

Thirty years of research on diagnostic and therapeutic thresholds for the self-measured blood pressure at home

Jan A. Staessen^{a,d}, Lutgarde Thijs^d, Takayoshi Ohkubo^e, Masahiro Kikuya^e, Tom Richart^{a,d}, José Boggia^{d,f}, Ahmet Adiyaman^{c,d}, Dirk G. Dechering^{c,d}, Tatiana Kuznetsova^d, Theo Thien^c, Peter de Leeuw^b, Yutuka Imai^e, Eoin O'Brien^g and Gianfranco Parati^{h,i}

Objective The goal of this review study is to summarize 30 years of research on cut-off limits for the self-measured blood pressure.

Methods We reviewed two meta-analyses, several prospective outcome studies in populations and hypertensive patients, studies in pregnant women, three clinical trials and the thresholds proposed in earlier and current hypertension guidelines.

Results In line with existing guidelines, prospective studies support that levels of the self-measured blood pressure at home of greater than or equal to 135 mmHg systolic or greater than or equal to 85 mmHg diastolic indicate hypertension. Circumstantial data suggest that levels of the self-measured blood pressure below 120/80 and 130/85 mmHg are optimal and normal, respectively. Therapeutic targets of the self-measured blood pressure to be attained on antihypertensive drug treatment are currently unknown, but should logically be lower (<135/85 mmHg) than those used to diagnose hypertension. Currently, there is no proof that therapeutic thresholds for the home blood pressure should be lower in high-risk compared with normal-risk patients. A large body of evidence, however, demonstrated that each millimetre of mercury of blood pressure lowering counts in the prevention of cardiovascular complications and that in high-risk patients even small decreases in blood pressure result in large absolute benefit.

Introduction

Already in 1971, investigators from Leuven promoted the use of blood pressure self-measurement at home in clinical research [1]. The development of cheap and properly validated devices for blood pressure self-measurement, over the past 20 years, carried this technique to clinical application [2–6]. Blood pressure self-measurement offers several of the well-recognized advantages of the more complex approach of ambulatory monitoring [7,8]. The greater number of readings [5,9] and the absence of the white coat effect [10] contribute to a better diagnostic accuracy, compared with conventional sphygmomanometry [11,12]. If automated devices are used [5], self-recorded blood pressure values are free

Conclusion The thresholds to diagnose hypertension from self-measured blood pressure readings at home remain unaltered since the 2000 consensus conference, but are currently supported by outcome data. Further studies need to establish what values of the self-measured blood pressure are optimal and normal in terms of cardiovascular outcome. *Blood Press Monit* 13:352–365 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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^aDepartment of Epidemiology, Maastricht University, ^bDepartment of Internal Medicine, University Hospital Maastricht, Maastricht, ^cDepartment of General Internal Medicine, Nijmegen Medical Centre, Radboud University, Nijmegen, The Netherlands, ^dDepartment of Cardiovascular Diseases, Division of Hypertension and Cardiovascular Rehabilitation, Studies Coordinating Centre, University of Leuven, Leuven, Belgium, ^eTohoku University Graduate School of Pharmaceutical Sciences and Medicine, Sendai, Japan, ^fDepartamento de Fisiopatología, Hospital de Clinicas, Universidad de la República, Montevideo, Uruguay, ^gConway Institute of Biomolecular and Biomedical Research, University College, Dublin, Ireland, ^hDepartment of Clinical Medicine and Prevention, University of Milano-Bicocca and ⁱDepartment of Cardiology, San Luca Hospital, Istituto Auxologico Italiano, Milan, Italy

Correspondence to Jan A. Staessen, MD, PhD, FESC, FAHA, Genetic Epidemiology Unit, Department of Epidemiology, Maastricht University, Peter Debyeplein 1, Box 616, Maastricht 6200 MD, The Netherlands
Tel: +31 43 388 2374; fax: +31 43 388 4128;
e-mail: jan.staessen@med.kuleuven.be

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of observer bias. Moreover, self-measurement of blood pressure increases adherence to antihypertensive treatment [13,14] and allows reducing the number of clinic visits required for the diagnosis and treatment of hypertension [15–17].

The goal of the current review study is to summarize over 30 years of research on cut-off limits for the self-measured blood pressure. We reviewed the literature in preparation of the second consensus meeting on the self-measured blood pressure, which took place in Verbania, Italy, on 13–14 June 2007. The European Society of Hypertension recently published its new guidelines, based on the second consensus conference [18].

For this study, we reviewed two meta-analyses [19,20], several prospective outcome studies in populations [21–31] and hypertensive patients [32–36], studies in pregnant women [37–41], children and adolescents [42–45], and three clinical trials [46–48] exploring adjustment of antihypertensive drug treatment guided by the self-measured blood pressure at home. We next reviewed the operational thresholds for the self-measured blood pressure as proposed by hypertension guidelines before June 2007 [49–62]. We conclude with the proposals we put forward for discussion at the second consensus meeting.

Evidence from two meta-analyses

In an attempt to define diagnostic thresholds for the self-measured blood pressure, we performed in collaboration with a large number of researchers two meta-analyses [19,20], which were respectively based on aggregate data extracted from published articles [19] and on individual patient data, made available to the International Database of Self-Recorded Blood Pressures [20].

Aggregate data extracted from published articles

In 1998, we reviewed 17 studies [1,63–78] including a total of 5422 participants. The number of participants in each of the individual studies ranged from 14 [63] to 1438 [75]. Eight reports did not apply any selection criteria based on blood pressure values [1,67,68,71,73,75,76,78]. Mean age ranged from 16 [72] to 47 years [78]. The participants measured their blood pressure by an automatic or semiautomatic oscillometric device in five studies [66–68,75,78], by a semiautomatic auscultatory device in four reports [64,72,76,77], or by a manual sphygmomanometer in eight reports [1,63,65,69–71,73,74]. In most studies, participants measured their blood pressure over several days (range, 1–63 days), usually in the morning and evening. The number of self-recorded blood pressures averaged for analyses ranged from 2 [75] to 252 [1].

With weighing for the number of participants included in the various studies, the self-recorded blood pressure averaged 115/71 mmHg in normotensive participants and 119/74 mmHg in untreated participants not selected on the basis of their blood pressure [19].

