Black Caribbean	Indian	Pakistani	Bangladeshi	Chinese	Irish	All
<i>Males</i>							
with CVD	78	59	61	45	64 ^c	61	71
without CVD	36	32	20	19	24	37	38
<i>Females</i>							
with CVD	67	62	51	43	35 ^c	53	65
without CVD	23	20	12	9	22	24	30

^a Defined as: on treatment for hypertension or with recorded blood pressure >140/90.

^b Defined as self-reported presence of angina, heart attack, stroke, heart murmur, irregular heart rhythm, 'other heart trouble' or diabetes.

^c Very small numbers of Chinese individuals with CVD were included in the survey.

Incidence of hypertension

In terms of a health care needs assessment for hypertension, prevalence is a much more useful concept than incidence. What is relevant in this context is ascertaining the number of people who, on the basis of their blood pressure and other risk factors for cardiovascular disease, would benefit from treatment to lower their blood pressure. Since treatment will usually be long-term, prevalence will be the major determinant of this need rather than incidence. However, incidence does give an indication of the numbers of new patients that warrant treatment over a given period of time.

The incidence of hypertension increases with age from <1–2% in people aged 20–29 to 4–8% aged 60–79.³⁵ Incidence is higher in younger men than women, but higher in older women than men. Factors associated with higher incidence of hypertension include obesity, excessive use of alcohol, salt consumption, and lack of exercise.³⁵

Trends in mean blood pressure in the population

As well as looking at number of 'cases', which is how prevalence and incidence data deal with hypertension, it is also useful to look at the mean level of blood pressure in the population. Firstly, as already emphasised, blood pressure is a continuous variable, and any cut-off between cases and non-cases is to some extent arbitrary. Secondly, in terms of population strategies to lower blood pressure (*see* 'Non-pharmacological' in section 5), the mean blood pressure is a more useful indicator.

Trends in age-specific systolic and diastolic blood pressure from 1994–98 in men and women are shown in **Figures 1–4**, drawing on data from the HSE.¹

Between 1994 and 1998, there is some evidence of small falls in the age-specific mean blood pressures of the English population. Over the five year period, the age-specific mean blood pressures for men went down on average by 1.7/0.9 mmHg, and for women by 2.7/1.2 mmHg. If real, these small declines in blood pressure would be clinically important in terms of leading to corresponding falls in the incidence of stroke and coronary heart disease (*see* section 6). The decline in blood pressure appeared to be slightly more pronounced in older people: in men, the blood pressure of people aged 75 and over went down by 2/2 mmHg, and in women by 4.5/2.8 mmHg. US data over a longer time scale (1960–1980) also offer evidence of a decline in blood pressure over time.³⁵ The age-adjusted mean systolic blood pressure went down by 4–8 mmHg in men and 6–8 mmHg in women. Again, the decline was greater in the older age groups.

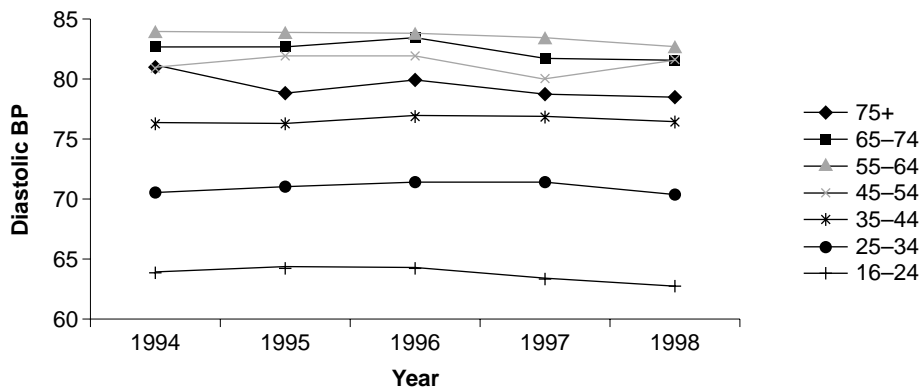


Figure 1: Trends in diastolic BP in men: 1994–98.

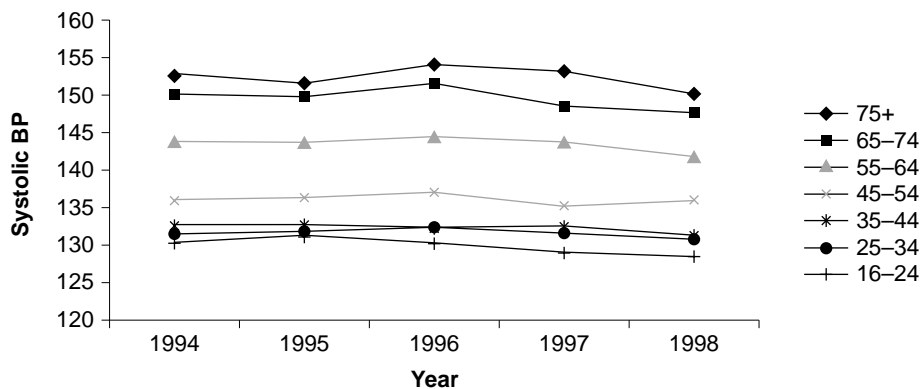


Figure 2: Trends in systolic BP in men: 1994–98.

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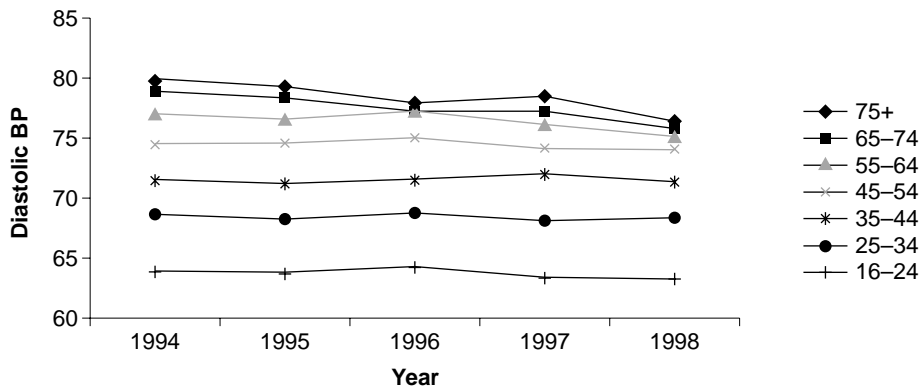


Figure 3: Trends in diastolic BP in women: 1994–98.

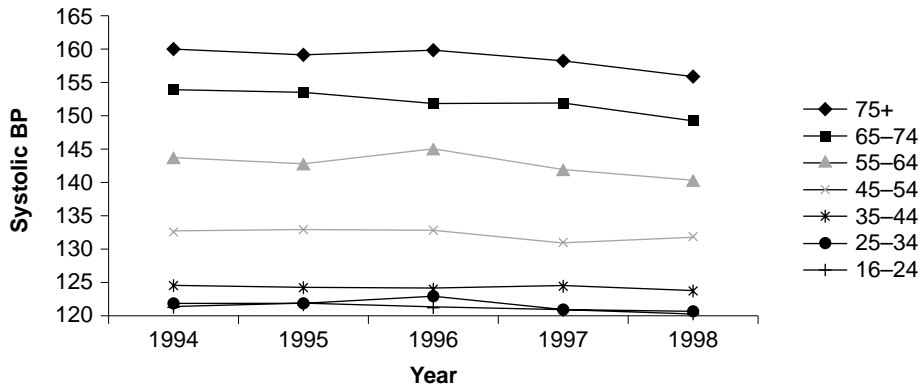


Figure 4: Trends in systolic BP in women: 1994–98.

Isolated systolic hypertension

Essential hypertension in the elderly commonly occurs in the form of isolated systolic hypertension and is worth considering separately. Isolated systolic hypertension is commonly defined as a systolic blood pressure of >160 mmHg with diastolic <95 mmHg. As with other cases of essential hypertension, prevalence rises with age – isolated systolic hypertension accounts for 25% of essential hypertension in people aged over the age of 80.³⁶

Diabetes and hypertension (sub-category 3)

Although diabetics with raised blood pressure commonly have essential hypertension, their overall increase in cardiovascular risk and the effect of hypertension on microvascular disease mean that it is helpful to consider this group separately. In the Hypertension in Diabetes Study, the prevalence in newly presenting adult diabetics was found to be 34.7% in men, and 46.5% in women.³⁷ In this study, hypertension was defined as a blood pressure >160/90, or on antihypertensive therapy. Therefore, the prevalence of hypertension appears higher in people with diabetes than those without, given the overall prevalence is similar to that obtained by the HSE which used the lower definition of >140/90 (see above).

Malignant or accelerated hypertension (sub-category 4)

Precise figures on the prevalence of malignant hypertension are rare. A series from one large hypertension unit in the West Midlands approximated a prevalence of 1–2/100 000 population.³⁸

Secondary hypertension (sub-category 5)

The prevalence of secondary hypertension was until recently thought to be around 5%. This was based on a number of 'classical series' but more recent work suggests that this is probably higher, at least 10%, with primary hyperaldosteronism an important cause. Secondary hypertension is important as treatment of the underlying cause may be life-saving and lead to normotension.

Two older studies provide data on the prevalence of secondary hypertension. Data from a Swedish population sample are available from a primary prevention trial in Goteborg.²⁹ 7455 men were initially screened, of whom 1159 were found to be hypertensive or already on treatment for hypertension (15.5%). Subsequent investigation of 689 of these patients revealed 40 to have secondary hypertension (5.8% of hypertensives). Secondary hypertension was further broken down into renal parenchymal disease (63%), renovascular disease (10%) and other forms of secondary hypertension (27%). The cut-off for hypertension was very high by modern standards (175/115 mmHg) and the series included four patients with renal tuberculosis so the numbers are not directly comparable with a current population.

A further Swedish series, this time in secondary care, (a retrospective analysis of 1000 consecutive patients attending another hypertension unit) found 47 (4.7%) to have an identifiable secondary cause of hypertension: renal parenchymal disease in 21, renal artery stenosis in 10, endocrine hypertension in 13 and hydronephrosis in 3.³⁰

More recent investigations into the prevalence of primary hyperaldosteronism have suggested that the prevalence of this abnormality amongst hypertensives may itself be as high as 3–18%.³⁹ The reason for this difference is that previous studies used hypokalaemia as a screening tool before looking for hyperaldosteronism, whereas more modern studies screen using direct measurement of serum aldosterone and the ratio of serum aldosterone to plasma renin activity. The upper limits of the prevalence range are disputed as there is concern as to selection bias in the populations concerned.³⁹ Overall it is probably reasonable to assume that around 5% of those thought previously to have essential hypertension have primary hyperaldosteronism.

A summary of the results of studies that investigated the epidemiology of secondary hypertension is shown in **Table 9**.

Table 9: Proportion of patients with secondary hypertension – summary of studies.

	Proportion in each category (range %)
Essential hypertension	72.6–95.3
Renal hypertension	2.4–17.2
Renovascular hypertension	0.6–6.1
Primary hypokalaemic aldosteronism	0.1–0.4
Primary normokalaemic aldosteronism	3–18
Phaeochromocytoma	0.2–0.7
Cushing's syndrome	0.1–0.3
Endocrine, other	0.1–0.4
Oral contraceptives	1.5–5.0
Coarctation of the aorta	0.2–0.6
Other	1.0–3.7

Adapted from Danielson and Dammstrom (1981).³⁰

White coat hypertension (sub-category 6)

Estimates of the prevalence of white coat hypertension vary between series from around 7–35%. A widely quoted secondary care series found a 21% (61/292 subjects) prevalence of normal daytime ambulatory blood pressure in patients with untreated borderline hypertension (persistently raised diastolic clinic measurements 90–104 mmHg).⁴⁰ A more recent Canadian series, again in secondary care, investigated patients with blood pressure above 140/90 mmHg despite taking at least two antihypertensive agents. They found 37/103 of these patients to have a white coat response.⁴¹ A primary care study using home blood pressure measurement rather than ambulatory monitoring found a 27% prevalence of white coat hypertension in an untreated population of 236 patients.⁴² This study also reported that 17% (45 of 258) of poorly-controlled hypertensives had white coat hypertension. The phenomenon of higher blood pressure in the presence of medical staff has also been reported in people with established hypertension.²²

Hypertension as a risk factor for disease

Observational studies have found a continuous relationship between level of blood pressure and risk of stroke and CHD. In a study combining the results of nine major prospective observational studies, a difference in blood pressure of 9/5 mmHg was associated with a difference in stroke risk of 34% and CHD risk of 21%.² An individual participant data meta-analysis including 61 prospective studies and 1 million adults found that between ages 40–69, each difference in usual systolic blood pressure of 20 mmHg was associated with a more than doubling of mortality rates from ischaemic heart disease and other vascular causes.⁴³

Similar results have been found when the risk reduction obtained by antihypertensive treatment is examined. A systematic review of antihypertensive treatment trials found a mean reduction in stroke of 38% (95% CI 31–45) for mean Diastolic Blood Pressure (DBP) reduction of 5–6 mmHg over 2–3 years. The equivalent mean reduction in CHD was 16% (8–23%). Given that CHD is more common than stroke, the absolute reduction in CHD events through treating hypertension is closer to the absolute reduction in stroke events, though the overall effect of treatment is still to prevent more strokes than coronary events (treatment vs control: 934 vs 1104 CHD events compared with 525 vs 835 strokes).⁶

The latest publication from the Blood Pressure Trialists Collaboration reports no significant difference in the relative risk reductions for total major cardiovascular events between Angiotensin Converting Enzyme Inhibitors (ACE inhibitors), calcium antagonists, diuretics and beta-blockers, so choice of agent within these classes does not appear to be a particular issue.⁴⁴

Benefit from blood pressure lowering also occurs in isolated systolic hypertension (ISH): a meta-analysis of trials of treatment of ISH found relative hazard ratios for 10 mmHg higher initial Systolic Blood Pressures (SBP) were 1.26 (p=0.0001) total mortality; 1.22 (p=0.02) stroke but only 1.07 (p=0.37) coronary events.⁴⁵

Summary of epidemiology at primary care trust level

Table 10 shows a breakdown of the number of people expected to suffer from hypertension by sub-category in a population of 100 000.

