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Home blood pressure during night-time sleep – a feasible treatment target for patients with hypertension: a proof-of-concept randomised controlled trial

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ABSTRACT

Background: This trial assessed the feasibility of titrating evening dosing of anti-hypertensive medications based on nighttime home blood pressure measurement (HBPM) readings in primary care for hypertensive (HT) patients.

Methods: 78 patients with nocturnal HT and stage I daytime HT were randomly assigned in a 1:1 ratio to either nighttime HBPM measurements (intervention group) or daytime HBPM measurements (control group). Nighttime blood pressure (BP) was measured 3x per night for at least two nights over 1 week using an automatic and validated HBPM device. The intervention group and control group aimed to achieve systolic BP <120 mmHg on nocturnal HBPM and systolic BP <135 mmHg on daytime HBPM respectively. All patients were seen every four weeks and followed the same drug titration algorithm.

Results: The trial achieved a recruitment rate of 6.5 persons per month and a retention rate of 96.1%. In the intervention group, patients provided ≥6 (considered adequate) and ≥9 nighttime HBPM readings for 77.5% and 63.8% of their follow-ups, respectively. At 6-month, both groups had similar nighttime, 24-hour, and daytime BP on ambulatory BP monitoring, as well as similar numbers of non-dippers and healthcare utilisation. Most patients

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reported that they learned more from their HBPM nighttime readings and found the intervention well-tolerated.
Conclusion: Adjusting evening dosage of anti-HT medications based on nighttime HBPM is a potential and feasible treatment approach for patients with nocturnal HT in primary care. This approach is well-accepted by patients and results in at least non-inferior BP control. Although titrating medications according to nighttime HBPM readings may improve nighttime BP, the small sample size limited statistical significance and the single-centre design restricted generalizability. Additionally, a few patients exhibited fair adherence to nighttime HBPM. Further randomised controlled trials are required to confirm that targeting nocturnal BP should be the primary treatment goal for HT.

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KEYWORDS Blood pressure; hypertension; home blood pressure measurement; randomised controlled trial

Background

Despite advances in treatment, hypertension (HT) remains the most common chronic condition and the leading cause of cardiovascular diseases, chronic kidney disease, and death globally (Zhou et al., 2021). Traditionally, HT management solely depended on daytime blood pressure (BP) values, often only measured in clinics. However, systolic BP (SBP) during nighttime sleep is consistently found to be the strongest predictor of cardiovascular events and death, even after controlling for daytime BP (Hansen et al., 2011; Kario et al., 2019). Furthermore, non-dipping, defined as a lack of a drop in BP during sleep by at least 10%, is also an independent predictor for cardiovascular diseases (Hansen et al., 2011). However, repeated or frequent monitoring (and therefore the treatment) of BP during nighttime sleep was previously difficult because the only way to measure nighttime BP was by 24-hour ambulatory BP monitoring (ABPM) (Wood et al., 2016). Despite being the 'gold standard' of BP measurements, ABPM is labor-intensive, expensive, and poorly accepted by some patients (e.g. disturbed sleep and disturbance to daily activities), making it infeasible to be repeated frequently (Fujiwara et al., 2018; Wood et al., 2016). Recently, this problem was overcome by a few models of home BP machines that can measure BP three times automatically (at 2, 3, and 4 o'clock) during sleep (Kario et al., 2019). This measurement schedule, which involved fewer measurements per night, was found acceptable by patients in a large nationwide Japanese cohort (the J-HOP study) and was adopted by the latest clinical trials (Kario et al., 2010; Kario et al., 2017; Lindroos, Jula, et al., 2016). The resultant nighttime HBPM readings were similar to those provided by ABPM (mean SBP difference = 1.4 mmHg, 95% confidence interval: 0.3–2.6 mmHg), and diastolic BP was not statistically different (Stergiou et al., 2020). Similar to ABPM (the current reference standard), nighttime HBPM readings can predict end-organ damage and

cardiovascular events, even after controlling for daytime BP (Ishikawa et al., 2012; Kario et al., 2019; Lindroos, Johansson, et al., 2016; Stergiou et al., 2020). Despite limited numbers of high-quality studies, recently published meta-analyses also suggested that evening dosing of anti-HT medications may be more effective to reduce nighttime BP than morning dosing (Lee et al., 2024; Maqsood et al., 2023). Therefore, nighttime readings from HBPM can potentially be the primary treatment target of HT.

The use of nighttime HBPM readings in this 'treatment-to-target' approach has not yet been examined in RCTs or recommended in international guidelines, making it a novel and promising approach. Prior RCTs had only compared the administration of the same drug in the morning or evening (without measuring nocturnal BP) or the administration of a fixed dose of antihypertensive medications to evaluate their impact on nocturnal BP (i.e. TIME trial). (Kario et al., 2010; Kario et al., 2017; Lindroos, Jula, et al., 2016; Mackenzie et al., 2022) Additionally, this is different from the study by Hermida et al. on chronotherapy, which titrated medications against daytime and nighttime ABPM values (not HBPM) and has yielded controversial results. (Kreutz et al., 2020) However, before progressing to a full-scale RCT to investigate the effectiveness of normalising nighttime HBPM, a pilot project is essential to demonstrate the feasibility of titrating evening dosing of anti-HT medications using nighttime HBPM readings. It is unclear if patients in primary care settings can accurately measure or comply to nighttime HBPM. Additionally, evening dosing of anti-HT medications may impair drug compliance in HT patients (Mackenzie et al., 2022). Furthermore, nighttime HBPM has exclusively been used in research conducted in European countries and Japan, which highlights the necessity for further investigation in various populations (Kario, 2018). This includes individuals in Hong Kong, where nighttime HBPM machines are not currently available.

This pilot and proof-of-concept RCT aimed to assess the feasibility of titrating evening dosing of anti-HT medications based on nighttime HBPM readings in Chinese primary care patients with nocturnal HT and stage I daytime HT. The study also aimed to examine the feasibility of procedures such as the acceptability of repeated ABPM, in preparation for a larger-scale RCT. Additionally, we hypothesised that using medications in the evening would not impair medication adherence and would not result in inferior daytime/24-hour blood pressure control on ABPM at the 6-month follow-up. This study primarily focused on systolic BP (SBP) rather than diastolic BP (DBP), as SBP is a stronger predictor of cardiovascular outcomes, particularly in older adults (Hansen et al., 2011).

Methods

This RCT was approved by the CUHK-NTEC ethics committee (2022.593) and was pre-registered (ClincialTrials.gov: NCT05031637). This parallel-arm RCT

involved 78 patients with nocturnal HT and stage I daytime HT. The patients were randomly assigned in a 1:1 ratio into the intervention group and the control group. Due to the nature of the intervention, the investigators and the patients cannot be blinded after group allocation, but the statistician remained blinded. All participants were followed up for six months.

