

**Resistance to Antihypertensive Treatment and Long-Term Risk:
the Atherosclerosis Risk in Communities (ARIC) study**

Supplementary Tables S1 – S6

Traditional BP goal (<140/90 mmHg)	Events Event rate	Unadjusted HR (95% CI) P value	Adjusted* HR (95 % CI) P value
No HT n=5029	467 events 5.1/1000 py	0.58 (0.50-0.67) P<0.001	0.70 (0.60-0.81) P<0.001
Controlled HT n=2306	332 events 8.6/1000 py	Ref. -	Ref. -
Untreated HT n=1110	160 events 8.8/1000 py	1.04 (0.86-1.25) P=0.71	1.09 (0.90-1.32) P=0.37
Uncontrolled HT n=1034	191 events 11.8/1000 py	1.41 (1.18-1.68) P<0.001	1.28 (1.07-1.53) P=0.007
Apparent resistant HT n=133	28 events 14.4/1000 py	1.75 (1.19-2.57) P=0.005	1.36 (0.92-2.01) P=0.12
Stricter BP goal (<130/80 mmHg)			
No HT n=3857	333 events 4.7/1000 py	0.52 (0.44-0.61) P<0.001	0.63 (0.53-0.75) P<0.001
Controlled HT n=1521	227 events 8.8/1000 py	Ref. -	Ref. -
Untreated HT n=2282	294 events 7.6/1000 py	0.86 (0.72-1.02) P=0.08	0.91 (0.76-1.08) P=0.28
Uncontrolled HT n=1759	286 events 10.1/1000 py	1.17 (0.98-1.39) P=0.08	1.08 (0.90-1.28) P=0.41
Apparent resistant HT n=193	38 events 13.1/1000 py	1.53 (1.09-2.16) P=0.015	1.28 (0.91-1.82) P=0.16

Supplementary Table S1. Outcomes (first hospitalization for incident myocardial infarction, or fatal coronary heart disease) by hypertension categories. *Adjusted for baseline age, sex, race and study center, BMI, heart rate, current smoking, eGFR, LDL, HDL, TG, and diabetes status.

Traditional BP goal (<140/90 mmHg)	Events/persons Event rate	Unadjusted HR (95% CI) P value	Adjusted* HR (95 % CI) P value
No HT n=5029	314 events 3.4/1000 py	0.67 (0.56-0.81) P<0.001	0.83 (0.69-1.00) P=0.05
Controlled HT n=2306	192 events 4.9/1000 py	Ref. -	Ref. -
Untreated HT n=1110	123 events 6.7/1000 py	1.39 (1.11-1.74) P=0.004	1.42 (1.13-1.79) P=0.003
Uncontrolled HT n=1034	130 events 8.0/1000 py	1.68 (1.34-2.10) P<0.001	1.44 (1.15-1.80) P=0.001
Apparent resistant HT n=133	18 events 9.2/1000 py	1.98 (1.22-3.22) P=0.005	1.45 (0.89-2.37) P=0.13
Stricter BP goal (<130/80 mmHg)			
No HT n=3857	232 events 3.2/1000 py	0.70 (0.56-0.87) P=0.002	0.87 (0.70-1.10) P=0.25
Controlled HT n=1521	117 events 4.4/1000 py	Ref. -	Ref. -
Untreated HT n=2282	205 events 5.2/1000 py	1.17 (0.93-1.46) P=0.18	1.24 (0.98-1.56) P=0.07
Uncontrolled HT n=1759	200 events 7.0/1000 py	1.60 (1.28-2.01) P<0.001	1.42 (1.13-1.79) P=0.003
Apparent resistant HT n=193	23 events 7.8/1000 py	1.83 (1.17-2.86) P=0.008	1.42 (0.91-2.23) P=0.13

Supplementary Table S2. Outcomes (first hospitalization for incident stroke) by hypertension categories.

*Adjusted for baseline age, sex, race and study center, BMI, heart rate, current smoking, eGFR, LDL, HDL, TG, and diabetes status.

