

Table 1. Baseline characteristics of participants by diabetes status at trial entry and follow-up, and by treatment group—chlorthalidone, amlodipine, and lisinopril (CVD Cohort)

	Chlorthalidone			Amlodipine			Lisinopril			Total		
	DM BL	Inc DM	No DM	DM BL	Inc DM	No DM	DM BL	Inc DM	No DM	DM BL	No DM	
N	5669	346	4282	3422	153	2578	3334	114	2520	12,425	613	9380
Age, y-mean(sd)	66.4(7.3)	66.1(7.4)	66.7(7.5) [†]	66.3(7.3)	65.4(7.0)	66.9(7.5) [†]	66.5(7.4)	66.2(7.5)	66.7(7.5)	66.4(7.3)	65.9(7.3)	66.8(7.5) [†]
Women-n(%)	2844(50.2)	115(33.2)	1838(42.9) [†]	1694(49.5)	67(43.8)	1121(43.5) [†]	1628(48.8)	34(29.8)	1041(41.3) [†]	6166(49.6)	215(35.2) [*]	4000(42.6) [†]
Black-n(%)	2211(39.0)	106(30.6)	1202(28.1) [†]	1345(39.3)	48(31.4)	749(29.1) [†]	1310(39.3)	32(28.1)	728(28.9) [†]	4866(39.2)	186(30.3)	2679(28.6) [†]
Current smoker-n(%)	756(13.3)	91(26.3)	1149(26.8) [†]	457(13.4)	40(26.1)	659(25.6) [†]	457(13.7)	26(22.8)	652(25.9) [†]	1670(13.4)	157(25.6)	2460(26.2) [†]
CHD-n(%)	1140(20.3)	116(33.7)	1267(29.8) [†]	615(18.2)	43(28.1)	750(29.3) [†]	646(19.5)	35(30.7)	725(29.1) [†]	2401(19.5)	194(31.8)	2742(29.5) [†]
ASCVD [§] -n(%)	2027(35.8)	219(63.3)	2617(61.1) [†]	1160(33.9)	99(64.7)	1564(60.7) [†]	1202(36.1)	74(64.9)	1535(60.9) [†]	4389(35.3)	392(64.0)	5716(60.9) [†]
LVH by ECG-n(%)	500(10.5)	35(11.3)	538(13.7) [*]	305(10.7)	18(12.7)	355(15.1) [*]	285(10.3)	16(15.5)	360(15.7) [†]	1090(10.5)	69 (12.4)	1253(14.6) [†]
Blood pressure, mm Hg-mean(sd)												
SBP	146.4(15.6)	147.3(15.5)	145.6(15.7)	146.4(15.6)	148.5(15.3)	145.6(16.0)	146.7(15.1)	147.8(15.1)	145.4(15.7) [†]	146.5(15.4)	147.7(15.4)	145.5(15.8) [†]
DBP	83.0(9.9)	84.3(10.7)	84.5(10.0) [†]	82.7(10.1)	85.2(9.4)	84.4(10.1) [†]	83.0(9.9)	86.0(9.6)	84.4(10.0) [†]	82.9(10.0)	84.7(10.2)	84.5(10.0) [†]
Body mass index, kg/m ² – mean (sd)	31.1 (6.4)	31.1 (6.3)	28.6 (5.6) [†]	31.3 (6.2)	29.8 (5.4)	28.6 (5.6) [†]	31.2 (6.2)	29.8 (5.2)	28.6 (5.8) [†]	31.2 (6.3)	30.5 (5.9)	28.6 (5.7) [†]
Cholesterol, mg/dL-mean(sd)												
Total	215.6(45.8)	215.4(39.3)	216.8(41.2)	216.8(45.3)	217.6(37.5)	215.3(42.2)	215.2(44.4)	216.0(42.4)	215.2(39.7)	215.8(45.2)	216.0(39.4)	216.0(41.1)
HDL	44.8(13.2)	43.0(13.6)	48.3(15.8) [†]	45.2(14.0)	42.0(12.0)	48.7(14.9) [†]	44.6(13.0)	42.4(11.6)	47.7(15.2) [†]	44.8(13.4)	42.6(12.9)	48.3(15.4) [†]
LDL	134.2(38.3)	136.0(34.6)	137.5(35.9) [†]	134.8(37.7)	137.8(33.0)	136.2(36.2) [*]	134.0(36.6)	136.6(36.0)	137.4(35.6) [†]	134.3(37.7)	136.6(34.4)	137.1(35.9) [†]
Fasting glucose, mg/dL-mean(sd)	169.1(70.0)	105.4(12.7)	91.8(10.2) [†]	167.2(67.2)	105.8(12.4)	91.9(10.5) [†]	168.3(65.3)	105.5(13.3)	92.6(10.8) [†]	168.4(67.8)	105.5(12.7)	92.0(10.5) [†]

* p<.05 comparing across diabetes subgroups.

