

SUPPLEMENTAL MATERIAL

Table S1. Characteristics of the included and excluded population *

Variables	Included population	Non-included population
N	16953	3749
Age, y	60.0 ± 7.4	59.8 ± 8.1
Male, No. (%)	6827 (40.3)	1670 (44.5)
Body mass index, kg/m ²	25.0 ± 3.7	24.5 ± 3.8
Current smoking, No. (%)	3882 (22.9)	987 (26.3)
Current alcohol drinking, No. (%)	3999 (23.6)	961 (25.6)
Family history of diabetes, No. (%)	750 (4.4)	143 (3.8)
Enalapril group, No. (%)	8504 (50.2)	1850 (49.3)
BP, mmHg		
SBP at baseline	167.2 ± 20.4	165.3 ± 20.1
DBP at baseline	94.2 ± 11.9	93.8 ± 12.0
Time-averaged on-treatment SBP	139.0 ± 10.6	141.4 ± 12.3
Time-averaged on-treatment DBP	82.7 ± 7.2	84.2 ± 8.3
Laboratory results		
Total cholesterol, mmol/L	5.5 ± 1.2	5.5 ± 1.2
Triglycerides, mmol/L	1.4 (1.1, 2.0)	1.4 (1.1, 1.9)
Fasting glucose, mg/dL	105.0 ± 30.9	101.3 ± 28.3
Creatinine, μmol/L	65.6 ± 17.1	67.9 ± 28.0
Folate, ng/mL	8.0 (5.6, 10.4)	8.3 (5.7, 11.0)
Medication use, No. (%)		
Antihypertensive drugs	7953 (46.9)	1583 (42.2)
Lipid lowering drugs	145 (0.9)	21 (0.6)
Antiplatelet drugs	522 (3.1)	85 (2.3)

*Continuous variables are presented as Mean ± SDs or medians (25th percentile, 75th percentile) Categorical variables are presented as n (%).

BP, blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein; *MTHFR*, methylenetetrahydrofolate reductase; SD, standard deviation; SBP, systolic blood pressure; tHcy, total homocysteine.

Table S2. Characteristics of participants with or without incident diabetes *

Variables	Participants with incident diabetes	Participants without incident diabetes	P value
N	1628	13350	
Age, y	60.4 ± 7.4	60.0 ± 7.4	0.020
Male, No. (%)	658 (40.4)	5452 (40.8)	0.744
Body mass index, kg/m ²	25.9 ± 3.9	24.8 ± 3.6	<0.001
Current smoking, No. (%)	389 (23.9)	3146 (23.6)	0.361
Current alcohol drinking, No. (%)	371 (22.8)	3212 (24.1)	0.106
Family history of diabetes, No. (%)	89 (5.5)	464 (3.5)	<0.001
Enalapril group, No. (%)	802 (49.3)	6700 (50.2)	0.481
BP, mmHg			
SBP at baseline	168.1 ± 21.1	166.8 ± 20.3	0.013
DBP at baseline	94.5 ± 11.8	94.2 ± 11.9	0.298
Time-averaged on-treatment SBP	141.0 ± 11.1	138.5 ± 10.4	<0.001
Time-averaged on-treatment DBP	83.2 ± 7.5	82.8 ± 7.2	0.034
Laboratory results			
Total cholesterol, mmol/L	5.5 ± 1.2	5.5 ± 1.1	0.063
Triglycerides, mmol/L	1.6 (1.1, 2.2)	1.4 (1.0, 1.9)	<0.001
Fasting glucose, mg/dL	104.3 ± 13.1	96.2 ± 12.1	<0.001
Creatinine, μmol/L	64.4 ± 15.2	66.0 ± 16.6	<0.001
Folate, ng/mL	7.7 (5.5, 10.0)	8.0 (5.6, 10.4)	0.005
Medication use, No. (%)			
Antihypertensive drugs	846 (52.0)	6042 (45.3)	<0.001
Lipid lowering drugs	12 (0.7)	101 (0.8)	0.932
Antiplatelet drugs	49 (3.0)	400 (3.0)	0.976

*Continuous variables are presented as Mean ± SDs or medians (25th percentile, 75th percentile) Categorical variables are presented as n (%).

BP, blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; *MTHFR*, methylenetetrahydrofolate reductase; SD, standard deviation; SBP, systolic blood pressure; tHcy, total homocysteine.

