Association between 24-hour systolic blood pressure time in target range and mortality

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Abstract

Background: Time in target range (TTR) reflects the proportion of time blood pressure (BP) remains within a defined range, integrating BP variability and control. We examined associations of systolic BP (SBP) TTR during ambulatory BP monitoring (ABPM) with cardiovascular (CV) and all-cause mortality.

Methods: Patients from the Spanish ABPM Registry who were receiving antihypertensive medications or who had sustained or masked hypertension without treatment, defined by office BP ≥140/90 mmHg and 24-hour BP ≥130/80 mmHg. TTR was estimated by linear interpolation between consecutive SBP recordings obtained from ABPM and expressed as the proportion of time SBP remained within 120-134 mmHg during daytime and 110-119 mmHg during nighttime, from which 24-hour TTR was derived. Associations with mortality were assessed by Cox regression adjusted for demographic and clinical variables.

Results: A total of 48,687 patients (46% women) were analyzed. Over a median follow-up of 9.7 years, 6,502 deaths occurred, including 2,185 CV deaths. Higher 24-hour TTR was associated with lower all-cause mortality (HR 0.83 per 1-SD increment; 95% CI 0.80-0.85). Similarly, higher 24-hour TTR was associated with lower CV mortality (HR 0.80 per 1-SD increment; 95% CI 0.76-0.84). Both associations remained significant after adjusting for mean 24-hour SBP and SBP variability.

Conclusions: Higher 24-hour SBP TTR derived from ABPM was independently associated with lower all-cause and CV mortality.

Keywords: Ambulatory blood pressure monitoring; hypertension; all-cause mortality; cardiovascular mortality; blood pressure variability

Abbreviations

ABPM	Ambulatory blood pressure monitor
BP	blood pressure
CI	confidence interval
CV	cardiovascular
DBP	diastolic blood pressure
SBP	systolic blood pressure
SD	standard deviation
TTR	time in target range

Introduction

Short-term blood pressure (BP) variability, as measured by 24-hour ambulatory BP monitoring (ABPM), is associated with an increased risk of cardiovascular (CV) outcomes, independent of the mean 24-hour BP level.(1-3) An emerging metric in assessing BP variability and control is time-in-target range (TTR), which has gained increasing attention in hypertension management. The concept of TTR originated in the fields of anticoagulation and diabetes care, where it is used both as a clinical target and outcome measure.(4,5) More recently, TTR has also been applied to hypertension.(6,7) TTR quantifies the proportion of time that systolic BP (SBP) remains within a predefined target range over multiple time points.(8) Unlike mean BP, TTR integrates information on BP levels and variability. For example, a patient may have a mean BP within the target range but exhibit high BP variability, resulting in fewer individual readings within the desired range. Since both elevated BP levels and increased BP variability are associated with all-cause and CV mortality,(9,10) TTR may offer additional prognostic value. In a post-hoc analysis of the Systolic BP (SBP) Intervention Trial (SPRINT), comparing intensive (unattended office SBP <120 mmHg) versus standard (unattended office SBP <140 mmHg) BP targets in patients with hypertension and increased CV risk, TTR calculated from 3 office BP recordings taken over the initial 3 months was associated with major adverse CV events, even after adjusting for mean SBP or BP variability.(6) The target SBP ranges were 110-130 mmHg and 120-140 mmHg in the intensive and standard treatment arms, respectively.(6)

When calculating TTR from home or office BP measurements using linear interpolation, this approach may inadequately capture rapid or non-linear fluctuations and is more susceptible to the influence of outliers due to the varying intervals between

measurements. Only three studies have used ABPM to estimate TTR. One study calculated 24-hour TTR in 228 patients with acute stroke,(11) another used ABPM to estimate between-visit TTR,(7) and a third large individual-participant meta-analysis of 14 population-based cohorts used 24-hour ABPM with linear interpolation to quantify the time spent within systolic and diastolic BP (DBP) targets. This latter analysis demonstrated a strong inverse association between TTR and long-term mortality and adverse CV outcomes.(12)

The present study assessed the association between TTR for SBP during 24-hour ABPM and both all-cause and cardiovascular mortality in patients with sustained and masked hypertension (treated or untreated), controlled hypertension, white-coat uncontrolled hypertension (both treated), based on office (≥140 and/or ≥90 mmHg) and 24-hour BP measurements (≥130 and/or ≥80 mmHg).

