Development of diagnostic thresholds for automated measurement of blood pressures in adults

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In clinical medicine, blood pressure is usually measured by conventional sphygmomanometry. Although it seems simple at first sight, this procedure is fraught with potential sources of error, which may arise from the subject, the observer, the sphygmomanometer or the overall application of the technique. Automated techniques of blood pressure measurement, such as ambulatory monitoring and self-measurement, reduce the limitations of conventional sphygmomanometry. However, the diagnostic thresholds applicable for conventional sphygmomanometry cannot be extrapolated to automated measurements. During the past 10 years criteria for normality have gradually been developed for ambulatory blood pressure (ABP) monitoring of adults. First, the distribution of the ABP in normotensive subjects and untreated hypertensive patients who had initially been recruited and classified on the basis of their conventional blood pressure was studied. Second, authors of various epidemiological studies investigated the distributions of the conventional blood pressure and the ABP in the population at large. Third, authors of several reports attempted to validate the preliminary thresholds for ambulatory monitoring by correlating the ABP to left ventricular hypertrophy, other intermediary signs of target-organ damage or the incidence of cardiovascular morbidity or mortality. Finally, clinical trials should be mounted to prove that it is beneficial to patients as well as cost-effective to diagnose and treat hypertension on the basis of ambulatory monitoring rather than solely under the guidance of conventional sphygmomanometry. For measurements of systolic/diastolic ABP in adults, the proposed upper limits of normotension are 130/80 mmHg for the 24 h blood pressure and 135/85 and 120/70 mmHg for the daytime and night-time blood pressures, respectively; for the self-measured blood pressure 135/85 mmHg might be the upper limit of normality. With regard to ABP monitoring, a large database already supports the proposed diagnostic thresholds in terms of their associations with left ventricular hypertrophy and with the incidence of cardiovascular complications; the evidence to validate the thresholds for the self-recorded blood pressure, to a large extent, must still be collected. In conclusion, the newer techniques of blood pressure measurement are now well established in the diagnosis and management of adult subjects with hypertension. *Blood Press Monit* 4:127–136
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Blood Pressure Monitoring 1999, 4:127–136

Keywords: ambulatory blood pressure monitoring, hypertension, normotension, self-recorded blood pressure

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Sponsorship: The Belgian population studies have been supported by the International Lead Zinc Research Organization (Research Triangle Park, North Carolina, USA), the municipality Hechtel–Eksel (Belgium) and the Nationaal Fonds voor Wetenschappelijk Onderzoek Vlaanderen (Brussels, Belgium). The ABP and Treatment of Hypertension (APTH) and the Treatment of Hypertension According to Home or Office Blood Pressure (THOP) trials are being conducted under the auspices of the Belgian Hypertension Committee and with financial support from AstraZeneca Inc. (Brussels, Belgium). The Systolic Hypertension in Europe (Syst-Eur) trial was a concerted action of the BIOMED Research Programme sponsored by the European Union. The Syst-Eur trial was carried out in consultation with the World Health Organization, the International Society of Hypertension, the European Society of Hypertension and the World Hypertension League. The trial was sponsored by Bayer A.G. (Wuppertal, Germany).

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Introduction

In most circumstances blood pressure is measured by conventional sphygmomanometry and by auscultation of the Korotkoff sounds [1]. This procedure is fraught with potential errors, which may arise from the subject, the observer, the sphygmomanometer or the overall application of the technique [2,3]. Terminal-digit preference refers to the phenomenon whereby the observer rounds off the blood pressure reading to an arbitrary digit, often to a zero or a five [4,5]. Observer bias is the practice whereby the observer simply adjusts the blood pressure reading to accord with a preconceived idea of what the blood pressure should be [4,6]. Observer prejudice is most likely to occur when an arbitrary division line is applied to diagnose hypertension, to recruit patients or to adjust treatment [6]. Moreover, the presence of an observer, such as a nurse or a doctor, can arouse the patient and increase the blood pressure [7–11]. This so-called 'white-coat phenomenon' can lead to an overestimation of the blood pressure and the artefactual diagnosis of hypertension. The seemingly elevated blood pressure in patients with white-coat hypertension is not sustained in the absence of the observer [7–11]. Another major drawback of conventional

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sphygmomanometry stems from the fact that blood pressure is highly variable [12] and, as was originally demonstrated by researchers in Oxford [13], is characterized by large diurnal fluctuations [14]. Single measurements or multiple readings taken by an auscultating observer at one or even several times throughout the day reflect a subject's true blood pressure only to a minor extent.

