

## Supplementary Appendix

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

Supplement to: Appel LJ, Wright JT Jr, Greene T, et al. Intensive blood-pressure control in hypertensive chronic kidney disease. N Engl J Med 2010;363:918-29.

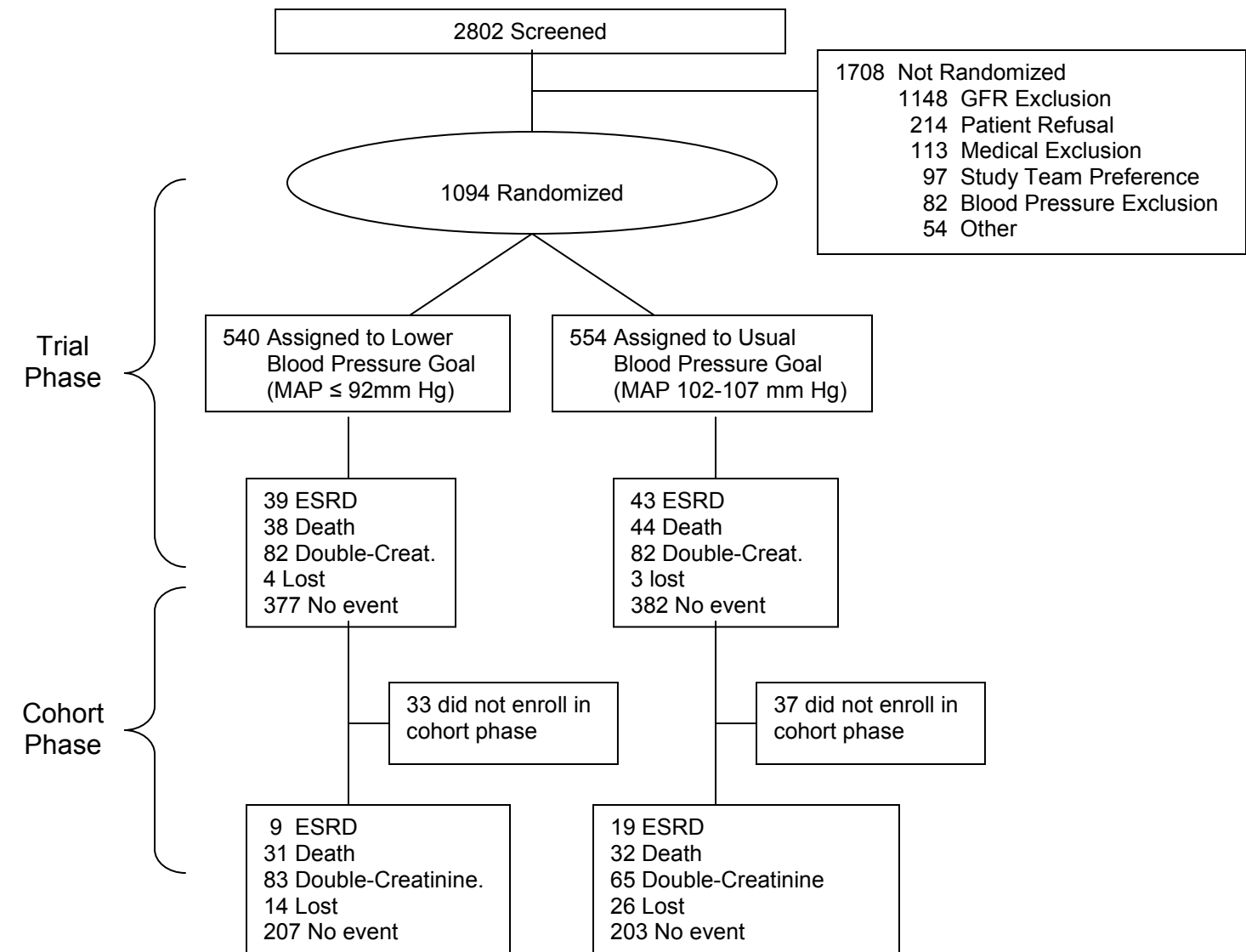
## Legend for Appendix Figures

Appendix Figure 1 – Participant flow in the trial and cohort phases of AASK

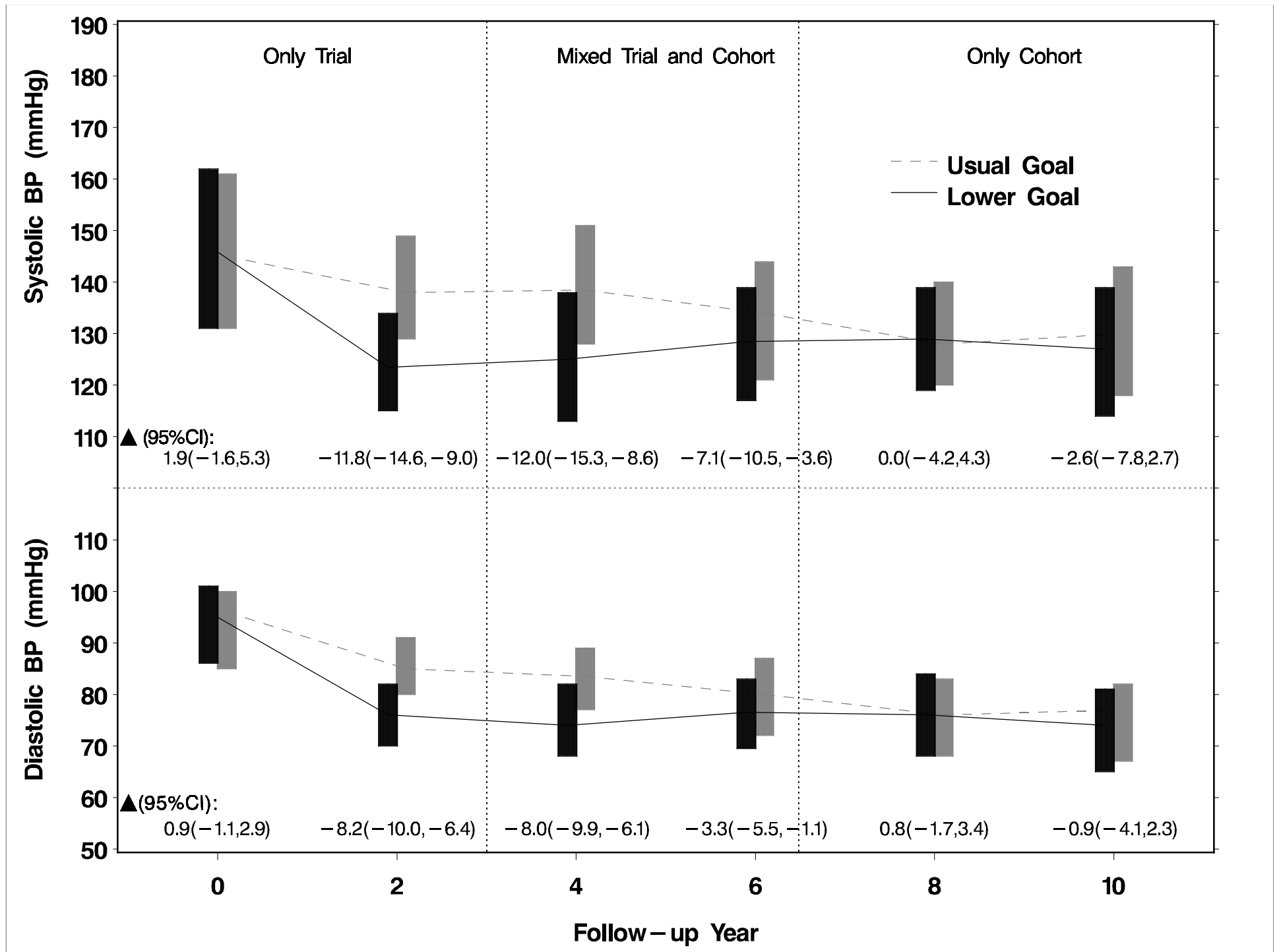
Appendix Figure 2 – Among participants with baseline  $UP/Cr \leq 0.22$ , BP levels in the usual BP group (light boxes) and lower BP group (dark boxes) over time in the trial and cohort phases of AASK among participants who had not yet experienced the primary study outcome (doubling of serum creatinine, ESRD or death). For each box, the upper edge corresponds to the 75<sup>th</sup> percentile and the bottom edge the 25<sup>th</sup> percentile. Note – All participants had at least 3 years of follow-up in the trial phase. The period between 3 and 6.5 years is a mixed period that is the trial phase for early enrollees and the cohort phase for the late enrollees. After 6.5 years, all data is from the cohort phase.