Methods

Study design

This study utilized data from the Spanish ABPM Registry, a nationwide observational cohort study conducted at 223 primary care centers within the Spanish National Health System. The baseline data, protocols, and inclusion-exclusion criteria have been previously reported.(9) A comprehensive database was created by requesting mortality information from the Spanish National Institute of Statistics and linking that data with the ABPM data. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study population

Between March 2004 and December 2014, the Spanish ABPM Registry included 51,942 adults aged 18 years or older with guideline-recommended indications for ABPM, including suspected white-coat hypertension, masked hypertension, high-risk hypertension, borderline hypertension, labile hypertension, and assessment of antihypertensive treatment efficacy. The study was sponsored by the Spanish Society of Hypertension, Lacer Laboratories, and European government agencies, which did not influence the study design, data analysis, or interpretation of results. Institutional review boards at each participating center approved the study protocols, and all patients provided written informed consent.

Because BP target ranges apply only to patients with an indication for antihypertensive therapy, the present analysis was restricted to patients fulfilling at least one of the following criteria:

i) sustained hypertension, defined as office BP ≥140 and/or ≥90 mmHg and 24-hour BP ≥130 and/or ≥80 mmHg, with or without antihypertensive medication.
ii) masked hypertension defined as office BP <140/90 mmHg but 24-hour BP ≥130 and/or ≥80 mmHg, with or without antihypertensive medication.
iii) white-coat hypertension in the presence of antihypertensive medication defined as elevated office BP (≥140 and/or ≥90 mmHg) and controlled 24-hour BP (<130/80 mmHg).
iv) controlled hypertension in the presence of antihypertensive medication, defined as office BP of <140/90 mmHg and 24-hour BP of <130/80 mmHg.

Procedures and blood pressure indices

Patient data were collected through standardized interviews and physical examinations during clinical visits. Office blood pressure (BP) and heart rate were measured following established protocols. In 85% of patients, validated oscillometric devices were used, while 15% were measured using calibrated mercury sphygmomanometers. BP readings were taken while the patients were seated and at rest. The mean of two BP readings was recorded.

ABPM was conducted using validated, automated devices (Spacelabs model 90207, Spacelabs Healthcare, Snoqualmie, WA, USA) with appropriate cuff sizes, recording BP every 20 minutes during the day and every 30 minutes at night. The same criteria as in previous analyses of the Spanish ABPM registry were applied: at least 70% of SBP and DBP successful readings during the daytime and nighttime periods, 24-h duration, and at least one BP measurement per hour.(9,13) Mean 24-hour, daytime, and nighttime SBP and DBP were examined. Day and night periods were based on the patients' self-reported sleeping and waking times. TTR was calculated using linear interpolation, which was performed on a per-minute basis between two consecutive SBP readings obtained from ABPM and determined the proportion of time spent in the target range defined as an SBP of 120-134 mmHg during daytime and an SBP of 110-119 mmHg during nighttime (**Figure S1**). TTR was calculated as the number of SBP values (observed and interpolated) within the target range divided by the total number of SBP values (observed and interpolated), multiplied by 100. Interpolation was performed only when the interval between two consecutive readings was <60 minutes. In the absence of universally accepted ambulatory and office treatment targets, the SBP target range used for this analysis was defined as 120-134 mmHg during daytime and 110-119 mmHg during nighttime. This ambulatory BP range approximates an

office SBP of 120-139 mmHg and aligns with the recommended office BP targets, which the 2024 European Society of Hypertension (ESH) Hypertension Guidelines recommend as a primary target for most patients.(14) The threshold of 120 mmHg was chosen because the ESH Guidelines advise against reducing office systolic BP <120 mmHg, and the 2024 European Society of Cardiology (ESC) Guidelines define 120 mmHg as the lower bound of the recommended office BP range for most treated patients.(14,15) For BP variability assessment, we chose 24-hour SBP coefficient of variation, calculated as the ratio between the standard deviation (SD) and the mean of the SBP (x 100).(16)

Mortality data

The primary outcomes were all-cause and CV mortality. Causes of death were determined from certificates coded according to the International Statistical Classification of Diseases. Follow-up began at the first recruitment visit and continued until the date of death or the end of the recruitment period on December 31, 2019. The Spanish National Institute of Statistics recorded the death data and verified its accuracy, completeness, and reliability.

