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Association between real-world home blood pressure measurement patterns and blood pressure variability among older individuals with hypertension: A community-based blood pressure variability study

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Abstract

Home blood pressure (BP) monitoring is a useful tool for hypertension management. BP variability (BPV) has been associated with an increased risk of cardiovascular events. However, little is known about the correlation between BPV and different measurement patterns of long-term home BP monitoring. This longitudinal cohort study aimed to assess the associations between dynamic BP measurement patterns and BPV. A total of 1128 participants (mean age, 77.4 ± 9.3 years; male, 51%) with 23 269 behavior measuring units were included. We used sliding window sampling to classify the home BP data with a regular 6-month interval into units in a sliding manner until the data are not continuous. Three measurement patterns (stable frequent [SF], stable infrequent [SI], and unstable [US]) were assessed based on the home BP data obtained within the first 3 months of the study, and the data in the subsequent 3 months were used to assess the BPV of that unit. We used linear mixed-effects model to assess the association between BP measurement patterns and BPV with adjustment for possible confounding factors including average BP. Average real variability and coefficient variability were used as measures of the BPV. No significant differences were observed in average BP between the SF, SI, and US patterns. However,

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BPV in the SF group was significantly lower than that in the US and SI groups (all *p*-values < .05). The BPV in SI and US groups was not significantly different. A stable and frequent BP measuring pattern was independently associated with a lower BPV.

1 | INTRODUCTION

High blood pressure (BP) is a leading risk factor of global disease burden and premature death.[1] In patients with hypertension, better BP control is associated with a lower risk of morbidity and mortality from cardiovascular diseases.[2] Previous studies have reported that home BP monitoring (HBPM) can help identify individuals with white-coat hypertension or worse BP control, provide guidance for treatment regimens, and reduce the incidence of vascular complications.[3–9] Regular home BP measurement can help achieve better long-term BP control.[10,11]

Previous studies have demonstrated that self-monitoring behavior in conjunction with co-interventions was associated with a clinically significant BP reduction.[12] Home BP monitoring (HBPM) may lead to a small but significant reduction in BP.[13] Studies have shown that long-term BP variability (BPV) might represent the stability of BP control in participants who received antihypertensive therapy rather than the immediate physiological change. More importantly, a high BPV may be associated with inaccurate dosing/titration of antihypertensive therapy or low adherence to antihypertensive therapy.[8] Moreover, long-term BPV and day-to-day BPV have been associated with adverse cardiovascular outcomes[14–22] and can be evaluated through HBPM or office BP monitoring.[23] However, no study has examined the association between BPV and regular home BP measurement or the frequency of BP measurements. Our study hypothesis is that different BP measuring patterns may be associated with the degree of BPV.

The sliding window method is a data preprocessing technique used to obtain time-series data, and it has been used in signal preprocessing,[24,25] genome sequence analysis,[26] climate science,[27] and finance.[28] This method can be used to capture the finite features of the data and prevent the loss of some critical features when whole data are utilized for analysis as a one-off procedure. Since the BP measurement pattern can vary from time to time, if we only categorize a participant's BP measurement pattern into one pattern based on the aggregate data, the important dynamic behavior may be overlooked. Thus, in the present study, the sliding window method was used for data preparation and analysis. Furthermore, Bauer and colleagues[29] have shown that the dynamic group models can fit the data significantly better than the traditional stable group models particularly when the multilevel mixed model is used to analyze dynamic group data.

This study aimed to assess whether long-term home BP measurement patterns are associated with BPV based on information from a community-based digitalized home BP measurement database in Taipei City.

2 | METHODS

2.1 | Population source

This community-based cohort study recruited adults from free preventive health examination for adults aged over 40 years every 3 years and aged over 65 years annually, supported by the Health Promotion Administration in Taiwan. The free health examination comprised blood/urine tests, medical examinations, and questionnaires about disease history, family medical history, medication history, health behavior, and depression. The study sample consisted of managed care cases in the Department of Health of the Taipei City Government between January 2014 and April 2017 (*N* = 1334). Public health nurses follow up patients with abnormal test results and recruited them for integrated health care management. They visit these individuals every few months, during which they perform a detailed physical examination, activity assessment, and focused evaluation of each participant's disease history. Some participants were then further enrolled (*N* = 1320) into an HBPM program. The study data were classified into two groups: home BP measurement data (HBPMD) and home visit data (HVD). Both data were digitalized and stored by the Taipei Health Cloud Project. The study only included participants with both HVD and HBPMD (Figure 1).

