

# Practice Guidelines For Primary Care Physicians: 2003 ESH/ESC Hypertension Guidelines

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- These guidelines are a concise summary of the more extensive ones prepared by the Expert Committee appointed by the European Society of Hypertension and the European Society of Cardiology, and published in the *Journal of Hypertension* 2003; 21:1011–1053. The extensive version of these guidelines can be consulted by readers preferring a more critical assessment of the evidence.
- These guidelines have been prepared on the basis of the best available evidence on all issues deserving recommendations, and with the consideration that guidelines should have an educational purpose more than a prescriptive one.
- The members of the Guidelines Committee have participated independently in the preparation of this document, drawing on their academic and clinical experience and utilizing an objective and critical

examination of all available literature. However, to ensure openness, their relations with industry, government and private health providers are listed in the extensive guidelines published in the *Journal of Hypertension*.

### Hypertension and total cardiovascular risk

#### Classification of hypertension

- Because of the continuous relationship between the level of blood pressure (BP) and cardiovascular risk, the definition of hypertension must be a flexible one, resulting from evidence of total risk and availability of effective and well-tolerated drugs (Table 1).

**Table 1 Definitions and classification of blood pressure levels (mmHg)**

Category	Systolic	Diastolic
Optimal	< 120	< 80
Normal	120–129	80–84
High normal	130–139	85–89
Grade 1 hypertension (mild)	140–159	90–99
Grade 2 hypertension (moderate)	160–179	100–109
Grade 3 hypertension (severe)	≥ 180	≥ 110
Isolated systolic hypertension	≥ 140	< 90

When a patient's systolic and diastolic blood pressures fall into different categories, the higher category should apply. Isolated systolic hypertension can also be graded (grades 1, 2, 3) according to systolic blood pressure values in the ranges indicated, provided diastolic values are < 90 mmHg.

**Stratification of hypertension**

- A simple approach to stratifying for total cardiovascular risk is suggested in Table 2. The terms low, moderate, high and very high added risk are calibrated to indicate an absolute 10-year risk of cardiovascular disease of < 15%, 15–20%, 20–30% and > 30%, respectively (Framingham criteria), or a 10-year risk of fatal cardiovascular disease of < 4%, 4–5%, 5–8% and > 8% (SCORE criteria). These categories can also be used as indicators of relative risk, the risk increasing by about 1.5 times going from a category to the next one.

**Factors influencing prognosis**

Decisions about the management of patients with hypertension should rarely be made on BP alone, but also on the presence or absence of other risk factors, target organ damage, diabetes, and cardiovascular or renal disease, as well as on other aspects of the patient's personal, medical, and social situation (Table 3).

**Diagnostic evaluation**

**Aims**

- Establishing BP values
- Identifying secondary causes of hypertension

- Searching for other risk factors, target organ damage, and associated or concomitant diseases

**Blood pressure measurement**

**Office blood pressure**

When measuring BP in your office:

- Allow the patient to sit quietly for several minutes
- Use a validated device
- Take at least two measurements spaced by 1–2 min
- Use a standard bladder (12–13 × 35 cm), but a larger one for big arms
- Have the cuff at the heart level
- Deflate the cuff slowly (2 mmHg/s)
- Measure BP also in standing position in elderly patients and diabetic patients

**Ambulatory blood pressure: when should it be measured?**

- Unusual variability of office BP
- Marked discrepancy between office and home BP
- High office BP with no organ damage
- Resistance to drug treatment
- Suspected sleep apnea

**Home blood pressure**

Pro:

- More information for the doctor's decision
- Improved patient's adherence to treatment

Con:

- May cause anxiety
- May induce self-modification of treatment

**Warning**

BP thresholds for definition of hypertension are different for:

- Office BP: 140/90 mmHg
- 24-h ambulatory BP: 125/80 mmHg
- Home BP: 135/85 mmHg

**Table 2 Stratification of risk to quantify prognosis**

	Blood pressure (mmHg)				
	Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 SBP 140–159 or DBP 90–99	Grade 2 SBP 160–179 or DBP 100–109	Grade 3 SBP ≥ 180 or DBP ≥ 110
Other risk factors and disease history					
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1–2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors or TOD or diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
ACC	High added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

ACC, associated clinical conditions; TOD, target organ damage; SBP, systolic blood pressure; DBP, diastolic blood pressure. Repeated blood pressure measurements should be used for stratification.

