

Clinical Investigations

**Blood Pressure Differences Between Home Monitoring and Daytime
Ambulatory Values and their Reproducibility in Treated Hypertensive Stroke
and TIA Patients**

Authors

William J Davison¹, Phyo Kyaw Myint², Allan B Clark³, John F Potter¹.

¹Ageing and Stroke Medicine Section, Norwich Medical School, Bob Champion Research and Education Building, James Watson Rd, Norwich Research Park, University of East Anglia, Norwich, NR4 7UQ.

²Ageing Clinical & Experimental Research Team (ACER), Institute of Applied Health Sciences, University of Aberdeen, AB25 2ZD.

³Norwich Medical School, University of East Anglia, Norwich, NR4 7TJ.

Short Title: Out-of-office blood pressure differences

Correspondence:

Professor John Potter

Ageing and Stroke Medicine Section

Bob Champion Research and Education Building,

James Watson Road, University of East Anglia,

Norwich, NR4 7UQ

Tel: +44 (0) 1603 591755

Email: john.potter@uea.ac.uk

Abstract

Background

Guidelines recommend ambulatory or home blood pressure monitoring to improve hypertension diagnosis and monitoring. Both these methods are ascribed the same threshold values, but whether they produce similar results has not been established in certain patient groups.

Methods

Adults with mild/moderate stroke or transient ischaemic attack (N=80) completed two sets of ambulatory and home blood pressure monitoring. Systolic and diastolic blood pressure values from contemporaneous measurements were compared and the limits of agreement assessed. Exploratory analyses for predictive factors of any difference were conducted.

Results

Daytime ambulatory blood pressure values were consistently lower than home values, the mean difference in systolic blood pressure for initial ambulatory vs first home monitoring was -6.6 ± 13.5 mmHg ($p < 0.001$), and final ambulatory vs second home monitoring -7.1 ± 11.0 mmHg ($p < 0.001$). Mean diastolic blood pressure differences were -2.1 ± 8.5 mmHg ($p = 0.03$) and -2.0 ± 7.2 mmHg ($p = 0.02$). Limits of agreement for systolic blood pressure were -33.0 to 19.9 mmHg and -28.7 to 14.5 mmHg for the two comparisons, and for DBP were -18.8 to 14.5 mmHg and -16.1 to 12.2 mmHg respectively. The individual mean change in systolic blood pressure difference was 11.0 ± 8.3 mmHg across the two comparisons. No predictive factors for these differences were identified.

Conclusions

Daytime ambulatory systolic and diastolic blood pressure values were significantly lower than home monitored values at both time points. Differences between the two methods were not reproducible for individuals. Using the same threshold value for both out-of-office measurement methods may not be appropriate in patients with cerebrovascular disease.

Key Words

Blood pressure, blood pressure measurement/monitoring, hypertension, stroke, cerebrovascular disease.

Introduction

Hypertension is a major modifiable risk factor for both primary and secondary stroke prevention.^{1, 2} Diagnosing hypertension and monitoring treatment response relies on being able to obtain an accurate and reproducible measurement of blood pressure (BP). Clinic BP measurement (CBPM) values taken manually by auscultation with a sphygmomanometer have been the traditional standardized method, yet they are limited by factors such as inadequate technique, observer bias, terminal digit preference, and blood pressure variability.^{3, 4} Whilst some of these limitations may be overcome by taking multiple clinic measurements over time, in patients with the white coat phenomenon or masked hypertension an accurate BP is unlikely to be obtained using CBPM alone.⁵ For these reasons, and because they better predict cardiovascular risk,⁶⁻⁸ current hypertension guidelines recommend the additional use of out-of-office measurements (either ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM)) to support diagnosis and for monitoring BP control.⁹⁻¹² Some authorities recommend ABPM as the “gold standard”,^{9, 13} but HBPM has become more popular as evidence indicating that its use can improve BP control has emerged.¹⁴ However, whether HBPM is effective in patients with cerebrovascular disease remains uncertain.¹⁵

Clinic BP values are frequently at variance with out-of-office values and so using the same diagnostic and monitoring threshold value for all BP measurement methods is not necessarily appropriate. Comparisons of daytime ABPM and CBPM suggest that for a CBPM of 140/90mmHg the equivalent readings from daytime ABPM are on average 4/3mmHg lower.¹⁶ The threshold set by several guideline groups for the upper limit of “normal” for daytime ABPM values is <135/85mmHg.^{9, 11, 12} The same

threshold value has been ascribed to HBPM though this has not been fully established,¹³ with recent studies suggesting the threshold should be lower.^{17, 18} Furthermore, there are limited comparisons of ABPM with HBPM, despite ABPM being considered the reference standard. Reports of their equivalence are inconsistent, have not investigated the reproducibility of any variation between the two methods, and have not assessed their equivalence in high-risk patient groups.¹⁹⁻

25

TEST-BP was a randomized controlled trial of HBPM with or without guided self-management of antihypertensive therapy in a population with cerebrovascular disease, with participants also undertaking daytime ABPM contemporaneously to HBPM. The aims of this study were to evaluate if there are differences between BP values measured using daytime ABPM and HBPM, assess their reproducibility, and explore factors that may relate to any differences.

Methods

The methodology used in TEST-BP has been previously reported.²⁶ Ethical approval was obtained from the NRES Committee East of England – Norfolk (ref: 11/EE/0147). The trial was registered with the ISRCTN trial database (ISRCTN 86192648) where the trial protocol is publicly available. The methodology as relevant to this analysis is summarized here. Adults with a history of stroke (National Institute of Health Stroke Scale (NIHSS) <15) or TIA, between 72 hours and twelve weeks post-event and requiring treatment for hypertension (defined as being on antihypertensive medications prior to the recent cerebrovascular event or having post-event untreated BP \geq 140/90mmHg from the mean of three clinic readings) were

included. Patients in atrial fibrillation, with life expectancy less than six months or with established cognitive impairment were excluded. Participants provided written informed consent before being randomised in a 1:1:1 ratio to treatment as usual, home monitoring only, or home monitoring with guided self-management of blood pressure. BP data from participants in both home monitoring groups have been used for this secondary analysis.

