Number and Timing of Ambulatory Blood Pressure Monitoring Measurements

Byron C. Jaeger, PhDa, Oluwasegun P. Akinyelure, MDb, Swati Sakhuja, MPHb, Joshua D. Bundy, PhD, MPHc, Cora E. Lewis, MD MSPHb, Yuichiro Yano, MD, PhDd, George Howard, DrPHa, Daichi Shimbo, MDe, Paul Muntner, PhDb, Joseph E. Schwartz, PhDe,f

1. Department of Biostatistics, University of Alabama at Birmingham, Birmingham, AL
2. Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL
3. Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA
4. Department of Medicine, Duke University, Durham, NC
5. Department of Medicine, Columbia University Irving Medical Center, New York City, NY
6. Department of Psychiatry, Stony Brook School of Medicine, Stony Brook, NY

**Word count exclusive of references, tables, and figure legends**

* Abstract:
* Text:

**Conflict of Interest**

PM received grant funding and consulting fees from Amgen Inc., unrelated to the current manuscript. All other authors have nothing to disclose.

# ABSTRACT

Ambulatory blood pressure (BP) monitoring (ABPM) may cause sleep disturbances. Some home BP monitoring (HBPM) devices are able to obtain a limited number of readings at specific times during sleep. Determining whether a small number of BP measurements taken at specific times could reliably assess sleep BP could inform the use of these devices. We used data from the Jackson Heart Study (JHS; N=621) and the Coronary Artery Risk Development in Young Adults (CARDIA; N=458) study to evaluate 74 approaches to sample BP measurements during sleep. We sampled 2 to 4 BP measurements from a full ABPM assessment (i.e., all ABPM measurements during sleep) obtained at specific clock times and times relative to the start of sleep. Sampling BP at 1, 2, 4, and 5 hours after falling asleep provided the highest agreement with full a ABPM in classification of nocturnal hypertension: Kappa statistic (95% CI) 0.84 (0.81, 0.87). There was no evidence of a difference in C-statistics for left-ventricular hypertrophy or albuminuria when BP was sampled at 1, 2, 4, and 5 hours after falling asleep compared to sampling BP throughout sleep (p = 0.67). Using four BP measurements at 1, 2, 4, and 5 hours after falling asleep provides high agreement with a full ABPM assessment.

Higher blood pressure (BP) levels during sleep have been associated with an increased risk for cardiovascular disease (CVD) and target organ damage, independent of BP measured in a clinical setting (1–6). Ambulatory BP monitoring (ABPM) typically measures BP every 15 to 30 minutes throughout the day and night (7). Although most people find ABPM acceptable, it may cause sleep disturbances for some individuals (8–10). Home BP monitoring (HBPM) is another approach for measuring BP outside of the office setting and some HBPM devices can be programmed to measure BP at specific times, including when someone is asleep. For instance, Kario et. al. and Ishikawa et. al. reported on an HBPM device that is put on before going to sleep and measures BP at 2:00, 3:00, and 4:00 AM (11,12).

Obtaining fewer BP readings during sleep with HBPM instead of ABPM devices may reduce discomfort and disrupted sleep. However, less frequent measurement of BP using HBPM instead of ABPM may result in a loss of information and a weaker association with outcomes (13). Few studies have considered the number and timing of BP measurements required to obtain an estimate of BP during sleep similar to that obtained by a full ABPM recording (i.e., using ABPM throughout sleep). Using data from participants in the Jackson Heart Study (JHS) and the Coronary Artery Risk Development in Young Adults (CARDIA) study who underwent 24‐hour ABPM, we evaluated a total of 74 variations on sampling BP during sleep. Each BP sampling variant selected a subset of 2 to 4 BP measurements from all of the BP measurements taken during sleep.

