

# **SUPPLEMENTAL MATERIAL**

**Table S1. Participant Characteristics, Overall,\* and for CEE-Alone vs. Placebo**

	<b>Total (n=1020)</b>		<b>Placebo (n=503)</b>		<b>CEE-Alone (n=517)</b>		<b>p-value</b>	
	Mean	SD	Mean	SD	Mean	SD		
	<b>Age, years</b>	55.13	2.87	55.14	2.94	55.11		2.80
<b>Age at scan</b>	64.38	2.89	64.38	2.92	64.39	2.85	0.94	
<b>Body Mass Index, kg/m<sup>2</sup></b>	30.56	6.04	30.58	6.28	30.54	5.79	0.91	
<b>Waist Circumference, cm</b>	91.65	14.33	91.52	14.33	91.77	14.34	0.79	
<b>SBP, mmHg</b>	124.54	15.70	125.20	16.60	123.90	14.77	0.18	
<b>DBP, mmHg</b>	77.79	8.86	78.06	8.81	77.53	8.91	0.34	
<b>log METs</b>	1.76	1.21	1.79	1.23	1.73	1.19	0.45	
<b>CAC score</b>	98.22	294.98	120.92	349.90	76.12	227.44	0.01	
<b>Categorical</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>p-value</b>	
<b>Diabetes</b>	no	957	93.92	470	93.63	487	94.20	0.70
	yes	62	6.08	32	6.37	30	5.80	
<b>Smoking</b>	never	496	48.92	248	49.60	248	48.25	0.76
	past	401	39.55	198	39.60	203	39.49	
	current	117	11.54	54	10.80	63	12.26	
<b>Hypertension</b>	no	698	68.63	348	69.32	350	67.96	0.64
	yes	319	31.37	154	30.68	165	32.04	
<b>High cholesterol</b>	no	786	90.45	386	90.61	400	90.29	0.87
	yes	83	9.55	40	9.39	43	9.71	
<b>MI in 1st degree relative</b>	no	505	52.06	251	51.75	254	52.37	0.85
	yes	465	47.94	234	48.25	231	47.63	
<b>CVD prior to scan</b>	no	931	91.27	454	90.26	477	92.26	0.26
	yes	89	8.73	49	9.74	40	7.74	
<b>CAC score</b>	0	550	53.92	256	50.89	294	56.87	0.05
	1-100	273	26.76	135	26.84	138	26.69	
	>100	197	19.31	112	22.27	85	16.44	

**Table S1. Cont'd**

CAC indicates coronary artery calcium; CEE, conjugated equine estrogen; CVD, cardiovascular disease; DBP, diastolic blood pressure; METs, metabolic equivalents; MI, myocardial infarction; and SBP, systolic blood pressure

\* excludes n=10 with surgical stent and n=44 without follow up data

p values from t-test, Wilcoxon rank sum test or chi square tests compare CEE-Alone vs. placebo.

<b>Table S2. Multivariable-adjusted HR(95%CI) for CHD by CAC Categories</b>		
		<b>CHD* HR(95%CI)</b>
<b>Model 1†</b>	CAC = 0	1.0 (ref)
	CAC 1-100 (ref=0)	2.13 (0.53, 8.54)
	CAC > 100 (ref=0)	<b>7.94 (2.40, 26.34)</b>
	Age	1.07 (0.89, 1.28)
<b>Model 2†</b>	CAC = 0	1.0 (ref)
	CAC 1-100 (ref=0)	2.67 (0.59, 12.11)
	CAC > 100 (ref=0)	<b>7.88 (1.94, 31.98)</b>
	Age	1.15 (0.92, 1.44)
	Diabetes	1.17 (0.14, 9.54)
	Smoking	0.71 (0.21, 2.38)
	Hypertension	1.32 (0.29, 5.98)
	High cholesterol	2.42 (0.74, 7.86)
<b>Model 3†</b>	CAC = 0	1.0 (ref)
	CAC 1-100 (ref=0)	2.64 (0.57, 12.22)
	CAC > 100 (ref=0)	<b>8.69 (2.11, 35.86)</b>
	Age	1.15 (0.92, 1.43)
	Diabetes	1.04 (0.12, 9.23)
	Smoking	2.40 (0.72, 8.05)
	Hypertension	0.77 (0.21, 2.78)
	High cholesterol	1.44 (0.32, 6.70)
	Hot flashes	0.88 (0.23, 3.36)
	BMI 25-29.9	0.40 (0.09, 1.80)
	BMI 30-34.9	1.06 (0.28, 4.08)
	BMI ≥35	0.19 (0.02, 1.79)
<p>BMI indicates body mass index; CAC, coronary artery calcium; and CHD, coronary heart disease. *Excludes women with CVD at baseline or prior to CAC scan, or no follow-up n=931. † Covariates include CEE-alone vs. placebo and the variables reported for each model. Statistically significant results are bolded.</p>		

