ORIGINAL RESEARCH

Age-Related Trends in Home Blood Pressure, Home Pulse Rate, and Day-to-Day Blood Pressure and Pulse Rate Variability Based on Longitudinal Cohort Data: The Ohasama Study

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***Background*—**Home blood pressure is a more accurate prognosticator than office blood pressure and allows the observation of day-to-day blood pressure variability. Information on blood pressure change during the life course links the prediction of blood pressure elevation with age. We prospectively assessed age-related trends in home blood pressure, home pulse rate, and their day-to-day variability evaluated as a coefficient of variation.

***Methods and Results*—**We examined 1665 participants (men, 36.0%; mean age, 56.2 years) from the general population of Ohasama, Japan. A repeated-measures mixed linear model was used to estimate the age-related trends. In a mean of 15.9 years, we observed 5438 points of measurements including those at baseline. The home systolic blood pressure linearly increased with age and was higher in men than in women aged <70 years. There was an inverse-U-shaped age-related trend in home diastolic blood pressure. The day-to-day home systolic blood pressure linearly increased with age in individuals aged >40 years. However, an U-shaped age-related trend in day-to-day diastolic blood pressure variability with the nadir point at 65 to 69 years of age was observed. No significant sex differences in the day-to-day blood pressure variability were observed ($P \geq 0.22$). The average and day-to-day variability of home pulse rate decreased with age but were lower and higher, respectively, in men than in women.

***Conclusions*—**The current descriptive data are needed to predict future home blood pressure and pulse rate. The data also provide information on the mechanism of day-to-day blood pressure and pulse rate variability. **(*J Am Heart Assoc*. 2019;8:e012121. DOI: 10.1161/JAHA.119.012121.)**

Key Words: blood pressure • blood pressure measurement/monitoring • epidemiology • heart rate/heart rate variability • home blood pressure

High blood pressure (BP) is still strongly related to health deterioration worldwide,[1] but is a preventable and modifiable risk factor. Information on the change in BP during the life course is essential from both clinical and public health standpoints because it is associated with the prediction and prevention of BP elevation with age. Previous prospective studies based on the general population indicate the age-related trends in office BPs.[2–6] However, recent guidelines

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Accompanying Tables S1 through S4 and Figures S1 through S11 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.012121

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Clinical Perspective

What Is New?

- The present study indicated for the first time the longitudinal changes in home blood pressure (BP), home pulse rate, and their day-to-day variability with a prospective cohort design.
- Home systolic BP linearly increased, but there was an inverse-U-shaped age-related trend in home diastolic BP.
- Day-to-day systolic BP variability linearly increased with age but there was a U-shaped association between day-to-day diastolic BP variability and age, without any significant sex differences, and the home PR and day-to-day PR variability decreased with age.

What Are the Clinical Implications?

- Present descriptive data are needed to predict the future home BP, home PR, and their day-to-day variability.
- The present findings may provide information on the mechanism of day-to-day BP and PR variability.

recommend the measurement of out-of-office BP[7–9] since it is a more reliable predictor of prognosis and strongly related to target organ damages than office BP.[10–12]

Home BP is the self-measured BP not in the office or clinic but in a home setting under a stable condition.[13] Home BP is a more accurate prognosticator than office BP because of the greater number of readings, elimination of the white-coat effect, and avoidance of measurement error through the use of automated BP monitors.[13] Furthermore, the multiple measurements of home BP allow the observation of home pulse rate (PR) as well as day-to-day BP and PR variability, which are associated with an elevated risk for cardiovascular disease.[14–18] Furthermore, day-to-day BP variability is a predictor for cognitive decline and dementia.[19,20]

Some previous cross-sectional studies including ours show the home BP, home PR, and their day-to-day variability across age groups.[21–23] However, since an elevated BP at a younger age results in fatal cardiovascular events in later life, the cross-sectional study design contributes to an underestimation of BP in elderly individuals. Moreover, in previous studies, the day-to-day variability in BP or PR was evaluated as the interindividual SD.[22,23] The SD is known to be strongly affected by the corresponding mean level. The information on sex difference between these age-related trends is also limited.

We assessed age-related trends in home BP, home PR, and day-to-day BP or PR variability according to sex using prospective data. The prospective cohort design can exclude survival bias[24] because interindividual changes in BPs with age can be observed. The day-to-day variability was evaluated as the coefficient of variation (CV), which is the SD divided by the mean level.

Methods

Because of the sensitive nature of the data from the Japanese cohort, the data and study materials will not be made available to other researchers for purposes of the reproduction of results or replication of the procedure. All analytical methods will be described in this section.

Study Design

This report was part of the Ohasama study, which is a prospective cohort study that was started in 1986. Details of the study including socioeconomic and demographic characteristics of this region have been described previously.[25,26] The study complied with the Declaration of Helsinki, and the study protocol was approved by the Institutional Review Boards of Teikyo University, Tohoku Medical and Pharmaceutical University, and Tohoku University.

We first performed the largest examination for home BP measurements between 1988 and 1995. After 1997, we conducted follow-up examinations every 4 years. For the current analyses, the data collected between 1988 and 1995 were used as the baseline, and those collected between 1997 and 2017 were used as the follow-up data.

Participants

We contacted all 4969 residents aged ≥35 years in Ohasama between 1988 and 1995. Residents were ineligible if they were not at home during working hours of study investigators or nurses (n=1057) or if they were hospitalized (n=166) or incapacitated (n=94). Of the remaining 3652 residents, 3090 (84.6%) participated at baseline. We further excluded 1425 participants from the analysis because they did not undergo home BP or home PR measurements ≥5 days at baseline (n=537), did not participate in the follow-up examinations for home BP measurements (n=829), or did not undergo home BP or home PR measurements ≥5 days at the follow-up examination (n=59). Thus, the total number of participants analyzed was 1665. All participants provided informed consent.

BP Measurements

Public health nurses or study investigators instructed participants how to measure their home BP using the Omron HEM 401C,[27] 701C, 747IC-N, or 7080IC cuff-oscillometric device (Omron Healthcare, Kyoto, Japan).[22,27–30] The last 3 devices are similar to HEM-705IT, which was previously validated.[22,29,30]

Participants were asked to measure their home BP for 4 weeks, after ≥2 minutes of rest in the morning within 1 hour after awakening, maintaining the arm-cuff position at heart level during rest, and, if applicable, before taking their

BP-lowering medications.[7,13,31] Although some participants measured BP twice or more per occasion, the first value from each measurement was used in order to exclude individual selection bias.[13] We defined home BP and PR as the mean of all measurements. Day-to-day variability of home BP or PR was computed as within-subject CV of measurements as well as SD.

Data Collection

At baseline, study nurses measured anthropometric characteristics and administered questionnaires inquiring into each participant's medical history, medication use, and smoking and alcohol consumption. Hypercholesterolemia was defined as a serum cholesterol level ≥5.68 mmol/L (220 mg/dL) or use of lipid-lowering drugs. Diabetes mellitus was defined as a random glucose level ≥11.1 mmol/L (≥200 mg/dL), a fasting glucose level ≥7.0 mmol/L (≥126 mg/dL), or the use of oral antidiabetic drugs or insulin.

Statistical Analysis

To analyze the differences in participant characteristics between groups, we compared means and proportions using a *t* test and the Fisher exact test for univariate analysis. For computing age-adjusted *P* values, we used logistic regression analysis.

We assessed adjusted age-related trends of BP, PR, and their day-to-day variability by a repeated-measures mixed linear model with autoregressive order 1 (AR (1)) correlation structure. AR(1) is a standard method for the covariance matrix in mixed model analyses of longitudinal data.[3] The mixed model included age, sex, an interaction term (age× sex), and the following parameters at baseline as the fixed effect: body mass index, current smoking, alcohol consumption, diabetes mellitus, hyperlipidemia, history of cardiovascular disease, and antihypertensive medication use.

The age at baseline and follow-up duration are dependent on the participants. Least-square means of each time point of 5-year increase subsets from those aged 35 and >80 years were used for age-related trends. We interpolated missing values of body mass index (n=27) from the regression slope on age after stratification for sex. For participants with unknown alcohol consumption status (n=346), we set design variables coded 1 or 0 if the data were missing or present. We included 7 participants with unknown smoking status into nonsmokers because of the small number of missing values. We performed the stratification analysis according to the use of antihypertensive medication. Our previous studies demonstrated that day-to-day BP and PR variability, home BP, and home PR were associated with each other.[32,33] Therefore, in a sensitivity analysis, the age-related trend in day-to-day BP variability was further adjusted for home BP, home PR, and day-to-day PR variability. Similarly, the age-related trend in day-to-day PR variability was further adjusted for home BP, home PR, and day-to-day BP variability. The mixed model computed the least-squares means as well as standard errors of BP, PR, and their day-to-day variability according to the category and tested the difference among all 20 sex-age groups after Tukey-Kramer adjustment. To assess the difference between actual measurements and estimated values, the calculated values from 1-way analysis of covariance (ANCOVA), in which missing data are not allowed, were compared with the estimated values from the mixed data. The present longitudinal data were treated as cross-sectional data when the 1-way ANCOVA analysis was used. Statistical significance was set at an α-level <0.05 on 2-tailed tests. Data are expressed as mean±SD, unless otherwise noted. SAS version 9.4 (SAS Institute, Cary, NC) was used in the statistical analysis.

Results

Participant Characteristics

Of the 1665 participants, 1065 (64.0%) were female. At baseline, 433 (26.0%) were treated with antihypertensive medications, and the mean values were 56.2±10.6 years for age, 121.6±13.9 mm Hg for home systolic BP, 74.1±9.8 mm Hg for home diastolic BP, 67.3±7.5 beats per minute for home PR, 6.8±2.2% for CV of home systolic BP, 8.7±3.1% for CV of home diastolic BP, and 8.4±3.2% for CV of home PR. Baseline characteristics according to sex and age at baseline are presented in Table S1. In both women and men, the proportion of participants receiving antihypertensive therapy, home systolic BP, and CV of home systolic BP consistently increased with an increase in the baseline age (Table S1).

The present study included a higher proportion of middle-aged to young or old individuals than observed in the population of Ohasama in 1990 (Figure S1). We compared 1665 participants included in the present analysis with 888 who did not visit for follow-up examination but for whom home BP and PR information at baseline was available. We found that the participants not visiting for follow-up examinations were significantly older, and after adjustment for age, had a significantly higher proportion of smokers, home systolic BP, and home PR, among both women and men (Table S2).