† p<.01 comparing across diabetes subgroups.

§ Atherosclerotic cardiovascular disease

|| Left ventricular hypertrophy: tall R wave on ECG with or without ST segment depression or T wave inversion

Inc DM= incident diabetes; DM=diabetes; SBP=systolic blood pressure; DBP=diastolic blood pressure

Table2. Mortality outcomes by treatment by diabetes status at 2 years among those with no diabetes at baseline

	Inc DM		No DM		Other Cause <2 Years n(%)	Unknown DM status		
	Death ≥2 Years n(%)	No Event ≥2 Years n(%)	Death ≥2 Years n(%)	No Event ≥2 Years n(%)		Death < 2 Years n(%)	Death ≥2 Years n(%)	No Event ≥2 Years n(%)
All-Cause Mortality								
Total	182(29.7)	431(70.3)	2477(26.4)	6903(73.6)		730(7.5)	2885(29.4)	6186(63.1)
Chlorthalidone	98(28.3)	248(71.7)	1142(26.7)	3140(73.3)		316(7.1)	1312(29.6)	2799(63.2)
Amlodipine	47(30.7)	106(69.3)	671(26.0)	1907(74.0)		198(7.6)	781(30.1)	1616(62.3)
Lisinopril	37(32.5)	77(67.5)	664(26.4)	1856(73.7)		216(7.8)	792(28.5)	1771(63.7)
		P = .67*		P=.84*				P=.59*
CVD Mortality								
Total	86(14.0)	527(86.0)	1063(11.3)	8317(88.7)	373(3.8)	357(3.6)	1228(12.5)	7843(80.0)
Chlorthalidone	42(12.1)	304(87.9)	479(11.2)	3803(88.8)	168(3.8)	148(3.3)	575(13.0)	3536(79.9)
Amlodipine	26(17.0)	127(83.0)	305(11.8)	2273(88.2)	94(3.6)	104(4.0)	307(11.8)	2090(80.5)
Lisinopril	18(15.8)	96(84.2)	279(11.1)	2241(88.9)	111(4.0)	105(3.8)	346(12.5)	2217(79.8)
		P=.30*		P=.84*				P=.60*
Non-CVD Mortality								
Total	92(15.0)	521(85.0)	1354(14.4)	8026(85.6)	393(4.0)	337(3.4)	1516(15.5)	7555(77.1)
Chlorthalidone	55(15.9)	291(84.1)	634(14.8)	3648(85.2)	162(3.7)	154(3.5)	680(15.4)	3431(77.5)
Amlodipine	18(11.8)	135(88.2)	347(13.5)	2231(86.5)	116(4.5)	82(3.2)	430(16.6)	1967(75.8)
Lisinopril	19(16.7)	95(83.3)	373(14.8)	2147(85.2)	115(4.1)	101(3.6)	406(14.6)	2157(77.6)
		P=.42*		P=.26*				P=.25*

*Contingency table analysis (3 x 2 or 3 x 4) of Treatment by outcome [Chi-square (2 or 6 df) or Fisher's exact]

Inc DM=incident diabetes; DM=diabetes

Table 3. Combined mortality and morbidity outcomes by treatment by diabetes status at 2 years among those with no diabetes at baseline

