Supplementary Online Content

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

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eMethods. Search Terms

("hypertension"[MeSH Terms] OR "hypertension"[All Fields]) AND (("antihypertensive agents"[Pharmacological Action] OR "antihypertensive agents"[MeSH Terms] OR "antihypertensive agents"[All Fields]) OR ("sodium chloride symporter inhibitors"[Pharmacological Action] OR "sodium chloride symporter inhibitors"[MeSH Terms] OR "sodium chloride symporter inhibitors"[All Fields]) OR "thiazide diuretics"[All Fields] OR ("adrenergic beta-antagonists"[Pharmacological Action] OR "adrenergic beta-antagonists"[MeSH Terms] OR "adrenergic beta-antagonists"[All Fields]) OR ("angiotensin-converting enzyme inhibitors"[Pharmacological Action] OR "angiotensin-converting enzyme inhibitors"[MeSH Terms] OR "angiotensin-converting enzyme inhibitors"[All Fields]) OR ("angiotensin receptor antagonists"[Pharmacological Action] OR "angiotensin receptor antagonists"[MeSH Terms] OR "angiotensin receptor antagonists"[All Fields]) OR ("calcium channel blockers"[Pharmacological Action] OR "calcium channel blockers"[MeSH Terms] OR "calcium channel blockers"[All Fields]) OR ("vasodilator agents"[Pharmacological Action] OR "vasodilator agents"[MeSH Terms] OR "vasodilator agents"[All Fields])) AND ((Controlled Clinical Trial[ptyp] OR Randomized Controlled Trial[ptyp]) AND "humans"[MeSH Terms] AND "adult"[MeSH Terms]) AND ("1990/01/01"[PDAT] : "2030/12/31"[PDAT])

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eTable 1. Cardiovascular Events and Outcomes by Randomized Treatment

Study	Sample Size	Follow-Up Time	Treatment	Cardiovascular Events				Age	Male, %	Region
				Death	MI	Stroke	CABG/PCI			
DEMAND, 2011[1]	126	3 years	ACEi/DH CCB*	0	-	-	-	60.2	61.9	Italy Slovenia
	127		ACEi	0	-	-	-	61.9	64.6	
	127		Placebo	2	-	-	-	60.4	69.3	
FEVER, 2005[2]	4841	40 months	DH CCB	73	-	177	4	61.5	61.8	China
	4870		Placebo	101	-	251	11	61.5	60.5	
MRC, 1992[3]	1081	5.8 years	Diuretics	66	-	45	-	70	42.0	UK
	1102		BB	95	-	56	-	70	41.4	
	2213		Placebo	180	-	134	-	70	41.8	
SHEP, 1991[4]	2365	4.5 years	Diuretics	90	50	96	49	71.6	43.7	US
	2371		Placebo	112	74	149	69	71.5	42.7	
STOP, 1991[5]	812	25 months	BB/Diuretics	36	19	26	-	75.6	37	Sweden
	815		Placebo	63	22	41	-	75.7	37	
Syst-China, 1998[6]	1253	2 years	DH CCB	33	4	35	-	66.4	63.6	China
	1141		Placebo	44	4	41	-	66.7	65	
Syst-Eur, 1997[7]	2398	2 years	DH CCB	59	26	34	-	70.3	32.5	Europe
	2297		Placebo	77	31	57	-	70.2	33.8	
Sun, Ming, 1997[8]	1040	10 years	DH CCB	-	-	37	-	51.8	53.0	China
	1040		Placebo	-	-	79	-			
Sun, Z. Q, 2010[9]	2530	15 months	ACEi/Diuretics/DH CCB	-	-	24	-	56.4	43.8	China
	2454		Education	-	-	52	-	56.2	41.8	
HYVET Pilot, 2003[10]	426	13 months	Diuretics	23	-	-	-	83.8	37.1	Europe
	431		ACEi	22	-	-	-	83.7	36.0	
	426		Standard	19	-	-	-	83.8	36.6	
UKPDS, 1998[11,12]	400	9 years	ACEi	-	61	21	-	56.3	51.0	UK
	358		BB	-	46	17	-	56	57.0	
	390		Standard	-	69	34	-	56.5	58.0	
ABCD, 1998[13]	235	67 months	DH CCB	10	22	11	-	57.2	68.1	US
	235		ACEi	5	5	7	-	57.7	66.8	
ACCOMPLISH, 2008[14]	5744	3 years	ACE/DH CCB	107	125	112	334	68.4	60.0	US Europe
	5762		ACE/Diuretics	134	159	133	386	68.3	61.0	
ALLHAT, 2002[15]	15255	4.9 years	Diuretics	992	-	675	1113	66.9	53.0	US
	9048		DH CCB	592	-	377	725	66.9	52.7	
	9054		ACEi	609	-	457	718	66.9	53.8	
ASCOT, 2005[16]	9639	5.5 years	DH CCB	263	429	327	167	63	77.0	Europe

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	9618		BB	342	474	422	214	63	77.0	

