Self-Measurement of Blood Pressure at Home Reduces the Need for Antihypertensive Drugs

A Randomized, Controlled Trial


Abstract—It is still uncertain whether one can safely base treatment decisions on self-measurement of blood pressure. In the present study, we investigated whether antihypertensive treatment based on self-measurement of blood pressure leads to the use of less medication without the loss of blood pressure control. We randomly assigned 430 hypertensive patients to receive treatment either on the basis of self-measured pressures (n=216) or office pressures (OPs; n=214). During 1-year follow-up, blood pressure was measured by office measurement (10 visits), ambulatory monitoring (start and end), and self-measurement (8 times, self-pressure group only). In addition, drug use, associated costs, and degree of target organ damage (echocardiography and microalbuminuria) were assessed. The self-pressure group used less medication than the OP group (1.47 versus 2.48 drug steps; \(P<0.001\)) with lower costs ($3222 versus $4420 per 100 patients per month; \(P<0.001\)) but without significant differences in systolic and diastolic OP values (1.6/1.0 mm Hg; \(P=0.25/0.20\)), in changes in left ventricular mass index (\(-6.5 \text{ g/m}^2\) versus \(-5.6 \text{ g/m}^2\); \(P=0.72\)), or in median urinary microalbumin concentration (\(-1.7 \text{ versus } -1.5 \text{ mg per 24 hours}; \ P=0.87\)). Nevertheless, 24-hour ambulatory blood pressure values at the end of the trial were higher in the self-pressure than in the OP group: 125.9 versus 123.8 mm Hg (\(P<0.05\)) for systolic and 77.2 versus 76.1 mm Hg (\(P<0.05\)) for diastolic blood pressure. These data show that self-measurement leads to less medication use than office blood pressure measurement without leading to significant differences in OP values or target organ damage. Ambulatory values, however, remain slightly elevated for the self-pressure group. (Hypertension. 2007;50:1-2.)

Key Words: blood pressure [hypertension] self-measurements [home monitoring] ambulatory blood pressure measurement [treatment]

As indications for lowering blood pressure (BP) become increasingly stringent, the associated medication use and costs rise markedly. This calls for proper diagnosis and careful selection of patients in whom treatment is really indicated. In this respect, conventional office BP measurements (OBPMs) have disadvantages, because they can easily elicit a white-coat effect, overestimation of a patient’s BP, and unnecessary drug prescription. Self-BP measurements (SBPMs) are less liable to the white-coat effect and may provide a more reliable estimate of a patient’s “true” BP. In addition, SBPM correlates better with the patient’s “true” BP. SBPM has the potential to identify subjects that may not need treatment. This could reduce drug use and lead to considerable costs savings. The Home Versus Office Measurement, Reduction of Unnecessary treatment Study (HOMERUS) was designed to determine whether treatment based on SBPM leads to a decreased drug prescription without an impaired BP control and TOD as compared with treatment based on OBPM.

Methods

The design of the HOMERUS has been described in detail elsewhere. Briefly, HOMERUS is a multicenter, prospective, randomized, double-blind trial with a parallel-group design. Patients, aged...
≥18 years whose office BP was ≥139 mm Hg systolic and/or 89 mm Hg diastolic were randomly allocated to either the self-pressure (SP) group or to the office pressure (OP) group using a procedure of minimization.10,11 If randomly assigned to the SP group, the patient was instructed to start self-measurements of BP at home. In this group, stepwise antihypertensive treatment was guided by the results of SBPM. In the OP group, stepwise treatment was based on office readings. The prescribing physician was kept blinded from random assignment and, therefore, remained unaware of whether the patient was treated according to OBPM or SBPM values.

