

Supplemental material

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

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Supplemental tables

Table S1. Baseline characteristics according to TTR quartiles

Variable	Total	TTR 1 st quartile (0-16.5)	TTR 2 nd quartile (16.5-29.5)	TTR 3 rd quartile (29.5-41.3)	TTR 4 th quartile (41.3-83.8)	TTR missing	p-value
Number of patients	48687	10947	12104	11977	12061	1598	
Female, No. (%)	22215 (45.6%)	4993 (45.6%)	5837 (48.2%)	5748 (48.0%)	4953 (41.1%)	684 (42.8%)	<0.0001
Age, years	59.7 (13.6)	61.3 (13.4)	61.8 (13.6)	60.4 (13.4)	55.3 (13.2)	60.5 (13.5)	<0.0001
Body mass index, kg/m ²	29.1 (4.8)	29.3 (4.9)	29.2 (4.8)	29.2 (4.9)	28.8 (4.6)	29.4 (5.2)	<0.0001
Tobacco smoker, No. (%)	7591 (15.6%)	1796 (16.4%)	1840 (15.2%)	1774 (14.8%)	1877 (15.6%)	304 (19.0%)	<0.0001
Diabetes mellitus, No. (%)	10014 (20.6%)	2695 (24.6%)	2545 (21.0%)	2441 (20.4%)	1918 (15.9%)	415 (26.0%)	<0.0001
Dyslipidemia, No. (%)	21278 (43.7%)	4878 (44.6%)	5531 (45.7%)	5408 (45.2%)	4792 (39.7%)	669 (41.9%)	<0.0001
CV disease, No. (%)	6961 (14.3%)	1862 (17.0%)	1934 (16.0%)	1696 (14.2%)	1206 (10.0%)	263 (16.5%)	<0.0001
Left ventricular hypertrophy, No. (%)	2840 (5.8%)	770 (7.0%)	746 (6.2%)	656 (5.5%)	547 (4.5%)	121 (7.6%)	<0.0001
Heart failure, No. (%)	1029 (2.1%)	286 (2.6%)	330 (2.7%)	216 (1.8%)	156 (1.3%)	41 (2.6%)	<0.0001
History of stroke, No. (%)	1972 (4.1%)	517 (4.7%)	518 (4.3%)	482 (4.0%)	381 (3.2%)	74 (4.6%)	<0.0001
Chronic kidney disease, No. (%)	984 (2.0%)	325 (3.0%)	285 (2.4%)	173 (1.4%)	139 (1.2%)	62 (3.9%)	<0.0001
Antihypertensive treatment							
Treatment status							<0.0001
None, No. (%)	13559 (27.8%)	3119 (28.5%)	3096 (25.6%)	3080 (25.7%)	3694 (30.6%)	570 (35.7%)	
Monotherapy, No. (%)	12543 (25.8%)	2433 (22.2%)	3075 (25.4%)	3180 (26.6%)	3541 (29.4%)	314 (19.6%)	
Combination therapy, No. (%)	22585 (46.4%)	5395 (49.3%)	5933 (49.0%)	5717 (47.7%)	4826 (40.0%)	714 (44.7%)	
Number of antihypertensive medications	1.5 (1.3)	1.6 (1.4)	1.6 (1.3)	1.5 (1.3)	1.3 (1.2)	1.5 (1.5)	<0.0001
Diuretic, No. (%)	17282 (35.5%)	4116 (37.6%)	4553 (37.6%)	4351 (36.3%)	3718 (30.8%)	544 (34.0%)	<0.0001