Age-Related Trends

The mean follow-up period between the baseline and final visit was 15.9±6.0 years (median, 14.5 years; 25th–75th percentiles, 10.3–21.7 years). The number of follow-up

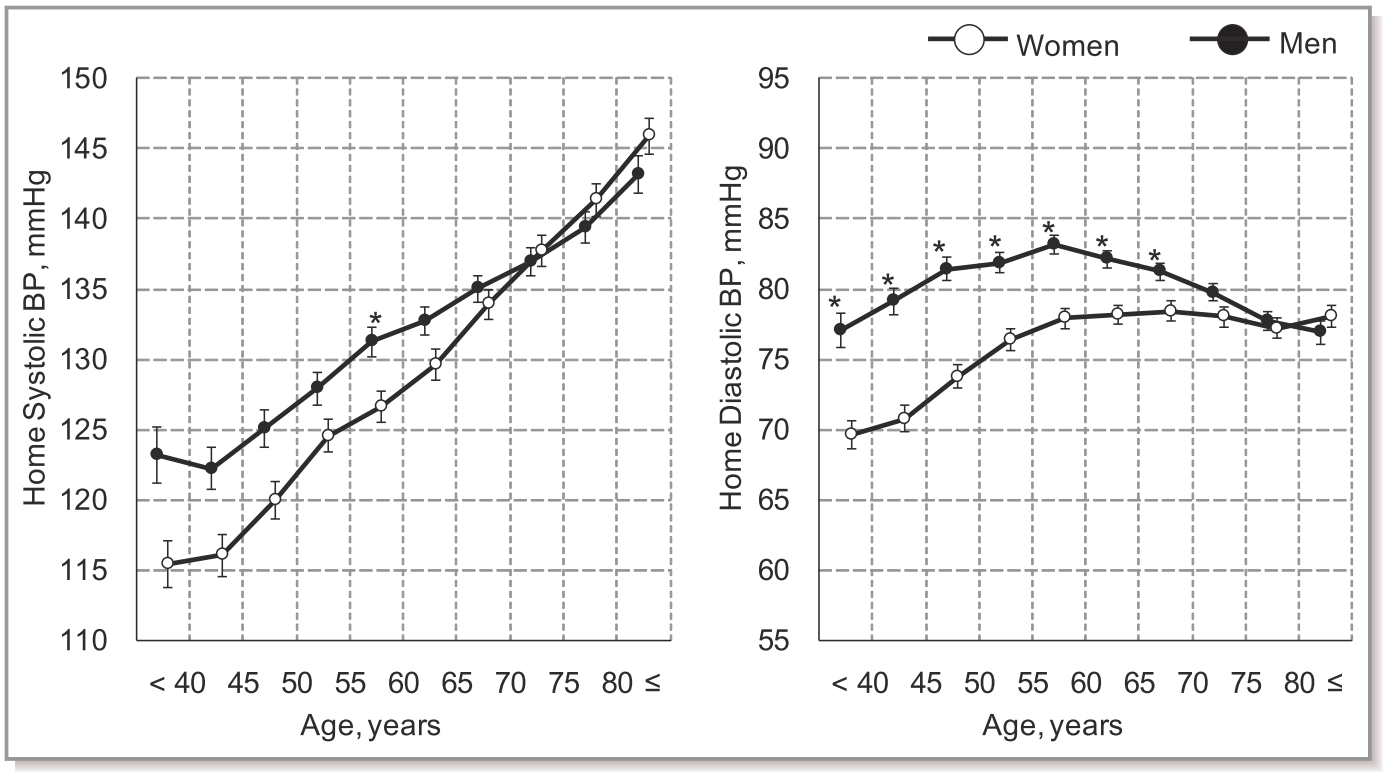

Figure 1. Age-related trends in home BPs according to sex. The mixed model included age, sex, interaction term (age×sex), and the following parameters at baseline: body mass index, current smoking status, alcohol consumption, diabetes mellitus, hyperlipidemia, history of cardiovascular disease, and antihypertensive medication use. BP indicates blood pressure. *P<0.05 vs women after adjusting with Tukey–Kramer test.

examinations without baseline visit was 1, 2, 3, 4, or 5 in 588, 447, 300, 259, and 71 participants, respectively. Numbers of observations according to age category are indicated in Table S3. Therefore, we used a total of 5438 points of measurements including those at baseline and follow-up examinations.

The age-related trends in home BPs are shown in Figure 1. The home systolic BP increased with age in both women and men. The home systolic BP in men were higher than those in women aged <70 years. Meanwhile, the sex difference in home systolic BP gradually diminished with age. The home diastolic BP in men increased to 83.2 mm Hg in those aged 55 to 59 years and decreased with age after the peak. In women, the home diastolic BP increased to 78.4 mm Hg in those aged 65 to 69 years and slightly decreased to 77.2 mm Hg in those aged 75 to 79 years (Figure 1).

The CV of home systolic BP consistently increased with age in those aged >40 years (Figure 2). The CVs of home diastolic BP decreased to 7.4% for men and 7.6% for women in those aged 65 to 69 years and increased with age after the points. No significant sex differences in the CVs of home BPs were observed (P≥0.22 after Tukey-Kramer adjustment) (Figure 2).

The home PR decreased with age, and the home PR in women aged 70 to 79 years was significantly higher than that in men with the same age (P≤0.014 after Tukey-Kramer adjustment) (Figure 3). The CV of home PR decreased with age in both women and men but tended to be higher in men than in women. The CV of home PR in men aged 50 to 59 years was significantly higher than that in women (P≤0.035 after Tukey-Kramer adjustment).

The results with no adjustments for confounding factors are shown in Figure S2. Similar results were observed in relation to the age-related trends of home PR and CVs of BP and PR, while the differences in systolic BP and diastolic BP between men and women were wider than those adjusted for confounding factors.

Sensitivity Analysis

Similar results were observed even after excluding the participants who visited <3 times for follow-up (Figure S3) or using data based on 4263 observations of 1232 participants untreated at baseline (Figure S4). In 680 untreated participants at baseline and during follow-up (2164 observations), the systolic BP in men and diastolic BP in women after 70 years seemed to increase more clearly than those in all participants, although the age-related trends in BP or PR indices are almost similar (Figure S5). In 433 participants treated at baseline (1175

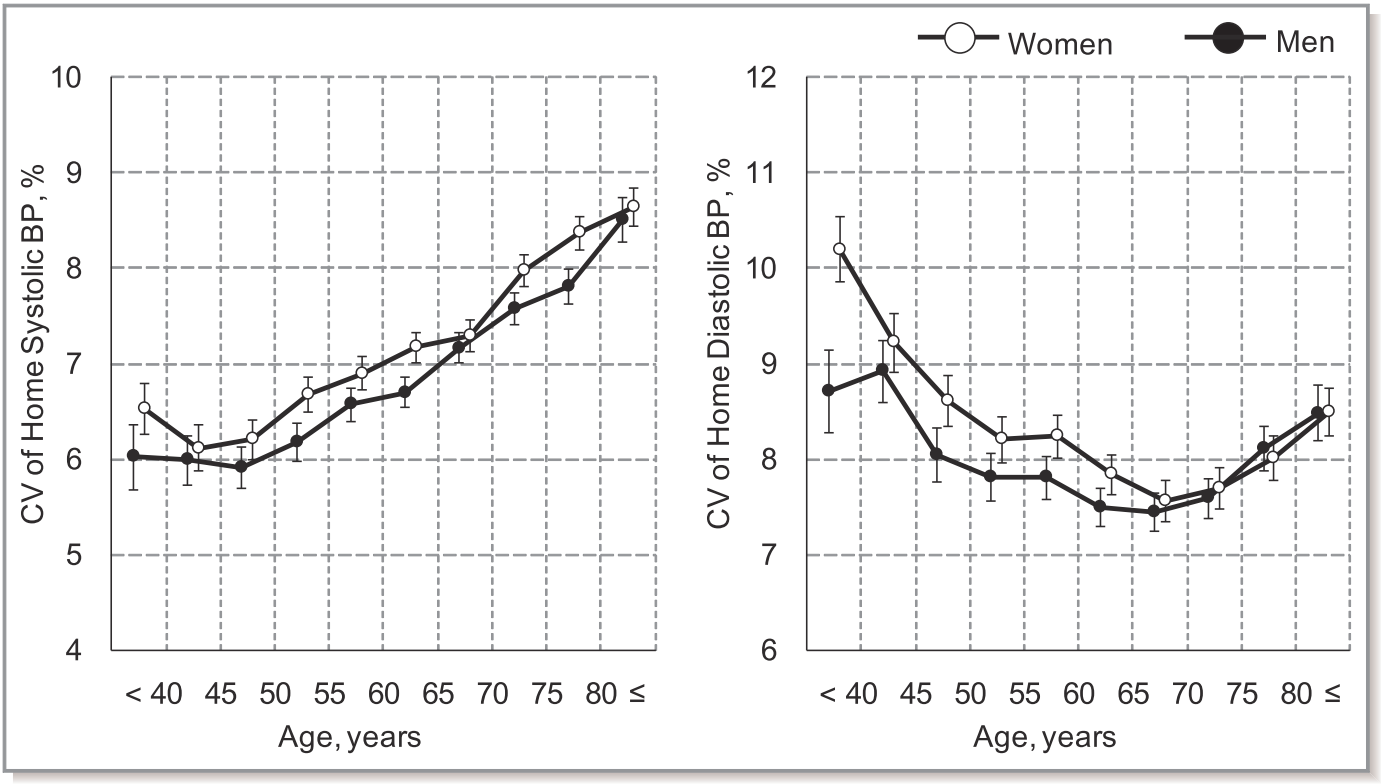

Figure 2. Age-related trends in CVs of home BPs according to sex. The mixed model included the same variables as those indicated in Figure 1. Bars indicate standard errors. There was no significant difference between women and men. BP indicates blood pressure; CV, coefficient of variation.

observations), the home systolic BP and CV of home systolic BP similarly increased with age, while the home diastolic BP decreased with age in those aged >45 years (Figure S6). Although age-related trends in home PR and CVs of home diastolic BP and PR appear to be similar, the ranges of standard errors were wide (Figure S6).