Statistical methods

Metric data were presented as means (standard deviations, SD) and categorical data as frequencies (percentages). Differences between groups were tested using ANOVA for metric data and the Chi-square test for categorical data. Cox regression analyses were adjusted for age, sex, body mass index, number of antihypertensive medications (zero or untreated vs. one vs. two or more), previous cardiovascular disease (previous

record of ischemic heart disease, stroke, or heart failure vs. no record), diabetes (previous record of diabetes vs. no record), dyslipidemia (previous record of dyslipidemia vs. no record), and tobacco smoking status (current vs. not) as recently reported.(9) Subgroup analyses were run for groups of mean 24-hour SBP, the same period as TTR, BP phenotype and treatment (no antihypertensive medications vs. one or more antihypertensive medications). There was no adjustment for the number of antihypertensive medications in subgroup analyses with BP phenotype and treatment because this variable would have limited the variance within the subgroups as the number of antihypertensive medications was zero for all patients in the no treatment group whereas, due to the exclusion criteria, included patients with normotension and white-coat hypertension were always on antihypertensive medications. The interaction between TTR and subgroup was tested with the likelihood-ratio test by adding the interaction to a model containing the adjustment variables, TTR and the subgroup. If a significant interaction was found, the data was further divided by subgroups and p-values for TTR were determined using the likelihood-ratio test by adding TTR to a model containing the adjustment variables. This procedure applies for the results shown in Figures 2 and 3. In Table 2 hazard ratios and confidence intervals for TTR are obtained from Cox regression when analyses were additionally adjusted for mean 24-hour SBP and SBP variability. All cox regression analyses were done for all-cause death and cardiovascular death. The trend of TTR over the lifespan was modeled with natural cubic splines using age terciles as knots and, in case of trend by sex, including an interaction. P-values are two-sided with a significance level of 0.05 and remain unadjusted, i.e., no correction for multiple testing was applied due to the exploratory nature of the analysis. All analyses were done with R version 4.4.1.

Results

Patient characteristics

A total of 59,124 patients (47.0% female) were recruited.(9) After excluding 10,437 (17.7%) patients with a 24-hour SBP <130 mmHg who were not receiving antihypertensive medication, 48,687 (82.3%) patients remained for the analyses. Among these, 45.6% were women. The mean age at baseline was 59.7 years (SD 13.6). The mean 24-hour SBP and DBP were 131.0 mmHg (SD 13.7) and 77.3 mmHg (SD 10.5) mmHg, respectively. During a median follow-up of 9.7 years, 6,502 deaths occurred, including 2,185 from CV causes. **Table 1** shows the baseline characteristics of the population used for this analysis. **Table S1-S3** summarize the baseline characteristics stratified by quartiles of 24-hour TTR, TTR <50% versus ≥50%, and hypertension phenotypes.

Time in target range

The mean 24-hour TTR was 29.3% (SD 16.6), ranging from 0% to 83.8%. During daytime (target range defined as SBP 120-134 mmHg), mean TTR was 32.7% (SD 19.7), while nighttime TTR (target range defined as SBP 110-119 mmHg) was 22.8% (SD 19.4). The 24-hour TTR decreased with age in both men and women (**Figure 1 and Figure S2**).

Association of time in target range with all-cause death

Higher 24-hour TTR was associated with a lower risk of all-cause death (HR 0.83 per 1-SD increment; 95% CI 0.80-0.85) in models adjusted for clinical confounders. This