**Table 3 Factors influencing prognosis**

Risk factors for cardiovascular disease used for stratification	Target organ damage (TOD)
<ul style="list-style-type: none"> <li>Levels of systolic and diastolic BP</li> <li>Men &gt; 55 years</li> <li>Women &gt; 65 years</li> <li>Smoking</li> <li>Dyslipidaemia (total cholesterol &gt; 6.5 mmol/l, &gt; 250 mg/dl* or LDL-cholesterol &gt; 4.0 mmol/l, &gt; 155 mg/dl*, or HDL-cholesterol M &lt; 1.0, W &lt; 1.2 mmol/l, M &lt; 40, W &lt; 48 mg/dl)</li> <li>Family history of premature cardiovascular disease (at age &lt; 55 years M, &lt; 65 years W)</li> <li>Abdominal obesity (abdominal circumference M ≥ 102 cm, W ≥ 88 cm)</li> <li>C-reactive protein ≥ 1 mg/dl</li> </ul>	<ul style="list-style-type: none"> <li>Left ventricular hypertrophy (electrocardiogram: Sokolow–Lyons &gt; 38 mm; Cornell &gt; 2440 mm/ms; echocardiogram: LVMI M ≥ 125, W ≥ 110 g/m<sup>2</sup>)</li> <li>Ultrasound evidence of arterial wall thickening (carotid IMT ≥ 0.9 mm) or atherosclerotic plaque</li> <li>Slight increase in serum creatinine (M 115–133, W 107–124 μmol/l; M 1.3–1.5, W 1.2–1.4 mg/dl)</li> <li>Microalbuminuria (30–300 mg/24 h; albumin-creatinine ratio M ≥ 22, W ≥ 31 mg/g; M ≥ 2.5, W ≥ 3.5 mg/mmol)</li> </ul>
Diabetes mellitus	Associated clinical conditions (ACC)
<ul style="list-style-type: none"> <li>Fasting plasma glucose ≥ 7.0 mmol/l (≥ 126 mg/dl)</li> <li>Postprandial plasma glucose &gt; 11.0 mmol/l (≥ 198 mg/dl)</li> </ul>	<ul style="list-style-type: none"> <li>Cerebrovascular disease: ischaemic stroke; cerebral haemorrhage; transient ischaemic attack</li> <li>Heart disease: myocardial infarction; angina; coronary revascularization; congestive heart failure</li> <li>Renal disease: diabetic nephropathy; renal impairment (serum creatinine M &gt; 133, W &gt; 124 μmol/l; M &gt; 1.5, W &gt; 1.4 mg/dl) proteinuria (&gt; 300 mg/24 h)</li> <li>Peripheral vascular disease</li> <li>Advanced retinopathy: haemorrhages or exudates, papilloedema</li> </ul>

M, men; W, women; LDL, low-density lipoprotein; HDL, high-density lipoprotein; LVMI, left ventricular mass index; IMT, intima-media thickness. \*Lower levels of total and LDL-cholesterol are known to delineate increased risk, but they were not used in the stratification.

### Isolated office hypertension (white-coat hypertension)

- Office BP persistently elevated (≥ 140/90 mmHg)
- Ambulatory or home BP values normal (24-h ambulatory < 125/80 mmHg, home < 135/85 mmHg)

In these subjects, cardiovascular risk is less than in individuals with raised office and ambulatory or home BP. However, it may not be an entirely innocent condition, and these subjects should be followed up rather closely.

### Diagnostic evaluation: what should be done besides measuring blood pressure

#### Family and clinical history

#### Physical examination

- Signs suggesting secondary hypertension
- Signs of organ damage (brain, retina, heart, peripheral arteries,

### Laboratory investigations

#### Routine tests

- Plasma glucose (preferably fasting)
- Serum total and high-density lipoprotein (HDL) cholesterol; fasting serum triglycerides
- Serum creatinine
- Serum uric acid
- Serum potassium
- Haemoglobin and haematocrit
- Urinalysis (dipstick test and urinary sediment)
- Electrocardiogram

#### Recommended tests

- Echocardiogram
- Carotid (and femoral) ultrasound
- Postprandial plasma glucose (when fasting value ≥ 6.1 mmol/l or 110 mg/l)
- C-reactive protein (high sensitivity)
- Microalbuminuria (essential test in diabetics)

