Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

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Supplement 1

This Appendix formed part of the original submission and has been peer reviewed.
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Expanded Methods

Study Participants

All studies received ethical approval and adhered to the principles of the Declaration of Helsinki.[1] Participants gave written informed consent. Previous publications describe the IDACO database in detail.[2] Population studies qualified for inclusion, if information on the office and the ambulatory blood pressure and cardiovascular risk factors was available at baseline and if follow-up included both fatal and nonfatal outcomes. Of the 13,111 people included in the database, we excluded 1976 because they were teenagers without events (n = 493), or had an ambulatory blood pressure recording with fewer than six daytime and three nighttime readings (n = 1483).[3] Thus, the number of individuals statistically analyzed was 11,135. **eTable 1** provides detailed information on the population sampling methods, timelines and country of recruitment.

Blood Pressure Measurement

eTable 2 provides detailed information on blood pressure measurement. Nurses or physicians measured the conventional blood pressure with a standard mercury sphygmomanometers,[4-11] or with validated auscultatory[12] (USM-700F, UEDA Electronic Works, Tokyo, Japan) or oscillometric[13,14] devices (OMRON HEM-705CP, Omron Corporation, Kyoto, Japan; Dinamap 8100, Critikon Inc., Tampa, FL), using the appropriate cuff size, with participants in the sitting[5-9,12-14] or supine[10] position. Hypertension was a conventional blood pressure of ≥140 mm Hg systolic or ≥90 mm Hg diastolic or use of antihypertensive drugs.[15]

For ambulatory blood pressure monitoring, portable monitors were programmed to obtain ambulatory readings at 30-minute intervals throughout the whole day,[4,12] or at intervals of

15[7-9,14], 20[5,6,10,11,13] or 30[10] minutes during daytime and at intervals of 20[10], 30[7-9,14], 40[5,13], 45[6,11] or 60[10] minutes during nighttime. All devices had passed validation and only oscillometric measurements were used for analysis. The same SAS macro processed all ambulatory recordings, which remained unedited or were only sparsely edited in Ohasama participants.[12] We defined daytime as the interval from 10 AM to 8 PM in Europeans[4,5,7-11] and South Americans[13,14] and from 8 AM to 6 PM in Asians.[6,12] The corresponding nighttime intervals ranged from midnight to 6 AM[5,7-9,13] and from 10 PM to 4 AM,[6,12] respectively. These short fixed clock-time intervals eliminate the transition periods in the morning and evening when blood pressure changes rapidly, resulting in daytime and nighttime blood pressure levels that are within 1–2 mm Hg of the awake and asleep levels.[16] We weighted the within-subject means of the ambulatory blood pressure by the time interval between successive readings. Furthermore, we also defined the awake and asleep periods of the day in 7133 participants (64.1%), who had kept a diary during ambulatory blood pressure monitoring. Automated office blood pressure was the mean of the ambulatory recordings during the first recording hour, when the monitors were applied in a medical environment.

The dipping ratio was the nighttime divided by the daytime blood pressure level. We focused on systolic blood pressure, because mean age was 53.4 years and in older adults systolic blood pressure is the predominant risk factor.[17] Diastolic pressure was analyzed to replicate findings for systolic pressure. Dipping ratio was defined as nighttime divided by daytime BP. In categorical analyses, extreme dipping, normal dipping, non-dipping and reverse dipping were dipping ratios of ≤0.80, >0.80 to ≤0.90, >0.90 to ≤1.00, and >1.00, respectively.[18]

Other Measurements

We used the questionnaires originally administered in each cohort to obtain information on each participant's medical history and smoking and drinking habits.[4-14] Body mass index was body weight in kilograms divided by height in meters squared. We measured serum total cholesterol and blood glucose by automated enzymatic methods. Diabetes mellitus was the use of antidiabetic drugs, a fasting blood glucose of ≥126 mg/dL (≥7.0 mmol/L),[5-13] a random blood glucose of ≥200 mg/dL (≥11.1 mmol/L),[5,6,12] a self-reported diagnosis,[5,11-13] or diabetes documented in practice or hospital records.[13]

References

1. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA.* 2013;310(20):2191-2194.

2. Thijs L, Hansen TW, Kikuya M, et al. The International Database of Ambulatory blood pressure in relation to Cardiovascular Outcome (IDACO): protocol and research perspectives. *Blood Press Monit.* 2007;12(4):255-262.

3. Yang WY, Thijs L, Zhang ZY, et al. Evidence-based proposal for the number of ambulatory readings required for assessing blood pressure level in research settings: An analysis of the IDACO database. *Blood Press.* 2018;27(6):341-350.

4. O'Brien E, Murphy J, Tyndall A, et al. Twenty-four-hour ambulatory blood pressure in men and women aged 17 to 80 years: the Allied Irish Bank Study. *J Hypertens.* 1991;9(4):355-360.

5. Staessen JA, Bieniaszewski L, O'Brien ET, Imai Y, Fagard R. An epidemiological approach to ambulatory blood pressure monitoring: the Belgian population study. *Blood Press Monit.* 1996;1(1):13-26.

6. Li Y, Wang JG, Gao HF, et al. Are published characteristics of the ambulatory blood pressure generalizable to rural Chinese? The JingNing population study. *Blood Press Monit.* 2005;10(3):125-134.

7. Kuznetsova T, Staessen JA, Kawecka-Jaszcz K, et al. Quality control of the blood pressure phenotype in the European Project on Genes in Hypertension. *Blood Press Monit.* 2002;7(4):215-224.

8. Hansen TW, Jeppesen J, Rasmussen S, Ibsen H, Torp-Pedersen C. Ambulatory blood pressure monitoring and risk of cardiovascular disease: a population based study. *Am J Hypertens.* 2006;19(3):243-250.

9. Kuznetsova T, Malyutina S, Pello E, Thijs L, Nikitin Y, Staessen JA. Ambulatory blood pressure of adults in Novosibirsk, Russia: interim report on a population study. *Blood Press Monit.* 2000;5(5-6):291-296.

10. Ingelsson E, Björklund K, Lind L, Ärnlöv J, Sundström J. Diurnal blood pressure pattern and risk of congestive heart failure. *JAMA.* 2006;295(24):2859-2866.

11. Tikhonoff V, Kuznetsova T, Thijs L, et al. Ambulatory blood pressure and long-term risk for atrial fibrillation. *Heart.* 2018;104(15):1263-1270.

12. Ohkubo T, Hozawa A, Yamaguchi J, et al. Prognostic significance of the nocturnal decline in blood pressure in individuals with and without high 24-h blood pressure: the Ohasama study. *J Hypertens.* 2002;20(11):2183-2189.

13. Schettini C, Bianchi M, Nieto F, Sandoya E, Senra H, Hypertension Working Group. Ambulatory blood pressure. Normality and comparison with other measurements. *Hypertension.* 1999;34(4 Pt 2):818-825.

14. Maestre GE, Pino-Ramírez G, Molero AE, et al. The Maracaibo Aging Study: population and methodological issues. *Neuroepidemiology.* 2002;21(4):194-201.

15. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC) *Eur Heart J.* 2013;34(28):2159-2219.

16. Fagard R, Brguljan J, Thijs L, Staessen J. Prediction of the actual awake and asleep blood pressures by various methods of 24 h pressure analysis. *J Hypertens.* 1996;14(5):557-563.

17. Franklin SS, Larson MG, Khan SA, et al. Does the relation of blood pressure to coronary heart disease change with aging? The Framingham Heart Study. *Circulation.* 2001;103(9):1245-1249.

18. O'Brien E, Parati G, Stergiou G, et al. European Society of Hypertension position paper on ambulatory blood pressure monitoring. *J Hypertens.* 2013;31(9):1731-1767.

eTable 1. Recruitment and Follow-Up by Cohort

Catchment Area	Sampling Frame	Recruitment		PR (%)	N° of Participants		Follow-Up	
		Timeline (Years)	Invitation		In Database	Analyzed	Last (Year)	Median in Years (5–95% Interval)
Ohasama, Iwate, Japan	People aged ≥40 years	1988–1994	Address list	78	1535	1535	2015	21.8 (4.7–26.8)
JingNing, Zhejiang, China	Family-based random sample	2003–2003	All villagers invited	62	360	352	2006	2.5 (2.3–2.6)
Oktyabrsky, Novosibirsk, Russian Federation	Family-based random sample	1999–2001	Address list	68	298	283	2009	8.8 (8.0–9.5)
Niepolomice, Kraków, Poland	Family-based random sample	1999–2008	Address list	54	413	355	2014	13.5 (6.1–14.3)
Gdańsk, Poland	Family-based random sample	2008–2010	Address list	90	215	202	2014	5.6 (4.7–6.7)
Pilsen, Czech Republic	Family-based random sample	2000–2001	Address list	82	174	159	2015	14.1 (13.8–14.4)
Padova, Italy	Family-based random sample	1999–2007	Address list	73	314	305	2013	13.3 (12.5–14.5)
Noordkempen, Belgium	Family-based random sample	1985–2008	Address list	78	2904	1430	12016	22.8 (7.9–26.2)
Uppsala, Sweden	Men aged 69–74 years	1991–1995	Population census	73	1143	1114	2015	15.1 (3.5–22.2)
Copenhagen County, Denmark	Stratified random sample of women and men aged 30, 40, 50 and 60 years	1993–1997	Population registry	83	2311	2148	2010	16.3 (5.1–17.3)
Dublin, Ireland	Bank employees working at branches across Ireland	1989–1991	All invited	14	981	933	2007	17.6 (16.4–18.2)
Maracaibo, Venezuela	City residents aged ≥55 years	1998–2008	Population census	71	604	590	2012	8.2 (1.7–13.7)
Montevideo, Uruguay	Age-stratified random sample	1995–1998	Members of a health insurance organization	78	1859	1729	2007	9.0 (4.2–10.7)

