



**MANAGEMENT OF ADULTS  
WITH ESSENTIAL HYPERTENSION**

**Clinical practice recommendations and economic data**

**APRIL 2000**

**ABSTRACT**

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## RECOMMENDATIONS

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**Since the ANDEM recommendations were published in 1997, new studies have confirmed some of the information they contained, such as managing hypertension as part of a more global approach to cardiovascular risk, the fundamental contribution of non-drug measures in preventing and treating hypertension, more specific indications for drug treatment, and specific aspects of hypertension in elderly subjects.**

**Table 1.** Summary of key points

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1. Lifestyle factors and the quality of patients' compliance with treatment (both non-drug and drug treatment) are fundamental components of the management of hypertensive patients (Grade B recommendation).
  2. The estimated cardiovascular risk governs whether or when drug treatment is prescribed for a hypertensive patient, based on whether there are other risk factors (Professional Agreement):
    - If there is a high risk, both drug and non-drug treatment should be started as soon as the diagnosis of hypertension has been confirmed.
    - If there is a low or average risk, drug treatment should be started if blood pressure values are still high after non-drug treatment alone and after any risk factors have been treated.
  3. The choice of initial drug treatment should be tailored to the patient's individual clinical situation, and will depend on the anticipated beneficial or harmful effects on certain concomitant indications or diseases; apart from these specific or compelling indications, the initial drug chosen should be one of the four categories of drugs which have been tested in controlled trials, i.e. low-dose thiazide diuretics, beta blockers, long-acting dihydropyridines and ACE inhibitors (Grade A recommendation).
  4. When the first drug is well tolerated but fails to control hypertension, a second active ingredient should be given, preferably a thiazide diuretic if the first drug was from one of the other categories (Professional Agreement).
  5. Target values are systolic blood pressure (SBP) < 140 mmHg and diastolic blood pressure (DBP) < 90 mmHg (Grade A recommendation).
  6. In elderly subjects, it is recommended that any isolated rise in SBP above 160 mmHg should be treated effectively to reduce it to below 150 mmHg (Grade A recommendation).
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## MEASURING BLOOD PRESSURE

**A routine clinical examination of an adult includes measurement of blood pressure. In the doctor's surgery, a validated electronic device with a suitable cuff can be used to take the measurement after the patient has been sitting or lying down for a few minutes. It can be useful to complete the examination by measuring blood pressure with the patient standing, to test for orthostatic hypotension.**

**Outside the surgery, ambulatory blood pressure monitoring and self-measurement of blood pressure can be valuable in providing a more accurate assessment of the true level of hypertension (Table 2) and in determining the risk of cardiovascular complications. It has not been shown that it improves the management of hypertension.**

**Table 2.** Indications for measuring blood pressure outside the doctor's surgery (ambulatory blood pressure monitoring, self-measurement of patient blood pressure)

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Suspected "white-coat" hypertension;  
 Management of hypertension which is resistant to treatment;  
 Symptoms of hypotension under antihypertensive treatment.

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## **EVALUATING THE HYPERTENSIVE PATIENT**

By definition, the term hypertension is used in relation to adults when systolic blood pressure (SBP) is usually 140 mmHg or over and/or diastolic blood pressure (DBP) is 90 mmHg or over when measured in the doctor's surgery. But many population studies have shown that there is a positive and continuous relationship between raised blood pressure and onset of cardiovascular disease, and this continuous relationship should be borne in mind when deciding on any threshold to define hypertension. Furthermore, blood pressure is only one component of cardiovascular risk, which requires a global management approach (scientific evidence level 1).

An evaluation of a hypertensive patient should include a history, clinical examination, laboratory tests and other diagnostic procedures, and has two objectives:

- To identify other determinants of cardiovascular risk or target-organ damage, so that the level of cardiovascular risk can be assessed individually for each patient. The global management strategy for a hypertensive patient will be based on this assessment;
- To try to find the cause of the hypertension: 1) when hypertension is discovered, if the initial assessment of the hypertensive patient has suggested that there is an aetiology which needs to be confirmed; 2) if there are no signs suggesting a specific cause, when initial blood pressure values are over 180/110 mmHg; 3) if the hypertension proves to be refractory to treatment (SBP > 140 or DBP > 90 mmHg) despite the use of an appropriate combination of three drugs from different categories, including one diuretic.