To maintain blinding during follow-up, medication was prescribed and, if necessary, adapted by a physician at the coordinating center who based his treatment decisions on the average OBPM or SBPM values. Patients picked up their treatment from their own pharmacist, who had been extensively informed about the trial and the importance of handing out the precise number of pills that were prescribed. Patients were asked not to tell their physician to which group they belonged. In accordance with recommendations at the time that this study started, the target BP was set at 140-mm Hg systolic and 90-mm Hg diastolic and the lower limit at 120-mm Hg systolic and 80-mm Hg diastolic for both groups. At entry into the study, any existing antihypertensive therapy was discontinued whenever possible, and patients entered a placebo run-in period of 4 weeks’ duration before study treatment was initiated. If the treating physician considered interruption of treatment to be too hazardous, the patient was switched immediately to trial medication. Twenty-four-hour ambulatory BP monitoring (ABPM), as a reference standard, and assessment of TOD (heart and kidney) took place at the end of the run-in period and at the end of the trial. Final results of the trial were analyzed in 2 domains: medication use and treatment costs and degree of BP control and TOD. The study was approved by an institutional review committee. Informed consent in accordance with the Declaration of Helsinki was obtained from all of the patients before entering the study, and the procedures followed were in accordance with institutional guidelines.

BP Measurements
At each visit, 3 consecutive OBPMs were performed in the hospital or at the general practitioner’s clinic. Patients of the SP group started SBPM 3 weeks after study entry. SBPM was performed 6 times a day (3 in the morning and 3 in the evening) for a 7-day period before every visit. Both OBPM and SBPM were always performed in the nondominant arm in sitting position after ≥5 minutes of rest using the same fully automated device (Omron HEM-705 CP).12 In addition, ABPM was performed with a SpaceLabs automatic device at the start and end of the trial. Measurements were taken every 15 minutes between 7 AM and 11 PM and every 30 minutes at night. The average daytime ABPM value was calculated from 9 AM and 9 PM hour on the first day without the initial hour. Average nocturnal ABPM was determined from 1 AM and 6 AM.

Additional Measurements
Treatment Costs
Treatment costs consisted of medication costs (ie, drug costs and pharmacist fee) and costs of the BP monitor. Medication costs were computed for each drug on each visit. Medication prices from May 2005 were taken for analysis. In the SP group, the costs of the BP monitor were calculated using the annuity method with a depreciation period of 3 years, an interest rate of 4.5%, and maintenance costs of 8% of the purchase price. Total treatment costs are reported in US$ (1 US$ is 0.76€ of 8% of the purchase price). Treatment costs consisted of medication costs (ie, drug costs and pharmacist fee) and costs of the BP monitor. Medication costs were computed for each drug on each visit. Medication prices from May 2005 were taken for analysis. In the SP group, the costs of the BP monitor were calculated using the annuity method with a depreciation period of 3 years, an interest rate of 4.5%, and maintenance costs of 8% of the purchase price. Total treatment costs are reported in US$ (1 US$ is 0.76€ of 8% of the purchase price). Total treatment costs are reported in US$ (1 US$ is 0.76€ of 8% of the purchase price). Total treatment costs are reported in US$ (1 US$ is 0.76€ of 8% of the purchase price).

Adherence to Treatment
At each visit, patients had to take their medication bottles to the clinic where the physician or nurse counted the number of pills left in the bottle in the presence of the patient. Feedback was given only when the number of pills left was extremely high. The scores were transmitted to the coordinating center, where the number of prescribed pills was registered so that intake could be calculated.

Adverse Effects of Medication
In a subscale of the Bulpitt questionnaire,13 symptoms of hypertension and adverse effects of medication were addressed. This was performed in 356 patients (179 from the SP group and 177 from the OP group) who were included before May 1, 2003.

Statistical Considerations
Data were analyzed according to the intention-to-treat principle. The last observation carried forward method was applied for missing values when data of ≥2 consecutive visits were available. Differences in BP between the 2 randomized groups were analyzed by a multivariate analysis adjusting for baseline BP values, center, age, gender, body mass index, smoking, antihypertensive drugs at baseline, run-in period, and setting of patient recruitment. Other between-group comparisons involved the following statistical methods: Student’s t test, Mann-Whitney (when data were not normally distributed), or χ² for proportions. A 2-sided P<0.05 was taken as statistical significance. All of the statistical calculations were performed using SPSS version 12.0 (SPSS, Inc.).

