

# Optimal Number of Days for Home Blood Pressure Measurement

Teemu J. Niiranen,<sup>1,2,\*</sup> Kei Asayama,<sup>3,4,\*</sup> Lutgarde Thijs,<sup>5</sup> Jouni K. Johansson,<sup>1</sup> Azusa Hara,<sup>5</sup> Atsushi Hozawa,<sup>6</sup> Ichiro Tsuji,<sup>7</sup> Takayoshi Ohkubo,<sup>3,4</sup> Antti M. Jula,<sup>1</sup> Yutaka Imai,<sup>3</sup> and Jan A. Staessen<sup>5,8;</sup> IDHOCO Investigators

## BACKGROUND

Current guidelines make no outcome-based recommendations on the optimal measurement schedule for home blood pressure (BP).

## METHODS

We enrolled 4,802 randomly recruited participants from three populations. The participants were classified by their (i) cross-classification according to office and home BP (normotension, masked hypertension, white-coat hypertension, and sustained hypertension) and (ii) home BP level (normal BP, high normal BP, grade 1 and 2 hypertension), while the number of home measurement days was increased from 1 to 7. The prognostic accuracy of home BP with an increasing number of home BP measurement days was also assessed by multivariable-adjusted Cox models.

## RESULTS

Agreement in classification between consecutive measurement days indicated near perfect agreement ( $\kappa \geq 0.9$ ) after the sixth measurement day for both office and home BP cross-classification (97.8% maintained classification,  $\kappa = 0.97$ ) and home BP level (93.6%

maintained classification,  $\kappa = 0.91$ ). Over a follow-up of 8.3 years, 568 participants experienced a cardiovascular event, and the first home BP measurement alone predicted events significantly ( $P \leq 0.003$ ). The confidence intervals (CIs) were too wide and overlapping to show superiority of multiple measurement days over the first measurement day (hazard ratios per 10 mm Hg increase in systolic BP at initial day, 1.11 [CI 1.07–1.16]; that at 1–7 days, 1.18 [CI 1.12–1.24]). Masked hypertension, but not white-coat hypertension, was associated with increased cardiovascular risk, irrespective of the number of home measurement days.

## CONCLUSION

Even a single home BP measurement is a potent predictor of cardiovascular events, whereas seven home measurement days may be needed to reliably diagnose hypertension.

**Keywords:** blood pressure; cardiovascular diseases; home blood pressure monitoring; hypertension; meta-analysis; prognosis.

doi:10.1093/ajh/hpu216

Blood pressure (BP) measurement at conventional settings is still the primary method for evaluating hypertension in primary care. However, the number of patients self-monitoring their BP at home is increasing steadily.<sup>1,2</sup> Home BP measurement provides a large number of readings over a period of several days that are free from digit preference and the white-coat effect, which translates into higher reproducibility and increased diagnostic accuracy compared with conventional measurement.<sup>3–6</sup> In addition to its diagnostic benefits, home

BP measurement is also highly acceptable to the patients and cost-effective.<sup>7–10</sup> Because of these advantages over conventional measurements, international and national guidelines currently recommend home BP monitoring for diagnosing and managing hypertension.<sup>11–13</sup>

Several studies have tried to define an optimal home measurement schedule, mainly based on the statistical reproducibility of the readings over multiple days.<sup>14–17</sup> Clinicians, however, make treatment decisions based on diagnostic

Correspondence: Jan A. Staessen ([jan.staessen@med.kuleuven.be](mailto:jan.staessen@med.kuleuven.be) or [ja.staessen@maastrichtuniversity.nl](mailto:ja.staessen@maastrichtuniversity.nl)).

\*These authors contributed equally to the work.

Initially submitted July 14, 2014; date of first revision August 20, 2014; accepted for publication October 7, 2014; online publication November 14, 2014.

<sup>1</sup>Population Studies Unit, Department of Chronic Disease Prevention, National Institute for Health and Welfare, Turku, Finland; <sup>2</sup>Department of Medicine, Turku University Hospital, Turku, Finland; <sup>3</sup>Department of Planning for Drug Development and Clinical Evaluation, Tohoku University Graduate School of Pharmaceutical Sciences, Sendai, Japan; <sup>4</sup>Department of Hygiene and Public Health, Teikyo University School of Medicine, Tokyo, Japan; <sup>5</sup>Studies Coordinating Centre, Research Unit Hypertension and Cardiovascular Epidemiology, KU Leuven Department of Cardiovascular Sciences, University of Leuven, Leuven, Belgium; <sup>6</sup>Department of Preventive Medicine and Epidemiology, Tohoku Medical Megabank Organization, Tohoku University, Sendai, Japan; <sup>7</sup>Department of Public Health, Tohoku University Graduate School of Medicine, Sendai, Japan; <sup>8</sup>VitaK Research and Development, Maastricht University, Maastricht, The Netherlands.

© American Journal of Hypertension, Ltd 2014. All rights reserved.

For Permissions, please email: [journals.permissions@oup.com](mailto:journals.permissions@oup.com)

categories. To our knowledge, no previous study has evaluated how an increasing number of home measurement days affects the reproducibility of the diagnostic BP categories. Furthermore, the few prognostic studies available have been performed in single populations and due to small sample size no subgroup analyses were possible.<sup>18,19</sup> No outcome-based recommendations therefore exist on how many days of self-measured home BP have been established.

The American Heart Association Scientific Statement on the Use and Reimbursement for Home Blood Pressure Monitoring<sup>1</sup> states that 2–3 readings should be taken, both in the morning and at night, over a period of 1 week for a recommended total of  $\geq 12$  readings. The recent Japanese Society of Hypertension guidelines recommend that the mean of the values measured 5–7 days per week should be used.<sup>12</sup> The European Society of Hypertension Guidelines for Home Blood Pressure Monitoring<sup>20</sup> also recommend 1-week's home measurement, while the measurements recorded on the first day should be discarded. One reason for these inconsistent recommendations is that the majority of studies that have tried to define an optimal home measurement schedule were based on the reproducibility of the home-measured blood pressure instead of prognostic and cross-sectional clinical data.