Within each study, we computed an operational threshold for the self-measured blood pressure separating normotension from hypertension from the mean + 2 standard deviations or from the 95th percentile of the self-recorded blood pressure in participants who were normotensive according to their office blood pressure (Table 1). For sake of comparability with the contemporary literature, we also extracted from published studies thresholds derived by the regression approach or the percentile method. The former consists of calculating the

Table 1 Operational cut-off points between 'normotension' and 'hypertension' for self-recorded blood pressure in individual studies

	Self-measured blood pressure corresponding to an office blood pressure of 140/90 mmHg		Upper limits of the distribution in normotensive participants only (mmHg)	
	Percentile method	Regression analysis	Mean + 2SD	95th percentile
Bättig <i>et al.</i> > [64]	NA	NA	138/94	?
Beckman <i>et al.</i> [65]	NA	NA	149/86	145/83
Brody and Rau [66]	NA	NA	140/90	133/87
De Gaudemaris <i>et al.</i> [67]	127/83	125/81	133/86	129/84
Imai <i>et al.</i> [68]	128/84	123/77	137/86	134/83
James <i>et al.</i> [63]	NA	NA	133/84	?
Johnson [69]	NA	NA	?	?
Joossens <i>et al.</i> [1]	?	?	?	?
Julius <i>et al.</i> [70]	NA	NA	139/90	?
Julius <i>et al.</i> [71]	?	?	133/89	?
Kawabe <i>et al.</i> [72]	NA	NA	137/95	134/91
Kesteloot <i>et al.</i> [73]	?	?	?	?
Kjeldsen <i>et al.</i> [74]	NA	NA	152/103	?
Mancia <i>et al.</i> [75]	?	126/79 ^a	141/90	138/87
Mengden <i>et al.</i> [76]	?	?	136/91	?
Saito <i>et al.</i> [77]	NA	NA	144/96	139/92
Weisser <i>et al.</i> [78]	133/86	?	?	?

NA indicates not applicable because the study included only normotensive participants. Question mark indicates that the information was unavailable. Reproduced with permission from ref. [19].

^aWeighed mean of reference values obtained in eight sex-age strata.

regression line between the self-recorded blood pressure and the clinic blood pressure in individual patients to estimate the self-recorded blood pressure that corresponds with a clinic blood pressure of 140 mmHg systolic or 90 mmHg diastolic [19]. The percentile method involves first the calculation of the percentile of the clinic blood pressure that corresponds to 140 mmHg systolic or 90 mmHg diastolic and next the determination of the self-recorded blood pressure that ranks at the same percentile value [19].

The reference values for the self-recorded systolic/diastolic blood pressures as derived from the mean + 2 standard deviations (137/89 mmHg) and the 95th percentile (135/86 mmHg) of the distribution in normotensive participants were concordant within 2 mmHg systolic and 3 mmHg diastolic. The cut-off points derived using the regression and percentile methods were considerably lower, that is, 129/84 and 125/79 mmHg, respectively [19].

Individual patient data as available in the international database

Thirteen research groups contributed 4668 untreated participants to the International Database [20], of whom 2401 were normotensive on office measurement. Participants had their office blood pressure measured at one (79%), two (18%) or three (3%) occasions. They were characterized by only one office blood pressure reading in a small minority (0.2%) or the average of two (39.7%),

three (38.9%), four (4.4%) or six (16.7%) office blood pressure readings. Participants recorded their blood pressure over a median of 3 days, obtaining from 1 to 159 readings (median, 14). The self-recorded blood pressure in the total study population averaged 129.9 mmHg systolic and 79.8 mmHg diastolic. Among 3221 participants, whose morning and evening blood pressures were separately available, systolic blood pressure was on average 1.9 mmHg higher ($P < 0.001$) in the morning with no diurnal difference in the diastolic blood pressure. Figure 1 illustrates the associations of the conventional and self-measured blood pressure with age.

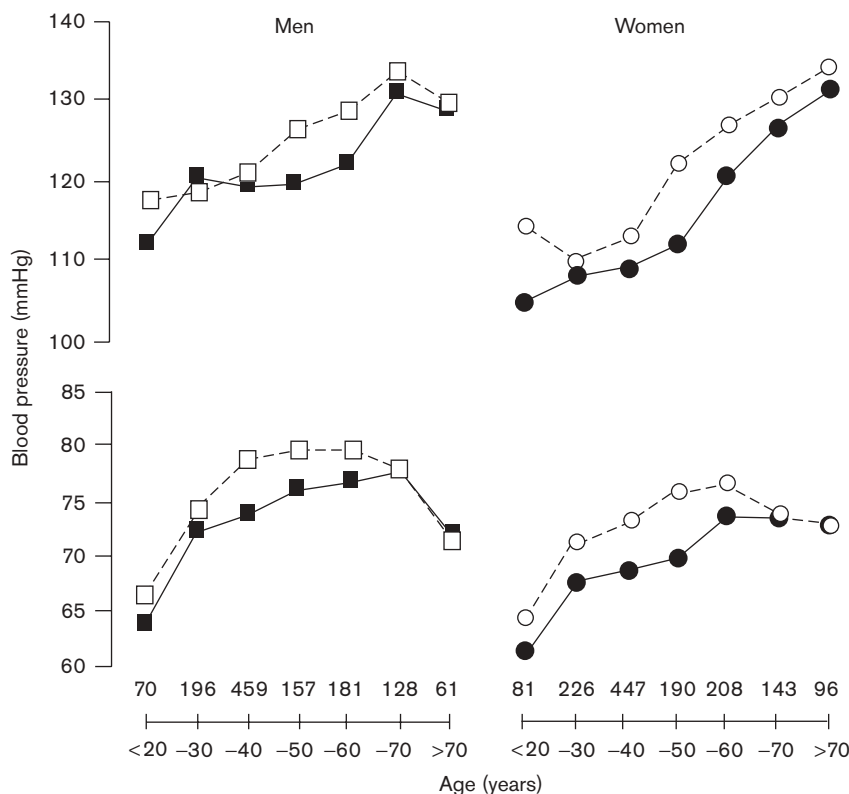
The mean self-recorded blood pressure in 2401 normotensive participants averaged 115.4 mmHg systolic and 70.7 mmHg diastolic. The 95th percentiles of their self-recorded blood pressures were 136 mmHg systolic and 85 mmHg diastolic in the morning, 139 and 86 mmHg in the evening and 137 and 85 mmHg over the whole day.

The database included 2267 hypertensive participants, of whom 494 participants had only a borderline elevation of their systolic or diastolic blood pressure (140–159/

90–94 mmHg), and 1773 participants were definitely hypertensive (≥ 160 systolic or ≥ 95 mmHg diastolic). By definition, there was a difference of at least 20 mmHg systolic or 5 mmHg diastolic between the office blood pressure of normotensive participants and patients with definite hypertension. Nevertheless, there was considerable overlap in the distributions of the self-measured blood pressure of normotensive and hypertensive participants (Fig. 2).