Randomisation

The randomisation sequence was generated by an independent statistician using the software 'Random Allocation Software'. Stratified block randomisation in randomised blocks of 3 or 6 was used to enhance balance of sex and age (≥60-year old or younger) between the two groups, because older patients may have difficulty using new technology, such as nighttime HBPM measurements. Additionally, sex differences in BP patterns on ABPM and adherence to HT medications have been well documented (Mihailidou et al., 2022; Omboni et al., 2023). The randomisation sequence was sealed in numbered, light-opaque envelopes. The respective envelope for each patient was opened only after eligibility was confirmed and consent was signed.

Intervention and control group

All patients were provided with the same validated HBPM machines (WatchBP Home N; details under *HBPM*). However, the control group was instructed to monitor only daytime HBPM readings, which guided drug treatment as recommended by international and local guideline (Lim et al., 2019; Mancia et al., 2023). Office BP measurements were not used for treatment decisions as they were consistently shown inferior to HBPM for predicting future cardiovascular events and were less reproducible (Mancia et al., 2023). After confirming eligibility, participants received instructions on proper HBPM techniques from the principal investigator or a trained research assistant. The data stored within the HBPM devices were reviewed at every follow-up for drug management.

Patients in the intervention group were instructed to use the HBPM to automatically measure their BP three times per night during sleep (at 2, 3, and 4am) for ≥3 nights in the week prior to the follow-up. This approach is based on a BP measuring algorithm used in a nationwide cohort study in Japan, and it has been found to be acceptable by Japanese patients (Kario, 2018). A minimum of 6 nighttime BP readings over 1 week were recommended for monitoring and management (Kario, 2018). Our approach would provide maximally 9 readings over 3 nights, accounting for potential measurement errors or missing readings. The average of all night-time BP readings from the preceding week was used for management. The titration of anti-HT medications was based solely on nighttime HBPM readings.

Management of patients in the control group followed the Hong Kong primary care office guideline, which involves measuring BP ≥2 times in the morning (with a one-minute interval) and ≥2 times in the evening (before dinner or bedtime) for one week prior to the follow-up. A minimum of HBPM readings from 3 days (i.e. 12 readings) was recommended for monitoring and management (Kario, 2021). The average of these BP values was used for management.

The principal investigator, EKPL, assessed all participants every four weeks to discuss lifestyle management for HT and adjust medication dosages until the study endpoint at six months. Assessments were conducted less frequently after achieving the target SBP. The 4-week assessment interval accounted for the typical duration required for most anti-HT medications to reach their maximum effectiveness (Lasserson et al., 2011). In the intervention group, drug treatment was titrated in the evening against HBPM SBP with the goal of achieving an SBP of <120 mmHg. In contrast, the control group had drug treatment titrated in the morning with the goal of achieving an SBP of <135 mmHg. These SBP targets were based on current international guidelines (Mancia et al., 2023). Both groups had suboptimal SBP levels during nighttime and daytime on recruitment and received same titration of anti-HT medications recommended by local Hong Kong guideline (Lim et al., 2019). The current Hong Kong Primary Care Office guideline recommended once-daily dosing of diuretics, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, or calcium channel blockers as first-line agents; it also provides guidance on compelling indications and contraindications for anti-HT medications (Lim et al., 2019). For the intervention group, participants already receiving anti-HT medications were shifted to evening administration to control nighttime HBPM SBP.

Participants

A total of 78 patients with HT were recruited for this study from publicly funded general outpatient clinics in the New Territories East Cluster of the Hospital Authority, as well as through newspaper advertisements. All recruited patients underwent a 24-hour ABPM to confirm their eligibility.

Patients were recruited if they had nocturnal HT (night-time SBP ≥120 mmHg) and stage I HT (daytime SB*P* = 135–159 mmHg) as detected by ABPM. The duration of sleep was determined using patients' diaries (refer to the ABPM section for more details). Patients who met any of the following exclusion criteria were not included: (i) presence of atrial fibrillation; (ii) daytime office SBP ≥180 mmHg or DBP BP ≥120 mmHg; (iii) known obstructive sleep apnea; (iv) presence of dementia or psychiatric illness that impairs patients' ability to perform HBPM; (v) patients with end-stage malignancies; (vi) night shift workers, due to their reverse BP patterns; (vii) patients who

slept after 2am or wake up before 4am, as these patients would not be asleep during nighttime HBPM; (viii) patients receiving ≥3 anti-HT medications at maximum tolerated doses, as there was limited room for drug titration and these patients might have secondary HT resulting from another underlying disease; and (ix) patients receiving anticoagulants, as ABPM can cause significant bruising (due to repeated cuff inflations) in these patients.

Sample size

Based on the latest review, a minimum of 70 patients (35 participants per arm) is recommended for parallel-arm pilot trials to obtain sufficient data for assessing feasibility of the main RCT (Teare et al., 2014). Accounting for an estimated dropout rate of 10%, a total of 78 patients were recruited.

Outcome

The primary outcomes of this study included the rate of recruitment, which was defined as the number of participants recruited per month during the recruitment period. Additionally, the feasibility of HBPM measurement and the feasibility of repeated ABPM were assessed. Feasibility of HBPM measurement was determined by the proportion of participants in the intervention group who complied with the measurement schedule. Furthermore, the dropout rate was also measured. Medication adherence was assessed using the validated Treatment Adherence Questionnaire for Patients with Hypertension (TAQPH) at baseline and at the 6-month. The medication domain of the TAQPH consists of nine questions and has been validated for use in Chinese patients with HT with good internal consistency (Cronbach's alpha = 0.86) (Ma et al., 2012).

ABPM

ABPM, which is the reference standard for BP measurements, was utilised in our study (Mancia et al., 2023). The ABPM machines used were the EnviteC PhysioQuant and WatchBP O3, both are validated (https://www.stridebp.org/). ABPM was performed on usual working days, from Mondays to Thursdays, and BP measurements were taken every 30 min throughout the monitoring period. Patients recorded their sleep duration in a diary to determine the actual sleep period.

HBPM

WatchBP Home N (Microlife, Switzerland) was used as it has been validated by several international societies (https://www.stridebp.org/bp-monitors). The

cuff size and measurement techniques adhered to the HK guideline (Lim et al., 2019).

Office BP measurements

This was collected using the automated office blood pressure (AOBP) device WatchBP Office (Microlife, Switzerland), which automatically measured BP at one-minute intervals for 3 times and provided a mean BP value.