Table S3. Concomitant medication usage during the treatment period by time-averaged on-treatment systolic blood pressure (SBP) categories *

Medication, No. (%)	Time-averaged on-treatment SBP Categories, mm Hg				P value
	<120	120 to <130	130 to <140	≥140	
N	263	2658	5878	6179	
Anti-hypertension drugs					
Calcium channel blockers	103 (39.2)	1677 (63.1)	4843 (82.4)	5652 (91.5)	<0.001
Diuretics	47 (17.9)	822 (30.9)	2797 (47.6)	4175 (67.6)	<0.001
Beta-blockers	0 (0.0)	6 (0.2)	17 (0.3)	14 (0.2)	0.746
Lipid-lowering drugs	0 (0.0)	3 (0.1)	11 (0.2)	7 (0.1)	0.625
Antiplatelet drugs	1 (0.4)	14 (0.5)	54 (0.9)	46 (0.7)	0.226

*Regular concomitant medication usage was defined as 180 or more cumulative days of taking the drug of interest.

Table S4. Concomitant medication usage during the treatment period in participants with or without the development of incident diabetes*

Medication, No. (%)	Participants with incident diabetes	Participants without incident diabetes	P value
N	1628	13350	
Anti-hypertension drugs			
Calcium channel blockers	1369 (84.1)	10906 (81.7)	0.018
Diuretics	898 (55.2)	6943 (52.0)	0.016
Beta-blockers	3 (0.2)	34 (0.3)	0.589
Lipid-lowering drugs	4 (0.2)	17 (0.1)	0.228
Antiplatelet drugs	10 (0.6)	105(0.8)	0.452

*Regular concomitant medication usage was defined as 180 or more cumulative days of taking the drug of interest.

Table S5. Association between time-averaged on-treatment blood pressure (BP) and incident diabetes, with further adjustment for the use of beta blockers, lipid-lowering drugs or antiplatelet drugs during the treatment period

BP, mmHg	N	No. of events (%)	Crude Model		Adjusted Model*	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	263	23 (8.7)	1.20 (0.76, 1.88)	0.435	1.24 (0.78, 1.99)	0.360
120 to <130	2658	197 (7.4)	<i>ref.</i>		<i>ref.</i>	
130 to <140	5878	606 (10.3)	1.44 (1.21, 1.70)	<0.001	1.37 (1.15, 1.64)	<0.001
≥140	6179	802 (13.0)	1.86 (1.58, 2.19)	<0.001	1.67 (1.39, 2.01)	<0.001
Time-averaged on-treatment DBP						
<70	491	42 (8.6)	0.80 (0.57, 1.11)	0.172	0.76 (0.53, 1.07)	0.115
70 to <80	4788	504 (10.5)	<i>ref.</i>		<i>ref.</i>	
80 to <90	7434	814 (10.9)	1.05 (0.93, 1.18)	0.461	1.13 (0.98, 1.30)	0.088
≥90	2265	268 (11.8)	1.14 (0.97, 1.34)	0.101	1.31 (1.06, 1.61)	0.012
Time-averaged on-treatment SBP/DBP						
<130 and <80	1603	125 (7.8)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	6618	651 (9.8)	1.29 (1.06, 1.58)	0.012	1.24 (1.01, 1.54)	0.044
≥140 and/or ≥90	6757	852 (12.6)	1.71 (1.40, 2.08)	<0.001	1.54 (1.24, 1.92)	<0.001

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB), diuretics, beta blockers, lipid-lowering drugs or antiplatelet drugs during the treatment period.

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S6. Association between time-averaged on-treatment blood pressure (BP) and incident diabetes, with further adjustment for the treatment (enalapril or enalapril-folic acid) compliance during the treatment period

BP, mmHg	N	No. of events (%)	Crude Model		Adjusted Model*	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	263	23 (8.7)	1.20 (0.76, 1.88)	0.435	1.26 (0.79, 2.01)	0.335
120 to <130	2658	197 (7.4)	<i>ref.</i>		<i>ref.</i>	
130 to <140	5878	606 (10.3)	1.44 (1.21, 1.70)	<0.001	1.35 (1.13, 1.62)	<0.001
≥140	6179	802 (13.0)	1.86 (1.58, 2.19)	<0.001	1.61 (1.33, 1.94)	<0.001
Time-averaged on-treatment DBP						
<70	491	42 (8.6)	0.80 (0.57, 1.11)	0.172	0.76 (0.54, 1.08)	0.124
70 to <80	4788	504 (10.5)	<i>ref.</i>		<i>ref.</i>	
80 to <90	7434	814 (10.9)	1.05 (0.93, 1.18)	0.461	1.10 (0.96, 1.27)	0.165
≥90	2265	268 (11.8)	1.14 (0.97, 1.34)	0.101	1.23 (1.00, 1.52)	0.053
Time-averaged on-treatment SBP/DBP						
<130 and <80	1603	125 (7.8)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	6618	651 (9.8)	1.29 (1.06, 1.58)	0.012	1.22 (0.99, 1.51)	0.065
≥140 and/or ≥90	6757	852 (12.6)	1.71 (1.40, 2.08)	<0.001	1.48 (1.18, 1.84)	<0.001

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB), diuretics or treatment (enalapril or enalapril-folic acid) compliance during the treatment period.

