Home Blood Pressure as Predictor of Adverse Health Outcomes

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4.1 Introduction

In the 1970s, home blood pressure measurement made its entry in clinical research [1, 2]. In the late 1980s, automated cuff-oscillometric home blood pressure monitors entered the market. Subsequently, studies highlighting the prognostic accuracy of the self-measured home blood pressure in populations and patients have paved the way for the widespread clinical application of this approach. The Lancet Commission on hypertension proposed better assessment of blood pressure as one of the key measures to be implemented to stop what has been named *the largest epidemic ever known to mankind* [3]. In this chapter, we review the prognostic studies regarding self-measured home blood pressure (Table 4.1), and clarify that self-measurement of the blood pressure at home is required to achieve the goal [3]. For the sake of comparability, we converted reported hazard ratios to express relative risk associated with a 10/5-mm Hg increment in systolic/diastolic blood pressure, when blood pressure was analysed on a continuous scale.

4.2 General Population

The Ohasama study (Hanamaki, Japan), initiated in 1986, is the first population study focusing on the prognostic accuracy of the self-measured home blood pressure. As reported in 1998, in Cox proportional hazard models including both the conventional office blood pressure and home blood pressure, the mean of multiple home systolic pressure measurements predicted cardiovascular mortality over and beyond the conventional systolic pressure (hazard ratio, 1.22; 95% confidence interval [CI], 1.00–1.48) [4]. While in the Ohasama cohort the incidence of stroke was closer associated with a single morning or evening home blood pressure on the first

Table 4.1 Characteristics of studies investigating cardiovascular outcome based on self-measured home blood pressure

Study type	Study name	Publication Year (ref)	Country	Sample size	Follow-up (years)
General population	Ohasama	1998 [4]	Japan	1789	6.6
	PAMELA	2005[14]	Italy	2051	10.9
	Didima	2007[11]	Greece	662	8.2
	Finn-Home	2010[13]	Finland	2081	6.8
Patient study	SHEAF	2004 [15]	France	4939	3.0
	HOMED-BP	2012 [16]	Japan	3518	5.3
	HONEST	2014 [18]	Japan	21,591	2.0
	J-HOP	2016 [19]	Japan	4278	4.0
Meta-Analysis	IDHOCO	2013 [21]	Multiple	6470	8.3

Publication year represents the first peer-reviewed publication. *PAMELA* the Pressioni Arteriose Monitorate e Loro Associazioni, *SHEAF* Self-Measurement of Blood Pressure at Home in the Elderly: Assessment and Follow-up, *HOMED-BP* Hypertension Objective Treatment Based on Measurement by Electrical Devices of Blood Pressures, *HONEST* Olmesartan Naive patients to Establish Standard Target blood pressure, *J-HOP* the Japan Morning Surge-Home Blood Pressure, *IDHOCO* the International Database of HOme blood pressure in relation to Cardiovascular Outcome monitoring day than the conventional blood pressure, the predictive accuracy of the home blood pressure increased with the number of monitoring days up to 2 weeks [5, 6]. The Ohasama investigators also reported the incidence of stroke according to the level of the office and home blood pressures after stratification for cardiovascular risk based on the criteria proposed by contemporary European and American guidelines [7, 8]. The key points emerging from these analyses (Fig. 4.1) were that

