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SHORT REPORT

Integrative Cardiovascular Physiology and Pathophysiology

Identifying an acceptable number of ambulatory blood pressure measurements for accuracy of average blood pressure and nocturnal dipping status

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Abstract

We aimed to identify the minimum number of ambulatory blood pressure (ABP) measures to accurately determine daytime and nighttime systolic blood pressure (BP) averages and nocturnal dipping status (i.e., relative daytime:nighttime change). A total of 43 midlife participants wore an ABP monitor for 24 h with measurements every 20/30 min during the daytime/nighttime, as identified by a sleep diary. We calculated daytime/nighttime systolic BP average and dipping status from all available measurements per participant (i.e., normative data). We then calculated daytime and nighttime BP per participant based on a random selection of 8–20 and 4–10 measurements and replicated random selections 1,000 times. We calculated accuracy by checking the proportion from 1,000 different randomly selected samples for a particular number of measurements that systolic BP was ±5 mmHg of normative data, and dipping status remained unchanged for each participant compared with the normative value. The best fit for the regression model estimated the minimal number of measurements for an accuracy of 95% in BP averages. For a 95% accuracy in estimating daytime and nighttime systolic BP, 11 daytime and 8 nighttime measurements were required. The highest accuracy for dipping status was 91.6 ± 13.4% using 20 daytime and 10 nighttime measures, while the lowest was (83.4 ± 15.1%) using 8 daytime and 4 nighttime measures. In midlife adults, 11 daytime and 8 nighttime measurements are likely enough to calculate average systolic BPs accurately. However, no minimum number is suggested to accurately calculate dipping status.

NEW & NOTEWORTHY We found that a minimum of 11 blood pressure (BP) measures are necessary to calculate an accurate average daytime BP, and 8 nighttime measures are necessary to calculate an accurate nighttime average if 95% accuracy is acceptable. Regarding BP dipping status, the current recommendations (20 daytime/7 nighttime) inaccurately classified the dipping status 10.5% of the time, suggesting that guidelines may need to be updated to classify patients as nocturnal dippers or nondippers correctly.

ambulatory blood pressure; awake blood pressure; cardiovascular risk; dipping and nondipping blood pressure; hypertension

INTRODUCTION

Hypertension (HTN) societies worldwide unanimously recommend ambulatory blood pressure monitoring (ABPM) as the most accurate screening test to confirm and help treat HTN (1–3).

The current recommendations for a valid ABPM exam require at least 80% successful ABPM readings across 24 h (1–3), and the European Society of HTN is the only organization that recommends a minimal number of readings ≥20/7 for daytime and nighttime, respectively (2). Notwithstanding its value, wearing an ABPM machine can be uncomfortable, disturb sleep, and restrain activities, with the frequency of measurements (i.e., every 20–30 min) indicated as the major complaint (4, 5). Along this line, Yang and colleagues recently proposed that the minimal number of ABPM readings may be reduced to ≥8/4 for daytime/nighttime periods to assign CV risk (6). If reproduced, these findings would substantially

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advance clinical practice by potentially increasing patient comfort and adherence. Surprisingly, these methods have already been used in large studies to categorize cardiovascular risk (7, 8), even though Yang and colleagues advised against it pending further studies on reliability and reproducibility (6), which still has not been tested.

So far, investigations on the number of ABPM readings have focused on risk prediction. This approach is highly relevant clinically, but its use remains limited without the understanding of whether the accuracy remains the same when performing a lower number of ABPM measures compared with when all readings are available (e.g., 48 during the day and 24 during the night). For instance, we recently showed that a reduced number of measurements during the biological night can affect average systolic BP and systolic dipping status (9).

In the current investigation, we aimed to identify the minimum number of BP readings to accurately estimate average daytime and nighttime BP and dipping status when compared with averages obtained using all measurements captured during the ABPM exam.

METHODS

These data were compiled from separate studies conducted between 2015 and 2021 that investigated sleep or circadian rhythms in individuals without severe sleep disorders, and some were published (10, 11). To be included in this analysis, participants' data had at least 80% successful readings and 20 daytime and 8 nighttime measurements. For those who participated in multiple studies or did multiple visits, only their first complete data set was included. Initially, our database had 121 files; we excluded 50 extra visit files (multiple studies or visits in one study) and 28 because of the unsuccessful percentage or number of readings criteria.