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S7. Association between time-averaged on-treatment blood pressure (BP) and incident diabetes with further adjustment for change in BMI (BMI at the exit minus that at baseline)

BP, mmHg	N	No. of events (%)	Crude Model		Adjusted Model*	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	263	23 (8.7)	1.20 (0.76, 1.88)	0.435	1.23 (0.76, 1.99)	0.395
120 to <130	2658	197 (7.4)	<i>ref.</i>		<i>ref.</i>	
130 to <140	5878	606 (10.3)	1.44 (1.21, 1.70)	<0.001	1.35 (1.12, 1.61)	0.001
≥140	6179	802 (13.0)	1.86 (1.58, 2.19)	<0.001	1.60 (1.32, 1.93)	<0.001
Time-averaged on-treatment DBP						
<70	491	42 (8.6)	0.80 (0.57, 1.11)	0.172	0.77 (0.54, 1.10)	0.150
70 to <80	4788	504 (10.5)	<i>ref.</i>		<i>ref.</i>	
80 to <90	7434	814 (10.9)	1.05 (0.93, 1.18)	0.461	1.12 (0.97, 1.29)	0.114
≥90	2265	268 (11.8)	1.14 (0.97, 1.34)	0.101	1.23 (0.99, 1.52)	0.057
Time-averaged on-treatment SBP/DBP						
<130 and <80	1603	125 (7.8)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	6618	651 (9.8)	1.29 (1.06, 1.58)	0.012	1.25 (1.01, 1.56)	0.044
≥140 and/or ≥90	6757	852 (12.6)	1.71 (1.40, 2.08)	<0.001	1.51 (1.21, 1.90)	<0.001

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB) or diuretics during the treatment period and change in BMI. DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S8. Association between time-averaged on-treatment blood pressure (BP) and incident diabetes with further adjustment for averaged BMI (BMI at the exit plus that at baseline divided by 2)

BP, mmHg	N	No. of events (%)	Crude Model		Adjusted Model*	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	263	23 (8.7)	1.20 (0.76, 1.88)	0.435	1.23 (0.76, 1.99)	0.395
120 to <130	2658	197 (7.4)	<i>ref.</i>		<i>ref.</i>	
130 to <140	5878	606 (10.3)	1.44 (1.21, 1.70)	<0.001	1.35 (1.12, 1.61)	0.001
≥140	6179	802 (13.0)	1.86 (1.58, 2.19)	<0.001	1.60 (1.32, 1.93)	<0.001
Time-averaged on-treatment DBP						
<70	491	42 (8.6)	0.80 (0.57, 1.11)	0.172	0.77 (0.54, 1.10)	0.150
70 to <80	4788	504 (10.5)	<i>ref.</i>		<i>ref.</i>	
80 to <90	7434	814 (10.9)	1.05 (0.93, 1.18)	0.461	1.12 (0.97, 1.29)	0.114
≥90	2265	268 (11.8)	1.14 (0.97, 1.34)	0.101	1.23 (0.99, 1.52)	0.057
Time-averaged on-treatment SBP/DBP						
<130 and <80	1603	125 (7.8)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	6618	651 (9.8)	1.29 (1.06, 1.58)	0.012	1.25 (1.01, 1.56)	0.044
≥140 and/or ≥90	6757	852 (12.6)	1.71 (1.40, 2.08)	<0.001	1.51 (1.21, 1.90)	<0.001

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB) or diuretics during the treatment period and averaged BMI.