The objective of our study was to determine how many days of home blood pressure measurement are needed to diagnose hypertension and to predict cardiovascular risk reliably. We addressed these issues in 4,802 participants from three populations and enrolled in the International Database on HOme blood pressure in relation to Cardiovascular Outcomes (IDHOCO).<sup>21</sup>

## METHODS

### Study participants

IDHOCO consists of prospective studies conducted in the general population. All studies contributing to the IDHOCO database received ethical approval and have been described in detail in peer-reviewed publications.<sup>21</sup> All participants gave informed written consent.

The IDHOCO<sup>21</sup> database has been constructed using individual participants' data including information on longitudinal follow-up of both fatal and nonfatal cardiovascular outcomes. Participants were recruited from Ohasama, Japan ( $n = 2,777$ ),<sup>4</sup> Finland (Finn-Home;  $n = 2,075$ ),<sup>3</sup> Tsurugaya, Japan ( $n = 836$ ),<sup>22,23</sup> Montevideo, Uruguay ( $n = 400$ ),<sup>24</sup> and Didima, Greece ( $n = 665$ ).<sup>25</sup> The Montevideo<sup>24</sup> and Didima<sup>25</sup> participants were excluded from this analyses because of an insufficient number of home measurements (Montevideo, two measurements) or measurement days (Didima, three days).

Of the remaining 5,688 participants, we excluded 658 and 228 participants because less than seven days of home measurements or less than two conventional BP values were available, respectively.<sup>3,4,22,23</sup> The number of participants available for the analysis therefore totaled 4,802.

### BP measurements and classification

Conventional BP was measured with a standard mercury sphygmomanometer or an automated device, using the

appropriate cuff size, after the participants had rested for at least 2 minutes in the sitting or supine position.<sup>21</sup> Participants measured their BP at home after at least 2 minutes of sitting rest with validated,<sup>21</sup> oscillometric devices in the sitting position. In the Finn-Home study, home BP was measured twice every morning and evening for seven consecutive days.<sup>3</sup> In the Tsurugaya study, home BP was measured once every morning for up to 1 month.<sup>22,23</sup> In the Ohasama study, home BP was measured once every morning and every evening for up to 1 month.<sup>4</sup> The first morning home BP measurements on seven days were included in the analyses to obtain a uniform measurement schedule for all cohorts.

Based on the mean of two conventional measurements and the mean BP of 1–7 measurement days, participants were classified in four categories according to (i) the cross-classification based on conventional and home BP measurement (normotension, white-coat hypertension, masked hypertension, and sustained hypertension) and (ii) home BP level (normal BP, high normal BP, grade 1 hypertension, and grade 2 hypertension). We defined white-coat hypertension as a conventional BP  $\geq 140$  mm Hg systolic or  $\geq 90$  mm Hg diastolic with a home BP  $< 135$  mm Hg systolic and  $< 85$  mm Hg diastolic.<sup>11–13</sup> We defined masked hypertension as a conventional BP  $< 140$  mm Hg systolic and  $< 90$  mm Hg diastolic with a home BP  $\geq 135$  mm Hg systolic or  $\geq 85$  mm Hg diastolic.<sup>11–13</sup> The remaining subjects were classified as normotensive or sustained hypertensive based on normality or elevation, respectively, of both conventional and home BPs. We also divided the participants into having normal BP (home BP  $< 125$  mm Hg systolic and  $< 80$  mm Hg diastolic), high normal BP (home BP 125–135 mm Hg systolic and/or 80–85 mm Hg diastolic), grade 1 hypertension (home BP 135–145 mm Hg systolic and/or 85–90 mm Hg diastolic), and grade 2 hypertension (home BP  $\geq 145$  mm Hg systolic and/or 90 mm Hg diastolic) according to previously published outcome-driven thresholds, which yield similar cardiovascular risks to the thresholds recommended by the Japanese and European Societies of Hypertension for conventional measurements.<sup>11,13,26</sup>

### Other measurements

In all cohorts, a questionnaire was used to obtain detailed information on each participant's medical history, intake of medications, and smoking and drinking habits. We defined smoking as the current use of smoking materials. Body mass index was body weight in kilograms divided by height in meters squared. Serum total cholesterol and blood glucose were determined by automated enzymatic methods on venous blood samples. Diabetes mellitus was a fasting or random blood glucose level of at least 7.0 or 11.1 mmol/l,<sup>21,27</sup> or the use of antidiabetic drugs.

### Ascertainment of events

We ascertained vital status and incidence of fatal and nonfatal diseases from the appropriate sources in each country, as described in detail in a previous publication.<sup>21</sup> The primary end point was a composite cardiovascular endpoint, including cardiovascular mortality, nonfatal myocardial infarction, surgical and percutaneous coronary revascularization, heart

failure, and stroke. Secondary analyses were conducted on cardiovascular mortality and cerebrovascular events (fatal and nonfatal stroke not including transient ischemic attacks). Only the first cardiovascular event for each category during the study follow-up was accepted for analysis.

### Statistical methods

For database management and statistical analysis, we used SAS software, version 9.3 (SAS Institute, Cary, NC). For comparison of means and proportions, we applied the large-sample Z test or analysis of variance and the  $\chi^2$  statistic, respectively. We used the kappa coefficient ( $\kappa$ ) to assess the level of agreement between BP classifications based on the cumulative means of successive days of home measurement. Near perfect agreement was defined as  $\kappa \geq 0.9$ .<sup>28</sup> We calculated incidence rates in each category, while standardizing by the direct method for sex and age (<40, 40–59, and  $\geq 60$  years). To analyze the association between endpoints and the home BP, we used Cox models adjusted for cohort, sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, and serum total cholesterol. We included home BP in the Cox models as the BP measured during one day, or the mean of a cumulatively increasing number of measurement days. In sensitivity analyses, we computed the differences in the hazard ratios between subgroups by introducing the appropriate interaction term in the Cox models. To determine the trend in the hazard ratios across the cumulative number of measurement days, we used a design variable coded from 1 to 7 in single regression analysis.