BENEDICT-B, 2011[17]	138	4.5 years	ACEi/Non-DH CCB	2	2	4	6	62.3	75.4	Italy
	143		ACEi	7	1	4	7	62.4	72.0	
COLM, 2014[18]	2568	3.3 years	DH CCB/ARB	13	9	60	-	73.6	51.5	Japan
	2573		Diuretics/ARB	18	16	62	-	73.6	51.7	
CONVINCE, 2003[19]	8179	3 years	Non-DH CCB	152	133	133	-	65.6	43.8	Multiple
	8297		BB/Diuretics	143	128	166	-	65.6	46.2	
ELSA, 2002[20]	1157	4 years	BB	8	17	14	-	55.9	55.4	Europe
	1177		DH CCB	4	18	9	-	56.1	54.2	
FACET, 1998[21]	189	3.5 years	ACEi	-	10	4	7	62.8	63.5	Italy
	191		DH CCB	-	13	10	8	63.3	55.5	
GLANT, 1995[22]	980	1 year	ACEi	1	1	5	-	60	44.4	Japan
	956		DH CCB	0	0	11	-	60	44.0	
INSIGHT, 2000[23]	3157	51 months	DH CCB	60	61	55	-	65	46.1	Europe
	3164		Diuretics	52	56	63	-		46.6	Israel
INVEST, 2003[24]	11267	2 years	Non-DH CCB	431	151	131	280	66	48.1	Multiple
	11309		BB	431	153	148	275	66.1	47.7	
J-MIND, 2001[25]	228	2 years	DH CCB	-	1	5	-	60.2	48.7	Japan
	208		ACEi	-	1	2	-	59.9	52.4	
JMIC-B, 2003[26]	828	3 years	DH CCB	6	16	16	81	65	67.6	Japan
	822		ACEi	6	13	16	75	64	70.0	
LIFE, 2002[27]	4605	4.8 years	ARB	204	198	232	261	66.9	46.0	US
	4508		BB	234	188	309	284	66.9	46.0	Europe
MAPHY, 1991[28]	1609	5 years	BB	29	82	21	6	40 to 64	100	Europe
	1625		Diuretics	34	109	18	8		100	
MIDAS, 1996[29]	442	3 years	DH CCB	3	6	6	11	58.2	79.9	US
	441		Diuretics	3	5	3	10	58.7	75.7	
MOSES, 2005[30]	681	2.5 years	ARB	-	-	236	-	67.7	53.6	Germany
	671		DH CCB	-	-	134	-	68.1	54.8	Austria
NAGOYA HEART, 2012[31]	575	3.2 years	ARB	-	7	13	29	63	66.0	Japan
	575		DH CCB	-	3	16	26	63	66.0	
NICS-EH, 1999[32]	204	5 years	DH CCB	2	2	1	-	69.7	40.2	Japan
	210		Diuretics	0	2	0	-	69.9	26.2	
NORDIL, 2000[33]	5410	4.5 years	Non-DH CCB	-	183	159	-	60.5	48.5	Sweden
	5471		Diuretics/BB	-	157	196	-	60.3	48.7	Norway
OSCAR, 2012[34]	578	3 years	ARB	-	-	24	-	73.6	43.9	Japan
	586		ARB/DH CCB	-	-	15	-	73.6	44.5	
PATE, 2000[35]	699	3 years	ACEi	-	1	11	-	70	38.3	Japan
	1049		DH CCB	-	5	17	-	69	43.3	

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SHELL, 2003[36]	940	32 months	Diuretics	13	14	38	4	72.4	37.8	Italy
	942		DH CCB	16	12	37	2	72.3	39.6	
STOP-2, 1999[37]	2213	4 years	Diuretics/BB	221	154	237	-	76	32.0	Sweden
	2205		ACEi	226	139	215	-	76.1	33.7	
	2196		DH CCB	212	179	207	-	75.9	34.0	
VALUE, 2004[38]	7649	4.2 years	ARB	304	369	322	-	67.2	57.6	Multiple
	7596		DH CCB	304	313	281	-	67.3	57.5	
VART, 2011[39]	510	3.4 years	ARB	0	2	10	-	60	56.9	Japan
	511		DH CCB	0	1	10	-	60	57.5	
VHAS, 1997[40]	707	2 years	Diuretics	4	5	4	3	53.9	50.1	Italy
	707		Non-DH CCB	5	5	3	4	54.5	47.8	
SANBPS, 2003[41]	3044	4.1 years	ACEi	84	50	91	-	72	50	Australia
	3039		Diuretics	82	71	94	-	71.9	48	
CTHPCETG, 2011[42]	1110	3.6 years	ARB	-	-	17	-	63	51.0	Japan
	1089		BB	-	-	27	-	63.2	50.5	
	1094		Diuretics	-	-	12	-	63.1	50.5	
E-COST, 2005[43]	1053	3.1 years	ARB	0	10	47	-	-	44.5	Japan
	995		Conventional	0	23	77	-	-	51.8	
HYVET, 2014[44]	1922	1.8 years	ACE/Diuretics	88	9	23	-	83.5	39.5	Multiple
	1900		Placebo	110	11	28	-			
CAPPP, 1999[45]	5492	6.1 years	ACEi	70	137	173	-	52.4	54.9	Sweden
	5493		BB/Diuretics	81	128	127	-	52.7	52.0	
SCOPE, 2003[46]	2477	3.7 years	ARB	145	54	68	-	76.4	35.2	Europe
	2460		Placebo	152	47	93	-	76.4	35.8	
HIJ-CREATE, 2009[47]	1024	4.2 years	ARB	28	29	45	256	65.0	81.8	Japan
	1025		ACEi	25	26	49	271	64.5	78.6	

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; DH CCB, dihydropyridine calcium channel blocker; nDH CCB: BB, beta blocker; ARB, angiotensin receptor blocker; MI, myocardial infarction; CABG, coronary artery bypass surgery; PCI, percutaneous coronary intervention.

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eTable 2. Absolute Risk Differences of Cardiovascular Events Comparing Each Type of Blood Pressure–Lowering Drug to Placebo From Network Meta-analysis

Drug	Cardiovascular Death	Myocardial Infarction	Stroke	Revascularization	Overall
ACEi vs. placebo	-0.005 (-0.027, 0.016)	**-0.024 (-0.036, -0.011)**	-0.035 (-0.070, 0.001)	**-**	-0.037 (-0.082, 0.009)
DH CCB vs. placebo	**-0.007 (-0.011, -0.003)**	-0.001 (-0.005, 0.003)	**-0.016 (-0.025, -0.006)**	-0.001 (-0.003, 0.0001)	-0.013 (-0.031, 0.005)
BB vs. placebo	0.005 (-0.015, 0.025)	-0.048 (-0.100, 0.003)	-0.020 (-0.048, 0.008)	-	-0.042 (-0.123, 0.039)
ARB vs. placebo	-0.000 (-0.002, 0.002)	-0.005 (-0.021, 0.011)	-0.020 (-0.041, 0.002)	-	-0.028 (-0.063, 0.007)
Diuretics vs. placebo	-0.010 (-0.022, 0.003)	**-0.010 (-0.019, -0.001)**	**-0.021 (-0.031, -0.011)**	-0.008 (-0.017, 0.0005)	-0.028 (-0.061, 0.005)

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; DH CCB, dihydropyridine calcium channel blocker; BB, beta blocker; ARB, angiotensin receptor blocker.

