Summary

Clinical Practice Guidelines on **Arterial Hypertension**

2007 Update

Clinical Practice Guidelines of Osakidetza

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Osakidetza

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These guidelines have the endorsement of the Basque Family and Community Medicine Society (Osatzen), of the Arterial Hypertension and Cardiovascular Risk Society of the Basque Country (Eusten) and of the Basque Hypertension and Cardiovascular Society (SovasAHT). Members of Osatzen and Eusten have collaborated in the authorship and review and members of SovasAHT in reviewing it.

1. Introduction

1.1 Justification for the guidelines

It is estimated that 20% of the population over 18 years of age can be considered hypertensive. Different estimates conclude that 42% of deaths from coronary heart disease and up to 46.4% of cerebrovascular diseases can be attributed to arterial hypertension (AHT).

In regards to the care of hypertensive people, there is still a wide margin for improvement. The dissemination and implementation of the previous version of the Clinical Practice Guidelines (CPG) were carried out according to some of the strategies that it recommended: presentation sessions in the centres (over 70), postal and electronic distribution, presentation in conferences and congresses, postal reminders and the development of indicators for the program and clinical management contracts. The evaluations on prescription antihypertensive drugs in our region have shown a change in accordance with the CPG's recommendations.

The publication of new evidence in the field of arterial hypertension is constant. The successive national and international CPGs regarding AHT are updated with new evidence; however, there is variability in their recommendations (1). The different methodology used by them can explain this fact (1). It is estimated that a CPG needs to be updated starting three years from its publication (2).

All these reasons are what led the Health Department and Osakidetza – Basque Health Care Service to update the CPG on AHT using the same methodological principles as in the first version.

1.2 Objectives

The objective of these guidelines is to serve as an instrument to improve health care for hypertensive persons within the framework of primary care. The main users of these guidelines are family doctors and the primary care nursing staff and other professionals: interns, cardiologists and nephrologists, who care for the patients on an outpatient basis.

The guidelines are centred on the care of the hypertensive adult. It does not deal with childhood AHT, AHT during pregnancy, or the study of secondary AHT.

The guidelines are structured to try to answer 39 questions that are raised from caring for hypertensive patients.

1.3 Methodology

This section is described in a very detailed form in Appendix 1. The updating process has led to the development of a methodology report, published by Osteba. The updating method is based on selecting quality CPGs by means of the AGREE instrument. The selected CPGs are the ones from NICE (3), Canada (4) and Britain (5), and constitute the "base" CPGs.

The classification of the evidence and the ranking of the recommendations have been carried out through a mixed system that uses the proposal of SIGN (Scottish Intercollegiate Guidelines Network) for all the questions except those regarding diagnosis, and that of the centre on evidence-based medicine from Oxford for the questions about diagnosis (Tables 1 and 2).

The elaboration system followed considers directly adopting recommendations from the selected base CPGs.

1.4 Use of the guidelines

This document is an update of the original guidelines published in 2002. To make the reading easier, at the beginning of each chapter there is a presentation of the new questions and an indication of whether there is any important change from the previous recommendations. There is a complete version of the CPG with all the appendixes and algorithms, a summarised version that has all the recommendations and that is intended to be the main tool for clinical use, and a quick guide to facilitate accessing information. The new recommendations and those substantially modified with regard to the guidelines' previous versions will be marked with an arrow 

Table 1. **SIGN evidence levels and recommendation grades**

EVIDENCE LEVELS

1++ High-quality Meta-analyses, systematic reviews of clinical trials or high-quality clinical trials with very little risk of bias.

1+ Well-conducted Meta-analyses, systematic reviews of clinical trials or well-conducted clinical trials with little risk of bias.

1- Meta-analyses, systematic reviews of clinical trials or clinical trials with high risk of bias.

2++ High-quality systematic reviews of cohort studies or of cases and controls. Cohort studies of cases and controls with very low risk of bias and with high probability of establishing a causal relation.

2+ Well-conducted cohort studies or those of cases and controls with low risk of bias and with a moderate probability of establishing a causal relation.

2 - Cohort studies or of cases and controls with high risk of bias and significant risk that the relation is not causal.

3 Non-analytic studies, such as reports of cases and series.

4 Experts' opinions.

RECOMMENDATION GRADES

A At least one Meta-analysis, systematic review or clinical study classified as 1++ and directly applicable to the guidelines' target population; or a volume of evidence comprised by studies classified as 1+ and with great consistency between them.

B A volume of evidence comprised by studies classified as 2++, directly applicable to the guidelines' target population and that shows great consistency among them; or evidence extrapolated from studies classified as 1 ++ or 1+.

C A volume of evidence comprised by studies classified as 2+ directly applicable to the guidelines' target population which demonstrates great consistency among them; or evidence extrapolated from studies classified as 2++.

D Evidence of level 3 or 4; or evidence extrapolated from studies classified as 2+.

Good clinical practice

✓ 1 Recommended practice based on clinical experience and the consensus of the editing team.

1. Upon occasion, the developing team notices important practical aspects that are necessary to highlight and for which there is probably no evidence. In general, they are related to an aspect of the treatment considered as good clinical practice that no one would normally question; they are aspects valued as points of good clinical practice. These messages are not an alternative to the recommendations based on the evidence, but must be considered only when there is no other way of highlighting said aspect.

Table 2. **Evidence levels and recommendation grades for diagnostic studies**

(Adapted from The Oxford Centre for Evidence-based Medicine - Levels of Evidence (2001) and the Centre for Reviews and Dissemination Report Number 4 (2001))

LEVELS OF EVIDENCE	TYPE OF EVIDENCE
Ia	Systematic review with homogeneity in **Level 1** studies
Ib	**Level 1** studies
II	**Level 2** studies Systematic review of **Level 2** studies
III	**Level 3** studies Systematic review of **Level 3** studies
IV	Consensus, experts' opinions without explicit critical evaluation
Level 1 Studies	They achieve: • Masked comparison with valid reference evidence ("gold standard") • Adequate patient spectrum
Level 2 Studies	They present only one of the following biases: • Non-representative population (the sample does not reflect the population where the sample will be applied) • Inadequate comparison with the reference standard ("gold standard") (the sample being evaluated is part of the gold standard or the result of the evidence being evaluated has influence on the performance of the gold standard) • Non-masked comparison • Case control studies
Level 3 Studies	They present two or more of the highlighted criteria in level 2 studies

Recommendation	Evidence
A	1a or 1b
B	2
C	3
D	4

2. Initial evaluation of hypertensive patients

2.1 Screening for arterial hypertension (AHT)

QUESTIONS TO ANSWER

- Is AHT screening effective in decreasing cardiovascular morbimortality?
- What is the optimum measurement frequency of BP in a healthy population?
- What is the most appropriate method as a screening instrument for AHT?
- Is there an age limit at which to interrupt the screening?

UPDATE 2007

1 new SR (6)
Update of consensus and groups of experts (7; 8)
No changes in the recommendation

The benefits on the screening effectiveness are indirectly deduced, in general, from the benefits in the prevention of cardiovascular morbimortality in the RCTs conducted on hypertensive patients. The opportunist strategy, which consists of measuring blood pressure (BP) in people that go to the primary care doctor's office, is especially effective when it is associated with trained professionals, protocols and reminder systems for the patients and professionals (9).

SR of RCT 1+

There is no established optimum interval for BP screening. Measuring BP in the regular clinical practice with the mercury sphygmomanometer, or lacking that, with validated electronic devices, continues to be the most adequate screening evidence (7). Measuring the BP must be done in the standardised manner (10). The most trustworthy measurements are those taken by the nursing staff, who are, therefore, the most appropriate persons in our field to carry out this task (10).

Expert's opinion 4

The screening activities in the cardiovascular area for the general population approved for our region are:

- BP measurement every 2 years.
- Calculation of coronary risk every 4 years (including BP, glycaemia, total cholesterol and HDL).

Recommendation	
B	Screening by means of an opportunist AHT strategy through periodic measuring of the clinical BP is recommended.
D	Following the PAPPS recommendations concerning AHT screening is advised: measuring BP at least once before reaching 14 years of age; every 4 or 5 years after 14 years of age until 40, and every 2 years from 40 years of age, taking advantage of occasional consultations.
✓	The BP measurements in health care centres are preferably taken by the nursing staff.

2.2. Definition and classification of AHT according to BP numbers and cardiovascular risk

QUESTIONS TO ANSWER

- What numbers define a person as hypertensive?
- How are hypertensive persons with higher cardiovascular risk selected?

UPDATE 2007

2 new cohort studies (11; 12) and 2 new SRs (13; 14)
Modified recommendation

The classification of a person as hypertensive is determined by the ratio of the BP numbers and cardiovascular morbimortality. In people over 18 years of age that do not receive pharmacological treatment, AHT is considered the permanent elevation of the BP numbers in the medical consultation, over 139 mmHg for the systolic BP (SBP) and 89 mmHg for diastolic BP (DBP) (10). In a patient with high BP, AHT must be confirmed by taking two readings in each visit in at least two additional consultations with a weekly interval (unless the SBP □180 mmHg or DBP □110 mmHg which requires immediate action). The readings of the three days must be averaged. AHT is diagnosed if their mean is higher than the abovementioned numbers.

In patients in stages 2 and 3 (Table 3) this frequency of consultations is sufficient. However, in patients with stage 1, performing at least two additional consultations in the following 4 weeks provides a better diagnosis of AHT, considering all the BP readings (10).

Table 3. **Classification of AHT in levels according to SBP and DBP numbers**

Category	SBP (mmHg)	And/or DBP (mmHg)
Stage 1 or Level 1	140 to 159	90 to 99
Stage 2 or Level 2	160 to 179	100 to 109
Stage 3 or Level 3	≥180	≥110

Isolated systolic hypertension is defined by systolic pressure values of 140 mmHg or higher and diastolic pressure lower than 90 mmHg, and it is classified according to its SBP level in the stages described above.

It is known that the risk of a hypertensive patient suffering a cardiovascular complication is also determined by the presence of other risk factors or by target organs being affected.

The BP numbers from which there is a cardiovascular benefit with pharmacological treatment are clear for stages 2 and 3, and for those patients with established cardiovascular disease (10).

In stage 1 the calculation of cardiovascular or coronary risk and the affection of target organs are two useful tools for decision-making in primary cardiovascular prevention.

In the case of detecting left ventricular hypertrophy (LVH), microalbuminuria, severe retinopathy or an ankle-arm index <0.9 in the level-1 AHT, using pharmacological treatment is recommended regardless of the cardiovascular risk, since these circumstances are related to greater cardiovascular risk (13-15).

SR of cohort studies
2+

The risk equations are clinical prevention rules (CPR) that relate a determined event, morbidity and/or coronary or total cardiovascular mortality, with a series of variables (risk factors). Coronary risk is a good estimator of cardiovascular risk, it is considered equivalent to two-thirds of the risk.

The original Framingham equation (16) overestimates coronary risk in the populations other than the original, including Spain (17-19).

The base guidelines propose the use of the cardiovascular (CV) risk tables adjusted to the epidemiological standards of the countries of each CPG. **CPR 2+**

In this sense, the REGICOR project offers an interesting alternative for the problem of overestimation since it has been able to adapt and validate Framingham tables to the epidemiological reality of our environment (17).

It must be noted that there is no evidence that proves the effectiveness of the use of CV risk tables as a strategy for decreasing morbimortality (20). The risk tables, therefore, with the current available evidence, have limited value in helping to make decisions on patients with no cardiovascular disease.

A consensus has been reached among the editing team of this CPG on a cut-off point of 10% (21) in these tables from which point it is recommended to start pharmacological treatment in level-1 hypertensive people (Appendix 14). In people with lower risk, it is necessary to make the decision individually taking into account the overall condition of the patient and other cardiovascular risk factors not included in the equation (such as family history of early cardiovascular disease) (Appendix 2). **Experts' opinion** **4**

RECOMMENDATION		
2007	**D**	Pharmacological treatment of level-1 AHT with target organ affection regardless of cardiovascular risk is recommended.
	C	The use of the REGICOR tables in the calculation of coronary risk in hypertensive patients is recommended.
	D	Pharmacological treatment of level-1 AHT with coronary risk 10% according to the REGICOR table is recommended.
	D	Patients with level-1 AHT with coronary risk <10% must be considered for pharmacological treatment depending on other additional risk factors.
2007	**D**	Patients with level-1 AHT with low coronary risk (<10%) and without other additional risk factors, must be treated with non-pharmacological measures for a year, after which the need for pharmacological treatment must be re-evaluated.

2.3. AHT diagnosis

QUESTIONS TO ANSWER

- Which are the BP values that define AHT according to the ABPM?
- What are the BP values that define AHT according to SMBP?
- What is the ideal number of measurements made with home SMBP?
- Is SMBP useful in the diagnosis of isolated clinical hypertension?
- What is the prognosis of WCH?
- Should patients with WCH receive pharmacological treatment?
- What must the initial study of hypertensive patients include?
- What devices are valid for their use in ABPM and in SMBP?

The AHT diagnosis is based on the measurement of BP in the medical consultation (clinical BP) in a standardized manner (see Appendix 3).

The alert reaction provoked by the BP being taken by the professional or in the health care setting (22) causes the so-called white coat effect (WCE), white coat phenomenon (WCP) and isolated or white coat hypertension (WCH) (10).

- **White coat effect (WCE):** is the increase in BP that the presence of health care personnel induces when measuring BP.

- **White coat phenomenon (WCP):** is produced when the difference between the BP in the doctor's office and that in the home is greater than 20 mmHg for the SBP and 10 mmHg for the DBP.

- **Isolated clinical hypertension or white coat hypertension (WCH):** is the clinical situation of AHT in the medical consultation and normotension with ABPM or SMBP.

In order to diminish the limitations in measuring the BP, there are strategies that try to minimize the bias of the observer and overcome the white coat effect.

When the BP measurements are taken by the patient himself or his family members in his home, one speaks of home self-measurements of blood pressure (SMBP). When the measurements are taken by means of automated devices, at pre-programmed intervals and during the daily activity of the person in a period that is usually 24 hours, one speaks of ambulatory blood pressure monitoring (ABPM).

2.3.1. Ambulatory blood pressure monitoring (ABPM): normal values and indications

Table 4 includes the update of the recommendations for the use of ABPM in our field. The instructions in the "masked" AHT were added. This phenomenon corresponds to patients with normal clinical BP numbers and high numbers by the ABPM. This phenomenon is associated with an increase in cardiovascular morbimortality (23-25) and constitutes a new indication for the ABPM. It should be suspected when discrepancies between the home and clinical numbers are observed or in the presence of target organ affection in patients with normal clinical BP numbers.

Cohort studies 2+

2007 UPDATE

3 new cohort studies (23-25)
Completed recommendation

Table 4. **Instructions for the use of the ABPM**

2007

- Suspicion of white coat phenomenon and white coat hypertension
- Suspicion of masked AHT
- Suspicion of hypertension in patients treated pharmacologically
- Hypertension resistant to pharmacological treatment
- As a guide to determine the effectiveness of the pharmacological treatment during 24 h

The normal BP values in the different periods are presented in Table 5 and have been kept the same as in the previous version of the CPG (10), including the "dipper" concept (drop of more than 10% in night time BP), which is accompanied by an increased cardiovascular risk (10).
The measurements must be taken by means of automatic sphygmomanometers and electronic oscillometers, validated by means of protocols from the American Association for the Advancement of Medical Instrumentation (AAMI) and/or the British Hypertension Society (BHS). Currently that of the European Society of Hypertension (ESH) has been added (26) (see Appendix 4).

Cohort studies 2+

Experts' opinion 4

Table 5. **BP numbers (means per period) in order to define AHT according to ABPM**

BP MEASUREMENT	AHT
SBP mmHg.	
Daytime Night time 24 h	≥135 ≥120 ≥135
SBP mmHg.	
Daytime Night time 24 h	≥85 ≥75 ≥80

"Dipper" phenomenon: decrease in the night time BP numbers □10% with respect to the daytime numbers.

RECOMMENDATION	
D	The ABPM must be conducted with independently validated instruments according to the international standards of the AAMI, BHS or ESH.
B	The ABPM is a method that can be useful in the diagnosis of AHT since its increase is correlated with cardiovascular morbimortality.
B	The mean BP numbers over a period of **24 h** measured by means of ABPM that define a person as hypertensive are SBP ≥135 mmHg and DBP ≥80 mmHg.
D	The mean **daytime** BP numbers measured by means of ABPM that define a person as hypertensive are SBP ≥135 mmHg and DBP ≥85 mmHg.
D	The mean **night time** BP numbers measured by means of ABPM that define a person as hypertensive are SBP≥120 mmHg and DBP ≥75 mmHg.

2.3.2. Self-measurement of blood pressure (SMBP): normal values and indications

2007 Update

1 new SR (27)
Completed recommendation (SMBP in the improvement of control of BP)

The SMBP provides numerous BP values in a context closest to the conditions of daily life. The measures must be made by means of validated automatic sphygmomanometers and electronic oscillometers (see Appendix 6).

In addition, BP measured with SMBP correlates better with cardiovascular morbimortality than the measurement in the medical consultation (27). The values proposed for classifying a patient as hypertensive were **SBP ≥135 mmHg or DBP ≥85 mmHg** (21; 10; 28) in the previous version of the CPG (10). These same values are those that are recommended in the only base CPG that takes up this subject (28). There is a recent systematic review (27), not included in any of the base CPGs, which studies this matter. Its BP limits for defining the AHT coincide with the values indicated above. As regards the indications of the SMBP, the possibility is added of using this technique to increase the degree of BP control (see compliance section later on). This new recommendation and those of the previous version of the CPG are included in Table 6.

SR of cross-sectional and cohort studies 2+/3

2007

Table 6. When SMBP should be used

- Suspicion of the white coat phenomenon or white coat hypertension
- Suspicion of hypotension in patients treated pharmacologically.
- It improves adherence to the treatment and control of BP in selected patients
- When a strict control is required of patient's BP numbers

Recommendation	
B	The SMBP must be done independently with instruments validated according to the international standards of the AAMI, BHS or ESH.
B	The SMBP is a method that can be useful in the diagnosis of AHT, since the values obtained by means of this technique are correlated to cardiovascular morbimortality.
B	The BP numbers measured by SMBP that define a patient as hypertensive are SBP □135 mmHg or DBP □85 mmHg.

2.3.3. Number of BP readings necessary with SMBP

2007

New question

In the papers on SMBP and diagnosis of WCH considered in these guidelines (29-31), schedules for measuring BP variables are followed. In all of them three measurements are used, morning and night, during at least three days, without excluding any measurement of the series and with schedules of a complete week or including three working days during two weeks. There are no comparisons between them. In a recent study (32) in a general population that included hypertensive patients, all the readings over a period of seven days were used.

Cross-sectional and cohort studies 2+/3

In long-term monitoring, the papers considered used measurements of 5 working days (three consecutive readings in the morning and at night, recording all the numbers) in the week prior to going to the clinical control (33) or the mean of the measurements of the previous week including the weekend (2 consecutive readings in the morning and two at night) (34). There are no studies that compare the different proposed schedules. In short, based on the available evidence, no firm proposal can be made on a definitive schedule with the ideal number of readings. If the number of days and the period of time in the diagnostic phase are increased, it is probable that the influence of the alert reaction of the first day of using the technique will not influence the diagnostic capacity of the SMBP.

Recommendation	
2007 **D**	When the SMBP is used for diagnostic purposes, a minimum schedule of BP self-measurements of at least three days with the readings taken every 12 hours is advised. The readings of the first day may not be taken into consideration.
2007 **D**	When the SMBP is used in the monitoring of the hypertensive patient, a minimum schedule of BP self-measurements on three days with three readings taken every 12 hours during the week prior to the medical consultation is advised.