Abbreviation: PR, participation rate. The European Project on Genes in Hypertension included participants recruited in Novosibirsk, Kraków, Gdańsk, Pilsen and Padova. Participants from Padova were recruited in Mirano in the province of Venice and in Torrebelvicino and Valli del Pasubio in the province of Vicenza.

eTable 2. Ambulatory Blood Pressure Monitoring by Cohort

Study Cohorts	N° of People	Monitoring Device	Programmed Reading Intervals minutes		N° of Readings					
			Day	Night	Programmed	Median	P5	P25	P75	P95
Ohasama, Iwate, Japan	1535	ABP-630, Nippon Colin	30	30	48	45	35	42	48	50
JingNing, Zhejiang, China	352	90207, SpaceLabs	20	45	65	56	52	55	56	57
Oktyabrsky, Novosibirsk, Russia	283	90202, SpaceLabs	15	30	76	71	56	65	75	78
Niepolomice, Kraków, Poland	355	90202, SpaceLabs	15	30	76	74	54	61	77	79
Gdańsk, Poland	202	TM-2430, A&D	20	45	65	62	50	59	64	64
Pilsen, Czech Republic	159	90202, SpaceLabs	20	45	65	75	54	70	80	82
Padova, Italy	305	90202, SpaceLabs	15	30	76	76	66	74	77	78
Noordkempen, Belgium	1430	90202, SpaceLabs	20	40	55	53	37	41	56	58
Uppsala, Sweden	1114	Accutracker II	20–30	20–60	41–72	65	44	52	75	84
Copenhagen County, Denmark	2148	TM-2421, A&D	15	30	80	80	67	78	81	83
Dublin, Ireland	933	90202 and 90207, Spacelabs	30	30	48	46	37	44	48	49
Maracaibo, Venezuela	590	90207, SpaceLabs	15	30	80	67	51	61	71	77
Montevideo, Uruguay	1729	90207, SpaceLabs	20	40	60	37	26	33	39	42

The TM-2421 and TM-2430 monitors implemented both an auscultatory and an oscillometric technique. However, only oscillometric readings were used for analysis. All devices passed validation.

eTable 3. Correlation Coefficients between Blood Pressure Measurements

	Conventional BP	Automated Office BP	24-Hour BP	Daytime BP	Nighttime BP
Systolic					
Conventional office BP	—				
Automated office BP	0.71	—			
24-hour BP	0.67	0.78	—		
Daytime BP	0.62	0.80	0.94	—	
Nighttime BP	0.60	0.62	0.89	0.72	—
Dipping ratio	0.09	–0.08	0.11	–0.20	0.54
Diastolic					
Conventional office BP	—				
Automated office BP	0.62	—			
24-hour BP	0.62	0.74	—		
Daytime BP	0.59	0.74	0.93	—	
Nighttime BP	0.53	0.56	0.85	0.64	—
Dipping ratio	0.06	–0.056	0.11	–0.22	0.59

Abbreviation: BP, blood pressure. Daytime and nighttime were defined using short fixed clock-time intervals (see Expanded Methods and reference 16). Dipping ratio is nighttime divided by daytime BP.
All correlation coefficients were significant ($P < .001$).

eTable 4. Incidence of End Points

End Point	Number of End Points		
	End Point	Fatal	Nonfatal
Total mortality	2836	2836	
Cardiovascular mortality	1073	1073	
Non-cardiovascular mortality		1611	
Death from renal failure		45	
Cause of death unknown		107	
All cardiovascular Outcomes	2049		
Coronary Outcomes	922		
Myocardial infarction		234	441
Coronary revascularization			180
Other ischemic heart disease		154	
Sudden death		83	
Heart failure		154	594
Stroke	822	283	684

Median follow-up of 11,135 participants was 13.8 years (5th to 95th percentile interval, 2.5–25.1 years). The nonfatal events do not add up, because within each category only the first event was analyzed.

eTable 5. Association of Outcomes With DBP Indexes Without or With Adjustment for 24-Hour or Nighttime DBP

Outcomes / DBP Indexes	Adjusted[a]		Additionally adjusted for 24-Hour DBP[b]		Additionally Adjusted for Nighttime DBP[b]	
	HR (CI)[c]	*P*	HR (CI)[c]	*P*	HR (CI)[c]	*P*
Total Mortality (n = 2836)						
Conventional DBP	1.07 (1.03 to 1.11)	<.001	1.02 (0.98 to 1.07)	.31	1.02 (0.98 to 1.06)	.40
Automated office DBP	1.04 (1.01 to 1.07)	.02	0.97 (0.93 to 1.01)	.11	0.99 (0.95 to 1.02)	.48
24-hour DBP	1.14 (1.09 to 1.19)	<.001	NA	NA	0.98 (0.90 to 1.06)	.61
Daytime DBP	1.09 (1.04 to 1.13)	<.001	0.86 (0.78 to 0.96)	.007	0.99 (0.94 to 1.05)	.77
Nighttime DBP	1.16 (1.11 to 1.21)	<.001	1.18 (1.09 to 1.27)	<.001	NA	NA
Dipping ratio[d]	1.09 (1.05 to 1.14)	<.001	1.09 (1.04 to 1.13)	<.001	1.01 (0.97 to 1.06)	.56
All CV Outcomes (n = 2049)						
Conventional DBP	1.14 (1.10 to 1.19)	<.001	1.03 (0.99 to 1.09)	.17	1.06 (1.01 to 1.11)	.02
Automated office DBP	1.10 (1.06 to 1.14)	<.001	0.96 (0.91 to 1.01)	.10	1.02 (0.98 to 1.06)	.31
24-hour DBP	1.30 (1.24 to 1.37)	<.001	NA	NA	1.16 (1.05 to 1.28)	.003
Daytime DBP	1.21 (1.15 to 1.27)	<.001	0.83 (0.73 to 0.93)	.002	1.07 (1.01 to 1.14)	.02
Nighttime BP	1.26 (1.20 to 1.32)	<.001	1.13 (1.04 to 1.23)	.005	NA	NA
Dipping ratio[d]	1.10 (1.05 to 1.15)	<.001	1.08 (1.04 to 1.13)	<.001	0.95 (0.90 to 1.01)	.07
CV Mortality (n = 1073)						
Conventional DBP	1.13 (1.07 to 1.20)	<.001	1.03 (0.96 to 1.10)	.38	1.04 (0.98 to 1.11)	.21
Automated office DBP	1.07 (1.02 to 1.13)	.007	0.92 (0.86 to 0.99)	.02	0.98 (0.93 to 1.04)	.56
24-hour DBP	1.29 (1.20 to 1.39)	<.001	NA	NA	1.09 (0.95 to 1.24)	.22
Daytime DBP	1.19 (1.12 to 1.28)	<.001	0.80 (0.67 to 0.94)	.007	1.04 (0.96 to 1.13)	.35
Nighttime DBP	1.28 (1.20 to 1.36)	<.001	1.20 (1.07 to 1.35)	.002	NA	NA
Dipping ratio[d]	1.13 (1.06 to 1.20)	<.001	1.11 (1.04 to 1.18)	<.001	0.98 (0.90 to 1.05)	.53
Coronary Outcomes (n = 922)						
Conventional DBP	1.08 (1.02 to 1.15)	.008	1.02 (0.95 to 1.09)	.66	1.02 (0.95 to 1.09)	.60
Automated office DBP	1.07 (1.01 to 1.13)	.02	0.98 (0.91 to 1.06)	.66	1.01 (0.95 to 1.07)	.79
24-hour DBP	1.18 (1.09 to 1.27)	<.001	NA	NA	1.02 (0.88 to 1.17)	.82
Daytime DBP	1.11 (1.04 to 1.20)	.003	0.84 (0.70 to 1.01)	.06	1.01 (0.92 to 1.10)	.91
Nighttime DBP	1.18 (1.10 to 1.26)	<.001	1.16 (1.03 to 1.32)	.02	NA	NA
Dipping ratio[d]	1.11 (1.03 to 1.18)	.003	1.09 (1.02 to 1.17)	.009	1.01 (0.93 to 1.10)	.81
Stroke (n = 822)						
Conventional DBP	1.19 (1.12 to 1.27)	<.001	1.06 (0.98 to 1.14)	.15	1.09 (1.01 to 1.17)	.02
Automated office DBP	1.15 (1.08 to 1.22)	<.001	0.98 (0.90 to 1.06)	.58	1.05 (0.99 to 1.13)	.11
24-hour DBP	1.41 (1.29 to 1.53)	<.001	NA	NA	1.24 (1.06 to 1.44)	.006
Daytime DBP	1.29 (1.19 to 1.39)	<.001	0.84 (0.70 to 1.02)	.08	1.12 (1.02 to 1.24)	.02
Nighttime DBP	1.34 (1.24 to 1.44)	<.001	1.15 (1.00 to 1.31)	.05	NA	NA
Dipping ratio[d]	1.10 (1.02 to 1.18)	.013	1.07 (1.00 to 1.15)	.05	0.89 (0.82 to 0.98)	.01

Abbreviations: CI, 95% confidence interval; CV, cardiovascular; DBP, diastolic blood pressure; HR, hazard ratio; NA, not applicable.

[a] All models accounted for cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus.

[b] Models including two correlated DBP indexes were constructed, using the residual method (see Statistical Analysis).

c Hazard ratios express the risk for increments of 10 mm Hg in DBP and 0.10 in the dipping ratio.