Further adjustments for home systolic/diastolic BP, home PR, and CV of home PR did not largely change the age-related trends in CVs of home systolic/diastolic BP (Figure S7). The age-related trends in CVs of home PR were also similar even after further adjustments for home PR, home systolic BP, and CV of home systolic BP at the same follow-up examinations (Figure S7).

The age-related trends in SDs of home BP and PR were similar to those in CVs (Figure S8). The SD of home systolic BP in women/men linearly increased from 7.3/7.3 mm Hg in those aged 40 to 44 years to 12.5/12.1 mm Hg in those aged >80 years. The SD of home diastolic BP in women/men decreased to 6.0/5.9 mm Hg in those aged 65 to 59 years but subsequently increased to 6.5/6.6 mm Hg in those aged >80 years. The SD of home PR decreased with age and was higher in men than in women. These age-related trends remained after further adjustments for home BP or PR at the same follow-up examinations (Figure S8).

We performed the stratified analysis according to the median follow-up of 14.5 years instead of sex (Figure S9). While age-related trends in the participants with longer follow-up period were similar to the main results in Figures 1 through 3, PR levels, day-to-day diastolic BP variability, and day-to-day PR variability in those with follow-up of <14.5 years were higher after ≈65 years (Figure S9). Participants with a short follow-up period had significantly older age, higher body mass index, higher proportions of diabetes mellitus, history of cardiovascular disease, used antihypertensive treatment, had higher home BP and PR levels, and elevated day-to-day systolic BP variability (Table S4). Although the stratified analysis was similarly performed according to the baseline year of 1992 (Figure S10), no significant difference was found in age-related trends in BP or PR indices between the 1998 to 1991 and 1992 to 1995 groups.

We compared the results from ANCOVA and the mixed model. The age-related trends in BP, PR, and the day-to-day variability obtained using the ANCOVA were similar to those from the mixed model (Figure S11).

Discussion

The present study indicated for the first time the longitudinal changes in home BP, home PR, and their day-to-day variability with a prospective cohort design. Home systolic BP linearly increased with age. There was an inverse-U-shaped age-

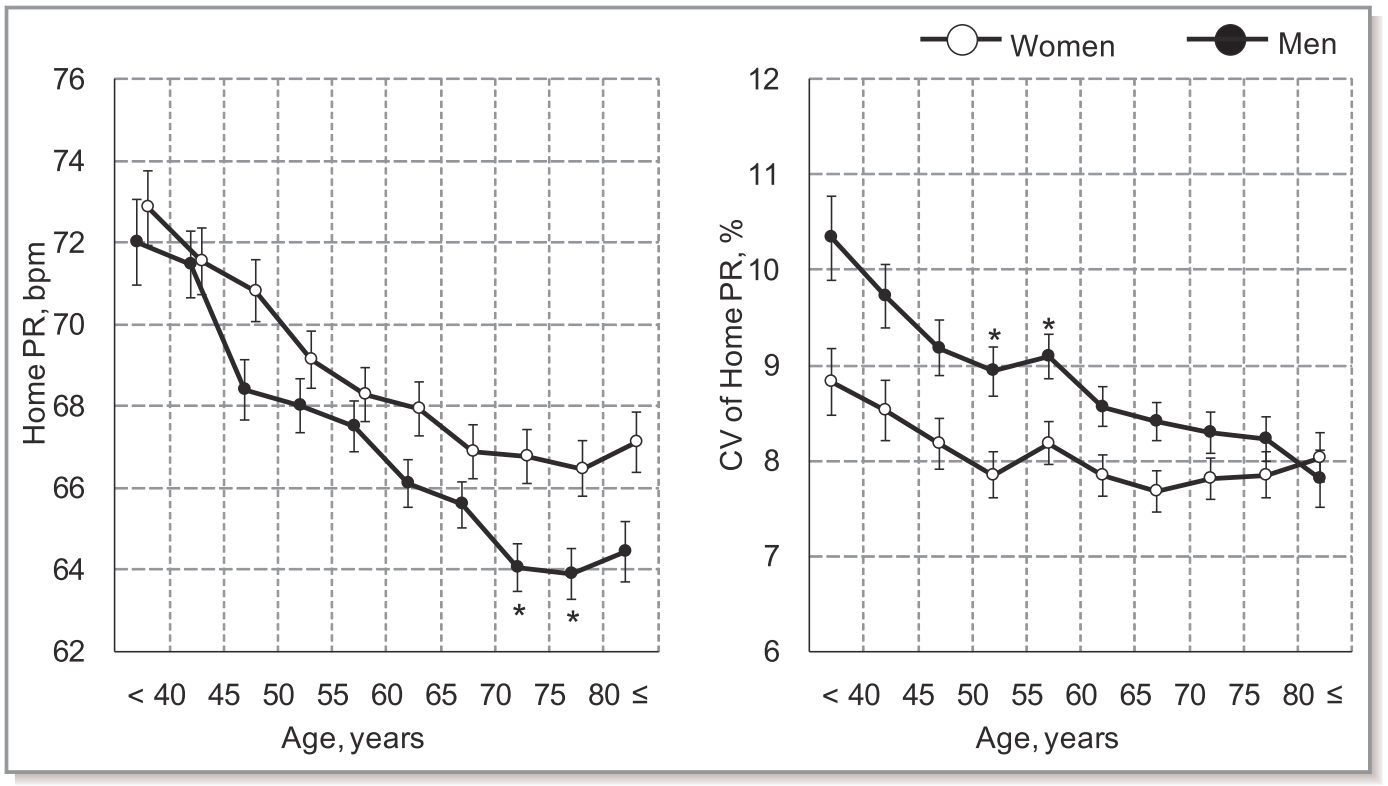

Figure 3. Age-related trends in home PR and CV of home PR according to sex. The mixed model included the same variables as those indicated in Figure 1. Bars indicate standard errors. CV indicates coefficient of variation; PR, pulse rate. *P<0.05 vs women after adjusting with Tukey–Kramer test.

related trend in home diastolic BP. Day-to-day systolic BP variability increased linearly with age, but a U-shaped association between day-to-day diastolic BP variability and age was observed. The home PR and day-to-day PR variability decreased with age.

The IDHOCO (International Database of Home Blood Pressure in Relation to Cardiovascular Outcome) study, which is a meta-analysis including the Ohasama study, demonstrated almost similar age-related trends in home systolic and diastolic BPs in untreated participants by a cross-sectional study design.[21] However, the sex difference and age-related trend in day-to-day BP and PR variability are not shown in the IDHOCO study.[21] As the present study indicated, women have lower home systolic and diastolic BPs <70 years of age, but the sex differences in home BPs seemed to be diminished in elderly individuals. Although 1 previous prospective cohort study based on office BP indicated a parallel shift in the time course of systolic BP by sex,[2] other results from several studies[5,34] were consistent with our findings. The peak of home diastolic BP was at 55 to 59 years in men but 65 to 69 years in women. Diastolic BP in women without treatment at baseline and during follow-up linearly increased without the peak (Figure S5). Since a decreased diastolic BP indicates atherosclerosis or target organ damage,[35] this result may imply that estrogen or other sex-related differences weaken the progression of atherosclerosis.[36]

The age-related linear trend of day-to-day systolic BP variability was observed even after further adjusting the home BP. Meanwhile, the day-to-day diastolic BP variability decreased until 65 to 69 years of age and increased thereafter. In relation to day-to-day diastolic BP variability, the mechanisms of age-related trend in those aged <65 and ≥65 years may be different. For those aged ≥65 years, both day-to-day systolic and diastolic BP variability increased with age. Previous prospective studies indicated the positive association of day-to-day systolic and diastolic BP variability with cognitive deterioration or dementia.[19,20] These studies were based on the population with a mean age of 63 years[19] or 71 years at baseline.[20] We also reported that common factors associated with higher day-to-day systolic and diastolic BP variability were older age, female sex, elevated home BP, low home PR, elevated home PR variability, alcohol consumption, and sedentary lifestyle.[32] These factors including cognitive function may be involved in age-related trends of day-to-day systolic and diastolic BP variability in those aged >65 years. However, the mechanisms of age-related trends in day-to-day diastolic BP variability in individuals aged <65 years are unclear. No specific factors associated with

day-to-day systolic or diastolic BP variability have been found. The difference in age-related trends between day-to-day systolic and diastolic BP variability may occur because of changes in adrenergic response or BP augmentation, which can cause isolated systolic hypertension in young adults.[37]

Similar to those in previous cross-sectional reports, the PR decreased with age and women had higher PR than men.[14,22,38] There is scarce information on day-to-day PR variability,[22] while many studies indicated the short-term heart rate variability such as R-R intervals measured by 24-hour ambulatory Holter echocardiography monitoring.[38–40] The short-term heart rate variability decreased with age and was higher in men than in women.[38–40] Therefore, the age-related trend in short-term heart rate variability appears to be similar to that of day-to-day PR variability. However, our previous study demonstrated that the correlation coefficient between within-day PR variability determined by ambulatory monitoring and day-to-day PR variability was only 0.08.[33] Factors associated with within-day PR variability differed from those associated with day-to-day PR variability. [33] Moreover, day-to-day PR variability was positively associated[16] but short-term PR variability was inversely associated with cardiovascular disease.[41] We recently reported the positive associations of day-to-day BP and PR variability with a high N-terminal pro-B-type natriuretic peptide level.[42] Based on these results,[16,42] an elevated day-to-day PR variability can be a risk factor for cardiovascular disease or target organ damage. There is a discrepancy between the associations of day-to-day PR variability with an elevated cardiovascular risk and age-related trend. This is also the case in PR level,[43] diastolic BP level, and day-to-day diastolic BP variability.[16] An intraindividual age-related trend can be distinguished from its predictive power assessed by a longitudinal analysis.

The short follow-up period was associated with higher PR, day-to-day diastolic BP variability, and day-to-day PR variability after ≈65 years (Figure S9). When compared with the participants with a long follow-up period, those with a short follow-up period had more risk factors of cardiovascular disease (Table S4), which can lead to a worse prognosis. This implies that the age-related trend in PR and day-to-day diastolic BP or PR variability might be associated with future health conditions.

