

Supplementary Online Content

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

eTable 1: Mortality Outcomes in the Women’s Health Initiative Hormone Therapy Trials During Cumulative 18 Year Follow-Up¹

Outcomes / Age	Events from randomization through December 31, 2014							Events from randomization through December 31, 2014							Pooled			
	No. (Annualized rate, %)		Hazard Ratio ²			P ³	No. (Annualized rate, %)		Hazard Ratio ¹			P ²	P-het ⁴	Hazard Ratio				
	CEE+MPA	Placebo	(95% CI)				CEE	Placebo	(95% CI)					(95% CI)	P ⁵			
All Cause Mortality	2244	(1.58)	2110	(1.57)	1.02	(0.96, 1.08)	0.51	1505	(1.73)	1630	(1.83)	0.94	(0.88, 1.01)	0.11	0.10	0.99	(0.94, 1.03)	0.60
50-59 y	307	(0.60)	294	(0.62)	0.97	(0.83, 1.14)	0.17	170	(0.58)	218	(0.73)	0.79	(0.64, 0.96)	0.18	0.87	0.89	(0.79, 1.01)	0.06
60-69 y	964	(1.50)	919	(1.51)	0.98	(0.90, 1.08)		650	(1.66)	694	(1.71)	0.97	(0.88, 1.08)			0.98	(0.91, 1.05)	
70-79 y	973	(3.64)	897	(3.42)	1.07	(0.98, 1.18)		685	(3.66)	718	(3.77)	0.97	(0.87, 1.07)			1.03	(0.96, 1.10)	
CVD Mortality	688	(0.49)	644	(0.48)	1.03	(0.92, 1.15)	0.61	547	(0.63)	577	(0.65)	0.97	(0.86, 1.09)	0.60	0.47	1.00	(0.92, 1.08)	0.98
50-59 y	75	(0.15)	70	(0.15)	0.99	(0.72, 1.38)	0.45	48	(0.16)	50	(0.17)	0.97	(0.65, 1.44)	0.69	0.43	0.98	(0.76, 1.27)	0.77
60-69 y	256	(0.40)	246	(0.40)	0.97	(0.82, 1.16)		226	(0.58)	233	(0.58)	1.01	(0.84, 1.21)			0.99	(0.87, 1.12)	
70-79 y	357	(1.34)	328	(1.25)	1.08	(0.93, 1.25)		273	(1.46)	294	(1.54)	0.94	(0.80, 1.11)			1.01	(0.91, 1.13)	
CHD Mortality	310	(0.22)	285	(0.21)	1.05	(0.89, 1.23)	0.57	240	(0.28)	277	(0.31)	0.89	(0.75, 1.05)	0.17	0.16	0.97	(0.86, 1.09)	0.60
50-59 y	40	(0.079)	34	(0.071)	1.09	(0.69, 1.73)	0.31	17	(0.058)	29	(0.098)	0.59	(0.32, 1.08)	0.77	0.66	0.87	(0.61, 1.24)	0.33
60-69 y	101	(0.16)	110	(0.18)	0.86	(0.66, 1.13)		111	(0.28)	115	(0.28)	1.00	(0.77, 1.30)			0.93	(0.77, 1.13)	
70-79 y	169	(0.63)	141	(0.54)	1.18	(0.95, 1.48)		112	(0.60)	133	(0.70)	0.85	(0.66, 1.10)			1.02	(0.87, 1.21)	
Stroke Mortality	188	(0.13)	161	(0.12)	1.12	(0.91, 1.38)	0.29	126	(0.14)	132	(0.15)	0.98	(0.77, 1.26)	0.89	0.42	1.06	(0.90, 1.24)	0.47
50-59 y	18	(0.035)	12	(0.025)	1.40	(0.68, 2.92)	0.66	13	(0.044)	9	(0.030)	1.47	(0.63, 3.45)	0.79	0.93	1.43	(0.82, 2.49)	0.61
60-69 y	80	(0.12)	68	(0.11)	1.10	(0.79, 1.52)		50	(0.13)	59	(0.15)	0.88	(0.60, 1.28)			1.00	(0.78, 1.27)	
70-79 y	90	(0.34)	81	(0.31)	1.09	(0.81, 1.48)		63	(0.34)	64	(0.34)	1.01	(0.71, 1.43)			1.06	(0.84, 1.33)	
Other known CVD Mortality	188	(0.13)	195	(0.14)	0.93	(0.76, 1.13)	0.47	174	(0.20)	164	(0.18)	1.08	(0.87, 1.34)	0.47	0.31	1.00	(0.86, 1.15)	0.97
50-59 y	17	(0.033)	24	(0.050)	0.65	(0.35, 1.22)	0.53	15	(0.051)	12	(0.040)	1.25	(0.59, 2.68)	0.57	0.40	0.85	(0.53, 1.36)	0.89
60-69 y	73	(0.11)	67	(0.11)	1.01	(0.73, 1.41)		64	(0.16)	59	(0.15)	1.13	(0.79, 1.61)			1.07	(0.84, 1.36)	
70-79 y	98	(0.37)	104	(0.40)	0.94	(0.71, 1.24)		95	(0.51)	93	(0.49)	1.03	(0.77, 1.37)			0.98	(0.80, 1.20)	
Cancer Mortality	706	(0.50)	638	(0.47)	1.06	(0.95, 1.18)	0.31	424	(0.49)	439	(0.49)	0.99	(0.86, 1.13)	0.86	0.44	1.03	(0.95, 1.12)	0.50
50-59 y	145	(0.29)	144	(0.30)	0.94	(0.75, 1.19)	0.22	70	(0.24)	85	(0.29)	0.83	(0.60, 1.14)	0.09	0.58	0.90	(0.75, 1.09)	0.05
60-69 y	348	(0.54)	310	(0.51)	1.06	(0.91, 1.24)		199	(0.51)	216	(0.53)	0.96	(0.79, 1.16)			1.02	(0.90, 1.15)	
70-79 y	213	(0.80)	184	(0.70)	1.14	(0.94, 1.39)		155	(0.83)	138	(0.72)	1.14	(0.91, 1.44)			1.14	(0.98, 1.33)	
Breast Cancer Mortality	61	(0.043)	40	(0.030)	1.44	(0.97, 2.15)	0.07	22	(0.025)	41	(0.046)	0.55	(0.33, 0.92)	0.02	0.003	N/R ⁶		
50-59 y	21	(0.041)	14	(0.029)	1.40	(0.71, 2.76)	0.50	5	(0.017)	11	(0.037)	0.46	(0.16, 1.32)	0.52	0.93	N/R		
60-69 y	26	(0.040)	20	(0.033)	1.23	(0.69, 2.20)		10	(0.026)	20	(0.049)	0.52	(0.25, 1.12)					
70-79 y	14	(0.052)	6	(0.023)	2.32	(0.89, 6.03)		7	(0.037)	10	(0.053)	0.72	(0.28, 1.90)					
Colorectal Cancer Mortality	53	(0.037)	50	(0.037)	1.01	(0.69, 1.49)	0.96	47	(0.054)	40	(0.045)	1.21	(0.79, 1.84)	0.38	0.54	1.10	(0.82, 1.46)	0.53
50-59 y	10	(0.020)	12	(0.025)	0.80	(0.34, 1.85)	0.80	5	(0.017)	8	(0.027)	0.65	(0.21, 2.00)	0.03	0.14	0.74	(0.38, 1.45)	0.08

¹ Median(IQR) for duration of follow-up was 17.7(16.6-18.6), 17.7(16.5-18.7) and 17.7(16.6-18.6) years in the CEE+MPA trial, CEE Alone trial and pooled, respectively.

