

Supplemental Material

Supplemental Table 1. Average blood pressure during the follow-up and its changes from first to the last visit

Average BP during the F-U	BP in mmHg	BP in mmHg	P-value
Average SBP during F-U, mmHg	129.4 ± 9.9	131.2 ± 10.5	<0.001
Average DBP during F-U, mmHg	72.4 ± 9.2	70.1 ± 10.1	<0.001

Legend: SBP, systolic blood pressure; DBP, diastolic blood pressure; F-U, follow-up.

Supplemental Table 2. Association of baseline variables with the primary outcomes in univariate and multivariate analyses

Univariate variable	HR	LCI	UCI	P-value	
Intensive vs. Control	0.75	0.64	0.89	0.001	
Age>75yr	2.16	1.83	2.55	<0.001	
Female sex	0.75	0.63	0.9	0.002	
Race					
White	Ref.				
Black	0.74	0.61	0.9	0.002	
Hispanic	0.58	0.42	0.81	0.001	
Other	0.78	0.4	1.51	0.47	
Smoking					
Never	Ref.				
Former	1.37	1.14	1.64	0.001	
Current	1.55	1.21	1.98	0.001	
BMI>30Kg/m ²	0.94	0.8	1.12	0.51	
SBP (mmHg)					
<120	1.26	0.94	1.67	0.12	
120-140	Ref.				
>140	1.25	1.05	1.49	0.013	
DBP (mmHg)					
<60	1.7	1.29	2.22	<0.001	
60-90	Ref.				
>90	0.96	0.75	1.23	0.76	
HR>75bpm	1.17	0.96	1.43	0.12	
eGFR<60ml/min	1.84	1.55	2.17	<0.001	
HDLc<40mg/dL	1.33	1.09	1.62	0.004	
TG>150mg/dL	1.16	0.96	1.39	0.12	
UACr>30mg/g	2.48	2.09	2.96	<0.001	
CV disease hx	2.76	2.32	3.29	<0.001	
No. anti-HT agents					
0	Ref.				
1	1.17	0.8	1.71	0.41	
2	1.55	1.08	2.23	0.018	
3+	2.12	1.47	3.05	<0.001	
Multivariate					Interaction P
Intensive vs. Control	0.75	0.63	0.88	0.001	
Age>75yr	1.9	1.59	2.27	<0.001	0.34
Female sex	0.8	0.67	0.97	0.02	0.43
Current smk	1.66	1.32	2.1	<0.001	0.28
eGFR<60ml/min	1.32	1.11	1.58	0.002	0.27
UACR>30mg/g	1.98	1.65	2.37	<0.001	0.9
CV disease hx	2.26	1.89	2.7	<0.001	0.22
3+ anti-HT agents	1.3	1.09	1.56	0.004	0.4

Legend: HR, hazard ratio; LCI, lower bound 95% confidence interval; UCI, upper bound 95% confidence interval; Interaction P, tested between each variable and the treatment arm.

Supplemental Table 3. Time updated univariate analysis for the primary outcome

Variable	HR	LCI	UCI	P-value
Time-updated SBP (mmHg)				
<120	0.79	0.65	0.95	0.015
120-140	Ref.			
>140	1.09	0.89	1.35	0.41
Time-updated DBP (mmHg)				
<60	1.7	1.4	2.07	<0.001
60-90	Ref.			
>90	1.08	0.74	1.56	0.69
Average SBP (mmHg)				
<120	0.68	0.53	0.87	0.002
120-140	Ref.			
>140	1.84	1.50	2.26	<0.001
Average DBP (mmHg)				
<60	1.79	1.42	2.26	<0.001
60-90	Ref.			
>90	2.20	1.46	3.32	<0.001
Time-updated anti-HT drugs				
ACEi/ARBs	0.82	0.69	0.98	0.028
Beta-blocker	1.91	1.62	2.25	<0.001
CCB	1.14	0.97	1.35	0.11
MRA	0.97	0.67	1.39	0.86
Thiazide diuretic	0.67	0.57	0.79	<0.001
Loop diuretic	2.84	2.28	3.55	<0.001
Central acting/Vasodilator	1.16	0.9	1.49	0.25
ACEi/ARBs/Thiazide combination	0.65	0.54	0.77	<0.001

Legend: HR, hazard ratio; LCI, lower bound 95% confidence interval; UCI, upper bound 95% confidence interval; anti-HT, anti-hypertensive.