# METHODS

## *Study population*

The JHS, a community-based prospective cohort study, was designed to evaluate the etiology of CVD among African Americans (14). The JHS enrolled 5,306 non-institutionalized African Americans aged ≥ 21 years from the Jackson, MS metropolitan area between 2000 and 2004. At the baseline JHS visit, 1,146 participants elected to undergo ABPM. The CARDIA study was designed to examine the development and determinants of clinical and subclinical CVD and their risk factors (15). The CARDIA study recruited 5,115 participants, 18 to 30 years of age, at four field centers in the United States (Birmingham, AL; Chicago, IL; Minneapolis, MN; and Oakland, CA) in 1985-1986. During the Year 30 Exam (2015-2016), 831 CARDIA participants enrolled in an ABPM ancillary study conducted in the Birmingham, AL and Chicago, IL field centers.

We included participants who slept ≥ 5 hours during their ABPM assessment and recorded ≥ 1 valid BP measurement every 30 minutes from midnight to 5:00 AM during their ABPM assessment (N = 621 JHS and 458 CARDIA participants; Table S1). Conduct of each study was approved by institutional review boards at the participating institutions and the current analysis was approved by the University of Alabama at Birmingham Institutional Review Board. Written informed consent was obtained from all participants.

## *Ambulatory blood pressure monitoring*

In the JHS, ABPM was conducted using the SpaceLabs model 90207 device (SpaceLabs Healthcare, Snoqualmie, WA), which has been previously validated, and BP was measured every 20 minutes over a 24-hour period (16). JHS participants self-reported the times they went to sleep and woke up while wearing the ABPM device. In CARDIA, ABPM was conducted using the SpaceLabs OnTrak model 90227 device (SpaceLabs Healthcare, Snoqualmie, WA), which has also been previously validated, with an appropriately sized cuff and BP was measured every 30 minutes over a 24-hour period (17). CARDIA participants also wore an Actiwatch activity monitor (Philips Respironics, Murrysville, PA) on the wrist of their non-dominant arm. In CARDIA, awake and asleep time periods were determined using the activity monitor data in conjunction with participants’ self-reported awake and asleep times.

## *Blood pressure sampling strategies and variations*

We considered ‘distributed’ and ‘consecutive’ strategies to sample BP during sleep (Figure 1). The distributed strategy sampled BP from the full ABPM assessment with intervals between measurements spanning at least 1 hour. The consecutive strategy sampled BP from the full ABPM assessment in consecutive measurements of BP. We considered 25 distributed and 12 consecutive BP sampling variations, and implemented each variation using hours since midnight and hours since falling asleep to identify sampling times. In total, we evaluated 74 different variations on sampling BP: (25 distributed variations + 12 consecutive variations) \* 2 time definitions = 74 variations in total.

## *Nocturnal hypertension*

For JHS and CARDIA participants, nocturnal hypertension according to ABPM was defined by a mean SBP ≥ 120 mm Hg or mean DBP ≥ 70 mm Hg based on all valid BP measurements during sleep. For all BP sampling variations, nocturnal hypertension was defined with the same BP thresholds but using the mean of the 2 to 4 BP measurements that were sampled from the full ABPM assessment.

*Left ventricular hypertrophy and albuminuria*

Echocardiograms and urine specimens were assessed during the Year 30 Exam for CARDIA participants and during the baseline study visit for JHS participants. Left ventricular mass was determined and indexed to body surface area to obtain left ventricular mass index (LMVI) according to recommendations from the American Society of Echocardiography and European Association of Cardiovascular Imaging (18). Left ventricular hypertrophy (LVH) was defined as LVMI > 95 g/m2 in women and > 115 g/m2 in men. Urine specimens were used to measure urinary albumin and creatinine excretion, which were used to calculate the urine albumin-to-creatinine ratio (ACR). ACR was quantified using a 24-hour urine sample in the JHS, if available. Otherwise, a spot urine sample was used. In CARDIA, a spot urine sample was collected for all willing participants. Albuminuria was defined as an ACR ≥ 30 mg/g.