² Main effect is from a proportional hazards model stratified by age group, trial, and dietary modification randomization arm. Time to event equals zero on date of randomization. For the subgroup analysis, hazard ratios are allowed to vary by age group by including an interaction term.

³ P-value corresponds to a test of whether the hazard ratios for the HT trials are statistically significant, or a 1-df test for trend.

⁴ P-value corresponds to a test of whether hazard ratios differ between trials, or whether the linear trends differ between trials.

⁵ P-value corresponds to a test of whether the pooled hazard ratio is statistically significant, or a 1-df test for trend of the pooled data.

⁶ The p-value corresponding to a test of heterogeneity between trial specific HRs was 0.05 or less, therefore pooled estimates for the corresponding HRs(95%CI) were not reported.

eTable 1: Mortality Outcomes in the Women’s Health Initiative Hormone Therapy Trials During Cumulative 18 Year Follow-Up¹

Outcomes / Age	Events from randomization through December 31, 2014							Events from randomization through December 31, 2014							P-het ⁴	Pooled	
	No. (Annualized rate, %)		Hazard Ratio ²			P ³	No. (Annualized rate, %)		Hazard Ratio ¹			P ²	Hazard Ratio	P ⁵			
	CEE+MPA	Placebo	(95% CI)				CEE	Placebo	(95% CI)						(95% CI)		
60-69 y	26 (0.040)	21 (0.035)	1.17 (0.66, 2.07)			15 (0.038)	19 (0.047)	0.81 (0.41, 1.60)				1.00 (0.65, 1.55)					
70-79 y	17 (0.064)	17 (0.065)	0.97 (0.50, 1.90)			27 (0.14)	13 (0.068)	2.13 (1.10, 4.12)				1.47 (0.92, 2.33)					
Other known Cancer Mortality	548 (0.39)	521 (0.39)	1.00 (0.89, 1.13)			0.94	336 (0.39)	345 (0.39)	1.00 (0.86, 1.16)			0.96	0.93	1.00 (0.91, 1.10)	0.98		
50-59 y	108 (0.21)	109 (0.23)	0.92 (0.71, 1.21)			0.50	59 (0.20)	63 (0.21)	0.94 (0.66, 1.34)			0.83	0.80	0.93 (0.75, 1.15)	0.51		
60-69 y	276 (0.43)	257 (0.42)	1.02 (0.86, 1.20)				169 (0.43)	172 (0.42)	1.02 (0.82, 1.26)					1.02 (0.89, 1.16)			
70-79 y	164 (0.61)	155 (0.59)	1.05 (0.84, 1.30)				108 (0.58)	110 (0.58)	1.00 (0.76, 1.30)					1.03 (0.87, 1.21)			
Other Mortality⁷	850 (0.60)	828 (0.61)	0.99 (0.90, 1.08)			0.77	534 (0.61)	614 (0.69)	0.89 (0.79, 1.00)			0.05	0.19	0.95 (0.88, 1.02)	0.14		
50-59 y	87 (0.17)	80 (0.17)	1.01 (0.75, 1.37)			0.48	52 (0.18)	83 (0.28)	0.63 (0.45, 0.89)			0.22	0.63	0.82 (0.65, 1.03)	0.18		
60-69 y	360 (0.56)	363 (0.60)	0.93 (0.80, 1.07)				225 (0.58)	245 (0.60)	0.96 (0.80, 1.15)					0.94 (0.84, 1.05)			
70-79 y	403 (1.51)	385 (1.47)	1.04 (0.90, 1.20)				257 (1.37)	286 (1.50)	0.91 (0.77, 1.08)					0.98 (0.88, 1.10)			
Alzheimer’s Disease or Other Dementia Mortality	223 (0.16)	233 (0.17)	0.93 (0.77, 1.11)			0.42	127 (0.15)	175 (0.20)	0.74 (0.59, 0.94)			0.01	0.14	0.85 (0.74, 0.98)	0.03		
50-59 y	13 (0.026)	10 (0.021)	1.19 (0.52, 2.72)			0.79	6 (0.020)	6 (0.020)	1.00 (0.32, 3.11)			0.72	0.91	1.12 (0.58, 2.19)	0.64		
60-69 y	82 (0.13)	85 (0.14)	0.90 (0.67, 1.22)				45 (0.12)	64 (0.16)	0.75 (0.51, 1.09)					0.84 (0.66, 1.06)			
70-79 y	128 (0.48)	138 (0.53)	0.92 (0.73, 1.17)				76 (0.41)	105 (0.55)	0.73 (0.54, 0.98)					0.84 (0.70, 1.01)			
COPD Mortality	108 (0.076)	100 (0.074)	1.03 (0.79, 1.36)			0.81	83 (0.095)	79 (0.088)	1.07 (0.78, 1.45)			0.68	0.88	1.05 (0.85, 1.29)	0.65		
50-59 y	9 (0.018)	8 (0.017)	1.04 (0.40, 2.70)			0.60	6 (0.020)	17 (0.057)	0.35 (0.14, 0.88)			0.005	0.10	0.57 (0.30, 1.09)	0.02		
60-69 y	58 (0.090)	57 (0.094)	0.95 (0.66, 1.37)				36 (0.092)	36 (0.089)	1.04 (0.65, 1.64)					0.98 (0.74, 1.31)			
70-79 y	41 (0.15)	35 (0.13)	1.17 (0.74, 1.83)				41 (0.22)	26 (0.14)	1.59 (0.97, 2.60)					1.35 (0.97, 1.88)			
Accident or injury Mortality	78 (0.055)	74 (0.055)	1.00 (0.73, 1.38)			0.98	39 (0.045)	35 (0.039)	1.13 (0.72, 1.79)			0.59	0.67	1.04 (0.80, 1.36)	0.74		
50-59 y	18 (0.035)	8 (0.017)	2.13 (0.92, 4.89)			0.19	5 (0.017)	9 (0.030)	0.56 (0.19, 1.67)			0.15	0.05	N/R ⁸			
60-69 y	31 (0.048)	35 (0.058)	0.82 (0.50, 1.33)				20 (0.051)	17 (0.042)	1.22 (0.64, 2.33)								
70-79 y	29 (0.11)	31 (0.12)	0.93 (0.56, 1.54)				14 (0.075)	9 (0.047)	1.60 (0.69, 3.70)								
Other known Mortality⁹	428 (0.30)	409 (0.30)	1.00 (0.87, 1.15)			0.98	277 (0.32)	313 (0.35)	0.91 (0.77, 1.07)			0.25	0.37	0.96 (0.87, 1.07)	0.47		
50-59 y	45 (0.089)	52 (0.11)	0.80 (0.54, 1.19)			0.07	34 (0.12)	46 (0.15)	0.75 (0.48, 1.17)			0.95	0.26	0.78 (0.58, 1.05)	0.16		
60-69 y	182 (0.28)	182 (0.30)	0.93 (0.76, 1.15)				121 (0.31)	124 (0.31)	1.02 (0.79, 1.31)					0.97 (0.82, 1.13)			
70-79 y	201 (0.75)	175 (0.67)	1.14 (0.93, 1.39)				122 (0.65)	143 (0.75)	0.86 (0.68, 1.10)					1.02 (0.87, 1.19)			