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S9. Association between time-averaged on-treatment blood pressure (BP) and incident diabetes with further adjustment for visit-to-visit variability (VTV) in blood pressure (BP) during the treatment period

BP, mmHg	N	No. of events (%)	Crude Model		Adjusted Model*	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	263	23 (8.7)	1.20 (0.76, 1.88)	0.435	1.24 (0.78, 1.98)	0.368
120 to <130	2658	197 (7.4)	<i>ref.</i>		<i>ref.</i>	
130 to <140	5878	606 (10.3)	1.44 (1.21, 1.70)	<0.001	1.37 (1.15, 1.64)	<0.001
≥140	6179	802 (13.0)	1.86 (1.58, 2.19)	<0.001	1.66 (1.38, 2.00)	<0.001
Time-averaged on-treatment DBP						
<70	491	42 (8.6)	0.80 (0.57, 1.11)	0.172	0.75 (0.53, 1.07)	0.109
70 to <80	4788	504 (10.5)	<i>ref.</i>		<i>ref.</i>	
80 to <90	7434	814 (10.9)	1.05 (0.93, 1.18)	0.461	1.13 (0.98, 1.30)	0.088
≥90	2265	268 (11.8)	1.14 (0.97, 1.34)	0.101	1.27 (1.03, 1.57)	0.025
Time-averaged on-treatment SBP/DBP						
<130 and <80	1603	125 (7.8)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	6618	651 (9.8)	1.29 (1.06, 1.58)	0.012	1.24 (1.01, 1.54)	0.043
≥140 and/or ≥90	6757	852 (12.6)	1.71 (1.40, 2.08)	<0.001	1.53 (1.23, 1.91)	<0.001

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB) or diuretics during the treatment period and VTV in SBP, VTV in DBP. DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S10. Association between time-averaged on-treatment blood pressure (BP) during the first 6-month treatment period and the subsequent incident diabetes

BP, mmHg	N	No. of events (%)	Crude Model		Adjusted Model*	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	565	47 (8.3)	1.04 (0.74, 1.47)	0.800	1.10 (0.77, 1.57)	0.591
120 to <130	2065	165 (8.0)	<i>ref.</i>		<i>ref.</i>	
130 to <140	4073	410 (10.1)	1.29 (1.07, 1.56)	0.009	1.23 (1.01, 1.49)	0.044
≥140	8249	988 (12.0)	1.57 (1.32, 1.86)	<0.001	1.41 (1.16, 1.70)	<0.001
Time-averaged on-treatment DBP						
<70	440	43 (9.8)	0.94 (0.67, 1.31)	0.721	0.96 (0.67, 1.36)	0.805
70 to <80	3614	373 (10.3)	<i>ref.</i>		<i>ref.</i>	
80 to <90	6958	746 (10.7)	1.04 (0.92, 1.19)	0.526	1.05 (0.91, 1.21)	0.495
≥90	3940	448 (11.4)	1.11 (0.96, 1.29)	0.143	1.15 (0.96, 1.37)	0.131
Time-averaged on-treatment SBP/DBP						
<130 and <80	1460	119 (8.2)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	4512	445 (9.9)	1.23 (1.00, 1.52)	0.052	1.18 (0.94, 1.47)	0.151
≥140 and/or ≥90	8980	1046 (11.7)	1.49 (1.22, 1.81)	<0.001	1.32 (1.06, 1.63)	0.013

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB) or diuretics during the treatment period.

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S11. Association between time-averaged on-treatment blood pressure (BP) during the first 24-month treatment period and the subsequent incident diabetes

BP, mmHg	N	No. of events (%)	Crude Model		Adjusted Model*	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	275	25 (9.1)	1.27 (0.82, 1.97)	0.291	1.34 (0.85, 2.12)	0.210
120 to <130	2176	159 (7.3)	<i>ref.</i>		<i>ref.</i>	
130 to <140	4979	486 (9.8)	1.37 (1.14, 1.65)	<0.001	1.28 (1.05, 1.56)	0.013
≥140	7490	902 (12.0)	1.74 (1.46, 2.07)	<0.001	1.54 (1.26, 1.87)	<0.001
Time-averaged on-treatment DBP						
<70	411	37 (9.0)	0.87 (0.61, 1.24)	0.449	0.88 (0.61, 1.28)	0.510
70 to <80	4076	415 (10.2)	<i>ref.</i>		<i>ref.</i>	
80 to <90	7394	772 (10.4)	1.03 (0.91, 1.17)	0.663	1.06 (0.92, 1.22)	0.428
≥90	3039	348 (11.5)	1.14 (0.98, 1.33)	0.087	1.24 (1.02, 1.51)	0.035
Time-averaged on-treatment SBP/DBP						
<130 and <80	1296	92 (7.1)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	5482	533 (9.7)	1.41 (1.12, 1.77)	0.004	1.31 (1.03, 1.67)	0.027
≥140 and/or ≥90	8142	947 (11.6)	1.72 (1.38, 2.15)	<0.001	1.51 (1.18, 1.93)	0.001

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB) or diuretics during the treatment period.

