Optimal Number of Days for Home Blood Pressure Measurement

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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.

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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.[1,2] 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.[3–6] In addition to its diagnostic benefits, home BP measurement is also highly acceptable to the patients and cost-effective.[7–10] Because of these advantages over conventional measurements, international and national guidelines currently recommend home BP monitoring for diagnosing and managing hypertension.[11–13]

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

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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.[18,19] 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[1] 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 ≥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.[12] The European Society of Hypertension Guidelines for Home Blood Pressure Monitoring[20] 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).[21]

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.[21] All participants gave informed written consent.

The IDHOCO[21] 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),[4] Finland (Finn-Home; n = 2,075),[3] Tsurugaya, Japan (n = 836),[22,23] Montevideo, Uruguay (n = 400),[24] and Didima, Greece (n = 665).[25] The Montevideo[24] and Didima[25] 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.[3,4,22,23] 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.[21] Participants measured their BP at home after at least 2 minutes of sitting rest with validated,[21] oscillometric devices in the sitting position. In the Finn-Home study, home BP was measured twice every morning and evening for seven consecutive days.[3] In the Tsurugaya study, home BP was measured once every morning for up to 1 month.[22,23] In the Ohasama study, home BP was measured once every morning and every evening for up to 1 month.[4] 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 ≥140 mm Hg systolic or ≥90 mm Hg diastolic with a home BP <135 mm Hg systolic and <85 mm Hg diastolic.[11–13] We defined masked hypertension as a conventional BP <140 mm Hg systolic and <90 mm Hg diastolic with a home BP ≥135 mm Hg systolic or ≥85 mm Hg diastolic.[11–13] 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 ≥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.[11,13,26]

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,[21,27] 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.[21] 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 (κ) 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 $\kappa \geq 0.9$.[28] We calculated incidence rates in each category, while standardizing by the direct method for sex and age (<40, 40–59, and ≥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.

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 1. Participants characteristics

Characteristic	Ohasama	Finn-Home	Tsurugaya	Total
Number of participants	2,377	1,855	570	4,802
Age, y	60.1 ± 12.0	57.3 ± 8.6	75.1 ± 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^2	23.5 ± 3.1	27.4 ± 4.4	23.9 ± 3.3	25.2 (4.2)
Serum total cholesterol, mmol/l	5.0 ± 0.9	6.1 ± 1.1	5.2 ± 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 ± 18.3	133.1 ± 22.6	143.5 ± 21.8	131.3 ± 21.2
1st day, diastolic home	76.2 ± 12.2	82.4 ± 11.7	78.6 ± 11.9	78.9 ± 12.3
7th day, systolic home	124.5 ± 17.6	127.7 ± 21.1	137.7 ± 22.0	127.3 ± 20.0
7th day, diastolic home	74.6 ± 12.1	79.8 ± 11.1	75.9 ± 11.0	76.7 ± 11.8
Systolic conventional	131.3 ± 18.2	137.2 ± 20.0	144.3 ± 19.5	135.1 ± 19.6
Diastolic conventional	74.5 ± 11.3	83.7 ± 10.5	83.0 ± 10.4	79.0 ± 11.8

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

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. ≥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.

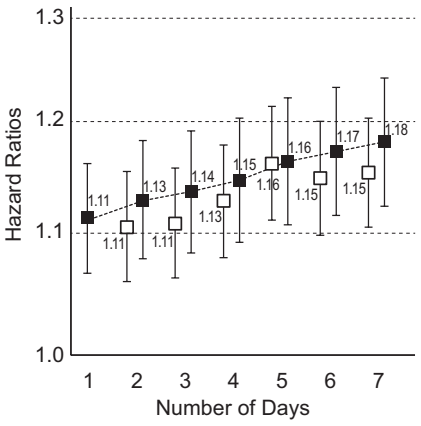

Figure 1. Predictive values of systolic home blood pressures (BPs). Hazard ratios express the increase in cardiovascular event risk per 10-mm Hg elevation of systolic BP on cumulative days (1 to the indicated times; filled square with dotted lines) and on individual days (open square) for cardiovascular 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.*[15] 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.[15] 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.[17] Furthermore, two studies by Stergiou *et al.*[14,16] 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.[3–5,25,29] Single measurements in the morning and evening were performed for up to 28 days in the Japanese Ohasama study,[4] single morning and evening measurements were performed on one day in the Italian Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study,[29] duplicate morning and evening measurements were collected during one week in the Finnish Finn-Home study,[3] duplicate morning and evening measurements during three days were performed in the Greek Didima study,[25] 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.[5]