Variable	Total	TTR 1 st quartile (0-16.5)	TTR 2 nd quartile (16.5-29.5)	TTR 3 rd quartile (29.5-41.3)	TTR 4 th quartile (41.3-83.8)	TTR missing	p-value
DHP calcium channel blocker, No. (%)	10029 (20.6%)	2326 (21.2%)	2481 (20.5%)	2576 (21.5%)	2348 (19.5%)	298 (18.6%)	0.0002
Non-DHP calcium channel blocker, No. (%)	1346 (2.8%)	371 (3.4%)	377 (3.1%)	316 (2.6%)	245 (2.0%)	37 (2.3%)	<0.0001
ACE inhibitor, No. (%)	11274 (23.2%)	2571 (23.5%)	2848 (23.5%)	2839 (23.7%)	2693 (22.3%)	323 (20.2%)	0.0029
Angiotensin receptor blocker, No. (%)	18945 (38.9%)	4382 (40.0%)	5020 (41.5%)	4771 (39.8%)	4195 (34.8%)	577 (36.1%)	<0.0001
Beta-blocker, No. (%)	8736 (17.9%)	2191 (20.0%)	2345 (19.4%)	2115 (17.7%)	1781 (14.8%)	304 (19.0%)	<0.0001
Alpha blocker, No. (%)	2656 (5.5%)	796 (7.3%)	726 (6.0%)	576 (4.8%)	408 (3.4%)	150 (9.4%)	<0.0001
Office BP							
SBP, mmHg	149.5 (18.9)	154.7 (21.0)	149.7 (18.7)	147.9 (17.1)	144.2 (15.5)	162.7 (24.5)	<0.0001
DBP, mmHg	87.0 (11.7)	87.8 (12.7)	86.1 (11.8)	86.1 (11.4)	87.3 (10.3)	90.5 (13.8)	<0.0001
Pulse rate, bpm	74.4 (14.2)	74.1 (14.7)	74.3 (14.2)	74.3 (14.1)	75.0 (13.8)	73.9 (14.6)	<0.0001
Ambulatory BP							
24-h SBP, mmHg	131.0 (13.7)	139.0 (18.5)	129.9 (11.6)	127.2 (7.5)	125.6 (4.7)	152.3 (22.6)	<0.0001
Daytime SBP, mmHg	134.0 (14.1)	141.9 (18.9)	132.8 (12.4)	130.4 (8.1)	128.9 (5.1)	155.3 (22.8)	<0.0001
Nighttime SBP, mmHg	122.3 (15.8)	131.0 (20.3)	121.7 (14.4)	118.3 (10.8)	116.0 (7.1)	143.6 (24.3)	<0.0001
24-h DBP, mmHg	77.3 (10.5)	79.5 (12.7)	75.7 (10.2)	75.3 (9.0)	77.7 (8.0)	85.7 (14.2)	<0.0001
Daytime DBP, mmHg	80.1 (11.1)	82.2 (13.3)	78.5 (11.0)	78.2 (9.7)	80.7 (8.5)	88.4 (14.7)	<0.0001
Nighttime DBP, mmHg	69.3 (10.4)	72.1 (12.5)	68.2 (10.2)	67.2 (9.0)	68.9 (7.9)	78.2 (14.1)	<0.0001
24-h pulse rate, bpm	71.9 (10.5)	71.6 (10.6)	71.5 (10.6)	71.6 (10.6)	72.9 (10.1)	71.6 (10.4)	<0.0001
Daytime pulse rate, bpm	74.6 (11.4)	74.1 (11.4)	74.1 (11.4)	74.3 (11.5)	75.8 (11.0)	73.9 (11.1)	<0.0001
Nighttime pulse rate, bpm	65.6 (9.8)	65.8 (10.0)	65.4 (9.9)	65.2 (9.9)	66.0 (9.3)	66.0 (9.8)	<0.0001

Data are presented as No. (%) or mean (standard deviations).

Abbreviations: BP, blood pressure; CV, cardiovascular; DBP, diastolic blood pressure; DHP, dihydropyridine; SBP, systolic blood pressure.

Table S2. Baseline characteristics according to TTR <50% versus ≥50%

Variable	Total	TTR <50%	TTR ≥50%	TTR missing	p-value
Number of patients	48687	42619	5551	517	
Female, No. (%)	22215 (45.6%)	22215 (45.6%)	19849 (46.6%)	2131 (38.4%)	<0.0001
Age, years	59.7 (13.6)	60.6 (13.5)	52.8 (12.8)	59.5 (13.7)	<0.0001
Body mass index, kg/m ²	29.1 (4.8)	29.2 (4.8)	28.6 (4.6)	29.2 (5.3)	<0.0001
Tobacco smoker, No. (%)	7591 (15.6%)	7591 (15.6%)	6630 (15.6%)	883 (15.9%)	0.7559
Diabetes mellitus, No. (%)	10014 (20.6%)	9165 (21.5%)	749 (13.5%)	100 (19.3%)	<0.0001
Dyslipidemia, No. (%)	21278 (43.7%)	19029 (44.6%)	2035 (36.7%)	214 (41.4%)	<0.0001
CV disease, No. (%)	6961 (14.3%)	6410 (15.0%)	476 (8.6%)	75 (14.5%)	<0.0001
Left ventricular hypertrophy, No. (%)	2840 (5.8%)	2570 (6.0%)	237 (4.3%)	33 (6.4%)	<0.0001
Heart failure, No. (%)	1029 (2.1%)	962 (2.3%)	57 (1.0%)	10 (1.9%)	<0.0001
History of stroke, No. (%)	1972 (4.1%)	1802 (4.2%)	150 (2.7%)	20 (3.9%)	<0.0001
Chronic kidney disease, No. (%)	984 (2.0%)	910 (2.1%)	53 (1.0%)	21 (4.1%)	<0.0001
Antihypertensive treatment					
Treatment status					<0.0001
None, No. (%)	13559 (27.8%)	11421 (26.8%)	1904 (34.3%)	234 (45.3%)	
Monotherapy, No. (%)	12543 (25.8%)	10760 (25.2%)	1659 (29.9%)	124 (24.0%)	
Combination therapy, No. (%)	22585 (46.4%)	20438 (48.0%)	1988 (35.8%)	159 (30.8%)	
Number of antihypertensive medications	1.5 (1.3)	1.6 (1.3)	1.2 (1.2)	1.1 (1.2)	<0.0001
Diuretic, No. (%)	17282 (35.5%)	15628 (36.7%)	1534 (27.6%)	120 (23.2%)	<0.0001
DHP calcium channel blocker, No. (%)	10029 (20.6%)	8958 (21.0%)	993 (17.9%)	78 (15.1%)	<0.0001
Non-DHP calcium channel blocker, No. (%)	1346 (2.8%)	1234 (2.9%)	104 (1.9%)	8 (1.5%)	<0.0001
ACE inhibitor, No. (%)	11274 (23.2%)	10016 (23.5%)	1171 (21.1%)	87 (16.8%)	<0.0001
Angiotensin receptor blocker, No. (%)	18945 (38.9%)	17034 (40.0%)	1761 (31.7%)	150 (29.0%)	<0.0001
Beta-blocker, No. (%)	8736 (17.9%)	7945 (18.6%)	732 (13.2%)	59 (11.4%)	<0.0001
Alpha blocker, No. (%)	2656 (5.5%)	2478 (5.8%)	158 (2.8%)	20 (3.9%)	<0.0001

