

# Blood pressure control based on office and ambulatory blood pressure monitoring: the European experience in hypertensive patients treated in clinical practice

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## Abstract:

It is currently well documented that blood pressure (BP) should be strictly controlled in hypertensive patients in order to provide optimal protection against cardiovascular and renal complications. The low target BP recommended today (i.e. <140/90 mm Hg in most patients) remains difficult to reach. Actually the BP control rate remains unsatisfactory worldwide. It is more difficult to normalize systolic than diastolic BP, and to control BP in older than in younger patients as well as in patients at high than in those at low cardiovascular risk. Combination antihypertensive therapy is necessary in most patients to normalize BP. Ambulatory BP monitoring is gaining increasing acceptance to detect patients who exhibit normal "out-of-office" BP levels while having still abnormally elevated BP values in the doctor's office despite ongoing antihypertensive therapy.

**Key words:** office blood pressure, primary care, 24-h ambulatory blood pressure monitoring, blood pressure variability, blood pressure control, cardiovascular risk.

## Introduction

The therapeutic benefits of blood pressure (BP) lowering have been demonstrated in a large number of morbidity-mortality trials [1-3]. A meta-analysis of 61 prospective observational studies involving one million adults has shown that cardiovascular risk is strongly and directly related to BP throughout middle and old age, with a doubling of cardiovascular death for every 20/10 mm Hg increase in usual BP, beginning at 115/75 mm Hg [4]. A large interventional trial including nearly 19 000 hypertensive patients, the Hypertension Optimal Treatment study, documented the lowest incidence of cardiovascular mortality at a mean achieved systolic and diastolic BP of 138.5 and 82.6 mm Hg, respectively [5]. This led international experts in the field of hypertension to recommend for the first time an intensive BP lowering in 1999, the aim being to bring BP <140/90 mm Hg in most patients [6]. This view was supported a few years later by other official guidelines, where even lower BP targets (<130/80 mm Hg) were recommended in patients with selected

diseases such as renal insufficiency and/or diabetes [7-9]). According to the last 2007 guidelines for the management of hypertension prepared jointly by the European Society of hypertension and the European Society of Cardiology, BP should be reduced below 130/80 mm Hg not only in patients with diabetes or renal dysfunction, but also in those with associated clinical conditions such as stroke and myocardial infarction [10]. The 140/90 mm Hg value was actually chosen as a goal in most recent randomized morbidity-mortality trials performed in hypertensive patients [11-19]. Notably, evidence for a better cardiovascular outcome was found in patients who achieved this target BP during the trial compared with those who failed to reach it [14, 20].

Major efforts have been directed in industrialized countries over the last decades at diagnosing and treating hypertension. How successful were these efforts in this privileged part of the world where patients are presumed to have easy access to health care? The present review aims to answer this question, taking as an example the experience accumulated in several countries across Europe. We decided to focus as much as possible on surveys performed after dissemination of the hypertension guidelines promoting as the treatment goal BP values <140/90 mm Hg, i.e. after 1999. We also made the choice of addressing the issue of BP control rate in hypertensive patients followed by physicians rather than observations made in population-based surveys. This option was taken to reflect everyday clinical practice, thus illustrating how difficult it is to normalize BP in most hypertensives. This should help to identify barriers to the achievement of satisfactory BP control as well as possible strategies to improve it. Finally, we searched for studies in which the BP control rate was assessed not only conventionally in an office setting, but also in "out-of-office" conditions, using 24-h ambulatory BP monitoring. This is of critical importance as "out-of-office" BP allows a better prediction of cardiovascular events [21-25] and has been endorsed by the latest European guidelines [10].

### Office blood pressure control rate in hypertensive patients

Several studies performed in different European countries were selected as representative of the BP control rate currently achieved in hypertensive patients followed by physicians in everyday practice. They are reported here according to the alphabetical order of the countries.

#### Belgium

In a prospective cross-sectional survey 253 general practitioners were asked to provide information on the first 15 men aged 55 years or

older who showed up in their office [26]. Data from 3761 subjects were obtained (Table I). Out of them 74% were considered to be hypertensive (of whom 80% were on antihypertensive therapy). BP was <140/90 mm Hg in 38% of the treated patients, and in 31% of all hypertensives. The hypertensive patients were classified into the different risk categories according to the 1999 WHO/ISH guidelines [6]. This could be done in 1316 patients. The proportion of patients who were treated was 47, 56 and 86% in the medium, high and very high risk groups, respectively. Among patients on antihypertensive therapy, BP was more frequently controlled in the medium (46%) than in the high (37%) and the very high risk group (31%). The BP control rate was significantly better among treated patients (n=92) with diastolic hypertension (defined as diastolic BP  $\geq$ 90 mm Hg irrespective of systolic BP) than among treated patients (n=837) with isolated systolic hypertension (defined as systolic BP  $\geq$ 140 mm Hg and diastolic BP <90 mm Hg), at 53 and 33%, respectively [27]. Notably, patients with isolated systolic hypertension were less frequently treated (25%) than those with diastolic hypertension (75%).