CEE indicates conjugated equine estrogens; MPA, medroxyprogesterone acetate; CI, confidence interval; CVD, cardiovascular disease; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; N/E, not estimable; N/R, not reported; and No., the number of events.

⁷ Mortality outcomes that were not due to CVD or cancer.

⁸ The p-value corresponding to a test of heterogeneity between trial specific HRs was 0.05 or less, therefore pooled estimates for the corresponding HRs(95%CI) were not reported.

⁹ Other mortality outcomes that were known, but not due to Alzheimer’s disease or other dementia, COPD, accident or injury.

eTable 2: Mortality Outcomes in the Women's Health Initiative Hormone Therapy Trials During the Intervention Phase¹

Outcomes / Age	Events from randomization through July 7, 2002				Events from randomization through Feb 29, 2004				P-het ⁴	Pooled	
	No. (Annualized rate, %)		Hazard Ratio ²		No. (Annualized rate, %)		Hazard Ratio ¹			Hazard Ratio	
	CEE+MPA	Placebo	(95% CI)	P ³	CEE	Placebo	(95% CI)	P ²		(95% CI)	P ⁵
All Cause Mortality	250 (0.51)	238 (0.52)	0.97 (0.82, 1.16)	0.77	301 (0.78)	299 (0.75)	1.04 (0.89, 1.22)	0.62	0.59	1.01 (0.90, 1.14)	0.86
50-59 y	35 (0.20)	48 (0.30)	0.67 (0.43, 1.04)	0.20	35 (0.28)	50 (0.39)	0.71 (0.46, 1.09)	0.04	0.62	0.69 (0.51, 0.94)	0.01
60-69 y	111 (0.51)	94 (0.46)	1.07 (0.82, 1.41)		130 (0.76)	134 (0.75)	1.02 (0.80, 1.30)			1.04 (0.87, 1.25)	
70-79 y	104 (1.06)	96 (1.01)	1.03 (0.78, 1.36)		136 (1.53)	115 (1.27)	1.22 (0.95, 1.56)			1.13 (0.94, 1.36)	
CVD Mortality	81 (0.17)	70 (0.15)	1.08 (0.78, 1.48)	0.65	110 (0.29)	113 (0.28)	1.01 (0.78, 1.31)	0.95	0.75	1.04 (0.85, 1.27)	0.73
50-59 y	10 (0.058)	12 (0.075)	0.77 (0.33, 1.79)	0.47	8 (0.063)	10 (0.077)	0.81 (0.32, 2.04)	0.34	0.24	0.79 (0.42, 1.47)	0.85
60-69 y	27 (0.12)	22 (0.11)	1.11 (0.63, 1.95)		57 (0.33)	46 (0.26)	1.30 (0.88, 1.92)			1.24 (0.90, 1.70)	
70-79 y	44 (0.45)	36 (0.38)	1.16 (0.74, 1.80)		45 (0.51)	57 (0.63)	0.81 (0.55, 1.20)			0.95 (0.71, 1.27)	
CHD Mortality	40 (0.082)	40 (0.087)	0.94 (0.60, 1.45)	0.77	66 (0.17)	67 (0.17)	1.02 (0.72, 1.43)	0.92	0.76	0.99 (0.75, 1.29)	0.92
50-59 y	8 (0.046)	6 (0.037)	1.27 (0.44, 3.67)	0.69	4 (0.032)	6 (0.046)	0.67 (0.19, 2.38)	0.94	0.81	0.98 (0.44, 2.17)	0.75
60-69 y	13 (0.060)	14 (0.069)	0.83 (0.39, 1.78)		34 (0.20)	30 (0.17)	1.18 (0.72, 1.93)			1.06 (0.71, 1.61)	
70-79 y	19 (0.19)	20 (0.21)	0.91 (0.49, 1.71)		28 (0.32)	31 (0.34)	0.93 (0.56, 1.55)			0.92 (0.62, 1.37)	
Stroke Mortality	27 (0.055)	16 (0.035)	1.58 (0.85, 2.94)	0.14	23 (0.060)	24 (0.060)	1.00 (0.57, 1.78)	0.99	0.29	1.24 (0.82, 1.89)	0.30
50-59 y	2 (0.012)	2 (0.012)	0.84 (0.12, 5.99)	0.74	0 (0)	2 (0.015)	N/E ⁶			0.44 (0.08, 2.43)	0.97
60-69 y	10 (0.046)	5 (0.025)	1.83 (0.62, 5.35)		14 (0.082)	9 (0.051)	1.67 (0.72, 3.87)			1.73 (0.89, 3.35)	
70-79 y	15 (0.15)	9 (0.095)	1.59 (0.69, 3.63)		9 (0.10)	13 (0.14)	0.71 (0.30, 1.66)			1.08 (0.60, 1.92)	
Other known CVD Mortality	14 (0.029)	14 (0.031)	0.91 (0.43, 1.91)	0.81	18 (0.047)	19 (0.048)	0.98 (0.52, 1.87)	0.96	0.88	0.95 (0.58, 1.55)	0.84
50-59 y	0 (0)	4 (0.025)	N/E		3 (0.024)	2 (0.015)	1.53 (0.26, 9.18)	0.27		0.49 (0.12, 1.96)	0.71
60-69 y	4 (0.018)	3 (0.015)	1.24 (0.28, 5.52)		9 (0.053)	7 (0.039)	1.34 (0.50, 3.61)			1.31 (0.57, 2.99)	
70-79 y	10 (0.10)	7 (0.074)	1.30 (0.49, 3.42)		6 (0.068)	10 (0.11)	0.62 (0.23, 1.71)			0.91 (0.46, 1.81)	
Cancer Mortality	133 (0.27)	111 (0.24)	1.10 (0.86, 1.42)	0.44	126 (0.33)	136 (0.34)	0.96 (0.75, 1.22)	0.72	0.42	1.03 (0.86, 1.22)	0.78
50-59 y	17 (0.099)	22 (0.14)	0.71 (0.38, 1.33)	0.37	20 (0.16)	26 (0.20)	0.78 (0.43, 1.40)	0.06	0.55	0.74 (0.48, 1.14)	0.05
60-69 y	72 (0.33)	52 (0.26)	1.26 (0.88, 1.80)		48 (0.28)	65 (0.37)	0.77 (0.53, 1.12)			1.00 (0.77, 1.28)	
70-79 y	44 (0.45)	37 (0.39)	1.13 (0.73, 1.75)		58 (0.65)	45 (0.50)	1.34 (0.90, 1.97)			1.24 (0.93, 1.66)	
Breast Cancer Mortality	5 (0.010)	4 (0.009)	1.08 (0.29, 4.03)	0.91	4 (0.010)	9 (0.023)	0.45 (0.14, 1.46)	0.17	0.33	0.66 (0.28, 1.54)	0.33
50-59 y	2 (0.012)	1 (0.006)	1.80 (0.16, 19.84)	0.70	1 (0.008)	3 (0.023)	0.34 (0.04, 3.30)	0.81	0.66	0.73 (0.16, 3.26)	0.92
60-69 y	2 (0.009)	2 (0.010)	0.81 (0.11, 5.84)		2 (0.012)	4 (0.023)	0.53 (0.10, 2.89)			0.63 (0.18, 2.26)	
70-79 y	1 (0.010)	1 (0.011)	0.96 (0.06, 15.35)		1 (0.011)	2 (0.022)	0.50 (0.05, 5.51)			0.66 (0.11, 3.92)	
Colorectal Cancer Mortality	11 (0.022)	12 (0.026)	0.87 (0.38, 1.98)	0.74	16 (0.041)	17 (0.043)	0.98 (0.50, 1.95)	0.96	0.83	0.94 (0.55, 1.58)	0.80
50-59 y	2 (0.012)	0 (0)	N/E		0 (0)	3 (0.023)	N/E			0.67 (0.11, 4.03)	0.04
60-69 y	7 (0.032)	7 (0.034)	0.94 (0.33, 2.68)		2 (0.012)	11 (0.062)	0.19 (0.04, 0.86)			0.49 (0.22, 1.10)	