Variable	Total	TTR <50%	TTR ≥50%	TTR missing	p-value
Office BP					
SBP, mmHg	149.5 (18.9)	150.3 (19.2)	142.8 (14.5)	151.7 (21.0)	<0.0001
DBP, mmHg	87.0 (11.7)	86.8 (11.9)	88.0 (10.0)	87.5 (11.3)	<0.0001
Pulse rate, bpm	74.4 (14.2)	74.3 (14.3)	75.3 (13.2)	73.9 (12.8)	<0.0001
Ambulatory BP					
24-h SBP, mmHg	131.0 (13.7)	131.7 (14.3)	125.2 (3.7)	134.3 (13.7)	<0.0001
Daytime SBP, mmHg	134.0 (14.1)	134.7 (14.7)	128.5 (4.0)	137.3 (14.2)	<0.0001
Nighttime SBP, mmHg	122.3 (15.8)	123.1 (16.5)	115.4 (5.7)	124.3 (15.2)	<0.0001
24-h DBP, mmHg	77.3 (10.5)	77.1 (10.8)	78.9 (7.5)	79.6 (10.1)	<0.0001
Daytime DBP, mmHg	80.1 (11.1)	79.9 (11.4)	81.9 (7.9)	82.3 (10.5)	<0.0001
Nighttime DBP, mmHg	69.3 (10.4)	69.3 (10.7)	69.7 (7.3)	70.9 (10.3)	<0.0001
24-h pulse rate, bpm	71.9 (10.5)	71.7 (10.6)	73.4 (9.9)	71.0 (8.7)	<0.0001
Daytime pulse rate, bpm	74.6 (11.4)	74.3 (11.4)	76.4 (10.8)	73.6 (9.3)	<0.0001
Nighttime pulse rate, bpm	65.6 (9.8)	65.5 (9.9)	66.2 (9.2)	64.6 (8.2)	<0.0001

Data are presented as No. (%) or mean (standard deviations).

Abbreviations: BP, blood pressure; CV, cardiovascular; DBP, diastolic blood pressure; DHP, dihydropyridine; SBP, systolic blood pressure.