Table 10: Prevalence of hypertension and sub-categories in primary care trust (PCT) of 100,000 population.^{1,29,30,38,41}

	Prevalence
All hypertension	29,100
Treated hypertension	7,500
Elderly isolated systolic hypertension (age >70)	900
Malignant hypertension	1
Secondary hypertension	375
White coat hypertension	750
Assuming 21% of the population are under the age of 16.	

5 Services available and their costs

This section describes the services that are available to diagnose and treat hypertension, and the different settings within which that care is provided. It also provides some data on current use of services and costs. It does not comment on whether these services are effective (covered in section 6) or whether they should be available (covered in section 7).

Diagnosis

Clinical evaluation

Patients with hypertension will have a process of evaluation consisting of history (including any symptoms, lifestyle factors, cardiovascular risk factors, past medical history, possible precipitants and family history), examination (of cardiovascular system) and repeated blood pressure measurements. In primary care this will typically be carried out by the general practitioner in conjunction with the practice nurse. The patient themselves may undertake self-monitoring of blood pressure as part of this process.⁴²

Routine diagnostic investigation

Routine investigations performed in primary care on patients with hypertension typically include urine testing, blood tests and electrocardiography (ECG). These aim to screen for end organ damage as well as test for other risk factors for cardiovascular disease. The precise tests used will depend on the suspicion of a secondary cause of hypertension and this will largely depend on the age of the patient. The evidence for routine investigation and recommendations for appropriate investigation are covered in subsequent sections. A summary of the tests which may be carried out in the investigation of hypertension is provided in **Table 11**.

418 Hypertension**Table 11:** Baseline investigations for hypertension (adapted from BHS Guidelines 1999 and The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI) 1997).^{16,18}

Investigation	Rationale
<i>Performed on most patients</i>	
Urinalysis: protein and blood	Evidence of end organ damage and investigation of possible secondary cause for hypertension (Renal)
Serum creatinine and electrolytes	Investigation of possible secondary cause for hypertension: Hypokalaemia/increased plasma sodium (Endocrine – Conn's syndrome) Elevated serum creatinine (Renal)
Blood glucose	Risk assessment (diabetes)
Serum total: HDL cholesterol	Risk assessment (Framingham Risk score for primary prevention)
ECG	Evidence of end organ damage and risk assessment (investigation of possible left ventricular hypertrophy)
<i>Performed on selected patients</i>	
Note: it is unlikely that all of these investigations would be performed on a single patient but rather that a clinician would be guided by the clinical picture	
Creatinine clearance	Further investigation of renal dysfunction (end organ damage and/or secondary cause of hypertension)
Microalbuminuria	Screening for evidence of early renal; dysfunction (end organ damage principally)
24-hour urinary protein	Further investigation of renal dysfunction (end organ damage and/or secondary cause of hypertension)
Urine microscopy and culture	Investigation of haematuria and/or proteinuria (possible urinary tract infection)
Urinary catecholamines	Investigation of possible secondary cause for hypertension: Pheochromocytoma
Aldosterone/renin ratio	Investigation of possible secondary cause for hypertension: Diagnosis of hyperaldosteronism
Uric acid	Investigation of possible secondary cause for hypertension: Gout
Thyroid stimulating hormone	Investigation of possible secondary cause for hypertension: Hyperthyroidism
Serum calcium	Investigation of possible secondary cause for hypertension: Hyperparathyroidism
Chest X-ray	Investigation of possible cardiomegaly (left ventricular hypertrophy)
Echocardiogram	Further investigation of possible left ventricular hypertrophy or other structural abnormality or dysfunction of heart

Special investigations for secondary hypertension

Patients referred to secondary care for consideration of possible secondary hypertension will typically have a more intensive and/or invasive set of investigations. These will again involve blood, urine and ECG but may also include chest X-ray, ultrasonography, echocardiography and other more complex screening tests. Key conditions that these screening tests will aim to test for are: renal artery stenosis, endocrine causes of hypertension (including pheochromocytoma, Conn's disease) and renal parenchymal disease (including glomerulonephritis, renal cystic disease). These tests and their rationale are summarised in **Table 11**.

Special investigations for white coat hypertension

Patients with suspected white coat hypertension will receive further evaluation of their blood pressure in a non-health care setting. Typically this might involve either home blood pressure monitoring or ambulatory blood pressure measurement. Both will usually involve automated electronic measurement. Ambulatory measurement consists of a portable device which measures blood pressure at regular intervals (half-hourly–hourly) over a 24 hour period. Results are usually expressed in terms of mean blood pressure (overall, day and night). Home measurement involves an individual recording their own BP over a period of days or weeks.

Cost of equipment is likely to be a barrier to the widespread adaptation of both these types of measurement. Ambulatory measurement is most often available in specialised settings and home measurement generally requires an individual to purchase equipment. Alternatives to this include short-term loaning until blood pressure is controlled or self-measurement at the practice.

Screening for hypertension

Routine health checks

Blood pressure is routinely checked in UK primary care in many different circumstances. These include health checks when a patient registers with a new general practice; contraceptive and obstetric encounters for women; Accident and Emergency encounters for non-minor injury; and private medical checks performed for insurance or other reasons.

Community screening programmes

No national community screening programme exists in the UK but various models have been studied both in the UK and US. These include schemes for blood pressure screening in pharmacies, work places and even door to door screening.⁸

Treatment

Non-pharmacological

Patients presenting with new hypertension are routinely offered advice on aspects of lifestyle to both lower blood pressure and affect other risk factors. This includes diet (increase fruit and vegetables, less salt, less alcohol, weight loss), exercise (increase) and smoking (stop). A summary of the effect of these treatments is presented in 'Non-pharmacological treatment of hypertension' in section 6 and **Table 21**.

Pharmacological: blood pressure lowering

Pharmacological treatment of blood pressure can be subdivided on the basis of class of drug. In the UK, the recent British Hypertension Society guidelines recommend the 'ABCD rule' for uncomplicated hypertension.⁴⁶ This is the use of ACE inhibitors or beta-blockers as first line in the under-55s and calcium antagonists or diuretics in the over-55s. Other choices may be relevant in the case of co-existing disease or lack of efficacy of first line drugs. The utilisation of various classes of antihypertensive is presented in **Table 12**. Figures from both the general practice research database 1998³³ and Health Survey for England 1996¹ are included. The former includes all patients receiving each class of drug and gives absolute numbers

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whereas the later is by proportion of patients with hypertension. Thus, the most commonly used class of agent are diuretics – 48% of treated hypertensives are on this class of drug. The GPRD data are not hypertension-specific, so are more difficult to interpret since each of these therapies have other indications (such as ischaemic heart disease).

Data from the HOT study suggest that less than one third of hypertensive patients will be adequately controlled on monotherapy and that a similar proportion will require three or more agents for control.²⁵ Overall the mean use of antihypertensive drugs was just under 2 per patient and depending on choice of drugs, costs can be expected to vary from £20 to £455.⁴⁷

Table 12: Choices of antihypertensive drugs by class.

Drug class	GPRD 1998 All persons prescribed drugs per 1000 patients ³³		Drug class	HSE 1996 ⁴⁸ % of persons on hypertensive medication		
	Male	Female		Males	Females	All adults
Diuretics	37.8	61.2	Diuretics	39	54	48
Beta-blockers	38.0	44.5	Beta-blockers	38	35	36
Drugs affecting the renin-angiotensin system	34.9	28.0	ACE inhibitors	25	19	22
Nitrates, calcium antagonists and potassium channel activators	45.0	36.6	Calcium antagonists	36	28	31
			Other drugs affecting blood pressure	4	3	1

Inevitably trends in drug prescription have changed over time both in terms of new classes of drugs (principally ACE inhibitors) gaining in popularity and also in the proportion of patients receiving combination therapy. **Table 13** shows the change in prescription over time for the classes of drug both by absolute number (rate of prescription per 1000 patients) and by net ingredient cost (NIC).

Pharmacological: other interventions to lower cardiovascular risk

Patients with hypertension, particularly those at highest overall risk, may benefit from other pharmacological measures to lower their cardiovascular risk, namely aspirin and cholesterol-lowering drugs.¹⁸

Setting of treatment

Hypertension is largely managed in primary care with only complicated or difficult-to-control cases being referred to hospital. A number of distinct models of care exist within either setting as described below.

Table 13: Change over time in prescription of antihypertensive drugs by rate³³ and cost (NIC data from Prescription Pricing Authority; Personal Communication Dr John J Ferguson).

Year		Diuretics	Beta-blocker	ACE inhibitor ^c	Calcium channel blocker ^d
1994	Rate ^a	35.7	35.7	24.1	42.5
	NIC ^b	60,954	88,428	147,023	160,161
1995	Rate	35.7	36.0	26.9	43.3
	NIC	55,590	81,511	170,364	178,918
1996	Rate	36.3	36.2	30.1	44.2
	NIC	51,641	79,283	193,297	197,796
1997	Rate	37.0	36.8	32.4	44.7
	NIC	48,349	77,361	200,003	212,031
1998	Rate	37.8	38.0	34.9	45.0
	NIC				

^a Rate of prescription per 1,000 patients.

^b Net ingredient cost (£000s). The NIC refers to the cost of the drug before discounts and does not include any dispensing costs or fees.

^c The rate data for ACE inhibitors includes all drugs in chapter 2.5 of the BNF including all renin-angiotensin system drugs, alpha-blockers.

^d Rate data includes nitrates and potassium channel activators.

Episodic treatment

Traditionally the standard method of care in primary care, this model depends on the patient attending periodically for blood pressure measurement as well as screening for end organ damage, consideration of management changes and other risk factor modification.

Structured care

This involves primary care teams following a structured care programme, typically using protocols and recording data on blood pressure, management changes and risk factors in a systematic fashion, perhaps using a computer template. A further key feature of structured care is systematic recall of patients. Structured care can be provided by both medical and/or nursing staff either within normal 'open' surgeries or at set times of the week in a special clinic.

Shared clinics

Shared clinics involve GPs and hospital specialists sharing the management of patients either with alternate visits, 'virtually' via IT links, or sometimes by sharing a clinic on the same site on a periodic basis.⁴⁹ This model allows specialist advice for complex cases while retaining the majority of patients within primary care.

Hospital clinics

Hospital clinics receive referrals from general practitioners and typically see either newly diagnosed patients where a secondary cause is suspected or patients with established hypertension where blood

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pressure control has proved hard to achieve. Length of follow-up of patients will depend on local workload and whether a secondary cause is established.

In-patient hospital care

Hypertension *per se* is an uncommon cause of hospital admission. Patients with malignant or accelerated hypertension are admitted to hospital, and uncontrolled hypertension may be a presenting feature of underlying disease such as renal or endocrine which may precipitate hospital admission. Hypertension is a co-morbidity in many other conditions that lead to hospital admission. This is illustrated by **Table 16** (see 'In-patient data' below) which shows Hospital Episode Statistics for England for 1996/7.

Data on service use

The overall consultation rate for all people with essential hypertension is 420 persons per 10 000 person years at risk. As expected this varies considerably with age and sex as can be seen in **Table 14**.

Table 14: Patient consulting rates for hypertension per 10,000 person years at risk.⁵⁰

	Total	0-4	5-15	16-24	25-44	45-64	65-74	75-84	85+
All essential hypertension	420	1	0	9	98	813	1,656	1,430	663
Male essential hypertension		1	1	9	100	760	1,488	1,118	511
Female essential hypertension		1	0	10	96	869	1,791	1,615	713

Uptake of treatment

Another way of looking at service use is to consider what proportion of people with hypertension have been diagnosed, and what proportion of people with hypertension are on antihypertensive therapy. The Health Survey for England provides some data on this, as shown in **Table 15**. In this survey, blood pressure was measured three times on one occasion and so the proportions of people found with untreated hypertension are likely to be overestimates if compared with the number with sustained raised blood pressure over a period of weeks or months. Nevertheless, only the minority of people with hypertension appear to be currently receiving treatment.

Table 15: Blood pressure status by age and sex.

