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Factors associated with intra-individual visit-to-visit variability of blood pressure in four countries: the INTERMAP study

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Abstract

Several studies demonstrated that visit-to-visit variability of blood pressure (BP) predicted future events of total death, stroke and cardiovascular disease. Little is known about factors associated with visit-to-visit BP variability in different countries. We recruited participants aged 40–59 years from four countries (Japan, the People's Republic of China [PRC], the United Kingdom [UK] and the United States [US]). At each study visit, BP was measured twice by trained observers using random zero sphygmomanometers after five minutes resting. We defined visit-to-visit BP variability as variation independent of mean (VIM) by using average systolic BP of 1st and 2nd measurement across four study visits. Data on 4680 men and women were analyzed. Mean ± standard deviation of VIM values among participants in Japan, the PRC, the UK and the US were 5.44 ± 2.88, 6.85 ± 3.49, 5.65 ± 2.81 and 5.84 ± 3.01, respectively; VIM value in the PRC

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participants was significantly higher. Sensitivity analyses among participants without antihypertensive treatment or past history of cardiovascular disease yielded similar results. Higher VIM value was associated with older age, female gender, lower pulse rate and urinary sodium excretion and use of antihypertensive agents such as angiotensin converting enzyme inhibitors, beta blockers and calcium channel blockers. The difference of visit-to-visit BP variability between PRC and other countries remained significant after adjustment for possible confounding factors. In this large international study across four countries, visit-to-visit BP variability in the PRC was higher than in the other three countries. Reproducibility and mechanisms of these findings remain to be elucidated.

Numerous cohort studies have reported that blood pressure (BP) predicts long-term future cardiovascular events [1–3], dementia [4] and disability [5]. Recent studies including meta-analyses indicate that visit-to-visit BP variability may also be an important risk factor for total mortality [6–8], cardiovascular diseases (CVD) [7–13], coronary heart disease [7–9, 13], stroke [8, 14], diabetic nephropathy [15], and dementia [16]. Most of these studies were based in populations carrying a high risk of CVD, and similar observations were reported in studies based on general and/or elderly populations [6, 8, 13, 14]. Recent studies have suggested that BP variability is a causal factor for atherosclerosis [17, 18] and diastolic function [17]. However, no studies compared visit-to-visit BP variability across Western and Asian countries, and little is known about race/ethnicity or differences in visit-to-visit BP variability between countries. Moreover, few studies have reported the factors associated with visit-to-visit BP variability [6, 19].

We therefore examined the distribution of visit-to-visit BP variability among middle aged men and women in Japan, the People's Republic of China (PRC), the United Kingdom (UK) and the United States (US), from the International Collaborative Study of Macronutrients, Micronutrients and Blood Pressure (INTERMAP) [20, 21], conducted with a highly standardized study protocol including BP measurements.

Methods

The INTERMAP study methods have been reported in detail [20, 21]. Briefly, INTERMAP surveyed 4680 men and women aged 40–59, from 17 population samples in Japan, the PRC, the UK and the US (1996–1999). Participants were selected randomly from communities or work-places. Participants visited study centers four times, with visits one and two on consecutive days, and visits three and four on consecutive days an average three weeks later. Trained staff measured BP twice per visit with a random-zero sphygmomanometer. Pulse was measured three times per visit. Height and weight were measured at the first and third visit. Each participant provided two 24-h urine collections with start and end times recorded by research staff. Twenty-four hour urinary excretions of sodium and potassium were means of two measurements. In the present study, four participants were excluded due to missing values of outside temperature. Thus, 4676 participants without missing values were included in this analysis. The study received institutional ethics committee approval for each site, and all participants gave written informed consent. The mean participation rate was 49%.

We defined within-individual visit-to-visit BP variability as variation independent of mean (VIM) of systolic BP since coefficient of variation is correlated with mean BP. VIM was derived from standard deviation(SD)/mean^{x} where the value of x was estimated from non-linear regression analysis for all individuals by the PROC NLIN procedure of SAS [20, 21]. With respect to the primary analysis, VIM of average BP by using average systolic BP of 1st and 2nd measurements across four study visits was calculated. With regard to the secondary analysis, we also calculated VIM of 1st and 2nd BP measurements by using systolic BP of 1st measurement and systolic BP of 2nd measurement across four study visits, respectively. We additionally calculated VIM of BP of all measurements by using BP of all measurements (eight). Finally, we calculated coefficient of variation (CV) of BP by using average systolic BP of 1st and 2nd measurements across four study visits.