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.[18,19,29,30] 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.[18,19] Increasing the number of measurements

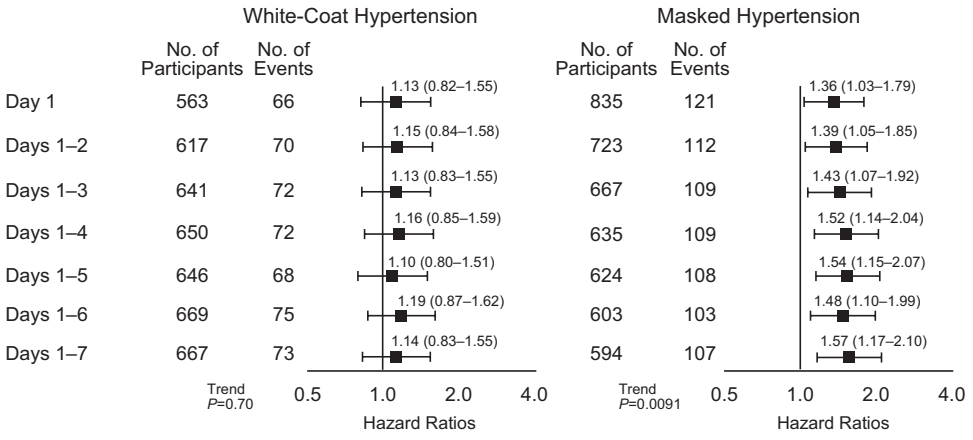

Figure 2. Risk of a cardiovascular endpoint associated with white-coat and masked hypertension vs. normotension. In this analysis, normotension was defined based on two conventional blood pressure (BP) readings and seven days of home BP measurement, which required that the conventional BP and all cumulative 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 ≥140/≥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 ≥135/≥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.[31,32] 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 a eight-year follow-up.[33]

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.oxfordjpurnals.org).

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DISCLOSURE

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Supplementary Information

Niiranen TJ, Asayama K, Thijs L, Johansson JK, Hara A, Hozawa A, Tsuji I, Ohkubo T, Jula AM, Imai Y, Staessen JA, for the IDHOCO investigators.

Number of Self-Measurement Days Required for Diagnosis and Prognostication Based on the Home Blood Pressure — an Outcome Driven Proposal
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This supplementary material has been provided by the authors to give readers additional information about their work.

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Table S1. Hazard Ratios for Cardiovascular Events with an Increasing Number of Home Measurement Days.

No. of Days	Systolic Pressure		Diastolic Pressure	
	Cumulative	Individual	Cumulative	Individual
Day 1	1.11 (1.07–1.16)‡	1.11 (1.07–1.16)‡	1.06 (1.02–1.09)*	1.06 (1.02–1.09)*
Days 1–2	1.13 (1.08–1.18)‡	1.11 (1.06–1.15)‡	1.08 (1.03–1.12)†	1.07 (1.03–1.11)†
Days 1–3	1.14 (1.08–1.19)‡	1.11 (1.06–1.16)‡	1.08 (1.04–1.12)†	1.06 (1.02–1.09)*
Days 1–4	1.15 (1.09–1.20)‡	1.13 (1.08–1.18)‡	1.08 (1.04–1.13)†	1.06 (1.02–1.10)*
Days 1–5	1.16 (1.11–1.22)‡	1.16 (1.11–1.21)‡	1.10 (1.05–1.14)‡	1.11 (1.07–1.15)‡
Days 1–6	1.17 (1.12–1.23)‡	1.15 (1.10–1.20)‡	1.10 (1.05–1.15)‡	1.08 (1.04–1.12)‡
Days 1–7	1.18 (1.12–1.24)‡	1.15 (1.11–1.20)‡	1.10 (1.06–1.15)‡	1.08 (1.04–1.12)‡
Trend *P*	<0.0001	0.012	0.0003	0.17

Hazard ratios (95% confidence intervals) reflect the risk associated with 10-mm Hg increase in systolic and 5-mm Hg increase in diastolic blood pressure. Hazard ratios were adjusted for sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, serum total cholesterol, and cohort. Significance of the hazard ratios: * $P<0.01$; † $P<0.001$; and ‡ $P<0.0001$.