[d] The dipping ratio is calculated by dividing nighttime by daytime DBP.

eTable 6. Association of Outcomes With 24-Hour or Nighttime DBP Adjusted for Other DBP Indexes

Outcomes	24-Hour DBP[a]		Nighttime DBP[a]	
DBP Indexes Adjusted For	HR (CI)[b]	*P*	HR (CI)[b]	*P*
Total Mortality (n = 2836)				
Conventional DBP	1.12 (1.06 to 1.19)	<.001	1.15 (1.10 to 1.20)	<.001
Automated office DBP	1.18 (1.11 to 1.25)	<.001	1.17 (1.11 to 1.22)	<.001
24-hour DBP	NA	NA	1.18 (1.09 to 1.27)	<.001
Daytime DBP	1.32 (1.17 to 1.48)	<.001	1.16 (1.10 to 1.22)	<.001
Nighttime DBP	0.98 (0.90 to 1.06)	.61	NA	NA
Dipping ratio[c]	1.13 (1.08 to 1.18)	<.001	1.15 (1.09 to 1.21)	<.001
All CV Outcomes (n = 2049)				
Conventional DBP	1.27 (1.19 to 1.35)	<.001	1.22 (1.16 to 1.29)	<.001
Automated office DBP	1.36 (1.26 to 1.46)	<.001	1.24 (1.18 to 1.31)	<.001
24-hour DBP	NA	NA	1.13 (1.04 to 1.23)	.005
Daytime DBP	1.58 (1.38 to 1.81)	<.001	1.21 (1.14 to 1.28)	<.001
Nighttime BP	1.16 (1.05 to 1.28)	.003	NA	NA
Dipping ratio[c]	1.29 (1.23 to 1.36)	<.001	1.30 (1.23 to 1.38)	<.001
CV Mortality (n = 1073)				
Conventional DBP	1.27 (1.16 to 1.38)	<.001	1.25 (1.17 to 1.34)	<.001
Automated office DBP	1.40 (1.27 to 1.54)	<.001	1.29 (1.20 to 1.38)	<.001
24-hour DBP	NA	NA	1.20 (1.07 to 1.35)	.002
Daytime DBP	1.63 (1.36 to 1.96)	<.001	1.25 (1.15 to 1.35)	<.001
Nighttime DBP	1.09 (0.95 to 1.24)	.22	NA	NA
Dipping ratio[c]	1.28 (1.19 to 1.38)	<.001	1.30 (1.20 to 1.40)	<.001
Coronary Outcomes (n = 922)				
Conventional DBP	1.16 (1.06 to 1.28)	.002	1.17 (1.08 to 1.26)	<.001
Automated office DBP	1.20 (1.08 to 1.33)	<.001	1.17 (1.09 to 1.26)	<.001
24-hour DBP	NA	NA	1.16 (1.03 to 1.32)	.02
Daytime DBP	1.40 (1.15 to 1.71)	<.001	1.17 (1.08 to 1.28)	<.001
Nighttime DBP	1.02 (0.88 to 1.17)	.82	NA	NA
Dipping ratio[c]	1.16 (1.08 to 1.26)	<.001	1.17 (1.08 to 1.27)	<.001
Stroke (n = 822)				
Conventional DBP	1.35 (1.23 to 1.49)	<.001	1.28 (1.18 to 1.39)	<.001
Automated office DBP	1.44 (1.28 to 1.61)	<.001	1.30 (1.20 to 1.41)	<.001
24-hour DBP	NA	NA	1.15 (1.00 to 1.31)	.05
Daytime DBP	1.67 (1.35 to 2.06)	<.001	1.25 (1.14 to 1.37)	<.001
Nighttime DBP	1.24 (1.06 to 1.44)	.006	NA	NA
Dipping ratio[c]	1.40 (1.28 to 1.52)	<.001	1.43 (1.31 to 1.57)	<.001

Abbreviations: CI, 95% confidence interval; CV, cardiovascular; DBP, diastolic blood pressure; HR, hazard ratio; NA, not applicable.

[a] All models accounted for cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus and were constructed, using the residual method (see Statistical Analysis).

[b] Hazard ratios express the risk for increments of 10-mm Hg in DBP and 0.10 in the dipping ratio.

[c] The dipping ratio is calculated by dividing nighttime by daytime DBP.

eTable 7. Association of Outcomes With SBP Indexes Without or With Adjustment for 24-Hour or Nighttime SBP Among 8873 Untreated Participants

Outcomes / SBP Indexes	Adjusted[a]		Additionally Adjusted for 24-Hour SBP[b]		Additionally Adjusted for Nighttime SBP[c]	
	HR (CI)[c]	*P*	HR (CI)[c]	*P*	HR (CI)[c]	*P*
Total Mortality (n = 1754)						
Conventional SBP	1.16 (1.10 to 1.22)	<.001	1.06 (1.00 to 1.13)	.06	1.07 (1.01 to 1.13)	.03
Automated office SBP	1.14 (1.09 to 1.20)	<.001	1.01 (0.95 to 1.08)	.66	1.05 (0.99 to 1.11)	.11
24-hour SBP	1.29 (1.21 to 1.38)	<.001	NA	NA	1.03 (0.90 to 1.18)	.69
Daytime SBP	1.22 (1.14 to 1.30)	<.001	0.84 (0.71 to 0.98)	.03	1.03 (0.95 to 1.12)	.45
Nighttime SBP	1.28 (1.21 to 1.36)	<.001	1.26 (1.12 to 1.41)	<.001	NA	NA
Dipping ratio[d]	1.13 (1.08 to 1.20)	<.001	1.10 (1.04 to 1.16)	<.001	0.98 (0.92 to 1.05)	.55
All CV Outcomes (n = 1227)						
Conventional SBP	1.26 (1.19 to 1.34)	<.001	1.07 (1.00 to 1.15)	.06	1.12 (1.05 to 1.20)	<.001
Automated office SBP	1.27 (1.20 to 1.35)	<.001	1.05 (0.97 to 1.13)	.25	1.14 (1.06 to 1.21)	<.001
24-hour SBP	1.54 (1.42 to 1.65)	<.001	NA	NA	1.37 (1.17 to 1.61)	<.001
Daytime SBP	1.43 (1.33 to 1.54)	<.001	0.90 (0.75 to 1.08)	.26	1.20 (1.09 to 1.33)	<.001
Nighttime BP	1.41 (1.33 to 1.51)	<.001	1.11 (0.97 to 1.28)	.12	NA	NA
Dipping ratio[d]	1.11 (1.04 to 1.19)	<.001	1.05 (0.98 to 1.11)	.14	0.86 (0.80 to 0.93)	<.001
CV Mortality (n = 604)						
Conventional SBP	1.27 (1.17 to 1.37)	<.001	1.04 (0.94 to 1.14)	.47	1.09 (1.00 to 1.19)	.06
Automated office SBP	1.35 (1.24 to 1.46)	<.001	1.08 (0.97 to 1.20)	.17	1.17 (1.07 to 1.28)	.001
24-hour SBP	1.65 (1.49 to 1.82)	<.001	NA	NA	1.36 (1.09 to 1.70)	.006
Daytime SBP	1.53 (1.38 to 1.68)	<.001	0.88 (0.68 to 1.14)	.33	1.22 (1.06 to 1.39)	.004
Nighttime SBP	1.51 (1.39 to 1.65)	<.001	1.20 (0.99 to 1.45)	.06	NA	NA
Dipping ratio[d]	1.16 (1.06 to 1.27)	<.001	1.08 (0.99 to 1.18)	.09	0.86 (0.77 to 0.96)	.008
Coronary Outcomes (n = 566)						
Conventional SBP	1.20 (1.10 to 1.30)	<.001	1.03 (0.92 to 1.14)	.61	1.07 (0.98 to 1.18)	.15
Automated office SBP	1.26 (1.16 to 1.37)	<.001	1.08 (0.96 to 1.22)	.19	1.14 (1.03 to 1.26)	.008
24-hour SBP	1.44 (1.29 to 1.61)	<.001	NA	NA	1.29 (1.01 to 1.64)	.04
Daytime SBP	1.37 (1.23 to 1.52)	<.001	0.91 (0.68 to 1.21)	.53	1.17 (1.01 to 1.35)	.04
Nighttime SBP	1.35 (1.23 to 1.49)	<.001	1.11 (0.90 to 1.37)	.31	NA	NA
Dipping ratio[d]	1.11 (1.01 to 1.22)	.04	1.05 (0.95 to 1.15)	.34	0.89 (0.79 to 1.00)	.05
Stroke (n = 463)						
Conventional SBP	1.41 (1.28 to 1.55)	<.001	1.18 (1.04 to 1.32)	.007	1.23 (1.11 to 1.38)	<.001
Automated office SBP	1.38 (1.25 to 1.51)	<.001	1.11 (0.98 to 1.26)	.10	1.21 (1.09 to 1.34)	<.001
24-hour SBP	1.69 (1.50 to 1.90)	<.001	NA	NA	1.45 (1.12 to 1.87)	.004
Daytime SBP	1.59 (1.41 to 1.78)	<.001	1.03 (0.77 to 1.38)	.84	1.30 (1.12 to 1.52)	.001
Nighttime SBP	1.52 (1.38 to 1.68)	<.001	1.16 (0.93 to 1.44)	.18	NA	NA
Dipping ratio[d]	1.12 (1.02 to 1.24)	.02	1.04 (0.94 to 1.15)	.41	0.81 (0.72 to 0.92)	.001

Abbreviations: CI, 95% confidence interval; CV, cardiovascular; HR, hazard ratio; SBP, systolic blood pressure; NA, not applicable.

[a] All models accounted for cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus.

[b] Models including two correlated SBP indexes were constructed, using the residual method (see Statistical Analysis).

[c] Hazard ratios express the risk for increments of 20 mm Hg in SBP and 0.10 in the dipping ratio.