Appendix Figure 3 – Among participants with baseline  $UP/Cr > 0.22$ , BP levels in the usual BP group (light boxes) and lower BP group (dark boxes) over time in the trial and cohort phases of AASK among participants who had not yet experienced the primary study outcome (doubling of serum creatinine, ESRD or death). For each box, the upper edge corresponds to the 75<sup>th</sup> percentile and the bottom edge the 25<sup>th</sup> percentile. Note – All participants had at least 3 years of follow-up in the trial phase. The period between 3 and 6.5 years is a mixed period that is the trial phase for early enrollees and the cohort phase for the late enrollees. After 6.5 years, all data is from the cohort phase.

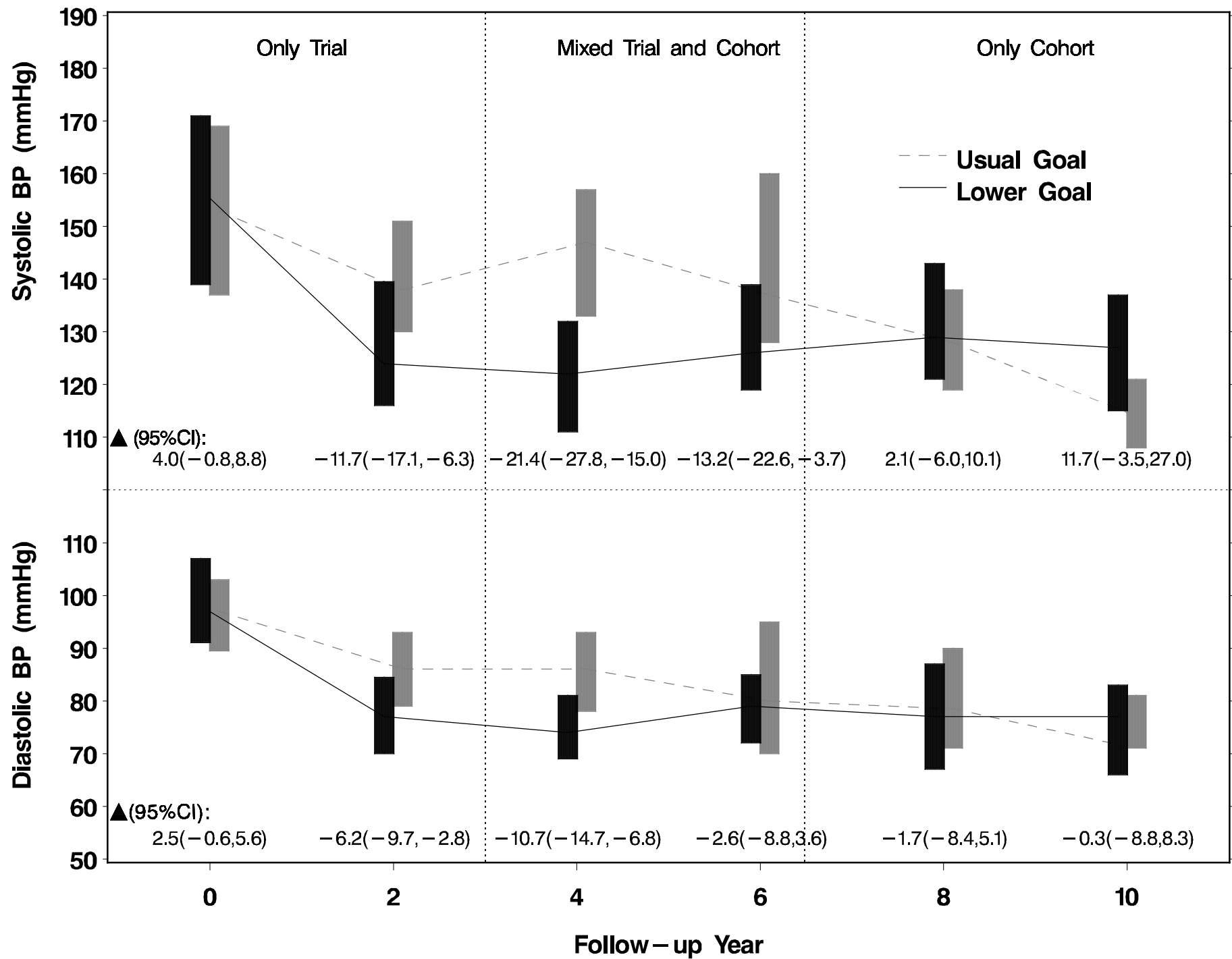
Appendix Figure 1



Appendix Figure 2



Appendix Figure 3



**Appendix Table 1: Characteristics of AASK Participants\* at Start of Cohort Phase by Randomized Group, Overall and Stratified by Baseline Urine Protein Excretion at Start of Trial**

Variable	All Participants		UP≤0.22		UP>0.22	
	Lower Goal	Usual Goal	Lower Goal	Usual Goal	Lower Goal	Usual Goal
	(N = 377)	(N = 382)	(N=290)	(N=312)	(N=86)	(N=68)
Age (yr)	60.5 ± 10.1	59.8 ± 10.3	61.8 ± 9.49	60.7 ± 9.64	56.3 ± 10.9	55.4 ± 12.1