Table S2. Hazard Ratios for Cardiovascular Events with an Increasing Number of Home Measurement Days When All Measurements Performed in All Cohorts Were Included in the Analyses

No. of Days	Systolic Pressure		Diastolic Pressure	
	Cumulative	Individual	Cumulative	Individual
Day 1	1.15 (1.09–1.20)†	1.15 (1.09–1.20)†	1.08 (1.04–1.12)*	1.08 (1.04–1.12)*
Days 1–2	1.17 (1.11–1.23)†	1.15 (1.09–1.20)†	1.10 (1.05–1.15)†	1.09 (1.05–1.14)†
Days 1–3	1.18 (1.12–1.24)†	1.16 (1.10–1.21)†	1.11 (1.06–1.16)†	1.10 (1.05–1.14)†
Days 1–4	1.19 (1.13–1.25)†	1.18 (1.12–1.24)†	1.12 (1.07–1.17)†	1.09 (1.05–1.14)†
Days 1–5	1.21 (1.15–1.27)†	1.21 (1.15–1.27)†	1.13 (1.08–1.18)†	1.14 (1.09–1.19)†
Days 1–6	1.22 (1.16–1.28)†	1.20 (1.15–1.26)†	1.13 (1.08–1.19)†	1.12 (1.07–1.16)†
Days 1–7	1.23 (1.16–1.29)†	1.20 (1.14–1.26)†	1.14 (1.09–1.19)†	1.11 (1.06–1.15)†
Trend *P*	<0.0001	0.005	0.0002	0.078

The maximum number of measurements per day per cohort was 1 for Tsurugaya, 2 for Ohasama, and 4 for Finn-Home. Hazard ratios (95% confidence intervals) reflect the risk associated with 10-mm Hg increase in systolic and 5-mm Hg increase in diastolic blood pressure. Hazard ratios were adjusted for sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, serum total cholesterol, and cohort. Significance of the hazard ratios: * $P<0.001$; and † $P<0.0001$.

Table S3. Hazard Ratios for Cerebrovascular Events and Cardiovascular Mortality with a Cumulatively Increasing Number of Measurement Days

No. of Days	Cerebrovascular Events (*n*=337)		Cardiovascular Mortality (*n*=221)	
	Systolic	Diastolic	Systolic	Diastolic
Day 1	1.16 (1.10–1.23)§	1.09 (1.04–1.14)‡	1.10 (1.03–1.18)†	1.03 (0.98–1.09)
Days 1–2	1.18 (1.11–1.26)§	1.10 (1.05–1.16)‡	1.10 (1.02–1.18)*	1.06 (1.00–1.13)
Days 1–3	1.20 (1.12–1.28)§	1.11 (1.06–1.17)§	1.10 (1.02–1.19)*	1.06 (0.99–1.13)
Days 1–4	1.22 (1.14–1.30)§	1.12 (1.06–1.18)§	1.12 (1.03–1.21)†	1.05 (0.98–1.12)
Days 1–5	1.23 (1.15–1.31)§	1.13 (1.07–1.19)§	1.12 (1.04–1.22)†	1.05 (0.98–1.12)
Days 1–6	1.24 (1.16–1.32)§	1.13 (1.07–1.20)§	1.13 (1.04–1.22)†	1.03 (0.97–1.11)
Days 1–7	1.25 (1.16–1.33)§	1.14 (1.08–1.20)§	1.14 (1.05–1.24)†	1.03 (0.97–1.11)

Hazard ratios (95% confidence intervals) reflect the risk associated with 10-mm Hg increase in systolic and 5-mm Hg increase in diastolic blood pressure. Hazard ratios were adjusted for sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, serum total cholesterol, and cohort. Significance of the hazard ratios: * $P<0.05$; † $P<0.01$; ‡ $P<0.001$; and § $P<0.0001$.