The study was approved by the research ethics committee of Taipei City Hospital (IRB approval number: TCHIRB-10607116) for collecting and using the data automatically unless study subjects actively dissent. The ethical committee also approved further analysis for research purposes. The data supporting the findings of this study are available from the corresponding author upon reasonable request.

2.2 | BP measurement

The public health nurses provided an ESH 2010 validated electronic sphygmomanometer (FORA D40 Blood Glucose plus Blood Pressure Monitoring System [TD-3261G])[30] to individuals who were enrolled in the HBPM program, and instructions on accurate measurement of BP were provided. The BP measurement instructions were based on the 2015 Taiwan Hypertension Guideline detailed elsewhere.[31] In brief, as suggested by the Taiwan Hypertension Society and Taiwan Society of Cardiology, subjects should avoid exercise for at least 30 min and sit calmly for 5 min before BP measurements. The participants were all requested to measure BP with an appropriate-sized cuff after waking up and before bed with twice measurements

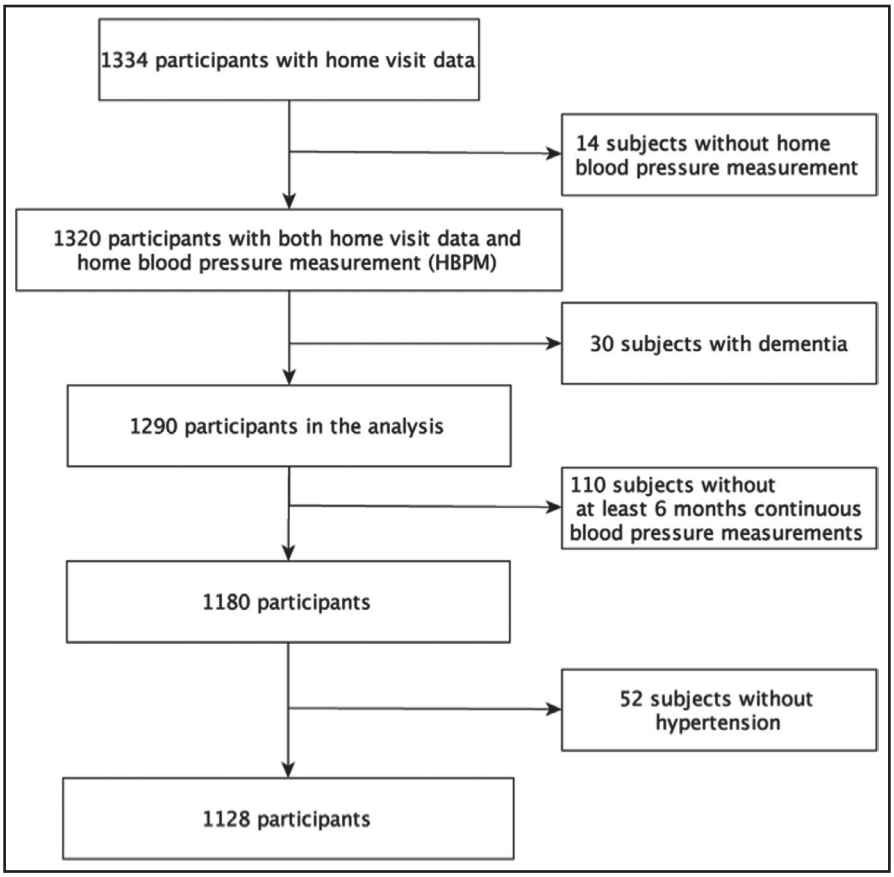

FIGURE 1 Flowchart of the recruitment of study participants: Details of the causes of exclusion are provided in the figure

each time. BP data were automatically uploaded to the Taipei Health Cloud.

2.3 | Sliding window method

Figure 2 presents the sliding window procedure. An illustration of the details of data handling is provided in Figure S1. The comparisons between the sliding window procedure and non-sliding window approaches are given in Figure S1 and Table S1. The sliding window method can be used for data preprocessing to investigate complex and dynamic measurement behaviors (Figure 3) and its relationship with BPV. The AHA Primary Prevention of Cardiovascular Disease guidelines[32] and Geriatric Practice books[33] recommend the assessment of adherence to and influence of non-pharmacological therapy within 3–6 months. Thus, long-term BP measurement patterns and BPVs were classified with 6-month interval as the window unit. Each participant had multiple window units of BP measurement data. Each unit included data with an uninterrupted BP measurement every month (at least one BP measurement/month). If no BP measurement was obtained during the whole month, this month was excluded, and the window unit was replenished by the BP data in the succeeding month to constitute a 6-month window unit. The first 3 months of each unit were used to characterize BP measurement patterns, and the succeeding 3 months (4th, 5th, and 6th months) were used to calculate BPV.

