## Prognostic Value of the Variability in Home-Measured Blood Pressure and Heart Rate The Finn-Home Study

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Abstract—The objective of the study was to assess the prognostic value of variability in home-measured blood pressure (BP) and heart rate (HR) in a general population. We studied a representative sample of the Finnish adult population with 1866 study subjects aged 45-74 years. BP and HR self-measurements were performed on 7 consecutive days. The variabilities of BP and HR were defined as the SDs of morning minus evening, day-by-day, and first minus second measurements. The primary end point was incidence of a cardiovascular event. The secondary end point was total mortality. During a follow-up of 7.8 years, 179 subjects had experienced a cardiovascular event, and 130 subjects had died. In Cox proportional hazard models adjusted for age, sex, BP/HR, and other cardiovascular risk factors, morning-evening home BP variability (systolic/diastolic relative hazard: 1.04/1.10 [95% CI: 1.01–1.07/1.05–1.15] per 1-mm Hg increase in BP variability) and morning day-by-day home BP variability (relative hazard: 1.04/1.10 [95% CI: 1.00–1.07/1.04–1.16] per 1-mm Hg increase in BP variability) were predictive of cardiovascular events. Morningevening home HR variability (relative hazard: 1.07 [95% CI: 1.02-1.12] per 1-bpm increase in HR variability) and morning day-by-day home HR variability (relative hazard: 1.11 [95% CI: 1.05-1.17] per 1-bpm increase in HR variability) were also independent predictors of cardiovascular events. Greater variabilities of morning home BP and HR are independent predictors of cardiovascular events. Because the variabilities of home BP and HR are easily acquired in conjunction with home BP and HR level, they should be used as the additive information in the assessment of cardiovascular risk. (Hypertension. 2012;59:212-218.) • Online Data Supplement

Key Words: home blood pressure measurement ■ home blood pressure variability ■ home heart rate variability ■ prognostic value of home heart rate ■ prognostic value of home blood pressure ■ cardiovascular risk

Hore blood pressure (BP) measurement has been reported to be more reliable than office measurement because it offers better reproducibility and is free from white-coat effect and observer dilution bias.<sup>1,2</sup> In addition, home BP measurement is more strongly associated with target organ damage<sup>3–5</sup> and offers better prognostic value in predicting mortality or cardiovascular (CV) events than office BP.<sup>1,6,7</sup> Variability of home BP and heart rate (HR) has been associated with several risk factors, including excessive use of alcohol, diabetes mellitus, and CV disease.<sup>8</sup>

Only a single study by the Ohasama investigators has suggested that higher day-by-day variability measured by single home BP and HR morning measurements over 10 to 30 days could be associated with CV and stroke mortality in the Japanese general population.<sup>9</sup> However, the prognostic value of the variability in self-measured BP and HR performed on 7 consecutive days (with duplicate measurements in the morning and in the evening), as suggested by the current international home monitoring guidelines, has not been assessed in the general population.<sup>10,11</sup> Our study provides the possibility to analyze the prognostic significance of the variability in home-measured BP and HR, obtained from 28 measurement points (measurements performed twice in the morning and in the evening over 7 days), in the Finnish general population. This makes a good basis for assessing the prognostic value of the variability between measurement days and between morning and evening measurements, as well as between individual measurement occasions.

### **Subjects and Methods**

#### **Study Population**

The study sample was drawn from the participants of a multidisciplinary epidemiological survey, the Health 2000 Study, which was carried out in Finland from autumn 2000 to spring 2001. The study population was a stratified 2-stage cluster sample of 8028 subjects drawn from the population register to represent Finnish adults aged  $\geq$ 30 years. The details of stratification and sampling procedures have been reported previously.<sup>12,13</sup>

There were 4388 individuals aged 45 to 74 years, of which 3672 (84%) agreed to participate in the interview and attended the health

Hypertension is available at http://hyper.ahajournals.org

Received June 22, 2011; first decision July 11, 2011; revision accepted December 5, 2011.