A prospective cross-sectional survey was recently performed in primary care with the aim of evaluating the prevalence of isolated uncontrolled systolic BP in treated hypertensive patients [28, 29]. A random sample of 770 physicians throughout Belgium included 11 562 patients on antihypertensive therapy (Table I). Table II shows the prevalence of hypertension types in these patients by age class. The prevalence of isolated systolic hypertension, defined as systolic BP at least 140 mm Hg and diastolic BP less than 90 mm Hg, increased with age, reaching 38.4% above the age of 80 years. The physicians in charge of the patients decided not to adapt antihypertensive therapy in 46% of patients with on-treatment isolated systolic hypertension, compared with 16% of uncontrolled patients in the other hypertension types.

#### France

A cross-sectional study was carried out in a sample of 3153 general practitioners who were requested to give information on the first 5 hypertensive patients presenting in their office [29]. Data from 14 066 treated patients were available for analysis (Table I). These patients were divided into 3 groups according to the cardiovascular risk stratification proposed by the 1999 WHO/ISH guidelines [6]. BP control (<140/90 mm Hg) was seen less frequently in patients with the highest risk (27%) than in those with the medium (31%) and the lowest risk (43%). A key observation was that the high risk patients received more frequently two or more drugs (56%) than their medium (44%) and

**Table I.** Blood pressure control rate (<140/90 mm Hg) and drug therapy in patients on antihypertensive treatment (from ref. [26, 28-36])

Study	Country	Period of data sampling	Number of patients	BP control rate [%]	Monotherapy [%]
Fagard et al., 2002 [26]	Belgium	2000	2210	38.0	54.5
Van der Niepen et al., 2008 [28]	Belgium	2003-2004	11 562	21.5	50.0
Amar et al., 2002 [29]	France	1999-2000	14 066	31.7	51.9
Roux et al., 2006 [31]	France	2001	4702	18.0	48.0
Steckelings et al., 2004 [32]	Germany	2001	14 647	31.7	45.0
Mancia et al., 2004 [33]	Italy	2000	2775	37.5	36.9
Mancia et al., 2005 [34]	Italy	2003	7512	18.4	NA
Banegas et al., 2004 [35]	Spain	2000	4049	42.0	48.0
Journath et al., 2008 [36]	Sweden	2002-2005	6537	Male PCPs: 26.6 Female PCPs: 31.0	NA

NA – not available, PCPs – primary care physicians

**Table II.** Prevalence of controlled and isolated systolic hypertension by age class in treated patients (from ref. [28])

Age class [year]	N	Controlled hypertension [%]	ISH [%]	IDH [%]	SDH [%]
≤40	459	21.8	18.5	4.4	55.3
40-50	1435	20.6	21.0	4.1	54.3
51-60	2784	20.9	22.7	2.4	54.0
61-70	3340	22.1	29.5	2.1	46.3
91-80	2773	20.9	35.8	1.3	42.0
>80	771	24.4	38.4	1.3	35.9
All	11 562	21.5	28.5	2.3	47.8

Controlled hypertension: systolic BP <140 mm Hg and diastolic BP <90 mm Hg

ISH – isolated systolic hypertension: systolic BP ≥140 mm Hg and diastolic BP <90 mm Hg

IDH – isolated diastolic hypertension: systolic BP <140 mm Hg and diastolic BP ≥90 mm Hg

SDH – systolic-diastolic hypertension: systolic BP ≥140 mm Hg and diastolic BP ≥90 mm Hg

low risk counterparts (34%). Thus, patients expected to benefit the most from BP normalization were also patients who were the most difficult to treat.

The BP control rate has also been evaluated in treated hypertensive patients known to have coronary heart disease [30]. A total of 1423 patients were recruited by general practitioners, and 2596 by cardiologists. Normal BP (<140/90 mm Hg) was observed more frequently among patients followed by cardiologists (40.8%) than among those followed in general practice (26.3%), and more often among patients in the lowest cardiovascular risk group (general practitioners: 26.3%, cardiologists: 32.4%). Among patients with uncontrolled hypertension, 67.4% were receiving ≥2 drugs when followed in

general practice, compared with 77.7% when followed in cardiological practice. In a multiple regression analysis, age, total cholesterol, obesity, current smoking, and diabetes were independently and negatively associated with hypertension control.