Other data collection

Demographic and clinical information were collected at baseline. Test results such as serum creatinine level, lipid levels (low-density lipoprotein [LDL], high-density lipoprotein [HDL], triglyceride [TG], total cholesterol [TC]), fasting glucose, and the presence of microalbuminuria were retrieved from the computerised medical system of the Hospital Authority (CMS). If these results were >3 months old, we conducted blood and urine tests for patients at baseline. We collected these clinical parameters, along with body mass index and the number and dosage of antihypertensive medications, at both baseline and the 6-month endpoint. Additionally, we retrieved the number of clinic visits, occurrences of death and hospitalisation during the study period from the CMS and through self-reporting. Any side effects experienced by the participants were self-reported and assessed by the investigator during follow-up.

To evaluate the acceptability of the intervention and assessments, we conducted interviews with 20 patients in the intervention group at 6-month. We asked the participants about their experience with home night-time HBPM, evening dosing of antihypertensive medications, trial procedures, and repeated ABPM. We used a semi-structured interview guide (Appendix 1). During the interviews, we also asked about any sleep disturbances experienced by the participants during the night-time HBPM and ABPM.

Statistical analysis

The demographic data, rate of recruitment, dropout rate, and adherence to home nocturnal BP measurement were presented as mean and standard deviation (if continuous) or by percentage (if discrete). We considered the following parameters to be feasible: (i) the rate of recruitment $\geq$15 participants per month, (ii) the dropout rate being < 20% from both arms, (iii) medication adherence not being statistically different between both arms, (iv) participants in the intervention group being adherent to the night-time HBPM schedule $\geq$80% of the time, and (v) $\geq$80% of participants completing ABPM at both time points.

All analyses were conducted by Stata (StataCorp. 2020. *Stata Statistical Software: Release 16.1*. College Station, TX: StataCorp LLC.). ANCOVA was used, where BP values on ABPM (daytime/night-time/24-hour), medication

adherence, fasting glucose level, lipid levels, creatinine levels, and BMI at 6 months were the dependent outcomes, and the baseline values and treatment group were used as covariates. Main analysis was conducted using the intention-to-treat approach. Sensitivity analyses were performed by using the per-protocol analysis, by excluding patients with resistant HT at the 6-month and by excluding patients who did not provide corresponding HBPM readings during the RCT period (i.e. no nighttime HBPM readings in the intervention group and no daytime HBPM readings in the control group). Statistical significance was defined as $p < 0.05$.

Data from the interviews were audio-recorded, transcribed, and coded. These codes were then grouped into various themes. The coding process was independently cross-checked for reliability by at least two researchers.

Results

Participants

The mean age of our participants was 63±8 years. Most patients were female (52.6%), had at least a secondary education (88.2%), were married (77.6%), and were dippers (52.6%). All patients had elevated BP during nighttime (mean B*P* = 129.4/74.7 mmHg), daytime (143.4/83.0 mmHg), 24-hour (139.2/80.4 mmHg), and during clinic visits (152.6/83.4 mmHg). Most demographic characteristics were balanced between both arms (Table 1). A list of anti-hypertensive drugs used by patients at study end-point can be found in Appendix 2.

Feasibility outcomes

Due to COVID-19 and its quarantine measures, 78 patients were recruited between June 2022 and June 2023, leading to a recruitment rate of 6.5 patients per month. During this time, a total of 1,315 individuals were screened for the research project, with the majority (76%) applying through newspaper advertisements. From this initial pool, 952 individuals completed ABPM, and ultimately, 78 were included in the study.

Only 3 participants (2 in the control group and 1 in the intervention group) were lost to follow-up (Figure 1), resulting in a retention rate of 96.1%.

In the intervention group, out of a total of 160 follow-ups, patients provided ≥6 and ≥9 nighttime HBPM readings for 77.5% and 63.8% of their follow-ups, respectively. In the control group, out of a total of 153 follow-ups, patients provided ≥12 and ≥28 daytime HBPM readings for 92.16% and 47.7% of their follow-ups, respectively.

All participants ($n = 74$) completed 6-month ABPM and participants in both arms had similar medication adherence scores (Table 2).

Table 1. Baseline characteristics of eligible participants.

Factor	Level	Control ($N = 38$)	Intervention ($N = 38$)	*p*-value
Demographic				
Age		62.6 (8.5)	62.7 (8.2)	0.92
Female		21 (55.3%)	19 (50.0%)	0.65
Education	Primary	8 (21.1%)	1 (2.6%)	0.026
	Secondary	14 (36.8%)	22 (57.9%)	
	University or above	15 (40.5%)	15 (39.5%)	
Occupation	Full time	9 (23.7%)	15 (39.5%)	0.22
	Part time	1 (2.6%)	2 (5.3%)	
	Unemployed	1 (2.6%)	0 (0.0%)	
	Housewife	10 (26.3%)	4 (10.5%)	
	Retired	16 (43.2%)	17 (44.7%)	
Marital status	Single	3 (8.1%)	5 (13.2%)	0.89
	Married	29 (78.4%)	30 (78.9%)	
	Divorced	3 (8.1%)	1 (2.6%)	
	Co-habit	1 (2.7%)	1 (2.6%)	
	Widowed	1 (2.7%)	1 (2.6%)	
Monthly income	No income	8 (24.2%)	7 (20.0%)	0.054
	< $5,000	7 (21.2%)	0 (0.0%)	
	$5,000–$9,999	0 (0.0%)	1 (2.9%)	
	$10,000–$19,999	4 (12.1%)	5 (14.3%)	
	$20,000–$29,999	3 (9.1%)	8 (22.9%)	
	$30,000–$39,999	3 (9.1%)	3 (8.6%)	
	$40,000 or above	7 (21.2%)	11 (31.4%)	
	Comprehensive Social Security Assistance	1 (3.0%)	0 (0.0%)	
Ambulatory blood pressure monitoring, mmHg				
24 h systolic blood pressure (SBP)		139.3 (5.5)	139.0 (5.4)	0.80
24 h diastolic blood pressure (DBP)		81.5 (8.3)	79.3 (9.1)	0.28
Daytime SBP		143.5 (5.9)	143.4 (6.5)	0.94
Daytime DBP		84.0 (8.9)	82.0 (9.5)	0.36
Nighttime SBP		129.6 (7.4)	129.3 (7.3)	0.86
Nighttime DBP		76.2 (8.4)	73.2 (8.6)	0.12
Dipping percentage, %		9.6 (4.8)	9.7 (5.2)	0.93
Number of non-dippers		18 (47.4%)	18 (47.4%)	1.00
Clinical measurement				
Office SBP, mmHg		155.5 (17.1)	149.6 (17.7)	0.14
Office DBP, mmHg		86.2 (13.3)	80.7 (11.8)	0.06
Body mass index, kg/m^2		24.6 (3.8)	25.2 (4.0)	0.47
Creatinine level, μmol/L		72.9 (14.3)	74.4 (14.8)	0.64
Low-density lipoprotein cholesterol, mmol/L		3.0 (1.1)	2.7 (0.8)	0.19
High-density lipoprotein cholesterol, mmol/L		1.6 (0.4)	1.5 (0.4)	0.28
Triglyceride, mmol/L		1.3 (0.9)	1.7 (1.3)	0.10
Total cholesterol, mmol/L		5.2 (1.1)	4.8 (1.0)	0.07
Fasting glucose level, mmol/L		5.5 (0.7)	5.7 (0.9)	0.29
Presence of microalbuminuria		4 (10.8%)	6 (15.8%)	0.53
Number of antihypertensive drugs		1.1 (1.1)	1.3 (0.9)	0.43
Adherence measured by Treatment Adherence Questionnaire for Patients with Hypertension				
Overall adherence score		95.9 (11.4)	94.4 (12.2)	0.62
Medication adherence score		33.4 (3.4)	33.3 (4.0)	0.91
Lifestyle adherence score		62.2 (9.3)	61.6 (9.9)	0.79
Diet score		29.9 (5.2)	29.6 (5.2)	0.85
Stimulation score		10.9 (1.4)	10.2 (2.5)	0.15
Exercise score		6.2 (1.8)	6.3 (1.8)	0.95
Weight control score		6.4 (1.4)	6.3 (1.4)	0.81
Relieving stress score		8.9 (2.2)	9.5 (1.8)	0.22