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examination. Home measurement of BP was not performed on all of the individuals willing to participate because of the limited number of home monitors (~800). Finally, 2103 individuals participated in the home BP measurement substudy (Finn-Home Study). Subjects with arrhythmias, such as atrial fibrillation and flutter, were not included in the Finn-Home Study. Subjects who had missing health examination or interview data (age, sex, body mass index [BMI], use of antihypertensive medication, smoking status, use of insulin injections or oral hypoglycemic agents or both, use of lipid modifying agents, and information on alcohol consumption; n=191), had not performed  $\geq 14$  valid home measurements of BP or HR (n=50), or had incomplete laboratory values (fasting cholesterol or glucose level; n=11) were also excluded. After removing subjects with  $\geq 1$ exclusion factor, the study population consisted of 1866 participants aged 45 to 74 years. The study protocol of the Health 2000 Study was approved by the epidemiology ethics committee of the Helsinki and Uusimaa hospital region, and all of the participants gave signed, informed consent.

#### Flow of the Study

At an initial health interview at the participant's home, basic background and sociodemographic information, information about health and illnesses, and information about the use of medication were gathered by centrally trained interviewers. Individuals who were willing to participate in the Finn-Home substudy received home monitors for measuring BP and HR during the week after the health interview. A physical examination was performed on each participant 1 to 6 weeks later at a local health center by centrally trained doctors and nurses. Each participant's height, weight, and body circumference were measured, and fasting blood samples for serum lipids and glucose were taken from the participants. Details of the methodology of the project have been published elsewhere.<sup>12,13</sup>

#### Home BP and Home HR Measurements

Home BP and HR were self-measured using a validated, automatic oscillometric device (Omron model HEM-722C; Omron Corp, Tokyo, Japan).<sup>14</sup> Participants received written instructions and individual guidance on how to measure BP and HR correctly. Seated BP and HR were measured twice, at an  $\approx$ 2-minute interval every morning between 6:00 AM and 9:00 AM (before breakfast and washing up) and every evening between 6:00 PM and 9:00 PM (eating was not allowed  $\geq$ 1 hour before measurements) on 7 consecutive days. The details of the methodology of the projects have been published elsewhere.<sup>12,13</sup>

#### Definitions

Diabetes mellitus, presence of hypercholesterolemia, smoking, use of alcohol, and past history of CV disease were defined according to previous publication.<sup>8</sup> Degree of physical activity was defined as follows: if the person answered that he/she is exercising at his/her free time (for  $\geq$ 30 minutes at a time and at least twice in a week so that he/she is at least slightly sweating), then the answer was considered as having sufficiently physical activity. Otherwise, the answer was considered not having sufficiently physical activity.

#### Follow-Up

The follow-up data were accumulated until December 31, 2008. Mortality data were obtained from the national mortality register based on death certificates.

Data on hospitalization attributed to heart failure and nonfatal coronary and stroke events, as well as the performed coronary interventions and coronary artery bypass graft surgeries, were obtained from the national hospital discharge register. Details of the follow-up phase have been published previously.<sup>7</sup>

The primary end point was the combination of CV mortality, nonfatal myocardial infarction, nonfatal stroke, hospitalization for heart failure, percutaneous coronary intervention, and coronary artery bypass surgery. Only the first event was included in the analysis. The secondary end point was the total mortality. Table 1. Baseline Characteristics of the Study Population

Variable	Data (n=1866)
Systolic home BP	129.5 (18.7)
Diastolic home BP	80.1 (9.2)
Home HR	68.3 (9.1)
Age, y	56.4 (8.5)
BMI, kg/m <sup>2</sup>	27.4 (4.5)
Alcohol use, g/wk	78.2 (147.7)
Male, %	43.9
Smokers, %	22.9
Antihypertensive medication, %	30.6
Past history of cardiovascular disease, %	6.7
Diabetes mellitus, %	6.7
Hypercholesterolemia, %	30.2
Sufficient physical activity, %	61.5

Values are expressed as mean (SD) or percentages as appropriate. BMI indicates body mass index; BP, blood pressure; HR, heart rate.