**Table 1.** Participants characteristics

Characteristic	Ohasama	Finn-Home	Tsurugaya	Total
Number of participants	2,377	1,855	570	4,802
Age, y	60.1 $\pm$ 12.0	57.3 $\pm$ 8.6	75.1 $\pm$ 4.5	60.8 (11.5)
Sex, women	1,462 (61.5)	1,004 (54.1)	293 (51.4)	2,759 (57.5)
Body mass index, kg/m <sup>2</sup>	23.5 $\pm$ 3.1	27.4 $\pm$ 4.4	23.9 $\pm$ 3.3	25.2 (4.2)
Serum total cholesterol, mmol/l	5.0 $\pm$ 0.9	6.1 $\pm$ 1.1	5.2 $\pm$ 0.8	5.5 (1.1)
Current smoking	452 (19.0)	413 (22.3)	68 (11.9)	933 (19.4)
Diabetes mellitus	238 (10.0)	117 (6.3)	85 (14.9)	440 (9.2)
Previous cardiovascular disease	179 (7.5)	231 (12.5)	91 (16.0)	501 (10.4)
Antihypertensive drug treatment	481 (20.2)	422 (22.8)	234 (41.1)	1,137 (23.7)
Blood pressure, mm Hg				
1st day, systolic home	126.9 $\pm$ 18.3	133.1 $\pm$ 22.6	143.5 $\pm$ 21.8	131.3 $\pm$ 21.2
1st day, diastolic home	76.2 $\pm$ 12.2	82.4 $\pm$ 11.7	78.6 $\pm$ 11.9	78.9 $\pm$ 12.3
7th day, systolic home	124.5 $\pm$ 17.6	127.7 $\pm$ 21.1	137.7 $\pm$ 22.0	127.3 $\pm$ 20.0
7th day, diastolic home	74.6 $\pm$ 12.1	79.8 $\pm$ 11.1	75.9 $\pm$ 11.0	76.7 $\pm$ 11.8
Systolic conventional	131.3 $\pm$ 18.2	137.2 $\pm$ 20.0	144.3 $\pm$ 19.5	135.1 $\pm$ 19.6
Diastolic conventional	74.5 $\pm$ 11.3	83.7 $\pm$ 10.5	83.0 $\pm$ 10.4	79.0 $\pm$ 11.8

Mean  $\pm$  SD, % in parentheses. All of the analysis of variance and  $\chi^2$  statistic *P* values for differences across the three cohorts were significant (*P* < 0.0001).

## RESULTS

Table 1 lists the characteristics of the participants. The mean home BP on the first day was 4.0 mm Hg higher for systolic (95% confidence intervals [CI], 3.5–4.4; *P* < 0.0001) and 2.1 mm Hg higher for diastolic (CI 1.9–2.4; *P* < 0.0001) than BP measured on the last day.

### BP cross-classification

We first examined how an increasing number of home measurement days modifies the classification into normotension, and white-coat, masked, and sustained hypertension (Table 2). When the number of home BP measurement days increased from 1 to 7, the classification remained the same in 4,073 participants (84.8%). Agreement in classification between consecutive measurement days indicated near perfect agreement ( $\kappa \geq 0.9$ ) already after the second measurement day (93.5% maintained classification,  $\kappa = 0.90$ ).

### Classification according to home BP level

Next, we examined how an increasing number of home measurement days modifies classification of the participants into normal BP, high normal BP, grade 1 hypertension, and grade 2 hypertension (Table 3). When the number of home BP measurement days was increased from 1 to 7, BP classification remained the same in 3,059 participants (63.7%). Agreement in classification between consecutive measurement days indicated near perfect agreement ( $\kappa \geq 0.9$ ) after the sixth measurement day (93.6% maintained classification,  $\kappa = 0.91$ ).

**Table 2.** Cross-classification of participants according to conventional blood pressure and the cumulative mean of home blood pressures measured on 1–7 days

Blood pressure cross-classification	Home measurement days						
	1	1–2	1–3	1–4	1–5	1–6	1–7
Normotension	2,015	2,127 (9.4)	2,183 (5.1)	2,215 (3.0)	2,226 (2.1)	2,247 (2.1)	2,256 (1.5)
White-coat hypertension	563	617 (21.1)	641 (13.4)	650 (8.3)	646 (6.8)	669 (6.4)	667 (3.3)
Masked hypertension	835	723 (12.2)	667 (8.3)	635 (5.4)	624 (5.6)	603 (4.5)	594 (4.2)
Sustained hypertension	1,389	1,335 (5.7)	1,311 (4.7)	1,302 (3.5)	1,306 (3.7)	1,283 (1.6)	1,285 (1.9)
Maintained classification, %		89.7	93.5	95.9	96.4	97.1	97.8
Kappa coefficient		0.85 (0.84–0.86)	0.90 (0.89–0.91)	0.94 (0.93–0.95)	0.95 (0.94–0.95)	0.96 (0.95–0.96)	0.97 (0.96–0.97)

Table is reported as the number of participants in each blood pressure category (% of participants who were reclassified compared with the classification of the previous day). Kappa coefficient (95% confidence intervals) indicates agreement with the classification of the previous day.