2.4 | Sliding window comparison analysis

To compare the reproducibility of BPV between different methods, we identified participants who comprehensively measured their BP for 28 months without any interruption and calculated the BPV of each month. The sliding window method used data from the 5th month to the 16th month as the first year and from the 17th month to the 28th month as the second year, while the non-sliding window method used the 5th to 7th and 14th to 16th months as the first year and 17th to 19th and 26 to 28th months as the second year. We calculated the intraclass correlation coefficient between the two methods. A total of 408 individuals met the criteria, and Table S2 presents the results of reproducibility. In general, the sliding window method had comparable reproducibility to the non-sliding window method (Table S2).

To compare the selection bias resulting from different sampling methods, we investigated the stability of the sliding window method in comparison with the non-sliding window method. We enrolled participants who measured their BP monthly for 12 months without interruption. A total of 986 participants met the criteria. The non-sliding window method used the first continuous 3 months to characterize BP measurement patterns and the last (10th, 11th, and 12th) months to compute the outcome and each participant with only one unit. The sliding window uses the 4th, 5th, and 6th months to compute, and each participant

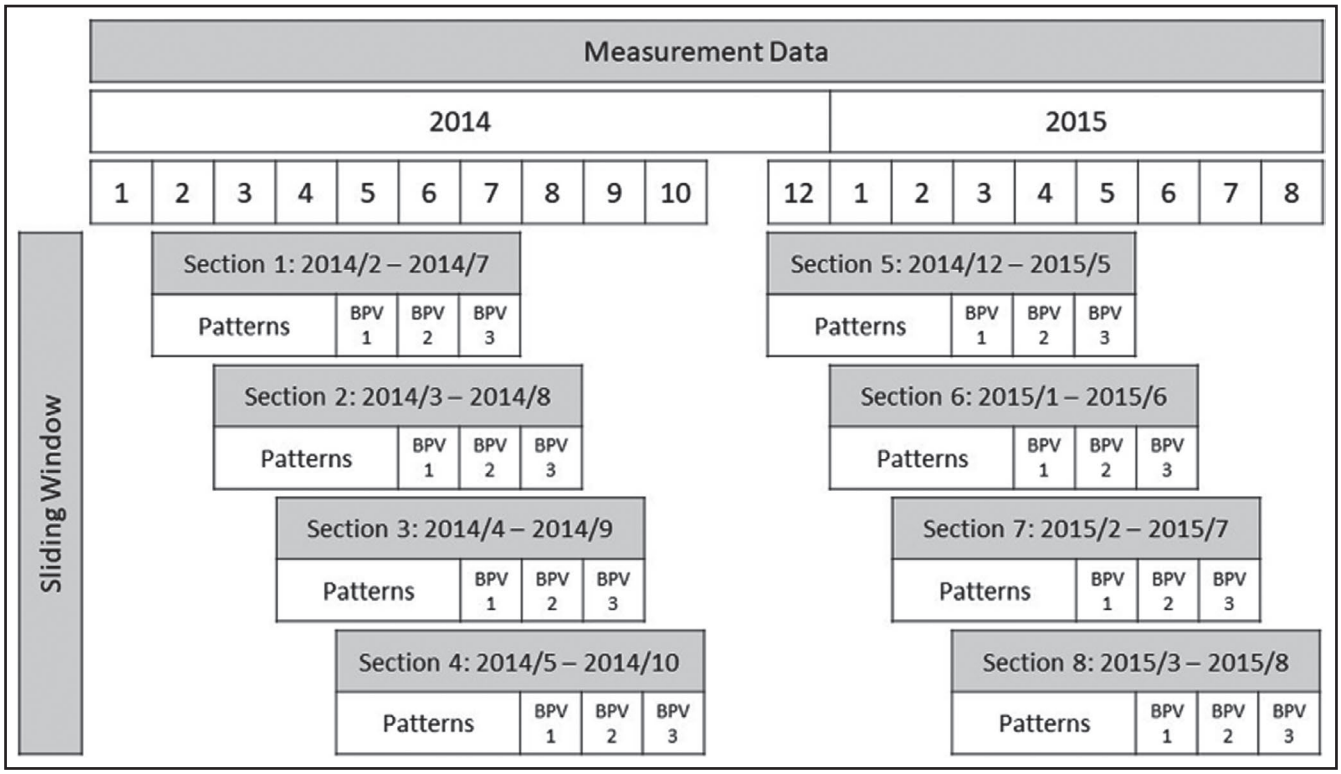

FIGURE 2 Sliding window technique. We used 6 months as a unit from an individual's entire data. The unit was dropped if there were no BP data in any month of the unit. For each unit, the first 3 months of each unit were used to characterize blood pressure measurement patterns, and the 4th, 5th, and 6th months were used to calculate BPV