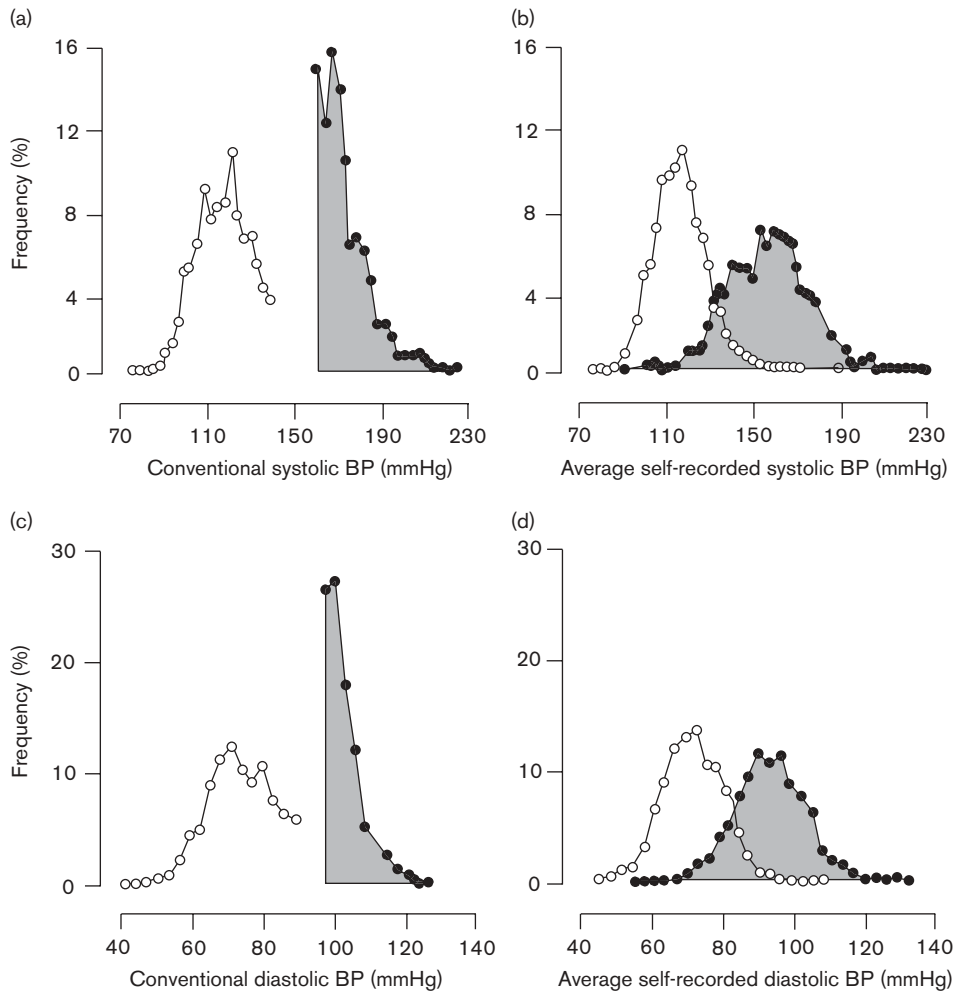
Of 1773 patients with definite systolic hypertension on office measurement (see above), 16% had a self-measured systolic blood pressure below 137 mmHg (the 95th percentile of the self-measured systolic pressure in normotensive participants). Similarly, 25% of those with definite diastolic hypertension had a self-measured diastolic blood pressure below 85 mmHg (the 95th percentile of the self-measured diastolic pressure in normotensive participants). The probability that participants with definite hypertension had a self-measured blood pressure below these thresholds (isolated office hypertension or white-coat hypertension [79]) was 34% (diastolic) to 62% (systolic) greater in women than in

Fig. 1



The office (dotted lines) and self-measured (full lines) blood pressure by sex and age class in 2643 untreated participants not selected by blood pressure criteria. Numbers along the horizontal axis indicate the number of participants in each age group. Reproduced with permission from ref. [20].

Fig. 2



Distributions of systolic (a, b) and diastolic (c, d) blood pressures on office (a, c) and self-measurement (b, d). Open circles denote 2323 participants normotensive according to their office blood pressure. Closed symbols represent 2067 patients with definite systolic hypertension (≥ 160 mmHg) and 2033 patients with definite diastolic hypertension (≥ 90 mmHg). Reproduced with permission from ref. [20].

men. It was two-fold to three-fold greater if fewer than three office blood pressure readings had been averaged to diagnose hypertension, and it increased by 50 (diastolic) to 126% (systolic) if the self-measured blood pressure had been measured on more than 3 days as opposed to fewer days (Table 2). In contrast, for each 10-mmHg increment in the systolic office blood pressure, the probability of isolated office systolic hypertension decreased by 35%; for each 5-mmHg increment in the diastolic office blood pressure, the probability of isolated office diastolic hypertension diminished by 36%. Finally, the probability of isolated office systolic hypertension fell by 31% for each 10-year increment in age (Table 2).

Evidence from prospective studies

Several longitudinal studies (Table 3) in populations [21–31] or patient cohorts [32–36] attempted to find a

justification for diagnostic cut-off limits of the self-measured blood pressure in terms of mortality [21–23,29,30,33] or fatal and nonfatal end points [24–28,32,34–36].

The Ohasama study

The Japanese investigators of the Ohasama study were the first to demonstrate that the self-measured blood pressure at home is a more precise predictor of outcome than the office blood pressure [21,22,25] and in consecutive publications [21–28] proposed and refined diagnostic thresholds for its use in clinical practice.

The Ohasama researchers initially proposed 137 mmHg systolic and 84 mmHg diastolic as acceptable upper limits for home blood pressure readings on the grounds that the risk of death increased above these thresholds [21].

These levels were comparable with the thresholds previously suggested by an international research consortium (137/85 mmHg [20]). Rounding these thresholds [20,21] to 135 mmHg systolic and 85 mmHg diastolic produced diagnostic limits similar to those in the meta-analysis of aggregate data [19] and in several guidelines [49,50,57,62].

The Japanese investigators subsequently published a subgroup analysis of Ohasama residents with and without cardiovascular risk factors, including diabetes mellitus, hypercholesterolaemia, habitual smoking and a history of cardiovascular disease [26]. In high-risk patients, pre-hypertension arbitrarily defined as a self-measured blood pressure ranging from greater than or equal to 115 mmHg to less than 135 mmHg systolic or from greater than or equal to 75 to less than 85 mmHg diastolic, compared with normotension, carried a two-fold higher risk of stroke. These observations suggested that the thresholds of the home blood pressure applicable to high-risk patients might be lower than 135/85 mmHg [26].