[d] The dipping ratio is calculated by dividing nighttime by daytime SBP.

eTable 8. Association of Outcomes With 24-Hour or Nighttime SBP Adjusted for Other SBP Indexes Among 8873 Untreated Participants

Outcomes	24-Hour SBP[a]		Nighttime SBP[a]	
SBP Indexes Adjusted For	HR (CI)[b]	*P*	HR (CI)[b]	*P*
Total Mortality (n = 1754)				
Conventional SBP	1.24 (1.14 to 1.34)	<.001	1.24 (1.16 to 1.32)	<.001
Automated office SBP	1.28 (1.17 to 1.40)	<.001	1.25 (1.17 to 1.33)	<.001
24-hour SBP	NA	NA	1.26 (1.12 to 1.41)	<.001
Daytime SBP	1.54 (1.30 to 1.82)	<.001	1.26 (1.17 to 1.36)	<.001
Nighttime SBP	1.03 (0.90 to 1.18)	.69	NA	NA
Dipping ratio[c]	1.27 (1.18 to 1.36)	<.001	1.30 (1.21 to 1.40)	<.001
All CV Outcomes (n = 1227)				
Conventional SBP	1.45 (1.33 to 1.60)	<.001	1.33 (1.24 to 1.43)	<.001
Automated office SBP	1.47 (1.33 to 1.63)	<.001	1.33 (1.23 to 1.43)	<.001
24-hour SBP	NA	NA	1.11 (0.97 to 1.28)	.12
Daytime SBP	1.70 (1.40 to 2.05)	<.001	1.27 (1.16 to 1.38)	<.001
Nighttime BP	1.37 (1.17 to 1.61)	<.001	NA	NA
Dipping ratio[c]	1.52 (1.41 to 1.64)	<.001	1.56 (1.44 to 1.70)	<.001
CV Mortality (n = 604)				
Conventional SBP	1.60 (1.42 to 1.81)	<.001	1.45 (1.32 to 1.60)	<.001
Automated office SBP	1.54 (1.34 to 1.77)	<.001	1.40 (1.27 to 1.54)	<.001
24-hour SBP	NA	NA	1.20 (0.99 to 1.45)	.06
Daytime SBP	1.86 (1.43 to 2.42)	<.001	1.35 (1.20 to 1.52)	<.001
Nighttime SBP	1.36 (1.09 to 1.70)	.01	NA	NA
Dipping ratio[c]	1.61 (1.46 to 1.79)	<.001	1.67 (1.50 to 1.86)	<.001
Coronary Outcomes (n = 566)				
Conventional SBP	1.41 (1.23 to 1.62)	<.001	1.30 (1.17 to 1.45)	<.001
Automated office SBP	1.34 (1.15 to 1.57)	<.001	1.26 (1.12 to 1.40)	<.001
24-hour SBP	NA	NA	1.11 (0.90 to 1.37)	.31
Daytime SBP	1.58 (1.17 to 2.11)	.002	1.23 (1.08 to 1.41)	.002
Nighttime SBP	1.29 (1.01 to 1.64)	.04	NA	NA
Dipping ratio[c]	1.43 (1.27 to 1.59)	<.001	1.46 (1.29 to 1.64)	<.001
Stroke (n = 463)				
Conventional SBP	1.51 (1.30 to 1.75)	<.001	1.38 (1.23 to 1.55)	<.001
Automated office SBP	1.54 (1.31 to 1.82)	<.001	1.39 (1.24 to 1.56)	<.001
24-hour SBP	NA	NA	1.16 (0.93 to 1.44)	.18
Daytime SBP	1.64 (1.21 to 2.22)	.001	1.31 (1.15 to 1.50)	<.001
Nighttime SBP	1.45 (1.12 to 1.87)	<.001	NA	NA
Dipping ratio[c]	1.67 (1.47 to 1.89)	<.001	1.76 (1.55 to 2.01)	<.001

Abbreviations: CI, 95% confidence interval; CV, cardiovascular; HR, hazard ratio; SBP, systolic blood pressure; NA, not applicable.

[a] All models accounted for cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus and were constructed, using the residual method (see Statistical Analysis).

[b] Hazard ratios express the risk for increments of 20 mm Hg in SBP and 0.10 in the dipping ratio.

[c] The dipping ratio is the nighttime divided by the daytime SBP.

eTable 9. Association of Outcomes With SBP Indexes During Wakefulness and Sleep in 7133 Participants Without or With Adjustment for 24-Hour or Asleep SBP

Outcomes / SBP Indexes	Adjusted[a,b]		Additionally Adjusted for 24-Hour SBP[a,c]		Additionally Adjusted for Asleep SBP[a,c]	
	HR (CI)[d]	*P*	HR (CI)[d]	*P*	HR (CI)[d]	*P*
Total Mortality (n = 1566)						
Conventional SBP	1.14 (1.08 to 1.21)	<.001	1.07 (1.00 to 1.14)	.05	1.07 (1.01 to 1.14)	.02
Automated office SBP	1.11 (1.05 to 1.17)	<.001	0.96 (0.89 to 1.04)	.35	1.00 (0.94 to 1.07)	.95
24-hour SBP	1.28 (1.19 to 1.39)	<.001	NA	NA	1.02 (0.87 to 1.19)	.82
Awake SBP	1.22 (1.13 to 1.32)	<.001	0.71 (0.55 to 0.93)	.01	1.02 (0.91 to 1.13)	.75
Asleep SBP	1.29 (1.20 to 1.38)	<.001	1.27 (1.10 to 1.47)	<.001	NA	NA
Dipping ratio[e]	1.14 (1.07 to 1.22)	<.001	1.12 (1.05 to 1.20)	<.001	1.00 (0.92 to 1.08)	.98
All CV Outcomes (n = 1048)						
Conventional SBP	1.25 (1.17 to 1.33)	<.001	1.06 (0.98 to 1.14)	.15	1.10 (1.02 to 1.18)	.009
Automated office SBP	1.25 (1.17 to 1.33)	<.001	0.94 (0.86 to 1.04)	.24	1.05 (0.97 to 1.14)	.21
24-hour SBP	1.65 (1.50 to 1.80)	<.001	NA	NA	1.29 (1.07 to 1.57)	.008
Awake SBP	1.54 (1.41 to 1.68)	<.001	0.69 (0.50 to 0.96)	.03	1.19 (1.04 to 1.35)	.009
Asleep BP	1.57 (1.45 to 1.70)	<.001	1.28 (1.08 to 1.52)	.005	NA	NA
Dipping ratio[e]	1.17 (1.08 to 1.27)	<.001	1.13 (1.04 to 1.23)	.004	0.89 (0.80 to 0.98)	.02
CV Mortality (n = 521)						
Conventional SBP	1.32 (1.20 to 1.44)	<.001	1.14 (1.02 to 1.27)	.02	1.17 (1.06 to 1.29)	.002
Automated office SBP	1.23 (1.12 to 1.35)	<.001	0.92 (0.81 to 1.05)	.22	1.02 (0.92 to 1.14)	.67
24-hour SBP	1.68 (1.48 to 1.91)	<.001	NA	NA	1.21 (0.93 to 1.58)	.16
Awake SBP	1.55 (1.37 to 1.76)	<.001	0.65 (0.42 to 1.01)	.06	1.15 (0.96 to 1.38)	.12
Asleep SBP	1.63 (1.45 to 1.83)	<.001	1.40 (1.10 to 1.78)	.006	NA	NA
Dipping ratio[e]	1.21 (1.08 to 1.35)	.001	1.17 (1.04 to 1.31)	.007	0.91 (0.79 to 1.04)	.18
Coronary Outcomes (n = 409)						
Conventional SBP	1.18 (1.06 to 1.31)	.002	0.98 (0.86 to 1.11)	.77	1.02 (0.91 to 1.15)	.71
Automated office SBP	1.22 (1.09 to 1.35)	<.001	0.93 (0.79 to 1.08)	.34	1.01 (0.89 to 1.15)	.83
24-hour SBP	1.55 (1.35 to 1.79)	<.001	NA	NA	1.15 (0.84 to 1.57)	.39
Awake SBP	1.46 (1.27 to 1.68)	<.001	0.59 (0.34 to 1.04)	.07	1.09 (0.88 to 1.36)	.42
Asleep SBP	1.52 (1.34 to 1.73)	<.001	1.36 (1.03 to 1.81)	.03	NA	NA
Dipping ratio[e]	1.21 (1.06 to 1.39)	.005	1.17 (1.02 to 1.34)	.03	0.94 (0.80 to 1.11)	.47
Stroke (n = 479)						
Conventional SBP	1.30 (1.18 to 1.43)	<.001	1.08 (0.97 to 1.21)	.17	1.13 (1.02 to 1.26)	.02
Automated office SBP	1.34 (1.22 to 1.48)	<.001	1.00 (0.87 to 1.15)	.97	1.12 (1.00 to 1.26)	.04
24-hour SBP	1.84 (1.61 to 2.10)	<.001	NA	NA	1.43 (1.09 to 1.88)	.01
Awake SBP	1.67 (1.47 to 1.90)	<.001	0.62 (0.39 to 0.98)	.04	1.25 (1.04 to 1.50)	.02
Asleep SBP	1.72 (1.52 to 1.94)	<.001	1.29 (1.01 to 1.66)	.04	NA	NA
Dipping ratio[e]	1.18 (1.05 to 1.33)	.005	1.14 (1.02 to 1.29)	.03	0.85 (0.74 to 0.98)	.03

Abbreviations: CI, 95% confidence interval; CV, cardiovascular; HR, hazard ratio; SBP, systolic blood pressure; NA, not applicable.

[a] In this analysis, we defined the awake and asleep periods of the day in 7133 participants (64.1%), who had kept a diary during ambulatory blood pressure monitoring.

[b] All models accounted for cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus.

[c] Models including two correlated SBP indexes were constructed, using the residual method (see Statistical Analysis).

[d] Hazard ratios express the risk for increments of 20 mm Hg in SBP and 0.10 in the dipping ratio.