#### **Statistical Analyses**

Data are expressed as mean (SD) or percentage. The variability of home BP and HR was calculated as follows, morning-evening variability as the SD of the difference between daily morning (mean of 2 readings) and evening (mean of 2 readings) home BP/HR of 7 consecutive days (SD of 7 morning-evening readings), day-by-day variability as the SD of daily BP mean (mean of 4 readings) of 7 consecutive days (SD of 7 day-by-day readings), and as the SD of all of the first minus second measurements (SD of 14 readings of first minus second measurements).

The average real variability method<sup>15</sup> was used when we calculated the relative hazards (RHs) between CV events and the variability of home BP and HR. The skewed distributions of home BP and HR variability were log-transformed for the t test analyses (in Table S3, available in the online Data Supplement, please see http://hyper.ahajournals.org). Cox proportional hazards model was used to test the association between CV events and individual covariates (age, sex, BMI, home BP/home HR [average of 7 days of duplicate morning and evening measurements], presence of diabetes mellitus, current smoking, use of alcohol, presence of hypercholesterolemia, past history of CV disease, degree of physical activity, and use of antihypertensive medication). Cox proportional hazards model was used as well for the multivariate analyses. Associations of the variability in home-measured BP and HR with the end points were analyzed by estimation of the RH and their 95% CI per 1-mm Hg or 1-bpm increase in BP or HR variability. Models were adjusted for age, sex, BMI, home BP/home HR, presence of diabetes mellitus, current smoking, use of alcohol, presence of hypercholesterolemia, past history of CV disease, degree of physical activity, and use of antihypertensive medication. A P value <0.05 was considered statistically significant. Statistical analyses were performed using SAS 9.1 software (SAS Institute, Cary, NC).

#### Results

The baseline characteristics of the study population are reported in Table 1. The follow-up period ended on December 31, 2008, and the mean follow-up time was 7.8 years (14 600 person-years; interquartile range: 96 days). During the follow-up there were 130 deaths and 179 CV events (fatal and nonfatal events). The causes of death and origins of CV events are reported by categories in Tables S1 and Table S2.

Baseline variabilities of home BP and HR in the study population with or without a CV event during the follow-up

Variable	Fatal and Nonfatal CV Events (n=179)*		Total Mortality (n=130)*	
	RH (95% CI)	Р	RH (95% CI)	Р
Systolic BP variability, mm Hg				
Morning-evening	1.04 (1.01–1.07)	0.006	1.04 (1.01–1.07)	0.01
Day-by-day	1.02 (0.98–1.07)	0.39	1.05 (1.00–1.11)	0.04
Morning day-by-day	1.04 (1.00–1.07)	0.03	1.05 (1.02–1.09)	0.006
Evening day-by-day	1.02 (0.98–1.06)	0.27	1.04 (0.99–1.08)	0.11
First minus second measurement	1.01 (0.97–1.06)	0.51	1.06 (1.01–1.10)	0.02
Diastolic BP variability, mm Hg				
Morning-evening	1.10 (1.05–1.15)	< 0.001	1.12 (1.07–1.16)	< 0.001
Day-by-day	1.09 (1.00–1.18)	0.04	1.19 (1.09–1.29)	< 0.001
Morning day-by-day	1.10 (1.04–1.16)	0.002	1.17 (1.11–1.23)	< 0.001
Evening day-by-day	1.05 (0.99–1.12)	0.11	1.09 (1.01–1.17)	0.03
First minus second measurement	1.09 (1.04–1.15)	< 0.001	1.09 (1.03–1.16)	0.003
HR variability, bpm				
Morning-evening	1.07 (1.02–1.12)	0.006	1.08 (1.03–1.13)	< 0.001
Day-by-day	1.05 (0.97–1.13)	0.26	1.07 (0.98–1.16)	0.12
Morning day-by-day	1.11 (1.05–1.17)	< 0.001	1.11 (1.05–1.17)	< 0.001
Evening day-by-day	1.01 (0.94–1.07)	0.85	1.00 (0.93–1.07)	0.91
First minus second measurement	1.02 (0.96–1.08)	0.49	1.03 (0.97–1.10)	0.30

Table 2. Multivariate Models of Relative Hazards for CV Events and Total Mortality With Systolic and Diastolic BP Variability Increase of 1 mm Hg and HR Variability Increase of 1 bpm

BP indicates blood pressure; CV, cardiovascular; HR, heart rate; RH, relative hazard.