**Table 3.** Classification of the participants according to the cumulative mean of home blood pressures measured on 1–7 days

Blood pressure level	Home measurement days						
	1	1–2	1–3	1–4	1–5	1–6	1–7
Normal blood pressure	1,655	1,775 (17.0)	1,851 (10.7)	1,887 (7.7)	1,934 (6.0)	1,955 (3.8)	1,990 (4.1)
Prehypertension	923	969 (47.6)	973 (32.0)	978 (23.3)	938 (16.9)	961 (15.1)	933 (10.9)
Grade 1 hypertension	753	770 (51.2)	788 (34.3)	792 (22.7)	821 (20.5)	807 (14.4)	810 (11.4)
Grade 2 hypertension	1,471	1,288 (9.0)	1,190 (5.8)	1,145 (5.1)	1,109 (4.5)	1,079 (3.6)	1,069 (3.1)
Maintained classification, %		73.5	82.3	87.3	89.7	92.2	93.6
Kappa coefficient		0.63 (0.62–0.65)	0.76 (0.74–0.77)	0.82 (0.81–0.84)	0.86 (0.85–0.87)	0.89 (0.88–0.90)	0.91 (0.90–0.92)

Table is reported as the number of participants in each blood pressure category (% of participants who were reclassified compared with the classification of the previous day). Kappa coefficient (95% confidence intervals) indicates agreement with the classification on the previous day.

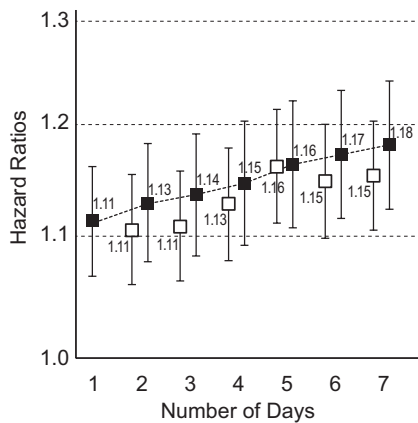
### Cardiovascular prognosis

Median follow-up was 8.3 years (5th–95th percentile interval, 4.2–16.8). During 46,037 person-years of follow-up, 568 participants experienced a fatal or nonfatal cardiovascular event (5.0 per 1,000 person-years), 221 died of cardiovascular causes, and 337 suffered a cerebrovascular event. All individual and cumulative systolic (Figure 1, Supplementary Table S1;  $P < 0.0001$ ) and diastolic (Supplementary Figure S1 and Table S1;  $P \leq 0.01$ ) BP measurements predicted the composite endpoint. When the home BP of the first measurement day was included in the Cox model, the hazard ratios per 10-mm Hg increase in systolic and per 5-mm Hg increase in diastolic BP were 1.11 (CI 1.07–1.16) and 1.05 (CI 1.02–1.09), respectively. The corresponding hazard ratios for the mean of seven measurement days were 1.18 (CI 1.12–1.24) in systolic pressure and 1.10 (CI 1.06–1.15) in diastolic pressure. The  $P$  values for the linear trends were

significant for systolic BP ( $P = 0.01$ ), but not for diastolic BP ( $P = 0.17$ ). However, the CIs were too wide and overlapping to show superiority of multiple measurements over a single measurement (Figure 1 and Supplementary Figure S1). No superiority of multiple over single days was observed even when the daily and cumulative mean BPs were calculated from all available measurements (one, two, and four measurements per day in the Tsurugaya, Ohasama, and Finn-Home cohorts, respectively; Supplementary Table S2).

Results were confirmatory when cerebrovascular events and cardiovascular mortality were used as the endpoint, although the hazard ratios of cardiovascular mortality in relation to diastolic BP were nonsignificant (Supplementary Table S3). Similar results were observed in subgroup analyses according to antihypertensive treatment status, sex, and age (<60 vs.  $\geq 60$  years; Supplementary Tables S4, S5, and S6). Excluding one cohort at a time confirmed the main analyses of systolic BP, as reported in Supplementary Table S7.





**Figure 1.** Predictive values of systolic home blood pressures (BPs). Hazard ratios express the increase in cardiovascular event risk per 10-mm Hg elevation of systolic BP on cumulative days (1 to the indicated times; filled square with dotted lines) and on individual days (open square) for cardiovascular events plotted on a log scale. Vertical lines represent 95% confidence intervals.

#### White-coat hypertension and cardiovascular events

Table 4 provides risk estimates for normotension, white-coat hypertension, masked hypertension, and sustained hypertension when the classification was based on the mean BP of 1–7 measurement days. In a multivariable-adjusted Cox model, white-coat hypertension was not significantly associated with cardiovascular risk irrespective of the number of home measurement days ( $P \geq 0.14$ ).

In Table 4, the normotensive reference group varies depending on how many days of measurement the classification is based on. In a further step of the analysis, we therefore applied the most stringent definition of normotension, which required that the conventional BP and all cumulative means of 1–7 home measurement days were within normal limits (Figure 2). The hazard ratios for white-coat hypertension vs. normotension were not statistically different ( $P \geq 0.27$ ), ranging from 1.10 to 1.19. Conversely, applying the most stringent definition of hypertension (Supplementary Figure S2) showed that the risk of white-coat hypertension was consistently lower than that of sustained hypertension ( $P < 0.01$ ) without any trend ( $P = 0.75$ ).

#### Masked hypertension and cardiovascular events

In multivariable-adjusted analyses (Table 4), the risk associated with masked hypertension compared with normotension was always significant ( $P \leq 0.03$ ) with estimates of excess risk ranging from 33% to 68%. Applying the most stringent definition of normotension (Figure 2) confirmed that the hazard ratios comparing masked hypertension with normotension were all significant ( $P < 0.03$ ), ranging from 1.36 to 1.57, with a significant linear trend ( $P = 0.01$ ). Conversely, applying the most stringent definition of hypertension (Supplementary Figure S2) showed that the risk of masked hypertension was lower than that of sustained hypertension when first and 1–2 days home measurements were used ( $P \leq 0.04$ ), whereas the significance disappeared when 1–3 days or more home measurements were averaged

( $P \geq 0.09$ ). The  $P$  value for linear trend was also significant ( $P = 0.01$ ).

#### DISCUSSION

In this study, we examined how many home BP self-measurement days are needed to diagnose hypertension and to predict cardiovascular risk reliably in an analysis of a combined sample of individual participant data. The results show that no significant changes in classification for BP level or cross-classification according to home and conventional BP occur after the sixth day. The predictive power of home BP for cardiovascular events does not materially increase within the range of 1–7 measurement days and most of the predictive power is obtained already on the first measurement day. Masked hypertension, but not white-coat hypertension, is associated with increased cardiovascular risk, irrespective of the number of home measurement days.