## *Statistical analyses*

Participant characteristics were summarized for the overall population and stratified by study cohort. The count and percent of missing values for each study variable were examined. Differences in mean SBP and DBP during sleep, LVH, and albuminuria were compared between study cohorts using t- and chi-square tests for continuous and categorical variables, respectively. Analyses were conducted using base R version 4.0.3 (Vienna, Austria) and a number of additional open-source R packages (19–23).

# RESULTS

# DISCUSSION

Table 1: Participant characteristics in the overall population and stratified by study.

|  | | **Study** | |
| --- | --- | --- | --- |
| **Characteristic\*** | **Overall (N = 1079)** | **CARDIA (N = 458)** | **JHS (N = 621)** |
| Age, years | 57.1 (8.57) | 54.7 (3.70) | 58.8 (10.5) |
| Male, % | 32.0 | 37.8 | 27.7 |
| Black, % | 81.0 | 55.2 | 100 |
| Education, % |  |  |  |
| College graduate | 62.3 | 61.1 | 63.2 |
| High School graduate/GED | 10.5 | 0.00 | 18.2 |
| Less than High School | 27.2 | 38.9 | 18.5 |
| Current smoker, %† | 10.8 | 12.9 | 9.25 |
| Diabetes, %‡ | 22.3 | 17.7 | 25.6 |
| Albuminuria, % | 8.06 | 6.99 | 9.09 |
| Left ventricular mass indexed to BSA, g/m2 | 77.5 (21.1) | 78.8 (20.2) | 76.7 (21.7) |
| Left ventricular hypertrophy, % | 9.78 | 8.59 | 10.6 |
| Sleep duration, hours | 8.00 (1.47) | 7.62 (1.43) | 8.29 (1.44) |
| Nocturnal hypertension, %§ | 46.9 | 36.7 | 54.4 |
| Antihypertensive medication use, % | 53.3 | 43.5 | 60.6 |
| Blood pressure, mm Hg | | | |
| Asleep systolic | 116 (15.6) | 111 (15.1) | 120 (14.7) |
| Asleep diastolic | 67.2 (8.95) | 66.3 (8.59) | 67.8 (9.16) |
| Clinic systolic | 124 (16.2) | 119 (15.1) | 128 (16.0) |
| Clinic diastolic | 73.8 (9.25) | 72.9 (9.86) | 74.5 (8.71) |
| \*Table values are mean (standard deviation) and percent for continuous and categorical variables, respectively. | | | |
| †Smoking status was defined as self-reporting cigarette use within the past year. | | | |
| ‡Diabetes was defined as fasting (8+ hours) glucose of at least 126 mg/dL or current use of anti-diabetes medication. | | | |
| §Nocturnal hypertension was defined as asleep systolic/diastolic blood pressure ≥120/70 mm Hg. | | | |
|  | | | |
| Missing counts (%): albuminuria: 148 (14%); left ventricular mass and hypertrophy: 57 (5.3%); antihypertensive medication use: 8 (0.74%); Smoking status: 6 (0.56%); diabetes: 2 (0.19%); education: 1 (0.09%) | | | |
| BSA = body surface area; CARDIA = Coronary Artery Risk Development in Young Adults; GED = General Educational Development; JHS = Jackson Heart Study | | | |

Table 2: summary of 12 blood pressure sampling variations that obtained the highest overall chance-corrected agreement (i.e., Kappa statistic) with ambulatory blood pressure monitoring throughout sleep.