Table S3. Baseline characteristics according to hypertension phenotype

Variable	Total	Controlled hypertension	White-coat hypertension	Sustained hypertension	Masked hypertension	p-value
Number of patients	48687	6105	10645	26938	4999	
Female, No. (%)	22215 (45.6%)	3264 (53.5%)	5767 (54.2%)	11164 (41.4%)	2020 (40.4%)	<0.0001
Age, years	59.7 (13.6)	61.5 (13.2)	62.9 (12.4)	58.5 (13.8)	56.9 (14.5)	<0.0001
Body mass index, kg/m ²	29.1 (4.8)	29.1 (4.9)	29.8 (5.1)	29.0 (4.7)	28.4 (4.6)	<0.0001
Tobacco smoker, No. (%)	7591 (15.6%)	733 (12.0%)	1155 (10.9%)	4779 (17.7%)	924 (18.5%)	<0.0001
Diabetes mellitus, No. (%)	10014 (20.6%)	1128 (18.5%)	2432 (22.8%)	5551 (20.6%)	903 (18.1%)	<0.0001
Dyslipidemia, No. (%)	21278 (43.7%)	2999 (49.1%)	5171 (48.6%)	11073 (41.1%)	2035 (40.7%)	<0.0001
CV disease, No. (%)	6961 (14.3%)	1224 (20.0%)	1730 (16.3%)	3301 (12.3%)	706 (14.1%)	<0.0001
Left ventricular hypertrophy, No. (%)	2840 (5.8%)	408 (6.7%)	697 (6.5%)	1458 (5.4%)	277 (5.5%)	<0.0001
Heart failure, No. (%)	1029 (2.1%)	192 (3.1%)	216 (2.0%)	513 (1.9%)	108 (2.2%)	<0.0001
History of stroke, No. (%)	1972 (4.1%)	378 (6.2%)	468 (4.4%)	911 (3.4%)	215 (4.3%)	<0.0001
Chronic kidney disease, No. (%)	984 (2.0%)	114 (1.9%)	216 (2.0%)	558 (2.1%)	96 (1.9%)	0.7213
Antihypertensive treatment						
Treatment status						<0.0001
None, No. (%)	13559 (27.8%)	0 (0.0%)	0 (0.0%)	11432 (42.4%)	2127 (42.5%)	
Monotherapy, No. (%)	12543 (25.8%)	(2364 (38.7%)	3749 (35.2%)	5291 (19.6%)	1139 (27.8%)	
Combination therapy, No. (%)	22585 (46.4%)	3741 (61.3%)	6896 (64.8%)	10215 (37.9%)	1733 (34.7%)	
Number of antihypertensive medications	1.5 (1.3)	2.0 (1.1)	2.1 (1.1)	1.3 (1.4)	1.2 (1.3)	<0.0001
Diuretic, No. (%)	17282 (35.5%)	2848 (46.7%)	5503 (51.7%)	7665 (28.5%)	1266 (25.3%)	<0.0001
DHP calcium channel blocker, No. (%)	10029 (20.6%)	1524 (25.0%)	2894 (27.2%)	4771 (17.7%)	840 (16.8%)	<0.0001
Non-DHP calcium channel blocker, No. (%)	1346 (2.8%)	205 (3.4%)	352 (3.3%)	663 (2.5%)	126 (2.5%)	<0.0001
ACE inhibitor, No. (%)	11274 (23.2%)	1913 (31.3%)	3530 (33.2%)	4924 (18.3%)	907 (18.1%)	<0.0001
Angiotensin receptor blocker, No. (%)	18945 (38.9%)	3158 (51.7%)	5644 (53.0%)	8647 (32.1%)	1496 (29.9%)	<0.0001
Beta-blocker, No. (%)	8736 (17.9%)	1599 (26.2%)	2637 (24.8%)	3843 (14.3%)	657 (13.1%)	<0.0001
Alpha blocker, No. (%)	2656 (5.5%)	318 (5.2%)	630 (5.9%)	1482 (5.5%)	226 (4.5%)	0.0033

Variable	Total	Controlled hypertension	White-coat hypertension	Sustained hypertension	Masked hypertension	p-value
Office BP						
SBP, mmHg	149.5 (18.9)	125.9 (10.1)	153.8 (14.2)	156.8 (16.4)	129.4 (8.2)	<0.0001
DBP, mmHg	87.0 (11.7)	75.7 (8.5)	87.3 (10.2)	90.9 (11.0)	78.8 (8.1)	<0.0001
Pulse rate, bpm	74.4 (14.2)	72.2 (14.3)	74.4 (14.2)	75.1 (14.3)	73.5 (13.2)	<0.0001
Ambulatory BP						
24-h SBP, mmHg	131.0 (13.7)	116.2 (7.9)	119.1 (7.5)	138.6 (11.1)	133.3 (8.8)	<0.0001
Daytime SBP, mmHg	134.0 (14.1)	118.7 (8.5)	122.0 (8.2)	141.9 (11.3)	136.2 (8.9)	<0.0001
Nighttime SBP, mmHg	122.3 (15.8)	109.5 (10.7)	111.3 (10.5)	129.0 (14.8)	124.7 (13.4)	<0.0001
24-h DBP, mmHg	77.3 (10.5)	68.9 (6.9)	69.1 (7.1)	81.8 (9.6)	80.5 (7.9)	<0.0001
Daytime DBP, mmHg	80.1 (11.1)	71.4 (7.5)	71.9 (7.7)	84.8 (10.2)	83.3 (8.7)	<0.0001
Nighttime DBP, mmHg	69.3 (10.4)	62.1 (7.5)	61.9 (7.7)	73.3 (9.7)	72.4 (8.5)	<0.0001
24-h pulse rate, bpm	71.9 (10.5)	70.1 (10.1)	70.0 (10.3)	72.8 (10.5)	73.2 (10.3)	<0.0001
Daytime pulse rate, bpm	74.6 (11.4)	72.7 (10.9)	72.6 (11.2)	75.5 (11.4)	75.9 (11.1)	<0.0001
Nighttime pulse rate, bpm	65.6 (9.8)	64.0 (9.5)	63.9 (9.5)	66.4 (9.8)	66.6 (9.8)	<0.0001

Data are presented as No. (%) or mean (standard deviations).

Abbreviations: BP, blood pressure; CV, cardiovascular; DBP, diastolic blood pressure; DHP, dihydropyridine; SBP, systolic blood pressure.