Table 2 Odds ratios expressing the probability that patients with definite hypertension have a self-measured blood pressure below the 95th percentile in participants with office normotension

Characteristic	Systolic hypertension	Diastolic hypertension
Number of patients in analysis	1070	1634
Odds ratios (95% confidence interval)		
Women versus men	1.62 (1.14–2.30)	1.34 (1.05–1.70)
10 years older	0.69 (0.59–0.81)	NS
5 kg/m ² higher body mass index	NS	NS
10 mmHg higher office systolic blood pressure	0.65 (0.53–0.80)	0.89 (0.82–0.97)
5 mmHg higher office diastolic blood pressure	NS	0.64 (0.56–0.73)
≤ 2 versus more office readings	2.99 (1.67–5.33)	2.29 (1.52–3.45)
>3 versus ≤ 3 days of self-measurement	2.26 (1.49–3.41)	1.50 (1.12–2.01)

The odds ratios were mutually adjusted for all explanatory variables in the Table. NS, nonsignificant.

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Table 3 Thresholds proposed in prospective cohort studies

Acronym	Year	Sample	Number	Age	Readings (days)	Threshold
Ohasama [21–23]	1997–2006	P	1913 (58.6)	60.8 (>40)	M (28)	<137/84
Kahoku [33,34]	1999	P	1186 (57.5)	73.5 (>65)	M/E (5)	125–134/...
	2005	P	461 (58.4)	80.0 (>75)	M/E (5)	<135/...
Rave <i>et al.</i> [32]	1999	DM	77 (48.0)	37	M/E (2)	<138/83
SHEAF [35]	2004	HT	4939 (51.1)	70	M/E (4)	<135/85
PAMELA [29,30]	2005–2006	P	2051 (49.4)	51.2 (25–75)	M/E (1)	<135/83
Agarwal [36]	2006	CKD	217 (3.7)	67.4	M/A/E (7)	<130/...
Didima [31]	2007	P	665 (58.2)	54.1	M/E (3)	<135/85

Number indicates the number of patients enrolled with the proportion of women given between parentheses. M, A and E stand for morning, afternoon and evening with the number of measurement days given between parentheses.

CKD, patients with chronic kidney disease; DM, patients with diabetes mellitus; HT, patients with hypertension; P, population sample; PAMELA, Pressioni Arteriose Monitorate e Loro Associazioni; SHEAF, Self-measurement of blood pressure at Home in the Elderly: Assessment and Follow-up.

The Ohasama investigators [27] also reported the incidence of stroke according to the level of the office and home blood pressures after stratification for cardiovascular risk based on the criteria jointly proposed by the European Society of Hypertension and the European Society of Cardiology [53]. The key points emerging from these analyses (Fig. 3) were that even in patients with low added risk both the office and self-measured blood pressures predicted stroke, and that across the strata of cardiovascular risk the probability of a first stroke rose steeper with the home than with the office blood pressure [27].

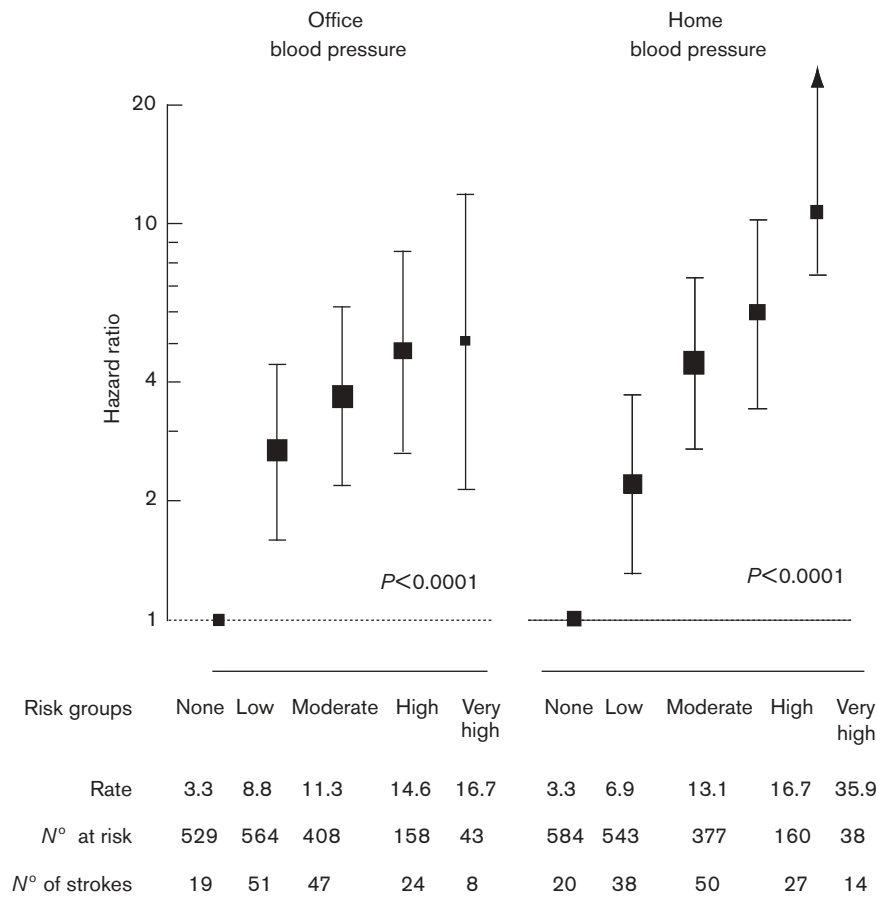
A recent Ohasama study noticed that the self-measured blood pressure predicted the risk of stroke, irrespective of whether it was measured in the morning or evening [28]. A level of 135/85 mmHg or higher was associated with a two-fold increase in the risk of stroke compared with the subgroup with levels of the home blood pressure below 135 mmHg systolic and 85 mmHg diastolic in the morning and evening. The multivariate-adjusted hazard ratios amounted to 2.66 (95% confidence interval, 1.64–4.33) for hypertension in the morning, and to 2.38 (1.65–3.45) for hypertension sustained from the morning to the evening [28].

The Kahoku study

A preliminary cross-sectional analysis of the Kahoku study considered a self-measured blood pressure of 135 mmHg systolic and 85 mmHg diastolic as the upper limit of normality, because these levels corresponded with the mean+1 standard deviation (79th percentile) in 708 untreated participants aged from 25 to 64 years [80].