The Institutional Review Board at the Oregon Health and Science University approved the studies for human subject protection. All methods concerning collecting ABPM data and sleep diary were identical as part of the standard screening process performed in our group studies. Participants were screened for chronic diseases by self-report of physical and psychological history, vital sign measurements plus 12-lead ECG in the laboratory, sleep apnea screening at home (WatchPAT; Itamar Medical, Ltd, Israel), and laboratory testing of hematologic and metabolic measures (e.g., basic blood chemistry and blood glucose). We excluded people who reported any chronic disease, including severe obstructive sleep apnea (i.e., apnea/hypopnea index $\geq$30 events/h or had abnormalities in their electrocardiogram at rest). Individuals were also excluded when they were pregnant (confirmed with a pregnancy test), had a smoking history (>3 packs/wk), or had recent use of nicotine confirmed by the presence of cotinine in the urine (NicAlert; Nymox Corporation, NJ) or use of recreational and opiated drugs verified by urinalysis (Drugsmart 12 panel cup; Speares Medical, Inc, SC).

Participants were instructed to wear an ABPM (Spacelabs Healthcare, 90207, Snoqualmie, WA) on their nondominant arms for 24 h. Participants were explained and demonstrated the procedures to don and doff the cuffs in a face-to-face meeting, and written instructions were provided, such as keeping the arm stable during each measurement. During the measurements, we asked participants to maintain a self-selected 8-h in-bed schedule beginning at their habitual sleep time (e.g., 11:00 PM to 7:00 AM) and avoid afternoon naps. Sleep and wake times were identified by self-report using detailed sleep diary data. BP was measured every 20 min during the 16-h daytime and every 30 min during the 8-h nighttime in each participant.

Systolic BP average values were calculated for daytime and nighttime. Systolic BP dipping (%) was calculated as the percent change between its average during daytime and nighttime BP. Dipping status was determined based on a threshold of $\geq$10% decline (dipper) or <10% decline in nighttime BP compared with daytime BP (nondipper) profile (12, 13).

Data Analysis

The analysis consisted of multiple steps run by a biostatistician (S.M.R.). Initially, we defined our "normative" values to allow us to evaluate the accuracy of using fewer measures. The normative average daytime and nighttime systolic BP and dipping status were calculated from each participant based on all available measurements. From this point to the end of the manuscript, these indices will be called normative daytime systolic BP, nighttime systolic BP, and dipping status.

Afterward, we took a series of intraparticipant random selections using fewer measurements to compare the accuracy of daytime and nighttime systolic BP and dipping status compared with their normative values. Specifically, we computed average systolic BP using a random selection of 8 through 20 daytime and 4 through 10 nighttime measures, respectively, to match the minimal criteria proposed by Yang et al. (6). We bootstrapped this process to produce 1,000 random samples of systolic BP averages using each of the identified number of measurements. Then, to avoid potentially dependent effects of a single random sample of 1,000 recorded average systolic BP values per person per measurement, we re-ran this sampling process such that each potential dipping status combination had a uniquely produced random sample of daytime and nighttime measurements. For instance, we replicated the 1,000 random samples of intraparticipant average systolic BP for 8 daytime measurements so that each could be paired with a corresponding random sampling of nighttime measurements 4–10 (e.g., dipping status accuracy computed for 8-day/4-night and 8-day/5-night measurements, respectively, used unique random samples for both daytime and nighttime). Note that one participant was excluded from all sampling that included 10 nighttime measurements as they only had a maximum of 9 measurements. From these random samples, accuracy was calculated by evaluating the proportion from 1,000 different randomly selected samples from each participant that SBP was within the clinically meaningful cutoff of ±5 mmHg from the normative average suggested in a previous consensus document (14), and the dipping status remained unchanged when compared with a participant's normative dipping status, respectively. Descriptive statistics (e.g., means and standard deviation) were computed for

accuracy, such that each participant's overall daytime and nighttime systolic BP accuracy proportion was averaged for each number of measurements used, respectively. Each participant's overall dipping status accuracy values were averaged for each combination (i.e., 8-day/4-night through 20-day/10-night). Finally, a mixed model approach was applied to develop predicted daytime and nighttime measurement accuracies. Data were nested within participants on the measurement level. Measurements were considered a continuous main effect (8–20 for daytime; 4–10 for nighttime) on accuracy. "Participant" was considered a random intercept with an unstructured covariance matrix. Linear, quadratic, and cubic functions were evaluated sequentially. The model with the highest order polynomial term at statistical significance ($P < 0.05$) was selected for plotting. Using estimated parameters, we plotted predicted empirical accuracy based on a given range of measurements used to measure systolic BP in the daytime or nighttime, respectively. All analyses were conducted using RStudio software (RStudio Team, 2020) and SAS 9.4.