All participants underwent CBPM at screening, ABPM at baseline and six months, and HBPM at six weeks, three and five months. HBPM data from the recordings at three months were not used in this study. Clinic BP was measured by the trial nurse using a semi-automated oscillometric BP monitor and appropriately sized cuff (Omron 705IT, Omron Healthcare UK Ltd., Milton Keynes, UK), with the subject seated, after five minutes rest following British Hypertension Society (BHS) guidelines,²⁷ taking the mean of three measurements. ABPM was measured with a Spacelabs 90207 monitor (Spacelabs Healthcare Ltd. (UK), Hertford, UK) set to measure BP every 20 minutes during the daytime and hourly overnight (2200-0700) following NICE guidelines.⁹ HBPM was performed following guideline recommendations with participants taking duplicate readings twice daily at home for seven consecutive days.^{9, 11} Morning measurements were taken prior to antihypertensive medication and all measurements were taken before meals. Readings from day one were discarded prior to analysis. The home monitoring only group used a validated BHS approved monitor with integrated memory and printer (Omron 705IT, Omron Healthcare UK Ltd., Milton Keynes, UK). The home monitoring and guided self-management group used a validated BHS approved monitor (A&D UA-767PBT, A&D Instruments Ltd., Abingdon, UK) with a linked

Bluetooth modem (iModem; Netmedical, Utrecht, Netherlands) that automatically transmitted readings to the trial team to allow for treatment decisions to be made in conjunction with the participant. Different monitors were used in order to incorporate telemonitoring of results into the intervention for the home monitoring with guided self-management group. Medication adherence was assessed using the Hill-Bone compliance questionnaire at baseline and six months. Participants were excluded from this analysis if any daytime ABPM recording had <14 readings or if any home monitoring period provided <21 readings. Medications were checked at each study visit and those who had their antihypertensive medications altered between recordings for comparison, or in the two weeks prior to any BP measurement were also excluded from this analysis.

Outcomes for this analysis were the comparison of mean systolic BP (SBP) and diastolic BP (DBP) from the baseline daytime ABPM readings with the first (six week) HBPM readings, the follow-up ABPM readings with the last (five month) HBPM readings, and the CBPM readings with both the baseline daytime ABPM and first HBPM readings.

Statistical Analysis

Data were analysed using SPSS version 23.0. A comparison of those included and excluded in the analysis was based on a two-sample Student's t-test and a chi-squared test. Mean SBP and DBP for each measurement method was calculated with the standard deviation (SD). Paired Student's t-tests were used to compare the mean difference in SBP and DBP between the measurement methods stated above. BP differences were first analysed for each intervention group separately and then

data from both groups was pooled when it was apparent that there were no significant differences between the separate analyses. Sensitivity and specificity of the diagnostic accuracy of HBPM was assessed against daytime ABPM (as the reference standard) using the kappa statistic with a diagnostic threshold for hypertension by both methods of $\geq 135/85$ mmHg.^{9, 11, 12} For the comparisons between contemporaneous ABPM and HBPM readings the limits of agreement for both SBP and DBP were assessed using Bland and Altman's method.²⁸ Exploratory univariate analyses were undertaken to investigate possible relationships between individual variance in SBP and DBP difference from ABPM and HBPM with potential predictor variables. Analyses were initially descriptive, using scatter plots for continuous variables and box and whisker plots for categorical variables, with formal testing using Pearson's correlation for continuous variables and independent samples t tests for categorical variables only where appropriate. The variables tested were age, sex, body mass index, baseline clinic BP, being on antihypertensive treatment, history of diabetes, diagnosis (TIA or stroke), baseline disability depicted by modified Rankin score (mRS), baseline cognition assessed using Montreal Cognitive Assessment score, and the number of measurements from daytime ABPM and HBPM.

Results

Ninety-nine subjects were randomised to one of the two intervention arms involving HBPM. 19 were excluded, eight due to insufficient HBPM measurements from one or both of the recording periods and 11 because they had their antihypertensive medications changed between the ABPM and HBPM recording periods, leaving 80 participants for this analysis. Demographics of those included compared to those

excluded showed no significant between-group differences (**Table I**). All participants were ambulant with a modified Rankin Score <2.

Mean SBP and DBP by CBPM were higher than both daytime ABPM and HBPM, with values from HBPM being higher than ABPM (**Table II**). The mean SBP and DBP from HBPM were higher than values from ABPM for both comparisons and the difference was consistent over time (**Figure 1**). BP differences were similar for both intervention groups and independent of the home monitor that was used (**Supplementary table I, online supplement**). Comparing the mean SBP and DBP from morning and evening HBPM recordings with daytime ABPM separately revealed greater differences with morning readings, but this did not significantly alter the findings (**Supplementary table II, online supplement**). Self-reported medication adherence was excellent throughout the trial (median Hill-Bone score 9.0 (interquartile range 1.0) at both baseline and follow-up).

The limits of agreement for SBP from ABPM vs. HBPM were -33.0 to 19.9mmHg for the first comparison and -28.7 to 14.5mmHg for the second comparison (**Figure 2**). Limits of agreement for DBP were -18.8 to 14.5mmHg and -16.1 to 12.2mmHg respectively. Although the difference in mean SBP and DBP from ABPM and HBPM for the whole cohort was consistent over time, the difference in BP recorded by each method was not consistent for individuals. The mean change in the difference between daytime ABPM SBP and HBPM SBP was 11.0 ± 8.3 mmHg (range 0.65 to 43.3mmHg). For DBP the mean change was 6.5 ± 5.1 mmHg (range 0.21 to 19.8mmHg (**Figure 3**)).

Using daytime ABPM as the reference standard and a diagnostic threshold value for hypertension of $\geq 135/85$ mmHg for both methods, HBPM had a diagnostic sensitivity of 76.1% and specificity of 55.9% ($k=0.36$, $p=0.004$) when comparing the baseline and first readings. At follow-up HBPM had a diagnostic sensitivity of 70.8% and specificity of 55.4% ($k=0.22$, $p=0.03$). From the baseline daytime ABPM recordings 46/80 (57.5%, 95% CI 46.3-67.9%) participants were classified as having uncontrolled hypertension and from the follow-up daytime ABPM the rate was 24/80 (30.0%, 95% CI 20.0-40.3%). For HBPM, 50/80 (62.5%, 95% CI 52.5-72.7%) were classified as uncontrolled hypertension on the first recording and 42/80 (52.5%, 95% CI 41.7-63.6%) on the second recording. For the first comparison 54/80 (67.5%, 95% CI 57.8-77.8%) participants were classified the same according to both daytime ABPM and HBPM (35 uncontrolled hypertension and 19 controlled hypertension). For the second comparison this proportion was 48/80 (60.0%, 95% CI 49.4-71.6% (17 uncontrolled hypertension and 31 controlled hypertension)).