2.3.4. SMBP in the diagnosis of isolated clinical hypertension or white coat AHT

2007 UPDATE

3 new studies on the validity of diagnostic tests (29-31)
Modified recommendation

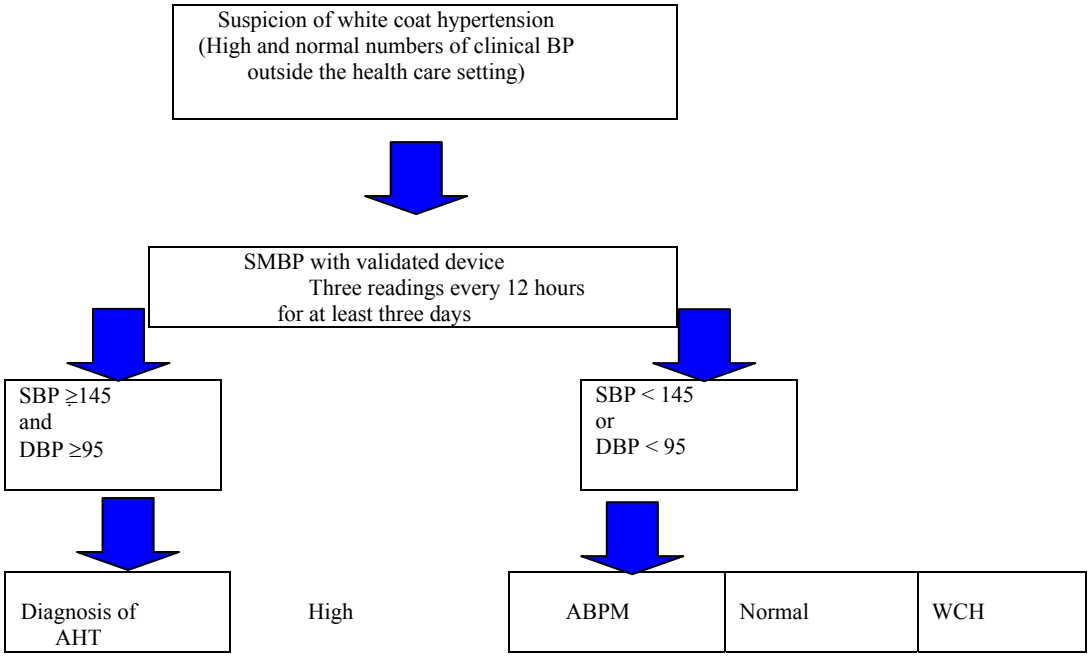
Studies of diagnostic tests
I/II

In the previous version of the CPG, using the SMBP as the first option in the diagnosis of WCH was recommended. If the SMBP values were normal, the use of the ABPM was recommended to confirm the diagnosis since the PPV (positive predictive values) obtained were discrete (60%) (10). This same proposal is included in the Canadian CPG (28) selected as the base CPG.

The aforementioned CPG cited data from the THOP study (30), in which an NPV (negative predictive value) of 97.1% and a PPV of 33.3% were obtained. However, there are two studies that contradict these results (20; 31). According to these two latter studies, in view of the suspicion of WCH, conducting the ABPM would be required.

An interesting question is the study of the diagnostic capacity of different BP cut-off points (35), instead of the SBP/DBP limits of 135/85 established as normal. One of the aforementioned works carried out in Cataluña drew an ROC curve for different values of B. Establishing 145/95 as SMBP limits, the NPV was 86.5%. This means that WCH could be excluded for the patients with BP above these limits; this group made up 30% of the cases.

Figure 1. **SMBP in the diagnosis of WCH**



Recommendation	
B	When the SMBP is used in light of the suspicion of WCH, the findings of some numbers higher than 145/95 mmHg diagnose a hypertensive person, while lower numbers require conducting an ABPM.

2.3.5. Clinical significance of white coat hypertension

2007 UPDATE

5 new cohort studies (25; 36-39)
No changes in the recommendation

Isolated clinical hypertension or white coat AHT is defined by the clinical situation of AHT in the doctor's office and normotension with the ABPM. It can affect at least 20% of the hypertensive patients (40).

The updating includes 5 new references (15; 36-39). All the studies evaluate different combinations of cardiovascular morbidity and general mortality. In all of them, except in a Danish cohort (39), no differences in the morbimortality were observed between normotensive patients and those with WCH.

Cohort studies 2+

However, it is known that the WCH can evolve towards maintained AHT in a variable proportion of patients (10).

Cross-sectional studies 3

RECOMMENDATION	
D	The monitoring of WCH must include non-pharmacological measures and the periodic evaluation of cardiovascular risk and of target organ affection.
C	Patients with isolated clinical AHT must be controlled by taking their BP in the doctor's office and by ABPM, if necessary, to identify its possible evolution to maintained AHT.

2.4. Initial study of the hypertensive patient

QUESTIONS TO ANSWER

- What must be included in the initial study of the hypertensive patient?
- Should the microalbuminuria of the hypertensive patients be measured?

Experts' opinion 4

The initial evaluation of the hypertensive patient is made for several objectives:

- To confirm the chronic elevation of the BP and to measure its magnitude
- To evaluate the impact of the hypertensive disease on target organs
- To detect possible causes of secondary AHT and co-morbidity
- To estimate the global cardiovascular risk of the patient
- To select the most appropriate pharmacological treatment in case it is necessary

These objectives are obtained from the anamnesis, physical examination and results of complementary tests.

In Table 7, some recommendations are summarized on the initial evaluation of the hypertensive patient based on the previous version of the CPG.

Table 7. **Initial evaluation of hypertensive patients**

Initial physical examination of hypertensive patients		
Initial examination	**Comments**	**D-level recommendation of the guide**
Examination of the ocular fundus	Reliability, precision and use not established	Recommended. A priority in the diabetic patient
BMI Calculation	For the monitoring and start of a hypocaloric diet if needed	Recommended
Jugular engorgement to detect volume overload	Reliable when combined with other findings	Recommended if the clinical situation suggests it
Cardiac auscultation to detect valvulopathy or arrhythmias	Reliable	Recommended
Neurological examination in search of hidden cerebrovascular disease	Use not established	Recommended if the clinical situation suggests it
Vascular examination of lower limbs (physical examination and AAI†)	Useful in evaluating affection of target organ	Recommended († selected patients)

(continued)

Table 7. **Initial evaluation of the hypertensive patient (Continuation)**

Complementary examinations		
Initial examination	**Comments**	**D-level recommendation of the guide**
Urine sediment	To rule out nephropathy as cause of secondary AHT	Recommended
Albumin/creatinine ratio	Related to cardiovascular morbidity. It can help in making a therapeutic decision	Recommended
Creatinine	Useful in selecting treatment and detecting lesion in target organs	Recommended if the clinical situation suggests it
Thoracic X-ray	Of little use in detecting cardiomegalia	Recommended
Echocardiogram	Useful in the evaluation of LVH and cardiac insufficiency	Recommended
ECG**	Poor diagnostic performance in detecting LVH (low sensitivity). Use in the case of CV risk and detection of rhythm disorders.	Only when there exists another circumstance that indicates it
Uric acid	Useful for selecting and monitoring some treatments	Recommended in selected patients*
Glucose	Clear relation to cardiovascular risk	Recommended
Lipid profile: cholesterol, HDL, TGC and LDL	Clear relation to cardiovascular risk	Recommended
Plasma sodium concentration	Poor diagnostic performance for detecting secondary AHT. Useful for monitoring some treatments	Recommended
Plasma potassium concentration	Poor diagnostic performance for detecting secondary AHT. Useful for monitoring some treatments.	Recommended

* Suspicion of ventricular dysfunction or associated coronary cardiopathy. Confirm LVH.
** See table 8.

Table 8. **Diagnostic performance of the electrocardiographic criteria of left ventricular hypertrophy**

Method	**Description**	**Sensitivity**	**Specificity**
Cornell	♂ S in V 3 + R aVL >28 mm ♀ S in V 3 + R aVL >20 mm	30 to 60%	80 to 90%
Sokolow-Lyon	S in V1 + RV5 □35 mm		

There is no evidence that carrying out different initial diagnostic strategies influences the degree of control of the AHT or the morbimortality of the hypertensive patient. This affirmation can be extended to the use of the echocardiogram. The Canadian CPG is the one that most specifies its instructions, limiting it to cases of suspicion of ventricular dysfunction, or associated coronary cardiopathy and to confirming left ventricular hypertrophy (28).

CPG

2.4.1. Measuring microalbuminuria in the hypertensive patient

2007 UPDATE

New question

Microalbuminuria is associated discretely with total mortality and with cardiovascular morbimortality (41-47).

No studies were located that evaluated whether the microalbuminuria treatment decreases cardiovascular morbimortality; only some RCTs of few patients and short monitoring evaluated different antihypertensive drugs in the reduction of microalbuminuria (41; 48).

Cohort studies 2+/2++

2007

Recommendation	
D	Measuring the albumin/creatinine ratio in hypertensive patients in stage 1 is recommended.
D	Conducting an echocardiogram is not recommended as initial study in all hypertensive patients.
D	The initial study of the hypertensive patient is comprised by the physical cardiovascular examination, blood analysis (haemogram, glycaemia, creatinine, sodium, potassium, total cholesterol, triglycerides, HDL, LDL, sediment and albumin/creatinine ratio), ocular fundus and ECG.

2.5. Monitoring proposal

2.5.1. Target numbers

RCT
1+

Based on the HOT study (49), in which no differences were observed in morbimortality between the three randomized groups in reaching DBP under 90 mmHg, 85 mmHg and 80 mmHg, the previous version of the CPG recommended target numbers of SBP <140 mmHg and DBP <90 mmHg for which reason, considering the absence of new evidence, this same recommendation is maintained.

Recommendation	
D	SBP numbers <140 mmHg and DBP <90 mmHg are recommended as the target of the treatment of the hypertensive patient.

2.5.2. Frequency of controls

RCT
1+

A clinical trial (50) that compared monitoring every 3 months to every 6 months did not find differences in the percentage of poorly controlled hypertensive patients or in patient satisfaction. It can be pointed out that nearly 60% controlled their BP in their homes. This RCT provided solidity to the half-yearly control recommendation in well controlled hypertensive patients. If there is difficulty in reaching the target numbers, suspicion of therapeutic non-compliance or presence of intercurrent disease, monitoring will be individualized with more frequent consultations.

The objectives of the medical consultations by the hypertensive patient are: achieving optimum BP numbers; assessment of the impact on target organs (TOL); supervision of compliance with the treatment, with detection of possible adverse effects and reassessment of cardiovascular risk. The activities proposed for the nurse or medical consultation are shown in Tables 9 and 10.

Table 9. **Content of the nurse consultation**

Nurse consultation (in case of high risk*, quarterly and the remainder half-yearly)

- Measuring BP, weight, pulse
- Detection of harmful habits: smoking, excessive intake of salt, fats or alcohol, sedentarism
- Supervision of the treatment (compliance and detection of adverse effects)
- Health education (importance of cardiovascular risk and advice on healthy habits)

*Associated disease (diabetes, ischaemic cardiopathy, etc.) and target organ affection.

Table 10. **Content of the medical consultation**

Annual medical consultation

- Cardiovascular examination
- Blood analysis:
  - Annual: glycaemia, creatinine, ions*, cholesterol, TGC, HDL, albumin/creatinine ratio and urine sediment **
- Annual ECG if there is a previous alteration and at least every 5 years in the remainder of the cases
- Reassessment of cardiovascular risk by means of the REGICOR tables
- Review of the suitability of the treatment according to the existing evidence

* Only in patients that are under treatment with diuretics, ACEI or ARA II
** More frequent measurement in case of hypertriglyceridaemia or nephropathy

Experts' opinion 4

The agreed consultation criteria on the specialized level by the guideline's editing team is based on the recommendations of the Catalan Family and Community Medicine Society and of the Spanish Hypertension Society and the Spanish League for the Fight against Arterial Hypertension (10) (Table 11).

Table 11. **Criteria for referral to specialized care**
D-level recommendation

- Study of secondary hypertension of non-pharmacological cause
- AHT associated with chronic kidney insufficiency or significant alterations of the kidney function as haematuria and maintained proteinuria (□0.5 g/day)
- Refractory AHT once WCH is ruled out
- AHT in pregnancy

Recommendation	
B	A half-yearly consultation is proposed to monitor hypertensive patients, once the target objective has been achieved.
D	In some patients selected according to their cardiovascular risk, target organ affection or compliance, this frequency can be quarterly.

2.5.3. Pharmacological therapeutic compliance

Questions to answer

- What interventions are effective in primary care in order to improve pharmacological compliance in hypertensive patients?

2007 UPDATE

2 new SRs (51; 52) and 1 updated SR, 1 new cohort study (54)

Modified Recommendation

Therapeutic compliance is understood as when the patient takes between 80% and 110% of the prescribed dosage (55). Pharmacological therapeutic non-compliance is one of the principal causes of failure to achieve proper numbers in BP.

SR of RCT 1 +

Two Cochrane SRs (51; 52) show that the simplification of the dosage and a combination of different strategies are the most effective measures for increasing compliance although their effects on lowering the BP numbers is not so conclusive.

Cohort study 2+

An observational study (54) carried out in the United States on 5,732 hypertensive patients showed that the combination at fixed doses of drugs in a single tablet improves compliance compared to the taking of single-component tablets separately but simultaneously.

RCT 1 +

In our area, several RCTs have been published that analyzed strategies to improve compliance, with the maximum monitoring of six months. Among them, group sessions with postal reinforcement (56), education or motivational interview in programmed consultations have been effective. The reminder by mobile telephone messages has not been effective and the data on the use of the SMBP for this purpose are inconsistent. A Meta-analysis not conducted in our area, which included an RCT with monitoring of up to 26 months found that the SMBP is effective in the control of BP numbers (57).

2007

Recommendation	
A	The antihypertensive pharmacological treatment has to be in a single daily dose whenever possible.
B	The health care professionals that treat the hypertensive patients must use different combined strategies that go beyond brief advice in order to improve the pharmacological therapeutic compliance.
A	Simplifying the dosage guidelines (reduction of dosage, combination of drugs in a single tablet, etc.) in order to enhance compliance of antihypertensive treatments is recommended.

3. Treatment of hypertensive patients

3.1. Non-pharmacological measures in the treatment of AHT

QUESTIONS TO ANSWER

- Are life-style changes effective in the control of the hypertensive patient?
- What is the magnitude of the decrease in SBP and DBP numbers that can be achieved through non-pharmacological measures in the hypertensive patient?

There are still no studies on the effectiveness of non-pharmacological measures in the treatment of AHT that evaluate the results in terms of cardiovascular morbimortality.

However, it is necessary to recall that small decreases in the BP numbers have been associated with significant reductions in cardiovascular morbimortality in cohort studies.

All the measures studied on life-style changes receive support from the advice of the health care personnel, some of them within a specific structured programme that requires a considerable investment of time. The primary care teams, the ones to whom these guidelines are aimed, must evaluate the feasibility of the proposed recommendations. The nursing personnel have an essential role in this area.

3.1.1. Consumption of salt

2007 UPDATE

2 new SRs (58; 59)
No changes in recommendations

The restriction of the consumption of salt can reduce the SBP and DBP numbers to a modest but significant degree in the overall hypertensive population.
Since the previous CPG, two Cochrane systematic reviews (58; 59) have been published. He's review (58) includes studies of at least four weeks of duration and found a reduction in the DBP numbers of 2.74 mmHg (3.2-2.3) and the SBP of 4.97 mmHg (5.8-4.2).

Jurgens' review (59) confirmed these findings with a reduction in SBP of 4.18 mmHg (3.3-5.1) and in DBP of 2 mmHg (1.3-2.5).

SR of RCT 1+

The evidence of the previous CPG continues to be valid on the greater effect of the low-sodium diet in persons over 45 years of age without pharmacological treatment, on which the restriction of salt is effective in the longer term (6 months-1 year), even at 3 years in the population between 60-80 years of age and on the need to make the recommendation in an individualized manner due to the different sensitivities to the effect of the intervention.

The nursing personnel are the suitable ones to facilitate the compliance of this measure for hypertensive patients. The evaluated studies use individual or group educational strategies. In our area, it can be done individually (see Appendix 9).

Recommendation	
A	The patients with essential AHT must receive professional advice in order to decrease the sodium content of the diet. This advice must be given even to those patients that follow a heart-healthy diet. This advice is especially important in the population over 45 years of age.

3.1.2. Physical exercise

2007 UPDATE

1 new SR (60)
Partially modified recommendation

SR of RCT 1+

Exercise of aerobic intensity has been the most studied. Available evidence points towards a decrease in BP numbers of a modest degree. The studies, given their duration between four weeks and one year, are not designed to demonstrate reductions in cardiovascular morbimortality. Exercise of aerobic intensity must be adapted to the characteristics of the patients.

A new SR (60) that included hypertensive and normotensive subjects analyzed the effect of resistance exercise three times a week for at least four weeks. Together, a significant reduction is obtained of 6 mmHg in SBP and 4.7 mmHg in DBP. The data of the subgroup of hypertensive patients are not conclusive.

Recommendation	
A	Hypertensive patients should receive advice through interventions structured on the practice of physical exercise of aerobic intensity adapted to their characteristics. The exercise should include, at least, three weekly sessions of 45-60 minutes of duration.

3.1.3. Weight control

2007 UPDATE

1 new SR (62) and 1 new Meta-analysis (63)
No changes to the recommendation

The new references (62; 63) found reaffirm the conclusions of the Cochrane review of the previous edition of these guidelines. The individual trials are not of great quality. The impact of the measure is modest as regards the BP numbers. It is estimated that a loss of 4-8% of the weight can decrease the SBP and DBP by 3 mmHg. The interventions that are evaluated are the hypocaloric diet and qualitative modifications to the diet supported by individual programmed interventions.

SR of RCT
1+

Recommendation	
A	The patients with essential AHT, including those that take antihypertensive drugs, must receive advice from the professionals on losing weight.

3.1.4. Stress control

2007 UPDATE

1 new SR (64) and a new cohort study (65)
No changes to the recommendation

The base CPGs (3-5) consulted hardly mention this measure and when they do they point to a marginal benefit. This can be explained by the heterogeneity of the measures used (biofeedback, meditation and other cognitive behavioural techniques) and by the limited quality of the experimental studies published.

RCT 1+

Recommendation	
B	Controlling stress is not recommended as a general measure in our area for the treatment of AHT.

3.1.5. Consumption of alcohol

2007 UPDATE

2 new cohort studies (66; 67)
No changes to the recommendation

The reduction of the consumption of alcohol in hypertensive patients who drink moderately/excessively (30 to 60 g/day) achieves a reduction in the SBP of 3.9 mmHg (CI 2.76 to 5.04) and the DBP of 2.41 mmHg (CI 1.57 to 3.25) (10).

SR of RCT 1+

The new RCTs were conducted on few patients, with brief monitoring and without evaluating morbimortality. It was considered advisable to include new cohort studies (66; 67) that studied the effect of alcohol consumption in hypertensive men. The results attribute a protective effect to the moderate consumption of alcohol on general and cardiovascular mortality. There are no data on hypertensive women.

The benefits of the reduction in alcohol consumption in hypertensive patients go beyond the cardiovascular area, for which reason this section must be a priority in the treatment of these patients. In general the guidelines recommend not exceeding 1-2 units/day in women and 2-3 units/day in men. There are some discrepancies regarding the grams that a unit of alcohol contains (8-12 g). The consumption advice given to the hypertensive patient must be the same as that which is given to the general population; in our area the PAPPS proposes consumption of less than 280 g/week (28 SDUs) for men and 170 g/week[1] (17 SDUs) for women (68).

2007

Recommendation	
A	Hypertensive excessive drinkers must receive advice on reducing alcohol consumption. The objective is to reduce the intake of alcohol by at least 60%.
B/D	Male hypertensive drinkers who consume amounts less than 17 units/week of alcohol do not require changes in their habits because of the possible cardioprotective effect of the moderate consumption of alcohol (B). This limit will be 11 units/week for women (D).

3.1.6. Consumption of potassium

2007 UPDATE

1 new RCT (69) and 1 new SR (70)
No changes to the recommendation

The new publications corroborate what was made known by the Meta-analysis referenced in the previous guidelines that evaluated the effect on blood pressure of a diet rich in potassium. Potassium administered in form of supplements of between 60-100 mmol/day can decrease BP by a modest amount in the hypertensive population. The effect is also greater in patients that do not follow a salt-free diet and in those of the black race (70). There does not seem to be differences among different potassium salts (69).

SR of RCT 1+

[1] 1 unit of alcohol = 1 glass of wine (100 ml) = 1 beer (200 ml) = shot of whisky (25 ml) = 8 to 10 g of alcohol
Exact calculation of g of alcohol = percentage of alcohol content x volume in ml x 0.79.

The usual potassium consumption in the diet is from 2 to 4 g/day. The DASH study (71) observed that a diet rich in vegetables and fruit with high potassium content significantly reduces the BP numbers.

The use of potassium supplements requires monitoring and can produce hyperpotassemia, especially in the elderly undergoing treatment with ACEI or with incipient renal insufficiency (10), for which reason advice on the consumption of a diet rich in vegetables and fruit seems the most reasonable option.

Recommendation	
A	A diet rich in fruit and vegetables with high potassium content is recommended for all patients with hypertension. Potassium supplements, after an individualized evaluation, can be recommended to some patients.

3.1.7. Consumption of calcium and magnesium

2007 UPDATE

2 new SRs (72; 73)
Modified Recommendation (magnesium is added)

As regards the consumption of calcium, two SRs (72; 73), subsequent to the previous version of this CPG, confirmed this recommendation despite the small decrease in SBP that was achieved with calcium supplements.

SR of RCT 1+

2007

Recommendation	
A	Neither calcium or magnesium supplements are generally recommended for hypertensive patients.

3.1.8. Consumption of Omega-3 fatty acids

2007 UPDATE
New question (74-77)

A Meta-analysis (74) and several clinical trials of variable quality (75-77), some conducted in primary care (75; 77), in which the Omega-3 fatty acids were administered in different forms (pills, fish, fish oil, etc.) found a very modest benefit in decreasing BP and also warned on possible digestive intolerance.