association remained significant after additional adjustment for mean 24-hour SBP (HR 0.90 per 1-SD increment; 95% CI 0.87-0.93) and SBP variability (HR 0.91 per 1-SD increment; 95% CI 0.88-0.94) (**Table 2**). Significant interactions were observed between mean 24-hour SBP groups (≥130, 115-129, and <115 mmHg) and 24-hour TTR (p for interaction = 0.0067) (**Figure 2**) and nighttime TTR (p for interaction <0.0001) in relation to all-cause mortality, whereas the interaction with daytime TTR was not significant (p for interaction = 0.3357) (**Figure S3**). Specifically, higher TTR was associated with lower all-cause death among patients with elevated (≥130 mmHg) and controlled (115-129 mmHg) mean 24-hour SBP, but not in those with low mean 24-hour SBP (<115 mmHg) (**Figure 2**). Similar interactions were observed for daytime and nighttime TTR with corresponding SBP levels (**Figure S3**). Higher TTR was associated with lower all-cause mortality in patients with elevated daytime and nighttime SBP, and in those with controlled daytime SBP, but not in those with low SBP levels (**Figure 2**). Moreover, higher TTR was associated with higher all-cause mortality when stratifying for mean 24-hour DBP (≥80 mmHg, 65-84 mmHg, and <65 mmHg), with the strongest association in the higher DBP groups (**Figure S4**). Across BP phenotypes, higher 24-hour TTR was associated with lower all-cause mortality in patients with masked hypertension, sustained hypertension (uncontrolled office and 24-hour BP, with or without antihypertensive medication), and controlled hypertension (controlled office and 24-hour BP while receiving antihypertensive medication), but not in those with white-coat uncontrolled hypertension receiving antihypertensive medication (p for interaction <0.0001) (**Figure 2**). There was no significant interaction between treatment status (with versus without antihypertensive medication) and 24-hour, daytime, or nighttime TTR (**Figure 2, Figure S3**).

Association of time in target range with CV death

Higher 24-hour TTR was also associated with a reduced risk of CV death (HR 0.80 per 1-SD increment; 95% CI 0.76-0.84). This association persisted after adjustment for mean 24-hour SBP (HR 0.91 per 1-SD increment; 95% CI 0.86-0.97) and SBP variability (HR 0.93 per 1-SD increment; 95% CI 0.88-0.99) (**Table 2**). A significant interaction was found between mean 24-hour SBP groups and nighttime TTR (but not 24-hour TTR or daytime TTR) for its association with CV death (**Figure 3, Figure S5**). As with all-cause mortality, high TTR was associated with reduced CV death in patients with elevated (≥130 mmHg) and controlled (115-129 mmHg) mean 24-hour SBP, but not in those with low mean 24-hour SBP (<115 mmHg) (**Figure 3**). Additionally, significant interactions were observed for daytime and nighttime TTR with corresponding SBP levels (**Figure S5**). Higher TTR during daytime and nighttime was associated with reduced risk of CV mortality only in patients with elevated SBP during the corresponding periods (**Figure S5**). There was no significant interaction between mean 24-hour DBP groups (≥80 mmHg, 65-84 mmHg, and <65 mmHg) and 24-hour, daytime, or nighttime SBP TTR in relation to CV mortality (**Figure S6**). Across BP phenotypes, higher 24-hour TTR was associated with lower CV mortality in patients with masked hypertension, sustained hypertension (uncontrolled office and 24-hour BP, with or without antihypertensive medication), but not in those with white-coat uncontrolled hypertension receiving antihypertensive medication (p for interaction 0.0002) or those with controlled hypertension receiving antihypertensive medication (**Figure 3**). There was no significant interaction between treatment status (with versus without antihypertensive medication) and 24-hour, daytime, or nighttime TTR (**Figure 3, Figure S5**).

Discussion

This analysis of 48,687 patients with hypertension from the Spanish ABPM Registry assessed the association between 24-hour TTR for SBP during ABPM and mortality outcomes. A higher 24-hour TTR was significantly associated with lower risks of both all-cause and CV mortality, independent of mean 24-hour SBP and SBP variability. This association was observed in patients with and without antihypertensive medication. Stratified analyses revealed that the benefit of higher TTR was evident in patients with elevated SBP (≥130 mmHg) and controlled SBP (115-129 mmHg), but not in those with low SBP (<115 mmHg). In addition, higher TTR was associated with lower mortality risk in patients with masked hypertension, sustained hypertension, and controlled hypertension in the presence of antihypertensive medication, whereas no such association was observed in patients with white-coat uncontrolled hypertension.