- Quantitative proteinuria (if dipstick test positive)
- Funduscopy (in severe hypertension)

**Extended evaluation (domain of the specialist)**

- Complicated hypertension
- Suspicion of secondary hypertension

**Searching for target organ damage**

- Target organ damage is important in determining the overall cardiovascular risk of the hypertensive patient (Table 2)
- Search carefully for organ involvement
- When treatment decisions are uncertain, cardiac and carotid ultrasound examinations and microalbuminuria measurement may help in more precisely classifying the overall risk of the hypertensive patient and in directing therapy

**When to initiate antihypertensive therapy**

Initiation of antihypertensive treatment (Table 4) is based on two criteria:

- Total level of cardiovascular risk
- Level of systolic and diastolic BP

**Goals of treatment**

- Achieve the maximum reduction in the total cardiovascular risk
- Treat all reversible risk factors (smoking, dyslipidaemia, diabetes, etc.) and the associated clinical conditions in addition to treating the raised BP
- Reduce both systolic and diastolic BP to below 140/90 mmHg and to lower values if tolerated
- Aim at values below 130/80 mmHg in diabetics

- Achieving systolic BP values below 140 mmHg may be difficult in the elderly

**Benefits of antihypertensive treatment**

Numerous trials of active antihypertensive treatment compared with placebo (Fig. 1) have shown that BP lowering reduces:

- Cardiovascular and total mortality
- Stroke
- Coronary events

Benefits have been proven:

- In patients with systolic–diastolic hypertension
- In elderly patients with isolated systolic hypertension

Benefits have been shown in placebo-controlled trials that have used all major antihypertensive drug classes:

- Diuretics
- Beta-blockers
- Calcium antagonists
- Angiotensin-converting enzyme (ACE)-inhibitors
- Angiotensin receptor antagonists

**Lifestyle changes**

- Lifestyle measures should be instituted wherever appropriate in all patients, including subjects with normal and high normal BP with additional risk factors, and in patients who require drug treatment.

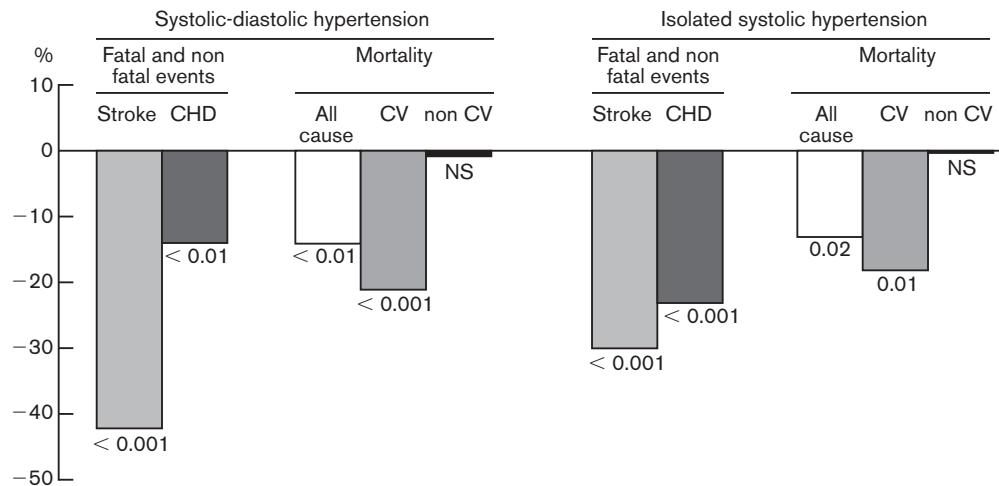
The purpose is to lower BP and to control other risk factors.