\*Data were adjusted for age, sex, use of antihypertensive medication, diabetes mellitus, body mass index, history of CV disease, use of alcohol, smoking, presence of hypercholesterolemia, and degree of physical activity, as well as systolic and diastolic home BP or home HR level (average of 7 d duplicate morning and evening measurements).

are reported in Table S3. Home BP variation was higher in subjects who had experienced a CV event than in healthy subjects. However, no difference was detected in home HR variability variables between the 2 groups.

## Correlation of Home BP/HR Variability Parameters With Each Other

The correlation matrix for home BP/HR variability parameters is presented in Table S4. The r values (Pearson) of home BP variability and home HR variability ranged from 0.29 to 0.79.

## Home BP Variability and Home HR Variability Covariates as Predictors of CV Events

In the univariate analyses, male sex (P < 0.001), higher age (P < 0.001), higher BMI (P = 0.001), diabetes mellitus (P < 0.001), hypercholesterolemia (P = 0.02), history of CV disease (P < 0.001), use of antihypertensive medication (P < 0.001), use of alcohol (P = 0.007), and higher systolic and diastolic home BPs (P < 0.001 for both) were associated with future CV events. Degree of physical activity (P = 0.58) was not associated with CV events. Smoking (P = 0.54) was not alone associated with future CV events, but when age was entered in the same model, smoking became predictive for CV events (P = 0.006). Home HR level alone was not associated with CV events (P = 0.52), but became predictive, after it was adjusted for age, sex, and history of CV disease (P = 0.03).

## Home BP Variability and Home HR Variability as Predictors of CV Events

In the unadjusted Cox regression models, all of the home BP variability variables were predictive of CV events (Table S5). Only morning home HR variability was predictive of CV events of the home HR variability variables.

After adjustments for other risk factors, both systolic and diastolic morning-evening home BP variability and morning day-by-day home BP variability remained as independent predictors of CV events (Table 2). In addition, diastolic day-by-day home BP variability and first minus second measurement of home BP variability were also predictive of CV events. When day-by-day first measurements of home BP variability and day-by-day second measurements of home BP variability were analyzed separately, only diastolic first and second day-by-day measurements predicted CV events. Diastolic second measurements were slightly better predictors of CV events than the diastolic day-by-day first measurements (Table S6).

Morning home HR variability predicted CV events both in the unadjusted and in the fully adjusted models (Table S5 and Table 2). Morning-evening HR variability became predictive of CV events in the adjusted models (Table 2). More specifically, morning-evening HR variability become predictive of CV events after age was added as the only covariate in the models (for morning-evening HR variability, RH: 1.07 [95% CI: 1.03–1.12]; P=0.003, per 1-bpm increase in HR variability). In the subgroup analyses by age group, the associations of the variability of home BP and home HR with CV events were stronger in the older participants' group (aged >60 years; CV events: n=103), whereas the associations were weaker or nonsignificant in the younger participants group (aged ≤60 years; CV events: n=76; data not shown). In the subgroup analyses of strokes, only diastolic first minus second measurement of home BP variability was predictive of stroke events (RH: 1.13 [95% CI: 1.03–1.25]; P=0.01, per 1-mm Hg increase in BP variability), in the adjusted model. None of the home HR variability measurements predicted strokes (data not shown). The cumulative risk between CV events and morning systolic/diastolic home BP variability and the CV risk between home HR variability at different BP levels are presented in the Figure.

## Home BP Variability and Home HR Variability as Predictors of Total Mortality

In the unadjusted Cox regression models, all of the home BP variability variables, as well as morning-evening, morning day-by-day, and day-by-day variables of home HR variability predicted total mortality (Table S5). In the adjusted models, all of the diastolic home BP variability variables were predictive of total mortality (Table 2). Systolic morning-evening, day-by-day, morning day-by-day, and first minus second measurement of home BP variability variables were predictive of total mortality. Moreover, morning-evening and morning day-by-day home HR variability variables were predictive of total mortality in the adjusted models.