SR of RCT 1+

2007

Recommendation	
B	The inclusion in the diet of food rich in Omega-3 fatty acids such as high-oil fish (3 times a week) can be recommended.

3.1.9. Consumption of fibre

2007 UPDATE

New question (78; 79)

None of the CPGs (3-5) consulted refer to this question. The two Meta-analyses found in the bibliographical search (78; 79) are on the general population, although they analyze the pre-established subgroup of hypertensive subjects. The evidence is weak given that the interventions are quite variable, the quality of the trials is not analyzed and the heterogeneity is not evaluated.

SR of RCT 1+

2007

Recommendation	
B	The consumption of fibre in the diet is recommended, the same as for the general population.

3.1.10. Consumption of coffee

2007 UPDATE

New question (80)

A systematic review (80) conducted on the normo- or hypertensive population compares the effect on BP and on the heart rate by the consumption of coffee or caffeine to decaffeinated coffee or to not consuming it. The results showed that the SBP increases 2.04 mmHg (CI 95% 1.18-2.99), the DBP increases 0.73 mmHg (CI 95% 0.14-1.31) and the difference on the heart rate is not significant.

SR of RCT 1+

The effect on the BP is more pronounced if the intake of caffeine is in a form other than coffee. The abovementioned cohort studies do not associate it to higher cardiovascular mortality.

2007

Recommendation	
B	It is not necessary to eliminate coffee in the diet of hypertensive patients; only the consumption of more than five cups a day can have effects on BP.

3.1.11. Life-style changes: combination of several non-pharmacological measures

2007 UPDATE

New question (81-85)

The variability of the different combinations makes their comparison difficult in order to obtain a firm conclusion, but the data point to the fact that the combination of several measures does not have an effect equivalent to the sum of each of them separately and this possibly is due to the complexity of carrying out the posed interventions (81-85). Some of them, such as those that require psychotherapists, are not at all applicable in our primary care organization.

SR of RCT 1++

Recommendation	
A	The combination of non-pharmacological measures is not effective in decreasing BP numbers.
D	The complexity of complying with it requires it to be proposed individually.

2007

2007

3.1.12. Educational or the organization's interventions

2007 UPDATE

New question (86)

A Cochrane review (86) shows that an organizative intervention that includes detection, monitoring, treatment algorithm, control of compliance and facilitation of access to services significantly reduced BP (up to 11.7 mmHg in SBP and 7.6 mmHg in DBP) and a decrease in mortality for any cause (absolute difference in risk of 1.4%).

SR of RCT 1++

The care in charge of nursing or pharmacy professionals, although it presents heterogeneous results, obtains favourable results in the majority of the cases. The reminders are associated with an improvement in the monitoring.

The most important result involves an intervention on so many levels that it is not easy to put it into practice.

All the results seem to point towards the convenience of making educational interventions, of involving the patient in his care, but there is insufficient evidence to determine which intervention is more effective.

Recommendation	
A	The organized care of hypertensive patients that also includes educational interventions and promotion of self-care is recommended.

2007

3.2. Pharmacological treatment of AHT in patients with no associated disease

QUESTIONS TO ANSWER

- What are the benefits of the pharmacological treatment of AHT for patients without associated disease?
- What are the benefits of the different drugs used as the first option in patients without associated disease?
- Are there differences in the effectiveness, morbimortality and safety among the different groups of antihypertensives?
- Which are the antihypertensive drugs of choice in hypertensive patients without associated pathologies?

2007 UPDATE

2 new Meta-analyses (87; 88)
No changes in the recommendations

The benefit of the pharmacological treatment of AHT compared to a placebo in the reduction of cardiovascular morbimortality is clearly demonstrated through many randomized clinical trials (RCT), included in different Meta-analyses (10; 87; 88).

The benefit of the treatment is consistent in young adults and the elderly, in men and women and in isolated systolic AHT. The benefit of the antihypertensive treatment is greater in the elderly than in young adults with AHT in stages 1 and 2.

SR of RCT 1++

Gender does not seem to influence the magnitude of the benefit of the antihypertensive treatment, but rather it is the basal cardiovascular risk that determines it. No decrease of cardiovascular morbimortality was detected in Caucasian women between 30 and 54 years of age at 5 years of treatment, probably due to a low basal CV risk, which makes the finding of statistically significant differences difficult (10).

Recommendation	
A	The treatment of hypertension is recommended independently of gender. With respect to age, it seems to be consistent in treating both young persons and adults under 80 years of age.

3.2.1. Diuretics

2007 UPDATE

1 new Meta-analysis (87)
No changes in the recommendations

Diuretics *vs.* beta blockers (BB)

According to the previous version of the guidelines, for hypertensive patients of 65-74 years of age, diuretics were slightly more effective than the beta blockers in the reduction of CVA and cardiovascular events; this difference was not observed in patients under 65 years of age (10).

A Cochrane SR (89) concluded that the BB are similar to diuretics in all the results evaluated although in some comparisons the heterogeneity was recorded, explained by the age or for the type of BB.

SR of RCT 1+

Diuretics *vs.* other families of antihypertensives

The ALLHAT study (90) showed the favourable effect of chlorathalidone in the prevention of cardiovascular morbidity compared to amlodipine and lisinopril. In a Meta-analysis (87), the diuretics presented a more favourable profile compared to calcium antagonists in cardiac insufficiency, reinforcing the results of the ALLHAT study.

SR of RCT 1+

The evidence on effectiveness seems consistent among the different thiazide diuretics, which suggest that there is a class effect.

RCT 1++

Recommendation	
A	In the initial treatment of uncomplicated AHT, thiazide diuretics at low doses are the drugs of first choice ahead of the remainder of the families of antihypertensives (ACEI, ARA II and calcium antagonists), in young hypertensive patients as well as those of a more advanced age and in isolated systolic AHT. They are also of choice in the initial treatment of hypertension in stages 1 and 2 associated with an additional risk factor.

3.2.2. Beta blockers

2007 UPDATE

5 new Meta-analyses (87; 89; 91-93) and 1 new RCT (94)
Modified Recommendation

In the previous version, the beta blockers were considered drugs of first choice in young hypertensive patients with uncomplicated AHT and in the older patients as alternative drugs or in association. In the search carried out, new evidence was found that modified these recommendations.

Beta blockers *vs.* placebo

According to the previous version of the guidelines, beta blockers reduce the incidence of CVA and cardiac insufficiency (10).

In a Meta-analysis (92), the added variable studied as the principal result (AMI, CVA or death) was only shown to be significantly favourable to the BB in patients under 60 years of age. A Cochrane SR (89) confirmed more clearly that the BB are shown favourable to a placebo in CVA (fatal or not) and in total CVD (which includes CVA), without differences in the remainder of the results.

SR of RCT 1+/1++

Beta blockers *vs.* other families of antihypertensives

Three Meta-analyses (87; 92; 93) and one Cochrane SR (89) presented the results including the rest of antihypertensive families *vs.* BB; these were not shown to be higher than the rest of the families in any of the results evaluated and, in any case, they present an unfavourable profile in the CVA (93).

RCT 1++

In the ASCOT study (94), which compares amlodipine with or without perindopril *vs.* atenolol with or without thiazides, no significant differences were found in the added variable studied as the principal result (non-fatal AMI, fatal coronary disease).

SR of RCT 1+

2007

Recommendation	
A	The use of beta blockers is not recommended as front-line drugs in the initial treatment of uncomplicated AHT.

3.2.3. ACEI

2007 UPDATE

5 new Meta-analyses (87; 88; 95-97)
No changes to the recommendation

ACEI *vs.* conventional treatment: diuretics / beta blockers

SR of RCT 1++

A Meta-analysis (97) concluded that there are no significant differences between ACEI and the conventional treatment with diuretics and/or beta blockers.

However, another Meta-analysis (87) concluded that the diuretics were shown to be more effective than the ACEI in CVA and cardiac insufficiency. Finally, another Meta-analysis (88), which compared new and previous antihypertensive drugs, found that the conventional treatment is better than ACEIs in the prevention of CVA, with the differences in the remainder of cardiovascular events being insignificant.

ACEI *vs.* calcium antagonists

SR of RCT 1++

According to the 2002 Guidelines, the ACEIs had better results than calcium antagonists in the prevention of ischaemic cardiopathy (10) but this finding is not confirmed in another Meta-analysis published in 2003 (97) that included new trials, among them was the ALLHAT study. In this Meta-analysis, ACEIs are shown to be similar in this variable, worse in CVA and better in the prevention of cardiac insufficiency.

Recommendation	
B	ACEIs can be used as alternative drugs to the diuretics with uncomplicated AHT, and in absence of stenosis of the renal artery.

3.2.4. Calcium antagonists

2007 UPDATE

4 new Meta-analyses (87; 88; 97; 98) and 2 new RCTs (94; 99)
Modified Recommendation

Calcium antagonists *vs.* conventional treatment: diuretics / beta blockers

SR of RCT 1+

Three Meta-analyses (87; 88; 97), subsequent to the 2002 guidelines, coincided in that the calcium antagonists are inferior to the conventional treatment and, especially, to the diuretics in the prevention of cardiac insufficiency, without finding differences in ischaemic cardiopathy.

The ASCOT study (94) compared amlodipine with or without perindopril *vs.* atenolol with or without bendroflumethiazide and did not find significant differences in the aggregate result of non-fatal AMI, including silent infarction, plus fatal coronary disease. In all the secondary variables, the branch of amlodipine was show to be more effective than that of atenolol in the prevention of CVA.

Calcium antagonists *vs.* ACEI

SR of RCT 1++

The calcium antagonists are more effective than ACEIs in the prevention of CVA and less effective in cardiac insufficiency (97) (see section ACEI).

Calcium antagonists *vs.* ARA II

RCT 1+

The VALUE study (99) that compared amlodipine to valsartan in high-risk hypertensive patients over 50 years of age (50% with ischaemic cardiopathy) showed results favourable to amlodipine in the prevention of infarction (secondary variable), with no differences in the principal result (cardiac event being mortal or not). See ARA II section.

Recommendation	
A	Dihydropyridines are an effective alternative to thiazide diuretics for the treatment of isolated systolic AHT in patients over 60 years of age.
B	Calcium antagonists can be an alternative treatment to the diuretics in uncomplicated hypertension.

2007

3.2.5. Alpha blockers

2007 UPDATE

No new references
No change to the recommendation

No new studies were published on this question. The branch of the ALLHAT study that compared doxazosin to chlorathalidone in patients with at least one risk factor was interrupted prematurely because of excessive cardiovascular disease with a risk two times greater of congestive cardiac insufficiency (10).

RCT
1++

Recommendation	
A	The alpha blockers are not recommended as treatment of first choice in single-drug therapy.
B	The use of alpha blockers in association must be reserved for cases in which the other combinations of drugs have failed.

3.2.6. ARA II

2007 UPDATE

11 new Meta-analyses (87; 88; 95-97; 100-105) and 4 new RCTs (106-109)
No changes to the recommendation

Several Meta-analyses (101; 102) compared the different antihypertensive drugs and, among them, ARA II. The Meta-analyses did not include the same studies, none were made on uncomplicated hypertension and some were in clinical situations other than AHT, which made reaching conclusions on this subject difficult.

SR of RCT
1+

ARA II *vs.* Placebo

The SCOPE study (106) that analyzed the effect of candesartan compared to a placebo in the elderly (mean age of 76 years) did not find a significant difference in the percentage of the first cardiovascular event (9.7% *vs.* 10.9%). For ethical reasons, nearly 80% of the patients of the control group ended the study with diuretics and/or beta blockers.

RCT 1+

ARA II *vs.* conventional therapy: diuretics / beta blockers

Two Meta-analyses (88; 97) coincided in that the ARA II are more effective than the conventional therapy in the prevention of CVA, with no differences in ischaemic cardiopathy and cardiovascular death.

There are no comparative studies with diuretics in patients with uncomplicated AHT. A Meta-analysis (87) that included three trials with ARA II in special situations concluded, through indirect comparison, that this pharmacological group is no better than the diuretics in decreasing cardiovascular events.

SR of RCT 1+

With respect to the comparison with BB, the LIFE study compared losartan to atenolol in hypertensive patients between 55 and 80 years of age, with high cardiovascular risk and left ventricular hypertrophy measured by ECG. Losartan was superior to atenolol in the reduction of CVA (109); no differences were observed in cardiovascular mortality.

SR of RCT 1+

ARA II *vs.* calcium antagonists

The VALUE study (99) compared valsartan to amlodipine in high-risk hypertensive patients over 50 years of age (nearly 50% with ischaemic cardiopathy). No significant differences were found in the principal result (cardiac event being mortal or not), but the infarctions were significantly more frequent in the group assigned to valsartan.

RCT 1+

ARA II *vs.* ACEI

The only Meta-analysis that contributed comparative data, up to now, on these two families (101) included five RCTs in other clinical situations and did not find significant differences in the total mortality, cardiovascular and non-cardiovascular, or in CVA or AMI.

RCT 1+

Recently the ONTARGET trial was published (110), which compared ARA II to ACEI in patients in secondary prevention and in diabetes; the hypertensive majority. No differences were observed in morbimortality. The ARA II produced less coughing and angioedema, but more hypotension.

RCT
1++

Relation to the appearance of AMI

As a result of the data observed in the VALUE study, several subsequent Meta-analyses (100; 101; 103-105) studied this subject from cases of infarction from the different trials on ARA II compared to a placebo or other treatments. The results are of difficult interpretation due to the variability of the RCTs included, to the populations and to the comparers.

SR
of RCT
1+

In the ONTARGET study, greater frequency of infarction with the ARA II was not observed.

RCT
1++

2007

Recommendation	
B	ARA II are not drugs of first choice in uncomplicated AHT, although they can be used as an alternative to the ACEIs in the case of intolerance.

3.2.7. Abandonment because of adverse effects

2007 UPDATE

3 new SR (89; 111; 112)
Modified Recommendation (expanded)

A Cochrane SR (89) found that the BB provoked more abandonment for adverse effects than the diuretics and that ACEI/ARA II, with no differences with the calcium antagonists. According to another SR (112) there does not seem to be significant differences in the serious adverse effects between the calcium antagonists and BB diuretics and the latter are better tolerated than the calcium antagonists. The ARA II are tolerated better than the ACEI; and the ACEI better than the alpha blockers (10).

SR of RCT 1+/1++

Other SRs (111) studied the relation of the dosage (half, standard, double) to the adverse effects in 354 RCTs and found that for the diuretics, BB and calcium antagonists there is a clear relation between these two variables, but not in the case of ACEI and ARA II. At half dosage, a lesser decrease in BP is achieved (20%) but there is an important reduction in the adverse effects from diuretics, BB and calcium antagonists. When the treatments are combined, the proportion of adverse effects was less than that expected by the addition (7.5% compared to 10.4%).

Some aspects under discussion are the relation of hyperglycaemia caused by the use of diuretics with the increase of CV morbimortality and the controversy that arose because of the hypothesis that ARA II drugs could increase the incidence of AMI. Post-hoc analysis of the ALLHAT and SHEP clinical trials (113; 114) confirmed an increase of new cases of diabetics with the diuretics, but that does not signify an increase in the risk of CV events.

Recommendation	
B	It is necessary to take into account the profile of adverse effects in the choice of antihypertensive drugs.
B	When antihypertensive associations are considered, the diuretics, BB and calcium antagonists can be used at half the standard dosage in order to minimize the adverse effects, keeping the ACEIs and ARA II at the usual dosage.

2007

3.2.8. Pharmacological treatment of the AHT in the elderly

2007 UPDATE

New question

The election of pharmacological treatment in this population will be done according to the general guidelines, since the large AHT clinical trials usually include a large proportion of patients over 60 years of age. More specific trials on this population, such as the ANBP-2 (115) and SCOPE (106) trials did not manage to show conclusively the superiority of one class of drugs over another.

RCT 1+

Recently, the BYVET trial was published that included 3,845 hypertensive patients (the majority without associated cardiovascular disease) over 80 years of age and with SBP □160 mmHg. In this study the patients were assigned to treatment with slow-release indapamide, 1.5 mg plus 2.4 mg of perindopril if necessary in order to achieve target numbers of SBP <150 mmHg and PAD <80 mmHg. The treatment showed a decrease of 30% in the CVA (principal variable) and 21% in mortality by any cause in comparison to the placebo. The secondary effects were less frequent in the branch of the pharmacological treatment (116).

RCT 1+

In this group of patients, the diuretics are the treatment of choice as the initial pharmacological treatment. If the elderly patient was already in treatment, continuing it is recommended (3-5).

Experts' opinion 4

Recommendation	
A	In patients between 60-80 years, it is recommended to follow the general guidelines of the antihypertensive treatment.
A	In patients □80 years with SBP □160 mmHg, indapamide is recommended as initial pharmacological treatment, adding perindopril up to 4 mg if it is necessary to control the BP.
D	In patients over 80 years of age, it is recommended to continue with the established treatments if they are well tolerated. In special situations the recommendations of the specific sections of this CPG will be followed.

2007

2007

2007

3.3. Pharmacological treatment in special situations

3.3.1. Diabetes mellitus without nephropathy

QUESTIONS TO ANSWER

- What are the target BP numbers of the hypertensive diabetic patient?
- What is the antihypertensive treatment of choice in diabetics?

2007 UPDATE

4 new SRs (117-120) and 1 new RCT (110)
Change in the target numbers
Completed recommendation on the pharmacological treatment of choice

Target numbers

The consulted base CPGs recommend target numbers of SBP of 130 mmHg and DBP of 80 mmHg. Both are based on the analysis of the same studies: the UKPDS (121) and the HOT (49) studies. The NICE CPG on diabetic nephropathy recommends numbers of 140/80 mmHg (122).

In the UKPDS 38 (122) the patients assigned to a strict BP control (objective: <150/85 mmHg; achieved: 144/82 mmHg) presented less risk of suffering any event related to diabetes and less mortality related to diabetes than the patients assigned a less strict BP control (objective: <180/105 mmHg; achieved: 154/87 mmHg). A non pre-established analysis of the diabetic patients of the HOT study showed that there are differences in the subgroup assigned a target diastolic BP of DBP <80 mmHg, compared to the subgroup assigned to a target DBP <90 mmHg. Although there are no differences in the total mortality, the patients with a less strict BP control objective have an increased risk of cardiovascular mortality.

RCT 1+

In a recent review of this subject (118) it was concluded that there is scarce evidence for recommending a specific number, and SBP <140 mmHg and DBP <80 mmHg numbers are preferred.

SR of RCT 1+

2007

Recommendation	
B/D	In the patients with essential AHT and Type 2 DM without nephropathy, treatment target numbers of SBP <140 mmHg (D) and DBP<80 mmHg (B) are recommended.

Pharmacological treatment

There is consistent evidence that cardiovascular benefits in the diabetic population do not differ from those observed in the general population (117). This fact supports the idea that, for cardiovascular events, there does not seem to be any class of medicine with especially beneficial effects on diabetic patients.

The ALLHAT (123) is the trial that included the largest number of diabetics (13,101 patients). In the diabetics no differences were observed between chlorathalidone *vs.* lisinopril or chlorathalidone *vs.* amlodipine in the principal result variable of cardiac-coronary disease, or in other variables of secondary results, except in cardiac insufficiency, in which chlorathalidone was superior to amlodipine and to lisinopril.

RCT 1+

For calcium antagonists, some small low-quality studies (124; 125) conducted on an exclusively diabetic population showed unfavourable results regarding cardiovascular morbimortality in comparison with ACEIs. In the analysis of the subgroup of diabetics of the INSIGHT trial (126), there were no differences between the diuretic (hydrochlorothiazide / amiloride) and nifedipine on cardiovascular morbimortality. Two low-quality Meta-analyses (117; 119) showed unfavourable results for the calcium antagonists in the result variable of cardiac insufficiency compared to the conventional treatment (diuretic/BB) or ACEI/ARA II.

RCT 1+

In regards to ARA II, the only favourable evidence in diabetes without nephropathy comes from the LIFE trial (109), in patients with LVH. Losartan reduced cardiovascular morbimortality to a greater extent than atenolol, an inadequate comparer, in light of current evidence (see text on the general population).

SR of RCT 1+

In the UKPDS (127) trial, there were no significant differences between beta blockers (atenolol) and ACEI (captopril) in the cardiovascular or renal results. However, the results of the LIFE trial, together with the latest evidence in the form of a systematic review on the general population led us not to recommend the beta blockers as treatment of AHT in DM 2 unless there are other firm indications for its use, such as ischaemic cardiopathy or cardiac insufficiency.

The independent nephroprotective effects of ACEI or ARA II, beyond the reduction of BP, have been questioned by a recent Meta-analysis (18).

ACEIs and ARA II have not been shown to be superior to other antihypertensives in the reduction of renal complications in diabetic patients. In one Cochrane review on the nephroprotective effect of ACEIs in diabetes, no differences were found between ACEIs and calcium antagonists or the placebo in the prevention of total mortality, terminal renal disease, or in the duplication of creatinine. There were differences in the appearance of microalbuminuria. The data compared to the remainder of the antihypertensives were not conclusive (120).