More recently the results of an observational cross-sectional epidemiological study aiming to assess the determinants of hypertension control have been published [31]. A total of 4966 hypertensive patients aged >18 years were included, followed by 2487 practitioners (Table I). The patients had to be pharmacologically treated with the same drug(s) for more than 1 month and less than 1 year. Half of them had two or more cardiovascular risk factors in addition to hypertension. BP was

<140/90 mm Hg in only a small fraction of patients (18%). Factors independently associated with poor BP control were advanced age, male gender, history of previous cardiovascular event, high heart rate and high body weight.

### Germany

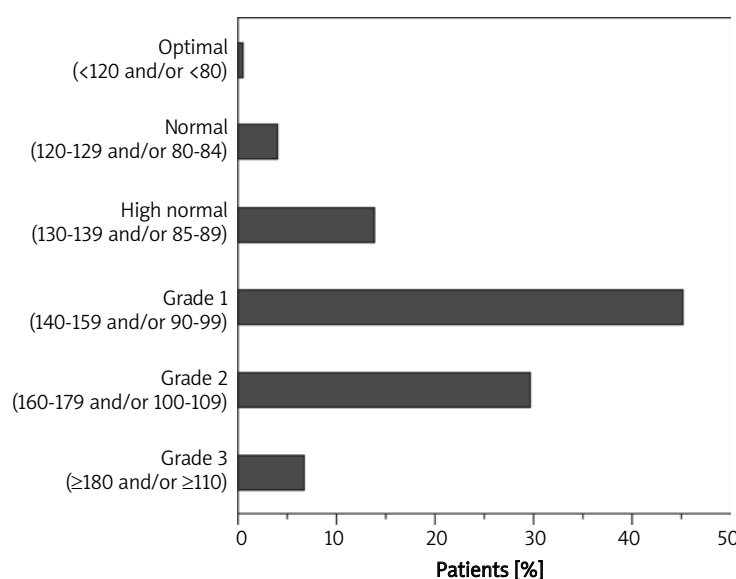
A cross-sectional prevalence study has been conducted in a representative nationwide sample of primary care doctors (n=1912) who were asked to give information on a total of 45 093 patients [32]. 17 485 patients were considered as having hypertension (39%) and 14 647 among those diagnosed as hypertensive were treated (84.5%), using a monotherapy in 45% of cases (Table I). The fraction of patients on antihypertensive therapy who had BP <140/90 mm Hg was 31.7%. When asked to estimate the success of their treatment, however, the doctors considered hypertension as “well controlled” in 52% of their patients.

### Italy

The BP control achieved in patients managed by specialist physicians has been studied in 131 outpatient centres located in northern (34.5%), central (28.1%) and southern (37.4%) Italy [33]. Each centre had the task of recruiting a minimum of 20 consecutive patients attending a routine visit (Table I). A total of 2775 patients with a mean age of 61 years were included. 36.9% were receiving monotherapy and the remainder combination therapy. The prevalence of BP <140/90 mm Hg was 37.5%. The control of systolic BP only was less frequent (40.2%) than the control of diastolic BP only (64.4%). The total cardiovascular risk profile was calculated according to the 2003 ESH/ESC

guidelines [9]. Low-medium risk, high risk and very high risk patients accounted for 37.3, 34.2 and 28.5% of the study population, respectively. The BP control rate (BP <140/90 mm Hg) was better in low-medium risk patients (43.2%) than in high (33.2%) and very high risk patients (34.9%). The BP control rate increased from the initial visit (41.2%) to the 6- and 12-month visits (46.2 and 52.3%, respectively). This improvement could hardly be explained by an intensification of drug consumption as the treatment remained unchanged during the 12-month follow-up in 78.3% of the patients, was stepped up in only 15.3% of the patients, and was even stepped down in 6.4% of the patients. Enhanced compliance with the prescribed treatment might have contributed to the better therapeutic effects observed with time. According to the latest ESH/ESC hypertension guidelines, target BP should be <130/80 mm Hg in high and very high risk patients [10]. Notably, such a low BP target was observed at the end of the 12-month follow-up in only a small fraction of high risk (16.3%) and very high risk patients (17.7%).