	Inc DM			No DM			Died or Lost <2 Years n(%)	Unknown		
	Event < 2 Years n(%)	Event ≥ 2 Years n(%)	No Event ≥2 Years n(%)	Event < 2 Years n(%)	Event ≥ 2 Years n(%)	No Event ≥2 Years n(%)		Event < 2 Years n(%)	Event ≥ 2 Years n(%)	No Event ≥2 Years n(%)
Non-fatal MI + Fatal CHD										
Total	6(1.6)	63(17.3)	296(81.1)	128(2.2)	655(11.0)	5148(86.8)	572(8.6)	137(2.1)	721(10.8)	5252(78.6)
Chlorthalidone	4(1.9)	29(14.0)	174(84.1)	61(2.3)	292(10.8)	2364(87.0)	248(8.2)	58(1.9)	333(11.0)	2379(78.8)
Amlodipine	0(0.0)	19(19.4)	79(80.6)	36(2.2)	193(11.8)	1407(86.0)	148(8.4)	36(2.0)	190(10.7)	1398(78.9)
Lisinopril	2(3.3)	15(25.0)	43(71.7)	31(2.0)	170(10.8)	1377(87.3)	176(9.3)	43(2.3)	198(10.5)	1475(78.0)
			P = .09*			P = .77*				P = .82*
CVD										
Total	14(3.8)	112(30.7)	239(65.5)	214(3.6)	1434(24.2)	4283(72.2)	572(8.6)	307(4.6)	1616(24.2)	4187(62.7)
Chlorthalidone	9(4.4)	61(29.5)	137(66.2)	95(3.5)	663(24.4)	1959(72.1)	248(8.2)	126(4.2)	742(24.6)	1902(63.0)
Amlodipine	1(1.0)	31(31.6)	66(67.4)	59(3.6)	413(25.2)	1164(71.2)	148(8.4)	84(4.7)	426(24.0)	1114(62.9)
Lisinopril	4(6.7)	20(33.3)	36(60.0)	60(3.8)	358(22.7)	1160(73.5)	176(9.3)	97(5.1)	448(23.7)	1171(61.9)
			P = .37*			P = .53*				P = .57*
Stroke										
Total	5(1.4)	38(10.4)	322(88.2)	56(0.9)	458(7.7)	5417(91.3)	572(8.6)	97(1.5)	500(7.5)	5513(82.5)
Chlorthalidone	4(1.9)	17(8.2)	186(89.9)	22(0.8)	210(7.7)	2485(91.5)	248(8.2)	39(1.3)	232(7.7)	2499(82.8)
Amlodipine	1(1.0)	15(15.3)	82(83.7)	13(0.8)	128(7.8)	1495(91.4)	148(8.4)	27(1.5)	125(7.1)	1472(83.1)
Lisinopril	0(0.0)	6(10.0)	54(90.0)	21(1.3)	120(7.6)	1437(91.1)	176(9.3)	31(1.6)	143(7.6)	1542(81.5)
			P = .33*			P = .48*				P = .72*
Heart Failure										
Total	4(1.1)	38(10.4)	323(88.5)	52(0.9)	498(8.4)	5381(90.7)	572(8.6)	110(1.7)	569(8.5)	5431(81.3)
Chlorthalidone	1(0.5)	27(13.0)	179(86.5)	17(0.6)	230(8.5)	2470(90.9)	248(8.2)	46(1.5)	260(8.6)	2464(81.6)
Amlodipine	0(0.0)	6(6.1)	92(93.9)	18(1.1)	148(9.1)	1470(89.9)	148(8.4)	30(1.7)	162(9.1)	1432(80.8)
Lisinopril	3(5.0)	5(8.3)	52(86.7)	17(1.1)	120(7.6)	1441(91.3)	176(9.3)	34(1.8)	147(7.8)	1535(81.1)
			P = .02*, †			P = .21*				P = .61*
ESRD										
Total	0(0.0)	10(1.6)	603(98.4)	1(0.01)	91(1.0)	9288(99.0)	730(7.5)	13(0.1)	148(1.5)	8910(90.9)
Chlorthalidone	0(0.0)	8(2.3)	338(97.7)	0(0.0)	40(0.9)	4242(99.1)	316(7.1)	10(0.2)	73(1.7)	4028(91.0)
Amlodipine	0(0.0)	0(0.0)	153(100.0)	0(0.0)	28(1.1)	2550(98.9)	198(7.6)	2(0.1)	42(1.6)	2353(90.7)
Lisinopril	0(0.0)	2(1.8)	112(98.3)	1(0.04)	23(0.9)	2496(99.1)	216(7.8)	1(0.04)	33(1.2)	2529(91.0)
			P = .16*			P = .61*				P = .16*

*Contingency table analysis (3 x 3 or 3 x 4) of Treatment by outcome [Chi-square (4 or 6 df) or Fisher's exact]

† P = .17 for 3 x 2 post two years ‡

Inc DM = incident diabetes; DM = diabetes; ESRD = end stage renal disease

Figure 1. Adjusted Kaplan-Meier plots by treatment group and diabetes status—chlorthalidone and amlodipine