Results
Altogether, 459 patients met the inclusion criteria and were considered eligible for the study. Of these, 29 did not start trial therapy because they withdrew or refused consent for various reasons. Consequently, 430 patients entered the study after a 4-week run-in period and started trial medication (Figure 1). Baseline characteristics at inclusion were comparable for the 2 groups (Table 1).

During the trial, 46 patients dropped out (OP group: 27; SP group: 19) because they withdrew consent (n=44), had an adverse event (n=1), or became pregnant (n=1). Reasons for withdrawing consent were that patients felt uncomfortable with the blinded medication, complained about adverse effects, found the frequent visits to the hospital too cumbersome, or thought that the additional examinations might be too hazardous. Patients who dropped out from the study did not differ in any characteristic from patients who completed follow-up either between or within groups.

Median follow-up time was 351 days (interquartile range: 336 to 366 days) for the OP group and 354 days (interquartile range: 340 to 369 days) for the SP group. Twenty patients (10 in each group) had no run-in period and switched immediately to the trial medication.

Figure 1. Flowchart of the trial.
Medication Use and Costs

Figure 2 shows that more patients from the SP group than from the OP group could permanently stop their medication because their BP values came below the present targets (10.7% versus 1.9%; log rank: \(P < 0.0001\)). Moreover, in the SP group, a greater proportion of patients reached a stable treatment level (treatment unchanged during the remaining part of the study) than in the OP group (54.0% versus 48.0%; log rank: \(P < 0.0001\)). On average, the SP group used 1 drug or 1 dose less in comparison with the OP group (\(P < 0.001\)).

Please see Table S1, available online at http://hyper.ahajournals.org, for more detailed information regarding medication use.

Significant differences for certain drugs were mainly caused by the fact that patients in the OP group were at a higher level of the treatment schedule. At the end of the trial, significantly more patients in the OP group than in the SP group received atenolol because of adverse effects to lisinopril (mostly dry cough).

Medication costs during the whole study amounted to $4147 in the OP group and $3023 in the SP group per 100 patients for 1 month of treatment, resulting in a saving in medication costs of $1124 (\(P < 0.001\)). With inclusion of the fees for pharmacist, costs amounted to $4420 and $3222 (\(P < 0.001\)) for the OP and SP group, respectively. The profit in the SP group is partially offset by the cost of the BP device, which was $490 for 100 patients for 1 month. However, when corrected for these costs, the SP group still has lower treatment costs than the OP group (\(P = 0.03\)). The total number of visits in the trial was similar in the SP and OP group, 2012 versus 2066, with a mean charge of $70 and $71 for the OP and SP group, respectively.

BP Control

Figure 3 illustrates the time course of BP patterns. Systolic OBPM increased after visit 1 when the run-in period started and regular antihypertensive treatment was discontinued. At visit 3, more patients were hypertensive according to their systolic BP than to their diastolic BP (n = 391 versus n = 342). Both groups showed almost similar BP patterns throughout the trial. Although SBPM followed the same pattern during follow-up as OBPM, at every visit SBPM was significantly lower than OBPM (\(P < 0.001\)). Of the 42 SBPMs that had to