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S12. Association between time-averaged on-treatment blood pressure (BP) and incident diabetes in participants without the use of diuretics during the treatment period

BP, mm Hg	N	No. of events (%)	Crude Model		Adjusted Model*	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	216	18 (8.3)	1.10 (0.66, 1.84)	0.712	1.14 (0.67, 1.94)	0.624
120 to <130	1836	140 (7.6)	<i>ref.</i>		<i>ref.</i>	
130 to <140	3081	311 (10.1)	1.36 (1.10, 1.68)	0.004	1.31 (1.05, 1.63)	0.018
≥140	2004	261 (13.0)	1.81 (1.46, 2.25)	<0.001	1.66 (1.31, 2.11)	<0.001
Time-averaged on-treatment DBP						
<70	304	29 (9.5)	0.95 (0.63, 1.42)	0.796	0.91 (0.59, 1.40)	0.662
70 to <80	2808	281 (10.0)	<i>ref.</i>		<i>ref.</i>	
80 to <90	3382	344 (10.2)	1.02 (0.86, 1.20)	0.831	1.11 (0.91, 1.35)	0.316
≥90	643	76 (11.8)	1.21 (0.92, 1.58)	0.174	1.38 (1.00, 1.92)	0.054
Time-averaged on-treatment SBP/DBP						
<130 and <80	1252	102 (8.2)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and /or 80-<90	3674	349 (9.5)	1.18 (0.94, 1.49)	0.152	1.14 (0.89, 1.46)	0.301
≥140 and/or ≥90	2211	279 (12.6)	1.63 (1.28, 2.07)	<0.001	1.50 (1.15, 1.95)	0.003

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB) during the treatment period.

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S13. Association between time-averaged on-treatment blood pressure (BP) and incident diabetes in participants with the use of diuretics during the treatment period[†]

BP, mm Hg	N	No. of events (%)	Crude Model		Adjusted Model*	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	47	5 (10.6)	1.60 (0.61, 4.20)	0.342	1.54 (0.57, 4.20)	0.396
120 to <130	822	57 (6.9)	<i>ref.</i>		<i>ref.</i>	
130 to <140	2797	295 (10.6)	1.58 (1.18, 2.13)	0.002	1.50 (1.10, 2.04)	0.010
≥140	4175	541 (13.0)	2.00 (1.50, 2.65)	<0.001	1.73 (1.28, 2.35)	<0.001
Time-averaged on-treatment DBP						
<70	187	213 (7.0)	0.59 (0.33, 1.05)	0.074	0.56 (0.31, 1.03)	0.061
70 to <80	1980	223 (11.3)	<i>ref.</i>		<i>ref.</i>	
80 to <90	4052	470 (11.6)	1.03 (0.87, 1.22)	0.700	1.13 (0.93, 1.38)	0.220
≥90	1622	192 (11.8)	1.06 (0.86, 1.30)	0.591	1.28 (0.97, 1.68)	0.083
Time-averaged on-treatment SBP/DBP						
<130 and <80	351	23 (6.6)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and /or 80-<90	2944	302 (10.3)	1.63 (1.05, 2.53)	0.029	1.59 (1.00, 2.51)	0.049
≥140 and/or ≥90	4546	573 (12.6)	2.06 (1.34, 3.17)	0.001	1.84 (1.16, 2.91)	0.009

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB) during the treatment period.

[†] There was no significant interaction between diuretics usage (no vs. yes) and time-averaged on-treatment SBP (130-<140 vs. 120-<130mmHg) on incident diabetes(*P*-interaction=0.323). DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S14. Post-matched participant characteristics according to propensity scores *

Variables	Time-averaged on-treatment SBP Categories, mmHg		Standardized Difference, %
	120 to <130	130 to <140	
N	2483	2483	
Age, y	58.97 ± 7.22	59.07 ± 7.31	1.4
Male, No. (%)	994 (40)	1003 (40.4)	0.7
Body mass index (mean ± SD)	24.55 ± 3.51	24.57 ± 3.52	0.4
Current smoking, No. (%)	529 (21.3)	546 (22.0)	1.7
Current alcohol drinking, No. (%)	563 (22.7)	572 (23.0)	0.9
Family history of diabetes, No. (%)	84 (3.4)	87 (3.5)	0.7
Enalapril group, No. (%)	1241 (50.0)	1270 (51.1)	2.3
BP, mmHg			
SBP at baseline	157.32 ± 15.70	156.93 ± 15.20	2.5
DBP at baseline	92.38 ± 10.69	91.98 ± 10.70	3.7
Laboratory results, mmol/L			
Total cholesterol	5.44 ± 1.12	5.44 ± 1.15	0.5
HDL-C	1.36 ± 0.36	1.36 ± 0.37	0.7
Triglycerides	1.57 ± 0.84	1.57 ± 0.83	0.6
Fasting glucose, mg/dL	95.61 ± 12.07	95.87 ± 12.27	2.1
Creatinine, µmol/L	65.37 ± 15.84	65.65 ± 16.94	1.7
Folate, ng/mL	8.72 ± 4.03	8.63 ± 4.02	2.3
tHcy, µmol/L	14.18 ± 8.34	14.17 ± 8.94	0.1
Medication use, No. (%)			
Antihypertensive drugs at baseline	1079 (43.5)	1116 (44.9)	3.0
Lipid lowering drugs at baseline	22 (0.9)	30 (1.2)	3.2
Antiplatelet drugs at baseline	68 (2.7)	76 (3.1)	1.9
CCB during the treatment period	1647 (66.3)	1631 (65.7)	1.4
Diuretics during the treatment period	790 (31.8)	841 (33.9)	4.4