	16-24	25-34	35-44	45-54	55-64	65-74	>75	Total
	%	%	%	%	%	%	%	%
<i>Men</i>								
Normotensive ¹ (untreated)	84	79.5	73.9	57.7	40.2	30.1	27.2	59.2
Treated hypertension ²	0	0.3	2.3	7	17.4	20.6	22.6	8.5
Untreated hypertension ³	16	20.2	23.8	35.4	42.4	49.3	50.2	32.3
<i>Women</i>								
Normotensive ¹ (untreated)	95.8	93.1	86.8	69.2	48.4	27.2	22.4	67.1
Treated hypertension ²	0.1	0.5	2.4	6.2	15.5	30	31.8	10.5
Untreated hypertension ³	4	6.4	10.8	24.6	36	42.9	45.8	22.5

¹ Normotensive: untreated and with mean BP <140/90.

² Treated hypertension: on treatment for hypertension.

³ Untreated hypertension: BP >140/90 and not receiving treatment for hypertension.

In-patient data

Table 16 shows Hospital Episode Statistics (HES) data relating to hospital admissions in England & Wales in 1996/97. Over this period, there were 20 times as many hospital episodes with hypertension coded as a secondary diagnosis as opposed to a primary diagnosis (i.e. the major reason for the admission). For the vast majority of cases where hypertension was a secondary diagnosis, this was coded as essential hypertension (96%). Where hypertension was the primary cause of the episode, essential hypertension remained the commonest cause (58%), but often in association with renal disease (35%).

Table 16: Hospital episodes associated with a primary or secondary diagnosis of hypertension. Hospital Episode Statistics Data for England & Wales 1996/7.

ICD-10 Diagnosis	Primary cause of episode		Secondary diagnosis	
	No. of admissions	(% of total hypertensive admissions)	No. of admissions	(% of total hypertensive admissions)
Essential hypertension (I10x)	8,716	(58.2)	283,016	(96.3)
Hypertension with heart disease (I11.0, I11.9)	771	(5.2)	1,574	(0.5)
Hypertension with renal disease (I12.0, I12.9, I15.0, I15.1)	5,249	(35.1)	8,632	(2.9)
Hypertension with heart & renal disease (I13.0, I13.1, I13.2, I13.9)	191	(1.3)	233	(0.1)
Hypertension with endocrine cause (I15.2)	4	(0)	22	(0)
Other secondary hypertension (I15.8, I15.9)	35	(0.2)	291	(0.1)
Totals	14,966	(100)	293,768	(100)

Source: National Casemix Office⁵¹

Estimated costs for hypertension detection and management

Drugs

A primary care trust (PCT) serving 100 000 patients would expect to spend over £1 million annually on drugs from the main classes used in hypertension. A more detailed breakdown is shown in **Table 17**.

Table 17: Estimated drug costs by antihypertensive drug class.

	Actual National NIC (£000s) 1997 data	Estimated PCT NIC (£000s) 1997 data ^a	Urban West Midlands PCT (£000s) 2000 data ^a
Diuretics	48,349	93	139
Beta-blockers	77,361	149	191
Drugs affecting the renin-angiotensin system	200,003	385	436
Nitrates, calcium antagonists and potassium channel activators	212,031	389	580
Total	537,744	1,016	1,346

Sources: Dr JJ Ferguson as above and Personal Communication Mr J Horgan, SW Birmingham PCT

^a Scaled for population of 100,000.

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The costs of the individual drugs for a 28 day course are shown in **Table 18**.

Table 18: Costs of commonly used antihypertensive agents.⁴⁷

	Example used for price (generic where relevant)	Cost of 28 days treatment (£)
Diuretics	Bendrofluazide 2.5mg	0.74
Beta-blockers	Atenolol 50mg	0.85
ACE inhibitors	Enalapril 10mg	5.20
AT II	Losartan 50mg	17.23
Calcium antagonists	Amlodipine 5mg	11.85
Alpha-blocker	Doxazosin 4mg	14.08

Source: BNF 44

ACE inhibitor: angiotensin converting enzyme inhibitor; AT II: angiotensin II receptor blocker.

GP time

A stable hypertensive patient will require approximately two consultations per year regarding hypertension plus blood and urine monitoring as a minimum. A consultation for hypertension with a GP or nurse practitioner has been estimated to cost in the order of £20.^{52,53}

Hospital time

Data for this are available from the National Reference Costs 2002.⁵⁴ The average cost of a first outpatient appointment for General Medicine (a typical route for referral) is £104 (range £66–143) with follow-up appointments considerably cheaper at £66 (£47–69).

Patient time

It is difficult to estimate this cost, due to the methodological problems such as what assumptions should be made with regard to loss of earnings. One study has suggested that the average costs incurred by patients attending a GP surgery are around £5, compared to £15 for attending medical outpatients.⁵⁵ These costs are made up from a survey of patients attending each type of clinic in terms of time and transport costs (both measured from origin of journey back to origin). Time was costed at 1996 average earnings. The greater costs incurred at outpatients reflects both longer time taken and greater transport costs.

6 Effectiveness of services and interventions

The grading of the quality of evidence in this section takes into account both the nature of the evidence (grade 1–4) and the size of the effect (A–E). The definitions are given in the introductory chapter to this series.

Diagnostic tests

Measurement of blood pressure

Natural variation in blood pressure

Blood pressure varies throughout the day and with the performance of various activities.⁵⁶ There is also often a variation between arms and with the technique used for measurement (*see Table 19*). In view of these variations, recommendations for blood pressure measurement include taking two or three readings of blood pressure at each office visit and only making a diagnosis on the basis of a sustained rise in blood pressure on three separate occasions.¹⁸

Table 19: Effect of routine activities on blood pressure.⁵⁷

Activity	Effect on blood pressure (mmHg)	
	Systolic Blood Pressure	Diastolic Blood Pressure
Attending a meeting	+20	+15
Commuting to work	+16	+13
Dressing	+12	+10
Walking	+12	+6
Talking on the telephone	+10	+7
Eating	+9	+10
Doing desk work	+6	+5
Reading	+2	+2
Watching television	+0.3	+1
Sleep	-10	-8

Mercury sphygmomanometers versus automated sphygmomanometers

Blood pressure has been measured indirectly using a mercury sphygmomanometer with little change for almost 100 years.⁵⁸ Measurements are taken using the appearance and disappearance of the Korotkoff sounds I and V.⁵⁹ The vast majority of treatment trials for hypertension have used this method of measurement as the basis for their end points.⁶ The use of mercury sphygmomanometers is however open to inaccuracy and bias.^{56,60,61}

Areas of potential bias include patient factors, operator error and machine error (*see Table 20*). Patient factors such as talking, ambient temperature variation or drinking alcohol can make significant differences to blood pressure. Avoidable operator errors include terminal digit preference (rounding of BP to nearest 0 or 5), threshold bias (avoidance of recording readings around a treatment or diagnostic threshold) and inability to accurately distinguish Korotkoff sounds. The position of a person's arm when performing a measurement as well as the size of cuff used can also make a significant difference. Considerable evidence exists regarding poor maintenance and lack of calibration of equipment.⁶² The effect of these on recorded blood pressure is harder to estimate but could certainly be significant.

Furthermore, mercury is an environmental pollutant that is due to be phased out.⁶³ A number of automated electronic sphygmomanometers now exist which are accurate enough to be recommended for routine use.⁶³ Transferring to electronic blood pressure measurement appears to be associated with a reduction in bias due to rounding but no consistent change in recorded blood pressure.⁶⁴

426 Hypertension**Table 20:** Potential sources of bias in blood pressure measurement (adapted from McAlister *et al.* 2001⁵⁶).

Source of bias	Mean variation of measured blood pressure from actual blood pressure	
	Systolic Blood Pressure	Diastolic Blood Pressure
<i>Operator factors</i>		
Terminal digit preference	Rounding to nearest 10 or 5 mmHg	Rounding to nearest 10 or 5 mmHg
Threshold bias	Increased frequency of recorded BP just below threshold	Increased frequency of recorded BP just below threshold
Inability to distinguish Korotkoff sounds	Wide variation	Wide variation
Position of patient's arm	↓ or ↑ 8 mmHg for every 10 cm above or below heart level	↓ or ↑ 8 mmHg for every 10 cm above or below heart level
Failure to support arm	↑ 2 mmHg	↑ 2 mmHg
Cuff too small	↓ 8 mmHg	↑ 8 mmHg
<i>Patient factors</i>		
Talking	↑ 17 mmHg	↑ 13 mmHg
Acute exposure to cold	↑ 11 mmHg	↑ 8 mmHg
Acute ingestion of alcohol	↑ 8 mmHg for ≤3 hours	↑ 7 mmHg for ≤3 hours
Supine rather than sitting	No effect; ↑ 3 mmHg in supine position	↓ 2–5 mmHg in supine position
<i>Equipment factors</i>		
Poorly calibrated machine	Unquantifiable but potentially clinically significant	Unquantifiable but potentially clinically significant

Setting of measurement: home versus office readings

The standard method of measuring blood pressure is in an 'office' setting (hospital outpatient or primary care surgery).¹⁸ Blood pressure measured in these circumstances may be affected by the 'white coat effect'.⁶⁵ The recent availability of relatively affordable accurate automated electronic sphygmomanometers has made self-measurement of blood pressure in the home a realistic alternative for some people.⁶⁶ Absolute values of home measurement tend to be lower than office measurements and so a different normal range needs to be adopted. A meta-analysis of home blood pressure measurement studies concluded that a threshold for normotension of ≤135/85 mmHg was appropriate for home measurement.⁶⁷ However, many machines currently on the market have not been adequately evaluated for accuracy.⁶³

One UK primary care study has evaluated the use of home blood pressure measurement by patients borrowing equipment from a practice and found this method to be feasible.⁴² A recent small study in Hampshire found self-measurement in the surgery to be broadly comparable with measurement by a nurse and acceptable to patients.⁶⁸ Key issues in self-measurement are the training of individuals to use the equipment satisfactorily and ongoing calibration of that equipment.⁶¹ Few long-term large scale randomised studies (>100 patients per group for >6 months) exist providing evidence with respect to the effectiveness of self-measurement compared to office.

Ambulatory versus one-off readings

The results of ambulatory blood pressure monitoring correlate more closely with target organ damage than those from office measurements.⁶⁹ Some consensus on reference ranges for ambulatory blood pressure monitoring has been achieved with 24-hour readings of $\leq 135/85$ mmHg considered normal.⁷⁰ The major issues with ambulatory measurement are the lack of availability due to cost even in very developed countries such as the USA and the paucity of evidence of effectiveness in treating individuals on the basis of ambulatory measurements as opposed to one-off readings.⁷¹

The accuracy of one-off readings can be improved by multiple readings on the same occasion although it may take several readings on more than one occasion to reach a steady state.⁷² The reasons for this include regression to the mean and cuff response. In the former, the natural variation in an individual's blood pressure means that a single measurement will not be a good representation of an individual's true mean blood pressure. In cuff response, the defence reaction of an individual to cuff inflation is attenuated over time as blood pressure measurement becomes more familiar. As a result, most consensus guidelines (see above, guidelines) recommend multiple readings over time before a diagnosis of hypertension is made, the number and time period recommended being dependent on the level of blood pressure recorded.

Tests for end organ damage and/or underlying cause

Tests performed are either to exclude a possible secondary cause for hypertension (for instance renal disease tested for using serum creatinine and urinalysis) or to look for end organ damage secondary to prolonged raised blood pressure (for instance the use of ECG or echocardiography to test for left ventricular hypertrophy). A list of standard and possible tests along with the rationale for doing them appears in section 5.

Screening for hypertension

Systematic versus opportunistic

Systematic screening aims to cover a population by systematically calling up a population to be screened in a clinic or by visiting them at home. Opportunistic screening is performed when a person presents themselves for some other reason (for instance attends the general practitioner for contraceptive advice). The latter may lead to similar rates of coverage provided that opportunistic attendance is high enough: in the UK around 90% of patients will visit their general practitioner over three years, and the consultation rate is rising.^{73,74} Trials that have examined the yield of unknown hypertensive patients from systematic compared to opportunistic methods have shown little difference in detection rates for hypertension.⁸

Different settings for systematic and opportunistic screening

Practice-based

An RCT of practice-based systematic screening (two invitations to attend for screening two years apart) compared to control (i.e. opportunistic detection) in two UK practices resulted in a 73% population coverage for the first round of screening and 66% for the repeat screening round. No difference was found compared to control in prevalence of diastolic blood pressure >95 mmHg five years after initial screening (10.8% vs 10.9%).⁷⁵ A Canadian RCT compared nurse-led case finding with usual care. After 5 years the nurses had measured blood pressure on 91% of the target population compared with 80% by usual care.⁷⁶ Case finding by Norwegian general practitioners was compared to systematic screening using a before and

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after design. Almost 90% of cases identified by screening had already been detected by case finding.⁷⁷ One study in Bristol examined the effect of calculating cardiovascular risk in patients with hypertension and found no effect in terms of a reduction of patients' cardiovascular risk (measured in terms of reducing risk below a prespecified threshold of a 10% 5 year cardiovascular risk).⁷⁸ However, a reduction in systolic blood pressure compared to usual care was seen in the group where risk had been calculated using a chart but not in those whose risk was calculated using a computer program.