### Table 1. Distribution of Clinical Characteristics at Inclusion

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=430)</th>
<th>OP Group (n=216)</th>
<th>SP Group (n=214)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males (%)</td>
<td>236 (55)</td>
<td>118 (55)</td>
<td>118 (55)</td>
</tr>
<tr>
<td>Age (SD), y</td>
<td>55 (11)</td>
<td>55 (11)</td>
<td>55 (11)</td>
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<tr>
<td>BMI (SD), kg/m²</td>
<td>28 (4)</td>
<td>28 (5)</td>
<td>28 (4)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>77 (18)</td>
<td>42 (19)</td>
<td>35 (16)</td>
</tr>
<tr>
<td>Alcohol, n (%)</td>
<td>329 (77)</td>
<td>169 (78)</td>
<td>160 (75)</td>
</tr>
<tr>
<td>Glucose (SD), mmol/L</td>
<td>5.5 (1)</td>
<td>5.4 (1)</td>
<td>5.6 (1)</td>
</tr>
<tr>
<td>Cholesterol (SD), mmol/L</td>
<td>5.7 (1)</td>
<td>5.7 (1)</td>
<td>5.7 (1)</td>
</tr>
<tr>
<td>Creatinine (SD), µmol/L</td>
<td>82 (16)</td>
<td>82 (14)</td>
<td>82 (17)</td>
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<td>Microalbuminuria, mg/24 h*</td>
<td>10.3</td>
<td>10.6</td>
<td>10.0</td>
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<tr>
<td>Treatment status, n (%)</td>
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<tr>
<td>Untreated</td>
<td>132 (31)</td>
<td>64 (30)</td>
<td>68 (32)</td>
</tr>
<tr>
<td>1 drug</td>
<td>160 (37)</td>
<td>85 (39)</td>
<td>75 (35)</td>
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<td>2 drugs</td>
<td>103 (24)</td>
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<td>≥3 drugs</td>
<td>35 (8)</td>
<td>17 (8)</td>
<td>18 (8)</td>
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<td>Previous antihypertensive</td>
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<tr>
<td>treatment, n (%)</td>
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<td></td>
<td></td>
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<tr>
<td>Diuretics</td>
<td>116 (27)</td>
<td>55 (25)</td>
<td>61 (29)</td>
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<td>ACE inhibitors</td>
<td>114 (27)</td>
<td>59 (27)</td>
<td>55 (26)</td>
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<tr>
<td>β-Blockers</td>
<td>120 (28)</td>
<td>57 (26)</td>
<td>63 (29)</td>
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<tr>
<td>Calcium channel blockers</td>
<td>51 (12)</td>
<td>27 (13)</td>
<td>24 (11)</td>
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<td>Angiotensin II receptor</td>
<td>65 (15)</td>
<td>35 (16)</td>
<td>30 (14)</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>α-Blockers</td>
<td>8 (2)</td>
<td>6 (3)</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

BMI indicates body mass index; ACE, angiotensin-converting enzyme.

*Results are given as medians.
At the end of the trial, 106 patients (50%) in the OP group had Target BP than in the SP group (38 [18%] versus 19 [9%]; 140 mm Hg systolic and/or 90 mm Hg diastolic) was significantly higher in the OP group whereas OBPM is still.

In the OP group, 409 treatment decisions (24%) were based on elevated systolic BP only, 48 (3%) on elevated diastolic BP only, and 699 (41%) on an elevation of both systolic and diastolic BP. In the SP group, these numbers were 357 (21%), 34 (2%), and 398 (23%), respectively. Both for systolic and diastolic BP, there was no significant difference in OBPM between the randomly assigned groups were found at the end of the trial for either absolute BP values (P=0.25 and P=0.20) or for changes in BP (P=0.77 and P=0.14).

Refractory or Resistant Hypertension

The number of patients with refractory or resistant hypertension (defined as the use of 3 different antihypertensives, whereas OBPM is still >140 mm Hg systolic and/or 90 mm Hg diastolic) was significantly higher in the OP group than in the SP group (38 [18%] versus 19 [9%]; P<0.01).

Target BP

At the end of the trial, 106 patients (50%) in the OP group had an OBPM value <140/90 mm Hg, whereas in the SP group, 160 patients (74%) had reached a final SBPM value that was <140/90 mm Hg (P<0.001). If we took the number of patients from the SP group who reached a SBPM value of 135/85 mm Hg, there were 112 patients (52%) who reached this target. At the last visit, 18 patients (8%) from the SBPM group had a normal OBPM but an elevated SBPM (masked hypertension).