Newer techniques, such as ambulatory blood pressure monitoring (ABPM) [15–17] and the self-measurement of blood pressure [18] are gradually gaining wide acceptance in clinical medicine as means that allow one to overcome some of the limitations of conventional sphygmomanometry. The goal of this review article is to describe how diagnostic thresholds for automated measurement of blood pressure in adults, in particular ABPM, were developed.

ABP measurement

ABPM makes it possible to record the blood pressure in patients engaged in their normal activities throughout the whole day and to provide within 24 h a reliable estimate of their blood pressure [19]. In order to collect the same information, conventional measurements must be repeated at intervals of a few weeks [20]. Furthermore, the ABP level is characterized by high reproducibility [21], is not subject to digit preference and observer bias [6] and avoids the transient rise of a patient's blood pressure in response to the clinic surroundings or the presence of the observer [10], the so-called white-coat effect [8,22].

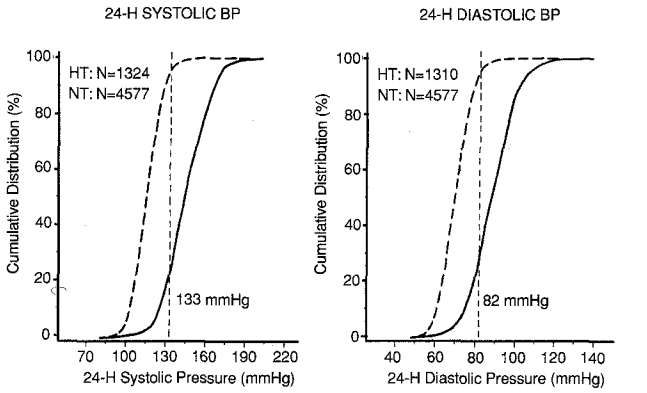
The association between blood pressure and cardiovascular risk is continuous without a threshold above which the risk suddenly increases [23,24]. However, clinical decisions must be based on diagnostic or operational thresholds. There is a general consensus that the thresholds currently applicable for conventional sphygmomanometry [25,26] cannot be extrapolated and used for automated blood pressure measurements. The guidelines [25–28] are also unanimous that only properly validated devices should be used for ABPM and for the self-measurement of blood pressure. The validation procedures have been standardized thoroughly [29–31]. Furthermore, when devices are to be used for special populations of patients, such as old subjects and pregnant women [32–34], or under special conditions, such as during exercise [35,36], a specific demonstration of accuracy for these defined subgroups and conditions is necessary [30,32].

During the past 10 years diagnostic thresholds for ABPM of adults have gradually been developed. First, the distribution of the ABP in normotensive subjects and untreated hypertensive patients who had initially been recruited and classified on the basis of their conventional blood pressure was studied [37–42]. Second, authors of various epidemiological studies investigated the distributions of the conventional blood pressure and the ABP in the population at large [43–57]. Third, authors of several reports attempted to validate the preliminary thresholds for ABPM by correlating ABP readings to left ventricular hypertrophy and other intermediary signs of target-organ damage [58–67] or to incidence of cardiovascular morbidity or mortality [68–70]. Finally, clinical trials should be mounted to prove that it is beneficial to patients as well as cost-effective to diagnose and to treat hypertension on the basis of ABPM rather than solely under the guidance of the conventional blood pressure [71,72].

Distributions of the ABP in normotensive and hypertensive subjects and in the general population

The early proposals for normality of the ABP in adults were largely based on the distributions of the ambulatory measurements for normotensive subjects and untreated hypertensive patients (Fig. 1). Initially, authors of several small studies described the distributions of ABP in healthy subjects and patients referred to specialized clinics to exclude the diagnosis of hypertension (for review, see Staessen *et al.* [39]). In these reports the average systolic blood pressure over the whole day ranged from 111 to 124 mmHg; the daytime averages ranged from 115 to 128 mmHg and the night-time means from 99 to 111 mmHg; the corresponding ranges for the diastolic blood pressure embraced 59 and 79 mmHg, 63 and 85 mmHg and 51 and 70 mmHg, respectively [39]. Results of further epidemiological studies concerning well-defined professional groups [37,38], normotensive and hypertensive subjects [39,42] and the population at large [43–57] subsequently led to various proposals for normality of blood pressure on ambulatory measurement.

Fig. 1



The cumulative distributions of the 24 h systolic (a) and diastolic (b) blood pressures in normotensive subjects (NT, n = 4577, full lines) and in untreated hypertensive patients (HT, systolic n = 1324 and diastolic n = 1310, broken lines). Normotension was a conventional systolic/diastolic blood pressure below 140/90 mmHg; hypertension was a conventional blood pressure of 160 mmHg systolic or 95 mmHg diastolic or higher. The dotted vertical lines indicate the 95th percentiles of the 24 h blood pressure for the normotensive subjects. Approximately 30% of the hypertensive patients had 24 h blood pressures below these thresholds. Reproduced with permission from Staessen *et al.* [76].