Female	145(38.5%)	152(39.8%)	119 (41.0%)	124 (39.7%)	26 (30.2%)	28 (41.2%)
Current Smoker	119(31.6%)	82 (21.5%)	90 (31.0%)	65 (20.8%)	28 (32.6%)	16 (23.5%)
No High School Education	156(41.4%)	153(40.2%)	124 (42.8%)	134 (43.1%)	32 (37.2%)	18 (26.5%)
Weight(Kg)	91.9 ± 22.7	92.1 ± 21.5	90.4 ± 22.5	91.1 ± 21.4	97.2 ± 22.8	96.6 ± 22.0
Body Mass Index (kg/m <sup>2</sup> )	31.4 ± 7.34	31.5 ± 6.86	30.9 ± 7.05	31.3 ± 6.90	33.2 ± 8.11	32.6 ± 6.73
Estimated GFR(ml/min/1.73m <sup>2</sup> )	47.0 ± 15.3	47.7 ± 15.0	49.1 ± 15.0	50.1 ± 14.0	39.4 ± 13.9	36.4 ± 14.1
Serum Creatinine (mg/dL)	1.99 ± 0.81	1.98 ± 0.80	1.87 ± 0.73	1.84 ± 0.68	2.44 ± 0.92	2.61 ± 0.98
Urine Protein (g/day)	0.07(0.04,0.25)	0.10(0.04,0.43)	0.06(0.03,0.14)	0.08(0.04,0.25)	0.45(0.16,1.17)	0.51(0.32,1.14)
U.Protein/Creatinine	0.06(0.03,0.20)	0.07(0.03,0.29)	0.04(0.02,0.09)	0.05(0.03,0.17)	0.35(0.11,0.80)	0.42(0.21,0.98)
U.Protein/Creatinine > 0.22	82 (24.0%)	102(30.3%)	39 (14.7%)	61 (21.9%)	43 (58.1%)	41 (70.7%)
Female	32 (24.6%)	38 (29.9%)	16 (15.1%)	21 (20.4%)	16 (66.7%)	17 (70.8%)
Male	50 (23.7%)	64 (30.5%)	23 (14.4%)	40 (22.9%)	27 (54.0%)	24 (70.6%)

\*Among participants who had not experienced the primary renal outcome and who therefore remained at risk