## **STRATEGY FOR MANAGING A HYPERTENSIVE PATIENT**

The objective of treatment is to reduce morbidity and mortality from cardiovascular disease in hypertensive patients, which means:

- Maintaining blood pressure values below 140 mmHg for SBP and 90 mmHg for DBP;
- Preventing, testing for and treating the complications of hypertension;
- Determining and managing risk factors that can be changed,
- Encouraging compliance.

Primary prevention of hypertension in the general population should be developed to complement this approach, as a reduction in the prevalence of hypertension in this way would mean a reduction in the number of hypertensives requiring treatment. In addition, people who are hypertensive would be more likely to comply with lifestyle and dietary measures if these measures were not very different from the lifestyle and food habits of the population as a whole.

### **1. Levels of intervention**

The strategy proposed is based on an individual assessment of cardiovascular risk (Professional Agreement), taking into account determinants of cardiovascular risk, target-organ damage and concomitant cardiovascular disease (*Table 3*).

**Table 3.** Principal determinants of cardiovascular risk and concomitant disease taken into account in the management of a patient with hypertension (adapted from WHO-ISH 1999). This list is neither hierarchical nor exhaustive.

Men > 45 years and women > 55 years;  
 Family history of premature cardiovascular disease (before age 55 in the father or age 65 in the mother);  
 Smoking;  
 Diabetes;  
 HDL-Cholesterol < 0.35 g/l (0.9 mmol/l), LDL > 1.90 g/l (4.9 mmol/l);  
 Excessive alcohol consumption  
 At-risk categories (particularly high-risk socioeconomic groups)\*;  
 No regular exercise;  
 Abdominal obesity;  
 Target-organ damage.

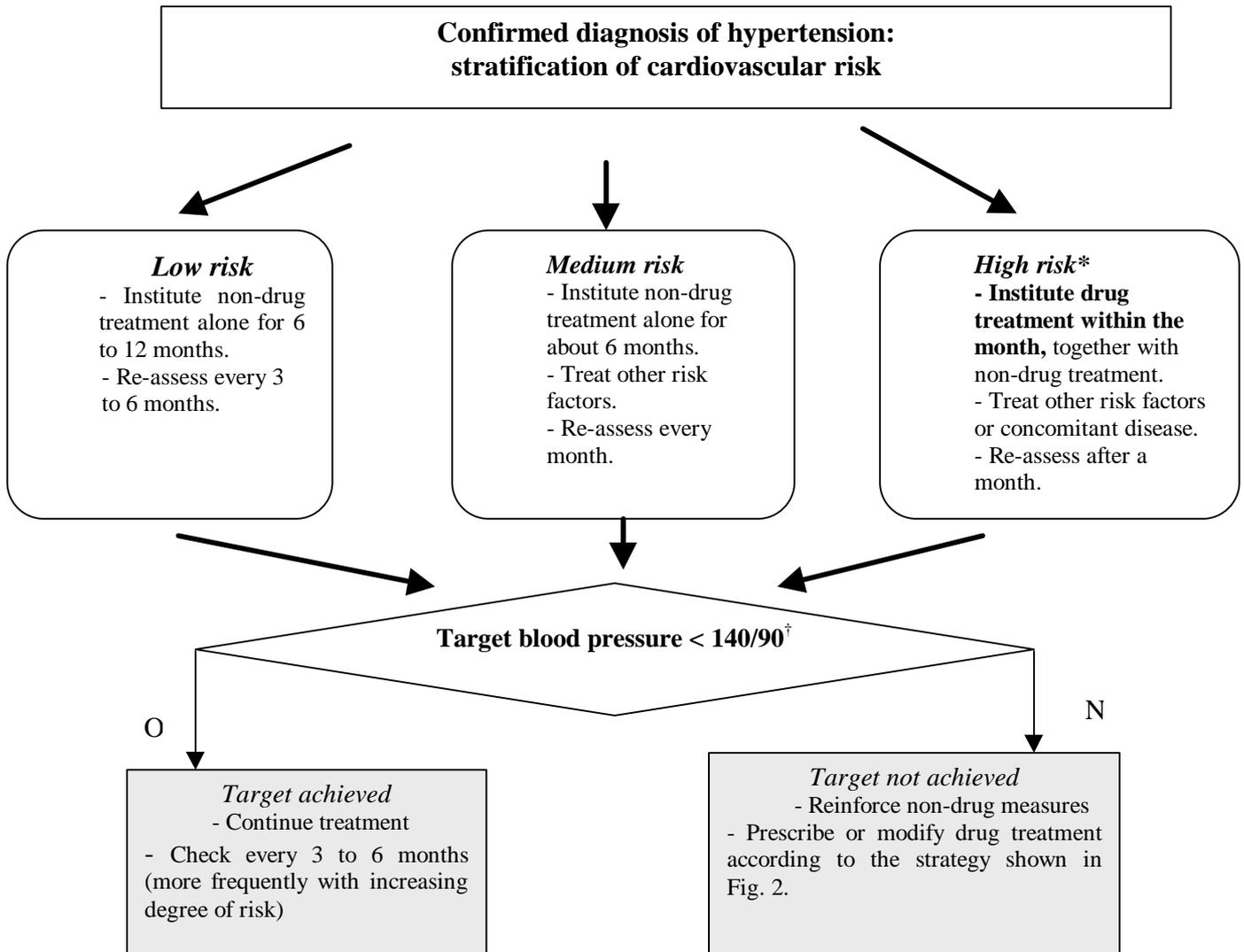
\* The 1999 JNC VI and WHO-ISH guidelines have also identified ethnicity and geographic region as risk factors, particularly African-Americans and people from the Caribbean. Clearly this would also include Guyana and the French Antilles. Many of these risk factors cannot be changed.