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eTable 3. Inconsistency Test Between Direct and Indirect Treatment Comparisons in Mixed Treatment Comparisons

Cardiovascular Mortality							
Side	**Direct**		**Indirect**		**Difference**		**p>z**
	Coefficient	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**	
ACEi placebo	0.04	0.30	-0.23	0.07	0.28	0.31	0.37
DH CCB placebo	-0.33	0.10	-0.18	0.07	-0.15	0.12	0.22
BB placebo	0.05	0.12	-0.03	0.08	0.08	0.15	0.57
ARB placebo	-0.05	0.11	-0.23	0.09	0.18	0.14	0.20
Diuretics placebo	-0.20	0.09	-0.30	0.08	0.10	0.13	0.42
Myocardial Infarction							
Side	**Direct**		**Indirect**		**Difference**		**p>z**
	Coefficient	SE	Coefficient	SE	Coefficient	SE	
ACEi placebo	-0.15	0.18	-0.41	0.13	0.26	0.22	0.24
DH CCB placebo	-0.20	0.26	-0.23	0.11	-0.03	0.28	0.91
BB placebo	-0.29	0.19	-0.19	0.13	-0.10	0.23	0.67
ARB placebo	-0.11	0.19	-0.12	0.13	0.01	0.23	0.95
Diuretics placebo	-0.39	0.20	-0.12	0.12	-0.27	0.23	0.25
Stroke							
Side	**Direct**		**Indirect**		**Difference**		**p>z**
	Coefficient	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**	
ACEi placebo	-0.54	0.30	-0.40	0.10	-0.15	0.32	0.56
DH CCB placebo	-0.46	0.11	-0.54	0.11	0.09	0.15	0.57
BB placebo	-0.29	0.17	-0.18	0.12	-0.12	0.21	0.58
ARB placebo	-0.43	0.15	-0.33	0.11	-0.09	0.19	0.63
Diuretics placebo	-0.41	0.14	-0.50	0.12	0.09	0.19	0.64
Revascularization							
Side	**Direct**		**Indirect**		**Difference**		**p>z**
	Coefficient	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**	
DH CCB placebo	-1.01	0.58	-0.27	0.20	-0.73	0.62	0.24
Diuretics placebo	-0.34	0.19	-1.07	0.59	0.73	0.62	0.24
Overall Cardiovascular Events							
Side	**Direct**		**Indirect**		**Difference**		**p>z**
	Coefficient	**SE**	**Coefficient**	**SE**	**Coefficient**	**SE**	
ACEi placebo	-0.18	0.18	-0.40	0.10	0.22	0.21	0.30
DH CCB placebo	-0.31	0.11	-0.31	0.10	-0.002	0.15	0.99
BB placebo	-0.19	0.15	-0.18	0.11	-0.01	0.18	0.97
ARB placebo	-0.30	0.15	-0.19	0.11	-0.11	0.18	0.56
Diuretics placebo	-0.26	0.13	-0.36	0.11	-0.10	0.17	0.56

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; DH CCB, dihydropyridine calcium channel blocker; BB, beta blocker; ARB, angiotensin receptor blocker.

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eTable 4. Bivariate Meta-regression on the 10 mm Hg Reduction of Blood Pressure and Change of Cardiovascular Events

10 mm Hg Systolic Blood Pressure Reduction	
Cardiovascular Events	**RR (95% CI)**
CVD mortality	**0.87 (0.77, 0.99)**
Myocardial infarction	0.95 (0.77, 1.17)
Stroke	**0.83 (0.72, 0.97)**
Revascularization	0.75 (0.50, 1.13)
Overall	**0.86 (0.78, 0.96)**
5 mm Hg Diastolic Blood Pressure Reduction	
Cardiovascular Events	**RR (95% CI)**
CVD mortality	**0.86 (0.74, 1.00)**
Myocardial infarction	0.95 (0.75, 1.21)
Stroke	**0.80 (0.67, 0.95)**
Revascularization	0.68 (0.42, 1.09)
Overall	**0.84 (0.74, 0.96)**

Abbreviation: RR, risk ratio.

