

SUPPLEMENTARY MATERIALS**COMT and alpha-tocopherol in cancer prevention: gene-supplement interactions in two randomized
clinical trials**

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Supplementary Table 1. Baseline characteristics of WGHS participants in the trial and post-trial (participants who were alive and opted in for the observational period) by randomized alpha-tocopherol and placebo allocation.

Characteristic	Trial Period				Post-trial Period			
	Alpha-tocopherol, No. (%)		Placebo, No. (%)		Alpha-tocopherol, No. (%)		Placebo, No. (%)	
Total No. of patients	11665	(100.0)	11629	(100.0)	10184	(100.0)	10131	(100.0)
Age, y (SD)	54.7	(7.1)	54.7	(7.1)	54.4	(6.8)	54.4	(6.8)
Smoking								
Current	1358	(11.7)	1352	(11.6)	1075	(10.6)	1052	(10.4)
Past	4392	(37.7)	4324	(37.2)	3825	(37.6)	3788	(37.4)
Never	5907	(50.7)	5943	(51.2)	5278	(51.9)	5283	(52.2)
Body Mass Index (SD)	25.9	(5.0)	25.9	(5.0)	25.9	(4.9)	25.9	(4.9)
Alcohol use, drink/wk								
< 1	6595	(56.6)	6571	(56.5)	5656	(55.6)	5658	(55.9)
> 1	5067	(43.5)	5057	(43.5)	4525	(44.5)	4472	(44.2)
Physical Activity, kcal/wk								
< 1000	7570	(65.7)	7426	(64.5)	6599	(65.6)	6404	(63.9)
> 1000	3961	(34.4)	4088	(35.5)	3467	(34.4)	3623	(36.1)
Menopausal Status								
Pre-menopause	3212	(27.6)	3215	(27.7)	2923	(28.8)	2896	(28.6)
Peri-menopause	2056	(17.7)	2108	(18.2)	1825	(18.0)	1856	(18.4)
Post, HRT now	3652	(31.4)	3675	(31.7)	3194	(31.4)	3253	(32.2)
Post, not HRT	2715	(23.3)	2602	(22.4)	2217	(21.8)	2105	(20.8)
Family Cancer History								
No	9569	(82.0)	9541	(82.0)	8351	(82.0)	8343	(82.4)
Yes	2096	(18.0)	2088	(18.0)	1833	(18.0)	1788	(17.7)
Aspirin Assignment								
Placebo	5863	(50.3)	5814	(50.0)	5113	(50.2)	5039	(49.7)
Active	5802	(49.7)	5815	(50.0)	5071	(49.8)	5092	(50.3)