**Table 4 Initiation of antihypertensive treatment**

Other risk factors and disease history	Blood pressure (mmHg)				
	Normal: SBP 120–129 or DBP 80–84	High normal: SBP 130–139 or DBP 85–89	Grade 1: SBP 140–159 or DBP 90–99	Grade 2: SBP 160–179 or DBP 100–109	Grade 3: SBP ≥ 180 or DBP ≥ 110
No other risk factors	No BP intervention	No BP intervention	Lifestyle changes for several months, then drug treatment if preferred by the patient and resources available	Lifestyle changes for several months, then drug treatment	Immediate drug treatment and lifestyle changes
1-2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several months, then drug treatment	Lifestyle changes for several months, then drug treatment	Immediate drug treatment and lifestyle changes
3 or more risk factors or TOD or diabetes	Lifestyle changes	Drug treatment and lifestyle changes	Drug treatment and lifestyle changes	Drug treatment and lifestyle changes	Immediate drug treatment and lifestyle changes
ACC	Drug treatment and lifestyle changes	Immediate drug treatment and lifestyle changes	Immediate drug treatment and lifestyle changes	Immediate drug treatment and lifestyle changes	Immediate drug treatment and lifestyle changes

ACC, associated clinical conditions; DBP, diastolic blood pressure; SBP, systolic blood pressure; TOD, target organ damage.

Fig. 1



Event reduction in patients on active antihypertensive treatment versus placebo or no treatment. CHD, coronary heart disease; CV, cardiovascular.

- The lifestyle measures lowering BP or cardiovascular risk are:
  - smoking cessation
  - weight reduction
  - reduction of excessive alcohol intake
  - physical exercise
  - reduction of salt intake
  - increase in fruit and vegetable intake
  - decrease in saturated and total fat intake

## Therapeutic strategies

### Principles of drug treatment

- Therapy should be started gradually, and target BP achieved progressively
- To reach target BP, a large proportion of patients will require combination therapy
- Therapy can be initiated either with a low dose of a single agent or with a low-dose combination of two agents (Fig. 2)

Two-drug combinations that have been found to be effective and well tolerated are indicated in Fig. 3. The most rational combinations are represented as thick lines. The frames indicate classes of agents proven to be beneficial in controlled trials.

### Choice of antihypertensive drugs

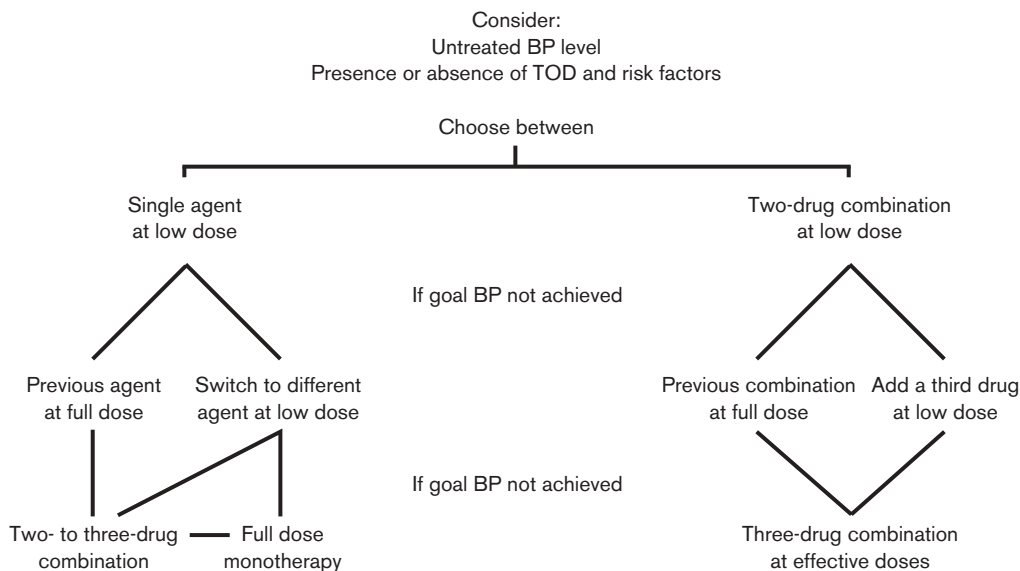
- The main benefits are due to lowering of BP *per se*
- However, specific drug classes may differ in some effect, or in special groups

- Drugs are not equal in terms of adverse disturbances in individual patients
- The major classes of antihypertensive agents (diuretics, beta-blockers, calcium antagonists, ACE-inhibitors, angiotensin receptor antagonists) are suitable for the initiation and maintenance of therapy
- Emphasis on a class of drugs to be used first is outdated by the need to use two or more drugs in combination in order to achieve goal BP
- The choice of drugs will be influenced by many factors, including:
  - previous experience of the patient with antihypertensive agents
  - cost of drugs (not to predominate over individual efficacy and tolerability)
  - risk profile, target organ damage, clinical cardiovascular or renal disease or diabetes
  - patient's preference
- Use long-acting drugs or preparations providing 24-h efficacy on a once daily basis

The physician should tailor the choice of drugs to the individual patient, after taking all these factors, together with the patient's preference, into account (see Table 5 for specific indications and contraindications).