In the exploratory analyses for independent predictor variables for the differences between daytime ABPM and HBPM values the descriptive testing only suggested possible relationships with baseline clinic SBP and being on antihypertensive treatment, with all other variables unrelated (**Supplementary figures 1 and 2, online supplement**). However, further testing for the relationship with baseline clinic SBP revealed no significant correlation with the first comparison and only a weak correlation ($r=-0.25$, $p=0.02$) with the second comparison. Further testing of the relationship with being on antihypertensive treatment was not possible due to the small number of untreated participants ($N=5$).

Discussion

This work aimed to assess if important differences exist, that may affect clinical management of BP levels in stroke or TIA patients, between the commonest methods of assessing out-of-office BP levels. We found that significant and prominent differences exist in BP values obtained from daytime ABPM compared to HBPM in this patient group. The mean differences in BP values were consistent between the two groups (who used different home monitors) and over the two measurement phases of the six month trial, however, the limits of agreement were wide-ranging and BP differences between the two measurement methods were not reproducible for individuals across the two measurement periods. This suggests that daytime ABPM and HBPM may not be interchangeable methods as BP values obtained using one method cannot be used to infer values from the other.

Furthermore, the difference between the methods was large enough to potentially affect patient management, with a mismatch in hypertension control at a threshold value of $\geq 135/85$ mmHg in 26/80 (32.5%) of participants at baseline and 32/80 (40.0%) at outcome. This indicates that there is the potential for discordant treatment decisions depending on which method is used to gauge treatment response. We were unable to demonstrate any predictive factors for the observed differences in BP between the two methodologies, with the significant correlation between baseline clinic SBP and SBP difference from the second comparison probably being a chance finding.

ABPM and HBPM have both been assessed against CBPM,^{16, 29} however, fewer studies have directly compared the two out-of-office methods using an HBPM protocol consistent with current guidelines. One randomised controlled trial of the

therapeutic effect of HBPM in a primary care cohort of treated hypertensive adults reported a difference between daytime ABPM and HBPM of $-3.1/+0.7$ mmHg at the end of the trial, though this difference was not assessed further.³⁰ Three cross-sectional studies in a mixture of treated and untreated hypertensive adults have shown differences ranging from -5 to -7 mmHg for SBP and -1 to -4 mmHg for DBP, with mean ABPM values lower than HBPM in each study, similar to our results.¹⁹⁻²¹ The limits of agreement we found are also comparable to those reported elsewhere.³¹ In contrast, one cohort study in untreated hypertensive adults reported no difference between BP values from HBPM and daytime ABPM.²³ This inconsistency may relate to the age of included participants as other studies have demonstrated that differences in BP values from out-of-office methods are not consistent across age groups, with daytime ABPM values being higher than HBPM values in children but lower or similar in adults over 60 years old.^{24, 25} The age of our cohort may therefore partly explain our findings and the narrow age range of participants may explain why age was not a predictive factor for the differences we found. Nevertheless, the findings potentially remain of relevance to managing stroke secondary prevention as many stroke patients experience their first cerebrovascular event at older ages. Importantly, none of these studies have performed repeated BP measures to investigate the reproducibility of any differences. Both ABPM and HBPM have been individually shown to be reproducible.³² However, they do not seem to provide the same BP information for individuals, with one study showing that, despite both methods diagnosing the same proportion of a cohort with masked hypertension, almost half of those diagnosed as masked hypertensive on daytime ABPM were not according to HBPM.³³

Using ABPM as the reference standard and with a diagnostic threshold value of $\geq 135/85$ mmHg, HBPM has been reported to have a diagnostic sensitivity of 86% and specificity 62% which is similar to our findings.²² Despite this, daytime ABPM and HBPM have been ascribed the same threshold values for hypertension diagnosis.^{9, 11, 12} Furthermore, they are deemed equivalent for categorizing patients by stage of hypertension.¹² This may not be the case as other studies have suggested that the difference between them may depend upon BP level.^{34, 35} This may relate to increased blood pressure variability, which has been shown to increase with BP level,³⁶ and could have a greater influence on mean BP from HBPM compared to ABPM due to the different number of measurements. Other factors which may be relevant include age, gender, and being on antihypertensive treatment.^{19, 35} Our data also suggested that the latter may be a relevant factor, but we were unable to formally test this due to our small sample size. A possible explanation for the relevance of antihypertensive treatment status is that morning HBPM measurements are routinely taken before antihypertensive medications, therefore capturing BP at the trough of antihypertensive activity. Due to the larger number of measurements obtained with ABPM throughout the day the influence of these 'trough values' will be diluted, resulting in a lower daytime mean BP than that obtained with HBPM. However, whilst our data did show that morning HBPM mean BP was higher than in the evening, the difference was not large enough to support this explanation.

This study is, to the best of our knowledge, the first to compare different out-of-office BP measurement methods and assess their limits of agreement in a population with cerebrovascular disease. Given the prevalence of stroke and the importance of BP management in secondary stroke prevention we believe the study is of importance.^{1,}

2, 37 Its main strength is that we were able to compare ABPM and HBPM measurements at two different time-points in the same population of patients who were treated but had not altered therapy between measurement timings, thereby investigating the consistency of any discrepancy and its reproducibility in individuals.