TTR reflects the proportion of time a patient remains within a predefined target range over multiple time points. Most prior studies assessing TTR have relied on infrequent office or home BP measurements, typically taken only a few times per year.(17) When TTR is calculated from sparse measurements using linear interpolation, it may fail to capture rapid or non-linear fluctuations, hence oversimplifying the data. Additionally, because the intervals vary, some interpolated segments may cover more time than others.(18) Therefore, calculating TTR based on only a few snapshot measurements can be more susceptible to outliers. These outliers may arise from intrinsic or extrinsic factors, such as stress, physical activity, dietary changes, seasonal variations, or improper blood pressure measurement techniques and can bias the estimates.(4,16) Moreover, when narrow target ranges are applied, TTR becomes inherently sensitive to both pathological and physiological BP variability.

Observational studies from large databases, including the Veterans Affairs system(19) and primary care records in England,(8) showed an inverse association between TTR (based on office SBP) and all-cause mortality at 10 years and incident CV disease through 5 years. Similarly, a post-hoc analysis of the SPRINT trial demonstrated that greater TTR, based on office SBP over 3 months, was associated with reduced risk of major CV events, even after adjustment for mean SBP and SBP variability.(6) In contrast to most previous studies that examined the relationship between TTR and CV outcomes based on a limited number of office BP measurements, the present study derived TTR from 24-hour ABPM, providing a more comprehensive and physiologically relevant assessment of BP exposure. Prior to this study, only three studies have used ABPM to estimate TTR. One study calculated 24-hour TTR in 228 patients with acute stroke,(11) another used ABPM to estimate between-visit TTR,(7) and a third individual-participant meta-analysis of 14 population-based cohorts used 24-hour ABPM with linear interpolation to quantify the time spent within SBP and DBP targets. This latter meta-analysis demonstrated a strong inverse association between TTR and long-term mortality and adverse CV outcomes.(12)

The present study extends these findings in several important ways. It included nearly three times as many participants as the meta-analysis (48,687 vs. 14,230) and was based on a contemporary cohort recruited from 223 primary care centers. Moreover, higher TTR was associated with a lower risk of all-cause and CV mortality even after adjusting for mean 24-hour SBP and SBP variability. Notably, when stratifying by SBP categories, the association between TTR and mortality was not only significant in patients with elevated SBP but also in those with controlled SBP. This highlights the immediate and clinically relevant added value of 24-hour TTR compared to mean 24-hour SBP, suggesting its potential clinical relevance in guiding hypertension

management. Importantly, the association between TTR and mortality remained significant across all DBP subgroups.

Although this analysis demonstrated a linear inverse association between 24-hour TTR and mortality, whether this relationship extends to adverse events remains uncertain. Notably, the SPRINT post-hoc analysis found no association between TTR (based on office SBP) and serious adverse events, including syncope and injurious falls.(6) Additionally, pooled data from the Action to Control CV Risk in Diabetes-BP (ACCORD-BP) trial and SPRINT showed that higher office-based TTR was linked to lower risks of major CV and adverse kidney events.(20) In contrast to the association between TTR and CV events, the relationship with renal events was non-linear, suggesting that modest increases in TTR may be sufficient to reduce risk, while further risk reduction only occurred at high TTR levels.(20) This has been attributed to renal autoregulation.(20) However, the potential influence of age, sex, comorbidities, and BP phenotypes (e.g., orthostatic hypotension or autonomic dysfunction) on the relationship between TTR and clinical outcomes remains to be fully elucidated. In such populations, mean 24-hour SBP may appear adequate, but significant BP variability, which is partly captured by 24-hour TTR, could be associated with symptoms and adverse clinical events.(21)

Limitations

Some limitations of this study warrant discussion. First, this analysis focused on SBP, given its superior prognostic value and current guideline emphasis on SBP as the primary treatment target.(14) Diastolic BP often declines with advancing age due to arterial stiffening. Second, although ABPM provides more frequent measurements

than office BP, the number of readings over 24 hours may still be insufficient to characterize TTR and BP variability in some patients fully.(22) Third, ABPM was performed only once at baseline, and acute or transient influences during monitoring could affect the results. Fourth, information on antihypertensive treatment was not captured during follow-up, limiting the ability to adjust for treatment changes over time. Fifth, data on symptomatic hypotension at baseline and on potential complications related to excessive BP lowering, such as symptomatic hypotension, syncope, falls, or acute kidney injury, were not capture in the Spanish ABPM Registry and therefore could not be assessed during follow-up. Sixth, the cause of death classification relied on death certificates, which may underestimate CV mortality due to misclassification. Seventh, the study cohort consisted exclusively of White individuals from Spain, and thus, it may not apply to other ethnicities or regions.