Analysis of variance for continuous variables or chi-square tests for proportions were used for comparing baseline characteristics. The associations between VIMs of BP and participant characteristics were assessed using multiple linear regression analysis. Participants from Japan were defined as reference group. We also examined the associations stratified by countries as sensitivity analyses. Characteristics included BMI, smoking status (never, past, current), drinking status (never, past, moderate [<300 g alcohol intake per week], heavy [≥300 g alcohol intake per week]), pulse, mean inside and outside temperature (Celsius) across four study visits, family history of high blood pressure, number of hours of moderate and heavy physical activity per day, 24-h urinary sodium and potassium excretion (mean of two 24-h urine collections), past history of CVD and treatment of hypertension (angiotensin converting enzyme [ACE] inhibitors, angiotensin II receptor blockers, beta blockers, calcium channel blockers, diuretics, direct vasodilators and others). The initial regression models (model 1) included age, sex, country, and study center. Subsequent models of association between BP variability and participant characteristics included variables in model 1 plus pulse, outside temperature, urinary potassium and sodium excretions, past history of CVD and anti-hypertensive medication drug class (model 2). In sensitivity analyses, we excluded participants with past history of CVD and/or antihypertension medication (N = 958). Analysis of covariance (ANCOVA) was used to compare the VIMs of the four countries, with adjustment for confounding factors using the Bonferroni adjustment for multiple comparisons.

All analyses were performed with SAS 9.4 (SAS, NC) and SPSS 18.0 (IBM, NY). A two-tailed P value of equal to or less than 0.05 was considered statistically significant.

Results

Characteristics of the study populations are shown in Table 1. By design, age and proportion of men were similar across the four countries. Compared with UK and US, Japan and PRC had lower BMI, higher prevalence of smoking, higher urinary sodium excretion and lower urinary potassium excretion. Prevalence of current drinker in Japan and the UK was higher than in the other two countries, approximately 90%. Highest average systolic BP was observed among participants in the PRC and lowest systolic BP in participants in Japan. Prevalence of anti-hypertensive treatment was highest in the US and lowest in Japan. The

pulse rate (PR) was higher in participants among the PRC and the US samples than the other two countries.

Table 2 shows the relationships between VIM of average BP across four study visits and various participant characteristics. In the age, sex and center adjusted model, older age, female gender, lower PR, past history of CVD, higher outside temperature, lower urinary sodium excretion, lower urinary potassium excretion, being PRC or the US participants and use of ACE inhibitors, beta blockers and calcium channel blockers were independently associated with higher VIM of BP. In multivariable models, older age, female gender, lower PR, lower urinary sodium excretion, being from the PRC and use of ACE inhibitors, beta blockers and calcium channel blockers were independently associated with higher VIM of BP. Being a PRC participant was independently associated with higher VIM after adjustment for these factors ($P < 0.001$). Similar results were found when stratified by countries (supplemental Table 2). Being PRC participant was independently associated with higher VIM after further adjustment for mean BP (data not shown).

We also examined the association between BP variability and various characteristics stratified by sex. The results were similar in men and women (Supplemental Table 4). Sensitivity analyses among participants without anti-hypertensive treatment or past history of CVD are shown in Table 3. In the age and center adjusted model, VIM of BP in PRC was significantly higher than the other countries, while further adjustment for other possible confounding factors did not affect the results ($P < 0.001$). In multivariable models, older age, female gender, lower PR, lower BMI and being a participant from the PRC were independently associated with higher VIM of BP.

Figure 1 shows the mean and SD of VIMs of average BP across four study visits stratified by country, age and sex. VIMs of BP were higher in older age groups.

Table 4 shows country-specific VIM values of BP. VIM values of visit-to-visit BP variability in the PRC (6.85 ± 3.49) were the highest among the four countries (5.44 ± 2.88 in Japan, 5.65 ± 2.81 in the UK and 5.84 ± 3.01 in the US). In multivariable adjusted models, VIM of BP in PRC remained significantly higher than that for the other countries. Further adjustment for other possible confounding factors did not affect the results. Stratified by sex, the results were similar (Supplemental Table 4).