The present study has several limitations. First, the present study excluded older participants with high BP or high PR and potentially included healthy individuals (Figure S1 and Table S2). Owing to this bias, the underestimation of home BP or home PR in older age could persist, although a longitudinal analysis was performed in the present study. Furthermore, since all study participants were Japanese, the external validity of the findings could be limited. However, a linear age-related trend in systolic BP and the inverse-U-shaped association between diastolic BP and age were cross-sectionally observed in Western populations.[6,21] The age-related trends in BP or PR indices found in the present study might be similar among Asian and Western populations. Second, the systolic BP decreased during the past decades.[44] The BPs in younger age, which were collected in an earlier period, may be overestimated because they could be affected by the baseline levels, which were collected around the 1990s. Furthermore, management guidelines for hypertension had also changed during the follow-up in the present study. The target office systolic/diastolic BP in patients aged ≥65 years was <140/90 mm Hg in the Japanese Society of Hypertension (JSH) 2009 guideline.[28] However, in the 2014 JSH guideline, the target office BP in those aged ≥75 years was changed to <150/90 mm Hg (if tolerance is present, <140/90 mm Hg).[7] The thresholds based on home BP is 5 mm Hg lower than these target values. These guideline changes might also have affected the present findings. Third, we could not consider participants' occupations, daily activities, or food consumption, which might also affect day-to-day BP variability in the present study. These factors can cause, for instance, differences in the age-related trend between diastolic BP level and its day-to-day variability. Frailty can also affect BP or PR, especially in individuals aged >70 years. Although frailty had not been investigated in the present study, most participants could measure their home BP and participate in our investigations. The present study includes few individuals with severe frailty or who were bedridden. Finally, comparing the results from ANCOVA and the mixed model (Figure S11), it appears that the estimation of missing values by the mixed model could be limited in the present study. However, it also suggests that the mixed model estimates robust values, not unrealistic ones.

Conclusions

We demonstrate the age-related trends in home BP, home PR, and their day-to-day variability by a prospective study based on the home BP data obtained in multiple examinations. The home BP was higher in men than in women, but the sex difference appears to diminish in elderly individuals. The age-related trends in day-to-day BP variability, especially day-to-day diastolic BP variability, differed from the mean values. Present descriptive data are needed to predict the future home BP and home PR. Furthermore, the present findings may provide information on the mechanism of day-to-day BP and PR variability.

Acknowledgments

All authors have contributed to this scientific work and approved the final version of the manuscript. Dr Satoh designed this study, performed the data analyses, and wrote the manuscript. Dr Metoki was deeply involved in the design

of the study and supervised the data analyses. Drs Asayama, Murakami, Hirose, Kikuya, Imai, and Ohkubo assisted with the data analyses and supervised the drafting of the manuscript. Drs Satoh, Kikuya, and Ohkubo were responsible for gathering and screening the data. Dr Ohkubo is the principal investigator of the Ohasama study. All authors were involved in data collection and had full access to all data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

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Disclosures

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Supplemental Material

Table S1. Characteristics of participants at baseline

	Age Category, Years Old			
	<40	40–59	60–69	≥70
Women	*n*=290	*n*=360	*n*=302	*n*=113
BMI, kg/m^2	23.5±3.1	23.9±3.2	23.8±3.1	22.9±3.5
Current smoking, %	2.4	2.2	1.3	1.8
Alcohol consumption, %	12.9	4.5	4.4	5.6
Diabetes, %	4.1	11.7	10.9	8.0
Hyperlipidemia, %	22.4	43.3	47.4	36.3
History of CVD, %	0.7	2.2	7.0	5.3
Antihypertensive treatment, %	5.2	21.4	37.7	59.3
Home systolic BP, mmHg	110.6±10.7	118.5±12.2	124.8±12.8	129.3±14.2
Home diastolic BP, mmHg	67.4±8.9	72.2±8.8	74±8.2	72.8±8.3
Home PR, bpm	69.3±6.8	66.8±6.4	67.1±7.2	66.6±7.9
CV of home systolic BP, %	6.4±2.1	6.9±2.0	7.2±2.1	8.1±2.6
CV of home diastolic BP, %	9.3±3.8	8.8±2.9	8.9±3.1	9.3±3.2
CV of home PR, %	8.1±3.0	7.9±2.8	7.9±2.9	8.6±3.3
Men	*n*=187	*n*=176	*n*=179	*n*=58
BMI, kg/m^2	24.0±2.7	23.6±2.8	23.0±2.5	22.5±3.0
Current smoking, %	57.2	42.3	43.3	34.5
Alcohol consumption, %	74.0	57.4	64.4	52.0
Diabetes, %	4.8	10.8	10.6	8.6
Hyperlipidemia, %	23.5	18.8	20.1	19.0
History of CVD, %	0.5	5.1	16.8	8.6
Antihypertensive treatment, %	7.5	23.3	41.9	51.7
Home systolic BP, mmHg	121.5±9.5	123.5±12.9	130.4±14.2	132.2±15.6
Home diastolic BP, mmHg	77.7±8.1	78.8±9.7	80.7±9.7	77.6±9.6
Home PR, bpm	69.5±7.5	66.7±7.4	65.4±9	62.1±7.1
CV of home systolic BP, %	6.1±2.1	6.4±2.0	6.6±2.0	7.7±2.2
CV of home diastolic BP, %	8.3±2.9	8.1±2.7	7.7±2.7	9.0±2.7
CV of home PR, %	9.4±3.2	9.1±4.2	8.5±3.4	8.9±3.0

Data on body mass index, smoking status, and alcohol consumption were unavailable for 27, 7, and 346 participants, respectively. CV, coefficient of variation; PR, pulse rate; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease.

Table S2. Characteristics in the followed and not followed participants.

	Follow-up Status		*P*	Age-Adjusted *P*
	Followed	Not Followed		
Women	*n*=1,065	*n*=472		
Age, years	56.4±10.6	65.8±13.9	<0.0001	-
BMI, kg/m^2	23.7±3.2	23.4±3.5	0.14	0.44
Current smoking, %	2.0	4.1	0.023	0.0053
Alcohol consumption, %	6.3	5.5	0.69	0.46
Diabetes, %	9.0	8.9	>0.99	0.63
Hyperlipidemia, %	38.0	32.8	0.058	0.0072
History of CVD, %	3.5	8.3	0.0002	0.058
Antihypertensive treatment, %	25.6	44.3	<0.0001	0.043
Home systolic BP, mmHg	119.3±13.8	127.8±15.7	<0.0001	<0.0001
Home diastolic BP, mmHg	71.5±9.0	73.4±9.5	<0.0001	0.14
Home PR, bpm	67.6±7.0	68.1±8.3	0.22	0.021
CV of home systolic BP, %	7.0±2.2	7.6±2.8	<0.0001	0.42
CV of home diastolic BP, %	9.0±3.2	9.5±4.0	0.038	0.19
CV of home PR, %	8.1±2.9	8.5±3.3	0.011	0.062
Men	*n*=600	*n*=416		
Age, years	55.9±10.7	63.2±13.6	<0.0001	-
BMI, kg/m^2	23.4±2.7	22.6±2.9	<0.0001	0.0066
Current smoking, %	46.5	47.0	0.90	0.041
Alcohol consumption, %	62.5	63.6	0.80	0.14
Diabetes, %	8.7	10.1	0.44	0.55
Hyperlipidemia, %	20.7	17.3	0.20	0.37
History of CVD, %	7.5	11.1	0.058	0.86
Antihypertensive treatment, %	26.7	35.8	0.0023	0.69
Home systolic BP, mmHg	125.8±13.3	131.4±16	<0.0001	0.0088
Home diastolic BP, mmHg	78.9±9.3	79.0±9.9	0.87	0.82
Home PR, bpm	66.8±8.2	67.9±8.6	0.037	<0.0001
CV of home systolic BP, %	6.5±2.1	6.8±2.5	0.028	0.82
CV of home diastolic BP, %	8.1±2.8	8.3±3.4	0.28	0.93
CV of home PR, %	9.0±3.5	8.7±3.4	0.27	0.47

Data on body mass index, smoking status, and alcohol consumption were unavailable for 155, 27, and 632 participants, respectively. CV, coefficient of variation; PR, pulse rate; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease.

Table S3. Number of observations according to age category

Number of observations, n	Age category									
	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	≥80
Women	94	118	194	309	437	599	592	558	382	243
Men	48	88	124	170	234	314	317	295	205	117

Data shows the number of observations from the baseline to the end of follow-up.

Table S4. Characteristics at baseline according to follow-up period

	Follow-up Period, Years		
	<14.5	≥14.5	*P*
n	827	838	
Age, years	61.0±10.2	51.5±8.8	<0.0001
Men, %	37.7	34.4	0.15
BMI, kg/m^2	23.4±3.1	23.8±3.0	0.0097
Current smoking, %	19.0	17.1	0.33
Alcohol consumption, %	23.5	23.7	0.92
Diabetes, %	11.4	6.4	0.0004
Hyperlipidemia, %	33.4	30.2	0.16
History of CVD, %	7.0	2.9	<0.0001
Antihypertensive treatment, %	36.5	15.6	<0.0001
Home systolic BP, mmHg	125.3±14.6	118.1±12.2	<0.0001
Home diastolic BP, mmHg	75.3±9.6	73.0±9.8	<0.0001
Home PR, bpm	67.0±7.7	67.6±7.3	0.094
CV of home systolic BP, %	7.0±2.2	6.5±2.0	<0.0001
CV of home diastolic BP, %	8.6±3.0	8.8±3.2	0.44
CV of home PR, %	8.3±3.1	8.5±3.3	0.084
Follow-up period, years	10.6±2.9	21.1±2.9	<0.0001

Data on body mass index, smoking status, and alcohol consumption were unavailable for 27, 7, and 346 participants, respectively. CV, coefficient of variation; PR, pulse rate; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease.