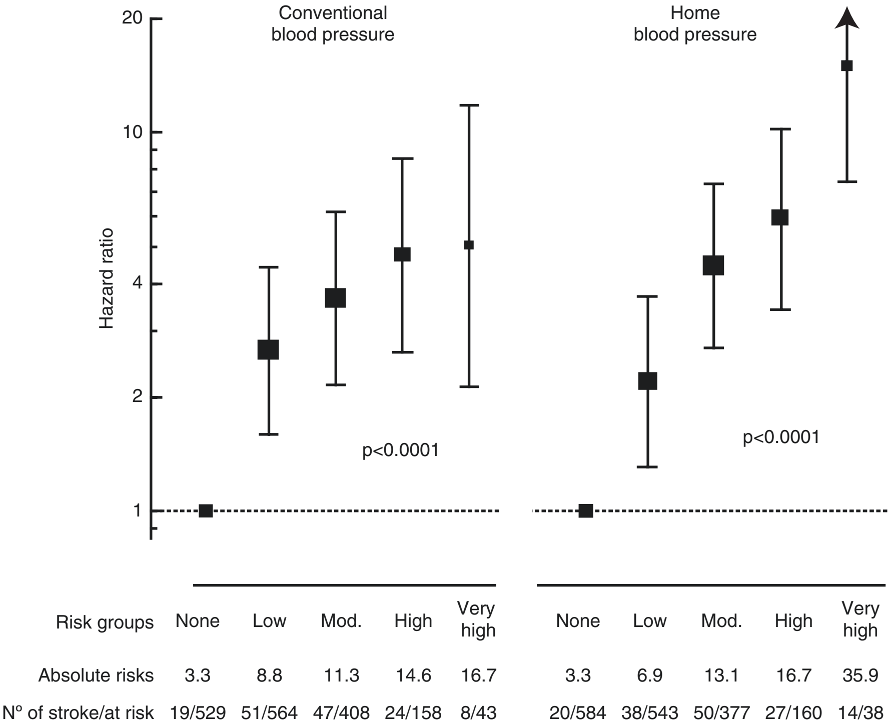

Fig. 4.1 Risk of stroke according to the multiple risk factor classification proposed by the 2003 European hypertension guideline. Risk factors include either the conventional or the self-measured blood pressure at home. The participants were first classified into one of six blood pressure categories as optimal (home, 115/75 mmHg; conventional, 120/80 mmHg), normal (home, 115/75–124/79 mmHg; conventional, 120/80–129/84 mmHg), high normal (home, 125/80–134/84 mmHg; conventional, 130/85–139/89 mmHg), grade 1 (home, 135/85–149/94 mmHg; conventional, 140/90–159/99 mmHg), grade 2 (home, 150/95–164/104 mmHg; conventional, 160/100–179/109 mmHg), or grade 3 hypertension (home, ≥165/105; conventional, ≥180/110 mmHg) based on the rate of participants from each level of home and conventional blood pressure classification. Based on the combination of the six blood pressure categories and the extent of cardiovascular risks—no risk factors, one or two risk factors, ≥2 risk factors or diabetes mellitus, or past history of cardiovascular disease—, they were finally assigned to one of five risk groups according to the 2003 European guidelines criteria, from none (reference group) to very high risk groups. Participants classified according to conventional and home blood pressure were analysed separately. The absolute risk is expressed in stroke events per 1000 person-years. Squares and vertical lines indicate the point estimate and 95% confidence interval of the hazard ratio in each subgroup, the size of the square being proportional to the number of events. p values are for trend across risk subgroups. Reproduced with permission from Asayama et al. [7]

even in patients with low added risk both the office and self-measured blood pressures predicted stroke, and that across the strata of cardiovascular risk the probability of a first stroke rose steeper with the home than with the conventional blood pressure [7]. Among treated patients with hypertension enrolled in the Ohasama population study, the risk of stroke remained associated with the home blood pressure, but not with the conventional blood pressure [9]. Another analysis of Ohasama data demonstrated that morning and evening blood pressure were equally predictive of stroke in all participants, but that morning compared with evening blood pressure was a better predictor in treated than untreated hypertensive patients, perhaps as a consequence of the dosing of antihypertensive drugs in the morning after measurement of the morning blood pressure [10].

The Didima study (Greece), initiated in 1997, involved 662 of its residents (58.2% women; mean age at enrolment, 54.1 years) [11]. Over 8.2 years of follow-up, 78 deaths, 42 of cardiovascular causes, and 67 fatal and non-fatal cardiovascular events occurred. The unadjusted hazard ratios for cardiovascular events were 1.41 ($p < 0.001$) and 1.40 ($p < 0.001$) for conventional office systolic and home systolic pressure, respectively; the corresponding estimates for diastolic pressure were 1.20 ($p < 0.01$) and 1.11 ($p = 0.07$). In contrast to the Ohasama findings [4], addition of the home blood pressure (average of duplicate readings in the morning and evening on three consecutive days) to Cox models already including the office blood pressure (average of six readings; three readings at each of two clinic visits) did not significantly improve the prediction of cardiovascular complications [11]. Confirmatory findings when the Didima participants were further followed-up for totalled 19.0 years, with 216 deaths (127 cardiovascular causes) and 174 cardiovascular events occurred, were later reported [12].