An observational study was performed by 1800 general practitioners who were asked to recruit 10 consecutive patients aged 54 to 84 years [34]. The diagnosis of hypertension was based on BP  $\geq$ 140/90 mm Hg or the current use of antihypertensive drugs. A total of 12 792 patients were included in the study (5280 were untreated and 7512 treated). Overall BP control in treated patients occurred in 18.4% of subjects (Table I). Among treated hypertensives, 23.1% had diabetes. BP was <140/90 mm Hg and <130/80 mm Hg in 14.9 and 3.0% of these patients, respectively. Figure 1 depicts the classification of the patients on anti-



**Figure 1.** Classification of patients treated for hypertension according to blood pressure criteria of the European Society of Hypertension/European Society of Cardiology hypertension guidelines (modified from [34])

hypertensive therapy according to the BP criteria of the ESH/ESC hypertension guidelines [9]. The majority of patients had grade 1 hypertension, meaning that their BP ranged from 140 to 159 mm Hg for systolic and/or 90 to 99 mm Hg for diastolic.

### Spain

A study was carried out to assess the BP control rate among special subgroups of hypertensives treated in 47 hospital-based hypertension units nationwide [35]. Out of the 4049 analyzed patients, 48% were on monotherapy and 42% had BP <140/90 mm Hg (Table I). The presence of diabetes, renal failure and proteinuria was observed in 893, 669 and 1757 patients, respectively. In these high risk patients, it is recommended to pursue the lowering of BP below 130/80 mm Hg [9]. This target was reached in only 10% of diabetics, 12% of patients with renal failure and 12% of proteinuric patients. Table III shows the physicians' management behaviour with regard to uncontrolled hypertension. Clinical inertia was a prominent finding, as it was observed in 56% of low or medium risk patients with BP  $\geq$ 140/90 mm Hg, and 61% of high or very high risk patients with BP  $\geq$ 130/85 mm Hg.

### Sweden

In a cross-sectional survey 6537 patients on antihypertensive therapy were recruited by 264 primary care physicians from across Sweden (187 men and 77 women) [36]. Blood pressure was normalized (<140/90 mm Hg) in a significantly greater fraction of patients when they were treated by a female (31.0%) than a male (26.6%) physician (Table I). The gender of the physician had no influence on BP control in hypertensive men. Significantly ( $P < 0.001$ ) more hypertensive women however reached the target BP when treated by a female physician (32.2%) rather than by a male physician (23.7%).

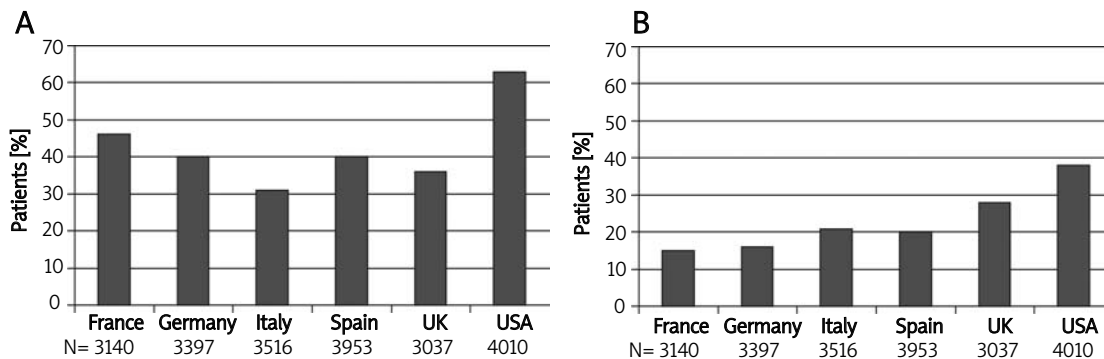
### International surveys

A large survey was performed in 2004 to explore international differences in hypertension treatment. It included 21 053 hypertensive patients followed by 291 cardiologists and 1284 primary care physicians in 5 western European countries (France, Germany, Italy, Spain, United Kingdom) and the United States [37]. The data were collected using identical procedures, allowing valid comparisons between countries. The left panel of Figure 2 depicts the percentage of treated hypertensive patients who had BP <140/90 mm Hg.