**Appendix Table 2: BP Levels and Medication Usage Among those with UP/Cr  $\leq 0.22^*$**

		Year Post- Randomization					
		Baseline	2	4	6	8	10
# Trial / # Cohort							
	Usual	376/0	326/0	214/32	44/155	0/185	0/107
	Lower	357/0	314/0	217/29	41/147	0/178	0/111
Mean SBP							
	Usual	147(22)	139(17)	139(17)	135(18)	131(20)	131(20)
	Lower	149(25)	127(19)	127(20)	128(16)	131(21)	128(20)
Mean DBP							
	Usual	94(13)	85(11)	83(10)	79(12)	76 (12)	75 (12)
	Lower	95(14)	77(13)	75(11)	76(10)	77 (13)	74 (12)
% with SBP <130 and DBP <80 mmHg							
	Usual	9.8	12.6	16.3	25.1	38.9	40.2
	Lower	9.5	51	53.7	44.1	39.9	48.6
% with SBP <140 and DBP <90 mmHg							
	Usual	22.9	40.5	43.5	61.8	73	70.1
	Lower	22.7	77.1	74	70.2	74.7	73
% with SBP ≥160 and DBP≥100 mmHg							
	Usual	16.2	3.4	2	2.5	3.2	0.9
	Lower	19	2.2	2.8	0.5	3.4	1.8
% on ACEI or ARB							
	Usual	39.7	39.3	47.6	82.9	90.3	82.2
	Lower	42	40.1	49.6	79.7	88.2	93.6
# of HTN Med Classes							
	Usual	2.3(1.1)	2.6(1.2)	3.0(1.4)	3.6(1.5)	3.9(1.5)	3.8(1.5)
	Lower	2.4(1.1)	3.4(1.1)	3.5(1.1)	3.6(1.4)	3.7(1.4)	4.1(1.3)

\*During the trial phase, mean BP was 128/77 mmHg in the lower BP group and 140/85 mmHg in the usual BP group. During the cohort phase, mean BP was 133/78 mmHg in the lower BP group and 131/77 mmHg in the usual BP group.

**Appendix Table 3: BP Levels and Medication Usage Among those with UP/Cr > 0.22\***

		Year Post- Randomization					
		Baseline	2	4	6	8	10
# Trial/ # Cohort							
Usual		176/0	121/0	56/7	2/28	0/22	0/9
Lower		181/0	140/0	74/8	15/42	0/41	0/22
Mean SBP							
Usual		154(22)	141(19)	147(19)	142(28)	129(12)	115(10)
Lower		158(24)	130(25)	125(20)	129(17)	131(17)	127(21)
Mean DBP							
Usual		97(15)	86(12)	87(11)	82(17)	78(12)	75(6)
Lower		99(15)	80(16)	76(13)	80(12)	77(13)	74 (12)
% with SBP <130 and DBP <80 mmHg							
Usual		5.7	11.6	6.3	23.3	27.3	55.6
Lower		1.1	51.4	59.8	42.1	36.6	45.5
% with SBP <140 and DBP <90 mmHg							
Usual		14.2	38	27	46.7	63.6	100
Lower		11.6	72.1	78	77.2	68.3	77.3
% with SBP ≥160 and DBP ≥100 mmHg							
Usual		22.2	5.8	7.9	13.3	0	0
Lower		29.3	7.9	4.9	5.3	0	0
% on ACEI or ARB							
Usual		39.4	42.1	52.4	76.7	95.5	100
Lower		34.6	42.1	45.1	77.2	87.8	81.8
# of HTN Med Classes							
Usual		2.5(1.2)	3.0(1.2)	3.0(1.2)	3.7(1.3)	4.0(1.8)	4.2(1.9)
Lower		2.5(1.2)	3.7(1.1)	3.7(1.1)	4.0(1.2)	4.1(1.2)	4.5(1.2)

\*During the trial phase, mean BP was 132/81 mmHg in the lower BP group and 144/87 mmHg in the usual BP group. During the cohort phase, mean BP was 132/80 mmHg in the lower BP group and 139/83 mmHg in the usual BP group.