The first publication with outcome data from the Kahoku study [33] included 1186 residents, aged 65 years or older, who in 1992 measured their blood pressure at home for 5 consecutive days and whose mortality (134 deaths) was recorded over 4 years. Okumiya and colleagues [33] applied arbitrary cut-off limits to delineate four categories according to the self-measured systolic (≤ 124, 125–134, 135–144, ≥ 145 mmHg) and diastolic (≤ 74, 75–79, 80–84, ≥ 85 mmHg) blood pressures. In multivariate-adjusted analyses across these groups, total mortality

Fig. 3



Risk of stroke according to the multiple risk factor classification proposed by the 2003 European hypertension guideline [45]. Risk factors include either the office or the self-measured blood pressure at home. None (referent group), low, moderate, high and very high indicate no risk factor (reference group), and low (no risk factor in addition to hypertension), moderate (one or two risk factors), high (two or more risk factors or diabetes mellitus) or very high added risk (past history of cardiovascular disease), respectively. The stroke rate is expressed in events per 1000 person-years. Squares and vertical lines indicate the point estimate and 95% confidence interval of the hazard ratio in each subgroup, the size of the square being proportional to the number of events. *P* values are for trend across risk subgroups. Reproduced with permission from ref. [27].

showed a significant U-shaped association with the home systolic blood pressure in men. The lowest risk occurred at levels ranging from 125 to 134 mmHg. The multivariate-adjusted associations of mortality with the categories of systolic blood pressure in women and those with the diastolic subgroups in both sexes were not statistically significant.

The 2005 Kahoku study included only 461 participants, who were at least 75 years old at enrollment (mean age, 80 years) and who were followed up for 9 years [34]. Nishinaga and colleagues [34] arbitrarily subdivided the study population in four subgroups of unequal size, depending on the level of the self-measured systolic blood pressure in the morning (< 135 vs. ≥ 135 mmHg) and the difference between the morning and evening systolic blood pressures (< 15 vs. ≥ 15 mmHg). Participants having both lower systolic blood pressure in the

morning and less diurnal variability in systolic pressure were used as reference group. With adjustments for confounders applied, high blood pressure in the morning with or without large differences between the morning and evening blood pressures predicted shorter survival and loss of independence.

The Pressioni Arteriose Monitorate e Loro Associazioni study

The Pressioni Arteriose Monitorate e Loro Associazioni study included 2051 residents of Monza (Italy), randomly recruited after stratification for sex and age (25–74 years). The participation rate was 64%. Participants obtained two readings of their self-measured blood pressure at home, one in the morning and one in the evening [29,30,75,81].

A cross-sectional analysis of 1438 participants [75], while recruitment was still ongoing, suggested that the systolic

blood pressure levels at home corresponding with a clinic level of 140 mmHg would across the age span (25–64 years) range from 127 to 132 mmHg (upper boundary of the 95% confidence interval, 128–134 mmHg) in men, and from 121 to 126 mmHg (125–129 mmHg) in women. For diastolic blood pressure, the corresponding thresholds varied from 75 to 81 mmHg (77–83 mmHg) in men and from 77 to 81 mmHg (80–83 mmHg) in women. A later cross-sectional analysis of 248 normotensive and untreated hypertensive participants, aged 65–74 years, suggested as thresholds for the self-measured blood pressure at home levels of 133 mmHg (95% confidence interval, 131–135 mmHg) systolic and 82 mmHg (80–83 mmHg) diastolic [81].

After an average follow-up of 131 months, 186 deaths occurred, of which 56 were cardiovascular (30.1%). Office and home blood pressures showed a significant relationship with cardiovascular and all-cause mortality, but the association was not tighter for the home than for the office blood pressure [29].

In a subsequent analysis [30], the *Pressioni Arteriose Monitorate e Loro Associazioni* investigators subdivided their cohort in four groups based on the office and home blood pressures, using as thresholds 140/90 and 135/83 mmHg, respectively. With normotension on both types of measurement as reference, the risk of cardiovascular and total mortality gradually increased if the office blood pressure, the home blood pressure, or both types of blood pressure were elevated. This trend was consistent in unadjusted and sex-adjusted and age-adjusted analyses.

The Didima study

Stegiou and colleagues [31] followed cardiovascular morbidity and cause-specific mortality over 8.2 years in 662 residents of Didima (Greece). Mean age at enrollment was 54.1 years and the proportion of women was 58.2%. During follow-up 78 deaths (42 cardiovascular) and 67 fatal and nonfatal events occurred. The unadjusted hazard ratios for cardiovascular events per 10 mmHg increase in the systolic blood pressure were 1.41 ($P < 0.001$) and 1.40 ($P < 0.001$) for office and home measurements, respectively. The corresponding estimates for a 5 mmHg increase in diastolic blood pressure were 1.20 ($P < 0.01$) and 1.11 ($P = 0.07$). The addition of the home blood pressure (average of duplicate readings in the morning and evening on 3 consecutive days) to Cox models already including the office blood pressure (average of six readings; three readings at each of two clinic visits) did not significantly improve the prediction of cardiovascular complications.

In categorical analyses, the Didima investigators defined office and home hypertension as systolic/diastolic blood pressure levels of 140/90 and 135/85 mmHg or higher, respectively [31]. Patients with hypertension on both

types of measurements (events/patients at risk, 26 of the 124 patients; 21.0%) and those with the white-coat phenomenon (nine of the 34 patients; 26.5%) had significantly higher cardiovascular risk than those who had a normal blood pressure in the office as well as at home (24 of the 452 patients; 5.3%). In contrast, masked hypertension was not associated with a significantly higher risk (eight of the patients 55; 14.5%).

Patient cohorts

The Self-measurement of blood pressure at Home in the Elderly: Assessment and Follow-up study [35] enrolled 4939 treated hypertensive patients aged 60 years or older. For the office and self-measured blood pressures, the targets to be reached on antihypertensive drug treatment were levels below 140/90 and 135/85 mmHg, respectively. The incidence of cardiovascular events in patients with elevated blood pressure in the office, but not at home, was the same as that in patients with controlled hypertension on both measurements: 11.1 versus 12.1 cases per 1000 patient-years, respectively. Conversely, the incidence of cardiovascular events in patients with elevated blood pressure at home, but not in the office, was high and similar to that of patients with uncontrolled hypertension on both measurements (30.6 vs. 25.6 cases per 1000 patient-years). In multivariate-adjusted models, using patients with normal office and normal self-measured blood pressures as the referent group, the hazard ratio of cardiovascular events doubled in patients with uncontrolled hypertension on both measurements (1.96; 95% confidence interval, 1.27–3.02) and in patients with an elevated blood pressure at home, but not in the office (2.06; 95% confidence interval 1.22–3.47). In contrast, patients with an elevated blood pressure in the office, but not at home, did not have an increased risk (1.18; 95% confidence interval, 0.67–2.10).

Agarwal and Andersen [36] followed 217 patients with chronic kidney disease for a median of 3.5 years, of whom 39 patients died. Of the 178 remaining patients, 38 patients developed end-stage renal disease. Poor control of the self-measured blood pressure at home, defined as a systolic level of 130 mmHg or higher, was a powerful predictor of end-stage renal disease. None of the patients with a self-measured blood pressure below 130 mmHg systolic, even in the presence of an elevated office blood pressure, progressed to end-stage renal disease.