**Identification of the principal determinants of cardiovascular risk makes it possible to stratify the risk (Table 4) and establish a stepwise strategy combining non-drug and drug treatment (Fig. 1).**

**Table 4.** Stratification of risk to quantify the prognosis for a patient with hypertension (adapted from WHO-ISH 1999).

Other risk factors and disease history	Grade 1 (mild hypertension) SBP 140-159 or DBP 90-99	Grade 2 (moderate hypertension) SBP 160-179 or DBP 100-109	Grade 3 (severe hypertension) SBP ≥180 or DBP ≥110
Group A: no other risk factors	Low risk	Medium risk	High risk
Group B: 1-2 risk factors	Medium risk	Medium risk	High risk
Group C: 3 or more risk factors or target-organ damage or diabetes*	High risk	High risk	High risk

\* Patients with concomitant cardiovascular disease should be regarded as being at very high risk irrespective of blood pressure value, and they require specific treatment.



\* except for hypertensive emergencies, which are not the subject of these recommendations.

† Or lower in the two special cases of diabetes and renal impairment.

**Fig. 1** Monitoring strategy for hypertensive patients.

## 2. Lifestyle measures

The following measures are recommended (Grade B recommendations):

- Lose weight, if the patient is overweight;
- Reduce alcohol consumption to less than 30 ml of ethanol a day (i.e. about 250 ml or wine or equivalent) for men of average weight, 15 ml for women and men of lower weight;
- Reduce salt intake to 5-6 g of salt a day.

Other basic measures are a moderate increase in aerobic physical activity if this is inadequate and reduced consumption of saturated dietary fat. Giving up smoking is an essential goal.

**In high-risk patients, effective antihypertensive treatment should not be delayed until these lifestyle changes have been implemented (Grade A recommendation).**

### 3. Choice of antihypertensive drugs and strategy for use

#### *Initial treatment*

As yet there is no proof that the principal benefits of hypertension treatment are due to a specific effect of treatment rather than to the lowering of blood pressure in itself. Initial drug treatment should be tailored to the individual clinical situation of each patient, their physiological makeup, and the anticipated beneficial or harmful effects on certain indications or concomitant disease (Grade A recommendation). Various elements to be taken into account when tailoring treatment to the individual are summarised in Tables 5 and 6.

Apart from these specific or compelling indications, the drug category chosen should be one which has been tested in controlled trials, i.e. low-dose thiazide diuretics, beta-blockers, long-acting dihydropyridines or ACE inhibitors (Grade A recommendation). The initial choice of drug may take into account the fact that, pending the results of studies in progress, there is currently more evidence relating to diuretics and beta-blockers. In many randomised studies, only low-dose thiazide diuretics have been shown to be effective in terms of total mortality, but two recent studies in hypertensive subjects aged over 60 have found that the efficacy of all four major therapeutic categories is similar. In terms of cardiovascular and cerebrovascular morbidity, all four categories cited have a similar degree of efficacy.

In addition, medicoeconomic studies have shown that treatment with diuretics or beta-blockers is not expensive.

Treatment should begin with monotherapy or a fixed combination which can be prescribed by first intention, preferably given in a single daily dose to encourage better compliance (Professional Agreement).

**Table 5.** Preferred indications for the principal categories of drugs used to treat hypertension, to be prescribed by first intention (if there are no contraindications\*) and continued if the target blood pressure is achieved.