TOD

Changes in left ventricular mass index were similar in both groups: 6.5±1.7 g/m² (from 98.3 to 91.8 g/m²) versus −5.6±1.7 g/m² (from 96.4 to 90.8 g/m²) for the OP and SP group, respectively (P=0.72). Median changes in urinary microalbuminuria concentration were also similar: from 10.0 to 8.3 mg per 24 hours and from 10.7 to 9.2 mg per 24 hours for the OP and SP group, respectively (P=0.87). Within-group reductions in left ventricular mass index and microalbuminuria concentrations were significant for both randomly assigned groups (P<0.001). No significant differences between groups were found for other laboratory variables.

Pill Count

Pill counts, which were assessed in all of the patients, indicated that medication intake was similar in both arms: 88.1% in the OP group versus 87.3% in the SP group (P=0.62).

Adverse Effects

For reported frequency of symptoms and adverse effects per visit, please see Table S2. Headaches, joint complaints, flushing of face or neck, light-headedness, and sleepiness were the most frequently mentioned symptoms (>35%).
Discussion

Our results show that adjustment of antihypertensive therapy based on SBPM can reduce the number of drugs without loss of OBPM control or an increase in the number of refractory hypertensive patients. Yet, a tendency toward slightly worse ABPM control was noted in patients of the SP group as compared with those of the OP group. Despite the latter, regression of TOD was comparable in the 2 groups. In addition, patients in the SP group had a similar chance to reach the target BP value as those in the OP group when this target was set at 135/85 mm Hg for SBPM. Finally, significantly more patients in the SP group could permanently stop their antihypertensive medication, suggesting that SBPM may be a valuable tool to prevent unnecessary drug prescription.

This study must be interpreted within the context of its limitations. BP measurements were not performed with a memory-equipped device, thus leaving room for observer bias; patients may have measured BP more often than needed and selected 3 preferred measurements. In some practices, OBPM was performed by a nurse instead of a physician, which may have resulted in lower BP values.14 Hence, some dilution cannot entirely be excluded, although patients were equally divided between the 2 groups in these practices.

The present study chose to take 140/90 mm Hg as the target of treatment for SBPM instead of the 135/85 mm Hg, which is presently recommended.15 This may have caused some undertreatment in the SP group relative to the OP group. However, at the time the protocol for HOMERUS was written, there was no agreement on what should be the upper limit for SBPM,16 because only some cross-sectional studies17–22 and 1 longitudinal study23 had addressed this subject by then. Second, the guidelines that recommend 135/85 mm Hg as the threshold for SBPM prescribe that OBPM is taken with a mercury sphygmomanometer and SBPM with an oscillometric automatic device. In the present study, both SBPM and OBPM have been performed with the same oscillometric automatic device so that there were no differences in BP values caused by the device. Third, the recommendations for OBPM prescribe that 2 measurements should be performed.24 In the present study, 3 measurements have been obtained, which generally leads to lower average OBPM values, because the first measurement is usually higher than subsequent ones.25 Lower OBPM values tend to dilute the differences between OBPM and SBPM.

Recently, the results of the Treatment of Hypertension based on home or Office blood Pressure (THOP) Trial26 were published which showed that patients whose medical treatment was based on SBPM had poorer OBPM and ABPM values than patients in whom treatment was based on OBPM. Although the THOP Trial seems largely similar to HOMERUS, there are some important differences. Firstly, in the THOP Trial, treatment was based on diastolic BP (<90 mm Hg) only, because at the time the World Health Organization still defined hypertension exclusively on the basis of diastolic BP. However, in the present study, more patients were hypertensive according to their systolic BP than to their diastolic BP at baseline. In addition, during follow-up, a quarter of all treatment decisions were based on elevated systolic BP only. For optimal management of hypertension, a well-controlled systolic BP is important, because it correlates significantly stronger with the risk of cardiovascular or all-cause death27 than diastolic BP. Second, in the THOP Trial, OBPMs were performed with a manual mercury sphygmomanometer, whereas an automatic device was applied for SBPM. The use of different devices complicates comparisons between both strategies, and, in addition, manual sphygmomanometers are more liable to observer bias.28 Third, in HOMERUS, patients in the OP group did not perform SBPM. Although this has the disadvantage that it is impossible to keep the patient blinded for randomization, it certainly better represents the normal clinical situation, which is important, because SBPM influences a patients’ behavior.29