¹ Median(IQR) for duration of follow-up was 5.6(4.9-6.5), 7.2(6.5-8.2) and 6.3(5.3-7.3) years in the CEE+MPA trial, CEE Alone trial and pooled, respectively.

² Main effect is from a proportional hazards model stratified by age group, trial, and dietary modification randomization arm. Time to event equals zero on date of randomization. For the subgroup analysis, hazard ratios are allowed to vary by age group by including an interaction term.

³ P-value corresponds to a test of whether the hazard ratios for the HT trials are statistically significant, or a 1-df test for trend.

⁴ P-value corresponds to a test of whether hazard ratios differ between trials, or whether the linear trends differ between trials.

⁵ P-value corresponds to a test of whether the pooled hazard ratio is statistically significant, or a 1-df test for trend of the pooled data.

⁶ Not estimable; no events observed, therefore HRs(95%CI) were not estimable.

eTable 2: Mortality Outcomes in the Women's Health Initiative Hormone Therapy Trials During the Intervention Phase¹

Outcomes / Age	Events from randomization through July 7, 2002				Events from randomization through Feb 29, 2004				P-het ⁴	Pooled			
	No. (Annualized rate, %)		Hazard Ratio ²		No. (Annualized rate, %)		Hazard Ratio ¹			Hazard Ratio			
	CEE+MPA	Placebo	(95% CI)		P ³	CEE	Placebo	(95% CI)		P ²	(95% CI)	P ⁵	
70-79 y	2 (0.020)	5 (0.053)	0.38 (0.07, 1.98)			14 (0.16)	3 (0.033)	4.91 (1.41, 17.12)			2.05 (0.87, 4.79)		
Other known Cancer Mortality	111 (0.23)	87 (0.19)	1.18 (0.89, 1.56)		0.26	97 (0.25)	104 (0.26)	0.96 (0.73, 1.27)		0.79	0.32	1.06 (0.87, 1.29)	0.54
50-59 y	12 (0.070)	18 (0.11)	0.60 (0.29, 1.25)		0.20	18 (0.14)	17 (0.13)	1.07 (0.55, 2.07)		0.98	0.34	0.82 (0.50, 1.34)	0.38
60-69 y	59 (0.27)	39 (0.19)	1.38 (0.92, 2.07)			42 (0.25)	49 (0.28)	0.89 (0.59, 1.35)				1.12 (0.84, 1.49)	
70-79 y	40 (0.41)	30 (0.32)	1.26 (0.78, 2.03)			37 (0.42)	38 (0.42)	1.01 (0.64, 1.58)				1.12 (0.81, 1.55)	
Other Mortality⁷	36 (0.074)	57 (0.12)	0.59 (0.39, 0.90)		0.01	65 (0.17)	50 (0.13)	1.34 (0.93, 1.94)		0.12	0.004	N/R⁸	
50-59 y	8 (0.046)	14 (0.087)	0.53 (0.22, 1.27)		0.65	7 (0.056)	14 (0.11)	0.51 (0.20, 1.26)		0.002	0.07	0.52 (0.28, 0.97)	0.01
60-69 y	12 (0.055)	20 (0.098)	0.55 (0.27, 1.13)			25 (0.15)	23 (0.13)	1.15 (0.65, 2.03)				0.86 (0.55, 1.34)	
70-79 y	16 (0.16)	23 (0.24)	0.67 (0.35, 1.26)			33 (0.37)	13 (0.14)	2.59 (1.36, 4.92)				1.35 (0.88, 2.08)	
Alzheimer's Disease or Other Dementia Mortality	0 (0)	0 (0)	N/E			5 (0.013)	6 (0.015)	0.90 (0.27, 2.95)		0.86		N/E	
50-59 y	0 (0)	0 (0)	N/E			0 (0)	0 (0)	N/E				N/E	
60-69 y	0 (0)	0 (0)	N/E			1 (0.006)	3 (0.017)	0.38 (0.04, 3.69)					
70-79 y	0 (0)	0 (0)	N/E			4 (0.045)	3 (0.033)	1.39 (0.31, 6.21)					
COPD Mortality	1 (0.002)	8 (0.017)	0.12 (0.01, 0.93)		0.01	6 (0.016)	8 (0.020)	0.76 (0.26, 2.20)		0.62	0.09	0.43 (0.18, 1.05)	0.06
50-59 y	0 (0)	1 (0.006)	N/E			2 (0.016)	1 (0.008)	1.96 (0.18, 21.68)		0.86	0.19	0.97 (0.14, 6.88)	0.75
60-69 y	0 (0)	5 (0.025)	N/E			1 (0.006)	4 (0.023)	0.27 (0.03, 2.43)				0.11 (0.01, 0.87)	
70-79 y	1 (0.010)	2 (0.021)	0.47 (0.04, 5.23)			3 (0.034)	3 (0.033)	1.03 (0.21, 5.09)				0.80 (0.21, 2.98)	
Accident or injury Mortality	12 (0.025)	17 (0.037)	0.65 (0.31, 1.36)		0.25	13 (0.034)	5 (0.013)	2.64 (0.94, 7.41)		0.05	0.03	N/R⁶	
50-59 y	6 (0.035)	4 (0.025)	1.38 (0.39, 4.91)		0.40	0 (0)	3 (0.023)	N/E				N/R	
60-69 y	2 (0.009)	7 (0.034)	0.25 (0.05, 1.20)			8 (0.047)	2 (0.011)	4.13 (0.88, 19.47)					
70-79 y	4 (0.041)	6 (0.063)	0.65 (0.18, 2.31)			5 (0.056)	0 (0)	N/E					
Other known Mortality⁹	22 (0.045)	29 (0.063)	0.72 (0.41, 1.25)		0.23	37 (0.096)	27 (0.068)	1.41 (0.86, 2.32)		0.17	0.07	1.05 (0.72, 1.51)	0.81
50-59 y	2 (0.012)	7 (0.044)	0.27 (0.06, 1.29)		0.42	5 (0.040)	8 (0.062)	0.64 (0.21, 1.95)		0.02	0.32	0.46 (0.19, 1.13)	0.03
60-69 y	9 (0.041)	8 (0.039)	1.06 (0.41, 2.76)			13 (0.076)	13 (0.073)	1.05 (0.49, 2.26)				1.05 (0.58, 1.92)	
70-79 y	11 (0.11)	14 (0.15)	0.75 (0.34, 1.65)			19 (0.21)	6 (0.066)	3.21 (1.28, 8.03)				1.48 (0.84, 2.60)	

