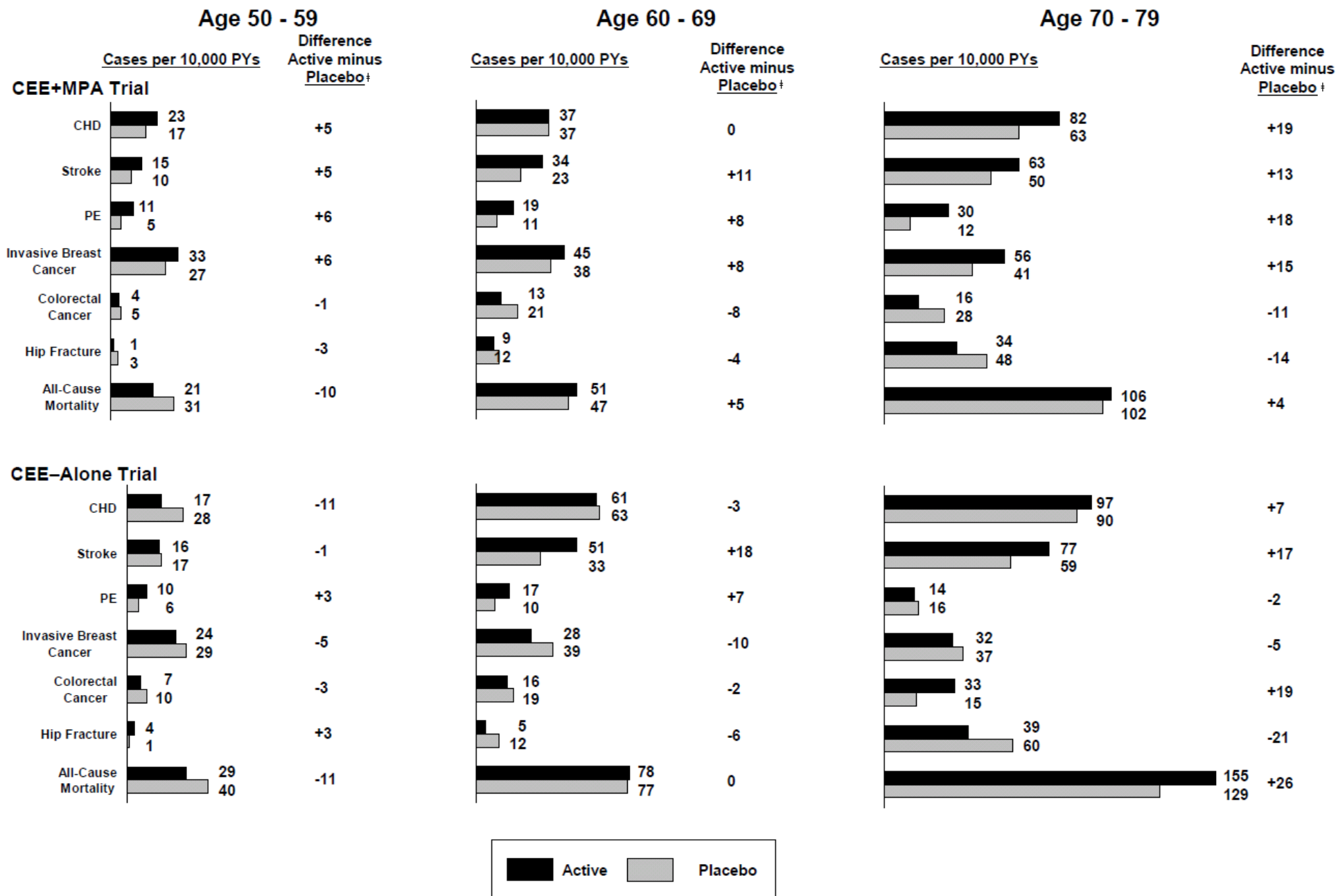