Table S4. Sensitivity Analysis for Cardiovascular Events by Antihypertensive Treatment Status

No. of Days	Untreated (E/R=329/3665)		Treated (E/R=239/1137)		Interaction *P*	
	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
Day 1	1.14 (1.08–1.21)§	1.05 (1.01–1.10)*	1.07 (1.01–1.15)*	1.06 (1.00–1.12)*	0.033	0.56
Days 1–2	1.17 (1.10–1.24)§	1.08 (1.03–1.14)†	1.08 (1.00–1.16)	1.06 (1.00–1.13)*	0.015	0.23
Days 1–3	1.17 (1.10–1.24)§	1.09 (1.03–1.14)†	1.09 (1.01–1.17)*	1.07 (1.00–1.14)*	0.023	0.27
Days 1–4	1.17 (1.10–1.25)§	1.09 (1.03–1.15)†	1.11 (1.03–1.20)†	1.07 (1.01–1.15)*	0.049	0.31
Days 1–5	1.19 (1.12–1.27)§	1.10 (1.04–1.16)‡	1.12 (1.04–1.22)†	1.09 (1.02–1.16)*	0.049	0.30
Days 1–6	1.20 (1.12–1.28)§	1.11 (1.05–1.17)‡	1.14 (1.05–1.23)†	1.09 (1.02–1.16)*	0.063	0.24
Days 1–7	1.21 (1.13–1.29)§	1.12 (1.05–1.18)‡	1.15 (1.06–1.24)‡	1.09 (1.02–1.17)*	0.076	0.21

E/R indicates the number of cardiovascular events/participants at risk. Hazard ratios (95% confidence intervals) reflect the risk associated with 10-mm Hg increase in systolic and 5-mm Hg increase in diastolic blood pressure. Hazard ratios were adjusted for sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, serum total cholesterol, and cohort. Significance of the hazard ratios: * $P<0.05$; † $P<0.01$; ‡ $P<0.001$; and § $P<0.0001$.

Table S5. Sensitivity Analysis for Cardiovascular Events by Sex

No. of Days	Women (E/R=246/2759)		Men (E/R=322/2043)		Interaction *P*	
	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
Day 1	1.10 (1.03–1.17)†	1.06 (1.00–1.12)*	1.12 (1.06–1.18)‡	1.05 (1.00–1.10)*	0.97	0.75
Days 1–2	1.11 (1.03–1.19)†	1.09 (1.03–1.16)†	1.14 (1.07–1.21)§	1.07 (1.01–1.12)*	0.95	0.83
Days 1–3	1.10 (1.02–1.19)*	1.09 (1.02–1.16)†	1.16 (1.09–1.23)§	1.07 (1.02–1.13)*	0.73	0.72
Days 1–4	1.12 (1.04–1.21)†	1.09 (1.03–1.17)†	1.16 (1.09–1.24)§	1.07 (1.02–1.14)*	0.96	0.84
Days 1–5	1.13 (1.04–1.22)†	1.11 (1.04–1.18)†	1.19 (1.11–1.27)§	1.09 (1.03–1.15)†	0.79	0.84
Days 1–6	1.14 (1.05–1.23)†	1.11 (1.04–1.19)†	1.20 (1.12–1.28)§	1.09 (1.03–1.15)†	0.79	0.93
Days 1–7	1.15 (1.06–1.24)‡	1.12 (1.05–1.20)‡	1.20 (1.12–1.28)§	1.09 (1.03–1.16)†	0.86	0.95

E/R indicates the number of cardiovascular events/participants at risk. Hazard ratios (95% confidence intervals) reflect the risk associated with 10-mm Hg increase in systolic and 5-mm Hg increase in diastolic blood pressure. Hazard ratios were adjusted for age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, serum total cholesterol, and cohort. Significance of the hazard ratios: * $P<0.05$; † $P<0.01$; ‡ $P<0.001$; and § $P<0.0001$.