CEE indicates conjugated equine estrogens; MPA, medroxyprogesterone acetate; CI, confidence interval; CVD, cardiovascular disease; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; N/E, not estimable; N/R, not reported; and No., the number of events.

⁷ Mortality outcomes that were not due to CVD or cancer.

⁸ The p-value corresponding to a test of heterogeneity between trial specific HRs was 0.05 or less, therefore pooled estimates for the corresponding HRs (95%CI) were not reported.

⁹ Other mortality outcomes that were known, but not due to Alzheimer's disease or other dementia, COPD, accident or injury.

eTable 3: Mortality Outcomes in the Women's Health Initiative Hormone Therapy Trials During the Postintervention Phase¹

Outcomes / Age	Events after July 7, 2002 through Dec 31, 2014				Events after Feb 29, 2004 through Dec 31, 2014				P-het ⁴	Pooled	
	No. (Annualized rate, %)	Hazard Ratio ²		P ³	No. (Annualized rate, %)	Hazard Ratio ¹		P ²		Hazard Ratio	
	CEE+MPA	Placebo	(95% CI)		CEE	Placebo	(95% CI)			(95% CI)	P ⁵
All Cause Mortality	1994 (2.15)	1872 (2.11)	1.04 (0.97, 1.10)	0.28	1204 (2.48)	1331 (2.69)	0.92 (0.85, 0.99)	0.03	0.02	N/R⁶	
50-59 y	272 (0.81)	246 (0.78)	1.04 (0.88, 1.24)	0.38	135 (0.81)	168 (1.00)	0.81 (0.64, 1.01)	0.61	0.88	N/R	
60-69 y	853 (2.01)	825 (2.04)	0.98 (0.89, 1.08)		520 (2.36)	560 (2.46)	0.96 (0.85, 1.08)				
70-79 y	869 (5.14)	801 (4.78)	1.09 (0.99, 1.20)		549 (5.58)	603 (6.05)	0.92 (0.82, 1.03)				
CVD Mortality	607 (0.65)	574 (0.65)	1.03 (0.92, 1.16)	0.59	437 (0.90)	464 (0.94)	0.96 (0.84, 1.09)	0.49	0.38	1.00 (0.92, 1.09)	0.96
50-59 y	65 (0.19)	58 (0.18)	1.05 (0.74, 1.50)	0.67	40 (0.24)	40 (0.24)	1.01 (0.65, 1.57)	0.99	0.77	1.04 (0.79, 1.37)	0.76
60-69 y	229 (0.54)	224 (0.55)	0.98 (0.81, 1.17)		169 (0.77)	187 (0.82)	0.93 (0.76, 1.15)			0.96 (0.83, 1.10)	
70-79 y	313 (1.85)	292 (1.74)	1.07 (0.91, 1.26)		228 (2.32)	237 (2.38)	0.96 (0.80, 1.16)			1.02 (0.91, 1.15)	
CHD Mortality	270 (0.29)	245 (0.28)	1.08 (0.91, 1.28)	0.39	174 (0.36)	210 (0.42)	0.84 (0.69, 1.03)	0.09	0.06	0.97 (0.85, 1.11)	0.65
50-59	32 (0.095)	28 (0.089)	1.07 (0.65, 1.78)	0.22	13 (0.078)	23 (0.14)	0.57 (0.29, 1.14)	0.71	0.63	0.85 (0.57, 1.28)	0.23
60-69	88 (0.21)	96 (0.24)	0.88 (0.66, 1.18)		77 (0.35)	85 (0.37)	0.93 (0.69, 1.27)			0.91 (0.73, 1.12)	
70-79	150 (0.89)	121 (0.72)	1.24 (0.98, 1.58)		84 (0.85)	102 (1.02)	0.82 (0.62, 1.10)			1.05 (0.87, 1.26)	
Stroke Mortality	161 (0.17)	145 (0.16)	1.08 (0.86, 1.35)	0.52	103 (0.21)	108 (0.22)	0.98 (0.75, 1.28)	0.86	0.59	1.03 (0.87, 1.23)	0.70
50-59 y	16 (0.048)	10 (0.032)	1.52 (0.69, 3.35)	0.50	13 (0.078)	7 (0.042)	1.89 (0.75, 4.75)	0.90	0.73	1.67 (0.92, 3.04)	0.55
60-69 y	70 (0.16)	63 (0.16)	1.06 (0.75, 1.48)		36 (0.16)	50 (0.22)	0.74 (0.48, 1.14)			0.92 (0.71, 1.20)	
70-79 y	75 (0.44)	72 (0.43)	1.03 (0.74, 1.42)		54 (0.55)	51 (0.51)	1.08 (0.73, 1.58)			1.05 (0.82, 1.34)	
Other known CVD Mortality	174 (0.19)	181 (0.20)	0.94 (0.76, 1.16)	0.55	156 (0.32)	145 (0.29)	1.08 (0.86, 1.36)	0.48	0.36	1.00 (0.86, 1.17)	0.97
50-59 y	17 (0.051)	20 (0.063)	0.79 (0.42, 1.51)	0.98	12 (0.072)	10 (0.059)	1.19 (0.52, 2.77)	0.82	0.85	0.92 (0.55, 1.54)	0.94
60-69 y	69 (0.16)	64 (0.16)	1.03 (0.73, 1.44)		55 (0.25)	52 (0.23)	1.09 (0.75, 1.59)			1.06 (0.82, 1.36)	
70-79 y	88 (0.52)	97 (0.58)	0.91 (0.68, 1.22)		89 (0.90)	83 (0.83)	1.06 (0.79, 1.44)			0.98 (0.80, 1.21)	
Cancer Mortality	573 (0.62)	527 (0.59)	1.05 (0.93, 1.18)	0.43	298 (0.61)	303 (0.61)	1.00 (0.85, 1.17)	1.00	0.64	1.03 (0.94, 1.13)	0.53
50-59 y	128 (0.38)	122 (0.39)	0.99 (0.77, 1.27)	0.37	50 (0.30)	59 (0.35)	0.85 (0.58, 1.24)	0.41	0.89	0.95 (0.77, 1.16)	0.23
60-69 y	276 (0.65)	258 (0.64)	1.02 (0.86, 1.21)		151 (0.69)	151 (0.66)	1.03 (0.82, 1.29)			1.02 (0.89, 1.17)	
70-79 y	169 (1.00)	147 (0.88)	1.15 (0.92, 1.44)		97 (0.99)	93 (0.93)	1.05 (0.79, 1.40)			1.11 (0.94, 1.33)	
Breast Cancer Mortality	56 (0.060)	36 (0.041)	1.50 (0.98, 2.27)	0.06	18 (0.037)	32 (0.065)	0.57 (0.32, 1.02)	0.06	0.008	N/R⁵	
50-59 y	19 (0.057)	13 (0.041)	1.40 (0.69, 2.84)	0.41	4 (0.024)	8 (0.048)	0.50 (0.15, 1.64)	0.56	0.99	N/R	
60-69 y	24 (0.057)	18 (0.044)	1.27 (0.69, 2.34)		8 (0.036)	16 (0.070)	0.52 (0.22, 1.20)				
70-79 y	13 (0.077)	5 (0.030)	2.64 (0.94, 7.39)		6 (0.061)	8 (0.080)	0.78 (0.27, 2.24)				
Colorectal Cancer Mortality	42 (0.045)	38 (0.043)	1.06 (0.68, 1.64)	0.80	31 (0.064)	23 (0.046)	1.36 (0.79, 2.34)	0.26	0.48	1.17 (0.83, 1.65)	0.36
50-59 y	8 (0.024)	12 (0.038)	0.64 (0.26, 1.56)	0.31	5 (0.030)	5 (0.030)	1.04 (0.30, 3.61)	0.88	0.61	0.75 (0.37, 1.55)	0.34
60-69 y	19 (0.045)	14 (0.035)	1.29 (0.65, 2.57)		13 (0.059)	8 (0.035)	1.65 (0.68, 3.98)			1.42 (0.82, 2.44)	