Community-based

A number of studies attempting case finding by 'health fairs' in shopping malls or housing blocks have been unsuccessful in achieving even modest rates of participation.⁸ A US RCT based on the population of three apartment blocks achieved 43% coverage with door to door screening compared with invitation to a central site of 8%.⁷⁹

Possible adverse consequences of screening

Labelling

There are conflicting results from studies studying the effect of labelling in hypertension suggesting that although labelling may have detrimental effects in terms of absenteeism following diagnosis, these effects can be mitigated by an intervention programme.⁸

Non-pharmacological treatment of hypertension (quality of evidence B I-2)

Evidence for the effectiveness of non-pharmacological intervention in hypertension comes from observational studies or small trials with end points in terms of blood pressure reduction rather than cardiovascular morbidity or mortality. The evidence for the effectiveness of exercise, weight loss, salt restriction and a low fat, high fruit and vegetable diet is presented in **Table 21**. Many of the trials of non-pharmacological interventions are relatively short in duration and individuals often find that exercise and weight loss in particular are difficult to maintain in the longer term.

Table 21: Effectiveness of lifestyle interventions for lowering blood pressure in people with primary hypertension.⁸⁰

Intervention	Mean decrease in BP (mmHg)	Number of RCTs (people)	Participants	Duration (weeks)	Mean change in targeted factor	Reference and evidence rank
Exercise	4/3	54 (2,419)	Sedentary adults >18	>2	At least 15 min aerobic 3x per week	⁸¹ BI-1
Salt restriction	4/2	58 (2,161)	Mean age 49	1-52	118 mmol/day	⁸² BI-1
	2/0.5	28 (1,131)	Mean age 47	4	60 mmol/day	⁸²
Weight loss	3/3	18 (2,611)	55% male, mean age 50	2-52	3-9% of body weight (mean weight 85 kg)	⁸³ BI-1
Low fat high fruit and vegetable diet	5.5/3	1 (459)	50% male, mean age 44	8		⁸⁴ BI-1

Exercise (quality of evidence B I-1)

The evidence from randomised studies for exercise reducing blood pressure shows small but significant reductions in the short term (regimes lasting at least 2 weeks) when compared to no exercise but trial evidence from longer studies (6 months or more) is equivocal with smaller non-significant reductions.^{81,85} One large observational study suggests that those performing regular exercise several times per week have lower all cause and cardiovascular mortality (all cause mortality RR 0.43, 95% CI 0.22 to 0.82; cardiovascular mortality RR 0.33, 95% CI 0.11 to 0.94).⁸⁶

Salt restriction (quality of evidence B I-1)

Randomised studies have shown that dietary salt restriction leads to small but significant reductions in blood pressure. The effect appears to be related to the extent of salt restriction with greater reductions in BP resulting from greater reductions in salt intake. A recent systematic review found that a mean reduction of 118 mmol/l (= 6700 mg; 2000 mg = one level teaspoon of salt) for 1 month led to a reduction of 3.9 mmHg (95% CI 3.0 mmHg to 4.8 mmHg) in systolic blood pressure and 1.9 mmHg (95% CI 1.3 mmHg to 2.5 mmHg) in diastolic blood pressure.⁸² Hooper *et al.* have looked at the longer term effects of salt restriction advice and found smaller but still significant reductions in systolic blood pressure but not diastolic blood pressure at follow-ups between 13 and 60 months.⁸⁷ Despite these robust findings of benefit in terms of blood pressure reduction, there is no satisfactory evidence of the effects of salt restriction on mortality and morbidity and subsequently there has been much debate in the literature regarding the 'real life' benefits.⁸⁸ Whilst there is debate on the efficacy of salt restriction on 'hard' end points, the evidence of any harm from salt restriction is weak due to methodological problems.⁸⁹

Weight loss (quality of evidence B I-1)

Relatively small reductions of weight (of the order of around 5 kg) over short periods of time have been shown to be associated with small reductions of blood pressure (around 3 mmHg) in hypertensive patients. A systematic review found that in 6 RCTs where antihypertensive regimens were not varied during the intervention period, losing weight (mean weight 85kg; mean reduction 3–9%) reduced blood pressure by 3.0/2.9 mmHg, compared to no weight loss.⁸³

Diet (quality of evidence B I-2)

One study has found that a diet low in fat and high in fruit and vegetables taken for 8 weeks lowered blood pressure by 5.5/3 mmHg compared to a 'control diet' low in magnesium and calcium. The results from this should be interpreted with caution due to the short duration and the fact that all food eaten by subjects in the study was prepared in a central kitchen, a setting unlikely to be reflected in usual daily life.⁸⁴ A systematic review on the effects of potassium supplementation on blood pressure found that supplementation (60–100 mmol per day) led to a mean reduction of blood pressure of 3/2 mmHg.⁹⁰ Fish oils taken in large quantities (3g daily) led to a reduction in blood pressure of 3/2 mmHg.⁹¹ There is insufficient evidence on the efficacy of other forms of dietary intervention including calcium and magnesium supplementation to judge effectiveness of blood pressure lowering in hypertensives.⁹²

Pharmacological treatment

Treatment of raised blood pressure leads to benefit in terms of total death rate, cardiovascular death rate, stroke, major coronary events and congestive heart failure. Absolute benefit is dependent on absolute risk, which depends on age and level of blood pressure.

Effects of lowering blood pressure

Various reviews and meta-analyses have been performed on the effects of treatment of hypertension. The data presented here are from Collins and Peto's 1994 update of their 1990 *The Lancet* meta-analysis and from a subsequent individual patient data analysis by Gueyffier.^{6,93} The Collins meta-analysis used data derived from four large and 13 small unconfounded randomised trials of pharmacological treatment reported between 1965 and 1992. Gueyffier used individual patient data from seven of the larger trials with considerable overlap between the two reviews. The sample sizes in the trials ranged from under 100 to over 17 000 with totals of 47 653 and 40 777 patients used by Collins and Gueyffier respectively. Most of the trials used a stepped approach to therapy with a diuretic being the main first line treatment used. Mean follow-up was for 4–5 years. Treatment was compared to either placebo or usual care. Treatment resulted in approximately a 5–6 mmHg reduction in diastolic blood pressure (reductions in systolic BP not available for all studies but likely to have been about double the diastolic reduction). Collins provides overall data for men and women whereas Gueyffier breaks down by gender.

Total death rate (quality of evidence C I-1)

Total mortality was significantly reduced but the absolute figures have not been quoted by Collins and Peto.⁶ They equate to approximately a 12% relative risk reduction. Gueyffier quotes OR for total mortality in favour of treatment for women of 0.91 (95% CI 0.81–1.01, $p=0.094$) and for men of 0.88 (0.8–0.97, $p=0.013$).⁹³

Cardiovascular death rate (quality of evidence A I-1)

Cardiovascular death rate was reduced by 21% in the treatment group compared to control in Collins and Peto's review.⁶ Gueyffier quotes ORs of 0.86 (0.74–1.01, $p=0.068$) for women and 0.80 (0.70–0.91, $p<0.001$) for mean, again in favour of treatment.⁹³

Stroke (quality of evidence A I-1)

A highly significant reduction in relative risk of stroke was seen of 38% (95% CI 31–45%). Results for fatal and non-fatal stroke were similar.⁶ Gueyffier's review also found highly significant reductions in stroke for both men and women (OR in favour of treatment 0.63 (0.52–0.73) women and 0.66 (0.56–0.78) for men, both $p<0.001$).⁹³

Major coronary events (quality of evidence A I-1)

A highly significant reduction in relative risk of major coronary events was seen of 16% (95% CI 8–23%).⁶ Gueyffier's review also found reductions in coronary events in favour of treatment (OR 0.85 (0.72–1.01, $p=0.059$) women and 0.82 (0.73–0.92, $p<0.001$)).⁹³

Congestive heart failure (quality of evidence A I-1)

No results for congestive heart failure are given by either Collins' or Gueyffier's reviews. A third meta-analysis also by Gueyffier (and using very similar trials to the Collins review) found an OR for congestive heart failure of 0.54 (0.43–0.68) in favour of treatment in trials on older people.⁹⁴ The result for younger people was non-significantly in favour of treatment but this is likely to be due to lack of power in view of very few events.

Adverse effects compared to placebo

Gueyffier's 1996 meta-analysis showed no increase in non-cardiovascular mortality or major morbidity in those receiving antihypertensive treatment as compared to placebo.⁹³ Treatment of hypertension *per se* does not appear to influence quality of life adversely: for patients in the HOT study, the lower the achieved blood pressure, the better the quality of life.

*What drugs have been shown to be effective?***Placebo controlled trials, or new drugs compared to old drugs of proven efficacy**

Most placebo controlled trials with major morbidity/mortality as end points have used diuretics and/or beta-blockers and it is this evidence that is presented above. Newer agents have typically been evaluated against secondary end points such as blood pressure reduction achieved or compared to older drugs of proven efficacy. The results of randomised comparisons and systematic reviews for the individual classes of antihypertensive are presented below. It is likely that the bulk of benefit from these drugs comes from their effect on blood pressure which lowers risk of cardiovascular disease and in particular stroke to levels approaching those expected from observational studies of the effect of blood pressure in populations.⁹⁵

Diuretics and beta-blockers (quality of evidence A I-1)

See above for results from meta-analysis of trials of diuretics (typically thiazide diuretics \pm amiloride) and/or beta-blockers compared with placebo in the treatment of hypertension. Of note is the fact that the doses of thiazides used in many of these trials was typically much higher than in common use today (e.g. bendrofluzide 10mg vs 2.5mg in current practice). Lower doses have a lower incidence of side effects albeit at marginally lower effects on blood pressure.⁹⁶ Two systematic reviews have compared diuretics with beta-blockers.^{97,98} No significant difference was found in terms of blood pressure reduction but although diuretics were found to reduce coronary events, no evidence was found that beta-blockers reduce coronary events. However, beta-blockers are known to reduce coronary events in other circumstances, e.g. post-myocardial infarction.⁹⁹

Angiotensin converting enzyme inhibitors (quality of evidence A I-1)

A systematic review of ACE inhibitors for lowering blood pressure found similar effects in terms of outcome to older drugs.¹⁰⁰ Recent RCTs have given conflicting results over whether ACE inhibitors confer benefit in addition to the direct effect on lowering blood pressure.^{101,102} The HOPE study compared an ACE inhibitor with placebo in people at high cardiovascular risk (history of ischaemic heart disease or diabetes plus a risk factor) but not necessarily with hypertension.¹⁰¹ This found significant benefit for the intervention group in terms of a composite primary end point of myocardial infarction, stroke, or death from cardiovascular causes despite only modest blood pressure reduction (136/76 in the ramipril group vs 139/77 in the placebo group at the end of the trial). Similarly, the PROGRESS post stroke trial found

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significant benefit in terms of the intervention comprising a diuretic and ACE inhibitor with a reduction in blood pressure of 9/4 mmHg.¹⁰² The benefits were seen in patients with high and 'normal' blood pressure at base line. Wing *et al.* from Australia performed an open label study in healthy older people comparing ACE inhibitors and diuretics as first line treatment with no limit on other classes of treatment used as 'add on' if required. Patients were included with blood pressures of over 140/90 without recent cardiovascular events, contraindications to ACE inhibitor or diuretics and without significant renal impairment. They found a hazard ratio for a cardiovascular event or death with ACE inhibitor treatment of 0.89 (95% CI 0.79–1.00; $p=0.05$) despite similar blood pressure reductions (26/12 mmHg), suggesting that ACE inhibitors might have additional beneficial effects apart from their impact on blood pressure.¹⁰³

However, the recently reported results from the ALLHAT study comparing a diuretic, ACE inhibitor and calcium antagonist have cast doubt on a special effect from ACE inhibitors, with no difference found in all cause mortality between the groups with over 33 000 people randomised.¹⁰⁴ Any differences between classes were in terms of secondary outcomes, in favour of the diuretic, and likely to be due to small differences in achieved blood pressure. Similarly, the prospective meta-analysis conducted by the Blood Pressure Lowering Treatment Trialists Collaboration, which included both ALLHAT and Wing *et al.*'s results, found no difference between ACE inhibitors and calcium antagonists, or diuretics or beta-blockers in terms of total major cardiovascular events.⁴⁴

Calcium antagonists (quality of evidence A I-1)

Calcium antagonists reduced blood pressure to equivalent levels compared with diuretics but considerable controversy has surrounded possible adverse effects in comparison with other classes of antihypertensive treatment. Evidence from previous observational studies, small RCTs and meta-analyses has suggested that calcium antagonists are inferior at protecting against heart failure and cardiovascular events, particularly MI, in comparison to other classes of drugs.^{105–107} However, data from the ALLHAT study suggests that the differences between calcium antagonists and other classes of drugs with respect to CHD, all cause mortality and cardiovascular disease are negligible and may have been due to either differences in achieved blood pressure or chance findings in previous smaller studies.¹⁰⁴ The one secondary outcome where the calcium channel blocker performed poorly in comparison to the diuretic was in terms of a 38% higher risk of heart failure. This secondary outcome included deaths, hospitalisations and treated non-hospitalised patients and may be in part explained by the fact that the use of diuretics may mask a clinical diagnosis of heart failure by reducing oedema. The latest publication by the Blood Pressure Trialists Prospective Meta-analysis Collaboration found no significant difference between calcium antagonists, ACE inhibitors, beta-blockers and diuretics in terms of cardiovascular events, death or total mortality but found that ACE inhibitors, beta-blockers and diuretics were all superior to calcium antagonists for heart failure that caused death or admission to hospital.⁴⁴

Alpha-blockers (quality of evidence B I-1)

The best evidence for the use of alpha-blockers in hypertension again comes from the ALLHAT trial, in which the alpha-blocker – diuretic arm was terminated and reported early.¹⁰⁸ This found that although no difference was seen in the main end point of fatal CHD or non-fatal MI, the alpha-blocker (doxazosin) performed significantly worse with respect to both the combined CVD end point (25% increase) and congestive heart failure (doubling of risk). These results need to be interpreted cautiously because the diuretic arm achieved a small but significantly greater reduction in systolic blood pressure (2 mmHg) which may be enough to explain some or all of the increased risk (especially in non-CHF CVD), and again the clinical diagnosis of CHF is likely to have been reduced in the diuretic group. Nevertheless, the degree

of increased risk is probably significant enough to avoid the first line use of alpha-blockers unless there is good reason in terms of drug intolerance or co-morbidity, particularly benign prostatic hypertrophy.