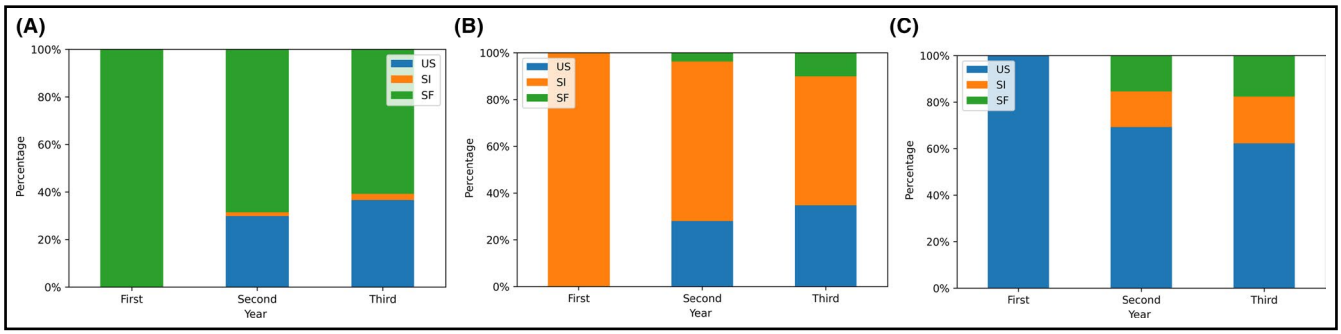

FIGURE 3 The dynamics of measurement behaviors during the follow-up periods of the study cohort. Subjects in the stable frequent (SF) group in the first year gradually shifted to the unstable (US) group or stable infrequent (SI) group in the succeeding years. Subjects in the SI group in the first year gradually shifted to the US group or SF group in the succeeding years. Subjects in the US group in the first year gradually shifted to SF or SI group in the subsequent years

had seven units. Figures S2–S5 present the variance of each BP measurement pattern, and Figures S5–S9 present the change frequency.

These two analysis results confirmed that the use of the sliding window procedure can help overcome the sampling bias problem and capture the dynamic behavior.

2.5 | Study populations

To understand long-term BP measurement behavior, only participants who had continuous BP measurements for at least 6 months were enrolled. To ensure the quality of home BP measurements, participants diagnosed with dementia were excluded. Hypertension was defined using the following criteria: participants who had a history of hypertension (n = 892), those who were taking antihypertensive medications (n = 685), and those who had an average systolic BP (SBP) or diastolic BP (DBP) >130/80 mmHg (n = 178). The comparison results between the excluded population and the whole study population are depicted in Table S3. A total of 1128 participants with 23 269 units were included, and the details of the inclusion process are presented in Figure 1. The average measurement days and measurement timeframe in 1128 participants were 484.5 and 857.2, respectively.

2.6 | Classification of the BP measurement patterns

Our primary parameter of interest was the BP measurement pattern. We first calculated the standard deviation (SD) of the number of days with BP measurement per week for 3 months (13 weeks). The median SD for 3 months was 1.12 (Figure S10). This median was then used to classify the measurement section into two patterns: unstable (US) (SD: ≥1.12) and stable measurement patterns (SD: <1.12). We presented the distribution of the mean BP measurement frequency per week in participants with stable and US measurement patterns. The stable and US measurement patterns had bimodal (Figure S11) and symmetric-like normal distributions, respectively (Figure S12). Therefore, only the frequent and infrequent measuring patterns in the stable measurement pattern were classified. The mean current BP measurement days per week in our study population was 4.28. The stable measuring pattern was classified into stable frequent (SF; mean days of BP measurements ≥4 days/week) and stable infrequent (SI; mean days of BP measurements <4 days/week). Figure 3 depicts the pattern of frequency changes between different BP measurement patterns (SF, SI, and US), which indicated that changes in BP measurement patterns were not unusual.

