

## SUPPLEMENTARY MATERIALS

### Supplementary Tables

**Supplementary Table 1.** Multivariate-adjusted hazard ratios and 95% confidence intervals of lung cancer by quintile of baseline serum alpha-tocopherol at baseline and at 3 years among Finnish male smokers in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study.\*

Characteristics	Event/ Total No. of participants	Lung cancer incidence rate <sup>†</sup>	HR (95% CI)
Serum alpha-tocopherol at baseline (range mg/L)			
Quintile 1: <9.5	695/4,623	10.38	1.00 (Ref)
Quintile 2: ≥9.5- <10.9	681/4,571	9.38	0.93 (0.84, 1.04)
Quintile 3: ≥10.9- <12.3	629/4,413	8.75	0.89 (0.80, 1.00)
Quintile 4: ≥12.3- <14.2	613/4,590	8.14	0.84 (0.74, 0.94)
Quintile 5: ≥14.2	566/4,584	7.67	0.82 (0.71, 0.94)
<i>P</i> <sub>trend</sub> <sup>‡</sup>			0.002
Serum alpha-tocopherol at 3 years (range mg/L)			
Quintile 1: <11.4	698/4,532	10.37	1.00 (Ref)
Quintile 2: ≥11.4- <13.6	646/4,601	8.71	0.87 (0.78, 0.97)
Quintile 3: ≥13.6- <15.9	632/4,505	8.66	0.85 (0.75, 0.96)
Quintile 4: ≥15.9- <19.0	609/4,594	8.22	0.80 (0.70, 0.92)
Quintile 5: ≥19.0	599/4,549	8.30	0.81 (0.70, 0.95)
<i>P</i> <sub>trend</sub> <sup>‡</sup>			0.02
Mean serum alpha-tocopherol at baseline and 3 years			
Quintile 1: <10.8	701/4,557	10.41	1.00 (Ref)
Quintile 2: ≥10.8- <12.5	663/4,611	9.00	0.87 (0.78, 0.98)

Quintile 3: $\geq 12.5$ - $< 14.1$	630/4,485	8.67	0.86 (0.77, 0.97)
Quintile 4: $\geq 14.1$ - $< 16.3$	608/4,555	8.21	0.83 (0.73, 0.94)
Quintile 5: $\geq 16.3$	582/4,573	7.98	0.80 (0.69, 0.92)
$P_{trend}^{\ddagger}$			0.005
Max serum alpha-tocopherol at baseline and 3 years			
Quintile 1: $< 11.7$	708/4,543	10.42	1.00 (Ref)
Quintile 2: 11.7-13.9	635/4,575	8.59	0.86 (0.77, 0.96)
Quintile 3: 13.9-16.1	626/4,503	8.63	0.85 (0.76, 0.96)
Quintile 4: 16.1-19.2	622/4,653	8.29	0.82 (0.72, 0.94)
Quintile 5: $\geq 19.2$	593/4,507	8.34	0.83 (0.71, 0.96)
$P_{trend}^{\ddagger}$			0.04

\*We used Cox proportional hazard regression, with time as the time metric, to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) of associations between measures of serum alpha-tocopherol (quintiles) and incidence of lung cancer, and adjusted for age at baseline, body mass index (BMI), years of cigarette smoking, number of cigarettes smoked daily, serum total cholesterol concentration, trial intervention group, family history of lung cancer, and education status. Ref=reference.

$\dagger$ Crude lung cancer incidence rate per 1000 person-years.

$\ddagger$  Two-sided  $P$  for trend is based on the statistical significance of the coefficient of the quintile variable (median value within each quintile).