The cost-effectiveness of SBPM has also been evaluated in the THOP Trial. Our study confirmed that a significant reduction in medication intensity and costs can be reached. The maximum difference in treatment costs was obtained at the end of the study. When these costs were extrapolated to the next year, this led to an even greater reduction in costs in favor of the SP group.

At the end of the trial, ABPM values were higher in the SP than in the OP group. Although this could mean that antihypertensive treatment based on SBPM leads to worse BP control as compared with OBPM-based treatment, we must realize that the reproducibility of ABPM is limited.30 Although differences in mean ABPM and OBPM values between both groups are small and perhaps not relevant for a patient as an individual, these results cannot be ignored, because even small differences can have serious consequences with respect to cardiovascular complications in the population at large. Indeed, a meta-analysis of individual data for 1 million adults in 61 prospective studies showed that a 2-mm Hg–lower systolic BP value would eventually lead to a 10% lower stroke mortality and ~7% lower mortality from ischemic heart diseases or other vascular causes in middle-aged patients.2

From these results, one may be inclined to think that it is better to base antihypertensive treatment on OBPM instead of SBPM. However, we believe that the present article offers several arguments that favor SBPM above OBPM. First of all, when we apply a threshold of 135/85 mm Hg as the treatment target in the SBPM patients, 52% actually reached this goal, which is quite similar to the 50% of OBPM patients who reached their target of 140/90 mm Hg OP. When using 135/85 mm Hg as a threshold value, there were 104 patients in the SP group who did not reach the target BP. Let us assume that these patients would need, on average, an additional treatment step to reach this target. If we consider the most expensive step at any occasion (Lisinopril, $15 for 1 month of treatment), the necessary additional costs for treatment would be 104 × $15 = $1560 for 1 month of treatment. For the whole SP population, this would equal $1560/216 = $7.22 per patient for 1 month of treatment. When added to the $3023, this would increase total costs in the SP group to $3745, which is still less than the $4147 for the OP group. This, together with the fact that half of the patients from the OP group also need additional treatment to reach their target BP of 140/90 mm Hg, indicates that it is most likely that treatment based on SBPM would lead to BP values similar to...
those in patients from the OP group with less medication. The second argument for using SBPM is the presence of masked hypertension, which is defined as a BP that is normal in the office but elevated when measured at home.\textsuperscript{32} In the present study, 18 patients (8\%) from the SP group had this phenomenon at the last visit. Other studies have shown that these patients have a similar risk of cardiovascular complications as “true” subjects with hypertension. Third, there were significantly less patients with refractory or resistant hypertension in the SP group than in the OP group. Finally, both the OP group and the SP group experienced a similar reduction in TOD (heart and kidney), which would imply that the SP group was not worse off.

Based on earlier data, one would expect that patients from the SP group would be more adherent to their medication than patients from the OP group, because SBPM increases patients’ awareness of their disease.\textsuperscript{33} However, the high overall adherence rate in both treatment groups as observed in the present study likely reflects some inherent motivation of patients who are willing to participate in a clinical trial. In this respect, SBPM had little additional value.