<b>Compelling indications*</b>	- Type 1 diabetes with proteinuria: ACE inhibitors - Heart failure: ACE inhibitors, diuretics - Isolated systolic hypertension in elderly subjects: thiazide diuretics, calcium antagonists (dihydropyridine (DHP) group) as alternative - Myocardial infarction: beta-blockers, ACE inhibitors (if there is systolic dysfunction)
<b>Specific indications</b>	see Table 6
<b>If there are no compelling or specific indications*</b>	Diuretics or beta-blockers

\* according to results from randomised studies

**Table 6. Factors to be taken into consideration when tailoring antihypertensive treatment to the patient. Adapted from JNC VI, and based on information contained in marketing authorisations -AFSSAPS (French agency for the safety of health products)**

Indication	Drug treatment
<i>Compelling indications if there are no contraindications</i>	
Diabetes (type 1) with proteinuria	ACE inhibitors
Heart failure	ACE inhibitors, diuretics
Uncomplicated hypertension in elderly subjects	first choice = thiazide diuretics, alternatively CA* (long-acting DHP)
Myocardial infarction	beta-blockers, ACE inhibitors (in systolic dysfunction)
<i>Possible beneficial effects on concomitant disease</i>	
Angina	beta-blockers, CA
Tachycardia and atrial fibrillation	beta-blockers, verapamil
Diabetes (types 1 and 2) with proteinuria	ACE inhibitors (first choice)
Diabetes (type 2)	cardioselective beta-blockers, low-dose diuretics, ACE inhibitors
Dyslipidaemia	alpha-blockers
Essential tremor	propranolol
Heart failure	bisoprolol, carvedilol (with very strict precautions), diuretics (notably spironolactone)
Hyperthyroidism	beta-blockers
Migraine	metoprolol, propranolol
Myocardial infarction	verapamil
Prostatism (benign prostatic hyperplasia)	alpha-blockers
Renal impairment (caution in renovascular hypertension or if blood creatinine is $\geq 150 \mu\text{mol/l}$ , i.e. 17 mg/l)	benazepril
<i>Possible adverse effects on concomitant disease<sup>†</sup></i>	
Bronchospasm	CI: non-cardioselective beta-blockers; cardioselective beta-blockers in severe cases.
Depression	P: beta-blockers, centrally-acting alpha-blockers CI: reserpine, methyldopa in severe cases
Diabetes (type 1 and 2)	P: beta-blockers
Gout	P: diuretics
Second or third degree atrioventricular block	CI: beta-blockers, CA (non-DHP)
Heart failure	P: beta-blockers <sup>‡</sup> (except carvedilol), CA (except amlodipine and felodipine)
Liver disease	P: labetalol hydrochloride; CI: methyldopa
Peripheral arterial disease	CI: non-cardioselective beta-blockers and cardioselective beta-blockers in severe cases.
Pregnancy	CI: ACE inhibitors, AII-ra
Renal impairment	P: potassium-sparing diuretics
Renovascular disease	P: ACE inhibitors, AII-ra

CI = contraindication; P = precautions; CA = calcium antagonists; DHP = dihydropyridine; ISA = intrinsic sympathomimetic action; CS = cardioselective; AII-ra = angiotensin II receptor antagonists.

\* With reference to the Syst-Eur trial. Low-dose thiazide diuretics are still the reference treatment for use by first intention;

<sup>†</sup> If there are no contraindications, the drugs listed may be used if the patient is monitored closely;

Great caution must be observed if beta-blockers (other than bisoprolol and carvedilol) are used in heart failure. While some patients will benefit from them, others will experience harmful effects, and there is no way of knowing how an individual patient will react. Strict monitoring is required, as a precautions.