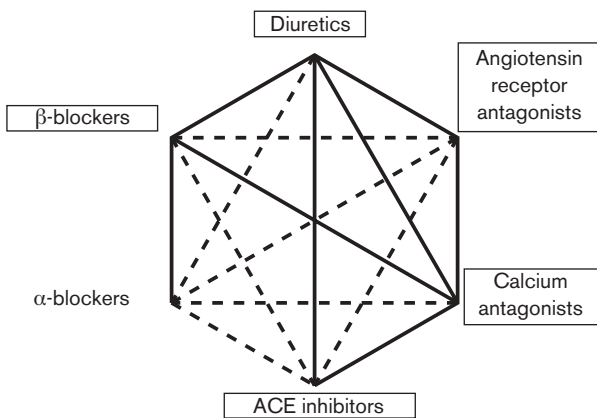
Particular attention should be given to adverse events, even to subjective disturbances, as these may be an important cause of non-compliance. Patients should always be asked about adverse events, and drugs or doses changed accordingly.

Fig. 2



Choice between monotherapy and combination therapy. BP, blood pressure; TOD, target organ damage.

Fig. 3



Possible combinations of different classes of antihypertensive agents. Among calcium antagonists, only dihydropyridines can be associated with betablockers. ACE, angiotensin-converting enzyme.

- Measure BP also in the erect posture to evaluate excessive postural effects
- Tailor therapy on concomitant risk factors and disease (frequent in the elderly)
- Use two or more drugs, if necessary
- In subjects aged  $\geq 80$  years, evidence of benefit from antihypertensive therapy is still weak

**Diabetic patients**

- Encourage lifestyle measures (particularly weight loss and reduction of salt intake in type 2 diabetics)
- Goal BP is below 130/80 mmHg
- Most often combination therapy is required
- All antihypertensive agents can be used, generally in combination
- Renoprotection benefits from the inclusion in these combinations of an ACE-inhibitor in type 1 diabetes, and of an angiotensin receptor antagonist in type 2 diabetes
- Microalbuminuria should be tested in all type 1 and type 2 diabetics, as it is an indication for antihypertensive treatment especially by a blocker of the renin-angiotensin system, irrespective of BP

**Therapeutic approaches in special conditions**

**Elderly**

- Cardiovascular events can be reduced by antihypertensive treatment also in older patients with isolated systolic hypertension
- BP lowering should be gradual particularly in frail patients

**Patients with previous cardiovascular disease**

- Patients who have suffered a previous stroke or transient ischaemic attack have a reduced recurrence of stroke if they receive antihypertensive therapy

**Table 5 Indications and contraindications for the major classes of antihypertensive drugs**

Class	Conditions favouring the use	Contraindications	
		Compelling	Possible
Diuretics (thiazides)	Congestive heart failure; elderly hypertensives; isolated systolic hypertension; hypertensives of African origin	Gout	Pregnancy
Diuretics (loop)	Renal insufficiency; congestive heart failure		
Diuretics (anti-aldosterone)	Congestive heart failure; post-myocardial infarction	Renal failure; hyperkalaemia	
$\beta$ -Blockers	Angina pectoris; post-myocardial infarction; congestive heart failure (up-titration); pregnancy; tachyarrhythmias	Asthma; chronic obstructive pulmonary disease; A–V block (grade 2 or 3)	Peripheral vascular disease; glucose intolerance; athletes and physically active patients
Calcium antagonists (dihydropyridines)	Elderly patients; isolated systolic hypertension; angina pectoris; peripheral vascular disease; carotid atherosclerosis; pregnancy		Tachyarrhythmias; congestive heart failure
Calcium antagonists (verapamil, diltiazem)	Angina pectoris; carotid atherosclerosis; supraventricular tachycardia	A–V block (grade 2 or 3); congestive heart failure	
Angiotensin-converting enzyme (ACE) inhibitors	Congestive heart failure; LV dysfunction; post-myocardial infarction; non-diabetic nephropathy; type 1 diabetic nephropathy; proteinuria	Pregnancy; hyperkalaemia; bilateral renal artery stenosis	
Angiotensin II receptor Antagonists (AT <sub>1</sub> -blockers)	Type 2 diabetic nephropathy; diabetic microalbuminuria; proteinuria; LV hypertrophy; ACE-inhibitor cough	Pregnancy; hyperkalaemia; bilateral renal artery stenosis	
$\alpha$ -Blockers	Prostatic hyperplasia (BPH); hyperlipidaemia	Orthostatic hypotension	Congestive heart failure

A–V, atrioventricular; LV, left ventricular.