SR of RCT 1+

In the subgroup of diabetics of the recent ONTARGET study, telmisartan was not superior to ramipril in the prevention of cardiovascular morbimortality (110).

RCT 1++

As regards isolated systolic AHT in diabetes mellitus, we refer to the previous version of the guidelines. The follow-up at 10 years of the SHEP (114) study added consistency to the benefits of the diuretics.

RCT 1+

	Recommendation
A	Thiazide diuretics or ACEIs are recommended as treatment of choice in hypertensive patients with DM 2 and the dihydropyridinic calcium antagonists and ARA II as alternative treatment.
B	Beta blockers are not recommended in the diabetic hypertensive patient, unless there is a firm indication for their use, such as ischaemic cardiopathy or cardiac insufficiency.
B	Elderly diabetic patients with isolated systolic AHT must be treated preferably with diuretics at low doses or with long-acting dihydropyridines (nitrendipine).

2007

2007

3.3.2. Diabetic nephropathy

QUESTIONS TO ANSWER

- What are the target BP numbers in the treatment of the diabetic hypertensive patient with diabetic nephropathy?
- What is the antihypertensive treatment of choice in diabetic nephropathy?

2007 UPDATE

3 new systematic reviews (117; 118; 128) and 2 new RCTs (129; 130)
Change in target numbers
No changes to the recommendation pharmacological treatment of choice

Target numbers

The natural history of diabetic nephropathy progresses from renal function disorders to terminal renal insufficiency, passing through intermediate stages marked by the appearance of microalbuminuria and proteinuria (Table 12).
The microalbuminuria phase involves incipient nephropathy.

Table 12. **Classification of diabetic nephropathy**

	24-hour albumin in urine (mg)	**Albumin/creatinine ratio (ACR) (mg/g)**
Normal	<30	<30
Microalbuminuria	30-299	30-299
Proteinuria	≥300	≥300

Localized evidence on the benefits of achieving different levels of BP in diabetic patients with nephropathy does not provide conclusive data. An SR (128) on type 1 and 2 diabetics with microalbuminuria or nephropathy did not find differences in the deterioration of the renal function or in the evolution to terminal renal insufficiency (TRI) among the different BP numbers achieved. However, the groups that reached lower BP numbers showed a decrease in the albumin excretion rate.

SR of RCT 1+

Two analyses were published after the IDNT (129) and RENAAL (130) studies that, due to their design, offered weak evidence. The first associated the greater benefits in mortality and renal results to keeping the SBP between 120 and 130 mmHg and did not find any correlation between the DBP and the renal results or mortality. In the second, it seems that there is no statistically significant differences in the progression of TRI while follow-up BP was kept below SBP <140 mmHg and DBP <90 mmHg.

RCT 1+

2007

Recommendation	
D	Patients with AHT and diabetic nephropathy must receive treatment to lower their BP until achieving BP under 140/80 mmHg.

Pharmacological treatment

There is evidence that the drugs that block the renin-angiotensin system (ACEI or ARA II) improve the parameters of renal function such as albuminuria and delay the progression of nephropathy (10), although a recent Meta-analysis questioned whether it is an independent effect of the hypotensive effect (131).

SR of RCT 1+

A Cochrane review (132) concluded that ACEIs and ARA II are effective as renal result variables (TRI, duplication of serum creatinine, progression of micro to macroalbuminuria). There does not seem to be any differences between the groups of drugs in these results, although direct comparisons are lacking on them.
Neither ACEIs nor ARA II reduced the total mortality compared to the placebo. Analyzing separately the studies that used ACEIs at full dosages, the reduction of mortality was indeed significant.

As for the combination of ACEIs and ARA II, the conducted studies included few patients and only intermediate variables were evaluated. These RCTs were included in a recent Meta-analysis (133) that showed a short-term improvement (12 weeks) in proteinuria, with a slight increase in the potassium levels.

SR of RCT 1+

If a patient is considered as a candidate for combination therapy, he must be treated in the specialized care area.

Recommendation	
A	The hypertensive patients with DM and nephropathy must be treated with an ACEI. ARA II is the alternative treatment.

3.3.3. Non-diabetic nephropathy

QUESTIONS TO ANSWER

- What are the target BP numbers in the treatment of the hypertensive patient with non-diabetic nephropathy?
- What is the antihypertensive treatment of choice in hypertension with non-diabetic nephropathy?
- Is the combination of ACEI and ARA II more effective than single-drug therapy in diminishing the progression of renal failure?

2007 UPDATE

1 new SR (131) and 1 new RCT (134)
Change of target BP numbers
No changes in the recommendation on the pharmacological treatment of choice

Target numbers

Several studies were published on the optimum blood pressure control numbers in non-diabetic nephropathy, which led to modifying the previous recommendations. A long-term follow up (up to 10 years) of the MDRD study (135) showed that the group assigned to BP with strict objective (equivalent to BP <125/75 mmHg) had less risk of renal failure. The follow up, however, was done outside the trial, without controlling the BP achieved in the branches of treatment, the concomitant use of ACEIs, or the results of the renal failure or death that was observed in databases outside the trial, which are important limitations to being able to generalize the results.

RCT 1+

In the AASK study (136) (mean basal proteinuria of 0.61 g/day), no significant differences were obtained in the renal result variables between a target BP under 125/75 mmHg and a BP target under 140/90 mmHg. In the REIN-2 study (134) (basal proteinuria over 1g/24h) no differences were observed in the progression to renal failure among the two branches of treatment: one, of intensive control, with the target BP <130/80 mmHg (SBP 129.6 mmHg and DBP 79.5 mmHg were achieved) and the other, with less strict control, with a target of DBP <90 mmHg (SBP of 133.7 mmHg and DBP of 82.3 mmHg were achieved). All the patients were in treatment with ramipril.

In summary, the studies have a certain degree of inconsistency regarding whether the strict control of BP achieves better results than the usual target numbers, probably due to their differences in methodology, the type of patients included (type of renal insufficiency, degree of basal proteinuria, etc.), pharmacological treatments used, target BP, and BP actually achieved in the studies, which make it difficult to establish firm recommendations on this subject. It is considered that achieving a target BP <130/80 mmHg could be a reasonable recommendation in view of the results of the clinical trials.

Cohort study 2+

Doubt remains on whether or not maintaining BP levels <140/90 mmHg is sufficient in cases of low proteinuria (less than 1 g/day), but it is reasonable to think that achieving somewhat greater reductions in BP will manage to decrease proteinuria and, consequently, the renal damage. For this group of patients, the recommendation of slightly higher numbers than those of the previous version of the guidelines (BP <130/85) (10) was considered.

Experts' opinion 4

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Recommendation	
D	In patients with non-diabetic nephropathy and gross proteinuria (>1 g/day), keeping the BP under 130/80 mmHg as long as they tolerate the treatment is recommended. In case of proteinuria <1 g/day the proposed numbers are 130/85 mmHg.

Pharmacological treatment

There is sufficient evidence that shows that in non-diabetic nephropathy of different types the ACEIs reduce the risk of progression to TRI and/or of duplicating the serum creatinine in comparison with the placebo (10). Whether there are differences between the different ACEIs has not been evaluated and, in general, the concomitant use of other antihypertensives was permitted.

With regard to other antihypertensives, different analyses subsequent to the ALLHAT trial did not show differences among chlorathalidone, lisinopril or amlodipine in the population with renal insufficiency in renal results or in cardiovascular results (137). However, the type of patient included, with high cardiovascular risk, as well as the trial's design, different from the others of specific nephropathy studies, could explain the absence of benefits of the ACEIs in this case.

RCT 1+

One Meta-analysis (131) questioned whether the benefits of ACEIs (or ARA II) are due to specific nephroprotective effects of the inhibition of the renin-angiotensin system by not finding significant differences between ACEIs or ARA II and other antihypertensives in the result variables of "creatinine duplication" or TRI. It suggested that, like the decrease in the BP numbers, there does not appear to be an additional benefit in the ACEI/ARA II (supposed "nephroprotective" effect). In the subanalysis of the patients with non-diabetic nephropathy these differences did not appear either, but the confidence intervals found are very wide and a beneficial effect of the ACEIs cannot be ruled out. In the ACEIs or ARA II analyses compared to the placebo, the difference for the TRI result variable is indeed significant.

SR of RCT 1+

One must take into account that the increases in the serum creatinine of up to 30% that are stabilized in the first two months of therapy with ACEIs are correlated to the long-term preservation of renal function, for which reason the ACEI treatment should only be interrupted when the serum creatinine concentration is over 30% of the basal number in the first two months or if hyperpotassemia develops (10).

As for ARA II, no study was found with sufficient duration to compare ARA II *vs.* placebo for clinically relevant result variables.

The base CPGs coincide in recommending ARA II in case the treatment with an ACEI produces secondary effects that require suspending the drug.

CPG

The majority of the trials that studied whether the combination of ACEI with ARA II is more effective than each drug alone only evaluate proteinuria as the result variable. The only RCT found that evaluates TRI or creatinine duplication is the COOPERATE study (138), in which the combination of losartan+trandolapril achieved a reduction in the combined result of TRI or creatinine duplication compared to losartan.

RCT 1++

In a systematic review that evaluated changes in BP and proteinuria (139), it was shown that there is a tendency towards a greater decrease in proteinuria with the combination of ACEI and ARA II (crossover trials of variable quality and maximum treatment duration of 16 weeks); nevertheless, they also show higher reductions in BP with the combined therapy than this result could explain.

RCT 1+

SR of RCT 1+

Recommendation	
A	The use of ACEI is recommended as the initial treatment for hypertensive patients with non-diabetic nephropathy.
B	In case of intolerance (secondary effects that require withdrawing the drug) of ACEIs, an ARA II is recommended as an alternative initial treatment.
✓	The ACEI or ARA II could be used whenever there is no bilateral stenosis of the renal arteries or unilateral stenosis in a single kidney.
✓	The combination of ACEI with ARA II can be useful in certain patients whose selection must be done in the specialized care area.

3.3.4. Congestive cardiac insufficiency (CCI)

QUESTIONS TO ANSWER

- What is the antihypertensive treatment of choice in the hypertensive patient with cardiac insufficiency for left ventricular systolic dysfunction?

2007 UPDATE

3 new RCTs (140-142) and 3 new SRs (143-145)
Recommendation completed

The RCTs in patients with cardiac insufficiency or left ventricular systolic dysfunction have evaluated drugs with antihypertensive properties but their benefits in patients with CCI and AHT were not specifically evaluated. The benefits of treating AHT in patients with CCI are not well known and the progression of CCI is frequently associated to a decrease in BP because of impairment of the cardiac function.

ACEI and ARA II

SR of RCT 1+/1++

Treatment with ACEIs reduces mortality by 20% and the risk of hospitalization by 33%, independently of the aetiology and the functional class of the CCI (10; 146).

The evidence is solid and consistent regarding the absence of additional benefits of ARA II on ACEIs (143). The evidence is solid for recommending an ARA II in case of intolerance of the ACEI, especially since the publication of the CHARM-alternative (141), which showed benefits precisely on this population.

RCT 1+

Questions and inconsistencies are posed regarding the combination of ACEI and ARA II. This combination does not produce benefits in mortality but it does in hospitalization for CCI (143). The inconsistencies basically arise in the subgroups of patients that in addition to an ACEI receive BB. In a systematic review (144) it is shown that in patients that do not take BB, the combination of ARA II and ACEI can have beneficial effects on morbimortality, due principally to the reduction in the hospitalization risk, although without differences in total mortality. In patients being treated with ACEI and BB, there is heterogeneity among the studies. While in the ValHeFT trial (147) (with valsartan) an increase in total mortality was produced with respect to the placebo, in the CHARM-added trial (140) on candesartan compared to a placebo, the risk of cardiovascular death and hospitalization for CCI were reduced and no differences in total mortality were given.

RCT 1+

In summary, the clinical impact of using the combination ARA II+ACEI is not clear. It does not provide benefits in total mortality but it can have benefits in reducing the risk of hospitalization for CCI, which is clearer in the population that is not taking added beta blockers. However, it presents an increase in the adverse effects, basically an increase in creatinine, hypotension and hyperpotassemia, provoking an absolute difference of 5.9% in the abandonments of the treatment.

These same effects were observed in the branch of the ONTARGET (110) study that compared the association of ACEI + ARA II (ramipril and telmisartan) to each of them in patients with high cardiovascular risk but without symptomatic cardiac insufficiency.

Beta blockers

The BB treatment (metoprolol, bisoprolol, carvedilol) reduces mortality and the risk of hospitalization in patients with stable cardiac insufficiency with functional class NYHA II-IV (10; 148; 149).

SR of RCT 1++

In patients over 70 years of age, nebivolol compared to a placebo reduced the combined result variable of total mortality and hospitalization for cardiovascular cause (142). Other published studies (150; 151) found benefits in the beta blockers in women and in diabetic patients, while in black patients no significant effects were found.

RCT 1+

Calcium antagonists

No new evidence has been found on calcium antagonists in cardiac insufficiency. Amlodipine and felodipine do not decrease mortality in patients with CCI and must be reserved for those patents as additional drugs for treating uncontrolled AHT, or as anti-anginal drugs (10).

Diuretics

A Cochrane review (145) on the use of diuretics (loop, thiazides, etc.) in CCI provided solid proof that diuretics relieve the symptoms, reduce the episodes of decompensation and increase the capacity to do exercise, but the tests are weak regarding an effect on the mortality in patients with chronic cardiac insufficiency. However, in all the broad clinical trials in which a reduction of mortality or of the risk of hospitalization for cardiac insufficiency has been shown for the different drugs, more than 90% of the patients received this type of diuretics as the base treatment.

SR of RCT 1+

Recommendation	
A	All hypertensive patients with CCI independently of its aetiology or functional class should be treated with ACEIs, as long as they do not present contraindications and their use is tolerated. In patients that do not tolerate their use, an ARA II is recommended.
A	All hypertensive patients with CCI in functional class II-IV, in stable phase and with previous standard treatment (ACEI, diuretics and/or digoxin) should be treated with beta blockers.
✓	The titration of the dosage of beta blockers should be done slowly and weekly to improve tolerance.
✓	The recommended beta blockers are: bisoprolol, carvedilol, metoprolol retard, nebivolol.
B*	The ACEI+ARA II combination (valsartan or candesartan) is recommended as an alternative in hypertensive patients with CCI in which beta blockers are not tolerated or are contraindicated.
✓	Monitoring of the adverse effects of the ACEI+ARA II combination (hypotension, hyperpotassemia and impairment of renal function) is recommended.

2007

2007

2007

B*	In case of poor control of AHT, despite optimizing the dosage of ACEI, beta blocker and diuretic, candesartan can be added.
B	Dihydropyridines should not be used in hypertensive patients with CCI as part of the standard treatment.
✓	Only long-acting dihydropyridines (amlodipine, felodipine) should be used if additional drugs are needed to control the BP or as anti-anginal drugs.

* The recommendation level is decreased due to being an analysis of subgroups.

3.3.5. Ischaemic cardiopathy

QUESTIONS TO ANSWER

- What is the treatment of choice in hypertensive patients with stable angina?
- What is the treatment of choice in hypertensive patients that have suffered myocardial infarction?

2007 UPDATE

2 new SRs (154; 155) and 6 new RCTs (110; 152; 153; 156-158)
Recommendation without substantial modifications

In recent decades, the natural history of ischaemic cardiopathy has been greatly modified, due to the great progress acquired in interventionist cardiology, so that at present it is usual to conduct an angiographic study on many of these patients, and, where applicable, the practice of coronary revascularization procedures. For this reason, different clinical trials have been designed, under the heading of stable coronary cardiopathy, that include patients with previous AMI and those with coronary cardiopathy documented angiographically (but without previous AMI), subjected or not to revascularization procedures, as well as patients with coronary cardiopathy without angiography.

RCT
1+

The majority of the RCTs published since 2002 in ischaemic cardiopathy have studied the effect of ACEIs or calcium antagonists.

Beta blockers

Studies that show a decrease in morbimortality with beta blockers were conducted on patients that had suffered an AMI, with or without systolic dysfunction and the results are consistent among the different Meta-analyses (10). In stable angina, they are recommended as the first option, ahead of the calcium antagonists, not only for their anti-anginal properties but also extrapolating the evidence of decrease of morbimortality by AMI.

SR of RCT 1+

ACEI and ARA II

The benefits of the ACEIs in patients that have suffered an AMI with systolic dysfunction are clear (10). Furthermore, there is proof of therapeutic equivalence between ACEI and ARA II in these patients, derived from the OPTIMAAL (154) and VALIANT (155) trials, conducted with losartan and valsartan, respectively. The ACEI+ARA II combination was studied in the VALIANT trial, finding no differences in the benefits of morbimortality, but differences were found in the adverse effects that caused the suspension of the treatment in the group treated with the combination.

RCT 1+

Two Meta-analyses (152; 153) in patients with ischaemic cardiopathy without systolic dysfunction showed that ACEIs added to the usual treatment (compared to a placebo) decreased total mortality and cardiovascular mortality. Within the included trials, those that obtained best results were the HOPE and EUROPA (159), where the dosages used were high, ramipril 10 mg and perindopril 8 mg respectively, and it was not clear if the same benefits could be obtained with lower doses. In the two trials with enalapril the dosages used were 10 mg/12 hours.

SR of RCT 1+

In the recent ONTARGET trial (110), telmisartan was not shown to be superior to ramipril in the prevention of cardiovascular morbimortality in patients in secondary prevention (74% with coronary disease and 49% post-infarction).

RCT 1++

Calcium antagonists

With calcium antagonists different heterogeneous studies were conducted. The INVEST trial (156) (hypertensive patients with ischaemic cardiopathy) compared the verapamil (+trandolapril) strategy to the atenolol (+hydrochlorothiazide) strategy. No differences were found in any of the result variables evaluated. Therefore, verapamil can be considered an alternative to the beta blockers in ischaemic cardiopathy if the latter are contraindicated (not associating both types of drugs due to the risk of bradycardia).

RCT 1+

For dihydropyridines, the only trial with favourable results is the CAMELOT (157), that compared amlodipine to a placebo and to enalapril in patients with ischaemic cardiopathy and "normal" BP (DBP <100 mmHg). Compared to enalapril, the differences were not significant.

RCT 1+

In patients with stable angina, in the ACTION study (158), nifedipine GITS (added to the usual treatment) was shown to be effective in the prevention of cardiovascular morbimortality in the subgroup of hypertensive patients.

RCT 1+

The reservations on the use of immediate-release nifedipine (10) are maintained.

Recommendation	
A	Beta blockers are the drugs of choice in the treatment of AHT in hypertensive patients with a history of AMI.
B*	Beta blockers are the drugs of choice in AHT treatment in patients with stable angina.
A	All hypertensive patients with previous AMI with or without left ventricular systolic dysfunction must be treated with ACEIs if there is no contraindication or intolerance of them.
A	An ARA II is recommended in all hypertensive patients with previous AMI and systolic dysfunction with intolerance of ACEIs.
B	The calcium antagonists should not form part of the initial treatment in hypertensive treatments that have suffered an AMI. They are recommended only if they are necessary as part of the antihypertensive treatment in achieving the target BP.
A	In all the patients with ischaemic cardiopathy and arterial hypertension, adding an ACEI to the treatment must be firmly considered.
B	In hypertensive patients with ischaemic cardiopathy, calcium antagonists (verapamil, amlodipine and nifedipine GITS) can be used as an alternative to the beta blockers.

2007

(continued)

2007

Recommendation (continuation)	
B	If another drug is required to be added to the beta blocker in hypertensive patients with ischaemic cardiopathy (to control the symptoms or to achieve the BP target numbers), the use of a dihydropyridine is recommended.
B	Immediate-release nifedipine should not be used in hypertensive patients with angina.
✓	If an ACEI is added to the hypertensive treatment with ischaemic cardiopathy, attempts should be made to reach the dosages used in the clinical trials (ramipril 10 mg, perindopril 8 mg), especially if the desired target BP has not been reached.

* It cannot be established conclusively that there are no differences between the beta blockers and the calcium antagonists as regards morbimortality.

3.3.6. Cerebrovascular disease

QUESTIONS TO ANSWER

- What is the treatment of choice in hypertensive patients that have suffered a cerebrovascular accident?

2007 UPDATE

1 new Meta-analysis (160)
No changes to the recommendation

A Meta-analysis (160) conducted on patients that had suffered a CVA (60-65% of hypertensive patients), and which included the PROGRESS (161) study, added consistency to the evidence that antihypertensive treatment reduces the risk of suffering a new CVA, although statistically significant differences in the reduction of the cardiovascular mortality or in total mortality were not shown. As regards the treatment of choice in these patients, diuretics and/or an ACEI could be a good choice according to the results of this Meta-analysis. The combination of ACEI+diuretic seems to be the one that obtains greater benefits,

SR of RCT 1+

decreasing the risk of a new CVA, of AMI and of vascular events (data of a single RCT, PROGRESS); diuretics alone (fundamentally indapamide) decrease the risk of a new CVA and of total vascular events, but not of AMI, and the ACEIs in single-drug therapy only decrease the risk of AMI (data of 2 RCTs, PROGRESS and HOPE).