## Comparison Between Subjects Who Completed the Whole Study Protocol With Those Who Completed 14 to 28 Readings

We also performed the analysis of the variability in home BP and home HR with subjects who had completed the whole study protocol (28 readings). The associations of the variability in home BP and home HR with CV events were slightly weaker compared with subjects who completed 14 to 28 measurements (data not shown).

#### The Additive Effect of Home BP Variability and Home HR Variability as Predictors of CV Events

When morning day-by-day home BP variability (systolic or diastolic) and morning day-by-day home HR variability were placed in the same model together with other CV risk covariates used in Table 2, diastolic morning day-by-day home BP variability (RH: 1.07 [95% CI: 1.00–1.14]; P=0.044 per 1-mm Hg increase in BP variability) and morning day-by-day home HR (systolic/diastolic model; RH: 1.09/1.08 [95% CI: 1.03–1.16/1.02–1.15]; P=0.003/0.008 per 1-bpm increase in HR variability) variability remained as independent determinants of CV events.

When morning-evening home BP variability (systolic or diastolic) and morning-evening home HR variability were placed in the same model together with other CV risk covariates used in Table 2, both systolic and diastolic morning-evening home BP variability (RH: 1.03/1.08 [95% CI: 1.00-1.07/1.03-1.14]; P=0.026/0.001 per 1-mm Hg increase in BP variability) remained as independent determi-



**Figure.** Variability (expressed as SD) of (**A**) systolic and (**B**) diastolic morning home blood pressure (BP)/(**C**) morning home heart rate (HR) and the percentage risk of cardiovascular (CV) events at different home BP levels. The upper cutoff point for SDs of home BP has been set to 99th percentile corresponding with 22/12 mm Hg of systolic/diastolic SD of morning home BP and with SD of home HR to 13 bpm. The percentage risk of CV events has been adjusted for age, sex, home BP/home HR, diabetes mellitus, smoking, use of alcohol, body mass index, history of CV disease, presence of hypercholesterolemia, degree of physical activity, and use of antihypertensive medication.

nants of CV events. Only morning-evening home HR variability (RH: 1.05 [95% CI: 1.00–1.10]; P=0.046 per 1-bpm increase in HR variability) remained as an independent determinant in the model adjusted with systolic morning-evening home BP and other CV risk covariates used in Table

2. The additive effect of diastolic morning home BP variability and morning home HR variability for CV risk at different home BP levels is presented in Figure S1.

# Interaction Between the Variability of Home BP and Home HR

When home BP variability variable (morning-evening, dayday-by, morning, evening, and first minus second measurement) and the corresponding home HR variability variable were placed in the same model, there were no interactions between the variability of home BP and home HR (data not shown). There were significant interactions between both systolic and diastolic morning-evening home BP variability and mean home BP and between systolic morning day-byday, diastolic day-by-day, and diastolic first minus second measurement of home BP variability (data not shown). None of the home HR variability variables had any significant interaction with mean home HR (data not shown).

## Coefficient of Variation and Average Real Variability

Using the coefficient of variation (data not shown) or average real variability (Table S7) instead of SDs of day-by-day and morning/evening day-by-day home BP and HR produced almost similar results.

#### Discussion

This study addressed for the first time the prognostic implications of the variability in home-measured BP and HR in European population and compared the prognostic value of the variability in home-measured BP and HR in different measurement settings (morning-evening, day-by-day, morning/evening day-by-day, and first minus second measurement of variability). The main finding of our study was that, in the fully adjusted models (adjusted for age, sex, BMI, home BP/home HR, presence of diabetes mellitus, current smoking, use of alcohol, presence of hypercholesterolemia, past history of CV disease, degree of physical activity, and use of antihypertensive medication), higher variability of morningevening and morning day-by-day home BP, as well as higher variability of morning-evening and morning home HR, predicted CV events in a Finnish middle-aged general population, whereas the variability of evening day-by-day home BP or HR did not. In addition, morning home HR variability predicted CV events independent of morning home BP variability and morning-evening home BP variability independent of morning-evening home HR variability. There was no interaction between the variability of home BP and home HR. Using the coefficient of variation or average real variability instead of SDs of home BP and HR produced similar results.