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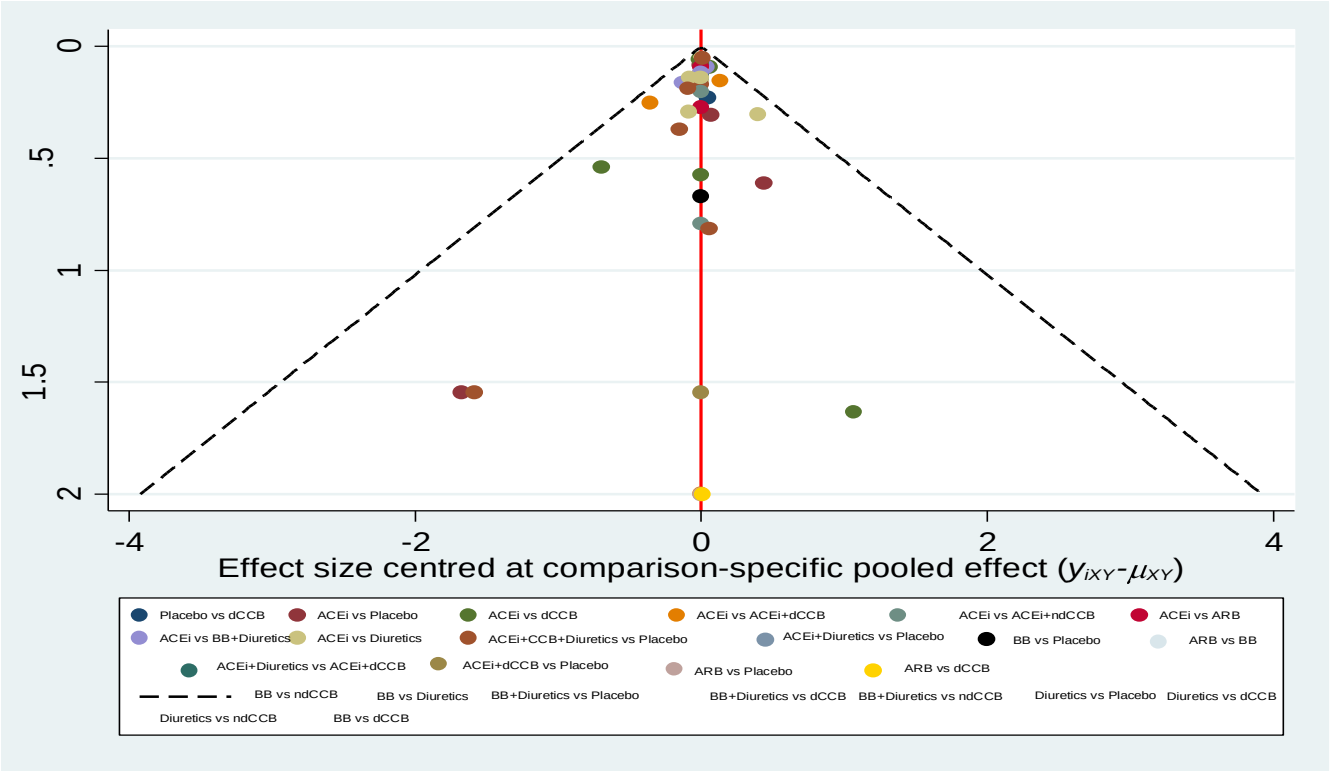
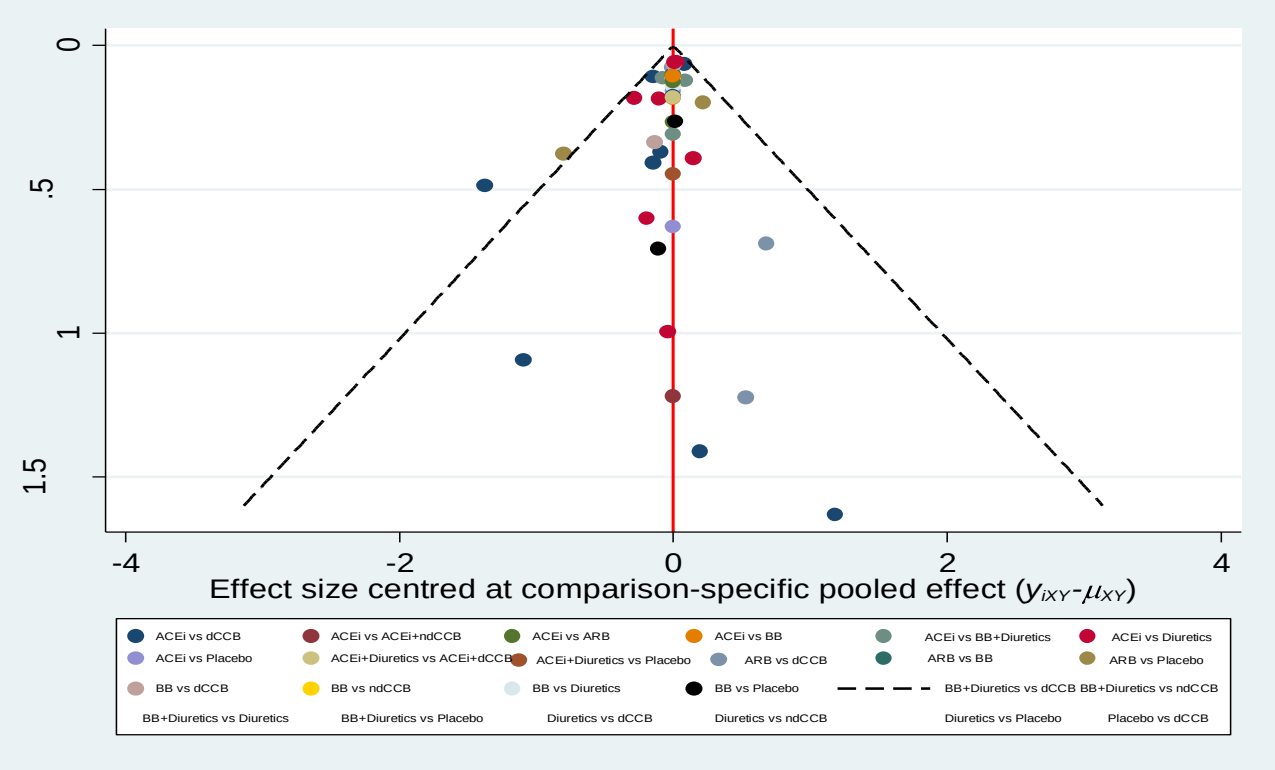
eFigure 1. Funnel Plots of Studies of Blood Pressure–Lowering Drugs and Effects of Prevention on Cardiovascular Death, Myocardial Infarction, Stroke, Revascularization, and Overall Cardiovascular Events