Rave and coworkers [32] studied the progression of nephropathy in 71 patients with type-1 diabetes, who were followed up for 6.2 years on average. Over this period, the office and the self-measured blood pressures dropped from 166/95 to 154/89 mmHg and from 159/93 to 138/83 mmHg, respectively. In multivariate-adjusted analyses, the self-measured blood pressure at baseline was a strong and independent predictor of the subsequent loss in renal function. As the renal function continued to

decline, Rave's findings [32] suggest that the level of the self-measured blood pressure to target on antihypertensive drug treatment in diabetic patients might be less than 138/83 mmHg.

Self-monitoring in pregnancy

Accurate measurement of blood pressure by automated techniques is feasible in pregnant women [40,82]. Ambulatory blood pressure monitoring [83] and self-measurement of blood pressure at home [37], compared with office measurement, are more predictive of severe hypertension or proteinuria. However, there is only indirect evidence to support operational thresholds for the self-measured blood pressure in antenatal care.

Ross-McGill and colleagues [38] randomized 80 women at 24–28 weeks of their pregnancy to a standard nine-visit schedule (30, 32, 34, 36–41 weeks) or to a reduced schedule (34, 38, 41 weeks). Women with multiple pregnancies, established hypertension or a history of preeclampsia before 34 weeks, or pregnancy loss were not eligible. Women in the home-monitoring group (reduced schedule group) measured their blood pressure weekly, using a portable sphygmomanometer. They were instructed to repeat self-measurement after 4 h, if the blood pressure level at the first reading was between 140 and 160 mmHg systolic or between 90 and 100 mmHg diastolic and to contact their midwife if the second reading was higher than 140 mmHg systolic or 90 mmHg diastolic. If any reading was higher than 160 mmHg systolic or 100 mmHg diastolic, women had to contact their midwife immediately. Although there were more unscheduled visits in the home monitoring group, this did not outweigh the reduction in scheduled visits (7.4 vs. 4.5; $P < 0.001$) and blood pressure was measured during more weeks (9 vs. 7; $P < 0.001$) in the experimental group. Most women expressed a preference for the reduced schedule both when the idea was first suggested, and after they had experienced it, and there were no significant between-group differences in anxiety.

In a subsequent study in 72 pregnant women at high risk of preeclampsia, Waugh and coworkers observed that of 979 self-measurements taken only 28 (2.9%) were inaccurate [39]. On further questioning, two women admitted that the device had been used by other family members, thus making comparison with the other measurements stored in memory impossible. Thus, the true nonconcordance rate amongst participants was 1/72 (1.4%). The same investigators, based on Stergiou's observation that on average the home blood pressure in nonpregnant hypertensive patients is 12/7 mmHg lower than the office blood pressure [5], recommended to use a threshold of 135 mmHg systolic and 85 mmHg diastolic to monitor the home blood pressure in pregnant women [37].

In a study by Denolle and colleagues [40], 45 healthy pregnant women measured their blood pressure for 1 week before 15 weeks of gestation, between weeks 15 and 27, and after 28 weeks for the last 3 months of gestation. The self-measured blood pressure was significantly lower during the second trimester and higher during the last trimester (102/59, 101/57, 105/62 mmHg, respectively) than during other trimesters. On the basis of the mean + 2 standard deviations, Denolle and colleagues [40], suggested as upper limits of normality 118/73, 117/73 and 121/80 mmHg for the three trimesters of pregnancy.

Self-monitoring in children and adolescents

Self-measurement of blood pressure by children and adolescents by means of semiautomatic [84] or automatic [85] devices, specifically validated in this age group, is feasible [43,44]. Whereas in adults the self-measured blood pressure and daytime blood pressure often have approximately similar levels, in children and adolescents, the self-measured blood pressure at home is apparently lower than the daytime ambulatory blood pressure [42]. In 23 normotensive children enrolled in Stergiou's study (mean age, 12.3 years), blood pressure levels averaged 112.8/63.1, 106.7/67.2 and 123.9/72.0 mmHg on conventional, home and daytime ambulatory measurement, respectively [42]. The 2004 guideline of the National Heart, Lung, and Blood Institute [86] defines a normal blood pressure in children and adolescents as systolic and diastolic levels below the 90th percentile, according to sex, age and height, and hypertension as systolic or diastolic levels above the 95th percentile. The German Working Group on Pediatric Hypertension developed similarly stratified reference tables from ambulatory blood pressure recordings in 949 healthy children and adolescents from 5 to 20 years old [87]. Stergiou and coworkers [45] recently published comparable reference tables for the self-measured blood pressure in 778 healthy youngsters (age range, 6–18 years) enrolled in the Arsakeion School study. Self-monitoring of blood pressure in children and adolescents, although potentially useful in the follow-up of young patients [43,44], should not be used for the diagnosis of hypertension. The amount by which, even in normotensive youngsters, the self-measured blood pressure is lower than the office and daytime blood pressures needs further clarification [42]. Only few studies documented the cross-sectional association in youngsters between early signs of target-organ damage and the home blood pressure. Finally, no study evaluated to what extent the self-measured blood pressure in children and adolescents predicts transition to hypertension or the risk of cardiovascular complications in young adults or later in life.

Evidence from clinical trials

Two clinical trials compared antihypertensive drug treatment guided by the self-measured blood pressure

as opposed to office blood pressure: the Treatment of hypertension based on Home or Office blood Pressure (THOP) trial [46] and the Home versus Office blood pressure measurements: Reduction of unnecessary treatment Study (HOMERUS [88]). The Hypertension Objective treatment based on Measurement by Electrical Devices of Blood Pressure (HOMED-BP) study [48] is still ongoing [89].

Treatment of hypertension based on Home or Office blood Pressure

In the THOP trial [46], antihypertensive drug treatment was adjusted in a stepwise manner based on either the self-measured diastolic blood pressure at home (average of six measurements per day during 1 week; 203 patients) or the average of three sitting diastolic readings at the doctor's office (197 patients). If the diastolic blood pressure guiding treatment was above (> 89 mmHg), at (80–89 mmHg) or below (< 80 mmHg) target, one physician-blinded to the patients' randomization intensified antihypertensive treatment, left it unchanged or reduced it, respectively.

The target blood pressure was the same in the two treatment groups. At the end of the study (median follow-up, 350 days; 5th–95th percentile interval, 153–586 days), more patients randomized to self-measurement had stopped antihypertensive drug treatment (25.6 vs. 11.3%; $P < 0.001$) with no significant difference in the proportions of patients progressing to multiple-drug treatment (38.7 vs. 45.1%; $P = 0.14$). The final office, home and 24-h ambulatory blood pressures were higher ($P < 0.001$) in patients randomized to self-measurement than in those treated according to the office blood pressure. The baseline-adjusted systolic/diastolic differences between these two groups averaged 6.8/3.5, 4.9/2.9 and 4.9/2.9 mmHg, respectively. Left ventricular mass and reported symptoms were similar in the two groups [46].