In conclusion, the findings in this randomized trial show that, in a population of mild-to-moderate hypertensive subjects without significant comorbidity, antihypertensive treatment based on SBPM is not associated with worse OBPM control, with more TOD, with an increased number of refractory hypertensive patients, or with a lower chance of reaching target BP as compared with treatment based on OBPM. In addition, SBPM does lead to decreased use of medication and, thus, less overall healthcare costs and adverse effects. Therefore, our findings support the use of SBPM in addition to OBPM in regular clinical care to improve overall BP control and to prevent unnecessary treatment prescriptions with associated healthcare costs. However, because the ambulatory BP was less well controlled in patients from the SP group than in patients from the OP group, the present study did not provide hard evidence that it is safe to base antihypertensive treatment on SBPM readings. Because this can be partly ascribed to using a threshold value of 140/90 mm Hg, we recommend the use of the proposed values of 135 mm Hg systolic and 85 mm Hg diastolic as the threshold values for normal SBPM.

Perspectives

Treatment based on SBPM using a threshold value of 140/90 mm Hg leads to less drug prescription than treatment based on OBPM. However, this also leads to slightly higher ABPM values that, in the long run and extended to a large population, may still lead to an increase in cardiovascular events. Therefore, large outcome trials with a longer follow-up period are necessary to confirm or refute the significance of our present findings. It should also be emphasized that our results are applicable only to the specific population of hypertensive patients that we included in our trial. It would be worthwhile to assess whether SBPM has the same implications in patients with comorbid conditions, such as diabetes mellitus or renal impairment, as well as in populations with a different racial background. Finally, the present data may serve as a starting point for more elaborate cost-effectiveness studies and reimbursement of BP monitoring devices.

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Disclosures

None.

References

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Home Versus Office Measurement, Reduction of Unnecessary Treatment Study Investigators

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## Table S1  Antihypertensive drugs for the two treatment groups used during follow-up

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<thead>
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<th></th>
<th>1 Month</th>
<th>2 Month</th>
<th>4 Month</th>
<th>6 Month</th>
<th>8 Month</th>
<th>10 Month</th>
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<tr>
<td><strong>Treatment score, mean (SD)</strong></td>
<td></td>
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<tr>
<td>OP</td>
<td>0.52 (0.21)</td>
<td>&lt;0.05</td>
<td>0.90 (0.39)</td>
<td>&lt;0.01</td>
<td>1.78 (0.91)</td>
<td>&lt;0.001</td>
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<tr>
<td>SP</td>
<td>0.47 (0.20)</td>
<td>0.75 (0.39)</td>
<td>1.27 (0.90)</td>
<td>1.45 (1.07)</td>
<td>1.57 (1.17)</td>
<td>&lt;0.001</td>
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<td><strong>Study medication, % of patients (median dose, mg/d)</strong></td>
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<tr>
<td><strong>Lisinopril</strong></td>
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<tr>
<td>OP</td>
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<td>66.8(20)</td>
<td>61.7(20)</td>
<td>44.2(20)</td>
<td>38.4(20)</td>
<td>34.2(20)</td>
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<tr>
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<td>53.3(20)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>OP</td>
<td>1.9 (12.5)</td>
<td>7.7(12.5)</td>
<td>63.3(12.5)</td>
<td>56.3(12.5)</td>
<td>46.3(12.5)</td>
<td>41.6(12.5)</td>
</tr>
<tr>
<td>SP</td>
<td>0.9 (12.5)</td>
<td>4.2(12.5)</td>
<td>48.5(12.5)</td>
<td>47.0(12.5)</td>
<td>42.5(12.5)</td>
<td>40.5(12.5)</td>
</tr>
<tr>
<td><strong>Amlo</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>OP</td>
<td>0</td>
<td>1.9 (5)</td>
<td>41.8(5)</td>
<td>50.5(5)</td>
<td>45.3(5)</td>
<td>37.4(5)</td>
</tr>
<tr>
<td>SP</td>
<td>0</td>
<td>0.9 (5)</td>
<td>26.0(5)</td>
<td>31.2(5)</td>
<td>35.5(5)</td>
<td>32.0(5)</td>
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<tr>
<td><strong>Atenolol</strong></td>
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<tr>
<td>OP</td>
<td>4.3 (50)</td>
<td>7.7 (50)</td>
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<td>15.3 (100)</td>
<td>16.3(100)</td>
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</tr>
<tr>
<td>SP</td>
<td>1.4 (50)</td>
<td>4.7 (50)</td>
<td>7.8 (100)</td>
<td>8.9 (100)</td>
<td>9.0(100)</td>
<td>10.0(100)</td>
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</table>
OP indicates the office pressure group; SP, self pressure group; HCTZ, hydrochlorothiazide; Amlo, amlodipine. Median daily doses of study drugs were compared between both groups;
### Appendix Table S2  Frequency of symptoms and side-effects in percentage per 100 patients