A. Cardiovascular death



B. Myocardial infarction



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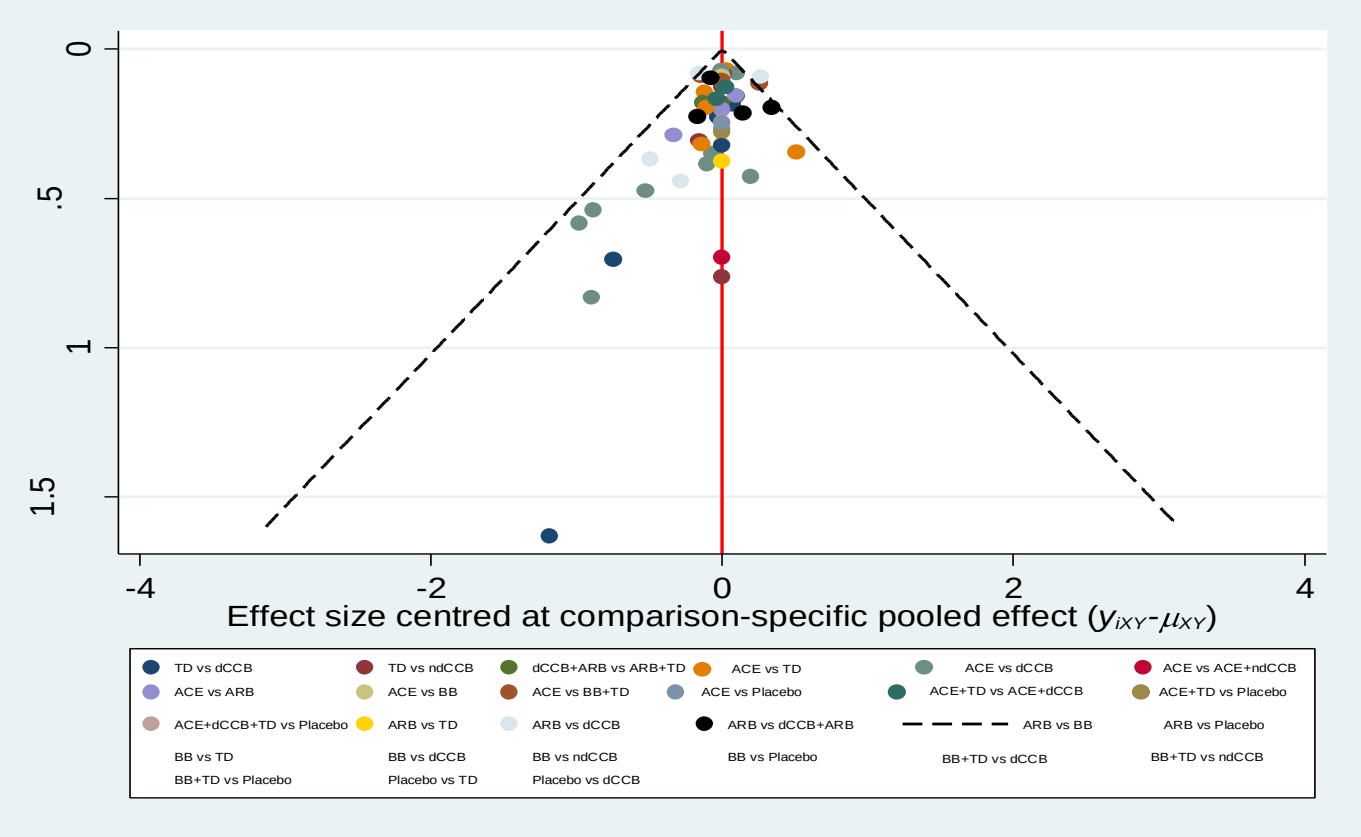
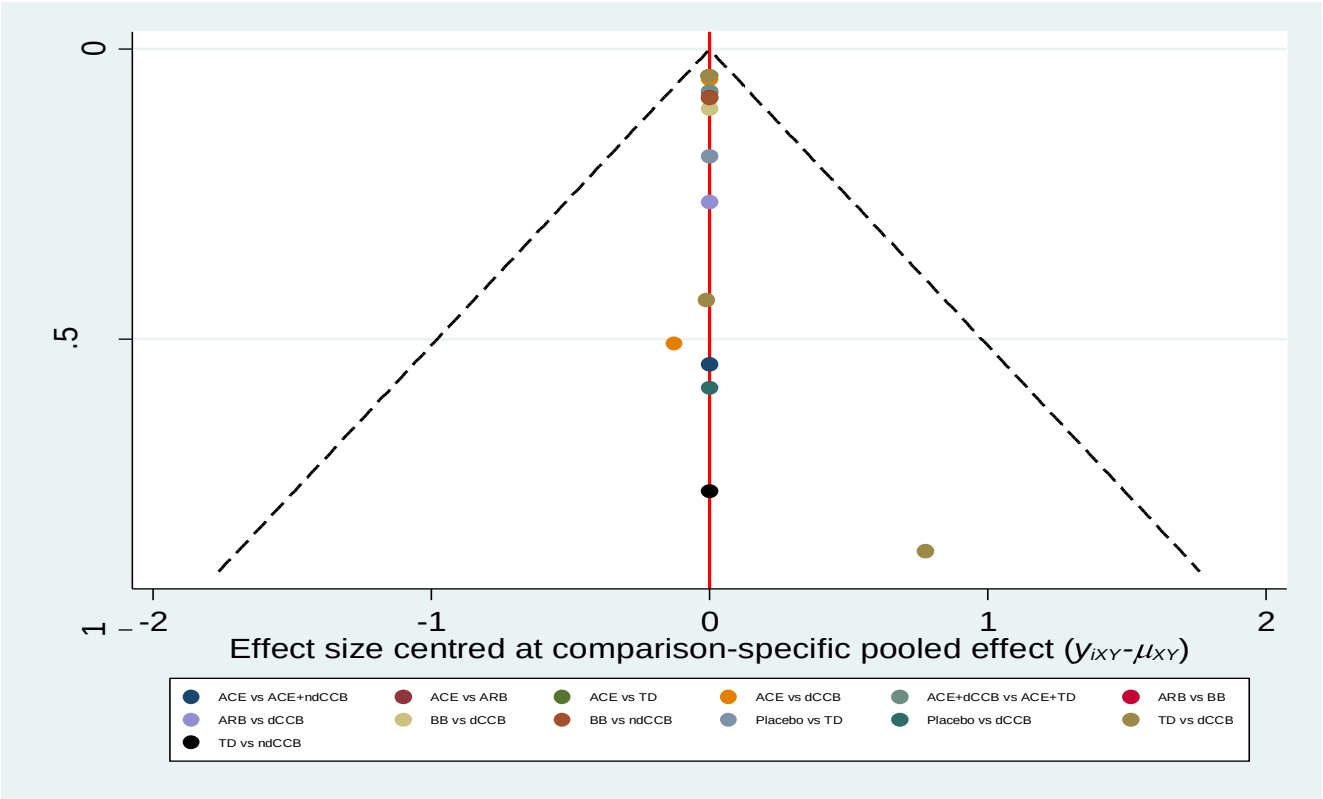
C. Stroke



D. Revascularization



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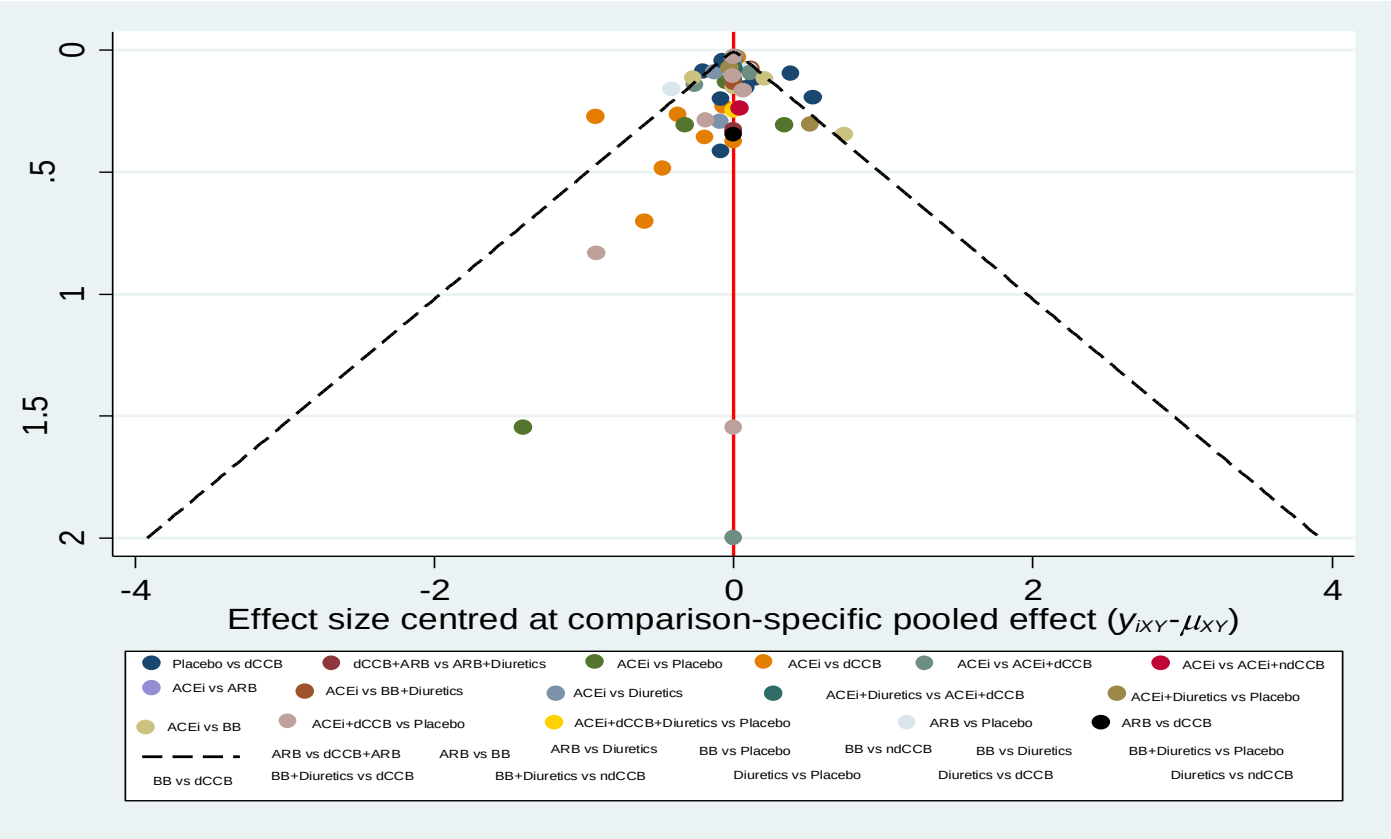
E. Overall cardiovascular events