Traditional BP goal (<140/90 mmHg)	Events/persons Event rate	Unadjusted HR (95% CI) P value	Adjusted* HR (95 % CI) P value
No HT n=5029	687 events 7.5/1000 py	0.44 (0.39-0.49) P<0.001	0.58 (0.52-0.65) P<0.001
Controlled HT n=2306	606 events 16.0/1000 py	Ref. -	Ref. -
Untreated HT n=1110	256 events 14.2/1000 py	0.90 (0.77-1.04) P=0.14	0.92 (0.79-1.07) P=0.27
Uncontrolled HT n=1034	338 events 21.5/1000 py	1.39 (1.22-1.59) P<0.001	1.21 (1.06-1.38) P=0.006
Apparent resistant HT n=133	64 events 36.6/1000 py	2.52 (1.95-3.26) P<0.001	1.83 (1.41-2.37) P<0.001
Stricter BP goal (<130/80 mmHg)			
No HT n=3857	498 events 7.0/1000 py	0.42 (0.37-0.48) P<0.001	0.57 (0.49-0.65) P<0.001
Controlled HT n=1521	392 events 15.6/1000 py	Ref. -	Ref. -
Untreated HT n=2282	445 events 11.5/1000 py	0.73 (0.63-0.83) P<0.001	0.79 (0.69-0.90) P=0.001
Uncontrolled HT n=1759	528 events 19.1/1000 py	1.26 (1.10-1.43) P=0.001	1.12 (0.98-1.28) P=0.09
Apparent resistant HT n=193	88 events 33.3/1000 py	2.32 (1.84-2.93) P<0.001	1.86 (1.47-2.35) P<0.001

Supplementary Table S3. Outcomes (first hospitalization for incident heart failure) by hypertension categories.

*Adjusted for baseline age, sex, race and study center, BMI, heart rate, current smoking, eGFR, LDL, HDL, TG, and diabetes status.

Traditional BP goal (<140/90 mmHg)	Events/persons Event rate	Unadjusted HR (95% CI) P value	Adjusted* HR (95 % CI) P value
No HT n=5029	1866 events 19.5/1000 py	0.66 (0.61-0.71) P<0.001	0.80 (0.74-0.87) P<0.001
Controlled HT n=2306	1147 events 28.0/1000 py	Ref. -	Ref. -
Untreated HT n=1110	574 events 29.8/1000 py	1.08 (0.98-1.19) P=0.14	1.04 (0.94-1.16) P=0.40
Uncontrolled HT n=1034	604 events 34.9/1000 py	1.30 (1.18-1.44) P<0.001	1.11 (1.01-1.23) P=0.039
Apparent resistant HT n=133	92 events 44.4/1000 py	1.75 (1.42-2.17) P<0.001	1.41 (1.14-1.75) P=0.002
Stricter BP goal (<130/80 mmHg)			
No HT n=3857	1374 events 18.6/1000 py	0.63 (0.57-0.68) P<0.001	0.77 (0.71-0.85) P<0.001
Controlled HT n=1521	757 events 27.9/1000 py	Ref. -	Ref. -
Untreated HT n=2282	1066 events 26.0/1000 py	0.92 (0.84-1.01) P=0.09	0.95 (0.87-1.05) P=0.30
Uncontrolled HT n=1759	960 events 31.9/1000 py	1.18 (1.07-1.30) P=0.001	1.05 (0.95-1.15) P=0.33
Apparent resistant HT n=193	126 events 40.7/1000 py	1.58 (1.31-1.91) P<0.001	1.35 (1.11-1.63) P=0.002

Supplementary Table S4. Outcomes (death) by hypertension categories.

*Adjusted for baseline age, sex, race and study center, BMI, heart rate, current smoking, eGFR, LDL, HDL, TG, and diabetes status.