Several cross-sectional studies with selected cohorts of hypertensive patients have tried to assess the optimal number of home BP measurements. Chatellier *et al.*<sup>15</sup> measured BP at home thrice in the morning and evening for 21 days in 79 hypertensive patients. They showed that 80% of the maximal reproducibility (reduction in the standard deviation of differences between the average values of two home BP sessions) is obtained by averaging 15 measurements on the first 5 days.<sup>15</sup> The Self-measurement for the Assessment of the Response to Trandolapril (SMART) study with 1,710 hypertensive patients also showed that, after six home BP measurements, only a small improvement in reproducibility is achieved.<sup>17</sup> Furthermore, two studies by Stergiou *et al.*<sup>14,16</sup> demonstrated that in hypertensive patients, at least 12 measurements taken on three days are needed for the reproducibility of home BP to be superior to that of conventional measurements. However, correct BP classification, on which treatment decisions are usually based, plays a much more important role in clinical practice than the statistical reproducibility of measurements. Our results demonstrate that no significant changes in classification for BP level or cross-classification are observed after the sixth measurement day as approximately 95% of the participants maintain classification after this.

Instead of only cross-sectional analyses based on statistical reproducibility, the optimal schedule for home BP measurement should also be determined based on outcome data. Several prospective large-scale population and patient studies using home BP measurements with a wide variety of monitoring schedules have been conducted during the past two decades.<sup>3–5,25,29</sup> Single measurements in the morning and evening were performed for up to 28 days in the Japanese Ohasama study,<sup>4</sup> single morning and evening measurements were performed on one day in the Italian Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study,<sup>29</sup> duplicate morning and evening measurements were collected during one week in the Finnish Finn-Home study,<sup>3</sup> duplicate morning and evening measurements during three days were performed in the Greek Didima study,<sup>25</sup> and triplicate morning and evening measurements for four days were used in the French Self-Measurement of Blood Pressure at Home in the Elderly: Assessment and Follow-up study.<sup>5</sup>

**Table 4.** Risk of cardiovascular endpoint by blood pressure cross-classification

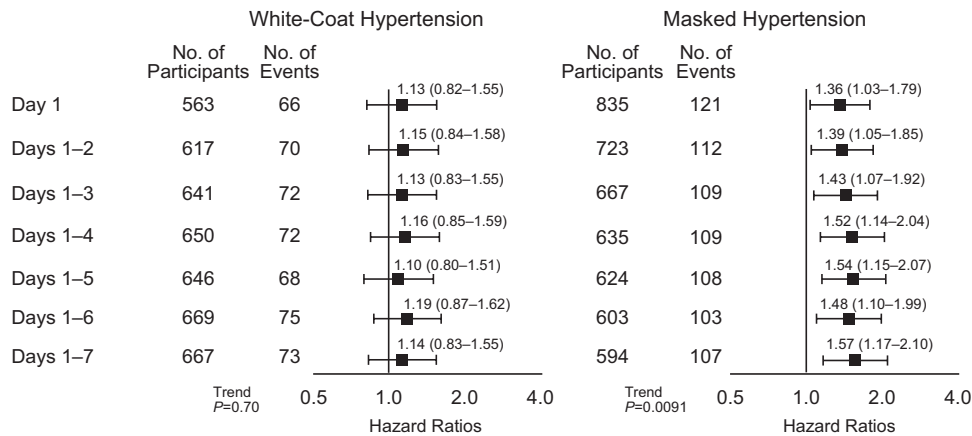
Blood pressure cross-classification	Number E/R	Rate (SE)	Hazard ratio (95% CI)	P
Day 1				
Normotension	149/2,015	9.7 (0.8)	1.00	
White-coat hypertension	66/563	13.5 (1.6)	1.20 (0.89–1.60)	0.23
Masked hypertension	121/835	14.8 (1.3)	1.33 (1.04–1.70)	0.025
Sustained hypertension	232/1,389	19.0 (1.2)	1.64 (1.31–2.05)	<0.0001
Days 1–2				
Normotension	158/2,127	9.6 (0.8)	1.00	
White-coat hypertension	70/617	13.0 (1.6)	1.16 (0.87–1.54)	0.32
Masked hypertension	112/723	15.4 (1.5)	1.38 (1.07–1.77)	0.012
Sustained hypertension	228/1,335	19.4 (1.3)	1.69 (1.35–2.11)	<0.0001
Days 1–3				
Normotension	161/2,183	9.5 (0.8)	1.00	
White-coat hypertension	72/641	13.0 (1.5)	1.16 (0.88–1.54)	0.30
Masked hypertension	109/667	16.2 (1.6)	1.44 (1.12–1.86)	0.005
Sustained hypertension	226/1,311	19.5 (1.3)	1.73 (1.38–2.16)	<0.0001
Days 1–4				
Normotension	161/2,215	9.3 (0.8)	1.00	
White-coat hypertension	72/650	13.2 (1.6)	1.20 (0.90–1.59)	0.22
Masked hypertension	109/635	17.0 (1.6)	1.59 (1.24–2.05)	0.0003
Sustained hypertension	226/1,302	19.4 (1.3)	1.80 (1.44–2.25)	<0.0001
Days 1–5				
Normotension	162/2,226	9.3 (0.8)	1.00	
White-coat hypertension	68/646	12.6 (1.5)	1.16 (0.87–1.54)	0.32
Masked hypertension	108/624	17.4 (1.7)	1.64 (1.28–2.12)	0.0001
Sustained hypertension	230/1,306	19.8 (1.3)	1.84 (1.47–2.29)	<0.0001
Days 1–6				
Normotension	167/2,247	9.4 (0.8)	1.00	
White-coat hypertension	75/669	13.5 (1.5)	1.23 (0.93–1.62)	0.14
Masked hypertension	103/603	17.0 (1.7)	1.54 (1.19–1.98)	0.001
Sustained hypertension	223/1,283	19.5 (1.3)	1.72 (1.38–2.15)	<0.0001
Days 1–7				
Normotension	163/2,256	9.1 (0.7)	1.00	
White-coat hypertension	73/667	13.3 (1.6)	1.24 (0.93–1.64)	0.14
Masked hypertension	107/594	18.0 (1.8)	1.68 (1.30–2.16)	<0.0001
Sustained hypertension	225/1,285	19.6 (1.3)	1.81 (1.45–2.26)	<0.0001

Abbreviations: CI, confidence interval; SE, standard error.