Limitations that should be considered include that this was a post-hoc analysis of data from a randomised controlled trial. The population recruited all had cerebrovascular disease and the majority were elderly and on treatment for hypertension. Consequently, our findings may not be generalizable to a broader population. Secondly, due to the relatively small sample size our findings should be interpreted with caution. Thirdly, due to the design of the trial, the two intervention groups used different home monitors and this could account for some of the difference with daytime ABPM values that was found. However, both types of monitor have been validated. Furthermore, we have shown that any differences with daytime ABPM values were not significantly different between the two groups and therefore are not likely to have been significantly influenced by the equipment. Fourthly, the majority of our participants were on antihypertensive treatment throughout the trial, which may have influenced BP readings. However, other studies discussed have also included participants on treatment and we have shown that poor adherence is unlikely to have been a confounding factor in our cohort.^{16, 19, 20, 30} Fifthly, the ABPM and HBPM measurements that we have compared were not precisely contemporaneous which may have introduced some natural variation. However, we excluded patients whose antihypertensive medications were changed in between measurements for comparison to try to ensure stability. Also, we have shown that the group variation between methods was consistent over time. Some

other studies discussed have also compared measurements up to four weeks apart. Finally, there was a larger than expected difference between the BP values from clinic measurement and out-of-office measurement in our group suggesting a marked white coat effect in some individuals. Home BP values, but not ABPM values, could also have been influenced by any anxiety around BP measurement thereby influencing our findings. However, the difference between clinic vs. ABPM and clinic vs. HBPM was consistent with the difference between ABPM vs. HBPM suggesting that any differences were not attributable to measurement differences from just one method. Furthermore, although we did not assess it in our cohort, there is evidence to show that patients with cerebrovascular disease do not experience additional anxiety due to HBPM and they can reliably measure their own BP at home.^{38, 39}

In this patient group with incident cerebrovascular events, we found significant differences between BP values obtained from ABPM and HBPM leading to inconsistency in hypertension control status if the current guideline threshold of $\geq 135/85$ mmHg is applied to both methods. This is clinically important because it creates the potential to over-treat individuals if relying on HBPM to assess treatment response, or conversely under-treat if relying on ABPM. The variation between methods is not consistent between individuals suggesting that ABPM and HBPM should not be considered interchangeable methods of BP evaluation. Considering this, the threshold value for monitoring BP treatment with HBPM may not be the same as that for initial diagnosis and at present may need to be individualised. Further work in larger cohorts of both treated and untreated hypertensive individuals

to establish values for HBPM with ABPM as the reference standard would be valuable.

Acknowledgements

We thank the participants of TEST-BP and Maggie Langley for her significant contribution to the completion of the study.

Source of Funding

TEST-BP was funded by the National Institute for Health Research (NIHR) Research for Patient Benefit Programme (RfPB) (grant reference PB-PG--0909-20246). This paper presents independent research funded by the NIHR under the RfPB. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Declarations of Interest: none.

Author Contributions: The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

References

1. Lawes CM, Bennett DA, Feigin VL, Rodgers A. Blood pressure and stroke: An overview of published reviews. *Stroke*. 2004;35:1024
2. Katsanos AH, Filippatou A, Manios E, Deftereos S, Parissis J, Frogoudaki A, Vrettou AR, Ikonomidis I, Pikilidou M, Kargiotis O, Voumvourakis K, Alexandrov AW, Alexandrov AV, Tsivgoulis G. Blood pressure reduction and secondary

- stroke prevention: A systematic review and metaregression analysis of randomized clinical trials. *Hypertension*. 2017;69:171-179
3. O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, Mengden T, Myers M, Padfield P, Palatini P, Parati G, Pickering T, Redon J, Staessen J, Stergiou G, et al. European society of hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens*. 2003;21:821-848
 4. Parati G, Ochoa JE, Lombardi C, Bilo G. Blood pressure variability: Assessment, predictive value, and potential as a therapeutic target. *Curr Hypertens Rep*. 2015;17:537
 5. Sheppard JP, Schwartz CL, Tucker KL, McManus RJ. Modern management and diagnosis of hypertension in the united kingdom: Home care and self-care. *Ann Glob Health*. 2016;82:274-287
 6. Ward AM, Takahashi O, Stevens R, Heneghan C. Home measurement of blood pressure and cardiovascular disease: Systematic review and meta-analysis of prospective studies. *J Hypertens*. 2012;30:449-456
 7. Fuchs SC, Mello RG, Fuchs FC. Home blood pressure monitoring is better predictor of cardiovascular disease and target organ damage than office blood pressure: A systematic review and meta-analysis. *Curr Cardiol Rep*. 2013;15:413
 8. Niiranen TJ, Maki J, Puukka P, Karanko H, Jula AM. Office, home, and ambulatory blood pressures as predictors of cardiovascular risk. *Hypertension*. 2014;64:281-286
 9. National Institute for Health and Care Excellence. Hypertension in adults: Diagnosis and management. 2011;2017
 10. Imai Y, Kario K, Shimada K, Kawano Y, Hasebe N, Matsuura H, Tsuchihashi T, Ohkubo T, Kuwajima I, Miyakawa M, Japanese Society of Hypertension Committee for Guidelines for Self-monitoring of Blood Pressure at H. The japanese society of hypertension guidelines for self-monitoring of blood pressure at home (second edition). *Hypertens Res*. 2012;35:777-795
 11. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, et al. 2013 esh/esc guidelines for the management of arterial hypertension: The task force for the management of arterial hypertension of the european society of hypertension (esh) and of the european society of cardiology (esc). *J Hypertens*. 2013;31:1281-1357
 12. Whelton PK, Carey RM, Aronow WS, Casey DE, Jr., Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC, Jr., Spencer CC, et al. 2017 acc/aha/aapa/abc/acpm/ags/apha/ash/aspc/nma/pcna guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: A report of the american college of cardiology/american heart association task force on clinical practice guidelines. *Hypertension*. 2017
 13. Stergiou GS, Parati G, Vlachopoulos C, Achimastos A, Andreadis E, Asmar R, Avolio A, Benetos A, Bilo G, Boubouchairopoulou N, Boutouyrie P, Castiglioni P, de la Sierra A, Dolan E, Head G, et al. Methodology and technology for peripheral and central blood pressure and blood pressure variability measurement: Current status and future directions - position statement of the european society of hypertension working group on blood pressure monitoring and cardiovascular variability. *J Hypertens*. 2016;34:1665-1677

