The most vital information related to hypertension in clinical / epidemiologic settings is conventional (casual / clinic / office / screening) blood pressure (BP). However, several issues have recently emerged regarding the true representativeness of conventional BP, and thus other methods of measuring BP, such as ambulatory BP monitoring and self-measured BP at home (home BP) have been examined. Each method of BP measurement has unique features.1

We have conducted an epidemiologic survey of hypertension using ambulatory BP and home BP since 1985 in general population of Ohasama, located in the northern part of Japan (the Ohasama study). The morbidity and mortality of the Ohasama population based on ambulatory BP and home BP have been monitored for 20 years and we demonstrated the unique prognostic significance of BP variabilities derived from these measurements. This study was approved by the Institutional Review Board at Tohoku University School of Medicine and by the Department of Health of Ohasama Town.

Public health nurses attached an ambulatory BP monitoring...
Blood Pressure Variability and Prognosis in the Ohasama Study

Device to the participants on a weekday morning and detached the device on the following morning. Participants diarized daily activities, including the time at which they went to bed and when they arose. Ambulatory BP data were included in the analysis when the monitoring period included more than 8 waking hours (daytime) and more than 4 hours in bed (night-time). These periods were estimated from the diaries maintained by the participants. Artifactual readings during ambulatory BP monitoring were defined according to the described criteria,1 and were omitted from the analysis. The averages of the 24-hour, daytime, and nighttime BP values were calculated for each individual. Ambulatory BP was monitored using an ABPM-630 (Nippon Colin, Komaki, Japan), which is a fully automatic device that was preset to measure BP every 30 minutes. Although systolic BP and diastolic BP were measured by both cuff-oscillometric and microphone methods, we only used data obtained using the former method in this analysis.

Home Blood Pressure
We used the following procedure to ascertain the accuracy of home BP. Briefly, physicians and public health nurses conducted health education classes to inform the population of the significance of home BP recording and to teach them how to measure their own blood pressure. The participants performed each step in the procedure under observation by a nurse. After verifying their ability to perform this task, participants were asked to measure their BP at home while seated once every morning within 1 hour after waking, after urination, before breakfast and after 2 or more minutes of rest, and to record the measurements for 4 weeks. If individuals were taking antihypertensive drugs, home BP was measured before medication. The participants also similarly measured their home BP once every evening just before going to bed. This scheme (multiple single measurements) was introduced to establish the most generalizable methods for home BP measurement.7 Home BP was measured using a semiautomatic device (HEM401C; Omron Healthcare Co., Ltd., Kyoto, Japan) based on the cuff-oscillometric principle.

Conventional Blood Pressure
Annual health check-ups that include conventional BP measurements are available to Japanese citizens from the age of 40 years. After remaining seated at rest for at least 2 minutes, nurses or technicians measure conventional BP. In Ohasama, BP was measured twice consecutively during the health check-up, using a semi-automatic device based on the microphone method (USM700F; Ueda Electronic Work Co., Ltd., Tokyo, Japan). We used data obtained from annual check-ups that proceeded within the same time period when home BP was first initiated as part of the study protocol.

Ohasama had a population of 9,400 in 1985; currently it is 6,800. Over the past 20 years, we have obtained 3,000 ambulatory BP measurements from individuals aged 20 years and over, and 5,000 home BP measurements from those aged 7 years and over, as well as outcome and information on risk factors and predictors. To prospectively investigate the association between BP levels and subsequent risk of outcomes (mortality and stroke incidence), we excluded individuals aged younger than 40 years at the time of BP measurement from the analysis because death or stroke occurrence were less common among younger people. Thus, ambulatory and home BP values were mainly prospectively analyzed in 1,542 and 1,913 participants, respectively, aged 40 or over.

Reference Values of Ambulatory Blood Pressure
Previous studies proposing reference values for ambulatory BP measurements derived from cross-sectional observations have been based on the statistical distribution of ambulatory BP values. We first proposed that the reference values for hypertension in 24-hour ambulatory BP measurement based on prognostic criteria should be 134/79 mmHg.4 These values were rounded up to 135/80 mmHg and included in the guidelines of the Japan Society of Hypertension.5 These values were recently modified to 130/80 mmHg according to the results of a meta-analysis of prospective studies including the Ohasama study.6

Comparison of Predictive Values between Ambulatory and Conventional Blood Pressure
Ambulatory BP was more closely associated with the risk of cardiovascular mortality / stroke morbidity than conventional BP measurements.7 Ambulatory BP and high ambulatory BP during daytime monitoring was associated with a worse prognosis for cardiovascular mortality / stroke morbidity.8 Systolic ambulatory BP was a better predictor of stroke than diastolic ambulatory BP and ambulatory pulse pressure.9