#### Home BP Variability as a Predictor of CV Events

The association between higher home BP variability and CV events may partly reflect underlying disease states. In our previous cross-sectional study, diabetes mellitus and past history of CV disease were independent determinants of higher home BP variability.<sup>8</sup> Aging and diabetes mellitus hasten the arterial stiffening process, leading to changes in

contents of arterial vessel wall (elastin is replaced by collagen).<sup>16,17</sup> This can magnify BP changes and increase BP variability. The same phenomenon was also seen in the subgroup analyses by age group in our study. In older study participants (aged >60 years), the associations between home BP variability and CV events were stronger than in the younger participants (aged ≤60 years). This is because of the fact that older participants have higher number of CV events than younger participants. They also have stiffer arteries, which further escalate oscillations in home BP and HR.<sup>16,17</sup>

Morning day-by-day home BP variability predicted CV events, whereas evening day-by-day BP variability did not. The prevalence of CV complications has been shown to be higher in the morning than at other times of day.<sup>18,19</sup> This has been linked to the activation of the sympathetic nervous system<sup>20</sup> and an increase in platelet aggregability.<sup>19</sup> Higher morning day-by-day home BP variability may, therefore, reflect greater hemodynamical instability and exposure to CV events. Higher morning-evening home BP variability also predicted CV events, which supports the theory of greater hemodynamical instability in subjects at risk of CV events. In the Japanese Ohasama Study, day-by-day home BP variability (measured in the morning) was predictive of CV mortality which is in accordance with our study.<sup>9</sup>

However, in the Ohasama Study, day-by-day BP variability was also predictive of stroke mortality, whereas in our study home day-by-day BP variability did not predict strokes. This may be partly attributed to the differences between study populations and to the smaller number of strokes in our study.

Diastolic first minus second measurement of home BP variability predicted CV events independently (Table 2). This variability variable can be generally considered to indicate better short-time variability than the other home variability variables, because there is only a gap of a few minutes between the measurements. Therefore, greater first minus second measurement of home BP variability indicates the reactivity of an individual, seen as a high variation of BP between the measurement occasions. The link between the reactivity and high variation between measurement occasions might be explained by the autonomic nervous system activation and arterial baroreflex, because short-term alteration in BP is regulated primarily by those 2 factors.<sup>18</sup>

When day-by-day first measurements of home BP variability and day-by-day second measurements of home BP variability were analyzed separately, diastolic day-by-day second measurements were slightly better predictors of CV events than the diastolic day-by-day first measurements (Table S6). This supports the hypothesis that second measurements are slightly more reliable than the first ones in assessing CV risk.

**Home HR Variability as a Predictor of CV Events** Morning day-by-day home HR variability predicted CV events both in the unadjusted model and in the fully adjusted model, although home evening day-by-day HR variability did not (Table S5 and Table 2). Moreover, morning-evening home HR variability was predictive of CV events in the fully adjusted model but not in the unadjusted model. Age was the primary covariate to explain this. As shown in our previous study, young age was an independent determinant of greater home HR variability.<sup>8</sup> Including age as a covariate in the analyses indicates that especially older subjects with high HR variation are at the greatest risk of a CV event, because older people generally are more likely to have an underlying CV disease, which could lead to hemodynamic instability seen as fluctuations in HR.

In addition, morning home HR variability predicted CV events independent of morning home BP variability. However, home HR level was not predictive of CV events in the univariate model but became predictive, after it was adjusted for age, sex, and history of CV disease. This result was similar to the finding in the Japanese Ohasama Study, where home HR predicted CV mortality in the general population.<sup>21</sup> The association between higher morning day-by-day HR variability and CV events may reflect as well a greater hemodynamical instability because of impairment in cerebral autoregulation.<sup>18</sup> Hemodynamical instability can be, as well, the underlying cause in the association between greater variability of morning-evening home HR and CV events. In the Japanese Ohasama Study, where home measurements were performed once every morning, day-by-day home HR variability was, as well as in our study, predictive of CV mortality, although in the Ohasama Study morning and evening HR variability was not separately examined.9 None of the home HR variability measurements were predictive of stroke events in our study. The similar finding was also made in the Ohasama Study where home HR variability did not predict stroke mortality.