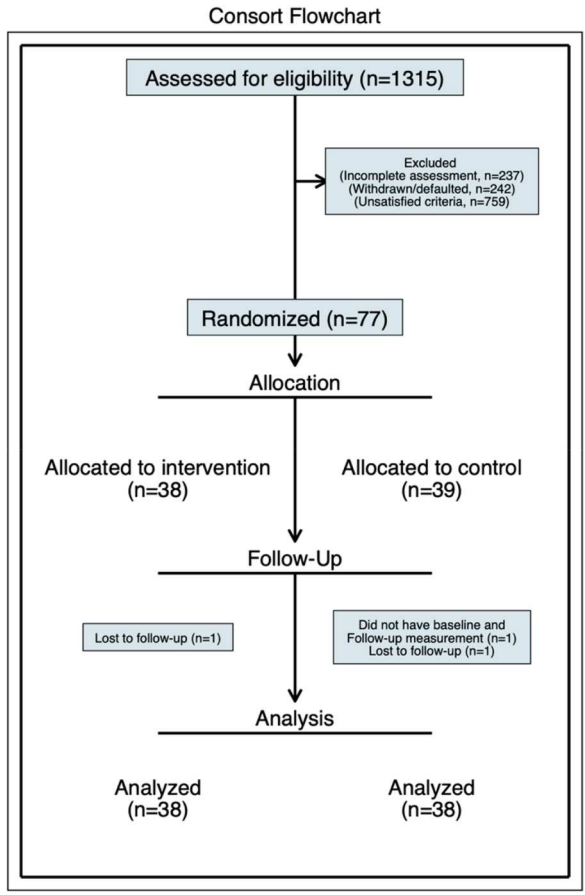

Figure 1. Patient flow chart.

Other secondary results

Nighttime SBP and DBP were similar between both arms (SBP: 115.9 mmHg versus 116.6 mmHg, $p = 0.80$; DBP: 64.8 mmHg versus 68.0 mmHg, $p = 0.48$). Both arms showed no significant differences in 24-hour and daytime BP on ABPM, as well as in the number of non-dippers. Office BP, lipid profile, fasting glucose, healthcare utilisation, and lifestyle adherence were also similar between both arms (Table 2). No serious adverse events were detected during the trial period.

Patients' interviews

Although most patients reported that they learned more from their HBPM nighttime readings and found nighttime BP measurements to be generally

Table 2. Comparison of primary and secondary outcome by intervention and control group at 6-month, following intention-to-treat principle.

Outcome	Control ($N = 38$)	Intervention ($N = 38$)	*p*-value
Ambulatory blood pressure monitoring, mmHg			
24 h systolic blood pressure (SBP)	124.6 (8.5)	125.7 (9.3)	0.60
24 h diastolic blood pressure (DBP)	73.3 (7.2)	71.7 (8.7)	0.98
Daytime SBP	128.2 (8.4)	130.1 (9.8)	0.38
Daytime DBP	75.7 (7.9)	75.0 (8.9)	0.60
Nighttime SBP	116.6 (10.7)	115.9 (10.9)	0.80
Nighttime DBP	68.0 (7.9)	64.8 (8.6)	0.48
Dipping percentage, %	9.0 (6.3)	10.7 (7.2)	0.27
Number of non-dippers	22 (58%)	17 (45%)	0.25
Home blood pressure monitoring, mmHg			
Daytime SBP	129.9 (11.7)	126.3 (8.1)	0.17
Daytime DBP	75.9 (5.3)	70.8 (7.5)	0.002
Nighttime SBP	126.5 (16.3)	117.5 (8.7)	0.18
Nighttime DBP	78.0 (19.8)	66.9 (9.7)	0.14
Clinical measurement			
Office SBP, mmHg	142.2 (15.4)	142.6 (18.6)	0.41
Office DBP, mmHg	80.1 (10.9)	76.3 (11.4)	0.71
Body mass index, kg/m^2	24.3 (3.6)	25.0 (3.6)	0.44
Creatinine level, μmol/L	74.9 (16.3)	76.6 (17.7)	0.98
Low-density lipoprotein cholesterol, mmol/L	2.9 (0.9)	2.6 (0.7)	0.35
High-density lipoprotein cholesterol, mmol/L	1.6 (0.5)	1.5 (0.4)	0.37
Triglyceride, mmol/L	1.3 (0.9)	1.4 (0.8)	0.56
Total cholesterol, mmol/L	5.0 (1.1)	4.7 (0.8)	0.64
Fasting glucose level, mmol/L	5.6 (1.1)	5.9 (1.0)	0.74
Presence of microalbuminuria	4 (11%)	2 (5%)	0.38
Healthcare utilisation			
Private doctor visit	0.3 (1.3)	0.2 (0.7)	0.57
General out-patient clinics visit	5.2 (1.2)	5.9 (1.8)	0.08
Hospitalisation	0.0 (0.0)	0.1 (0.3)	0.08
Accident & emergency visit	0.1 (0.2)	0.3 (1.1)	0.15
Increased dosing of antihypertensive drugs	31 (82%)	33 (87%)	0.50
Adherence measured by Treatment Adherence Questionnaire for Patients with Hypertension			
Overall adherence score	94.5 (8.9)	94.6 (10.0)	0.70
Medication adherence score	34.2 (2.5)	34.6 (2.4)	0.78
Lifestyle adherence score	60.3 (7.9)	60.2 (8.8)	0.68
Diet score	28.5 (4.3)	28.3 (5.5)	0.99
Stimulation score	10.8 (1.4)	10.6 (1.7)	0.75
Exercise score	5.9 (1.7)	6.1 (1.6)	0.48
Weight control score	6.0 (1.5)	6.0 (1.3)	0.89
Relieving stress score	9.2 (1.9)	9.2 (1.4)	0.56