14. Uhlig K, Patel K, Ip S, Kitsios GD, Balk EM. Self-measured blood pressure monitoring in the management of hypertension: A systematic review and meta-analysis. *Ann Intern Med.* 2013;159:185-194
15. Tucker KL, Sheppard JP, Stevens R, Bosworth HB, Bove A, Bray EP, Earle K, George J, Godwin M, Green BB, Hebert P, Hobbs FDR, Kantola I, Kerry SM, Leiva A, et al. Self-monitoring of blood pressure in hypertension: A systematic review and individual patient data meta-analysis. *PLoS Med.* 2017;14:e1002389
16. Head GA, Mihailidou AS, Duggan KA, Beilin LJ, Berry N, Brown MA, Bune AJ, Cowley D, Chalmers JP, Howe PR, Hodgson J, Ludbrook J, Mangoni AA, McGrath BP, Nelson MR, et al. Definition of ambulatory blood pressure targets for diagnosis and treatment of hypertension in relation to clinic blood pressure: Prospective cohort study. *BMJ.* 2010;340:c1104
17. Niiranen TJ, Asayama K, Thijs L, Johansson JK, Ohkubo T, Kikuya M, Boggia J, Hozawa A, Sandoya E, Stergiou GS, Tsuji I, Jula AM, Imai Y, Staessen JA, International Database of Home blood pressure in relation to Cardiovascular Outcome I. Outcome-driven thresholds for home blood pressure measurement: International database of home blood pressure in relation to cardiovascular outcome. *Hypertension.* 2013;61:27-34
18. Park JS, Rhee MY, Namgung J, Lee SY, Cho DK, Choi TY, Kim SY, Kim JY, Park SM, Choi JH, Lee JH, Kim HY. Comparison of optimal diagnostic thresholds of hypertension with home blood pressure monitoring and 24-hour ambulatory blood pressure monitoring. *Am J Hypertens.* 2017;30:1170-1176
19. Gaborieau V, Delarche N, Gosse P. Ambulatory blood pressure monitoring versus self-measurement of blood pressure at home: Correlation with target organ damage. *J Hypertens.* 2008;26:1919-1927
20. Nasothimiou EG, Tzamouranis D, Roussias LG, Stergiou GS. Home versus ambulatory blood pressure monitoring in the diagnosis of clinic resistant and true resistant hypertension. *J Hum Hypertens.* 2012;26:696-700
21. Nunan D, Thompson M, Heneghan CJ, Perera R, McManus RJ, Ward A. Accuracy of self-monitored blood pressure for diagnosing hypertension in primary care. *J Hypertens.* 2015;33:755-762; discussion 762
22. Hodgkinson J, Mant J, Martin U, Guo B, Hobbs FD, Deeks JJ, Heneghan C, Roberts N, McManus RJ. Relative effectiveness of clinic and home blood pressure monitoring compared with ambulatory blood pressure monitoring in diagnosis of hypertension: Systematic review. *BMJ.* 2011;342:d3621
23. Stergiou GS, Skeva, II, Baibas NM, Kalkana CB, Roussias LG, Mountokalakis TD. Diagnosis of hypertension using home or ambulatory blood pressure monitoring: Comparison with the conventional strategy based on repeated clinic blood pressure measurements. *J Hypertens.* 2000;18:1745-1751
24. Ishikawa J, Ishikawa Y, Edmondson D, Pickering TG, Schwartz JE. Age and the difference between awake ambulatory blood pressure and office blood pressure: A meta-analysis. *Blood Press Monit.* 2011;16:159-167
25. Stergiou GS, Ntineri A, Kollias A, Destounis A, Nasothimiou E, Roussias L. Changing relationship among clinic, home, and ambulatory blood pressure with increasing age. *J Am Soc Hypertens.* 2015;9:544-552
26. Davison WJ, Myint PK, Clark AB, Kim LG, Wilson EC, Langley M, Potter JF. Does self-monitoring and self-management of blood pressure after stroke or transient ischemic attack improve control? Test-bp, a randomized controlled trial. *Am Heart J.* 2018

27. Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, Sever PS, Mc GTS, British Hypertension S. Guidelines for management of hypertension: Report of the fourth working party of the british hypertension society, 2004-bhs iv. *J Hum Hypertens*. 2004;18:139-185
28. Giavarina D. Understanding bland altman analysis. *Biochem Med (Zagreb)*. 2015;25:141-151
29. Thijs L, Staessen JA, Celis H, de Gaudemaris R, Imai Y, Julius S, Fagard R. Reference values for self-recorded blood pressure: A meta-analysis of summary data. *Arch Intern Med*. 1998;158:481-488
30. Verberk WJ, Kroon AA, Lenders JW, Kessels AG, van Montfrans GA, Smit AJ, van der Kuy PH, Nelemans PJ, Rennenberg RJ, Grobbee DE, Beltman FW, Joore MA, Brunenberg DE, Dirksen C, Thien T, et al. Self-measurement of blood pressure at home reduces the need for antihypertensive drugs: A randomized, controlled trial. *Hypertension*. 2007;50:1019-1025
31. Carney S, Gillies A, Garvey L, Smith A. Direct comparison of repeated same-day self and ambulatory blood pressure monitoring. *Nephrology (Carlton)*. 2005;10:151-156
32. Viera AJ, Lin FC, Tuttle LA, Olsson E, Stankevitz K, Girdler SS, Klein JL, Hinderliter AL. Reproducibility of masked hypertension among adults 30 years or older. *Blood Press Monit*. 2014;19:208-215
33. Hanninen MR, Niiranen TJ, Puukka PJ, Jula AM. Comparison of home and ambulatory blood pressure measurement in the diagnosis of masked hypertension. *J Hypertens*. 2010;28:709-714
34. Shimada K, Kario K, Kushiro T, Teramukai S, Ishikawa Y, Kobayashi F, Saito I. Differences between clinic blood pressure and morning home blood pressure, as shown by bland-altman plots, in a large observational study (honest study). *Hypertens Res*. 2015;38:876-882
35. Verberk WJ, Kroon AA, Kessels AG, Lenders JW, Thien T, van Montfrans GA, Smit AJ, de Leeuw PW. The optimal scheme of self blood pressure measurement as determined from ambulatory blood pressure recordings. *J Hypertens*. 2006;24:1541-1548
36. Veloudi P, Sharman JE. Methodological factors affecting quantification of blood pressure variability: A scoping review. *J Hypertens*. 2017
37. The Stroke Association. State of the nation: Stroke statistics january 2017. 2017;2017
38. Ovaisi S, Ibison J, Leontowitsch M, Cloud G, Oakeshott P, Kerry S. Stroke patients' perceptions of home blood pressure monitoring: A qualitative study. *Br J Gen Pract*. 2011;61:e604-610
39. Shaw J, Kerry S, Adjei-Gyamfi Y, Tulloch J, Coster D, Sharma S, Oakeshott P. Are stroke patients' reports of home blood pressure readings reliable? Cross-sectional study. *Fam Pract*. 2011;28:118-122

Table I: Baseline demographics of those included and excluded from analysis. Data presented are mean (SD) or frequency (%). Modified Rankin score is presented as median (interquartile range). No significant differences between groups.