¹ Median(IQR) for duration of follow-up was 12.5(12.5-12.5), 10.8(10.7-10.8) and 10.8(10.8-12.5) years in the CEE+MPA trial, CEE Alone trial and pooled, respectively.

² Main effect is from a proportional hazards model stratified by age group, trial, and dietary modification randomization arm. Time to event equals zero on respective dates trials were stopped. For the subgroup analysis, hazard ratios are allowed to vary by age group by including an interaction term.

³ P-value corresponds to a test of whether the hazard ratios for the HT trials are statistically significant, or a 1-df test for trend.

⁴ P-value corresponds to a test of whether hazard ratios differ between trials, or whether the linear trends differ between trials.

⁵ P-value corresponds to a test of whether the pooled hazard ratio is statistically significant, or a 1-df test for trend of the pooled data.

⁶ The p-value corresponding to a test of heterogeneity between trial specific HRs was 0.05 or less, therefore pooled estimates for the corresponding HRs(95%CI) were not reported.

eTable 3: Mortality Outcomes in the Women’s Health Initiative Hormone Therapy Trials During the Postintervention Phase¹

Outcomes / Age	Events after July 7, 2002 through Dec 31, 2014				Events after Feb 29, 2004 through Dec 31, 2014				P-het ⁴	Pooled	
	No. (Annualized rate, %)		Hazard Ratio ²		No. (Annualized rate, %)		Hazard Ratio ¹			Hazard Ratio (95% CI)	P ⁵
	CEE+MPA	Placebo	(95% CI)	P ³	CEE	Placebo	(95% CI)	P ²			
70-79 y	15 (0.089)	12 (0.072)	1.22 (0.57, 2.61)		13 (0.13)	10 (0.10)	1.31 (0.57, 2.98)			1.26 (0.72, 2.21)	
Other known Cancer Mortality	437 (0.47)	434 (0.49)	0.97 (0.85, 1.11)	0.66	239 (0.49)	241 (0.49)	1.01 (0.84, 1.21)	0.93	0.74	0.98 (0.88, 1.09)	0.77
50-59 y	96 (0.29)	91 (0.29)	0.99 (0.75, 1.33)	0.97	41 (0.25)	46 (0.27)	0.89 (0.58, 1.35)	0.76	0.82	0.96 (0.76, 1.22)	0.83
60-69 y	217 (0.51)	218 (0.54)	0.95 (0.79, 1.15)		127 (0.58)	123 (0.54)	1.06 (0.83, 1.36)			0.99 (0.85, 1.15)	
70-79 y	124 (0.73)	125 (0.75)	0.99 (0.78, 1.27)		71 (0.72)	72 (0.72)	1.00 (0.72, 1.38)			1.00 (0.82, 1.21)	
Other Mortality⁷	814 (0.88)	771 (0.87)	1.03 (0.93, 1.14)	0.58	469 (0.97)	564 (1.14)	0.84 (0.75, 0.95)	0.006	0.01	N/R⁸	
50-59 y	79 (0.24)	66 (0.21)	1.13 (0.82, 1.57)	0.73	45 (0.27)	69 (0.41)	0.65 (0.45, 0.95)	0.68	0.93	N/R	
60-69 y	348 (0.82)	343 (0.85)	0.96 (0.83, 1.12)		200 (0.91)	222 (0.98)	0.93 (0.77, 1.12)				
70-79 y	387 (2.29)	362 (2.16)	1.07 (0.93, 1.24)		224 (2.28)	273 (2.74)	0.83 (0.69, 0.98)				
Alzheimer’s Disease or Other Dementia Mortality	223 (0.24)	233 (0.26)	0.94 (0.78, 1.13)	0.52	122 (0.25)	169 (0.34)	0.73 (0.58, 0.92)	0.008	0.09	0.85 (0.74, 0.99)	0.03
50-59 y	13 (0.039)	10 (0.032)	1.24 (0.54, 2.83)	0.73	6 (0.036)	6 (0.036)	1.00 (0.32, 3.10)	0.66	0.89	1.15 (0.59, 2.24)	0.56
60-69 y	82 (0.19)	85 (0.21)	0.92 (0.68, 1.25)		44 (0.20)	61 (0.27)	0.74 (0.50, 1.09)			0.85 (0.67, 1.07)	
70-79 y	128 (0.76)	138 (0.82)	0.93 (0.73, 1.19)		72 (0.73)	102 (1.02)	0.71 (0.52, 0.96)			0.84 (0.69, 1.01)	
COPD Mortality	107 (0.12)	92 (0.10)	1.13 (0.85, 1.49)	0.41	77 (0.16)	71 (0.14)	1.09 (0.79, 1.51)	0.60	0.89	1.11 (0.90, 1.37)	0.33
50-59 y	9 (0.027)	7 (0.022)	1.20 (0.45, 3.22)	0.78	4 (0.024)	16 (0.095)	0.24 (0.08, 0.73)	0.002	0.04	N/R	