[e] The dipping ratio is calculated by dividing asleep by awake SBP.

eTable 10. Association of Outcomes with 24-Hour or Asleep SBP Adjusted for Other SBP Indexes in 7133 Participants

Outcomes	24-Hour SBP[a]		Asleep SBP[a]	
SBP Indexes Adjusted For	HR (CI)[b]	*P*	HR (CI)[b]	*P*
Total Mortality (n = 1566)				
Conventional SBP	1.23 (1.12 to 1.34)	<.001	1.25 (1.16 to 1.34)	<.001
Automated office SBP	1.33 (1.19 to 1.48)	<.001	1.29 (1.19 to 1.40)	<.001
24-hour SBP	NA	NA	1.27 (1.10 to 1.47)	<.001
Awake SBP	1.81 (1.37 to 2.39)	<.001	1.27 (1.15 to 1.41)	<.001
Asleep SBP	1.02 (0.87 to 1.19)	.82	NA	NA
Dipping ratio[c]	1.27 (1.17 to 1.37)	<.001	1.29 (1.19 to 1.40)	<.001
All CV Outcomes (n = 1048)				
Conventional SBP	1.58 (1.42 to 1.76)	<.001	1.49 (1.36 to 1.63)	<.001
Automated office SBP	1.74 (1.53 to 1.98)	<.001	1.52 (1.38 to 1.67)	<.001
24-hour SBP	NA	NA	1.28 (1.08 to 1.52)	.005
Awake SBP	2.38 (1.70 to 3.34)	<.001	1.39 (1.23 to 1.57)	<.001
Asleep BP	1.29 (1.07 to 1.57)	.008	NA	NA
Dipping ratio[c]	1.62 (1.48 to 1.78)	<.001	1.68 (1.52 to 1.85)	<.001
CV Mortality (n = 521)				
Conventional SBP	1.54 (1.33 to 1.79)	<.001	1.52 (1.34 to 1.72)	<.001
Automated office SBP	1.81 (1.52 to 2.16)	<.001	1.61 (1.41 to 1.84)	<.001
24-hour SBP	NA	NA	1.40 (1.10 to 1.78)	.006
Awake SBP	2.60 (1.63 to 4.15)	<.001	1.48 (1.25 to 1.75)	<.001
Asleep SBP	1.21 (0.93 to 1.58)	.16	NA	NA
Dipping ratio[c]	1.66 (1.45 to 1.88)	<.001	1.72 (1.50 to 1.98)	<.001
Coronary Outcomes (n = 409)				
Conventional SBP	1.58 (1.32 to 1.88)	<.001	1.50 (1.30 to 1.74)	<.001
Automated office SBP	1.68 (1.36 to 2.07)	<.001	1.51 (1.29 to 1.76)	<.001
24-hour SBP	NA	NA	1.36 (1.03 to 1.81)	.03
Awake SBP	2.62 (1.47 to 4.65)	.001	1.43 (1.17 to 1.75)	<.001
Asleep SBP	1.15 (0.84 to 1.57)	.39	NA	NA
Dipping ratio[c]	1.53 (1.32 to 1.76)	<.001	1.57 (1.34 to 1.83)	<.001
Stroke (n = 479)				
Conventional SBP	1.74 (1.5 to 2.03)	<.001	1.62 (1.42 to 1.84)	<.001
Automated office SBP	1.83 (1.52 to 2.21)	<.001	1.60 (1.39 to 1.84)	<.001
24-hour SBP	NA	NA	1.29 (1.01 to 1.66)	.04
Awake SBP	2.97 (1.84 to 4.80)	<.001	1.48 (1.24 to 1.76)	<.001
Asleep SBP	1.43 (1.09 to 1.88)	.01	NA	NA
Dipping ratio[c]	1.81 (1.59 to 2.07)	<.001	1.88 (1.63 to 2.18)	<.001

Abbreviations: CI, 95% confidence interval; CV, cardiovascular; HR, hazard ratio; SBP, systolic blood pressure; NA, not applicable.

[a] In this analysis, we defined the awake and asleep periods of the day in 7133 participants (64.1%), who had kept a diary during ambulatory blood pressure monitoring. All models accounted for cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus and were constructed, using the residual method (see Statistical Analysis).

[b] Hazard ratios express the risk for increments of 20 mm Hg in SBP and 0.10 in the dipping ratio.

[c] The dipping ratio is calculated by dividing asleep by awake SBP.

eTable 11. Sensitivity Analysis Excluding Cohorts

Outcomes / Population	N° Event/ N° at Risk	24-Hour SBP		Nighttime SBP	
		HR (CI)[a]	*P*	HR (CI)[a]	*P*
Total Mortality					
All Cohorts[b]	**2836/11,135**	**1.22 (1.16 to 1.28)**	**<.001**	**1.23 (1.17 to 1.28)**	**<.001**
Excluding[c]					
Ohasama	2115/9600	1.21 (1.15 to 1.29)	<.001	1.22 (1.16 to 1.28)	<.001
Small cohorts	2787/9479	1.22 (1.16 to 1.29)	<.001	1.22 (1.17 to 1.28)	<.001
Noordkempen	2527/9705	1.21 (1.14 to 1.27)	<.001	1.21 (1.16 to 1.27)	<.001
Uppsala	1907/10,021	1.32 (1.23 to 1.41)	<.001	1.33 (1.25 to 1.41)	<.001
Copenhagen	2297/8987	1.19 (1.13 to 1.26)	<.001	1.21 (1.15 to 1.27)	<.001
Dublin	2800/10,202	1.22 (1.16 to 1.28)	<.001	1.22 (1.17 to 1.28)	<.001
Maracaibo	2697/10,545	1.19 (1.13 to 1.26)	<.001	1.20 (1.15 to 1.26)	<.001
Montevideo	2722/9406	1.23 (1.16 to 1.29)	<.001	1.23 (1.17 to 1.28)	<.001
CV Outcomes					
All Cohorts[b]	**2049/11,135**	**1.45 (1.37 to 1.54)**	**<.001**	**1.36 (1.30 to 1.43)**	**<.001**
Excluding[c]					
Ohasama	1681/9600	1.42 (1.34 to 1.51)	<.001	1.34 (1.28 to 1.42)	<.001
Small cohorts	1995/9479	1.44 (1.36 to 1.53)	<.001	1.35 (1.29 to 1.42)	<.001
Noordkempen	1768/9705	1.44 (1.35 to 1.53)	<.001	1.35 (1.29 to 1.42)	<.001
Uppsala	1363/10,021	1.62 (1.50 to 1.75)	<.001	1.53 (1.43 to 1.64)	<.001
Copenhagen	1683/8987	1.42 (1.34 to 1.52)	<.001	1.33 (1.26 to 1.40)	<.001
Dublin	2030/10,202	1.45 (1.37 to 1.54)	<.001	1.36 (1.30 to 1.43)	<.001
Maracaibo	1919/10,545	1.45 (1.37 to 1.54)	<.001	1.36 (1.29 to 1.43)	<.001
Montevideo	1904/9406	1.45 (1.36 to 1.54)	<.001	1.36 (1.30 to 1.43)	<.001

Abbreviations: CI, confidence interval; CV, cardiovascular; HR, hazard ratio; SBP, systolic blood pressure.

[a] Hazard ratios express the risk per 20 mm Hg increment in 24-hour or nighttime SBP. HRs accounted for cohort (random effect), sex, age, body mass index, smoking and drinking, serum total cholesterol, antihypertensive drug intake, history of CV disease and diabetes mellitus.

[b] The analyses included 11,135 participants.

[c] Identifies the excluded cohort. All cohorts with fewer than 500 participants were excluded in a single run. These cohorts included JingNing (n = 352), Novosibirsk (n = 283), Kraków (n = 355), Gdańsk (n = 202), Pilsen (n = 159) and Padova (n = 305).

eTable 12. Improvement in Model Performance by Adding 24-Hour or Nighttime SBP to Another SBP Index

Outcomes SBP Index to Which 24-Hour or Nighttime SBP Was Added	AUC (CI) Basic Model[a]	ΔAUC (CI)[b]	
		Adding 24-Hour SBP	Adding Nighttime SBP
Total Mortality (n = 2836)			
Conventional SBP	0.83 (0.82 to 0.85)	0.0013 (0.0001 to 0.0024)	0.0024 (0.0010 to 0.0038)
Automated office SBP	0.83 (0.82 to 0.85)	0.0016 (0.0003 to 0.0029)	0.0027 (0.0010 to 0.0044)
24-hour SBP	0.83 (0.82 to 0.85)	*NA*	0.0013 (0.0001 to 0.0024)
Daytime SBP	0.83 (0.82 to 0.85)	0.0016 (0.0001 to 0.0032)	0.0023 (0.0006 to 0.0040)
Nighttime SBP	0.83 (0.82 to 0.85)	*NC*[c]	*NA*
Dipping ratio[d]	0.83 (0.82 to 0.85)	0.0017 (0.0003 to 0.0032)	0.0018 (0.0002 to 0.0032)
All CV Outcomes (n = 2049)			
Conventional SBP	0.84 (0.83 to 0.85)	0.0057 (0.0033 to 0.0082)	0.0058 (0.0034 to 0.0082)
Automated office SBP	0.84 (0.83 to 0.85)	0.0048 (0.0025 to 0.0071)	0.0050 (0.0028 to 0.0072)
24-hour SBP	0.84 (0.83 to 0.86)	*NA*	0.0005 (–0.0002 to 0.0012)
Daytime SBP	0.84 (0.83 to 0.86)	0.0034 (0.0015 to 0.0052)	0.0031 (0.0014 to 0.0048)
Nighttime SBP	0.84 (0.83 to 0.86)	0.0006 (–0.0002 to 0.0015)	*NA*
Dipping ratio[d]	0.84 (0.83 to 0.85)	0.0075 (0.0047 to 0.0103)	0.0071 (0.0043 to 0.0099)
CV Mortality (n = 1073)			
Conventional SBP	0.87 (0.86 to 0.89)	0.0037 (0.0012 to 0.0062)	0.0046 (0.0019 to 0.0073)
Automated office SBP	0.87 (0.86 to 0.89)	0.0047 (0.0020 to 0.0074)	0.0052 (0.0022 to 0.0082)
24-hour SBP	0.88 (0.86 to 0.89)	*NA*	0.0009 (–0.0004 to 0.0023)
Daytime SBP	0.88 (0.86 to 0.89)	0.0025 (0.0002 to 0.0048)	0.0029 (0.0004 to 0.0054)
Nighttime SBP	0.88 (0.86 to 0.89)	*NC*[c]	*NA*
Dipping ratio[d]	0.87 (0.86 to 0.89)	0.0055 (0.0023 to 0.0087)	0.0055 (0.0022 to 0.0087)
Coronary Outcomes (n = 922)			
Conventional SBP	0.86 (0.85 to 0.87)	0.0038 (0.0014 to 0.0063)	0.0033 (0.0011 to 0.0055)
Automated office SBP	0.86 (0.85 to 0.88)	0.0023 (0.0002 to 0.0044)	0.0022 (0.0002 to 0.0042)
24-hour SBP	0.86 (0.85 to 0.88)	*NA*	0.0001 (–0.0007 to 0.0009)
Daytime SBP	0.86 (0.85 to 0.88)	0.0014 (–0.0002 to 0.0029)	0.0011 (–0.0004 to 0.0027)
Nighttime SBP	0.86 (0.85 to 0.88)	*NC*[c]	*NA*
Dipping ratio[d]	0.86 (0.84 to 0.87)	0.0049 (0.0018 to 0.0079)	0.0045 (0.0016 to 0.0074)
Stroke (n = 822)			
Conventional SBP	0.84 (0.82 to 0.86)	0.0073 (0.0028 to 0.0118)	0.0068 (0.0025 to 0.0110)
Automated office SBP	0.84 (0.82 to 0.86)	0.0076 (0.0027 to 0.0124)	0.0069 (0.0026 to 0.0112)
24-hour SBP	0.85 (0.83 to 0.87)	*NA*	0.0002 (–0.0012 to 0.0016)
Daytime SBP	0.85 (0.83 to 0.87)	0.0037 (0.0004 to 0.0069)	0.0034 (0.0002 to 0.0066)
Nighttime SBP	0.84 (0.83 to 0.86)	0.0017 (–0.0004 to 0.0038)	*NA*
Dipping ratio[d]	0.83 (0.82 to 0.85)	0.0138 (0.0080 to 0.0196)	0.0135 (0.0077 to 0.0193)