	Included (N=80)	Excluded (N=19)
Age	74.1 (10.3)	75.4 (8.8)
Male	53 (66%)	12 (63%)
Diagnosis of TIA*	53 (66%)	14 (74%)
Time from event to recruitment (weeks)	8.9 (3.5)	9.1 (3.3)
Baseline mRS[†] (stroke only)	1.0 (1.0)	1.0 (1.0)
BMI	28.6 (5.3)	26.8 (2.1)
Never smoked	36 (45%)	6 (32%)
Alcohol (units/week)	9.4 (12.0)	7.1 (8.3)
On antihypertensive therapy	75 (94%)	17 (89%)
Antihypertensive monotherapy	35 (44%)	7 (37%)
Dual antihypertensive therapy	24 (30%)	8 (42%)
Triple antihypertensive therapy	14 (17%)	1 (5%)
ACEi[‡]/ARB[§]	63 (79%)	14 (74%)
Beta blocker	15 (19%)	6 (32%)
Calcium channel blocker	33 (41%)	6 (32%)

Thiazide diuretic	14 (18%)	3 (16%)
--------------------------	----------	---------

*Transient ischaemic attack

†Modified Rankin Score

‡Angiotensin-converting enzyme inhibitor

§Angiotensin receptor blocker

Table II: Mean group systolic and diastolic blood pressure from each measurement method. Data presented are mean (SD).

Measurement method	Number of measurements	Mean systolic BP* (mmHg)	Mean diastolic BP* (mmHg)
Baseline CBPM [†]	3 (0)	150.8 (20.2)	85.1 (11.8)
Baseline daytime ABPM [‡]	38.1 (9.1)	133.5 (13.7)	76.4 (8.5)
Home BP* at six weeks	27.3 (1.4)	140.1 (15.8)	78.5 (8.7)
Home BP* at five months	26.8 (3.1)	134.7 (13.7)	76.2 (9.7)
Daytime ABPM [‡] at six months	37.2 (8.4)	127.6 (12.2)	74.2 (9.2)

*Blood pressure

[†]Clinic blood pressure measurement

[‡]Ambulatory blood pressure monitoring

Figure Legends

Figure 1: Mean differences in blood pressure for head-to-head comparisons of out-of-office measurement methods. Error bars are 95% confidence intervals. P values represent paired Student's t-tests comparing the difference between measurement methods. ABPM denotes ambulatory blood pressure monitoring; HBPM, home blood pressure monitoring; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Figure 2: Bland-Altman plots to show the limits of agreement for within-individual blood pressure recorded by ambulatory monitoring (ABPM) and home monitoring (HBPM). Thick lines show the mean difference, dotted lines the 95% confidence interval for the mean difference, and dashed lines the limits of agreement (± 2 standard deviations). **A** shows systolic blood pressure (SBP) comparing baseline ABPM and the first HBPM. **B** shows SBP comparing follow-up ABPM and the last HBPM. **C** shows diastolic blood pressure (DBP) comparing baseline ABPM and the first HBPM. **D** shows DBP comparing follow-up ABPM and the last HBPM.

Figure 3: Histograms to show the change in the blood pressure difference recorded by ambulatory blood pressure monitoring and home blood pressure monitoring from the first to the second comparison for individuals. **A** shows the change in systolic blood pressure (SBP). **B** shows the change in diastolic blood pressure (DBP).

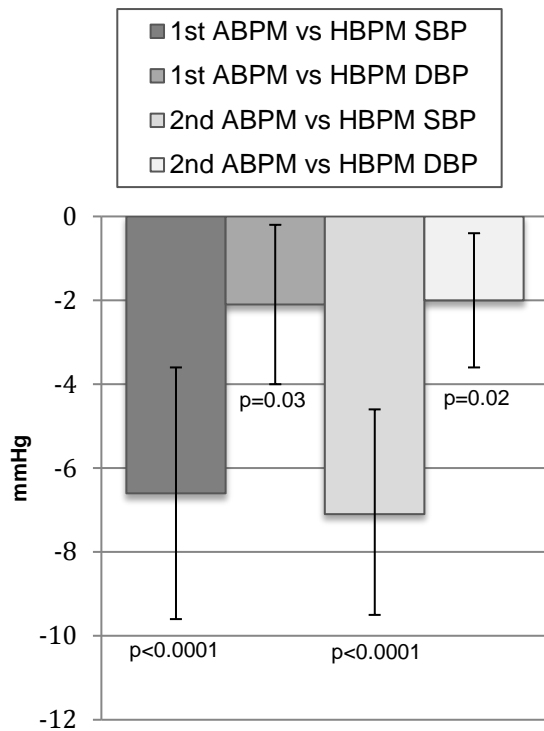


Figure 1: Mean differences in blood pressure for head-to-head comparisons of out-of-office measurement methods. Error bars are 95% confidence intervals. P values represent paired Student's t-tests comparing the difference between measurement methods. ABPM denotes ambulatory blood pressure monitoring; HBPM, home blood pressure monitoring; SBP, systolic blood pressure; DBP, diastolic blood pressure.