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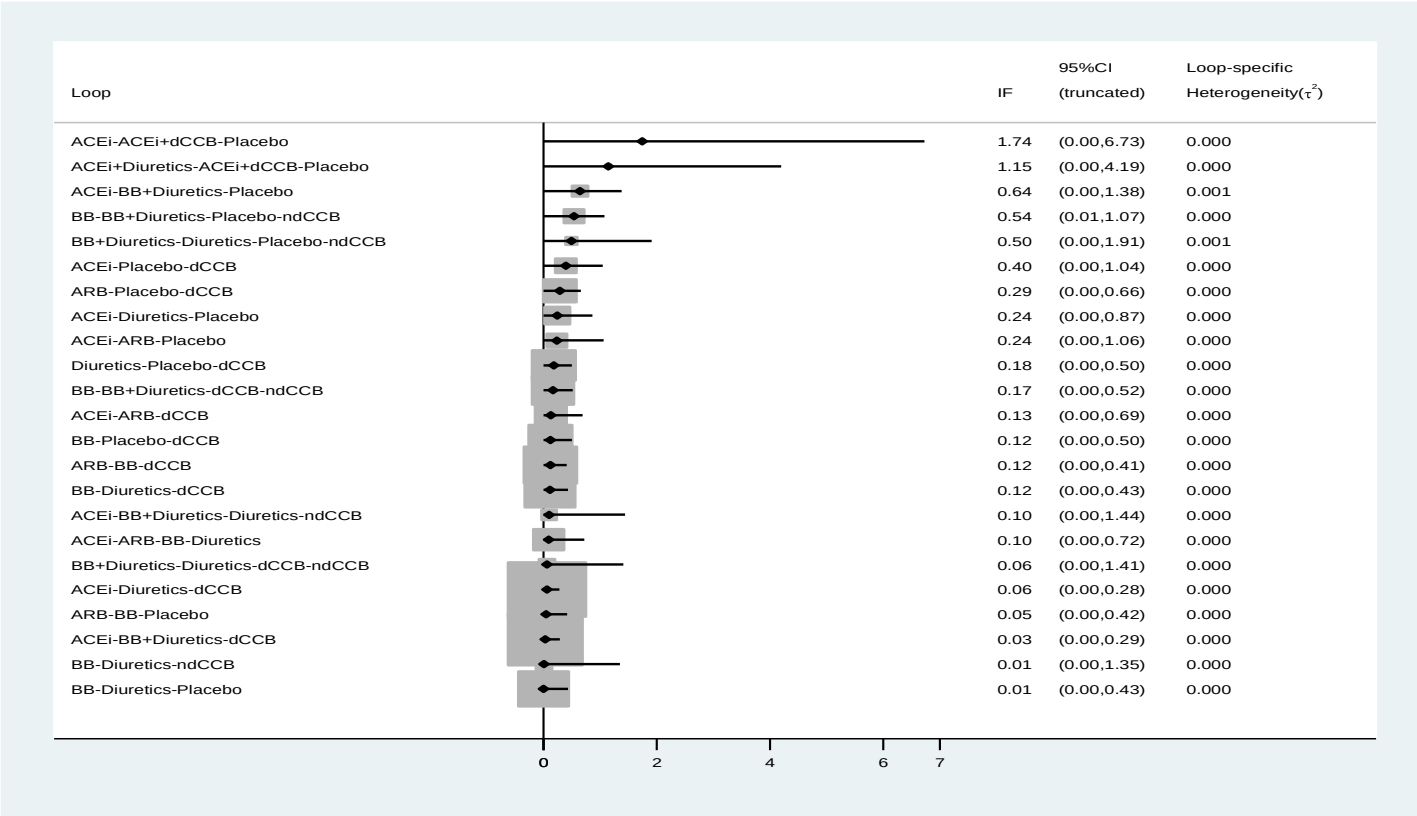
eFigure 2. Inconsistency Plots of Studies of Blood Pressure–Lowering Drugs and Effects of Prevention on Cardiovascular Death, Myocardial Infarction, Stroke, Revascularization, and Overall Cardiovascular Events