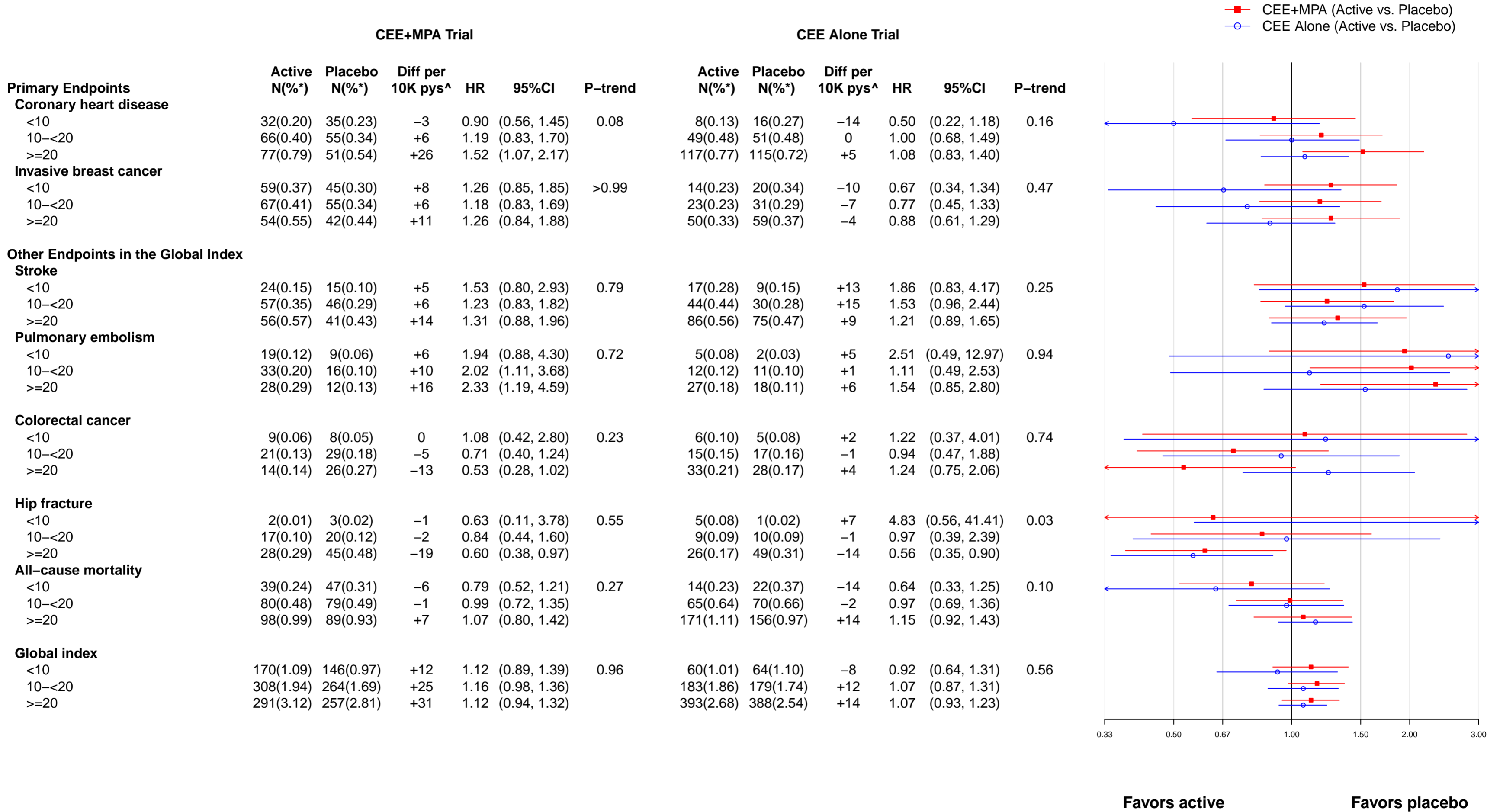