RESULTS

A total of 43 participants were included in the analysis. The characteristics of the participants are shown in Table 1. Descriptive statistics of participants' ABPM data set are shown in Supplemental Table S1 (https://doi.org/10.6084/m9.figshare.25962124.v1). Most participants' data were in the range of normality according to skewness and kurtosis coefficient.

Accuracy in Determining Average Systolic Blood Pressure

Daytime systolic BP was accurately identified in 99.7 ± 0.7% of the samples using 20 measures and 89.4 ± 6.9% using 8 measures (Fig. 1*A*). A cubic mixed-effects model fitted on daytime measurements estimated that a 95% accuracy threshold would be achieved with 11 measurements (Fig. 1*C*). Nighttime systolic BP was accurately identified in 98.8 ± 2.6% of the samples using 10 measures and accuracy at 78.2 ± 11.7% using 4 measures (Fig. 1*B*). A quadratic mixed-effects model fitted on nighttime measurements estimated that a 95% accuracy threshold would be achieved with eight measurements (Fig. 1*D*).

Table 1. *Demographic and participants' characteristics*

N	43
Females, *n* (%)	17 (39.5)
Age, yr	50 ± 10
Height, cm	176.2 ± 11.0
Body mass, kg	83.8 ± 16.1
Body mass index, kg/m^2	27.0 ± 4.5
Systolic blood pressure, mmHg	121 ± 13
Diastolic blood pressure, mmHg	69 ± 9
Blood glucose mg/dL	93 ± 10
Apnea-hypopnea index, events/h	9.2 ± 7.4
Average time to bed, hh:mm	22:46 ± 1:06
Average wake time, hh:mm	06:48 ± 1:07

Values are means ± SD or *n* (%); *N*, *n*, number of participants. Blood pressures were measured in triplicate in the office during screening visits. Hours:minutes (hh:mm) refer to average bedtime and wake time reported by participants.

Accuracy in Determining Systolic Blood Pressure Dipping Status

Systolic dipping status was accurately identified in 91.6 ± 13.4% of the samples using 20/10 measures and 83.4 ± 15.1% using 8/4 measurements of daytime/nighttime, respectively (Fig. 2).

A demonstrative graph presented in Fig. 3 reveals that accuracy in determining dipping status reduced as close the individual is to the 10% threshold of calculating the dipping status (Fig. 3).

DISCUSSION

We aimed to identify the number of measures needed for an accurate ABPM exam based on daytime and nighttime averages and the dipping status of systolic BP when compared against all available measurements throughout 24 h. With 95% accuracy, the main findings in the current study are: *1*) ≥11 daytime measures are necessary for an accurate daytime average systolic BP, and ≥8 measures during nighttime are required to determine the nighttime average. *2*) The accuracy of calculating a dipping status is lower than 95% regardless of the number of measures and is more sensitive to changes in nighttime BP than daytime BP. Clinicians can use our findings to evaluate the number of ABPM measures needed for an accurate decision depending on the level of accuracy personally deemed satisfactory (Fig. 1).

Even though our focus was solely on methodological accuracy and not risk prediction, our results are somewhat different from those published by Yang et al. (6). The discrepancy in findings is not altogether unexpected because of the differences in our statistical approaches. For instance, Yang et al.'s approach of averaging the individual bootstrapped BP means for each data reduction likely produced an arbitrarily deflated standard deviation of the difference for each full-reduced data comparison. In contrast, our approach used the proportion of bootstraps for everyone that differed within a clinically meaningful margin (e.g., ±5 mmHg). This makes our method not as susceptible to the normal sampling distribution because we selected clinical cutoffs that reduce the possible effect of standard sampling error based on standard deviation due to the margin of different existent outside of the bootstrapping (i.e., consistency was based on non-statistical criteria). We also present results from a range of data reductions for clinicians to be able to make individual decisions based on how much error they are comfortable with on a case-by-case basis (see Fig. 1, *C* and *D*). This may be particularly important in clinical assessment to guarantee good measures of BP as an important clinical biomarker to identify patients at different risk levels (15). Not restricted to HTN, an accurate ABPM exam will positively influence decisions on the treatment of other diseases, such as chronic kidney disease (16) and obstructive sleep apnea (17).