Number E/R indicate the number of events/participants at risk. Definition of the blood pressure cross-classifications is given in the Methods. Rates (SE) of events per 1,000 person-year were standardized by the direct method for sex and age. Hazard ratios (95% confidence interval) express the risk compared with normotension and were adjusted for sex, age, body mass index, smoking, drinking, total cholesterol, diabetes, history of cardiovascular disease, and cohort.

Despite such differences in monitoring schedules, these studies consistently showed strong prognostic value of home BP. Some of these studies have also demonstrated that only two home BP readings predict the risk of cardiovascular events.<sup>18,19,29,30</sup> Our study demonstrates that even a single

home BP measurement is a strong predictor of cardiovascular disease. In our study, as in previous studies, the prognostic value of home BP within the range of 1–7 days increased only slightly and no significant differences in hazard ratios were observed.<sup>18,19</sup> Increasing the number of measurements



**Figure 2.** Risk of a cardiovascular endpoint associated with white-coat and masked hypertension vs. normotension. In this analysis, normotension was defined based on two conventional blood pressure (BP) readings and seven days of home BP measurement, which required that the conventional BP and all cumulative means of 1–7 home measurement days were within normal limits. Hazard ratios express the risk compared with normotension and were adjusted for sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, serum total cholesterol, and cohort. Horizontal bars denote the 95% confidence interval of the hazard ratios. White-coat hypertension was a conventional BP  $\geq 140/\geq 90$  mm Hg and a home BP  $<135/<85$  mm Hg. Masked hypertension was a conventional BP  $<140/<90$  mm Hg and a home BP  $\geq 135/\geq 85$  mm Hg.

days from one adds only little to the predictive accuracy of the self-measured BP, but most likely also results in lower patient compliance and increased measurement errors.

Some previous studies have observed that the risk of cardiovascular disease increases from normotension to white-coat hypertension to masked hypertension to sustained hypertension.<sup>31,32</sup> Our results show that masked hypertension carries an elevated cardiovascular risk, even when the diagnosis is based on the mean of one or seven home measurements. White-coat hypertension carried a cardiovascular risk comparable with normotension in our study, although with a larger study this difference could become statistically significant. Furthermore, the hazard ratios for masked hypertension showed an increasing trend when the diagnosis was based on an increasing number of measurements, whereas the hazard ratios for white-coat hypertension remained the same. Our findings emphasize the need to recognize and actively treat masked hypertension although white-coat hypertensive individuals also need close follow-up because nearly half of them have been shown progress to sustained hypertension during an eight-year follow-up.<sup>33</sup>

This study must be interpreted within the context of some potential limitations. Only the Finn-Home participants took their BP in duplicate in the morning and evening. We could not assess whether home BP should be measured twice, instead of once, at one measurement occasion. Therefore, the generalizability of the results to other procedures for home BP measurement is unknown. Furthermore, the original home monitoring schedules differed between studies, which might have affected the findings. Nevertheless, the current analysis of a combined sample is based on the individual participant data from unselected population cohorts. The external validity and generalizability of population-based results must be larger than those emerging from cohorts of selected hypertensive patients, and the large sample size of IDHOCO enables us to provide sensitivity analyses. Finally, although there was wide overlap in the CIs of the hazard ratios of the Cox models, this is not necessarily evidence of non-association. However,

because of the strong correlation between BP values based on the mean of consecutive number of measurements, there is no perfect method for comparing these hazard ratios.

In conclusion, even a single home BP measurement is a potent predictor of cardiovascular events. Hypertension may be reliably diagnosed by using a mean of seven readings performed during seven days as no significant reclassification occurs after day 6, although the differences between various measurement schedules limit the generalizability of our results. A longer period of measurement could slightly increase diagnostic accuracy. Nevertheless, the clinical relevance of adding more measurements needs to be carefully evaluated because the probability of lower compliance and errors in a generalized use increases at the same time. The present information could inform future guidelines in creating a unified recommended scheme for home BP measurement.

#### SUPPLEMENTARY MATERIAL

Supplementary materials are available at the *American Journal of Hypertension* (<http://ajh.oxfordjournals.org>).

#### FUNDING

This work was supported by The European Union (grants IC15-CT98-0329-EPOGH, LSHM-CT-2006-037093 InGenious HyperCare, HEALTH-F4-2007-201550 HyperGenes, HEALTH-F7-2011-278249 EU-MASCARA, HEALTH-F7-305507 HOMAGE, and the European Research Council Advanced Research Grant 294713 EPLORE) and the Fonds voor Wetenschappelijk Onderzoek Vlaanderen, Ministry of the Flemish Community, Brussels, Belgium (G.0734.09, G.0881.13, and G.0880.13N) supported the Studies Coordinating Centre (Leuven, Belgium). The Ohasama study was supported by the Grants for Scientific Research (23249036, 23390171, 24591060, 24390084,

24591060, 22590767, 22790556, 23790718, 23790242, and 24790654) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan; Health Labour Sciences Research Grant (H23-Junkankitou [Seishuu]-Ippan-005) from the Ministry of Health, Labour and Welfare, Japan; the Japan Arteriosclerosis Prevention Fund; and the grant from the Daiwa Securities Health Foundation. The Finn-Home project organization created for the study involved the Finnish Centre for Pensions, the Social Insurance Institution, the National Public Health Institute, the Local Government Pensions Institution, the National Research and Development Centre for Welfare and Health, the Finnish Dental Society and the Finnish Dental Association, Statistics Finland, the Finnish Institute for Occupational Health, the UKK Institute for Health Promotion, the State Pensions Office, and the State Work Environment Fund. The Tsurugaya study was supported by a Health Sciences Research Grant for Health Service (H21-Choju-Ippan-001) from the Ministry of Health, Labour, and Welfare, Japan, and the Japan Arteriosclerosis Prevention Fund.