Discussion

Main finding of this study was: VIM values of visit-to-visit BP variability in the PRC (6.85) was the highest among four countries (5.44 in Japan, 5.65 in UK and 5.84 in US). Visit-to-visit BP variability was higher in older, female, PRC participants and users of ACE inhibitors, beta blockers and calcium channel blockers, and was inversely associated with PR and urinary sodium excretion. The difference of visit-to-visit BP variability between PRC and the other countries remained significant after adjustment for those associated factors.

Visit-to-visit BP variability is a relatively new risk factor for total mortality [6] and CVD [7, 9–14], and differences in visit-to-visit BP variability in different countries have not been examined. To compare visit-to-visit BP variability among different regions, high

standardization of BP measurements is needed. The INTERMAP study was carried out using highly standardized methods including random zero mercury manometers in all four countries [22, 23]. Participants were selected randomly from communities or workplaces. In the present study, we assessed differences in visit-to-visit variability among participants in Japan, the PRC, the UK and the US. Therefore, the INTERMAP study is suitable to investigate differences in visit-to-visit BP variability in Asian and Western regions. Japan had the lowest visit-to-visit BP variability and PRC the highest. With adjustment for possible confounding factors, visit-to-visit BP variability in the PRC was significantly higher than in the other countries. We did not find any significant association between BP variability and education, a marker of socioeconomic status.

There were few studies to report the short-term visit-to-visit BP and future events [6]. Both long-term (every several months or annually) visit-to-visit BP variability [7] and day-by-day BP variability [24] has been reported as a predictor of future morality and/or CVD events. These findings may indicate the association between short-term visit-to-visit BP variability and future CVD events. However, the evidence for short-term visit-to-visit BP variability assessed at weekly intervals is limited. Further studies are needed to clarify the association between short-term visit-to-visit BP variability and CVD.

BP variability is commonly calculated as the SD or CV of BP. However, these indices are dependent on BP levels. The VIM of BP is a relatively new index of BP variability and is independent of mean of BP [20]. Thus to avoid the confounding by BP level, we used VIM of BP as an index of BP variability in this study. Three indices of BP variability (SD, CV and VIM) are derived from the same formula ($SD/mean^x$). Although the values of x for SD and CV are fixed (0 for SD and 1 for CV), the value of x for VIM is estimated for study population and different in different study population. Therefore, VIM values might be affected by the distribution of mean BP in the study population. In the present study, similar results were observed both for VIM and for CV of visit-to-visit BP variability indicating that our findings are not dependent on the method of variability estimation.

Previous studies reported that white coat hypertension or masked hypertension are associated with BP variability [22, 23]. These factors might influence the BP variability in different countries. Further studies are needed to clarify mechanisms, including those underlying the between-country differences.

In the present study, we found that older age and female sex were independently associated with visit-to-visit BP variability, consistent with results from previous studies [6, 19]. We did not find significant associations between visit-to-visit BP variability and smoking status and physical activity, also consistent with previous results [6].

In multivariable adjusted models, higher 24 h urinary excretion of sodium was significantly associated with lower visit-to-visit BP variability. The association was similar, but not significant, when stratified by countries. However, this inverse association was not found among participants without past history of CVD and/or hypertension medication. Therefore, the inverse association between urinary sodium excretion and visit-to-visit BP variability may be due to reverse causality. An intervention study reported that weight reduction and

salt reduction did not reduce visit-to-visit BP variability of persons with high normal DBP [25].

The use of ACE inhibitor, beta blocker, and calcium channel blocker were associated with visit-to-visit BP variability, a finding consistent with a previous observational study [6]. Recent clinical trials reported the use of calcium channel blocker was associated with lower visit-to visit BP variability [26, 27]. Our result was not consistent with these recent results. The discrepancy might be due to the different characteristics of participants with or without using calcium channel blocker and/or the different combination of antihypertensive drug type.

Although we did not find a significant association between visit-to-visit BP variability and diuretic use, a previous study reported a significant association between thiazide-type diuretic and SD of visit-to-visit BP [6]. Due to lack of information about type of diuretic, we could not examine the association between visit-to-visit BP variability and loop and thiazide-type diuretic.