| **BP sampling variation\*** | **Kappa statistic (95% CI) for nocturnal hypertension†‡** | | | **Mean absolute error (95% CI) for mean systolic BP during sleep** | | | **Mean absolute error (95% CI) for mean diastolic BP during sleep** | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Overall** | **CARDIA** | **JHS** | **Overall** | **CARDIA** | **JHS** | **Overall** | **CARDIA** | **JHS** |
| *2 Consecutive BP measurements* | | | | | | | | | |
| starting at 4 hours after midnight | 0.72 (0.68, 0.76) | 0.72 (0.65, 0.79) | 0.71 (0.65, 0.76) | 5.32 (5.06, 5.58) | 5.47 (5.08, 5.88) | 5.20 (4.87, 5.54) | 4.55 (4.33, 4.76) | 4.65 (4.32, 5.00) | 4.47 (4.19, 4.76) |
| starting at 2 hours after sleep | 0.73 (0.69, 0.77) | 0.72 (0.65, 0.79) | 0.72 (0.66, 0.77) | 5.52 (5.25, 5.80) | 5.42 (5.00, 5.88) | 5.58 (5.23, 5.94) | 4.53 (4.30, 4.76) | 4.44 (4.09, 4.81) | 4.59 (4.29, 4.89) |
| *2 Distributed BP measurements* | | | | | | | | | |
| at 1 and 3 hours after midnight | 0.74 (0.70, 0.78) | 0.78 (0.72, 0.84) | 0.70 (0.65, 0.76) | 4.86 (4.64, 5.10) | 4.72 (4.37, 5.09) | 4.97 (4.68, 5.26) | 3.96 (3.75, 4.16) | 3.75 (3.44, 4.09) | 4.10 (3.83, 4.37) |
| at 1 and 5 hours after sleep | 0.77 (0.73, 0.81) | 0.79 (0.73, 0.85) | 0.75 (0.69, 0.80) | 4.67 (4.46, 4.89) | 4.54 (4.21, 4.88) | 4.77 (4.50, 5.06) | 3.80 (3.61, 3.99) | 3.56 (3.27, 3.86) | 3.99 (3.75, 4.23) |
| *3 Consecutive BP measurements* | | | | | | | | | |
| starting at 1 hours after midnight | 0.74 (0.70, 0.78) | 0.75 (0.68, 0.81) | 0.72 (0.66, 0.77) | 4.88 (4.64, 5.13) | 4.78 (4.41, 5.17) | 4.95 (4.63, 5.29) | 4.08 (3.87, 4.30) | 3.97 (3.65, 4.30) | 4.16 (3.88, 4.44) |
| starting at 1 hours after sleep | 0.76 (0.72, 0.80) | 0.77 (0.71, 0.83) | 0.73 (0.68, 0.78) | 5.27 (5.02, 5.54) | 4.78 (4.42, 5.15) | 5.63 (5.29, 6.00) | 4.27 (4.06, 4.48) | 3.87 (3.59, 4.18) | 4.55 (4.27, 4.86) |
| *3 Distributed BP measurements* | | | | | | | | | |
| at 1, 2 and 4 hours after midnight | 0.79 (0.75, 0.83) | 0.80 (0.74, 0.86) | 0.77 (0.72, 0.82) | 3.82 (3.64, 4.00) | 3.93 (3.65, 4.22) | 3.73 (3.49, 3.98) | 3.25 (3.09, 3.42) | 3.24 (2.98, 3.51) | 3.27 (3.06, 3.48) |
| at 1, 2 and 4 hours after sleep | 0.82 (0.78, 0.85) | 0.83 (0.78, 0.89) | 0.80 (0.75, 0.84) | 4.01 (3.82, 4.20) | 4.01 (3.73, 4.29) | 4.01 (3.76, 4.27) | 3.31 (3.16, 3.47) | 3.07 (2.85, 3.30) | 3.48 (3.28, 3.69) |
| *4 Consecutive BP measurements* | | | | | | | | | |
| starting at 1 hours after midnight | 0.77 (0.73, 0.81) | 0.80 (0.74, 0.86) | 0.74 (0.69, 0.79) | 4.31 (4.10, 4.51) | 4.09 (3.79, 4.40) | 4.46 (4.18, 4.75) | 3.66 (3.47, 3.84) | 3.40 (3.13, 3.70) | 3.85 (3.60, 4.10) |
| starting at 1 hours after sleep | 0.78 (0.74, 0.81) | 0.78 (0.72, 0.84) | 0.76 (0.71, 0.81) | 4.58 (4.36, 4.81) | 4.16 (3.86, 4.47) | 4.89 (4.58, 5.22) | 3.72 (3.53, 3.90) | 3.32 (3.08, 3.56) | 4.01 (3.76, 4.26) |
| *4 Distributed BP measurements* | | | | | | | | | |
| at 1, 2, 4 and 5 hours after midnight | 0.82 (0.78, 0.85) | 0.85 (0.81, 0.90) | 0.78 (0.73, 0.83) | 3.17 (3.01, 3.32) | 3.15 (2.93, 3.38) | 3.18 (2.98, 3.38) | 2.61 (2.48, 2.75) | 2.60 (2.38, 2.85) | 2.62 (2.46, 2.78) |
| at 1, 2, 4 and 5 hours after sleep | 0.84 (0.81, 0.87) | 0.84 (0.79, 0.89) | 0.83 (0.79, 0.88) | 3.11 (2.97, 3.26) | 3.10 (2.89, 3.33) | 3.12 (2.93, 3.32) | 2.66 (2.53, 2.78) | 2.48 (2.30, 2.67) | 2.79 (2.62, 2.96) |
| BP = blood pressure; CARDIA = Coronary Artery Risk Development in Young Adults; JHS = Jackson Heart Study | | | | | | | | | |
| \*Blood pressure sampling variations were compared to other variations that measure blood pressure the same number of times (i.e., 2, 3, or 4) using the same strategy (i.e., Consecutive or distributed) and the same time reference (i.e., midnight or onset of sleep). Each of these 12 comparison groups had one variation with the highest overall Kappa statistic, and those variations are presented here. | | | | | | | | | |
| †Kappa statistics measure the chance-corrected agreement in classification of nocturnal hypertension between ambulatory blood pressure monitoring throughout sleep and a blood pressure sampling variation. | | | | | | | | | |
| ‡Nocturnal hypertension was defined as asleepsystolic/diastolic blood pressure ≥120/70 mm Hg. | | | | | | | | | |