2.7 | Home BP and BPV

To describe day-to-day BPV, three parameters were used: SD, coefficient variability (CV), and average real variability (ARV). The detailed formula for calculating these parameters is presented in Table S4. We calculated the average SBP or DBP by obtaining the average of all BP measurements on the same day and by calculating the SD of the average BP per day within 1 month. Moreover, the CV and ARV were calculated using all the measurement days of the average BP. To understand whether the measurement patterns influence the average BP, the average BP obtained during the latter 3 months was calculated.

2.8 | Potential confounders

The baseline measurements upon enrollment were considered potential confounding factors. Body height (cm) and weight (kg) were self-reported, and body mass index (BMI, kg/m^2) was calculated. Drinking and smoking habits and history of stroke, hypertension, hyperlipidemia, heart disease, and diabetes mellitus were also self-reported. Moreover, the records of prescription medications were reviewed and recorded. Only antihypertensive medications were considered as confounding factors. The type of antihypertensive agent was also considered as a confounding factor, including calcium channel blockers (CCB), renin-angiotensin system (RAS) blockade, diuretics, beta-blockers, alpha-blockers, and central-acting agents. If the record of prescription medications was altered, we documented changes in the antihypertensive treatment composition. Socioeconomic status (SES)

TABLE 1 Baseline characteristics of all the participants

	Hypertension participants (*N* = 1128)
Male, *N* (%)	572 (50.7)
Age[a], mean(SD)	77.4 (9.3)
BMI mean(SD)	24.5 (4.0)
Antihypertensive medication and diuretics, *N* (%)	696 (61.7)
CCB, *N* (%)	324 (28.7)
RAS inhibitor, *N* (%)	331 (29.3)
Diuretics, *N* (%)	52 (4.6)
Beta-Blocker, *N* (%)	142 (12.6)
Alpha-Blocker, *N* (%)	21 (1.9)
Central-Acting Agent, *N* (%)	12 (1.1)
The changing antihypertensive treatment composition, *N* (%)	8 (0.7)
Charlson comorbidity index	
Stroke, *N* (%)	51 (4.5)
Hypertension, *N* (%)	892 (79.1)
Hyperlipidemia, *N* (%)	131 (11.6)
Heart disease, *N* (%)	396 (0.35)
Diabetes mellitus, *N* (%)	282 (25)
Habits of smoking, *N* (%)	104 (9.2)
Habits of drinking, *N* (%)	28 (2.4)
Education	
Illiteracy, *N* (%)	491 (43.5)
Elementary school, *N* (%)	106 (9.4)
Junior high school, *N* (%)	163 (14.5)
Senior high school, *N* (%)	181 (16.0)
College, *N* (%)	187 (16.6)
General-income family, *N* (%)	1102 (97.7)
Beneficiary of social welfare, *N* (%)	418 (37.1)
Residence area	
Wanhua District, *N* (%)	163 (14.5)
Shilin District, *N* (%)	123 (10.9)
Da'an District, *N* (%)	106 (9.4)
Zhongshan Area, *N* (%)	105 (9.3)
Beitou District, *N* (%)	87 (7.7)
Songshan District, *N* (%)	105 (9.3)
Zhongzheng District, *N* (%)	87 (7.7)
Wenshan District, *N* (%)	81 (7.2)
Xinyi District, *N* (%)	82 (7.3)
Datong District, *N* (%)	80 (7.1)
Nangang District, *N* (%)	71 (6,3)
Neihu District, *N* (%)	54 (4.8)

Note: Data were presented as number (%) or mean (SD).

Abbreviations: CCB, calcium channel blocker; RAS, renin-angiotensin system.

[a]The age of the participants ranged from 45 and 102 years.