Abbreviations: AUC, area under the receiver operating characteristic curve for the 10-year absolute risk; CI, 95% confidence interval; CV, cardiovascular; ΔAUC, change in AUC; SBP, systolic blood pressure; NA, not applicable.

[a] Basic models included cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus and another SBP index identified by the row label.

[b] ΔAUC for adding 24-hour or nighttime SBP to a basic model already including covariables and another SBP index. Models were constructed using the residual method (see Statistical Analysis).

[c] NC indicates that the improvement in model performance was not calculated, because the hazard ratio for 24-hour SBP did not attain significance in multivariable-adjusted models already including nighttime SBP (**Table 3**).

[d] The dipping ratio is calculated by dividing nighttime by daytime SBP.

eTable 13. Improvement in Model Performance by Adding 24-Hour or Nighttime DBP to Another DBP Index

Outcomes DBP Index to Which 24-Hour or Nighttime DBP Was Added	AUC (CI) Basic Model[a]	ΔAUC (CI)[b]	
		Adding 24-Hour DBP	Adding Nighttime DBP
Total Mortality (n = 2836)			
Conventional DBP	0.83 (0.82 to 0.84)	0.0007 (–0.0001 to 0.0015)	0.0018 (0.0005 to 0.0030)
Automated office DBP	0.83 (0.82 to 0.85)	0.0007 (–0.0003 to 0.0017)	0.0018 (0.0005 to 0.0032)
24-hour DBP	0.83 (0.82 to 0.85)	*NA*	0.0012 (0.0002 to 0.0022)
Daytime DBP	0.83 (0.82 to 0.85)	0.0009 (–0.0001 to 0.0020)	0.0017 (0.0004 to 0.0030)
Nighttime DBP	0.83 (0.82 to 0.85)	*NC*[c]	*NA*
Dipping ratio[d]	0.83 (0.82 to 0.85)	0.0009 (–0.0001 to 0.0019)	0.0011 (0.0001 to 0.0021)
All CV Outcomes (n = 2049)			
Conventional DBP	0.84 (0.83 to 0.85)	0.0028 (0.0009 to 0.0047)	0.0034 (0.0014 to 0.0053)
Automated office DBP	0.84 (0.83 to 0.85)	0.0028 (0.0011 to 0.0045)	0.0033 (0.0014 to 0.0053)
24-hour DBP	0.84 (0.83 to 0.85)	*NA*	0.0006 (–0.0002 to 0.0014)
Daytime DBP	0.84 (0.83 to 0.85)	0.0025 (0.0007 to 0.0042)	0.0024 (0.0007 to 0.0041)
Nighttime DBP	0.84 (0.83 to 0.86)	0.0001 (–0.0006 to 0.0008)	*NA*
Dipping ratio[d]	0.84 (0.83 to 0.85)	0.0042 (0.0020 to 0.0063)	0.0039 (0.0018 to 0.0059)
CV Mortality (n = 1073)			
Conventional DBP	0.87 (0.86 to 0.89)	0.0019 (–0.0000 to 0.0038)	0.0032 (0.0009 to 0.0056)
Automated office DBP	0.87 (0.86 to 0.89)	0.0028 (0.0004 to 0.0053)	0.0038 (0.0011 to 0.0066)
24-hour DBP	0.87 (0.86 to 0.89)	*NA*	0.0012 (–0.0002 to 0.0027)
Daytime DBP	0.87 (0.86 to 0.89)	0.0024 (0.0003 to 0.0044)	0.0027 (0.0005 to 0.0050)
Nighttime DBP	0.88 (0.86 to 0.89)	*NC*[c]	*NA*
Dipping ratio[d]	0.87 (0.86 to 0.89)	0.0022 (–0.0002 to 0.0046)	0.0020 (–0.0003 to 0.0043)
Coronary Outcomes (n = 922)			
Conventional DBP	0.86 (0.85 to 0.87)	0.0017 (0.0003 to 0.0032)	0.0016 (0.0002 to 0.0031)
Automated office DBP	0.86 (0.85 to 0.87)	0.0015 (–0.0001 to 0.0031)	0.0014 (–0.0001 to 0.0029)
24-hour DBP	0.86 (0.85 to 0.88)	*NA*	0.0000 (–0.0008 to 0.0009)
Daytime DBP	0.86 (0.85 to 0.87)	0.0009 (–0.0005 to 0.0024)	0.0007 (–0.0006 to 0.0020)
Nighttime DBP	0.86 (0.85 to 0.88)	*NC*[c]	*NA*
Dipping ratio[d]	0.86 (0.84 to 0.87)	0.0024 (0.0005 to 0.0044)	0.0022 (0.0004 to 0.0039)
Stroke (n = 822)			
Conventional DBP	0.84 (0.82 to 0.86)	0.0055 (0.0013 to 0.0096)	0.0049 (0.0010 to 0.0089)
Automated office DBP	0.84 (0.82 to 0.86)	0.0054 (0.0014 to 0.0094)	0.0049 (0.0013 to 0.0085)
24-hour DBP	0.85 (0.83 to 0.87)	*NA*	0.0005 (–0.0009 to 0.0019)
Daytime DBP	0.85 (0.83 to 0.87)	0.0031 (0.0001 to 0.0062)	0.0028 (–0.0002 to 0.0058)
Nighttime DBP	0.84 (0.83 to 0.86)	0.0016 (–0.0003 to 0.0034)	*NA*
Dipping ratio[d]	0.83 (0.82 to 0.85)	0.0094 (0.0045 to 0.0143)	0.0090 (0.0041 to 0.0140)

Abbreviations: AUC, area under the receiver operating characteristic curve for the 10-year absolute risk; CI, 95% confidence interval; CV, cardiovascular; ΔAUC, change in AUC; DBP, Diastolic blood pressure; NA, not applicable.

[a] Basic models included cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus and another DBP index identified by the row label.

[b] ΔAUC for adding 24-hour or nighttime to a basic model already including covariables and another DBP index. Models were constructed using the residual method (see Statistical Analysis).

[c] NC indicates that the improvement in model performance was not calculated, because the hazard ratio for 24-hour DBP did not attain significance in multivariable-adjusted models already including nighttime DBP (**eTable 6**).

[d] The dipping ratio is calculated by dividing nighttime by daytime DBP.

eTable 14. Improvement in Model Performance by Adding a SBP Index to 24-Hour or Nighttime SBP