Appendix eFigure 1. Absolute Risks and Risk Differences for Outcomes in the Trials (Intervention Phase by Age Group)



† Difference in estimated absolute excess risk (active minus placebo). Numbers may not add up precisely due to rounding error.

Appendix eFigure 2. Absolute Risks and Hazard Ratios for Outcomes in the Trials (Intervention Phase by Time Since Menopause)



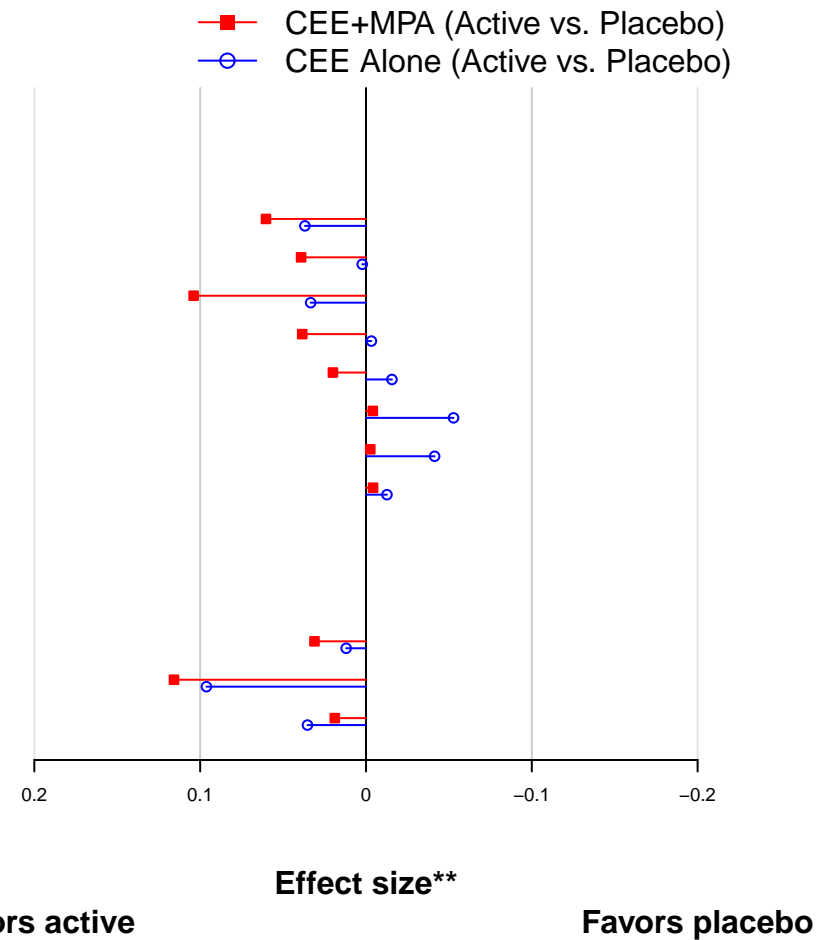
CEE indicates conjugated equine estrogens; and MPA, medroxyprogesterone acetate.

* Annualized percentage

^Difference in estimated absolute excess risk (active minus placebo) per 10,000 person years. Numbers may not add up precisely due to rounding error.

Appendix eFigure 3. Results for Other Health-Related Quality of Life Variables in the WHI Hormone Therapy Trials (Intervention Phase)

	CEE+MPA Trial			CEE Alone Trial		
	Active Mean(95%CI)	Placebo Mean(95%CI)	P-val	Active Mean(95%CI)	Placebo Mean(95%CI)	P-val
RAND-36*						
Physical functioning	82.6(82.3, 82.9)	81.8(81.5, 82.1)	<0.001	76.0(75.5, 76.4)	75.4(75.0, 75.8)	0.08
Role physical	77.4(76.7, 78.0)	76.2(75.5, 76.9)	0.02	69.0(68.0, 70.0)	68.9(68.0, 69.9)	0.91
Bodily pain	77.6(77.2, 78.0)	75.6(75.2, 76.1)	<0.001	69.8(69.2, 70.4)	69.1(68.5, 69.7)	0.10
General health	76.6(76.3, 76.9)	76.1(75.8, 76.4)	0.02	72.2(71.8, 72.6)	72.2(71.9, 72.6)	0.87
Vitality	65.2(64.9, 65.6)	64.9(64.6, 65.3)	0.22	60.9(60.5, 61.3)	61.1(60.7, 61.6)	0.45
Social Functioning	89.9(89.5, 90.3)	90.0(89.6, 90.4)	0.80	85.8(85.3, 86.4)	86.9(86.3, 87.4)	0.01
Role emotional	85.3(84.7, 85.9)	85.4(84.8, 86.0)	0.87	81.0(80.2, 81.8)	82.2(81.4, 83.0)	0.04
Mental health	80.7(80.4, 80.9)	80.7(80.5, 81.0)	0.79	78.5(78.2, 78.9)	78.7(78.3, 79.0)	0.54
Other						
Self-reported health^	2.27(2.26, 2.29)	2.29(2.28, 2.31)	0.06	2.53(2.51, 2.55)	2.54(2.52, 2.55)	0.56
Sleep disturbance#	6.13(6.05, 6.20)	6.51(6.44, 6.59)	<0.001	6.92(6.81, 7.02)	7.25(7.15, 7.36)	<0.001
Depressive symptoms@	2.21(2.16, 2.26)	2.25(2.20, 2.30)	0.25	2.58(2.51, 2.65)	2.66(2.59, 2.73)	0.09



CEE indicates conjugated equine estrogens; and MPA, medroxyprogesterone acetate.