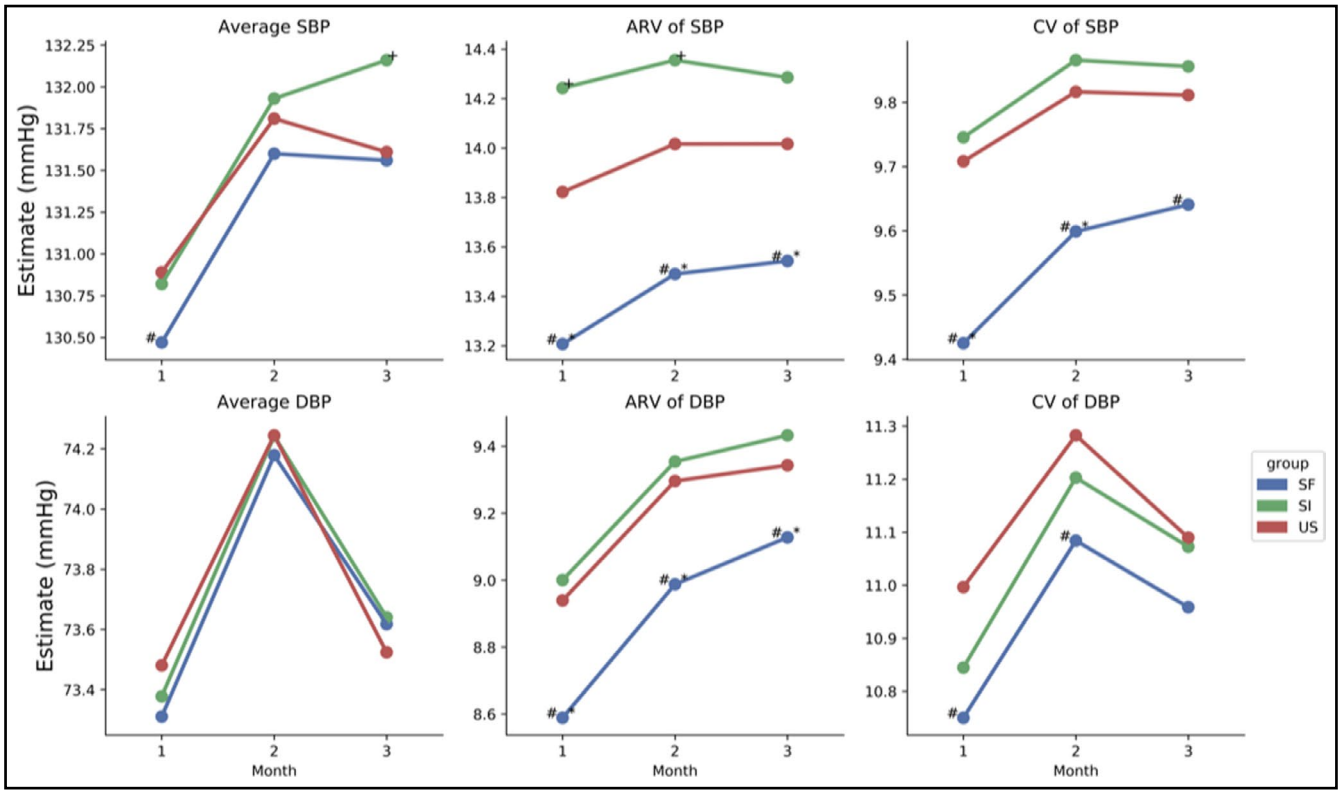

FIGURE 4 Comparison of the average blood pressure (BP) and blood pressure variabilities according to three different measurement patterns in the population with hypertension. The criterion used in the stable frequent (SF) group was blood pressure measurement obtained more than 4 days per week. The left, middle, and right columns represent the average BP, average real variability (ARV), and coefficient variability (CV), respectively. The upper and bottom rows were the parameters derived using systolic BP and diastolic BP, respectively. The symbol (*) on the blue line indicates that the difference between SF and SI was statistically significant. The symbol (#) on the blue line indicates that the difference between SF and US was statistically significant. The symbol (+) on the orange line shows that the difference between SI and US was statistically significant ($p < .0028$ for ARV and CV, $p < .0083$ for average BP)

and information on whether the participant received any social welfare benefit were obtained from the Department of Social Welfare Department in Taipei City. SES was classified as follows: low-income, low-middle–income, and general-income families. It was reclassified according to whether a participant's family had general income. The area of residence included 12 administrative areas in Taipei City.

2.9 | Statistical analysis

Continuous and categorical variables were compared using Student's *t*-test and chi-square test, respectively. All statistical analyses were conducted by SAS Institute Inc (2015), and SAS 9.4 for Windows 10 was used.[34] The SAS output format for the figure was organized using Python 3.6.8 for Red Hat 4.8.5-36. Data collection was performed using Pandas v0.23.4,[35] and the figures were plotted using Matplotlib v2.2.3[36] and Seaborn v0.9.0.[37] Because each participant had multiple units of BP measurements, the linear mixed-effects model was used to investigate the associations between BP measurement patterns and BPV. A random intercept was used to account for within-individual correlation and was fitted with an unstructured covariance structure. Adjustment for age, sex, BMI, education, SES, receipt of social welfare benefit, area of residence, drinking habits, smoking habits, drugs, type of drugs (CCB, RAS blockade, diuretics, beta-blockers, alpha-blockers, and central-acting agents), the changing antihypertensive treatment composition, and history of stroke, hypertension, heart disease, and diabetes mellitus was performed. For the association between BP measurement patterns and BPV, we also adjusted the average SBP and DBP for the BPV of SBP and DBP, respectively.