Supplemental Figures

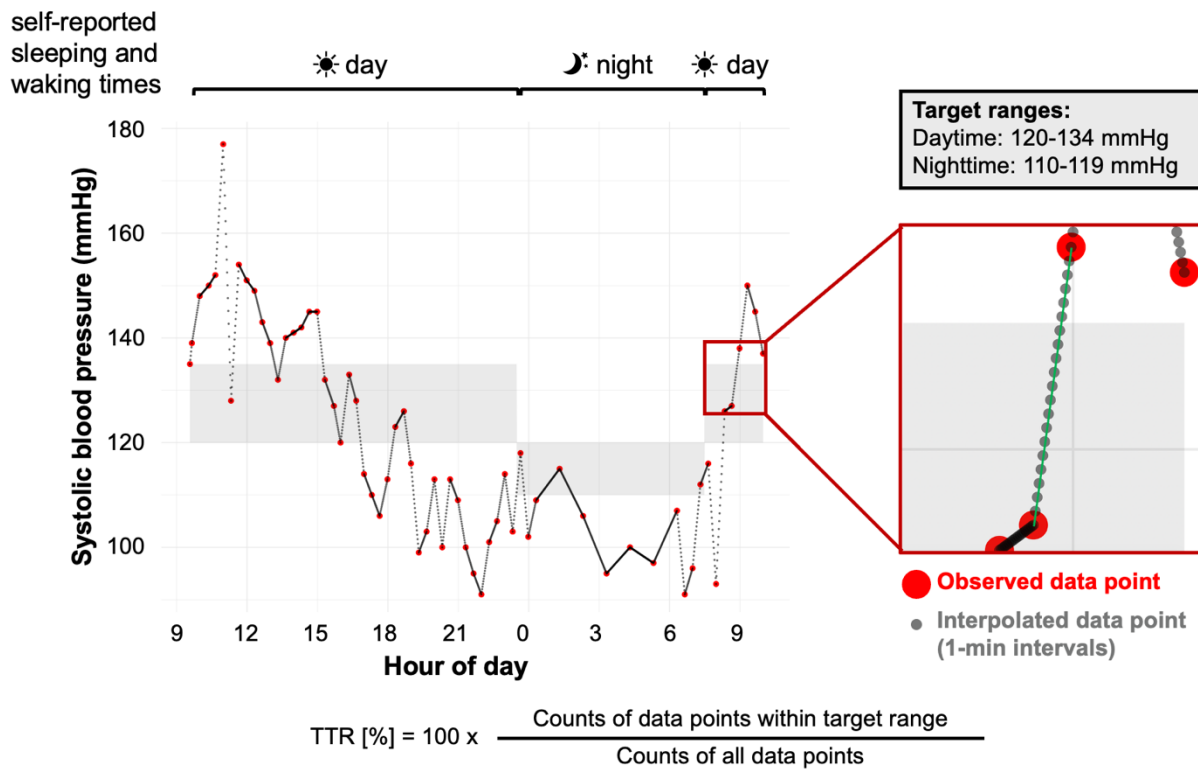


Figure S1. Example calculation of 24-hour systolic blood pressure time in target range (TTR).

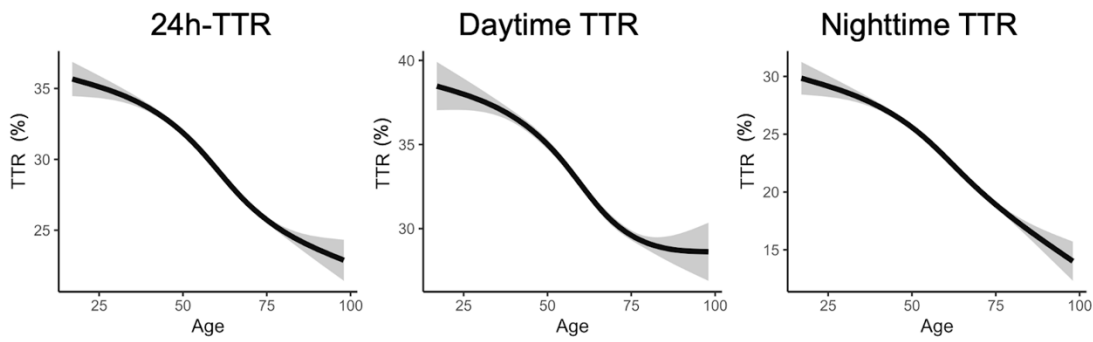
This example patient had 63 valid systolic blood pressure (SBP) measurements (red points) obtained during ambulatory blood pressure monitoring (ABPM), from 09:34 to 09:59 the following day. Linear interpolation was applied between consecutive measurements by connecting consecutive measurements with straight lines (green line in red box), generating interpolated SBP values (light grey points) at one-minute intervals along each segment. Interpolation was performed only when the interval between consecutive readings was <60 minutes.

The light grey shaded area represents the SBP target range, defined as 120-134 mmHg during daytime and 110-119 mmHg during nighttime. Daytime and nighttime

periods were determined using patient self-reported waking and sleeping times; in this example, daytime began at 07:30 and nighttime at 23:30.

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. In this example, $TTR_{\text{mean}} = 314 / 1,466 \times 100 = 21.42\%$. The same approach was used to calculate daytime and nighttime TTR.