Outcomes SBP Index Added to 24-Hour or Nighttime SBP	Added to 24-Hour SBP		Added to Nighttime SBP	
	Basic Model AUC (CI)[a]	**ΔAUC (CI)**[b]	**Basic Model AUC (CI)**[a]	**ΔAUC (CI)**[b]
Total Mortality (n = 2836)				
Conventional SBP	0.83 (0.82 to 0.85)	0.0001 (–0.0004 to 0.0007)	0.84 (0.82 to 0.85)	0.0000 (–0.0006 to 0.0005)
Automated office SBP	0.83 (0.82 to 0.85)	*NC*[c]	0.84 (0.82 to 0.85)	*NC*[c]
24-hour SBP	0.83 (0.82 to 0.85)	*NA*	0.84 (0.82 to 0.85)	*NC*[c]
Daytime SBP	0.83 (0.82 to 0.85)	0.0006 (–0.0004 to 0.0016)	0.84 (0.82 to 0.85)	*NC*[c]
Nighttime SBP	0.83 (0.82 to 0.85)	0.0013 (0.0001 to 0.0024)	0.84 (0.82 to 0.85)	*NA*
Systolic dipping ratio	0.83 (0.82 to 0.85)	0.0010 (–0.0005 to 0.0024)	0.84 (0.82 to 0.85)	*NC*[c]
All CV Outcomes (n = 2049)				
Conventional SBP	0.85 (0.83 to 0.86)	*NC*[c]	0.85 (0.83 to 0.86)	0.0001 (–0.0007 to 0.0009)
Automated office SBP	0.85 (0.83 to 0.86)	*NC*[c]	0.85 (0.83 to 0.86)	0.0003 (–0.0003 to 0.0010)
24-hour SBP	0.85 (0.83 to 0.86)	*NA*	0.85 (0.83 to 0.86)	0.0006 (–0.0002 to 0.0015)
Daytime SBP	0.85 (0.83 to 0.86)	0.0006 (–0.0003 to 0.0014)	0.85 (0.83 to 0.86)	0.0004 (–0.0002 to 0.0011)
Nighttime SBP	0.85 (0.83 to 0.86)	0.0005 (–0.0002 to 0.0012)	0.85 (0.83 to 0.86)	*NA*
Systolic dipping ratio	0.85 (0.83 to 0.86)	0.0010 (–0.0005 to 0.0024)	0.85 (0.83 to 0.86)	0.0004 (–0.0003 to 0.0010)
CV Mortality (n = 1073)				
Conventional SBP	0.88 (0.86 to 0.89)	*NC*[c]	0.88 (0.86 to 0.89)	0.0002 (–0.0008 to 0.0012)
Automated office SBP	0.88 (0.86 to 0.89)	*NC*[c]	0.88 (0.86 to 0.89)	*NC*[c]
24-hour SBP	0.88 (0.86 to 0.89)	*NA*	0.88 (0.86 to 0.89)	*NC*[c]
Daytime SBP	0.88 (0.86 to 0.89)	0.0006 (–0.0006 to 0.0017)	0.88 (0.86 to 0.89)	*NC*[c]
Nighttime SBP	0.88 (0.86 to 0.89)	0.0009 (–0.0004 to 0.0023)	0.88 (0.86 to 0.89)	*NA*
Systolic dipping ratio	0.88 (0.86 to 0.89)	0.0007 (–0.0002 to 0.0015)	0.88 (0.86 to 0.89)	*NC*[d]
Coronary Outcomes (n = 922)				
Conventional SBP	0.86 (0.85 to 0.88)	*NC*[c]	0.86 (0.85 to 0.88)	*NC*[d]
Automated office SBP	0.86 (0.85 to 0.88)	*NC*[c]	0.86 (0.85 to 0.88)	0.0007 (–0.0003 to 0.0017)
24-hour SBP	0.86 (0.85 to 0.88)	*NA*	0.86 (0.85 to 0.88)	*NC*[c]
Daytime SBP	0.86 (0.85 to 0.88)	*NC*[c]	0.86 (0.85 to 0.88)	*NC*[c]
Nighttime SBP	0.86 (0.85 to 0.88)	0.0001 (–0.0007 to 0.0009)	0.86 (0.85 to 0.88)	*NA*
Systolic dipping ratio	0.86 (0.85 to 0.88)	0.0003 (–0.0005 to 0.0011)	0.86 (0.85 to 0.88)	*NC*[c]
Stroke (n = 822)				
Conventional SBP	0.85 (0.83 to 0.87)	0.0004 (–0.0010 to 0.0019)	0.85 (0.83 to 0.86)	0.0014 (–0.0006 to 0.0034)
Automated office SBP	0.85 (0.83 to 0.87)	*NC*[c]	0.85 (0.83 to 0.86)	0.0009 (–0.0006 to 0.0023)
24-hour SBP	0.85 (0.83 to 0.87)	*NA*	0.85 (0.83 to 0.86)	0.0017 (–0.0004 to 0.0038)
Daytime SBP	0.85 (0.83 to 0.87)	*NC*[c]	0.85 (0.83 to 0.86)	0.0014 (–0.0006 to 0.0033)
Nighttime SBP	0.85 (0.83 to 0.87)	0.0002 (–0.0012 to 0.0016)	0.85 (0.83 to 0.86)	*NA*
Systolic dipping ratio	0.85 (0.83 to 0.87)	0.0002 (–0.0012 to 0.0016)	0.85 (0.83 to 0.86)	0.0014 (–0.0007 to 0.0034)

Abbreviations: AUC, area under the receiver operating characteristic curve for the 10-year absolute risk; CI, 95% confidence interval; CV, cardiovascular; ΔAUC, change in AUC; SBP, systolic blood pressure; NA, not applicable.

[a] Basic models included cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus and 24-hour or nighttime SBP.

[b] ΔAUC for adding a SBP index identified by the row label to a basic model already including covariables and 24-hour or nighttime SBP. Models were constructed using the residual method (see Statistical Analysis).

[c] NC indicates that the improvement in model performance was not calculated, because the hazard ratio for the SBP index did not attain significance in multivariable-adjusted models already including either 24-hour or nighttime SBP (**Table 2**).

eTable 15. Improvement in Model Performance by Adding a DBP Index to 24-Hour or Nighttime DBP

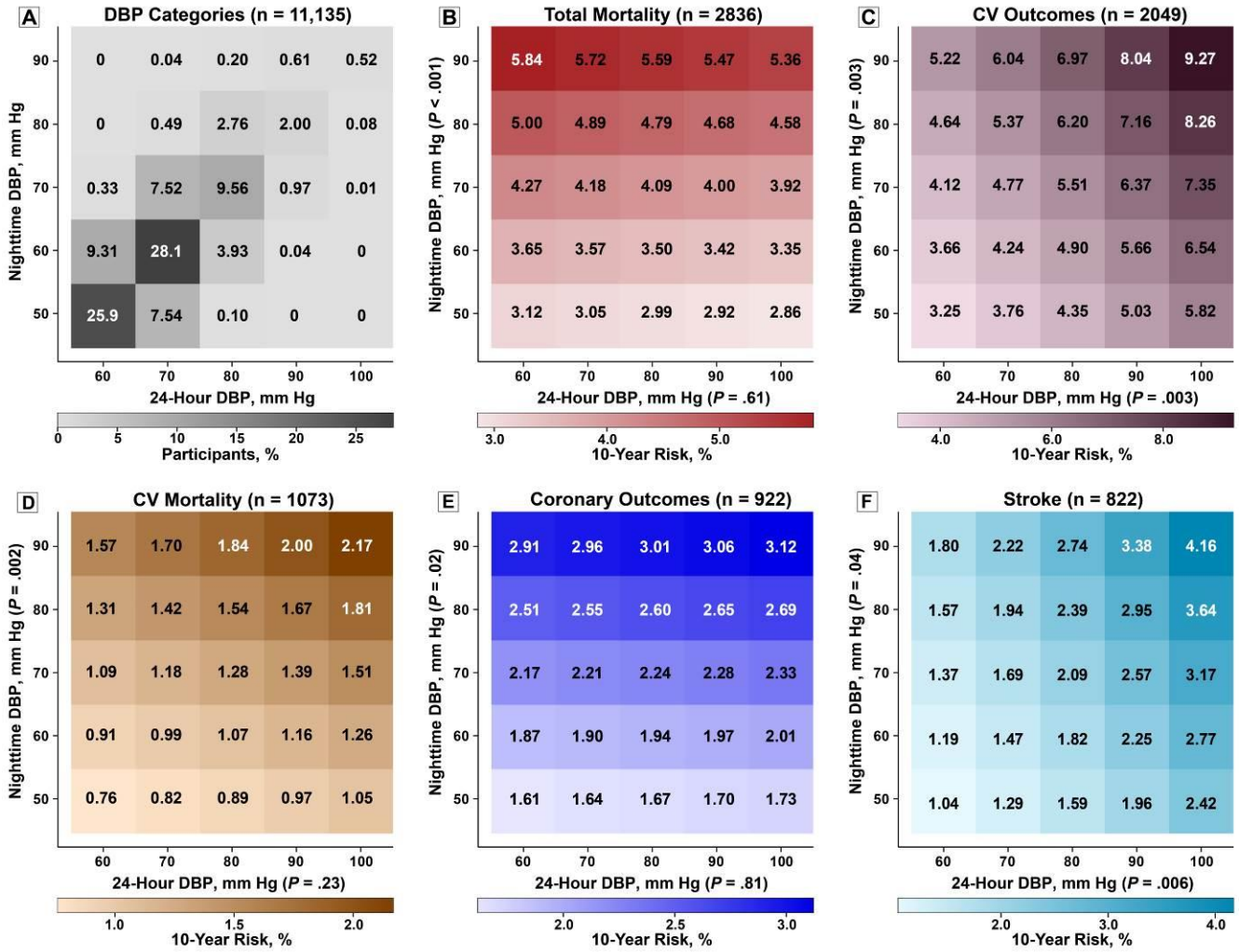
Outcomes DBP Index Added to 24-Hour or Nighttime DBP	Added to 24-Hour DBP		Added to Nighttime DBP	
	Basic Model AUC (CI)[a]	**ΔAUC (CI)**[b]	**Basic Model AUC (CI)**[a]	**ΔAUC (CI)**[b]
Total Mortality (n = 2836)				
Conventional DBP	0.83 (0.82 to 0.85)	*NC*[c]	0.83 (0.82 to 0.85)	*NC*[c]
Automated office DBP	0.83 (0.82 to 0.85)	*NC*[c]	0.83 (0.82 to 0.85)	*NC*[c]
24-hour DBP	0.83 (0.82 to 0.85)	*NA*	0.83 (0.82 to 0.85)	*NC*[c]
Daytime DBP	0.83 (0.82 to 0.85)	0.0004 (–0.0003 to 0.0011)	0.83 (0.82 to 0.85)	*NC*[c]
Nighttime DBP	0.83 (0.82 to 0.85)	0.0012 (0.0002 to 0.0022)	0.83 (0.82 to 0.85)	*NA*
Diastolic dipping ratio	0.83 (0.82 to 0.85)	*NC*[c]	0.83 (0.82 to 0.85)	*NC*[c]
All CV Outcomes (n = 2049)				
Conventional DBP	0.84 (0.82 to 0.85)	*NC*[c]	0.84 (0.83 to 0.86)	0.0001 (–0.0005 to 0.0006)
Automated office DBP	0.84 (0.82 to 0.85)	*NC*[c]	0.84 (0.83 to 0.86)	*NC*[c]
24-hour DBP	0.84 (0.82 to 0.85)	*NA*	0.84 (0.83 to 0.86)	0.0001 (–0.0006 to 0.0008)
Daytime DBP	0.84 (0.82 to 0.85)	0.0006 (–0.0003 to 0.0014)	0.84 (0.83 to 0.86)	0.0000 (–0.0005 to 0.0005)
Nighttime DBP	0.84 (0.82 to 0.85)	0.0006 (–0.0002 to 0.0014)	0.84 (0.83 to 0.86)	*NA*
Diastolic dipping ratio	0.84 (0.82 to 0.85)	*NC*[c]	0.84 (0.83 to 0.86)	*NC*[c]
CV Mortality (n = 1073)				
Conventional DBP	0.87 (0.86 to 0.89)	*NC*[c]	0.88 (0.86 to 0.89)	*NC*[c]
Automated office DBP	0.87 (0.86 to 0.89)	0.0005 (–0.0005 to 0.0016)	0.88 (0.86 to 0.89)	*NC*[c]
24-hour DBP	0.87 (0.86 to 0.89)	*NA*	0.88 (0.86 to 0.89)	*NC*[c]
Daytime DBP	0.87 (0.86 to 0.89)	0.0010 (–0.0003 to 0.0022)	0.88 (0.86 to 0.89)	*NC*[c]
Nighttime DBP	0.87 (0.86 to 0.89)	0.0012 (–0.0002 to 0.0027)	0.88 (0.86 to 0.89)	*NA*
Diastolic dipping ratio	0.87 (0.86 to 0.89)	*NC*[d]	0.88 (0.86 to 0.89)	*NC*[d]
Coronary Outcomes (n = 922)				
Conventional DBP	0.86 (0.85 to 0.88)	*NC*[c]	0.86 (0.85 to 0.88)	*NC*[c]
Automated office DBP	0.86 (0.85 to 0.88)	*NC*[c]	0.86 (0.85 to 0.88)	*NC*[c]
24-hour DBP	0.86 (0.85 to 0.88)	*NA*	0.86 (0.85 to 0.88)	*NC*[c]
Daytime DBP	0.86 (0.85 to 0.88)	*NC*[c]	0.86 (0.85 to 0.88)	*NC*[c]
Nighttime DBP	0.86 (0.85 to 0.88)	0.0000 (–0.0008 to 0.0009)	0.86 (0.85 to 0.88)	*NA*
Diastolic dipping ratio	0.86 (0.85 to 0.88)	*NC*[d]	0.86 (0.85 to 0.88)	*NC*[c]
Stroke (n = 822)				
Conventional DBP	0.84 (0.82 to 0.86)	*NC*[c]	0.85 (0.83 to 0.86)	0.0011 (–0.0005 to 0.0028)
Automated office DBP	0.84 (0.82 to 0.86)	*NC*[c]	0.85 (0.83 to 0.86)	*NC*[c]
24-hour DBP	0.84 (0.82 to 0.86)	*NA*	0.85 (0.83 to 0.86)	0.0016 (–0.0003 to 0.0034)
Daytime DBP	0.84 (0.82 to 0.86)	*NC*[c]	0.85 (0.83 to 0.86)	0.0012 (–0.0003 to 0.0028)
Nighttime DBP	0.84 (0.82 to 0.86)	0.0005 (–0.0009 to 0.0019)	0.85 (0.83 to 0.86)	*NA*
Diastolic dipping ratio	0.84 (0.82 to 0.86)	0.0005 (–0.0008 to 0.0019)	0.85 (0.83 to 0.86)	0.0013 (–0.0004 to 0.0029)