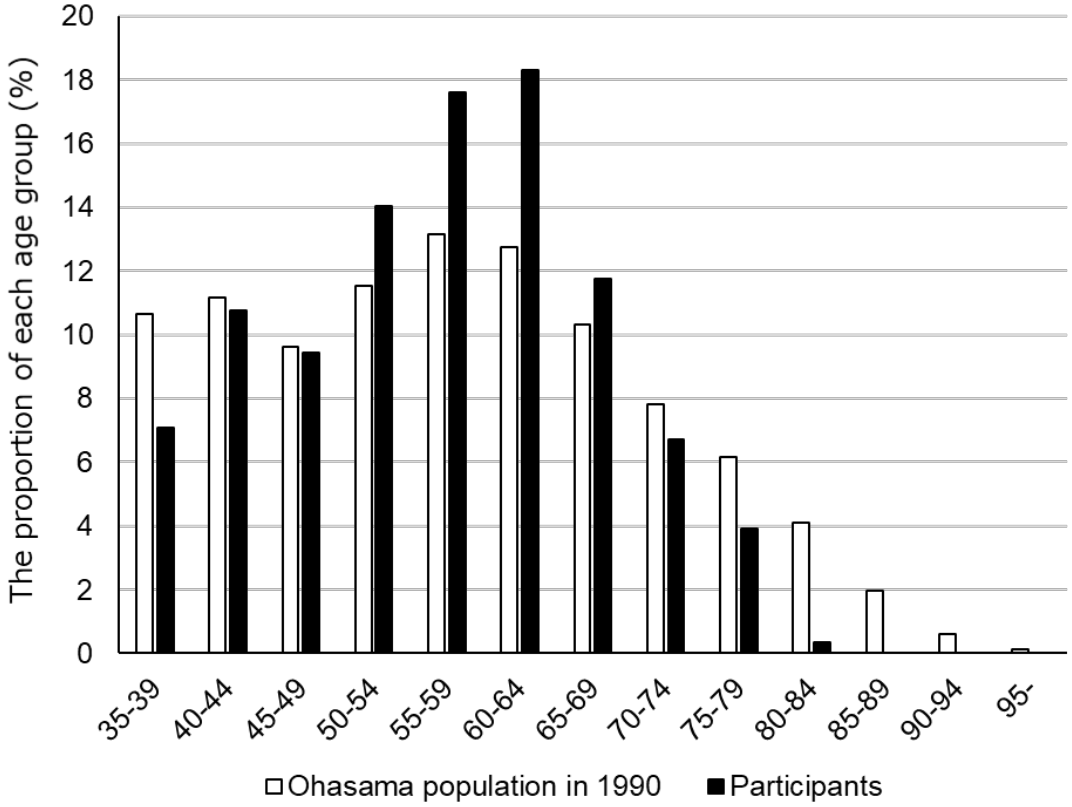

Figure S1. Age distribution of the population in 1990 and of the study cohort.

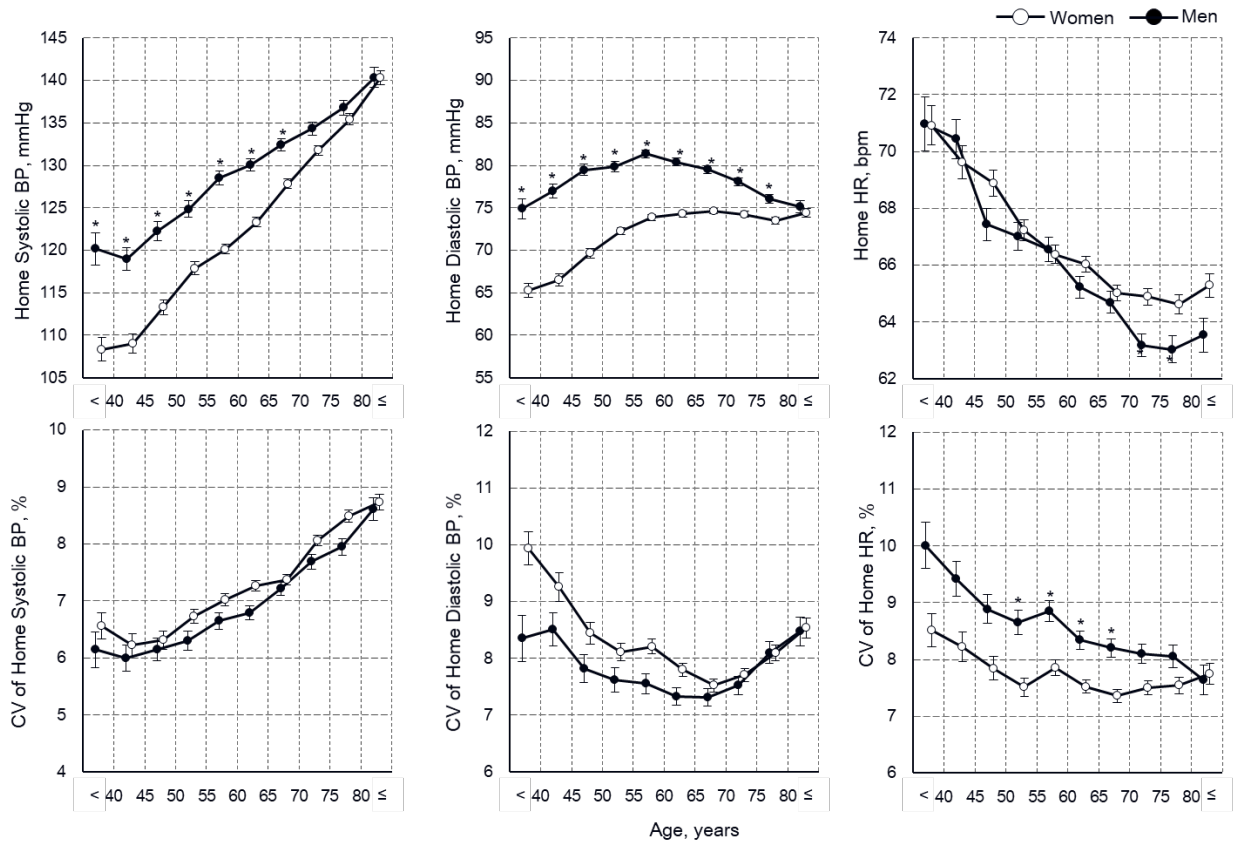

Figure S2. Age-related trends in home BP and home PR, and CVs of home BP and PR without adjustment for covariates.

The mixed model included age, sex, and interaction term (age × sex). Bars indicate standard errors. BP, blood pressure; CV, coefficient of variation; PR, pulse rate. *P<0.05 vs women in the same age group after adjusting with Tukey-Kramer test.

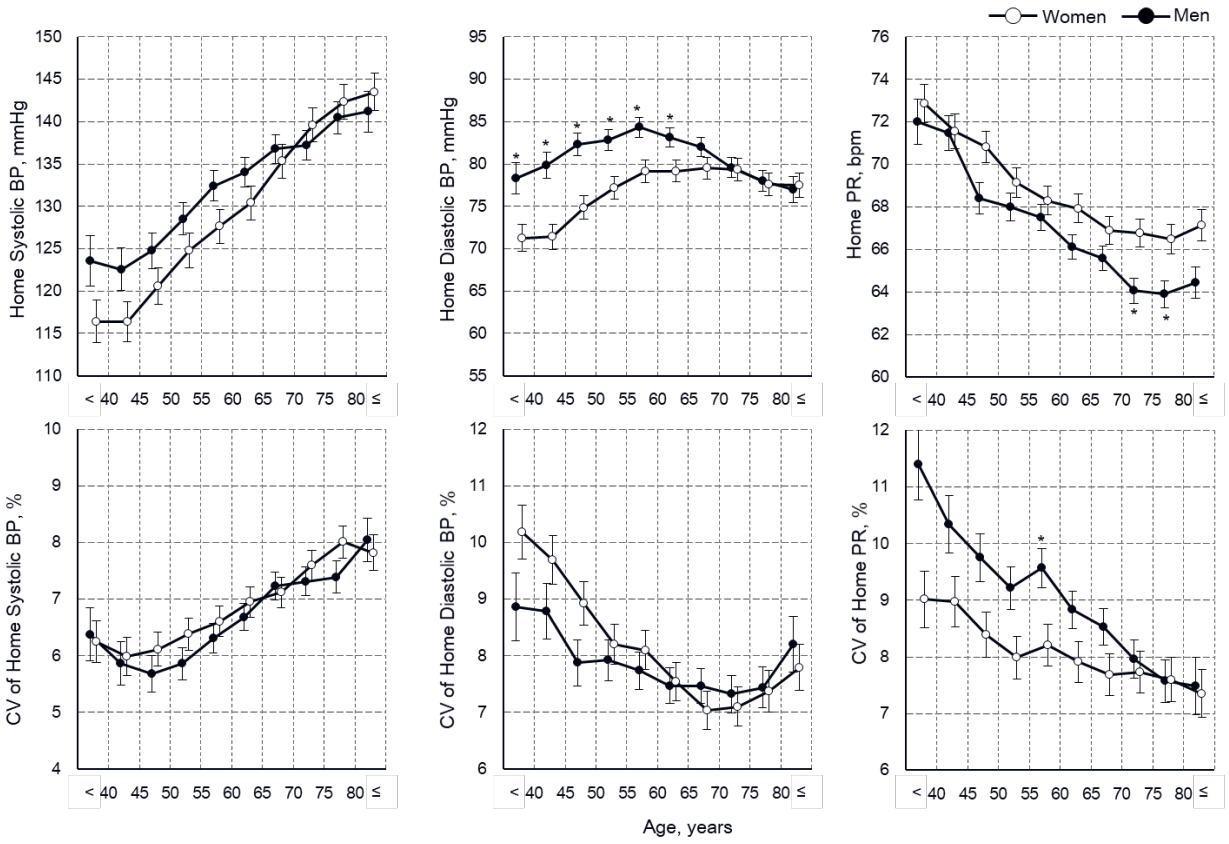

Figure S3. Age-related trends in participants who visited for ≥3 times during the follow-up period.

The results were based on 630 participants (2,921 observations) who visited ≥3 times for follow-up. The mixed model included age, sex, interaction term (age × sex), and the following parameters at baseline: body mass index, current smoking status, alcohol consumption, diabetes, hyperlipidemia, history of cardiovascular disease, and antihypertensive medication use. Bars indicate standard errors. BP, blood pressure; CV, coefficient of variation; PR, pulse rate. *P<0.05 vs. women in the same age group after Tukey-Kramer adjustment.