well-tolerated, some patients still reported sleep disturbances. Similarly, although some patients reported good adherence to evening dosing of medications and subjectively experienced better symptom control, some patients occasionally forgot to take their medications before going to sleep. Additionally, some patients found that follow-up visits every 4 weeks could impose a burden on their daily lives. Lastly, while most patients reported that ABPM was acceptable and potentially helpful for their BP management, they also noted that it could be disruptive to their daily routine (Table 3).

Sensitivity analyses

Sensitivity analyses found similar results. (Appendix 3–5).

Discussion

Main findings

Adjusting the evening dosage of anti-HT medications with repeated nighttime HBPM was acceptable to patients, offering at least non-inferior BP control on ABPM, as well as similar healthcare utilisation and medication adherence compared to usual care. There was excellent acceptability to repeated ABPM and both groups had <5% dropout rate.

Although we initially set a compliance threshold of 80%, where patients in the intervention group were required to provide ≥6 nighttime HBPM readings in the week prior to index consultations, our patients achieved compliance of 77.5%. However, our interview results indicated that some patients needed time to learn the nighttime HBPM technique. On average, each patient in the intervention group had only 4.3 office visits, which means that missing HBPM measurements during just 1 office visit would lower their compliance below the 80% threshold. Furthermore, the nighttime ABPM at the 6-month were similar between the intervention and control groups, suggesting adequate number of nighttime BP readings for drug titration. However, a small subgroup of patients (n = 4, 10.8%) in the intervention group did not provide any nighttime BP measurements during all follow-up visits due to sleep disturbances, compared to n = 2 (5.6%) in the control group. This suggests that nighttime HBPM may be impractical for this subgroup of patients who experienced sleep disturbances during nighttime HBPM. Post-hoc analyses did not identify consistent characteristics among these patients, except that they were all married and had at least a secondary education. To enhance compliance with nighttime HBPM in the future RCT, the research assistant can check for any issues with HBPM after the first consultation and remind participants to conduct HBPM and bring their results one to two weeks before subsequent consultations.

Although the rate of recruitment (6.5 participants per month) was slower than our predefined threshold of 15 participants per month, the RCT was conducted during the COVID-19 outbreak in Hong Kong and was affected by quarantine measures. Many patients were reluctant to visit the office and placed less emphasis on managing chronic diseases. In future definitive RCTs, it will be necessary to monitor the recruitment rate and consider including more recruiting sites, such as general practices or hospitals.

The time of administration of anti-HT medications remain subject to controversy. For example, the Hygia trial reported a >50% relative risk reduction

Table 3. Facilitators and barriers to the intervention, classified by implementation step.

Facilitators	Barriers
Nighttime home blood pressure monitoring	
Acquired knowledge about BP management (e.g. nighttime BP dipping)	Potential negative effects on sleep quality or sleep duration
'Through this project, I gained insights that nighttime BP should be 10% lower (than daytime BP). This awareness has prompted me to pay attention to the nighttime BP dipping.'	'The difficulty that I encountered is waking up when the cuff inflated, which affected my sleep quality.'
Improved nighttime BP monitoring	Concerns about accuracy due to personal habits
'Nighttime BP readings provided records and helped me gain better understanding of nighttime BP status.'	'I usually take a shower right before going to bed. I am not sure whether it affects the accuracy of my (nighttime) BP readings, especially since I fall asleep quickly.'
Facilitated clinical decision-making based on nighttime BP readings	Can be inconvenient if patients use the toilet during the night.
'I shared my nighttime BP readings with my doctor, and they adjusted my medication dosage accordingly.'	'One challenge is that I having to bring the HBPM machine with me when using the toilet during the night, which could be inconvenient.'
Modified lifestyle based on nighttime BP readings	Arm was uncomfortable
'After discussing (nighttime BP readings) with my doctor, I paid more attention to my lifestyle choices including diet and physical activities … I increased my exercise routine and made modifications to my diet.'	'I experienced discomfort and numbness in my arm during the BP measurement, as the cuff felt tight. However, I was hesitant to loosen the cuff, concerned that it might affect the accuracy of the readings.'
Accustomed to nighttime HBPM measurement over a period of measurement	
'Initially, I felt unused to the measurement, but everything turned out fine later.'	
Evening dosing of antihypertensive drugs	
Easy to remember evening dosing	Potential side effects such as feet edema and nocturia
'I may forget to take daytime medication, especially when I am engaged in outdoor activities. In contrast, I hardly forget to take my medication before going to bed.'	'At the beginning, I experienced edema in my feet. The symptom subsided after taking edema medications.'
Improved BP control	Forgetfulness due to unaccustomedness
'The evening dosing helped me maintain good control over my BP, particularly the nighttime BP. Lately I visited primary care physicians due to a cold, and they commended me for effectively managing my BP.'	'One difficulty is that I am unaccustomed to taking medication at night. There are times when I forgot to take evening dosing, and occasionally I wake up during the night, realising that I have missed my pills.'
Less likely to experience symptoms such as dizzy and headache	BP was initially unstable during initial transition to nighttime dosing
'After taking evening medication, I was less likely to experience morning dizziness upon wake up.'	'During the initial transition from daytime dosing to nighttime dosing, my BP was not stable. But after drug titration, I found it was acceptable.'
Nighttime dosing was preferred when participant took Chinese medicine in daytime	
'I prefer taking medications in the evening as it helps me better manage my medication schedule. Evening dosing allows for a convenient time gap of at least two hours between taking Chinese and Western medications, which is necessary for proper administration.'	
Had better sleep after drug titration	

(*Continued*)

Table 3. Continued.