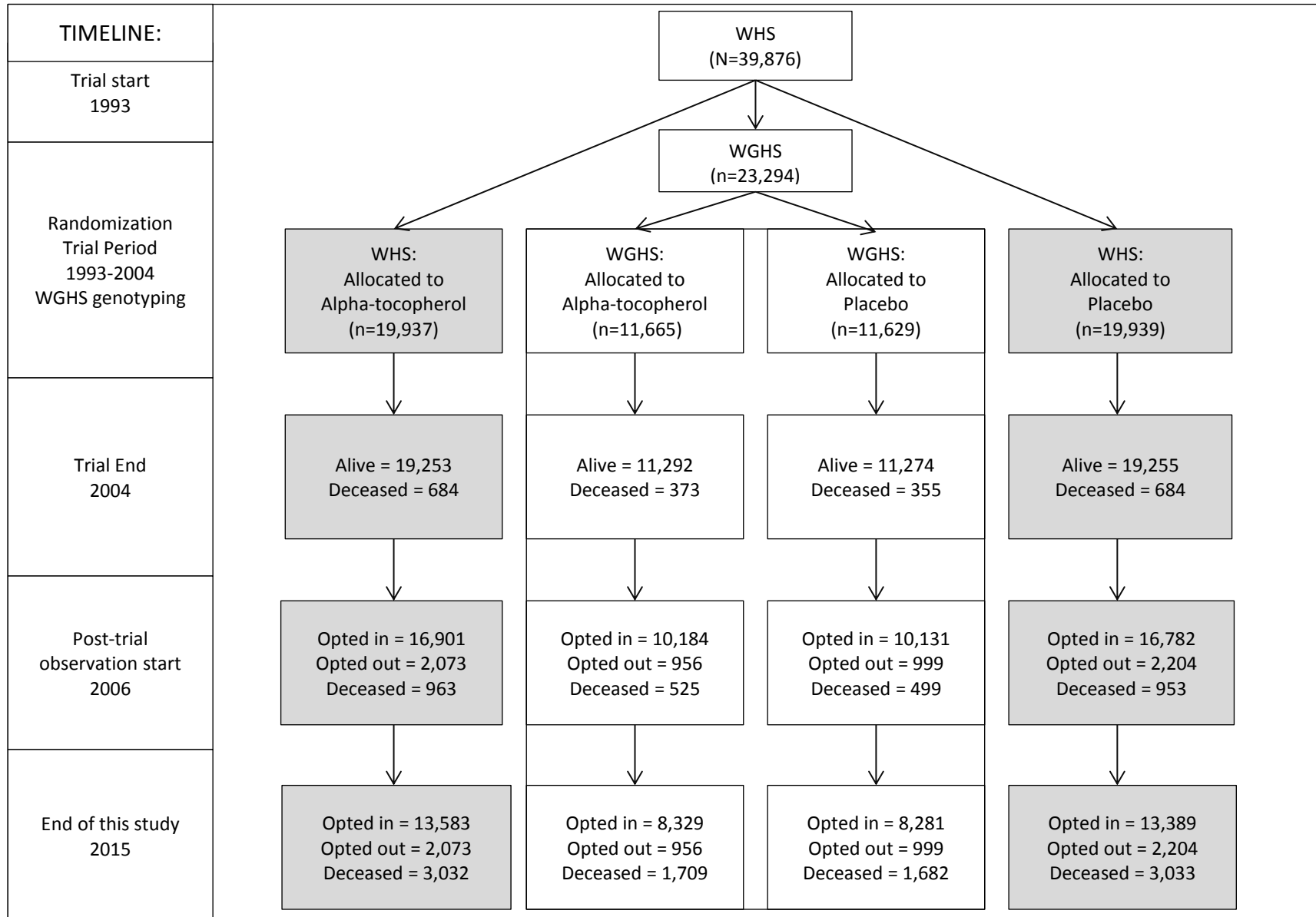
Beta-carotene Assignment

Placebo	5858	(50.2)	5834	(50.2)	5112	(50.2)	5083	(50.2)
Active	5807	(49.8)	5795	(49.8)	5072	(49.8)	5048	(49.8)

Supplementary Table 2. Baseline characteristics of participants in the ATBC cancer case control set.

Characteristic	Alpha-tocopherol (n=2,287)	Placebo (n=2,344)
Mean Age, y (SD)	58.0 (5.0)	58.0 (5.0)
Current Smoking, %	100	100
Mean Body Mass Index, kg/m ² (SD)	26.2 (3.7)	26.2 (3.7)
Mean Alcohol use, g ethanol/day (SD)	16.5 (19.4)	16.4 (19.8)
Physical Activity (leisure exercise), %		
Unknown	0.2	0.3
< 3 times per week	78.7	80.9
≥ 3 times per week	21.2	18.9
Beta-carotene Assignment, %		
No	50.1	50.2
Yes	49.9	49.8
rs4680		
met/met	674	690
val/met	1144	1177
val/val	469	477
rs4818		
C/C	1063	1099
C/G	1001	1017
G/G	223	228

Supplementary Figures 1. CONSORT Flow Diagram for the Women’s Health Study (WHS) and Women’s Genome Health Study (WGHS) genetic subset.



Supplementary Figure 2. Kaplan-Meier curves comparing cumulative incidence of first cancer which was lymphoma and leukemia by *COMT* genotype. Results are shown for rs4680 (A-C) and rs4818 (D-F) genotype strata among WGHS participants randomized to alpha-tocopherol or placebo in the overall period (trial plus 10-years). Differences between genotype strata were tested using the log-rank test; P-values were two-sided.