Supplemental Table 4. Multivariable outcome associations (for outcomes other than the primary)

Multivariate	HR	LCI	UCI	P-value	Interaction P
Cardiovascular death or heart failure					
Time-updated SBP (mmHg)					
<120	0.85	0.6	1.2	0.36	
120-140	Ref.				0.007
>140	0.97	0.7	1.35	0.84	
Time-updated DBP (mmHg)					
<60	1.31	0.95	1.82	0.1	
60-90	Ref.				0.96
>90	1.24	0.69	2.21	0.47	
Average SBP (mmHg)					
<120	0.97	0.63	1.48	0.87	
120-140	Ref.				0.012
>140	1.43	1.04	1.98	0.030	
Average DBP (mmHg)					
<60	0.93	0.63	1.37	0.72	
60-90	Ref.				0.45
>90	2.28	1.18	4.41	0.014	
Time-updated anti-HT drugs					
ACEi/ARBs	0.83	0.62	1.1	0.19	0.33
Beta-blocker	1.31	0.98	1.75	0.069	0.55
Thiazide diuretic	0.8	0.59	1.08	0.14	0.21
Loop diuretic	2.85	2.02	4.01	<0.001	0.64
ACEi/ARBs/Thiazide combination *	0.74	0.53	1.03	0.076	0.7
Heart failure hospitalization					
Time-updated SBP (mmHg)					
<120	0.68	0.45	1.03	0.070	
120-140	Ref.				0.009
>140	0.81	0.54	1.22	0.314	
Time-updated DBP (mmHg)					
<60	1.53	1.05	2.23	0.028	
60-90	Ref.				0.7
>90	1.01	0.46	2.26	0.972	
Average SBP (mmHg)					
<120	0.91	0.54	1.53	0.72	
120-140	Ref.				0.10
>140	1.29	0.87	1.92	0.21	
Average DBP (mmHg)					
<60	1.11	0.72	1.70	0.64	
60-90	Ref.				0.30
>90	1.79	0.71	4.50	0.21	
Time-updated anti-HT drugs					
ACEi/ARBs	0.82	0.58	1.15	0.245	0.51
Beta-blocker	1.41	0.98	2.01	0.061	0.93

Thiazide diuretic	0.62	0.43	0.91	0.014	0.21
Loop diuretic	2.81	1.88	4.20	0.000	0.61
ACEi/ARBs/Thiazide combination *	0.63	0.42	0.95	0.029	0.99
Myocardial infarction					
Time-updated SBP (mmHg)					
<120	0.85	0.60	1.20	0.351	
120-140	Ref.				0.38
>140	0.99	0.68	1.42	0.940	
Time-updated DBP (mmHg)					
<60	1.49	1.05	2.11	0.026	
60-90	Ref.				0.68
>90	1.03	0.54	1.96	0.940	
Average SBP (mmHg)					
<120	0.72	0.47	1.11	0.14	
120-140	Ref.				0.89
>140	1.50	1.05	2.15	0.025	
Average DBP (mmHg)					
<60	1.46	0.99	2.17	0.059	
60-90	Ref.				0.81
>90	2.93	1.59	5.41	0.001	
Time-updated anti-HT drugs					
ACEi/ARBs	0.79	0.59	1.07	0.135	0.89
Beta-blocker	1.27	0.97	1.65	0.081	0.83
Thiazide diuretic	0.77	0.57	1.05	0.097	0.56
Loop diuretic	1.22	0.78	1.91	0.384	0.86
ACEi/ARBs/Thiazide combination *	0.73	0.53	1.01	0.055	0.85
Stroke					
Time-updated SBP (mmHg)					
<120	0.70	0.44	1.11	0.128	
120-140	Ref.				0.79
>140	1.45	0.94	2.23	0.089	
Time-updated DBP (mmHg)					
<60	1.49	0.95	2.33	0.081	
60-90	Ref.				0.72
>90	0.89	0.40	1.99	0.775	
Average SBP (mmHg)					
<120	0.64	0.36	1.14	0.13	
120-140	Ref.				0.004
>140	2.39	1.57	3.64	<0.001	
Average DBP (mmHg)					
<60	1.39	0.84	2.30	0.20	
60-90	Ref.				0.68
>90	1.69	0.67	4.27	0.27	
Time-updated anti-HT drugs					
ACEi/ARBs	0.80	0.55	1.18	0.263	0.12
Beta-blocker	1.24	0.85	1.82	0.267	0.51