A. Cardiovascular death



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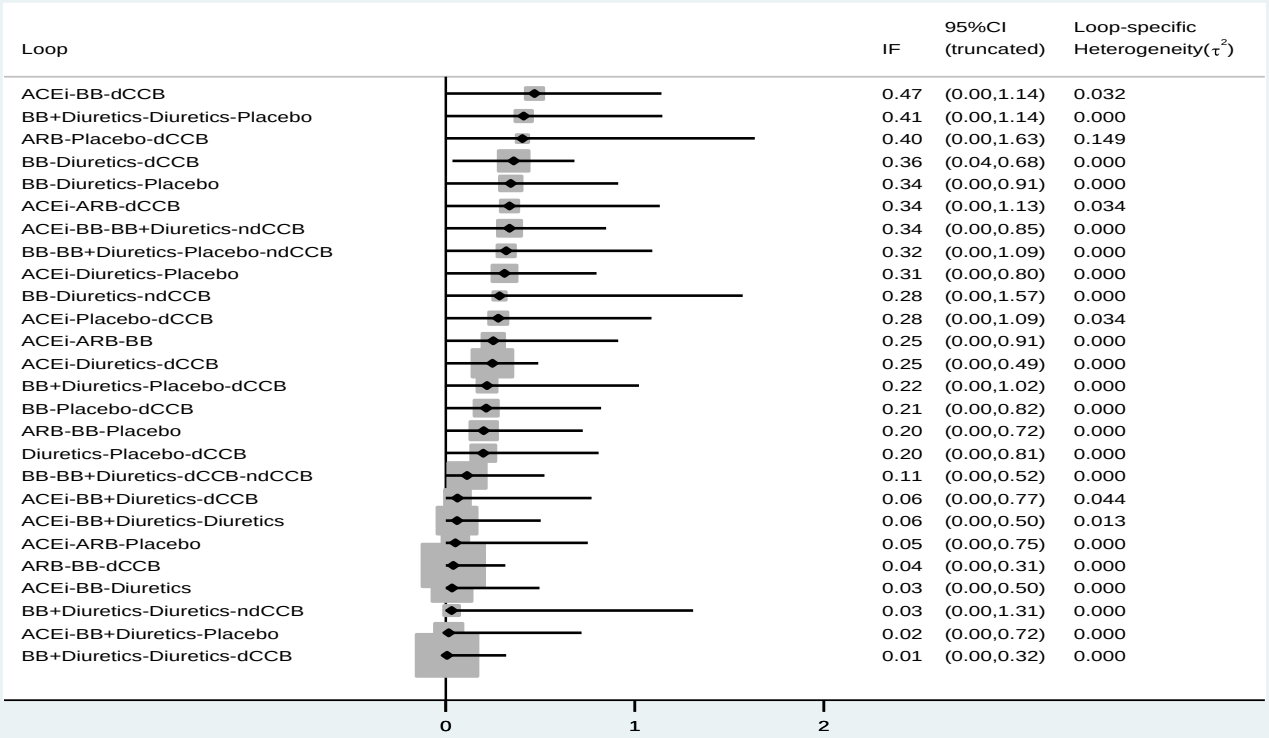
B. Myocardial infarction



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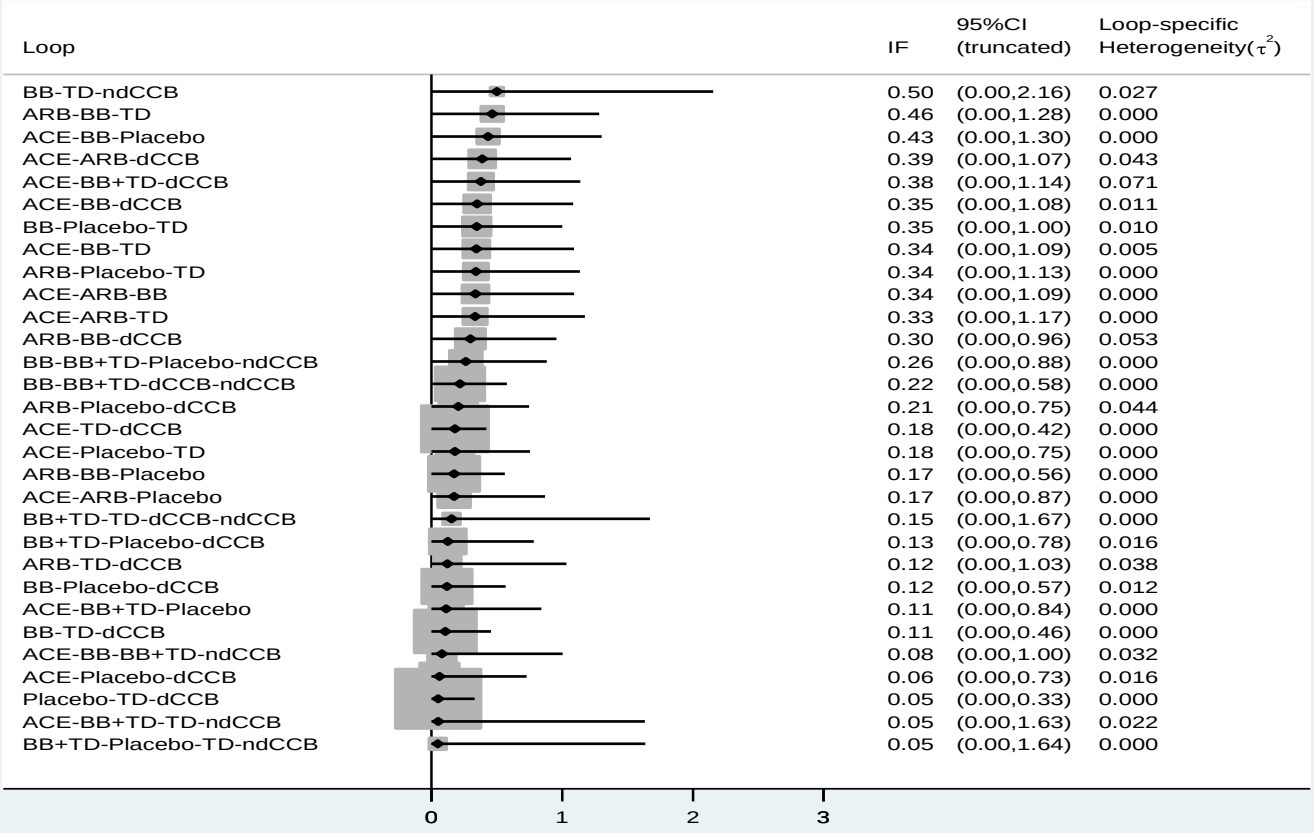
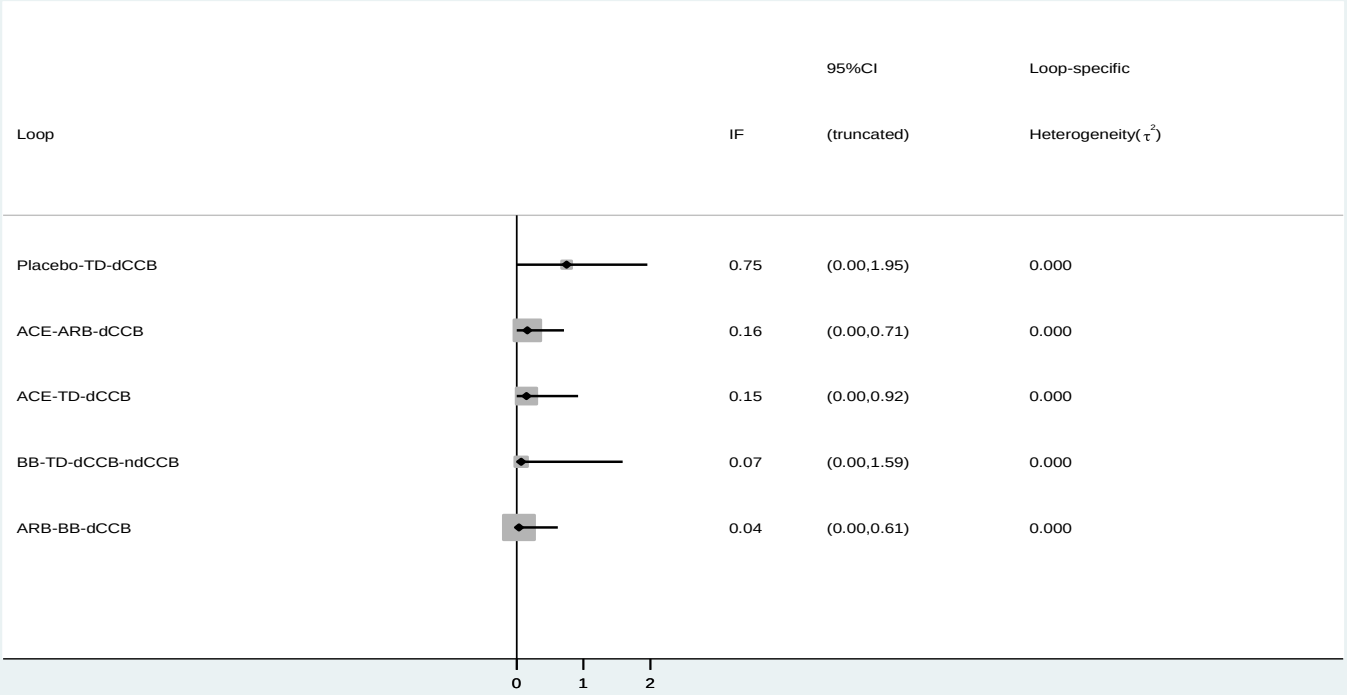
C. Stroke