A Overall



B Subgroups by sex

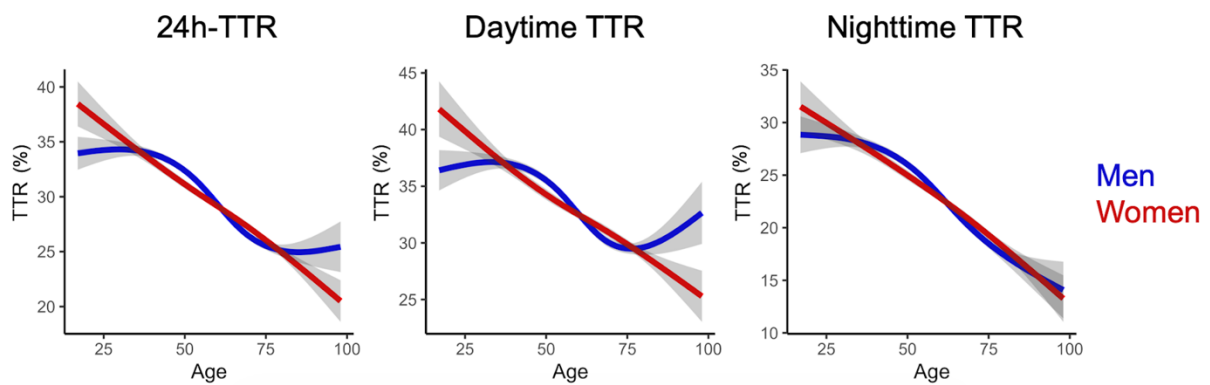


Figure S2. TTR for SBP during 24-hour ABPM according to age and sex

Panel A shows the overall association between age and TTR for SBP measured by ambulatory blood pressure monitoring over 24 hours, during daytime, and during nighttime. TTR declines with increasing age across all periods. Panel B presents age-related trends in TTR stratified by sex. While both men (blue) and women (red) exhibit age-related declines in TTR, sex-specific differences are observed, particularly during daytime hours. Shaded areas represent 95% confidence intervals.

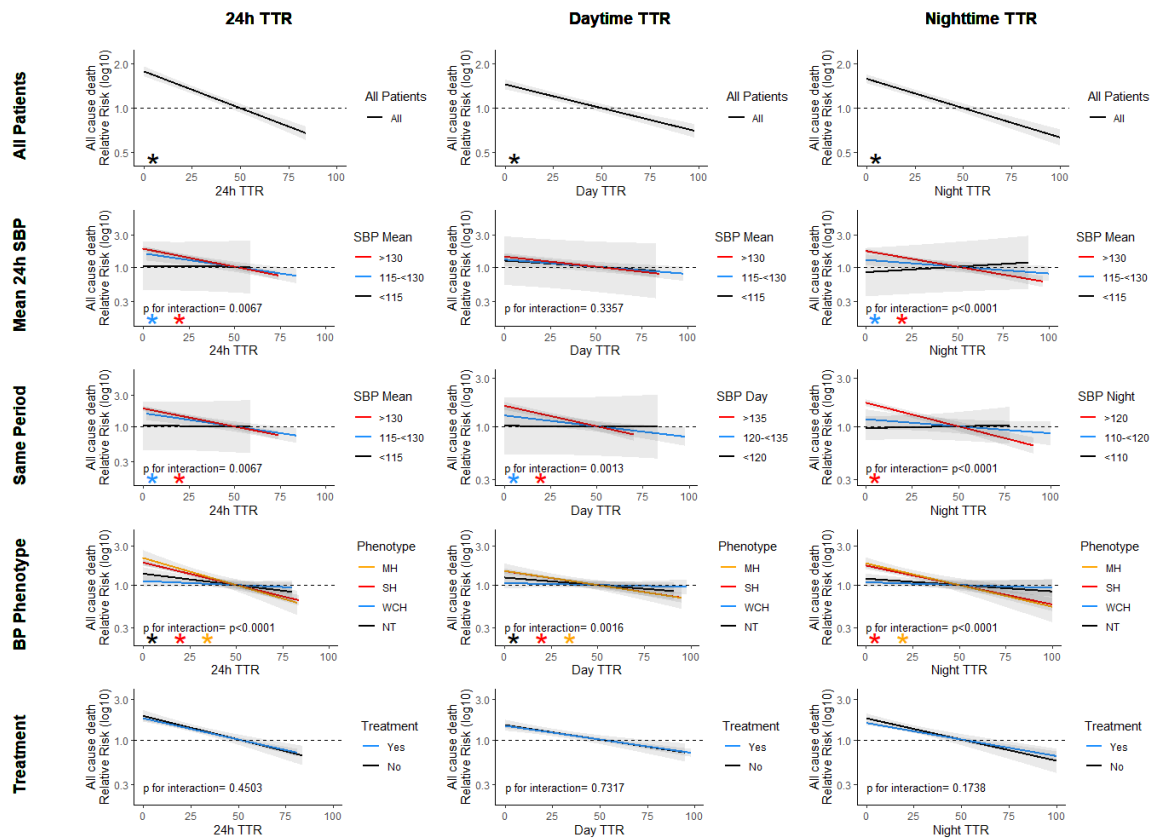


Figure S3. Association of TTR for SBP during ABPM and relative risk for all-cause death

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. 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 SBP levels, hypertension phenotype, and treatment status. 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.