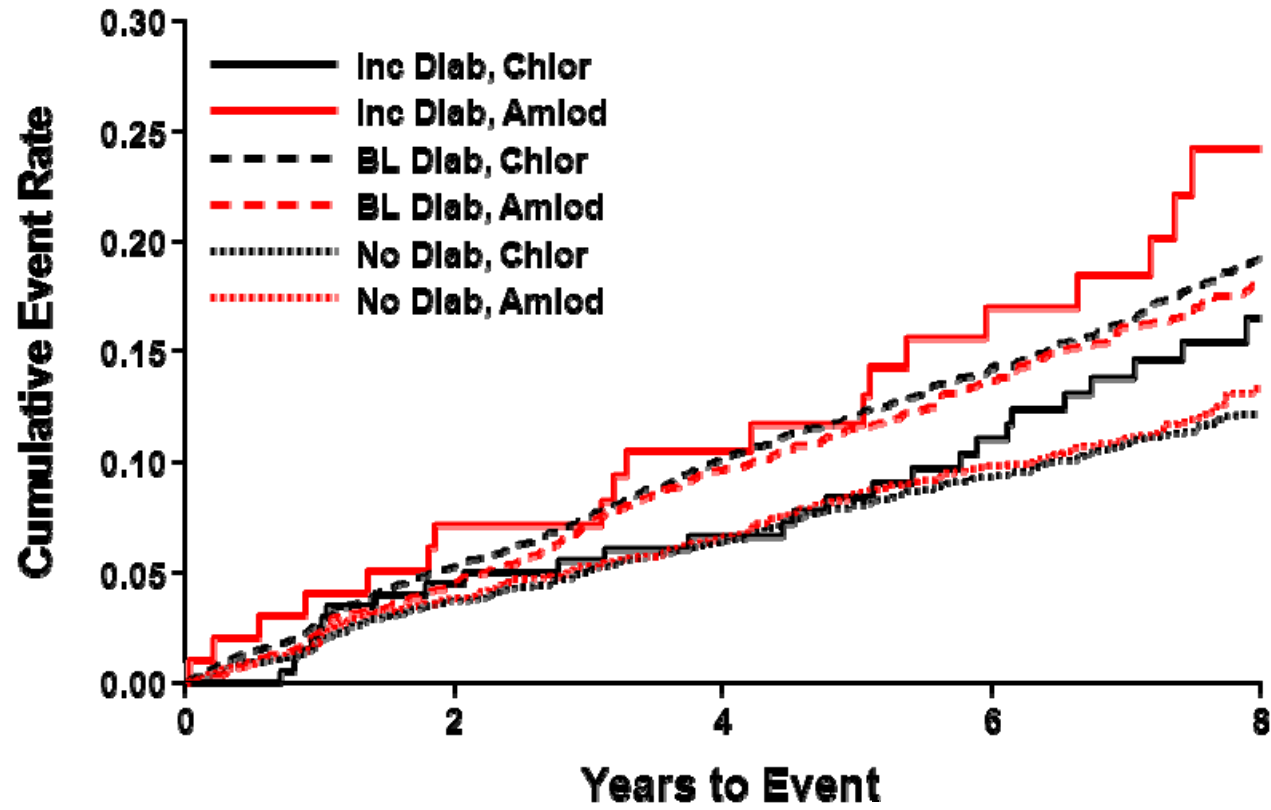


Figure 2. Adjusted Kaplan-Meier plots by treatment group and diabetes status—chlorthalidone and lisinopril