The present study has limitations. We used systolic BP measurements across only four study visits on average of only 3 weeks apart: i.e., only the distribution of short term visit-to-visit BP variability. Moreover, the first and second study visits, and third and fourth study visits, were on consecutive days. Previous findings on short-term visit-to-visit BP variability and day-by-day BP variability indicated that both one associated with future CVD events.

In summary, from a highly standardized international collaborative study, INTERMAP, we found that visit-to-visit BP variability in Japan was lowest and that in the PRC was highest among the four study countries.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Summary Table

What is known about topic

- Recent studies including meta-analyses indicate that visit-to-visit BP variability may also be an important risk factor for total mortality, cardiovascular diseases, coronary heart disease, stroke, diabetic nephropathy and dementia.
- However, no studies compared visit-to-visit BP variability across Western and Asian countries and few studies have reported factors associated with BP variability.

What this study adds

- Variation independent of mean (VIM) values of visit-to-visit BP variability was significantly higher in participants from the People's Republic of China (PRC) than in participants from other countries.
- VIM value was associated with age, gender, pulse rate and urinary sodium excretion and use of antihypertensive agents.
- The difference of visit-to-visit BP variability between PRC and other countries remained significant after adjustment for these possible confounding factors.

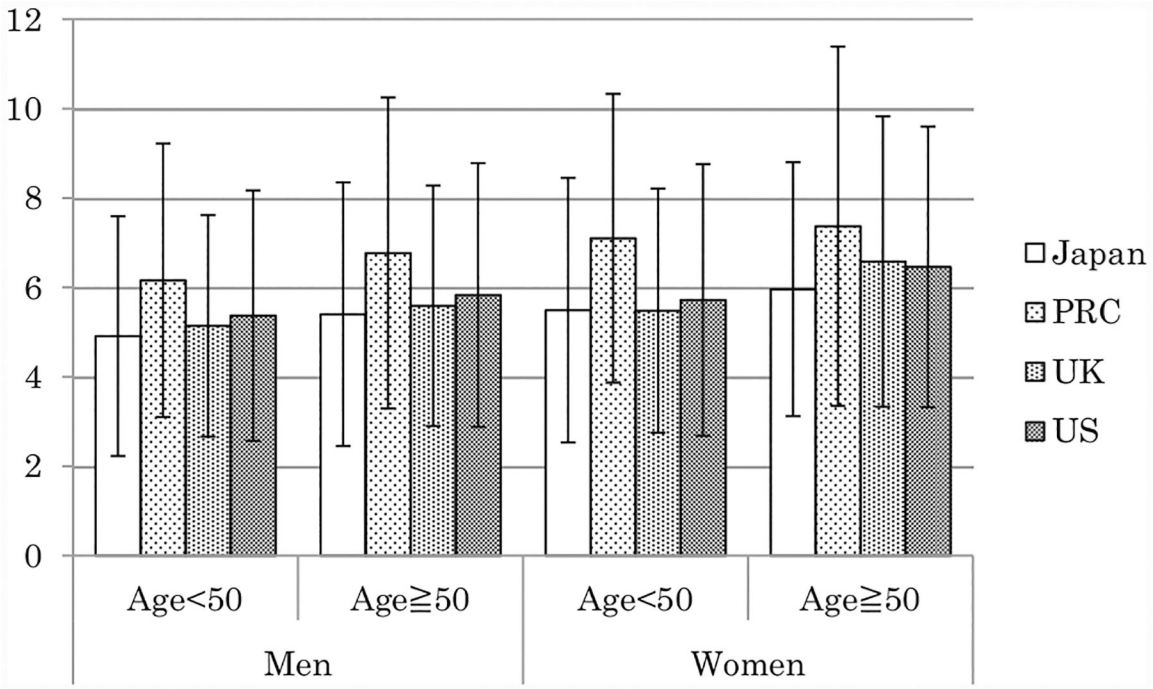

Fig. 1.