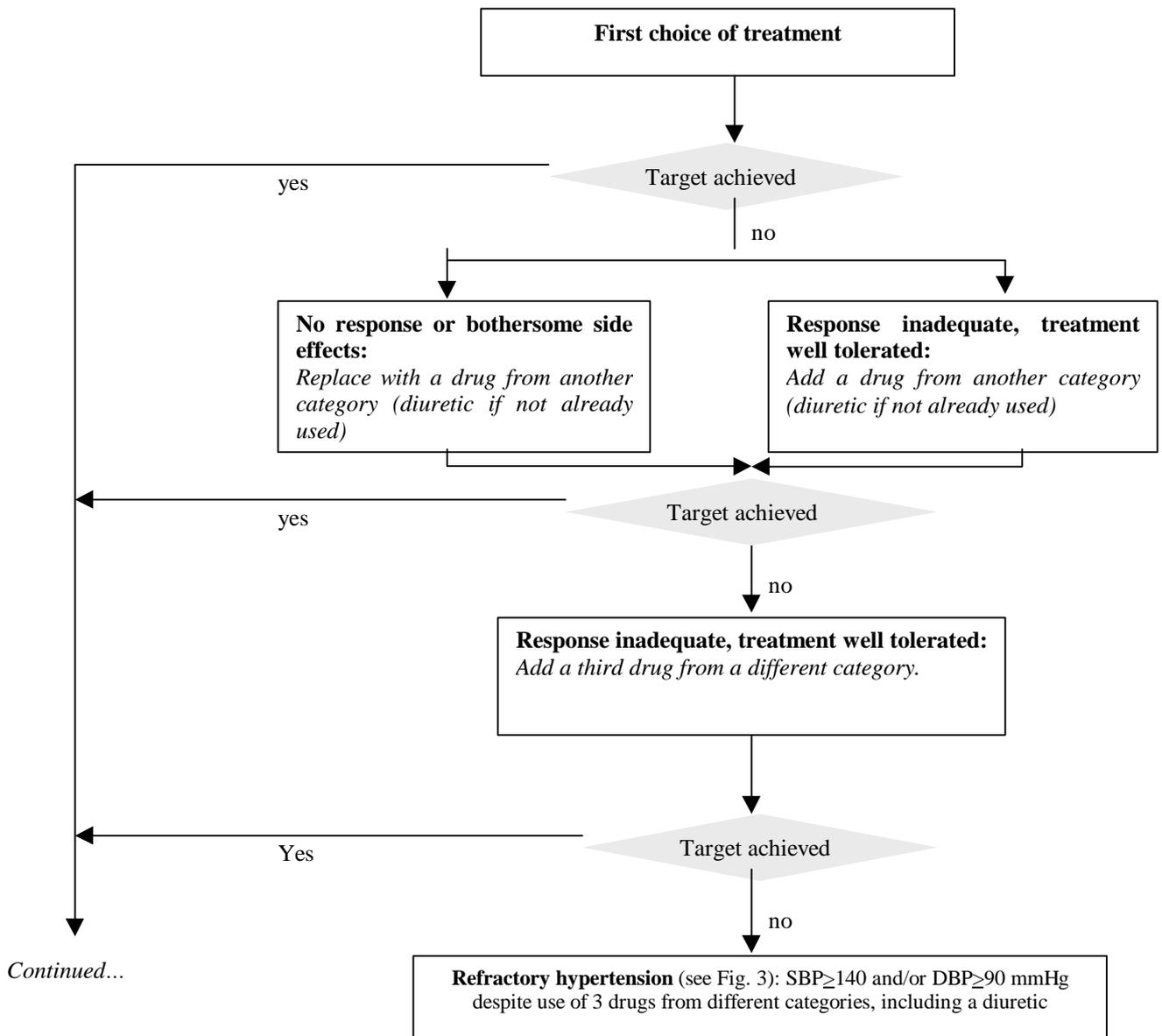
***Evaluation and adjustment of initial treatment***

**Treatment should be evaluated after 4-8 weeks to assess how effective it is and how well it is being tolerated; this period will vary according to the estimated level of risk (Professional Agreement). The target blood pressure is SBP < 140 mmHg and DBP < 90 mmHg.**