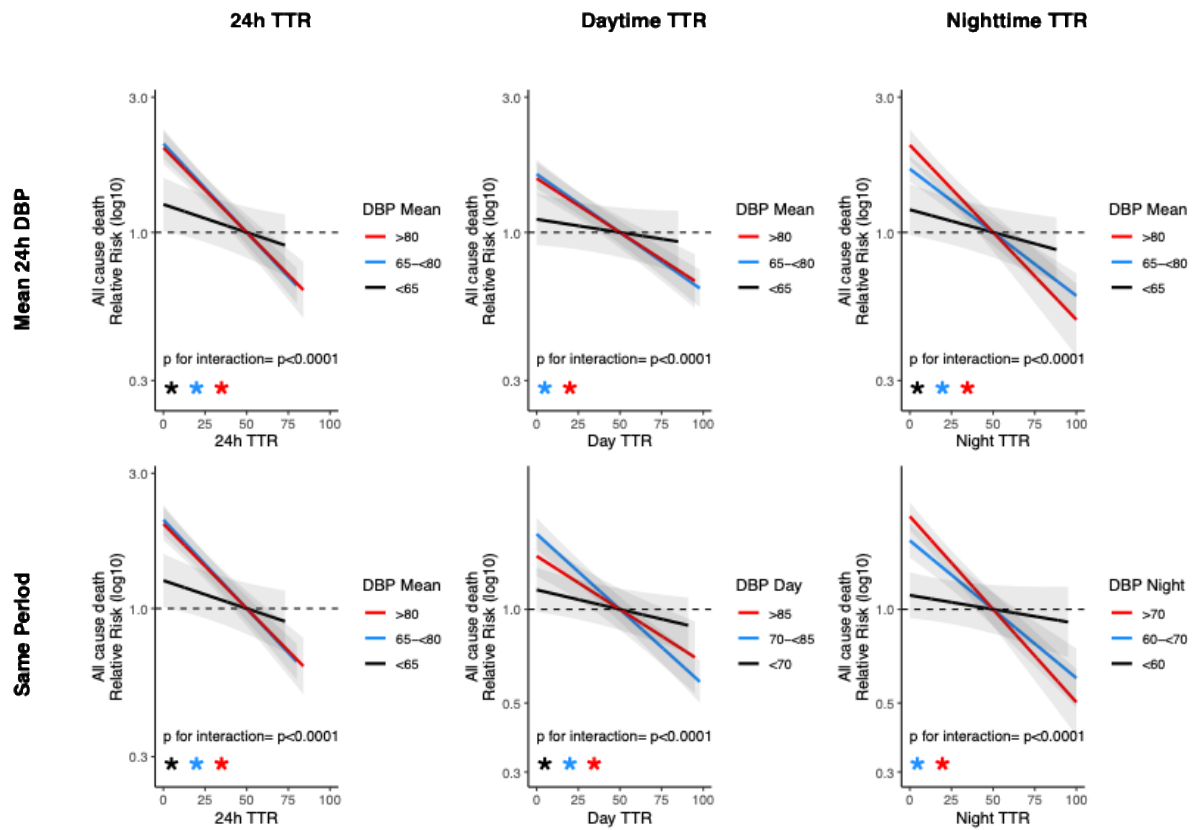


Figure S4. Association of TTR for SBP during ABPM and relative risk for all-cause death across different DBP levels

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. 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. 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.