It is known that systolic BP fluctuates during sleep. This occurs because of slight variations in sleep architecture that have two main sleep patterns: non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. Such variation in BP may directly affect its averaged values measured during sleep. Our group recently showed that the chronological distribution of a small number of measurements (i.e., four) during the biological night impacts systolic BP's

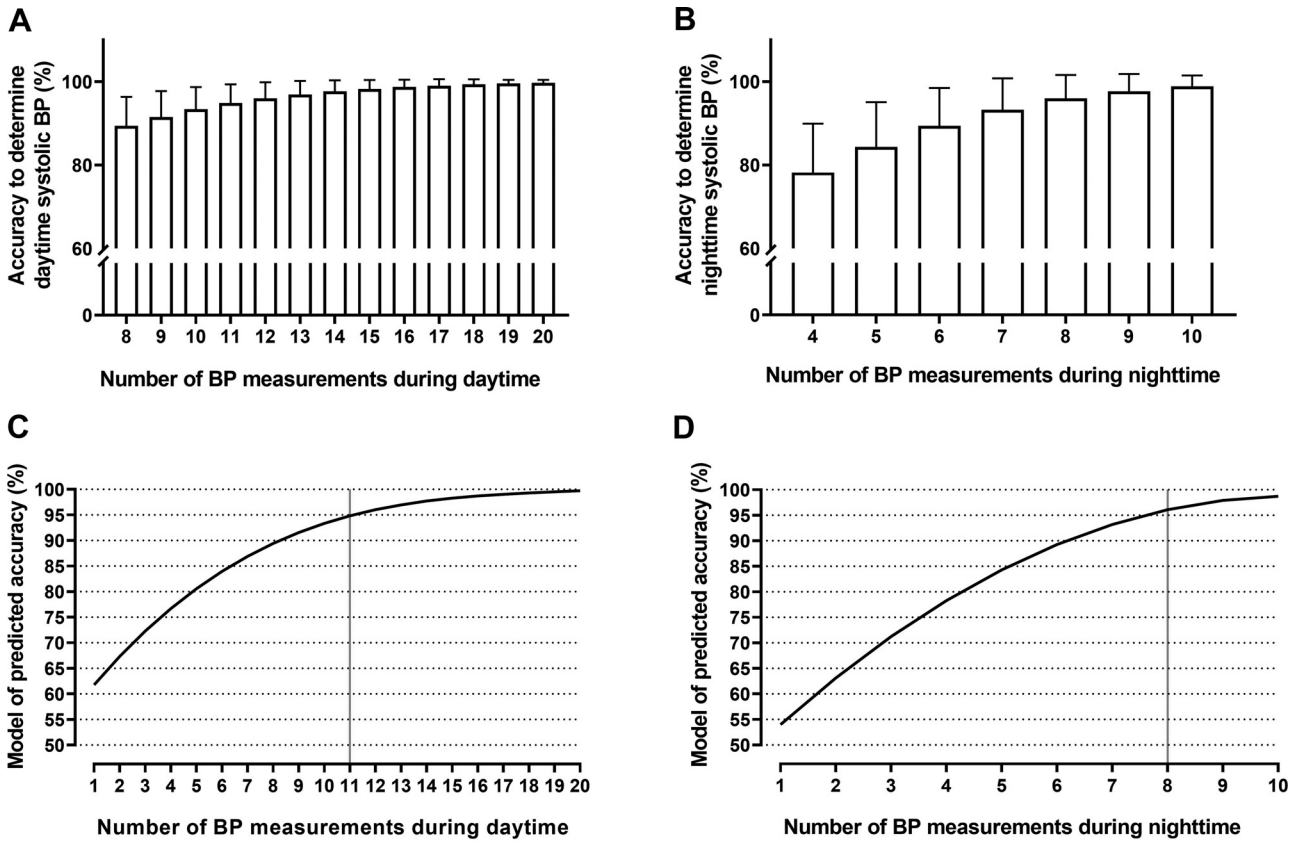

Figure 1. Average accuracy in determining systolic blood pressure was based on 1,000 random samples compared with normative average calculated from all measurements available from each participant. *A*: daytime means ± SD accuracy from 8 to 20 measurements. *B*: nighttime means ± SD accuracy from 4 to 10 measurements. *C*: cubic mixed-effects model fitted on daytime measurements (red line indicates 95% of accuracy). *D*: quadratic mixed-effects model fitted on nighttime measurements (red line indicates 95% of accuracy).

average and dipping status (9). Variation from the daytime average has been previously associated with physical activity in people with hypertension assessed during their free daily living activities (18). In addition, daytime measures are also subject to other confounders that increase the variability measure to measure ABPM, such as arm movement, driving, environmental stress, and work, among others (15). To minimize that confounder in our data set, we instructed the participants to have a stable 8 h in bed and avoid strenuous physical effort one day before and during the exam in the current study. Such sample characteristics may explain why the daytime average was not greatly affected by fewer numbers, whereas the mechanisms affecting the stability of BP measures across the night need further investigation.