D. Revascularization



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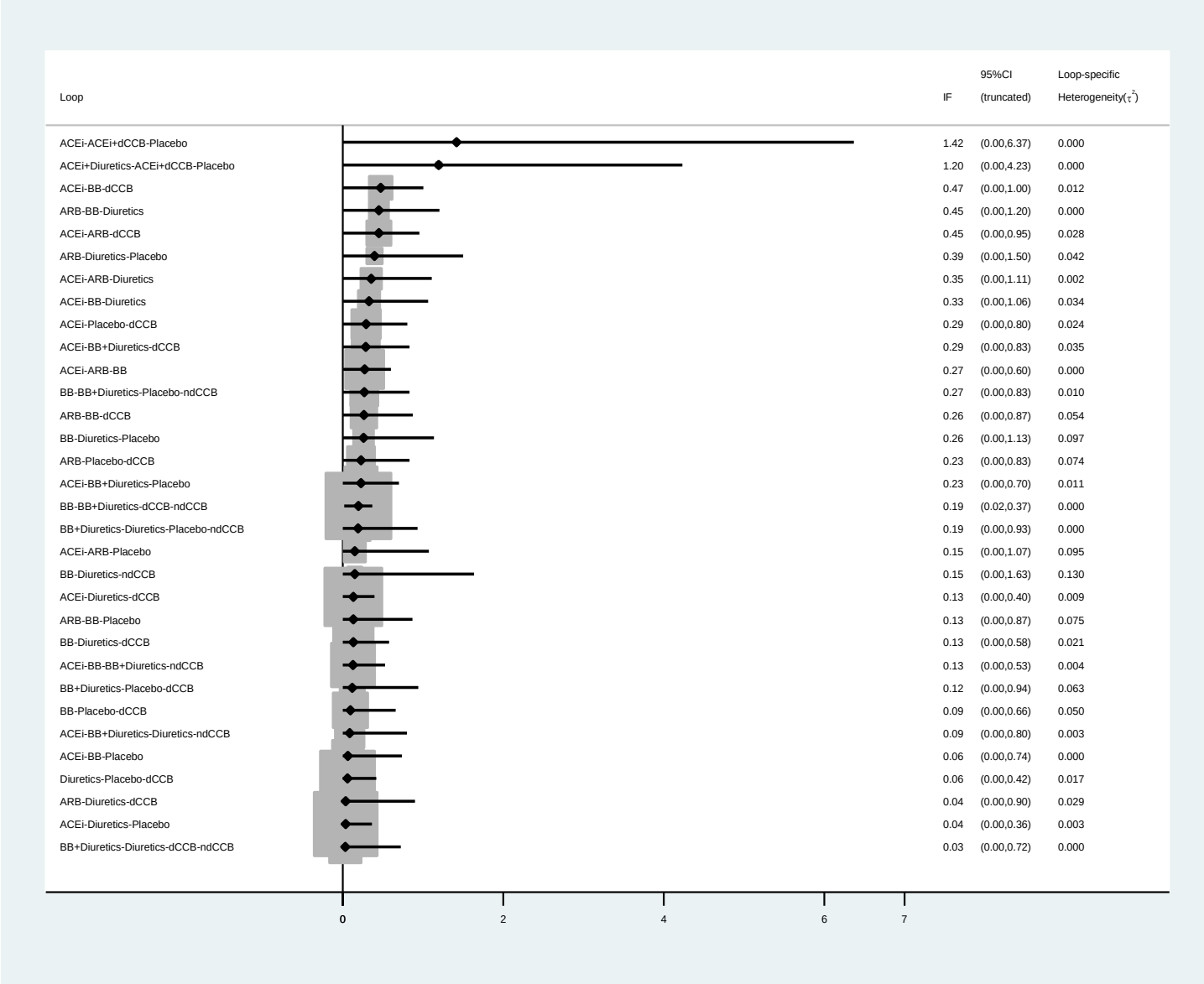
E. Overall cardiovascular events



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