Circadian Blood Pressure Variation
Circadian BP variation (higher and lower BP during daytime and nighttime, respectively) is a feature of both normotensive individuals and those with essential hypertension. However, circadian BP variation is diminished under several pathophysiological conditions, even in patients with essential hypertension; for example, inversion sometimes occurs, resulting in nocturnal BP elevation.1 Those with a normal nocturnal dip were referred to as dippers, whereas those with diminished nocturnal dipping or nocturnal BP elevation (inverted dippers) were classified as non-dippers. The term ‘extreme dipper’ was applied to those with a nocturnal dip of 20% or more in diurnal BP.

Non-dippers in the Ohasama study are associated with a significantly higher risk of cardiovascular mortality, independently of 24-hour ambulatory BP levels.10 Recent analyses of stroke inci-
dence have further demonstrated that non-dipping is associated with cerebral infarction, whereas extreme dipping and a large morning pressor surge, which are analogous to a large diurnal increase in BP, are both associated with a risk of cerebral hemorrhage.14

Recent analysis using 2-h moving averages of BP (a total of 24 average BP measurements for two consecutive hours based on four BP readings taken every 30 min) to compare the predictive power of BP taken during a 24-h period given the same number of measurements have confirmed those findings; hemorrhagic stroke mortality is significantly associated with elevated daytime 2-h moving averages of systolic BP (2 h-SBP), whereas mortality due to cerebral infarction and heart disease is significantly associated with elevated night-time 2 h-SBP, indicating that high BP at various times of the day is associated with different subtypes of cerebrovascular and cardiovascular disease risk.15

Blood Pressure Variability and Heart Rate Variability
Ambulatory BP monitoring provides information on variability in BP and in heart rate. We estimated the variability of BP and heart rate from the Ohasama Study as the standard deviation of the daytime or night-time average measured every 30 min. Daytime systolic ambulatory BP variability was significantly related in a linear fashion with the risk of cardiovascular mortality, whereas the risk linearly increased with the decrease in daytime and nighttime heart rate variability.16 Variabilities in both BP and heart rate are independently associated with cardiovascular mortality.16

Ambulatory Arterial Stiffness Index
The ambulatory arterial stiffness index (AASI) is a novel reflection of arterial stiffness defined as 1 minus the regression slope of diastolic over systolic BP in individuals, which can be determined from 24-h ambulatory BP recordings. In the Ohasama study, AASI was significantly associated with risk for cardiovascular and stroke mortality in a U-shaped fashion, whereas pulse pressure did not yield any prognostic information.17

Reference Values of Home Blood Pressure
Previous studies proposing reference values for home BP measurements derived from cross-sectional observations were based on the statistical distribution of home BP values. We first proposed that the reference values for hypertension of home BP measurement based on prognostic criteria should be 137/84 mmHg.16 These values were rounded to 135/85 mmHg and were subsequently included in several guidelines.1, 2, 5

Comparison of Predictive Values between Home and Conventional Blood Pressure
Home BP was more closely associated with the risk of cardiovascular mortality/stroke (including subtypes) morbidity than conventional BP measurements.20-21 Systolic home BP was a better predictor of cardiovascular mortality than diastolic home BP.22

Number of Home Blood Pressure Measurements Relative to the Predictive Power of Stroke
An increased number of measurements improved the predictive values of home BP. No threshold for the number of home BP measurements within the range of 1-14 measurements was evident for increasing the predictive power of stroke risk. Interestingly, even the initial home BP values (1 measurement) were significantly more closely related to stroke risk than conventional BP values (mean of 2 measurements).20 These results suggest that in addition to the number of measurements, other factors such as the absence of the white-coat effect are associated with the superior predictive power of home BP measurements.

Use of Guidelines for Predicting Stroke Using Home Blood Pressure
Guidelines based on individualized categorizations, such as the 2003 European Society of Hypertension – European Society of Cardiology (ESH-ESC) guidelines,23 are more useful for predicting stroke24 than those based on simple BP-oriented categorizations, such as those of the Joint National Committee (JNC)-7.25, 26 Home BP increased the predictive power of guideline categorizations compared with conventional BP.