Angiotensin II receptor antagonists (quality of evidence A I-I)

Angiotensin II antagonists (AT II blockers) are a more recent development in hypertension and work by blocking a different part of the renin-angiotensin pathway than ACE inhibitors. A systematic review has examined the evidence for efficacy in terms of blood pressure reduction and found the various compounds in this group to be broadly similar.¹⁰⁹ One large RCT has compared cardiovascular end points for an AT II blocker with that of a beta-blocker in patients with hypertension and left ventricular hypertrophy and found a reduction in the primary end point of combined cardiovascular mortality and morbidity.¹¹⁰ These results need to be interpreted with caution in view of the fact that the AT II group attained slightly lower blood pressure and the major effect seen was on stroke which is most affected by blood pressure reduction. In addition, patients in the AT II group were more likely to have received other drugs including a thiazide diuretic (see above for comments regarding the efficacy of diuretics in the ALLHAT study).

Nitrates and potassium channel activators (quality of evidence B III)

Both these classes of drugs tend to reduce blood pressure but are not routinely used or licensed for the treatment of hypertension. Both medications have their main role in the treatment of ischaemic heart disease which is a common co-morbidity in people with hypertension. No RCTs exist of these therapies in terms of effects on morbidity and mortality but it would be expected that any blood pressure reduction achieved from their use would lead to similar effects as seen in other classes of medication.

Other antihypertensive classes (quality of evidence A III)

Three other classes of antihypertensive medication are in use in the UK but usually as third line therapy or on a historical basis. These are vasodilator antihypertensive drugs (e.g. hydralazine), centrally acting antihypertensives (e.g. clonidine, moxonadine) and adrenergic neurone blocking drugs (e.g. guanethidine). These older classes of drugs have not in general been used in any of the modern randomised comparisons although hydralazine, clonidine and reserpine were part of the titration scheme used in the ALLHAT study.¹⁰⁴ Again, on the basis of blood pressure lowering, the effects of these medications on cardiovascular effects would be expected to be similar to diuretics and beta-blockers.

Other pharmacological interventions to lower cardiovascular risk

Evidence exists for the use of both aspirin and cholesterol-lowering drugs in patients with hypertension. The following section refers to the use of these interventions in the primary prevention of cardiovascular disease, i.e. in patients without other indications such as previous stroke or myocardial infarction.

Anti-platelet therapy (quality of evidence A I-1)

The evidence for the use of anti-platelet therapy (in most cases low dose aspirin) in patients at increased cardiovascular risk (hypertension or other risk factor) has been summarised in a systematic review.⁸⁰ This gives an estimate of approximately 1.2 events avoided per 1000 person years in a total pool of over 50 000 patients. Treatment is associated with a risk of haemorrhage (major extracranial and intracranial) of similar magnitude. The choice to treat asymptomatic patients with aspirin must therefore depend both on absolute risk of cardiovascular event and likelihood of haemorrhage. The BHS guidelines recommend

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treatment with aspirin only in individuals over the age of 50, with blood pressure controlled below 150/90 and a 10 year cardiovascular risk of $\geq 15\%$.¹⁸

Cholesterol lowering (quality of evidence A I-1)

Several systematic reviews and subsequent RCTs have shown that although cholesterol lowering therapy reduces CHD risk when used for primary prevention, it does not have an effect on overall mortality.¹¹¹ This is likely to be due to the fact that the absolute risk of cardiovascular disease in patients with hypertension (or other risk factors) but not frank cardiovascular disease is too low for benefit to be clear-cut. The ALLHAT study, which in addition to antihypertensives studied the use of pravastatin 40 mg against 'usual care', found no benefit in terms of either all cause mortality or CHD.¹¹² Prior to the landmark '4S' study, concerns had been raised regarding a possible excess of violent death due to cholesterol lowering.^{113,114} The '4S' study randomised 4444 people with coronary heart disease and moderately raised cholesterol to simvastatin or placebo and was the first cholesterol lowering study to find a reduction in all cause mortality (30%). Subsequent meta-analysis of statin cholesterol lowering trials has found no evidence of increased risk of accidental death, suicide or trauma.¹¹⁵ Jackson *et al.* have attempted to quantify the level of risk at which the potential harm from cholesterol lowering might outweigh potential benefits.¹¹⁶ The conclusions reached were that for those at low CHD risk (<13% 10 year CHD risk) the evidence for an overall benefit in terms of mortality was poor and that absolute safety had not been demonstrated for this group. Above this level, however, benefits outweighed risk. However, the results of the recent ASCOT trial cholesterol lowering arm showed benefit from lipid lowering (atorvastatin 10 mg) compared to placebo in terms of non-fatal MI and fatal CHD for patients with a 10 year CHD risk of approximately 10% (although off antihypertensive treatment this risk would have been approximately doubled).¹¹⁷ These results, along with those from the Heart Protection Study (simvastatin 40 mg vs placebo for 20 536 UK adults (aged 40–80 years) with coronary disease, other occlusive arterial disease, or diabetes), suggest that benefit from statins is still present at lower risks, with little evidence of significant adverse effects.¹¹⁸

Adverse effects of drug therapy

Trial data on adverse effects suggests that with modern therapies, around 2% of patients will suffer adverse effects from treatment.²⁵ These are mostly dose-related and clearly linked to the individual drug classes, for instance ankle swelling with calcium channel blockers, cough with ACE inhibitors or cold extremities with beta-blockers. Most trial designs are not appropriate for identifying rare events which may only occur after years of treatment. Case control or cohort designs are most appropriate in these circumstances.

A systematic review of individual patient data from RCTs found no evidence of increased non-cardiovascular mortality in patients treated with diuretics or beta-blockers compared to placebo.⁹⁴

A systematic review investigated the association between diuretic use and renal cell carcinoma.¹¹⁹ 12 studies were reviewed, 9 case control and 3 cohort. A small but significant increase in renal cell carcinoma was found (OR in case control studies 1.55 (95% CI 1.421.71, $p < 0.00001$)). The significance of these results is unclear: renal cell carcinoma is rare, many millions of people worldwide take diuretics, and there is a possibility that the results are confounded by an effect of hypertension on renal cell carcinoma or vice versa.

A secondary analysis of the treatment of mild hypertension study examined the differences in rate of sexual dysfunction between acebutolol, amlodipine, chlorthalidone, doxazosin, enalapril or placebo.¹²⁰ After 2 years chlorthalidone was associated with a higher rate of erectile problems than the other groups or placebo. Baseline levels of erectile dysfunction (ED) were 14% and related to age. Although the chlorthalidone group had higher rates of ED, the absolute numbers were small due to small sample sizes.

Numerous other side effects have been reported from the various classes of antihypertensive and are summarised in **Table 22**.

Table 22: Side effects of commonly used classes of antihypertensive.⁴⁷

Drug class and example	Side effects
Thiazide diuretics <i>Bendroflumazide</i>	Postural hypotension and mild gastrointestinal effects; impotence (reversible on withdrawal of treatment); hypokalaemia (see also notes above), hypomagnesaemia, hyponatraemia, hypercalcaemia, hypochloreaemic alkalosis, hyperuricaemia, gout, hyperglycaemia and altered plasma lipid concentration; less commonly rashes, photosensitivity; blood disorders (including neutropenia and thrombocytopenia – when given in late pregnancy neonatal thrombocytopenia has been reported); pancreatitis, intrahepatic cholestasis and hypersensitivity reactions (including pneumonitis, pulmonary oedema, severe skin reactions) also reported.
Beta-blockers <i>Propranolol</i>	Bradycardia, heart failure, hypotension, conduction disorders, bronchospasm, peripheral vasoconstriction (including exacerbation of intermittent claudication and Raynaud's phenomenon), gastrointestinal disturbances, fatigue, sleep disturbances; rare reports of rashes and dry eyes (reversible on withdrawal), exacerbation of psoriasis; see also notes above.
Alpha-blockers <i>Doxazosin</i>	Postural hypotension; dizziness, vertigo, headache, fatigue, asthenia, oedema, somnolence, nausea, rhinitis; less frequently abdominal discomfort, diarrhoea, vomiting, agitation, tremor, rash, pruritus; rarely blurred vision, epistaxis, haematuria, thrombocytopenia, purpura, leucopenia, hepatitis, jaundice, cholestasis and urinary incontinence; isolated cases of priapism and impotence reported.
ACE inhibitors <i>Captopril</i>	ACE inhibitors can cause profound hypotension and renal impairment (in patients with severe bilateral renal artery stenosis), and a persistent dry cough. They may also cause angioedema (onset may be delayed), rash (which may be associated with pruritus and urticaria), pancreatitis and upper respiratory-tract symptoms such as sinusitis, rhinitis and sore throat. Gastrointestinal effects reported with ACE inhibitors include nausea, vomiting, dyspepsia, diarrhoea and constipation. Altered liver function tests, cholestatic jaundice and hepatitis have been reported. Blood disorders including thrombocytopenia, leucopenia, neutropenia and haemolytic anaemia have also been reported. Other reported side-effects include headache, dizziness, fatigue, malaise, taste disturbance, paraesthesia, bronchospasm, fever, serositis, vasculitis, myalgia, arthralgia, positive antinuclear antibody, raised erythrocyte sedimentation rate, eosinophilia, leucocytosis and photosensitivity, tachycardia, serum sickness, weight loss, stomatitis, maculopapular rash, photosensitivity, flushing and acidosis.
AT II blockers <i>Candesartan</i>	Side-effects are usually mild. Symptomatic hypotension may occur, particularly in patients with intravascular volume depletion (e.g. those taking high-dose diuretics). Hyperkalaemia occurs occasionally; angioedema has also been reported with some angiotensin-II receptor antagonists. See notes above; also upper respiratory-tract and influenza-like symptoms including rhinitis and pharyngitis; abdominal pain, back pain, arthralgia, myalgia, nausea, headache, dizziness, peripheral oedema, rash also reported; rarely urticaria, pruritus, blood disorders reported.
Calcium antagonists <i>Amlodipine</i>	Headache, oedema, fatigue, nausea, flushing, dizziness, gum hyperplasia, rashes (including rarely pruritus and very rarely erythema multiforme); rarely gastrointestinal disturbances, dry mouth, sweating, palpitations, dyspnoea, drowsiness, mood changes, myalgia, arthralgia, asthenia, peripheral neuropathy, impotence, increased urinary frequency, visual disturbances; also reported, jaundice, pancreatitis, hyperglycaemia, thrombocytopenia, vasculitis, angioedema, alopecia, gynaecomastia.

Comparisons between different drug classes (quality of evidence A I-1)

As discussed above in the individual drug class sections, there is little convincing evidence of a differential effect in terms of cardiovascular morbidity and mortality or all cause mortality between the various classes of antihypertensives, at least with regard to diuretics, beta-blockers, ACE inhibitors and calcium channel blockers. For an individual person with hypertension the choice may well be influenced by co-morbidities such as heart failure, diabetes or benign prostatic hypertrophy. Blood pressure lowering in patients with hypertension and co-existing heart failure in particular is more effectively treated with diuretics, ACE inhibitors or beta-blockers rather than calcium antagonists. Furthermore, individuals may achieve better results in terms of blood pressure lowering with different drugs: in one small trial, 56 hypertensive patients were randomised between and then rotated in turn through four drug classes comprising a diuretic, beta-blocker, ACE inhibitor and calcium antagonist.¹²¹ Rotation around the four classes doubled the chance of controlled blood pressure on monotherapy as compared to the first drug randomised to.

Class effects vs specific drugs (quality of evidence A I-1)

The effect of antihypertensive drugs in reducing stroke and coronary heart disease risk appears to be largely due to the blood pressure lowering properties of these drugs and so would be expected to be a class effect rather than specific to a given drug.¹⁰⁴ This is in keeping with epidemiological studies showing the association of lower blood pressure with lower cardiovascular risk. The recent HOPE trial using the ACE inhibitor ramipril found a significant reduction in its combined outcome of myocardial infarction, stroke or cardiovascular death despite apparently very modest blood pressure effects (2.4 mmHg/1 mmHg).¹²² However, a sub-study of HOPE involving 24-hour blood pressure monitoring of a sample of the subjects found that the mean blood pressure lowering achieved by ramipril was sufficiently lower than that of the control group to explain the reduction in risk seen.¹²³ Thus, the 'additional' benefits of ramipril can probably be explained by blood pressure lowering alone.