The THOP trial [46] confirmed that the cut-off limit for the diastolic blood pressure should be lower on home than office measurement and suggested that one should account for both systolic and diastolic blood pressures to adjust antihypertensive drug treatment.

Home versus Office blood pressure measurements: Reduction of unnecessary treatment Study

In the randomized HOMERUS trial [47,88], the office blood pressure and the self-measured blood pressure guided antihypertensive drug treatment in the control and experimental group, respectively. In contrast to the THOP trial [46], HOMERUS patients randomized to office blood pressure measurement, did not record their blood pressure at home [88]. The patients underwent ambulatory blood pressure monitoring at entry and at closeout. After a standardized treatment schedule, investigators had to reach the target blood pressure levels of

120–139 mmHg systolic and 80–89 mmHg diastolic. This goal was similar in both treatment groups [47]. A blinded physician at the coordinating centre took the treatment decisions. The stated hypothesis [88] was that at the end of the 1-year follow-up period, patients in both groups would have the same blood pressure, at the expense of more medication in the office blood pressure group.

The patients randomized to self-measurement ($n = 216$) used less medication than those ($n = 214$) allocated to office blood pressure measurement (1.47 vs. 2.48 drug steps; $P < 0.001$) with lower costs (\$3222 vs. \$4420 per 100 patients per month; $P < 0.001$), but without significant differences in systolic and diastolic blood pressures on office measurement (1.6/1.0 mmHg; $P = 0.25/0.20$), in changes in left ventricular mass index (-6.5 vs. -5.6 g/m²; $P = 0.72$), or in median urinary microalbumin concentration (-1.7 vs. -1.5 mg/24 h; $P = 0.87$). Nevertheless, the 24-h ambulatory blood pressure was higher (125.9/77.2 vs. 123.8/76.1 mmHg; $P < 0.05/0.05$) in the self-measurement than the office group [47].

Hypertension Objective treatment based on Measurement by Electrical Devices of Blood Pressure

The primary objective of the HOMED-BP study is to determine the optimal level of the self-measured blood pressure, to which hypertensive patients should be treated to achieve the best protection against cardiovascular complications [48]. A secondary objective is to investigate which of the newer antihypertensive drug classes (calcium-channel blockers, angiotensin-converting enzyme inhibitors or angiotensin type-1 receptor blockers) is best suited to initiate blood pressure lowering treatment in Japanese [48]. The study has a 2×3 factorial randomized open design with blinded end point validation. The study will include 9000 untreated patients with essential hypertension, aged 40–78 years, whose self-measured blood pressure at home is 135/85 mmHg or higher. Eligible patients are randomized to one of the two home blood pressure target groups (125–134/80–84 vs. $\leq 125/80$ mmHg), and to initial treatment with one of the three drug classes [48].

By the end of March 2003, a total of 1086 patients (12.1% of those planned) had been randomized [89]. Among 653 patients who had been followed for more than 6 months, the self-measured blood pressures at randomization averaged 149/89, 150/89 and 149/88 mmHg in the calcium-channel blocker, angiotensin-converting enzyme and angiotensin II receptor blocker groups, respectively. After 6 months, these levels had decreased to 134/81, 135/80 and 133/80 mmHg, respectively, with no significant between-group differences. In the intensive and usual treatment groups, the self-measured blood pressures at randomization and at 6 months were 149/88 and 150/89 mmHg and 134/80 and 135/80 mmHg, respectively without significant between-group differences. In the

less-intensive treatment group, 45% of the 304 patients achieved a systolic blood pressure below 135 mmHg, whereas 60% achieved a diastolic blood pressure of less than 85 mmHg. In the intensive treatment group, 22% of the 349 patients achieved a systolic blood pressure below 125 mmHg, and 42% reached a diastolic blood pressure of less than 80 mmHg. These results [89] prove that, even under the standardized conditions of a clinical trial, it is very difficult to control blood pressure and that doctors should at least strive to lower the self-measured blood pressure at home to levels below the commonly accepted [49,50,57,62] therapeutic target of 135/85 mmHg. In the Japan Home versus Office blood pressure Measurement Evaluation study, only 34% of 3400 hypertensive patients achieved these levels [90].

Current guidelines

We reviewed the diagnostic thresholds for the self-measured blood pressure (Table 4) in the guidelines for the management of hypertension, published in 2000 at the occasion of the first consensus meeting on the self-measured blood pressure [49] or later [50–52,54,56–62]. Self-monitoring refers to the blood pressure measured at home in all guidelines [49–52,54,56–62], whereas the American recommendations [56,61] leave the possibility open for self-monitoring at the work place. The results of our review of guidelines are summarized in Table 4.

Proposal for diagnostic and therapeutic thresholds

The association between blood pressure and cardiovascular risk is continuous, without a threshold above which the risk suddenly increases. Clinical decisions, however, must be based on operational thresholds. Worldwide consensus is that the cut-off limits applicable for conventional sphygmomanometry cannot be extrapolated without further validation to the self-measured blood pressure at home, because studies in unselected populations [21–30] and hypertensive patients [32–36] demonstrated that the self-measured blood pressure, compared with the office blood pressure, is lower.

Diagnostic thresholds

Definition of normality for the self-measured blood pressure at home is following the same path as that for defining normality of the ambulatory blood pressure [91,92]. The first reference values for the self-measured blood pressure started from its distributional characteristics in participants with a normal office blood pressure [19,20]. Subsequent cross-sectional studies demonstrated stronger association of target-organ damage with the self-measured than with the office blood pressure. It, however, took over 20 years to collect the necessary prospective data (Table 3) to define normality in terms of cardiovascular risk [21–23,29,30,32–36].

Table 4 Diagnostic thresholds in guidelines for the management of hypertension

Guideline	Year	Target group	Systolic/diastolic threshold (mmHg)
First consensus meeting [49]	2000	Adults	≥ 130/85 (HT) ≥ 135/85 (D-HT) ≥ 135/85 (HT)
		Older age	...
		Pregnancy	...
Japanese elderly [50]	2002	≥ 65 years	< 125/80 (NT) ≥ 135/85 (HT)
JSH [51]	2003	Adults	< 125/75 (D-NT) < 125/80 (NT) ≥ 135/80 (HT) ≥ 135/85 (D-HT) ≥ 135/85 (HT)
ESH [52]	2003	Adults	...
WHO/ISH [54]	2003
US Task Force [55]	2003	Adults	...
JNC7 [56]	2003	Adults	< 130/80 (NT)
ESH Working Group [57]	2004	Adults	< 130/80 (NT) ≥ 135/85 (HT)
BHS [58]	2004	Adults	< 130/80 (NT)
CHEP [59]	2004	Adults	> 136/83 (HT)
ESH [60]	2005	Adults	< 130/80 (NT) ≥ 135/80 (HT)
AHA [61]	2005	Adults	< 130/80 (NT)
BJS [62]	2006	Adults	> 135/85 (HT)

An ellipsis indicates that the guideline did not provide any concrete recommendation.