The Finn-Home study included 2081 individuals aged 45 to 74 years, representative for the whole of Finland [13]. After 6.8 years of follow-up, 162 participants had experienced a cardiovascular event. In multivariable-adjusted analyses, the systolic/diastolic hazard ratios were 1.13/1.13 (CI, 1.05–1.22/1.05–1.22) for conventional office blood pressure and 1.23/1.18 (CI, 1.13–1.34/1.10–1.27) for home blood pressure. However, when both types of blood pressure estimates were simultaneously entered in the models, only the hazard ratios for home blood pressure (1.22/1.15; 1.09–1.37/1.05–1.26), not office blood pressure (1.01/1.06; CI, 0.92–1.12/0.97–1.16), retained significance.

High prognostic ability of 1-day home blood pressure measurements for cardiovascular mortality was reported from the Pressioni Arteriose Monitorate e Loro Associazioni (PAMELA) study [14]. Among 2051 Italian participants, 56 of 186 observed deaths during 11.9 years of follow-up were cardiovascular. Risk of cardiovascular death increased more with a given increase in home than in conventional blood pressure, and a significant improvement of the prediction model was obtained by adding home blood pressure to the initial model with conventional blood pressure (Goodness of Fit, 15.039; $p < 0.001$) [14].

4.3 Patient Studies

The "Self-Measurement of Blood Pressure at Home in the Elderly: Assessment and Follow-up" (SHEAF) study involved a 3-year follow-up of 4939 patients with antihypertensive drug treatment in general practice (women, 51.1%; mean age, 70.0 years), who experienced 324 cardiovascular endpoints [15]. The systolic/diastolic multivariable-adjusted hazard ratios for home blood pressure were 1.17/1.12 (CI, 1.11–1.24/1.06–1.18), whereas the corresponding associations with the office blood pressure were not significant ($p \geq 0.09$). In a multivariable model with patients having controlled hypertension as the reference, the hazard ratios were 2.06 (CI, 1.22–3.47) in patients with normal office blood pressure (threshold 140/90 mmHg) and elevated home blood pressure (threshold 135/85 mm Hg), 1.18 (CI, 0.67–2.10) in patients with elevated office, but normal home blood pressure, and 1.96 (CI, 1.27–3.02) in patients with elevated blood pressure on both types of measurement.

The multicentre Hypertension Objective Treatment Based on Measurement by Electrical Devices of Blood Pressure (HOMED-BP) included 3518 patients (women, 50%; mean age, 59.6 years) [16]. Over 5.3 years of follow-up, the major adverse cardiovascular event consisting of cardiovascular death, stroke and myocardial infarction occurred in 51 participants. In fully adjusted models, the hazard ratios associated with systolic home blood pressure before the initiation of antihypertensive drug treatment and on treatment were 1.32 (CI, 1.05–1.66) and 1.34 (CI, 1.11–1.61), respectively [16]. There was a log-linear increase of the risk across thirds of the distributions of the untreated home systolic pressure at baseline and the achieved home systolic pressure during follow-up (Fig. 4.2) [17]. Across thirds of the baseline systolic pressure before treatment, levels averaged 138.2, 150.4 and 166.1 mmHg; the corresponding mean levels on treatment were 116.8, 128.2 and 144.4 mmHg. These observations highlight the potential of monitoring blood pressure at home before and after initiation of antihypertensive drug treatment as well as the importance of strict blood pressure control.

The Olmesartan Naive patients to Establish Standard Target blood pressure (HONEST) study [18] was a surveillance of 21,591 patients (women, 50.6%; mean age, 64.9 years) receiving the angiotensin receptor blocker olmesartan on top of other antihypertensive drugs. After 2 years of follow-up, 280 cardiovascular events had occurred. Patients with morning home systolic blood pressure 145 mmHg or higher had a significantly higher risk (hazard ratio, 2.47; CI, 1.20–5.08) than patients with morning home systolic blood pressure of less than 125 mmHg. The Japan Morning Surge-Home Blood Pressure (J-HOP) study confirmed the prognostic accuracy of the morning blood pressure [19]. This multicentre study involved 4278 patients with a history of and/or risk factors for cardiovascular disease (women, 65.6%; mean age 64.9 years). Over a mean follow-up of 4.0 years, stroke or coronary artery disease had occurred in 74 and 77 patients, respectively. The morning systolic pressure improved the discrimination of incident stroke (C statistics, 0.802; CI, 0.692–0.911) beyond traditional risk factors, including office systolic pressure (C statistics, 0.756; CI, 0.646–0.866); this was not the case for prediction of coronary artery disease. In the same J-HOP population [19], masked hypertension