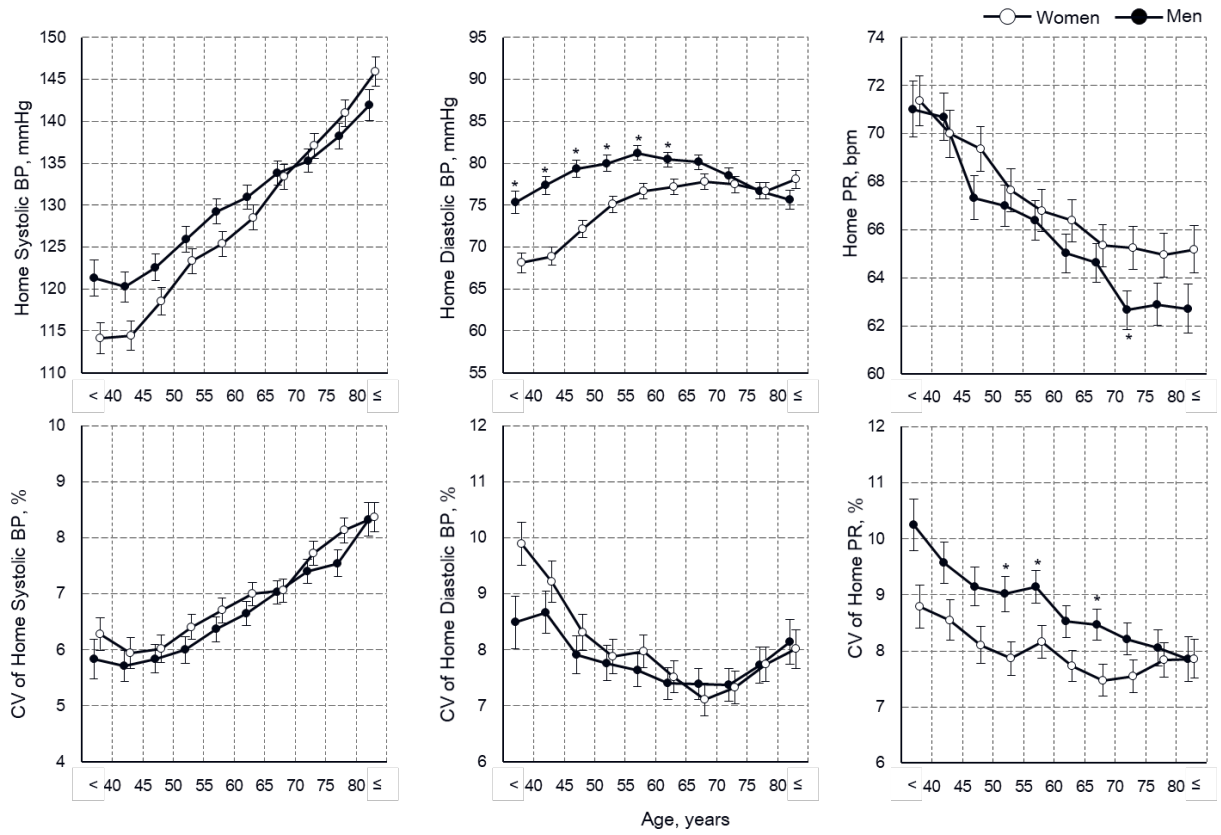

Figure S4. Age-related trends in home BP and home PR, and CVs of home BPs and home PR in the untreated participants at baseline.

The results were based on 1,232 participants (4,263 observations) untreated at baseline and during follow-up. The mixed model included age, sex, an interaction term (age × sex), and the following parameters at baseline: body mass index, current smoking, alcohol consumption, diabetes, hyperlipidemia, and history of cardiovascular disease. Bars indicate standard errors. BP, blood pressure; CV, coefficient of variation; PR, pulse rate. *P<0.05 vs women in the same age group after adjusting with Tukey-Kramer test.

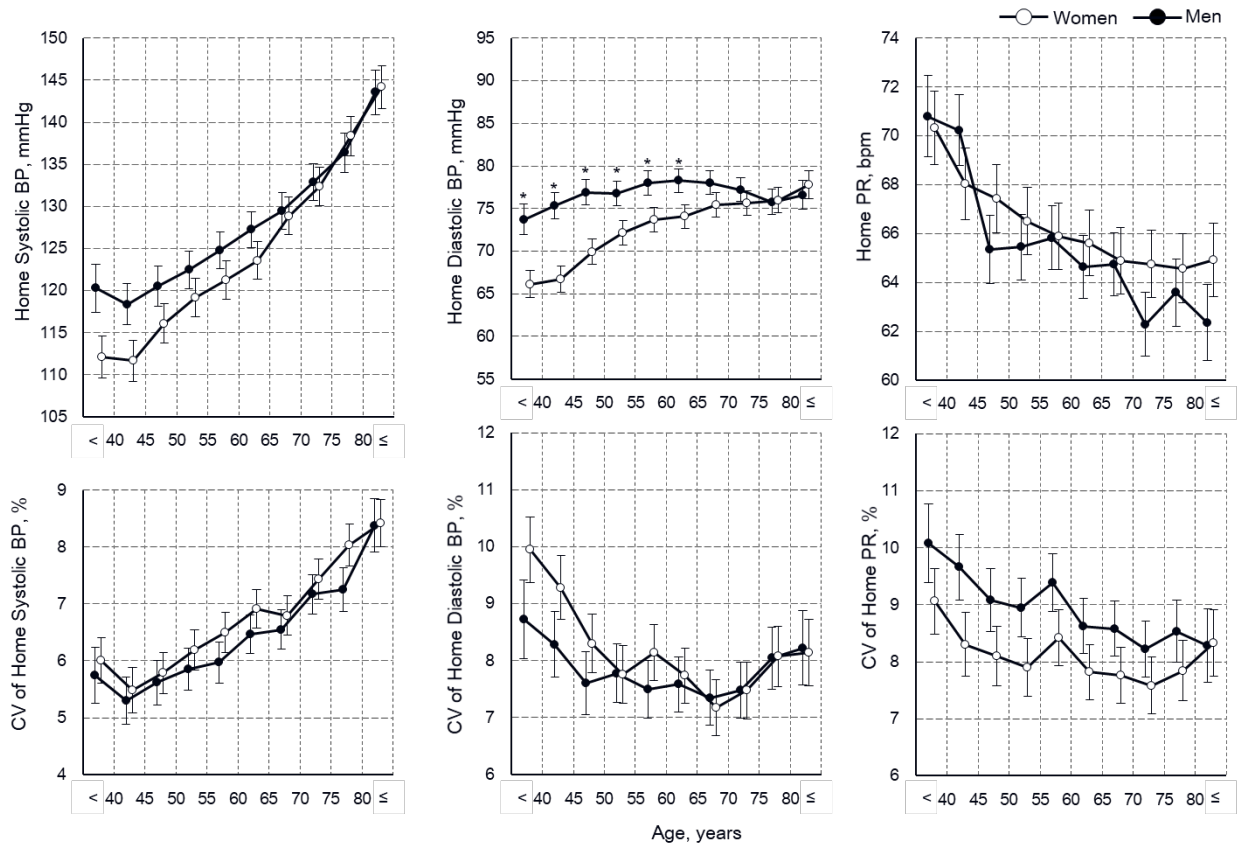

Figure S5. Age-related trends in home BP and home PR and CVs of home BPs and home PR in the untreated participants at baseline and during follow-up.

The results were based on 680 participants (2,164 observations) untreated at baseline and during follow-up. The mixed model included age, sex, interaction term (age × sex), and the following parameters at baseline: body mass index, current smoking status, alcohol consumption, diabetes, hyperlipidemia, and history of cardiovascular disease. Bars indicate standard errors. BP, blood pressure; CV, coefficient of variation; PR, pulse rate. *P<0.05 vs women in the same age group after adjusting with Tukey-Kramer test.

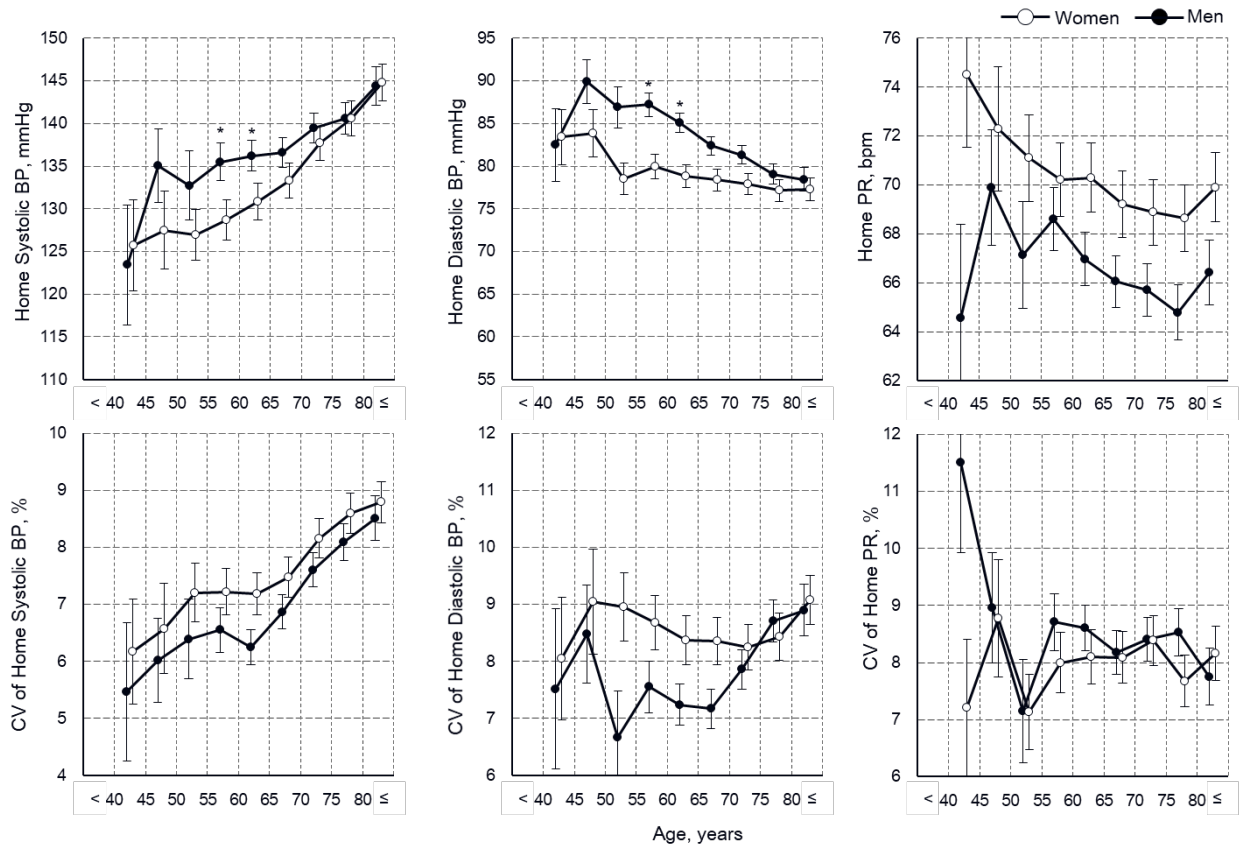

Figure S6. Age-related trends in home BP and home PR, and CVs of home BPs and home PR in the treated patients at baseline.