Older drugs vs newer drugs

The best evidence for benefit from the treatment of hypertension comes from studies of the older classes of drugs, namely diuretics and beta-blockers. See above for further details. The evidence from the ALLHAT study and meta-analyses suggests that little if any important differences exist between old and new drugs given equivalence of blood pressure lowering.¹⁰⁴

Treatment in specific circumstances

Isolated systolic hypertension (quality of evidence A I-1)

A meta-analysis has investigated the effects of treating isolated systolic hypertension (systolic >160 mmHg and diastolic <95 mmHg) in patients aged 60 years or more.⁴⁵ Eight trials containing 15 963 patients were examined with a median follow-up of 3.8 years. The relative hazard associated with a 10 mmHg higher initial systolic blood pressure was 1.26 (p=0.0001) for total mortality and 1.22 (p=0.02) for stroke but not significantly raised for coronary events. Treating systolic hypertension reduced total mortality by 13% (95% CI 2–22, p=0.02), cardiovascular mortality by 18%, all cardiovascular complications by 26%, stroke by 30% and coronary events by 23%. Absolute benefits of treatment were increased for men vs women (NNT 18 vs 38), at or above age 70 (NNT 19 vs 39) and in patients with previous cardiovascular complications (NNT 16 vs 37).

Older people (quality of evidence A I-1)

Older people are at higher absolute risk for all types of cardiovascular disease and so will tend to receive greater benefit in terms of absolute risk reduction for any given reduction in blood pressure. Gueyffier's meta-analysis which included seven trials in older patients (mean age >65) found significant risk reductions in terms of congestive heart failure (46% risk reduction), stroke (34% risk reduction), cardiovascular mortality (23% risk reduction), major coronary events (21% risk reduction) and all cause mortality (10% risk reduction).⁹³ The absolute risk reduction was of the order of 10 events avoided for 1000 patients treated for one year (all end points combined, NNT 100). This is in contrast to the results in the same review for younger patients where the only significant reduction was seen in terms of stroke risk (down 49% vs placebo), but even this was a small reduction in absolute terms (NNT 1000 for one year to prevent one event). Messerli examined ten trials involving over 16 000 patients aged ≥ 60 and compared results from those using diuretics with those using beta-blockers.⁹⁸ The diuretics were found to be superior in terms of preventing all outcomes studied (cerebrovascular events, fatal stroke, coronary heart disease, cardiovascular mortality, and all cause mortality) and beta-blockers were found only to have a significant effect in stroke prevention, not CHD. This study was not a formal meta-analysis but rather a comparison of the results from the individual trials.

Insufficient evidence currently exists with respect to patients aged over 80 of the efficacy of blood pressure lowering, particularly in terms of mortality. A meta-analysis using data from 1670 elderly people included in trials of blood pressure lowering found that treatment prevented 34% (95% CI 8–52) of strokes. There was a significant decrease in the rate of major cardiovascular events and heart failure, by 22% and 39%, respectively. No treatment benefit was seen for cardiovascular death, and a non-significant 6% (–5 to 18) relative excess of death from all causes.¹²⁴

Minority ethnic groups (quality of evidence A I-1)

Many of the large randomised trials in hypertension have previously included few patients from minority ethnic groups. Responses to the standard classes of antihypertensive will be different depending on ethnicity: African and African-Caribbean people respond better to diuretics and calcium antagonists than to beta-blockers, ACE inhibitors or AT II blockers.^{125–128} This applies only to monotherapy and these differences in efficacy are eliminated when used in combination. The recent consensus statement on the management of high blood pressure in African Americans differs in two key ways from guidelines for other ethnic groups: lower blood pressure targets are recommended for diabetes or non-diabetic renal disease (namely <130/80) and combination therapy is recommended first line for patients presenting with blood pressure $\geq 150/100$ mmHg.¹²⁹ The ALLHAT study included 35% black and 19% Hispanic patients. Results for chlorthalidone vs amlodipine showed no difference in outcomes for black vs non-black but lisinopril showed poorer blood pressure response, which presumably explains the observed increased risk of stroke and combined CVD for blacks receiving lisinopril compared to those receiving chlorthalidone.¹⁰⁴

Secondary prevention of stroke (A I-1)

The effect of blood pressure reduction post stroke is covered in detail in the stroke chapter, but briefly, the PROGRESS study has recently confirmed the benefit of blood pressure reduction in this group of people.¹³⁰

Diabetes

See under 'Treatment by sub-category' below.

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Treatment targets (quality of evidence A I-1)

The Hypertension Optimal Treatment Trial (HOT) investigated the effect of treating blood pressure in over 18 000 hypertensives to three predetermined treatment targets, namely 90, 85 and 80 mmHg.²⁵ No significant difference was found between the groups in terms of major cardiovascular events, stroke or total mortality, but a small difference in terms of myocardial infarction was achieved when comparing the 80 and 90 mmHg target groups. This apparent paucity of effect was probably due to a combination of small differences in achieved blood pressure between the three groups (85.5, 83.2 and 81.2 mmHg) and fewer than expected cardiovascular events, which lowered the power of the study. A secondary analysis of events in relation to achieved blood pressure found the lowest incidence of major cardiovascular events at a mean achieved BP of 130–140/80–85 mmHg. Reduction of blood pressure below these values was not associated with further reduction in event incidence.

Achieving currently recommended levels of blood pressure reduction will require combination therapy in the majority of patients. For example, in the HOT study, the mean number of drugs per patient at final follow-up was 1.8, with almost 60% needing two or more medications (see **Table 23**).

Table 23: The proportion of patients taking antihypertensive drugs at the final visit of the HOT Study

Number of medications	Proportion taking
0 drug	1.9%
1 drug	37.9%
2 drugs	43.8%
3 drugs	13.6%

Source: data on file, Astra Zeneca. Personal communication from Paul Sellwood

Treatment by sub-category

This section refers back to the sub-categories defined in section 3.

Groups 1 & 2 (essential hypertension) (A I-1)

The absolute effect of treatment is directly proportional to absolute level of baseline risk. Older (>65 years) patients are in general at higher risk. On average, treating 1000 older adults for 1 year can be expected to prevent five strokes (95% CI 2–8), three coronary events (95% CI 1–4) and four cardiovascular deaths (1–8). Similar blood pressure reductions in middle aged (<65) hypertensives prevent only one stroke (0–2) per thousand person years of treatment, with no significant effect on coronary events or mortality.⁹³

Group 3 (hypertension and diabetes) (A I-1)

Treatment of blood pressure in patients with diabetes is at least as effective as in those without, due to increased absolute risk of cardiovascular disease.¹³¹ Elderly hypertensive diabetics have double the risk of stroke, cardiovascular events and all cause mortality compared to non-diabetics.

With regard to target blood pressure, the BHS guidelines recommend 140/80 as goal BP for diabetics, based on a sub-group analysis of the HOT trial.^{18,25} This same data has been interpreted by others as suggesting lower targets (130/80 or lower).¹³²

Tighter blood pressure control in patients with diabetes has been associated with reduction in risk of deaths and complications related to diabetes (progression of diabetic retinopathy and reduction in visual acuity).²⁶ Sub-group analysis of the 1501 patients with diabetes in the Hypertension Optimal Treatment Trial found a reduction in major cardiovascular events (RR 2.06 (95% CI 1.24–3.4)), and cardiovascular mortality (RR 3.0 (1.28–7.08), $p=0.016$) in the group randomised to a target diastolic blood pressure of 80 mmHg compared to a target of 90 mmHg. These reductions were not seen in the study population as a whole but this is likely to be due to the much higher event rate in the diabetic population.¹³³ The benefit of intensive treatment appears to be independent of whether low-dose diuretics, beta-blockers, angiotensin-converting enzyme inhibitors or calcium antagonists are used as first line treatment.¹³⁴ Diabetics with proteinuria or impaired renal function benefit from even lower BP (systolic <125 mmHg).¹³⁵

Group 4 (malignant hypertension) (A I-1)

Patients with malignant hypertension need emergency treatment of their blood pressure. Early trials of lowering very high blood pressure leave no doubt as to the efficacy of treatment.¹³⁶

Group 5 (secondary hypertension) (A II-1)

Treatment of the underlying cause of secondary hypertension may lead to improvements in blood pressure. In a retrospective study of 1000 secondary care hypertensive patients, 47 were found to have some form of secondary hypertension, of whom 18 had blood pressure improved or normalised after operative treatment of the underlying cause or cessation of oral contraception.¹²⁰

Group 6 (white coat hypertension) (C III)

Treatment of white coat hypertension is generally considered unnecessary and there is evidence that although clinic BP may be lowered by treatment, little effect is seen on ambulatory BP.¹³⁷

Population approaches to lower blood pressure (C I-I)

Population level interventions to reduce blood pressure are attractive in theory. Evidence from both observational studies and treatment trials shows that lower blood pressure is associated with better prognosis from a wide range of cardiovascular outcomes. Initiatives might include programmes aimed at smoking cessation, increasing exercise, reducing salt in processed foods (for example bread) or healthier eating (the 'five fruit a day' campaign). Higher cigarette prices (e.g. by higher taxes) have been shown to reduce cigarette consumption.¹³⁸ The evidence from the effect of instituting smoke-free workplaces shows a reduction in overall tobacco consumption.¹³⁹ A modelling exercise published this year suggested that salt reduction on a population basis (possibly by legislation for processed food) was one of the most cost-effective methods of reducing blood pressure.¹⁴⁰ A number of supermarket chains have now agreed to reduce the salt content in processed food in response to concerns raised by amongst others the Department of Health.¹⁴¹ A systematic review of physical activity promotion (11 studies) found that interventions that encouraged walking and did not require attendance at a central facility were most likely to lead to sustainable increases in overall physical activity.¹⁴² Initial evaluations of the 'five-a-day' programme suggest that it is possible to increase fruit and vegetable intake.¹⁴³

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Cost-effectiveness studies

When considering the cost-effectiveness of blood pressure lowering treatment a number of factors need to be taken into account. Many of these have already been considered earlier in this section, and include:

- treatment threshold
- treatment target
- perspective of costs
- blood pressure lowering vs effect on cardiovascular risk
- antihypertensive vs other interventions to lower cardiovascular risk.

Pearce *et al.* performed a cost minimisation analysis based on the number needed to treat (NNT) to prevent one stroke, MI or death from a meta-analysis of 15 major trials of antihypertensive treatment.¹⁰ This US study found an NNT of 86 for middle aged patients with uncomplicated mild hypertension and 29 for elderly patients. The results are presented in **Table 24**. The drugs used and costs are based on US prices, but the price differentials are similar in the UK. Diuretic therapy remained most cost-effective, even under the unlikely assumption that newer drugs were 50% more effective at preventing these events than diuretics.

Table 24: Wholesale drug acquisition costs to prevent one MI, stroke or death among patients with uncomplicated mild-to-moderate hypertension.^a

Drug class	Most common treatment			Least expensive treatment		
	Treatment	Middle aged	Elderly	Treatment	Middle aged	Elderly
Diuretic	HCTZ	£3,400	£1,100	HCTZ	£3,400	£1,100
β -blocker	Atenolol	£75,000	£25,300	Propranolol	£39,100	£13,200
ACE inhibitor	Enalapril	£111,500	£37,700	Trandolapril	£67,300	£22,700
α -blocker	Terazosin	£138,800	£46,800	Doxazosin	£108,000	£36,400
Calcium blocker	Nifedipine GITS	£247,300	£83,400	Nisoldipine	£91,800	£31,000

^a Costs converted from dollars at rate of \$1.4=£1.

The cost-effectiveness of antihypertensive treatment in the UK has recently been evaluated in a modelling exercise by Montgomery and colleagues.¹⁴⁴ They produced a Markov model comparing the effects of treatment for hypertension versus non-treatment and taking into account age, sex, cardiovascular risk, costs and patient preferences. The range of cardiovascular risk considered was from <0.1% per year to almost 30%. The costs of antihypertensive treatment used were fairly conservative, being less than £80 per year for all groups. Antihypertensive treatment resulted in gains in life expectancy for all groups considered but these were small in those at low risk of cardiovascular disease. In all but the oldest age groups, treatment was effective but cost more. In the oldest high risk group, treatment resulted in cost savings. Incremental cost-effectiveness for those at low risk ranged from £1000 to £3300 per quality adjusted life year (QALY) gained and from £30 to £250 per QALY in those at higher risk.