RCT 1+

One of limitations of these trials is that lower BP numbers are achieved in the branch of treatment than in that of the placebo, for which reason one cannot rule out a large part of the benefits are explained by the decrease in the BP.

Recommendation	
A	All hypertensive patients that have suffered a cerebrovascular accident must be treated with antihypertensives.
A	The combination of indapamide with perindopril is appropriate for the treatment of hypertensive patients with previous CVA.

3.3.7. Peripheral arteriopathy

QUESTIONS TO ANSWER

- What is the guideline for antihypertensive treatment in patients with intermittent claudication?

2007 UPDATE

1 new SR (162)
No changes to the recommendation

A Cochrane review (162) on the treatment of the AHT in peripheral arteriopathy did not find any study in which cardiovascular events were evaluated as a result variable. No statistically significant differences were observed in the claudication distance variables or changes in the ankle-arm index.

SR of RCT 1+

In the analysis of the subgroup of the HOPE trial (163) on patients with peripheral arteriopathy (50% hypertensive patients), the treatment with ramipril 10 mg is associated with a reduction of the cardiovascular events in patients with symptomatic as well as asymptomatic peripheral arteriopathy. In another study (164) of only 40 patients (not hypertensive or diabetic), ramipril 10 mg increased the time of walking free of pain and total. These studies have many limitations and it was considered that there is insufficient evidence for recommending an ACEI specifically in this indication.

RCT 1+

As for the use of beta blockers, we refer to the evidence indicated in the previous version of the guidelines (10).

SR of RCT 1+

Recommendation	
B	The AHT treatment in patients with peripheral arteriopathy should follow the general recommendations.
B	The cardioselective beta blockers can be used in stable peripheral arteriopathy in the mild or moderate phase whenever there is a firm indication for use.

3.3.8. Left ventricular hypertrophy

QUESTIONS TO ANSWER

- What is the treatment of choice for AHT with LVH?

2007 UPDATE

New question

In the LIFE study (165), there were no differences between losartan and atenolol in cardiovascular mortality (principal variable of the study), although losartan was superior in reducing CVA. In the subgroup of the diabetic patients (109), the benefit from losartan compared to atenolol was greater, also observing a decrease in total mortality.

RCT 1++

Cohort study 2+

A sub-study of the LIFE clinical trial that included monitoring for 4.6 years found that the regression of LVH is related to the decrease in cardiovascular and total mortality (166).

A Meta-analysis (167) analyzed the effects of the different classes of antihypertensive patients in the regression of the left ventricular mass. The ARA II decreased it by 13% (CI 8-18%), calcium antagonists by 11% (CI 9-13%), ACEIs by 10% (CI 8-12%), diuretics by 8% (CI 5-10%) and beta blockers by 6% (CI 3-8%). There were no significant differences in the comparisons by pairs except for the beta blockers, which reduced the left ventricular mass in a lesser proportion than the ARA II, calcium antagonists and ACEIs.

In the previous version of the CPG, the use of losartan was considered preferable to atenolol in the treatment of hypertensive patients with LVH, particularly in diabetics. However, in light of current evidence, and since it can be less effective in the regression of the LVH (see the beta blockers section), atenolol cannot be considered an adequate comparer, for which reason trials are needed among the different families of antihypertensives in order to be able to make firm recommendations in this situation.

2007

Recommendation	
D	The treatment of AHT if there is left ventricular hypertrophy must follow the general recommendations.

3.3.9. Asthma and COPD

QUESTIONS TO ANSWER

- What is the antihypertensive treatment guideline for the patient with asthma or COPD?

2007 UPDATE

2 updated Cochrane SRs (168; 169) and 2 new observational studies (170; 171)
No changes to the recommendation

Two Cochrane reviews (184; 185) showed that the use of short-term cardioselective beta blockers does not significantly alter pulmonary function in patients with asthma or COPD in mild or moderate phases. Data from observational studies (170; 171) in patients with asthma or COPD and associated cardiovascular diseases, under treatment with beta blockers, showed that these do not increase mortality by all causes or the risk of respiratory exacerbations compared to other antihypertensives, although as they are observational studies, bias is not ruled out. Therefore, the beta blockers could be used in these patients in case of firm indications (ischaemic cardiopathy or congestive cardiac insufficiency).

SR of RCT 1+

Observational studies 3

Recommendation	
B	The general recommendations for antihypertensive treatment should be followed in patients with asthma or COPD.
B	In patients with asthma or COPD in mild or moderate phases, the cardioselective beta blockers can be used with precaution, whenever there is a firm indication for their use (ischaemic cardiopathy or congestive cardiac insufficiency).
✓	In case of severe COPD and asthma associated with ischaemic cardiopathy, the use of beta blockers must be individualized, evaluating the benefits and risks of the measure.

3.4. Combined drug therapy

QUESTIONS TO ANSWER

- In case of not achieving the target BP numbers, is it preferable to increase the dosage of the antihypertensive in a single drug or combine it with another drug?

2007 UPDATE

1 new SR (111) and 2 new RCTs (94; 110)
Modified recommendation

SR of RCT 1+

An SR (111) found that, in single-drug therapy, duplicating the dosage of the drugs did not improve the control of the BP numbers in a directly proportional way; however, with the diuretics, BB and calcium antagonists, the frequency of adverse effects increased considerably; this is not so with the ACEI and ARA II. On the contrary, used at half the dosage, a lesser decrease in BP (around 20%) was achieved but with a more significant reduction of the adverse effects with the first three families of the cited antihypertensives.

This same SR provided data on six combinations (diuretic+ACEI, diuretic+BB, diruetic+calcium antagonist, diuretic+ARA II, calcium antagonist+ACEI, and calcium antagonist+BB). The results showed that the control of the BP numbers is only somewhat less than expected by the additive effect, even using them at half dosage, with the advantage of the decrease in the adverse effects (10.4% at standard doses *vs.* 7.5% at half doses). For these reasons, the review concluded that the antihypertensives in combination can be considered, at half the standard dosage in the case of diuretics, BB and calcium antagonists, and at usual dosages in the case of the ACEI and ARA II.

The question about which combination to choose is fundamentally based on the pharmacological characteristics of the different antihypertensives, in an attempt to strengthen the antihypertensive effectiveness, minimizing the secondary effects (Figure 2). From this perspective, the drugs of the first column are considered for combination with any of the second column and vice versa. The combination between those of the same column is less recommendable unless there is a specific indication for a disease associated with AHT (10).

The ACEI+ARA II combination (telmisartan and ramipril) in the ONTARGET study (110) reduced the SBP by 2.4 mmHg and the DBP by 1.4 mmHg with respect to ramipril, but at the expense of a significant increase in the impairment of the renal function (1.1%) and of the abandonment of the treatment for adverse effects (29.3%) in a cardiovascular high-risk population. This association is not an advisable option for increasing the degree of decrease of the BP, as advanced in a recent Meta-analysis (172).

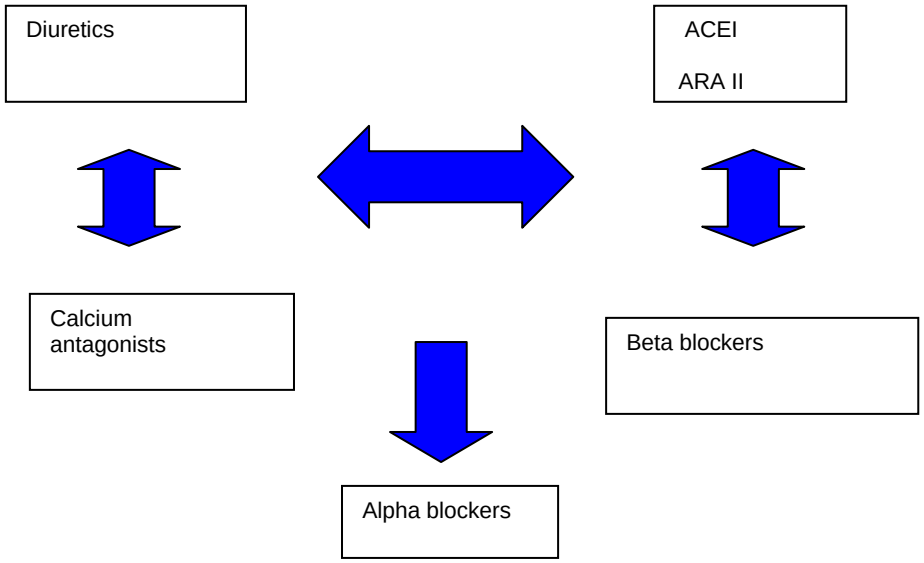
RCT 1++

SR of RCT 1+

Finally, the alpha blockers can be combined with any, but this strategy must be used only when other associations fail or cannot be used (10).

RCT 1++

Figure 2. **Diagram for the association of antihypertensives**



Recommendation	
A	When single-drug therapy is insufficient, it is better to combine antihypertensives at half dosages in the case of diuretics, BB or calcium antagonists or with usual dosages of ACEI or ARA II, than to double the single-drug dosage.
D	The choice of the combination of antihypertensive drugs among the associations on which studies have been conducted will be according to professional criteria, taking into account their pharmacological characteristics and their profile of adverse effects.
A	The use of the ACEI+ARA II combination is not recommended for increasing the degree of decrease of the BP.

2007

2007

2007

3.5. Hypertensive urgency

QUESTIONS TO ANSWER

- Must severe BP numbers be treated in a patient with no target organ affection?

2007 UPDATE

New question

The definition of hypertensive urgency as a situation that requires immediate treatment to decrease the BP numbers is a question for debate and the majority of the proposals are the product of consensus or are based on observational studies, case series or low-quality RCTs. There is agreement on calling it a **hypertensive emergency** when, besides the high BP numbers (>180/120 mmHg (173) or >180/110 mmHg (174)), there is target organ affection (hypertensive encephalopathy, CVA, acute lung oedema, left ventricular failure, aortic dissection, ischaemic cardiopathy, renal insufficiency and/or eclampsia). If there is no affection, one speaks of **hypertensive urgency** or **severe hypertension.** (174).

Experts' opinion 4

The usual clinical presentation of these high BP numbers is known through observational studies (175; 176) conducted in emergency rooms. Seventy-six percent correspond to urgencies and 24% to emergencies. The most frequent symptoms reported in the hypertensive urgencies are: cephalea (22%), epistaxis (17%) and weakness (10%). The most frequent symptoms in the emergencies are: thoracic pain (27%), dyspnoea (22%) and neurological deficit (21%).

Observational studies 3

With respect to the prognostic involvement of high BP without target organ affection of the data from the VA Cooperative Trial, a low risk of developing cardiovascular complications in the short term (177) was reported.

The remainder of the RCTs found that compare treatment *vs.* placebo measure only intermediate results on the BP control (178).

RCT 1+

Before dealing with high BP numbers without target organ affection, one must take into account that:

1) The repetition of the BP readings can lower blood pressure to moderate numbers, according to RCT conducted on a few patients (179), to a retrospective study (180) and from the fact that a large part of the spontaneous decrease in BP can be explained by the regression-to-the-mean phenomenon (181).

RCT 1+

2) A rapid lowering of the initial BP does not improve the control at 24 hours or at one week (182).

3) The rapid reduction of the BP is not exempt from risks such as hypotension, sedation, cephalea or facial erythema, the majority of which are resolved without consequences (178). However, the use of sublingual nifedipine has been related to serious effects of the appearance or worsening of ischaemic processes (178), AMI (183; 184) or left ventricular failure (185), generally caused by rapid drops in BP (>25% of the initial value).

Descriptive and cohort studies 2+/3

Despite the weak evidence, there is agreement in questioning the urgent treatment of high blood pressure without target organ affection and on considering that the best control of this elevation is the intensification of long-term control of their BP.

Shayne (186) considers progressively lowering BP over 24-48 h in patients without criteria of target organ affection but with a high probability of having it (patients with history of cardiac insufficiency, angina, CVD, renal insufficiency, CVA).

Experts' opinion 4

Recommendation	
C	In view of a high AHT number in an asymptomatic patient or with symptoms that do not suggest target organ affection, this value must be confirmed with various subsequent measurements, after eliminating aggravating factors.
D	In view of high AHT in an asymptomatic patient or without suggestive signs of target organ affection, a gradual decrease in BP should be attempted, seeing the patient in the following days to adjust the treatment.

2007

2007

APPENDIX 1.
Methodology in updating the CPG

This work has attempted to bring together the best evidence on the questions posed on the care of the hypertensive patient.

The update was done according to a structured plan from the CPG on AHT published by Osakidetza in 2002, following the same methodological principles as in the original version.

After the formation of the CPG editing team and of a "committee of experts" in AHT, a list of **clinical questions** was drawn up starting principally with the questions of the previous version with the inclusion of proposals by the editing team after group discussions and the proposals of the committee of experts through a previously designed instrument.

Previously, at the start of the work, some "base" CPGs were selected by applying the AGREE instrument to different **national** and **international CPGs** on AHT published in the 2002-2006 interval.

The three guidelines that obtained the highest score based on the AGREE instrument were: the Canadian CPG, the one from the NICE and the BHS guidelines. These three CPGs were used in the successive steps.

For the new questions, not included in the 2002 CPG, these CPGs were initially consulted.

The following possibilities could occur:

- Question answered and updated in the base guidelines
- Question with the need to be updated
- Question not answered

For the questions included in the previous version, the bibliography provided by the committee of experts and that included in the selected CPGs were used and the systematic **search** of the literature limited to the 2002-2007 period was updated. A bibliographic alert service was maintained to incorporate relevant studies up to the time of publishing the CPG.

For all the searches, the **information sources** used were: Clinical Evidence, Evidence-Based Reviews, Cochrane Library, Medline, Embase, Índice Médico Español, IBECS, UpToDate and Tripdatabase. The publications were prioritized according to the following order: systematic reviews, clinical trials, cohort studies, case-control studies, descriptive studies and experts' opinion.

The considered references were **evaluated** independently by at least two reviewers with the explicit criteria of the NICE (National Institute for Clinical Excellence) for the questions about diagnoses and of SIGN (Scottish Intercollegiate Guidelines Network) for the questions on prognosis, aetiology and treatment. The differences were resolved by means of consensus.

For those questions not directly adapted from the base CPGs, the evaluated references were summarized in the form of **evidence tables,** which served to draw up a "formal evaluation" or "reasoned opinion" which is the basis for formulating the **final recommendations.**

With regard to the previous recommendations, the update has supposed:

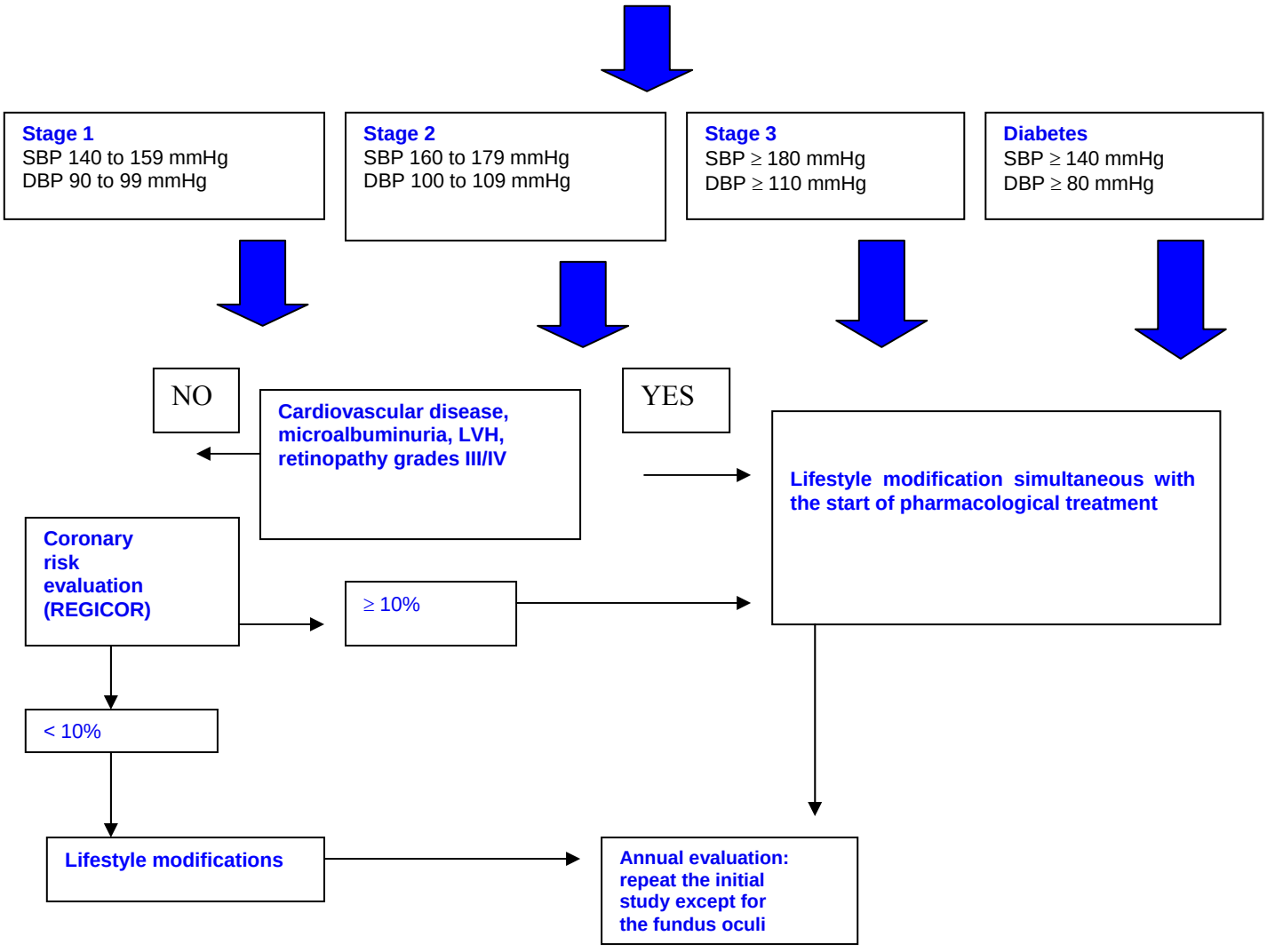
- Recommendation not modified: it **coincides** with the one recommended in the previous CPG.
- Recommendation completed: the recommendation goes **along the same line** as the previous version but the new evidence completes or expands the previous recommendation.
- Modified Recommendation: the new evidence means a **relevant change** in the recommendation.

These Guidelines have been evaluated by **external reviewers** who are experts in the area of hypertension as well as in the methodology field, by means of a previously designed instrument, so that each proposal for modification must be justified with its corresponding bibliographical reference.

APPENDIX 2.

Initial study and monitoring of hypertensive patients

D	The **initial study** proposed for hypertensive patients is comprised by a cardiovascular physical examination, blood analysis (glycaemia, creatinine, sodium, potassium, uric acid, cholesterol, HDL, TGC, LDL, urine sediment, albumin/creatinine ratio), ocular fundus and ECG.



Target numbers (mmHg)	
General	SBP <140 DBP <90
Diabetes	SBP <140 DBP <80
Renal insufficiency Proteinuria <1g	SBP <130 DBP <85
Renal insufficiency Proteinuria ≥1g	SBP <130 DBP <80

APPENDIX 3.

Rules for the correct measuring of blood pressure

(based on the previous version of the CPG and modified from *)

BP measurement should be done under the subject's normal conditions for which reason we must make sure that he rests at least 5 minutes, repeating the measurement at the end of the consultation if necessary.

Examined subject:

- **Position:** seated, back supported, arm relaxed without clothing that compresses it and resting on a table or support, with the palm of the hand upwards and the elbow slightly flexed at the height of the heart.
- **Psychophysical and environmental conditions:** minimum rest of 5 minutes in a calm room and with warm temperature. Avoid: prior efforts, anxiety, smoking, vesical distension, pain, or eating in the half hour before measuring.

Observer

- Appropriate training, good visual and acoustic conditions. Visualization of the mercury column at the height of the eyes.
- No rounding of numbers. Note the exact number.

Measuring equipment

- Cuff or sleeve of fabric or synthetic material, in whose interior is the inflatable tubing, with dimensions (referring to the tubing) of:

– Width: 40-50% of the total circumference of the arm. The width multiplied by 2.5 defines the ideal circumference of the arm for this cuff. Example: Width 12 cm x 2.5 = 30 cm. An arm of 30 cm in circumference needs a cuff whose rubber tubing is 12 cm.
– Length: the relation between the length and width must be 2:1. The cuffs are printed with the maximum and minimum of the admissible circumference.

- The inflating system, the release valve and the connector tube must be checked periodically to avoid air leaks or malfunctioning.