Perspectives

In patients with treated or untreated sustained or masked hypertension, white-coat uncontrolled hypertension, and controlled hypertension, a higher TTR for SBP, as measured by ABPM, was independently associated with lower risks of both all-cause and CV mortality. These associations remained significant even after adjustment for mean 24-hour SBP and SBP variability. These findings underscore the potential value of 24-hour TTR as a complementary metric of BP level and variability for risk stratification in hypertension. Future studies are warranted to determine whether interventions specifically aimed at increasing 24-hour TTR translate into improved clinical outcomes and to explore the role of TTR in guiding treatment strategies.

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Supplemental material

- Supplemental Table S1-S3
- Supplemental Figures S1-S6

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Novelty and Relevance

What Is New?

- Spending more time within the target range during ambulatory blood pressure monitoring was associated with lower risks of all-cause and cardiovascular death, independent of mean blood pressure and its variability.
- This benefit was observed in patients with elevated or well-controlled blood pressure, but not in those with low levels.
- The association was seen across most hypertension phenotypes, except white-coat uncontrolled hypertension.

What Is Relevant?

- Time in target range provides additional prognostic information beyond mean blood pressure and variability for mortality risk assessment.

Clinical/Pathophysiological Implications?

- Future studies should evaluate whether interventions that increase time in the target range lead to improved patient outcomes.

Figure legends

Figure 1. TTR for SBP during 24-hour ABPM according to age and sex

Associations between age and systolic blood pressure (SBP) time in target range (TTR) measured by 24-hour ambulatory blood pressure monitoring for the overall cohort (panel A) and stratified by sex (panel B). Both men (blue) and women (red) exhibit age-related declines in TTR. Shaded areas represent 95% confidence intervals.

Figure 2. Association of TTR for SBP during ABPM and relative risk for all-cause death

Cox regression analyses were used to examine the association between SBP TTR and all-cause mortality, adjusted for age, sex, body mass index, number of antihypertensive medications, history of cardiovascular disease, diabetes, dyslipidemia, and smoking status (panel A). Solid lines represent adjusted Cox model-estimated hazard ratios across increasing SBP TTR, and shaded areas indicate 95% confidence intervals. Hazard ratios are expressed relative to the predicted hazard at a 50% TTR within each subgroup. Analyses were stratified by mean 24-hour SBP levels (panel B), hypertension phenotype (panel C), and treatment status (panel D). Interaction between TTR and subgroup was assessed using likelihood-ratio tests by adding an interaction term to a model containing the adjustment variables, TTR, and the subgroup. When a significant interaction was identified, subgroup-specific associations were evaluated, and p-values for TTR were derived by adding TTR to a model containing the adjustment variables. Asterisks denote statistically significant

associations (p <0.05) between TTR and all-cause mortality in subgroups with a significant interaction.

Abbreviations: CH, controlled hypertension; MH, masked hypertension; SH, sustained hypertension; WCH, white-coat hypertension.

Figure 3. Association of TTR for SBP during ABPM and relative risk for CV death

Cox regression analyses were used to examine the association between SBP TTR and CV mortality, adjusted for age, sex, body mass index, number of antihypertensive medications, history of cardiovascular disease, diabetes, dyslipidemia, and smoking status (panel A). Solid lines represent adjusted Cox model-estimated hazard ratios across increasing SBP TTR, and shaded areas indicate 95% confidence intervals. Hazard ratios are expressed relative to the predicted hazard at a 50% TTR within each subgroup. Analyses were stratified by mean 24-hour SBP levels (panel B), hypertension phenotype (panel C), and treatment status (panel D). Interaction between TTR and subgroup was assessed using likelihood-ratio tests by adding an interaction term to a model containing the adjustment variables, TTR, and the subgroup. When a significant interaction was identified, subgroup-specific associations were evaluated, and p-values for TTR were derived by adding TTR to a model containing the adjustment variables. Asterisks denote statistically significant associations (p <0.05) between TTR and CV mortality in subgroups with a significant interaction.

Abbreviations: CH, controlled hypertension; MH, masked hypertension; SH, sustained hypertension; WCH, white-coat hypertension.