Table S6. Sensitivity Analysis for Cardiovascular Events by Age Group

No. of Days	<60 years (E/R=133/2307)		≥60 years (E/R=435/2495)		Interaction *P*	
	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
Day 1	1.14 (1.03–1.25)*	1.06 (0.98–1.14)	1.10 (1.05–1.16)§	1.05 (1.01–1.09)*	0.19	0.19
Days 1–2	1.18 (1.06–1.31)†	1.07 (0.98–1.16)	1.11 (1.06–1.17)§	1.08 (1.03–1.12)†	0.10	0.30
Days 1–3	1.20 (1.07–1.33)†	1.07 (0.98–1.17)	1.12 (1.06–1.18)§	1.08 (1.03–1.13)†	0.073	0.29
Days 1–4	1.20 (1.07–1.34)†	1.08 (0.99–1.18)	1.13 (1.07–1.19)§	1.08 (1.03–1.13)†	0.11	0.22
Days 1–5	1.23 (1.09–1.37)‡	1.10 (1.00–1.20)*	1.15 (1.08–1.21)§	1.09 (1.04–1.15)‡	0.078	0.19
Days 1–6	1.24 (1.11–1.40)‡	1.11 (1.02–1.22)*	1.15 (1.09–1.22)§	1.10 (1.04–1.15)‡	0.060	0.14
Days 1–7	1.25 (1.12–1.41)‡	1.12 (1.02–1.23)*	1.16 (1.10–1.23)§	1.10 (1.05–1.15)‡	0.057	0.13

E/R indicates the number of cardiovascular events/participants at risk. Hazard ratios (95% confidence intervals) reflect the risk associated with 10-mm Hg increase in systolic and 5-mm Hg increase in diastolic blood pressure. Hazard ratios were adjusted for sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, serum total cholesterol, and cohort. Significance of the hazard ratios: * $P<0.05$; † $P<0.01$; ‡ $P<0.001$; and § $P<0.0001$.

Table S7. Sensitivity Analysis in Systolic Blood Pressure for Cardiovascular Events with One Cohort Excluded

No. of Days	Ohasama Excluded (E/R=227/2425)		Finn-Home Excluded (E/R=390/2947)		Tsurugaya Excluded (E/R=519/4232)	
	Cumulative	Individual	Cumulative	Individual	Cumulative	Individual
Day 1	1.09 (1.02–1.15)*	1.09 (1.02–1.15)*	1.13 (1.07–1.19)‡	1.13 (1.07–1.19)‡	1.12 (1.07–1.17)‡	1.12 (1.07–1.17)‡
Days 1–2	1.12 (1.05–1.19)†	1.12 (1.05–1.19)†	1.13 (1.06–1.20)‡	1.09 (1.03–1.16)*	1.14 (1.08–1.19)‡	1.11 (1.06–1.16)‡
Days 1–3	1.12 (1.05–1.20)*	1.09 (1.02–1.16)*	1.14 (1.08–1.22)‡	1.12 (1.06–1.18)‡	1.15 (1.09–1.20)‡	1.11 (1.06–1.17)‡
Days 1–4	1.13 (1.05–1.21)†	1.12 (1.05–1.19)†	1.16 (1.09–1.23)‡	1.14 (1.08–1.21)‡	1.15 (1.10–1.21)‡	1.13 (1.08–1.18)‡
Days 1–5	1.15 (1.07–1.23)†	1.17 (1.10–1.25)‡	1.17 (1.10–1.25)‡	1.15 (1.08–1.21)‡	1.17 (1.11–1.24)‡	1.17 (1.12–1.23)‡
Days 1–6	1.16 (1.08–1.25)‡	1.15 (1.08–1.23)‡	1.18 (1.10–1.26)‡	1.14 (1.08–1.21)‡	1.18 (1.12–1.25)‡	1.15 (1.10–1.21)‡
Days 1–7	1.17 (1.09–1.25)‡	1.15 (1.08–1.22)‡	1.19 (1.11–1.27)‡	1.15 (1.09–1.22)‡	1.19 (1.13–1.26)‡	1.16 (1.11–1.22)‡

E/R indicates the number of cardiovascular events/participants at risk. Hazard ratios (95% confidence intervals) reflect the risk associated with 10-mm Hg increase in systolic blood pressure. Hazard ratios were adjusted for sex, age, body mass index, smoking, history of cardiovascular disease, diabetes mellitus, treatment with antihypertensive drugs, serum total cholesterol, and cohort. Significance of the hazard ratios: * $P<0.01$; † $P<0.001$; and ‡ $P<0.0001$.