2.10 | Sensitivity analyses

We conducted another sensitivity analysis by adopting different criteria for the diagnosis of hypertension (SBP/DBP > 135/85 mmHg). Moreover, the relationships between different measurement frequencies in the whole population or participants in the stable group and the average BP or BPVs were investigated.

3 | RESULTS

Table 1 shows the demographic characteristics of the participants in this study. The mean age was 77.4 ± 9.3 (range 45–102) years. Most

participants were illiterate (43.1%), and approximately 81.8% had a history of hypertension. As regards the proportions of participants classified under a particular BP measurement pattern, the median was 74%, indicating that more than 50% of the participants had at least 74% probability of having the same measurement pattern (Figure S13). Moreover, only 14% of the participants were classified under the same measurement pattern (Figure S14). In addition, the characteristics of each group are presented in Table S5.

Figure 4 depicts the associations between different BP measurement patterns and the average BP or BPVs of SBP and DBP. In general, no significant differences were observed in terms of average BP among individuals with the SF, SI, and US patterns. In SBP, an SF pattern is better than a US pattern in the first month, and US and SF patterns are better than an SI pattern in the third month. In contrast, the BPVs in individuals with the SF pattern were significantly lower than those with the US pattern, and the differences slightly decreased from the first month to the third month (4th, 5th, and 6th months in a 6-month unit). The BPVs in individuals with the SF pattern were also significantly lower than those with the SI pattern (all p-values < .01). For the BPVs of DBP, the differences remained similar to time. However, the BPVs in individuals with SI and US patterns were not significantly different.

3.1 | Sensitivity analysis

By adopting a different threshold for the diagnosis of hypertension (SBP/DBP ≥ 135/85 mmHg), consistent results are demonstrated in Figure S15. The comparisons between the average BP and BPVs between individual measurement frequency (days per week) showed similar results (Figures S16–S18).

4 | DISCUSSION

To the best of our knowledge, this community-based cohort study is the first study to explore this relationship and the first study using the sliding window technique in the home BP cohort study. This study addressed important findings and contributions. First, in these community-dwelling hypertensive older individuals, a stable and frequent home BP measurement pattern was found to be associated with a decrease in long-term BPV. Second, the sliding window method is used to investigate the association between dynamic behavior and BPV and to avoid the sampling bias problem.

Previous studies usually categorize participants into a fixed status and request them to join the entire project. However, in the real world, the participants' behaviors can be highly variable and usually change over time. The sliding window approach can slice the data by a reasonable size to observe the different states within a subject. This method does not need the participants to join the project entirely, can use the data more sufficiently, and does not discard valuable data in reasonable data preprocessing. It is a better data preprocessing approach to be used in real-world registry data with long-term follow-up as compared to the non-sliding window method (Table S1 and Figure S1). Moreover, a series of sensitivity and simulation studies were used to examine the robustness of our conclusions. A consistent relationship was observed between an SF monitoring pattern and a lower BPV. An optimal BP control includes not only a lower BP level but also a BP profile with fewer fluctuations. As such, the present study may provide evidence to support the recommendations about regular BP measurements at home for patients with hypertension.

Our results are consistent with those of other studies. A systematic review and meta-analysis included 52 prospective comparative studies of self-monitoring BP measurement, and results showed that self-managed BP monitoring with or without additional support is more effective than usual care in lowering BP at 6 months, but not at 12 months.[38] However, the studies included in this review had substantial heterogeneity in the use of HBPM, BP targets, and management. Another study based on self-reported BP recording by mobile phone indicated that a higher engagement in measuring BP is associated with a more significant reduction in BP.[39] More importantly, using the sliding window technique, our studies analyzed the behaviors rather than the participants with different BP measuring patterns. Thus, a participant can have different BP measurement patterns during the follow-up period using different sliding windows of observation (Figures 2 and 3). Using this unique approach, the dynamics of BP measurement behaviors can be identified and analyzed.