Abbreviations: AUC, area under the receiver operating characteristic curve for the 10-year absolute risk; CI, 95% confidence interval; CV, cardiovascular; ΔAUC, change in AUC; DBP, Diastolic blood pressure; NA, not applicable.

[a] Basic models included cohort, sex, age, body mass index, smoking and drinking, serum cholesterol, antihypertensive drug intake, history of cardiovascular disease and diabetes mellitus and 24-hour or nighttime DBP.

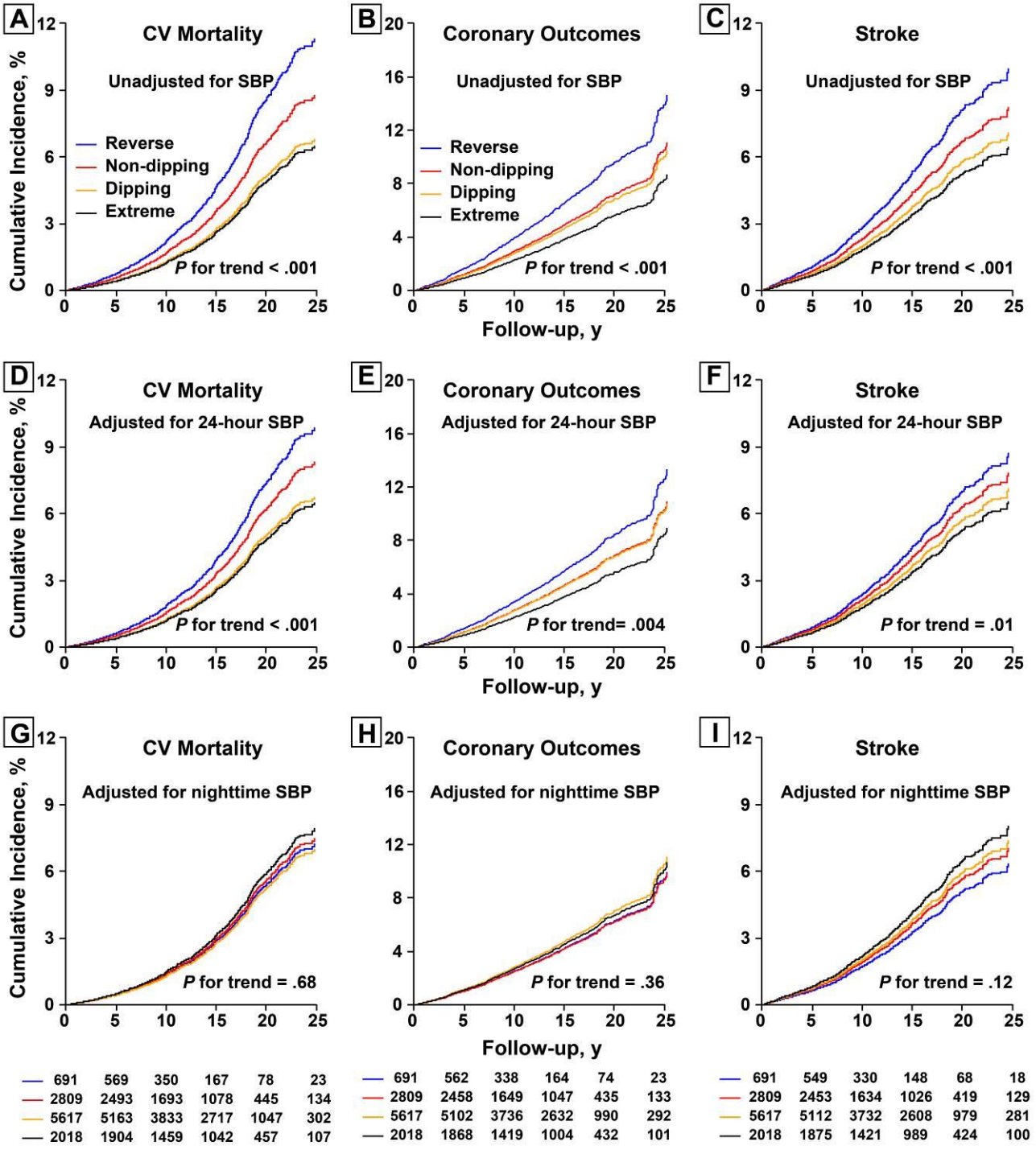
[b] ΔAUC for adding a DBP index identified by the row label to a basic model already including covariables and 24-hour or nighttime DBP. Models were constructed using the residual method (see Statistical Analysis).

[c] NC indicates that the improvement in model performance was not calculated, because the hazard ratio for the DBP index did not attain significance in multivariable-adjusted models already including either 24-hour or nighttime DBP (**eTable 5**).



eFigure 1. Heat Map Depicting 10-Year Risk in Relation to 24-Hour and Nighttime Diastolic Pressure in 11,135 Study Participants

Heat maps were derived by Cox proportional hazards regression with 24-hour and nighttime diastolic blood pressure (DBP) analyzed as continuous variables. Estimates of 10-year risk were standardized to the average of the distributions in the whole study population (mean or ratio) of cohort identifier, sex, age, body mass index, smoking and drinking, antihypertensive drug treatment, serum cholesterol, history of cardiovascular (CV) disease and diabetes mellitus. Numbers in the grids in Panel A represent the percent of participants within each cross-classification category. Numbers in colored grids (Panels B–F) the 10-year risk of an end point. Along the vertical axis, the risks of all Outcomes (B–F) were significantly greater with higher nighttime DBP ($P \leq .04$), but along the horizontal axis only the risk of the composite CV outcomes (C; $P = .003$) and stroke (F; $P = .006$) were significantly greater with higher 24-hour DBP. Risks of total mortality (B), CV mortality (D) and coronary outcomes (E) were not significantly associated with 24-hour DBP ($P \geq .23$).



eFigure 2. Cumulative Incidence of Cardiovascular Mortality, Coronary Outcomes and Stroke by Dipping Status

Participants were categorized in extreme dippers (≤0.80), normal dippers (>0.80 to ≤0.90), non-dippers (>0.90 to ≤1.00) and reverse dippers (>1.00) based on the systolic dipping ratio. Tabulated data are the number of participants at risk by dipping status at 5-year intervals. *P*-values for trend were derived by Cox proportional hazards regression. All estimates accounted for sex and age (Panels A–I). Additional adjustment for 24-hour SBP (Panels D, E and F) did not remove significance, whereas additional adjustment for nighttime SBP did (Panels G, H and I).