Because the cost-effectiveness of antihypertensive medication varies with absolute risk of stroke and CHD, the costs involved in the intensive treatment of non-insulin dependent diabetics, a high risk group, has been examined. The study was part of the long running UKPDS trial and found that the cost-effectiveness ratio of intensive treatment compared favourably to many accepted health care programmes. The incremental costs are shown in **Table 25**.¹⁴⁵

Table 25: Incremental costs associated with tight blood pressure control compared to less tight control.¹⁴⁵

	Costs and effects discounted at 6% per year	Costs discounted at 6% per year, effects not discounted
Incremental cost per extra year free from end points	£1,049	£434
Incremental cost per life year gained	£720	£291

7 Models of care and recommendations

Summary of guidelines for hypertension treatment

Diagnostic thresholds

There is variation in national and international recommendations with respect to diagnostic thresholds in hypertension. The following strategy represents a degree of consensus between the international guidelines and importantly reflects the BHS guideline.¹⁸ Patients with sustained blood pressure over 160/100 need treatment, but the decision for those in the range 140–159/90–99 will depend on the presence of other factors, namely evidence of end organ damage, diabetes or a raised 10 year CHD risk.

No data exist on the proportions of patients requiring treatment in a UK population and the effect of treatment in terms of events prevented, but a group from New Zealand have performed a modelling exercise by extrapolating data from a risk factor survey to the population of Auckland residents.¹⁴⁶ This study showed that a change to treatment on the basis of cardiovascular risk would result in a greater number of cardiovascular events being averted with fewer patients treated, compared to current treatment (largely on the basis of absolute level of blood pressure), even if a conservative threshold of 20% 5 year cardiovascular (CVS) risk were used.

A Swedish review has considered treatment thresholds in the light of cost-effectiveness.¹⁴⁷ For patients aged over 45 cost savings result at a threshold above 100 mmHg, whereas in younger patients, even blood pressure above 105 mmHg was associated with costs per life year gained as high as £28 300–42 200 (1992 prices).

Treatment targets

The various guidelines give similar recommendations on treatment targets as indicated in **Table 26**. One study of 876 patients from 18 UK general practices found that the proportion of patients with controlled hypertension varied between 17.5% and 84.6%, depending on which guidelines were used.¹⁴⁸

Choice of antihypertensive drug

The latest guideline from the British Hypertension Society regarding treatment choice is the 'ABCD algorithm'.⁴⁶ The recommendations for choice of first line antihypertensive drug are as follows:

- 1 In younger non-black patients either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (A) or in some circumstances beta-blockers (B) should be used as an initial therapy.

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Table 26: Target blood pressure and first line treatment for uncomplicated hypertension (adapted and updated from Swales, 1994¹⁴).

Guideline	Target diastolic blood pressure (mmHg)	Target systolic blood pressure (mmHg)	First line treatment
Canada ²³	<90	<140	In uncomplicated cases, low dose thiazide diuretics, β -blockers, or ACE inhibitors in under 60s; low dose thiazide or long acting hydropridine calcium antagonists in over-60s
Britain ¹⁸	<85	<140	ABCD algorithm (<i>see</i> section 5)
USA ²⁴	<90	<140	Thiazide diuretics alone or in combination with ACE inhibitors, or beta-blockers (uncomplicated hypertension)
DM/Renal Dis	<80	<130	
New Zealand ¹⁷	70–80	120–140	Low dose thiazide diuretics or β -blockers
WHO/ISH ²²			Patient factors determine choice from: diuretics, β -blockers, ACE inhibitors, calcium antagonists, α adrenoceptor blockers or angiotensin II antagonists
(older)	<90	<140	
(younger)	<85	<130	

In older or black (i.e. African-Caribbean) patients calcium channel blockers (C) or diuretics (D) should be used initially.

- The majority of patients need a combination of drugs in order to achieve a blood pressure target of 140/85 mmHg (140/80 mmHg in diabetics).
- When two drugs are needed, A (or B) should be combined with C or D, and for triple therapy A+C+D should be used.

The guideline goes on to recommend the use of fixed dose combinations, provided appropriate cost-effective choices are available.

Additional treatments to lower cardiovascular risk

The BHS guideline recommends the addition of aspirin and/or a statin to people with hypertension at higher risk of cardiovascular disease:¹⁸

- aspirin:** over 50 years of age, CHD risk >15% over 10 years and BP controlled below audit threshold of 150/90
- statin:** cholesterol >5mmol/l if current cardiovascular disease, otherwise in the presence of CHD risk >30% over 10 years.

Table 27: Compelling and possible indications, contraindications and cautions for major classes of antihypertensive drug (taken from Guidelines for management of hypertension, BHS).¹⁸

Class of drug	Compelling indications	Possible indications	Possible contraindications	Compelling contraindications
α -blockers	Prostatism	Dyslipidaemia	Postural hypotension	Urinary incontinence
ACE inhibitors	Heart failure LV dysfunction Type 1 diabetic Nephropathy	Chronic renal disease Type 2 diabetes Nephropathy	Renal impairment ^a Peripheral vascular disease ^b	Pregnancy Renovascular disease
AT 2 blockers	ACE inhibitor-induced cough	Heart failure Intolerance of other antihypertensive drugs	PVD ^b Pregnancy Renovascular disease	
β -blockers	Myocardial infarction Angina	Heart failure ^c	Heart failure Dyslipidaemia PVD	Asthma/COPD Heart block
Calcium antagonists (dihydropyridine)	Elderly ISH	Elderly Angina		
Calcium antagonists (rate limiting)	Angina	Myocardial infarction	Combination with β -blockade	Heart block Heart failure
Thiazides	Elderly		Dyslipidaemia	Gout

^a ACE inhibitors may be beneficial in chronic renal failure but should only be used with caution, close supervision and specialist advice when there is established and significant renal failure.

^b Caution with ACE inhibitors and AT II blockers in peripheral vascular disease because of the association with renovascular disease.

^c Beta-blockers may worsen heart failure but may also be used to treat heart failure.

COPD: chronic obstructive pulmonary disease; ISH: isolated systolic hypertension; PVD: peripheral vascular disease.

Follow-up

Site of follow-up

The vast majority of hypertensive patients will be followed up in the community under the care of a general practitioner. Follow-up clinics may often be run by a practice nurse. Patients requiring continued follow-up in a secondary care setting may include those with poorly controlled hypertension, those with secondary hypertension and those requiring special monitoring.

Frequency of follow-up

The BHS guideline recommends follow-up of people receiving treatment for hypertension at between 3–6 month intervals once stable but points out that the frequency of follow-up for an individual will depend on multiple factors including severity of hypertension, variability of blood pressure and compliance with treatment.¹⁸

Those not currently receiving treatment who have previously been hypertensive or who have borderline blood pressures should be reviewed yearly.

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Follow-up regime

The BHS guideline recommends the following routine for follow-up visits:

- measure BP and weight
- enquire about general health, side effects and treatment problems
- reinforce non-pharmacological measures
- test urine for proteinuria (annually)
- systematic follow-up including computerised recall for patients not otherwise attending.

Special groups

Diabetes mellitus

Treatment targets for those people suffering from diabetes are lower following evidence for this from the HOT study.²⁵ The BHS recommends a treatment target of <140/80 and commencement of treatment with a sustained blood pressure of $\geq 140/90$ in diabetics.¹⁸

Elderly

Treatment targets and thresholds for the elderly are no different than for other groups.¹⁸ However, as increasing age is a key risk factor for CHD, people will be eligible for risk-based care at lower levels of blood pressure. Furthermore, many older people will have isolated systolic hypertension. The evidence for treating this group of people is good, particularly with respect to stroke protection (*see* 'Hypertension as a risk factor for disease' in section 4, p.416).

Pregnancy

The BHS guideline recommends that careful distinction be made between those with new onset (or newly recognised) chronic hypertension (i.e. BP $\geq 140/90$ mmHg before 20 weeks gestation) and pre-eclampsia.¹⁸ Raised BP prior to 20 weeks usually means that hypertension preceded pregnancy. If chronic hypertension is diagnosed then secondary causes should be sought. Exclusion of phaeochromocytoma using urinary catecholamines is particularly important as it can cause sudden death in pregnancy.

Sub-categories

Guideline recommendations for people falling in sub-categories 1–3 have been covered above. The BHS guideline recommends admission for immediate treatment for people in group 4 (malignant or accelerated hypertension).¹⁸ Recommendations for diagnosis and treatment of group 5 (secondary hypertension) will depend on the underlying cause (for example surgery for those with phaeochromocytoma). The BHS guideline recommends referral to secondary care of those where such a secondary cause is suspected. The BHS guideline does not give specific recommendations for people in group 6 (white coat hypertension). JNC VI states that in people in whom a raised clinic blood pressure is the only abnormality, ambulatory blood pressure monitoring may identify a group at relatively low risk of morbidity.¹⁶

Towards a quantified model

Figure 5 (page 448) represents a simple model for the detection and treatment of hypertension encompassing community and secondary care facilities. Figures from the Health Survey for England suggest that around 36.5% of the adult population screen positive for hypertension (or are already receiving treatment) using a threshold of 140/90 for mean blood pressure taken three times on one occasion (*see* section 4, **Table 4**).¹ Only 26% of those screening positive for hypertension were currently being treated, which suggests that around a quarter (27%) of the adult population require further follow-up to determine whether or not their blood pressure requires treatment.

Detecting hypertension

Detecting of previously unrecognised hypertension could be done opportunistically, using a systematic untargeted screening system or by using targeting to prioritise systematic screening. A recent modelling exercise compared non-targeted and targeted systematic screening and concluded that targeting people for primary prevention in order of estimated coronary heart disease risk (calculated using known patient data or population estimates where this was not available) was more efficient.¹⁴⁹ However, as discussed in section 6, over 90% of a primary care population will consult their GP in a three-year period. The initial screening of blood pressure could feasibly be done opportunistically in a consultation without the need for systematic screening, apart from chasing up low attenders as required. The BHS guidelines suggest a five-yearly opportunistic screen.¹⁸

Guidelines recommend making a diagnosis of hypertension over a period of time (3–6 months) unless the BP on presentation is particularly high. This is because many people's blood pressure will reduce over time due to a combination of accommodation to the measurement procedure and regression to the mean. For example, one study found that in a group with mild to moderate untreated hypertension, mean blood pressure dropped by 8.5/4.5 mmHg between two readings taken one week apart. In this study around 20% of patients were misclassified as hypertensive or not after four readings at weekly intervals.⁷²

For example, a population of 100 000, of which 21% are below the age of 16 will contain 71 500 adults not currently taking antihypertensives (**Figure 5**). Screening this population on a five year cycle would require 14 300 additional blood pressure readings per year. Data from the Health Survey for England suggest that 4260 (27%) would screen positive (*i.e.* BP >140/90 and not currently on treatment). Each person screening positive will need at least two additional screening visits to confirm or refute the diagnosis of hypertension requiring an additional 8500 nurse appointments per year. Assuming that each visit takes 10 minutes (to take account of lifestyle advice and appropriate rest periods prior to measurement) then at £10 per consultation, this will cost £85k per year or £0.43m over five years (**Table 28**).⁵³

It is not clear what proportion of hypertension screen positive adults will be categorised as hypertensive after such a period of monitoring. Using current BTS guidelines then those with sustained blood pressure of $\geq 160/100$ mmHg would be treated automatically with those falling between 140–159/90–99 being treated on the basis of their coronary heart disease risk or other risk factors (pre-existing cardiovascular disease or diabetes).¹⁸ However, blood pressure tends to drop on repeated measurement and only a proportion of those screening positive will be high risk and so this will reduce the number requiring treatment.⁷² The HSE found that a third of those screening positive at a threshold of 140/90 had a blood pressure $\geq 160/95$. For the purposes of this example, it will be assumed that half of those screening positive to a BP >140/90 will require treatment after further evaluation (*i.e.* 2100 per year or 10 500 over five years) (**Figure 5**).

Each newly diagnosed person with hypertension will need baseline investigations at the very least. Costs for investigation are likely to be low for the majority of patients comprising urinalysis, simple blood tests

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and ECG. The actual costs of these in primary care are difficult to quantify but using the NHS reference costs then a figure of £100 (£90 for the ECG and £10 for the blood and urine tests) is appropriate.⁵⁴ If 2100 additional patients require investigating then this will equate to £210,000 of additional baseline investigations costs per year (**Table 28**).

Between 5–10% are likely to require referral for additional investigation and/or treatment. Assuming 200 are referred per year then each will require a consultation and further costs for investigation. These will include the baseline consultation (£79), and ECG (£100 as above), and may include an echocardiogram (£72–103), further pathology tests such as 24-hour urinary protein collection (£5–20 depending on number and type of test ordered) or 24-hour blood pressure monitoring (cost not available but likely to be of the order of £100 based on ECG/echo costs). It would seem realistic to assume that an average secondary care consultation with associated investigation will cost of the order of £200 (i.e. £80,000–160,000). Ongoing costs will depend on frequency of follow-up.

The additional treatment costs incurred by detecting new cases will depend to a great extent on the classes of drug used. Assuming each patient requires two medications to adequately control blood pressure (1.8 was the mean in the HOT study) then the mean additional yearly cost could range from (BNF 44: BDZ 2.5 mg £9.67 + atenolol 50mg £11.08) £20 per patient per year to (losartan 50mg £224.61 + amlodipine 10 mg 230.73) £455 per patient per year. Aspirin and cholesterol lowering medication will inflate this further (**Table 28**).