**Appendix Table 4: Mortality, CVD Events, and Hospitalizations by Randomized Group, All Participants**

	Lower Goal		Usual Goal		Lower vs Usual*	
	# events	Rate	# events	Rate	HR	P-value
Total Mortality						
Trial Phase	44/540	1.8	61/554	2.4	0.71 (0.48,1.05)	0.09
Cohort Phase	81/492	3.5	68/490	3	1.14 (0.82,1.57)	0.44
Both	125/540	2.6	129/554	2.7	0.94 (0.73,1.20)	0.62
CV Death						
Trial Phase	16/540	0.7	15/554	0.6	1.00 (0.49,2.02)	0.99
Cohort Phase	19/350	1.3	9/341	0.6	1.86 (0.84,4.13)	0.13
Both	35/540	0.9	24/554	0.6	1.32 (0.78,2.23)	0.3
CV Composite						
Trial Phase	71/540	3.2	78/554	3.5	0.87 (0.63,1.21)	0.41
Cohort Phase	45/322	3.4	31/307	2.6	1.22 (0.77,1.94)	0.39
Both	116/540	3.3	109/554	3.2	0.98 (0.75,1.27)	0.87
Stroke Event						
Trial Phase	26/540	1.1	29/554	1.3	0.87 (0.51,1.47)	0.6
Cohort Phase	15/337	1.1	15/327	1.1	0.87 (0.43,1.79)	0.71
Both	41/540	1.1	44/554	1.2	0.87 (0.57,1.33)	0.52
Heart Failure Event						
Trial Phase	27/540	1.2	23/554	1	1.11 (0.63,1.94)	0.71
Cohort Phase	22/341	1.5	17/329	1.3	1.13 (0.60,2.14)	0.71
Both	49/540	1.3	40/554	1.1	1.12 (0.73,1.71)	0.6
Major CAD Event						
Trial Phase	19/540	0.8	23/554	1	0.80 (0.44,1.48)	0.48
Cohort Phase	18/339	1.3	7/329	0.5	2.29 (0.95,5.50)	0.06
Both	37/540	1	30/554	0.8	1.16 (0.71,1.88)	0.55
Overall rate of CV Events						
Trial Phase	108/540	4.1	94/554	3.5	1.11(0.78 ,1.56)	0.57
Cohort Phase	70/350	4.7	58/341	4.1	1.08(0.72 ,1.70)	0.74
Both	178/540	4.6	152/554	4	1.03 (0.89,1.20)	0.55
First hospitalization (any cause)						
Trial Phase	256/540	15.3	256/554	14.3	1.05 (0.88,1.24)	0.62
Cohort Phase	84/205	11.8	77/201	11.4	0.99 (0.73,1.35)	0.95
Both	340/540	14.3	332/554	13.4	1.03 (0.89,1.20)	0.67
Overall rate of hospitalization (any cause)						
Trial Phase	518/540	19.9	519/554	19.4	0.98 ( 0.81 ,1.2)	0.87
Cohort Phase	321/350	21.6	352/341	25.1	0.83(0.77 ,1.26)	0.13
Both	839/540	21.9	870/540	23.1	0.92(0.78 ,1.08)	0.32

**Appendix Table 5: Mortality, CVD Events, and Hospitalizations by Randomized Group, UP/Cr  $\leq 0.22$** 

	<b>Lower Goal</b>		<b>Usual Goal</b>		<b>Lower vs Usual*</b>	
	<b># events</b>	<b>Rate</b>	<b># events</b>	<b>Rate</b>	<b>HR</b>	<b>P-value</b>
Total Mortality						
Trial Phase	23/357	1.4	34/376	1.9	0.66 (0.39,1.12)	0.12
Cohort Phase	52/331	3.3	46/339	3	1.09 (0.73,1.62)	0.68
Both	75/357	2.3	80/376	2.4	0.91 (0.66,1.24)	0.54
CV Death						
Trial Phase	10/357	0.6	9/376	0.5	1.14 (0.46,2.81)	0.78
Cohort Phase	17/266	1.5	7/274	0.6	2.31 (0.95,5.60)	0.06
Both	27/357	1	16/376	0.5	1.66 (0.89,3.09)	0.11
CV Composite						
Trial Phase	43/357	2.8	49/376	3	0.88 (0.58,1.33)	0.54
Cohort Phase	38/245	3.7	25/247	2.4	1.44 (0.87,2.39)	0.16
Both	81/357	3.1	74/376	2.8	1.07 (0.78,1.47)	0.66
Stroke Event						
Trial Phase	20/357	1.3	22/376	1.3	0.93 (0.50,1.70)	0.8
Cohort Phase	12/254	1.1	13/262	1.2	0.89 (0.40,1.95)	0.77
Both	32/357	1.2	35/376	1.3	0.91 (0.56,1.47)	0.7
Heart Failure Event						
Trial Phase	12/357	0.7	11/376	0.6	1.12 (0.49,2.54)	0.79
Cohort Phase	17/261	1.5	13/268	1.1	1.32 (0.64,2.72)	0.46
Both	29/357	1.1	24/376	0.8	1.23 (0.71,2.11)	0.46
Major CAD Event						
Trial Phase	11/357	0.7	15/376	0.9	0.73 (0.33,1.60)	0.43
Cohort Phase	16/259	1.4	6/264	0.5	2.62 (1.02,6.72)	0.05
Both	27/357	1	21/376	0.7	1.28 (0.72,2.28)	0.39
Overall rate of CV Events						
Trial Phase	66/357	3.8	61/376	3.4	1.11(0.72 ,1.73)	0.63
Cohort Phase	54/266	4.6	47/266	3.9	1.13(0.68 ,1.82)	0.63
Both	120/357	4.3	108/376	3.7	1.12(0.79 ,1.58)	0.52
First hospitalization (any cause)						
Trial Phase	163/357	13.9	168/376	12.8	1.08 (0.87,1.34)	0.5
Cohort Phase	66/158	11.8	61/160	10.7	1.08 (0.76,1.53)	0.67
Both	229/357	13.2	228/376	12.1	1.08 (0.90,1.30)	0.43
Overall rate of hospitalization (any cause)						
Trial Phase	302/357	17.6	336/376	18.5	0.94(0.73 ,1.21)	0.63
Cohort Phase	257/266	22	276/266	23.1	0.94(0.73 ,1.21)	0.66
Both	559/357	20	611/376	20.9	0.94(0.78 ,1.14)	0.55