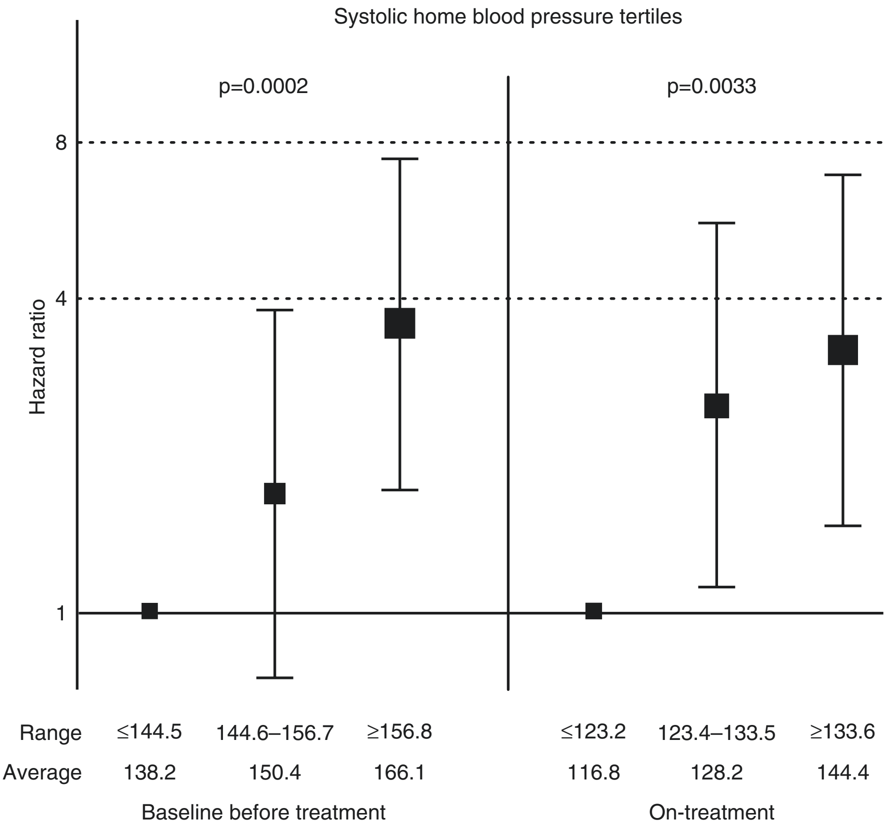

Fig. 4.2 Hazard ratios for major adverse cardiovascular events across thirds of the pretreatment (left) and on-treatment (right) home systolic pressure. Squares representing the hazard ratios are sized proportionally to the number of cardiovascular endpoints. Vertical bars indicate 95% confidence intervals for comparison with the lowest third. For each plotted point, the range and average of the home systolic pressure are given (mm Hg). p values express the significance of the log-linear trend. The analyses accounted for sex, age, body mass index, hypercholesterolaemia, smoking and drinking, diabetes mellitus and history of cardiovascular disease. Models including the pretreatment blood pressure were adjusted for the on-treatment blood pressure and vice versa. Reproduced with permission from Asayama et al. [17]

diagnosed based on the 14-day averaged morning and evening home blood pressures was associated with higher stroke risk (hazard ratio for masked hypertension vs. normotension on office and home measurement, 2.77; CI, 1.20–6.37) [20].

4.4 The IDHOCO Participant-Level Meta-Analysis

The International Database of HOme blood pressure in relation to Cardiovascular Outcome (IDHOCO) is a collaborating research project involving seven population studies (in 2018) where participants had measured their home blood pressure and follow-up data with fatal and non-fatal outcomes were fully supplied [21]. Based on the 6470 participants (women, 56.9%; mean age, 59.3 years), we determined home blood pressure thresholds, which yielded 10-year cardiovascular risks similar to those associated with stages 1 (120/80 mmHg) and 2 (130/85 mmHg) prehypertension, and stages 1 (140/90 mmHg) and 2 (160/100 mmHg) hypertension on conventional office measurement [21]. During a median of 8.3 years of follow-up, 716 cardiovascular endpoints occurred. The rounded outcome-driven systolic/diastolic thresholds for the home blood pressure corresponding with stages 1 and 2 prehypertension and stages 1 and 2 hypertension amounted to 120/75, 125/80, 130/85, and 145/90 mmHg, respectively. Population-based outcome-driven thresholds for home blood pressure are slightly lower than those provided in contemporary hypertension guidelines [22, 23].