The results were based on 433 participants (1,175 observations) untreated at baseline and during follow-up. There are no data on individuals aged <40 years. The mixed model included age, sex, an interaction term (age × sex), and the following parameters at baseline: body mass index, current smoking status, alcohol consumption, diabetes, hyperlipidemia, and history of cardiovascular disease. Bars indicate standard errors. BP, blood pressure; CV, coefficient of variation; PR, pulse rate. *P<0.05 vs women in the same age group after adjusting with Tukey-Kramer test

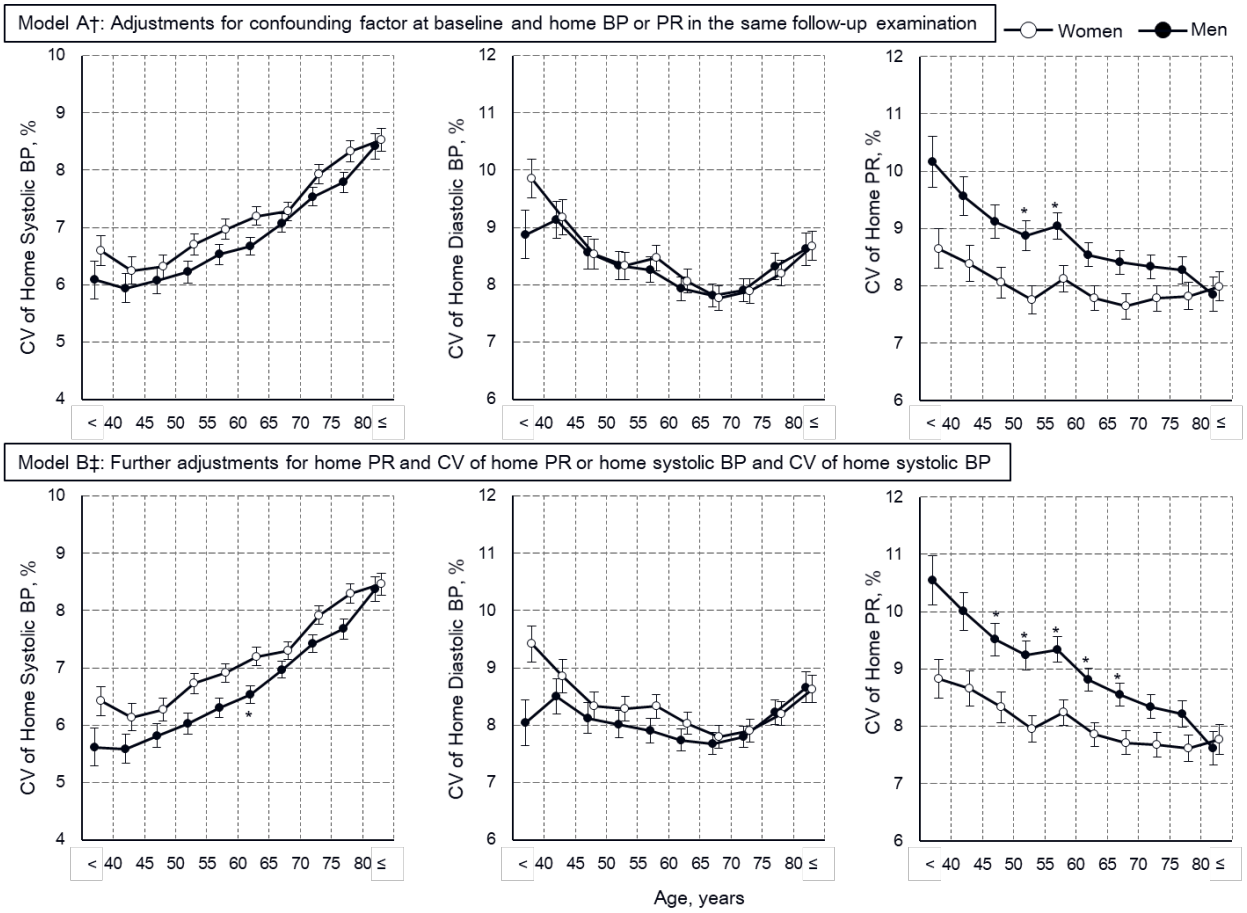

Figure S7. Age-related trends in CVs of home BP and PR after further adjustments for the corresponding mean values.

Bars indicate standard errors. BP, blood pressure; CV, coefficient of variation; PR, pulse rate. *P<0.05 vs. women in the same age group after adjusting with Tukey-Kramer test.
†In addition to the model in Figure 1, home systolic BP, diastolic BP, or PR at the same follow-up examinations was included in model A for the estimation of CVs of home systolic BP, diastolic BP, or PR.
‡In addition to model A, home PR and CV of home PR at the same follow-up examinations were included in model B for the estimation of CVs of home BPs. Home systolic BP and CV of home systolic BP at the same follow-up examinations were included in model B for the estimation of CVs of home PR.

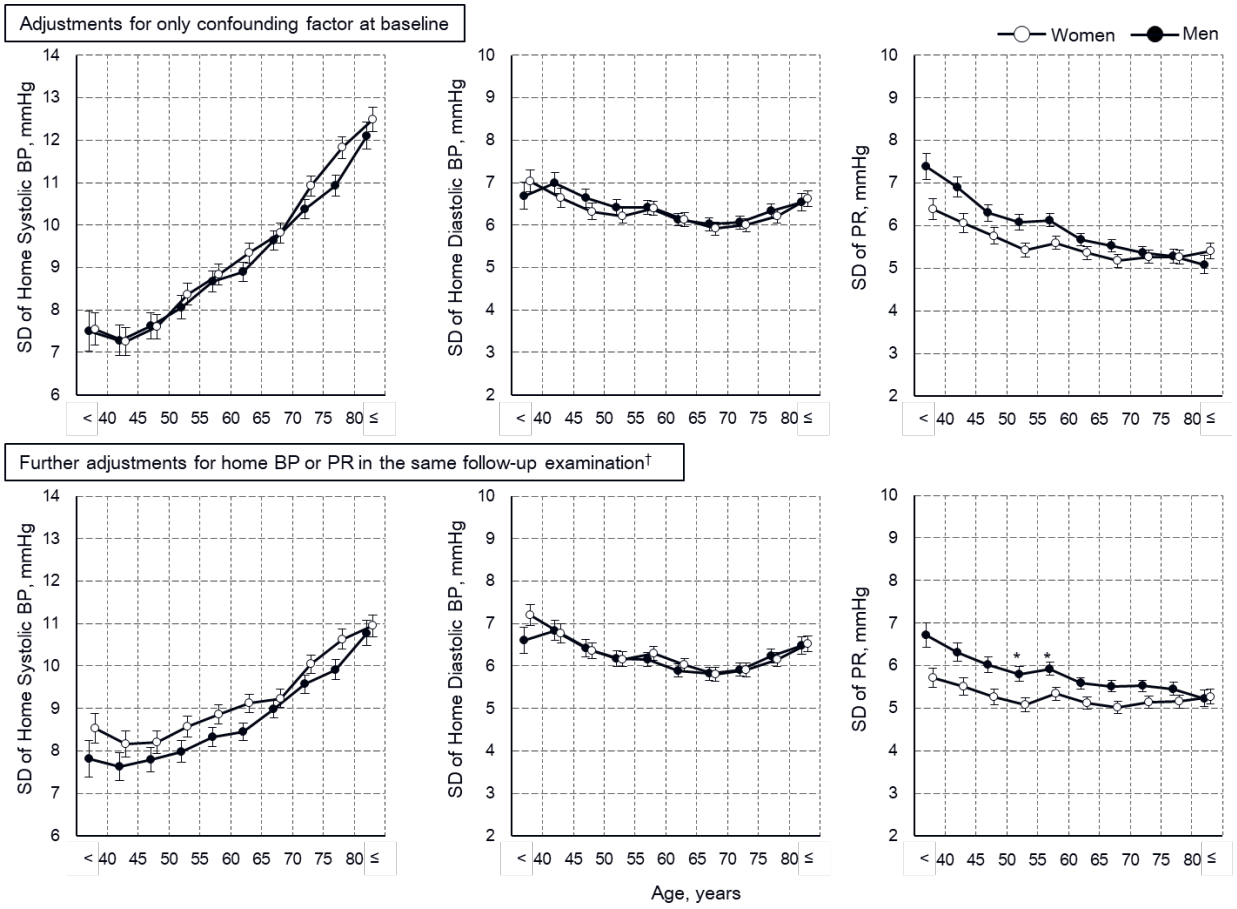

Figure S8. Age-related trends in SDs of home BPs and PR before and after further adjustments for the corresponding mean values.

Bars indicate standard errors. BP, blood pressure; SD, standard deviation; PR, pulse rate.

*P<0.05 vs. women in the same age group after adjusting with Tukey-Kramer test.

†In addition to the model in Figure 1, home systolic BP, diastolic BP, or PR at the same follow-up examinations was included in the model for the estimation of SDs of home systolic BP, diastolic BP, or PR.