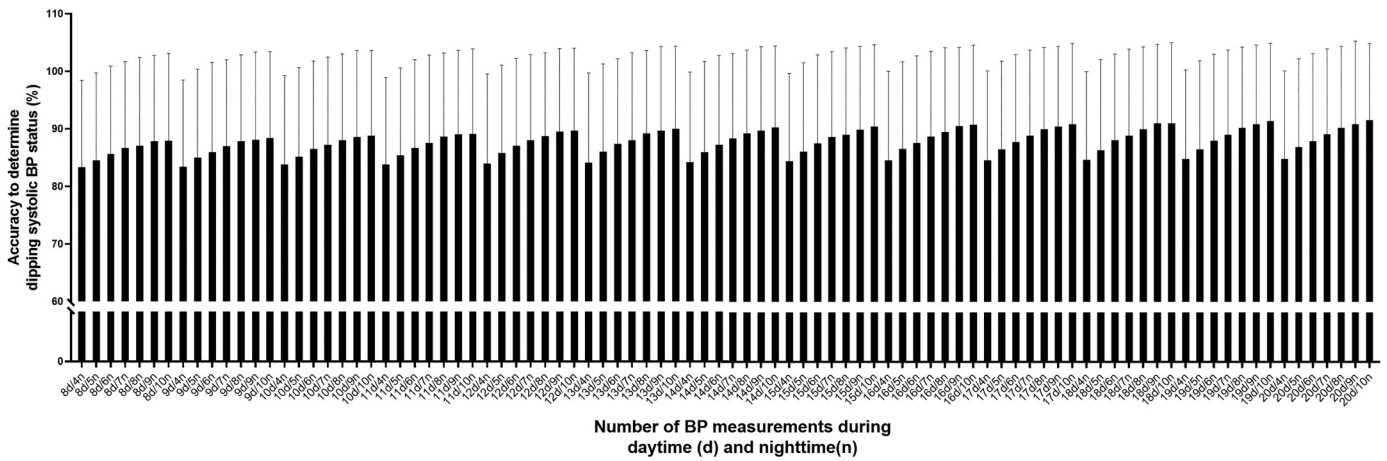

Figure 2. Means ± SD accuracy to determine the dipping statuses of systolic blood pressure based on 1,000 random samples of all possible combinations between 8 and 20 measurements during daytime with all possible combinations between 4 and 10 measurements during nighttime compared with normative dipper status calculated from all measurements available from each participant.