**Table III.** Physicians' behaviour in patients with uncontrolled hypertension, classified according to their global cardiovascular risk\* (from ref. [35])

	No drug treatment modification [%]	Drug treatment modification		
		Dose increase [%]	Addition of another drug [%]	Switch to another drug [%]
Low or medium risk with BP $\geq$ 140/90 mm Hg (n=809)	56	16	20	8
High or very high risk with BP $\geq$ 130/85 mm Hg (n=2107)	61	14	18	7

\*Based on the 1999 WHO/ISH guidelines [6]



**Figure 2.** A – percentage of hypertensive patients having their blood pressure controlled (<140/90 mm Hg) during antihypertensive therapy. B – percentage of hypertensive patients with uncontrolled hypertension having their treatment intensified (modified from [37])

Large differences were observed across some countries. The best BP control rate was observed in the United States, where the use of combination therapy was highest (64 vs. 44-59% across European countries). Notably, only a small fraction of patients with inadequately controlled BP had their treatment intensified during the visit, indicating that physicians' inertia may account for the persistence of high BP in many patients on antihypertensive therapy (Figure 2B). Physicians in the United States were clearly more prompt in modifying the treatment (38 vs. 15-28% across European countries).

Finally, the results of a survey aiming to investigate in hypertensive patients the cardiometabolic profile according to the control of BP have been published very recently [38]. A total of 3370 hypertensive patients were included in this observational, cross-sectional survey which was carried out in 12 European countries (Belgium, Germany, Hungary, Italy, the Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, Turkey and the United Kingdom) by 289 physicians (general practitioners: 61%, internists: 24%, cardiologists: 14%, hypertension specialists: 1%). Blood pressure was controlled (<140/90 mm Hg) in 28.1% of patients. Metabolic syndrome and type 2 diabetes were seen in 57.8 and 25.6% of the total population, respectively, whereas metabolic syndrome and type 2 diabetes co-existed in 25.6% of the patients. Notably, the prevalence of metabolic syndrome was significantly ( $P < 0.001$ ) greater in patients with uncontrolled hypertension (66.5%) than in those with controlled hypertension (35.5%). This was also true regarding the prevalence of type 2 diabetes (41.1 vs. 9.8%,  $P < 0.001$ ). Most patients received only monotherapy (29.5 and 28.4% of patients with controlled and uncontrolled BP, respectively).

The surveys described above provide an overview of the current management of hypertension in European countries with well developed health systems. Several points should be emphasized:

- the control of BP in treated hypertensive patients remains unsatisfactory,
- it is more difficult to normalize BP in patients with higher than in those with lower cardiovascular risk,
- the control of systolic BP is more difficult to achieve than that of diastolic BP,

- BP control is achieved with greater difficulty in older than in younger patients,
- BP is difficult to control in patients with metabolic syndrome and type 2 diabetes,
- combination therapy is required in most patients to normalize BP,
- poor compliance with the prescribed drug regimen may contribute to the unsatisfactory BP seen in the community,
- clinical inertia is a major cause of unsatisfactory BP control.

#### Office versus "out-of-office" blood pressure control

The BP control rates achieved either conventionally (i.e. using office BP as a criterion) or relying on ambulatory BP monitoring have been compared in 12 897 hypertensive patients, recruited by 1124 physicians from 210 primary healthcare clinics, as part of a nationwide project developed by the Spanish Society of Hypertension [39]. Observations were sent to a central database from June 2004 to July 2005. There was less than 1 month interval between the office BP measurements and the 24-h ambulatory BP monitoring. Office BP was controlled (<140/90 mm Hg) in 23.6% of patients (Table IV). The daytime ambulatory BP control rate (<135/85 mm Hg) was 51.5%. Among patients who had daytime ambulatory BP  $\geq 135/85$  mm Hg, only 5.4% had their office BP controlled. These findings indicate that the BP control rate in treated hypertensives is substantially better when relying on BP readings taken outside the medical setting rather than on standard office-based measurements. This is important since ambulatory BP is known to reflect more closely cardiovascular risk than BP determined in a medical setting [21-24, 40].

#### Conclusions

There is strong evidence that tight BP control in hypertensive patients allows maximal protection against cardiovascular and renal diseases [1-3]. The BP control rate observed today in everyday practice is improving, but remains unsatisfactory. In order to normalize BP in most hypertensive patients, it appears necessary to extend the use of drug combinations. This is especially true in older patients

**Table IV.** Blood pressure (BP) control rate based on office BP readings and daytime ambulatory BP monitoring (from ref. [39])

Daytime ambulatory BP	Clinic-based BP controlled (<140/90 mm Hg) [%]	Clinic-based BP not controlled ( $\geq 140/90$ mm Hg) [%]
controlled (<135/85 mm Hg)	18.2	33.4
not controlled ( $\geq 135/85$ mm Hg)	5.4	43

and in those at high cardiovascular risk, in whom it is particularly difficult to bring BP under control.

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