565 **Table 1. Baseline characteristics**

Variable	**Statistic**
Number of patients	48687
Female, n (%)	22215 (45.6)
Age, years	59.7 (13.6)
Body mass index, kg/m^2	29.1 (4.8)
Tobacco smoker, n (%)	7591 (15.6)
Diabetes mellitus, n (%)	10014 (20.6%)
Dyslipidemia, n (%)	21278 (43.7%)
History of disease	
CV disease, n (%)	6961 (14.3%)
Left ventricular hypertrophy, n (%)	2840 (5.8%)
Heart failure, n (%)	1029 (2.1%)
Stroke, n (%)	1972 (4.1%)
Chronic kidney disease, n (%)	984 (2.0%)
Antihypertensive treatment	
Treatment status	
None, n (%)	13559 (27.8%)
Monotherapy, n (%)	12543 (25.8%)
Combination therapy, n (%)	22585 (46.4%)
Number of antihypertensive medications prescribed†	1.5 (1.3)
Diuretic, n (%)	17282 (35.5%)
DHP calcium channel blocker, n (%)	10029 (20.6%)
Non-DHP calcium channel blocker, n (%)	1346 (2.8%)

Variable	Statistic
ACE inhibitor, n (%)	11274 (23.2%)
Angiotensin receptor blocker, n (%)	18945 (38.9%)
Beta-blocker, n (%)	8736 (17.9%)
Alpha blocker, n (%)	2656 (5.5%)
Office BP	
SBP, mmHg	149.5 (18.9)
DBP, mmHg	87.0 (11.7)
Pulse rate, bpm	74.4 (14.2)
Ambulatory BP	
24-h SBP, mmHg	5515 (11.3%)
24-h SBP <115 mmHg, n (%)	17541 (36.0%)
24-h SBP 115-129 mmHg, n (%)	25631 (52.6%)
24-h SBP ≥130 mmHg, n (%)	134.0 (14.1)
Daytime SBP, mmHg	7378 (15.2%)
Daytime SBP <120 mmHg, n (%)	18827 (38.7%)
Daytime SBP 120-134 mmHg, n (%)	22482 (46.2%)
Daytime SBP ≥135 mmHg, n (%)	122.3 (15.8)
Nighttime SBP, mmHg	10487 (21.5%)
Nighttime SBP <110 mmHg, n (%)	12777 (26.2%)
Nighttime SBP 110-119 mmHg, n (%)	25423 (52.2%)
Nighttime SBP ≥120 mmHg, n (%)	5515 (11.3%)
24-h DBP, mmHg	77.3 (10.5)
Daytime DBP, mmHg	80.1 (11.1)

Variable	Statistic
Nighttime DBP, mmHg	69.3 (10.4)
24-h pulse rate, bpm	71.9 (10.5)
Daytime pulse rate, bpm	74.6 (11.4)
Nighttime pulse rate, bpm	65.6 (9.8)

566 Data are presented as n (%) or mean (standard deviations).

567 † Number of antihypertensive medications prescribed represents the mean (standard
568 deviations) count of antihypertensive medications per patient and does not account
569 for dose.

570 Abbreviations: ACE, angiotensin-converting enzyme; BP, blood pressure; CV,
571 cardiovascular; DBP, diastolic blood pressure; DHP, dihydropyridine; SBP, systolic
572 blood pressure.

573

Table 2. Association of time in target range for 24-hour SBP and risk for all-cause and CV death

	Model 1*	**Model 2** (additionally adjusted for mean 24-hour SBP)	**Model 3** (additionally adjusted for mean 24-hour SBP and SBP variability)
	HR per 1-SD increment (95% CI)	HR per 1-SD increment (95% CI)	HR per 1-SD increment (95% CI)
All-cause death	0.83 (0.80-0.85)	0.90 (0.87-0.93)	0.91 (0.88-0.94)
CV death	0.80 (0.76-0.84)	0.91 (0.86-0.97)	0.93 (0.88-0.99)

Values are hazard ratios (HR) per 1-standard deviation (SD) increment with 95% confidence intervals.

* Model 1 was adjusted for age, sex, body mass index, number of antihypertensive medications, previous cardiovascular disease, diabetes, dyslipidemia, and tobacco smoking status.

Abbreviations: CV, cardiovascular; SBP, systolic blood pressure.