Facilitators	Barriers
'After the medication titration, I achieved good control over my blood pressure. I have been experiencing better sleep and an overall improved sense of well-being.'	
More frequent follow-up, monitoring and measurement compared to usual care	
Helped BP monitoring and management	Affect daily schedule
'Throughout the 6-month period, I maintained close monitoring of my blood pressure. I measured and recorded my BP readings, which I shared with my physician before each consultation. I paid more attention during this period.'	'I may not be able to engage in outdoor activities or go travelling. It affected my daily schedule, and I need to make adjustments to accommodate the intervention schedule.'
The frequency is acceptable	Concerns about forgetfulness
'The frequency is manageable for me. While measuring nighttime BP every week might be challenging, I find it easy to monitor my BP only during the week prior to my consultation with the doctor.'	'I was concerned about potentially forgetting to measure BP. It led to a sense of unease, similar to the feeling of not being able to complete an assignment.'
Repeated ABPM measurement	
Helped BP monitoring and management	Affected daily schedule and mobility
'The ABPM measurement was helpful because previously I did not realise that my BP was so high during the nighttime. But after taking medications and being more attentive to BP control, my BP returned to normal levels.'	'Although I can work as usual, I must be cautious about my movements, such as avoiding activities that involve running, maintaining a calm state of mind, and taking quick showers. I was not able to go out freely. I felt a bit restricted.'
Wearing ABPM machine is acceptable	Potential negative effects on sleep quality or sleep duration
'I only wore ABPM machine for a single day (each time). The duration was relatively short to me. I did not experience much pressure from wearing it.'	'In terms of sleep quality, it may not be drastically different, but there was indeed some disruption caused by it.'
Accustomed to the ABPM measurement through repeated measurement	Concern about physical appearance of the ABPM machine
'Except for the first time, I have become accustomed to the ABPM measurements.'	'Having a device attached to me made me feel a bit strange. Therefore, I wore a light jacket to cover the device.'

in cardiovascular events by shifting ≥1 anti-HT medications to bedtime (Hermida et al., 2020). However, the TIME trial found no significant change in cardiovascular events associated with evening anti-HT medications (Mackenzie et al., 2022). This discrepancy may be explained by these landmark RCTs not adjusting medication dosage based on nighttime BP levels (Maqsood et al., 2023). Although this approach may be beneficial for patients with nocturnal HT, for patients with nocturnal normotension, excessive reduction of nighttime BP (along with excessive dipping and morning surge) can increase cardiovascular risk (Burnier et al., 2020). Our findings indicate that titrating medications according to home nighttime BP is a feasible strategy in primary care settings. This approach also allows for more targeted and personalised care, ensuring that patients with nocturnal HT receive the optimal dosage of anti-HT medications based on their nighttime BP.

Strength and weakness

This RCT is the first proof-of-concept RCT to show that nocturnal HT can be monitored and managed by night HBPM and that this approach can be feasible in primary care settings, where most HT patients are being managed.

Furthermore, our results suggested a better control of nighttime BP and its associated pattern (our secondary outcomes) in the intervention group. However, statistical significance was limited by the small sample size in this pilot RCT. For instance, patients in the intervention group exhibited potentially lower nighttime SBP (115.5 mmHg versus 116.5 mmHg), lower nighttime DBP (64.8 mmHg versus 68 mmHg), higher dipping ratio (10.8% versus 8.9%), and were less likely to be non-dippers (43% versus 59%). Despite these trends, none of these differences reached statistical significance, possibly due to the limited size of our study population.

Since all patients are treated by a single clinician, this may limit the generalizability of our results. In future definitive RCTs, multiple clinicians can be involved. Similarly, only 11.8% of the participants had an education level at or below primary school. The acceptability or feasibility of using nighttime HBPM in patients with lower education levels, such as those below secondary school, is currently unknown and is likely lower. Additionally, due to the nature of the intervention, it was inherently impossible to blind both the intervener and the participant. For instance, patients took their HBPM readings and could observe changes in their BP. However, in the future definitive RCTs, the primary outcome can be ABPM readings, which are objective. This approach also better resembled the 'real-life' clinical situation.

Clinical and research implications

Clinicians should be aware that nocturnal HT is currently underdiagnosed and undertreated. Results from both local and international studies indicated that >60% of patients with diagnosed HT have undiagnosed nocturnal HT, despite good daytime HT control in around 50% of these patients (Lee et al., 2022; Li et al., 2021). This is likely caused by monitoring and treating daytime HT without measuring nocturnal BP in routine clinical practice. Our findings suggest that nighttime HBPM is well accepted by HT patients and can play a crucial role in diagnosing, monitoring, and managing nocturnal HT (with or without daytime HT) in primary care. Moreover, our results indicate that the evening dosing of anti-HT medications does not hinder medication adherence in most patients and does not lead to additional side effects. Nevertheless, further investigation through RCTs is necessary to substantiate these findings.

At the time of writing, only a limited number of validated models of nighttime HBPM devices were available (none in Hong Kong). One such device, the WatchBP Home N, was utilised in our study and offers three different modes: 'usual,' 'diagnostic,' and 'nocturnal.' In the 'diagnostic' mode, patients can take dual measurements and record their daytime HBPM for seven days prior to their consultation. This mode automatically provides the clinician with a seven-day average, eliminating the need for manual calculation. Similarly, the 'nocturnal mode' of the device measures BP at 2.00am, 3.00am, and 4.00am during the patient's sleep, providing an average for clinician management. Overall, we found that the WatchBP Home N is user-friendly and suitable for managing HT in primary care settings. However, a subset of patients still had difficulty sleeping, even with fewer readings taken compared to ABPM per night. A newer and silent wrist-based nighttime HBPM device (ORMON Nightview) is validated and being marked, which may prove to be more suitable for these patients (Imai et al., 2018). However, cuff from the Nightview device cannot be replaced and may be more difficult to cleanse.

As the feasibility has now been demonstrated, adequately-powered RCTs should be conducted to investigate whether nocturnal BP, the strongest predictor to cardiovascular events among BP indices, can be a primary treatment target for HT. These RCTs can have a longer duration ($\geq$1 year) and incorporate surrogate cardiovascular outcomes (e.g. pulse wave velocity) or hard cardiovascular outcomes (e.g. myocardial infarction), while utilising ABPM as the primary outcome. Furthermore, additional studies are needed to explore the role of nighttime HBPM (e.g. its usefulness in screening for nocturnal HT) and to facilitate its implementation in primary care. Moreover, the 'treatment-to-target' approach and evening administration of anti-HT medications should be examined in patients with isolated nocturnal HT, as it remains unclear this may lead to daytime hypotension.

Conclusion

Nocturnal HT is prevalent among patients with diagnosed HT and represents an untreated cardiovascular risk. Adjusting the evening dosage of anti-HT medications based on repeated nighttime HBPM represents a potential treatment approach for patients with nocturnal HT. This intervention was well accepted by patients and resulted in at least non-inferior BP control on ABPM, as well as similar healthcare utilisation and medication adherence compared to usual care. Further RCTs should be adequately powered and include long-term cardiovascular outcomes to confirm if targeting nocturnal BP, rather than daytime BP, should be the primary treatment goal for HT and if it offers greater cardioprotection.