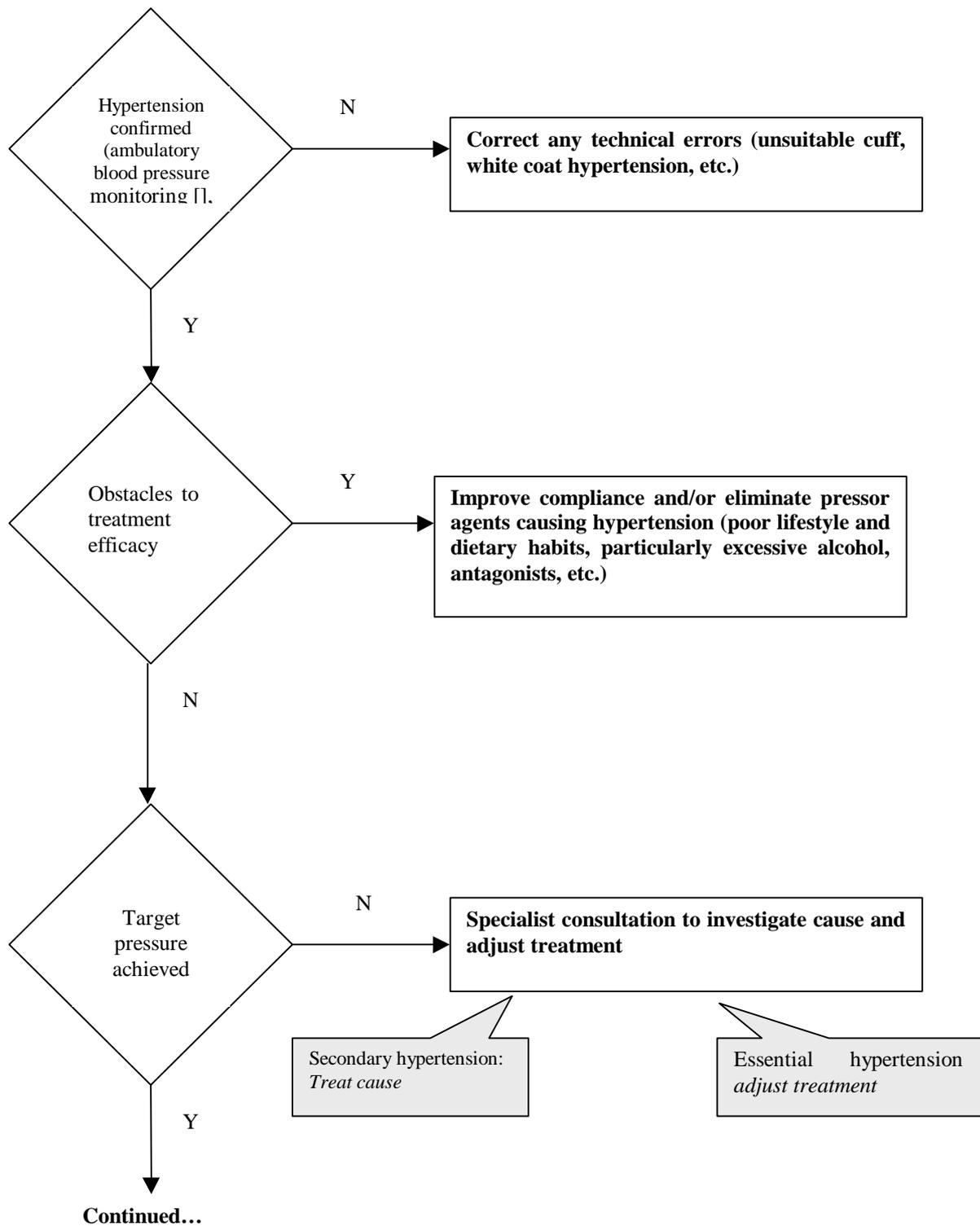
**When the first drug is well tolerated but fails to control hypertension, a second active ingredient should be given, preferably a thiazide diuretic if the first drug was from one of the other categories (Professional Agreement). Fixed-dose combinations simplify prescription and compliance at lower cost.**

**Table 7.** Additive combinations of antihypertensives (these combinations have not been tested in comparative trials)

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- Beta-blocker + diuretic
  - Beta-blocker + calcium antagonist (dihydropyridine)
  - ACE inhibitor + diuretic
  - ACE inhibitor + calcium antagonist
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**Figure 2.** Strategy for adjusting drug treatment



**Figure 3.** Diagnostic and treatment strategies if treatment produces inadequate control.

### *Stopping treatment*

An attempt to decrease the dose and number of antihypertensives prescribed can be safely made when blood pressure values have been normal for at least 6 to 12 months (Grade B recommendation). Drugs should be reduced slowly and gradually, and treatment should be monitored carefully. Success is more likely if the earlier hypertension was only moderate or if there have been major changes in lifestyle (weight loss, reduced alcohol consumption, decreased salt intake or increased physical exercise).

## 4. Compliance

Compliance with treatment presupposes that the relationship between doctor and patient includes a component of very practical education which is tailored to the individual (Grade B recommendation)

- Information about hypertension, its complications and how it is treated, based on the what the patient knows and thinks about their disease;
- Negotiated goals for weight loss and exercise duration;
- Simplification of the dose, a single daily dose being preferable for most patients.

Compliance with treatment is also governed by practical aspects of follow-up of a hypertensive patient, in particular on the co-ordination between the various health professionals involved with them.