## ACKNOWLEDGMENTS

We thank Mrs Annick De Soete (Studies Coordinating Centre, Leuven, Belgium) who provided expert clerical assistance. We acknowledge the International Database on Home blood pressure in relation to Cardiovascular Outcome Investigators.

## DISCLOSURE

The authors declared no conflict of interest.

## REFERENCES

- Pickering TG, Miller NH, Ogedegbe G, Krakoff LR, Artinian NT, Goff D; American Heart Association; American Society of Hypertension; Preventive Cardiovascular Nurses Association. Call to action on use and reimbursement for home blood pressure monitoring: a joint scientific statement from the American Heart Association, American Society of Hypertension, and Preventive Cardiovascular Nurses Association. *Hypertension* 2008; 52:10–29.
- Ostchega Y, Berman L, Hughes JP, Chen TC, Chiappa MM. Home blood pressure monitoring and hypertension status among US adults: the National Health and Nutrition Examination Survey (NHANES), 2009–2010. *Am J Hypertens* 2013; 26:1086–1092.
- Niiranen TJ, Hänninen MR, Johansson J, Reunanen A, Jula AM. Home-measured blood pressure is a stronger predictor of cardiovascular risk than office blood pressure: the Finn-Home study. *Hypertension* 2010; 55:1346–1351.
- Ohkubo T, Imai Y, Tsuji I, Nagai K, Kato J, Kikuchi N, Nishiyama A, Aihara A, Sekino M, Kikuya M, Ito S, Satoh H, Hisamichi S. Home blood pressure measurement has a stronger predictive power for mortality than does screening blood pressure measurement: a population-based observation in Ohasama, Japan. *J Hypertens* 1998; 16:971–975.
- Bobrie G, Chatellier G, Genes N, Clerson P, Vaur L, Vaisse B, Menard J, Mallion JM. Cardiovascular prognosis of “masked hypertension” detected by blood pressure self-measurement in elderly treated hypertensive patients. *JAMA* 2004; 291:1342–1349.
- Kikuya M, Ohkubo T, Satoh M, Hashimoto T, Hirose T, Metoki H, Obara T, Inoue R, Asayama K, Hoshi H, Totsune K, Satoh H, Staessen JA, Imai Y. Prognostic significance of home arterial stiffness index derived from self-measurement of blood pressure: the Ohasama study. *Am J Hypertens* 2012; 25:67–73.
- Little P, Barnett J, Barnsley L, Marjoram J, Fitzgerald-Barron A, Mant D. Comparison of acceptability of and preferences for different methods of measuring blood pressure in primary care. *BMJ* 2002; 325:258–259.
- Fukunaga H, Ohkubo T, Kobayashi M, Tamaki Y, Kikuya M, Obara T, Nakagawa M, Hara A, Asayama K, Metoki H, Inoue R, Hashimoto J, Totsune K, Imai Y. Cost-effectiveness of the introduction of home blood pressure measurement in patients with office hypertension. *J Hypertens* 2008; 26:685–690.
- Staessen JA, Den Hond E, Celis H, Fagard R, Keary L, Vandenhoven G, O'Brien ET. Antihypertensive treatment based on blood pressure measurement at home or in the physician's office: a randomized controlled trial. *JAMA* 2004; 291:955–964.
- Caccioliati C, Tzourio C, Dufouil C, Alperovitch A, Hanon O. Feasibility of home blood pressure measurement in elderly individuals: cross-sectional analysis of a population-based sample. *Am J Hypertens* 2012; 25:1279–1285.
- Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F, Redon J, Dominiczak A, Narkiewicz K, Nilsson PM, Burnier M, Viigimaa M, Ambrosioni E, Caulfield M, Coca A, Olsen MH, Schmieder RE, Tsoufis C, van de Borne P, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Clement DL, Coca A, Gillebert TC, Tendera M, Rosei EA, Ambrosioni E, Anker SD, Bauersachs J, Hitij JB, Caulfield M, De Buyzere M, De Geest S, Derumeaux GA, Erdine S, Farsang C, Funck-Brentano C, Gerc V, Germano G, Gielen S, Haller H, Hoes AW, Jordan J, Kahan T, Komajda M, Lovic D, Mahrholdt H, Olsen MH, Ostergren J, Parati G, Perk J, Polonia J, Popescu BA, Reiner Z, Rydén L, Sirenko Y, Stanton A, Struijker-Boudier H, Tsoufis C, van de Borne P, Vlachopoulos C, Volpe M, Wood DA. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013; 34:2159–2219.
- Shimamoto K, Ando K, Fujita T, Hasebe N, Higaki J, Horiuchi M, Imai Y, Imaizumi T, Ishimitsu T, Ito M, Ito S, Itoh H, Iwao H, Kai H, Kario K, Kashihara N, Kawano Y, Kim-Mitsuyama S, Kimura G, Kohara K, Komuro I, Kumagai H, Matsuura H, Miura K, Morishita R, Naruse M, Node K, Ohya Y, Rakugi H, Saito I, Saitoh S, Shimada K, Shimosawa T, Suzuki H, Tamura K, Tanahashi N, Tsuchihashi T, Uchiyama M, Ueda S, Umemura S; Japanese Society of Hypertension Committee for Guidelines for the Management of Hypertension. The Japanese society of hypertension guidelines for the Management of Hypertension (JSH 2014). *Hypertens Res* 2014; 37:253–387.
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003; 42:1206–1252.
- Stergiou GS, Baibas NM, Gantzaru AP, Skeva II, Kalkana CB, Roussias LG, Mountokalakis TD. Reproducibility of home, ambulatory, and clinic blood pressure: implications for the design of trials for the assessment of antihypertensive drug efficacy. *Am J Hypertens* 2002; 15:101–104.
- Chatellier G, Day M, Bobrie G, Menard J. Feasibility study of N-of-1 trials with blood pressure self-monitoring in hypertension. *Hypertension* 1995; 25:294–301.
- Stergiou GS, Skeva II, Zourbaki AS, Mountokalakis TD. Self-monitoring of blood pressure at home: how many measurements are needed? *J Hypertens* 1998; 16:725–731.
- Chatellier G, Dutrey-Dupagne C, Vaur L, Zannad F, Genès N, Elkik F, Ménard J. Home self blood pressure measurement in general practice. The SMART study. Self-measurement for the Assessment of the Response to Trandolapril. *Am J Hypertens* 1996; 9:644–652.
- Ohkubo T, Asayama K, Kikuya M, Metoki H, Hoshi H, Hashimoto J, Totsune K, Satoh H, Imai Y; Ohasama Study. How many times should blood pressure be measured at home for better prediction of stroke