The mean and standard deviation of VIMs of average BP measurement across four study visits stratified by country, age-group and sex are shown. BP, blood pressure; VIM, variation independent of mean; PRC, People's Republic of China; UK, United Kingdom; US, United States

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Table 1

Characteristics of study participants by country: INTERMAP, 1996–1999

	Japan		PRC		UK		US		*P* value[a]
Total (*n*)	1145		839		497		2195		
Men (*n*)	574	(50.1)	416	(49.6)	264	(53.1)	1103	(50.3)	0.627
Age (years)	49.4	(5.3)	49.0	(5.8)	49.2	(5.6)	49.1	(5.4)	0.423
Body mass index (kg/sq.m)	23.4	(2.9)	23.1	(3.4)	27.5	(4.6)	28.9	(5.9)	<0.001
Pulse rate									
Mean of 4 visits (beats/min)	71.4	(8.8)	73.9	(8.4)	71.3	(9.4)	73.3	(9.4)	<0.001
1st visit (beats/min)	71.4	(10.1)	74.2	(9.9)	70.0	(10.4)	72.6	(10.6)	<0.001
2nd visit (beats/min)	71.5	(9.8)	73.6	(9.8)	71.5	(10.5)	73.8	(11.0)	<0.001
3rd visit (beats/min)	71.2	(10.1)	74.0	(9.9)	71.5	(10.8)	73.0	(10.6)	<0.001
4th visit (beats/min)	71.4	(10.0)	73.9	(9.9)	72.2	(10.4)	73.9	(10.4)	<0.001
Systolic blood pressure									
Mean of 4 visits (mmHg)	117.2	(13.8)	121.3	(17.4)	120.4	(14.6)	118.6	(13.9)	<0.001
1st visit (mmHg)	119.5	(15.5)	124.7	(20.3)	123.8	(16.6)	120.7	(15.8)	<0.001
2nd visit (mmHg)	116.6	(14.6)	120.2	(18.1)	119.2	(15.3)	118.2	(14.7)	<0.001
3rd visit (mmHg)	116.5	(14.4)	120.8	(18.7)	120.2	(15.5)	118.1	(14.9)	<0.001
4th visit (mmHg)	116.3	(14.4)	119.3	(17.6)	118.3	(14.5)	117.3	(14.6)	<0.001
VIM of average BP across four study visits	5.44	(2.88)	6.85	(3.49)	5.65	(2.81)	5.84	(3.01)	<0.001
CV of average BP across four study visits	6.58	(3.53)	7.07	(3.54)	6.64	(3.41)	6.50	(3.82)	0.002
Diastolic blood pressure									
Mean of 4 visits (mmHg)	73.6	(10.3)	73.2	(10.2)	77.2	(9.9)	73.4	(9.7)	<0.001
1st visit (mmHg)	74.7	(11.4)	74.3	(11.8)	78.8	(11.1)	74.4	(10.9)	<0.001
2nd visit (mmHg)	73.5	(11.1)	72.7	(11.4)	76.7	(10.8)	73.1	(10.5)	<0.001
3rd visit (mmHg)	73.1	(11.0)	73.1	(11.0)	77.1	(10.4)	73.1	(10.5)	<0.001
4th visit (mmHg)	73.4	(11.0)	72.6	(10.9)	76.3	(10.7)	73.0	(10.4)	<0.001
Urinary sodium (mmol/24 h)	198.3	(56.2)	227.5	(100.3)	145.0	(49.1)	162.6	(59.4)	<0.001
Urinary potassium (mmol/24 h)	48.9	(13.6)	38.3	(12.7)	68.2	(20.1)	57.7	(20.9)	<0.001
Drinking status									
Heavy drinker (*n*)	236	(20.6)	78	(9.3)	63	(12.6)	98	(4.5)	<0.001