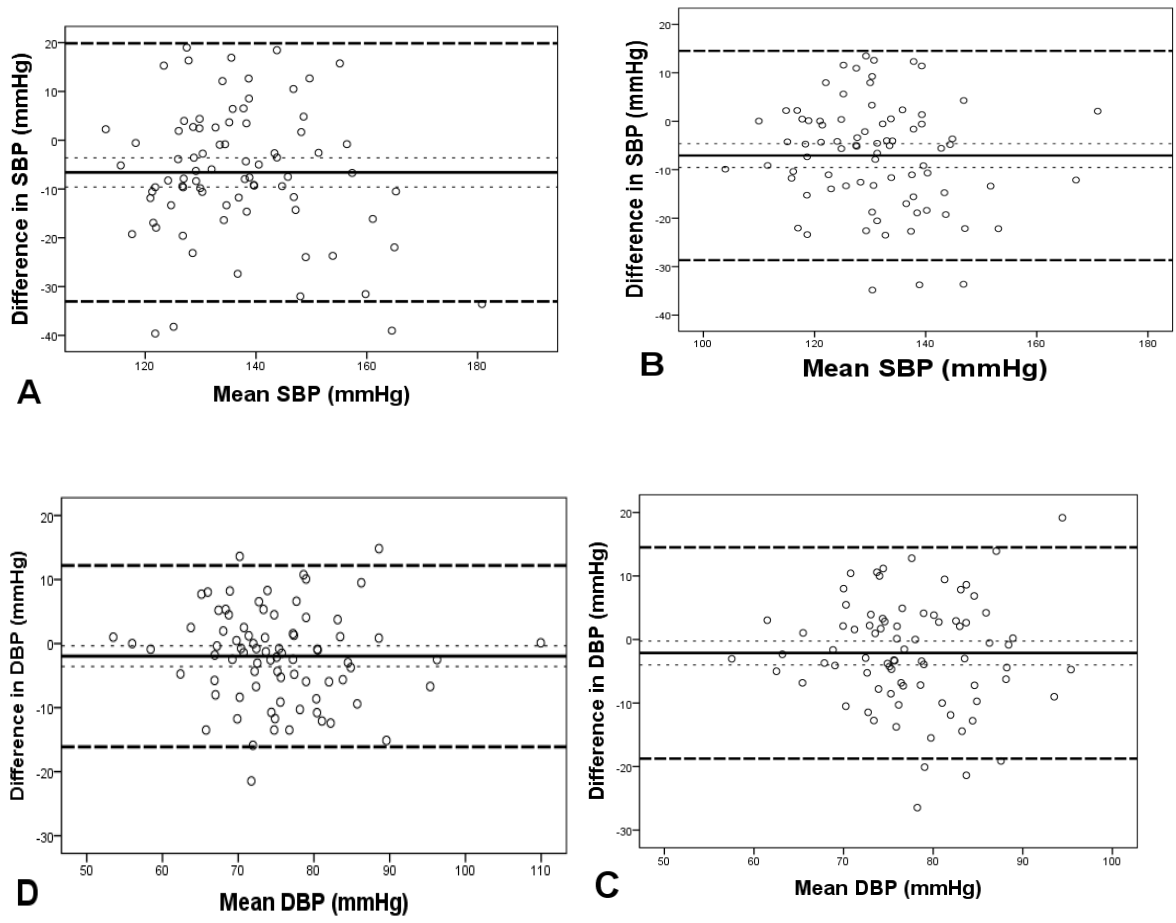


Figure 2: Bland-Altman plots to show the limits of agreement for within-individual blood pressure recorded by ambulatory monitoring (ABPM) and home monitoring (HBPM). Thick lines show the mean difference, dotted lines the 95% confidence interval for the mean difference, and dashed lines the limits of agreement (± 2 standard deviations). **A** shows systolic blood pressure (SBP) comparing baseline ABPM and the first HBPM. **B** shows SBP comparing outcome ABPM and the last HBPM. **C** shows diastolic blood pressure (DBP) comparing baseline ABPM and the first HBPM. **D** shows DBP comparing outcome ABPM and the last HBPM.

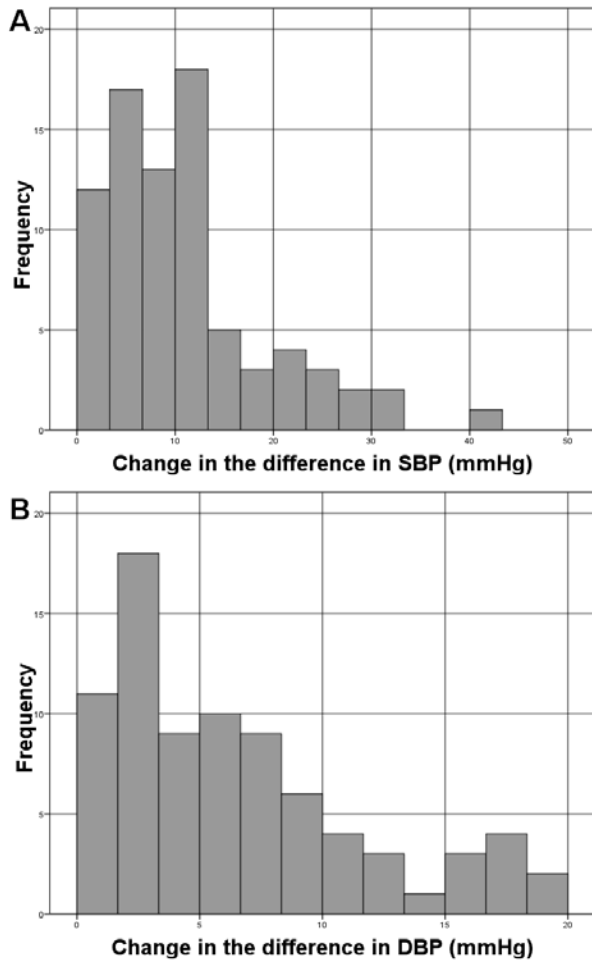


Figure 3: Histograms to show the change in the blood pressure difference recorded by ambulatory blood pressure monitoring and home blood pressure monitoring from the first to the second comparison for individuals. **A** shows the change in systolic blood pressure (SBP). **B** shows the change in diastolic blood pressure (DBP).

Online Supplement

**Blood Pressure Differences Between Home Monitoring and Daytime
Ambulatory Values and their Reproducibility in Treated Hypertensive Stroke
and TIA Patients**

Authors

William J Davison¹, Phyo Kyaw Myint², Allan B Clark³, John F Potter¹.

¹Ageing and Stroke Medicine Section, Norwich Medical School, Bob Champion Research and Education Building, James Watson Rd, Norwich Research Park, University of East Anglia, Norwich, NR4 7UQ.

²Ageing Clinical & Experimental Research Team (ACER), Institute of Applied Health Sciences, University of Aberdeen, AB25 2ZD.

³Norwich Medical School, University of East Anglia, Norwich, NR4 7TJ.

Short Title: Out-of-office blood pressure differences

Correspondence:

Professor John F Potter

Ageing and Stroke Medicine Section

Bob Champion Research and Education Building,

James Watson Road, University of East Anglia,

Norwich, NR4 7UQ

Tel: +44 (0) 1603 591755

Email: john.potter@uea.ac.uk

Additional Results

Supplementary table I: Mean differences in systolic and diastolic blood pressure between different out-of-office measurement methods at different time-points according to intervention group and type of home monitor used. Data presented are mean (SD) or mean (95% confidence intervals). P values represent independent samples t-tests to investigate the mean difference in blood pressure between the two groups.