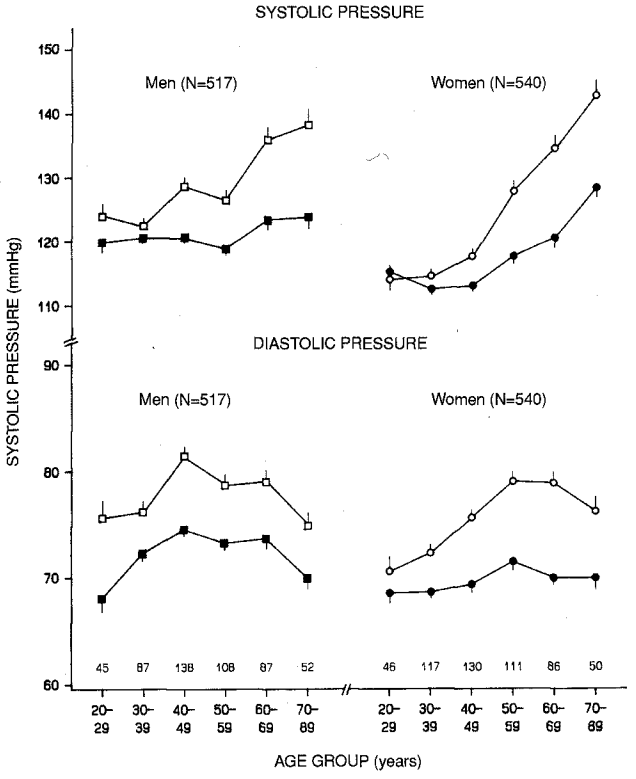
Table 1 **The 95th percentiles as the upper limits of the distribution of the ambulatory blood pressure in normotensive subjects**

	IDB	AIBS	BPS	JPS	DPS	IPS	All
References	[40,73]	[38]	[48,52]	[43,44]	[53]	[56,57]	
Subjects							
All	7320	815	1057	705	352	1438	11 687
Normotensive subjects[a]	3188[b]	807	729	324[c]	238[c]	1402	5 286
Systolic blood pressure (mmHg)							
Conventional	140	136	136	136	137	137	137
Whole day	134	131	129	134	136	128	132
Daytime	141	138	137	138	139	134	138
Night-time	128	120	121	128	122	121	123
Diastolic blood pressure (mmHg)							
Clinic	87	88	86	86	89	89	88
Whole day	82	82	80	79	86	82	82
Daytime	88	89	88	83	88	88	87
Night-time	77	72	72	74	77	74	74

IDB, International Database; AIBS: Allied Irish Bank Study; BPS, Belgian population study; JPS, Japanese population study; DPS, Danish population study; IPS, Italian population study. [a]Ninety-fifth percentiles were determined for normotensive subjects whose conventional blood pressures were lower than 140 mmHg systolic and 90 mmHg diastolic. [b]This group excludes participants of the AIBS and the BPS, data for whom were analysed separately. [c]The authors generated the 95th percentiles from the databases [44,53].

The most prominent feature of the larger studies on ABPM [38–40,44,47,48,55,73–75] is the striking concordance of their reported statistics, be it the mean + 2SD (for review, see Staessen *et al.* [76]) or the 95th percentile (Table 1). Averaging the 95th percentiles for the normotensive subjects and rounding the resulting boundaries downwards or upwards to the nearest value ending in 0 or 5 produced working definitions of normality for ABPM, which could be easily remembered (Table 2). According to these procedures, the upper limits of normotension, calculated by rounding downwards, were 130/80 mmHg for the 24 h blood pressure and 135/85 and 120/70 mmHg for the daytime and night-time blood pressures [76,77]. Abnormality, obtained by rounding upwards, corresponded to blood pressures exceeding 135/85, 140/90 and 125/75 mmHg, respectively [76,77] . These preliminary threshold values did not account for sex and age. However, the boundaries currently in use for normotension and hypertension on conventional blood pressure measurement and jointly endorsed by expert panels from World Health Organization/International Society for Hypertension (WHO/ISH) [26] and the sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI) [25], namely 140 mmHg systolic and 90 mmHg diastolic, are also uniformly applicable to adult men and women regardless of age. Moreover, age is a stronger correlate of the conventional than it is of the ABP in adults (Fig. 2) [44,46,57].