Technique for measuring the BP

- Subject in correct position and conditions following the above instructions.
- **Use a cuff with the proper width for the size of the arm. In case of a brachial perimeter > 32 cm** the use of the wide cuff ("for obese arms") is required.

- Locate the brachial artery by palpation along the inside face of the arm.
- Place the cuff so that the inflatable tubing is located above the arterial beat, then adjust it carefully. The lower edge must be 2 cm above the antecubital fossa.
- The cuff must surround the circumference of the arm at the midpoint between the shoulder and the elbow. The tubing of the cuff must surround 80% of the arm.
- Phonendoscope on the brachial artery in the cubital fossa (inside face of the elbow fold), applying mild pressure. Never insert the phonendoscope under the cuff.
- Inflate the tubing rapidly up to 70 mmHg and then increase the pressure by 10 mmHg increments, palpating the radial pulse. Note the level of pressure at which the pulse disappears and again returns by deflating.
- The observer must correctly put on the phonendoscope, and then place its head using the position of low frequency (membrane) above the pulse of the brachial artery.
- Inflate the tubing rapidly 20 or 30 mmHg above the number detected previously. Then partially open the valve, deflating the tubing at a rate of 2 mmHg/second.
- The pressure level at which the first dry and repetitive sound appears is the Korotkoff phase I and constitutes the SBP. The disappearance of the sound is the Korotkoff phase V and constitutes the DBP.
- After the disappearance of the last sound, slowly deflate another 10 mmHg to be sure you will hear no further sounds.
- Record the SBP (phase I) and DBP (phase V) as accurately as possible (discriminating at intervals of 2 mmHg).
- Repeat the BP measurement after making sure of the complete emptying of the tubing. It is necessary to wait between one and two minutes before taking a new reading.
- Measure the BP in both arms and take into consideration the highest result.
- *No. of readings: **obtain the mean of the first 2 consecutive BP measurements between which there is no more than a 5-mmHg difference.**

The most common causes of incorrect BP readings are:
• Use of narrow cuffs for obese arms • Lack of prior rest • Rapid deflating • Rounding the numbers obtained to zero or to five

APPENDIX 4.

Recommended Ambulatory Blood Pressure Monitoring (ABPM) Devices

(Oscillometrics, validated according to the protocols of the Association for the Advancement of Medical Instrumentation (AAMI), of the British Hypertension Society (BHS) or European Society of Hypertension (ESH*))

Device	Type	AAMI	BHS	ESH	Circumstance
A&D TM-2430	Osc	Passed	A/A		At rest
IEM Mobil O Graph (version 12)	Osc	Passed	B/A		At rest
Meditech ABPM-04	Osc	Passed	B/B		At rest
Save 33, Model 2	Osc	Passed	B/B		At rest
Spacelabs 90207	Osc	Passed Passed Passed	B/B B/B A/B		At rest In pregnancy Elderly standing and SBP <161 mmHg
Spacelabs 90217	Osc	Passed	A/A		At rest
Suntech AGILIS	Osc			Passed	At rest
Suntech Medical OSCAR 2	Osc			Passed	At rest
Tensioday	Osc	Passed	A/A		At rest

Association for the Advancement of Medical Instrumentation=AAMI, British Hypertension Society=BHS. TM= Takeda Medical. In order to pass the criteria of the AAMI, the difference of systolic and diastolic blood pressure between the studied device and the mercury device must be ≤5 mmHg and the standard deviation must be ≤8 mmHg. The validation following the criteria of the BHS must be at least grade B for the systolic and diastolic blood pressure. The grades signify a percentage of BP readings within 5, 10 and 15 mmHg (A, B, C) with respect to the mercury sphygmomanometer. All the percentages must be less than or equal to the values shown in order to reach a specific grade. There are other devices that do not meet both criteria and are not included in the above table.

*Consult updates in the Web page http://www.dableducational.com

Absolute difference between the standard and the studied device (%)			
Grade	**≤ 5 mmHg**	**≤ 10 mmHg**	**≤ 15 mmHg**
A	≤ 60%	≤ 85%	≤ 95%
B	50-59%	75-84%	90-94%
C	40-49%	65-74%	85-94%
D		Less than C	

APPENDIX 5.

Instructions for the use of ambulatory blood pressure monitoring (ABPM)

(Recommendation of the British AHT Society 2000)

1. Programme the monitor so that it takes BP readings every 30 minutes.
2. The patient must be relaxed in a calm room.
3. Measure the BP in both arms.
4. If the difference in the systolic BP of both arms is < 10 mmHg, place the ABPM on the non-dominant arm.
5. If the difference is ≥10 mmHg, place the monitor on the arm that has the highest BP.
6. Select the appropriate cuff. The tubing of the cuff should surround 80% of the arm.
7. Deactivate the display of the BP readings.
8. Give the patients the written instructions.
9. Teach the patient how to disconnect the device after 24 hours.
10. More than 14 readings of systolic and diastolic BP are necessary during the day and more than 7 readings of the systolic and diastolic BP during the night.

Explain to the patient:

1. The procedure.
2. The frequency of inflating and deflating.
3. How to manually deflate the device.
4. That in case of failure to read, the device will repeat the measurement.
5. That the arm must be kept quiet and at the height of the heart while measuring.
6. That the normal activities must be carried out between the measurements.
7. That the monitor must be kept in place during the night, putting it under the pillow.
8. That the health centre can be contacted telephone if there is any problem.
9. Give him the journal sheet so that he may note:
    - His activities at the time of the measurement.
    - When he goes to bed.
    - When he gets up.
    - When he takes the antihypertensive treatment.
    - Any symptom.

APPENDIX 6.

Recommendable automatic oscillometric devices for home self-measurement of blood pressure (SMBP)

(Brachial or wrist models, valid according to the protocols of the Association for the Advancement of Medical Instrumentation/AAMI, of the British Hypertension Society/BHS or European Society of Hypertension/ESH*)

Brachial device	Type	AAMI	BHS	ESH	Use
A&D UA-631 (UA-779 Life Source)	Osc			Passed	At rest
A&D UA-705	Osc		A/A		At rest
A&D UA-767	Osc	Passed	A/A		At rest; no high BP
A&D UA-774 (UA-767 Plus)	Osc		A/A		At rest; Incomplete tables
A&D UA-787	Osc			Passed	
Colson MAM BP3AA1-2	Osc			Passed	At rest
Microlife BP 3AC1-1	Osc			Passed	At rest
Microlife BP 3AC1-1 PC	Osc			Passed	BP 3AC1-1 Equivalence
Microlife BP 3AC1-2	Osc			Passed	BP 3AC1-1 Equivalence
Microlife BP 3AG1	Osc		A/A		BP 3BT0-A Equivalence
Microlife BP 3BTO-1	Osc		A/A		BP 3BT0-A Equivalence
Microlife BP 3BTO-A		Osc	A/A Passed Passed Passed	A/B BB A/B	In normotensive pregnant women En absence of proteinuria Pre-Eclampsia
Microlife BP 3BTO-A(2)	Osc		A/A		BP 3BT0-A Equivalence
Microlife BP 3BTO-AP	Osc		A/A		BP 3BT0-A Equivalence
Microlife BP A 100	Osc		Passed		BP A 100 Plus Equivalence
Microlife BP A 100 Plus	Osc		Passed		At rest
Microlife RM 100	Osc		A/A		BP 3BT0-A Equivalence

(continued)

Brachial device	Type	AAMI	BHS	ESH	Use
Omron 705IT	Osc	Passed	A/A	Passed	Reasonable adaptation in children and adolescents
Omron M5-I	Osc		Passed		
Omron M6				Passed	At rest
Seinex SE-9400	Osc			Passed	At rest

Wrist device	AAMI	BHS	ESH	Circumstance
Braun BP 3550			Passed	At rest. Questionable for very high BP numbers.
Braun PrecisionSensor BP2550 (UG)			Passed	At rest
Omron 637IT			Passed Passed Passed	Adults Obese adults Obese elderly patients
Omron R7			Passed	At rest

The empty cells indicate that up to now the validation has not been made.

Association for the Advancement of Medical Instrumentation=AAMI, British Hypertension Society=BHS. In order to pass the criteria of the AAMI the difference in both systolic and diastolic blood pressure between the device studied and the mercury device must be ≤5 mmHg and the standard deviation must be ≤8 mmHg. The validation following the criteria of the BHS must be at least level B for the systolic and diastolic blood pressure. ESH: grading according to the international protocol of the European Society of Hypertension, Overall pass or fail.

Consult updates in the Web page: www.dableducational.com

APPENDIX 7.

Rules for the home self-measurement of blood pressure*

Remember these rules for measuring blood pressure in your home

Before beginning...

1. Do not measure during the hour after eating or physical exercise, or in situations of stress or pain.
2. Avoid coffee, alcohol and tobacco for half an hour prior to measuring.
3. Empty the bladder.
4. Remain seated for at least five minutes before.
5. Adopt a comfortable and relaxed position, with your back supported and avoid crossing your legs.
6. Room with a comfortable temperature (the cold can increase the BP numbers).

To measure …

1. The rubber tubing inside the cuff must be between 80 and 100% of the circumference of the arm. Excessively large cuffs measure the blood pressure lower than the actual numbers and the reverse if they are small.
2. Place the cuff in the centre of the arm, 2-3 cm above the elbow fold.
3. Support the arm on the table, without clothing that compresses it, and keeping it approximately at the height of the heart. The blood pressures should be measured in the arm that the health centre indicated to you as the control arm.
4. Follow the instructions of the device in making the measurement.
5. Do not move or squeeze the arm while the pressure is being measured. Do not speak.
6. Read the numbers or data correctly that appear on the monitor screen, which correspond to the maximum pressure (systolic), to the minimum pressure (diastolic) and to the pulse rate per minute (heart rate).
7. Take two blood pressure readings separated by at least two minutes. If the difference between them is more than 5 mmHg, take more readings until the blood pressure is stabilized. Consider the mean of the two last readings as the definitive value.
8. Always write down the above data, next to the date and the time of the reading.

In case of …

1. If the pulse is irregular, take several readings (from three to five) and use the mean.
2. If for any reason you must repeat any reading, wait at least two or three minutes.

Remember

1. The devices for measuring blood pressure can be arm or wrist models, automatic and be validated according to the criteria of the British Hypertension Society with at least grade B and the "American Association for the Advancement of Medical Instrumentation".
2. Check the devices every six months, calibrating them in comparison to a mercury sphygmomanometer.
3. The majority of the experts consider home blood pressure numbers over 135/85 mmHg as high.

*We thank Eduardo Mayoral for authorization for the use of this material.

APPENDIX 8.

Instructions for the patient on ambulatory blood pressure monitoring

- This device will measure your blood pressure every 30 minutes. During the day you will be warned by a beep before the measurement.
- During the reading you should remain quiet and hold your arm at the height of your heart.
- In case of failure to read, the device will repeat it.
- You should carry out your normal activities between readings, although you should not perform intensive exercise.
- You should keep the monitor on during the night and put it under your pillow.
- In the daily sheet you should write down:
  1. Your activities at the time of each measurement.
  2. Type of activity during the day.
  3. When you go to bed and when you get up. Also if you take a nap.
  4. When you take the antihypertensive treatment.
  5. Any symptom.
- In the morning, at the same time that the device was placed the previous day, disconnect it and remove the device from your arm and take it to the health centre.

You can call the health centre if you have any problem.

APPENDIX 9.

Low-sodium diet

(Modification of the recommendations of the Spanish Hypertension Society Association – Spanish League for the Fight against Arterial Hypertension, available at: http://www.seh-lelha.org/informpa.htm)

Considerations for professionals

- Not all the patients respond in the same way to the low-sodium diet. It is estimated that up to 30% of the patients can respond with decreases of less than 5 mmHg in the BP numbers. Older patients are more sensitive to the measure.
- The salt (sodium) content of the diet comes from the content of the food that we consume, plus the salt that we add in cooking the food and supplements at the table ("salt shaker").
- The consumption of salt must be decreased little by little, so that the palate becomes accustomed to it, which usually occurs in the majority of the people in a short time.
- In case of recommending potassium or magnesium salt, the risk of hypermagnesemia and hyperpotassemia in the case of renal insufficiency must be taken into account.

Advice for patients

- Use less salt when you cook or do not use the salt shaker at the table.
- In order to increase the flavour of the meals, use pepper and other spices, lemon juice, aromatic herbs, fresh garlic, or powdered garlic or onion. Use oil with flavour such as olive oil.
- Use low-sodium products (examine the labels of packaged foods).
- Eat the smallest amount possible of foods in which a large amount of sodium has been used in processing them, such as canned foods, pre-cooked foods, nuts and stock cubes.
- Avoid too much salted or smoked meats, such as pork belly, ham, sausages and bacon.
- In restaurants, choose the meal from the menu that best adjusts to these recommendations. Ask that the food served to you is not salted.
- Read the labels carefully, some indicate the amount of sodium that each portion contains.
- Ask those that prepare your meals to help you not to consume salt. It is possible that they will also benefit from this.

APPENDIX 10.

Antihypertensive drugs: adverse effects, interactions and precautions

GROUPS	ADVERSE EFFECTS (AE)	CONTRAINDICATIONS/ PRECAUTIONS/ INTERACTIONS/PREGNANCY/BREAST FEEDING	COMMENTS
DIURETICS			
Thiazides	At low doses, minimum AE	Do not use in case of advanced IRC, hypocalcaemia, allergy to sulphonamides.	Recommend diet rich in potassium and low in sodium.
	Biochemical alterations: K+, Na+, Mg++, ↑ uric acid and calcium.	Precautions: hyperuricaemia, gout.	Effects on lipids or glycaemia: minimum at low doses and prolonged use.
	↑ Short-term glucose and cholesterol levels (C-total and LDL).	Interactions: digoxin: ↑ risk of toxicity (if there is hypopotassaemia); lithium (risk of intoxicity); NSAID: ↑ risk of nefrotoxicity and antihypertensive effect; antidiabetic drugs: hypoglycaemic effect; antiarrhythmic drugs: ↑ toxicity of amiodarone, disopyramide, flecainide and quindine (if there is hypopotassaemia).	In the elderly, begin with lower doses.
	Impotence (reversible)	Possibly safe in pregnancy. Chlorthalidone, hydrochlorothiazide: compatible with breast feeding.	
	Rare AE: cholestasis, blood dyscrasias, photosensitivity, pancreatitis, hypersensitivity reactions.	↑ Ototoxicity with aminoglycosides and vancomycin. Pregnancy: furosemide indicated in serious situations. Breast feeding: it can inhibit breast feeding during the first month.	
Loop	Ototoxicity. Other AE: see thiazides, except that they increase excretion of calcium.	Other precautions: see thiazides.	In AHT, indicated in case of IRC.
Potassium-sparing agents	AE other than the thiazide diuretics.	Contraindicated in renal insufficiency.	They are usually used in combinations with the above to decrease the risk of hypopotassaemia.
	Hyperpotassaemia	Interactions: ACEI, ARA II, tacrolimus: ↑ hyperpotassaemic risk; NSAID and cyclosporine: ↑ hyperpotassaemic and nefrotoxicity risk; litium: risk of intoxication.	
	Spironolactone: gynecomastia, menstrual alterations.	Spironolactone: avoid in pregnancy. Compatible with breast feeding.	
Beta blockers	Bronchospasm (less with cardioselective drugs), bradycardia (less with ISA), cardiac insufficiency, coldness in limbs, sleep disorders and nightmares, dysponea, asthenia, masking of symptoms of hypoglycaemia, hypo and hyperglycaemia, and HDL (less with ISA and carvedilol), sexual dysfunction.	Contraindications: cardiac blockage, intense bradycardia, cardiogenic shock. Precautions: asthma, COPD (non cardioselective drugs contraindicated), intermittant claudication, Raynaud's syndrome, diabetics. In RI, use those that are excreted by hepatic means. Change the dosage in case of serious RI or HI. Interactions: verapamil, diltiazem, amiodarone and other antiarrhythmic drugs, ↑ risk of severe hypertension (especially with non-cardioselective drugs); NSAID: antihypertensive effect. Avoid in first trimester of pregnancy. They seem safe in 2nd and 3rd trimesters. Compatible with breast feeding.	The interruption of the treatment must be gradual (risk of precipating an AMI, angina). Cardioselective drugs: atenolol, betaxolol, bisoprolol, celiprolol, metoprolol, acebutolol. At high dosages, they lose cardioselectivity. ISA: acebutolol, carteolol, celiprolol, oxprenolol. Dilating action: labetalol, metoprolol, propranolol. Basically renal elimination: atenolol, celiprolol.

APPENDIX 10.

Antihypertensive drugs: adverse effects, interactions and precautions

(Continuation)

GROUPS	ADVERSE EFFECTS (AE)	CONTRAINDICATIONS/ PRECAUTIONS/ INTERACTIONS/PREGNANCY/BREAST FEEDING	COMMENTS
ACEI			
	Hypertension, renal function impairment, persistent dry cough, angioedema, skin rash, dysgeusia, hyperpotassaemia (especially in IRC, with potassium supplements and/or potassium-sparing diuretics), cephalea, nausea, gastrointestinal alterations, neutropenia, agranulocytosis.	Contraindications: bilateral renal stenosis or unilateral in single kidney, history of angioedema associated with ACEI. Precautions: renovascular disease. Adjust dosage in renal insufficiency. Potassium: risk of hyperpotassaemia; lithium: ™ toxicity; sulphonylureas: ↑ hypoglycaemic effect with captopril; cyclosporine: ↑ risk of hyperpotassaemia, NSAID: hypotensor effect and ↑ risk of RI. Contraindicated in pregnancy. Catopril and enalapril compatible with breast feeding.	Evaluate renal function and during the treatment. Closely watch if hypotension appears with first dose, especially in patients with volume depletion, CCI, treatement with diuretics.
ARA II			
	Angioedema (rare), hyperpotassaemia.	Like ACEI	Like ACEI.
Calcium antagonist			
DHP	Ankle oedema, blushing, cephalea, gingival hypertrophy, reflex tachycardia.	Contraindications: cardiogenic shock, unstable angina, recent AMI; porphyia (nifedipine). Precautions: CCI, aortic stenosis. Reduce dosage in HI.	The use of rapid-release nifedipine is not recommended for the treatment of AHT or of the blood since it has been associated with serious adverse effects.
Non DHP	Defects of conduction of the heart, worsening of systolic dysfunction, gingival hyperplasia. Diltiazem: nausea, cephalea. Verapamil: constipation.	Contraindications: AV blockage (without pacemaker), sick sinus syndrome (without pacemaker), severe bradycardia, left cardiac insufficiency. Contraindications: avoid their association with BB due to the risk of blockages.	Recommend correct oral hygiene to avoid gingival hyperplasia.
DHP and non DHP		Interactions of calcium antagonists: Antiarrhythmic drugs (amiodarone, disopyramide, flecainide) and verapamil or diltiazem: ↑ risk of cardiac adverse effects; rifampcin: antihypertensive effect; phenobarbital and phenytoin: antihypertensive effect; carbamazepine: effect of DHP; verapamil and diltiazem increase the effect of carbamazepine; digoxin: ↑ toxicity; beta blockers: do not associate with verapamil or nicardipine; theophylline: ↑ toxicity risk. Do not use in pregnancy (safety unclear). Nifedipine, verapamil, diltiazem compatible with breast feeding.	
Alpha blockers			
	Orthostatic hypertension	"First dose" effect: syncope or collapse due to hypertension: administer at night, reduce dosage in the elderly. ↑ Risk of hypertension of 1st dose with other antihypertensive drugs.	They are not treatment of choice for use in single-drug therapy. Combinations: only when other associations have failed.

RI: Renal insufficiency. **HI:** Hepatic insufficiency. **DHP**: dihydropyridines. **IRC:** Chronic renal insufficiency.

APPENDIX 11.
Selection of antihypertensive drugs

The different antihypertensive drugs marketed in our country are presented below.
The **drugs marked in bold letters** are the drugs of choice based on the following criteria agreed by the editing team of the Guidelines:

1. Benefits demonstrated through randomized clinical trials with results of morbimortality that have been considered in the evaluation of the evidence in these guidelines.
2. Class effect: if it is a heterogeneous group, criterion 1 will be the principal selection criterion.
3. Profile and frequency of adverse reactions
4. Number of doses/day
5. Cost

The criterion for inclusion of the associations is that all their active ingredients are selected.