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author, LEKP.

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Appendix

Table A1. Interview guide for participants in the intervention group (home night-time BP measurement group).

Area to explore	Sample questions
Opening question/ understanding background	• Before joining this trial, how do you manage your hypertension? • How do you usually monitor your blood pressure before joining this trial? • If you used to measure home blood pressure, how did you measure it previously?
Experience with night-time home blood pressure	• After joining this trial, can you tell me how you measure your night-time blood pressure? • What are the barriers or difficulties of measuring home blood pressure at night? • How does measuring blood pressure at night affect your daily living? • How does measuring blood pressure at night affect your sleep (if any)? • How do you interpret the home BP results? In what ways do these readings help your hypertension management, if any?
Evening doses of anti-hypertensive medications	• The doctors managed your blood pressure, in the past 6 months, by changing the drug regimen in the evening. How do you feel about that? • Does it cause any difficulties, including remembering to take the drugs, if any? • Are there any side effects from this drug treatment? If so, what are they?
Trials related matters	• There were possibly more frequent follow-ups, assessments and monitoring than your usual treatment. How did you feel about it? How did this impact your life? • You have received two 24-hours blood pressure monitoring. How do you feel about it? (if not mentioned: how does it affect your sleep, if any?) • Will you recommend your friend (who has hypertension) to participant in this trial? Why?
Closing	• Thank you very much for your information. This is really helpful. Is there anything that you would like to add, regarding your treatment in last 6 months?

Table A2. Anti-hypertensive drug used.

Drug name	Brand name in Hong Kong
ACEI/ARB	
Losartan (25–100 mg)	Cozaar
Lisinopril (10–20 mg)	Zestril
Beta-blocker*	

(*Continued*)

Table A2. Continued.

Drug name	Brand name in Hong Kong
Atenolol (25–100 mg)	Tenormin
Carvedilol (25 mg)	Coreg
CCB	
Amlodipine (2.5–10 mg)	Norvasc
Felodipine extended release (5–10 mg)	Plendil
Diltiazem sustained release (100 mg)	
Diuretics	
Indapamide SR (1.5–2.5 mg)	Natrilix SR
Frusemide (40 mg)	Lasix
Potassium sparing diuretics*	
Spironolactone (12.5–25 mg)	Aldactone
Alpha blockers*	
Terazosin (1–10 mg)	Hytrin
Doxazosin (4–8 mg)	Cardura XI
Others*	
Hydralazine (50 mg)	
Methyldopa (500 mg)	Aldoment

ACEI/ARB = Angiotensin-converting enzyme/ Angiotensin receptor blockers, CCB = calcium channel blocker.

*considered non-first line medications by Hong Kong guidelines. Only used in this trial for patients with resistant hypertension or with compelling indications.

Table A3. Comparison of primary and secondary outcome by intervention and control group at 6-month, following per-protocol principle.

Outcome	Control ($N = 37$)	Intervention ($N = 37$)	*p*-value
Ambulatory blood pressure monitoring, mmHg			
24 h systolic blood pressure (SBP)	124.3 (8.3)	125.3 (9.1)	0.61
24 h diastolic blood pressure (DBP)	73.1 (7.2)	71.1 (7.9)	0.84
Daytime SBP	127.8 (8.1)	129.7 (9.6)	0.37
Daytime DBP	75.5 (7.8)	74.4 (8.3)	0.67
Nighttime SBP	116.5 (10.8)	115.5 (10.6)	0.72
Nighttime DBP	68.0 (7.9)	64.8 (8.6)	0.48
Dipping percentage, %	8.9 (6.3)	10.8 (7.3)	0.23
Number of non-dippers	22 (59%)	16 (43%)	0.16
Home blood pressure monitoring, mmHg			
Daytime SBP	129.6 (11.6)	126.3 (8.1)	0.17
Daytime DBP	76.1 (5.4)	70.8 (7.5)	0.002
Nighttime SBP	126.5 (16.3)	117.8 (9.1)	0.18
Nighttime DBP	78.0 (19.8)	67.4 (10.1)	0.14
Clinical measurement			
Office SBP, mmHg	141.7 (15.3)	142.3 (18.8)	0.39
Office DBP, mmHg	79.9 (11.0)	75.9 (11.2)	0.66
Body mass index, kg/m^2	24.3 (3.7)	24.8 (3.5)	0.47
Creatinine level, μmol/L	74.9 (16.5)	76.4 (18.0)	0.98
Low-density lipoprotein cholesterol, mmol/L	2.9 (0.9)	2.5 (0.7)	0.28
High-density lipoprotein cholesterol, mmol/L	1.6 (0.5)	1.5 (0.4)	0.37
Triglyceride, mmol/L	1.4 (0.9)	1.4 (0.8)	0.50
Total cholesterol, mmol/L	5.1 (1.0)	4.7 (0.8)	0.53
Fasting glucose level, mmol/L	5.6 (1.1)	5.8 (0.9)	0.69
Presence of microalbuminuria	4 (11%)	2 (6%)	0.39
Healthcare utilisation			
Private doctor visit	0.3 (1.3)	0.2 (0.7)	0.57
General out-patient clinics visit	5.2 (1.2)	5.9 (1.8)	0.08
Hospitalisation	0.0 (0.0)	0.1 (0.3)	0.08

(*Continued*)

Table A3. Continued.

Outcome	Control ($N = 37$)	Intervention ($N = 37$)	p-value
Accident & emergency visit	0.1 (0.2)	0.3 (1.1)	0.15
Increased dosing of antihypertensive drugs	31 (84%)	33 (89%)	0.50
Adherence measured by Treatment Adherence Questionnaire for Patients with Hypertension			
Overall adherence score	94.1 (8.5)	95.2 (9.8)	0.44
Medication adherence score	34.2 (2.5)	34.9 (1.8)	0.36
Lifestyle adherence score	59.9 (7.6)	60.4 (8.9)	0.53
Diet score	28.3 (4.2)	28.4 (5.6)	0.90
Stimulation score	10.7 (1.4)	10.7 (1.7)	0.92
Exercise score	5.8 (1.7)	6.1 (1.6)	0.40
Weight control score	6.0 (1.5)	6.0 (1.3)	1.00
Relieving stress score	9.1 (1.9)	9.2 (1.4)	0.68

Table A4. Comparison of primary and secondary outcome by intervention and control group at 6-month, excluding participants with resistant hypertension.