Fig. 2



The conventionally measured blood pressure (mean of five consecutive readings during one home visit) and the 24 h ambulatory blood pressure plotted by 10-year age classes for 1057 participants in a population study in Belgium. Values are means ± SEM. Reproduced with permission from Staessen *et al.* [52].

Methodological issues

The diagnostic thresholds presented in Table 2 are in line with the recommendations of JNC VI [25] and those of

Table 2 ***Proposed thresholds for automated blood pressure measurements***

	95th percentiles	Normotension[b]	Hypertension[c]
Ambulatory blood pressure (mmHg)			
24 h	132/82[a]	≤ 130/80	> 135/85
Daytime	138/87[a]	≤ 135/85	> 140/90
Night-time	123/74[a]	≤ 120/70	> 125/75
Self-recorded blood pressure (mmHg)			
Morning	136/85	≤ 135/85	> 140/90
Evening	139/86	≤ 135/85	> 140/90
Morning and evening	137/85	≤ 135/85	> 140/90

[a]Mean value for the 95th percentiles for normotensive subjects (see Table 1). [b]Obtained by rounding downwards to the next blood pressure ending in 0 or 5 mmHg. [c]Obtained by rounding upwards to the next value ending in 0 or 5 mmHg.

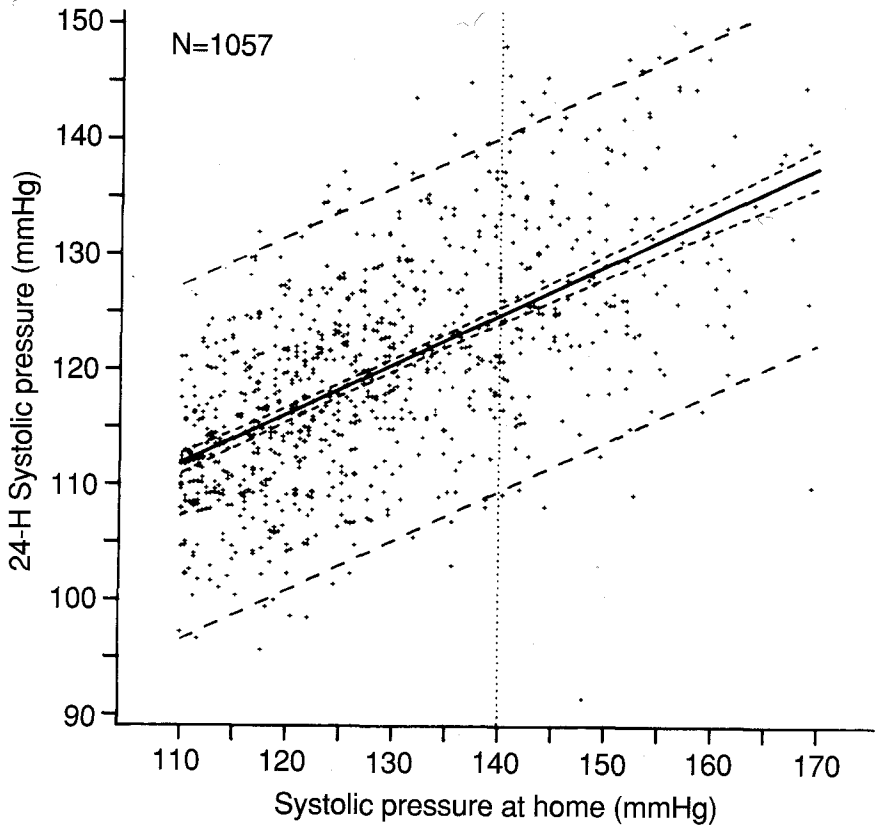
many other national expert committees [27], but they are higher than those proposed by the PAMELA investigators both in their own publications [54] and in the WHO/ISH guidelines [26]. The Italian group concluded that the upper limits of a normal 24 h ABP would probably be lower than 120–130 mmHg systolic and 75–81 mmHg diastolic [54]. Just like in another, German, study [78], these thresholds were derived by regressing the 24 h blood pressure on the clinic blood pressure and by determining the 24 h level that would correspond to a clinic blood pressure of 140 mmHg systolic or 90 mmHg diastolic. However, the 95% confidence intervals about the regression lines from which the PAMELA investigators derived the upper limits of normality for the ABP were those for the prediction of population means [54]. Such intervals were determined in various strata according to sex and age. These confidence bands were then juxtaposed to obtain an overall interval estimate of the upper normal limits. However, the 95% confidence intervals for the prediction of the 24 h ABP in individual subjects, which reflect the scatter of individual 24 h values to be expected with a clinic blood pressure of 140 mmHg systolic or 90 mmHg diastolic (Fig. 3), are much wider than 120–130 mmHg and 75–81 mmHg, respectively [52]. Moreover, data for normotensive subjects and untreated hypertensive patients were pooled in the regression analysis [54]. Because the white-coat phenomenon is substantial for the latter but almost nonexistent for the former [40], it remains to be demonstrated that the regression lines for these two subgroups were coincident and that normotensive and hypertensive subjects could be pooled in the regression analysis.