The continuous nature of the relation with blood pressure not only holds true in hypertensive patients, but in normotensive people as well. Among 5008 untreated participants in the IDHOCO database (women, 56.6%; mean age, 57.1 years) [24], using 135/85 mm Hg as a threshold for the home blood pressure, the number with masked hypertension amounted to 42 (3.1%), 131 (12.9%), and 233 (22.5%) among participants with optimal (<120/<80 mmHg), normal (120–129/80–80 mmHg), and high-normal (130–139/85–89 mmHg) conventional blood pressure. Across these three categories of patients with masked hypertension (Fig. 4.3), using optimal conventional blood pressure without masked hypertension as reference, the

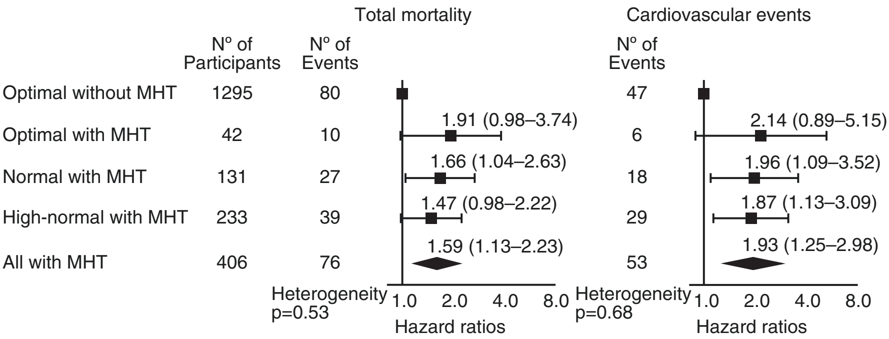

Fig. 4.3 Hazard ratios associated with masked hypertension (MHT; ≥135/85 mm Hg) on home blood pressure monitoring in participants with optimal, normal, or high-normal office blood pressure. Participants with optimal blood pressure without elevated home blood pressure was the reference group. Systolic/diastolic thresholds for the conventional blood pressure were optimal (<120/80 mm Hg), normal (120–129/80–84 mm Hg), and high-normal (130–139/85–89 mm Hg). When a systolic or diastolic blood pressure was in a different category, the participant was assigned to the higher category. Systolic/diastolic thresholds for hypertension on home measurement were ≥ 135/85 mm Hg. The hazard ratios were adjusted for cohort, sex, age, body mass index, smoking, total cholesterol, diabetes mellitus, and history of cardiovascular disease. Horizontal lines denote the 95% confidence interval. The diamond represents the pooled estimate in all patients with MHT. The p value for heterogeneity was derived by testing an ordinal variable in Cox proportional hazard regression coding for the 3 subgroups among patients with MHT. Reproduced with permission from Asayama et al. [24]

multivariable-adjusted hazard ratios for a composite cardiovascular endpoint were 2.14 (CI, 0.89–5.15), 1.96 (CI, 1.09–3.52), and 1.87 (CI, 1.13–3.09), respectively. Thus, home blood pressure refines risk stratification in apparently healthy people with a normal or high-normal office blood pressure, and is therefore an essential information to diagnose hypertension and to initiate or adjust antihypertensive drug treatment.

The IDHOCO database of diverse populations enables us to provide robust subgroup analysis beyond each cohort. Multivariable-adjusted analysis with a bootstrap procedure to determine home blood pressure levels yielding 10-year cardiovascular risks similar to those associated with established systolic/diastolic thresholds for the conventional blood pressure supported that single blood pressure thresholds can be indiscriminately applied in both sexes and across the age range up to 80 years of age [25]. A systolic home blood pressure of 152 mmHg or more and a diastolic home blood pressure of less than 65 mmHg entailed increased cardiovascular risk, whereas a diastolic home blood pressure above 82 mmHg minimized risk among untreated octogenarians [26]. In treated octogenarians in which overtreatment is certainly an issue, total mortality was curvilinearly associated with systolic home blood pressure, i.e., levels below 127 mmHg were associated with increased total mortality with 149 mmHg being associated with lowest risk of death.

4.5 Variability in the Home Blood Pressure

The HOMED-BP extended dataset (median of 7.4 years follow-up) allowed studying the association between a composite cardiovascular endpoint and seasonal variability in the home blood pressure [27]. The study investigators defined seasonal variability as an average of all increases in home blood pressure from summer to winter combined with all decreases in home blood pressure from winter to summer throughout the follow-up period. Compared with the small-to-middle seasonal variability in the home blood pressure (0–9.1/0–4.5 mm Hg), composite cardiovascular outcome was worse in the large variability group (≥9.1/≥4.5 mm Hg; hazard ratio, 2.02/1.95; CI, 1.03–3.97/1.00–3.79) as well as in the inverse variability group (<0/<0 mm Hg; hazard ratio, 3.07/2.81; CI, 1.44–6.54/1.41–5.61) variability group (Fig. 4.4) [27].