Prediction of Stroke by Home “Morning” versus “Evening” Blood Pressure Values
Home BP in the morning (morning BP) and in the evening (evening BP) provided equally useful information for stroke risk, whereas morning hypertension, which is observed specifically in the morning, might be a good predictor of stroke, particularly among individuals using anti-hypertensive medication.27

White Coat Hypertension as a Transient State to Hypertension outside Medical Settings
Individuals with white-coat hypertension whose home BP was normal but whose conventional BP was high had an approximate-ly 3-fold higher risk of eventually manifesting sustained home hypertension after 8 years compared with those having sustained normotension, indicating that patients with white-coat hypertension should be carefully monitored.29

Predictive Values of Home Heart Rate
The advantages of home BP were also applicable to resting heart rate values assessed at home using a device designed for home BP measurement. Home heart rate was significantly associated with the risk of cardiovascular mortality. This relationship was statistically significant after adjustment for home BP values, indicating that home BP and heart rate represent simple sources of useful clinical information with which to assess cardiovascular risk.29
In the Ohasama study, we demonstrated that ambulatory BP and home BP variabilities provide a variety of useful prognostic information. Ambulatory BP and home BP are useful tools with which to examine the prognostic significance of BP variabilities in clinical and epidemiologic settings. These variabilities also bias the diagnosis and treatment of hypertension in that the phasic, as well as tonic component of BP, must be considered for effective management of hypertension.

The author is grateful to Professor Yutaka Imai, the principal investigator of the Ohasama study, as well as all of the collaborating mentors, colleagues, foundations and individuals. The author also acknowledges the Japan Epidemiological Association and the Editorial Board of the Journal of Epidemiology for the opportunity to write this article.

1. O'Brien E, Asmar R, Bellin L, Imai Y, Mallion JM, Mancia G, et al. European Society of Hypertension Working Group on Blood Pressure Monitoring. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens 2003; 21: 821-48.
2. Imai Y, Nihei M, Abe K, Sasaki S, Minami N, Munakata M, et al. A finger volume-oscillometric device for monitoring ambulatory blood pressure: laboratory and clinical evaluation. Clin Exp Hypertens A 1987; 9: 2001-25.
3. Imai Y, Otsuka K, Kawano Y, Shimada K, Hayashi H, Tochikubo O, et al. Japanese Society of Hypertension (JSH) Guidelines for Self-Monitoring of Blood Pressure at Home. Hypertens Res 2003; 26: 771-82.
4. Ohkubo T, Imai Y, Tsuji I, Nagai K, Ito S, Satoh H, et al. Reference values for 24-hour ambulatory blood pressure monitoring based on a prognostic criterion: the Ohasama Study. Hypertension 1998; 32: 255-9.
5. Japanese Society of Hypertension. Japanese Society of Hypertension guidelines for the management of hypertension (JSH 2004). Hypertens Res 2006; 29 Suppl: S1-105.
6. Kikuya M, Hansen TW, Thijs L, Bjorklund-Bodegard K, Kuznetsova T, Ohkubo T, et al. on behalf of the IDACO Investigators. Diagnostic thresholds for ambulatory blood pressure monitoring based on 10-year cardiovascular risk. Circulation 2007; 115: 2145-52.
7. Ohkubo T, Imai Y, Tsuji I, Nagai K, Watanabe N, Minami N, et al. Prediction of mortality by ambulatory blood pressure monitoring versus screening blood pressure measurements: a pilot study in Ohasama. J Hypertens 1997; 15: 357-64.
8. Ohkubo T, Hozawa A, Nagai K, Kikuya M, Tsuji I, Ito S, et al. Prediction of stroke by ambulatory blood pressure monitoring versus screening blood pressure measurements in a general population: the Ohasama study. J Hypertens 2000; 18: 847-54.
9. Kikuya M, Ohkubo T, Asayama K, Metoki H, Obara T, Saito S, et al. Ambulatory blood pressure and 10-year risk of cardiovascular and noncardiovascular mortality: the Ohasama study. Hypertension 2005; 45: 240-5.
10. Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, Hashimoto J, et al. Prognosis of "masked" hypertension and "white-coat" hypertension detected by 24-hour ambulatory blood pressure monitoring: 10-year follow-up from the Ohasama study. J Am Coll Cardiol 2005; 46: 508-15.
11. Inoue R, Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, et al. Predicting stroke using 4 ambulatory blood pressure monitoring – derived blood pressure indices: the Ohasama study. Hypertension 2006; 48: 877-82.
12. Ohkubo T, Imai Y, Tsuji I, Nagai K, Watanabe N, Minami N, et al. Relation between nocturnal decline in blood pressure and mortality: the Ohasama Study. Am J Hypertens 1997; 10: 1201-7.
13. Ohkubo T, Hozawa A, Yamaguchi J, Kikuya M, Ohmori K, Michimata M, et al. Prognostic significance of the nocturnal decline in blood pressure in individuals with and without high 24-h blood pressure: the Ohasama study. J Hypertens 2002; 20: 2183-9.
14. Metoki H, Ohkubo T, Kikuya M, Asayama K, Obara T, Hashimoto J, et al. Prognostic significance of stroke for a morning pressor surge and a nocturnal blood pressure decline: the Ohasama Study. Hypertension 2006; 47: 149-54.
15. Metoki H, Ohkubo T, Kikuya M, Asayama K, Obara T, Hara A, et al. Prognostic significance of night-time, early morning, and daytime blood pressures on the risk of cerebrovascular and cardiovascular mortality: the Ohasama Study. J Hypertens 2006; 24: 1841-8.
16. Kikuya M, Hozawa A, Ohkubo T, Tsuji I, Michimata M, Matsubara M, et al. Prognostic significance of blood pressure and heart rate variabilities: the Ohasama study. Hypertension 2000; 36: 901-6.
17. Kikuya M, Staessen JA, Ohkubo T, Thijs L, Metoki H, Asayama K, et al. Ambulatory arterial stiffness index and 24-hour ambulatory pulse pressure as predictors of mortality in Ohasama, Japan. Stroke 2007; 38: 1161-6.
18. Tsuji I, Imai Y, Nagai K, Ohkubo T, Watanabe N, Minami N, et al. Proposal of reference values for home blood pressure measurement: diagnostic criteria based on a prospective observation of the general population in Ohasama, Japan. Am J Hypertens 1997; 10: 409-18.
19. Ohkubo T, Imai Y, Tsuji I, Nagai K, Kato J, Kikuchi N, et al. Home blood pressure measurement has a stronger predictive power for mortality than dose screening blood pressure measurement: a population-based observation in Ohasama, Japan. J Hypertens 1998; 16: 971-5.
20. Ohkubo T, Asayama K, Kikuya M, Metoki H, Hoshi H, Hashimoto J, et al. How many times should blood pressure be measured at home for better prediction of stroke risk? Ten-year follow-up results from the Ohasama study. J Hypertens 2004; 22: 1099-104.