Thiazide diuretic	1.04	0.71	1.51	0.841	0.21
Loop diuretic	0.68	0.34	1.36	0.277	0.4
ACEi/ARBs/Thiazide combination *	0.79	0.53	1.18	0.251	0.51
Cardiovascular death					
Time-updated SBP (mmHg)					
<120	1.07	0.62	1.83	0.811	
120-140	Ref.				0.018
>140	1.55	0.96	2.51	0.074	
Time-updated DBP (mmHg)					
<60	1.22	0.73	2.04	0.456	
60-90	Ref.				0.58
>90	1.32	0.61	2.89	0.481	
Average SBP (mmHg)					
<120	1.02	0.53	1.96	0.94	
120-140	Ref.				0.014
>140	2.14	1.35	3.41	0.001	
Average DBP (mmHg)					
<60	1.08	0.61	1.93	0.79	
60-90	Ref.				0.74
>90	3.59	1.59	8.10	0.002	
Time-updated anti-HT drugs					
ACEi/ARBs	0.79	0.51	1.21	0.280	0.27
Beta-blocker	1.29	0.83	2.01	0.255	0.4
Thiazide diuretic	1.36	0.86	2.14	0.193	0.48
Loop diuretic	4.55	2.70	7.67	0.000	0.83
ACEi/ARBs/Thiazide combination *	1.05	0.64	2.03	0.85	0.79
All-cause death					
Time-updated SBP (mmHg)					
<120	1.20	0.92	1.57	0.172	
120-140	Ref.				<0.001
>140	1.23	0.94	1.61	0.139	
Time-updated DBP (mmHg)					
<60	1.28	0.98	1.66	0.067	
60-90	Ref.				0.21
>90	1.15	0.71	1.86	0.573	
Average SBP (mmHg)					
<120	1.00	0.73	1.37	0.99	
120-140	Ref.				<0.001
>140	1.42	1.08	1.86	0.012	
Average DBP (mmHg)					
<60	1.15	0.85	1.55	0.36	
60-90	Ref.				0.30
>90	2.13	1.22	3.70	0.008	
Time-updated anti-HT drugs					
ACEi/ARBs	0.73	0.58	0.91	0.005	0.45
Beta-blocker	1.30	1.03	1.65	0.025	0.54

Thiazide diuretic	0.78	0.61	0.98	0.037	0.15
Loop diuretic	2.31	1.73	3.08	0.000	0.34
ACEi/ARBs/Thiazide combination *	0.72	0.55	0.94	0.015	0.55

Legend: HR, hazard ratio; LCI, lower bound 95% confidence interval; UCI, upper bound 95% confidence interval; anti-HT, anti-hypertensive.

Models adjusted on baseline treatment allocation (intensive vs. control), age (≤ 75 yr vs. >75 yr), sex, smoking, renal function (eGFR <60 ml/min vs. ≥ 60 ml/min), albuminuria (UACR ≤ 30 mg/g vs. >30 mg/g), history of cardiovascular disease, use of 3 or more anti-HT agents at baseline.

For statistically significant interactions, see also the Supplemental Table 5 depicting the differential blood pressure impact on intensive and standard therapy, separately.

Supplemental Table 5. Adjusted association of systolic blood pressure with outcomes on standard and intensive groups, separately

<120	0.76	0.10	5.59	0.79	0.72	0.39	1.34	0.30	
120-140	Ref.				Ref.				0.004
>140	1.36	0.80	2.32	0.26	6.45	3.34	12.5	<0.001	
Cardiovascular death									
Time-updated									
<120	2.31	1.18	4.50	0.014	0.52	0.24	1.14	0.11	
120-140	Ref.				Ref.				0.018
>140	1.61	0.90	2.88	0.11	1.58	0.67	3.76	0.30	
Average									
<120	2.52	0.86	7.41	0.093	0.96	0.43	2.18	0.93	
120-140	Ref.				Ref.				0.014
>140	1.64	0.94	2.86	0.080	5.05	2.18	11.7	<0.001	
All-cause death									
Time-updated									
<120	2.54	1.79	3.60	<0.001	0.65	0.45	0.93	0.020	
120-140	Ref.				Ref.				<0.001
>140	1.24	0.89	1.74	0.20	1.35	0.84	2.16	0.22	
Average									
<120	3.25	1.92	5.51	<0.001	0.75	0.51	1.10	0.14	
120-140	Ref.				Ref.				<0.001
>140	1.18	0.85	1.64	0.33	2.53	1.56	4.11	<0.001	

Legend: HR, hazard ratio; LCI, lower 95% confidence interval; UCI, upper 95% confidence interval;

SBP, systolic blood pressure; HFH, heart failure hospitalization; CVD, cardiovascular death; MI, myocardial infarction; ACM, all-cause mortality; SBP, systolic blood pressure.

Models adjusted on baseline treatment allocation (intensive vs. control), age (≤ 75 yr vs. >75 yr), sex, smoking, renal function (eGFR <60 ml/min vs. ≥ 60 ml/min), albuminuria (UACR ≤ 30 mg/g vs. >30 mg/g), history of cardiovascular disease, use of 3 or more anti-HT agents at baseline.