BP ≥140/90 mmHg	Events Event rate	Mean SBP (mmHg) Mean DBP (mmHg)	Unadjusted HR (95% CI)	Adjusted* HR (95 % CI)
Untreated HT n=1110	706 events 41.7/1000 py	152±12 79 ±10	Ref. -	Ref. -
Uncontrolled HT with 1 drug n=660	451 events 47.7/1000 py	153±14 78±11	1.17 (1.04-1.31) P=0.010	1.05 (0.93-1.19) P=0.40
Uncontrolled HT with 2 drugs n=359	251 events 49.8/1000 py	154±13 78±12	1.22 (1.05-1.41) P=0.007	1.16 (1.00-1.35) P=0.046
Uncontrolled HT with ≥ 3 drugs n=130	109 events 70.6/1000 py	157±16 78±14	1.83 (1.49-2.24) P<0.001	1.50 (1.21-1.85) P<0.001
BP ≥130/80 mmHg				
Untreated HT n=2282	1319 events 36.0/1000 py	141±14 77±9	Ref. -	Ref. -
Uncontrolled HT with 1 drug n=1143	736 events 43.0/1000 py	145±15 77±10	1.23 (1.12-1.35) P<0.001	1.08 (0.98-1.18) P=0.11
Uncontrolled HT with 2 drugs n=597	410 events 47.9/1000 py	145±15 77±11	1.38 (1.24-1.55) P<0.001	1.28 (1.14-1.44) P<0.001
Uncontrolled HT with ≥ 3 drugs n=202	158 events 62.1/1000 py	148±18 76±12	1.89 (1.60-2.22) P<0.001	1.62 (1.36-1.92) P<0.001

Supplementary Table S5. Outcomes (first hospitalization for incident myocardial infarction or stroke or heart failure, or death) and baseline blood pressure levels by number of antihypertensive drug classes used, in participants with baseline blood pressure ≥140/90 mmHg, and in participants with baseline blood pressure ≥130/80 mmHg. *Adjusted for baseline age, sex, race and study center, BMI, heart rate, current smoking, eGFR, LDL, HDL, TG, and diabetes status.

BP<140/90 mmHg	Events Event rate	Mean SBP (mmHg) Mean DBP (mmHg)	Unadjusted HR (95% CI)	Adjusted* HR (95 % CI)
No HT n=5029	2328 events 26.3/1000 py	118±12 68±9	Ref. -	Ref. -
Controlled HT with 1 drug n=1436	828 events 35.4/1000 py	122±11 69±9	1.41 (1.30-1.52) P<0.001	1.21 (1.11-1.31) P<0.001
Controlled HT with 2 drugs n=716	458 events 42.8/1000 py	122±11 70±9	1.75 (1.58-1.93) P<0.001	1.46 (1.31-1.62) P<0.001
Controlled HT with ≥ 3 drugs n=172	127 events 54.4/1000 py	123±11 69±10	2.33 (1.95-2.78) P<0.001	1.73 (1.44-2.08) P<0.001
BP<130/80 mmHg				
No HT n=3857	1715 events 24.9/1000 py	114±10 66±7	Ref. -	Ref. -
Controlled HT with 1 drug n=953	543 events 34.6/1000 py	116±9 67±8	1.45 (1.31-1.59) P<0.001	1.26 (1.14-1.39) P<0.001
Controlled HT with 2 drugs n=478	299 events 41.6/1000 py	117±9 67±8	1.80 (1.59-2.04) P<0.001	1.45 (1.28-1.65) P<0.001
Controlled HT with ≥ 3 drugs n=100	78 events 58.4/1000 py	116±9 65±8	2.66 (2.12-3.33) P<0.001	1.71 (1.36-2.17) P<0.001

Supplementary Table S6. Outcomes (first hospitalization for incident myocardial infarction or stroke or heart failure, or death) and baseline blood pressure levels by number of antihypertensive drug classes used, in participants with baseline blood pressure <140/90 mmHg, and in participants with baseline blood pressure <130/80 mmHg. *Adjusted for baseline age, sex, race and study center, BMI, heart rate, current smoking, eGFR, LDL, HDL, TG, and diabetes status.