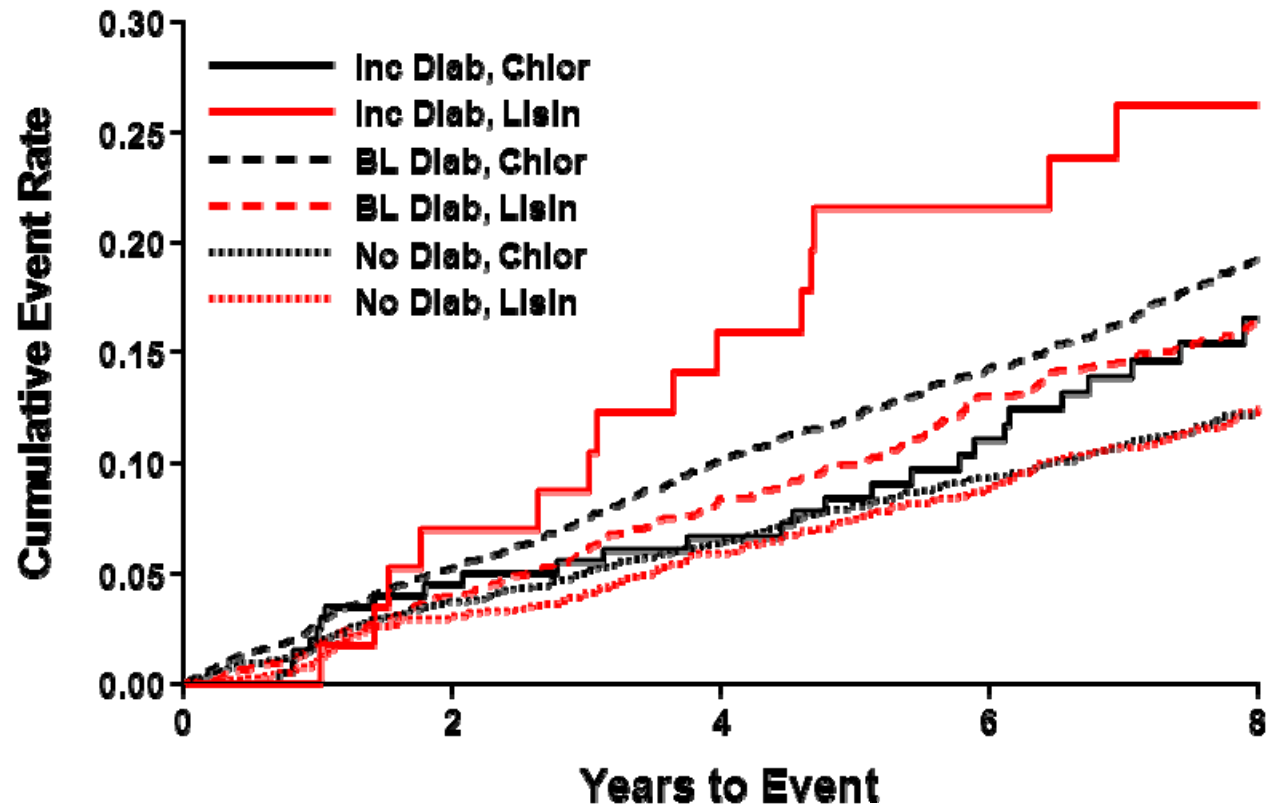
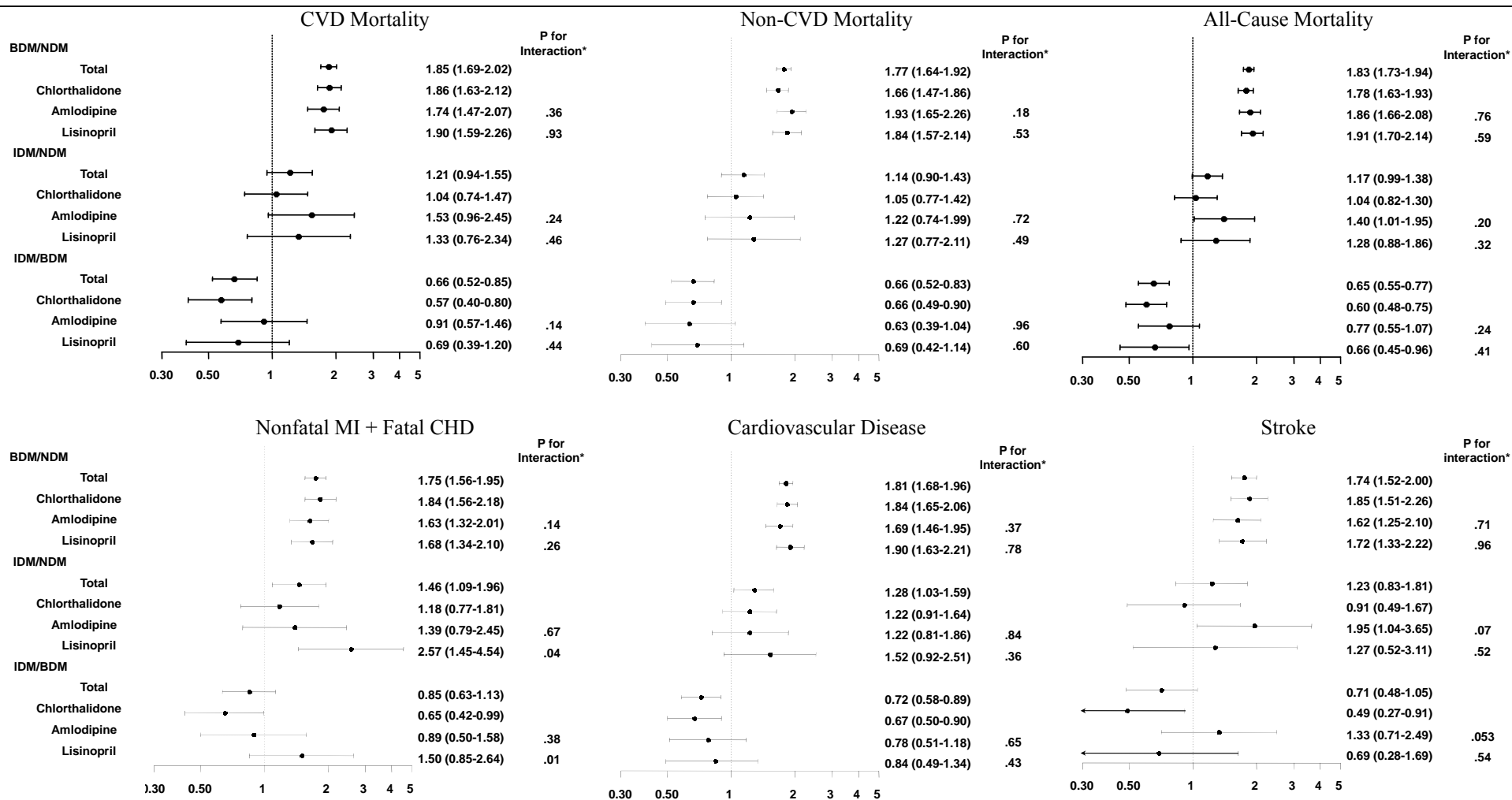