*Variables are presented as Mean ± SD or n (%).

BP, blood pressure; CCB, Calcium channel blockers; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; SBP, systolic blood pressure; tHcy, total homocysteine.

Table S15. Association between time-averaged on-treatment blood pressure (BP) and incident impaired fasting glucose*

BP, mmHg	N	No. of events (%)	Crude Model		Adjusted Model [†]	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<120	170	60 (35.3)	0.92 (0.66, 1.29)	0.640	0.94 (0.66, 1.32)	0.701
120 to <130	1649	612 (37.1)	<i>ref.</i>		<i>ref.</i>	
130 to <140	3349	1416 (42.3)	1.24 (1.10, 1.40)	<0.001	1.17 (1.03, 1.33)	0.019
≥140	3299	1466 (44.4)	1.36 (1.20, 1.53)	<0.001	1.19 (1.04, 1.37)	0.012
Time-averaged on-treatment DBP						
<70	301	113 (37.5)	0.79 (0.62, 1.02)	0.066	0.77 (0.60, 1.00)	0.050
70 to <80	2780	1197 (43.1)	<i>ref.</i>		<i>ref.</i>	
80 to <90	4146	1712 (41.3)	0.93 (0.84, 1.03)	0.145	0.98 (0.87, 1.10)	0.690
≥90	1240	532 (42.9)	0.99 (0.87, 1.14)	0.927	1.07 (0.89, 1.27)	0.483
Time-averaged on-treatment SBP/DBP						
<130 and <80	1002	377 (37.6)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	3814	1568 (41.1)	1.16 (1.00, 1.34)	0.045	1.12 (0.96, 1.30)	0.159
≥140 and/or ≥90	3651	1609 (44.1)	1.31 (1.13, 1.51)	<0.001	1.18 (1.01, 1.39)	0.043

*Subjects with baseline FG<100 mg/dL and without incident diabetes during follow-up were included in the analysis.

[†] Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB) or diuretics during the treatment period.

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S16. Association between time-averaged on-treatment blood pressure (BP) and physician-diagnosed diabetes or use of glucose-lowering drugs during follow-up[†]

BP, mm Hg	N	No. of events (%)	Crude Model		Adjusted Model*	
			HR (95%CI)	P value	HR (95%CI)	P value
Time-averaged on-treatment SBP						
<130	2921	22 (0.8)	<i>ref.</i>		<i>ref.</i>	
130 to <140	5878	56 (1.0)	1.26 (0.77, 2.07)	0.354	1.47 (0.88, 2.45)	0.143
≥140	6179	89 (1.4)	1.95 (1.22, 3.10)	0.005	2.34 (1.39, 3.93)	0.001
Time-averaged on-treatment DBP						
<80	5279	55 (1.0)	<i>ref.</i>		<i>ref.</i>	
80 to <90	7434	76 (1.0)	1.01 (0.71, 1.43)	0.951	1.25 (0.84, 1.87)	0.270
≥90	2265	36 (1.6)	1.64 (1.08, 2.51)	0.021	2.67 (1.52, 4.69)	<0.001
Time-averaged on-treatment SBP/DBP						
<130 and <80	1603	12 (0.8)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	6618	61 (0.9)	1.25 (0.67, 2.32)	0.477	1.43 (0.74, 2.74)	0.285
≥140 and/or ≥90	6757	94 (1.4)	1.93 (1.06, 3.53)	0.031	2.40 (1.24, 4.65)	0.009

*Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel blockers (CCB) or diuretics during the treatment period.