21. Ohkubo T, Asayama K, Kikuya M, Metoki H, Obara T, Saito S, et al. Prediction of ischaemic and haemorrhagic stroke by self-measured blood pressure at home: the Ohasama study. Blood Press Monit 2004; 9: 315-20.

22. Hozawa A, Ohkubo T, Nagai K, Kikuya M, Matsubara M, Tsuji I, et al. Prognosis of isolated systolic and isolated diastolic hypertension as assessed by self-measurement of blood pressure at home: the Ohasama study. Arch Intern Med 2000; 160: 3301-6.

23. European Society of Hypertension-European Society of Cardiology Guideline Committee. 2003 European Society of Hypertension – European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003; 21: 1011-53.

24. Asayama K, Ohkubo T, Kikuya M, Metoki H, Obara T, Hoshi H, et al. Use of 2003 European Society of Hypertension – European Society of Cardiology guidelines for predicting stroke using self-measured blood pressure at home: the Ohasama study. Eur Heart J 2005; 26: 2026-31.

25. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr et al. The National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The JNC 7 Report. JAMA 2003 21: 2560-72.

26. Asayama K, Ohkubo T, Kikuya M, Metoki H, Hoshi H, Hashimoto J, et al. Prediction of stroke by self-measurement of blood pressure at home versus casual screening blood pressure measurement in relation to the Joint National Committee 7 classification: the Ohasama study. Stroke 2004; 35: 2356-61.

27. Asayama K, Ohkubo T, Kikuya M, Obara T, Metoki H, Inoue R, et al. Prediction of stroke by home ‘morning’ versus ‘evening’ blood pressure values: the Ohasama study. Hypertension 2006; 48: 737-43.

28. Ugajin T, Hozawa A, Ohkubo T, Asayama K, Kikuya M, Obara T, et al. White-Coat hypertension as a risk factor for the development of home hypertension: the Ohasama study. Arch Intern Med 2005; 165: 1541-6.

29. Hozawa A, Ohkubo T, Kikuya M, Ugajin T, Yamaguchi J, Asayama K, et al. Prognostic value of home heart rate for cardiovascular mortality in the general population: the Ohasama study. Am J Hypertens 2004; 17: 1005-10.