**Appendix Table 6: Mortality, CVD Events, and Hospitalizations by Randomized Group, UP>0.22**

	Lower Goal		Usual Goal		Lower vs Usual*	
	# events	Rate	# events	Rate	HR	P-value
Total Mortality						
Trial Phase	21/181	2.5	27/176	3.4	0.72 (0.41,1.29)	0.27
Cohort Phase	29/159	4	21/149	3.1	1.32 (0.74,2.33)	0.34
Both	50/181	3.2	48/176	3.3	0.98 (0.65,1.46)	0.91
CV Death						
Trial Phase	6/181	0.8	6/176	1	0.90 (0.28,2.85)	0.86
Cohort Phase	2/83	0.6	2/66	1	0.69 (0.09,5.08)	0.72
Both	8/181	0.8	8/176	1	0.84 (0.31,2.30)	0.73
CV Composite						
Trial Phase	27/181	4.1	29/176	4.9	0.82 (0.48,1.40)	0.46
Cohort Phase	7/76	2.5	6/59	3.3	0.61 (0.20,1.87)	0.39
Both	34/181	3.6	35/176	4.5	0.79 (0.49,1.28)	0.34
Stroke Event						
Trial Phase	6/181	0.9	7/176	1.1	0.69 (0.23,2.09)	0.51
Cohort Phase	3/82	1	2/64	1	0.69 (0.10,4.50)	0.69
Both	9/181	0.9	9/176	1.1	0.71 (0.28,1.84)	0.48
Heart Failure Event						
Trial Phase	14/181	2	12/176	2	1.00 (0.45,2.20)	1
Cohort Phase	5/79	1.7	4/60	2.1	0.68 (0.18,2.64)	0.58
Both	19/181	1.9	16/176	2	0.92 (0.46,1.82)	0.8
Major CAD Event						
Trial Phase	7/181	1	8/176	1.3	0.75 (0.26,2.12)	0.58
Cohort Phase	2/79	0.7	1/64	0.5	0.41 (0.03,6.54)	0.53
Both	9/181	0.9	9/176	1.1	0.76 (0.29,2.00)	0.58
Overall rate of CV Events						
Trial Phase	41/181	4.7	33/176	3.8	1.05(0.6,1.83)	0.86
Cohort Phase	16/83	5.1	11/66	5.4	0.95(0.44,2.52)	0.91
Both	57/181	5.5	44/176	5.3	1.01(0.60,1.70)	0.97
First hospitalization (any cause)						
Trial Phase	92/181	18.5	87/176	18.4	1.00 (0.74,1.35)	0.9997
Cohort Phase	17/46	11.4	16/40	15.2	0.67 (0.34,1.35)	0.266
Both	109/181	16.9	103/176	17.8	0.95 (0.72,1.25)	0.7252
Overall rate of hospitalization (any cause)						
Trial Phase	214/181	24.3	182/176	21.2	1.1(0.8,1.52)	0.55
Cohort Phase	63/83	20.2	76/66	37.1	0.54 (0.58,2.1)	0.06
Both	277/181	27	258/176	30.9	0.91(0.66,1.26)	0.58