	Home monitoring only (N=42)	Home monitoring with guided self- management (N=38)	Mean difference between groups	P value
Baseline daytime				
ABPM* vs first HBPM†	-7.6 (14.4)	-5.5 (12.6)	-2.1 (-8.1 to 4.0)	0.49
SBP‡ (mmHg)				
Baseline daytime				
ABPM* vs first HBPM†	-1.5 (8.9)	-2.8 (8.1)	1.3 (-2.5 to 5.1)	0.50
DBP§ (mmHg)				
Follow-up daytime				
ABPM* vs last HBPM†	-8.1 (11.2)	-5.9 (10.9)	-2.2 (-7.1 to 2.7)	0.38
SBP§ (mmHg)				
Follow-up daytime				
ABPM* vs last HBPM‡	-1.1 (7.0)	-2.9 (7.4)	1.8 (-1.4 to 5.0)	0.27
DBP§ (mmHg)				

*Ambulatory blood pressure monitoring

†Home blood pressure monitoring

‡Systolic blood pressure

§Diastolic blood pressure

Supplementary table II: Mean differences in systolic and diastolic blood pressure between different out-of-office measurement methods at different time-points, comparing morning and evening home readings separately. Data presented are mean (SD) or mean (95% confidence intervals). P values represent paired samples

t-tests to investigate the mean difference in blood pressure between the two methods.

	Mean difference	P value
Baseline daytime ABPM* vs first HBPM†		
morning SBP‡ (mmHg)	-7.8 (14.8)	<0.0001
Baseline daytime ABPM* vs first HBPM†		
evening SBP‡ (mmHg)	-5.5 (14.8)	0.001
Baseline daytime ABPM* vs first HBPM†		
morning DBP§ (mmHg)	-3.0 (8.5)	0.003
Baseline daytime ABPM* vs first HBPM†		
evening DBP§ (mmHg)	-0.8 (9.6)	0.48
Follow-up daytime ABPM* vs last HBPM†		
morning SBP§ (mmHg)	-8.3 (12.9)	<0.0001
Follow-up daytime ABPM* vs last HBPM†		
evening SBP§ (mmHg)	-5.9 (11.8)	<0.0001
Follow-up daytime ABPM* vs last HBPM†		
morning DBP§ (mmHg)	-3.5 (7.9)	<0.0001
Follow-up daytime ABPM* vs last HBPM†		
evening DBP§ (mmHg)	-0.5 (7.6)	0.59

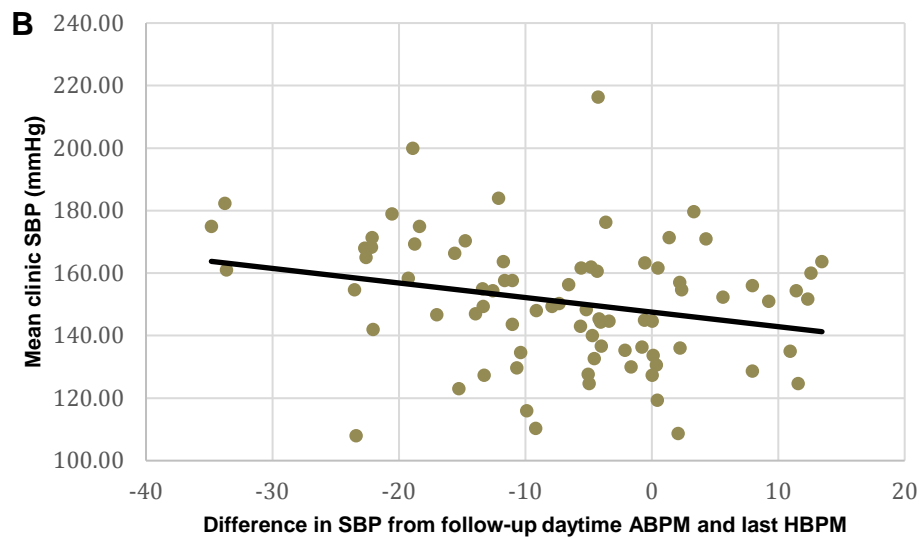
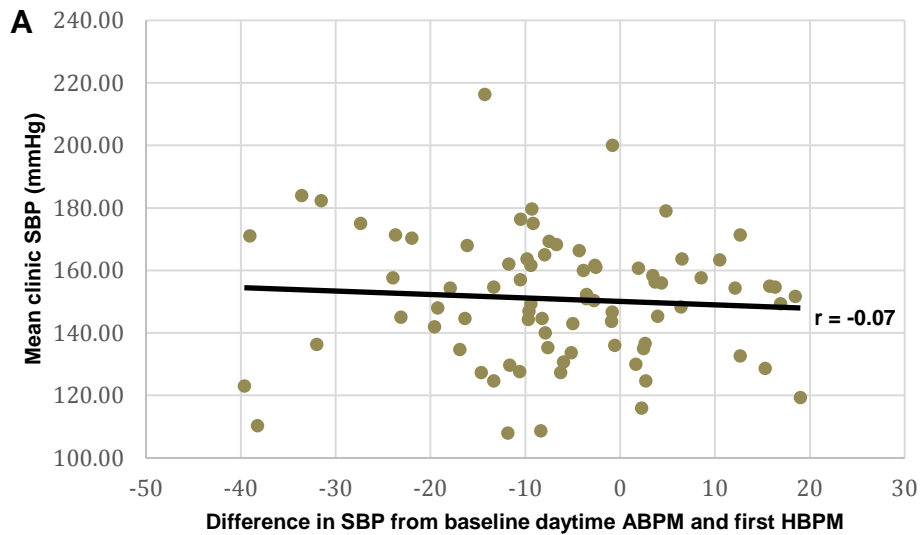
*Ambulatory blood pressure monitoring

†Home blood pressure monitoring

‡Systolic blood pressure

§Diastolic blood pressure

Supplementary figure 1: Scatter plots showing mean clinic systolic blood pressure (SBP) at baseline plotted against the difference in SBP from daytime ABPM and HBPM. Fit lines and r values represent Pearson's correlation between the two values. **A** is the SBP difference from the first comparison. **B** is the SBP difference from the second comparison.



Supplementary figure 2: Box and whisker plots showing the difference in blood pressure between baseline daytime ambulatory blood pressure monitoring and the first home blood pressure monitoring according to whether individuals were taking antihypertensive treatment. **A** is the difference in systolic blood pressure (SBP). **B** is the difference in diastolic blood pressure (DBP).