(diuretics and ACE-inhibitors), even if their BP is in the normal or high normal range only

- Whether BP in acute stroke should be lowered is still disputed
- Several antihypertensive agents have been proven beneficial post-myocardial infarction
- In congestive heart failure, diuretics, anti-aldosterone agents, beta-blockers, ACE-inhibitors, and angiotensin receptor antagonists have been proven beneficial

#### **Patients with deranged renal function**

- Renal protection in diabetes requires strict BP control (to less than 130/80 mmHg), but also in patients with non-diabetic nephropathy it appears prudent to lower BP intensively
- Proteinuria should be lowered to values as near to normal as possible
- To reduce proteinuria either an angiotensin receptor antagonist or an ACE-inhibitor (or the combination of both) is required

- To achieve the BP goal, combination therapy is usually required, with the addition of a diuretic, a calcium antagonist and other antihypertensive agents
- Consider an integrated therapeutic intervention (anti-hypertensives, statins, antiplatelet therapy, etc.)

#### **Hypertension in pregnancy**

- For pregnant women with pre-existing hypertension:
  - non-pharmacological treatment when BP is 140–149/90–99 mmHg
  - weight reduction contraindicated (associated with reduced neonatal weight)
  - low-dose aspirin in women with a history of early pre-eclampsia
- Thresholds for initiating antihypertensive treatment are:
  - systolic BP 140 mmHg or diastolic BP 90 mmHg in gestational hypertension or pre-existing hypertension with organ damage

- thresholds in other circumstances are 150/95 mmHg
- systolic BP  $\geq$  170 or diastolic BP  $\geq$  110 mmHg in pregnancy should be considered an emergency (hospitalization essential)
- Methyldopa, labetalol, calcium antagonists and (though less effective) beta-blockers are the drugs of choice

#### **Resistant hypertension**

- Definition: when lifestyle measures and combination of at least three drugs in adequate doses have failed to lower systolic and diastolic BP sufficiently
- Causes:
  - unsuspected secondary cause
  - poor adherence to therapeutic plan
  - intake of drugs raising BP (steroids, anti-inflammatory drugs, oral contraceptives, cocaine, etc.)
  - failure to modify lifestyle (weight gain, alcohol, etc.)
  - volume overload (insufficient diuretic dose, renal insufficiency, high salt intake)
  - sleep apnea
  - spurious hypertension (e.g. small cuff on large arms, isolated office hypertension)

#### **Treatment of associated risk factors**

##### **Lipid-lowering agents**

- Statins should be given to:
  - hypertensive patients with or without overt cardiovascular disease, whose estimated 10-year cardiovascular risk is  $\geq$  20% (high or very high risk in Table 2), if their total cholesterol is  $>$  3.5 mmol (135 mg/dl), with the goal of reducing it by about 30%

##### **Antiplatelet therapy**

- Use low-dose aspirin in hypertensive patients older than 50 years with an even moderate increase in serum creatinine, or with a 10-year cardiovascular risk  $\geq$  20% (high or very high risk in Table 2)
- In hypertension, low-dose aspirin administration should be preceded by good BP control

#### **Implementation of guidelines**

Despite major efforts to diagnose and to treat hypertension, this condition remains a leading cause of morbidity and mortality worldwide, and goal BP levels are seldom achieved. It is therefore highly desirable to improve this unsatisfactory delivery of care.

This requires the participation of all professionals

involved in health care, from governmental levels to the individual physician.

These guidelines have been prepared and distributed as a help toward improving hypertension management in common medical practice, with the awareness that it is easier to prepare guidelines on a medical condition in general than to deal with individual patients.

Rigid rules have been avoided, and responsibility for managing individual patients, widely differing in their personal, medical and cultural characteristics, is obviously left to the individual physician.



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