Ongoing costs in terms of follow-up and follow-up investigation once blood pressure has been controlled will comprise two consultations per year (one GP (£15) and one practice nurse (£10)), urea and electrolytes (£5) for those on a diuretic or drug affecting the renin angiotensin system (likely to be the majority) and urinalysis (<£1 so ignored). This gives a total of £30 per year non-drug ongoing costs.

Table 28 and **Table 29** show a breakdown of likely costs of such a screening programme. Overall, a five year screening programme will cost approximately £2.4 million–£8.9 million per 100 000 population over and above current costs, depending on the drugs used (i.e. more than doubled).

Table 28: Additional yearly costs of screening and treating for hypertension over and above current costs using 5-year rolling programme.

Activity	Number of people ^a	Unit cost	Cost per year
Adult population not currently taking antihypertensives	71,500		
Initial screening for hypertension	14,300 per year		Assume zero additional cost as opportunistic
Follow-up screening (2 visits @ £10 each)	4,260 per year	£20	£85,000
Baseline investigations	2,100 per year	£100	£210,000
Secondary ref/investigations	200 per year	£200	£40,000
Low cost combination drug treatment	2,100 per year	£20	£42,000
High cost combination drug treatment	2,100 per year	£455	£956,000
Ongoing monitoring	2,100 per year	£30	£63,000
Yearly additional non-drug costs			£398,000
Yearly additional drug costs			£42,000–£956,000
Yearly total additional costs			£440,000–£1,350,000

^a Assumes population of 100,000 of which 79,000 are adults of which 7,500 are currently receiving antihypertensive treatment.

Table 29: Estimated additional cost of 5 year programme to screen and treat hypertension.

	Non-drug costs (screening, investigation & monitoring) ^a	Drug costs ^b
Year one	£398,000	£42,000–£956,000
Year two	£461,000	£84,000–£1,910,000
Year three	£524,000	£126,000–£2,870,000
Year four	£587,000	£168,000–£3,820,000
Year five	£650,000	£210,000–£4,780,000
Total five year costs ^c	£2,620,000	£630,000–£13,380,000

^a Ongoing monitoring costs are cumulative as more people require monitoring each year (£63,000 extra per year).

^b Ongoing drug costs are cumulative as more people are treated each year of the cycle.

^c An assumption has been made that both the population and cost remain static throughout. (See Figure 5 overleaf.)

Treating hypertension

The Health Survey for England showed that only between a quarter and a third of treated hypertensives are currently being treated adequately (to below 140/90 mmHg in this case).¹ Data from the HOT study (see ‘Treatment targets’ in section 6) found that for non-diabetics the optimum blood pressure in terms of morbidity and mortality was 138/83.²⁵ For those with diabetes, benefit was gained from still lower pressures. Subsequently the British Hypertension Society has recommended a target of below 140/85 for people without diabetes and below 140/80 for those with diabetes. Data from the HOT study suggest that most people will require two or more medications to achieve this target.

So, returning to the population of 100 000 used in the example above, 7500 patients from the adult population already receiving treatment will require monitoring at a yearly cost of £30 and £20–£455 depending on treatment chosen. This equates to £1.13 million monitoring and £750 000–£17.06 million treatment over 5 years.

Conclusions for the model

The two main priorities for purchasers in the management of hypertension are therefore to extend the current reach of detection using a largely opportunistic model and then to ensure that those being treated are receiving adequate medication to control blood pressure below recommended limits. This should be done in the context of an individual’s overall cardiovascular risk unless blood pressure is above 160/100. Given that current provision is limited, treatment of people at the highest risk, namely those with current cardiovascular disease (coronary heart disease, vascular disease or stroke) should be the first priority. This exercise is likely to require significant funding of the order of several million pounds per PCT. The largest influence on cost over and above this level is the choice of drug. The BHS recommendations of ‘ABCD’ can be achieved with both low cost or high cost combinations and choice will depend at least in part on individual patient characteristics. However, given the evidence of equivalence of benefit from the four major classes, low cost combinations will be more cost-effective.^{46,104} For those patients with side effects or poor control, new more expensive medications will be appropriate.

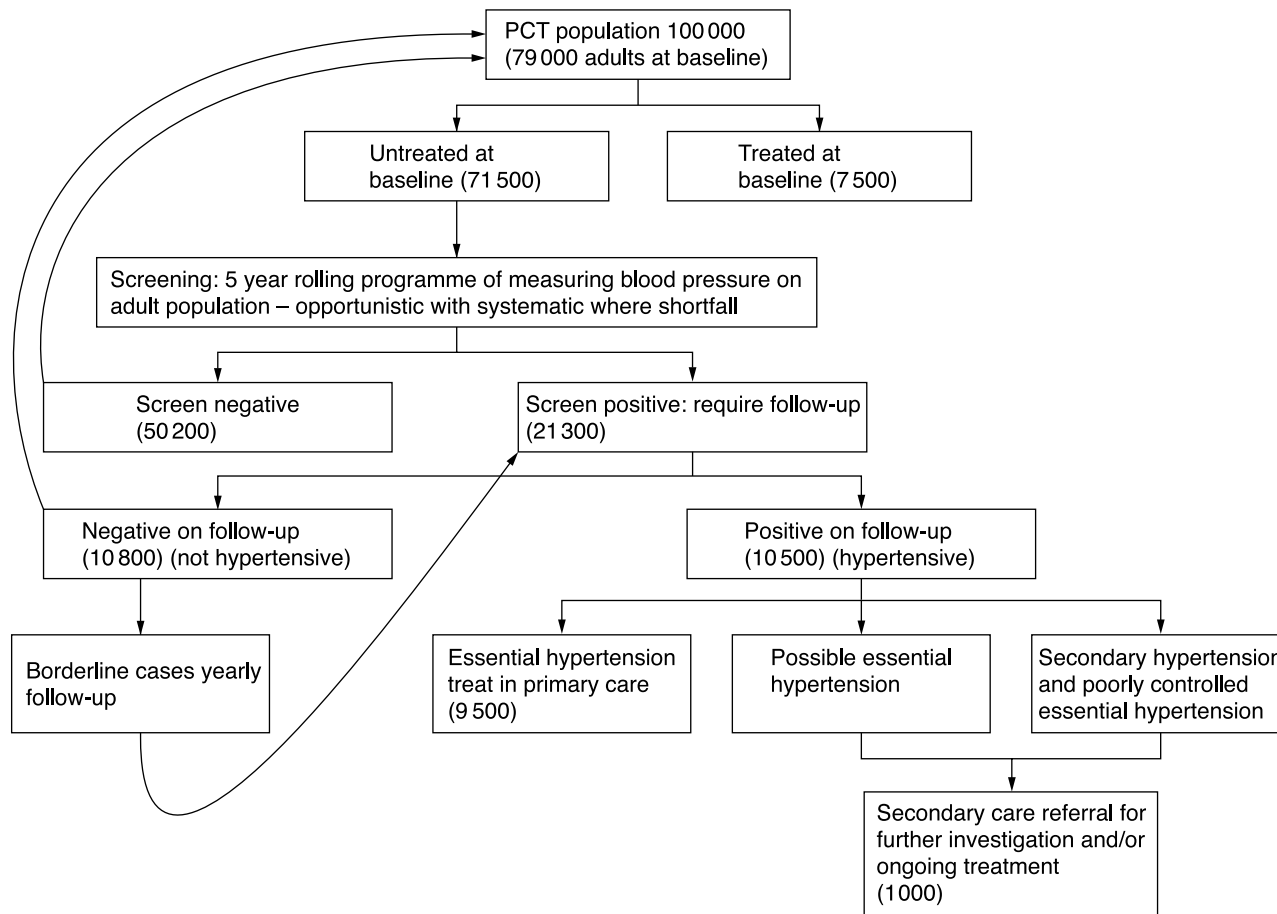


Figure 5: Model for the detection and treatment of hypertension (numbers indicate population screened in a 5 year cycle).

8 Outcome measures

A number of national audit and outcome indicators are currently in use by various primary care organisations.

British Hypertension Society Guideline

The British Hypertension Society Guideline recommends the following audit criteria for primary care:¹⁸

- the proportion of all adults in the practice who have had a blood pressure measurement in the last 5 years
- the proportion of all hypertensives given non-pharmacological advice
- the proportion of all hypertensives given antihypertensive therapy
- the proportion of hypertensives receiving antihypertensive therapy who have suboptimal control, i.e., blood pressure levels >150 mmHg systolic and >90 mmHg diastolic BP
- the proportion of patients lost from follow-up; or of treated patients who have not been reviewed within the last 6 months
- the use of aspirin and statins by those who require secondary prevention; or their use when indicated for primary prevention, i.e. when the estimated 10 year CHD risk is >15% (aspirin) or >30% per year (statins).

New General Medical Services Contract

The new General Medical Services Contract for General Practitioners has, since April 2004, awarded quality points and therefore resources to practices performing the following criteria for people with hypertension:

- **BP 1:** The practice can produce a register of patients with established hypertension (Yes/No).
- **BP 2:** The percentage of patients with hypertension, whose notes record smoking status at least once (standard max 90%).
- **BP 3:** The percentage of patients with hypertension who smoke, whose notes contain a record that smoking cessation advice has been offered at least once (standard max 90%).
- **BP 4:** The percentage of patients with hypertension in which there is a record of the blood pressure in the past 9 months (standard max 90%).
- **BP 5:** The percentage of patients with hypertension in whom the last blood pressure (measured in last 9 months) is 150/90 or less (standard max 70%).

The performances of practices in respect of these criteria are likely to become the major data from audit available on a national scale in England due to the fact that every practice with a GMS contract will be paid according to them.

National Service Framework for Coronary Heart Disease

Standard four of the National Service Framework for Coronary Heart Disease states:¹⁵⁰

General practitioners and primary health care teams should identify all people at significant risk of cardiovascular disease but who have not yet developed symptoms and offer them appropriate advice and treatment to reduce their risks.

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The relevant NSF milestones with respect to hypertension are contained in the second step, which concerns those at high risk for CHD (>30% 10 year CHD risk) but without evidence of frank disease at present:

- **Milestone 2:** Every practice should have:
 - a systematically developed and maintained practice-based register of people with clinical evidence of CHD, occlusive vascular disease *and* of people whose risk of CHD events is >30% over ten years in place and actively used to provide structured care to those at high risk of CHD.
- **Milestone 3:** Every practice should have:
 - a protocol describing the systematic assessment, treatment and follow-up of people at high risk of CHD, including those without evidence of existing arterial disease but whose risk of CHD events is >30% over 10 years, agreed locally and being used to provide structured care to people with CHD.
- **Milestone 4:** Every practice should have:
 - clinical audit data no more than 12 months old available that describes all the items listed below
 - clinical audit data recording the following interventions and risk factors:
 - advice about how to stop smoking including advice on the use of nicotine replacement therapy
 - information about other modifiable risk factors and personalised advice about how they can be reduced (including advice about physical activity, diet, alcohol consumption, weight and diabetes)
 - advice and treatment to maintain blood pressure below 140/85 mmHg
 - add statins to lower serum cholesterol concentrations *either* to less than 5 mmol/l (LDL-C to below 3 mmol) *or* by 30% (whichever is greater)
 - meticulous control of blood pressure and glucose in people who also have diabetes.

Overview of audit criteria and National Standards

At the time of writing, none of these audit criteria have been in widespread use, nor have there been nationally available figures for the performance of practices with respect to the various criteria. The new GP contract is the most likely to change this state of affairs in that as GP income will be directly related to performance against these criteria, it is likely that at least summary figures will be available.

9 Information and research requirements

Key areas for research in hypertension include:

- robustly powered studies with appropriate clinically relevant end points (i.e. mortality and major morbidity) to determine the efficacy of non-pharmacological measures in the treatment of hypertension
- further studies examining the effect of increased user involvement in the treatment and control of hypertension
- community-based studies evaluating the benefit of generic antihypertensive medication post stroke
- long-term community-based studies with clinically relevant end points evaluating the implementation of treatment for hypertension on the basis of risk rather than blood pressure thresholds.

The bulk of this chapter was written in 2003/4 prior to both the implementation of the new General Medical Services (nGMS) Contract for General Practitioners and the publication of the most recent guidelines from the National Institute for Clinical Excellence (NICE) and the British Hypertension Society

(BHS). Furthermore, these guidelines are now in the process of being updated again following publication of several new studies, particularly relating to the use of beta-blockers in hypertension.

Key recent changes relevant to the chapter include:

- National prevalence of recognised hypertension has increased to around 11% (Quality and Outcomes Framework of nGMS; slightly lower in the 2003 version of Health Survey for England due to different definitions).
- Two systematic reviews and the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) trial results have cast doubt on the efficacy of beta-blockers in the treatment of hypertension as compared to other classes of antihypertensive.
- The forthcoming update of the NICE hypertension guideline will use a cost-effectiveness model to dictate choice of antihypertensive therapy taking into account both benefits (in terms of reduction of cardiovascular events) and significant side effects (principally in terms of risk of diabetes). It is expected to relegate beta-blockers to fourth line treatment behind calcium channel blockers, thiazide diuretics and ACE inhibitors to bring NICE and BHS guidance together.

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Acknowledgements

The authors would like to thank Dr JJ Ferguson and Mr J Horgan for access to prescribing data.