Figure 3. Forest plots – chlorthalidone, amlodipine, lisinopril – comparisons of diabetes groups



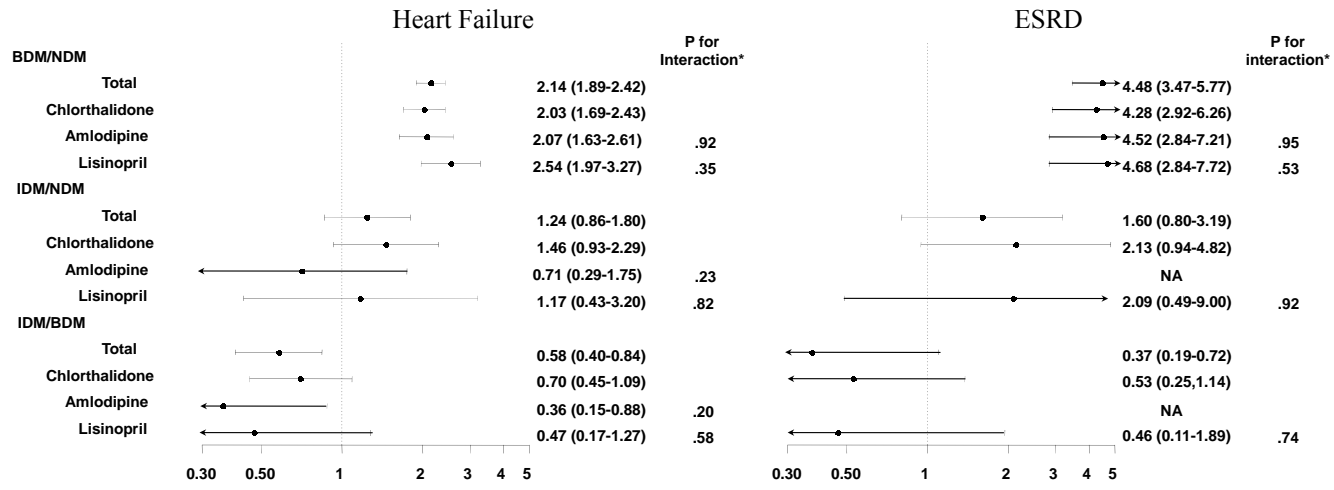


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Figure 1: Adjusted Kaplan-Meier plots by treatment group and diabetes status—chlorthalidone and amlodipine

Figure 2. Adjusted Kaplan-Meier plots by treatment group and diabetes status—chlorthalidone and lisinopril

Figure 3. Forest plots – chlorthalidone, amlodipine, lisinopril – comparisons of diabetes groups