†The proportional hazards' assumption was checked using global statistical tests based on the scaled Schoenfeld residuals in each model. No clear evidence was found against the proportional hazards' assumption in the model for time-averaged on-treatment SBP ($P=0.154$), time-averaged on-treatment DBP ($P=0.070$) and time-averaged on-treatment SBP/DBP ($P=0.140$).

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table S17. Association between time-averaged on-treatment blood pressure (BP) and regression to normal fasting glucose (FG) levels (<100mg/dL)*

BP, mm Hg	N	No. of events (%)	Crude Model		Adjusted Model [†]	
			OR (95%CI)	P value	OR (95%CI)	P value
Time-averaged on-treatment SBP						
<130	990	311 (31.4)	<i>ref.</i>		<i>ref.</i>	
130 to <140	2275	543 (23.9)	0.68 (0.58, 0.81)	<0.001	0.76 (0.63, 0.90)	0.002
≥140	2555	548 (21.4)	0.60 (0.51, 0.70)	<0.001	0.69 (0.57, 0.84)	<0.001
Time-averaged on-treatment DBP						
<70	168	43 (25.6)	1.01 (0.70, 1.45)	0.954	1.15 (0.78, 1.69)	0.493
70 to <80	1776	451 (25.4)	<i>ref.</i>		<i>ref.</i>	
80 to <90	2973	693 (23.3)	0.89 (0.78, 1.02)	0.104	0.81 (0.69, 0.95)	0.009
≥90	903	215 (23.8)	0.92 (0.76, 1.11)	0.370	0.77 (0.61, 0.99)	0.038
Time-averaged on-treatment SBP/DBP						
<130 and <80	530	178 (33.6)	<i>ref.</i>		<i>ref.</i>	
130 to <140 and/or 80 to <90	2526	623 (24.7)	0.65 (0.53, 0.79)	<0.001	0.71 (0.57, 0.89)	0.002
≥140 and/or ≥90	2764	601 (21.7)	0.55 (0.45, 0.67)	<0.001	0.64 (0.51, 0.81)	<0.001