- risk? Ten-year follow-up results from the Ohasama study. *J Hypertens* 2004; 22:1099–1104.
19. Niiranen TJ, Johansson JK, Reunanen A, Jula AM. Optimal schedule for home blood pressure measurement based on prognostic data: the Finn-Home study. *Hypertension* 2011; 57:1081–1086.
  20. Parati G, Stergiou GS, Asmar R, Bilo G, de Leeuw P, Imai Y, Kario K, Lurbe E, Manolis A, Mengden T, O'Brien E, Ohkubo T, Padfield P, Palatini P, Pickering T, Redon J, Revera M, Ruilope LM, Shennan A, Staessen JA, Tisler A, Waerber B, Zanchetti A, Mancia G; ESH Working Group on Blood Pressure Monitoring. European Society of Hypertension guidelines for blood pressure monitoring at home: a summary report of the Second International Consensus Conference on Home Blood Pressure Monitoring. *J Hypertens* 2008; 26:1505–1526.
  21. Niiranen TJ, Thijs L, Asayama K, Johansson JK, Ohkubo T, Kikuya M, Boggia J, Hozawa A, Sandoya E, Stergiou GS, Tsuji I, Jula AM, Imai Y, Staessen JA; IDHOCO Investigators. The International Database of HOme blood pressure in relation to Cardiovascular Outcome (IDHOCO): moving from baseline characteristics to research perspectives. *Hypertens Res* 2012; 35:1072–1079.
  22. Niu K, Hozawa A, Awata S, Guo H, Kuriyama S, Seki T, Ohmori-Matsuda K, Nakaya N, Ebihara S, Wang Y, Tsuji I, Nagatomi R. Home blood pressure is associated with depressive symptoms in an elderly population aged 70 years and over: a population-based, cross-sectional analysis. *Hypertens Res* 2008; 31:409–416.
  23. Nakagawa H, Niu K, Hozawa A, Ikeda Y, Kaiho Y, Ohmori-Matsuda K, Nakaya N, Kuriyama S, Ebihara S, Nagatomi R, Tsuji I, Arai Y. Impact of nocturia on bone fracture and mortality in older individuals: a Japanese longitudinal cohort study. *J Urol* 2010; 184:1413–1418.
  24. Schettini C, Bianchi M, Nieto F, Sandoya E, Senra H. Ambulatory blood pressure: normality and comparison with other measurements. Hypertension Working Group. *Hypertension* 1999; 34:818–825.
  25. Stergiou GS, Baibas NM, Kalogeropoulos PG. Cardiovascular risk prediction based on home blood pressure measurement: the Didima study. *J Hypertens* 2007; 25:1590–1596.
  26. Niiranen TJ, Asayama K, Thijs L, Johansson JK, Ohkubo T, Kikuya M, Boggia J, Hozawa A, Sandoya E, Stergiou GS, Tsuji I, Jula AM, Imai Y, Staessen JA; International Database of Home Blood Pressure in Relation to Cardiovascular Outcome Investigators. Outcome-driven thresholds for home blood pressure measurement: International Database of Home Blood Pressure in Relation to Cardiovascular Outcome. *Hypertension* 2013; 61:27–34.
  27. Expert Committee on the Diagnosis Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 2003; 26(Suppl 1):S5–S20.
  28. Dunn G. *Design and Analysis of Reliability Studies: The Statistical Evaluation of Measurement Errors*. Oxford University Press: New York, 1989.
  29. Segà R, Facchetti R, Bombelli M, Cesana G, Corrao G, Grassi G, Mancia G. Prognostic value of ambulatory and home blood pressures compared with office blood pressure in the general population: follow-up results from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study. *Circulation* 2005; 111:1777–1783.
  30. Stergiou GS, Nasothimiou EG, Kalogeropoulos PG, Pantazis N, Baibas NM. The optimal home blood pressure monitoring schedule based on the Didima outcome study. *J Hum Hypertens* 2010; 24:158–164.
  31. Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, Hashimoto J, Totsune K, Hoshi H, Satoh H, Imai Y. Prognosis of “masked” hypertension and “white-coat” hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama study. *J Am Coll Cardiol* 2005; 46:508–515.
  32. Mancia G, Facchetti R, Bombelli M, Grassi G, Segà R. Long-term risk of mortality associated with selective and combined elevation in office, home, and ambulatory blood pressure. *Hypertension* 2006; 47:846–853.
  33. Ugajin T, Hozawa A, Ohkubo T, Asayama K, Kikuya M, Obara T, Metoki H, Hoshi H, Hashimoto J, Totsune K, Satoh H, Tsuji I, Imai Y. White-coat hypertension as a risk factor for the development of home hypertension: the Ohasama study. *Arch Intern Med* 2005; 165:1541–1546.