# SUPPLEMENT

Table S1: Participant inclusion cascade.

| **Inclusion criteria** | **Overall** | **CARDIA participants** | **JHS participants** |
| --- | --- | --- | --- |
| All study participants | 10,421 | 5,115 | 5,306 |
| Participants who underwent 24-hour ABPM. | 1,977 | 831 | 1,146 |
| Participants with ≥5 asleep systolic and diastolic blood pressure measurements. | 1,729 | 788 | 941 |
| Participants who were asleep for all measurements between 1am and 5am. | 1,499 | 645 | 854 |
| Participants with at least 1 systolic and diastolic blood pressure measurement within 30 minutes of all sampling times | 1,079 | 458 | 621 |
| ABPM = ambulatory blood pressure monitoring; CARDIA = Coronary Artery Risk Development in Young Adults; JHS = Jackson Heart Study | | | |

# REFERENCES

1. O’Brien E, Parati G, Stergiou G, et al. European society of hypertension position paper on ambulatory blood pressure monitoring. *Journal of hypertension*. 2013;31(9):1731–1768.

2. Parati G, Stergiou G, O’Brien E, et al. European society of hypertension practice guidelines for ambulatory blood pressure monitoring. *Journal of hypertension*. 2014;32(7):1359–1366.

3. Shimamoto K, Ando K, Fujita T, et al. The Japanese society of hypertension guidelines for the management of hypertension (JSH 2014). *Hypertension Research*. 2014;37(4):253–390.