The conventional blood pressure and ABP are not normally distributed in the population [52]. Taking the mean and adding twice the SD is therefore a method less suited to describing the upper tail of the blood pressure distribution. It overestimates the high-end thresholds. For the normotensive subjects enrolled in the International Database [40,55] , the mean + 2SD for the systolic and diastolic blood pressure on conventional measurement were 143 and 91 mmHg, respectively, whereas in fact all conventional readings had been below 140 and 90 mmHg, respectively. For this reason non-parametric statistics, such as the 95th percentile, constitute the preferred way to delineate the upper tail of the non-normal blood pressure distribution. The mean + 2SD roughly corresponds to the 97–98th percentile of the underlying distribution.

Validation of the diagnostic thresholds in terms of left ventricular hypertrophy

Devereux *et al.* [61] contrasted the ambulatory measurements of normotensive subjects with normal left ventricular geometry with those of patients with concentric left

Fig. 3



Regression line relating 24 h systolic blood pressure to the conventional systolic blood pressure in 1057 participants in a Belgian population study. For clarity the plot depicts only the results for conventional blood pressure values ranging from 110 to 170 mmHg, but all data were used to calculate the regression line. The 95% confidence interval for the prediction of the average 24 h systolic blood pressure corresponding to a conventional systolic blood pressure of 140 mmHg is much smaller than the 95% confidence interval for the prediction of the 24 h systolic blood pressures in individual subjects. Reproduced with permission from Staessen *et al.* [52].

ventricular hypertrophy, the morphological pattern associated with the worst prognosis [79]. These investigators suggested that awake ABP below 139/86 mmHg in adult men and women be considered normal, whereas values over 145/95 mmHg should be viewed as pathological [61]. Along similar lines, Gosse *et al.* [58] found that the left ventricular mass index increased with increasing daytime blood pressure, but not with increasing white-coat effect defined as the difference between the clinic and the daytime blood pressure. In Gosse *et al.*'s study [58] left ventricular mass index was on average not greater than normal (< 125 g/m^2) for the patients in the bottom quartile of the daytime blood pressure, in whom during the day the maximal value of the systolic blood pressure was 133 mmHg and that of the diastolic 89 mmHg. In addition, results of two recent studies [62,65] showed that regression of left ventricular hypertrophy under antihypertensive drug treatment was correlated more closely to the changes in the ABP than it was to those in the conventional blood pressure.

Validation of the diagnostic thresholds in terms of morbidity and mortality

Perloff *et al.* [69,70] started the validation of ABPM in terms of hard cardiovascular end points. These investigators used the patient-activated Remler M-2000 recorder (Remler Corporation, San Francisco, California, USA). They showed for the first time that the portion of the daytime ABP which was not already explained by systolic or diastolic clinic blood pressure could discriminate high-risk from low-risk hypertensive patients [69]. These results obtained with 1076 hypertensive patients by life-table analysis were later confirmed by Cox regression for a subgroup of 761 patients, who were untreated at baseline [70]. With stratification for previous cardiovascular complications and with cumulative adjustments for clinic blood pressure, sex, age, electrocardiographic left ventricular hypertrophy, hypertensive retinopathy and subsequent antihypertensive drug therapy, a higher systolic ABP was still a harbinger of a worse cardiovascular outcome [70]. Furthermore, a smaller study of 137 newly referred hypertensive patients revealed that intra-arterial measurement of blood pressure over 24 h significantly improved upon the prognostic accuracy of conventional blood pressure readings [68]. A recent report from the same centre concerned 479 patients who underwent 24 h intra-arterial blood pressure monitoring and were followed up for an average of 9.1 years [67]. White-coat hypertension, defined as a clinic systolic blood pressure of 140–180 mmHg associated with a 24 h blood pressure of less than 140 mmHg systolic and 90 mmHg diastolic, was present in 126 patients; compared with the patients with sustained hypertension (n = 353), the former had a 71% lower risk [95% confidence interval (CI) 10–91%, $P = 0.04$) of experiencing cardiovascular events [67].