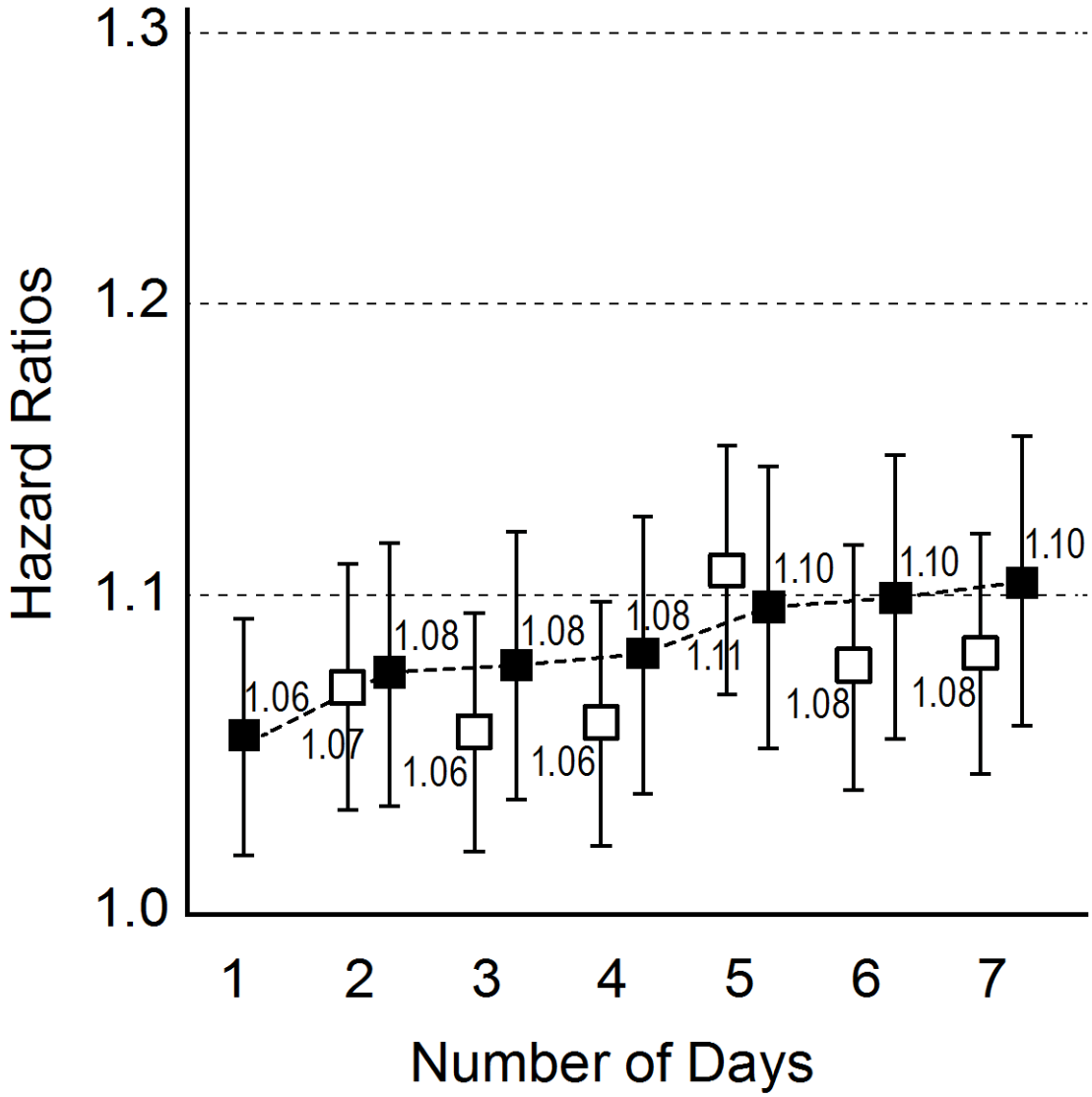

Figure S1. Predictive values of diastolic home blood pressures. Hazard ratios express the increase in cardiovascular event risk per 5 mm Hg elevation of diastolic blood pressure on cumulative days (1 to the indicated times; filled square with dotted lines) and on individual days (open square) for cardiovascular events plotted on a log scale. Vertical lines represent 95% confidence intervals.