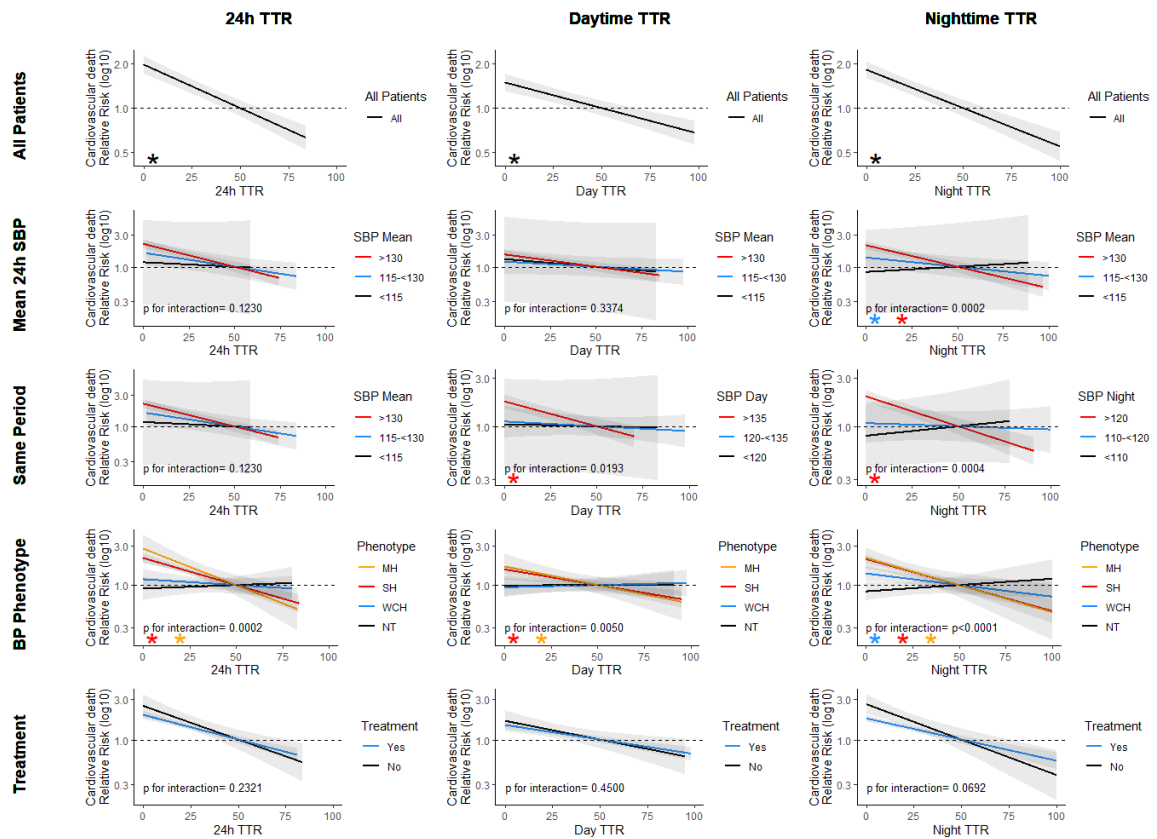


Figure S5. Association of TTR for SBP during ABPM and relative risk for CV death

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. 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 SBP levels, hypertension phenotype, and treatment status. 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.

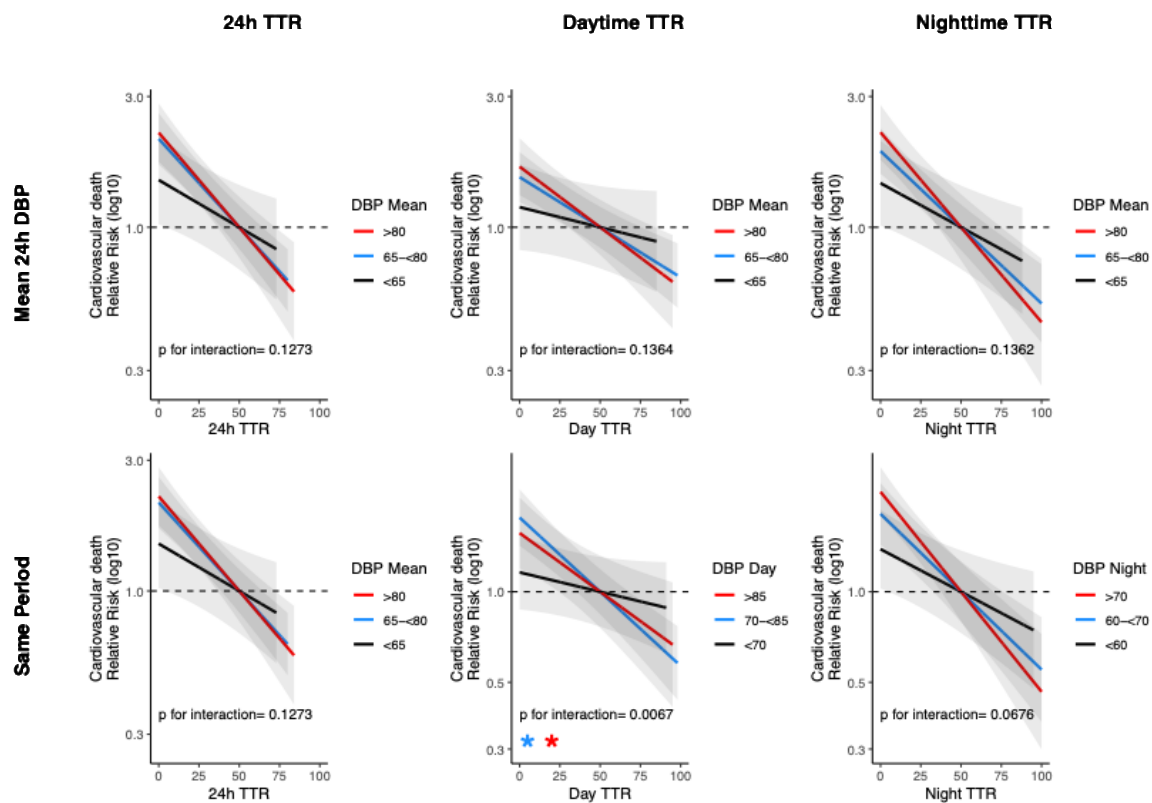


Figure S6. Association of TTR for SBP during ABPM and relative risk for CV death across different DBP levels

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. 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. 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.