Verdecchia's group followed up for up to 7.5 years (mean 3.2 years) 1187 subjects with essential hypertension and 205 healthy normotensive control subjects, all of whom underwent baseline off-therapy 24 h non-invasive ABPM [60]. The prevalence of white-coat hypertension, defined as an average daytime blood pressure lower than 136/87 mmHg for men and 131/86 mmHg for women, among the hypertensive patients was 19.2%. After adjustment for traditional markers of cardiovascular risk, morbidities of the normotensive subjects and the white-coat hypertensive group did not differ ($P = 0.83$) [60]. Ohkubo *et al.* [66] recently found that the 24 h systolic and diastolic blood pressures in 1542 residents of a rural Japanese community, aged 40 years and more, were significantly and curvilinearly correlated to total mortality. This second-order relationship persisted after cumulative adjustments for sex, age, smoking status, use of antihypertensive medication at baseline and history of cardiovascular disease, diabetes and hypercholesterolaemia. However, the Japanese group did not report whether the correlation between all-cause mortality and the 24 h blood pressure was also spared by adjustment for the conventional blood pressure at baseline or by excluding the non-cardiovascular deaths [66]. Furthermore, Redón *et al.* [63] studied patients with refractory hypertension, defined as a diastolic blood pressure of more than 100 mmHg, while they were taking three or more antihypertensive medications. Patients were classified into three groups according to their daytime ABP; those in the lowest tertile (< 88 mmHg) had a significantly lower rate of morbidity over the next 4 years than did those in the middle (88–97 mmHg) and highest (> 97 mmHg) tertiles. No differences in office blood pressure among these three groups were observed either at baseline or at the time of the last evaluation [63].

In a substudy [42,80,81] of the double-blind placebo-controlled Systolic Hypertension in Europe (Syst-Eur) Trial [59,64] , the prognostic significances of conventional and ABP measurement for older patients with isolated systolic hypertension were compared. The conventional blood pressure at random allocation to groups was the mean of six readings (two measurements with the patient sitting during three visits 1 month apart). The baseline ABP was recorded with a non-invasive intermittent technique. Old (aged ≥ 60 years) patients whose untreated blood pressure on conventional measurement at baseline was 160–219 mmHg systolic and less than 95 mmHg diastolic were randomly allocated to administration of 10–40 mg/day nitrendipine with the possibility of addition of 5–20 mg/day enalapril or 12.5–25 mg/day hydrochlorothiazide, or both, or to matching placebos [59]. With cumulative adjustments applied for sex, age, previous cardiovascular complications, smoking and residence in western Europe [82], higher systolic blood pressure at randomization predicted a worse prognosis, whereas the association between diastolic blood pressure and outcome was not significant. For patients in the placebo group (n = 393), the 24 h, daytime (1000–2000 h) and night-time (0000–0600 h) systolic ABP

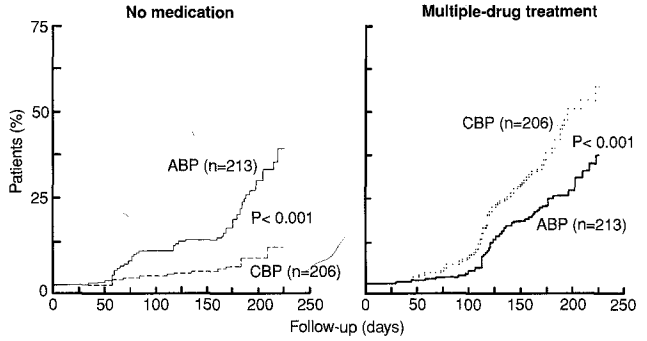
predicted the incidence of cardiovascular complications even after further adjustment for the conventional blood pressure [81]. At randomization, the cardiovascular risk conferred by a conventional systolic blood pressure of 160 mmHg was similar to that associated with 24 h, daytime and night-time systolic blood pressures of 142 mmHg (95% CI 128–156 mmHg), 145 mmHg (95% CI 126–164 mmHg) and 132 mmHg (95% CI 120–145 mmHg), respectively [81]. For patients in the active-treatment group (n = 415), systolic blood pressure at randomization did not significantly predict cardiovascular risk, regardless of the technique of blood pressure measurement. This observation confirmed that active treatment had reduced the excess risk conferred by hypertension.