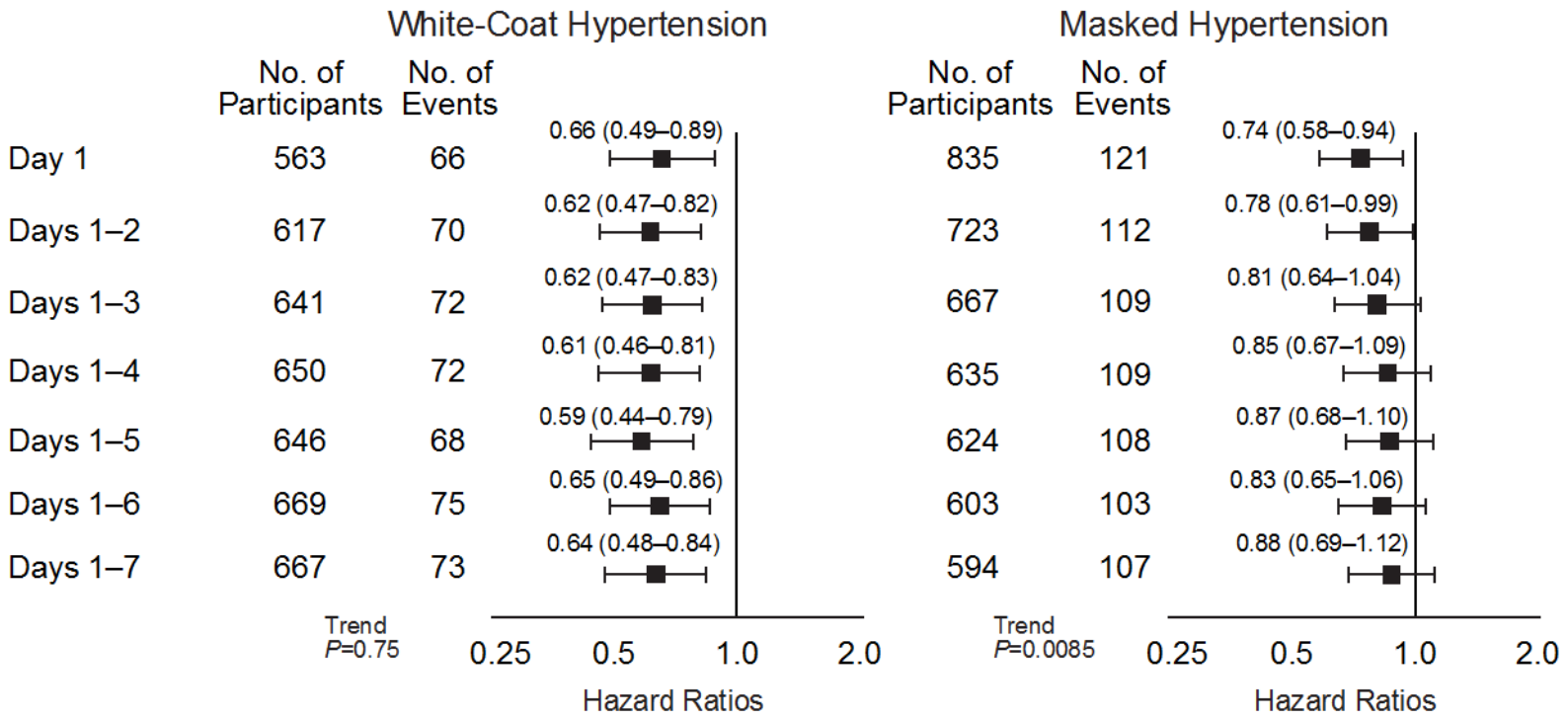

Figure S2. Risk of a cardiovascular endpoint associated with white-coat and masked hypertension *vs.* hypertension. In this analysis, hypertension was defined based on two conventional blood pressure readings and seven days of home blood pressure measurement, which required that the conventional blood pressure and all cumulative means of 1 to 7 home measurement days were elevated. Hazard ratios express the risk compared to hypertension 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 blood pressure ≥140/≥90 mm Hg and a home blood pressure <135/<85 mm Hg. Masked hypertension was a conventional blood pressure <140/<90 mm Hg and a home blood pressure ≥135/≥85 mm Hg.

Appendix 1. IDHOCO investigators.

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