* Scored from 0 (worst) to 100 (best).

^ Scored from 1 (best) to 5 (worst).

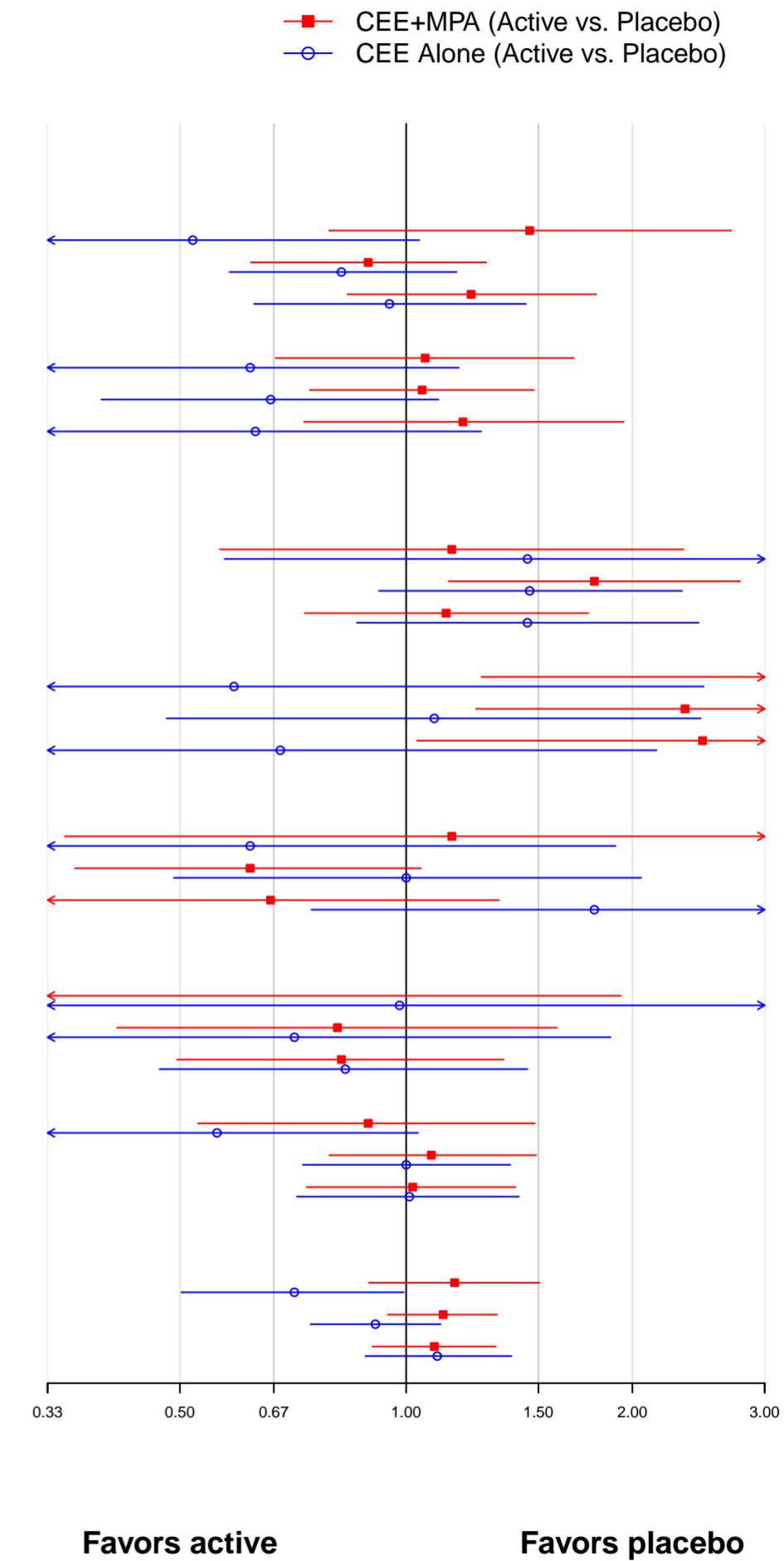
Scored from 0 (best) to 20 (worst).