4. Friedman O, Logan AG. Can nocturnal hypertension predict cardiovascular risk? *Integrated blood pressure control* [electronic article]. 2009;2:25. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3172086/>). (Accessed October 14, 2017)

5. Yano Y, Tanner RM, Sakhuja S, et al. Association of daytime and nighttime blood pressure with cardiovascular disease events among african american individuals. *JAMA Cardiol* [electronic article]. 2019;(<https://jamanetwork.com/journals/jamacardiology/fullarticle/2747607>). (Accessed August 15, 2019)

6. Kario K. Nocturnal hypertension: New technology and evidence. *Hypertension*. 2018;71(6):997–1009.

7. Pickering TG, Shimbo D, Haas D. Ambulatory blood-pressure monitoring. *New England Journal of Medicine*. 2006;354(22):2368–2374.

8. Ernst ME, Bergus GR. Favorable patient acceptance of ambulatory blood pressure monitoring in a primary care setting in the united states: A cross-sectional survey. *BMC family practice*. 2003;4(1):15.

9. Degaute JP, Kerkhofs M, Dramaix M, et al. Does non-invasive ambulatory blood pressure monitoring disturb sleep? *Journal of hypertension*. 1992;10(8):879–885.

10. Agarwal R, Light RP. The effect of measuring ambulatory blood pressure on nighttime sleep and daytime activity—implications for dipping. *Clinical Journal of the American Society of Nephrology*. 2010;5(2):281–285.

11. Kario K, Hoshide S, Haimoto H, et al. Sleep blood pressure self-measured at home as a novel determinant of organ damage: Japan morning surge home blood pressure (J-HOP) study. *The Journal of Clinical Hypertension*. 2015;17(5):340–348.

12. Ishikawa J, Shimizu M, Edison ES, et al. Assessment of the reductions in night-time blood pressure and dipping induced by antihypertensive medication using a home blood pressure monitor. *Journal of hypertension*. 2014;32(1):82–89.

13. Kario K, Saito I, Kushiro T, et al. Home blood pressure and cardiovascular outcomes in patients during antihypertensive therapy: Primary results of HONEST, a large-scale prospective, real-world observational study. *Hypertension*. 2014;64(5):989–996.

14. Taylor Jr HA, Wilson JG, Jones DW, et al. Toward resolution of cardiovascular health disparities in african americans: Design and methods of the jackson heart study. *Ethn Dis*. 2005;15(4):S6–4.

15. Friedman GD, Cutter GR, Donahue RP, et al. CARDIA: Study design, recruitment, and some characteristics of the examined subjects. *Journal of clinical epidemiology*. 1988;41(11):1105–1116.

16. O’Brien E, Mee F, Atkins N, et al. Accuracy of the SpaceLabs 90207 determined by the British Hypertension Society protocol. *J Hypertens*. 1991;9(suppl 5):S25–S31.

17. Greef A de, Shannan AH. Validation of spacelabs 90227 OnTrak upper arm blood pressure monitor, for clinical use, according to the European Society of Hypertension International Protocol 2010 and the British Hypertension Society Protocol. (<http://www.dableducational.org/Publications/2014/ESH-IP%202010%20and%20BHS%20Validation%20of%20Spascelabs%2090227%20OnTrak.pdf>)

18. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Heart Journal-Cardiovascular Imaging*. 2015;16(3):233–271.

19. R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2020.(<https://www.R-project.org/>)

20. Wickham H, Averick M, Bryan J, et al. Welcome to the tidyverse. *Journal of Open Source Software*. 2019;4(43):1686.

21. Landau WM. The drake r package: A pipeline toolkit for reproducibility and high-performance computing. *Journal of Open Source Software* [electronic article]. 2018;3(21). (<https://doi.org/10.21105/joss.00550>)

22. Buuren S van, Groothuis-Oudshoorn K. Mice: Multivariate imputation by chained equations in r. *Journal of statistical software*. 2010;1–68.

23. Jaeger B. table.glue: Make and apply customized rounding specifications for tables. 2020.(<https://github.com/bcjaeger/table.glue>)