Outcome	Control ($N = 35$)	Intervention ($N = 35$)	p-value
Ambulatory blood pressure monitoring, mmHg			
24 h systolic blood pressure (SBP)	124.2 (8.6)	125.5 (9.3)	0.55
24 h diastolic blood pressure (DBP)	73.5 (7.3)	72.7 (8.2)	0.92
Daytime SBP	127.9 (8.4)	130.0 (9.8)	0.35
Daytime DBP	76.0 (7.9)	76.0 (8.3)	0.52
Nighttime SBP	116.0 (10.8)	115.5 (10.8)	0.86
Nighttime DBP	68.1 (8.0)	65.5 (8.5)	0.61
Dipping percentage, %	9.3 (6.4)	11.0 (7.4)	0.28
Number of non-dippers	20 (57%)	15 (43%)	0.23
Home blood pressure monitoring, mmHg			
Daytime SBP	129.2 (11.6)	125.6 (8.0)	0.19
Daytime DBP	76.2 (5.2)	71.6 (7.1)	0.005
Nighttime SBP	126.5 (16.3)	117.9 (8.8)	0.21
Nighttime DBP	78.0 (19.8)	68.1 (9.3)	0.18
Clinical measurement			
Office SBP, mmHg	142.6 (15.9)	142.5 (19.4)	0.54
Office DBP, mmHg	80.4 (11.0)	77.3 (11.3)	0.74
Body mass index, kg/m^2	24.2 (3.8)	24.9 (3.8)	0.13
Creatinine level, μmol/L	74.5 (16.3)	74.5 (16.7)	0.91
Low-density lipoprotein cholesterol, mmol/L	2.9 (0.9)	2.6 (0.8)	0.52
High-density lipoprotein cholesterol, mmol/L	1.6 (0.5)	1.5 (0.4)	0.41
Triglyceride, mmol/L	1.3 (0.9)	1.5 (0.8)	0.80
Total cholesterol, mmol/L	5.1 (1.1)	4.8 (0.8)	0.89
Fasting glucose level, mmol/L	5.5 (0.9)	5.8 (1.0)	0.32
Presence of microalbuminuria	4 (12%)	2 (6%)	0.37
Healthcare utilisation			
Private doctor visit	0.2 (0.9)	0.2 (0.7)	0.88
General out-patient clinics visit	5.1 (1.1)	5.7 (1.8)	0.08
Hospitalisation	0.0 (0.0)	0.1 (0.3)	0.08
Accident & emergency visit	0.1 (0.2)	0.4 (1.2)	0.15
Increased dosing of antihypertensive drugs	28 (82%)	30 (88%)	0.49
Adherence measured by Treatment Adherence Questionnaire for Patients with Hypertension			
Overall adherence score	94.7 (9.1)	93.8 (9.9)	1.00
Medication adherence score	34.1 (2.6)	34.5 (2.5)	0.71
Lifestyle adherence score	60.6 (8.0)	59.6 (8.7)	0.99
Diet score	28.5 (4.5)	27.9 (5.5)	0.82

(*Continued*)

Table A4. Continued.

Outcome	Control ($N = 35$)	Intervention ($N = 35$)	p-value
Stimulation score	10.9 (1.2)	10.6 (1.8)	0.34
Exercise score	5.9 (1.8)	6.0 (1.6)	0.22
Weight control score	6.1 (1.6)	5.9 (1.3)	0.99
Relieving stress score	9.2 (2.0)	9.1 (1.4)	0.44

Table A5. Comparison of primary and secondary outcome by intervention and control group at 6-month, excluding participants who did not measure HBPM during the study period.

Outcome	Control ($N = 35$)	Intervention ($N = 33$)	p-value
Ambulatory blood pressure monitoring, mmHg			
24 h systolic blood pressure (SBP)	124.2 (8.5)	126.1 (9.3)	0.39
24 h diastolic blood pressure (DBP)	72.6 (7.0)	70.9 (8.2)	0.97
Daytime SBP	127.8 (8.3)	130.5 (9.9)	0.23
Daytime DBP	74.9 (7.7)	74.4 (8.5)	0.45
Nighttime SBP	116.5 (11.0)	116.2 (11.0)	0.91
Nighttime DBP	67.4 (7.8)	64.4 (8.9)	0.44
Dipping percentage, %	8.8 (6.3)	10.8 (7.6)	0.25
Number of non-dippers	21 (60%)	15 (45%)	0.23
Home blood pressure monitoring, mmHg			
Daytime SBP	129.9 (11.7)	127.0 (8.4)	0.29
Daytime DBP	75.9 (5.3)	70.5 (7.6)	0.002
Nighttime SBP	126.5 (16.3)	117.5 (8.7)	0.18
Nighttime DBP	78.0 (19.8)	66.9 (9.7)	0.14
Clinical measurement			
Office SBP, mmHg	142.2 (15.5)	143.3 (19.3)	0.42
Office DBP, mmHg	79.3 (11.0)	75.7 (11.6)	0.68
Body mass index, kg/m^2	24.3 (3.8)	24.8 (3.6)	0.47
Creatinine level, μmol/L	74.3 (16.7)	75.8 (17.7)	0.94
Low-density lipoprotein cholesterol, mmol/L	2.9 (0.9)	2.5 (0.7)	0.32
High-density lipoprotein cholesterol, mmol/L	1.6 (0.5)	1.6 (0.4)	0.23
Triglyceride, mmol/L	1.3 (0.9)	1.4 (0.9)	0.43
Total cholesterol, mmol/L	5.1 (1.1)	4.7 (0.9)	0.64
Fasting glucose level, mmol/L	5.6 (1.1)	5.9 (1.1)	0.66
Presence of microalbuminuria	4 (11%)	2 (6%)	0.44
Healthcare utilisation			
Private doctor visit	0.2 (0.9)	0.2 (0.7)	0.84
General out-patient clinics visit	5.2 (1.2)	5.9 (1.9)	0.054
Hospitalisation	0.0 (0.0)	0.1 (0.3)	0.07
Accident & emergency visit	0.1 (0.2)	0.4 (1.2)	0.13
Increased dosing of antihypertensive drugs	30 (86%)	30 (91%)	0.51
Adherence measured by Treatment Adherence Questionnaire for Patients with Hypertension			
Overall adherence score	93.5 (8.4)	93.9 (10.2)	0.53
Medication adherence score	34.1 (2.6)	34.5 (2.5)	0.75
Lifestyle adherence score	59.4 (7.4)	59.7 (9.1)	0.49
Diet score	28.0 (4.2)	27.9 (5.7)	0.90
Stimulation score	10.7 (1.4)	10.6 (1.7)	0.82
Exercise score	5.8 (1.8)	6.2 (1.7)	0.23
Weight control score	5.9 (1.5)	5.9 (1.3)	0.93
Relieving stress score	9.0 (1.9)	9.1 (1.5)	0.75