@ Scored from 0 (best) to 18 (worst).

** Estimated Mean Difference at Year 1, adjusting for baseline, divided by the root-mean-square error. For all measures, the sign of the effect size has been flipped (if necessary) so that adverse effects (favors placebo) extend to the right and favorable effects (favors active) extend to the left.

Appendix eFigure 4. Results Among Women in the Trials with No Prior HT Use (Intervention Phase by Age Group)

	CEE+MPA Trial						CEE Alone Trial					
	Active N(%*)	Placebo N(%*)	Diff per 10K pys^	HR	95%CI	P-trend	Active N(%*)	Placebo N(%*)	Diff per 10K pys^	HR	95%CI	P-trend
Primary Endpoints												
Coronary heart disease												
50–59	25(0.21)	17(0.15)	+6	1.46	(0.79, 2.71)	0.50	12(0.19)	23(0.37)	–18	0.52	(0.26, 1.04)	0.96
60–69	59(0.36)	60(0.40)	–4	0.89	(0.62, 1.28)		59(0.69)	69(0.81)	–13	0.82	(0.58, 1.17)	
70–79	59(0.83)	49(0.71)	+12	1.22	(0.84, 1.79)		43(0.95)	46(0.99)	–4	0.95	(0.63, 1.44)	
Invasive breast cancer												
50–59	39(0.33)	35(0.31)	+2	1.06	(0.67, 1.67)	0.81	15(0.24)	24(0.39)	–15	0.62	(0.32, 1.18)	0.98
60–69	70(0.43)	61(0.41)	+2	1.05	(0.74, 1.48)		24(0.28)	36(0.42)	–14	0.66	(0.39, 1.10)	
70–79	36(0.50)	29(0.42)	+9	1.19	(0.73, 1.95)		13(0.28)	21(0.45)	–17	0.63	(0.32, 1.26)	
Other Endpoints in the Global Index												
Stroke												
50–59	17(0.14)	14(0.12)	+2	1.15	(0.57, 2.34)	0.83	11(0.18)	8(0.13)	+5	1.45	(0.57, 3.67)	0.69
60–69	58(0.36)	30(0.20)	+16	1.78	(1.14, 2.78)		44(0.51)	30(0.35)	+16	1.46	(0.92, 2.33)	
70–79	44(0.62)	38(0.55)	+7	1.13	(0.73, 1.75)		34(0.75)	24(0.51)	+23	1.45	(0.86, 2.45)	
Pulmonary embolism												
50–59	16(0.14)	4(0.04)	+10	3.77	(1.26, 11.29)	0.07	3(0.05)	5(0.08)	–3	0.59	(0.14, 2.49)	0.34
60–69	33(0.20)	13(0.09)	+12	2.35	(1.24, 4.47)		12(0.14)	11(0.13)	+1	1.09	(0.48, 2.47)	
70–79	18(0.25)	7(0.10)	+15	2.48	(1.03, 5.93)		5(0.11)	7(0.15)	–4	0.68	(0.22, 2.15)	
Colorectal cancer												
50–59	6(0.05)	5(0.04)	+1	1.15	(0.35, 3.78)	0.71	5(0.08)	8(0.13)	–5	0.62	(0.20, 1.90)	0.70
60–69	23(0.14)	34(0.23)	–9	0.62	(0.36, 1.05)		15(0.17)	15(0.17)	0	1.00	(0.49, 2.06)	
70–79	13(0.18)	19(0.27)	–9	0.66	(0.32, 1.33)		14(0.30)	8(0.17)	+13	1.78	(0.75, 4.25)	
Hip fracture												
50–59	1(0.01)	4(0.04)	–3	0.21	(0.02, 1.93)	0.87	1(0.02)	1(0.02)	0	0.98	(0.06, 15.67)	0.23
60–69	16(0.10)	18(0.12)	–2	0.81	(0.41, 1.59)		7(0.08)	10(0.12)	–4	0.71	(0.27, 1.87)	
70–79	29(0.41)	34(0.49)	–9	0.82	(0.50, 1.35)		22(0.48)	27(0.58)	–10	0.83	(0.47, 1.45)	
All-cause mortality												
50–59	28(0.24)	30(0.26)	–3	0.89	(0.53, 1.48)	0.14	16(0.26)	28(0.45)	–19	0.56	(0.30, 1.04)	0.73
60–69	85(0.52)	70(0.46)	+5	1.08	(0.79, 1.49)		76(0.87)	76(0.88)	–1	1.00	(0.73, 1.38)	
70–79	77(1.07)	73(1.04)	+3	1.02	(0.74, 1.40)		66(1.42)	67(1.42)	0	1.01	(0.72, 1.41)	
Global index												
50–59	125(1.08)	103(0.92)	+16	1.16	(0.89, 1.51)	0.58	57(0.93)	80(1.33)	–40	0.71	(0.50, 0.99)	0.49
60–69	304(1.93)	249(1.70)	+22	1.12	(0.94, 1.32)		188(2.27)	200(2.45)	–18	0.91	(0.75, 1.11)	
70–79	229(3.37)	204(3.07)	+30	1.09	(0.90, 1.32)		159(3.69)	149(3.35)	+34	1.10	(0.88, 1.38)	