Some studies have shown that age, BMI, income-to-poverty ratio, history of hypertension and diabetes mellitus, race, health insurance, number of health care visits, and education had a significant effect on the frequency of HBPM.[40,41] Another study revealed that age, sex, day of the week, and seasonal variations were correlated with BPV.[42] In our study, after adjusting for all confounding factors, including age, sex, BMI, education, SES, receipt of social welfare benefit, area of residence, drinking habit, smoking habit, drugs, changing antihypertensive treatment composition, and history of stroke, hypertension, hyperlipidemia, heart disease, and diabetes mellitus, significant differences were still observed in BPVs according to different BP measurement patterns. These associations remained consistent and robust in a series of sensitivity analyses.

4.1 | Mechanism

Previous studies have shown that co-intervention with HBPM can be beneficial in controlling BP.[12,43,44] This improvement in BP control might be correlated with the modification in medication advised by their primary doctors. However, in the present study, the primary doctors did not access the cloud data of HBPM; this indicates that the improvement in BPV was independent of medical treatment but was associated with BP measurement behavior. Moreover, individuals with stable and frequent monitoring patterns may have a better health awareness. Thus, they can have better lifestyle and visit physicians more often for adjustment of medical treatment or modification of unhealthy lifestyles. On

another perspective, long-term BPV might not reflect immediate physiological change; instead, it was considered as the representation of the stability of BP control in participants who received antihypertensive therapy. A high BPV may be associated with inaccurate dosing/titration of antihypertensive therapy or low adherence to antihypertensive therapy.[45] However, in our mixed effect model, we adjusted for many possible confounding factors including the types of antihypertensive medications. Therefore, the mechanism of lower BPV in the stable frequent group was independent of the type of medication. Subjects with the stable and frequent measurement pattern may have attributes, including higher health awareness and literacy about BP control. Another cause might be the alerting effect of measuring behavior. Individuals with a stable and frequent BP measurement pattern might have sufficient knowledge about BP fluctuations and adopt relevant behavioral changes accordingly. These factors might lead to lower BPV.[45] Another plausible cause is the measurement error, and some studies have indicated that it could have a possible regression dilution effect.[46–49] More frequent BP measurements can obtain a more precise estimate of BPV. However, some studies have shown that HBPM is free from dilution bias.[4,50] Figure S15 shows that the variance owing to the sampling ratio was extremely low; therefore, regression dilution was not responsible for the association between different BP measurement patterns and BPVs.

4.2 | Strengths and weaknesses

Our study has some strengths. This is a longitudinal follow-up cohort study in which temporality between exposure (BP measurement patterns) and outcome (BPV) was established. A seemingly dose-response relationship between US, SF, and SI BP measurement patterns and BPV supports this speculation. We used the sliding window method to identify dynamic measurement patterns at different periods; this method can utilize real-world data in a more efficient manner. The BP measurement record was uploaded to the cloud platform in real time, thereby decreasing recall and handwriting errors. We recruited participants based on a community-based project, which increases the generalizability of our study population. We also adjusted for numerous factors in the linear mixed effect model. However, the study also had several limitations. That is, the average age of the participants was 77 years. Whether similar findings could be reproduced in younger participants should be further investigated. However, hypertension is common among older individuals; most participants may well represent patients with hypertension in the real world. The BP measurement patterns were determined based on the descriptive analysis of our study cohort, which may have limited generalizability in other study populations. However, the consistent results of these sensitivity analyses supported the robustness of the study conclusion. Some confounding factors were self-reported, which may have some residual confounding effects. In addition, given that there is a single-payer National Health Insurance in Taiwan and the participants were almost of the same ethnicity, some possible confounding factors, such as race, health insurance, and number of healthcare visits, were not considered in our study.

5 | CONCLUSIONS

In our study, we found that regular and frequent BP measurements at home among older individuals with hypertension were associated with lower BPV, which indicated that regular BP measurements at home may be correlated with BP profiles with less fluctuations.

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CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTION

Conceived and designed the analysis: Jia-You Lin, Kuan-Liang Kuo, Yi-Hsin Kuo, Yi-Fang Chuang, Hao-Min Cheng; Performed the analysis: Jia-You Lin; Wrote the paper: Jia-You Lin, Yi-Hsin Kuo, Kun-Pin Wu, Hao-Min Cheng; Collected the data: Kuan-Liang Kuo, Kuo-Chung Chu; Contributed data or analysis tools: Kuan-Liang Kuo, Kun-Pin Wu, Kuo-Chung Chu, Yan-Chen Jiang, Hao-Min Cheng; Other contribution: Yi-Fang Chuang, Hao-Min Cheng.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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