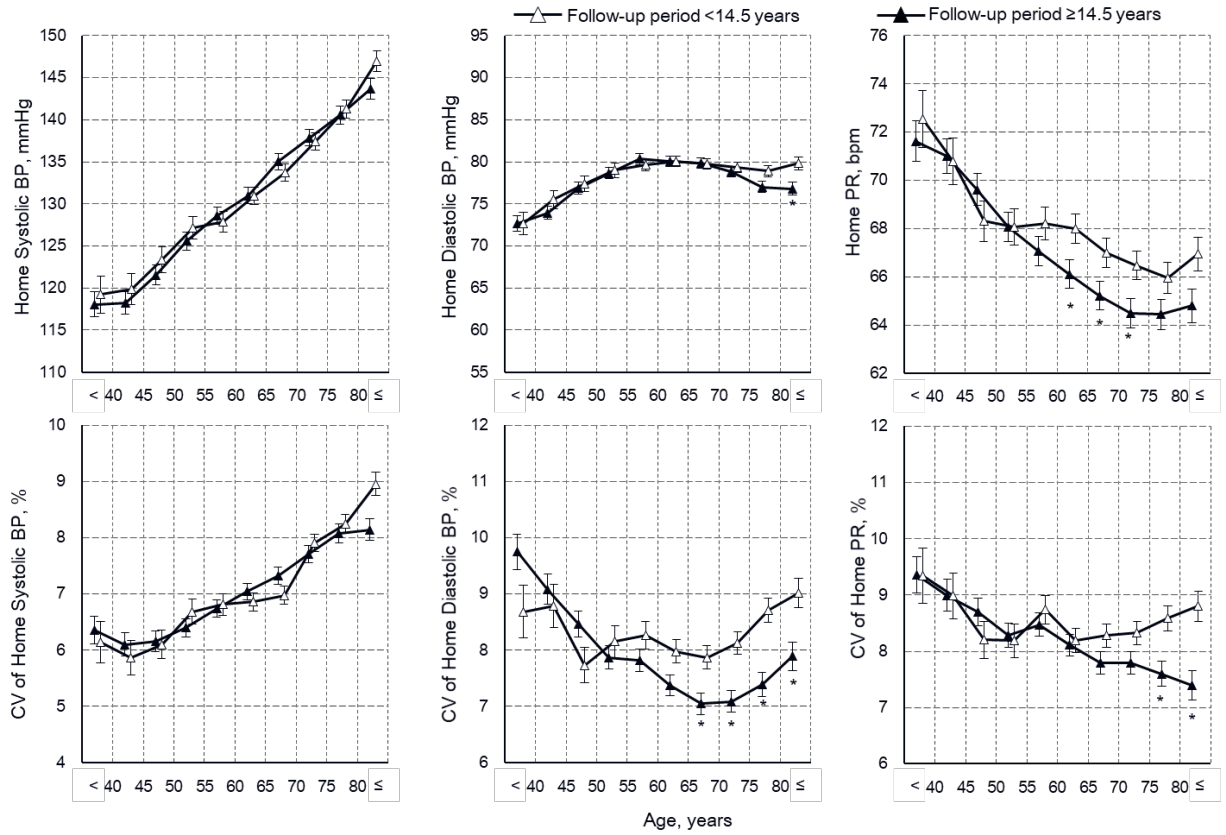

Figure S9. Age-related trends in home BP and home PR and CVs of home BPs and home PR after stratification by the median follow-up of 14.5 years.

The mixed model included age, median follow-up of 14.5 years, interaction term (age × the median follow-up), and the following parameters at baseline: sex, body mass index, current smoking status, alcohol consumption, diabetes, hyperlipidemia, history of cardiovascular disease, and antihypertensive medication use. Bars indicate standard errors. BP, blood pressure; CV, coefficient of variation; PR, pulse rate. *P<0.05 vs the follow-up period ≥14.5 years in the same age group after adjusting with Tukey-Kramer test.

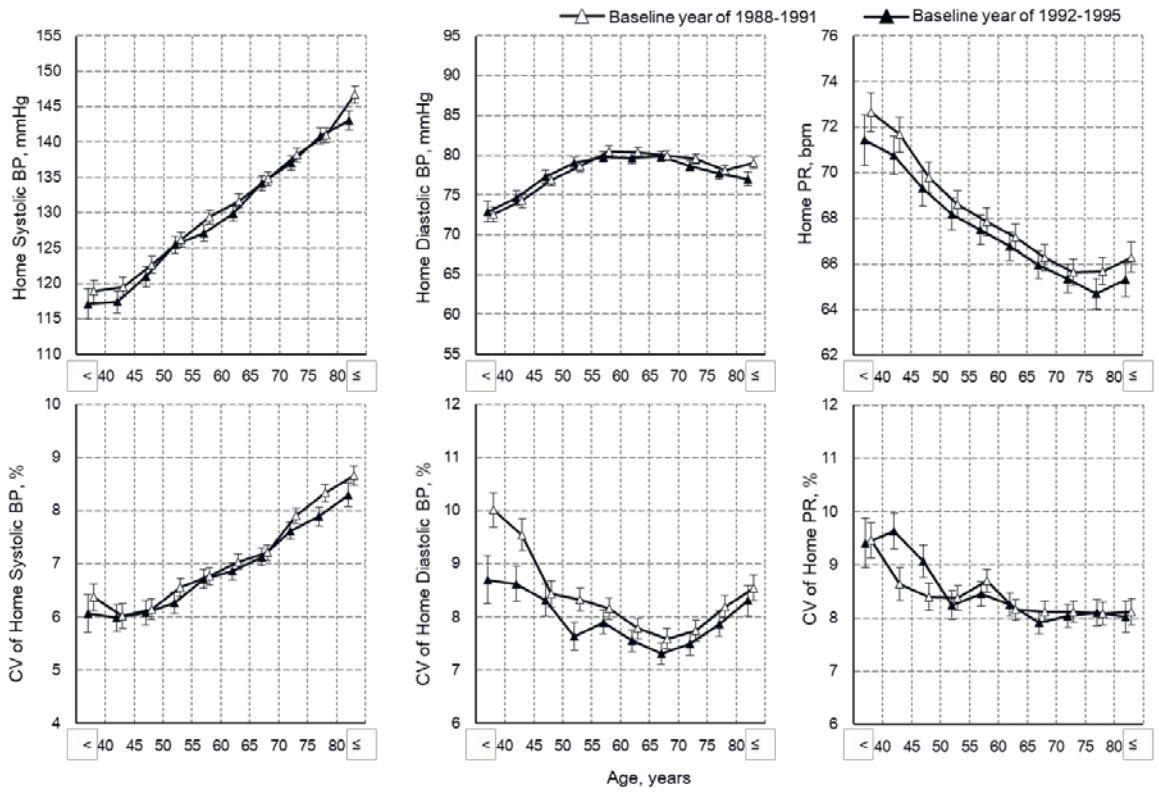

Figure S10. Age-related trends in home BP and home PR and CVs of home BPs and home PR after stratification by the baseline year of 1992.

The mixed model included age, baseline year (after 1991 or not), interaction term (age ×the baseline year), and the following parameters at baseline: sex, body mass index, current smoking status, alcohol consumption, diabetes, hyperlipidemia, history of cardiovascular disease, and antihypertensive medication use. Bars indicate standard errors. BP, blood pressure; CV, coefficient of variation; PR, pulse rate. No significant differences were observed between the two in the same age group after adjusting with Tukey-Kramer test.

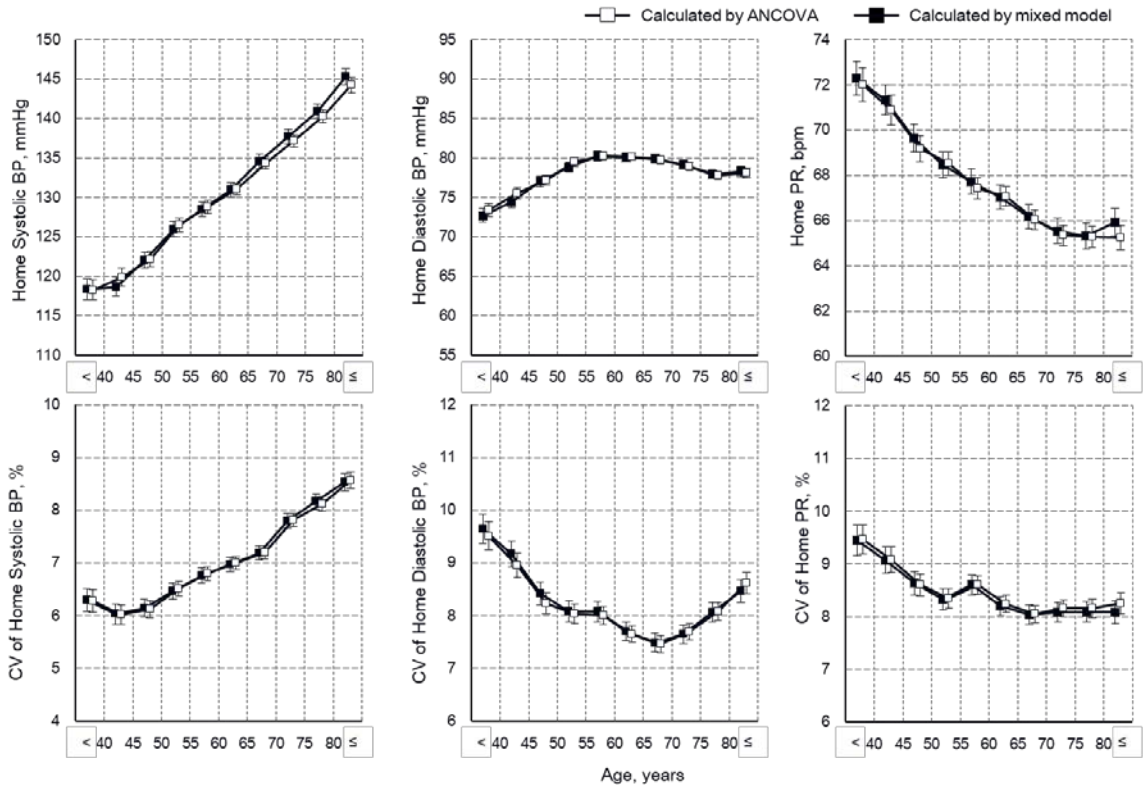

Figure S11. Age-related trends calculated by ANCOVA and the mixed model.

The data represent the values calculated by ANCOVA and those estimated by the mixed model. The present longitudinal data were treated as cross-sectional data when the one-way ANCOVA analysis was used. All participants were included in both models. ANCOVA: analysis of covariance.