Evidence from a clinical trial

Investigators in the ABPM and Treatment of Hypertension (APTH) trial [71,72] tested the hypothesis that the use of ABPM in the management of hypertensive patients would lead to less intensive drug treatment with fewer side effects and that, in spite of the reduction in treatment, control of blood pressure throughout the day and protection against left ventricular hypertrophy would be preserved. The patients were randomly allocated to be treated on the basis of the average daytime (1000–2000 h) ABP (ABP group) or on the basis of the average of three sitting readings obtained by conventional sphygmomanometry by the clinical investigators (CBP group). After random allocation, all patients started to be administered 10 mg/day lisinopril (step I). Follow-up visits after random allocation were scheduled for after 1 month (visit one), 2 months (visit two), 4 months (visit three) and 6 months (visit four). The same standardized treatment regimen was applied to both groups with the goal of reaching the same target range of diastolic blood pressure, namely 80–89 mmHg [71]. The possible treatment steps at visits one to four involved increasing dosage of lisinopril to its standard daily dose of 20 mg (step II), the addition of 12.5 mg hydrochlorothiazide in the morning (step III) and the association of 5 mg/day amlodipine (step IV). For patients with known contra-indications to administration of converting enzyme inhibitors, lisinopril could be substituted by 50 (step I) or 100 mg/day (step II) atenolol. If the diastolic blood pressure guiding treatment was above target (> 89 mmHg), medical treatment was intensified by one step. If the diastolic blood pressure was within the target range (80–89 mmHg), medical treatment was left unchanged. If the diastolic blood pressure guiding treatment was below target (< 80 mmHg), medical treatment was reduced by one step.

After random allocation, more ABP than CBP patients ceased to be administered antihypertensive drug treatment (Fig. 4), because their diastolic blood pressures were less than 80 mmHg and thereafter remained below or within the target range (4.7 versus 1.3 patients per 100 followed up for 1 month, $P < 0.001$). The opposite trend (Fig. 4) was observed for patients proceeding to sustained multiple drug treatment (4.8 versus 8.3 patients per 100 followed up for 1 month, $P < 0.001$). Low daytime ABP at random allocation and female sex independently predicted the cessation of antihypertensive drug treatment of patients in the ABP group [72].

Fig. 4



Kaplan–Meier estimates modelling the probability that patients would permanently stop needing antihypertensive drug treatment (a) or would proceed to sustained multiple-drug treatment (b) during follow-up. The differences between the patients randomly allocated to conventional blood pressure (CBP, broken line) or ambulatory blood pressure (ABP, full line) measurement were significant ($P < 0.001$). Reproduced with permission from Staessen *et al.* [72].

Blood pressures in patients in both groups decreased ($P < 0.001$) after random allocation. During the first follow-up visit, the decreases for patients in the two treatment groups were the same, averaging 16.5/10.2 mmHg for the conventional blood pressure and 11.2/7.5 mmHg for the daytime blood pressure. Thereafter, decrease in blood pressure in the CBP patients tended to be slightly greater than that in patients in the ABP group. The final conventional and 24 h ABP averaged 144/90 and 129/80 mmHg for patients in the ABP group and 140/90 and 128/79 mmHg for patients in CBP group (P values for the between-group differences ranged from 0.16 to 0.02). At the end of follow-up, electrocardiographic and echocardiographic left ventricular mass and symptoms reported by patients in the two groups were similar. The APTH findings demonstrated that adjustment of antihypertensive treatment on the basis of ABPM instead of conventional sphygmomanometry leads to less intensive drug treatment with preservation of control of blood pressure, maintenance of general well-being and inhibition of enlargement of left ventricle.

Clinical application of ABPM to adults

ABPM is most clinically helpful and most commonly used for assessing patients suspected to have white-coat hypertension [25–27] . The prevalence of clinic or office hypertension in industrialized countries is nearly 15% of the whole population and can exceed 30% among subjects

aged > 70 years [83]. The prevalence of white-coat hypertension (isolated clinic hypertension) among these patients varies from 20% [8,84] to 35% [40]. The APTH trial [72] demonstrated that by using ABPM, antihypertensive drug treatment of 25% of the hypertensive-patient population can be postponed and that multiple-drug treatment of 15% can be avoided. The APTH results do not imply that patients with white-coat hypertension should be left untreated. However, if no cardiovascular complications are present at diagnosis, treatment could be limited to further follow-up and the implementation of cardiovascular-hygienic measures, such as regular exercise, reduction of excessive consumption of alcohol and intake of sodium and slimming of overweight subjects. Initial treatment should also account for other cardiovascular risk factors, such as smoking, hypercholesterolaemia and diabetes mellitus. Whether white-coat hypertensive patients have a higher than normal risk of developing sustained hypertension is still being debated [85,86] , although there is a growing database suggesting that apart from the few cases misclassified at initial diagnosis, white-coat hypertension is really a benign condition.

ABPM is superior to conventional sphygmomanometry not only for selecting adult patients for antihypertensive drug treatment but also for assessing the effects of such treatment, for instance on left ventricular mass [62,65]. Antihypertensive medications lower the clinic blood pressure but not the ABP in patients with white-coat hypertension [80,87–89]. ABPM is therefore an excellent technique for evaluating treatment-resistant hypertension. According to the JNC VI guidelines [25], other indications for ABPM are hypotensive symptoms under antihypertensive drug treatment, episodic hypertension and autonomic dysfunction [90].