	Japan		PRC		UK		US		*P* value[a]
Moderate drinker (*n*)	803	(70.1)	304	(36.2)	377	(75.9)	1435	(65.4)	
Ex-drinker (*n*)	26	(2.3)	41	(4.9)	24	(4.8)	427	(19.5)	
Nondrinker (*n*)	80	(7.0)	416	(49.6)	33	(6.6)	235	(10.7)	
Smoking status									
Smoker (*n*)	346	(30.2)	305	(36.4)	87	(17.4)	369	(16.8)	<0.001
Ex-smoker (*n*)	157	(13.7)	69	(8.2)	146	(29.4)	677	(30.8)	
Non-smoker (*n*)	642	(56.1)	465	(55.4)	264	(53.1)	1149	(52.3)	
Mean inside temperature (°C)	22.5	(3.3)	16.3	(3.4)	21.4	(1.9)	23.1	(1.1)	<0.001
Mean outside temperature (°C)	14.5	(6.9)	12.3	(5.0)	8.6	(4.5)	18.8	(9.9)	<0.001
Physical activity (hours/week)[a]	2.6	(3.6)	6.0	(3.8)	2.2	(2.4)	3.2	(3.2)	<0.001
Year of education									
6 years or less	0	(0.0)	580	(69.1)	6	(1.2)	17	(0.8)	<0.001
12 years or less	894	(78.1)	257	(30.6)	267	(53.7)	522	(23.8)	
More than 13 year	251	(21.9)	2	(0.2)	224	(45.1)	1656	(75.4)	
Past history of CVD (*n*)	98	(8.6)	45	(5.4)	45	(9.1)	193	(8.8)	0.013
Family history of HBP (*n*)	528	(46.1)	298	(35.5)	241	(48.5)	1491	(67.9)	<0.001
Anti-hypertension drug class									
ACE inhibitor (*n*)	20	(1.7)	11	(1.3)	26	(5.2)	196	(8.9)	<0.001
Angiotensin II receptor blocker (*n*)	0	(0.0)	0	(0.0)	5	(1.0)	18	(0.8)	0.001
Beta blocker (*n*)	13	(1.1)	4	(0.5)	24	(4.8)	116	(5.3)	<0.001
Calcium channel blocker (*n*)	50	(4.4)	23	(2.7)	16	(3.2)	137	(6.2)	<0.001
Diuretic (*n*)	5	(0.4)	19	(2.3)	19	(3.8)	160	(7.3)	<0.001
Direct vasodilators (*n*)	5	(0.4)	14	(1.7)	0	(0.0)	9	(0.4)	<0.001
Other (*n*)	5	(0.4)	3	(0.4)	2	(0.4)	27	(1.2)	0.017

Values are number (proportion [%]) or mean (standard deviation)

[a]Analysis of variance for continuous variables or chi-square tests for proportions. Physical activity was defined as number of hours with moderate and heavy physical activity per week

BP blood pressure, *VIM* variation independent of mean, *CV* coefficient of variation, *CVD* cardiovascular disease, *HBP* high blood pressure, *PRC* People's Republic of China, *UK* United Kingdom, *US* United States

Table 2

Relationship between VIM of average BP across four study visits and various characteristics: INTERMAP, 1996–1999

	VIM of average BP			
	Model 1		Model 2	
	Beta	*P*-value	Beta	*P*-value
Age (5 years)	0.312	<0.001	0.256	<0.001
Women	0.576	<0.001	0.497	<0.001
Country				
Japan	Reference		Reference	
PRC	1.358	<0.001	1.377	<0.001
UK	0.061	0.817	−0.058	0.836
US	0.591	0.017	0.308	0.230
BMI	−0.014	0.122		
Pulse rate (10 beats/min)	−0.209	<0.001	−0.204	<0.001
Smoking				
Non-smoker	Reference			
Ex-smoker	0.010	0.934		
Smoker	0.061	0.603		
Drinking				
Non-drinker	Reference			
Ex-drinker	−0.187	0.311		
Moderate drinker	−0.118	0.396		
Heavy drinker	−0.222	0.266		
Mean inside temperature (°C)	−0.001	0.964		
Mean outside temperature (°C)	0.014	0.036	0.012	0.086
Physical activity (h/week)[a]	0.002	0.876		
Years of education				
6 years or less	Reference			
12 years or less	−0.009	0.968		
More than 13 years	0.115	0.636		
Family history of hypertension	0.126	0.171		
Past history of CVD	0.498	0.002	0.287	0.075
Urinary Sodium (20 mmol/24 h)	−0.038	0.011	−0.036	0.022
Urinary Potassium (10 mmol/24 h)	−0.051	0.049	−0.033	0.233
Antihypertensive medication drug class				
ACE inhibitor	0.478	0.017	0.527	0.009
Angiotensin II receptor blocker	0.603	0.340	0.625	0.322
Beta blocker	0.993	<0.001	0.805	0.001
Calcium channel blocker	0.826	<0.001	0.843	<0.001
Diuretic	0.248	0.281	0.289	0.207
Vasodilation drug	0.789	0.167	0.750	0.188

	VIM of average BP			
	Model 1		Model 2	
	Beta	*P*-value	Beta	*P*-value
Other	1.091	0.028	1.074	0.030