## HYPERTENSION AND CONCOMITANT CARDIOVASCULAR RISK

### 1. Smoking

The patient should give up smoking as soon as possible, and abstain from smoking for as long as possible, and it remains beneficial regardless of age (Grade B recommendation).

All hypertensives who smoke should be offered help in giving up. This consists of an evaluation of their dependence on nicotine using the Fagerström test, prescription of nicotine patches to dependent patients and, for very highly dependent patients, specialist treatment in a centre dealing with smoking dependence or a centre for the treatment of addiction.

### 2. Metabolic disorders

It is recommended that blood glucose and lipid profile should be determined at least every three years when the first determination is normal and when there has been no change in weight or lifestyle.

#### *-Type 2 diabetes*

The definition of hypertension is the same as for the general population, that is, over 140/80 mmHg (Professional Agreement), but it is not known what the optimum target pressure is for a hypertensive diabetic in order to prevent onset or progression of micro- and macroangiopathic complications. A target blood pressure of 140/80 is recommended (Grade C recommendation).

It is recommended that the initial choice of drug should be either a cardioselective beta-blocker or a low-dose diuretic, or an ACE inhibitor (Grade B recommendation). Type 2

diabetics often require multiple drug treatment for hypertension. A specialist assessment is recommended (Professional Agreement).

*- Dyslipidaemia*

When dyslipidaemia is combined with hypertension, both diseases must be treated effectively (Grade A recommendation). After 6 months of appropriate diet and after the best possible control of blood pressure has been obtained, the LDL-cholesterol value is used as a reference value when instituting lipid-lowering drug treatment.

## **HYPERTENSION AND TARGET ORGANS**

### **Hypertension and the brain**

Antihypertensive treatment is effective in preventing stroke (scientific evidence level 1) and decline in cognitive function (scientific evidence level 2) in hypertensives. It satisfies the general rules for drug treatment described above (Grade A recommendation).

Cerebrovascular disease is an indication for antihypertensive treatment, using the same target blood pressure values as for the general population (Grade A recommendation).

### **Hypertension and the cardiovascular system**

Patients must be screened for cardiovascular disease associated with hypertension. The diagnosis of such disease implies a very high risk irrespective of blood pressure level, and requires specific management.

The following clinical examination should be carried out once a year:

- History to detect typical or atypical signs suggesting angina, heart failure and/or intermittent claudication and/or transitory ischaemic attack;
- Palpation of pedal and posterior tibial pulses; abdominal palpation;
- Auscultation to detect carotid, femoral or abdominal murmurs.

A resting electrocardiogram (ECG) should be done during the initial work-up of a hypertensive patient. It is recommended if any symptoms occur during follow-up. It may be offered routinely every 3 years (Professional Agreement). No other further studies are recommended for asymptomatic patients with a normal resting ECG, except in special circumstances (Professional Agreement).

### **Hypertension and the kidney**

The purpose of screening for renal impairment is to prevent or delay the onset of renal failure, which is a serious complication of hypertension.

Fasting blood creatinine and potassium should be determined every three years, and creatinine clearance should be calculated using the Cockcroft formula, when the first determination is normal (Professional Agreement). In patients whose treatment may change creatinine values (diuretics, ACE inhibitors and angiotensin II receptor antagonists), creatinine and blood electrolytes should be determined on an annual basis. Proteinuria should be tested at least every five years when the first test is negative, using

standard urine test strips or laboratory tests. Routine testing for microalbuminuria is only recommended in diabetic hypertensives; if it is found, treatment should be reinforced in all areas. Confirmed proteinuria, and micro-albuminuria in diabetics, should be quantified by means of 24-hour urine testing.

Routine annual urine culture is not recommended.

Further studies starting with measurement of endogenous creatinine clearance should be undertaken in the following circumstances (Professional Agreement): proteinuria, haematuria or urinary infection; blood creatinine > 105 µmol/l (11.8 mg/l) in women and > 135 µmol/l (15.2 mg/l) in men; calculated clearance (Cockcroft)  $\leq$  60 ml/min.

Hypertensives with renal impairment should be treated with an ACE inhibitor if there are no contraindications, usually combined with a thiazide diuretic (ineffective when blood creatinine is higher than 190 µmol/l, i.e. 20 mg/l) or a loop diuretic. Strict blood pressure control is recommended in hypertensives with renal impairment, to delay dialysis. Whatever treatment is required, the target blood pressure in renal impairment is < 130/85 mmHg, and < 125/75 mmHg if proteinuria is > 1 g/24h (Grade C recommendation). In renal impairment (blood creatinine higher than 135 µmol/l in men and 105 µmol/l in women), ACE inhibitors or angiotensin II receptor antagonists should be prescribed, with strict laboratory monitoring of blood creatinine and blood potassium.