Selection of antihypertensive drugs

SINGLE-DRUG TREATMENT

Active ingredient	Dose/day (mg) Range	Number doses/day	Commercial names and presentation
DIURETICS			
Thiazides and related products			
CHLORATHALIDONE	12.5-50	1	Higrotona 50 mg 30 comp
HYDROCHLOROTHIAZIDE	12.5-50	1	Esidrex 25 mg 20 comp, Hidrosaluretil 50 mg 20 comp
INDAPAMIDE	2.5-5	1	Indapamida EFG, Extur, Tertensif: 2.5 mg 30 comp
	1.5(retard)	1	Extur Retard, Tertensif Retard: 1.5 mg 30 comp lib prol.
XIPAMIDE	20-40	1	Diurex: 20 mg 30 and 60 comp
Loop			
FUROSEMIDE	20-240	1-3	Furosemida EFG, Seguril: 40 mg 10 and 30 comp
TORASEMIDE	2.5-10	1-2	Torasemida EFG, Dilutol HTA, Isodiur HTA, Sutril HTA: 2.5 mg 30 comp; Torasemida EFG, Dilutol, Isodiur, Sutril, Tadegan: 5 mg 30 comp, 10 mg 30 comp; Sutril Neo 5 mg 30 comp lib prol., 10 mg 30 comp lib prol.
Potassium-sparing agents			
SPIRONOLACTONE	25-100	1	Espironolactona EFG, Aldactone A: 25 mg 20 and 50 comp; Espironolactona EFG, Aldactone 100: 100 mg 20 comp
*** See table of associations**			

BETA-BLOCKERS

Cardioselective drugs			
ATENOLOL	50-100	1-2	Atenolol EFG, Blokium, Neatenol, Tanser, Tenormin: 50 mg 30 comp and 60 comp, 100 mg 30 comp and 60 comp
BISOPROLOL	5-10	1	Bisoprolol EFG, Emconcor, Euradal: 5 mg 30 and 60 comp, 10 mg 30 and 60 comp; Emconcor Cor 2.5 mg 28 comp, 5 mg 28 comp and 10 mg 28 comp
CELIPROLOL	200-400	1	Cardem 200 mg 30 and 60 comp
METOPROLOL	50-200	1-2	Beloken, Lopresor: 100 mg 40 comp; Beloken Retard: 100 mg 30 comp retard, 200 mg 30 comp retard
NEBIVOLOL	2.5-5	1	Lobivon, Silostar: 5 mg 28 comp
Not cardioselective			
CARTEOLOL	2.5-10	1	Arteolol 5 mg 40 comp
NADOLOL	40-320	1	Solgol: 40 mg 60 comp, 80 mg 30 comp
OXPRENOLOL	80-320	1-2	Trasicor 80 mg 30 comp, Trasicor Retard 160 mg 28 comp
PROPRANOLOL	40-320	2	Sumial 10 mg 50 comp, 40 mg 50 comp, Sumial Retard 160 mg 20 caps
Alpha-Beta Blockers			
CARVEDILOL	12.5-50	2	Carvedilol EFG, Coropres: 6,25 mg 28 comp and 25 mg 28 comp
LABETALOL	200-1200	2	Trandate 100 mg 30 comp, 200 mg 30 comp

Active ingredient	Dose/day (mg) Range	Number doses/day	Commercial names and presentation
ACEI			
BENAZEPRIL **CAPTOPRIL**	10-40 25-150	1-2 2-3	Cibacen, Labopal: 10 mg 28 comp, 20 mg 28 comp Captopril EFG, Capoten, Captosina, Cesplon, Dilabar, Garanil, Tensoprel: 25 mg 60 comp, 50 mg 30 comp, 100 mg 15 comp;
CILAZAPRIL **ENALAPRIL**	1.25-5 5-40	1 1-2	Captopril EFG, Capoten Cor, Cesplon Cor: 12.5 mg 20 comp Inhibace, Inocar: 1 mg 30 comp, 2.5 mg 28 comp, 5 mg 28 comp Enalapril EFG, Acetensil, Baripril, Bitensil, Clipto, Controlvas, Crinoren, Dabonal, Ditensor, Herten, Hipoartel, Iecatec, Insup, Naprilene, Neotensin, Pressitan, Reca, Renitec: 5 mg 10 and 60 comp, 20 mg 28comp; Enalapril Davur, Enalapril Belmac: 2.5 mg 10 comp, 10 mg 28 and 56 comp,
SPIRAPRIL FOSINOPRIL IMIDAPRIL **LISINOPRIL**	3-6 10-40 5-20 5-40	1 1 1 1-2	Renormax, Renpress: 6 mg 28 comp Fosinopril EFG, Fositens, Hiperlex, Tenso-stop: 20 mg 28 comp; Hipertene 5 mg 28 comp, 10 mg 28 comp and 20 mg 28 comp Lisinopril EFG, Doneka, Likenil, Prinivil, Tensikey, Zestril: 5 mg 60 comp, 20 mg 28 comp
PERINDOPRIL **QUINAPRIL**	2-8 5-80	1 1	Coversyl 4 mg 30 comp Quinapril EFG, Acuprel, Ectren, Lidaltrin: 5 mg 60 comp, 20 mg and 40 mg 28 comp
RAMIPRIL	1.25-20	1-2	Ramipril EFG, Acovil, Carasel: 2.5 mg 28 comp, 5 mg 28 comp and 10 mg 28 comp; Acovil, Carasel: 1,25 mg 28 comp
TRANDOLAPRIL	1-4	1	Gopten, Odrik: 0.5 mg 28 comp, 2 mg 28 comp and 4 mg 28 comp
ARA II			
CANDESARTAN	4-16	1	Atacand, Parapres: 4 mg 14 comp, 8 mg 28 comp, 16 mg 28 comp
EPROSARTAN	600-800	1	Futuran, Navixen, Regulaten, Tevetens: 600 mg 28 comp Eprosartan SmithKline 300 and 400 mg 56 comp
IRBESARTAN **LOSARTAN** OLMESARTAN **TELMISARTAN** **VALSARTAN**	75-300 25-100 10-40 20-80 80-160	1 1-2 1 1 1	Aprovel, Karvea: 75 mg, 150 mg 300 mg 28 comp Losartan EFG, Cozaar 12.5 mg 7 comp, 50 mg 28 comp, 100 mg Ixia, Olmetec, Openvas: 10 mg, 20 mg and 40 mg 28 comp Micardis, Pritor: 20 mg, 40 mg, 80 mg 28 comp Diovan, Kalpress, Miten, Vals: 40 mg (Cardio), 80 mg; 160 mg 28 caps
Calcium antagonists			
Dihydropyridines			
AMLODIPINE BARNIDIPINE **FELODIPINE** LACIDIPINE LERCANIDIPINE MANIDIPINE NIFEDIPINE RETARD **NIFEDIPINE GITS** NISOLDIPINE **NITRENDIPINE**	2.5-10 10-20 2.5-20 2-6 10-20 10-20 40-120 60-120 10-40 10-20	1 1 1 1 1 1 2 1 1-2 1-2	Amlodipino EFG, Astudal, Norvas: 5 mg 30 comp, 10 mg 30 comp Libradin 10 mg 28 caps lib control, 20 mg 28 caps lib control Felodipino Sandoz, Perfudal, Plendil: 5 mg 30 comp Lacimen, Lacipil, Motens: 4 mg 28 comp Lercadip, Lerzam, Zandip: 10 mg 28 comp, 20 mg 28 comp Artedil: 10 mg 28 comp, 20 mg 28 comp Nifedipino EFG, Adalat retard: 20 mg 40 and 60 comp Adalat oros, Pertensal: 30 and 60 mg 28 comp Syscor: 10 mg 30 comp; Sular: 10 and 20 mg lib sost 30 comp Nitrendipino E.F.G., Balminil, Baypresol, Gericin, Niprina, Sub tensin, Tensogradal, Trendinol: 10 and 20 mg 30 comp

(continued)

SINGLE-DRUG TREATMENTS

Active ingredient	Dose/day (mg) Range	Number doses/day	Commercial names and presentation
Calcium antagonists			
Non dihydropyridines			
DILTIAZEM LIB RETARD	120-360	1-2	Angiodrox R: 90 mg 30 and 60 caps, 120 mg 30 and 60 caps, 180 mg 30 and 60 caps, 300 mg 30 caps; Cardiser R: 120 mg 60 caps, 300 mg 28 caps, 240 mg 30 comp; Carreldon: 120 mg 40 caps, 240 mg 20 and 30 comp; Corolater R: 60 mg 30 and 60 caps, 90 mg 30 and 60 caps, 120 mg 40 caps; Cronodine: 120 mg 30 and 60 caps, 240 mg 30 caps; Dilaclan HTA: 90 mg 30 and 60 caps, 120 mg 60 caps, 180 mg 60 caps, HTA 300 mg 30 caps; Diltiwas R: 120 mg 40 caps, Dinisor R: 120 mg 40 comp, 180 mg 30 comp, 240 mg 30 caps; Doclis R: 120 mg 60 caps, 240 mg 30 caps; Lacerol R: 120 mg 40 caps, 300 mg 20 and 30 caps; Lacerol HTA 240 mg 20 and 30 caps; Masdil R: 120 mg 60 comp, 300 mg 28 caps; Tilker R: 120 mg 40 comp, LIB SOST 200 and 300 mg 28 caps; Uni masdil R: 200 mg 28 caps.
VERAPAMIL RETARD AHT	120-480 240-480	1-2 1	Manidon R 120 and 180 mg 60 comp, Manidon HTA 240 mg 30 comp retard
Alpha blockers			
DOXAZOSIN	2-16	1	Doxazosina EFG, Carduran, Doxatensa, Propangol: 2 mg 28 comp and 4 mg 28 comp Carduran Neo, Propandol Neo: 4 mg and 8 mg 28 comp lib controlada
PRAZOSIN	2-30	2-3	Minipres 1 mg 60 comp, 2 mg 60 comp, 5 mg 30 comp

R: retard

The active ingredients in bold letters are those selected by the editing group of the Guidelines.

ASSOCIATIONS

Associations	Dose (mg)	Commercial presentations
Among diureticos		
Amiloride/hydrochlorothiazide Spironolactone/althizide Spironolactone/bendroflumethiazide Spironolactone/chlorathalidone Triamterene/furosemide xantinol	5/50 25/15 50/2.5 50/50 25/40	Ameride, Diuzine 20 and 60 comp Aldactacine 40 comp Spirometon 20 and 60 comp Aldoleo 20 comp Salidur 20 and 60 comp

ASSOCIATIONS

Association	Dose (mg)	Commercial presentation
Beta-blockers with diuretics		
Atenolol/bendroflumethiazide	100/5	Neatenol Diu 28 comp
Atenolol/chlorathalidone	100/25	Blokium Diu, Normopresil, Tenoretic 28 and 56 comp
Atenolol/hydrochlorothiazide/amiloride	50/25/2.5	Kalten 28 caps
Bisoprolol/hydrochlorothiazide	10/25	Emcoretic 28 and 56 comp
Oxprenolol/chlorathalidone	160/20	Trasitensin Retard 28 grag
IECA with diuretics		
Benazepril/hydrochlorothiazide	10/12.5	Cibadrex, Labodrex 28 comp
	20/25	Cibadrex, Labodrex 28 comp
Captopril/hydrochlorothiazide	50/25	Captopril/HCTZ EFG, Cesplon Plus, Dilabar Diu, Ecadiu, Ecazide 30 comp
Cilazapril/hydrochlorothiazide	5/12.5	Inhibace Plus, Inocar Plus 28 comp
Enalapril/hydrochlorothiazide	20/12.5	Enalapril/HCTZ EFG, Acediur, Acetensil Plus, Baripril Diu, Bitensil Diu, Co-Renitec, Crinoretic, Dabonal Plus, Ditenside, Herten Plus, Hipoartel Plus, Neotensin Diu, Pressitan Plus 28 comp
		Renitecmax 28 comp
	20/6	Fositens Plus, Hiberlex Plus, Tenso Stop Plus 28 comp
Fosinopril/hydrochlorothiazide	20/12.5	Doneka Plus, Iricil Plus, Prinivil Plus, Secubar Diu, Tensikey Complex, Zestoretic 28 comp
Lisinopril/hydrochlorothiazide	20/12.5	Preterax 30 comp
		Bipreterax 30 comp
Perindopril/indapamide	2/0.625	Acuretic, Bicetil, Lidaltrin Diu 28 comp
	4/1.25	
Quinapril/hydrochlorothiazide	20/12.5	
ARA II with diuretics		
Candesartan/hydrochlorothiazide	16/12.5	Atacand Plus, Parapres Plus 28 comp
Eprosartan/hydrochlorothiazide	600/12.5	Eprosartan/hidroclorotiazida Tora, Futuran Plus, Navixen Plus, Regulaten Plus, Tevetens Plus
		Coaprovel, Karvezide 28 comp
Irbesartan/hydrochlorothiazide	150/12.5	Coaprovel, Karvezide 28 comp
	300/12.5	Cozaar Plus 28 comp
Losartan/hydrochlorothiazide	50/12.5	Fortzaar 28 comp
	100/25	Micardis Plus, Pritor Plus
Telmisartan/hydrochlorothiazide	40/12.5	Micardis Plus, Pritor Plus
	80/12.5	Co Diovan, Co Vals, Kalpress Plus, Miten Plus
Valsartan/hydrochlorothiazide	80/12.5	Co Diovan, Co Vals, Kalpress Plus, Miten Plus
	160/12.5	Co Diovan Forte, Co Vals Forte, Kalpres Plus Forte,
	160/25	Miten Plus Forte
Calcium antagonists with beta blockers		
Metoprolol/felodipine	50/5	Logimax 50/5 mag 30 comp
Calcium antagonists with ACEI		
Verapamil/trandolapril	180/2	Tarka, Tricen 28 caps retard
Nitrendipine/enalapril	10/20	Eneas, Enit, Vipres 30 comp
Calcium antagonists with ARA II		
Amlodipine/valsartan	5/160	Exforge 28 comp
	10/160	Exforge 28 comp
Other associations		
Atenolol/hydralazine/bendroflumethiazide	100/50/5	Neatenol diuvas 30 and 60 comp

APPENDIX 12.
Individualization of the antihypertensive treatment according to associated pathologies

Clinical situation	Treatment of choice	Alternative treatment	Trearment not recommended	Observations
General Population	Thiazide at low doses	ACEI, calcium antagonists, ARA II	BB unless there is a specific recommendation	Thiazide or nifedipine in isolated systolic AHT >80 years of age.
Elderly	Thiazide + ACEI at low doses	ACEI, calcium antagonists, ARA II		Evidence for indapamide and perindopril
Diabetes WITHOUT nefropathy	ACEI / Thiazide	ARA II, calcium antagonists DHP	BB unless there is a specific recommendation	Thiaziade or nifedipine in isolated systolic AHT >80 years of age.
Diabetic WITH nephropathy	ACEI at full doses	ARA II		ARA II: Evidence for losartan, irbesartan ACEI + ARA II (Specialized Care)
Non-diabetic nephropathy	ACEI	ARA II		ACEI + ARA II (Specialized Care)
Cardiac insufficiency	ACEI BB (bisoprolol, carvedilol, metoprolol retard, nebivolol)	ARA II if there is intolerance to ACEI	Calcium antagonists (if required, add as antihypertensive therapy use only amlodipine, felodipine)	ARA II: Candesartan, losartan, valsartan ACEI + ARA II (Specialized Care)
After recent AMI WITH systolic dysfunction	BB ACEI	BB + ARA II if there is intolerance to ACEI	DHP calcium antagonists	The ACEI and ARA II association is not justified. ARA II: Indication approved for valsartan
After recent AMI WITHOUT systolic dysfunction	BB ACEI	ARA II	DHP calcium antagonists	ARA II: Telmisartan
Stable ischaemic cardiopathy	BB ACEI	Verapamil, other calcium antagonists, ARA II	Rapid-release Nifedipine	ACEI: Better evidence for ramipril 10 mg; perindopril 8 mg. ARA II: Telmisartan Avoid association BB with diltiazem Avoid association of ACEI with ARA II
CVA	Thiazide Thiazide + ACEI	ARA II		Evidence for indapamide and perindopril
Peripheral arteriopathy	= General population			Cardioselective BB not contraindicated in low/moderate doses
Asthma/COPD	= General population			Cardioselective BB: use only if there is firm indication
LHV	= General population			

Ischaemic cardiopathy, cardiac insufficiency
In very special cases its use can be considered, always in the Specialized Care Area.
AMI: acute myocardial infarction. **CVA:** Cerebrovascular accident. **HVI:** Left ventricle hypertrophy ACEI: angiotensin-converting enzyme inhibitors **BB**: Beta blockers **ARA II:** angiotensin II receptor antagonists **DHP:** Dihydropyridines

APPENDIX 13.
Evaluation proposal for the care given to hypertensive patients

The authors of these Guidelines, in coordination with the editing team of the indicators of the preferred offer included in the PAP, have designed some indicators that can be useful for the clinics and managers in evaluating the care given to the hypertensive patient.

The indicators refer to the different subjects dealt with in the Guidelines and are calculated as a percentage of patients that meet the different criteria.

The denominator is comprised by patients with their medical history open in the health centre in the case of screening and patients with a diagnosis recorded of hypertension in the remainder of the cases. The indicators refer to a specific period of time that the evaluator must choose according to his objectives.

Screening

- The proportion of patients between 14 and 40 years of age with determination of BP numbers every 5 years.
- The proportion of patients over 40 years of age with determination of BP numbers every 2 years.

Diagnosis of the AHT patient

- The proportion of patients with new AHT diagnosis that have carried out the basic study.
- The proportion of patients with evaluation of cardiovascular risk according to the proposed method.
- The existence in the centre of standards of quality in the BP measuring systems that include the use of calibrated sphygmomanometers subject to annual periodic inspections and that the use of the devices for SMBP and ABPM validated by the BHS, the AAMI or the ESH.

Treatment

- The proportion of hypertensive patients to which the lifestyle modifications recommended in these guidelines has been indicated: changes in the diet including the low consumption of sodium, decrease in the consumption of alcohol, stop smoking, practice physical exercise, and loss of weight, if applicable.
- The proportion of hypertensive patients without associated complications under pharmacological treatment that receive diuretics.
- The proportion of hypertensive patients without associated complications under pharmacological treatment that receive ARA II.
- The proportion of hypertensive patients with microalbuminuria and/or diabetic nephropathy that receive treatment with ACEI or ARA II.
- The proportion of elderly hypertensive patients without associated diseases that receive treatment with diuretics.
- The proportion of hypertensive patients that receive alpha blockers.

Monitoring

- The proportion of hypertensive patients with BP numbers <140/90 mmHg.
- The proportion of patients in single-drug therapy with SBP □140 mmHg or DBP □90 mmHg
- The proportion of diabetic hypertensive patients with BP <140/80 mmHg.
- The proportion of hypertensive patients that have gone to the nurse consultation in the last 6 months.
- The proportion of hypertensive patients that have carried out a specific annual medical visit.

APPENDIX 14.