### Comparison Between Subjects Who Completed the Whole Study Protocol With Those Who Completed 14 to 28 Readings

The associations with CV events with subjects who completed the whole study protocol (28 readings) compared with those who completed 14 to 28 readings were mainly similar. However, in real life, it is rare that all of the subjects measuring home BP will have complete home BP readings (28 measurements). Therefore, we believe that having study subjects who had 14 to 28 home readings in the analyses better reflects the situation in real life.

## Correlation of Home BP/HR Variability Parameters With Each Other

The results of the correlation matrix (Table S4) indicate that morning-evening, day-by-day, and first minus second measurements of variability parameters are quite "independent" from other day-by-day parameters. This emphasized the role of morning-evening variability as an indicator of diurnal variation and first minus second measurement variability as an indicator of short time variability.

## The Additive Effect of Home BP Variability and Home HR Variability as Predictors of CV Events

There were no interactions between any of the variability parameters of home BP and home HR. In addition, morning home HR variability predicted CV events independent of morning home BP variability, when they were placed in the same multivariate model. Systolic and diastolic morningevening and diastolic morning home BP variability variables predicted CV events independent of morning-evening/morning home HR variability, when they were in the same multivariate model. There were as well some interactions between the variability of home BP and mean home BP. These results can be interpreted that increased home BP variability, together with increased mean home BP, has an additive effect on CV events. These novel results validate that both the variability of home BP and home HR have an independent and additive role in predicting CV events.

#### **Study Limitations**

Although the home BP and HR measurements were carefully assessed, the study results must be interpreted with caution. The interview data and laboratory measurements were gathered at the baseline of the study, and, therefore, the possible changes in the person's health status were not updated during the follow-up. Participants measured their BP and HR under relatively controlled conditions and received individual guidance on how to perform the measurements correctly. However, it is still possible that measurement procedure could have affected BP variability. The associations of the home BP and home HR variability parameters with CV events were slightly weaker when analyzing subjects with the complete measurement protocol (28 readings) compared with subjects with 14 to 28 readings. This might depend on the fact that there were less CV events in those subjects who had complete measurement protocol. Furthermore, the population was smaller when analyzing only those subjects with complete measurement protocol, which as well might produce weaker associations with CV events.

There was no association between sedentary lifestyle and CV events in our study. This might be because of the identification criteria used in our study, which probably was not accurate enough to distinguish subjects with sedentary lifestyle and active lifestyle. In addition, there might be some associations of variability parameters and CV events by chance. Although this study assessed the prognostic value of the variability in home-measured BP and HR based on the CV outcome, additional research is warranted for examining whether CV prognosis can be improved by making lifestyle adjustments (eg, reducing alcohol consumption, giving CV disease prevention counseling, and adjusting medication). This remains to be assessed in future studies.

#### Perspectives

Numerous studies indicate that home BP measurement is more reliable than office measurement because it offers better reproducibility and is free from white-coat effect and observer dilution bias. Furthermore, home BP measurement offers better prognostic value than office BP. In addition to the BP and HR level, several measurement points acquired from home measurements offer the analysis of variability in home-measured BP and HR. Prognostic data from this study based on the 7 days consecutive monitoring of home BP and HR show that the variabilities of home-measured BP and HR both are independent predictors of CV events. Because the variabilities of home BP and HR both are predictive of CV events, and they are as well easily acquired in conjunction with home BP and HR level, they should be used as additive information in the assessment of CV risk.

### Sources of Funding

The project organization created for the study involved the National Institute for Health and Welfare, the Finnish Centre for Pensions, the Social Insurance Institution of Finland, the Local Government Pensions Institution, Statistics Finland, the Finnish Work Environment Fund, and the Finnish Institute for Occupational Health.

None.

## Disclosures

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