## HYPERTENSION IN THE ELDERLY

There is a higher risk of cardiovascular complications in an elderly subject with hypertension, even SBP hypertension alone, than in a younger subject. It has been shown that the risk is reduced when the hypertension is treated. SBP is a better predictor than DBP of the risk (serious cardiovascular, cerebrovascular and renal events, and mortality from any cause) and this is increasingly so as patient age increases.

It is recommended (Grade A recommendation) that effective treatment should be given whenever SBP rises above 160 mmHg. The target to be achieved is to lower SBP to < 150 mmHg (Grade B recommendation).

**Table 8.** Management strategy for patients over 65 without concomitant cardiovascular disease.

Criteria on which the treatment decision is based	Management strategy
1. SBP < 160 and DBP < 95.	1. Non-drug treatment and monitoring.
2. SBP 160-179 and DBP < 95.	2. Non-drug treatment and monitoring for 3 months. Then institute drug treatment if SBP remains $\geq$ 160. The target pressure is SBP < 150.

Non-drug treatment is crucial and has been shown to be effective. If appropriate, it should be completed with drug treatment tailored to each patient's clinical situation, and should take into account concomitant disease and multiple drug treatment, which is particularly common in elderly subjects. Apart from specific or compelling indications, the initial choice of drug should be a low-dose thiazide diuretic (Grade A recommendation), because they have been shown to be effective in reducing morbidity and mortality. **If there are any contraindications to treatment with a low-dose thiazide diuretic or if such treatment is ineffective, beta blockers, ACE inhibitors and long-acting dihydropyridines are possible alternatives.**

**Elderly hypertensives on antihypertensives should be tested routinely for orthostatic hypotension. Particular attention should be paid to the risk of renal impairment, particularly if potentially nephrotoxic drugs are prescribed or if the patient is taking a number of different drugs. Monitoring of blood creatinine concentration and of creatinine clearance is particularly important in elderly subjects (Grade A recommendation).**

**Very few elderly hypertensives over the age of 80 are included in therapeutic trials, but the findings of these trials conclude that if antihypertensive treatment has already been started, it should be continued after the age of 80. Iatrogenic risks and the complexity of treatment in patients who frequently have concomitant disease mean that priorities have to be established; hypertension is only relevant if it represents a short-term risk. If hypertension is discovered after the age of 80, the most important points in reaching a decision are the preservation of quality of life and an assessment of the patient's physiological rather than chronological age.**

### **MONITORING A CONTROLLED HYPERTENSIVE PATIENT**

**How often a controlled hypertensive patient needs to be seen depends on an assessment of their level of cardiovascular risk and their compliance. It is not based on any studies of strategy. An annual pattern of 3 to 4 appointments would seem to correspond to a professional consensus which tends to be based on normal practice. The aim of these consultations is to verify the following points throughout the follow-up period, using clinical examination and a few simple further studies:**

- Achievement of blood pressure goals (self-measurement of blood pressure and ambulatory blood pressure monitoring are relevant here);**
- Real compliance both in terms of lifestyle changes (reduction in modifiable risk factors) and with taking prescribed medication; educational aspects, checking whether there any side effects from the drugs (particularly orthostatic hypotension in elderly patients);**
- There are no new cardiovascular risk factors nor concomitant disease.**

## **CONCLUSION**

**Achieving these targets depends mainly on implementing them in primary care. All the measures required should be taken to ensure that professionals use these recommendations to improve the treatment of hypertensives, which is still inadequate, from screening to the implementation of a follow-up strategy leading to better prevention of cardiovascular risk .**

**The working group recommends that further studies be carried out, primarily in the following areas:**

- Primary prevention of hypertension;**
- Education of hypertensive patients;**
- Evaluation of predictive factors such as microalbuminuria and left ventricular hypertrophy;**
- Clinical and economical evaluations of the various strategies for treating uncomplicated hypertension, and comparison of the various intervention thresholds in relation to cardiovascular risk;**
- Economic evaluations which take the patient's quality of life into account ;**
- Cost effectiveness evaluation of self-measurement of blood pressure and ambulatory blood pressure monitoring;**
- Evaluation of the benefits of calculating cardiovascular risk in treating hypertensive patients;**
- Organisation and evaluation of care networks for treating hypertension .**

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