The associations between VIMs of BP and participant characteristics were assessed using multiple linear regression analysis. Model 1 included adjustment for age, sex, countries and study centers. Model 2 included age, sex, countries, study centers and all variables associated with VIM of visit-to-visit BP variability ($P < 0.05$) in Model 1

[a]Physical activity was defined as number of hours with moderate and heavy physical activity per week

BP blood pressure, *VIM* variation independent of mean, *CVD* cardiovascular diseases, *BMI* body mass index, *PRC* People's Republic of Chin, *UK* United Kingdom, *US* United States, *h* hour, *ACE* angiotensin-converting-enzyme

Table 3

Relationship between VIM of average BP across four study visits and various characteristics among participants without antihypertensive treatment or past history of CVD: INTERMAP, 1996–1999

	VIM of average BP			
	Model 1		Model 3	
	Beta	*P*-value	Beta	*P*-value
Age (5 years)	0.231	<0.001	0.229	<0.001
Women	0.631	<0.001	0.589	<0.001
Country				
Japan	Reference		Reference	
PRC	1.225	<0.001	1.276	<0.001
UK	−0.024	0.931	−0.025	0.931
US	0.235	0.392	0.262	0.365
BMI (kg/sq.m)	−0.038	0.001	−0.031	0.008
Pulse (10 beats/min)	−0.145	0.008	−0.122	0.029
Smoking				
Non-smoker	Reference			
Ex-smoker	−0.003	0.985		
Smoker	0.075	0.548		
Drinking				
Non-drinker	Reference			
Ex-drinker	−0.354	0.085		
Moderate drinker	−0.185	0.218		
Heavy drinker	−0.327	0.125		
Mean inside temperature (°C)	0.003	0.919		
Mean outside temperature (°C)	0.015	0.039	0.014	0.062
Physical activity (h/week)[a]	0.018	0.249		
Years of education				
6 years or less	Reference			
12 years or less	0.025	0.909		
More than 13 years	0.174	0.496		
Family history of hypertension	−0.003	0.972		
Urinary sodium (20 mmol/24 h)	−0.035	0.031	−0.022	0.192
Urinary potassium (10 mmol/24 h)	−0.036	0.203		

The associations between VIMs of BP and participant characteristics were assessed using multiple linear regression analysis

BP blood pressure, *VIM* variation independent of mean, *CVD* cardiovascular disease, *BMI* body mass index, *PRC* People's Republic of China, *UK* United Kingdom, *US* United States, *h* hour

[a]Physical activity was defined as number of hours with moderate and heavy physical activity per week. Model 1 included age, sex, countries and study centers. Model 3 included age, sex, countries, study centers and all variables associated with VIM of visit-to-visit BP variability (*P* 0.05) in Model 1

Table 4

VIM values of BP stratified by country: INTERMAP, 1996–1999

Number	Japan		PRC		UK		US	
	1145		839		497		2195	
VIM of average SBP of 1st and 2nd measurement across 4study visits	5.44	± 2.88[b]	6.85	± 3.49[a,c]	5.65	± 2.81[b]	5.84	± 3.01[b]
VIM of 1st SBP measurement across 4 study visits	6.14	± 3.15[b]	7.20	± 3.62[a,c]	6.10	± 2.97[b]	6.39	± 3.22[b,c]
VIM of 2nd SBP measurement across 4 study visits	5.89	± 3.02[b]	7.02	± 3.51[a,c]	5.92	± 3.01[b]	6.22	± 3.16[b]
VIM of SBP of all measurement (8 times)	5.92	± 2.53[b,c]	6.76	± 3.13[a,c]	5.82	± 2.53[a,b]	6.14	± 2.67[b,c]

Values are number or mean ± SD

ANCOAVA was used to tests for differences of VIMs of BP among countries

Adjusted for age, sex, study centers, pulse, outside temperature, urinary potassium excretion, urinary sodium excretion, past history of CVD and antihypertensive medication drug class

[a]Significantly different from Japan (Followed by Bonferroni post hoc testing)

[b]Significantly different from PRC (Followed by Bonferroni post hoc testing)

[c]Significantly different from UK (Followed by Bonferroni post hoc testing)

BP blood pressure, *VIM* variation independent of mean, *SBP* systolic blood pressure, *PRC* People's Republic of China, *UK* United Kingdom, *US* United States, *SD* standard deviation, *ANCOVA* analysis of covariance