<table>
<thead>
<tr>
<th>Symptoms and side effects</th>
<th>1 month</th>
<th>3 months</th>
<th>7 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SBPM</td>
<td>OPBM</td>
<td>SBPM</td>
<td>OPBM</td>
</tr>
<tr>
<td>Light-headedness</td>
<td>43</td>
<td>37</td>
<td>36</td>
<td>39</td>
</tr>
<tr>
<td>Sleepy during the day</td>
<td>42</td>
<td>44</td>
<td>41</td>
<td>42</td>
</tr>
<tr>
<td>Weakness in the limbs</td>
<td>22</td>
<td>22</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>Blurring of vision</td>
<td>38</td>
<td>32</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Short of breath</td>
<td>8</td>
<td>13</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Swollen ankles</td>
<td>19</td>
<td>13</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>Loose or liquid motions</td>
<td>18</td>
<td>21</td>
<td>21</td>
<td>25</td>
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<tr>
<td>Constipation</td>
<td>6</td>
<td>5</td>
<td>7</td>
<td>4</td>
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<tr>
<td>Dry mouth</td>
<td>34</td>
<td>29</td>
<td>27</td>
<td>24</td>
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<tr>
<td>Bad taste</td>
<td>15</td>
<td>10</td>
<td>8</td>
<td>11</td>
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<tr>
<td>Blocked or runny nose</td>
<td>37</td>
<td>36</td>
<td>36</td>
<td>39</td>
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<tr>
<td>Dry cough</td>
<td>26</td>
<td>29</td>
<td>38</td>
<td>43</td>
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<tr>
<td>Flushing face or neck</td>
<td>44</td>
<td>39</td>
<td>40</td>
<td>38</td>
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<tr>
<td>Nightmares</td>
<td>11</td>
<td>7</td>
<td>10</td>
<td>11</td>
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<tr>
<td>Sick or vomited</td>
<td>10</td>
<td>8</td>
<td>9</td>
<td>10</td>
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<tr>
<td>Rash</td>
<td>13</td>
<td>22</td>
<td>19</td>
<td>13</td>
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<tr>
<td>Itching</td>
<td>22</td>
<td>24</td>
<td>24</td>
<td>19</td>
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<tr>
<td>White fingers</td>
<td>17</td>
<td>20</td>
<td>14</td>
<td>18</td>
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<tr>
<td>Headaches</td>
<td>55</td>
<td>58</td>
<td>45</td>
<td>39</td>
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<tr>
<td>Dry painful eyes</td>
<td>23</td>
<td>19</td>
<td>21</td>
<td>18</td>
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<tr>
<td>Condition</td>
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<td>29</td>
<td>20</td>
<td>26</td>
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<tr>
<td>---------------------------------</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>Non-adherence because of side effects</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>3</td>
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<tr>
<td>Muscle spasm</td>
<td>24</td>
<td>27</td>
<td>21</td>
<td>26</td>
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<tr>
<td>Joint complaints</td>
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<td>35</td>
<td>38</td>
<td>35</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>20</td>
<td>22</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>To doctor for complaints</td>
<td>41</td>
<td>38</td>
<td>25</td>
<td>26</td>
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</tbody>
</table>

SBPM indicates self blood pressure measurement; ABPM, ambulatory blood pressure measurement.
Acknowledgments

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