60-69 y	58 (0.14)	52 (0.13)	1.06 (0.73, 1.54)		35 (0.16)	32 (0.14)	1.12 (0.69, 1.81)				
70-79 y	40 (0.24)	33 (0.20)	1.22 (0.77, 1.93)		38 (0.39)	23 (0.23)	1.65 (0.98, 2.77)				
Accident or injury Mortality	66 (0.071)	57 (0.064)	1.12 (0.78, 1.59)	0.54	26 (0.054)	30 (0.061)	0.87 (0.51, 1.47)	0.59	0.43	1.03 (0.77, 1.38)	0.83
50-59 y	12 (0.036)	4 (0.013)	2.90 (0.94, 9.01)	0.19	5 (0.030)	6 (0.036)	0.83 (0.25, 2.73)	0.78	0.32	1.67 (0.76, 3.64)	0.41
60-69 y	29 (0.068)	28 (0.069)	0.97 (0.58, 1.64)		12 (0.055)	15 (0.066)	0.82 (0.38, 1.75)			0.92 (0.60, 1.41)	
70-79 y	25 (0.15)	25 (0.15)	1.00 (0.57, 1.73)		9 (0.091)	9 (0.090)	1.00 (0.40, 2.53)			1.00 (0.62, 1.60)	
Other known Mortality⁹	406 (0.44)	380 (0.43)	1.04 (0.90, 1.19)	0.61	240 (0.49)	286 (0.58)	0.86 (0.72, 1.02)	0.08	0.09	0.96 (0.86, 1.07)	0.47
50-59 y	43 (0.13)	45 (0.14)	0.90 (0.59, 1.37)	0.12	29 (0.17)	38 (0.23)	0.77 (0.48, 1.25)	0.49	0.12	0.84 (0.61, 1.16)	0.46
60-69 y	173 (0.41)	174 (0.43)	0.94 (0.76, 1.16)		108 (0.49)	111 (0.49)	1.01 (0.77, 1.31)			0.97 (0.82, 1.14)	
70-79 y	190 (1.12)	161 (0.96)	1.18 (0.96, 1.46)		103 (1.05)	137 (1.37)	0.76 (0.59, 0.98)			0.99 (0.84, 1.16)	

CEE indicates conjugated equine estrogens; MPA, medroxyprogesterone acetate; CI, confidence interval; CVD, cardiovascular disease; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; N/E, not estimable; N/R, not reported; and No., the number of events.

⁷ Mortality outcomes that were not due to CVD or cancer.

⁸ The p-value corresponding to a test of heterogeneity between trial specific HRs was 0.05 or less, therefore pooled estimates for the corresponding HRs(95%CI) were not reported.

⁹ Other mortality outcomes that were known, but not due to Alzheimer’s disease or other dementia, COPD, accident or injury.

eTable 4. All-Cause Mortality: Comparison of Hazard Ratios¹ (HRs) in Younger vs Older Women During the Intervention and Cumulative Follow-up Phases of the WHI Hormone Therapy Trials

	Younger women (age 50-59y)			Older women (age 70-79y)			Ratio of HRs ² (95% CI)
	Number of Deaths (Annualized Rate, %)		Hazard Ratio (95% CI)	Number of Deaths (Annualized Rate, %)		Hazard Ratio (95% CI)	
	HT	Placebo		HT	Placebo		
Intervention Phase							
CEE+MPA Trial	35 (0.20)	48 (0.30)	0.67 (0.43, 1.04)	104 (1.06)	96 (1.01)	1.03 (0.78, 1.36)	0.65 (0.39, 1.10)
CEE Alone Trial	35 (0.28)	50 (0.39)	0.71 (0.46, 1.09)	136 (1.53)	115 (1.27)	1.22 (0.95, 1.56)	0.58 (0.35, 0.96)
Pooled Cohort	70 (0.23)	98 (0.34)	0.69 (0.51, 0.94)	240 (1.28)	211 (1.14)	1.13 (0.94, 1.36)	0.61 (0.43, 0.87)
Cumulative 18-year Follow-up							
CEE+MPA Trial	307 (0.60)	294 (0.62)	0.97 (0.83, 1.14)	973 (3.64)	897 (3.42)	1.07 (0.98, 1.18)	0.91 (0.75, 1.09)
CEE Alone Trial	170 (0.58)	218 (0.73)	0.79 (0.64, 0.96)	685 (3.66)	718 (3.77)	0.97 (0.87, 1.07)	0.81 (0.65, 1.02)
Pooled Cohort	477 (0.60)	512 (0.66)	0.89 (0.79, 1.01)	1658 (3.65)	1615 (3.57)	1.03 (0.96, 1.10)	0.87 (0.76, 1.00)

HT indicates menopausal hormone therapy; CEE, conjugated equine estrogens; MPA, medroxyprogesterone acetate; and y, year.

¹ Hazard ratios(95%CI) and their corresponding ratios(95%CI) are from a proportional hazards model stratified by age group, trial and dietary modification randomization arm; time to event equals zero on date of randomization.