**Supplemental Table 2.** Multivariate-adjusted hazard ratios and 95% confidence intervals for associations between quintile of baseline serum alpha-tocopherol and lung cancer, stratified by age at baseline, smoking, and BMI according to alpha-tocopherol supplementation, among the Finnish male smokers in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study\*

Stratified characteristics	Serum alpha-tocopherol at baseline (range mg/L)					<i>P</i> <sub>trend</sub> †	<i>P</i> <sub>interaction</sub> ‡
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5		
	<9.5 mg/L	9.5-10.9 mg/L	10.9-12.3 mg/L	12.3-14.2 mg/L	≥14.2 mg/L		
	HR (95%CI)	HR (95%CI)	HR (95%CI)	HR (95%CI)	HR (95%CI)		
Age at baseline, year							
<60							
Alpha-tocopherol Yes	1.00 (Ref)	0.85 (0.70, 1.04)	0.84 (0.69, 1.04)	0.77 (0.62, 0.96)	0.68 (0.53, 0.88)	0.003	1.00
Alpha-tocopherol No	1.00 (Ref)	0.85 (0.70, 1.03)	0.79 (0.65, 0.97)	0.74 (0.60, 0.92)	0.65 (0.51, 0.84)	<0.001	
≥60							
Alpha-tocopherol Yes	1.00 (Ref)	1.06 (0.84, 1.35)	0.91 (0.70, 1.19)	0.90 (0.68, 1.18)	0.92 (0.68, 1.26)	0.41	0.86
Alpha-tocopherol No	1.00 (Ref)	0.98 (0.76, 1.25)	1.00 (0.77, 1.31)	0.83 (0.62, 1.11)	0.95 (0.70, 1.30)	0.57	
Year smoked							
<40							
Alpha-tocopherol Yes	1.00 (Ref)	0.84 (0.67, 1.05)	0.81 (0.64, 1.01)	0.66 (0.51, 0.84)	0.58 (0.44, 0.77)	<0.001	0.94
Alpha-tocopherol No	1.00 (Ref)	0.80 (0.64, 1.00)	0.74 (0.58, 0.93)	0.67 (0.53, 0.86)	0.58 (0.43, 0.77)	<0.001	
≥40							
Alpha-tocopherol Yes	1.00 (Ref)	1.03 (0.83, 1.27)	0.93 (0.74, 1.17)	1.00 (0.79, 1.27)	1.00 (0.76, 1.30)	0.94	0.68
Alpha-tocopherol No	1.00 (Ref)	0.98 (0.79, 1.21)	1.00 (0.79, 1.25)	0.87 (0.68, 1.11)	0.94 (0.73, 1.23)	0.51	
Body mass index, kg/m <sup>2</sup>							
<27.6							
Alpha-tocopherol Yes	1.00 (Ref)	0.94 (0.79, 1.12)	0.89 (0.74, 1.07)	0.84 (0.68, 1.02)	0.68 (0.54, 0.86)	<0.001	0.60
Alpha-tocopherol No	1.00 (Ref)	0.87 (0.73, 1.04)	0.86 (0.71, 1.04)	0.71 (0.57, 0.87)	0.70 (0.56, 0.89)	0.001	
≥27.6							
Alpha-tocopherol Yes	1.00 (Ref)	0.93 (0.68, 1.27)	0.87 (0.63, 1.20)	0.78 (0.56, 1.09)	0.98 (0.70, 1.39)	0.90	0.59
Alpha-tocopherol No	1.00 (Ref)	1.00 (0.74, 1.35)	0.88 (0.64, 1.22)	0.99 (0.71, 1.37)	0.91 (0.64, 1.28)	0.59	

\*We used Cox proportional hazard regression, with time as the time metric, to calculate hazard ratios (HRs) and 95% confidence interval (CIs) of associations between baseline serum alpha-tocopherol (quintiles) and incidence of lung cancer, adjusted for age at baseline, body mass index (BMI), years of cigarette smoking, number of cigarettes smoked daily, serum total cholesterol concentration, and trial intervention group.

† Two-sided  $P$  for trend is based on the statistical significance of the coefficient of the quintile variable (median value within each quintile).

‡ Two-sided  $P$  for interaction is based on the statistical significance of the cross-product term added to multivariate models.