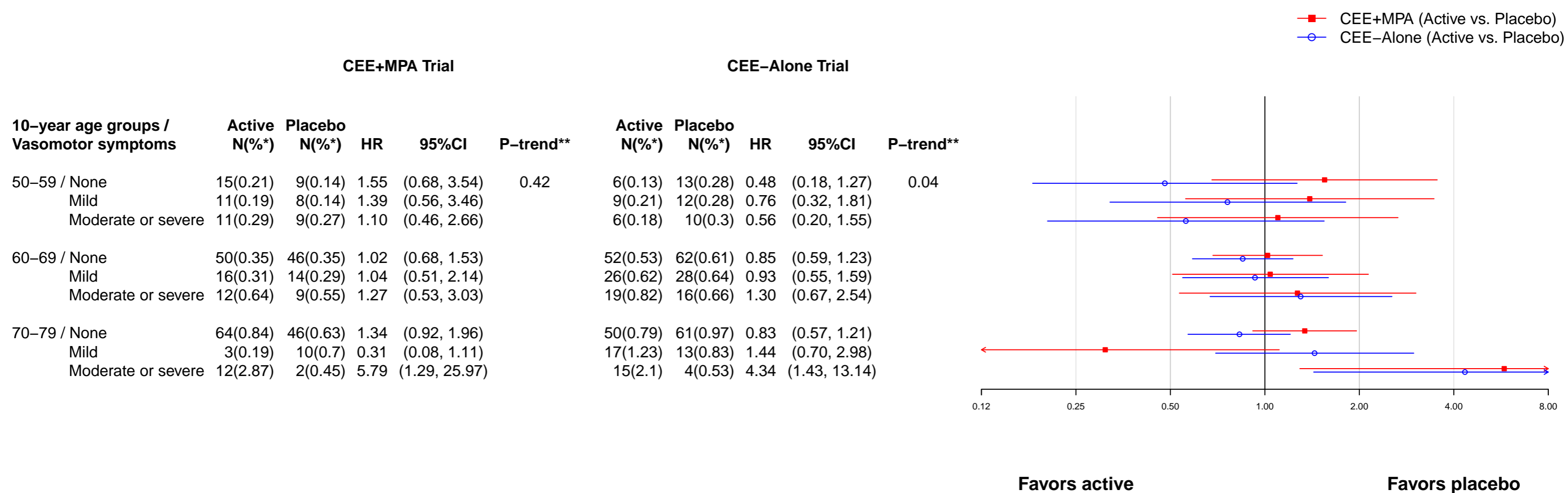


CEE indicates conjugated equine estrogens; and MPA, medroxyprogesterone acetate.

^ Difference in estimated absolute excess risk (active minus placebo) per 10,000 person years. Numbers may not add up precisely due to rounding error.

* Three-way trend test between randomization assignment, age group, and prior HT use

Appendix eFigure 5. CHD Results Among Women in the Trials (Intervention Phase, According to Vasomotor Symptoms and Age Group)



CEE indicates conjugated equine estrogens; and MPA, medroxyprogesterone acetate.

* Annualized percentage

** Three-way trend test between randomization assignment, age group, and vasomotor symptoms