**Table S3. Multivariable-adjusted HR(95%CI) for CVD\* with Recategorized Current Smoking and Systolic Blood Pressure**

		<b>HR (95% CI)</b>
<b>Model 1†</b>	CAC 1-100 (ref=0)	<b>1.91 (1.05, 3.47)</b>
	CAC >100 (ref=0)	<b>4.41 (2.49, 7.82)</b>
	Age , years	1.01 (0.93, 1.10)
<b>Model 2†</b>	CAC 1-100 (ref=0)	1.58 (0.79, 3.14)
	CAC >100 (ref=0)	<b>4.05 (2.12, 7.75)</b>
	Age , years	1.02 (0.93, 1.13)
	Diabetes (ref=no)	1.84 (0.78, 4.36)
	Current smoker: # cigarettes 1-14 (ref=no current smoking)	0.48 (0.12, 2.01)
	Current smoker: # cigarettes 15+ (ref=no current smoking)	2.27 (0.94, 5.49)
	SBP 118-130 mmHg (ref =SBP<118)	1.25 (0.63, 2.46)
	SBP >130 mmHg (ref =SBP<118)	1.44 (0.74, 2.81)
	High cholesterol (ref=no)	1.76 (0.86, 3.64)
<b>Model 3†</b>	CAC 1-100 (ref=0)	1.51 (0.75, 3.01)
	CAC >100 (ref=0)	<b>3.96 (2.07, 7.57)</b>
	Age , years	1.03 (0.93, 1.13)
	Diabetes (ref=no)	1.67 (0.70, 4.00)
	Current smoker: # cigarettes 1-14 (ref=no current smoking)	0.50 (0.12, 2.06)
	Current smoker: # cigarettes 15+ (ref=no current smoking)	2.32 (0.94, 5.68)
	SBP 118-130 mmHg (ref =SBP<118)	1.19 (0.60, 2.35)
	SBP >130 mmHg (ref =SBP<118)	1.35 (0.69, 2.63)
	High cholesterol (ref=no)	1.78 (0.87, 3.68)
	BMI 25-29.9 (ref= BMI<25)	1.38 (0.54, 3.54)
	BMI 30-34.9 (ref= BMI<25)	1.94 (0.76, 4.93)
BMI ≥35 (ref= BMI<25)	1.50 (0.56, 4.05)	

BMI indicates body mass index; CAC, coronary artery calcium; CEE, conjugated equine estrogen; CVD, cardiovascular disease; and PY, person-years

\*Excludes women with CVD at baseline or prior to CAC scan, or no follow-up n=931.

† Each model is adjusted for CEE vs. placebo (not shown) as well as the predictors reported for that model. Statistically significant results are bolded.

**Table S4. All Incident CVD Outcomes from WHI Baseline by CAC Categories for E-Along, Placebo and Total (combined), n=1074\***

Event	CAC	E-Along Control				E-Along Intervention				All (E-Along + Placebo)			
		Total n	Events n	%	Age-adjusted rate/1000 PY	Total n	Events n	%	Age-adjusted rate/1000 PY	Total n	Events n	%	Age-adjusted rate/1000 PY
<b>MI</b>	all	529	19	3.59	2.09 (0.99,4.61)	545	17	3.12	1.80 (0.79,4.16)	1074	36	3.35	1.93 (1.10,3.43)
	0	267	4	1.50	0.69 (0.10,4.91)	301	4	1.33	0.75 (0.20,3.19)	568	8	1.41	0.69 (0.21,2.65)
	1-100	142	5	3.52	2.01 (0.60,6.86)	152	3	1.97	0.79 (0.11,5.58)	294	8	2.72	1.40 (0.50,3.96)
	>100	120	10	8.33	4.94 (1.79,16.51)	92	10	10.87	7.13 (2.47,21.30)	212	20	9.43	5.94 (2.81,13.15)
<b>Stroke</b>	all	529	15	2.84	1.74 (0.75,4.16)	545	14	2.57	1.52 (0.63,3.79)	1074	29	2.70	1.64 (0.88,3.07)
	0	267	5	1.87	1.22 (0.32,5.52)	301	8	2.66	1.57 (0.53,5.30)	568	13	2.29	1.43 (0.59,3.60)
	1-100	142	4	2.82	1.77 (0.44,7.06)	152	2	1.32	0.79 (0.11,5.61)	294	6	2.04	1.21 (0.32,5.09)
	>100	120	6	5.00	2.61 (0.91,9.28)	92	4	4.35	3.05 (0.63,16.06)	212	10	4.72	2.85 (0.99,8.94)
<b>CVD</b>	all	529	70	13.23	8.04 (5.36,12.14)	545	70	12.84	7.41 (4.87,11.30)	1074	140	13.04	7.73 (5.77,10.37)
	0	267	18	6.74	4.21 (1.91,9.42)	301	20	6.64	3.77 (1.73,8.21)	568	38	6.69	3.94 (2.25,6.90)
	1-100	142	16	11.27	7.01 (3.03,16.61)	152	21	13.82	7.56 (3.48,16.97)	294	37	12.59	7.25 (4.08,13.05)
	>100	120	36	30.00	19.21 (10.49,35.92)	92	29	31.52	22.08 (11.57,42.30)	212	65	30.66	20.63 (13.24,32.31)

BMI indicates body mass index; CAC, coronary artery calcium; CEE, conjugated equine estrogen; CHD, coronary heart disease; CVD, cardiovascular disease; HF, heart failure; HT, hormone therapy; TIA, transient ischemic attack; PAD, peripheral artery disease; and PY, person-years

\* no exclusions; follow up time: from study entry to event or end of follow up.