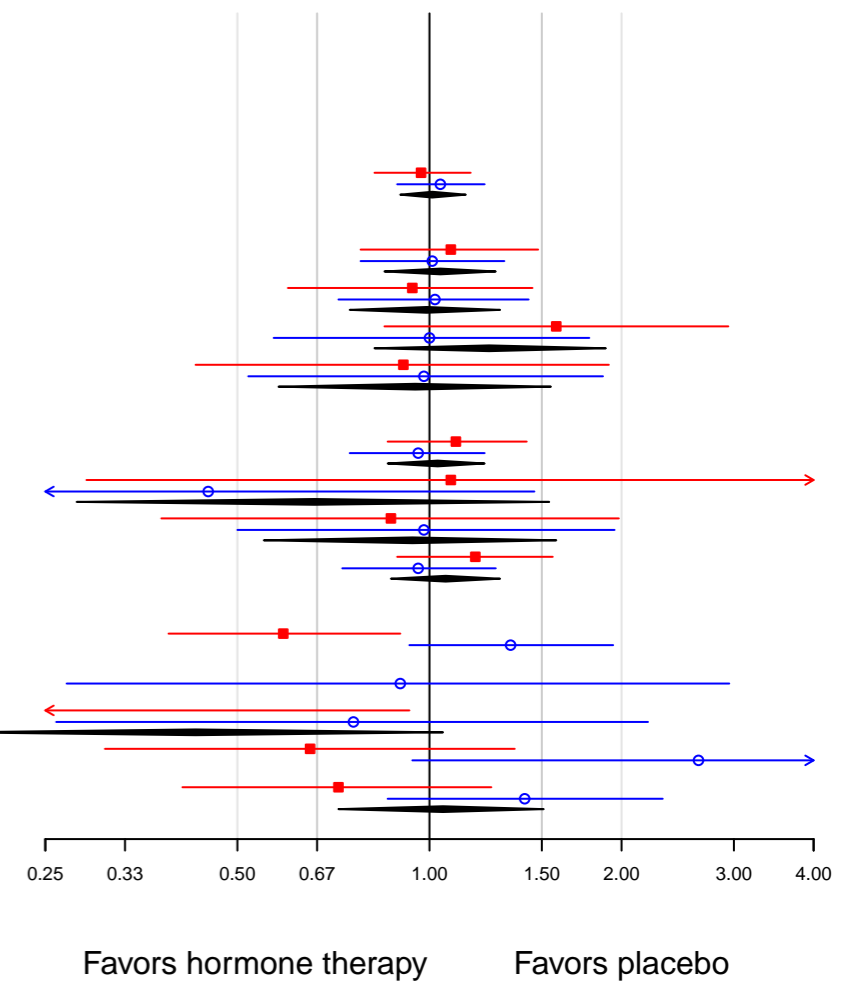
² HR(HT vs. placebo; among youngest women) divided by HR(HT vs. placebo; among oldest women) . The ratio of hazard ratios (rHR) quantifies the interaction between HT and these age groups. An rHR < 1.0 indicates a more favorable HT effect for younger women than older women. The rHRs are solely intended to aid interpretation. Since rHRs were derived from HRs, statistical significance corresponds to the P-value for the test of interaction by age group, and is presented in Figures 3 and 4;.

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eFigure. Overall Mortality Outcomes in the Women's Health Initiative Hormone Therapy Trials During the Intervention Phase*

■ CEE+MPA trial (CEE+MPA vs. Placebo)
○ CEE Alone trial (CEE Alone vs. Placebo)
◆ Pooled (Hormone Therapy vs. Placebo)

Endpoints	CEE+MPA Trial				CEE Alone Trial				Pooled	
	No. of Events	Annualized Rates, %	HR(95%CI)	P	No. of Events	Annualized Rates, %	HR(95%CI)	P	HR(95%CI)	P
	CEE+MPA	Placebo			CEE Alone	Placebo				
All-cause mortality	250(0.51)	238(0.52)	0.97(0.82,1.16)	0.77	301(0.78)	299(0.75)	1.04(0.89,1.22)	0.62	1.01(0.90,1.14)	0.86
CVD mortality	81(0.17)	70(0.15)	1.08(0.78,1.48)	0.65	110(0.29)	113(0.28)	1.01(0.78,1.31)	0.95	1.04(0.85,1.27)	0.73
CHD mortality	40(0.082)	40(0.087)	0.94(0.60,1.45)	0.77	66(0.17)	67(0.17)	1.02(0.72,1.43)	0.92	0.99(0.75,1.29)	0.92
Stroke mortality	27(0.055)	16(0.035)	1.58(0.85,2.94)	0.14	23(0.060)	24(0.060)	1.00(0.57,1.78)	0.99	1.24(0.82,1.89)	0.30
Other known CVD mortality	14(0.029)	14(0.031)	0.91(0.43,1.91)	0.81	18(0.047)	19(0.048)	0.98(0.52,1.87)	0.96	0.95(0.58,1.55)	0.84
Cancer mortality	133(0.27)	111(0.24)	1.10(0.86,1.42)	0.44	126(0.33)	136(0.34)	0.96(0.75,1.22)	0.72	1.03(0.86,1.22)	0.78
Breast cancer mortality	5(0.010)	4(0.009)	1.08(0.29,4.03)	0.91	4(0.010)	9(0.023)	0.45(0.14,1.46)	0.17	0.66(0.28,1.54)	0.33
Colorectal cancer mortality	11(0.022)	12(0.026)	0.87(0.38,1.98)	0.74	16(0.041)	17(0.043)	0.98(0.50,1.95)	0.96	0.94(0.55,1.58)	0.80
Other known cancer mortality	111(0.23)	87(0.19)	1.18(0.89,1.56)	0.26	97(0.25)	104(0.26)	0.96(0.73,1.27)	0.79	1.06(0.87,1.29)	0.54
Other mortality†	36(0.074)	57(0.12)	0.59(0.39,0.90)	0.01	65(0.17)	50(0.13)	1.34(0.93,1.94)	0.12	N/R^	
Alzheimer's or dementia mortality‡	0(0)	0(0)	N/E**		5(0.013)	6(0.015)	0.90(0.27,2.95)	0.86	N/E**	
COPD mortality	1(0.002)	8(0.017)	0.12(0.01,0.93)	0.01	6(0.016)	8(0.020)	0.76(0.26,2.20)	0.62	0.43(0.18,1.05)	0.06
Accident or injury mortality	12(0.025)	17(0.037)	0.65(0.31,1.36)	0.25	13(0.034)	5(0.013)	2.64(0.94,7.41)	0.05	N/R^	
Other known mortality^^	22(0.045)	29(0.063)	0.72(0.41,1.25)	0.23	37(0.096)	27(0.068)	1.41(0.86,2.32)	0.17	1.05(0.72,1.51)	0.81



CEE indicates conjugated equine estrogens; MPA, medroxyprogesterone acetate; HR, hazard ratio; CI, confidence interval; CVD, cardiovascular disease; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; N/E, not estimable; N/R, not reported; and IQR, interquartile range.

* Median(IQR) for duration of follow-up was 5.6(4.9–6.5), 7.2(6.5–8.2) and 6.3(5.3–7.3) years in the CEE+MPA trial, CEE Alone trial and pooled, respectively.

† Mortality outcomes that were not due to CVD or cancer.

^ The p-value corresponding to a test of heterogeneity between trial specific HRs was 0.05 or less, therefore pooled estimates are not displayed in forest plot and the corresponding HRs (95%CI) are not reported.

‡ Alzheimer's disease or other dementia mortality.

** No events observed in the CEE+MPA trial, therefore HRs(95%CI) were not estimable.

^^ Other mortality outcomes that were known, but not due to Alzheimer's disease or other dementia, COPD, accident or injury.