Table e-1: Baseline characteristics of participants who completed the follow-up 3 years after the end of the mHT phase and those who participated in the longitudinal MRI study during mHT, but did not complete the follow-up and therefore excluded from the current study

	Did not complete follow-up (excluded) (N=20)	Completed follow-up (N=75)	P-value
Education, n (%)			>0.99
High school or less	1 (5%)	6 (7%)	
Some college / College graduate	13 (65%)	46 (65%)	
Some graduate / Graduate	6 (30%)	20 (28%)	
Smoking status, n (%)			0.29
Non-smoker	11 (55%)	52 (69%)	
Smoker (past or current)	9 (45%)	23 (31%)	
APOE ε4 carrier, n (%)	6 (33%)	18 (25%)	0.55
Global Cognitive function z-scores	0.10 (0.70)	0.03 (0.74)	0.73
Whole brain, cm^3	1324 (111)	1314 (86)	0.13
White matter hyperintensities, cm^3	2.3 (1.1)	2.1 (1.3)	0.45

Data are n (%) or mean (sd). Pairwise p-values were assessed using Fisher's Exact and analysis of variance followed by Tukey pairwise tests

Table e-2: Percentage of change in whole brain volumes, ventricular volumes, and the mean change in white matter hyperintensity volumes and global cognition per year in the17β-estradiol (tE2) and the oral conjugated equine estrogen (oCEE) groups compared to placebo during the mHT (0-48 months), during the 3 years after the mHT (48-84 months), and during the entire 7 years of follow-up (0-84 months).

Months	Whole Brain				Ventricular				WMH				Global Cognition			
	CEE mean change (%/year)	Placebo mean change (%/year)	Mean % difference (95% CI)	P-value*	CEE mean change (%/year)	Placebo mean change (%/year)	Mean % difference (95% CI)	P-value*	CEE mean change per year	Placebo mean change per year	Mean difference (95% CI)	P-value*	CEE mean change per year	Placebo mean change per year	Mean difference (95% CI)	P-value*
0 - 48	-0.20	-0.08	-0.12 (-0.31, 0.07)	0.22	3.05	1.52	1.52 (0.35, 2.70)	0.01	0.12	0.05	0.07 (-0.01, 0.16)	0.10	-0.05	0.05	-0.10 (-0.65, 0.45)	0.71
48 - 84	-0.11	-0.27	0.16 (0.03, 0.30)	0.02	-2.43	-2.62	0.19 (-2.36, 2.74)	0.88	0.22	0.10	0.13 (-0.02, 0.27)	0.09	0.04	0.05	-0.01 (-0.53, 0.51)	0.97
0 - 84	-0.17	-0.16	0.00 (-0.10, 0.09)	0.96	2.65	2.23	0.43 (-0.43, 1.28)	0.32	0.15	0.07	0.08 (0.01, 0.15)	0.03	-0.02	0.04	-0.06 (-0.36, 0.24)	0.68

Months	Whole Brain				Ventricular				WMH				Global Cognition			
	tE2 mean change (%/year)	Placebo mean change (%/year)	Mean % difference (95% CI)	P-value*	tE2 mean change (%/year)	Placebo mean change (%/year)	Mean % difference (95% CI)	P-value*	tE2 mean change per year	Placebo mean change per year	Mean difference (95% CI)	P-value*	tE2 mean change per year	Placebo mean change per year	Mean difference (95% CI)	P-value*
0 - 48	-0.16	-0.08	-0.08 (-0.26, 0.09)	0.35	2.02	1.52	0.50 (-0.58, 1.56)	0.36	0.14	0.05	0.09 (0.00, 0.19)	0.06	-0.02	0.05	-0.07 (-0.61, 0.48)	0.81
48 - 84	-0.28	-0.27	-0.01 (-0.13, 0.12)	0.90	-1.98	-2.62	0.64 (-1.14, 2.42)	0.47	0.17	0.10	0.07 (-0.11, 0.25)	0.44	-0.03	0.05	-0.08 (-0.50, 0.33)	0.69
0 - 84	-0.21	-0.16	-0.04 (-0.14, 0.05)	0.36	2.17	2.23	-0.06 (-1.08, 0.96)	0.90	0.14	0.07	0.07 (-0.03, 0.18)	0.17	-0.04	0.04	-0.07 (-0.39, 0.25)	0.65

* P-values are from t-tests comparing the change in each of the mHT groups to placebo at each follow-up time point