Self-recorded blood pressure

A survey of a general medical practice in Michigan demonstrated that on the basis of the prevailing costs of antihypertensive drug treatment and the prevalence of white-coat hypertension, the break-even cost for performing ABPM would be around £115 [91]. However, in Europe [72], ABPM did not reduce the short-term costs of antihypertensive treatment. Whether these conclusions [72,91] would still hold true in the long run, especially after accounting for morbidity and mortality, remains to be elucidated. Regardless of any cost–benefit consideration, the investment in equipment and software still prevents the large-scale implementation of ABPM in primary care, the first line in diagnosing and treating hypertension, in most countries. However, the self-measurement of blood pressure [90,92,93] , using standardized procedures, might provide a valid and less expensive alternative.

The development of cheap, automated and properly validated devices stimulated the clinical application of the self-recording of blood pressure [94–98]. Variation of blood pressure throughout the day can be monitored only by ambulatory measurement, but several advantages of the latter approach can also be obtained by self-measurement [99,100] . The greater number of readings [97,101] , which can be obtained in a practical way, and the absence of the white-coat effect [102] contributes to making diagnostic accuracy better than that with conventional sphygmomanometry [90,103,104]. Furthermore, self-measurement of blood pressure has been shown to increase compliance to prescribed drugs [105,106] and to reduce the number of clinic visits required for the diagnosis and the treatment of hypertension [107–109]. When automated devices are used [97], self-recorded blood pressures are also free of observer bias.

The widespread clinical use of self-measurement is still limited by the lack of a generally accepted reference frame and operational thresholds for initiating and adjusting antihypertensive treatment. A meta-analysis of the summary statistics of published articles demonstrated that the self-recorded blood pressure averaged 115/71 mmHg in normotensive persons and 119/74 mmHg in untreated subjects not selected on the basis of their blood pressures [18]. In an international database of self-recorded blood pressures [110], the 95th percentile for 2401 normotensive persons was 136/85 mmHg for the measurements taken in the morning, 139/86 mmHg for the measurements obtained in the evening and 137/85 mmHg for the self-recorded blood pressure regardless of the time of day. Authors of this meta-analysis concluded that a self-recorded blood pressure above 137 mmHg systolic or 85 mmHg diastolic should be considered hypertensive. These thresholds are in close agreement with those for the daytime ABP (Table 2) and with other proposals for self-recorded measurements [18,50,111–113]. However, they must be further validated in clinical trials and prospective outcome studies.

Few studies with the goal of validating self-recorded blood pressure measurements in terms of cardiovascular complications have been published. In a prospective Japanese-population study, the self-recorded blood pressure had a stronger predictive power for subsequent mortality than did the screening blood pressure [114]. Mancia *et al.* [62] found that ABP measurements were correlated better to regression of left ventricular hypertrophy in hypertensive patients than were clinic and self-recorded blood pressure measurements. However, in this study the self-recorded blood pressure was measured on 1 day only , once in the morning and once in the evening [62]. Had the self-recorded blood pressure been taken over multiple days, the results might have been different. Investigators in the Treatment of Hypertension According to Home or Office Blood Pressure (THOP) trial [115] are currently investigating whether antihypertensive treatment guided by the

self-measured blood pressure would be more beneficial and cost-effective than treatment based on conventional sphygmomanometry.

Conclusions

The technique of non-invasive ABPM is now well established in clinical research and as a diagnostic tool in clinical practice. Self-measurement of blood pressure might become a more cost-effective alternative for diagnosing white-coat hypertension in the near future, but cannot provide information on the blood pressure during sleep. These techniques minimize misclassification of subjects due to the white-coat effect and have found wide acceptance in the management of hypertensive patients during the past two decades, especially in Europe.

Relatively few studies on ABPM [116–118] have concerned youngsters. Definitions of hypertension on conventional blood pressure measurement for children and adolescents take into account sex, age and height [119]; within each stratum values greater than the 95th percentile are considered hypertensive [119]. Defining diagnostic thresholds for the ABP in children and adolescents is difficult, because of the large variation in blood pressure with sex, age and height, and because long-term outcome results are difficult to obtain. A nonparametric approach [40,110] based on the distribution of the ABP in a large database of children and adolescents currently classified as normotensive on the basis of their conventional blood pressure will probably prove to be the most practical way to proceed in the short run.

Acknowledgement

The authors gratefully acknowledge the expert technical and secretarial assistance of Sylvia Van Hulle and Renilde Wolfs in preparing this manuscript.

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