Framingham Tables for estimating coronary risk at 10 years adapted to the Spanish population (REGICOR)

Men

Non smokers

mmol/L <4.1 4.7 5.7 6.7 ≥ 7.2
mg/dl <160 180 220 260 ≥ 280

≥160/100	5	8	10	13	15	Age 65 - 74
140-159/90-99	4	7	9	12	14	
130-139/85-89	3	6	7	9	11	
120-129/80-84	2	5	5	7	8	
<120/80	3	5	5	7	8	
≥160/100	3	5	6	8	10	Age 55 - 64
140-159/90-99	3	5	6	8	9	
130-139/85-89	2	4	5	6	7	
120-129/80-84	2	3	4	5	5	
<120/80	2	3	4	5	5	
≥160/100	2	3	4	5	6	Age 45 - 54
140-159/90-99	2	3	4	5	6	
130-139/85-89	2	3	3	4	5	
120-129/80-84	1	2	2	3	4	
<120/80	1	2	2	3	4	
≥160/100	1	2	3	4	4	Age 35 - 44
140-159/90-99	1	2	3	3	4	
130-139/85-89	1	2	2	3	3	
120-129/80-84	1	2	2	2	2	
<120/80	1	2	2	2	2	

mmol/L <4.1 4.7 5.7 6.7 ≥7.2
mg/dl <160 180 220 260 ≥280
Cholesterol

Smokers

<4.1 4.7 5.7 6.7 ≥ 7.2 mmol/L
<160 180 220 260 ≥ 280 mg/dl

7	13	15	20	23	≥160/100
7	12	14	19	21	140-159/90-99
5	10	11	15	17	130-139/85-89
4	7	9	12	14	120-129/80-84
4	7	9	12	13	<120/80
5	8	10	13	15	≥160/100
4	8	9	12	14	140-159/90-99
4	6	7	10	11	130-139/85-89
3	5	6	8	9	120-129/80-84
3	5	6	8	9	<120/80
3	5	6	9	10	≥160/100
3	5	6	8	9	140-159/90-99
2	4	5	6	7	130-139/85-89
2	3	4	5	6	120-129/80-84
2	3	4	5	6	<120/80
2	4	4	6	6	≥160/100
2	3	4	5	6	140-159/90-99
2	3	3	4	5	130-139/85-89
1	2	3	3	4	120-129/80-84
1	2	3	3	4	<120/80

mmol/L <4.1 4.7 5.7 6.7 ≥7.2
mg/dl <160 180 220 260 ≥280
Cholesterol

If HDL cholesterol <35 mg/dL the real risk ≈ risk x 1.5
If HDL cholesterol ≥60 mg/dL the real risk ≈ risk x 0.5

Risk at 10 years
Very high > 39%
High 20-39%
Moderate 10-19%
Slight 5-9%
Low <5%

(available in http://www.regicor.org/fitxers_generals/tablas.pdf)

Women

Non smokers

mmol/L <4.1 4.7 5.7 6.7 ≥ 7.2
mg/dl <160 180 220 260 ≥ 280

≥160/100	5	6	8	8	10	Age 65 - 74
140-159/90-99	4	5	6	6	8	
130-139/85-89	3	4	5	5	6	
120-129/80-84	3	4	5	5	6	
<120/80	2	3	3	3	4	
≥160/100	5	6	8	8	10	Age 55 - 64
140-159/90-99	4	5	6	6	8	
130-139/85-89	3	4	5	5	6	
120-129/80-84	3	4	5	5	6	
<120/80	2	3	3	3	4	
≥160/100	3	4	5	5	7	Age 45 - 54
140-159/90-99	3	3	4	4	5	
130-139/85-89	2	3	3	3	4	
120-129/80-84	2	3	3	3	4	
<120/80	2	2	2	2	3	
≥160/100	2	1	2	2	3	Age 35 - 44
140-159/90-99	1	2	2	2	2	
130-139/85-89	1	1	2	2	2	
120-129/80-84	1	1	2	2	2	
<120/80	1	1	1	1	1	

mmol/L <4.1 4.7 5.7 6.7 ≥7.2
mg/dl <160 180 220 260 ≥280
Cholesterol

Smokers

<4.1 4.7 5.7 6.7 ≥ 7.2 mmol/L
<160 180 220 260 ≥ 280 mg/dl

6	8	10	10	12	≥160/100
5	7	8	8	11	140-159/90-99
4	5	6	7	9	130-139/85-89
4	5	6	7	9	120-129/80-84
3	3	4	4	5	<120/80
6	8	10	10	13	≥160/100
5	7	8	8	11	140-159/90-99
4	5	6	7	9	130-139/85-89
4	5	6	7	9	120-129/80-84
3	3	4	4	5	<120/80
4	5	6	7	9	≥160/100
4	4	5	5	7	140-159/90-99
3	4	4	4	6	130-139/85-89
3	4	4	4	6	120-129/80-84
2	2	3	3	4	<120/80
2	2	2	3	3	≥160/100
2	2	2	2	3	140-159/90-99
1	2	2	2	2	130-139/85-89
1	2	2	2	2	120-129/80-84
1	1	1	1	2	<120/80

mmol/L <4.1 4.7 5.7 6.7 ≥7.2
mg/dl <160 180 220 260 ≥280
Cholesterol

If HDL cholesterol <35 mg/dL the real risk ≈ risk x 1.5
If HDL cholesterol ≥60 mg/dL the real risk ≈ risk x 0.5

Risk at 10 years
Very high > 39%
High 20-39%
Moderate 10-19%
Slight 5-9%
Low <5%

Diabetic Men

Non smokers

mmol/L <4.1 4.7 5.7 6.7 ≥ 7.2
mg/dl <160 180 220 260 ≥ 280

≥160/100	7	12	14	20	21	Age 65 - 74
140-159/90-99	6	11	13	17	20	
130-139/85-89	5	9	10	14	16	
120-129/80-84	4	7	8	11	12	
<120/80	4	7	8	11	12	
≥160/100	4	8	9	12	14	Age 55 - 64
140-159/90-99	4	7	8	11	13	
130-139/85-89	3	6	7	9	10	
120-129/80-84	3	4	5	7	8	
<120/80	3	4	5	7	8	
≥160/100	3	5	6	8	9	Age 45 - 54
140-159/90-99	3	5	5	7	8	
130-139/85-89	2	4	4	6	7	
120-129/80-84	2	3	3	5	5	
<120/80	2	3	3	5	5	
≥160/100	2	3	4	5	6	Age 35 - 44
140-159/90-99	2	3	4	5	5	
130-139/85-89	2	3	3	4	4	
120-129/80-84	1	2	2	3	3	
<120/80	1	2	2	3	3	

mmol/L <4.1 4.7 5.7 6.7 ≥7.2
mg/dl <160 180 220 260 ≥280
Cholesterol

Smokers

<4.1 4.7 5.7 6.7 ≥ 7.2 mmol/L
<160 180 220 260 ≥ 280 mg/dl

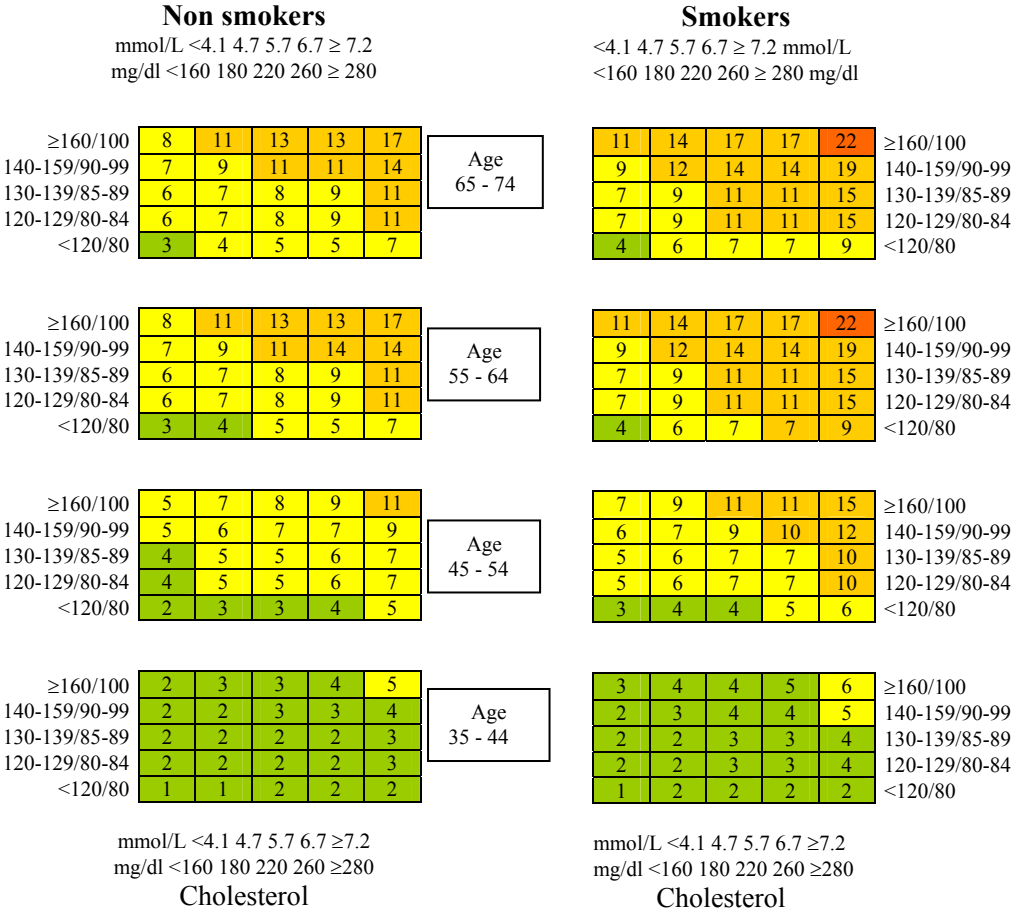
11	19	22	29	33	≥160/100
10	18	21	27	31	140-159/90-99
8	14	17	22	25	130-139/85-89
6	11	13	17	20	120-129/80-84
6	11	13	17	20	<120/80
7	12	15	20	22	≥160/100
6	11	13	18	20	140-159/90-99
5	9	11	14	17	130-139/85-89
4	7	8	11	13	120-129/80-84
4	7	8	11	13	<120/80
4	8	9	13	15	≥160/100
4	7	9	12	13	140-159/90-99
3	6	7	9	11	130-139/85-89
3	5	5	7	8	120-129/80-84
3	5	5	7	8	<120/80
3	5	6	8	9	≥160/100
3	5	6	8	9	140-159/90-99
2	4	5	6	7	130-139/85-89
2	3	4	5	5	120-129/80-84
2	3	4	5	5	<120/80

mmol/L <4.1 4.7 5.7 6.7 ≥7.2
mg/dl <160 180 220 260 ≥280
Cholesterol

If HDL cholesterol <35 mg/dL the real risk ≈ risk x 1.5
If HDL cholesterol ≥60 mg/dL the real risk ≈ risk x 0.5

Risk at 10 years
Very high > 39%
High 20-39%
Moderate 10-19%
Slight 5-9%
Low <5%

Diabetic Women



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Risk at 10 years
Very high > 39%
High 20-39%
Moderate 10-19%
Slight 5-9%
Low <5%

APPENDIX 15.
Glossary and abbreviations

AGREE Appraisal of Guidelines, Research and Evaluation for Europe; an international initiative to facilitate the design and evaluation of the CPG.

Intention-to-treat analysis Strategy for evaluating the results of a clinical trial that consists of analyzing each patient in the group to which he was assigned at the start of the study, independently of the intervention received.

Cochrane Library Database on effectiveness produced by the Cochrane Collaboration that includes the original systematic reviews of this organization.

EMBASE European database (Dutch) produced by Excerpta Médica with clinical medicine and pharmacology content.

Randomized clinical trial A study design in which the subjects are randomly assigned to two groups: one (experimental group) receives the treatment that is to be tested and the other (comparison or control group) receives a standard treatment (or sometimes a placebo). The two groups are monitored to observe any difference in the results. In this way the effectiveness of the treatment is evaluated.

Specificity The proportion (or the percentage) of truly healthy people that have a negative test result. That is, the proportion of true negative results.

Case-control study A study that identifies people with a disease (cases), for example lung cancer, and it compares them to a group without the disease (control). The ratio between one or several factors (for example, tobacco) related to the disease is examined, comparing the frequency of exposure to this and other factors between the cases and the controls.

Cohort study The monitoring or one or more cohorts of individuals that present different degrees of exposure to a risk factor in whom the appearance of the disease or condition under study is measured.

Heterogeneity See “Homogeneity”.

Homogeneity Means "similarity". Studies are called homogeneous if their results do not vary with each other more than what can be expected by chance. The opposite of homogeneity is heterogeneity.

Confidence interval The interval in which the true magnitude of the effect is found (never known exactly) with a preset degree of confidence. Often one speaks of "95% confidence interval" (or "confidence limits of 95%"). It means that the true value is found within this interval in 95% of the cases.

Medline Database of clinical predominance produced by the United States National Library of Medicine. Free access through PubMed.

Meta-analysis A statistical technique that permits integrating the results of different studies (of diagnostic tests, cohorts, cases-control, RCT, etc.) in a single estimator.

NICE National Institute for Health and Clinical Excellence, whose purpose is to provide professionals and patients with the best evidence available. One of its strategies is the drawing up of the CPG.

NNT/NNH A measurement of the effectiveness of a treatment. It is the number of persons that are needed to treat with a specific treatment (for example, aspirin in secondary prevention) in order to avoid an additional event (for example, a new ischaemic event). In the same way, the number needed to harm (NNH) is defined in order to evaluate undesirable effects.

Odds Ratio (OR) A measurement of the effectiveness of a treatment. If it is equal to 1, the effect of the treatment is no different from the control effect. If the OR is higher (or lower) than 1, the effect of the treatment is greater (or lesser) than that of the control. Note that the effect that is being measured can be adverse (death, disability) or desirable (stop smoking).

PROBE (design) A design used in many trials on antihypertensive patients. It is characterized by only the evaluators of the results being blind to the treatment received by the patients.

Relative risk reduction The ratio from the difference of risk in the treatment group and the risk in the control group.

Clinical Prediction Rule (CPR) This is a clinical tool that quantifies the individual contribution of various components of the clinical history, physical examination and laboratory results or other variables on the diagnosis, prognosis or the most probable response to a treatment in a specific patient.

Systematic Review (SR) A review in which the evidence on a subject has been systematically identified, evaluated and summarized in accordance with predetermined criteria. It may or may not include the Meta-analysis.

Relative Risk (RR) The ratio of the rate of events in the treatment and the control group. Its value follows the same interpretation as the OR.

Sensitivity (SE) The proportion (or the percentage) of truly ill patients that have a positive test result. In other words, it is the proportion of true positives.

Positive Predictive Value (PPV) The probability that a subject is truly ill when the result of the test is positive.

Negative Predictive Value (NPV) The probability that a subject is truly healthy when the result of the test is negative.

The glossary is based on the glossary of CASPe (Critical Appraisal Skills Programme Español) which we thank for permission to use it. Available in: http://www.redcaspe.org/homecasp.asp

Abbreviations

AAMI American Association of Medical Instrumentation

CVA Cerebrovascular accident

SMBP Self-measurement of blood pressure

ARA II Angiotensin II receptor antagonists

ISA Intrinsic sympathomimetic activity

BB Beta blockers

BHS British Hypertension Society

CAPV Basque Country Autonomous Region

IC Ischaemic cardiopathy

HC Health Care Centre

CV Cardiovascular

DHP Dihydropyridines

DM Diabetes mellitus

DM 2 Diabetes mellitus type 2

WCE White coat effect

CT Clinical trial

RCT Randomized clinical trial

ECG Electrocardiogram

CVD Cardiovascular disease

COPD Chronic obstructive pulmonary disease

EUSTEN Arterial hypertension and cardiovascular society of the Basque Country

WCP White coat phenomenon

FEV1 Forced expiratory volume in one second

FO Ocular fundus

CPG Clinical Practice Guidelines

WCH White coat hypertension or isolated clinical hypertension

HDL High density lipoproteins

AHT Arterial hypertension

LVH Left ventricle hypertrophy

AMI Acute myocardial infarction

CI Confidence interval

CCI Congestive cardiac insufficiency

ACEI angiotensin-converting enzyme inhibitors

BMI Body mass index

TRI Terminal renal insufficiency

JNC Joint National Committee

LDL Low density lipoproteins

TOL Target organ lesion

ABPM Ambulatory blood pressure monitoring

mmHg Millimetres of mercury

NICE National Institute for Clinical Excellence

NNT Number needed to treat

NYHA New York Heart Association

WHO World Health Organization

OR Odds ratio

OSATZEN Basque Society of Family and Community Medicine

BP Blood pressure

DBP Diastolic blood pressure

PAPPS Program of Preventive Activities and of Promotion of Health

SBP Systolic blood pressure

PROBE Prospective Randomized Open Blinded Endpoint

CVR Cardiovascular risk

RR Relative risk

RRR Relative risk reduction

SR Systematic review

SD Standard deviation

SEMFYC Spanish Society of Family and Community Medicine

SIGN Scottish Intercollegiate Guidelines Network

SOVASAHT Basque Hypertension and Cardiovascular Risk Society

TGC Triglycerides

PCU Primary Care Unit

PPV Positive predictive value

NPV Negative predictive value

Vs. Versus

Studies

NAME	TYPE OF STUDY	DESCRIPTION
AASK	Clinical trial	Antihypertensives and progression of the renal disease
ABCD	Clinical trial	ACEI (enalapril) *vs.* Dihydropyridine (nisoldipine) in diabetic hypertensive patients.
ALLHAT	Clinical trial	Doxazosin, chlorthalidone, lisinopril and amlodipine in AHT with another CV risk factor.
ACTION	Clinical trial	Nifedipine GITS *vs.* placebo in stable ischaemic cardiopathy
ANBP-2	Clinical trial	Enalapril *vs.* hydrochlorothiazide in the elderly
ASCOT	Clinical trial	Perindopril (+ Amlodipine) *vs.* Atenolol (+ diuretic) in high-risk hypertensive patients
CAMELOT	Clinical trial	Amlodipine *vs.* placebo *vs.* enalapril in stable ischaemic cardiopathy and normotension
CAPPP	Clinical trial	Captopril *vs.* diuretics and/or beta blockers in hypertensive adults
CHARM	Clinical trial	Candesartan *vs.* placebo or ACEI in cardiac insufficiency
COPERNICUS	Clinical trial	Carvedilol added to conventional treatment in patients with stage IV CCI evaluated in terms of mortality and hospital admittance
COMET	Clinical trial	Carvedilol *vs.* metoprolol in cardiac insufficiency
CONTROLPRESS	Cohorts	Evolution of the control of BP in Spain
COOPERATE	Clinical trial	ACEI + ARA II combination in non-diabetic nephropathy
DASH	Clinical trial	Effect on AHT of a qualitative low-sodium diet rich in vegetables and fruit.

NAME	TYPE OF STUDY	DESCRIPTION
EUROPA	Clinical trial	Perindopril in stable ischaemic cardiopathy
FRAMINGHAM	Cohorts	Monitoring of a cohort in USA on cardiovascular morbimortality
HOPE	Clinical trial	Study of an ACEI on the morbimortality of adult patients with high CVR (47% AHT)
HOT	Clinical trial	Comparison of three stategies (three objective levels of AHT)
HYVET	Clinical trial	Hypertension in the very elderly
IDNT	Clinical trial	Irbesartan *vs.* amlodipine *vs.* placebo in type-2 diabetic patients (hypertensive) with nephropathy evaluating renal function and mortality
INSIGHT	Clinical trial	Nifedipine *vs.* amiloride/hydrochlorothiazide in CV morbimortality
INVEST	Clinical trial	Calcium antagonists *vs.* non-calcium antagonists in patients with coronary disease
IRMA 2	Clinical trial	Irbesartan 150 mg *vs.* irbesartan 300 mg *vs.* placebo in type-2 diabetic patients with microalbuminuria evaluating development of diabetic nephropathy
LIFE	Clinical trial	Losartan *vs.* atenolol in AHT with LVH and high CVR evaluating morbimortality
MIDAS	Clinical trial	Isradipine *vs.* hydrochlorothiazide evaluating carotide arteriosclerosis and CV events
MDRD	Clinical trial	Effect of different target numbers of BP in the progression of renal insufficiency in hypertensive patients with renal insufficiency
MOSES	Clinical trial	Eprosartan *vs.* nitrendipine in secondary prevention of ictus
NAVIGATOR	Clinical trial	Valsartan and nateglinide in persons with glucose intolerance

NAME	TYPE OF STUDY	DESCRIPTION
NORDIL	Clinical trial	Diltiazem *vs.* diuretics and/or beta blockers evaluating CV morbimortality
OCTAVE II	Cohorts	Study on the CV morbimortality in a French cohort of WCH
OHASAMA	Cohorts	Study on Japanese population in ABPM and SMBP evaluating morbimortality
ONTARGET	Clinical trial	Telmisartan *vs.* ramipril and their combination in process of high-risk patients
OPTIMAL	Clinical trial	Losartan *vs.* captopril in the post-infarction patient
PATS	Clinical trial	Effect on the diuretic treatment of patients with CVA
PIUMA	Cohorts	Effect on the CV morbimortality in an Italian cohort of WCH
PRAISE	Clinical trial	Amlodipine in CCI evaluating CV morbimortality
PROGRESS	Clinical trial	Perindopril and indapamide in patients with CVA
REGICOR	Cohorts	Study on the incidence of CV disease in a Catalan population
RENAAL	Clinical trial	Effect of losartan on diabetic patients with nephropathy on CV morbidity and progression to renal insufficiency
SAVE	Clinical trial	Captopril in patients with recurring AMI, evaluating new episodes of ischaemic disease
SCOPE	Clinical trial	Candesartan *vs.* placebo in the elderly
SENIOR	Clinical trial	Effect of nebivolol in the elderly with cardiac insufficiency
SHEP	Clinical trial	Diuretics *vs.* placebo in isolated systolic AHT of the elderly

NAME	TYPE OF STUDY	DESCRIPTION
SOLVD-1	Clinical trial	Effect of enalapril on the CV morbimortality in patients with CCI and diminished ejection fraction
SOLVD-2	Clinical trial	Effect of enalapril on the CV morbimortality in asymptomatic patients with diminished ejection fraction
STOP-2	Clinical trial	ACEI and calcium antagonists *vs.* beta blockers and diuretics in the elderly
SYST-EUR	Clinical trial	Nitrendipine *vs.* placebo in isolated systolic AHT of the elderly
TONE	Clinical trial	Effect of a salt-free diet on BP, need for pharmacological treatment and morbimortality in the elderly
TRACE	Clinical trial	Trandolapril in patients after AMI with diminished ejection fraction evaluating CV morbimortality
TRANSCEND	Clinical trial	Telmisartan *vs.* placebo in high-risk hypertensive patients with intolerance to ramipril (not published)
UKPDS 38	Clinical trial	Effect of the control of BP on CV morbimortality in the diabetic population
UKPDS 39	Clinical trial	Effect of atenolol and captopril on hypertensive diabetic patients in terms of morbimortality
VALIANT	Clinical trial	Valsartan, captopril or both in infarction with systolic dysfunction
VALUE	Clinical trial	Valsartan *vs.* amlodipine in high-risk hypertensive patients
V-HeFT	Clinical trial	Felodipine in patients with CCI evaluated in CV morbidity and quality of life.

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