Day-to-day (day-by-day) home blood pressure variability in relation to cardiovascular complications is described in Chap. 15 "Home BP Variability". Meanwhile, the day-to-day home blood pressure variability is considered to be a risk factor for the development of cognitive decline [28] and dementia [29]. After a median 7.8 years of follow-up of the 485 Ohasama participants (women, 71.8%; mean age, 63.3 years), home systolic pressure at baseline was significantly associated with cognitive decline (n = 46; odds ratio, 1.31; CI, 1.03–1.65) [28]. However, the conventional systolic pressure was not (odds ratio, 1.12; CI, 0.95–1.32) [28]. Furthermore, cognitive decline was positively associated with the day-to-day standard deviation of home systolic pressure in models including the home systolic

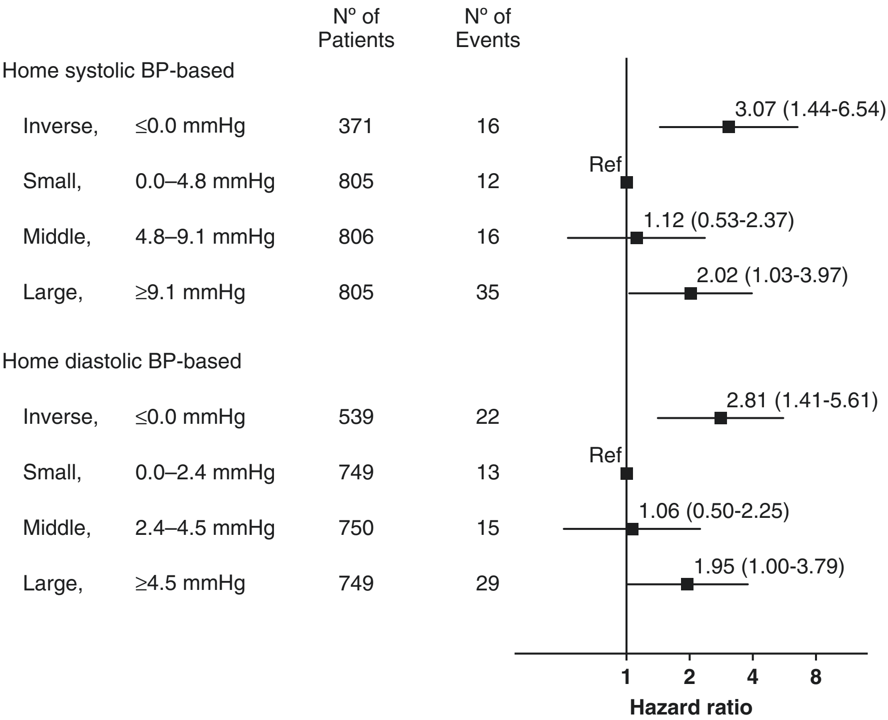

Fig. 4.4 Hazard ratios associated with seasonal home blood pressure (BP) variability for a composite cardiovascular outcome.The seasonal variability in an individual was defined as an average of observed seasonal changes in home blood pressure, i.e., all increases in home blood pressure from summer (July–August) to winter (January–February) combined with all decreases from winter to summer throughout the follow-up period. Hazard ratios for comparison with the reference group were given with 95% confidence interval with adjustments applied for sex, age, the pretreatment and on-treatment home blood pressure, body mass index, smoking and drinking, hypercholesterolaemia, diabetes mellitus and history of cardiovascular disease. Reproduced with permission from Hanazawa et al. [27]

pressure level (odds ratio per 2.6 mmHg increase of SD, 1.51; CI, 1.07–2.12) [28]. The Hisayama study involved a population-based cohort recruited in Fukuoka, Japan [29]. Over a follow-up of 5.3 years, 194 of 1674 participants all aged 60 years or more (women, 55.9%) developed vascular or neurodegenerative dementia. Compared with participants in the bottom fourth of the distribution of the coefficient of variation, the risks of dementia was significantly higher in those in top fourth (multivariable-adjusted hazard ratio, 2.27; CI, 1.45–3.55), thereby confirming the Ohasama results [28].

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