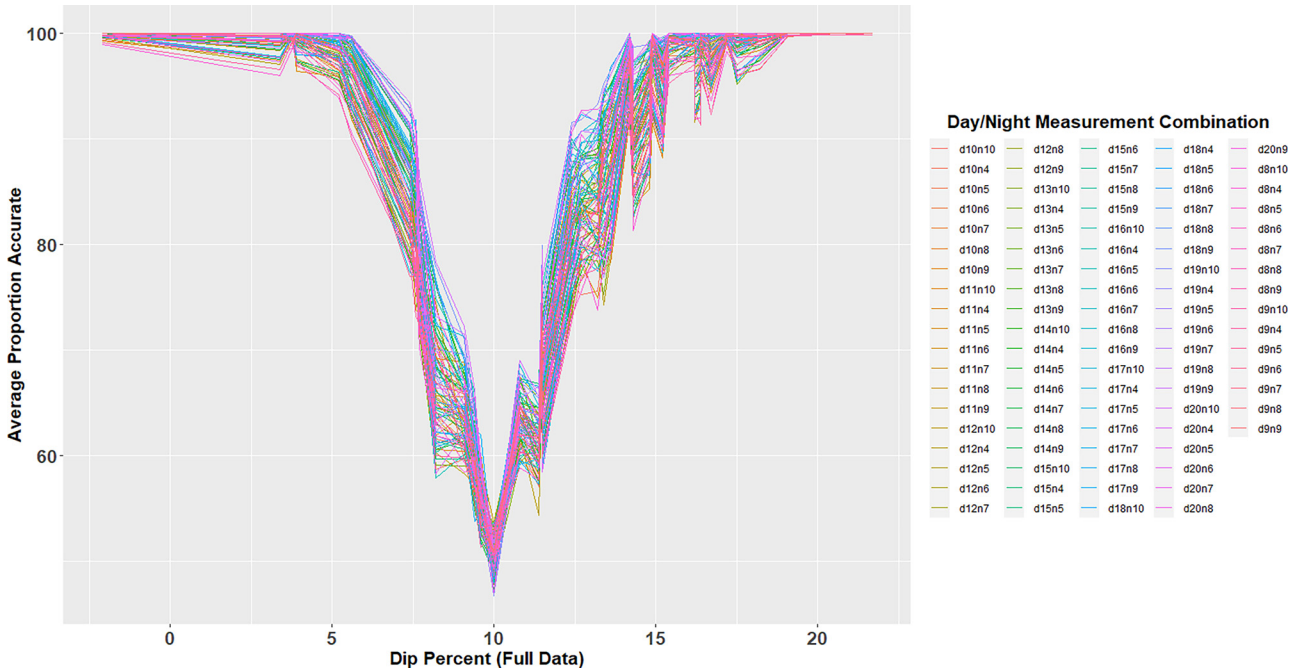

Figure 3. Demonstrative graph presenting the level of accuracy to predict percent dipping status for each random combination of daytime and nighttime number of readings (*y*-axis) by the normative percent dipping status previously found using all available readings (*x*-axis).

The current study presents several strengths but also has a few limitations. As the main strength, bedtime and wake time were self-selected and verified accurately using each participant's sleep diary rather than an arbitrary fixed "nighttime." This methodology aligns with previous ABPM studies reporting consistency in bedtime and wake times obtained from diaries and actigraphy (19). In addition, a recent study identified that ABPM averages were more reproducible using participants' diaries than the actigraphy (20). Due to the self-selected 8 h in bed, the nighttime period was 8 h for each participant. The limitations include: *1*) our study is descriptive and does not establish future cardiovascular risk; *2*) the generalizability of the findings is limited to young and midlife adults, but not older adults; *3*) We included people with common disorders such as untreated hypertension and untreated moderate sleep apnea (21–23), which could potentially confound data interpretation, although this increases generalizability as both disorders are present in more than 1 billion adults worldwide (24); *4*) we cannot provide mechanistic data to explain differences in accuracy; *5*) we could not address how low versus high accuracy could affect risk prediction since all studies are cross-sectional design in this data sets and the participants were not followed longitudinally; and *6*) we could not investigate if a different number of measurements, less or more, would burden the participants differently and affect activity and/or sleep, as well as ABPM accuracy.

In conclusion, the current recommendation of 20 measurements has an optimal accuracy of 99.7% for daytime, and 7 measurements provided 93.3% accuracy for nighttime. However, the use of 11 and 8 measurements during daytime and nighttime, respectively, can be considered as an option if a minimum of 95% accuracy is acceptable. Dipping status is a volatile index that increases its variability as it gets closer to the 10% cutoff value. Future studies where this metric is the primary outcome may aim for as many measurements as possible. Our results emphasize that a small number of measures should be interpreted with extreme caution, and more studies should be conducted to evaluate the accuracy and prognosis among different numbers of ABP measurements in parallel.

SUPPLEMENTAL DATA

Supplemental Table S1: https://doi.org/10.6084/m9.figshare.25962124.v1.

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DISCLOSURES

A.W.M. reports consulting for Pure Somni, Inc. None of the other authors has any conflicts of interest, financial or otherwise, to disclose.

AUTHOR CONTRIBUTIONS

L.C.B. and S.S.T. conceived and designed research; N.P.B., M.P.B., A.W.M., J.S.E., S.A.S., and S.S.T. performed experiments; L.C.B. and S.P.M.R. analyzed data; L.C.B., S.P.M.R., N.P.B., M.P.B., A.W.M., J.S.E., S.A.S., and S.S.T. interpreted results of experiments; L.C.B. prepared figures; L.C.B. drafted manuscript; L.C.B., S.P.M.R., N.P.B., M.P.B., A.W.M., J.S.E., S.A.S., and S.S.T. edited and revised manuscript; L.C.B., S.P.M.R., N.P.B., M.P.B., A.W.M., J.S.E., S.A.S., and S.S.T. approved final version of manuscript.

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