AHA, American Heart Association; BJS, British Joint Societies; CHEP, Canadian Hypertension Education Program; D-NT, definite normotension; ESH, European Society of Hypertension; HT, hypertension; ISH, International Society of Hypertension; JNC7, Joint National Committee, version 7; JSH, Japanese Society of Hypertension; NT, normotension.

Table 5 Updated proposals for thresholds

Blood pressure	Optimal (mmHg)	Normal (mmHg)	Hypertension (mmHg)
Office	< 120/80	< 130/85	≥ 140/90
Daytime ambulatory	< 120/80	< 130/85	≥ 135/85
Self-measured (home)	< 120/80	< 130/85	≥ 135/85

For evidence in support of the thresholds, see text.

Table 5 shows an updated proposal for diagnostic thresholds for the self-measured blood pressure at home. Two meta-analyses [19,20], prospective studies in populations [21–30], hypertensive patients [32–36] and pregnant women [37,38], as well as the consensus in current guidelines (Table 4, [49–54,56–62]) support the idea that hypertension on self-monitoring at home starts at blood pressure levels of 135 mmHg systolic or 85 mmHg diastolic.

The evidence for optimal and normal blood pressure levels on self-measurement is much weaker. In the Kahoku study [33], men with systolic levels from 125 to 134 mmHg were at the lowest risk of death. International databases of individual-patient data demonstrated that the difference between automated [20,91] and conventional blood pressure readings increases with the level of the office blood pressure. In participants with normotension on office blood pressure measurement, the mean differences between the office and self-measured blood

pressures (116.9/72.8 vs. 115.4/70.7 mmHg [20]) and between the office and the daytime ambulatory blood pressures (119/73 vs. 122/75 mmHg [91]) were only 1.5/2.1 [20] and 3.0/2.0 mmHg [91], respectively. Recent analyses found that levels of 120/80 and 130/85 mmHg carried similar 10-year cardiovascular risks on both office and daytime ambulatory measurement [93]. Until more prospective data become available, it seems reasonable to propose values below 120/80 mmHg and below 130/85 mmHg as optimal and normal, respectively, also for the self-measured blood pressure at home.

Current diagnostic thresholds for the conventionally measured office blood pressure and ambulatory blood pressure are applicable irrespective of sex and age. In line with the recommendation of the 2000 consensus meeting [49], the thresholds in Table 5 might be used for adult as well as older patients and for women and men alike.

Therapeutic thresholds

The target levels of the self-measured blood pressure to be attained on antihypertensive drug treatment are currently unknown. The HOMED-BP study is still ongoing [89]. Therapeutic targets for the home blood pressure (< 135/85 mmHg), however, should logically be lower than those used to diagnose hypertension (\geq 135/85 mmHg). As for the office blood pressure [53], lower treatment targets might be advisable in high-risk patients, such as those with diabetes mellitus, a history of stroke, coronary heart disease or renal dysfunction. Direct evidence, however, supporting these lower targets is not yet available. The Japanese experience [89] shows how difficult it is even under the best possible conditions to lower the self-measured blood pressure to less than 135 mmHg systolic and 85 mmHg diastolic.

Two considerations might be helpful in titrating antihypertensive drug treatment according to the self-measured blood pressure. First, in keeping with large-scale prospective observational studies [94,95], meta-regression analyses published by us [96–98] and other research consortia [99–101] demonstrated that small gradients in the achieved systolic office blood pressure explained most of the differences in the cardiovascular outcomes, as observed in randomized clinical trials. This association was particularly strong for the prevention of stroke [99], the complication most directly associated with blood pressure [102] and weakest for heart failure [99]. Any reduction in the systolic conventional blood pressure by 3 mmHg will reduce the incidence of stroke, myocardial infarction and cardiovascular events by approximately 20, 15 and 15%, respectively [103]. Any reduction in the conventional blood pressure will also be accompanied by a decrease in the self-measured blood pressure at home. As already shown for the daytime ambulatory blood pressure in the Systolic Hypertension in Europe trial (systolic daytime vs. office, 9.3 vs. 16.6 mmHg; diastolic, 4.9 vs. 7.3 mmHg; systolic/diastolic daytime-to-

office ratio, 0.59/0.67) [104], estimates of the treatment-induced blood pressure lowering effects are smaller on automated than office measurement. In the Ambulatory blood Pressure monitoring and Treatment of Hypertension trial [105], this ratio was 0.64 systolic (14.3 vs. 22.4 mmHg) and 0.70 diastolic (9.5 vs. 13.7 mmHg). In the THOP trial [46], the home-to-office ratios in the blood pressure lowering effect were 0.73 systolic (13.5 vs. 18.6 mmHg) and 0.71 diastolic (8.7 vs. 12.2 mmHg). These findings suggest that relative risk reductions might be approximately equivalent for any decrease in the systolic blood pressure by 2 mmHg at home or by 3 mmHg at the office.

Second, in the light of the low control rates in the HOMED-BP trial [89], absolute benefit might override the importance of lower therapeutic goals in high-risk compared with normal-risk patients. As suggested above, one might assume that lowering the home systolic blood pressure by 2 mmHg would result in a 20% reduction in the incidence of stroke, independent of the risk at baseline. At a rate of 35.9 strokes per 1000 person-years (Fig. 3, [27]) lowering systolic blood pressure at home by a mere 2 mmHg in 1000 patients for 1 year would approximately prevent seven strokes. At a rate of 6.9 strokes per 1000 person-years (Fig. 3, [27]), the corresponding estimate would be only one stroke.

Rather than underscoring the importance of lower therapeutic thresholds in high-risk patients, it might be more encouraging to highlight that each millimetre of mercury counts in the prevention of cardiovascular complications by blood pressure lowering treatment and that absolute benefit and therefore the number to treat is proportional to the absolute risk. Nevertheless, even if every millimetres of mercury counts in prevention, opinion leaders should convince physicians to adopt a more aggressive approach in the control of blood pressure, irrespective of the way it is measured.

Conclusion

The thresholds to diagnose hypertension from the self-measured blood pressure at home remain basically unaltered since the 2000 consensus conference [49], but they are currently supported by evidence from prospective outcome data in populations [21–30] and patients [32–36]. Moreover, two recently published studies [106,107] proved that the introduction of the self-measured blood pressure in the management of hypertensive patients reduces medical costs. In contrast, further studies must establish what values of the self-measured blood pressure are optimal and normal in terms of cardiovascular outcome.

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