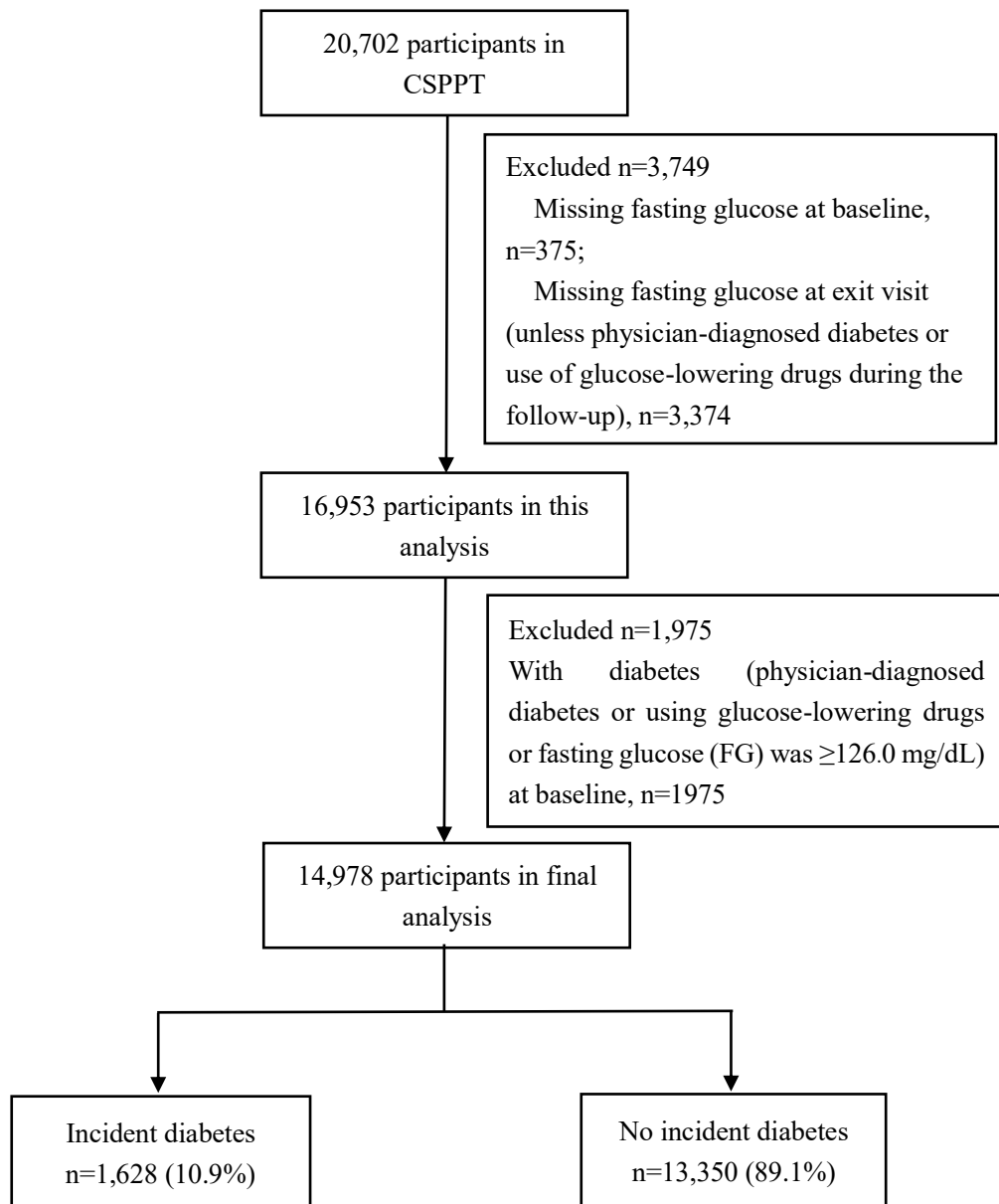
*

Subjects with baseline FG ≥100 and <126 mg/dL, and without physician-diagnosed diabetes, or use of glucose-lowering drugs during follow-up were included.

[†] Adjusted for age, sex, study center, body mass index (BMI), smoking, family history of diabetes, SBP, DBP, fasting glucose (FG), total cholesterol (TC), triglycerides (TG), creatinine, folate and the use of antihypertensive drugs at baseline, as well as use of calcium channel or diuretics during the treatment period.

Abbreviations: DBP, diastolic blood pressure; SBP, systolic blood pressure.

Figure S1. Flow chart of the study participants.



CSPPT, China Stroke Primary Prevention Trial; FG, fasting glucose.

Figure S2. Standardized differences of participant characteristics before and after matched according to propensity scores by the degree of time-averaged on-treatment SBP (120-<130 vs. 130-<140 mmHg) control.

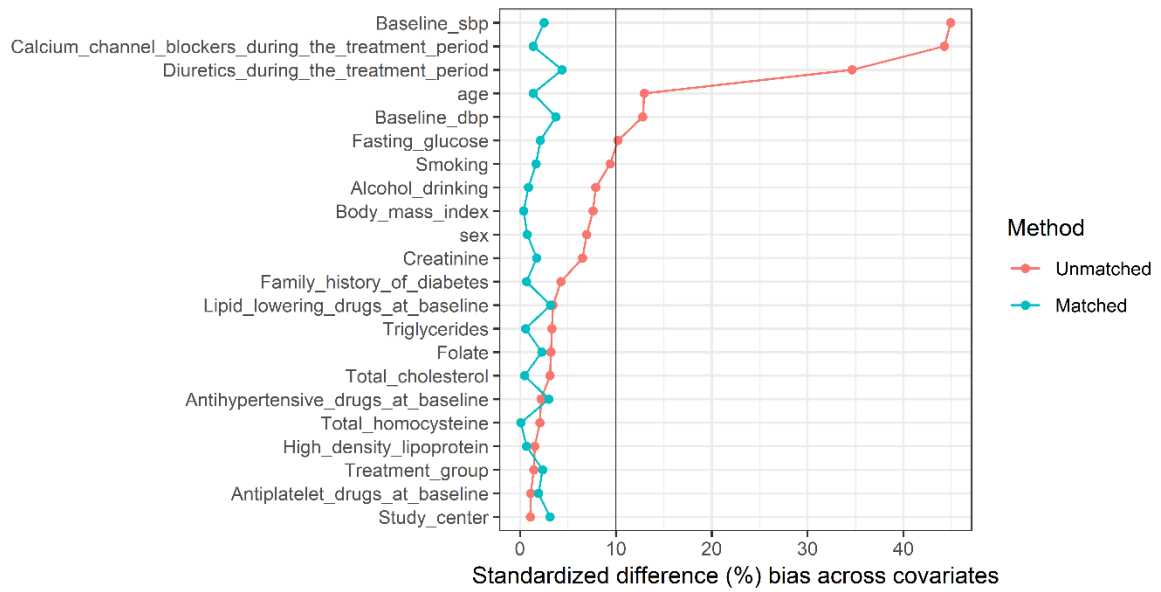


Figure S3. Tight blood pressure control and the risk of incident diabetes.

